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PL1. NEW TECHNIQUES FOR THE NON INVASIVE ASSESSMENT OF BONE QUALITY

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Noninvasive and/or nondestructive techniques can provide structural information about bone, beyond standard bone mineral densitometry (BMD). While the latter provides important information about osteoporosis diagnosis and fracture risk assessment, considerable evidence indicates that BMD only partially explains bone strength and fracture resistance. Quantitative assessment of macrostructural characteristics such as geometry and section modulus, and microstructural features such as relative trabecular volume, and trabecular spacing, number and connectivity may improve our understanding of osteoporosis and our ability to estimate bone strength and predict fractures. The rationale for imaging bone macro/micro structure, therefore, is to obtain information beyond BMD, improve fracture risk prediction, clarify the pathophysiology of skeletal disease, define the skeletal response to therapy, and assess biomechanical relationships.

The methods for quantitatively assessing the macrostructure of bone include, (besides conventional radiography) computed tomography, especially high resolution computed tomography (hrCT) at 100–400μ and volumetric quantitative computed tomography (vQCT), and high resolution magnetic resonance imaging (hrMR) at 100–200μ. The strengths of these approaches include they are widely available, non-invasive and non-destructive methods, providing both macro structure and bone density information, are moderately precise and accurate, and permit serial measurement of most any body site, while their limitations include, for vQCT, the modest exposure to ionizing radiation and the lack of derived microstructural information and, for hrCT and hrMR, the provision of only approximations of microstructural parameters, with considerable threshold and resolution dependence.

The methods for assessing the microstructure of bone noninvasively and/or nondestructively include, micro computed tomography (μCT) at 1–100μ, and micro magnetic resonance imaging (μMR) at 20–200μ. The strengths of the former, μCT, are the automated 2D and 3D evaluation, the nondestructive nature of the imaging, permitting mechanical or other testing of the sample, and the highly precise and accurate measurement, while the limitations are the high exposure to ionizing radiation, the requirements for invasive biopsy with large sampling errors or for animal studies, and the expense and limited availability of the equipment. The strengths and weaknesses of μMR are similar, except for the absence of ionizing radiation, and the greater complexity and expense of this technology.

Despite the considerable progress made in bone imaging over the past decade, a number of challenges remain. Technically, the challenges reflect the balances and trade-offs between spatial resolution, sampling size, signal-to-noise, radiation exposure and acquisition time, or between the complexity and expense of the imaging technologies versus their availability and accessibility. Clinically, the challenges for bone imaging include balancing the advantages of standard densitometric information versus the more complex architectural features of bone, or the deeper research requirements in the laboratory versus the broader needs in clinical practice. The biological differences between the peripheral appendicular skeleton and the central axial skeleton and their impact on the relevant bone imaging methods must be further clarified. Finally, the relative merits of these sophisticated imaging techniques must be weighed with respect to their applications as diagnostic procedures, requiring high accuracy or reliability, versus their applications as monitoring procedures, requiring high precision or reproducibility.

PL2. ULTRASTRUCTURAL DEFECTS, BONE MINERALIZATION AND RESPONSE TO TREATMENT

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Current pharmacologic agents used to treat osteoporosis have effects on mineralization and microdamage accumulation that are independent of change in bone mineral density.

A high degree of mineralization can reduce the amount of energy required to cause fracture. Agents that suppress bone remodeling can increase the normal age-related elevation of mineralization. Anti-resorptive agents also increase the homogeneity of the bone tissue at the microscopic level as more of the tissue becomes mineralized to the same degree. The increased mineralization can be associated with a greater propensity to initiate microdamage; the increased homogeneity will make the tissue matrix less effective at stopping microcracks once they have begun. Agents such as teriparatide that accelerate bone turnover make the matrix transiently less mineralized and more heterogeneous, which may limit microdamage initiation and growth.

Anti-resorptive agents increase the cross-linking of collagen in the bone matrix, and reverse the osteoporosis-related reduction in non-reducible cross-linking. This may provide an added benefit in fracture risk reduction.

Microdamage is naturally initiated in bone tissue, and is normally repaired through physiologic bone remodeling processes. Microdamage accumulation in bone reduces the strength, elastic modulus and fracture energy of the bone tissue. The microdamage burden in bone increases with age, perhaps because there is an inherent fragility of the tissue matrix that allows initiation of cracks to occur more readily. The impact of pharmacologic interventions for osteoporosis on microdamage accumulation depends on the degree of remodeling suppression, which partly determines the balance between damage initiation and repair. Over-suppression of bone remodeling is associated with increased microdamage and decreased bone toughness, properties that are highly correlated in a non-linear fashion to the rate of bone turnover. The overall efficacy of a compound in reducing fracture risk is partly dependent on its effects on the matrix, and this may help to explain the observation that all pharmacologic agents have about the same efficacy on vertebral fracture risk even though they each are associated with larger or smaller changes in BMD.

PL3. BONE–SYNOVIUM INTERACTION

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Rheumatoid arthritis (RA) represents a paradigm for investigating the role of synovial inflammation on articular and systemic bone remodeling. In RA, proliferation of the synovial lining of diarthrodial joints is accompanied by progressive localized articular bone loss manifest radiographically by the development of focal joint erosions. The joint inflammation is also associated with systemic bone loss, and patients with RA exhibit an increased risk of hip and vertebral fracture. Histopathological analysis of joint tissues from patients with RA indicates that osteoclasts participate in the pathogenesis of the focal joint erosions. Animal models of inflammatory arthritis, including adjuvant arthritis (Kong et al. Nature 1999; 402:304), serum transfer arthritis (Pettit et al. Am J Pathol 2001;159:1689); TNF-transgenic mice with spontaneous arthritis (Redlich et al. Arthritis Rheum 2002; 46:785); and collagen-induced arthritis (Romas et al. Am J Pathol 2002, 161:1419–27), confirm that osteoclasts are the principal cell type responsible for the pathogenesis of focal joint erosions. Additional studies have helped to identify the cytokines and inflammatory mediators that are involved in the recruitment and activation of bone resorbing cells associated with inflammatory arthritis. Tumor necrosis factor alpha, interleukin-1, receptor activator of NF-kβ ligand (RANKL) and a number of other products of activated T cells, macrophages and synovial fibroblasts are among the factors implicated in the increased focal articular and systemic bone loss. Pro-inflammatory cytokines that regulate bone remodeling represent rational therapeutic targets for specifically inhibiting or slowing the progressive bone loss associated with RA and related inflammatory disorders.

PL4. OSTEOCYTES AND MECHANICAL TRANSDUCTION

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As osteoblasts become embedded in osteoid, they undergo a dramatic change in morphology and function to become osteocytes. Long dendritic processes are generated that travel through canaliculi to connect with the dendritic tips of existing osteocytes creating a three dimensional syncytium within the mineralized matrix. Osteocytes can send signals of both resorption and formation depending on the 'window' of mechanical strain such as 1) low or no strain resulting in disuse-associated bone loss, 2) physiological strain that maintains homeostasis, 3) high-end physiological strain that results in modeling, and 4) supra-physiological strain that causes injury-associated repair. The osteocyte is ideally suited to translate strain into biochemical signals and to orchestrate the resulting complex biological responses.

Osteocytes appear to respond to strain individually or as a population. Osteocytes may act individually in response to strain where a specific magnitude of strain elicits a specific gene response, especially for antigens highly expressed in osteocytes such as dentin matrix protein 1, OF45/MEPE, or E11/gp38. Whereas the function of E11/gp38 appears to be in the generation of dendritic processes, the function of Dentin Matrix Protein 1 or OF45/MEPE in osteocytes is unknown. When osteocytes respond as a population, the overall strain may be averaged to generate a specific response in all cells. With either of these two types of responses, gene expression is not detectable until a particular threshold is reached, demonstrating that gene expression can be strain threshold dependent. Hormones such as estrogen and parathyroid hormone can modulate these thresholds.

Osteocyte viability is essential for the maintenance of bone integrity. Osteocytes, unlike osteoblasts and osteoclasts, are long lived, for decades, and make up over 90% of all bone cells. Osteocyte programmed cell death occurs with 1). immobilization or space flight 2). damage in the form of microcracks, and 3). post-menopausal and steroid induced osteoporosis. Although all three conditions are characterized by osteocyte apoptosis and bone resorption, the mechanisms for induction of cell death and signals of resorption are distinctly different. The mechanisms for induction of cell death include hypoxia, physical cell damage, decreased viability due to a lack of estrogen, cytokines such as Interleukin-1 or tumor necrosis factor-induced apoptosis, or steroid-induced apoptosis. These observations emphasize the importance of considering osteocyte viability and function in the development of drug and/or exercise regimens to prevent or treat bone loss.

PL5. NEUROTRANSMITTERS IN BONE: NEW PLAYERS IN BONE PHYSIOLOGY

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Recent interest in the role of the CNS in providing an inhibitory influence on bone formation has raised interest in the activity of neurotransmitters on the skeleton. This discovery is significant because it demonstrates that the dogma of regulation of bone mass by interactions of local and circulating systemic osteotropic mediators is flawed. However, as functionally adaptive responses occur in cells that are not innervated, and there is not sufficient neural bandwidth to account for many of the responses of bone to osteotropic influences, it is still unlikely that the highly focused regulation of site specific remodelling that provides the link between skeletal form and function can be mediated by other than local effects.

In addition to the effects of what can be termed "extrinsic" neurotransmitters, acting via central and peripheral innervation, there is in addition a history of the effects of the actions of "intrinsic" neurotransmitters directly on their receptors on bone cells. Studies on the actions of classical neurotransmitters such as bradykinin, neuropeptide Y and substance P on receptors on osteoblasts show that paracrine interactions in the bone microenvironment involve many molecules originally thought to be specific to the nervous system. Recently the role of the excitatory neurotransmitter glutamate has been explored in this context. Originally conceived to be involved as a result of studies to identify genes regulated by mechanical loading in vivo that identified a glutamate transporter known only in the CNS before, it is now clear that glutamate has a multitude of functions in bone. Glutamate signalling mediates bone formation and bone resorption, by direct effects on glutamate receptors on osteoblasts and osteoclasts. In addition, glutamate signalling between osteoblasts and osteoclast precursors regulates osteoclast precursor differentiation, while multipotent bone marrow osteoblast precursors are incapable of differentiation down osteoblastic lineages if glutamate signalling is inhibited. Furthermore, specific temporal and spatial regulation of glutamate receptor expression and function in mesenchymal condensations in developing limbs controls the chondrogenesis that is a prerequisite for skeletogenesis.

One further feature of the skeleton's response to external stimuli may involve mechanisms that parallel those in the CNS. It has been clear for some time that only brief periods of time are needed to saturate the response of bone to loading, so that a few seconds or minutes of loading in each day initiate the same changes as longer periods. This suggests that there is a retention of loading history by bone that persists for between 24 and 48 hours. Interestingly the molecules underlying the long term potentiation (LTP) that is the basis for memory formation are also expressed in osteoblasts. Loading in vitro induces the same changes in CAM kinase II in osteoblasts from a calcium dependent to a calcium independent state that are seen in LTP in the CNS.

Like so many "tissue specific" agents, neurotransmitters may have been misnamed, in that their sites of expression and function are becoming found to be steadily more ubiquitous. Such discoveries have significant impact on possible drug development as agents discovered and tested for neuroscience applications, may have utility in the skeleton for the control of bone cell function.

PL6. ROLE OF SEX HORMONES IN BONE GROWTH

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A substantial amount of bone mineral is acquired during a relatively short pubertal period of rapid skeletal growth. This phase of accelerated skeletal modeling is essential to meet the mechanical loads imposed on the skeleton by the growing body.

During puberty, greater periosteal than endosteal bone expansion results in longer and wider, but also in thicker bones. To this end, sex steroids provide a disproportionately stronger stimulus to osteoblastic bone formation than to osteoclastic bone resorption, as a result of interaction with specific sex steroid receptors in different bone compartments and regions. Not surprisingly, puberty represents a vulnerable period during which deficiency or even delay of sex steroid activity may have a deleterious and potentially irreversible impact on bone mass and structure.

In both genders, estrogens (in males resulting from conversion of androgens) have biphasic, estrogen receptor (ER)-alpha mediated effects on growth: in early puberty, estrogens stimulate both longitudinal and radial growth; by the end of puberty, on the other hand, they induce closure of the epiphyseal growth plates and limit length growth and ultimate bone size. During this process, site-specific differences emerge with axial growth continuing longer than appendicular growth.

Skeletal sexual dimorphism may in part result from estrogen-mediated inhibitory effects on female skeletal growth with relatively less exposure to growth-stimulatory estrogen effects. Estrogens interact with the growth hormone-insulin-like growth factor-I (GH-IGF-I) axis, stimulating (both directly and indirectly) GH and IGF-I at the start of puberty. Moreover, estrogen reduces the bone marrow cavity by endosteal bone contraction in the female. Thickening of trabeculae in the axial skeleton may also be partially estrogen-mediated.

To accommodate to the increasing mechanical demands during puberty ,androgens stimulate periosteal bone formation through the androgen receptor (AR) . AR-mediated androgen action has no major direct effect on the growth plate and non-aromatisable androgens do not interact with GH-IGF-I axis. However, direct AR-mediated anabolic effects on muscle tissue have been well-documented; the resulting increase in mechanical loading is thought to be important in upregulating skeletal modeling during male puberty.

In summary, AR-activation by androgens and ER-alpha-activation by estrogens have both direct and indirect anabolic effects on the development of the skeleton during puberty. In line with the increasing mechanical loading of bone – due to pubertal changes in body size and body composition – bone mass increases. Sex steroids are critically involved in this continuous, time- and site-specific adaptation process. Clinicians should take great care to detect and correct deficiencies and/or delays in sex steroid activity during puberty.

PL7. WHAT HAS GENETICS CONTRIBUTED TO OSTEOPOROSIS?

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What do we want genetics to contribute? The clinical goals of genetic research are to identify persons likely to fracture, persons with low peak bone mass, rapid bone loss, sensitive to corticosteroids, responsive to drugs, exercise, or calcium. These goals have not been achieved, partly because of problems in defining the phenotype and the questions. The relevant phenotype is structural failure. However, fractures are uncommon and involve varying trauma and bone fragility so that little evidence for heritability of fracture exists, except perhaps for the Col1A1 gene. In lieu of fracture, bone mineral density (BMD) is the accepted surrogate of bone strength because BMD predicts fracture and its variance is largely genetic. However, allelic variants in 'candidate' genes account for little of the genetic variance. Associations between a genotype and BMD or rates of BMD 'loss' are usually negative or contradictory, and when positive (eg COL1A1 gene), differences in the mean BMD between genotypes are small and the scatter of values is large so that the BMD difference attributable to the genotype is 1–2%; few of the fractures in the community are explained by this genotype. Genotype specific responses to drugs, calcium, or exercise are not based on trials with prior stratification by genotype then randomisation to placebo or intervention, so differences in response may be due to covariates unevenly distributed by genotype, *not* the genotype. These results do not support genotyping in diagnosis, risk assessment or therapy.

Revealing the genetic regulation of bone in man with mice. The limited success may be, in part, a problem of the ambiguity of BMD, a phenotype that is the product of a multitude of genetic factors that regulate the cellular activity on bone's periosteal and endosteal surfaces throughout life. By contrast, many insights into the central, systemic and local regulation of skeletal growth and ageing in mice have been obtained by studying the genetic regulation of specific phenotypes. Leptin controls bone mass through central sympathetic nervous regulation and neuropeptide receptorY4 may contribute to the sex specific regulation of trabecular density. Knockouts (KOs) of the genes for receptors for PTHrP, growth hormone, estrogen, provide insights into the regulation of trabecular and cortical bone, and sex specific regulation of bone growth. The lipoxygenase gene (Alox15) is associated with low peak bone mass and gene deletion produces high peak bone mass. Genetic ablation of products promoting osteoclastogenesis (RANK, RANKL) produce osteopetrosis. Genetic ablation of inhibitors of osteoclastogenesis (OPG) produce osteoporosis, while KO of genes producing osteoblasts results in mice with a cartilaginous skeleton. Family studies of individuals with a high bone mass reveal linkage to a mutation in the LDL receptor related protein 5. Studies of families with fractures and low BMD reveal linkage to variants in BMP 2 gene, an interesting finding given that BMPs participate in skeletogenesis, and over expression of the gene for noggin, a BMP 2 antagonist, produces osteoporosis and fractures in mice.

What do we want from the Genie before we rub the bottle? Integrating these and other insights into bone physiology obtained in mice to whole bone strength in human subjects remains a challenge. The purpose of genetic regulation is to construct a whole bone with properties suited to the contradictory functions it must perform as both a lever and spring – stiffness for leverage, yet flexibility (deformability) for energy absorption, lightness for movement yet strength for loading. Thus, the unifying purpose of genetic regulation may be to orchestrate the central, systemic and local regulators of the cellular activity on the periosteal and endosteal surfaces to adapt bone's material composition (mineral, collagen) and structure (trabecular number, thickness, connectivity, cortical thickness, porosity) to the prevailing loads imposed on it throughout life. Adaptation by one trait in the face of a defect in another can maintain whole bone strength. For example, collagen defects in the MOV 13 mouse are compensated by structural adaptations (periosteal apposition) but collagen defect in the Brittle IV mouse are compensated for by material adaptations (mineral/collagen ratio). Severe defects in oim/oim mice result in failed adaptive increases in remodelling because the tissue produced is defective.

So, what genes regulate and co-regulate endosteal remodelling, BMU balance and periosteal bone formation to keep whole bone 'just right'? Why is adaptation so successful during growth, not ageing? There is no 'osteoporosis' gene. Is bone fragility a genetic disease of failed adaptation, a problem in which the cellular events that adapt bone's material and structural properties to prevailing loads fail, so bone deforms too much during its function as a lever or too little during its function as a spring.

PL8. INDICATIONS TO TREATMENT

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The objective of any treatment strategy in osteoporosis is to identify those who will most benefit from treatment and to avoid

unnecessary treatment in those at low risk. The implied treatment threshold depends upon costs and consequences of fracture and the costs, effects and side effects of intervention. Where interventions are inexpensive and safe, global strategies can be envisaged, for example the use of calcium and vitamin D in the institutionalised elderly. More widespread global strategies, such as avoidance of smoking, physical exercise and other lifestyle measures have not been tested. For this reason high risk strategies are the most viable option where individuals are identified on the basis of high fracture risk.

To date, assessment of bone mineral density (BMD) has been the corner-stone for the diagnosis of osteoporosis, and the WHO definition of osteoporosis, based on the T-score, is widely accepted as an intervention threshold for drug development and in practice guidelines. The recommended diagnostic test is BMD at the proximal femur by dual energy X-ray absorptiometry. The same BMD threshold for osteoporosis for diagnosis (a T-score for BMD of -2.5 SD or less in young healthy women) can be used in both men and women.

Since the determinants of osteoporotic fracture are multifactorial, risk prediction will always be imperfect. Hip fracture prediction with BMD alone is, however, at least as good as blood pressure readings to predict stroke. Like blood pressure tests, the test has high specificity, but its sensitivity (detection rate) for fracture outcome is low over most reasonable assumptions. When the WHO thresholds are used, the majority of fractures will occur in those individuals characterised to be at low risk.

The predictive value of BMD can be enhanced by the use of other factors such as biochemical indices of bone resorption and clinical risk factors. In meta-analyses of prospectively studied cohorts, several risk factors have been identified that contribute to fracture risk independently of BMD. They include age, previous fragility fracture, secondary causes of osteoporosis, smoking, high intakes of alcohol, a family history of hip fracture and the prolonged use of corticosteroids. Since the presence of such factors increases fracture risk over and above that which can be explained on the basis of BMD, thresholds for intervention that are based on the use of these risk factors can be less stringent than those based on BMD alone. The choice of risk factors to use depends on whether they identify a risk that is amenable to the treatment envisaged. With this caveat, diagnostic thresholds differ from intervention thresholds.

Because of the many techniques available for fracture risk assessment, the absolute (e.g. ten year) probability of fracture is the desirable parameter to determine intervention thresholds. The setting of intervention thresholds is ultimately dependent on health economic considerations. Intervention can be directed to individuals cost-effectively where hip fracture probability ranges from 2% to 10% (depending on age). When BMD is used as a test alone, an intervention threshold of -2.5 SD is cost-effective. These thresholds, derived from Sweden, require modification in different countries to take account of different costs and risks that vary markedly in different regions of the world.

OC1. A META-ANALYSIS OF BMD AS A PREDICTOR OF FRACTURE RISK

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The aim of this study was to quantify the relationship between hip bone mineral density (BMD) and fracture risk (all, osteoporotic, hip fractures) and examine the influence of this relationship with age, gender and time since assessment of BMD.

We studied nearly 39000 men and women from twelve population-based cohorts comprising Rotterdam, EVOS/EPOS, CaMos, Rochester, Sheffield, DOES, EPIDOS, OFELY, two cohorts from Gothenburg, Kuopio and Hiroshima with a total follow-up of almost 170,000 person-years. The effect of BMD on fracture risk was examined using a Poisson model in each cohort separately. Results of the different studies was then merged using weighted coefficients.

BMD was a strong predictor of fractures, especially hip fractures with a similar predictive value observed between men and women. At the age of 65 years, hip fracture risk increased in men by 2.94 (2.02–4.27) and in women by 2.88 (2.31–3.59) for each SD decrease in BMD. However, the effect was dependent on age with a significantly higher gradient of risk at age 50 than at age 80 years. For any fracture and for osteoporotic fractures, the gradient of risk was lower than for hip fractures, and predictive value increased with age. At age 65 years, osteoporotic fracture risk increased in men by 1.41 (1.33–1.51) and in women by 1.38 (1.28–1.48) for each SD decrease in BMD. For hip fractures, there was a non-significant reduction of predictive ability with time after measurement. For the prediction of osteoporotic fractures (and any fracture) there was a higher predictive ability the lower the BMD value. At a T-score –4 SD the risk ratio was 2.10 (1.63–2.71), and at a T-score of –1 SD the risk ratio was 1.73 (1.59–1.89). A similar but less pronounced and non-significant effect was observed for hip fractures. We conclude that BMD is a risk factor for fracture of substantial importance, and is similar in both sexes. This validation on an international basis permits its use in case-finding strategies. Its use should, however, take account of the variations in predictive value with age and BMD.

OC2. ASSESSING VERTEBRAL FRACTURE RISK USING BIOMECHANICAL PRINCIPLES: FRACTURE RISK INDEX

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Aims: Structural failure becomes increasingly likely as the load on bone approximates or exceeds the bone's ability to withstand it. The vertebral fracture risk index (FRI) expresses the risk for structural failure as a ratio of the load per unit area/strength. The purpose of this study was to determine whether the FRI provides a more sensitive and specific predictor of vertebral fracture risk than spinal areal BMD (aBMD) or volumetric BMD (vBMD).

Methods: We conducted two studies, a case-control study of 89 postmenopausal women with vertebral fractures and 306 postmenopausal controls in Melbourne, Australia, and a prospective study of 30 postmenopausal women with incident vertebral fractures and 150 age-comparable controls in Lyon, France. FRI and vBMD of the third lumbar vertebral body and spine aBMD were derived from dual x-ray absorptiometry

Results: In the cross-sectional analysis, after adjusting for age, each SD increase in FRI was associated with 2.1-fold (95% CI, 1.55–2.73) increase in the risk of fracture, while each SD reduction in aBMD or vBMD was associated with 4.0-fold (95% CI, 2.69–6.18 and 2.65–6.94, respectively) increase in the risk. Using ROC analysis, the FRI had a lower sensitivity and specificity than aBMD in discriminating cases and controls (area under ROC curve, 0.76 vs 0.84, $p < 0.01$), but was similarly compared to vBMD (0.76 vs 0.79). Prospective analysis suggested that the FRI was no better predictor than aBMD [HR, 1.2 (95% CI:0.9–1.7) vs 2.4 (95% CI:1.5–3.8); area under ROC, 0.64 vs 0.79, $p < 0.01$]. There was also lower sensitivity using a cut off of FRI $> = 1$ compared with aBMD T-score of −2.5 SD in both studies. FRI was inversely associated with aBMD T-score in patients with prevalent but not incident fractures. There was poor agreement (Kappa = 0.11–0.18) between FRI and aBMD T-scores in diagnosing osteoporotic fractures.

Conclusion: Within the constraints of the small sample size, we concluded that applying biomechanical index such as FRI at the spine did not provide a better discriminatory ability to distinguish fracture cases and controls than aBMD or vBMD.

OC3. FALL INDEX PREDICTS HIP FRACTURE INDEPENDENT OF AGE AND BONE DENSITY

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Hip fracture risk is related to several factors, including bone mineral density (BMD), bone distribution, age, height, and weight. Modern bone densitometers can measure structural parameters beyond BMD, including cross sectional moment of inertia (CSMI) and cross sectional area (CSA) at the femoral neck. Models have been proposed that combine density, structure, age, height, and weight to produce a Fall Index (FI). FI estimates the ability of a hip to withstand a fall on the greater trochanter, with larger values indicating greater strength and decreased risk (Yoshikawa et al, JBMR 9:1053–1064).

In this study, we compared femoral BMD with CSMI, CSA, and FI for assessing hip fracture risk. DXA scans were obtained in 422 women, 58 with prior hip fracture and 364 controls using the Lunar Prodigy (GE Medical Systems). For the fracture subjects, DXA measurements were performed on the non-fractured femur. BMD of the femoral neck was determined, as well as CSMI, CSA, and FI using the Lunar Hip Strength Analysis program.

	Age	Height	Weight	Neck BMD	CSMI	CSA	FI
Fracture	77 yrs	160 cm	61.7 kg	0.659 g/cm^2*	10689	149 cm^2	1.54*
Controls	76 yrs	157 cm	62.6 kg	0.748 g/cm^2	10284	148 cm^2	1.62

*Significantly different than controls ($p < 0.01$)

There was no significant trend with age for the BMD-adjusted CSA, CSMI and FI values. Results for fracture cases and controls were compared using an unpaired t-test. Femoral neck BMD was significantly lower in the fracture group compared to controls. After adjustment for BMD, neither CSMI nor CSA were significantly different between groups. However, FI was significantly lower in the fracture group, consistent with a reduced capacity to withstand a fall.

We conclude that femoral neck BMD is an important predictor of femoral fracture. Measurements of femoral geometry, which are based on BMD distribution, did not provide additional predictive power compared to BMD alone. The Fall Index, which combines BMD, geometry, age, height, and weight into a single risk factor, is a significant predictor of hip fracture, even after adjustment for age and BMD.

OC4. EFFECT OF DIFFERING VERTEBRAL AREAS ON INTERPRETATION OF SERIAL DENSITOMETRY IN CLINICAL PRACTICE

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Background: In comparing serial BMD measurements, the ISCD recommends vertebral projected areas should not differ by $> 2\%$ to avoid measurement error from change in apparent bone size. This study assessed whether this guideline is followed in routine densitometry.

Methods: Analysis of 103 consecutive paired BMD reports performed by qualified radiologists. Scans were excluded if technical errors present. We analyzed the difference between projected areas of individual vertebrae in serial scans from individual patients. We excluded all vertebrae differing by >2% and recalculated both scans, provided at least 2 vertebrae were suitable for analysis. After re-calculating the results, we compared corrected BMD to the original reported change using 0.025 g/cm2 for least significant change.

Results: Mean differences in projected areas of L1, L2, L3 and L4 were 5.6%, 3.8%, 3.6% and 4.6% respectively. Only 4.9% of scans had all 4 vertebrae differ by <2%. Despite greatest variability, a change in L1 area only accounted for 33% of "failed" scans. 12% of scans were unacceptable, having 3 or more vertebrae differing by >5%.

Analysis excluding all vertebrae differing by >2% showed a mean 0.012 g/cm2 change from the original reported change. However, 11% had results differing from reported change by >0.025 g/cm2. If analysis requires at least 2 vertebrae with areas differing by <2%, 55.3% of DXA's were either unsuitable for analysis, or re-analysis changed results by >0.025 g/cm2. Of the 12% of paired DXA having 3 or more vertebrae with >5% areal difference, 66% changed by >0.03 g/cm2.

To determine clinical impact, we re-analyzed scans excluding vertebrae >2% different and using LSC of 0.025 g/cm2. After re-analysis, 26% of reports changed clinical interpretation: clinically significant increase or decrease became non-significant or vice versa.

Conclusions: Half of serial DXA measurements did not meet ISCD criteria. This resulted in 20% of DXA reports being inaccurate in quantifying the true BMD change. 26% of properly performed DXA erroneously reported the significance of an observed change by not excluding vertebrae with large differences in projected areas. Serial densitometry results should be used with caution in patient management if projected area analyses are not performed.

OC5. NON-DESTRUCTIVE ASSESSMENT OF TRABECULAR MICROSTRUCTURE IN THE LUMBAR SPINE

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Aim: Structural bone parameters like trabecular thickness and trabecular number predict the mechanical properties of cancellous bone better than bone mineral density. Accurate data are required to test new spinal instrumentations especially for the treatment of the osteoporotic spine. Since conventional DXA provides BMD data only for L1 to L4 and does not distinguish between cancellous and cortical bone, 3D high-resolution peripheral quantitative computer tomography (3D-pQCT) was employed to quantify structural parameters non-destructively prior to mechanical testing.

Methods: Thirteen human cadaveric spines ranging from T11 to L5 were measured with DXA and 3D-pQCT. DXA measurements (Hologic QDR 4500 W) included AP view from L1 to L4 and lateral view for L2 and L3. PQCT was performed using a new generation in vivo 3D-pQCT scanner (Radios, Scanco Medical, Switzerland) providing an isotropic nominal resolution of 93 μm measuring all levels (Fig. 1). Subsequently, direct 3D morphometry was used to compute cancellous bone volume density (BV/TV), trabecular thickness (Tb.Th), number (Tb.N) and separation (Tb.Sp). Correlations between DXA and pQCT and between structural parameters and BV/TV were calculated.

Results: Whereas AP and lateral view in the DXA correlated only moderately ($r = 0.77$; $r2 = 0.59$), 3D-pQCT values for cancellous bone density (BV/TV) correlated well with AP DXA ($r = 0.86$; $r2 = 0.72$). Tb.Th ranged from 0.14 to 0.27 mm, Tb.N from 0.13 to 0.97 per mm. BV/TV was linearly correlated to Tb.N ($r = 0.97$) and an inversely correlated to Tb.Sp ($r = -0.83$). Additionally, two cysts and one intraosseous calcification were discovered.

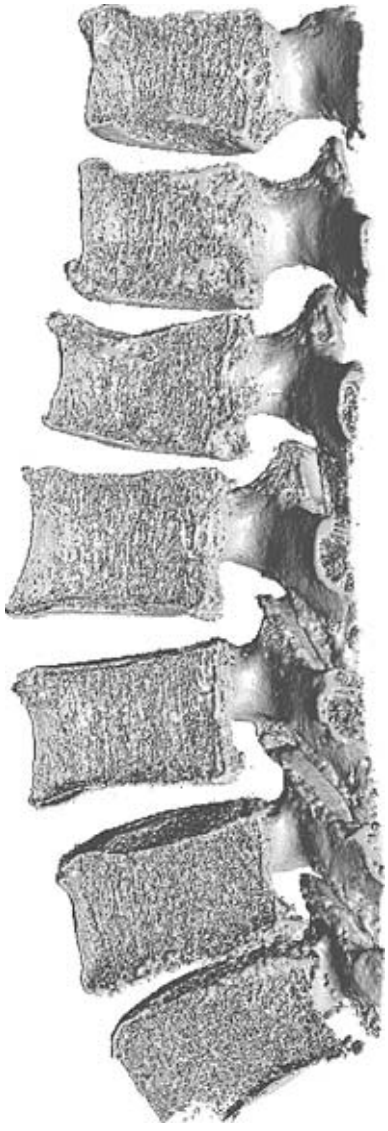

Fig. 1 3D-pQCT reconstruction of a lumbar spine from a 84-year-old female

Conclusions: The findings suggest a good correlation between 3D-pQCT and DXA. However, the microtomography-based evaluation allows scanning of the whole spine segment at once, detects pathological alterations and provides additional structural parameters. Although the technique is currently suitable for cadaveric spines only it offers a great potential for in vivo measurements of the distal radius or the heel.

OC6. ESTROGEN HAS SITE SPECIFIC EFFECTS ON TRABECULAR AND TOTAL BONE DENSITY AND BONE AREA MEASURED BY PQCT AND IS DEPENDENT ON WEIGHTBEARING

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Aims: Endogenous estrogen levels decline after menopause and accelerate bone loss. We propose the magnitude of this estrogen effect is site specific and is dependent on weight bearing. Estrogen may affect the trabecular bone density and mechanical distribution of bone mass by influencing periosteal bone apposition.

Methods: We examined the predictive effect of Estradiol, Sex Hormone Binding Globulin (SHBG) and Free Estradiol Index (FEI) on Peripheral Quantitative Computed Tomography (pQCT) parameters in a prospective 5-year population based, randomised controlled trial of calcium supplementation in 1076 women. Total Bone Mineral Density (TotBMD), Trabecular Bone Mineral Density (TrBMD) and Total Bone Area (TotA) were measured at the distal radius and distal tibia using a Stratec XCT-2000 pQCT machine in women mean age 80(±25.6) who had blood testing for estradiol and SHBG (n = 958). A pixel size of 0.15 micrometer and slice of 1mm was used, and radiation dosimetry was determined to be less than 0.3 microsieverts for both scans. The coefficient of variation (CV) was ≤5% for all parameters, determined by a precision sub-study in 77 patients.
Results: In linear correlation, FEI was positively associated with total and trabecular BMD in both limbs, but negatively associated with TotA tibia. After adjustment for age, weight and height, the (FEI) remained a significant predictor of total and trabecular BMD in both the radius and tibia, but was negatively associated with TotA tibia (see table 1).
Conclusions: This study suggests that there are site specific effects of estrogen on bone area, total and trabecular BMD. Low postmenopausal estrogen levels are associated with low BMD at the radius and tibia. Low estrogen levels are associated with increased bone area only at the tibia. We hypothesise that the effect of estrogen on BMD, periosteal bone apposition and bone remodelling is mediated and augmented by weight bearing.

Table 1 Standardised regression coefficients for determinants of PQCT bone density and bone area, controlled for age, weight and height in elderly women.

PQCT BMD (g/cm3)	R Square	FEI	Weight	Height
Tot BMD Radius	0.124	0.229**	0.195**	−0.068*
Tr BMD Radius	0.091	0.213**	0.133**	−0.077*
Tot A Radius	0.072			0.236**
Tot BMD Tibia	0.195	0.279**	0.247**	−0.124**
Tr BMD Tibia	0.163	0.231**	0.256**	−0.092*
Tot A Tibia	0.288	−0.177**	0.250**	0.418**

Denotes significance of: **p ≤ 0.001, *p ≤ 0.05.

OC7. HIGH BURDEN FACED BY FAMILIES OF THE PATIENTS 2 YEARS AFTER A HIP FRACTURE: THE PICAROS PROSPECTIVE STUDY

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Aim: The assessment of the mean cost of hip fracture (HF) is often focused on short-term events, directly linked to surgery. Our aim was to estimate the long term morbidity for dependent people who return to their individual homes after being discharged from orthopedic or geriatric wards

Methods: We analyzed the burden of help among patients living at home 24 months after a HF. This study is part of the Picaros Study, which included all the patients (n = 1512) hospitalized for a HF in all public or private surgical centers in Picardie, one of the 22 regions of France. All patients were face-to-face interviewed by our technicians, and we analyzed the data collected at the last visit (24 months after the fracture). We classified help of 4 types as either "total" or "partial": 1) eating, 2) going to the toilet, 3) washing (oneself), and 4) getting dressed.

Results: 599 of the people surviving after 2 years were living in individual accommodation, 179 (38%) needed one or more helpers at home. Those who were living with their spouse or with other members of their family at the time of the fracture were less likely to have moved into communal accomodation than to be receiving help at home. Half of the dependent people in individual accomodation were receiving 1 or 2 types of help, virtually always help with washing and/or dressing. The other half were receiving 3 or 4 types of help, including help with eating and going to the toilet. Approximately 3 providers(257) were needed for every 2 patients(179). The unpaid providers were able to provide a mean maximum of 1.5 types of help and above this threshold the help was partly paid. Unpaid help was mainly provided by members of the family and women, wives and daughters, provided the bulk of this help.

In conclusion, families were heavily involved in providing unpaid and collaborative help for people living in individual accomodation who had survived 2 years after hip fracture. This highlights the fact that in addition to its direct cost, hip fracture also has a high intangible cost for the family.

OC8. HYPOVITAMINOSIS D IN EUROPE

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The optimal level of vitamin D for establishing an optimal bone health and preventing osteoporosis is subject to debate these years. The aim of this study was to follow the vitamin D status throughout a year in groups of adolescent girls and elderly women in different European countries to estimate the relative contributions of sun exposure, dietary habits including food fortification and vitamin D supplementation, to vitamin D status. The data presented here are baseline measurements from the study, which was simultaneously conducted in four European countries (Denmark, Finland, Ireland, and Poland) during winter and early spring (February and March). The best measurement of vitamin D status is serum 25-hydroxy vitamin D (S-25OHD). All S-25OHD analyses were performed by HPLC in the same laboratory. Here deficiency is defined as S-25OHD < 25 nmol/l and insufficiency as S-25OHD < 50 nmol/l. Only data from the girls are included in this abstract.

The table shows the median and percentile values of the S-25OHD concentrations, the percentages of the girls with S-25OHD below 25 and 50 nmol/l, the explanatory variables used

Girls	Denmark	Finland	Ireland	Poland
Latitude	55°N	60°N	52°N	52°N
Number of subjects (*n*)	59	57	17	61
Age (years)[a]	12.5 (11.6–13.6)	12.7 (12.1–13.7)	12.1 (11.1–13.8)	12.5 (11.6–13.5)
Weight (kg)[b]	47.7 (12.8)	48.4 (7.9)	49.7 (12.8)	46.9 (9.7)
Height (cm)[b]	157.2 (7.9)	158.7 (6.2)	152.4 (10.3)	157.7 (6.7)
BMI (kg/m^2)[b]	19.1 (3.8)	19.1 (2.4)	21.2 (4.3)	18.8 (3.4)
S-25OHD (nmol/l)[a c d1 e]	24.4 (9.1–86.1)	29.2 (11.3–53.8)	41.3 (18.6–59.3)	30.6 (14.3–88.5)
Percentile 5	10.2	13.9	18.6	15.9
Percentile 10	13.4	16.3	20.0	16.4
Percentile 25	16.5	23.9	32.9	21.5
Percentile 75	36.4	36.0	45.1	38.2
Percentile 90	45.3	41.6	55.1	51.3
Percentile 95	55.1	47.9	59.3	56.0
S-25OHD < 25 nmol/l	51%	33%	18%	33%
S-25OHD < 50 nmol/l	93%	96%	88%	89%
Dietary vitamin D intake (μg/day)[a d2 f]	2.4 (0.3–5.1)	5.0 (1.2–16.2)	2.4 (1.2–7.5)	6.1 (1.6–17.2)
Dietary calcium intake (mg/day)[a d2 f]	831 (181–2646)	1092 (424–2676)	728 (54–2259)	524 (60–1895)
Taking vitamin D supplements *n* (%)	20 (34%)	7 (12%)	3 (18%)	7 (11%)
S-25OHD (nmol/l) eating supplements	38.0	37.9	41.3	32.8
S-25OHD (nmol/l) not eating supplements	21.6	27.6	41.0	28.9
Started period *n* (%)	16 (27%)	33 (58%)	9 (53%)	19 (31%)
Time since period started (months)	11	9	12	9
Prefer to stay in sun during summer *n* (%)[g]	26 (44%)	31 (54%)	9 (53%)	9 (15%)

[a]Median (range).
[b]Mean (SD).
[c]Analysed by HPLC. Significant difference between countries
[d1](P < 0.01)
[d2](P < 0.0001).
[e]Morning blood samples were taken after an overnight fast during February and March.
[f] The dietary intake are calculated from food frequency questionnaires using the same food database and calculation system.
[g] Opposed to avoid sun or sometimes in sun.
BMI: body mass index, S-25OHD: serum 25-hydroxoy vitamin D.

in the multiple regression analyses performed to explain the S-25OHD levels, which are log-transformed in the statistical analyses. The only significant determinants of vitamin D status were country ($P < 0.05$) and use of vitamin D supplements ($P < 0.001$). As shown in the table girls not eating supplements had lower S-25OHD concentration compared to girls eating supplements.

Nine out of ten girls were vitamin D insufficient and possibly in risk of not reaching optimal peak bone mass with increased risk of osteoporosis later in life.

Acknowledgment: The study is part of the OPTIFORD-project 'Towards a strategy for optimal vitamin D fortification', financed by EU, the 5th Framework Programme (QLK1-CT-2000-00623).

OC9. LOW 25-HYDROXYCHOLECALCIFEROL (25OHD) LEVEL IS A RISK FACTOR OF ACCELERATED BONE LOSS IN ELDERLY MEN: THE MINOS STUDY

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We have shown that 25OHD is a determinant of BMD and bone turnover in elderly men *(Szulc et al. Calcif Tissue Int, 2003)*. We hypothesised that low 25OHD level is a risk factor of accelerated bone loss in elderly men. We assessed the bone loss in 699 men aged 50 to 85 followed up prospectively for 58 ± 18 months. BMD was measured at the hip by the HOLOGIC 1000 W device and at the distal forearm with OSTEOMETER DTX 100 device. Average bone loss varied from 0.11%/year at the femoral neck to 0.31%/year at the distal radius. Rate of bone loss in ten-year age groups accelerated with ageing (total hip – $p < 0.003$, distal forearm – $p < 0.001$). After the age of 70, bone loss was twice as high than before the age of 60 (hip - 0.39 vs 0.21%/year, $p < 0.0001$). After adjustment for age and season, bone loss was more rapid in men with baseline 25OHD level below 27 ng/ml. We defined accelerated bone loss as > 1%/year. After adjustment for age and season, 25OHD below the median (≤ 26 ng/ml) was predictive of the accelerated bone loss at the total hip (n = 53, O.R. = 2.2, 95% C.I. - 1.36, 3.69) and at the distal forearm (n = 62, O.R. = 2.85, 95% C.I. - 1.29 - 5.34). Baseline level of parathyroid hormone, calcium intake and leisure physical activity (associated with sunlight exposure) did not correlate with the rate of bone loss at any site of measurement nor interacted with 25OHD.

We conclude that the concentration of 25OHD ≤ 26 ng/mL (65 pmol/L) predicts accelerated bone loss at the hip and distal radius in elderly men.

25OHD (ng/ml)	Distal forearm (%/yr)	Total hip (%/yr)
QI – ≤ 19	−0.44 ± 0.71	−0.34 ± 0.53
QII −19.1–26	−0.36 ± 0.60	−0.34 ± 0.51
QIII −26.1–34	−0.23 ± 0.47	−0.22 ± 0.39
QIV – > 34.1	−0.21 ± 0.35	−0.22 ± 0.36
	p = 0.002	p = 0.02

Supported by a contract INSERM/Merck Sharp & Dohme Chibret, France

OC10. EFFECT OF ANNUAL INTRAMUSCULAR VITAMIN D SUPPLEMENTATION ON FRACTURE RISK: POPULATION-BASED, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Aims: To determine the effect of an annual intramuscular vitamin D injection on fracture rate among men and women aged 75 years and over, living in the general population.

Methods:

(a) *Design:* Randomised, double-blind placebo-controlled trial of 300,000 IU intramuscular vitamin D (ergocalciferol) injection or matching placebo administered every autumn over three years.
(b) *Subjects:* 9,440 people (4,354 men and 5,086 women) aged 75 years and over, living in the general community, recruited from the patient registers of general practitioners in Wessex, England.
(c) *Outcome measures:* Hip, wrist and all non-vertebral fractures.

Results: After three years of follow up, 609 men and women had incident fractures (hip 110, wrist 107, ankle 24). Hazard ratios in the vitamin D group compared with the placebo group were 1.10 (95% CI 0.94–1.29 $p = 0.25$) for any first fracture and 1.48 (95% CI 1.01–2.17, $p = 0.04$) for first hip fracture; and 1.17 (95% CI 0.80–1.71, $p = 0.43$) for first wrist fracture, controlling for age and sex. Although the findings were similar among men and women, the difference between treatment groups for hip fracture appeared more pronounced among those aged 80 years and over, and among those without previous fractures. No apparent protective effect was observed when the cohort was stratified by age, previous fracture, or level of mobility. Analysis of serum PTH and 25-hydroxyvitamin D concentrations in a subset of subjects suggested that the intervention achieved a 20% suppression in peak winter PTH levels.

Conclusion An annual intramuscular injection of 300,000 IU vitamin D is not effective in preventing hip and other non-spine fractures among elderly men and women resident in the general population.

OC11. HIGH RISK OF FALLS RELATED TO LOW D-HORMONE SYNDROME AND ITS TREATMENT WITH ALFACALCIDOL

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Aims: Treatment with D-hormone analogues significantly reduces the number of fallers and falls in elderly. Since impaired renal function is detrimental to the activation of calcitriol (D-hormone) we determined the cutoff levels of creatinine clearance (CrCl) at which D-hormone serum levels decline and investigated if other risk factors are associated with low D-hormone. Using the determined cutoff, we further investigated in post hoc analyses of a double-blind randomized study, if CrCl is associated with the risk of falls and whether treatment with Alfacalcidol can reduce this risk.

Methods: 378 community-dwelling elderly men and women received for 36 weeks randomly 1μg Alfacalcidol (Alpha-D3® TEVA) or placebo daily. Serum calcitropic hormones were regularly measured by radioimmunoassay Falls were assessed by a questionnaire. The risk of becoming a faller and the risk of falling were assessed in multivariate-controlled logistic regression models according to treatment groups and according to a CrCl cutoff at 65ml/min. The results are from ITT analyses.

Results: D-hormone serum levels were in multivariate-controlled analyses, significantly associated with CrCl ($p < 0.0001$) and steadily declined below a CrCl of 65ml/min. A CrCl of < 65ml/min, the use of diuretics and a diagnosis of adult-onset diabetes were in multivariate controlled analyses associated with significantly low D-hormone serum levels ($p = 0.0008$, $p = 0.001$ res. $p = 0.003$). In the Placebo group we observed significantly more fallers in participants having a CrCl of < 65ml/min as compared to participants with a CrCl of ≥65ml/min (OR 4.01, 95%CI 1.48-10.98, $p = 0.006$). In participants with a CrCl of < 65ml/min the 36 weeks of treatment with Alfacalcidol was, compared to placebo, associated with a significant reduction in the number of fallers (OR 0.26, 95%CI 0.08-0.80, $p = 0.019$), and a reduction of the number of falls (OR 0.29, 95%CI 0.09-0.88, $p = 0.028$). We observed no clinically relevant hypercalcemia.

Conclusion: Within other risk factors (serum-cytokines, glucocorticoid-treatment) associated with low D-hormone, a reduced

CrCl of <65ml/min is also associated with a significant increased risk of falls. In a community-dwelling elderly population with a CrCl of <65ml/min, treatment with Alfacalcidol can significantly and safely reduce the low CrCl associated increased number of fallers and the high risk of falls.

OC12. BONE ANABOLIC RESPONSE TO PTH(1-34) TREATMENTS IS ATTENUATED IN RATS FED AN ISOCALORIC LOW PROTEIN DIET

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Stimulators of bone formation can improve bone structure and increase bone strength, being thereby particularly suitable for the management of patients with severe osteoporosis. This condition is frequently associated with malnutrition in elderly. Whether protein intake could influence the response to PTH is unknown. To address this issue, six-month old female rats were fed isocaloric diets containing 2.5% (low Protein) or 15% (normal Protein) casein for 2 weeks. Then, PTH(1-34) (5 or 40 μg/kg BW) or its solvent were given subcutaneously to rats on either diet daily for 4 weeks. Effect on bone strength and its determinants like BMD, geometry and microarchitecture were measured at the level of the proximal and midshaft tibia. PTH(1–34) treatment dose-dependently increased ultimate strength ($+55.3\% \pm 14.3$* and $+96.5\% \pm 16.1$*) and BMD ($10.0\% \pm 2.2$* and $+21.5\% \pm 2.2$*), in rats treated with 5 or 40 μg/kg BW and fed the normal protein diet. In rats fed a low protein diet only the higher dose of PTH significant increased ultimate strength ($+4.2\% \pm 8.4$ and $+43.8\% \pm 13.0$*) and BMD ($+4.12\% \pm 1.98$ and $+11.0\% \pm 2.7$*). At the level of the midshaft tibia, the highest dose of PTH significantly increased ultimate strength and BMD in rat fed a normal casein diet; but not in rat fed low protein diet. MicroCT analysis indicated a dose-dependent increment of trabecular bone volume and thickness in rat fed the normal protein diet. This change was less pronounced in rat fed a low protein diet. At the midshaft tibia level, a dose-dependent significant increment of external diameter, bone volume and cortical thickness was observed in rats fed the normal protein diet but not in those fed the low protein diet. These observations suggest that under a low protein diet, bone formation and thus anabolic effect of PTH is reduced. The changes on bone geometry and micro-architecture, depending on the various protein intakes, could explain most of the attenuated PTH effect on bone strength in rats fed a low protein diet. These results indicate that an isocaloric protein restriction attenuates the anabolic response to PTH by reducing its positive effect on bone formation and thus bone geometry and micro-architecture.

OC13. FRACTURES AND ALL-CAUSE MORTALITY IN A POPULATION SAMPLE OF ELDERLY WOMEN: OBSERVATIONS FROM THE MRC HIP STUDY

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Hip fracture is associated with increased mortality, a significant proportion of which is due to co-morbidity. The association between other fracture types, co-morbidity and mortality has not been widely reported. We studied the contribution of several clinical risk factors and incident fractures to all-cause mortality in a cohort of elderly women.

5212 women aged 75 years or over participated in the MRC HIPS study, a community based study of risk factors for hip fractures combined with a placebo controlled trial of clodronate (Bonefos®). Self-reported medical history was recorded at study entry. Incident fractures were confirmed independently and definite high trauma fractures were excluded from analysis.

The incidence of fracture and mortality was lower than predicted for this population reflecting a "healthy participant" bias. After a median follow-up of 4 years, 184 (3.5%) participants sustained hip fractures, 76 (1.5%) sustained clinical vertebral fractures, and 448 (8.6%) sustained appendicular (non-hip) fractures. Of the latter, 380 (7.3%) sustained exclusively limb fractures. 755 (14.5%) subjects died of various causes in the study period. At baseline, the mortality group were older, had lower body-mass index, and lower hip and forearm bone mineral density (BMD) (all $P < 0.01$). In univariate analysis rheumatoid arthritis (relative risk, 95% CI, 1.80, 1.13–2.85), current corticosteroid (CS) use (1.79, 1.24–2.57), stroke (2.70, 1.84–3.98), Parkinson's disease (2.04, 1.03–4.07), type 1 diabetes (2.26, 1.12–4.54), type 2 diabetes (1.82, 1.32–2.49), hip fracture (2.71, 1.96–3.75), and limb fracture (0.41, 0.28–0.62) were significantly associated with mortality. In multivariate logistic regression models, age (odds ratio, 95% CI, 1.09, 1.07–1.11), 1 standard deviation decrease in hip BMD (1.30, 1.20–1.42), CS use (1.74, 1.19–2.55), stroke (2.51, 1.68–3.75), type 1 diabetes (2.64, 1.26–5.52), type 2 diabetes (2.04, 1.46–2.83), hip fracture (2.20, 1.56–3.10), and limb fracture (0.42, 0.28–0.64) were independently associated with mortality. Limb fracture remained significant even when classified as upper limb (0.44, 0.27–0.70) and lower limb fracture (0.37, 0.16–0.87).

The study confirms the independent associations between hip fracture, co-morbidity and increased mortality. The mechanism of the association between incident limb (non-hip) fracture and decreased mortality requires further investigation and examination in other population samples.

OC14. STRUCTURAL BASIS FOR DIFFERENCES IN FEMORAL NECK FRAGILITY IN CHINESE AND CAUCASIANS

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Aims: We hypothesized that structural characteristics may be better maintained in Chinese than Caucasians in old age, accounting for the lower hip fracture rates in Chinese. A faster rate of periosteal apposition maintains bending strength, while a slower rate of endocortical resorption reduce the increased risk of buckling with age.

Methods: We measured femoral neck (FN) dimensions and BMD using DXA, estimated endocortical diameter, cortical thickness, section modulus, and buckling ratio in 738 Chinese (490 females) and 1181 Caucasians (788 females) aged 18–93 years.

Results: In young women, after adjusting for racial differences in height and weight, FN axis length and diameter remained 4–8% lower in Chinese, while cortical thickness and vBMD were no different by race. Thus, growth produced racial differences in FN geometry; the same cortical thickness was distributed further from the FN neutral axis conferring 22.3% greater bending strength in Caucasians than Chinese. However, buckling ratio was 5.2% lower in Chinese than Caucasian women. In young men, bending strength was 12.5% lower while buckling ratio was no different in Chinese compared to Caucasians. From young (~30yrs) to old age (~70yrs), FN periosteal diameter (height and weight adjusted) increased less in Chinese than Caucasian men (1.0% vs. 9.1%), but increased similarly in Chinese and Caucasian women (4.6% vs. 3.3%). Endocortical diameter increased less in Chinese than Caucasian men (2.6% vs. 12.5%), but similarly in Chinese and Caucasian women (8.5% vs. 6.5%). Bending strength decreased by 6.9% in Chinese men but maintained in Caucasian men, while bending strength decreased similarly in Chinese and Caucasian women (4.0% vs 6.9%). Buckling ratio increased less in Chinese than Caucasian men (14.5% vs 28.4%) but increased similarly among Chinese and Caucasian women (28.8% vs 31.2%). These changes produced 17.4–25.0% lower bending strength and 6.9–8.7% lower buckling ratio in elderly Chinese than Caucasians in both sexes.

Conclusion: Despite the smaller FN diameter and lower bending strength, the relatively thicker cortex in a narrower diameter in elderly Chinese suggest a lower risk of structural failure by local buckling than Caucasians. These structural differences are likely to be established during both growth and aging.

OC15. HOW CAN WE IDENTIFY OSTEOPENIC WOMEN AT HIGH RISK OF FRACTURE : THE OFELY STUDY

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Although a low BMD is the most important fracture risk factor in postmenopausal women, about half of patients with fractures have a T score > -2.5. Bone turnover markers (BTM) and prior fracture are BMD independent fracture risk factors. Aim : to identify within osteopenic women, those at risk of fracture. Methods : We measured BMD by DXA at the spine and total hip and BTM in 668 postmenopausal women (mean age : 62 yr). Women were categorized in 3 groups : normal (T score spine and hip > -1), osteopenic ($-2.5 <$ T score < -1) and osteoporotic (T score spine or hip $= -2.5$). During a median 9.1 yr (IQ :2.9) of follow-up, 158 incident fractures including 50 vertebral fractures were recorded in 116 women : 8% in normal, 48% in osteopenic and 44% in osteoporotic women.

Ten well known predictors of fractures were tested in osteopenic women and except for BMD, three of them were independently associated with a increased fracture risk (age, BMD, prior fracture, BTM). Prior fractures, high levels of bone ALP and their combination were associated with a 2.2 to 2.6 increased fracture risk ($p < 0.01$).The ten years probability of fracture is 29 % if at least one predictor is present contrasting with 19% in all osteopenic and 38% in osteoporotic women. Among osteopenic women, 59% of incident fractures could be identified with assessment of prior fractures and a single BTM measurement (Table). Similar results were obtained with serum osteocalcin or CTX, and in women below or above the age of 65 yr.

Predictors	n	HR (95% CI)*	Fracture probability/ 10yr	Sensitivity	Specificity
Prior fracture	44	2.2 (1.2–4.3)	38%	29	89
Bone ALP (highest quartile)	90	2.2 (1.4–3.8)	28%	43	75
Bone ALP and/or prior fracture	122	2.6 (1.5–4.5)	29%	59	66

*age-adjusted

Conclusion: In postmenopausal women with osteopenia, an increased BTM and prior fracture allow to identify a subgroup of women at high risk of vertebral and non vertebral fracture. Their assessment may play an important role in identifying osteopenic women who may benefit from a therapeutic intervention.
Fracture risk in osteopenic women.

OC16. LARGE WAIST CIRCUMFERENCE AND RELATED LOW APO-A PREDICT ACCELERATED BONE LOSS FROM THE HIP: RESULTS FROM A 9-YEAR PROSPECTIVE STUDY

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Aims: Recent observations implicated low hip bone mineral density (BMD) as an independent predictor of cardiovascular morbidity and mortality. Linking mechanisms to atherogenesis, however, remain obscure. The aim was to investigate whether central obesity and related dyslipidemia are among the common underlying mechanisms.

Methods: Participants were 457 women with mean age 60 ± 7 years. Follow-up period was 9 years. Study parameters were baseline measures of waist and hip circumference, serum glucose and lipids (triglyceride, total cholesterol, LDL-C. HDL-C, apo-A, apo-B), which were related to the 9-year changes in bone markers (s-CTx and s-osteocalcin) and in hip BMD (DEXA). The impact on atherogenesis was estimated by follow-up measure of the severity of aortic calcification (lateral x-rays).

Results: Baseline waist circumference was directly correlated with both baseline and follow-up measures of serum glucose, triglyceride, and LDL, whereas it was inversely correlated with HDL and apo-A (all $p < 0.001$) independetly of years since menopause (YSM), BMI, smoking, and previous hormone therapy. Under the same boundaries, waist circumference was inversely correlated with the 9-year changes in s-CTx and hip BMD ($p < 0.05$). Of the different metabolic factors, apo-A was inversely correlated with baseline s-CTx and s-OC and directly correlated with the 9-year change in hip BMD. Furthermore, the change in apo-A was also inversely correlated with the simultaneous 9-year changes in s-CTx and s-OC. In a backward multiple regression analysis, the independent predictors of the variation in the change of hip BMD were YSM, baseline LDL, apo-A, and CTx ($R = 0.34$, $p < 0.001$). Finally, low apo-A predicted severe AC.

Conclusion: Central obesity is associated with low apo-A, which in turn appears to accelerate not only atherogenesis, but also bone turnover and bone loss from the hip.

OC17. SMOKING AND FRACTURE RISK: A META-ANALYSIS

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Smoking is widely considered to be a risk factor for future fracture. The aim of this study was to quantify this risk on an international basis and to explore the relationship of the risk with age, sex and bone mineral density (BMD).

We studied 59,232 men and women (74% female) from ten prospectively studied cohorts comprising EVOS/EPOS, DOES, CaMos, Rochester, Sheffield, Rotterdam, Kuopio, Hiroshima and two cohorts from Gothenburg. Cohorts were followed for a total of 250,000 person-years. The effect of current or past smoking on the risk of any fracture, any osteoporotic fracture and hip fracture alone was examined using a Poisson model for each sex from each cohort. Covariates examined were age, sex, body mass index (BMI) and BMD. The results of the different studies were merged by using the weighted b-coefficients.

Current smoking was associated with a significantly increased risk ratio (RR) for any fracture compared to non-smokers (RR = 1.25; 95% CI = 1.15–1.36). The RR was marginally downward adjusted when account was taken of BMD (RR = 1.13). For an osteoporotic fracture, the risk was marginally higher (RR = 1.29; 95% CI = 1.13–1.28). The highest risk was observed for hip fracture (RR = 1.84; 95% CI = 1.52–2.22), but this was also somewhat lower after adjustment for BMD (RR = 1.60; 95% CI = 1.27–2.02) or BMI. Low BMD accounted for only 23% of the risk of hip fracture conferred by smoking. The RR was significantly higher in men than in women for all fractures and osteoporotic fractures, but not for hip fracture. For osteoporotic fracture, the RR increased with age, but decreased with age for hip fracture. A smoking history was associated with a significantly increased risk of fracture compared with individuals with no smoking history, but the RR was lower than for current smoking.
We conclude that a history of smoking confers a risk of fracture of substantial importance beyond that explained by measurement of BMD. Its validation on an international basis permits the use of this risk factor in case finding strategies.

OC18. HIP FRACTURE RISK IN STATIN USERS: A POPULATION BASED DANISH CASE-CONTROL STUDY

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Background: Statins have been suggested as potential agents in the treatment of osteoporosis. In some but not all previous epidemiological studies, treatment with statins has been associated with a reduced fracture risk.

Aim: To examine associations between statin treatment and hip fracture risk.

Subjects and methods: In a population-based case-control study design, a total of 6,660 subjects with hip fracture and 33,274

age-matched population controls were retrieved using the Hospital Patient Register in North Jutland County, Denmark and the Danish Central Personal Registry, respectively. Data on redeemed prescriptions for statins within the last five years before the index date were retrieved from a population-based prescription database. We used conditional logistic regression to estimate odds ratios (ORs) for hip fracture according to use of statin prescriptions adjusted for potential confounding factors, i.e., gender, diseases and use of other drugs known to affect bone metabolism and fracture risk.

Results: Risk of hip fracture decreased as number of statin prescriptions increased. After adjustment for potential confounders, statin treatment was associated with a reduced hip fracture risk (OR 0.68; 95% CI 0.49–0.92) for those who had redeemed more than three prescriptions for a statin drug. Stratified analyses on gender and age did not reveal any major differences between men and women or between different groups on the association between use of statins and hip fracture risk.

Conclusion: Our finding supports an effect of statin treatment on hip fracture risk. A reduced fracture risk may be a positive side effect of statin treatment. Further studies are needed to determien whether this association is causal.

OC19. LASOFOXIFENE: A NEXT GENERATION SELECTIVE ESTROGEN RECEPTOR MODULATOR (SERM) FOR THE PREVENTION OF BONE LOSS IN POSTMENOPAUSAL WOMEN

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Aims: In an initial phase 2 study, lasofoxifene doses ranging from 0.4–10 mg/d resulted in statistically significant reductions in markers of bone turnover and LDL-C and statistically significant increases in lumbar spine BMD at 3 months and 1 year compared with placebo. We conducted a second phase 2 study to explore the efficacy and safety of 1 year of lasofoxifene treatment at doses lower than those previously studied.

Methods: Healthy postmenopausal women (n = 394) aged 50–74 years were randomized to receive lasofoxifene 0.017 mg/d, 0.05 mg/d, 0.15 mg/d, 0.5 mg/d, or placebo, in addition to calcium and vitamin D for 1 year. The primary efficacy end point was percentage change from baseline in lumbar spine BMD at 1 year. Secondary analyses included percentage change from baseline in biochemical markers of bone turnover and LDL-C at 6 months.

Results: All lasofoxifene doses resulted in statistically significant increases in lumbar spine BMD compared with placebo at 1 year ($P < 0.001$). Approximately 75% of lasofoxifene- and 43% of placebo-treated subjects experienced increases in lumbar spine BMD. At 6 months, lasofoxifene therapy resulted in statistically significant decreases in secondary efficacy parameters including *N*-telopeptide, deoxypyridinoline, alkaline phosphatase, osteocalcin, and LDL-C compared with placebo. No cases of endometrial cancer, hyperplasia, or other abnormal histopathology were reported. At 1 year, mean endometrial thickness in the lasofoxifene groups ranged from 3.25–4.09 mm compared with 2.51 mm for placebo ($P = 0.007$). Vasodilatation, leg cramps, and leukorrhea were the most frequently reported adverse events among lasofoxifene-treated subjects. No clinically significant mammographic changes or breast cancer cases were observed during the trial.

Conclusions: One year of lasofoxifene therapy is well tolerated in postmenopausal women, has an acceptable safety profile, and produces significant increases in lumbar spine BMD and significant decreases in biochemical markers of bone metabolism and LDL-C over a broad range of doses.

Percentage Change From Baseline	Lasofoxifene 0.017 mg/d	Lasofoxifene 0.05 mg/d	Lasofoxifene 0.15 mg/d	Lasofoxifene 0.5 mg/d	Placebo	*P* Value*
Lumbar spine BMD† (percentage of responders)	1.75 (76.7)	1.80 (78.0)	1.97 (74.1)	2.19 (78.7)	−0.25 (42.6)	< 0.001
N-telopeptide‡	−27.5 ± 33.7	−27.1 ± 30.8	−37.1 ± 24.5	−35.6 ± 31.0	−0.8 ± 43.3	≤ 0.001
Deoxypyridinoline‡	−5.9 ± 20.7	−15.3 ± 22.9	−14.0 ± 18.0	−16.0 ± 16.5	0.2 ± 23.2	< 0.001§
Alkaline phosphatase‡	−9.3 ± 23.2	−16.7 ± 16.3	−19.8 ± 17.1	−23.6 ± 17.5	−4.1 ± 23.4	< 0.001§
Osteocalcin‡	−4.3 ± 18.7	−14.2 ± 15.5	−14.3 ± 20.6	−18.9 ± 14.0	3.1 ± 23.9	< 0.001§
LDL-C‡ (raw value [mg/dL] ± SD)	−12.8 ± 13.0 (119.2 ± 25.2)	−16.3 ± 11.7 (111.0 ± 25.9)	−20.6 ± 12.3 (107.3 ± 26.4)	−21.1 ± 14.3 (106.5 ± 23.2)	−6.1 ± 15.5 (128.9 ± 29.9)	< 0.001§

*P value for each of the lasofoxifene dose groups vs placebo.
†Percentage change from baseline at Month 12; least squares means value.
‡ Percentage change from baseline at Month 6; raw mean value ± SD.
§$P < 0.001$ vs placebo for all doses of lasofoxifene except 0.017 mg/d.

OC20. RISK ASSESSMENT TOOLS FOR OSTEOPOROSIS: SCOPE AND LIMITS

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Objectives: Several indices have been developed and validated to identify individuals at risk of osteoporosis: OST,ORAI,SCORE and OSIRIS. This study was designed to compare their discriminatory performances in identifying osteoporotic postmenopausal women.

Material and methods: The data needed to calculate all indices and corresponding BMD values for the total hip, femoral neck and lumbar areas, were obtained from 4035 postmenopausal Caucasian women. The OST, ORAI, SCORE and OSIRIS indices were derived according to the algorithms suggested by their developers. The following cutoffs for DXA referral were used: < 2 for OST, > 7 for SCORE, > 8 for ORAI and < 1 for OSIRIS. Also, 3 risk categories were used for each index, according to their developer's recommendations. BMD were obtained using dual X-Ray absorptiometry (DXA) technology (Hologic QDR series equipment) and converted into t-scores using local reference values. Internal and external validity of the four tools were investigated using sensitivity/specificity and positive/negative predictive values (PPV, NPV), respectively. ROC curves were drawn for each tool as well and for bone status categories of −2 and −2.5 standard normal deviates to t-score.

Results: At the recommended cutoffs, OST showed the highest sensitivity (81–97%) and NPV (77–99%) for predicting osteoporosis or severe osteopenia at the femoral, hip or lumbar levels, followed by SCORE, ORAI and OSIRIS. Conversely, OSIRIS reached the highest specificity level (63–69%), followed by ORAI, SCORE and OST. Using these tools to predict osteoporosis at any site, OST and SCORE were found to be equivalent in sensibility (78–86%) and NPV (71–86%) whilst OSIRIS was the only indice to reach 50–65% in PPV. Notwithstanding OST, OSIRIS and SCORE truly identified 81,2–85% of osteopenic or osteoporotic subjects of their respective high risk categories.

Conclusions: The high NPV at all skeletal sites demonstrated the usefulness of these indices to exclude women from DXA testing. The OST performed at least as well compared to the other indices, even if its calculation rule is simpler. We conclude that these tools are effective in referring high-risk subjects to DXA and to exclude those with very low risk ones, in two-steps mass screening enterprises.

OC21. USEFULNESS OF BODY SWAY IN PREDICTING FALLS IN OLDER WOMEN WITH VERTEBRAL FRACTURES: A PROSPECTIVE STUDY

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Introduction: Vertebral fracture patients have an increased risk of hip fractures. Identifying those at increased falls risk in this population should allow targeting of fall and fracture prevention measures. Body sway (BS) has been advocated as a measure for predicting falls. This study aimed to assess if BS could predict falls in women with vertebral fractures.

Methods: Women aged ≥60 years with ≥1 vertebral fracture were recruited. Baseline demographics and previous falls history

was ascertained. BS was measured by a swayometer (Lord et al; JAGS 1991;39:1194–1200). Prospective falls data were collected at 3-monthly intervals (telephone) and final clinic interview at 12 months.

Results: 104 women (mean age 78 ± 7 years) were recruited. 84 completed follow up (7 died). 46.4% (n = 39) of women had at least one fall after 1 year. The median BS (interquartile range) was 81.6cm2 (31.1–164.8). Univariate logistic regression using fallers (≥1 fall) at 12 months as the dependent variable, showed that a history of recurrent falls (2 or more in previous year) [OR 6.5, 95%CI 1.7–25.2, p = 0.007] and BS quartiles [OR 1.8, 95%CI 1.7–2.7, p = 0.007] significantly predicted falls. Receiver Operator Characteristics curve showed that the optimal cut-off for BS was 125 cm2. Using this cut-off the OR for BS in fall prediction was 6.3 [95%CI = 2.3–17.6, p < 0.001], and the sensitivity, specificity, positive predictive value and negative predictive value were 54%, 84%, 75% and 68% respectively. Combining this BS cut-off with recurrent falls history (both present), the OR increased to 43.7, and the specificity and positive predictive values both increased to 100% (although at the expense of a lower sensitivity of 21% and negative predictive value of 59%). With the either/or method of combining previous recurrent falls with the 125 cm2 BS cut-off, the sensitivity and negative predictive value were improved to 64% and 72% respectively.

Conclusion: These data suggest that the measurement of BS can predict falls in older women with vertebral fractures, thus potentially allowing the clinician to target fall and fracture prevention measures to those at highest risk. Fall prediction can be further improved by combining BS with a previous history of recurrent falls.

OC22. BONE MASS MEASUREMENT PREDICTS MORTALITY IN ELDERLY WOMEN: THE PERF STUDY

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Aim: To investigate the predictive value of bone mass for risk of total and disease-specific mortality in postmenopausal women.

Methods: We followed 6544 postmenopausal women aged 45-70 years old at baseline for an average of 10 years. At baseline, bone mineral density (BMD) at the spine and hip or bone mineral content (BMC) at the forearm were measured with DEXA. During the follow-up period, 724 women had died. Causes of death assigned by ICD 8 and ICD 10 codes were obtained from the Danish Ministry of Health.

Results: 217 women died of cardiovascular diseases (CVD), 43 of breast cancer, 290 of other types of cancer, and 174 of other diseases/conditions. Women who died during the follow-up period were slightly older at baseline than survivors (65.5 vs. 63.8 yrs, p < 0.05). When adjusting for age, those who died during the follow-up period had significantly lower bone mass at all sites (Fig. 1, left). Women who died of breast cancer had significantly higher bone mass at all sites (mean 4.5%, p < 0.05) compared with those died of other causes. When comparing survivors with those who died of other causes, but not breast cancer or CVD, the difference in bone mass became even greater (Figure 1, right). When stratifying the population into categories of normal, osteopenic and osteoporotic (WHO criteria), women with T score below -2.5 at the spine, hip and forearm had significantly increased risk for total mortality with odds ratio 1.5, 2.1 and 1.6, respectively after adjustment for age (p < 0.001). Women with normal BMD (T score > −1) were at 1.9-5.1 times increased risk of breast cancer mortality.

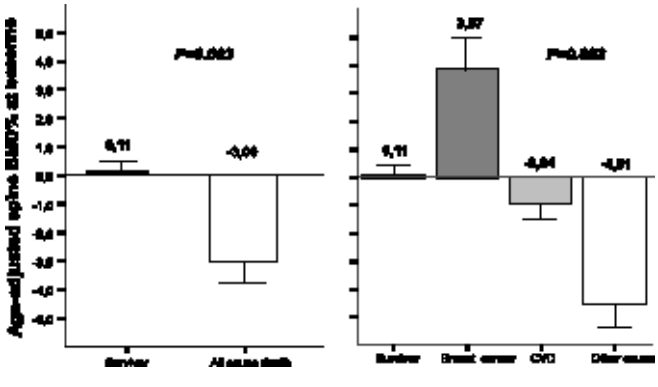

Fig. 1 Age-adjusted spine BMD% at baseline between survivor and dead population

Conclusion: Lower bone mass after menopause is a risk factor for increased total mortality in later life. High BMD increases the relative risk for breast cancer mortality.

OC23. HIP FRACTURE PROBABILITY AND ABILITY TO PAY FOR TREATMENT: A WORLDWIDE PERSPECTIVE

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There are very large differences in the risk of hip fracture in different regions of the world. So too are there large disparities in health care priorities and the ability to pay for health care. Thus, the intervention threshold – i.e. the hip fracture risk above which treatment can be recommended – needs to take account of this heterogeneity. The aim of this study was to examine the relationship between hip fracture risk and economic prosperity.

Ten-year hip fracture probabilities were computed for 30 countries where recent data (from 1990) were available on incidence and mortality. These covered all WHO regions of the world (Africa, Asia, Europe, North America, Oceania and South America). Affordability of treatment was expressed as Gross Domestic Product (GDP) per capita for each country. The relationship was examined by regression analysis (GLM).

Ten-year hip fracture probability ranged from 0.3 to 5.7% and GDP/capita from ,700-$ 37,600. There was a highly significant relationship between GDP/capita and 10-year hip fracture probability for men, women and both sexes combined (p < 0.001). For each $ 10,000 increase in GDP/capita, the 10-year probability of hip fracture was increased by + 1.3%.

A similar increase was observed for increasing latitude. Interestingly, both GDP and latitude was related to 10-year hip fracture probability independently.

The finding of this relationship provides a mechanism for computing affordable intervention thresholds in different regions of the world.

OC24. SPINE OSTEOARTHRITIS IS ASSOCIATED WITH AN INCREASED VERTEBRAL FRACTURE RISK IN POSTMENOPAUSAL WOMEN: THE OFELY STUDY

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Although osteoarthritis (OA) and osteoporosis both increased with age, their coexistence is unusual. A higher bone mineral density (BMD) in OA is well documented but the reduction of fracture risk is controversial. Aim : To analyze the risk of fracture in postmenopausal women with spine OA.

Methods : Spine OA was evaluated by lateral radiographs according to the method of Lane and BMD was measured by DXA in 559 postmenopausal women from the OFELY cohort, mean age 68 ± 8 yrs, eight years after their inclusion into the study. Previous fragility fractures were registered during the annual follow-up and vertebral fractures were evaluated with radiographs. Severity of OA was assessed according to the presence of osteophytes and disc narrowing using a scale from score 0 (normal) to 3 (severe) and

graded from 0 to 2 (moderate or severe osteophyte and/or narrowing).

Results : Osteophytes and disc narrowing were present in 75 and 64% of women at the lumbar spine and in 88 and 51% at the thoracic spine, increasing with age. BMD increased with severity of osteophytosis at the lumbar spine, hip and whole body whereas severity of narrowing was associated with a higher BMD only at the spine. Ninety-six fractures, including 48 vertebral fractures, occurred before OA assessment, representing 19% of women with OA grade 2 and 16 % with grade 0 or 1. No significant association was found between spine OA and all fragility fractures. In contrast, disc narrowing was associated with an increased risk of vertebral fracture with odds-ratio (95% CI) of 3.2 (1.1–9.3) after adjusting for age, BMI and BMD. The risk of vertebral fracture increased with the aggravation of narrowing. In comparison with the score 0, the odds-ratio varied from 2.8 (0.9–8.7) to 4.6 (1.2–16.9) according to the narrowing score. There was no association between fracture risk and the osteophytosis score.

Conclusions : despite a higher BMD, women with spine OA do not have a reduced risk of fracture. Disc narrowing is associated with a significant increased vertebral fracture risk. The risk of osteoporotic fracture should not be underestimated in women with spine OA.

OC25. INFLUENCE OF PHYSICAL ACTIVITY AND VITAMIN D ON BONE MINERAL GAIN AMONG PERIPUBERTAL FINNISH GIRLS: A 3-YEAR PROSPECTIVE STUDY

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Aims: To investigate the influence of physical activity on bone mineral content (BMC) accrual at the femoral neck and lumbar spine.

Methods: A total of 171 healthy peripubertal girls aged 9–15 years (62 gymnasts, 58 runners, and 51 nonathletic controls) were included. Weight, height, and the type and the amount of physical activity were recorded at 6-months' intervals over 3 year. Serum 25-hydroxyvitamin D (S-25(OH)D) was measured at baseline. BMC of the femoral neck and lumbar spine were measured by dual-energy x-ray absorptiometry (DXA).

Results: By stepwise linear regression analysis the increase of bone area and weight, the amount of physical activity, and the baseline BMC presented as significant variables and accounted for 67.3% of the variation of the 3-year change of BMC (dBMC) at the femoral neck. At the lumbar spine, the increase of bone area, height and weight, the amount of physical activity, S-25(OH)D and baseline BMC were the significant predictors for dBMC and accounted for 90.6%. The adjusted (for increase of height, weight, and bone area) dBMC was 41.7% ($P < 0.001$) and 13.6% ($P < 0.001$) greater in the physically most active tertile than in the physically least active tertile of the participants at the femoral neck and at the lumbar spine, respectively. The corresponding figures for the physically most active tertile compared with the middle tertile were 37.7% ($P < 0.001$) and 12.1% ($P < 0.05$) greater at the femoral neck and lumbar spine, respectively.

Conclusions: High-impact loading during the peripubertal years is extremely important and beneficial for the growing skeleton, and particularly for the acquisition of BMC of the femoral neck. Vitamin D has effect on BMC at the lumbar spine.

OC26. UNIQUE EVIDENCE FOR LOAD INDUCED MODIFICATION IN TRABECULAR BONE ARCHITECTURE AS WELL AS INCREASED CORTICAL BONE FORMATION IN A NON-INVASIVE AXIAL LOADING OF MOUSE TIBIAE

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Although bone's response to mechanical loads can be studied in several in vivo models, axially loading the murine tibia, non-invasively, through its articulations would have advantages. These include: i) larger bone size; ii) scope to apply disuse; iii) larger region of cancellous bone volume, and iv) scope to apply strain distributions similar to those engendered during locomotion. Herein, we explore such a model in which cortical and cancellous bone adaptation to mechanical loading is examined.

We used 8 groups of female, 14 week old C57Bl/J6 mice: 5 groups were loaded so that 1200–2000με were produced on the lateral midshaft cortex. 2 groups were submitted to sciatic neurectomy (SN, 114 days) with and without loading. 1 group was sham-operated. Animals were loaded on alternate days for 3 weeks. They received fluorochrome label on third and last days and were killed 3 days later. Tibiae (+contralateral controls) were embedded; transverse confocal images from 5 diaphyseal sites were analysed histomorphometrically. Proximal tibial epiphyses were analysed by μCT scans, which extended 0.75 mm distally of the growth plate.

We found that murine tibia midshaft exhibited low physiological strains during normal locomotion (< 300 με). Loading at 2000 με significantly increased periosteal bone formation at all sites. Increased endosteal formation was only evident at sites distal to the midshaft. In contrast, an increase in cortical bone formation was not observed in tibiae loaded at less than 1200 με. μCT scans showed that loading induced significant increases in trabecular bone thickness; SN-induced 'disuse' significantly decreased bone volume fraction and increased trabecular spacing, while loading after 'disuse' also increased trabecular thickness.

We show that: i) loading induces an osteogenic response of trabecular bone architecture and, at least partly, rescues the effects of SN, ii) tibial cortices, which encounter low strains during locomotion, require these to be exceeded during axial loading to induce bone formation. These results suggest that the murine tibia offers a novel model for studying the effects of loading on cortical and cancellous bone. To our knowledge this is the first evidence for direct load-induced changes in trabecular architecture in an animal model.

OC27. INTERACTION BETWEEN CALCIUM INTAKE AND MENARCHEAL AGE ON BONE MASS GAIN: AN 8-YEAR FOLLOW-UP STUDY FROM PREPUBERTY TO POST-MENARCHE

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Both late menarche and low Ca intake during growth are considered as risk factors for osteoporosis, probably by impairing optimal peak bone mass achievement. We investigated whether the response of bone mineral mass accrual to increased Ca intake could vary according to menarcheal age and, conversely, whether Ca intake could influence menarcheal age. In an initial study girls aged 7.9 ± 0.1 years (mean ± sem) were randomized in a double blind controlled trial to receive either a Ca supplement (Ca-suppl.) of 850 mg/d or placebo during one year. We now report on results obtained when subjects were 16.4 ± 0.1 years. Areal bone mineral density (aBMD) was determined by DXA at 6 skeletal sites: radius metaphysis, radius diaphysis, femoral neck, trochanter, femoral diaphysis and L2–L4 vertebrae. During the intervention the mean yearly aBMD gains at these 6 sites were 21 ± 2 and 27 ± 2 mg/cm2 ($p < 0.005$) in the Placebo and Ca-suppl. group, respectively. Subjects were re-examined at 1.0, 3.5 and 7.5 years after the end of intervention and menarcheal age was recorded. Spontaneous Ca intake was assessed by frequency questionnaires at baseline, 6 and 12 months and at each follow-up visit. A significant earlier mean age of menarche was observed in the Ca-suppl as compared to the placebo group ($p < 0.05$) and a

significant negative correlation was found between menarcheal age and Ca intake ($R = -0.35$, $p < 0.0001$), and between gain in aBMD from age 8.0 to 16.4 years and menarcheal age at all 6 skeletal sites (R range: from −0.41 to −0.22, $p < 0.0001$ – $p < 0.016$). The positive effect of Ca-suppl. on mean aBMD gain (mg/cm2) from baseline remained significantly greater in girls below but not in those above the median of menarcheal age (13.0 years). Early menarcheal age (12.1 ± 0.1): placebo: 286 ± 8; Ca-suppl. 317 ± 8, $p < 0.01$. Late menarcheal age (13.9 ± 01): placebo 284 ± 10, Ca-suppl. 276 ± 16, $p > 0.05$. This study suggests that the level of Ca intake during pre-puberty could influence the timing of menarche which in turn, appears to influence long term bone mass gain in response to Ca supplementation. Thus, both early menarcheal age determinants and high Ca intake may positively interact on bone mineral mass accrual.

OC28. POSTTRANSLATIONAL MODIFICATIONS OF COLLAGEN CONTRIBUTE TO BONE STRENGTH INDEPENDENTLY OF BONE MINERAL DENSITY (BMD)

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Bone strength depends on its mass and geometry, but also on the material properties of its matrix.Mineral accounts for the stiffness of bone and collagen mainly influences its toughness although the relative contribution of each is unclear.

Aim: To analyze the role of posttranslational modifications of collagen on the mechanical properties of cortical bone using an in vitro model where the extent of crosslinking can be modified, keeping constant the size and the mineral content of bone.

Methods: Calibrated fetal bovine cortical bone specimens (11 animals, 41 samples in total) characterized by a low degree of postranslational modifications were incubated for 0, 60, 90 and 120 days at 37 °C to induce collagen crosslinking. At each time, 3 point bending mechanical test was performed to determine the stiffness and the yield strength. The concentration of enzymatic (PYD, DPD) and non-enzymatic (pentosidine) crosslinks was measured by HPLC and the extent of C-telopeptide (CTX) isomerisation was evaluated by ELISA of native (α CTX) and isomerised (β CTX) forms.

Results: After 60 days of incubation, yield strength was decreased by 40% ($p = 0.01$) whereas no effect was observed on stiffness and BMD. The decline of yield strength was associated with increases of PYD (+98%, $p = 0.005$), DPD (+42%, $p = 0.013$), pentosidine (+ 55 fold, $p = 0.005$) and β/α CTX ratio (+4.9 fold, $p = 0.005$). In multivariate analyses, the prediction of yield strength was significantly improved by combining BMD ($r2 = 0.36$) with PYD (r2 increasing to 0.58, $p = 0.0003$), pentosidine ($r2 = 0.58$, $p < 0.0001$) or β/α CTX ($r2 = 0.49$, $p = 0.003$. The β/α CTX ratio highly correlated with PYD ($r = 0.63$), DPD ($r = 0.60$) and pentosidine ($r = 0.7$), ($p < 0.001$ for all). We measured the urinary ratio β/α CTX in 404 postmenopausal women followed for 7 years and found that it was associated with incident fracture independently of BMD and bone turnover.

Conclusion: These data indicate that the degree of posttranslational modifications of collagen matrix plays an independent role in determining the mechanical competence of cortical bone. The ratio of β/α CTX may reflect the extent of posttranslational modifications of collagen and its measurement in urine could provide an in vivo marker of bone collagen quality.

OC29. LEPTIN RECEPTOR (LEPR) POLYMORPHISMS CONTRIBUTE TO BONE MASS IN HEALTHY PRE-PUBERTAL BOYS

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The adipocyte-derived satiety factor, Leptin, also appears to negatively regulate bone formation in mice. However, its contribution to bone mass determination in humans remains unclear. A Gln223Arg missense polymorphism (c.668A > G) in the leptin receptor gene (LEPR) and a promoter polymorphism (−2548G > A) in the leptin gene (LEP), both previously associated with leptin levels and obesity in humans, were investigated for their association with bone mass in healthy European-Caucasian boys (n = 235, 7.4 ± 0.4 yrs).

LEPR A > G (MspI) and LEP −2548G > A (HhaI) polymorphisms were determined by PCR. Bone mineral content (BMC, gm) was measured by DXA at the lumbar spine (LS), femoral neck (FN), total hip (TH), midshaft femur (FS), distal and ultradistal radius (DR, UR). Dietary intake of calcium (Ca) and proteins, and the level of physical exercise (PE) were recorded.

Frequency of the LEPR G and LEP –2548A allele was 0.30 and 0.43, respectively. LEP promoter genotypes were not associated with any variable. In contrast, LEPR genotypes were significantly associated with height ($p = 0.044$) and BMC at FN ($p = 0.035$), TH ($p = 0.022$), FS ($p = 0.027$), DR ($p = 0.007$), and marginally at UR ($p = 0.066$) and LS ($p = 0.099$). Thus, BMC was 8–12% significantly lower in GG (n = 21) compared to AA (n = 108), and intermediate in GA. BMI, age, Ca and protein intake were similar among LEPR genotypes. However, PE significantly differed among genotypes ($p = 0.021$) and was significantly related to BMC at all sites (by multiple regression further including age, Ca and proteins). Subsequently, significant p values for interaction between PE and LEPR genotypes were found at several skeletal sites (by 2F-ANOVA). Indeed, BMC was significantly lower in GG compared to AA among children with low PE (≤median, 222 kcal/d), but not with higher PE levels. After adjustment for age, height, BMI, PE and dietary intakes, LEPR alleles contribution to FN BMC variance was 1.5% in all boys and 2.9% in those with low PE.

In conclusions, LEPR Gln223Arg polymorphism is associated with BMC in healthy pre-pubertal boys, particularly in those with low levels of physical exercise. These data support the possibility that the leptin system may influence bone mass in humans in relation to energy expenditure.

OC30. ACIDIFICATION OF THE OSTEOCLASTIC RESORPTION LACUNAE IMPINGES ON THE COUPLING OF BONE RESORPTION TO BONE FORMATION

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Bone resorption is tightly coupled to bone formation in normal healthy adults. However, in autosomal dominant osteopetrosis II (ADOII) caused by a mutation in the ClC-7 chloride channel gene essential for acidification of the osteoclastic resorption lacunae and resorption, decreased levels of bone resorption, normal levels of bone formation, but 5 fold-increased levels of osteoclasts are detected. This strongly suggests that bone turnover has been uncoupled in these patients.

We found that osteoclastogenesis of ADOII osteoclasts was normal, albeit the resorption was reduced to 10–25%. When mature osteoclasts were cultured on bovine bone slices, osteoclast viability was augmented either by 20% in ADOII osteoclasts or by 50–80% through complete abrogation of acidification by either a chloride channel inhibitor (NS5818 10microM) or an inhibitor of the proton pump, Bafilomycin 30nM. This suggests that attenuated osteoclast apoptosis is responsible for the increased osteoclast levels in the ADOII patients.

To investigate if decreased resorption is compatible with unaffected bone formation, we used a chloride channel inhibitor in the rat OVX model. We observed a significant 40% decrease in the resorption marker (Dpd), but no effect on the bone formation marker (osteocalcin). Moreover, we found a significant increase in serum TRAP levels, in alignment with the attenuated ClC-7 activity in ADOII patients.

In conclusion, osteoclasts with attenuated dissolution of the inorganic phase of bone have prolonged viability. The increased

levels of inactive osteoclasts generate formation signals to osteoblasts, either directly or by an increased area of bone surface exposed to resorption. These results suggest that acidification of the osteoclastic resorption compartment may be involved in the coupling of bone resorption to bone formation.

OC31. RNA PROFILING OF ANTIRESORPTIVES REVEAL ALENDRONATE AND ESTROGEN DECREASE BONE FORMATION GENES WHILE RALOXIFENE MAINTAINS THEIR INCREASE IN THE OVARIECTOMIZED RAT

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The preservation of bone by three classes of compounds (Estrogen, SERMS, and bisphosphanates) have been well described in the ovariectomized rat model by histomorphometric and histological analysis but a global analysis comparing their effects on gene expression has not yet been described. This study utilized an Affymetrix microarray to analyze RNA from the OB-enriched proximal femur of sham, ovariectomized rats, and ovariectomized rats treated for 1 day and 5 weeks with 17α-ethinyl estradiol (E) at 0.1 mg/kg, Raloxifene (Ral) at 3.0 mg/kg, EM652 at 0.1 mg/kg, and Alendronate (Ald) at 8 μg/kg. Genes significantly changed ($p < 0.05$) from sham levels following ovariectomy, which were also changed by any drug following 5 weeks of treatment, were identified and subjected to clustering analysis. Genes associated with bone formation (i.e. type I collagen α 1 & 2, osteocalcin, osteonectin, and biglycan) clustered together indicating a similar pattern of regulation. Ovariectomy, known to increase the rate of bone formation, induced these genes within 12 d and sustained this over time. Following 5 weeks, Ral only slightly lowered the levels of these genes while E and Ald suppressed them below that of sham. EM652 suppressed these genes to a level intermediate between Ral and Ald. At the earlier timepoint Ald began decreasing some of these formation genes but E did not. It can be concluded that at the molecular level the three classes of antiresorptives can be identified by contrasting their effects on mRNA levels of osteoblastic genes. Ald began turning down the expression of osteoblastic genes within 24 h and then lowered them below sham levels with time. E did not alter expression at 24 h, but suppressed these genes below that of sham at 5 weeks. The SERMS were also differentiated by a partial suppression of formation genes at both timepoints with EM652 and a negligible change by Ral only at 5 weeks. In summary, ovariectomy rapidly induced markers of bone formation and these levels are maintained with Ral treatment but are suppressed with Ald and E. Additionally, these data provide evidence that treatment with Ald not only inhibits resorption but also suppresses osteoblastic activity.

OC32 POSITIVE CORRELATIONS BETWEEN EARLY CHANGES IN BIOCHEMICAL MARKERS OF BONE FORMATION AND VOLUMETRIC BMD AFTER TERIPARATIDE THERAPY: FURTHER EVIDENCE FOR DIVERGING EFFECTS OF ALENDRONATE AND TERIPARATIDE ON BONE

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We conducted an 18-month randomized controlled trial comparing the effects of teriparatide 20 mcg/day [rhPTH (1-34),TPTD20] and alendronate 10 mg/day (ALN10) on bone in postmenopausal women with osteoporosis. Previously reported results have shown significant increases of 100 to 300% in bone turnover markers (BTM) during the first 6 months of TPTD20 treatment compared with decreases of 60 to 70% during ALN10 treatment (McClung et al. ASBMR 2003). Both lumbar spine areal BMD (aBMD) by DXA and trabecular volumetric BMD (vBMD) by QCT increased in each treatment group. However, while increases in aBMD were nearly 2-fold, vBMD increases were 4 to 5-fold greater in TPTD20 versus ALN10 treated patients.

Aims: To assess the correlation of early changes in BTM and improvements in bone mass as reflected in lumbar spine aBMD and vBMD changes after 18 months of ALN10 or TPTD20 therapy.

Methods: Early changes in the collagen bone formation markers (PINP, PICP) were assessed using the area under the curve (AUC) from the first 6 months of treatment. Spearman's correlation coefficient was calculated between 6-month AUC values and last observed aBMD and vBMD.

Results: In TPTD20-treated patients, early changes in PINP and PICP had similar significant positive correlations with lumbar spine aBMD and vBMD (Table). After ALN10 therapy, early changes in PINP and PICP had significant negative correlations with lumbar spine aBMD, but lesser negative and nonsignificant correlations with lumbar spine vBMD.

BMD parameter Biochemical marker	Spearman Correlation	
	ALN10	TPTD20
Change in Lumbar spine aBMD (DXA) at study endpoint	(N = 89)	(N = 90)
PINP first 6-months AUC	−0.51*	0.53*
PICP first 6-months AUC	−0.27*	0.42*
Change in Lumbar spine vBMD (QCT) at study endpoint	(N = 23)	(N = 26)
PINP first 6-months AUC	−0.20	0.51*
PICP first 6-months AUC	−0.19	0.55*

*$P < 0.01$

Conclusions: Early changes in PICP and PINP correlate positively to ultimate aBMD and vBMD response in teriparatide-treated patients and inversely to aBMD in alendronate-treated patients. In alendronate-treated patients no correlation to vBMD was demonstrable. These results highlight the differences in mechanism of action between the two therapies, and indicate that PINP and PICP are good markers for the skeletal response to teriparatide.

OC33. BONE TURNOVER AFTER ONE YEAR OF ALENDRONATE AND FRACTURE RISK: THE FRACTURE INTERVENTION TRIAL

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Short-term changes in biochemical markers of bone turnover predict subsequent spine and non-spine fractures among bisphosphonate treated women, but the utility of a single on-treatment measurement is unknown. In addition, some have hypothesized that very low turnover on therapy may be associated with impaired bone quality and increased fragility.

In the Fracture Intervention Trial we measured bone specific alkaline phosphatase (bone ALP, Hybritech) and N-terminal propeptide (P1NP, Orion) after 1 year of therapy with alendronate (ALN), 5 mg/d (n = 3105) or placebo (n = 3081). Among ALN-treated women, during a mean follow-up of 3.6 years after baseline, 226 non-spine fractures (including 15 hip fractures), and 119 incident vertebral fractures on paired lateral spine x-rays were documented. Age-adjusted logistic and hazard models were used to examine the relationship between marker level after 1 yr. of ALN therapy and subsequent spine and non-spine fracture.

After 1 year of ALN, lower bone ALP levels (per SD) were associated with fewer vertebral fractures (OR = 0.75, 95% CI: 0.65, 0.86) but not non-spine fractures (RH = 0.99, 95% CI: 0.87, 1.14).

Lower bone ALP levels were also associated with a reduced risk of hip fracture, but this did not reach statistical significance (RH = 0.72, 95% CI: 0.50, 1.02). Among women in the lowest quintile of bone ALP after 1 yr. of ALN (< 6.4 mg/dl), there was no evidence of an increase in fracture risk (Fig. 1). Further adjustment for baseline BMD and prevalent VF had no effect. Results were similar with PINP.

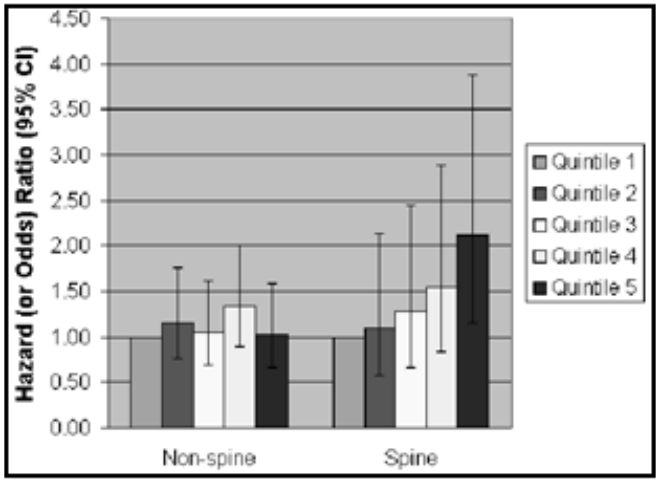

Fig. 1 Risk of Fracture by Quintile of Bone ALP After 1 Year of ALN

We conclude that a single on-therapy measurement of bone turnover is associated with the risk of vertebral and possibly hip fracture among alendronate-treated women. The lack of an association with non-spine fracture deserves further study. We found no evidence that women in the lowest quintile of turnover after 1 yr. of ALN were at increased risk of fracture.

OC34. RAPID RESOLUTION OF THE REDUCTION OF BONE TURNOVER MARKERS AFTER DISCONTINUATION OF RISEDRONATE IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS PREVIOUSLY TREATED FOR 2 YEARS

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In women with postmenopausal osteoporosis, 35 mg risedronate once weekly and 5 mg once daily have similar effects on bone mineral density (BMD) and bone turnover markers (BTM). We evaluated resolution of BTM effects after discontinuation of risedronate in women previously treated for 2 years.

Subjects were recruited from women completing a 2-year study evaluating risedronate 35 mg once weekly, risedronate 50 mg once weekly and risedronate 5 mg daily. All were ambulatory, 50 years or older, postmenopausal for at least 5 years, naïve to bisphosphonate therapy, and with either a BMD T-score of −2.5 or lower (lumbar spine or proximal femur) or a T-score lower than –2 and at least one vertebral fracture. Subjects agreeing to participate in this extension study were block randomized to receive risedronate 35 mg once weekly or no active treatment for 6 months. All subjects received 1 g elemental calcium supplementation daily, and vitamin D (up to 500 IU/day) if supplemented during the first 2 years.

Time to resolution of the BTM effects after discontinuing risedronate therapy (duration 2 years) was compared with continuing risedronate therapy. We measured serum CTx (sCTx), urinary NTx (uNTx), and serum BSAP (sBSAP) after 2 years of risedronate therapy. Time to resolution of effect for the resorption markers was defined as the earliest time point where the median percent increase in sCTx or uNTx was greater than 100% compared to the baseline value obtained after 2 years of risedronate dosing. If the prior treatment with risedronate over 2 years led to a 50% reduction in sCTx and uNTx, resolution within 3 months was observed after discontinuing risedronate therapy.

BTM v. baseline	Treatment	1 mo % (SEM)	2 mo % (SEM)	3 mo % (SEM)	6 mo % (SEM)
SCTX	Rise 35 mg OaW	+7.3% (7.9) n = 44	+10.5% (10.5) n = 42	+18.1% (8.5) n = 45	+24.4% (24.4) n = 42
	Control	+ 54.4% (9.2) n = 44	+76.9% (9.2) n = 44	+101,8% (9.5) ¥ n = 44	+117.4% (14.5) ¥ n = 42
uNTX/Creat	Rise 35 mg OaW	+5.4% (6.4) n = 42	+7.8% (8.9) n = 42	−0.4% (11.9) n = 43	+5.8% (8.9) n = 40
	Control	+28.2% (8.9) n = 42	+44.2% (10.9) n = 43	+48.7% (36.5) ¥ n = 44	+71.3% (19.2) ¥ n = 42
BSAP	Rise 35 mg OaW	−0.7 % (2.6) n = 44	+3.8% (2.6) n = 42	+3.0% (5.3) n = 45	+2.4% (3.0) n = 41
	Control	+0% (7.7) n = 44	+10.3% (2.9) n = 44	+13.7% (4.2) n = 44	+22.1% (3.9) ¥ n = 41

¥ p value < 0. 0001

We conclude that bone resorption markers resolve rapidly after discontinuation of risedronate therapy in postmenopausal women with osteoporosis previously dosed with risedronate for 2 years.

OC35. BONE TURNOVER MARKERS IN PATIENTS WITH OSTEOGENESIS IMPERFECTA

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Osteogenesis Imperfecta (OI) is a heterologous group of rare inherited bone disorders resulting from defect in collagen synthesis and/or function. In previous studies bone turnover has been found either increased or low-normal. These contradictory findings might result from the study population made of children with prior recent fractures. We measured serum total and bone alkaline phosphatase (total and bone AP) serum osteocalcin (sOC), serum type I collagen C-telopeptide breakdown products (sCTX), urinary free-deoxypyridinoline (ufDPD) and urinary cross-linked N-telopeptides of type I collagen (uNTx) in 39 male and 38 premenopausal patients with different types of OI aged between 18 to 51 years who had not experienced new clinical fracture during 12 months preceding the laboratory assessment. The study includes also a control group of 29 men and 26 women, matched for age and gender.

Most bone markers were 50 to 200% higher in patients than in controls. Only sCTX was comparable to that found in controls. From a sub-analysis of the data a trend for higher bone resorption markers was observed for any OI type, but patients with OI type III and IV had significantly higher values in ufDPD and uNTX than patients with type I OI and their sOC levels were not significantly higher than in controls.

These results provide a strong rationale for the use of bisphosphonates for the treatment of OI.

OC36. ANOTHER HORMONAL UPSTREAM FACTOR IN THE OPG/RANKL SYSTEM? EFFECTS OF THE THYROID STIMULATING HORMONE TSH ON BONE METABOLISM

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Aims: In vitro evidence indicates that the human thyroid stimulating hormone (TSH, thyrotropin) may be involved in regulation of bone metabolism. Recently, a highly purified recombinant human TSH alpha (THYROGEN) has been registered for diagnostic purpose in patients with well-differentiated thyroid cancer. These patients usually are thyroidectomized, and in addition, they are on TSH suppressive thyroid hormone therapy, in order to avoid endogenous TSH production. The administration of

THYROGEN allows to look at the effects of TSH during follow up for recurrent cancer, without changes in the serum levels of free thyroid hormones (triiodothyronin, thyroxin). We therefore saught to investigate the effects of THYROGEN on markers of bone metabolism and the osteoprotegerin (OPG)/receptor activator of NF-kB ligand (RANK-L) system.

Methods: We investigated 25 patients who underwent total thyroidectomy because of well-differentiated thyroid cancer. All patients received suppressive thyroid hormone therapy. Thyrogen was administered at a dosage of 0.9 mg IM daily on two consecutive days. Blood samples were drawn right before the first injection, 120 min thereafter, and 24 h (i.e right before the second injection), 48 h, and 72 h after the 1st injection. All patients continued receiving their usual dosage of thyroid hormone.

Results: TSH (μU/mL): 0.14 ± 0.07; 100.8 ± 10.8 ($p \leq 0.0001$); 141.9 ± 6.7 ($p \leq 0.0001$); 141.8 ± 7.4 ($p \leq 0.0001$); 58.6 ± 7.9 ($p \leq 0.0001$); Interleukin-6 (pg/mL): 1.95 ± 0.36; 2.54 ± 0.47 ($p \leq 0.01$); 2.28 ± 0.42; 2.05 ± 0.39; 1.98 ± 0.43; Osteocalcin (ng/mL): 21.8 ± 2.6; 21.1 ± 2.6; 22.9 ± 2.6 ($p \leq 0.05$); 23.1 ± 2.4 ($p \leq 0.01$); 21.3 ± 1.7; CrossLaps (pmol/L): 3593 ± 676; 3609 ± 710; 4514 ± 673 ($p \leq 0.05$); 4465 ± 716 ($p \leq 0.001$); 3709 ± 541; RANKL (pmol/L): 1.65 ± 0.61; 1.78 ± 0.70; 1.64 ± 0.61; 1.76 ± 0.66; $P < 1.54 \pm 0.71$.

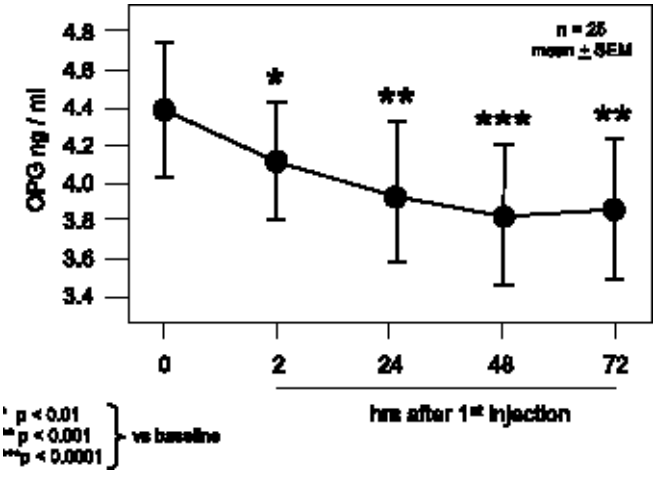

Fig. 1 Serum OPG Levels Following THYROGEN Injection.

Conclusion: These data suggest that TSH may affect bone metabolism by increasing bone turnover. This effect appears to be mediated via changes in the OPG/RANK-L system. We therefore consider TSH to be another hormonal upstream factor in this osteoclast-regulating system. Our findings also may explain accelerated bone loss in hyperthyroidism associated with elevated serum TSH-receptor antibodies (e.g. Graves' disease).

OC37. MISSENSE SUBSTITUTIONS IN LDL RECEPTOR-RELATED PROTEIN 5 (LRP5): A NEW GENETIC SUSCEPTIBILITY FACTOR FOR IDIOPATHIC OSTEOPOROSIS IN MEN

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Idiopathic osteoporosis in men (IOM) is a non-mendelian disorder with strong poly-genetic determinants. IOM results from decreased bone formation leading to low peak bone mass, particularly in the vertebrae. Mutations in LDL receptor-related protein 5 (LRP5), which mediates the effects of Wnt on osteoblasts, cause osteoporosis-pseudoglioma (OPPG) and "high bone mass" syndromes. We previously reported that LRP5 polymorphisms are associated with vertebral bone mass in healthy males. We now hypothesize that LRP5 polymorphisms could play a role in IOM.

We conducted a case-control study in 67 European-Caucasian men with IOM (mean age: 50.7 yrs, range 23–70) and in 65 age-matched controls. IOM was defined in absence of secondary causes of osteoporosis by areal (a)BMD at the spine (LS) or hip (FN) below −2.0 T-score using DXA and/or by a low-energy fracture. LRP5 missense substitutions in exon9 (c.2047G > A, p.V667M) and 18 (c.4037C > T, p.A1330V) were determined by pyrosequencing and haplotypes reconstructed by computer algorythm.

Compared to controls, cases had significantly lower height, weight, LS and FN aBMD, and LS BMC, and 70% had a low energy fracture. Carriers of the exon 18T allele (frequency, 37%) had significantly lower aBMD (-0.084 ± 0.035 g/cm2, $p = 0.018$) and BMC (-4.83 ± 2.06 g, $p = 0.021$) at LS, but not FN, compared to CC (adjusted for age, height and weight by multiple regression analysis). LRP5 9/18 haplotypes (GC, GT and AT) were also significantly associated with LS aBMD ($p = 0.027$) and BMC ($p = 0.034$). Vertebral bone mass was the lowest among carriers of the AT haplotype (frequency, 20%). Sixty-one percent of 18T carriers were among cases, compared to 44% of CC homozygotes ($p = 0.064$ by Chi-square analysis), and the 18T allele was associated with a significantly higher risk of IOM (OR, 2.3, 95%CI, 1.01–5.21, $p = 0.046$ by logistic regression including age, height and weight). Moreover, the AT haplotype was associated with a marginally increased risk of osteoporotic fractures (OR, 2.2, 95%CI, 0.87–5.85, $p = 0.092$).

In conclusion, these data suggest that LRP5 missense substitutions in exon 9 and 18 are a first identified genetic susceptibility factor for IOM. To confirm these observations, forty-two additional cases and controls are currently being investigated.

OC38. GLOBAL TRANSCRIPTION PROFILING OF ESTROGEN ACTIVITY: ESTROGEN REGULATES GENE EXPRESSION IN THE MOUSE BONE

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Introduction: Estrogen has beneficial effects on the maintenance of bone mass, however, its effect on gene expression is not fully understood. The aim of this study was to search for possible effects of estrogen on the expression of bone-related genes in mice using the microarray technique.

Materials and Methods: We examined the expression profiles of over 3,200 genes in the femurs and tibiae of sham operated (CTR), ovariectomized (OVX), and ovariectomized plus estrogen-replaced mice (ERT).

Results: Using strict analysis criteria, 1038 genes showed significant intensity ratios and 6.7% showed altered expression: 30 genes exhibited significant up-regulation and 28 were down-regulated. We focused on those genes that showed alterations in their expression patterns both in OVX and ERT mice. Altogether 905 data points could be evaluated, from which 5.2% showed altered expression: 23 genes exhibited significant up-regulation and 23 had down-regulation. In order to confirm the differential expression of genes revealed by microarray analysis of mouse bones after OVX with and without estrogen treatment, 12 genes were analyzed by QRT-PCR. We have identified genes such as L1cam, and non-muscle tropomyosin-5, cathelin-like protein, heparin cofactor II, protein synthesis elongation factor Tu, and small GTP-binding protein Rab1a that have not been reported to have bone-specific regulation of their transcription. We have also shown genes that have been reported to be expressed in bone but have not been reported to participate in the mediation of estrogen action on bone.

Conclusion: By using the microarray technique, we have found novel estrogen-regulated genes of potential importance for the bone-sparing effect of estrogen in mouse bone.

OC39. PATIENTS AT HIGH RISK OF HIP FRACTURE BENEFIT FROM TREATMENT WITH STRONTIUM RANELATE

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The lifetime risk of a hip fracture from age 50 years has been estimated at 17% for Caucasian women and the incidence rises exponentially in women over 74 yearsold.

Strontium ranelate has been shown to significantly reduce the risk of vertebral fracture in women with established post-menopausal osteoporosis by 41% (SOTI study) and by 45% in those patients without prevalent vertebral fracture (TROPOS study) over 3 years.

The international TROPOS study was designed to evaluate the efficacy of strontium ranelate in reducing the risk of non-vertebral fractures. A total of 5091 patients aged above 70 years, with a low femoral neck BMD (T-score < -2.5 SD) were randomized to receive strontium ranelate 2g daily orally over 3 years. A significant reduction of 16% ($p = 0.04$) and 19% ($p = 0.031$) respectively in the relative risk of non-vertebral osteoporotic fracture and major osteoporosis-related fracture was demonstrated in the intention to treat population. The efficacy of strontium ranelate in reducing the risk of hip fracture was investigated in a subset of particular medical interest, namely women of 74 years and above and with a baseline femoral neck BMD T-score lower or equal to −3 (calculated according to the centralized normative data). A total of 1977 patients are represented in this subset: 982 patients in the strontium ranelate group and 995 patients in the placebo group. The main baseline characteristics of this subset were similar between treatment and control groups and were as follows: mean (SD) age of 79.6 (4.5) years; menopause duration of 31.5 (7.0) years; femoral neck BMD T-score of −3.6 (0.5)..

In ITT, over 3 years, a significant reduction of 36% in the relative risk of hip fracture risk was observed (RR = 0.64, 95%CI [0.412;0.997]; $p = 0.046$).

These results demonstrate that strontium ranelate is a new and innovative anti-osteoporotic treatment which is effective in reducing hip fracture in high risk, osteoporotic postmenopausal women.

OC40. BONE TURNOVER MARKER FEEDBACK AND LONG-TERM PERSISTENCE WITH RISEDRONATE: IMPROVING MEASUREMENTS OF PERSISTENCE ON ACTONEL TREATMENT (IMPACT) STUDY

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Aim: Long-term persistence is important for treating postmenopausal osteoporosis. The IMPACT study assessed the effect of physician reinforcement using urinary N-telopeptide [uNTX] changes on persistence and BMD responses with risedronate (RIS).

Methods: 2302 osteoporotic women (65–80 years; spine/hip T-score ≤ -2.5 or spine/hip T-score ≤ -1.0 with a low-traumatic fracture > 45 years) received RIS 5 mg/d for 1 year. Centers were randomized into reinforcement (RE+; feedback based on uNTX) or non-reinforcement (RE-) groups. In the RE+ group, 3 reinforcement messages were given based on uNTX changes from baseline at weeks 10 and 22: positive, $> 30\%$ decrease; neutral, -30% to $+30\%$ change; negative, $> 30\%$ increase. Electronic caps measured daily compliance. Persistence, defined as the number of days from first dose until discontinuation, was compared between groups using a Cox proportional hazard model adjusted for a cluster-randomized design.

Results: The type of message significantly affected persistence ($P = 0.017$). Compared to RE- patients, a positive message increased persistence (HR = 0.7, $P = 0.02$) while a negative message decreased persistence (HR = 2.24, $P = 0.005$). BMD followed a similar pattern; concordant BMD changes were observed in the positive and negative message groups ($P < 0.05$), with no BMD change in the neutral message group. To ensure these differences were due to the reinforcement message and not a differential RIS response, we compared the 3 RE+ groups to RE- groups with similar uNTX changes. Reinforcement increased persistence in patients with a positive uNTX response (HR = 0.89, $P = 0.044$) or neutral uNTX response (HR = 0.91, $P = 0.058$) and decreased persistence in patients with a negative uNTX response (HR = 1.19, $P = 0.025$), compared to their respective RE- groups. The neutral and negative uNTX groups displayed a concordant BMD response. In the positive uNTX group, there was no further increase in BMD despite improved persistence at 1 year.

Conclusions: These data indicate the effect of reinforcement on patient persistence depends on the type of reinforcement. Positive and neutral uNTX response reinforcement improves persistence on treatment; negative uNTX response reinforcement decreases persistence. We conclude that either positive or neutral reinforcement improves overall persistence in postmenopausal women treated with RIS.

OC41. TOPICAL NATURAL PROGESTERONE CREAM EFFECT ON POSTMENOPAUSAL BONE LOSS: A TWO YEAR DOUBLE BLIND, RANDOMISED, PLACEBO CONTROLLED TRIAL

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Concern about Hormone Replacement Therapy (HRT) has attracted attention to alternative interventions at the menopause. Observational data suggesting progesterone cream increases bone mass in postmenopausal women has encouraged widespread use to prevent osteoporosis.

This study investigated the efficacy and safety of 1.5% USP progesterone cream on postmenopausal bone loss.

We randomised 45 non-hysterectomised postmenopausal women (aged 49–70) to apply topical progesterone cream twice daily containing progesterone 40mg/d [Group (1)] or placebo [Group (2)] for one year. In the second year (open-label) Group (1) doubled the dose applied (progesterone 80 mg/d), whilst Group 2 started using progesterone 40mg/d plus an oral mineral and vitamin supplement. A parallel group of 15 postmenopausal women [(Group (3)] used transdermal continuous combined HRT (oestradiol 50mcg; norethisterone 170 mcg/d) throughout the study. Bone mineral density (BMD) was assessed by DXA at baseline, 6, 12 and 24 months. Urine NTX to creatinine ratio was measured to assess bone turnover. Blood, saliva and urine assays were measured to determine absorption of progesterone. Endometrial assessments were made annually. A validated Womens Health Questionnaire was completed at each visit.

Results: Mean lumbar spine BMD in Groups (1) and (2) had decreased by 12 months. Mean change Group (1) −1.38% (95% CI −2.50, −0.26); mean change Group (2) −2.58% (95% CI −4.41, −0.75) [n/s difference ($p = 0.23$)], compared to an increase in BMD in Group (3) of 5.54% (95% CI 2.10, 8.97). Decrease in BMD for Group (1) after 24 months was −1.93% (95%CI −3.38, −0.47). Urine NTX/creatinine did not significantly change from baseline in Groups (1) or (2) throughout the 2yr study, but had decreased in Group (3) by 35% at 12 months.

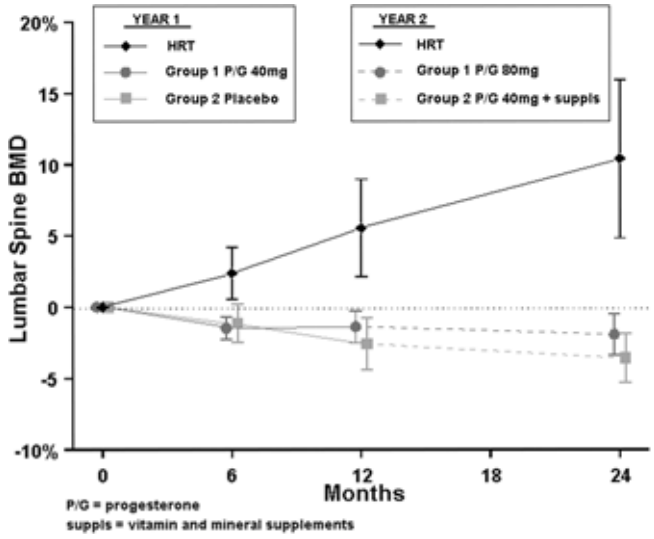

Fig. 1 Lumbar Spine BMD - Mean Percentage Change (95% CI).

Conclusion: Topical progesterone cream containing 40–80 mg progesterone, used daily for 2 years, does not prevent bone loss or increase bone mass in postmenopausal women, although well absorbed.

OC42. TERIPARATIDE EFFECTS ON BONE GEOMETRY ARE INDEPENDENT OF MUSCLE AREA AND RADIUS LENGTH

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We had previously reported that, as compared with placebo, teriparatide-treated patients had significantly higher axial (Ix) and polar (Ip) moments of inertia at mid-distal radius. These improvements in bone geometry were not associated with differences in age, height or weight. However, several other factors may affect bone geometry. We assess here the influence of muscle cross-sectional area (CSA) and forearm length (L) in the effects of teriparatide on cortical bone architecture.

pQCT scans were performed in 72 postmenopausal osteoporotic women after a median 18 months of treatment with teriparatide at doses of either 20 ($n=29$) or 40 ($n=21$) ug or placebo ($n=22$); and in a control group of 28 healthy men ($n=8$) and premenopausal women ($n=20$), at a site corresponding to 15% the length of the ulna from the distal radius end. Ix and CSMA were calculated from the scan images. L was measured between the ulnar styloid and the olecranon process.

Linear regression analysis showed a strong relationship between CSMA and Ix in the control group ($r=0.85$, $p<0.001$), but not in postmenopausal patients ($r=0.18$, $p=$ns). Comparison of regression lines for the placebo and teriparatide groups showed no differences in slope, but elevation was significantly higher in the treatment group ($F=5.1$, $p=0.027$). CSMA was not significantly different between the placebo and treatment groups, but both showed significantly lower CSMA than the control group. Despite differences in CSMA, and in agreement with the results of the regression analysis, Ix values were not significantly different between controls and teriparatide patients, and both showed significantly higher Ix values than placebo. Similarly, a significantly relationship between L and Ix was found for the control group ($r=0.65$. $p<0.01$), but not in patients ($r=0.19$, $p=$ns). Regression lines for the placebo and teriparatide patients showed no differences in slope, but elevation was significantly higher in the treatment group ($F=6.8$, $p=0.011$). L was not different between treatment groups but both showed significantly lower L values than the control group.

These results suggest that the improvements in bone geometry associated with teriparatide treatment are independent of cross-sectional muscle area and bone length.

OC43. THERAPEUTIC EFFICACY OF RISEDRONATE IN MEN WITH PRIMARY AND SECONDARY OSTEOPOROSIS: ONE YEAR RESULTS IN 316 PATIENTS

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Aims: In the current study, we examine the effects of Risedronate on vertebral fractures and BMD mean change in lumbar spine, femoral neck and total hip BMD only in men with primary and secondary osteoporosis. Secondary endpoints include non-vertebral fractures, height, pain, safety, and tolerability.

Methods: In this single center, open label, matched pair controlled prospective clinical study, we enrolled 316 male patients with T-score values of lower than minus 2.5 SD at lumbar spine (LS) and lower than minus 2.0 SD at the femoral neck (FN) with or without prevalent vertebral fractures (vert-fx). The patients were allocated in pair-wise fashion into two treatment groups. Patients in Group A ($n=158$; 81 with, 77 without prevalent vert-fx) received Risedronate 5 mg plus calcium 1000 mg and 800 IU Vit. D daily. Group B comprised equally 158 men. Those with a prevalent vert-fx (subgroup B1 $n=81$) were treated with alfacalcidol 1 mg plus calcium 500 mg daily, whereas patients without prevalent vert.-fx (subgroup B2, $n=77$) were treated with calcium 1000 mg plus 800 IU plain vitamin D daily. In group A 64 patients (41%) and in group B 66 (42%) had secondary osteoporosis. BMD measurements and x-rays were performed at baseline and 12 months thereafter.

Results: After this first year of treatment men receiving Risedronate showed a mean LS-BMD increase of 4.7% compared with a mean increase of 1.0% in Group B patients ($p<0.001$). The mean change of total hip BMD was 2.7% and 0.4% for groups A and B, respectively ($p<0.001$). Corresponding changes at the FN were 1.8% and 0.3% for the respective groups ($p<0.001$). During the 12 months of therapy in 5% (8/158) of patients of Group A and in 12.7% (20/158) of Group B new vert-fx were recorded (RR 0.4, Fisher exact test; $p<0.028$). The corresponding incidences for patients with new non-vert-fx were 10 and 17, (RR 0.59, n.s due to insufficient power). Both therapies were well tolerated.

Conclusions: We conclude that Risedronate therapy reduces the risk of new vertebral fractures by 60% and significantly increases of BMD at all measurement sites in men with osteoporosis within one year.

P100SA. DIGITAL X-RAY RADIOGRAMMETRY (DXR) AS A NEW METHOD FOR MEASUREMENT OF PERIARTICULAR DEMINERALIZATION ON PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS AND COMPARED TO PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (PQCT)

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Aims: As a generalized inflammatory disease rheumatoid arthritis involves several joints as well as synovial sheaths of tendons and bursae. Both, rheumatoid arthritis and its extended treatment (i.e. cortisone therapy) cause a significant systemic bone loss in a high number of patients and additionally a periarticular disease-related osteoporosis, especially at the hands and feet in an early stage of the disease. To evaluate changes of bone mineral density (BMD) using a radiogrammetrically based bone densitometric technology on patients suffering from rheumatoid arthritis with and without corticoid therapy. To compare this method with peripheral Quantitative Computed Tomography.

Patients and Methods: 90 patients underwent a prospective analysis of BMD via DXR and pQCT. Radiographs have been subjected to DXR for estimating BMD from a plain radiograph of the nondominant hand using Pronosco X-Posure System (Sectra, Sweden), which digitizes a radiograph with a scanner and subsequently derives a BMD of the three middle metacarpals; pQCT calculated BMD (total, trabecular, cortical) regarding distal radius.

All patients were divided into a subgroup ($n = 52$) with (5 mg cortisone/d for 6 months) and without corticoid therapy ($n = 38$).

Results: The mean value of DXR-BMD decreased from 0.57 g/cm2 $\pm$0.08 (Larsen Score 1) to 0.45 g/cm2 $\pm$0.11 (Larsen Score 5). The relative decrease of BMD measured by DXR between the highest and lowest score was 20% ($p < 0.05$). The relative decrease of BMD (pQCT) from Larsen-Score 1 to Score 5 showed a significant result regarding pQCT-BMD (trabecular, representative for metabolic active bone tissue) with 16% ($p < 0.05$). No significant demineralization confirmed for pQCT-BMD (total) with 12% and pQCT-BMD (cortical) with 2%. Correlation between DXR-BMD and pQCT-BMD (total and trabecular) demonstrated a significant result ($R = 0.53$ vs 0.55; $p < 0.01$) for the cortisone-subgroup. Correlation of DXR-BMD with pQCT-BMD (cortical) was lower ($R = 0.37$, $p < 0.05$). Equal results were verified for patients without corticoid therapy.

Conclusion: The digital radiogrammetry can exactly measure cortical differences of bone mineralization on patients suffering from rheumatoid arthritis and seems to be able to quantify disease-related periarticular loss of bone mineral density depend on severity and independent from corticoid influence.

P101SU. BODY COMPOSITION CHANGES IN A HEALTHY POPULATION OF 2 TO 21 YEAR OLDS ASSESSED BY WHOLE BODY DXA

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There are limited data about body composition changes during growth using radiological absorptiometry.

Objectives: Assess the changes in bone mineral content (BMC) bone density (BMD), fat mass (FM) and lean mass (LM) from childhood to youth and allow for the influence of sex maturation (2 to 21 years).

Methods: BMC, BMD, FM and LM were measured by dual energy x-ray absorptiometry (DXA, Prodigy, GE-Lunar. version 6.5) in 1072 healthy caucasian volunteers (302 male, 780 female) residents in an urban area of Barcelona. Puberal stage was assessed by the Tanner method. Total and regional measurements were analized in absolute values and as percentages of total amount of tissues.

Results: BMC and BMD values increased progressively and mean values were similar for both sexes up to the age of 10 years. BMD mean values were similar for both sexes (2–21 years). However, total BMC values between 11 and 16 years were higher in girls than in boys ($p < 0.001$). Regional analysis showed higher BMC values between 10 and 16 years in arms and legs in boys than girls ($p < 0.0001$ and $p < 0.03$, respectively), whereas girls showed higher values in pelvis BMC ($p < 0.08$). Total body fat and lean mass in girls followed the same trend for each age group (2–21 years of age). Conversely, total body fat mass in boys decreased significantly altogether with a significant increase in lean mass over the years.

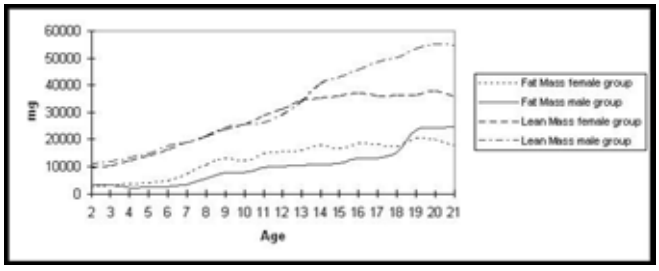

Fig. 1 Body Composition.

Conclusion: No gender-related significant differences were found in BMD evolution from 2 to 21 years. However, the BMC differences between sexes might be due to bigger skeletal size achieved in boys by the end of their puberal period. Both, physical activity and sex hormones, could explain the different trend in total fat mass and lean mass changes with BMD and BMC regional measurements during 14–18th period.

P102MO. QUANTIFICATION AND DIFFERENTIATION OF PERIARTICULAR DEMINERALIZATION IN PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS VIA DIGITAL X-RAY RADIOGRAMMETRY (DXR) AND DUAL-ENERGY X-RAY ABSORPTIOMETRY (DXA)

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Aims: To evaluate the ability to measure variations of bone mineral density (BMD) using DXR on patients with rheumatoid arthritis (RA) and to differentiate systemic from disease-related demineralization. To compare this method with DXA including comparison between patients with and without corticoid therapy.

Patients and Methods: 152 patients with verified RA underwent analysis of BMD by DXR, which calculated BMD and Metacarpal Index (MCI) from a plain radiograph of the non dominant hand using Pronosco X-Posure System (Sectra, Sweden). This technique digitized a radiograph with a scanner and subsequently calculated cortical thickness of the three middle metacarpals. Based on the mean bone volume per area and the estimated porosity of the cortical bone, DXR-BMD was computed. DXA (Hologic QDR-4500) measured BMD regarding total femur and lumbar spine.

Results: Correlation of BMD-DXR vs BMD-DXA were significant (femur: $R = 0.59$, $p < 0.01$; lumbar spine: $R = 0.47$, $p < 0.01$). The mean value of BMD decreased from 0.55 g/cm^2 $\pm$0.08 (Larsen Score 1) to 0.44 g/cm^2 $\pm$0.11 (Larsen Score 5). Equal results were verified for the Steinbroker Stage and MCI. The relative decrease of BMD measured by DXR between the highest and lowest score was 20% for both scores ($p < 0.05$), whereas DXA showed no significant results depending on severity. Correlation regarding BMD-DXR versus BMD-DXA (femur) was $R = 0.60$ ($p < 0.01$) in patients with corticoid therapy and $R = 0.34$ (n.s.) without corticoid influence.

Conclusion: Calculated by DXR a significant reduction of BMD depending on severity of RA has been verified, whereas DXA-BMD has been demonstrated no significant results. These results indicate that the progress of RA itself allows a quantification of the sum of disease-related periarticular cortical demineralization via DXR. Furthermore the correlation between DXR-BMD and DXA-BMD (total femur) shows only a closed and significant association in patients with steroid therapy. This result points at the ability of DXA and DXR for exact determination of systemic bone mineral density loss, but also this fact maybe shows the lack of DXA in the detection of periarticular disease-related demineralization. Possible application of DXR

should be the additional BMD-calculation on routinely performed follow-up radiographs for quantification and monitoring of demineralization.

P103SA. DESCRIPTIVE STUDY OF BONE MINERAL DENSITY MEASURED BY PERIPHERAL DENSITOMETRY: ARGENTINE EXPERIENCE

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Aim: To describe the prevalence of osteopenia and osteoporosis by peripheral densitometry in women aged 50 years or older in Argentina.

Methods: Secondary analysis of data from a database with 41,118 ambulatory subjects (38,525 women) from 180 primary care centers from 7 regions of the Argentine Republic participating in a free campaign for osteoporosis detection. The examination was performed by Norland p-DXA equipment, in the no-dominant distal forearm.

Results: Demographics: Age: 63.9 (+/− 9.2) years; Weight: 69 (+/− 12.3) kg; Height: 158 (+/− 0.07) cm; BMI (Body Mass Index): 27.6 (+/− 4.8). Age distribution : 50–59 years: n = 14374 (37.3% of the sample); 60 to 69 years: n = 13194 (34.2%); 70 to 79 years: n = 9057 (23.5%); 80 years or older: n = 1899 (5%). Diagnosis (World Health Organization (WHO) criteria): Osteoporosis (T-score < −2.5): n = 6731, 17.47%; Osteopenia (T-score of −1 to −2.49): n = 17034, 44.22%; Normal (T-score > to −1): n = 14760, 38.3%. The prevalence of osteoporosis increased in accordance with the age progression and it was similar between different regions of the country. Using National Osteoporosis Foundation (NOF) criteria, the high-risk group (30.7 %) was bigger than the osteoporotic group using WHO criteria (17.47%) (Table 1).

Conclusions: We observed a significant difference in the percentage of potential treated patients according to the criteria used. Our results presents some differences with the results of the National Osteoporosis Risk Assessment (NORA) study, performed with the same method, peripheral densitometry, and identical age distribution in the sample, but with different racial composition of the sample (we dońt include black subjects). Given the lower costs and the accessibility of p-DXA, we are in agreement with other international authors that this method seems to be a useful screening tool to detect subjects with low bone mineral density.

P104SU. CHANGES IN BONE MASS IN ADOLESCENTS WITH SEVERE OBESE DURING WEIGHT REDUCTION

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Background: Osteoporosis and obesity become a major public health concern in many countries. Primary preventive method of osteoporosis is to reach an optimal peak bone mass which is taken place during adolescence. In obese adults, some studies indicated that weight loss is associated with bone mass loss but the interpretation of these results are often controversial. Little known about the changes of bone mass during weight reduction in obese adolescents.

Aim: The aim of this investigation is to evaluate the effects of a marked weight loss resulting from dietary and physical activites interventions on total and regional bone mass in obese adolescents.

Methods: Thirty three girls and 22 boys, aged 13.4 ± 3.6 y with BMI 34.6 ± 3.6 kg/m2 were included in a 9 ± 3 months multidisciplinary weight reduction programme including a slight caloric restriction and submaximal aerobic physical training. Total and regional (lumbar spine and femoral neck) were measured by DEXA Hologic QDR 1000 at baseline and after treatment.

Results: Mean weight loss was 23.5 ± 8.9 kg ($p < 0.0001$), height growth was 2.7 ± 1.6 cm ($p < 0.001$). Fat mass decreased ($p < 0.0001$) whereas lean mass maintained. In whole body: BMC and bone area decreased significantly by 253 ± 131 g and 212 ± 14 cm^2 (both $p < 0.0001$) whereas BDM did not vary ($p = 0.3$). The changes of total BMC was highly correlated to the diminution of fat mass ($r = 0.88$, $p < 0.0001$).At lumbar spine: BMC, bone area and BMD increased significantly in both sexes. At femoral neck: BMC, bone area and BMD did not vary.

Conclusions: Total and regional areal BMD maintained during major weight loss resulting from a dietary and physical activities programme in obese adolescents. Total BMC decreased whereas regional BMC (both trabecular and cortical bone) increased or maintained may suggest the limitation of interpretation of DEXA in assessing bone mass during a marked weight loss.

P105MO. CAN FEMUR BMD AND STIFFNESS INDEX PREDICT FUTURE OSTEOPOROTIC FRACTURE IN BRAZILIAN ELDERLY WOMEN? A 5 YEAR FOLLOW-UP.

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Previous studies have suggested that low bone mineral density (BMD) is associated with increased risk of fracture and mortality. However, the relationship between quantitative ultrasound (QUS) and fracture and mortality is still controversial. Our aim was evaluate the ability of the BMD and QUS to predict future osteoporotic fracture in 275 Brazilian postmenopausal women.

Patients and methods: Spine and femur BMD (Lunar) and heel QUS (Lunar) measurements were performed in all patients. Risk factors to osteoporosis and fractures were evaluated by a specific questionnaire. Patients were followed-up for 5 years and new fracture or death were investigated as main outcomes. Lateral thoracic and lumbar radiographs were taken at baseline and 5 years later to survey for the presence of vertebral fractures. All reported deaths were confirmed by review of the hospital records and classified according to the ICD- 9 code.

Results: 208 (75.6%) women completed the protocol study, 42 (15.3%) died and 25 (9.1%) lost follow-up. Mean age, height, weight and bone mass index (BMI) for the group were 75.2 ± 6.5 years, 60.3 ± 10.2 kg, 1.50 ± 0.8 m and 26.9 ± 4.2 kg/ m^2, respectively. Forty-two patients (20.2%) had new osteoporotic fracture at any skeletal site. After adjustments for age, weight, previous fracture, familiar history of hip fracture, smoking, physical activity, drugs and others diseases, each 1 SD reduction in stiffness index was associated with hazard ratio of 2.2 (95% CI 1.3; 3.8) of future fracture. Femural neck BMD (HR 2.0) [95% CI 1.3; 3.2] and trochanter BMD (HR 1.62) [95% CI 1.1; 2.4] were also significantly associated with the risk of future fracture. The most relevant hazard ratio to death were trochanter BMD (HR 1.59) [95% CI 1.1; 2.4], stiffness index (HR 1.57) [95% CI 1.1; 2.4] and femural neck BMD (HR 1.44) [95% CI 1.1; 2.2]. Mortality from cancer, cardiovascular or infectious diseases was not significantly associated with BMD or QUS measurements.

In conclusion, low QUS and femur BMD measurements were able to predict future osteoporotic fracture and mortality, independently of the age, health status and other associated diseases in this cohort of Brazilian elderly women.

P106SA. PREVALENCE AND IDENTIFICATION OF VERTEBRAL FRACTURES: COMPARISON OF VISUAL INSPECTION, DIGITAL COMPUTERIZED MORPHOMETRY AND VISUAL SEMIQUANTITATIVE ASSESSMENT

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This study aimed to determine the percentage of vertebral fractures eluding x-ray reports and to calculate the precision of the digital morphometric system used for vertebral body heights x-ray evaluation.

We analyzed 233 postmenopausal women (aged 63.9 ± 0.5) who have undergone clinical evaluation in a bone metabolic diseases outpatient service. They had lateral and posterior-anterior thoracic and lumbar spine x-ray assessment; radiology reports described the presence of at least one vertebral fracture in 12% of the subjects.

The T4-L4 film analysis was performed by digital computerized morphometry [DCM] (Spine-X Analyser, CAM Diagnostics, Milan, Italy), calculating vertebral height ratios on the basis of the identification method of 6 standard points of 3 vertebral heights; a 20% reduction of any vertebral heights ratio was chosen as threshold value to assess vertebral deformity. Thus, a prevalence of fractures of 46.25% was observed. Furthermore, Genant's semi-quantitative grading scheme for the assessment of vertebral fractures [VQA] was performed by an expert radiologist. A fractures prevalence of 49.75% was observed.

By comparing both methods, it was deduced that most fractures usually occur in the T6-T9 interval and that end-plate fractures are the most common (68.9% by DCM, 58.4% by VQA).

Thus, a good agreement (0.839) between the VQA and the DCM method by using k-score was found.

Sensitivity (0.655) and specificity (0.957) of vertebral fractures identification by VQA, were calculated in connection with DCM method, the latter considered as the gold standard.

We suggest that in clinical practice, vertebral fractures are often undiagnosed and not adequately reported by inspection of radiographs. Moreover, both the methods, DCM and VQA, represent effective tools to be applied to clinical research enabling the demonstration of higher prevalence of vertebral fractures.

P107SU. REFERENCE DATA OF BONE MINERAL MASS AND DENSITIES AS WELL AS MUSCLE-BONE RELATIONSHIP INDICATORS ASSESSED USING DXA METHOD IN HEALTHY POLISH CHILDREN

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Aim: To assess total body, spine and hip bone mineral mass and density reference data for healthy Polish children using DXA method and to compare established reference data with data provided by DXA manufacturer and reference data-sets published elsewhere.

Methods: 500 healthy children (250 girls) aged 5–18 years were measured using DPX-L machine. Age and sex-matched means and SDs were calculated for BMD and BMC of total body, lumbar spine and femoral neck. Total lean body mass (LBM) and body height (BH)/LBM, TBBMC/LBM, spine (S)BMC/LBM ratios were calculated. The relationships between BMD, BMC, BH/LBM, TBBMC/LBM, SBMC/LBM and chronological age (CA), height age (HA), bone age (BA), body height (BH), weight (W) were analyzed using correlation analysis. 24 DXA children's reference data-sets from 12 countries and reference provided by DXA manufacturer were compared with our results (mainly BMD) using ANOVA.

Results: Gender related differences were noted for the tempo of bone mineralization evaluated on the basis of BMC and BMD values of analyzed ROIs. Stronger relationship was noticed between BH($r = 0.92$;$r = 0.93$), W($r = 0.95$;$r = 0.95$), CA($r = 0.90$; $r = 0.88$), HA($r = 0.88$;$r = 0.90$), BA($r = 0.89$;$r = 0.89$) and TBBMC than TBBMD (BH:$r = 0.84$;$r = 0.87$;W:$r = 0.90$;$r = 0.90$;CA:$r = 0.87$; $r = 0.87$;HA:$r = 0.80$;$r = 0.80$;BA:$r = 0.88$;$r = 0.88$), for girls and boys respectively. The muscle-bone relationship analysis based on BMC, LBM values and TBBMC/LBM, SBMC/LBM ratios revealed that pubertal and post-pubertal girls stored more bone per LBM unit than boys ($p < 0.0001$). Lack of major differences was found between BMD reference data-sets provided by DXA manufacturer or published elsewhere and our results only for total body and spine, but not for femoral neck BMD, probably as an effect of markedly lower number of studies which provide femoral neck BMD data and technical problems with bone edge detection for hip measurements in children.

Conclusion: Data from healthy children are essential to evaluate bone mineralization during childhood as well as for proper diagnosis when bone disorder is suspected. Complete and unified children's reference data is strongly needed. Lack of reference for hip bone mineralization and still, only one normative study of muscle-bone treated as a unit in children are available. Therefore, we provide age and gender related reference BMD and BMC data expanded by hip bone mineralization parameters and muscle-bone relationship indicators.

P108MO. BONE LOSS AFTER CHEMOTHERAPY IN WOMEN WITH EARLY BREAST CANCER

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Our aim was evaluate the impact of the chemotherapy (CT) on bone mineral density (BMD) and quantitative ultrasound (QUS) measurements in patients with early breast cancer (EBC).

Patients and methods: 154 women were enrolled (54 with EBC and 100 healthy controls matched to age, body mass index [BMI] and status menopausal). Patients with history of another cancer, previous CT or metastatic disease were excluded. Spine and femur BMD (Lunar, DPX-L) and heel QUS (Achilles+, Lunar) were performed in all patients.

Results: 46 (85.2%) patients with EBC and 83 (83%) healthy controls completed follow-up. The mean age, weight, height and BMI of the EBC patients were 52.1 ± 10 years, 68.2 ± 14.3 kg, 1.57 ± 0.7 m and 27.6 ± 5.4 kg/m2, respectively. Twenty (43.5%) patients with EBC were premenopausal and six (13%) had previous atraumatic fracture. The protocols of the CT used were [fluorouracil, doxorubicin, cyclophosphamide] (71.7%) or [cyclophosphamide, methotrexate, fluorouracil] (28.3%) with mean number of 5.8 ± 1.8 or 7.7 ± 2.1 cycles, respectively. At baseline, the patients with EBC had BMD and QUS measures 5% higher than healthy controls. After CT (8.5 ± 2.7 months), the women with EBC lower BMD and QUS measurements (table below).

Table. 1 BMD and QUS measures before and after the chemotherapy in women with EBC compared to healthy controls.

	Baseline		After CT		Δ%	
	EBC	Controls	EBC	Controls	EBC	Controls
Spine BMD (g/ cm^2)	1.170 ± 0.2	1.092 ± 0.2*	1.141 ± 0.2	1.104 ± 0.2*	−2.5	1.1*
Femur BMD (g/cm^2)	0.940 ± 0.1	0.871 ± 0.1*	0.919 ± 0.1	0.884 ± 0.1*	−2.2	1.5*
BUA (dB/ MHz)	114 ± 11	108 ± 10*	112 ± 9	110 ± 9*	−1.7	1.8*
SOS (m/s)	1561 ± 30	1532 ± 28*	1554 ± 32	1539 ± 29*	−0.5	0.7*
Stiffness Index	93 ± 13	88 ± 13*	90 ± 13	89 ± 13*	−3.2	1.1*

Δ% (% difference between measures); *$p < 0.05$

In conclusion, women with EBC lost 2% and 3.2% on spine BMD and QUS measurements, respectively, after chemotherapy.

P109SA. TWO YEAR FOLLOW-UP STUDY OF BONE MODELING IN CYSTIC FIBROTIC CHILDRENS AND ADOLESCENTS

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Cystic fibrosis (CF) is caused by mutations of CF-transmembrane-conductance-regulator (CFTR) gene, and is the most common lethal autosomal recessive (AR) genetic disease (1). Several data suggest that an inherited genetic susceptibility contributes to the development of bone deficit.

Aim: To investigate bone mineral density (BMD) and bone turnover (BTM) in cystic fibrosis (CF) patients in a two-year period, and to test the role of inheritance (Inh +/−).

Methods: Thirty-eight clinically stable CF patients (11 children, 16 adolescents, 11 young adults) were enrolled. None of the patients was treated with corticosteroids prior to or during the study. Weight (a) and the height (b) Z-scores and bone mineral density (BMD) Z-score (c) values at the femoral neck (FN) and

the lumbar spine (LS) were recorded at the beginning of the study and two years later. Bone turnover markers (BTM) including osteocalcin and cross-link (DPR) excretion were also measured. The correlations between BMD, bone turnover parameters, disease severity, pubertal stage and nutritional state were investigated. As an extension of the study, BMD values of the mothers of patients (carriers of CFTR gene) were also determined and related to patients' BMD.

Results: Height and weight Z-scores were normal in children, while decreased in adolescents. Puberty was delayed in most of patients. Bone age was lower than chronological age in adolescents. Lumbar spine and femoral neck BMD Z-scores were lower than normal in each age group. Disease severity (i.e. Schwachman scores) correlated with lumbar BMD ($r = 0.45$, $p < 0.02$). Mother and patient lumbar and femoral BMD correlated significantly ($r = 0.51$, $p < 0.01$, and $r = 0.54$, $p < 0.01$, respectively).

Conclusion: Bone mineral and turnover decrease was present in cystic fibrosis (CF) adolescent patients without steroid treatment. The genetic factors additionally to chronic inflammation might be responsible for the delayed puberty. Correlation of BMD values between homozygous patients, and heterozygous mothers support the presence of genetic factors in the pathogenesis (Inh+).

P110SU. BONE MINERAL DENSITY, HIP STRENGTH PARAMETERS AND FALL INDEX FOR HIP FRACTURE PREDICTION

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Introduction: It is accepted that BMD is not the only predictor for hip fracture. Other parameters such as age, height and weight also should be taken into account.

Femur structure factors such as Cross Sectional Area (CSA), and Cross Sectional Moment of Inertia (CSMI) now can be measured by modern DXA equipment. As some investigators have proposed, it is possible that combining bone mineral density, structure, age, height, and weight in a Fall Index (FI) that might predict hip fracture more accurately than BMD or age alone. As published by Yoshikawa et al, (JBMR 9:1053–1064,1994) FI can estimate the ability of a hip to withstand the impact of a fall on the greater trochanter.

Methods: Femoral Neck BMD, CSMI, CSA, and FI were evaluated for assessing hip fracture risk in a group of fractured subjects and compared to non-fracture controls. DXA scans were obtained in 362 women, 72 with prior hip fracture and 289 controls, using Lunar Prodigy (GE Medical Systems). BMD of the femoral neck, CSMI, and CSA were determined using the Hip Strength Analysis software (version 8.00.256), and FI was calculated according to the equations developed by Yoshikawa et al. Geometric results were adjusted for BMD, and the fractured and control subjects were compared using a unpaired t-test.

Results: Both Femur Neck BMD and the Fall Index were significantly lower in the fracture group when compared to controls ($p < 0.001$).

Conclusions: According to the results of this sample, we conclude that fractured subjects have a reduced capacity to withstand the impact of a fall without fracturing. Additionally, the **Fall Index**, which combines BMD, femur geometry, age, weight and height, is a significant predictor of hip fracture.

Table 1: Summary of the main results

Age	Height	Weight	Average BMD Neck	CSMI	CSA	Median FI
Fracture Group n = 72						
71.8	154.6	58.5	0.684*	6985.11	100.6	1.4930*
No Fracture Group n = 289						
69.9	152.56	59.7	0.804*	7149.86	114.25	1.7140*

*Significantly different than controls ($p < 0.001$)

P111MO. PATIENT EDUCATION AND TREATMENT FOLLOWING BONE DENSITOMETRY

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Introduction: Treatment of osteoporosis is often inadequate. One reason can be insufficient patient education following diagnostic bone densitometry (DEXA). Therefore we studied how patients are informed and treated following their first DEXA. Individuals who had DEXA at a rural hospital in Wisconsin, USA were surveyed with a questionnaire regarding their post-test education and prescribed treatment. Their DEXA results and the specialty of their clinician were also recorded.

Results: Eighty percent of the 1014 participants were informed of their results. Of the 341 participants who had normal BMD, 63% reported correct results, 31% of the 309 who had osteopenia and 50% of the 364 who had osteoporosis. Accuracy in reporting was not affected by the patients' age or the specialty of their clinician. Calcium supplements were recommended to 65% of those not taking calcium prior to DEXA. Internists were more likely than family practitioners to recommend calcium ($p = 0.0003$). Following DEXA, 339 patients were started on medications (33%), 86% of those remained on some prescribed therapy, but 140 (41%) did not continue the original medication. Reasons for discontinuation included sideffects (48%) and cost (26%). Patients with low BMD, who correctly reported their results, were more likely to have received a medication and to continue to take it ($p < 0.0001$).

Conclusions: While most participants are informed of the results of their DEXAs, the retained information may not be accurate. Participants who correctly reported the results of their DEXAs were more likely to have received a medication and to remain on treatment.

P112SA. THE USE OF FINGERNAIL AS A MEANS OF ASSESSING BONE HEALTH: A PILOT STUDY

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Aim: Patients report increasing hardness of their nails within months of starting treatment for osteoporosis. A pilot study was undertaken to assess if the properties of nail and bone could be linked in a comparable, measurable way.

Methods: Two groups of ten subjects were identified. The first group were diagnosed, by DEXA (Lunar Prodigy GE, Medical systems), as osteoporotic. The second group were non-osteoporotic. Fingernail clippings were obtained from all subjects. A dedicated, laboratory-built nano-indenter was employed to measure hardness and elastic modulus of the nail. Raman Spectroscopy (Labram Integrated system) was configured to analyze between 300 and 700 cm^{-1}. This is where disulphide bond breakdown and C-S bond shift would be detectable.

Results: The mean moduli of fingernails from patients with low BMD are about 25% lower than those with normal BMD. The mean difference in mean modulus between the groups was found to be 0.996 but this was not significant at the 5% level ($p = 0.147$). This p value is quite low and indicates that a significant difference might be found if a further study is undertaken which is sufficiently powered. The spectroscopy data also showed differences between the two sets of nails. The disulphide bond content of the nails sourced from osteoporotic patients was much lower than those from healthy patients. There was also a significant shift in c-s bond detection.

Conclusion: We hypothesise that whilst bone collagen and nail keratin are two distinct structural proteins, they share the need for protein sulphation and disulphide bond formation for their structural integrity. A disorder of either process may lead to disordered

collagen and keratin synthesis. The relationship between nail and bone may exist in a measurable way. Nail may therefore prove to be a valuable adjunct to diagnosis in osteoporosis.

P113SU. LOWERED JUMP POWER AND FORCE ARE RISK FACTORS FOR POSTMENOPAUSAL OSTEOPOROSIS: THE OSTEOPOROSIS RISK FACTOR SURVEY

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We examined the association of muscle force and power with bone mineral density and fracture prevalence in a population based sample of 1197 postmenopausal women aged 60 to 95 years. These women were examined in the ''Osteoporosis Risk Factor Survey'' in July and August 2002 in 20 different cities throughout Germany. The Osteoporosis Risk Factor Survey was conducted in order to develop a high risk score for osteoporosis based on clinical tests.

In all women a bone mineral density measurement of the lumbar spine and the proximal femur was performed (DPX-NT, GE Lunar Corp). Each woman answered a questionnaire including detailed questions on fracture status. Muscle force and power were tested by squatter and counter movement jumps using the Ground Reaction Force Plate (Novotec Medical, Pforzheim, Germany), data of the maximum force (in N/kg body weight) and power (in Watt/kg body weight) were analysed. In addition a variety of clinical tests such as chair rising, Up & Go, Tandem, Semi-Tandem, measurements of height change and body mass index (BMI) were conducted (data not presented).

Significant lower results for maximum jump power and force ($p < 0.001$) were seen in women with a T-score ≤ -2.5 SD at the lumbar spine or the femoral neck and women with postmenopausal fractures. Odds ratios per decrease by one standard deviation of the results were calculated for the age groups 60–69, 70–79 and ≥80. The maximum force and power discriminated 1. women with and without postmenopausal fractures (OR ranging from 1.31–1.96 for power and 1.47-1.60 for force), 2. women with a spinal T-score ≤ -2.5 SD (OR ranging from 1.12–1.50 for power and 1.95–2.09 for force), 3. women with a femoral T-score ≤ -2.5 SD (OR ranging from 1.31–2.71 for force). Maximum power did not discriminate this group (OR 0.919–0.989).

In conclusion, measurements of muscle force and power significantly separate postmenopausal women with and without osteoporosis and therefore serve as a risk factor for postmenopausal osteoporosis. Maximum jump power and force should be implemented in the clinical testing and screening for postmenopausal osteoporosis.

P114MO. DENSITOMETRIC ANALYSIS OF BMC/LEAN MASS RELATIONSHIPS IN THE WHOLE BODY AND LIMBS OF 2,265 NORMAL MEN AND PRE- AND POST-MENOPAUSAL WOMEN

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A whole-body DEXA study of 1,450 normal Caucasian individuals [Bone 22:683, 1998] found that mineral mass, either crude (BMC) or statistically adjusted to fat mass (FA-BMC) correlated linearly with lean mass (LM, proportional to muscle mass), showing similar slopes but decreasing intercepts in the order: pre-MP women > men > post-MP women > children. This supported the control of bone status by muscle strength in humans (bone ''mechanostat'' theory) and the positive interaction of sex hormones with that control. Now we further study those relationships in 2,265 normal Hispanic adults (60 men, 753 pre-MP women, 1,452 post-MP women), including separate determinations in upper and lower limbs.

In all studied regions the slopes of the BMC or FA-BMC vs LM relationships were parallel. However, the intercepts of the curves showed regional differences. In the whole body, the crude-BMC/LM relationships showed the same intercept differences observed previously. In the lower limbs, those differences were smaller but highly significant, showing the order: pre-MP women > men = post-MP women. In the upper limbs, the decreasing intercept order was: men > pre-MP women > post-MP women. After fat-adjustment of the BMC, the intercept order in both limbs was men > pre-MP women > post-MP women. Parallelism of the curves was maintained in all cases. A larger independent influence of LM than FM, body weight or age on these results was shown.

The parallelism of the curves further supports a common biomechanical control of bones by muscles in humans. Results suggest that the sex-hormone-associated differences in the DXA-assessed muscle-bone proportionality in humans could vary in different regions, perhaps because of the different weight-bearing nature of the musculoskeletal structures studied. Besides the obvious anthropometric associations, the FM would exert a mechanical effect as a component of body weight, evident in the lower limbs, while muscle contractions would induce a more significant, dynamical effect in both lower and upper limbs. Muscles seem to exert a larger influence than FM, body weight and age on BMC in the whole body and lower limbs, regardless of the gender and reproductive status of the individual.

P115SA. PRECISION COMPARISON OF TWO DXA DENSITOMETERS – PRODIGY AND DELPHI

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Precision error in BMD measurement can be caused by many factors: differences in patient positioning, variations in scan analysis, automation of software, and both short- and long-term fluctuations of the densitometry equipment. Minimization of these errors is essential for accurate assessment of BMD change over time. We compared the short-term precision error of two DXA devices, the Prodigy (GE Medical Systems Lunar) and the Delphi (Hologic). Both are fan-beam DXA devices predominantly used to measure BMD of the spine and proximal femur. In this study, 93 women (mean age 61.6 ± 8.9 years) were measured in duplicate, with repositioning, on both Prodigy and Delphi systems at one of three clinical centers. The DXA technologists were ISCD-certified and used manufacturer recommended scanning and analysis procedures. All scans were performed using 30-second scan modes. BMD precision error was calculated as the RMS standard deviation and coefficient of variation (RMS-%CV) for the repeated measurements. Data from right and left femora were evaluated individually (single femur precision) and using the combined value (dual femur precision). The precision

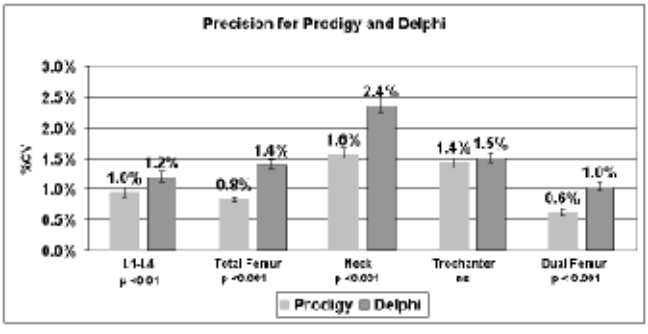

Fig. 1 Precision Comparison between Prodigy and Delphi

error of the Prodigy and Delphi measurements at each measurement region was compared using an F-test to determine the significance of any observed differences. Prodigy precision errors were significantly lower than the Delphi at L1–L4 spine, total femur, femoral neck, and dual total femur. There was no significant difference in precision error at the trochanter. Using dual femur measurements, precision errors were improved for both systems by approximately 25% compared to the single femur results. We conclude that there are skeletal site-specific differences in precision error depending on whether a Prodigy or Delphi is used. In clinical practice, these differences should be considered when determining a) the minimum time interval between baseline and follow-up scans, and b) whether a statistically significant change in the patient's BMD has occurred.

P116SU. MEASUREMENT OF FOOT BONE MINERAL DENSITY BY DUAL ENERGY X-RAY ABSORPTIOMETRY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND NORMAL VOLUNTEERS: DEVELOPMENT OF THE METHOD, ITS APPLICATION AND CLINICAL RELEVANCE

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Background: Hand and foot joints are primary target in rheumatoid arthritis (RA) and changes in periarticular bone mineral density (BMD) is one of the earliest and prominent feature of rheumatoid involvement of the joint.

Objective: This case-control study proposed to assess the relationship between foot BMD measured by DXA with BMD at axial sites, clinical indices of disease activity, functional status and quality of life in patients with RA. Healthy volunteers were enrolled for the development and assessment of method and its application.

Methods: 48 patients (4M, 44F, mean age 52 and disease duration 9 years.) and 40 age-and sex-matched healthy controls (3M, 37F, mean age 52) were included into the study. Patients' CRP, ESR, Ritchie articular index (RAI), HAQ, Foot Function Index (FFI) were noted. Axial, hand and fBMD were measured by DXA on a Lunar densitometer. fBMD measurements were performed using Lunar software for hand BMD measurement with little modifications.

Results: There was not a significant difference between right and left side in foot or hand BMD measurements. Bilateral foot and hand BMD and axial (spinal and femoral) BMD were significantly lower in patients compared to controls. Right fBMD significantly correlated with right hand ($r = 0.87$, $p = 0.0001$) and axial BMD (L2–L4, $r = 0.54$, femur Ward's, $r = 0.71$, $p = 0.0001$). But fBMD (right and left) did not correlate with disease duration and activity indices, RAI or FFI. Nevertheless right fBMD negatively correlated with Sharp erosion scores of right foot ($r = -0.38$, $p = 0.007$). The short-term precision error for fBMD measurements assessed by DXA (14 volunteers, 3 repeated measurement) was very small with a coefficient of variation 2.18%.

Conclusion: Foot joints are commonly involved and frequently disabled in RA and should not be overlooked by the physicians. Our results showed for the first time that foot BMD by DXA is an accurate and precise method. fBMD reflects BMD at other skeletal sites in patients with RA, and may be an outcome marker particularly in patients with prominent foot involvement. Longitudinal studies are required to examine the fact that foot BMD measurement is a sensitive marker of disease progression and response to therapeutic intervention.

P117MO. SENSIBILITY AND SPECIFICITY OF SPINE AND FEMUR BONE MINERAL DENSITY AND HEEL QUANTITATIVE ULTRASOUND TO IDENTIFY OSTEOPOROTIC FRACTURE RISK IN ELDERLY WOMEN ARE SIMILAR

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Spine and femur bone mineral density (BMD) measurements are gold standard techniques to diagnose osteoporosis. Work from the past decade suggest that quantitative ultrasound (QUS) measurements can be an alternative for the screening of patients at risk of osteoporosis. The purpose of this study was to evaluate the performance of the BMD and QUS (BUA, SOS, Stiffness index) measurements to identify osteoporotic fracture risk in Brazilian elderly women.

Patients and methods: 275 Brazilian elderly women were recruited to participate in this study. 122 had had previous osteoporotic fracture. Spine and femur BMD (DXA, Lunar) and heel QUS (Achilles+, Lunar) measurements were performed in all patients. Lateral thoracic and lumbar radiographs were taken at baseline and 5 years later to survey for presence of vertebral fractures.

Results: The performances of the BMD measurements at different sites were similar to one another. The area under the curve (AUC) for spine, femoral neck and trochanter BMD measurements were 0.739, 0.773 and 0.772, respectively. QUS performance was also comparable to that observed for BMD measurements, however stiffness index performance was slightly better than BUA and SOS (table below). The cutoff values for each method as well as their sensibility and specificity are also listed in the table below.

Performance of the BMD and heel QUS (area under the curve – AUC, cutoff values and sensibility and specificity)

Measure	AUC	95% Confidence Interval	Cutoff value	Sensibility (%)	Specificity (%)
Spine BMD (g/cm^2)	0.739	0.659; 0.819	0.870	71.4	63.3
Neck femur BMD (g/cm^2)	0.773	0.698; 0.847	0.710	71.4	66.9
Trochanter BMD (g/cm^2)	0.772	0.703; 0.842	0.590	73.8	73.4
BUA (dB/MHz)	0.770	0.697; 0.843	100	73.8	67.5
SOS (m/s)	0.757	0.678; 0.836	1504	71.4	69.8
Stiffness Index	0.783	0.709; 0.856	67	71.4	72.2

In conclusion, the performance of BMD and heel QUS measurements to identify osteoporotic fracture risk in elderly women are similar.

P118SA. EVALUATION OF BONE MASS BY QUANTITATIVE ULTRASOUND (BUA) IN A VENEZUELAN POPULATION OF 12,965 PATIENTS

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Objectives: Determine the bone mass with peripheral quantitative ultrasound of calcaneus in a Venezuelan population.

Methods: Between 2001–2003, 12,965 patients in ages between 20 to 93 years were evaluated by peripheral ultrasound in the right calcaneus, previous application of a epidemiologist survey. The collected data (T score, Z score, peripheral bone mass) were compiled and analyzed using dispersion measures.

Results: Of a total of 12,965 patients, 12,752 were females and 213 were males (average 55 years). 60.9% were positive for osteopenia and osteoporosis. Of this population with positive results, 81,14% of the patients had osteopenia and 18.85% had osteoporosis. 49.7% of the females had osteopenia and 11.6% had osteoporosis. 37.1% of the males had osteopenia and 7.5% had osteoporosis.

Conclusion: We recommend the use of the peripheral ultrasound in the search and early detection of patients with this pathology because is a reliable, fast, low cost and an affordable method for big groups of population in the detection of osteoporosis and the prognosis of fracture.

P119SU. INFLUENCE OF CHEMOTHERAPY (AC) ON BONE MINERAL DENSITY AND BONE ULTRASONOMETRY (QUS) IN WOMEN WITH BREAST CANCER

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Introduction: The aim of this prospective, case-control pilot study was to investigate the influence of chemotherapy (Adriamycin/Cyclophosphamid) on BMD and QUS in pre- and postmenopausal women with breast cancer.

Material and Methods: We included 32 premenopausal patients, mean age 37.1 ± 8.3 years with an incident diagnose of breast cancer who received a chemotherapy (4 cycles of AC) and 32 age- and BMI-matched controls. Women with metastases, a history of osteoporosis with or without fracture, diseases or treatments known to affect bone metabolism were excluded from the study. BMD was measured by DXA (DPX-L, GE/Lunar) at spine and hip. QUS was performed at the os calcaneus using the Achilles device (GE/Lunar) and at the phalanges using the Bone-Profiler (IGEA). Measurements were performed at baseline (before chemotherapy), after 6 and 12 months and were compared with measurement results of the age- and BMI-matched control group.

Results: DXA results of the spine and hip showed a significant decrease of T- and Z-score in patients with chemotherapy compared to controls ($p \leq 0.001$). In accordance to QUS results, measurement at the os calcaneus showed a similar, significant, linear decrease of T- and Z-score ($p \leq 0.001$). QUS results of the phalanges also showed a significant decrease of AD-SOS, for T- and Z-Score ($p \leq 0.001$), with the largest difference between baseline and 12 months T-score ($p \leq 0.001$).

Conclusion: The result of our prospective, case controlled pilot study confirms the deleterious influence of chemotherapy on BMD in women with breast cancer. This effect could be observed by DXA and additionally by QUS for the first time in this regard. Further, large scale longitudinal studies are needed to improve our understanding of the mechanism of bone changes during chemotherapy.

P120MO. T-SCORES FROM STANDARD REFERENCES ARE INADEQUATE FOR BRAZILIANS: A MULTI-ETHNIC POPULATION BASED STUDY FROM RIBEIRAO PRETO, SAO PAULO

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Aims: To determine peak bone mineral density (BMD) in a multiethnic cohort born in 1978/79 and compare with reference values used to calculate T scores.

Methods: 529 subjects answered structured interviews and performed anthropometric and biochemical tests. Healthy 226 females (**F**) and 221 males (**M**) with BMI from 18 to 30 kg/m^2 had BMD determined by qualified technicians at L1-L4 vertebrae (LS), femoral neck (FN) and total femur (TF) in a DXA scanner, HOLOGIC QDR 4500A®. Analyses were done by the author. LS T scores were derived from Hologic's references and the femoral regions from NHANES' data. Ethnicity was self-determined according to Brazilian census criteria. White (**w**) and Mixed-race (**m**) persons were compare to caucasian Americans and Blacks (**b**) to Afro-Americans.

Results: 81.4% were **w**, 7.8% **b** and 10.7% **m**, similar to the cohort and city age-ethnic distributions. BMI did not differ in the subgroups. Table 1 shows BMD values as mean ± SD. Brazilian **M** have higher peak BMD than **F** in all bone sites. Brazilian **F** have similar LS BMD despite ethnicity. **bF** and **mF** have higher FN and TF BMD than **wF**. **wM** and **mM** have similar BMD values but lower than **bM** in all sites. T scores differences from standards are in table 2. Brazilian **wF** and **bF** have significantly lower scores in all bone regions. **mF** have lower values only at LS. Brazilian **M** have lower T scores only at LS. **wM** had significantly higher scores at femoral sites. **mM** show similar scores but not significant.

Table 1. (*) g/cm^3

BMD*	WF n = 190	bF n = 14	mF n = 22	wM n = 174	bM n = 21	MM n = 26
LS	.991 ± .098	.997 ± .087	.991 ± .129	1.056 ± .118	1.126 ± .162	1.055 ± .135
FN	.833 ± .104	.859 ± .093	.854 ± .122	.991 ± .147	1.101 ± .158	.986 ± .160
TF	.898 ± .104	.916 ± .073	.926 ± .147	1.076 ± .142	1.188 ± .155	1.076 ± .158

Table 2. (*) significant differences from mean reference values, $p < .01$

T−scores	wF	bF	mF	wM	bM	mM
LS	−.47*	−1.38*	−.54*	−.31*	−.66*	−.33
FN	−.15*	−.65*	.04	.42*	.18	.41
TF	−.35*	−.73*	−.13	.28*	.06	.28

Conclusions: our findings indicate that Brazilians have important variations in peak BMD due to gender and ethnicity. These differences translated into T scores derived from values gathered elsewhere may exagerate the assessment of fragility fracture risk and contribute to erroneous medical decisions.

P121SA. DISCORDANCE WITHIN BONE MINERAL DENSITY VALUES IN LUMBAR SPINE AND FEMORAL NECK: IS IT VALID TO ANALYZE A SINGLE AREA IN ORDER TO MAKE THERAPEUTIC DECISIONS?

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Aims: Different medical insurance systems sustain the reliabilty of assessing bone mineral density (BMD) of a single area to perform the diagnosis of a patient presumably osteoporotic. We decided to carry out this study in order to evaluate the power to discriminate risk populations of a single area assessment, by determining if are there discrepancies between both sites, lumbar spine (L2L4) and femoral neck (FN), BMD.

Methods: 687 postmenopausal women between 45–79 years old, free of medication and other risk factors known to affect bone mass were studied. Values of BMD in L2L4 and FN were evaluated by DEXA using a Lunar DPX IQ equipment. Total predictive value (PV) of BMD in L2L4 and FN was determined.

Results: Results are displayed in table 1. Of the 687 patients screened, 462 of them showed low bone mass (LBM) in L2L4 and it PV was 89% whereas 413 had LBM in FN and it PV was 82.6%.

Table 1 Discordance between L2L4 an FN values: normal bone mass (NBM) vs. low bone mass(LBM). Distribution of the discordant areas.

Age (years)	n	NBM in both areas	LBM in both areas	Discordants		
				n	LBM in L2L4	LBM in FN
45–49	113	53 (46.9%)	32 (28.3%)	28 (24.8%)	20 (71.4%)	8 (28.6%)
50–54	98	32 (32.6%)	35 (35.7%)	31 (31.76%)	18 (58%)	13 (42%)
55–59	142	25 (17.6%)	65 (45.8%)	52 (36.6%)	37 (71.1%)	15 (28.9%)
60–64	133	18 (13.53%)	82 (61.65%)	32 (24.06%)	19 (59.4%)	13 (40.6%)
65–69	130	17 (13.07%)	80 (61.53%)	34 (26.15%)	18 (52.9%)	16 (47.1%)
70–74	44	4 (9%)	26 (59%)	14 (32%)	6 (42.8%)	8 (57.2%)
75–79	27	1 (3.7%)	23 (85%)	3 (11.3%)	1 (33.3%)	2 (66.6%)
Total	687	150 (21.8%)	343 (50%)	194 (28.2%)	119 (61.3%)	75 (38.7%)

Conclusions: According to the results obtained in this study, there is an important percentage of patients showing discordance in their BMD values, having one site as normal and the other one pathologic between 45–74 years old, and only lowering the percentage of discordance in the 75–79 years old group. The PV of L2L4 BMD as a sole investigated site was 89%, whilst if the chosen area was FN the PV of the assessment would be 82.6%. Therefore, evaluating one zone excludes from a proper diagnosis a large part of an otherwise affected population. Moreover, if the decision of evaluating a single area is mantained, it is difficult to select the right one given the data distribution between both areas among the different groups. We conclude that according to our results evaluating a single zone will led to suboptimal disease diagnosis.

P122SU. A COMPARISON OF SUPINE LATERAL AND DECUBITUS LATERAL MORPHOMETRY

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Aims: The aim of this study was to compare vertebral morphometry on a supine lateral DXA scanner (GE Lunar Expert) with a scanner that only allowed decubitus lateral mophometry (GE Lunar Prodigy).

Methods: 25 patients (19F, 6M, mean age 68, range 50–84) were recruited. Morphometry was carried out on each machine. Patients completed a questionnaire on comfort during scanning. The operator analysing the scans was blinded to the acquisition, and completed a questionnaire on the image quality.

Results: Two patients had unsatisfactory scans on the Prodigy, one due to operator error and one because of pins and plates in the lumbar spine. There was no significant difference between the scanners in terms of patient comfort. 19/25 reported that comfort was very good or better on the Expert compared with 17/25 on the Prodigy. There was no significant difference between the scanners in perceived image quality or in the ability to identify osteophytes or aortic calcification. The image quality was significantly worse in the thoracic (median 4, range 1–6) compared to the lumbar spine (median 5, range 2–6, $p < 0.001$). T4 was the highest vertebra assessed in 83% of cases on the Expert compared to 67% of cases on the Prodigy. There was no significant difference in vertebral dimensions or Z-score at L3. At T8, the posterior vertebral heights significantly higher on the Expert. (19.3 ± 1.6mm on the Expert compared to 18.2 ± 1.8mm on the Prodigy, $p < 0.001$). The average Z-scores for vertebral height were not significantly different, but the A/P and M/P ratios and Z-scores were, e.g. A/P ratio 0.88 ± 0.08 Expert and 0.91 ± 0.07 Prodigy. The Z-score was, on average, 0.5 lower on the Expert. The Expert identified 14 fractures, 3 in a patient not scanned on the Prodigy and 1 not seen on the Prodigy. The Prodigy identified 13, of which 3 were not identified on the Expert.

Conclusions: There are no qualitative differences between the Expert and Prodigy in patient comfort or image quality. Measurements in the lumbar spine are identical, but there are differences in the thoracic spine and the number of fractures identified that requires further study.

P123MO. THE VALIDATIONAL AND COMPARISIONAL STUDY OF SEVERAL RISK INDICES FOR PREDICTION OF OSTEOPOROSIS IN PERI- AND POSTMENOPAUSAL KOREAN WOMEN

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Aims: The objective of this study is to evaluate which risk index is preferred to identify peri- and postmenopausal Korean women at increased risk of osteoporosis by performing several clinical tools (SCORE; Simple Calculated Osteoporosis Risk Estimation, ORAI; Osteoporosis Risk Assessment Instrument, OSTA; Osteoporosis Self-Assessment Tool for Asians) for osteoporosis risk assessment.

Methods: A total of 1001 peri- and postmenopausal Korean women aged 45 years or more who had undergone testing with dual-energy x-ray absorptiometry (DEXA) at both the femoral neck and the lumbar spine (L1–L4). Osteoporosis was defined by T-score ≤ -2.5 at either the femoral neck or lumbar spine. Performances of SCORE, ORAI, and OSTA were calculated respectively in terms of DEXA.

Results: Among participants, 7.6% had osteoporosis at the femoral neck and 13.3% had osteoporosis at the lumbar spine. Validation of several risk indices for selecting women with osteoporosis at the femur neck showed that SCORE, ORAI, and OSTA had 94.7%, 92.1%, and 98.7% sensitivity and 75.2%, 75.4%, and 73.4% specificity, respectively. Validation of several risk indices for selecting women with osteoporosis at the lumbar spine showed that SCORE, ORAI, and OSTA had 74.4%, 72.2%, and 78.2% sensitivity and 76.7%, 76.7%, 75.0% specificity, respectively. Validation of several risk indices for selecting women with osteoporosis at either the femoral neck or lumbar spine showed that SCORE, ORAI, and OSTA had 76.8%, 75.6%, and 81.7% sensitivity and 79.1%, 79.2%, and 77.7% specificity, respectively.

Conclusions: SCORE, ORAI and OSTA are useful clinical tools for assessing risk of osteoporosis and effective in decreasing the need to undergo DEXA testing for peri-and postmenopausal Korean women, although SCORE and ORAI were risk indices developed for Caucasian women.

P124SA. DIFFERENTIATION BETWEEN POSTMENOPAUSAL WOMEN WITH AND WITHOUT OSTEOPOROTIC FRACTURES USING T-SCORES FROM VARIOUS SPINE AND HIP REGIONS

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Introduction: BMD is reported for several hip and spine regions of interest. It is not clear whether any of these regions perform better than others in assessing fragility. The present study examined which BMD T-score best separated subjects with and without osteoporotic fractures.

Methods: Subjects were 302 postmenopausal women (age 66 ± 10 years) with no secondary causes of osteoporosis (133 with radiographic vertebral fractures and/or peripheral osteoporotic fractures, and 169 without any fractures). T-scores were obtained using Lunar Prodigy: at the lumbar spine for L1–L4 (LS1–4), L2–L4 (LS2–4), L1–L4 with exclusion of artifact laden vertebrae (LS clean) and lowest of L1 to L4 vertebra (LS min); and at the proximal femur for right and left femoral neck and total hip, the lower of the two femoral neck (FN min) and total hip measurements (TH min), and the mean of the two femoral neck (FN mean) and total hip measurements (TH mean). Statistical analysis: logistic regression with presence of osteoporotic fractures as binary outcome and T-scores as single predictors. Results are expressed as: odds ratio (OR) of having a fracture per 1 unit decrease in T-score, 95% confidence interval (CI) for odds ratio, p value for significance of the regression coefficient; and area under the Roc curve (Az) with its standard error (SE), as a test of the ability of a given T-score to separate subjects with and without fractures.

Results: see table. Age had a significant effect in all regression analyses. Combining hip and spine T-scores did not improve the separation of subjects with and without fractures.

Table 1 Ability of T-scores from various sites to differentiate subjects with and without osteoporotic fractures

T-score	OR (95% CI)	P value	ROC Az + SE
LS1–4	1.17 (1.01–1.36)	0.033	0.568 + 0.03
LS2–4	1.16 (1.01–1.34)	0.033	0.569 + 0.03
LS min	1.21 (1.04–1.41)	0.016	0.577 + 0.03
LS clean	1.23 (1.05–1.43)	0.011	0.578 + 0.03
FN min	1.73 (1.35–2.20)	0.000	0.658 + 0.03**
FN mean	1.71 (1.34–2.18)	0.000	0.658 + 0.03**
TH min	1.42 (1.16–1.74)	0.001	0.638 + 0.03*
TH mean	1.42 (1.16–1.75)	0.001	0.638 + 0.03*

* $p < 0.05$ and ** $p < 0.01$ compared to spine

Conclusion: In this study of postmenopausal women, proximal femur measurements, particularly femoral neck, outperformed lumbar spine measurements in separating subjects with and without osteoporotic fractures. For spine measurements there was no clear advantage to using the lowest vertebra or eliminating artifact laden vertebrae.

P125SU. RELATIONSHIP OF OSTEOPOROSIS WITH GONADAL STATUS AND DISEASE ACTIVITY CHANGES IN PATIENTS WITH ANKYLOSING SPONDYLOSIS

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Aim: Osteoporosis (OP) is very common in patients with ankylosing spondylosis (AS). There are different opinions about gonadal changes in patients with (AS). Our aim in this study was to analyze relationship of OP with gonadal status and disease activity.

Method: The study group consisted of 51 male patients diagnosed with AS according to Modified New York Criteria and 32 patients followed with pain complaints formed the control group. Exclusion criteria were discovery of any disorders that could cause OP or hypogonadism.

Lumbar spine and femoral neck areas were assessed with Lunar DPX. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were used to identify the disease activity of the cases. The follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone and sex hormone binding globulin (SHBG) levels of the control and study groups were measured. Testosterone free index values were calculated. Graphpad Prisma V.3 program package was used for the statistical analyze of the data.

Results: The femoral neck bone mineral density (BMD) values of the study group were lower than the control group. However the lumbar spine values were not significantly different between the two groups. ESR and CRP values were higher in the study group. Femoral neck BMD values were correlated with ESR but not with CRP. FSH levels of the study group were lower than the control group. Total testosterone, LH, SHBG levels were not different in both control and study groups. There was a negative correlation between the SHBG and femoral neck BMD values of the study group but the SHBG values were not statistically different between the two groups.

Conclusions: The BMD measurements of the femoral neck are lower in patients with AS and are in correlation with disease activity (ESR). The absence of gonadal status changes in patients with AS suggests that gonadal status is not relative in these patients.

P126MO. QUANTITATIVE MORPHOMETRY OF T12 THORACIC VERTEBRAL BODY IN DETECTION OF PREVALENT FRACTURE: SHOULD MEASUREMENT ON LUMBAR SPINE FILM FOR THOARCIC DEPICTION OF T12 BE AN ALTERNATIVE TECHNIQUE?

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Aims: Quantitative morphometry (QM) of the 12th thoracic vertebral body (T12) on poorly projected lateral thoracic spine film could lead to mis-measurement of the vertebral body height. We compared the measurements of T12 from both thoracic and lumbar films and validated the solution of using lumbar film as an alternative method.

Methods: Women with a suspected osteoporotic vertebral fracture participating in a clinical trial by visual assessment were retrospectively investigated. Of a total of 103 women, 83 women were confirmed to have a prevalent fracture by an experienced radiologist using a semiquantitative (SQ) method. The anterior (Ha), middle (Hm), and posterior heights (Hp) at T12 were measured on thoracic spine film using six points technique corresponding to the contour of the vertebral body and the measurements were repeated on lumbar spine film. The vertebral heights were used to assess fracture prevalence using a form of the widely adopted Melton method: height ratio reduction ÿ ≥ 3 standard deviation (SD) at the level from normal reference data.

Results: The three vertebral dimensions measured on either the thoracic or lumbar film were on average all within 1% different (Ha = 0.27 ± 6.86%; Hm = 0.60 ± 8.00%; Hp = 0.45 ± 7.01%). Vertebral heights measured on lumbar film are found highly correlated with thoracic film (Ha: R2 = 0.94, Hm: R2 = 0.88) with the exception of Hp (R2 = 0.62). Although QM on both thoracic and lumbar films provided very similar vertebral dimensions, assessing T12 on the lumbar film was overall equal or better than on the thoracic film (Table).

Conclusions: Measurement of T12 vertebral dimension with lumbar spine film provides equal or better results than the same measurement on the thoracic film. QM measurement on the lumbar spine film when T12 is poorly depicted on the thoracic film is an acceptable alternative technique.

Table 1 Comparison of T12 measurements on thoracic and lumbar spine films

	N	Thoracic Film	Lumbar Film
T12 depiction: adequate / poor	103	50/53	75/28
QM Fracture Rate (3 SD reduction from normal)	103	57	56
Agreement with SQ (Kappa Score)	103	0.42	0.45
Overall Anterior height reduction (%)	103	29.45 ± 14.71	29.1 ± 14.76
Overall Middle height reduction (%)	103	25.08 ± 13.18	24.53 ± 13.62
Anterior height reduction (%) related to SQ Grades:			
SQ = 0.5 (questionable height reduction)	20	19.15 ± 4.74	19.03 ± 4.91
SQ = 1 (Mild height reduction 20–25%)	32	23.05 ± 5.59	22.70 ± 4.55
SQ = 2 (Moderate height reduction 25–40%)	40	30.79 ± 8.02	30.29 ± 8.56
SQ = 3 (Severe height reduction > 40%)	11	61.96 ± 17.46	61.86 ± 17.59

P127SA. COMPARISON OF QUANTITATIVE ULTRASONOGRAPHY WITH DUAL ENERGY ABSORPTIOMETRY AND INVESTIGATION OF THE CORRELATION BETWEEN QUANTITATIVE ULTRASONOGRAPHY PARAMETERS

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Aims: To evaluate the correlation between the two QUS parameters: broadband ultrasound attenuation (BUA) and speed of sound (SOS), and also to investigate correlation of QUS and dual energy X-ray absorptiometry (DEXA) measurements.

Methods: Calcaneal QUS measurements were performed in a standard fashion in a total of 1755 patients. Then BMD measurements using DEXA were performed in 485 (444 females and 41males) of the QUS patient population. Sensitivity, specificity, and positive and negative accuracy were calculated for BUA and SOS values and correlation of QUS and DEXA values were calculated by Pearson correlation coefficient.

Results: Calcaneal QUS measurements showed a positive moderate correlation ($r = 0.43$, $p < 0.01$) for SOS and BUA amplitudes, and a positive low correlation ($r = 0.37$, $p < 0.01$) for SOS and BUA T-scores. By taking SOS values as reference, sensitivity and negative accuracy were found to be 0.88, and specificity and positive accuracy 0.47 and 0.45, respectively, for BUA values. These results suggest a higher probability for accuracy of the findings when either SOS measurements show osteoporosis or BUA gives normal values, whereas they also suggest that a positive result with BUA or a negative result with SOS should be approached with suspicion. A low correlation ($r = 0.13$–0.37, $p < 0.001$) between DEXA and BUA amplitudes and T-scores was found. Correlation was also low ($r = 0.16$–0.29, $p < 0.001$) between DEXA and SOS T-scores and not significant between DEXA and SOS amplitudes. Separate evaluation of men, premenopausal women, and postmenopausal women showed a significant correlation ($r = 0.25$–0.36, $p < 0.001$) only for the postmenopausal group.

Conclusion: The results of our study suggest that QUS can give results comparable in reliability to those of DEXA particularly in the postmenopausal women. However, the overall low to moderate correlation between QUS and DEXA results emphasizes the need for further research for delineation of the definitive role of QUS in diagnosing osteoporosis and predicting fracture risk.

P128SU. QUALITY OF LIFE IN POSTMENOPAUSAL OSTEOPOROTIC WOMEN

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The aim of study was to assess quality of life in postmenopausal women (PMW) with low bone mineral density (BMD) and in PMW with fracture. We compare Health assessment Questionnaire (HAQ), Osteoporosis Quality of Life Questionnaire (OQLQ) and Short Form 36-item Health Survey Questionnaire (SF-36). BMD was measured on lumbar spine using dual x-ray absorptiometry. HAQ was used to assess physical disability in 8

categories of function. OQLQ is a specific measure and includes 30 questions, which are grouped into five domains: Symptoms, Emotional function, Physical function, Activities of Daily living (ADL), Leisure and Social activities with a score between 1 and 7. The SF-36 is a generic measure, and assessed 8 areas of general health each with a score between 0 and 100. High scores reflect better quality of life, and may also be converted to 2 summary scales: the physical and mental component summary scores. Spearman's rank method and Kruskal-Wallis Anova by ranks test were used to analyse the strength of relationships between variables. We assessed 114 PMW stratified in 4 groups: I (22) with normal BMD (T-0.19), mean age 52.6, HAQ 0.79; II (33) with Osteopenia (T-1.71), mean age 59.8, HAQ 0.57; III (27) with osteoporosis (T-3.28), mean age 62.1, HAQ 0.84 and IV (32) with fracture (T-2.49), mean age 65.9, HAQ 0.95. Results are on the graph. There was significant correlation between HAQ index, OQLQ and SF-36 in all groups. There were significant lower values of HAQ index ($p < 0.001$), OQLQ ($p < 0.001$) and SF-36 median scores ($p < 0.01$) in group with fracture, as might be expected. The study showed that both, the SF-36 and OQLQ are potentially useful measures on wider aspects of quality of life in PM osteoporotic women.

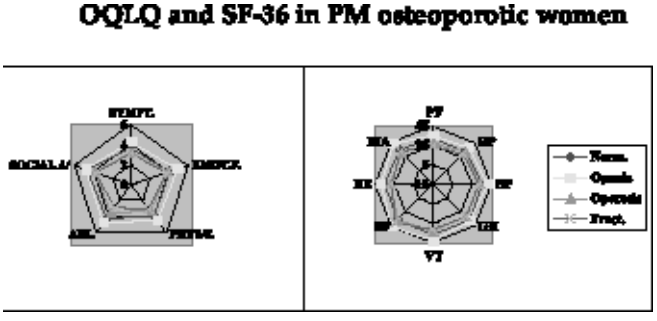

Fig. 1 Precision Comparison between Prodigy and Delphi

P129MO. EVALUATION OF CORTICAL BONE BY PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (PQCT) IN PERITONEAL DIALYSIS (PD) PATIENTS

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Peripheral QCT allows the non-invasive evaluation of cortical and trabecular bone separately as well as the geometrical properties of the radius. We investigated cortical bone by pQCT in 22 patients (6 males and 16 females) on maintenance PD; comparisons were made with 28 normal controls. Peripheral QCT (XCT 960, Stratec, Pforheim, Germany) was performed at distal radius of the nondominant forearm (15% the length of the ulna from endplate). We evaluated Total and cortical bone mineral density (TBMD, cBMD), Total (cross-sectional) and cortical area (TA, cA), cortical thickness (cThk), endosteal and periosteal perimeters and buckling ratio. Intact PTH levels were measured by IRMA. Correlations were made with age, total time in dialysis and serum iPTH. DP patients had a marked decrease in cThK (1.90 vs 2.95 mm; $p < 0.0001$) and a marked increase in endosteal perimeter (31.2 vs 23.9 mm; $p < 0.0001$) Buckling ratio [r/cThK] (3.81 vs 2.21; $p < 0.0001$) and TA. TBMD and cBMD correlated negatively with total time in dialysis ($p < 0.01$); no correlations were found between cA, cBMD and cThk with iPTH. Age correlated positively with TA, endosteal and periosteal perimeter and negatively cBMD. Our results show a cortical thinning of the radius with cortical parameters correlating predominantly with total time in dialysis and that bone adaptations to aging (peripherization) occur despite disturbances in endocrine-metabolic environment of dialysis.

P130SA. ANALYSIS OF BONE MINERAL DENSITY IN PATIENTS WITH HYPERPARATHYROIDISM SECONDARY TO END-STAGE RENAL DISEASE AND INDICATION OF PARATHYROIDECTOMY

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Background: Patients with hyperparathyroidism secondary to end-stage renal disease (HPT2) have moderate to severe bone disease and increased fracture risk compared to normal population. Some reports had demonstrated marked improvement in bone mass after successful parathyroidectomy (PTX).

Aims: To evaluate bone density in patients with HPT2 immediately before PTX.

Methods: 34 patients with HPT2 and indication for parathyroidectomy were studied. Serum PTH was above 600 pg/mL in all patients, and half of them had hypercalcemia. Serum gonadotrophins, testosterone and estradiol were evaluated by routine methods. Bone densitometry was performed to evaluate whole body density and composition, using dual x-ray absorptiometry (DXA). All exams were performed in the same densitometer, Lunar Corporation. Any evidence of aluminium intoxication such as high serum levels or a compatible bone biopsy was considered excluding criteria. Other factors, chronic diseases and medications that can alterate BMD were also valuated.

Results: Hypogonadism was present in 14 patients (41.2%), low body mass index in 10 (29.4%), HCV infection in 10 (29.4%), chronic smoking in 8 (23.5%), immobilization in 6 (17.6%), chronic glucocorticoid exposure in 2 (5.9%), one patient had hyperthyroidism and another systemic lupus erythematosus. No case of HIV infection or alcoholism was found. All patients had increased bone resorption in skeletal radiographs. 8 patients (23.5%) reported pathologic fractures. The median value of Z-score of total body, arms, legs and trunk were respectively −3.1; −2.7; −3.85; e −1.9. All these differences were statistically significant.

Conclusions: The severe bone loss observed in all patients is mainly due to HPT2, but comorbidities usually found in patients with end-stage renal disease also contribute. Bone densitometry was useful to quantitatively estimate bone loss and to demonstrate that skeletal sites rich in cortical bone were mostly affected, which is compatible with PTH's effects on bone.

P131SU. PAMIDRONATE AND ZOLEDRONATE EFFECTS IN THE INCREMENT OF BONE MINERAL DENSITY: COMPARING CONTROL, PROTEIC AND APROTEIC DIETS, OOPHORECTOMIZED AND NON- OOPHORECTOMIZED FEMALE RAT GROUPS

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Aims: Compare the increment of bone mineral density (BMD) with pamidronate, zoledronate and the isolated effect of protein diet, with bone densitometry and histomorphometry, in malnutrition oophorectomized and not oophorectomized female rats; and validate the indexes of BMD.

Methods: 60 young female Lewis rats divided in 5 experimental and a control group with and without oophorectomy and the administration of the drugs were submitted to two diets (proteic and aproteic). The variables were: weight, densitometry, histological and biochemistry evolution.

Results: Weight Evaluation: 1st interval (after 1st dose) showed increase in all groups, statically significant in the groups oophorectomized. 2nd interval (2nd dose) showed decrease, not significant, in all groups. Densitometric Evaluation: 1st interval (after aproteic diet) showed decrease in all groups, significant in the 4 medicated groups. 2nd interval (after 1st dose) showed increase in all groups.

3rd interval (after 2nd dose) showed increase in all groups, significant in the two not oophorectomized. Laboratorial Evaluation: the interval (at the beginning and at the end of medications) showed: increase of total proteins and globulin, confirming that there was not more malnutrition, decrease of alkaline phosphatase (except for the two ophorectomized groups), decrease of phosphorus and calcium in the four medicated groups and increase of phosphorus and calcium in the two groups not medicated, confirming that the medications cause hypocalcemia. Histomorphometric Evaluation: the ophorectomized group had smaller increment than that of not ophorectomized, confirming the discoveries of densitometric study.

Conclusions: The pamidronate and zoledronate were shown effective in the increment of BMD, in malnutrition and oophorectomized or not oophorectomized rats. These preliminary results indicate that the proteic diet, separately, possesses therapeutic effect in BMD, however in a significant less way, compared with the medicated animals. The results of histomorphometry, allows validating the bone densitometry, in this experimental model.

P132MO. THE LUNAR ACHILLES AS A SCREENING TOOL FOR OSTEOPOROSIS: COMPARISON WITH SPINE DXA

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Quantitative ultrasound of the os calcis is accepted as an effective, low-cost method to assess osteoporotic fracture risk. Recently the International Society for Clinical Densitometry (ISCD) recommended the use of peripheral densitometry (such as heel ultrasonometry) to identify patients who might have osteoporosis and should therefore undergo BMD testing at the hip and spine. This recommendation requires the use of a device specific T-score cutpoint on the peripheral device that detects 90% of individuals with osteoporosis (T-score ≤ -2.5) at either the spine or hip. In this study, we wished to determine the 90% sensitivity cutpoint that could be used with the Achilles bone ultrasonometer.

A total of 1087 women aged 50 years and older (mean age 68 ± 10 years) had DXA measurements of the spine (L1–L4) using a Lunar Prodigy (GE Medical Systems) or a Lunar DPX-NT, as well as heel ultrasound measurement using Achilles Solo. The heel T-score cutpoint with 90% sensitivity for identifying subjects with osteoporosis (T-score ≤ -2.5) at the spine was determined using ROC analysis with the ROCKIT program (Charles Metz, University of Chicago).

From the DXA results, 332 out of the 1087 patients were classified as osteoporotic in the spine. At a heel T-score of −1.4, sensitivity was 91% and specificity was 38%. Higher specificity of nearly 50% could be obtained with a T-score cutpoint of −1.8, which has a sensitivity of 85%. We conclude that the Achilles bone ultrasonometer can be used as a valid screening tool for osteoporosis according to ISCD recommendations. In situations where central DXA measurements are not ready available, the Achilles is a useful device to identify those patients who should be considered for spine and hip bone density assessment.

Sensitivity and Specificity of Osteoporosis at Spine Based on Heel T-Score

Heel T-Score	Sensitivity	Specificity
−0.6	95%	20%
−0.8	94%	24%
−1.0	94%	27%
−1.2	91%	31%
−1.4	91%	38%
−1.6	88%	43%
−1.8	85%	49%
−2.0	82%	55%

P133SA. DENSITOMETRIC DIFFERENTIAL DIAGNOSIS BETWEEN "DISUSE" AND "SYSTEMIC" OSTEOPENIAS: REFERENCE CHARTS AND CLINICAL APPLICATIONS

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DEXA assessment of bone mass (BMC) can be complemented by measuring lean mass (LM, regarded as proportional to muscle mass within certain limits) in either the whole body (WB) or selected regions. This little-profitted resource may provide a differential diagnosis between "disuse" and "systemic" osteopenias. We have showed linear, parallel BMC(y)-vs-LM(x) relationships in the WB and limbs of 1,450 Argentine and 3,000 Colombian normal boys/girls, men, and pre- and post-MP women. Parallelism of the curves would reflect the biological control of bones by muscles (bone mechanostat theory). However, the intercepts of the graphs differed between groups, in the order: boys/girls < post-MP women < men < pre-MP women, suggesting a positive modulation of that control by sex hormones. The variance of the BMC/LM relationship was substantially lower in lower limbs than in WB.

These results allowed performing z-scored graphs, specific for gender, reproductive status, region studied, race, and DEXA equipment employed, suitable for evaluating the bone/muscle mass proportion. They may allow evaluating whether an eventually low BMC value is or not adequately proportionate to the individual's WB or regional muscle mass. "Disuse-related" osteopenias (as well as small or lean, normally active individuals) should show a normal z-score for the BMC/LM relationship. "Systemic" osteopenias caused by alterations of bone cells (either primary or secondary to changes in their endocrine-metabolic environment) should show low BMC/LM z-scores. Such cases ought to be further studied employing other technologies to determine whether bone strength is or not affected; i.e. for diagnosing an osteoporosis as a (metabolic) "osteopenic fragility" (NIH criterion, out of the DEXA scope).

We have tested the ability of our WB or lower-limb BMC/LM z-score reference charts to detect "metabolic" osteopenias in a. haemodialysis patients (z-scores decaying as time on dialysis or serum PTH increased); b. obese hyperinsulinemic euglycemic patients (z-scores diminishing as body-mass index or fasting plasma insulin increased, or insulin sensitivity decreased); c. female ballet dancers (z-scores decaying as calciuria increased presumably because of a disturbed estrogen metabolism), and d. hypopituitary men and women before and after treatment with GH (z-scores improving as serum IGF-I levels increased).

P134SU. ASSESSMENT OF TRABECULAR BONE TEXTURE IN THE DISTAL RADIUS USING PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (PQCT)

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Aim: The purpose of this study was to investigate the distribution of bone and the changes in trabecular bone texture along the distal radius using peripheral quantitative computed tomography (pQCT) and to assess the accuracy of such measurements using micro-computed tomography (μCT) as a gold standard. It is well established that trabecular bone architecture, in addition to bone mineral density, is an important indicator for people at risk of fracture.

Methods: 12 dry human cadaver radii, of unknown gender or age, were imaged in air using a Stratec XCT-2000 pQCT scanner. Consecutive transaxial images were acquired with an in-plane pixel resolution of 0.2×0.2 mm and a slice thickness of 2.2 mm, covering 12% of bone length proximal from the radioulnar joint. μCT scans were performed on those two radii, determined from x-ray radiographs, to be the most and least osteoporotic. μCT images were acquired using a GE eXplore RS system with an isotropic

voxel resolution of 47 μm covering a 40 mm section at the distal radius. All texture analyses were performed using an in-house algorithm, which determined the mean hole size, number of holes and a connectivity index.

Results: The accuracy of pQCT assessment of texture is directly influenced by partial volume averaging due to the limited spatial resolution of the image data. Preliminary results indicate similar trends for connectivity index, number of holes and average hole size for all bones along their length as measured by pQCT (Fig).

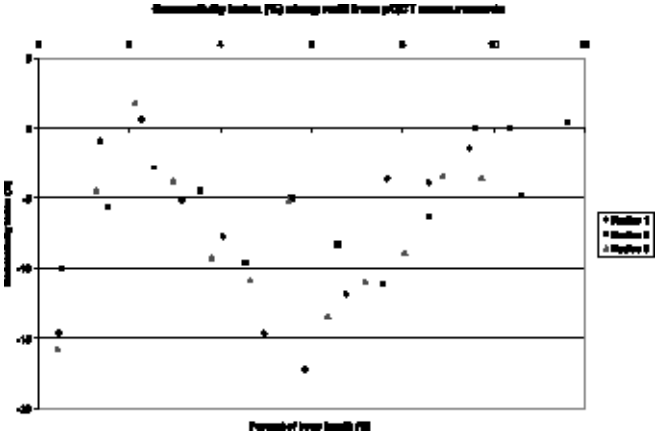

Fig. 1 Connectivity Index (%) along radii from pQCT measurements

Conclusions: The similar patterns of change in connectivity and mean hole size between radii will allow the distal radius to be used clinically as a site for trabecular bone texture measurement. Differences between sequential measurements of texture will be attributable to changes in bone architecture and will not be the consequence of poor reproducibility arising from patient positioning uncertainties.

P135MO. BONE MINERAL DENSITY IN PATIENTS WITH PARKINSON'S DISEASE

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Objective: This study proposed to assess bone mineral density (BMD) - lumbar spine, femoral and hand - and the relationship between BMD and disease duration, Hoehn and Yahr staging in Turkish patients with Parkinson's disease (PD).

Background: PD is mainly a disease of elderly adults and can cause severe disability and injury resulting from falls. Osteoporosis is a serious problem for older adults, especially for postmenopausal women leads to disabling falls and fractures. To best of our knowledge this report is the first assesing hand BMD in PD.

Methods: Twenty-four PD patients and age- and sex- matched 27 control were recruited from outpatient clinic of Neurology of our hospital. We evaluated lumbar spine (L2–L4), femoral (neck, Ward's triangle, trochanteric) and bilateral hand BMD using dual-energy x-ray absorbsiometry (DXA) in both groups and Hoehn and Yahr staging (HYS) in patients.

Results: There was no significant difference in right hand BMD (rHBMD), L2–L4 spinal BMD, and right femoral (neck, ward's triangle, trochanteric) BMD between patients and controls. However, female patients' hand BMD and right femoral neck BMD were significantly lower than female controls ($p < 0.05$). Male patients had no significant difference in BMD measurements in all sites with respect to controls. Patients' HYS and disease duration were negatively correlated with BMD at all sites except L2–L4 BMD.

Conclusions: We underscore an increased risk for osteoporosis in female patients with PD that is more prominent in femoral and hand BMD measurements. Female patients should be carefully examined for osteoporosis to prevent bone loss and associated disability.

P136MO. AGE RELATED DECLINE IN BONE MASS MEASURED BY DUAL ENERGY X-RAY ABSORPTIOMETRY AND QUANTITATIVE ULTRASOUND IN A POPULATION BASED SAMPLE OF BOTH SEXES: IDENTIFICATION OF USEFUL ULTRASOUND VALUES FOR SCREENING FOR OSTEOPOROSIS

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Aims: The aim of this population based study was to compare age related changes in bone mass measured by quantitative ultrasound (QUS) and dual x-ray absorptiometry (DXA) in order to identify a useful QUS values for screening for osteoporosis.

Methods: The study population was a random sample of 1630 individuals (1041 females, 589 males) age 30-85 years. Bone mass was measured by DXA (Hologic QDR 4500) in lumbar spine and proximal end of femur (total hip) and in calcaneus by QUS (Lunar, Achilles+). Biochemical bone markers (serum osteocalcin and serum CTX) were measured and fractures were reported. Individuals with DXA t-score < -2.5 at the lumbar spine or hip were identified and receiver operating curves (ROC) were used to calculate cut-off points for QUS. Sensitivity, specificity and kappa statistics were calculated.

Results: Age related decline in bone mass was significantly larger with calcaneal QUS than DXA at both sites in women. For men, the curves were similar for QUS and DXA in the hip. Similar correlations were found between QUS and DXA in different age groups of both sexes (0.45–0.53). Bone markers correlated inversely and similarly with QUS and DXA measurements. For women age 50–65 years a QUS t-score > -0.5 was found the most applicable for identifying normal BMD by DXA. In the age group 70–85 years, t-score > -2.0 for women and > -1.0 for men seemed reasonable cut-offs for identifying normal BMD (sensitivity around 90%, specificity 30–40%, discordance rate around 50%).

Conclusions: Calcaneal QUS cannot be used for the diagnosis of osteoporosis according to WHO criteria for DXA but can be of use to exclude osteoporosis in 30–40% of our cases.

P137SU. COMPARISONS OF BMD, BMC AND BONE AREA IN PENCIL AND FAN BEAM DENSITOMETRY WITH THE USE OF ANTHROPOMETRIC SPINE PHANTOM

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Aim: Introduction of newer DXA technology replaced earlier pencil beam x-ray by fan beam. The new fan beam devices ensure a high resolution images at multiple sites of skeleton. Changes in the hardware and software allowed assessments of bone mineral densities of various regions with much increased speed of measurement. However, little is known about the concordance between densitometric results established using pencil and fan beam devices. To address this issue, we performed a repeated measurements of anthropometric spine phantom using pencil- and fan-beam densitometers.

Methods: 440 measurements of anthropometric spine phantom performed using DPX-L and Prodigy machines were analyzed. Bone mineral densities and contents, as well as areas were evaluated in L1, L2, L3, L4, L1–L4, L2–L4, L3–L4 regions of interest.

Results: The stability of BMD measurements was very high in both devices (range of results within 1.5%). Significant differences between Prodigy and DPX-L assessed densities, contents and areas were found in all analyzed ROIs ($p < 0.0001$). Evaluation of mean values revealed lower densities, contents but not areas established using fan beam technology (Prodigy) when compared to pencil beam (DPX-L). The differences (in g/cm^2) between means of BMD assessed in L1-L4, L2-L4 and L3-L4 tended to increase with decreasing number of analyzed vertebrae (-0.0365 ± 0.0004, $p < 0.0001$; -0.0417 ± 0.0004, $p < 0.0001$; and -0.0429 ± 0.0006, $p < 0.0001$), respectively. In opposite, the differences (in g) between

means of BMC tended to decrease with decreasing number of analyzed vertebrae (-2.053 ± 0.0177, $p < 0.0001$; -1.544 ± 0.0166, $p < 0.0001$; and -0.998 ± 0.0134, $p < 0.0001$), respectively. Similar tendency has not been found for differences between means of areas. Coefficients of variations for all data sets of analyzed parameters were lower for Prodigy, indicating lower variability of measurement results reflecting improved edge detection when compared to DPX-L.

Conclusion: On the basis of our results it can be concluded that there is substantial need to establish correction algorithms which allow comparison of measurements performed using fan and pencil beam devices what is essential in time when increasing number of fan beam machines is being installed.

P138MO. STUDY OF BONE MINERAL DENSITY IN PATIENTS WITH THYROTOXICOSIS

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Aim and objectives: To evaluate bone density in patients with uncontrolled thyrotoxicosis and to study the impact of various factors like severity and duration of thyrotoxicosis, parity, duration of lactation, socioeconomic status, nutritional factors, physical activity, vitamin D status on bone density in study population.

Materials and methods: A total of 45 premenopausal female patients having Graves disease with untreated or uncontrolled thyrotoxicosis between age group 30–50 yrs were studied. In addition to clinical parameters, hormonal and biochemical parameters like serum T3, T4, TSH, calcium, phosphorus, alkaline phosphatase, albumin, 25-OH D3 and urinary calcium and creatinine values were evaluated. Bone density was obtained by dual energy x-ray absorptiometry (DXA; Hologic Inc.) and was compared with the Indian normative data.

Results: As compared to Indian normative data, the study population had significantly reduced bone density. The mean Z score was −0.69 and −0.65 at lumbar spine and femoral neck respectively. 37.78% and 35.55% of patients had Z scores less than −1.0 at lumbar spine and femoral neck, respectively. 78% patients had hypovitaminosis D (≤20 ng/ml).

Weight, body mass index, total caloric and calcium intake per day correlated positively with bone densities at various sites. Sr. T3, parity, lactation, correlated negatively with bone density at various sites.

Physical activity, sunlight exposure, socioeconomic status, vitamin D status and other biochemical parameters did not show significant correlation with bone density at any site.

Conclusion: Bone density is reduced in patients with thyrotoxicosis as compared to the general population. In addition to thyrotoxicosis, a combination of various other factors contribute to low bone mass observed in this condition. In the absence of universal guidelines to treat bone disease in thyrotoxicosis, optimum control of thyrotoxicosis, as well as maintenance of proper nutrition, adequate vitamin D and calcium intake and control of other risk factors for osteoporosis appears to be the correct strategy.

P139SA. BONE MINERAL DENSITY, SERUM MARKERS OF BONE TURNOVER AND THEIR RELATIONSHIPS IN PERITONEAL DIALYSIS

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Background: The usefulness of bone mass measurements and bone turnover markers to estimate fracture risk or the type of underlying renal osteodystrophy are not well established in patients on peritoneal dialysis (PD).

Objective: To asses bone mass using total and regional bone densitometry in a group of patients on PD and to determine if serum markers of bone turnover identify patients with low bone mass.

Methods: Bone densitometry was studied by dual-energy X-ray absorptiometry (DXA) and bone turnover using several serum markers in 65 patients on PD. Bone mass was classified as normal, osteopenic or osteoporotic according to World Health Organization criteria based on bone mineral density T scores.

Results: T scores in osteopenic range were present in 44.6% (45% of men and 44.4% of females) of patients at the lumbar spine (LS) and in 56% (55% of men and 58% of females) at the femoral neck (FN). T scores in the osteoporotic range were present in 13% of patients (10% of men and 15.5% of women) at the LS and in 21% (30% of men and 17.7% of women) at the FN. Patients with BMD T scores in osteoporotic range at both regions had increased serum iPTH levels compared to patients in the osteopenic/normal range. TBMC correlated negatively with iPTH ($r = -0.34$) and with total time in dialysis ($r = -0.26$); in multivariate analysis only iPTH correlated negatively with TBMC ($B = -0.26$; $p = 0.03$). No correlations were found between the other bone markers and BMD T scores at the FN or LS. There were no significant differences in absolute BMD or BMD T scores at the LS or FN between patients with or without fractures.

Conclusions: BMD T scores in osteopenia osteoporosis range were observed in 58.4% of these patients on PD at the LS and in 78.4% at the FN. TBMC correlated negatively with iPTH. There were no correlations between markers of bone turnover and bone mass measurements at the two skeletal regions, although patients with BMD T scores in osteoporotic range had increased serum iPTH levels. Bone mass measurements were not different between patients with or without fractures.

P140SU. PREDICTION OF LUMBAR SPINE BONE MINERAL DENSITY FROM WHOLE BODY DUAL-ENERGY X-RAY ABSORPTIOMETRY

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Whole body Dual-energy x-ray absorptiometry (DXA) is used most often in studies of body composition analysis. Bone mineral density (BMD) values are then generated for different body parts including the lumbar spine.

Aim: The present study compared BMD values (in g/cm^2) yielded in standard DXA of the antero-posterior spine with lumbar spine BMD derived from whole body scans.

Methods: 100 women aged 52.6 (SD 12.1) years were included. Their mean body mass index was 30.5 (SD 6.6) kg/m^2. 55 of them were postmenopausal with mean age at menopause 46.3 years. All participants received consecutively standard AP spine DXA and whole body scans on a Hologic QDR 4500 A bone densitometer. The manufacturer's reference database for white women was used. Correlation analysis was performed.

Results: AP DXA usually yielded higher values for bone mineral content (BMC, g) and scanned area (cm^2). As BMD represents BMC divided by the area, the difference in BMD was partly corrected. BMD correlations derived from both measurements were strong and statistically significant ($r = 0.88$). The correlation was weaker in those participants with very high BMI.

Conclusions: Whole body DXA may be used for lumbar spine BMD prediction. This approach would be particularly useful in cases when a DXA whole body scan had been performed at a younger age without standard AP spine DXA. Results derived from the whole body scan may be extrapolated to lumbar spine BMD measured at an older age by AP spine DXA to allow comparison.

P141MO. BONE MINERAL DENSITY IN ACQUIRED IMMUNODEFICIENCY SYNDROME

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Acquired immunedeficiency syndrome (AIDS) patients present several comorbidities; endocrine abnormalities as adrenal insufficiency, hypogonadism and hypothyrodism. This study aimed to assess bone mineral density (BMD) and its correlation with the complex universe of AIDS patients during highly active antiretroviral therapy (HAART). We evaluated 24 males with AIDS, aged 37.4 yr (range = 24–55 yr), BMI was $22.4 \pm 3{,}6$ kg/m^2, 10 healthy men were considered as normal control, aged 34.7yr (range = 25–49 yr), BMI was $23.8 \pm 4{,}7$ kg/m^2. All of them were submitted to bone mineral density determination employing a double photon emission densitometer (HOLOGIC QDR 1000 Plus). BMD was evaluated at the level of lumbar spine (L1–L4) and standardized femoral sites: T score between −1 and −2.5 SD was indicative of osteopenia and T score ≤ 2.5 negative SD was indicative of osteoporosis. Mann-Whitney's test was used to compare the results between groups and Chi square-test was used to compare frequencies. Normal control patients had normal BMD at spine and femoral level. Decreased BMD was found in 15 (62.5%) patients: 4 (16.6%) with osteopenia at lumbar spine, 1 (4.1%) with osteopenia at femoral level, 1(4.1%) with osteoporosis at lumbar spine, 4 (16.6%) with osteoporosis at lumbar spine and osteopenia at femoral level, and 5 (20.8%) osteopenia at lumbar and femoral level. We concluded that AIDS patients have decreased BMD of multiple etiologies to be further investigated.

P142SA. DENSITOMETRIC EVALUATION OF ORAL PAMIDRONATE ON JAW OF PATIENTS WITH PERIODONTOPATHIES

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Bisphosphonates are compounds used in different osteopathies like osteoporosis. However, the effects of bisphosphonates have only been quantified in a limited number of skeletal sites. The availability of a quantitative densitometric technique, the peripheral quantitative computing tomography (pQCT, XCT 3000-D, Stratec. Pforzheim) allows easy access to specific skeletal sites like jaw peridental bone.

Twenty adult patients (male and female, range 30–60 years old) with periodontal disease were studied after corresponding periodontal treatment and the administration of 200 mg/d of oral pamidronate (AMINOMUX® provided by Gador S.A.) during 6 months. Clinical studies, x-ray and pQCT studies were performed before and after the bisphosphonate treatment. Clinical controls showed the absence of new infections during the 6-month follow-up. X-ray studies showed no apparent change while the pQCT study showed changes of bone mineral density (BMD) in cortical bone from 572.9 ± 64.1 mg cm3 to 588.8 ± 39.5 mg cm^3 (+1.1%, p:n.s.) and BMD changes in underlying trabecular bone from 240.8 ± 21.6 mg cm3 to 242.7 ± 14.6 mg cm^3 (+1.1%, p:n.s.). The conservation of regional bone mass under these conditions is considered a positive finding.

P143SU. SCINTIGRAPHIC QUANTITATIVE DETERMINATION OF THE BONE METABOLIC ACTIVITY AT THE HUMAN MANDIBLE

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The bone metabolic activity of mandibles is affected by loading derived from regional muscles, teeth and the hormonal environment as well. Bone turnover is much higher than in other skeletal sites and uptake of bone binding substances as bisphosphonates is also remarkable. In order to study such metabolism, quantitatively, and by a practical non invasive method, we studied 10 volunteers who gave consent to participate. They were all adults, from 31 to 50 years old, in good health conditions, and normal parameters of bone metabolism. All participants were clinically examined, including panoramic x-ray of the mandible and maxilla, ionic calcium and serum alkaline phosphatase. Three hours before scintigraphy, a 40 microcuries/kg b.w. dose of MDP-Tc^{99m} was injected. Tracer activity was explored at whole body, facial region, and both humeri by an SPECT system (Siemens). Small regions of interest (ROI) were elected at each mandible, separating the basal portion from the peri-alveolar portion (peri-dental). Vertical ROIs were defined in order to distinguish alveolar bone surrounding dentate from edentate portions. Using the system software figures are expressed as counts/pixel. The activity at mandible was found always higher than in humeri (1.7 fold, $P < 0.05$), average values 31.6 at mandible and 18.6 at humerus. Comparing basal vs. peri-alveolar portions of the mandible, a higher tracer uptake was observed in the later. Mean activity at basal portion was 17.8; and at peri-alveolar bone portions of 27.5 ($p < 0.05$). Activity was also higher in peri-alveolar bone at dentate sites than at edentate sites ($p < 0.05$). Therefore it is shown that the higher metabolic sites at mandible can be identified and quantified with SPECT, mostly at peri-alveolar portions. The higher activity could be attributed to vascularity and high bone turnover. This technique deserves development, combined with absorptiometric systems, it may provide useful quantitative regional information on bone turnover changes.

P144MO. HISTOMORPHOLOGY IN YOUNG WOMEN WITH SUSPECTED OSTEOPATHIES

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Background: Osteoporosis (OPO) is the most common osteopathy in postmenopausal women. But there are clinically relevant osteopathies in young/premenopausal women, too.

Methods: We reviewed 272 women with max. age of 50 years (18–50, mean 41 years). They suffered from back pain and height loss or atraumatic fractures. We detected common risk factors for OPO. Bone mineral density (BMD) with DXA Hologic QDR 2000 at lumbar spine (LS) and hip, laboratory tests and bone histomorphology (Yamshidi punction) were performed.

Results: 200/272 patients (74%) had OPO by histomorphology (66 high-turnover, 79 low-turnover, 55 not differentiated). 30 showed osteomalacia (11%), another 25 had "osteomalacial components". 11 of those 55 patients were mediterranean immigrants. 6 cases had primary hyperparathyreoidism. And 5% of the patients had severe bone marrow diseases: systemic mastocytosis, plasmocytoma, chronic lymphatic leucaemia, hairy cell leucaemia, immunocytoma and toxic bone marrow changes. 23 women had normal biopsies (8%).

In OPO by histomorphology, mean T-score at LS was −2.26, at lowest vertebra −2.90 and at hip −1.84. Patients with osteomalacia had lower BMD (LS −3.21, lowest −3.88 and hip –3.13).

Following risk factors for OPO were found: positive familiar anamnesis (23%), smoking > 10 cigarettes/day (23%), systemic steroids (17%), rheumatism (6%), menopause < 40th year (15%), thyroid diseases (9%), low intake of calcium/vitamin D (10%). Other risk factors were rare, like anorexia, inflammatory bowel diseases, history of malignant tumors. 24% had no risk factors for bone diseases.

10% of our OPO patients had elevated levels of cholesterol (> 300 mg/dl), but a low BMI of 20,8 kg/m^2.

One third had prevalent low-trauma fractures with no difference between the diseases, even 4 premenopausal low-energy hip fractures.

Discussion:

- Normal BMD or osteopenia does not exclude histomorphologic OPO.
- Risk factors are comparable in pre- and postmenopausal OPO, but there was no group for comparison to healthy controls.
- Hypercholesterolaemia in thin premenopausal women could play a pathogenetic role and might have possible theurapeutic consequences. Prospective studies on this point should be done.

- In unclear back pain, height loss and fractures without trauma in younger women differential diagnosis including bone histomorphology should be performed, especially to exclude malignant bone marrow diseases.

P145SA. ULTRASONOMETRY, MECHANICAL TEST AND SCATTERING ELECTRONIC MICROSCOPY IN STUDY OF HUMAN TRABECULAR BONE

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Aims: The aim of this study was to determine the correlation between the found values through ultrasonometry and compression mechanical tests. Besides this, scattering eletronic microsopy was used for the analysis of the microarchitecture of trabecular bone.

Methods: Ten human cadavers (men and women, age 60 ± 16 years old) were examined with a ultrasonometry device (SONOST-2000, Osteosys/Medison) at the Os calcis. Trabecular cilinders samples were taken out from the calcaneus, these samples were submitted to compression test. Ultrasonometry variables, speed of sound (SOS), broadband ultrasound attenuation (BUA), and the bone quality index (BQI) were correlated to the variables of mechanical test: Young Modulus (E), stiffness and maximum strain. The samples were submitted to scattering eletronic microcospy and trabecular thickness, trabecular number and conectivies were analysed.

Results: Found ultrasonometry variables were BQI = 93.5 ± 27.26, SOS = 1661.24 ± 45.58 m/s, BUA = 60.77 ± 23.59 dB/mHz and the mechanical test variables were E = 105.89 ± 86.56 Mpa, Stiffness = 754.95 ± 589.98 and maximum strain = 2.48 ± 1.8 Mpa. The correlation between BQI and maximum strain was statistically significant ($r = 0.703$). Through scattering eletronic microsopy, it was able to differ health bone from osteoporotic bone.

Conclusion: BQI variable can be used as an indirect method to evaluate important properties during the analysis of the fracture risk, such as the analysis of the maximum strain supported on the bone. Scattering eletronic microsopy was able to show the deterioration of trabecular architecture according to the ultrasonometry results. Calcaneus ultrasonometry was noticed as a good method to predict the bone state.

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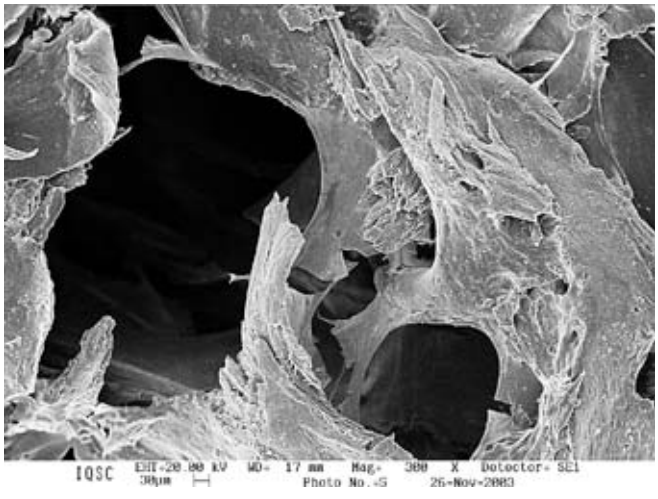

Fig. 1 Scattering eletronic microcospy of osteoporotic trabecular bone. 300x

P146SU. REGIONAL APPROACH OF THE VOLUMETRIC BONE DENSITY OF THE ADULT HUMAN MANDIBLE

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The structure and volumetric bone mineral density (vBMD) of the human mandible shows significant regional variations, depending on the history of its mechanical usage, metabolic activity and loading from teeth or prosthesis. The macro-structures can be assessed by different equipments, and vBMD can be complementary used in order to achieve non invasive data at selected small regions of interest (ROI). Indeed, ROIs at cortical areas may indicate degree of porosity, and at medullar areas may reflect the content of trabecular packages. Therefore, we describe vBMD values shown at selected ROIs in healthy adults, in comparison with values shown at the whole region. A sample of 36 subjects, of both gender, older than 50 years were analysed following Capiglioni et al criteria (Diagnóstico, 1998,7:898–901). Likely, an axial scan was performed with a peripheral quantitative tomograph, pQCT (XCT3000-D, Stratec), x-rays: 10 mrem. Regional densities were overall assessed through the software provided with the system, and selected ROIs, from 3 to 16 mm^2 at different sites, were manually analysed. Table shows mean ($\pm$SD) values in mg/cm^3. Whole region cortical values were found underestimated, while medullar values were overestimated compared to selected ROIs. It is concluded that the regional variables calculated by the software may be affected, perhaps by partial effect; or sub-cortical tissue. Hence the manual exploration of the scans should be performed in order to assess specific cortical and/or medullar vBMDs.

P147MO. MANDIBLE CORTICAL AND MEDULLAR DENSITY ASSESSED BY PQCT IN PATIENTS WITH BRUXISM

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Bruxism is a condition in which psychological factors affects mandible and teeth due to compulsive and protracted rubbing and pressing. Aiming to study the effects of this atypical loading on mandible we study a group of 9 patients with clinical diagnosis of bruxism. They all were accepted if a silent period over 20 ms was detected. Both genders were included, being between 18–60 years old. A low radiation, peripheral quantitative computarized tomography (pQCT) Stratec XCT 3000-D system (Pforzheim) was adapted for head assessments. Each scan was placed below the dental interference line (admitted $< 5\%$ of the total scanned area) following R. Capiglioni et al procedures (Diagnóstico 1998,7:898–901). By means of the provided software, volumetric bone mineral density (vBMD) was obtained at cortical (mean assessed area = 504.3 mm^2) and trabecular (mean area = 3290.0 mm^2) regions. Considering the diameters between the labial and lingual cortex, at each scan, the polar stress-strain index (SSI_{polar}) was estimated, as an indicator of the local structural stability against deforming forces. Bone quality was determined following Horner classification (types I to IV), and its equivalence to pQCT units (Roldán et al JBMR2001, 16(Supp1): S244).The findings were compared to historical values available at our unit. vBMD cortical was 1429.5 ± 127.5 mg/cm^3 (overnormal, tissue quality type I); vBMD trabecular was 105.5 ± 3.02 mg/cm^3 (osteopenia, tissue quality type IV); and SSI_{polar} was 7993.7 ± 7057.5 mm^3 (no references available yet). In conclusion, in all cases medullar density was found diminished (osteopenia; dispersion 5.5%), with concomitant increase of cortical density (dispersion 17.2%). It can be suggested a decrease in porosity, and a probable loss of cortical ductility affecting mandible

strength in these patients. Peridental tissue could be even more affected, but was not assessed in this sample. If these observations are confirmed the mandible of patients suffering bruxism could be mechanically less elastic. According to our present data the mandible, is indeed, different from the one of normal dentate adults.

P148SA. INFLUENCE OF AGE ON THE MECHANICAL EVALUTION OF BENDING-COMPRESSION IN INTACT AND OVARIECTOMIZED RATS

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Aim: Evalute the influence on two different ages in intact and ovariectomized rats using bending-compression on the proximal femur.

Methods: This study evaluated the age influence of overload in 37 female Wistar rats. The overload was compared between intact rats at 5 and 7 months of age, after that they were compared to 7 months ovariectomized rats. A surgery was made in order to induce osteopenia and the animals were sacrificed after two months. The overload was got through the bending-compression test on the proximal femur and was used as a evaluation criteria.

Results: The analysis of the maximum overload in intact animals between 5 months and 7 months of age showed an increasing bone resistance, as well as weight increasing, but with a non-significant difference. Ovariectomized animals at 5 and 7 months of age showed a significant decreasing of maximum overload in relation to the intact rats at the same age. A nonsignificant difference between 5 and 7 months ovariectomized rats was found.

Conclusion: There was a decreasing on bone resistance, which was evaluated through maximum overload, between 5 and 7 months ovariectomized animals and their control group (5 and 7 months intact animals). This study showed that age does not have a significant influence on 5 and 7 months of age intact animals, as well as on 5 and 7 months of age ovariectomized rats.

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P149SU. THE DIAGNOSIS OF OSTEOPOROSIS BY STANDARD SPINE DUAL-ENERGY X-RAY ABSORPTIOMETRY AND WHOLE BODY SCANS

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In whole body dual-energy x-ray absorptiometry (DXA) bone mineral density (BMD) values are generated for different body parts and whole body T- and Z-scores are then calculated.

Aim: The present study compared T- and Z-scores (in SDs) yielded in standard DXA of the antero-posterior spine and in DXA whole body scans.

Methods: 100 women aged 52.6 (SD 12.1) years were included. Their mean body mass index was 30.5 (SD 6.6) kg/m^2. 55 of them were postmenopausal with mean age at menopause 46.3 years. All participants received consecutively standard AP spine DXA and whole body scans on a Hologic QDR 4500, a bone densitometer. The manufacturer's reference database for white women was used as well as the WHO definition for osteoporosis. Correlation analysis was performed.

Results: AP DXA yielded similar proportions of osteopenic and osteoporotic women as standard AP spine DXA. But only in 50% of the cases a woman was classified in the same BMD group by both methods. The T-score correlation was weaker ($r = 0.75$) than the Z-score correlation ($r = 0.85$).

Conslusions: Whole body BMD T-scores possibly reflect mineralization of the whole skeleton including both cortical and trabecular bone. Heterogeneity of bone loss is inherent in the process of ageing. This may be the reason why the trabecular-rich lumbar spine does not always yield the same T-score in a particular person as the whole body scan. We conclude that whole body BMD T-scores may be more useful in studies of the growing skeleton in children and adolescents as they reflect the integral process of bone mineralization.

P150MO. EVALUATION OF THE BRAVO: PRECISION AND ACCURACY OF A NEW COMPACT BONE DENSITOMETER

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The Bravo (GE Medical Systems) is a new DXA bone densitometer designed to fit into smaller offices that cannot accommodate a full-sized DXA system. The Bravo scan arm swings 90 degrees to the side for easy access to the scan table. Bone mineral density (BMD) of the spine and bilateral femurs are measured in one exam, using the OneScan acquisition protocol that eliminates the need to reposition the patient between scans. We compared the precision and accuracy of the Bravo measurements with a full size densitometer, the Lunar Prodigy (GE Medical Systems). Thirty women aged 45 to 60 years (mean age 52.6; SD 6.4 years) had spine/bilateral femur scans twice with the Bravo and once with the Prodigy. Patients were repositioned between the Bravo scans. One subject was removed from the study because of considerable positioning differences between scans. BMD precision error was calculated as the root-mean-square coefficient of variation for repeated measurements. Paired T-tests were used to determine significance of BMD differences between Bravo and Prodigy measurement results. Left and right femur results were averaged for bilateral total femur ($n = 29$), and were pooled ($n = 58$) for femur neck, trochanter and total femur. Bravo BMD precision error (CV) ranged from 0.7% for spine L1-L4 and 1.0% for total femur to 1.9% for femur neck. Average differences in measured BMD were negligible for femur sites and were clinically insignificant at the spine site ($< 2\%$). Regression of Bravo BMD with Prodigy BMD showed very high correlations ($r = 0.99$) with no significant differences in the regression slopes or intercepts. We conclude that the Bravo provided accurate BMD for spine and femur measurement sites, with precision that compared favorably with published values for full size DXA systems.

Comparison of Bravo with Prodigy densitometer

	Femur Neck	Trochanter	Total Femur	Bilateral Total Femur	Spine L1-L4
Bravo (%CV)	1.9%	1.6%	1.0%	0.9%	0.7%
Bravo BMD (g/cm^2)	0.96	0.80	0.99	0.99	1.21
Prodigy BMD (g/cm^2)	0.96	0.81	1.00	1.00	1.23
BMD Difference (p)	ns	ns	< 0.01	< 0.05	< 0.001

P151SA. IN THE SEARCH OF OPTIMAL DIAGNOSTIC AND MONITORING PROCEDURES IN CHILDREN USING DXA METHOD: THE STUDY OF IDIOPATHIC JUVENILE OSTEOPOROSIS SUBJECTS

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Aim: Various diagnostic approaches to interpret and monitor DXA results in IJO cases were compared and utilized in the aim of developing optimal evaluation scheme of studied cases.

Methods: Study population comprised 61 IJO and 481 healthy children. IJO cases were analyzed according to type of IJO (mild, moderate, severe) and stage (acute, chronic). DXA derived LBM, as a surrogate of muscle mass, total and L2-L4 BMC (TBBMC, SBMC) and densities were assessed. Lumbar spine volumetric density (BMAD, g/cm^3) was calculated according to Carter's algorithm. Utilizing mechanostat thesis, body height (BH)/LBM, TBBMC/LBM, SBMC/LBM ratios were employed as diagnostic indicators of musculoskeletal system. Regression curves fitted to age-dependent data were assessed in healthy or moderate IJO cases and the results of each mild or severe IJO subject were converted to the % of expected value what allowed to monitor skeleton in relation to healthy or typical IJO cases. Additionally, data were adjusted for age, height and weight as the second possible approach for monitoring of skeleton to avoid influence of growth.

Results: The highest deficits of analyzed parameters (except BH/LBM) were observed during acute phase of severe type of IJO. Percentages of expected values for TBBMC/LBM and SBMC/LBM

ratios, in severe type of IJO, but not mild, were low according to expected values for healthy and moderate IJO. Significant differences were found between adjusted TBBMD, SBMD, TBBMC, SBMC,BMAD, TBBMC/LBM and SBMC/LBM, but not BH/LBM, calculated in moderate vs. severe ($p < 0.001$), moderate vs. mild ($p < 0.05$) and mild vs. severe ($p < 0.001$) types of IJO and between acute and chronic phases ($p < 0.001$), in both genders. Lack of major differences between healthy and mild type of IJO was noted.

Conclusion: Percentages of expected values allowed diagnosis and monitoring of single individual IJO case not only in relation to healthy but also to typical IJO (moderate type) what seems to be essential for proper therapeutical management. Anthropometrical correction of DXA results allowed to diagnose and monitor changes in bone mineralization regardless of changing body size. Type-phase-dependent impact of IJO on skeleton, but not on muscles, was noted and primary bone disorder diagnosed utilizing BH/LBM, TBBMC/LBM and/or SBMC/LBM ratios.

P152SU. OSTEOPOROSIS SCREENING: COMPARISON OF THE HEEL ULTRASOUND MEASUREMENT TO CALCULATED RISK ASSESSMENT TOOLS

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Quantitative ultrasound of the os calcis is accepted as an effective, low-cost method to identify women likely to have osteoporosis at the hip or spine as measured by DXA. In this study, we wished to determine the specific T-score cutpoint on the Lunar Achilles InSight (GE Medical Systems) that detects 90% of individuals with osteoporosis (T-score ≤ -2.5) at either the spine or hip. The Achilles InSight is an imaging heel ultrasonometer with 8–10 second measurement time. We also compared the performance of ultrasound screening to a simple risk assessment tool based on weight and age.

A total of 272 women aged 40 to 83 years (mean age 58 ± 7 years) had DXA measurements of the spine and hip using a Lunar DPX (GE Medical Systems) and heel ultrasound measurement using the Achilles InSight. Osteoporosis was diagnosed if the lowest DXA T-score at spine (L1–L4) or hip (total femur) was ≤ 2.5. The heel T-score cutpoint with 90% sensitivity was determined using ROC analysis. For each subject the value of the osteoporosis risk assessment tool, risk tool ((Weight in kg – age)*0.2) was also calculated.

From the DXA results, 54 of 272 patients were classified as osteoporotic. At a heel T-score of −1.0, sensitivity was 91% and specificity was 46%. Based on ROC analysis, the area under the curve (AUC) for the heel T-score was 0.79, which was significantly greater than the AUC for the risk tool, 0.69 ($p < 0.05$).

We conclude that the Achilles bone ultrasonometer can be used as a valid screening tool for osteoporosis, with 90% sensitivity at a T-score of −1.0 and good specificity. Moreover, the Achilles performs significantly better in identifying those patients who should be considered for spine and hip bone density assessment compared to the calculated osteoporosis risk assessment tool.

AUC values, sensitivity and specificity for osteoporosis screening tools

	AUC	90% Sensitivity Cutpoint	Sensitivity	Specificity
Heel T-score	0.79 (0.72–0.85)	−1.0	90.7%	46.3%
Risk Tool	0.69 (0.62–0.77)	2.4	90.7%	28.9%

For the combination of the Heel T-score and Risk Tool the AUC is 0.81 (0.75–0.87).

P153MO. CHANGES IN BONE MINERAL DENSITY IN SUBJECTS WITHOUT OSTEOPOROSIS TREATMENT

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Aim: Evaluate the bone mineral density (BMD) behavior in subjects without osteoporosis treatment, submitted to a new bone scan.

Materials and Methods: A total of 392 women aged above 44 underwent a second lumbar spine and hip bone mineral density measurement between April and November of 2001 by dual energy x-ray absorptiometry (DXA), DPX-L device. None of the subjects received bone protective treatment.

Results: Among the 392 patients, 326 (83.2%) were Caucasian, 52 (13.3%) Mulatto and 14 (3.6%) Asian descent. The mean age was 60.1 ± 9.4 yrs (45–87). Surprisingly, 220 (56.1%) subjects presented osteopenia or osteoporosis at the first bone scan. The BMD was measured at an interval of 33.3 ± 15.8 months. Regarding longitudinal changes in BMD, it was $-1.6 \pm 4.5\%$ in L2–L4 and $-1.4 \pm 4.1\%$ in femoral neck. Significant correlations were observed between BMD and age or measurement interval ($p < 0.001$). No correlations were observed between BMD and race or body mass index.

Conclusion: These results would suggest that the losses of BMD are increased in younger subjects and with longer interval between measurements. Unfortunately, most of patients were not in osteoporosis treatment, besides previous diagnosis of low bone mass.

P154SA. LUMBAR AND FEMORAL BONE MINERAL DENSITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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This study was carried out to determine the bone mineral density (BMD) values of the lumbar spine and femoral neck in ankylosing spondylitis (AS) patients. Eighteen outpatients who fulfilled the modified New York criteria for AS and also 18 healthy controls were consecutively included in the study. BMD of lumbar spine and femoral neck was evaluated by dual energy x-ray absorptiometry (DEXA). Laboratory parameters included erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The demographic variables such as age,-sex-and BMI were similar between patients and controls ($p > 0.05$). The biochemical parameters ESR and CRP were found to be different between the patient and control groups ($p < 0.001$ for both).

BMD values of lumbar and femoral regions in AS patients were 0.98 ± 0.2 g/cm2 and 0.87 ± 0.1 g/cm2. BMD values of lumbar and femoral area in control subjects were 1.02 ± 0.13 g/cm2 and 0.97 ± 0.12 g/cm2. Patients with AS had reduced BMD in their lumbar spine and femoral neck regions ($p < 0.05$, $p < 0.01$ respectively). Femoral measurements exhibited greater severity of reduced BMD than lumbar values when average BMD scores were compared. Consequently, related to the structural possible changes seen in the lumbar area, the lumbar region BMD measurements can be misleading when evaluating the extent of bone mass loss in AS patients. Therefore, alternative sites or the femoral region should be used to evaluate bone mass in AS patients.

P155SA. THE RELATIONSHIP BETWEEN BODY COMPOSITION AND REGIONAL BONE MINERAL DENSITY IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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Objective: This study was performed to investigate whether the body composition parameters and disease characteristics had any effect on bone mineral density (BMD) of regional, total body, lumbar spine and femoral neck in premenopausal women with rheumatoid arthritis (RA).

Material and Methods: 23 premenopausal women with RA who were diagnosed according to the criteria of the American College of Rheumatology and with disease duration of more than 1 year and 31 age and sex-matched healthy controls with right side dominance were recruited. Disease duration, morning stiffness duration, patient's pain evaluation (VAS), assessments of joints (Ritchie articular index) and functional disability (HAQ), erythrocyte

sedimentation rate (ESR) and C reactive protein (CRP) were recorded in RA patients. BMD (arms, legs, L1–L4 lumbar spine, femoral neck and total body) and body composition (lean mass of regional-total body, fat mass of regional-total body and percentage of body fat) were measured by whole-body scanning with dual x-ray absorptiometry (DXA).

Results: BMD values of all body sites were significantly lower in premenopausal women with RA compared with the healthy controls, while body composition determinants were no different between the two groups. However, BMD of arms was correlated with any of regional lean or fat mass, while BMD of legs, femoral neck and total body were affected by lean mass of legs and total body as independent from body weight in RA patients. Only disease duration and HAQ scores were correlated with BMD among the disease characteristics. HAQ scores were inversely correlated with BMD of all body sites, except for lumbar spine and total body. Disease duration was negatively correlated with BMD of lower limbs (legs and femoral neck) and lean mass of legs.

Conclusion: Lean mass of legs and total body may be significant determinants of BMD on the regions of femoral neck, total body and legs. Also, the measuring of regional BMD by DXA may be useful to determine functional disability and risk of morbidity and mortality in premenopausal women with RA.

P156MO. THE EFFECT OF A SHORT DURATION OF LOW INTENSITY EXERCISE ON QUANTITATIVE ULTRASOUND MEASUREMENTS IN HEALTHY YOUNG ADULTS

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The aim of this study was to examine the influence of a short duration of low intensity exercise on bone tissue as measured by calcaneal quantitative ultrasound(QUS).

40 nonathletic young adults (20 men and 20 women, aged 19–30 years) were allocated either to a group who received exercise trainining (walking on a treadmill for 30 minutes three times a week for three months) or to a group who did not. Calcaneal QUS parameters (BUA-in dB/MHz, SOS-in m/s, QUI, and estimated heel BMD in g/cm^2) were measured in all subjects using a gel coupled device at the beginning and after three months. In statistical analyses, before and after values were compared using ''paired t-test''. ''Chi-square analysis'' was used to compare the number of subjects who showed improvement greater than that would be expected from the root-mean-square coefficient of variation (RMSCV) in the exercise and control groups. The short and long-term precision of the measurements were also examined with duplicate measurements.

No significant difference was observed between before and after mean values of QUS indices in either the exercise or the control group.The number of subjects who showed improvement greater than RMSCV % for QUS indices was similar in both groups. The short-term precision of this device was satisfactory, but the long-term precision was poor, enabling us to detect subtle differences which occured during time.

In conclusion, we were not able to show favorable effects of a short duration of low intensity exercise on bone properties as measured by calcaneal QUS. This issue remains to be elucidated by studies including larger size of subjects and/or different duration and/or different intensity of exercise.

P157SA. BONE MINERAL DENSITY AND OSTEOPROTEGERIN (OPG) IN PATIENTS AFFECTED BY THALASSEMIA MAJOR

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Bone disease is an important cause of morbidity in patients affected by Thalassemia Major; it is a multifactor disease: massive bone marrow expansion, delayed puberty, hypogonadotropic hypogonadism, other hormonal disorder (hypothyroidism, hypoparathyroidism, diabetes mellitus), iron overload and deleterious effects of chelant therapy on osteoblasts. OPG is a soluble decoy-receptor, and is produced in different tissues, e.g. bone, skin, liver, stomach, intestine and lung. As a so-called ''decoy receptor'' OPG inhibits the binding of RANK to RANKL (OPG-L, osteoclast differentiation factor, ODF) and thus inhibits the recruitment, proliferation and activation of osteoclasts.

The main aims of this study are to evaluate the bone mineral density in 31 patients affected by Thalassemia Major (12 males and 19 females); age average 24.5 (range 15–38) and the OPG serum concentrations.

Methods and materials: Bone mineral density has been measured by BMD of lumbar spine (L2–L4), femoral neck and distal radius using the ACN Unigamma x-ray Plus. OPG serum concentrations have been determined using the ''sandwich ELISA'' method. In order to examine the level of OPG in serum, we considered 82 healthy subjects, equally divided between male and female, with an average age of 15–38. Correlation between variables has been calculated according to Pearson's method. The differences between the two considered groups have been analysed using Student's test.

Results and conclusions: Analysing the results, we have found this evidence. The two groups could be easily compared as for the age parameter ($t = 1.11$, $p = 0.27$). Bone mineral density loss appears first of all at the distal radius level in all patients tested. In fact distal radius T-score mean is –2.23, and it is significant inferior to the normality limit that is –1 ($t = -7.53$, $p < 0.01$). OPG serum concentrations mean in healthy subjects is 2.45 pmol/l with standard deviation of 0.63, while in patients it is 3.95 with standard deviation of 1.51. The difference between the two groups is significant ($t = -5.39$, $p < 0.001$). We have found a kind of correlation statistically significant between distal radius T-score and OPG serum concentrations.

P158SU. COMPARATIVE EVALUATION OF BONE MINERAL DENSITY MEASURED IN DIFFERENT SITES AND INCIDENCE OF VERTEBRAL FRACTURES

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The aim of this study was to evaluate correlation between bone mineral densities (BMD) measured by dual energy x-ray absorptiometry of bilaterally forearm (DTX-200 Osteometer-Denmark), femoral neck and lumbar vertebral body (L2–L4) using Lunar DPX-L device. We also aimed to examine the frequency of vertebral bone fracture using thoracic and lumbar lateral x-rays.

We were studing 130 patients, 125 female (aged 45–83, 61.9 ± 9.35) and 5 male. All of 125 investigated women were in menopause (ranged from 33–58 years, 47.9 ± 5.04). In investigated group we devided the patients according to the osteoporosis (46.9%), osteopenia (29.23%) and referent values (23.87%). Having used Spearman's test we confirmed highly positive correlation between dominant and nondominant forearm ($n = 128$, $p < 0.0001$), forearm and lumbar spine ($n = 113$, $p < 0.0001$) and spine vs. femoral neck ($n = 30$, $p = 0.01$), but we didn't find correlation between neck and forearm ($n = 45$, $p > 0.05$). In 39 (30%) cases we registered the fractures of thoracic or lumbar spine. The frequency of fractures in the examined sample is biggest in the group with BMD on the level of osteopenia. We found positive correlation between age and fracture ($p < 0.01$).

In the cases with osteoporosis at the forearm we found the osteoporosis at the lumbar spine and osteopenia in the femoral neck, in cases with osteopenia in forearm we found also osteopenia on femoral neck and on spine, but in cases with osteopenia in the neck we registered the cases of osteoprosis on both forearm and spine. More complicated situation we found in cases within referent values (measured on any of the three different measuring points)-because we noticed same possibility of appearance of the cases with lowered BMD on any of the two other measuring spots. (General linear modeling – GLM, Statistica for Windows 6.0)

So it can be concluded that if we get referent values for BMD on one measuring spot, the measuring should be done on, at least, one more spot. And according to the examined sample it seems that measuring of BMD on the level of the forearm and lumbar spine is better prediction of the loss of BMD than BMD measured on the femoral neck.

P159MO. BONE MINERAL DENSITY AND SERUM OSTEOCALCIN ARE REDUCED IN YOUNG ADULTS WITH IDIOPATHIC SHORT STATURE

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Aim: To examine differences in risks of osteoporosis, we measured the bone mineral density (BMD) and the serum osteocalcin in four groups of young adults with different growth patterns as part of the PROGRAM study. The PROGRAM study (PROgramming factors for GRowth And Metabolism) is unique in determining risk profiles for diabetes, cardiovascular disease and osteoporosis in four groups, distinguishing weight and heigth at birth, and weight and height in young adulthood.

Methods: Our four study groups: 1.Small for Gestational Age (SGA;birth length and/or birth weight <-2SDS) with no catch up(current height <-2SDS) 2. SGA with catch up (current height >-2 SDS) 3. Idiopathic Short Stature (ISS;birth length and/or birth weight $>$-2SDS but current height <-2 SDS) 4. control group(birth length and/or birth weight as well as current height >-2sds). Up to now, we completed group 3 and 4. 27 young adults with ISS (13 girls, 14 boys) were included. Our control group consisted of 31 young adults (17 girls, 14 boys). All were healthy Caucasian 18-23 years'old, and born after 37 weeks'of gestation. BMDs(g/cm3)of the lumbar spine (LS) and the total body (TB) were measured using dual energy x-ray absorptiometry. Osteocalcin was measured using radioimmuno-assay.

Results: We found the mean BMD to be significantly lower in girls of group 3 than of girls in group 4 for both the LS and TB ($p=0.005$, $p=0.004$). Boys of group 3 had significantly lower TBMD ($p=0.015$) and serum osteocalcin ($p=0.026$) than boys of group 4. After adjustment for birth length, birth weight, age, BMI, cigarette smoking, alcohol comsumption and sports participation, these differences remained significant.

Conclusions: Our results indicate that girls and boys with ISS have a significant reduction in TB BMD, that girls with ISS have a significant reduction in LS BMD, and that serum osteocalcin is significantly lower in boys with ISS. We suggest that ISS children be carefully monitored in order to start preventive care for osteoporosis at an early age.

P160SA. OSTEOPOROSIS IN VENEZUELAN MEN: QUANTITATIVE ULTRASOUND STUDY

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Objective: Evaluate the osteoporosis frequency in the Venezuelan male population by quantitative calcaneus ultrasound.

Methods: Of a total of 12,965 patients, the bone mass of 213 Venezuelan males in ages between 35 and 83 years was evaluated. The collected data was analyzed by chi square, average, DS and standard error.

Results: Of the 213 evaluated males, 79 had osteopenia (37.1%) and 16 had osteoporosis (7.5%) representing a 44.6% of positive patients in screening. The higher frequency of positive results was obtained in males 55 years old or older.

Conclusions: The peripheral ultrasound is a reliable, fast, low cost and a affordable method for big groups of population. There is not a comparative data of males evaluated with DXA equipment against ultrasound. 44.6% of our patients had positive results, which represents a high frequency and reveals the importance of the evaluation of the male population. A follow up of this group of patients and confirmation by other methods is required.

P161SU. DIAGNOSTIC ABILITY OF THE PERIPHERAL MEASUREMENTS OF BONE DENSITY: ANALYSIS BY ROC CURVES

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Aims: Identify postmenopausal women with osteoporosis in the axial and peripheral skeleton, look for a correlation between the different measured regions and evaluate the diagnostic ability of the peripheral measurements using ROC curves.

Methods: We measured bone density (BD) in 105 postmenopausal women in forearm(FA) with an Osteometer DTX-200 equipment, and simultaneously in lumbar spine (LS) and femoral neck (FN) with a DEXA equipment. We analyzed FA by ROC curves, established the cut-offs and calculated Sensibility, Specificity, Predictive Positive Value(PPV), and Predictive Negative Value(PNV). We considered the measurement in FN as gold standard to diagnosis osteoporosis by WHOs criteria.

Results: Average age 58.6 ± 10.2 years, menopause period 13 ± 7 years, correlation between FA and FN $r=0.46$ ($p<0.05$), correlation between FA and LS $r=0.65$ ($p<005$). Area under curve (AUC) for FA is 0.83 ($SE=0.014$) ($CI=0.80$-0.86). For a cutoff -2.5 in FA: Sensibility 59% (CI 39-76), Specificity 88%.(CI 79–94), PPV 64%.(CI 43–81), and PNV 86%.(CI 76–92).For a cutoff -1 in FA: Sensibility is 76% (CI 65–85), Specificity 78% (CI 59–90), PPV 88% (CI 78–95), and PNV 58% (CI 43–74).

Table 1 Results of Forearm

Cut-offs	Sensibility (CI)	Specificity (CI)	PPV (CI)	PNV (CI)
<-1	76% (65–85)	78% (59–90)	88% (78–95)	58% (43–74)
<-2.5	59% (39–76)	88% (79–94)	64% (43–81)	86% (76–92)

Conclusions: BD measurement in forearm is useful for initial screening of osteoporosis and for identifying patients who require additional investigation with axial DEXA. There is a moderate correlation between FA, LS and FN. Could be no proper to consider DEXA cutoffs for peripheral measurements in all patients with possible osteoporosis.

P162MO. MEASUREMENTS OF BONE CALCIUM THROUGH THE TOTAL BODY DENSITOMETRY

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Objectives: To measure bone calcium through the total body densitometry with normal levels of bone mineral density. To compare the bone calcium results in different levels of bone mineral density (osteopenia and osteoporosis levels).

Methods: We evaluated the total body densitometry at the Catholic University of Brasilia with DEXA Lunar® DPX-IQ during the period from January 2002 to October 2003. The inclusion criteria were: age above 20 years, with no visual evidence of bone breaking, bone deformity or alteration of the bone distribution in the carried bone densitometry. Analysis statistics were made with MSExcel XP®.

Results: We analyzed 300 total body densitometry in men and women from 20–82 years of age (average of 47.4 ± 20.7 years). Based on the World Health Organization criteria (WHO) for the bone density classification (normal, osteopenia and osteoporosis), we used as a base the T-Score. We divided the examinations into three groups: a) Normal, with 212 examinations; b) Osteopenia, with 68 examinations; c) Osteoporosis, with 20 examinations. In each group, we verified the average value of bone calcium, finding the following results: normal, 1084.9 ± 214.4 g of calcium (varying

of 678–1588 g); osteopenia, 720.8 ± 97.0 g of calcium (varying of 528–1012 g); osteoporosis, 594.7 ± 54.4 g of calcium (varying of 529–706 g). Comparing the three groups, we obtained a significant difference between them with $p < 0.001$. In normal group, we verified the value of bone calcium in men and women, with the respective average: 1247.1 and 906.6.

Conclusions: The value of the bone calcium measurements in the results of the total body densitometry is a value not used in the results of the densitometry. We verified the existence of different and significant values when we compared examinations with different levels of bone density. This suggests that this value must be more understood as a form to be used in the evaluations of the bone mineral density.

P163SA. COMPARISON OF BONE MINERAL DENSITY IN CHILRDEN FROM MANY POPULATIONS: A LITERATURE REVIEW

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Aim: To compare bone mineral density data assessed in healthy children from different populations in the aim to evaluate whether or not the substantial differences between children's bone mineralization datasets provided worldwide are present.

Methods: A literature search was performed for papers published during last ten years. 184 papers providing BMD data assessed in healthy children were found. To be eligible for the further analysis papers must to fit to chosen criteria such as: DXA pencil beam device used for total body and lumbar spine measurements, BMD data presented as g/cm^2, Caucasian children aged 4–20 yrs. Finally, 57 papers matched our criteria and BMD datasets were analyzed according to age and gender as well as the origin of DXA devices (Hologic and Lunar). 142 groups of datasets were analyzed using Statistica 5.0 software.

Results: Significant differences in age-, gender and device-matched BMD data were found in 45 of 145 analyzed groups (32%). Only 1 population specific BMD data assessed in healthy children markedly differed from the other datasets in whole analyzed age range. The apparent differences found in 32% of analyzed datasets suggested that the tempo of bone mineralization as well as amount of achieved BMD might be population specific. However, those differences might be also the consequence of different study design (cohort, prospective) as well as various scientific purposes. Moreover, the number of children included into age and sex groups was markedly different, ranging from 1 to 455.

Conclusion: Our results indicated that substantial differences in BMD data are existent at least in some age groups of healthy children. However, those differences might be also the effect of different study purposes and study designs. Therefore, there is substantial need to establish population specific reference BMD data basing on well prepared studies and than unify BMD reference for whole children.

P164SU. ANALYSIS OF ANTHROPOMETRICAL AND MECHANICAL PROPERTIES OF CORTICAL BONE IN FEMUR OF OSTEOPENIC FEMALE RATS

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Aim: Osteoporosis is the progressive fragility of bones, which are more and more induced to suffer fractures. Although it can happen to men and women, it is more common in the second group due to the decreasing of the female hormone, estrogen. Osteoporosis is a "slow-motion" disease, without symptom and it is usually noticed only after a fracture. Once osteoporosis is in the bone, it is necessary to avoid bone lack in order to prevent fractures. The treatment is based on inibitory drugs for bone resorption, which cannot supply what has already been destroyed, it can only help to stop the process. The aim of this study is to evalute the effects of ovariectomy on cortical bones of 29 female rats in different periods of osteopenia.

Methods: Osteopenia caused by ovariectomy was analysed in rats at 3 months of age during six different periods: 5 animals were sacrified 30 days after surgery; and the other animals, every 15 days until 105th day after surgery. The symptoms of osteopenia were evaluated through bending test of the femurs.

Results: The results found were compared using statistical methods: t-Student for body weights and ANOVA and Student-Newmam-Keuls for femur length and weight, cross-sectional area, maximum overload, stiffness and tensile.

Conclusion: Ovarectomy is a factor that does not cause significant alterations in cortical bone of femur in osteopenic rats.

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P165MO. PERFORMANCE OF COMPUTER ASSISTED DENSITOMETRY (CAD) IN SPINE AND FEMUR ANALYSIS: COMPARISON WITH VISUAL ASSESSMENT BY EXPERIENCED DENSITOMETRISTS

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Although DXA systems provide semi-automated analysis of spine and femur bone mineral density (BMD), visual assessment by the user is necessary to a) assure proper acquisition and positioning, b) assure accurate identification of regions of interest (ROI), and c) identify abnormalities that could artificially elevate BMD. Recently, automated software known as Computer Assisted Densitometry (CAD) (GE Medical Systems Lunar) was introduced to identify scans with common acquisition and analysis irregularities. We examined whether CAD agreed with the assessment of experienced DXA users, and whether CAD identified abnormalities missed by visual assessment. A total of 71 spine and 70 femur scans were analyzed, with 67% exhibiting abnormal conditions flagged by CAD. An ISCD-certified team (densitometrist and technologist) evaluated the scans for abnormalities, unaware of the CAD results. The team's blinded assessment was compared to CAD. Scans where CAD and the team disagreed were reviewed to determine if an abnormality was missed by the team. Results showed strong agreement between CAD and visual assessment. Experienced users agreed with CAD assessment in 76% to 86% of spine scans and 63% to 97% of femur scans, prior to knowing the CAD result. Review of scans where disagreement was present, after revealing the CAD recommendations, resulted in an assessment change by the team in 20% to 40% of spine cases, and in 0% to 79% of femur cases. After CAD assessment was known, spine scan agreement increased to 83% to 92%, and femur scan agreement increased to 66% to 97%. One potential source of disagreement is a stricter expectation of the ideal scan by experienced users. We conclude

Agreement (%) between cad and expert evaluation of spine and femur scans

CAD vs. Experts	Blinded to CAD Results	After CAD Results Known
SPINE		
Spine Centered (%)	86	92
Spine Straight (%)	79	83
ROIs Accurate (%)	82	86
No Unusual High Density (%)	80	87
No Unusual T-Score Variation (%)	76	86
No Spine Curvature (%)	83	90
FEMUR		
Shaft/Pelvis Separation (%)	71	94
Shaft Straight (%)	63	66
ROIs Accurate (%)	80	89
Tissue Regions Accurate (%)	97	97
Edges, Point Typing Accurate (%)	86	97
No Unusual High Density (%)	83	83

that use of CAD can 1) provide valuable information for inexperienced users regarding DXA scan quality and 2) assist experienced densitometrists in identifying potentially abnormal scans which might be missed by visual assessment alone.

P166SA. BONE MINERAL DENSITY IN LONG TERM HEMODIALYSIS PATIENTS

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Aims: The purpose of this study was to report the bone mineral density and the hip joint radiographic findings in 18 patients who have been undergoing hemodialysis for 20 or more years.

Methods: Ten male and eight female patients on maintenance hemodialysis treatment for more than 20 years were enrolled in this study from the outpatient clinic of our institution. The mean age was 56 years, and the mean duration of hemodialysis 286 months at the investigation. Bone mineral density was measured at the 1/3 distal radius by dual-energy X-ray absorptiometry. The radiographs of the hip joint were evaluated for the presence of bone cysts and joint space narrowing. Serum levels of total calcium, phosphorus, alkaline phosphatase, intact-parathyroid hormone, and beta-2-microglobulin were measured.

Results: The mean bone mineral density was 0.462 g/cm^2. Bone cysts were found in 12 patients (67%) and joint space narrowing was found in 4 patients (22%). The radiographic abnormalities were frequently bilateral in bone cysts (82%) and joint space narrowing (92%). The mean values of calcium, phosphorus, alkaline phosphatase, intact-parathyroid hormone, and beta-2-microglobulin were 4.4 mEq/L, 6.7 mg/dl, 294.1 IU/L, 12.9 pg/ml, and 39.2 μg/ml, respectively. Beta-2-microglobulin was significantly high, with other values being within normal limits. Hip arthroplasties were performed in 6 patients (33%) suffering from femoral neck fracture associated with bone cysts (4 patients) and joint space narrowing (2 patients). All of 4 femoral neck fracture patients showed marked bone loss (mean 0.371 g/cm^2).

Conclusions: Bone mineral density was markedly decreased in long-term hemodialysis patients. Bone cysts and joint space narrowing were found in the hip joints of 16 of 18 patients (89%). Thus, we concluded that measures should be taken to prevent hip arthropathy in patients undergoing long-term hemodialysis.

P167SU. ACCURACY OF THE HOLOGIC QDR EXPLORER WHOLE BODY DENSITOMETER

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The QDR Explorer is an axial linear scanning fan beam densitometer that supports Whole Body applications. A BMD correlation was performed to compare the Explorer to another Hologic fan beam densitometer, the Discovery, as well as a Hologic pencil beam densitometer, the QDR-4000.

Twenty-three subjects ages 25 to 85 years old were scanned at the spine, hip, forearm and whole body on both the Explorer and Discovery. Linear correlation was done with the intercepts unrestricted and results were highly correlated and reported in the table. Since the intercepts were not statistically significant, the slopes and RMSE results are reported with the intercept restricted to zero. None of the slopes were statistically different from unity. See table for full results.

The same twenty-three subjects were also measured at the spine on the QDR-4000. Linear correlation between the Explorer and the QDR-4000 was similiarly high (r = 0.992). The slope was 0.995 and was not statistically different from unity. The RMSE was 0.025 g/cm^2.

Precision of the Explorer was also measured *in vivo* on fourteen subjects, with triplicate measurments with complete repositioning. The coefficient of variation was found to be 0.80% at the AP spine, 0.86% at the total hip, 0.94% at the forearm, and 0.85% for the whole body BMD and BMC.

Table 1 Linear correlation between the Explorer and Discovery densitometers. N.S. is not significant.

Region	r	Slope ± SEE	Intercept	RMSE
AP Spine	0.993	0.999 ± 0.004	N.S.	0.019
Total Hip	0.996	1.004 ± 0.003	N.S.	0.016
Femoral Neck	0.995	0.993 ± 0.004	N.S.	0.016
Radius + Ulna	0.993	0.998 ± 0.003	N.S.	0.008
Total Body BMD	0.991	1.000 ± 0.003	N.S.	0.016
Total Body BMC	0.998	1.000 ± 0.003	N.S.	31 g

The QDR Explorer measures BMD equivalently to other Hologic fan beam and pencil beam densitometers and has better than 1% precision *in vivo*.

P168MO. COMPARISON OF RIGHT AND LEFT FEMUR MEASUREMENTS WITH DEXA

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Measurement of femur bone density with DXA is the gold standard for assessing hip fracture risk. Recent enhancements to hip densitometry include the ability to automatically measure bone mineral density (BMD) at both the right and left femora in a single scan sequence, without the time consuming repositioning and scan set up. Bilateral femur scans may be useful in cases of femoral BMD asymmetry to detect patients with low BMD and elevated fracture risk that could be missed if only one femur was measured. We measured bilateral femur BMD with the Lunar Prodigy densitometer (GE Medical Systems) in 120 women (mean age 57.5, SD 12.6 years) who presented at an osteoporosis clinic. Paired T-tests were used to identify significant side-to-side differences. World Health Organization (WHO) guidelines were used to indicate osteoporosis and osteopenia. A T-score of < -2.0 was used as the threshold for treatment. Results showed significant side-to-side difference in average BMD at femur neck and trochanter, but not total femur. Left vs. right T-scores differed by more than 0.5 units in 14%, 13%, and 8% of subjects at the neck, trochanter, and total femur, respectively. Diagnoses using WHO guidelines disagreed in 12% and 15% of subjects at neck and total femur, respectively. For all subjects, there was a 96% agreement in treatment decision using the 2.0, T-score threshold. However, of the 18% of subjects with a total femur T-score less than −2.0, 23% were less than −2 at only one femur. Thus, approximately 12% of subjects with low femur T-score would not receive treatment if BMD were measured on only one femur. We conclude that there were significant side-to-side BMD differences at some femur sites. WHO diagnoses would differ in 12% to 15% of subjects if single rather than bilateral femoral BMD was measured.

Right vs. Left	Neck	Trochanter	Total
Mean BMD Difference	0.03 g/cm^2	0.03 g/cm^2	0.03 g/cm^2
Mean T-score Difference	0.3	0.3	0.2
T-score Difference > 0.5	14%	13%	8%
Subjects with R/L Diagnosis Discordance	12%	16%	15%
Subjects with R/L Treatment Discordance	4%	11%	4%

P169SA. OSTEOPOROSIS SCREENING FOR HIGH AND LOW RISK PATIENTS USING HEEL ULTRASOUND

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Heel ultrasound can provide low-cost measurements to identify women likely to have osteoporosis at the hip or spine as measured by DXA. We determined T-score cutpoints for the Achilles bone ultrasonometer to identify women at high and low risk for

osteoporosis. The Lunar Achilles InSight (GE Medical Systems) is an imaging ultrasonometer with 8–10 second measurement time; the complete examination takes 3–5 minutes.

A total of 163 women (mean age 67 ± 12 years) who presented for spine/femur BMD testing were assessed. Each subject had DXA measurements of the spine and both femurs (Lunar Prodigy) and a heel ultrasound measurement (Achilles InSight). Osteoporosis was diagnosed if the lowest DXA T-score at spine (L1–L4) or left or right femur (neck, trochanter or total) was ≤−2.5. Using the binormal fit to the ROC data, InSight T-score cutoffs for a likelihood ratio for a positive test (LR+) ≥ 5 and negative test (LR−) ≤ 0.2 were calculated.

We found 86% of the women with InSight T-score > −1.0 did not have osteoporosis at the spine/hip (negative DXA). The 88% sensitivity for a negative test is statistically not different from the 90% level recommended by the ISCD for referring subjects from peripheral ultrasonometry to central DXA. Also, 83% of the women with an InSight T-score = −1.8 had osteoporosis at the spine or hip. Women with InSight T-Scores ≤ −1.8 are at high risk, and could be considered for treatment and DXA monitoring measurements. Women with InSight T-scores > −1.0 could be considered at low risk and scheduled for retesting in future depending on risk factors. Women with an InSight T-score between −1.8 and −1.0 should be referred for DXA assessment.

DXA Test	InSight T-score	Sensitivity	Specificity	LR+	LR−
Negative	> −1.0	88%	58%	2.1	0.2
Positive	≤ −1.8	58%	89%	5.0	0.5

We conclude that the Achilles InSight can be used as a valid screening tool to select candidates for axial DXA.

P170SU. COMPARISON OF 10-SECOND AND 30-SECOND SCAN MODES ON LUNAR PRODIGY

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Clinicians rely on knowledge of instrument precision to determine whether a measured change in bone mineral density (BMD) indicates a significant change in that patient's BMD. Precision errors result from improper positioning, inconsistent analysis, and short and long-term instability in densitometry equipment. Precision may also be affected by scan mode attributes. Faster scans may exhibit somewhat lower precision due to differences in photon flux or pixel size. In this study, we compared BMD and precision of two scan modes on the Lunar Prodigy (GE Medical Systems).

A total of 60 women aged 50 to 78 years (mean age 59.8; SD 8.5 yrs) were measured at the spine and both femora with the Prodigy. Each subject was measured twice using the standard 30-second scan mode, and twice using the 10-second QuickView mode, with repositioning between each scan. BMD precision was calculated as the root-mean-square coefficient of variation for repeated measurements. Right and left femur values were pooled (n = 120) and paired T-tests assessed significance of BMD differences between the modes.

	Standard		Quick View		r	BMD Difference
	BMD	%CV	BMD	% CV		p
Femur Neck	0.88	1.3	0.89	1.8	0.98	ns
Trochanter	0.74	1.1	0.74	1.4	0.99	ns
Femur Total	0.91	0.7	0.92	1.0	0.99	<0.01
Bilateral Total Femur	0.91	0.5	0.92	0.8	0.99	<0.05
Spine L1-L4	1.13	1.2	1.13	1.3	0.99	ns

Precision for the 10-second mode ranged from 0.8% for bilateral total femur to 1.8% for single femur neck, compared with 0.5% and 1.3% for corresponding precision with standard (30-second) mode. Values for BMD were highly correlated (r > 0.98) between scan modes and differences were not statistically significant, except for total femur, which showed slightly lower (~0.8%) values with the 10-second mode that were not considered clinically significant.

In conclusion, spine precision with the 10-second mode was equivalent to standard mode, and femur precision error was 1% or lower for total femur and only modestly higher than Standard mode at other sites. QuickView BMD results were virtually identical to those measured with Standard mode.

P171MO. EVALUATION OF BONE MINERAL DENSITOMETRY IN POST-MENOPAUSAL WOMEN WITH BACK PAIN

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Objective: Osteoporosis(OP)is the most prevalent metabolic bone disease and important cause of morbidity and mortality in the elderly. Backpain(BP), the most presenting symptom of OP, may be a heralding sign of vertebral fracture. The frequency of occurence of fractures vary widely among patients. To determine the frequecy of bone loss in postmenopausal women with BP in a geographic region in north of iran. This study was designed.

Methods: BMD at spine and hip of postmenopausal patients presented with BP was measured with DXA by Norland scanner. These patients attended at Shahid Beheshti clinic from November 2001 to December 2002. T-score and Z-score at regions of L2–L4 and total hip were evaluated with respect to age and duration of menopause. Patients with history of using hormones, inflammatory arthritis and ovarectomy were excluded from the study.

Results: 111 patients with mean(SD) age of 64(8.4) years and the menopausal duration of 19(17) years were studied. The frequency of osteopenia and OP (T-score of <-1 and -2.5 respectively) were detected in 48%, 27% and 26% < 49% for l2–l4 and hip regions respectively. There were sighnificant differences in the age and the menopausal duration of patients with and without OP [65(11.6), 18.6(11.6) years and 58(13.2)10.4(9) years, $P<0.01$, and <0.001 respectively]. Menopause duration over than 10 years was associated with OP risk of 5.62. Conclusion: In north of Iran the majority of postmenopausal women presenting with BP are osteoporotic and are at increased risk for fracture.

P172SA. PRECISION AND ACCURACY OF THE HOLOGIC DISCOVERY DENSITOMETER

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A BMD correlation and precision study was performed to examine the relationship between the Hologic Discovery and Delphi models. The Discovery is a new densitometer which supports a 10s scan with reduced radiation dose (30%) to the patient.

For the correlation study, BMD at the AP spine and hip of 50 women, age range 28 to 88 years old, was measured using the "Express" 10 second scanning mode on a Discovery and using the "Fast" 30 second scanning mode on a Delphi. Linear regression of the BMD's was performed with the BMD measured with Discovery as the dependent variable. If the intercept was not significantly different than zero at the 95% confidence level, the intercept was restricted to zero.

The two models were very highly linearly correlated and did not have offsets different from zero. See Table.

The precision was measured on Discovery by measuring 30 women, age 41 to 70 years old in triplicate with them getting off from the table after each hip and spine measurement. The precision for this 10 second scan was 1.06% at the AP Spine and 0.93% for the total hip.

Table 1 Linear correlation results. N.S. is not significant.

Region	r	Slope ± SEE	Intercept	RMSE
AP Spine	0.99	1.000 ± 0.003	N.S.	0.021
Total Hip	0.99	0.997 ± 0.004	N.S.	0.022
Femoral Neck	0.98	1.015 ± 0.007	N.S.	0.036

The Discovery's 10 second Express scan mode was found to be precise and highly linearly correlated to the Delphi's 30 second Fast scan. No significant offsets were detected between the two scanners, and slopes were not statistically different from unity for the spine and total hip. Other studies have found similar results when comparing the 30 second Fast scan mode and the 60 second Array scan modes, and when comparing the QDR Delphi to the QDR-4500. Therefore, all of these models and scan modes provide equivalent diagnostic and BMD information, however, the scanning time and radiation dose has been significantly decreased on the Discovery.

P173SU. BONE MINERAL DENSITY AND PREVALENCE OF OSTEOPOROSIS IN A HEALTHY POPULATION OF PHYSICALLY ACTIVE WOMEN OLDER THAN 50 LIVING IN SÃO CAETANO DO SUL CITY, BRAZIL

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Aims: São Caetano do Sul (SCS) is a suburb of Sao Paulo having the highest per capita income of Brazil and has one of the highest life expectancies (78 years). Osteoporosis increases with the aging, phenomenon that occurs also in Brazil. This study aims to assess the prevalence of osteoporosis and to analyze the factors that would influence BMD in a healthy physically active women population older than 50 living in SCS.

Methods: 107 postmenopausal women 50–84 years (68.0 ± 7.2 years) involved in an exercise program participated in this study. Bone mineral density (BMD) (g/cm2) of the lumbar spine (LS), proximal femur (femoral neck, FN), total hip (TH) and trochanter (T), and the body composition were assessed by DEXA. Osteopenia and osteoporosis were defined in according to WHO criterion. The results were expressed as mean ± standard deviation, and linear regression was used to determine the factors would influence BMD. The level of significance was set at $P < 0.05$.

Results: BMD was not evaluated in 3 participants at proximal femur and in 3 at LS due to anatomical limitations. The prevalence of osteopenia and osteoporosis, as expected, was higher at LS (40.4% and 26.0%, respectively). While 6 (5.7%) women had osteoporosis at FN, only 3 (2.9%) had it at TH and 4 (3.8%) at T. No one with normal BMD at LS had osteoporosis at FN or T, but 1 at TH. Out of 6 women with osteoporosis at FN, 3 had osteopenia, and the other 3 osteoporosis at LS. There was a significant correlation of LS BMD with weight and height, but not with age, lean mass index (LMI) or body mass index (BMI). Weight, BMI, age and LMI significantly correlated with BMD at all sites from proximal femur.

Conclusions: Osteoporosis in at least one of the investigated sites was detected in 30% of the physically active women older than 50 living in SCS. FN showed to be more sensitive to diagnosis osteoporosis at proximal femur than TH. If we had used BMD at TH only, we would miss the half of the patients with osteoporosis at FN.

P174MO. THE LIFESTYLE FACTORS IN POSTMENOPAUSAL WOMEN AND QUANTITATIVE ULTRASOUND VALUES OF CALCANEUS

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Aum: From the viewpoint of preventive medicine, we hope to find a convenient, accurate tool by which to screen communities based bone mass for high risk groups of osteoporosis or osteopenia in developing countries such as Brazil. Calcaneal QUS system was selected because it is simple, safe, low cost. The purpose of this study was evaluate the correlation between quantitative ultrasound values of calcaneus and lifestyle factors in postmenopausal women.

Materials and methods: Samples were obtained from subjects included in the Genesis Program, composed of 108 postmenopausal women from Gravatai City, aged 56–79 years. The subjects were divided into two groups (G1: below −2.0 T-score and G2: above −2.0 T-score). They were interviewed about smoking, physical activity, calcium intake, nutritional screening initiative, age of menopause, body mass index, hormone replacement therapy. The measure QUS was obtained in right foot with the Achilles Express by Lunar Corp.

Results: In G1 was allocated 28 subjects and 81 in G2. Mean age G1: 68.8 (± 5.03) and G2: 66.7(± 5.43) years. The mean of T score of G1 was −2.46 (± std 0.45) and G2, −0.66 (± 1.03); mean BMI was 29.07 (± 4.93) in G1 and G2 29.87 (± 4.58); mean menopause age, 44.7 (± 7.2) in G1 and G2, 48.9 (± 4.3); calcium intake in G1, 545.6 mg/d (± 219.5) and G2 was 769.1 mg/d (± 100.8); In the group G1 only 13.8% subjects realized regular physical activity, while in G2 17.6% realized it. Variables with differences between two groups: menopause age ($p = 0.01$), calcium intake ($p = 0.05$) and physical activity ($p = 0.03$). The another variables, smoking, hormone replacement and BMI dont have differences between two groups.

Conclusion: Our results suggest that women that realized regular physical activity and have higher calcium intake and late menopause age, showed increase calcaneal ultrasound values. However, studies with greater sample will be implemented to confirm these results, and this technical screening can serve to reinforce the indication for bone densitometry in this kind of population.

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P175SA. THE DIFFERENCE OF BONE MINERAL DENSITY BETWEEN BOTH HIPS INFLUENCES THE WHO CLASSIFICATION

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Aims: Some articles have shown a good correlation between the BMD of both hips. However a significant number of women have difference between sides. We wanted to know if this difference could alter the WHO classification.

Methods: We prospectively studie the BMD of both hips (Lunar Prodigy) of 115 postmenopausal women. The presence of scoliosis and previous treatments were exclusion criteria. They were classified in Normal(n), osteopenia(op) or Osteoporosis(OP) in both sides. We report the difference in % and T-Score, in Femoral neck(FN), Ward(W), Trochanter(Troch), and Total Hip(TH). We study the group as a whole and divided in tertils of age and weight.

Results:

Age: 60.2 (SD: 9.8) years. Menop: 48.6(4.5) years. Weight: 67.9 (13) kg.

- Difference mean: FN:4.1% (4.1SD), W:4.3% (4.4), Troch:4.7% (3.9), TH:3.0% (2.8)
- Correlation between sides: FN:0.88, W:0.90, Troch:0.92, Shaft:0.95, TH:0.95
- % patients with difference between sides:

in FN > 5% in 22% of the women and > 0.5 SD in 15%
in TH > 5% in 16% of the women and > 0.5 SD in 9.6%

In FN 83.5% of the women have concordance between both sides (n-n, op-op or OP-OP) and 16.5% have discordance (n-op in 12.2% and op-OP in 4.3%)

In TH 85.2% of the women have concordance between both sides (n-n, op-op or OP-OP) and 14.8% have discordance (n-op in 10.4% and op-OP in 4.4%)

In older women (> 60 years) discordance were present in 28% of 47 women in FN, and in 15% in TH.

Dividing them into tertiles, heavier (> 71 kg) and older (> 60 years) women have more difference between both sides in Troch and TH.

In multivariate analysis the difference between both Troch and between both TH increases when weight and age increases.

Conclusion: Although the correlation between both hips is high, a significant number of patients without scoliosis have difference between sides and nearly 15–16% is classified in a different way if we choose only one side. Bilateral DXA measurements are recommended, especially in older and heavier patients.

P176SU. OSTEOPOROSIS IN TURKISH HIV/AIDS PATIENTS: COMPARATIVE ANALYSIS BY DUAL ENERGY X-RAY ABSORPTIOMETRY AND DIGITAL X-RAY RADIOGRAMMETRY

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Aims: Recently, the concept of osteoporosis has gained an intriguing concern among the physicians treating AIDS patients. With its yet uncovered exact etiology, many factors are assumed to play a role in the pathogenesis. This study was run to assess the bone mineral density measurements (BMD) of our HIV/AIDS patients using two methodologies: dual energy x-ray absorptiometry (DXA) and digital x-ray radiogrammetry (DXR) – a relatively new, convenient and less expensive method.

Methods: The study comprised 27 AIDS patients (15 male, 12 female) who were recruited from our infectious diseases department among those under routine follow up. Bone mineral density measurements using DXA (HOLOGIC QDR-4500) were performed from lumbar spine, femur and distal radius. DXR evaluations were done by Pronosco X-posure system using the x-ray graphies of the patients' nondominant hands. The patients were diagnosed to have osteopenia (T score between –2.5 and –1) and osteoporosis (T score < –2.5) according to the DXA measurements. Estimated BMD, metacarpal index, cortical thickness and bone width parameters were recorded by DXR evaluations. The statistical analysis were carried out using SPSS (Statistical Package for Social Sciences)10 for windows.

Results: The ages of the patients ranged between 21–62 years (39.48 ± 12.47). The disease duration ranged between 0–2846 days (869.66 ± 743.59). Their antiretroviral treatment protocols included 2 nucleoside analogues and 1 protease inhibitor ($n = 23$) or 2 nucleoside analogues with 1 non-nucleoside analogue ($n = 2$) and 2 patients were not receiving any treatment. Nine patients were found to have osteoporosis, 14 osteopenia and 4 were normal. Estimated BMD results of DXR evaluations were significantly correlated with lumbar, femoral and radial DXA measurements (all $p < 0.05$ and $0.54 < r < 0.66$).

Conclusions: Overall, we imply that digital x-ray radiogrammetry (DXR), being a convenient and less expensive technique, can well be used during the follow up of HIV/AIDS patients' bone mineral density evaluations. This way we believe that our patients might become more compliant in their follow up that is actually full of a surplus of diagnostic investigations.

P177MO. QUANTIFICATION OF BONE MINERAL DENSITY OF THE HAND IN WOMEN

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Objectives: To determine the bone mineral density in the hand of young women.

Methods: We evaluated the results of hand densitometry studies at the Catholic University of Brasilia with DEXA Lunar® DPX-IQ during the period from October 2002 to May 2003. Inclusion criteria included: feminine gender, age between 20–35 years, and no black racial characteristics. The exclusion was due to the presence of reduction of bone mineral density in the femoral neck, Wards or total femur observed by densitometry of the proximal femur. Analysis statistics were done with MSExcel XP®.

Results: We analyzed 50 results of hand densitometry in women from 20–35 years of age (mean = 22.10 ± 3.35 years). Hand densitometry values were evaluated for women who presented normal values in proximal femur densitometry in the femoral neck, Wards, or total femur according to criteria of the World Health Organization (WHO) based on T-score and within the range of Z-score. 42 examinations with normal values of proximal femur densitometry in relation to young adults (T-score) and age-matched (Z-score) were verified. The results of the bone mineral density of the hand presented an average of 0.407 g/cm^2 with a standard deviation of 0.030 g/cm^2.

Conclusions: Bone mineral density of the hand is a non-standard aspect of bone densitometry; therefore, if it is found to be relevant, research must be done to standardization because in the literature of rheumatic diseases there exist reports of a reduction of bone mineral density of the hand that precedes alterations of lumbar spine densitometry and proximal femur densitometry.

P178SA. MARKED IMPROVEMENT IN BONE MASS AFTER PARATHYROIDECTOMY IN SEVERE HYPERPARATHYROIDISM SECONDARY TO END-STAGE RENAL DISEASE: CASE REPORT

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Background: Hyperparathyroidism is a common complication of end-stage renal insufficiency and lead to severe osteoporosis. Several reports show marked improvement in bone mass after successful parathyroidectomy (PTX) in primary hyperparathyroidism, ranging from 5–10% in the first year.

Aim: To evaluate the postoperative effects of parathyroidectomy in bone density in a patient with hyperparathyroidism secondary to end-stage renal disease.

Methods: We report the case of a 22-year-old white woman with end-stage renal disease, on maintenance haemodialysis for nine years, that developed severe and symptomatic secondary hyperparathyroidism (HPT2). She presented with bone pain refractory to medical treatment that caused immobilization, pathologic fracture of the right arm, blood vessels and soft-tissue calcifications, bone deformities, serum intact parathyroid hormone (PTH) higher than 10 times the upper limit of normality (3300; normal, 7–53 pg/ml) and maxillary brown tumor that caused local destruction and discomfort. Severe osteitis fibrosa cystica was detected in skeletal radiographs. Total parathyroidectomy was successfully performed, and serum PTH level fell to 44.8 pg/ml. Whole body mineral density was evaluated using dual x-ray absorptiometry (DXA) before and one year after PTX. Both exams were performed in the same densitometer, Lunar Corporation.

Results: In few months after total parathyroidectomy bone pain disappeared enabling her to walk again and the brown tumor gradually diminished. Total body BMD increased 23%, from 0.767 to 0.945 g/cm^2, corresponding to a change in Z-score from −4.5 to −2.4. Arms BMD increased 21%, from 0.544 to 0.657 g/cm^2, corresponding to a change in Z-score from −4.0 to −2.7. Legs BMD showed a 23.5% increase, from 0.493 to 0.609 g/cm^2, corresponding to a change in Z-score from −7.4 to −6.2. Trunk BMD increased 22.5%, from 0.767 to 0.945 g/cm^2, corresponding to a change in Z-score from −3.0 to −1.1. Total bone calcium increased from 441 to 648 g.

Conclusion: The case reported here illustrates the postoperative benefits in severe secondary hyperparathyroidism, including the rapid and marked improvement in bone density and deformities. Skeletal sites where cortical bone predominates were mostly affected, but the percentual increase in bone density was similar in all sites.

P179SU. NORMAL VALUES OF VERTEBRAL HEIGHTS IN A REPRESENTATIVE POPULATION SURVEY IN HUNGARY

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Aims: The authors' aim was to derive Hungarian normal vertebral heights, height ratios and threshold values.

Methods: The mean -3 SD of these ratios give them the threshold values for defining normal vertebrae. They examined the standardized vertebral morphometric measurements obtained in a cross-sectional population survey. Radiographs were taken according to standardized protocol and morphomeric measurements of anterior, central and posterior heights from thoracic 4 to lumbar 4 were made with a semiautomatic technique. The anterior, central, posterior I and posterior II height ratios were calculated for each vertebra. The mean and standard deviation of these ratios for each sex were derived using a statistical procedure to normalize the distribution. From the normally distributed vertebral height ratios the mean and standard deviation give us the threshold values for defining normal vertebraes. Anterior and central vertebral height ratios were smaller in males than females. The authors compared the ratios and threshold values in different European centers using the same method.

Results: The data confirm that vertebral height ratios vary between and within populations and the authors suggest that normal values for vertebral height ratios should be derived separately for males and females at each vertebral level. Having the normal values the knowledge of the Hungarian normal vertebral height ratios gives the possibility to carry on multicentre clinical, therapeutic and epidemiologic studies of vertebral deformity in Hungary.

Conclusions: The authors suggest the widespread use of morphometry to evaluate vertebral osteoporosis because it can be done in every radiology unit, it is a cheap and easy method for measuring the bone mineral content.

P180MO. THE EFFECT OF OSTEOPOROSIS RISK FACTORS ON QUANTITATIVE ULTRASOUND MEASUREMENTS AT RADIUS

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Osteoporosis is a disease that culminates with fragility fractures and therefore, imposes a major burden on health economy. In dealing with this worldwide condition, it is prudent to use a reliable, inexpensive, portable diagnostic means that does not use ionizing radiation and is capable of measuring bone properties at several sites. Quantitative ultrasound (QUS) techniques have been shown to be as good as bone mineral density (BMD) assessed by dual-energy x-ray. QUS technique at radius could increase substantially the accessibility to a reliable bone osteoporosis risk evaluation, but little is known regarding the relationship of QUS to risk factors that have been found to predict DXA-BMD values.

The aim of the study was to evaluate the relationship between the most relevant risk factors for osteoporosis and speed of sound (SoS) measurements at radius. We report the reference database for speed of sound (SoS) at the radius with Sunlight Omnisence 7000S.

We studied 87 postmenopausal women between 40–77 years of age with a mean age of 52.7 ± 0.17. All participants were questioned on lifestyle habits and on their medical history. After a physical examination SoS was measured by Omnisence distal third of the radius.

The SoS at radius was significantly related with T radius ($p \leq 0.01$) and, body mass index ($p \leq 0.01$) and, reduced body height ($p \leq 0.05$) and, dairy calcium intake and, tea consumption were significantly related with SoS at radius ($p \leq 0.05$). The age at menopause and, the duration of menopause were negatively correlated with SoS ($p \leq 0.05$). Daily coffee intake and smoking, the time spent outdoors exercising had no effect on SoS.

In conclusion, the most of the risk factors for osteoporosis are associated with SoS. It should be pointed out that the SoS value is predictive method in detecting patients with osteoporosis. Prospective studies are needed to support the role of Omnisence in assessing the risk factors of osteoporosis.

P181SA. CORRELATION BETWEEN THE AMOUNT OF BLEEDING AND BONE MINERAL DENSITY IN PATIENTS UNDERGOING TOTAL HIP ARTHROPLASTY

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Aims: Evaluation of correlation between amount of bleeding and bone mineral density (BMD) in patients undergoing total hip arthroplasty.

Methods: In group of 48 patients, prior to procedure of total hip replacement we performed BMD test of the neck of femur and vertebral bodies. We monitored postoperative bleeding.

Results: Mean bone density in the neck of femur amounted −0.41.Both superficial and deep draining systems within 12, 24 h after operation and later presented blood loss increase related to the growth of BMD score.Mean BMD score in the area of Ward's triangle of the neck of femur was −0.84.Postoperative bleeding increases together with the growth of BMD in Ward's triangle.Mean value of BMD around the area of greater trochanter was −;0.12.We have not ascertained the influence of BMD score in greater trochanter on the amount of postoperative bleeding. Mean value of BMD for neck of femur was −0.33.The increase of postoperative blood loss is related to the growth of mean BMD values for the neck of femur.The increased mean BMD value for the neck of femur implicated more abundant bleeding at 12th and 24th h period as well as greater total amount of blood loss after surgery.Mean value of BMD for the neck of femur was 1.18.We have observed the tendency to increased bleeding relative to growth of BMD around the proximal femur.Total drainage amount in the first 24 h after operation was greatest in patients with normal spinal BMD score, and smallest in operated osteoporotic patients.As BMD score decreases according to a patient's age, we attempted to evaluate amount of bleeding in relation to that factor. Blood loss in elderly patients is smaller than in operated patients of younger age.

Conclusions: Smaller postoperative bleeding occured at the downfall of BMD. Blood loss in the period of the first 24 h after operation was most intense in patients with normal values of BMD compared to patients with decreased level of BMD. The age of operated patients does not have an effect on postoperative drainage amount significantly. BMD test should be considered as one of the prognostic factors of the amount of postoperative blood loss.

P182SU. DXA AND QUS CAN COMPARABLY DISCRIMINATE PATIENTS WITH OSTEOPOROTIC HIP FRACTURE FROM MATCHED CONTROLS

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Introduction: The aim of this pilot study was to evaluate the ability to discriminate patients with hip fracture from healthy controls using DXA and QUS in postmenopausal women.

Material and Methods: We included 22 patients mean age 76.5 ± 5.4 years with an incident osteoporotic hip fracture and 22 age and BMI matched controls. Women in the control group with a history of osteoporosis or with a fracture or diseases or treatments known to affect bone metabolism were excluded from the study. BMD was measured by DXA (Prodigy, GE/Lunar) at the spine and hip. QUS was performed at the os calcaneus using the Achilles+ device as well as the Insight device (GE/Lunar).

Results: DXA results of women with hip fractures at the femoral neck showed statistically significant lower T-score of −2.6 and Z-score of −0.8 compared to T-score of −1.7 and a Z-score of 0.1 in healthy controls ($p \leq 0.008$ and $p \leq 0.01$). In women with hip fracture, DXA results of the spine (L1–L4) showed a T-score of −2.1 and a Z-score of −0.3, compared to age and BMI matched

controls who showed a T-score of −1.4 (L1-L4) and a Z-score of 0.3 (L1–L4) (difference not significant). In accordance to QUS results, measurement at the os calcaneus (Achilles + and Insight) also showed significant differences between the groups. The T-score was −3.3 and −2.6 in women with hip fracture compared to a T-score of −2.3 and −1.6 ($p \leq 0.01$) in controls. The Z-score was −0.9 and −0.3 in women with hip fracture compared to 0.1 and 0.8 ($p \leq 0.01$ and $p \leq 0.005$) in controls.

Conclusion : The results of our pilot study confirm the capability of DXA and QUS devices to discriminate patients with prevalent hip fracture from healthy controls. This significant difference could be observed by DXA at the hip and both QUS devices measuring at the os calcaneus but not for DXA of the spine. Further large scale longitudinal studies are needed to evaluate the diagnostical capabilities of DXA and QUS.

P183MO. IS THERE A SIGNIFICANT DIFFERENCE BETWEEN BONE MINERAL DENSITY OF MAJOR DEPRESSIVE PATIENTS AND NORMAL SUBJECTS?

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Aims: Osteoporosis is one of the important diseases of metabolic bone diseases and is characterized by a decrease in bone mineral density (BMD) which results in an increase in bone fracture. Its etiology is still unknown. Depression is associated with alteration in behavior and hypothalamic dysfunction that are risk factors for decreased BMD. Some studies demonstrated that major depression was associated with marked osteoporosis. Hypercortisolism is a frequent finding in depressed patients and cause bone loss.

Methods: We measured BMD at lumbar vertebrae and femur neck in 39 patients (19 males and 20 females) with major depression and 23 normal subjects (11 males and 12 females) matched for age and gender. BMD was measured by dual energy x-ray absorptiometry (DEXA). The patients with the diseases or risk factors may cause osteoporosis were excluded from the study.

Results: There was not a statistically significant difference between the ages of the groups (mean age 36.07 ± 7.41, age range 18–45 years in depression group; mean age 33.73 ± 7.16, age range 20–45 years in control group). There was not also significant difference according to gender distribution with Chi-square test. The lumbar and femoral neck BMDs were 0.96 ± 1.26 g/cm^2 and 0.85 ± 0.20 g/cm^2 in depression group and 0.99 ± 0.09 and 0.82 ± 0.12 g/cm^2 in control groups. We did not find statistically significant difference between the values of BMDs and t-scores of lumbar vertebra and femoral neck in depression and control groups ($p < 0.05$).

Conclusion: Although we and also some other studies did not find a correlation between depression and osteoporosis, many studies demonstrated that major depression is a risk factor for bone loss. However it can be explained by some neuroendocrin mechanism, and there are still unknown mechanisms. Further studies including more patients, more parameters and longer observations are needed.

P184SA. PERFORMANCE EVALUATION OF A COMPACT DXA SYSTEM: THE LUNAR BRAVO

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The Lunar Bravo (GE Medical Systems) is a small footprint spine/hip DXA scanner designed for offices with limited space. The Bravo scanner arm swings to the side for easy patient access and positioning. It includes several features designed for simplified scan acquisition and analysis. These include a combined spine and dual femur measurement in a single exam without patient repositioning, and analysis software that automatically identifies scans with potential irregularities. We compared the performance of the Bravo with a full-size table bone densitometer.

Twenty-six women (average age 55 ± 10 years) had spine and dual femur measurements on Bravo and on the Lunar Prodigy (GE Medical Systems). Each subject was measured 3 times on Bravo and on Prodigy using standard patient positioning (legs-elevated for the spine scan, dual femur positioner for the femur). Subjects were repositioned between scans. BMD results were determined using manufacturer-recommended analysis protocols. Precision error was calculated as the RMS standard deviation for the repeat measurements (%CV). Bravo spine and hip BMD values were compared to Prodigy values using a two-tailed, paired t-test based on the first measurement obtained from each densitometer.

Bravo precision error was slightly higher than with the Prodigy but consistent with published values for other fan-beam DXA systems. Bravo and Prodigy spine BMD values and femur neck BMD values were highly correlated ($r = 0.98$ and 0.99 respectively) and not significantly different. There were small but significant differences (~2%) in Bravo and Prodigy trochanter and total femur BMD values. We conclude that the Bravo provides accurate and precise spine and hip DXA measurements, consistent with results from other bone densitometers, making it a valuable alternative for practices with space limitations.

Table 1

	L1-L4 Spine	Femur Neck	Femur Troch	Total Femur	Dual Total Femur
Bravo Precision (%CV)	1.5%	1.7%	1.4%	0.9%	0.6%
Prodigy Precision (%CV)	1.1%	1.1%	1.1%	0.8%	0.5%
Bravo BMD (g/cm^2)	1.091	0.868	0.740	0.925	0.926
Prodigy BMD (g/cm^2)	1.096	0.865	0.753	0.943	0.943

P185SU. BONE MINERAL DENSITY IN CHRONIC AUTOIMMUNE THYROIDITIS AND CALCITONIN DEFICIENCY

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We evaluated bone mineral density (BMD) in euthyroid patients on l-thyroxine replacement therapy presenting Chronic Autoimmune Thyroiditis (CAT) and calcitonin (CT) deficiency. Conjugated estrogens were given when they entered the climacteric period. Four groups were studied: Group 1, composed by 9 normal women, median age 32 years (23–53), median BMI 24.0 kg/m^2 (21.4–31.3), matched to a CAT diffuse goiter group (DGG); Group 2 constituted of 12 normal women, median age 47 years (31–55), median BMI 26.9 kg/m^2 (20.9–32.7), matched to a CAT group presenting the atrophic form (AFG). The DGG and AFG groups were composed by 9 and 12 women, with ages between 22–53 years (median: 32) and 32–55 years (median: 47.5), and median BMI 25.0 (19.1–30.9) and 26.1 kg/m2 (20.4–34.1), respectively. BMD was evaluated at lumbar spine (L1–L4) and standardized femoral sites by a HOLOGIC QDR 1000 PLUS densitometer: T-score between −1 and −2.5 SD was indicative of osteopenia, and > 2.5 SD negative was indicative of osteoporosis. Serum measures of biochemical markers of bone formation, osteocalcin (OC) and bone alkaline phosphatase (BAP), and bone resorption in the urine, deoxypyridinoline (DPD), were also obtained, as well as the daily calcium intake. Statistical analysis was performed by: analysis of variance, to compare BMD and T-score between groups; the Kruska Wallis test, to compare the results of OC, BAP and DPD between groups; correlations by Spearman test, to study the relationship between BMD and CT measurement before and after the secretagogues infusion (calcium and pentagastrin), and Chi-square test, to compare the frequency of osteopenia and osteoporosis between controls and affected. BMD of patients suffering from CAT and CT deficiency did not differ from the controls ($p = 0.137$), however T-score

demonstrated larger prevalence of osteopenia and osteoporosis ($p < 0.05$) in the affected group mainly in lumbar spine. There was no correlation between CT and BMD or T-score ($p > 0.05$), but CT deficiency seems to play a role regarding osteopenia and osteoporosis events, especially when associated with estrogen deficiency. Biochemical markers of bone formation and resorption didn't demonstrate acceleration of bone remodeling cycle.

P186MO. BONE MINERAL DENSITY AND HORMONAL CHANGES IN THE PATIENTS MAJOR DEPRESSION: A PRELIMINARY REPORT

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Aims: Osteoporosis is characterized by decreased bone mineral density (BMD). Decreased BMD has recently been reported in patients suffering from several mental disorders, including schizophrenia and major depression. Endocrine factors such as depression-induced hypersecretion of corticotropin-releasing hormone and hypercortisolism, hypogonadism, growth hormone deficiency and increased concentration of circulating interleukin 6, might play a crucial role in the bone loss observed in subjects suffering from major depression.

Accelerated decrease in BMD can be attributed to also drug-induced decreases in levels of estrogen and testosterone, and to hyperprolactinemia and hypercortisolemia. We aimed to measure and correlate BMD and the level of some hormones such as prolactin, growth hormone (GH) and leptin in the patients with major depression.

Methods: We included patients with major depression in the study to measure BMD, body mass index (BMI), the levels of prolactin, GH and leptin. Patients having other risk factors or diseases for osteoporosis were not included. BMD was measured at lumbar spine and hip. The results from ten patients with major depression are presented.

Results: The results of ten patients (8 males, 2 females) were evaluated and correlated with each other. The mean age: 41.40 ± 9.85 (25–55) years, BMI 26.61 ± 4.04 (20.82–32.88) kg/m^2, BMD at lumbar spine 0.91 ± 0.14 (0.74–1.16) g/cm^2, GH: 0.88 ± 1.69 (0.04–5.29) mU/L, prolactin: 15.10 ± 11.75 (3.21–30.84) mU/L, leptin: 10.80 ± 10.27 (0.78–32.54) ng/ml were found. There was a positive correlation between age and BMI, GH level and lumbar BMD. We found also negative correlation between age and BMD, age and GH. There was no significant correlation between the other parameters.

Conclusions: Because correlation in BMD and GH-prolactin levels is well known, the decrease in BMD in depressive patients can be explained with hormonal alterations in depression. Further studies are needed to investigate the presence of osteoporosis and its mechanism in depressive patients.

P187SA. ULTRASOUND DENSITOMETRY PARAMETERS OF UKRAINIAN WOMEN IN POSTMENOPAUSAL PERIOD: NORMATIVE DATA

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In order to create a normative database for ultrasound densitometry parameters 302 healthy postmenopausal women were examined. The following methods were used: ultrasound densitometry, height and weight determination. Ultrasound characteristics of structural-functional bone state depending on age and duration of postmenopausal period were presented for Ukrainian women (Table 1). It was found out that the ultrasound parameters characterizing state of spongy bone tissue and its density decrease after 45 years old. A most loss of bone mass in Ukrainian women from data of ultrasound densitometry was observed during first period (from 1 to 2–3 years) after menopause. The SOS accordingly decrease on 0.9%, BUA – on 3.5%; Stiffness – on 7.2%. The temp of bone loss gradually decreased to 12 years postmenopausal period. For period from one to 12 years observed the SOS index lowering is on 2.2%, BUA – on 5.0% and to Stiffness – on 13.9%. In further statistically dynamics in SOS, BUA and Stiffness dependency on duration postmenopausal period (from 12 to 21 years) was not founded.

Table 1 Data of ultrasound densitometry of postmenopausal women.

Data	All group	45–49 years	50–54 years	55–59 years	60–64 years	65–70 years
SOS, m/s	1541.3 ± 29.1**a**	1547.5 ± 27.0**a**	1554.3 ± 30.0**a**	1544.4 ± 29.3**a,b**	1534.7 ± 22.2**a,b,c**	1520.5 ± 28.5**a,b,c**
BUA, dB/MG	106.5 ± 11.0**a**	107.6 ± 10.8**a**	110.5 ± 10.4**a**	106.9 ± 10.1**a,b**	104.9 ± 10.5**a,b,c**	101.1 ± 13.0**a,b,c**
Stiffness, %	82.6 ± 13.7**a**	84.9 ± 12.8**a**	88.7 ± 14.0**a**	83.8 ± 12.8**a,b**	76.9 ± 11.1**a,b,c**	73.2 ± 14.8**a,b,c**

Notes: $p < 0.05$ (**à**– compared with women aged 40–44 years in premenopausal period, **â**- compared with women aged 50–54 years in postmenopausal period, **c**- compared with women aged 55–59 years in postmenopausal period).

P188SU. BONE MINERAL DENSITY AND VERTEBRAL FRACTURES

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Aim: Analyze the results of bone mineral density (BMD) from 48 patients that evolved with new vertebral fractures in region of interest (L1 to L4).

Materials and Methods: We reviewed the archived exams since 1994 that showed densitometric fracture characteristics: a significant increase of BMD of one or more vertebrae and height reduction. We evaluated BMD of lumbar spine and femoral neck before and after the fractures, by dual-energy x-ray absorptiometry, DPX-L device. Some radiographies were obtained to confirm fracture.

Results: We studied 48 patients (44 women, 4 men), ages 46 to 88 years. Among them, 42 (87.5%) were Caucasian and 6 (12.5%) were Asian descents. BMD was measured at an interval of 22.0 ± 10.6 months. Nine patients had more than one vertebral fracture. The most fractured vertebra was L1 (28 in 59 fractures, $p < 0.007$). Initial mean BMD was 0.794 ± 0.17 g/cm^2 in lumbar spine before fracture and increased to 0.878 ± 0.17 g/cm^2 ($p < 0.001$). Femoral neck BMD evolved from 0.673 ± 0.13 g/cm^2 to 0.660 ± 0.13 g/cm^2 ($p < 0.05$). Initial mean T score was -3.25 ± 1.4 SD in lumbar spine and -2.64 ± 1.2 SD in femoral neck. Regarding longitudinal changes in BMD, it was $12.12 \pm 12.2\%$ ($p < 0.001$) in L1–L4 and $-1.12 \pm 5.4\%$ ($p < 0.005$) in femoral neck. Most of patients (72.9%) had initial T score less than −2.5 SD.

Conclusion: We concluded that low BMD in the past was a good prediction of fractures. It was well established that thoracolumbar transition is positively correlated with fractures, with L1 being the most affected vertebra. Femoral neck measurement can represent a better parameter for follow up in these patients.

P189MO. BONE TURNOVER & BONE MASS IN HIGH–RISK NEONATES

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Hundred newborns were chosen to determine the level of osteocalcin (reflecting osteoblastic activity) to denote the state of bone formation and BMC, to denote state of bone mass and correlate them with different health parameters. According to their gestational age and weights, they were classified into 4 groups: 20 normal control infants (PGA), 20 large for gestational age (LGA), 20 small for gestational age(SGA), and 40 preterm infants. Serum osteocalcin (denoting osteoblastic activity) levels were reduced in group II (LGA) and group III (SGA), and markedly reduced in prematures ($P < 0.001$); i.e. osteoblastic activity (bone formation) are reduced in LGA and SGA, and markedly reduced in prematures. T-scores were parallel and compatible to osteocalcin levels, whereas T-scores were reduced in LGA and SGA, and markedly reduced in prematures ($P < 0.001$).

P190SA. BONE DENSITOMETRY AND RADIOLOGIC IMAGES IN LUMBAR AND FEMORAL AFFECTIONS

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Aim: Illustrative cases of diseases affecting lumbar and femoral regions, with radiographic correlations, were presented.

Materials and Methods: Bone scans were selected from Bone Densitometry Division of HSPE, by using dual x-ray absorptiometry (DXA), DPX-L device.

Results: Some different diseases were presented, including osteoarthritis, scoliosis, vertebral and femoral fractures, laminectomy, ankylosing spondylitis, Paget's disease, bone tumors, lithiasis, and several forms of abdominal calcifications. All cases were correlated with radiographies or computed tomography scans.

Conclusion: It was considered that DXA scan images cannot replace radiographs. There is, however, much information in these images which can aid the correct interpretation of bone mineral density results.

P191SU. CASE REPORT OF HUNGRY BONE SYNDROME AFTER ABLATION OF THE PARATHYROID INTRATHYMIC ADENOMA WITH SEVERAL BONE AND RENAL DISEASE

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A boy 16 years old with normal pubertal and growth development, presented hyperparathyroidism due to a parathyroid intrathymic adenoma.

He had nephrolithiasis at pyelocaliceal and ureteral stones, it was promoting partial urinary obstruction tract and hydronephrosis.

He presented osteitis fibrosa cystica too, and great reduction in bone mineral density at trabecular bone (BMD IN SPINE = 0.699 g/cm^2).

Previously 13 years old he had slipped capital femoral epiphysis, which was treated with pinning in situ, it was impossible to determine BMD at cortical bone in HIP.

Endocrine investigation showed intact pth = 1.258 pg/ml (7–53), serum total calcium = 12.3 mg/dl (8.8–10.8), serum phosphorus = 2.6 mg/dl, alkaline phosphatase = 1331 u/l, urinary calcium = 237 mg/24 h (60–200) and creatinine clearance = 73 ml/min/1.73 m^2 (60–120).

99mTc-Sestamibi spect scan showed intense uptake in mediastinal region and absence of uptake in cervical region.

He was submitted to radio guided sternotomy to hand-held gamma probe that localize the adenoma in right lobe of the thymus, which was removed successful.

Immediate before sternotomy, examinations were intact PTH = 2.172 pg/ml, total calcium = 10.7 mg/dl (8.4–10.2), ionized calcium = 1.40 mmol/l (1.12–1.32), phosphorus = 3.0 mg/dl (2.5–4,8) and magnesium = 1.3 mg/dl (1.9–2.5).

Intraoperative PTH 10 and 20 min after removal the thymus was respectively 146 pg/ml (6.72% of preoperative value) and 109 pg/ml (5.01%). after 38 hours removal PTH = 66.8 pg/ml (3.07%).

25 Hours after surgery he presented hungry bone syndrome, with serum total calcim = 7.3 mg/dl, ionized calcium = 1.12 mmol/l , phosphorus = 1.7 mg/dl, magnesium = 1.3 mg/dl, when started calcium supplementation iv and oral with total daily doses of the elemental calcium changed 0.63–2.3 g.

He presented only one time chvostek's sign 94 hours after surgery, and he keeps hypocalcemia, hypophophastemia and hypomagnesemia until 111 hours.

Calcium supplementation iv was suspended in fourth and discharge from hospital in sixth postoperative day with prescription of 2.3 g elemental calcium by calcium carbonate.

P192MO. CASE REPORT OF PRIMARY HYPERPARATHYROIDISM DUE ECTOPIC PARATHYROID INTRATHYMIC ADENOMA IN BOY 16 YEARS OLD, WITH SEVERAL BONE AND RENAL DISEASE

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A Boy 16 years old, with normal pubertal and growth development, presented sporadic macroscopic hematuria 2 years ago, and 15 months later nephrolithiasis due to bilateral pyelocaliceal and ureteral stones.

Partial urinary tract obstruction with elevation of plasma creatinine to 2.3 mg/dl (0.4–1.4 mg/dl), promoted hydronephrosis, resolved through introduction of bilateral ureteral catheter pig tail type, following lithotripsy.

Endocrine investigation showed ionized calcium = 5.65 mg/dl (4.2–5.5), intact PTH = 858 pg/ml (7–53), phosphorus = 2.44 mg/dl (2.7–4.5), alkaline phosphatase = 844 u/l (37–147).

Evaluate was repeated 4 months after and showed serum total calcium = 12.3 mg/dl (8.8–10.8), intact PTH = 1.258 pg/ml, serum phosphorus = 2.6 mg/dl, alkaline phosphatase = 1.331 u/l, urinary calcium = 237 mg/24 h (60–200) and was normalized creatinine clearance = 73 ml/min/1.73m^2 (60–120), that discarded secondary hyperparathyroidism due renal insufficiency.

Ultrasonography revealed normal thyroid gland and hypoecoic nodular lesion below left thyroid lobe. chest CT and MRI confirmed nodular lesion behind left clavicle and next subclavian vessels and also another intrathymic nodular lesion.

99mTc-Sestamibi spect scan showed intense uptake in mediastinal region and absence of uptake in cervical region.

X-Ray revealed osteitis fibrosa cystica.

Great reduction BMD at trabecular bone (BMD in spine = 0.699 g/cm^2) was detected in densitometry that was not made at cortical bone due to slipped capital femural epiphysis treated with pinning in situ.

Preoperative sestamibi scintigraphy and marking of focal adenoma uptake followed sternotomy with intraoperative hand-held gamma probe localized adenoma in right lobe of the thymus, which was removed.

Intact PTH immediate before sternotomy was 2.172 pg/ml, and intraoperative 10 min, 20 min and 38 h after removal of the thymus was respectively 146 pg/ml, 109 pg/ml and 66.8 pg/ml.

25 Hours after surgery, the patient presented hungry bone syndrome.

The tracer uptake ratio thymic adenoma/cervical = 3.5; thymic adenoma/precordium = 1.8.

Anatomicophatologic examination of the tissue confirmed an ectopic parathyroid adenoma in right lobe of the thymus.

P193SA. COMPARISON OF THE SENSITIVITY, PRECISION, ACCURACY BETWEEN QUANTITATIVE CT AND DXA IN MEASUREMENT OF BONE MINERAL DENSITY

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Objective: From statistical analysis of the sensitivity, precision, accuracy of quantitative CT(QCT) and DXA(dual energy x-ray absorptiometry) in measurement of bone mineral density(BMD), the measuring value of QCT and DXA in BMD changes were investigated.

Methods: If there were no fracture or other malformation, the BMD of nearby vertebra would be getting close and the BMD of inferior vertebra would be higher than that of the superior. For had been confirmed with no malformations such as fracture by posteroanterior and lateral x-ray pictures, 75 Han postmenopause females had been measured the BMD of lumbar vertebra 2 to 4 (L2–4) by QCT or DXA, among them, 32 cases were measured by QCT (the QCT group) and 43 cases by DXA(the DXA group). The average and standard deviation of BMD of L2, L3 and L4 in every individual by groups were calculated and it would reflect the vicariance degree in the three nearby vertebra and its regression was indirect of the precision of the two methods. The average and standard deviation of the

two groups were calculated and the vicariance degree of the BMD between every individual would reflect the sensitivities of the two methods indirectly. The accuracy of QCT and DXA were showed by the ratio of cases whose BMD L2 < L3 < L4 in two groups and compared with X2 test in statistics. Supposed the sensitivity, precision and accuracy of QCT was 100%, those of DXA would be calculated, respectively.

Results: There were no difference in age, sex and race between two groups. The average BMD of L2 to L4 were 98.63 ± 35.15(mg/cm^3), 0.816 ± 0.121(g/cm^2) and the standard deviation of L2 to L4 BMD were 5.92 ± 3.23, 0.0477 ± 0.0314 by QCT and DXA respectively. Supposed the sensitivity, precision and accuraty of QCT was 100%, those of DXA were 40.8%, 82.8% and 82.8%. There was no difference in accuraty by QCT or DXA.

Conclusions: For measuring the BMD of lumbar, the sensitivity of QCT was higher markedly than that of DXA, the precision and accuracy of QCT were a little higher than those of DXA also. For reflecting the change of BMD, QCT was more sensitive than DXA.

P194SU. THE RISK OF FOREARM FRACTURE AMONG 6801 POST-MENOPAUSAL WOMEN

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Background: In general the prediction of fracture among younger women is poorer than among older, where hip fractures are more common. Studies have shown that a prior fracture is an independent risk factor for new fractures. Forearm fracture is the first osteoporotic fracture with a mean age of 64 years in Swedish women.The question is if it is possible to predict a forearm fracture with BMD and risk factors. Population and methods: 6801 women, mean age 59.0 years,were participating in a simultaneously screening of breast cancer (mammography) and osteoporosis (forearm BMD, Osteometer-200). The woman were followed for 44893 person years. Fractures were collected from a register at the X-ray department. 733 new fractures were registered,198 women had a forearm fracture. A set of risk variables were studied with respect to their ability to predict forearm fractures among women. Besides age the variables were BMD at radius,previous fracture, area at radius, corticosteroids, BMI, body height, body weight, smoking, number of walkings per week and coffee intake per day.

Results: Age, BMD and previous fracture were the only variables contributing significantly to the prediction of forearm fracture. The gradient of risk per 1 standard deviation was 1.41 for BMD. The risk ratio of forearm fracture for a woman with previous fracture versus a woman without a previous fracture was 1.77(95%CI:1.30–2.41) provided that age and BMD were equal.The increase of forearm fracture risk was 5.6% per year of age(95%CI:3.5–7.9%).

Conclusions: In this prospective study only age, forearm BMD and prior fracture contributed to the prediction of forearm fracture.

P195MO. IS THE RISK OF NON-VERTEBRAL FRACTURE ASSOCIATED WITH TYPE I DIABETES GENDER SPECIFIC?

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Aim: In a follow up of 12270 young subjects from a general population (1988–95), lean diabetic females and females with type I diabetes were at high risk of non-vertebral fractures. Due to lack of power, we could not stratify on all three variables of interest. A new larger cohort of 27159 persons with a larger age range became available. The aim was to test the hypothesis of a high gender specific fracture risk in lean type I diabetics.

Methods: This is a population based study of all those who attended the fourth survey (1994/95) in the Tromsø Study, followed until the 31st of December 2000 with respect to non-vertebral fractures. Diabetes mellitus cases were defined by self-report in questionnaires, then validated in hospital records. All non-vertebral fractures were registered by computerized search in radiographic archives in the sole provider of radiographic service in the area.

Results: We validated 390 cases of diabetes mellitus (191 women, 199 men), and 1251 non-vertebral fracture cases (799 women, 452 men). The crude relative risk (RR) of fracture was 2.1 (95% confidence interval (CI) 1.4–3.3) and 2.0 (95% CI 1.3–3.8) for diabetic women and men respectively compared to the reference group of non-diabetics. No increased risk was found among women with either type of diabetes or among lean (BMI < 25 kg/m^2) women when adjusting for age. Among lean men the independent RR of fracture was 2.8 (95% CI 1.4–5.6) when adjusting for age. Lean men with type I diabetes had a RR of 3.9 (95% CI 1.2–12.1). Type II diabetic men had no increase fracture risk.

Conclusion: This study found a higher risk of non-vertebral fractures in lean male type I diabetics as compared to non-diabetic controls. The contradictory results in the two studies could be caused by the first cohort being a much younger one, as all variables of interest as well as fracture risk are closely linked to age. There is a need for pooling of the two datasets enabling stratified analysis on all variables of interest and examining age interactions in a larger population with a longer follow up period.

P196SA. EVALUATION OF THE RELATIONSHIP BETWEEN IGF-I, IGF-BP3, BMD AND AGE IN MEN PRESENTING AT A MULTIPLE RISK DETECTION CAMPAIGN

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Background: Bone loss related to aging or unloading is characterised by diminished osteoblast proliferation and reduced local concentrations of IGFs.

Objectives: To evaluate the relationship between IGF-I, IGF-BP3 and BMD in a population of men between 50 and 70 years old who presented at an age related multiple risk detection campaign.

Population and methods: The Province of Liège has organized a multiple risk detection campaign for men aged 50 to 70. 183 were screened. The tests consisted, in a prostate cancer screening, an andropause screening, a physical performance tests and osteporosis screening. Participants had to be fasting. Total IGF-I and IGF-BP3 levels were determined. The osteoporosis screening was performed by DEXA (Hologic, QDR1000+) at the total hip and at the femoral neck. 110 participants had both a BMD, IGF-I and IGFBP-3 assessed. The study population was stratified by age into five groups. Group 1 (50–54 years old, n = 28), group 2 (55–59 years old, n = 32), group 3 (60–64 years old, n = 17), group 4 (65–70 years old, n = 20) and group 5 (= 70 years old, n = 4).

Results: The general characteristics are: mean age (SD) was 59.1($\pm$5.8) years, mean Total hip BMD was 1.007 ($\pm$0.170) g/cm^2, mean T-score at the hip was –0.172 ($\pm$1.128), mean femoral neck BMD was 0.821 ($\pm$0.130), mean T-score at the femoral neck was 0.145 ($\pm$ 0.951). The mean IGF-I level was 212.409 ($\pm$59.489) ng/ml and the IGFBP-3 level was 3063.818 ($\pm$587.730) ng/ml. Mean IGF-I levels positively correlated with BMD at the femoral neck ($r = 0.25$, $p < 0.005$) and to a lesser extend at the Total hip ($r = 0.19$, $p < 0.005$). No correlations were observed between IGFBP-3 and BMD at either sites. The IGF-I/IGFBP-3 ratio positively correlates with the BMD at the femoral neck site($r = 0.24$, $p < 0.005$). Total IGF-I levels and IGFBP-3 decreased significantly with age.

Conclusion: Bone loss related to aging in men could be related to alterations in the production of and or in cell responsiveness to local IGFs. Several studies show that growth factors may stimulate bone formation. These findings could lead to new therapeutic opportunities for the prevention of osteopenia and osteoporosis.

P197SU. EFFECT OF SEASONAL DIFFERENCES IN SERIAL DENSITOMETRY ON POSTMENOPAUSAL BONE LOSS

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The aim of the present study was to investigate the effect of DXA densitometry season on bone mineral density (BMD) and bone loss.

The study population, 954 peri- and postmenopausal women, was a random sample of the OSTPRE-study cohort (n = 13 100) in Kuopio, Finland. A 3-category season of densitometry variable was formed: Group 1 (January-April), Group 2 (May-August) and Group 3 (September-December). The seasonal difference index (SDI) was computed as follows: SDI = (season group number at baseline)-(season group number at follow-up). Accordingly, the numeric values of SDI were −2, −1, 0, 1 and 2. BMD at lumbar spine (LS) and femoral neck (FN) was measured with dual x-ray absorptiometry at baseline in 1989–91 and at the five year follow-up in 1994–97. All measurement prints were manually reviewed by specialists to exclude any measurement errors or severe bone deformities.

There were no differences between season and LS or FN BMD at either baseline or follow-up. In contrast, women with low SDI had significantly greater bone loss than women with high SDI ($p < 0.001$ between SDI groups −2 and 1 or 2) (Fig. 1). Adjustment for age, height, weight, months since menopause, calcium intake, use of HRT, duration of follow-up, exercise level and use of bone affecting medications or diseases did not change any of the results. As an example, the protective effects of HRT on bone loss were found highly dependent on SDI (e.g., $p < 0.001$ within SDI 0 in contrast to p = ns within SDI 1 for bone loss rate between HRT users and non-users).

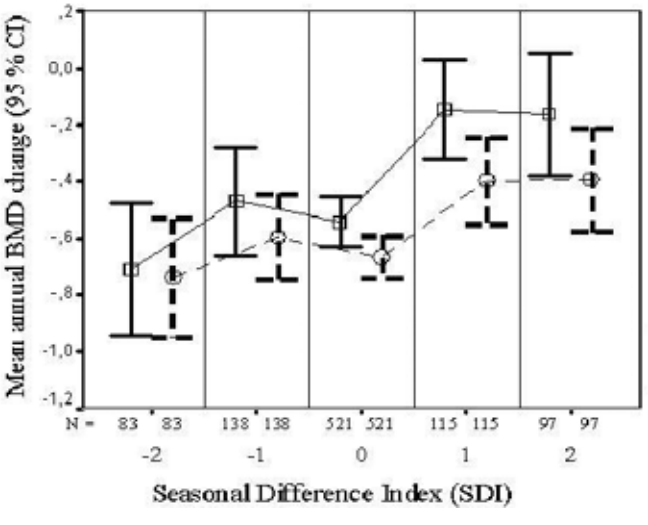

Fig. 1 Effect of SDI on mean annual LS and FN (dotted line) BMD change (%), n = 954

In summary, seasonal difference between two successive DXA measurements may significantly distort the evaluation of postmenopausal bone loss rate. This supports seasonal matching of the follow-up measurements or adjustments for seasonal differences in RCTs, treatment monitoring and follow-up studies.

P198MO. PREVALENCE OF VERTEBRAL FRACTURES IN MEXICO: A POPULATION-BASED STUDY

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The rate of vertebral fractures in Latin America has never been studied in population-based samples.

Objective: We designed the Latin American Vertebral Osteoporosis Study (LAVOS) to determine the prevalence of vertebral fractures in women over 50 years in several countries. We report here preliminarily results from the Mexico survey.

Methods: An age-stratified sample of 400 randomly selected women from Puebla Mexico was surveyed in a face-to-face interview. A questionnaire to get information on demographics, OP conventional risk factors, and some lifestyles were applied. BMD in two regions and lateral dorsal/lumbar x-rays were obtained in all cases accordingly with international protocols to be able to have cross-national comparisons. Digital Morphometry was used to determine vertebral deformities by Eastell criterion.

Results: The overall prevalence of vertebral fractures was 17.5% and increased exponentially with age. Comparing to studies that used very similar methods and criteria, the rate in Mexican women is very similar to that in Caucasian women and higher then the prevalence found in African American and Chinese women.

Conclusion: This first population-based study of radiographically confirmed vertebral fractures in a Latin American country that shows indicates that Mexican women have a risk of vertebral fracture that is similar to white US women and greater than the risk of Chinese and African-American women. Treatments to prevent vertebral fracture as important for Mexican as for US women.

Table 1 Demographic data for the four groups ,Figure 6 Comparetive study between control group and all studied groups regarding T-score

Age	SOF Whites Prev (IC95%)	SOF AA Prev (IC95%)	Beijing Prev (IC95%)	Mexico Prev (IC95%)
50–59	–	–	3.9 (0.2–7.7)	8.3 (2.7–13.8)
60–69	14.5* (13.4–15.5)	–	10.5 (4.6–16.3)	12.6 (6.1–19.1)
70–79	22.0 (20.8–23.3)	9.4 (6.3–12.6)	15.0 (8.0–22.0)	18.6 (10.7–26.4)
80 +	33.9 (30.9–36.9)	17.4 (11.0–23.9)	31.2 (21.8–40.6)	37.9 (28.3–47.4)

* > 65 years

P199SA. RISK FACTORS FOR OSTEOPOROSIS IN A UK MALE COMMUNITY-DWELLING POPULATION: THE NOTTINGHAM MALE OSTEOPOROSIS (NOMOS) STUDY

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Osteoporosis in men is increasingly recognized as a major public health problem. Few studies address this issue in community-dwelling men.The NOMOS study comprises older men recruited from General Practice age-sex registers as part of the longitudinal Nottingham Community Osteoporosis (NOCOS) Study. At baseline, the dataset consists of basic demographics, risk factors for fracture and falls using standardised questionnaires, heel BMD (GE Lunar PIXI) and assessment of social deprivation (Jarman score). Previous analysis in women from this cohort showed that the least socially deprived were protected from osteoporosis. The aim of this analysis was firstly to assess the extent of osteoporosis in this male population, and secondly to determine which baseline factors, including deprivation levels, predict osteoporosis. As the WHO criteria cannot be applied to the heel, osteoporosis and osteopenia were diagnosed using the manufacturer's recommended WHO-equivalent T-score thresholds of T-1.6 and T-0.6 respectively. 325 men (mean age 70, range 52–89) were studied.The prevalence of osteoporosis and osteopenia was 18% and 32% respectively. In this group of community dwelling elderly men, the

Table 1 Risk factors for osteoporosis

Risk Factor	Odds ratio (95%CI)
Age (yrs) 70 or more	1.8 (1.0–3.2)
Postural hypotension	3.0 (1.4–6.4)
Four or more drugs	2.4 (1.2–4.7)
Mobility problems	4.2 (1.3–12.9)
Tandem walk	3.4 (1.3–9.2)
Previous wrist fracture	3.3 (1.2–8.9)

study identified a number of risk factors for osteoporosis (Table 1). Degree of social deprivation did not constitute a risk. Logistic regression identified weight, presence of postural hypotension, previous non-wrist fracture and tandem walk as significant predictors of osteoporosis. ROC analysis showed that these four variables identified osteoporosis with a sensitivity and specificity of 73%. The area under the ROC curve was 0.78 (95% CI 0.71–0.85).

This study identifies the magnitude of this neglected health problem in a UK population. The risk factors identified should be considered in the case-finding approach, for identifying older males at high risk of osteoporosis. These data also suggest that, in contrast to women from this UK population, social deprivation levels in men had no relationship to the presence of osteoporosis.

P200SU. DO PATIENTS WITH OSTEOPOROTIC HIP FRACTURE RECOVER THEIR INITIAL HEALTH-RELATED QUALITY OF LIFE?

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Objective: To document the loss of health-related quality of life (HRQoL) in osteoporosis (OP) patients having experienced a hip fracture.

Methods: The SF-36, the QUALEFFO and the WOMAC hip physical function scale were administered to OP outpatients without any event of hip fracture and consulting an OP referral clinic for routine examination (N = 104). Concomitantly, medical records from 4 orthopedic units from the same area were scrutinized to identify patients treated for osteoporotic hip fracture 3 (N = 38) or 6 (N = 41) months ago. Once identified, these patients were contacted to be administered with the same instruments than the outpatients. Each HRQoL dimension was scored on a 0 (worst) to 100 (best) scale. Regression equations were estimated using the outpatients sample to explain the different HRQoL scores with age, sex, comorbid conditions and socioeconomic status. The regression coefficients were then assigned to the orthopedic sample to assess a theoretical level (i.e., without hip fracture) for each HRQoL dimension. Paired-samples analyses were then performed in the orthopedic sample to compare the theoretical scores with the 3 and 6 months post-fracture scores.

Results: At 3 months, three scales of the SF-36 were still deteriorated: physical function (delta3–0 = −15.0, $p < 0.05$), social function (delta3–0 = −13.0, $p < 0.05$) and vitality (delta3–0 = −11.5, $p = < 0.001$). Four scales of the QUALEFFO remained impaired: physical function (delta3-0 = −19.7, $p < 0.001$), social function (delta3–0 = −14.8, $p < 0.001$), general health perception (delta3–0 = −11.1, $p < 0.001$) and mental health (delta3–0 = −9.7, $p < 0.05$). The hip function as assessed by the WOMAC was also decreased (delta3–0 = −13.3, $p < 0.001$). At 6 months, the physical and the social function dimensions of the SF-36 continued to be altered (delta6–0 = −22.6, $p < 0.001$ & delta6–0 = −17.3, $p < 0.001$ respectively). Significant decreases were noted in the physical function (delta6–0 = −24.8, $p < 0.001$), the social function (delta6–0 = −21.9, $p < 0.001$), the general health perception (delta6–0 = −16.2, $p < 0.001$) and the mental health (delta6–0 = –8.6, $p < 0.05$) dimensions of the QUALEFFO. The WOMAC hip function revealed that patients still suffered from hip dysfunction at 6 months (delta6–0 = −20.8, $p < 0.001$).

Conclusion: OP patients experiencing hip fracture do not recover their initial HRQoL and hip function at 3 and 6 months post-fracture. Given advanced age of OP sufferers, this finding suggests that hip fracture definitively damages HRQoL.

P201MO. ENVIRONMENTAL DETERMINANTS OF BONE MINERAL DENSITY: RESULTS FROM THE HUNGARIAN OSTEOPOROSIS RISK ASSESSMENT (HORA) STUDY

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Background: It is widely accepted that race and geography significantly affect the risk for osteoporosis. However, most of our knowledge on risk factors was derived on populations from Western-Europe and the United States. Much less is known about similar associations in Eastern European people. The aim of our present study was to describe the frequency and risk factors for osteoporotic fractures and osteoporosis in a female population in a cross-sectional, multi-center study performed under the auspices of the Hungarian Society for Osteoporosis and Osteoarthrology.

Patients and methods: From 5 randomly selected regional and 5 local osteoporosis centers, altogether 2606 women over 18 years of age, referred to the given center with any osteoarthrological reason, participated. During the office visit, detailed risk factor assessment questionnaire was filled in and blood pressure, weight, height and bone mineral density were measured.

Results: Using the results of a univariate analysis the following variables were made available for further examination: older age, longer duration since menopause, lower femoral T-score, positive family history of bone fracture, less physical activity, fall in the previous year, lower diastolic blood pressure and smoking habit. Using multiple regression analysis, only older age, lower diastolic blood pressure, family history of bone fracture, fall in the previous year and lower T-score were independently related to fractures ($p < 0.05$). In comparison the univariate risk factors for femoral osteoporosis were higher age, lower weight, lower BMI, positive family history of bone fracture, fall in the previous year, glucocorticoid treatment, lower parity, lower diastolic blood pressure, longer duration since menopause and less physical activity. The multiple regression analysis revealed the following independent associates ($p < 0.05$) from the previous list: older age, lower weight, family history of bone fracture, less physical activity, fall in the previous year and glucocorticoid treatment.

Conclusion: Our study is the first large-scale epidemiological survey describing risk factors of osteoporosis and fractures in a Hungarian female population. Our data suggest that lower diastolic blood pressure might be a new risk factor related to osteoporotic fractures; however, it needs further examinations.

P202SA. THYROXIN TREATMENT AND BONE MINERAL DENSITY IN 1 285 70-YEAR OLD WOMEN: THE NORDOS STUDY

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Background. Excessive thyroxin levels either by endogenous or exogenous reasons is known to increase bone turnover and bone loss leading to osteoporosis and increased risk for fracture.

Thyroxin. as a metabolic active hormone also afflicts body composition, corresponding against weight loss. Our two main objectives for this study were to investigate eventful differences in

body weight between women with or without thyroxin treatment and also bone mineral density against treatment.

Population and Methods. 1 285 women randomly selected 70-year old women in Island (n = 305) and Sweden (n = 980) participated in this population-based study. Body composition and bone mineral density was measured with DXA technique; Hologic 4500 A. Blood samples were collected in the morning under fasting condition. Data were obtained from an extensive enquire were the women self reported medication, medical condition, earlier fracture and lifestyle factors. Women with the diagnosis of osteoporosis were medically examined and evaluated for treatment.

Results. 138 (10.7%) reported thyroxin treatment. Thyroxin treated women reported significantly greater body mass 59.9–58.1 kg ($p = 0.008$) were taller 165.8–164.2 cm ($p = 0.004$) at age 25 than controls. Current weight and height showed a consistent significant difference at age 70 weight 73.0–69.0 kg ($p = 0.0006$). Bone mineral density in total hip was 2.6% higher among thyroxin treated but ns, in spine (L2-L4) BMD was 3.7% higher $p = 0.0246$ and when adjusting for weight and height BMD was still higher among thyroxin treated 0.5% and 1.8% respectively but not significant.

Conclusion. Women with thyroxin treatment in this representative population study from Island and Sweden had 3.7% higher BMD in spine $p = 0.0246$. Women on thyroxin treatment also had significant higher body height and weight this difference was also present in those women at age 25.

P203SU. SIMPLE INDICES ON PLAIN X-RAYS STRONGLY PREDICT RISK OF HIP FRACTURES IN MEXICAN MEN AND WOMEN

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Hip x-rays are universally available, even where densitometry is not affordable. We postulated that simple measurements on hip x-rays may be powerful predictors of hip fracture in men and women. We conducted a study to test the hypothesis that simple measurements on hip x-rays could predict hip fractures and identify women and men at high risk of fracture. A total of 254 pelvic radiographs from a case control study on hip fractures and risk factors in individuals over 45 years old were included for this study; 184 women (78 cases and 106 controls) and 70 men (33 cases and 37 controls) Two measurements were performed by two trained observers in all studies: Singh index, a measure of the quality and connectivity of bundles of trabecular bone of the proximal end of the femur were the change in trabecular patterns is graded in six categories from 6 normal pattern to 1 the worst, and the Cortical Index obtained by dividing the sum of the thickness of the internal and external cortices by the total diameter of the shaft at the distal limit of the sub trochanteric region, measurements of 0.20 to 0.49 are associated with osteoporotic changes. In age-adjusted generalized logit models, for every 1 unit decrease in Singh Index, men and women had a 45.5 (7.6–273.2) and 6.8 (3.7–12.5) increased risk of trochanteric fracture. For cervical fracture a risk of 23.8(4.0–143.2) for men and 21.0(7.8–56.3) for women was found. After adjusting for Cortical Index, Singh index remained predictive of trochanteric fractures in men 52.5(7.4–370.0) and women 5.3(2.6–10.9) and cervical fractures in men 13.1(1.9–90.9) and women 25.8 (7.8–86.1). For Cortical Index alone, a 0.1 decrease was also associated with increased risk of trochanteric [3.1 (1.6–6.3) men, 3.2 (2.1,4.9) women] and cervical fractures [4.1 (1.7–9.7) men, 3.2 (1.8,5.8) women], but not when Singh Index was included in the model.

P204MO. INCIDENT RATES OF HIP FRACTURES IN MEXICANS OVER 50 YEARS

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We have recently shown that the rate of vertebral fractures is similar in Mexico and Whites in the US. The rates of hip fracture in Mexico have never been determined in a population-based study.

Objective: To describe rates of hip fractures in urban Mexico in individuals over 50 years,

Methods: Individuals over 50 years of age diagnosed with hip fracture were identified from institutional registers of all hospitals with hip surgery facilities from the two largest Health Systems in Mexico City (Instituto Mexicano del Seguro Social IMSS and Ministry of Health Ssa).Cases were verified against surgical and x-ray logs. Age, sex, type of fracture, ICD-10 coding and place of residence were obtain. Age stratified incident rates were developed using the CENSUS 2000 population data.

Results: The rates of hip fracture increase exponentially with age in both genders. Age-standardized rates in Mexico (206 for women and 108 for men) were 2.5 lower than the rates in US non-Hispanics for women and 1.6 times lower for men (510 and 174/100 000 for women and men, respectively) but similar to rates found in urban Chinese and US Hispanics.

Table 1 Hip 2003

Age group	Total No. Cases		Population per thousands		Annual rate × 100 000 (IC)	
	Men	Women	Men	Women	Men	Women
50–59	29	38	145.99	192.21	20(13–30)	20(14–28)
60–69	52	105	99.70	138.61	52(36–73)	76(58–98)
70–79	95	236	58.62	79.92	162(115–227)	295(228–385)
80+	143	369	20.77	32.44	688(429–1134)	

Conclusion: This first population based study in Mexicans shows that the risk of hip fracture in Mexican women and men are lower than the US and Europe and similar to several other developing countries.

P205SA. VALIDATION OF THE QUALITY OF LIFE INSTRUMENT QUALEFFO PROPOSED BY THE EUROPEAN FOUNDATION FOR OSTEOPOROSIS IN THE MEXICAN POPULATION

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Pain, social isolation, depression and disability are described in patients with vertebral fractures due to osteoporosis (OP) and have an impact in their quality of life (QL). No specific instrument has been validated in Spanish and adapted transculturally to evaluate the QL in patients with vertebral fractures due to OP in Mexican population.

Objective: To validate the European Questionnaire for Life Quality (QUALEFFO) in Mexican population with osteoporosis (OMS criteria) with and without vertebral fractures determined morphometrically by the Eastell Method.

Methodology: The QUALEFFO was translated into Spanish and cultural adaptation was performed by consensus with an expert team; then, we tested its content validity in a pilot study. The SF36 was applied at the same time to verify concurrent validity. Both instruments were applied by the same trained interviewer at the Centro Nacional de Rehabilitación (CNR) in Mexico City, and the vertebral fracture sample group from LAVOS Mexico (Vertebral Fractures Prevalence Study) in the City of Puebla City in a face to face interview.

Results: The total sample was 160 OP patients, 80 with OP and fractures and 80 only with OP; the patients average age was 71.9 (11.19). Content validity was assessed by expert consensus and global internal consistency of the sample was very good (Cronbach's Alpha .9281). Reproducibility was very high (Ri = .94) and the concurrent validity showed a significant correlation of Pearson $p < 0.001$. The discriminatory validity between the groups was significant in the following areas: pain domains ($p < 0.05$), social activities and physical condition ($p < 0.001$), and mental condition ($p < 0.05$).

Conclusion: The QUALEFFO had excellent psychometric characteristics in our sample of Mexican patients; it proved to be consistent and homogeneous and to have discriminatory potential in 3 different domains of QL. We conclude that the QUALEFFO can be used in Mexican population to measure QL due to Vertebral Fractures attributable to OP.

P206SU. THE ASSOCIATION BETWEEN NUTRITIONAL RISK DETERMINED BY MINI-NUTRITIONAL ASSESSMENT (MNA) AND OSTEOPOROSIS IN ELDERLY WOMEN: A CROSS-SECTIONAL STUDY

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Aims: The aim of this study was to investigate the association between bone mineral density and the nutritional risk determined by Mini Nutritional Assessment (MNA) questionnaire in a group of home living elderly Swedish women.

Methods: The study sample consists of 584 women. 60% or 351 women (mean age 73 years) participated. Their nutritional status was determined by MNA, a test consisting of 18 point-weighted questions in four categories: anthropometric measurements, clinical and functional evaluations, assessment of dietary intake and self-assessment of nutritional status and health. 30 points is the maximum, a score <17 indicates malnourished, >17 and <24 at risk of malnutrition and >24 well nourished.

Bone mineral density (BMD) values were determined at the left hip and the lumbar spine, L1-L4, using HologicQDR 4500 equipment for dual energy x-ray absorptiometry (DXA). The data were analysed by logistic regression.

Results: The median score of MNA was 27. Only 7.4% of the women were at risk of malnutrition and only one subject was classified as malnourished. Osteoporosis in the femoral neck was found in 52.9% of the women and 31% had a history of fracture after the age of 50 years. Those with <23.5p at MNA had a 70% larger age-adjusted risk of having osteoporosis than those with normal scores but this finding was not statistically significant ($p=0.24$). ROC analysis showed an AUC of 0.67 and a high specificity of 95% combined with a very poor sensitivity of 9%. The following items in the MNA questionnaire had the strongest association with osteoporosis at the femoral neck: age (OR = 1.12; CI = 1.02–1.24) per 1 year increase, calf circumference (OR = 0.91; CI = 0.83–0.99) per 1 cm increase and BMI over 26 (OR = 0.19; CI = 0.04–0.93). Reduced appetite (OR = 2.55; CI = 0.79–8.20) and the highest protein score (OR = 0.41; CI = 0.11–1.48) were not statistically significantly associated with osteoporosis.

Conclusions: The anthropometric measurements of the MNA questionnaire were highly associated with osteoporosis but the MNA questionnaire is not sensitive enough to detect osteoporosis.

P207MO. THE INFLUENCE OF FAMILY HISTORY OF OSTEOPOROTIC FRACTURE ON THE RISK OF VERTEBRAL OSTEOPOROSIS IN WOMEN

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Introduction Bone mass is an important determinant of bone strength and risk for osteoporotic fractures (OF). The majority of family studies of bone mass indicates that it is under strong genetic control. However, there are few data exploring clustering of osteoporosis within families in Latin America.

Objectives The aim of this study was to determine the influence of family history of OF on the risk of vertebral osteoporosis and occurrence of OF in a set of Brazilian women included in Lavos Study.

Material and Methods 407 women aged 50 and over, were recruited from population based sampling across Vitória metropolitan area, Brazil. Subjects were invited to participate, signed an informed consent form and a trained interviewer applied a standardized questionnaire. A DXA measurement at L-Spine and Hip was performed, as well as an X-Ray of Thoracic and L-Spine. Vertebral osteoporosis was defined using NIH criteria (T-score = –2.0SD)

Results A family history of OF was associated with a 14% increased risk of vertebral osteoporosis [odds ratio (OR) 1.14 (95%CI:1.127–1.166)] and with a 44% increased risk of personal OF [OR 1.44 (95%CI:1.424–1.461)]. We also observed significantly lower BMD in subjects who reported OFs ($n=62$), with a mean BMD of 0.897 (+0.037) and of 0.974 (+0.021) ($p=0.00026$) in the groups with and without history of OF ($n=345$), respectively. The number of relatives with past of OF as well as the number of OF these relatives suffered, was statistically correlated with BMD ($r=-0.33$, $p=0.009$ and $r=-0.285$, $p=0.025$).

When the mean BMD of subjects who reported relatives with OF was compared with those without family history of OF, the correlation was not statistically significant (mean BMD of $0.947+0.188$ and $0.958+0.204$ [$p=0.36$]) in the groups with and without family history of OF, respectively).

Conclusion As seen in other populations, family history of OF appears to be an important risk factor for OF in Brazilian women. This risk factor seems to be determined not only by BMD genetic hereditariness. As the risk of OF increases with the number of relatives with past of OF, this particular information should be considered when looking for risk factors for osteoporosis and fractures.

P208SA. THE GLOBAL BURDEN OF HIP FRACTURE

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The aim of this study was to quantify the global burden of osteoporosis as judged by hip fracture and the burden in different socio-economic regions of the world. The population mortality in 1990 and the incidence of hip fracture in different regions were identified, where possible in 1990. Excess mortality from hip fracture used data for Sweden, and disability weights were assigned to survivors from hip fracture.

In 1990 there were 1.31 million new hip fractures and the prevalence of hip fractures with disability was 4.48 millions. There were 738,116 deaths associated with hip fracture and 1.7 million life-years lost reduced to 951 thousands with weighting for age. Disability adjusted life years lost accounted for 1.75 million disability adjusted life years, representing 0.1% of the global burden of disease world wide and 1.4% of the burden amongst women from the established market economies. We conclude that hip fracture is a significant cause of morbidity and mortality world-wide.

P209SU. COSTS AND QUALITY OF LIFE RELATED TO VERTEBRAL FRACTURES: PRELIMINARY RESULTS BASED ON AN ONGOING SWEDISH PROSPECTIVE STUDY

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Aims: There are few studies investigating the consequences of osteoporotic (low bone density) fractures in terms of costs and health outcomes. A previous Swedish pilot study assessed the costs and quality of life related to fractures of the hip, spine, wrist and shoulder in the southern part of Sweden. Data were collected using a questionnaire administered by a nurse at Malmö University Hospital in the south of Sweden. The study indicated that spine fractures are associated with higher costs and lower quality of life than previously assumed. Based on the pilot study a large-scale prospective study was designed in a Swedish setting. The purpose of this ongoing study is to collect cost and health effect data related to osteoporotic fractures of the hip, wrist and spine for a large number of patients, e.g. to be able to assess the determinants of costs and quality of life.

Methods: In total data for 2 000 patients at 7 study centres will be included. The patient enrolment started in June 2002 and will continue during the year 2003 and 2004. In September (2003), 103 spine fracture patients were enrolled in the study, out of which 76 were hospitalised and 27 were discharged the same day as the first contact with the health care.

Results: Preliminary results show that spine fractures are associated with lower quality of life levels than previously assumed, and that the quality of life of spine fracture is similar to the quality of life for hip fracture. It is also indicated that spine fracture patients being hospitalised have higher costs during the period 4 months after fracture compared to patients not being hospitalised (SEK 56 000 vs SEK 44 000). The quality of life measured by the EuroQol 5D social tariff method amounted to 0.70 (just before fracture), 0.12 (just after fracture) and 0.38 four months after spine fracture for the group being hospitalised. The corresponding values for non-hospitalised spine fracture patients were 0.76, 0.28, and 0.37.

Conclusions: The completed study will provide important inputs for health economic evaluations assessing the cost-effectiveness of the treatment and prevention of osteoporosis.

P210MO. RELATIONSHIP BETWEEN LIPIDS AND BONE MASS IN HEALTHY WOMEN AND MEN

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A number of recent finding seems to indicate that fat and bone metabolism are strictly connected. We investigated the relationship between lipid profile and bone mineral density (BMD) first in 236 either pre or postmenopausal women, aged 35 to 81 years, attending our osteoporosis center (''osteoporosis center group'') and then, in order to verify the consistency of the results, in 265 men and 481 women aged 68 to 75 years participating in a population-based epidemiological investigation (''elderly cohort''). Lumbar spine, femoral neck BMD, total body fat, % fat mass and lean mass were measured using dual energy x-ray absorptiometry (DXA). In the women of the ''osteoporosis center group'' lumbar spine and hip BMD Z score values were both strongly related to all measured serum lipids: the relationship was negative for HDL cholesterol ($p \leq 0.05$) and Apo A lipoprotein ($p \leq 0.000$) and positive for LDL cholesterol ($p \leq 0.05$) , Apo B lipoprotein ($p \leq 0.001$) and triglycerides ($p \leq 0.05$). When BMD values were adjusted for body weight and BMI most relationships remained statistically significant. In the subjects of the ''elderly cohort'' total body and hip BMD values were strongly related in both men and women to age, body weight, height, BMI, fat mass, lean mass, % fat mass. Total body and hip BMD were significantly related to serum lipids in both women and men. The relationship was negative for HDL cholesterol and positive for total cholesterol, triglycerides and LDL cholesterol. Most of these relationships (triglycerides, HDL cholesterol, LDL/HDL cholesterol ratio in women, and all measured lipids in men) remained statistically significant (p values ranging from 0.000 to 0.03) when the BMD values were adjusted also for anthropometric measures (body weight, height, fat mass). This study demonstrates for the first time that the lipid profile is strictly related to bone mass both in men and women: the individuals with the worse lipid profile are those with the highest BMD values. The interpretation of this association remains hypothetical but it might open new perspectives for understanding the mechanisms controlling for bone metabolism.

P211SA. PREVALENCE OF OSTEOPOROSIS IN BRAZILIAN WOMEN

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Aims: The prevalence of osteoporosis in Brazilian women has never been estimated before. Using the Brazilian sample of the LAVOS – Latin American Vertebral Osteoporosis Study, our aim was to determine the prevalence of Osteoporosis and Osteopenia, according to WHO criteria, in Brazilian women.

Methods: 407 women, aged 50 or more, were randomly selected using the survey zones defined by the IBGE, (Brazilian Institute of Statistics and Geography) from the metropolitan area in Vitoria and Vila Velha, (total population of about 700,000). The women were stratified in 4 groups: from 50 to 59.9 years old (n = 107) group 1, 60 to 69.9 years old (n = 102) group 2, from 70 to 79.9 years old (n = 100) group 3 and 80 years old and over (n = 99) group 4. For each woman a questionnaire was applied by trained interviewers, in their homes, and lumbar and femoral DXA scans were performed (Prodigy GE/Lunar, Madison USA). The prevalence of osteoporosis, osteopenia and normal BMD were calculated according to the WHO's criteria for each category using T scores. The analysis of the scans were made by a single, well trained operator using the same criteria for positioning profiles, vertebral exclusion and scans acceptance.

Results: We found 33.6% of osteoporotic and 33.8% osteopenic women in this sample. Table 1 shows the results by age strata and region of interest. As expected BMD decreases with age in every region studied being the most affected region with osteoporosis the lumbar spine in all four groups.

Table 1

LSpine L1-4	50–59,9	60–69,9	70–79,9	80-up
% Normal	46	29	21	20
% Osteopenia	38	42	33	21
% Osteoporosis	16	28	46	59
Left Femoral Neck	50–59,9	60–69,9	70–79,9	80-up
% Normal	64	43	21	8
% Osteopenia	35	47	57	43
% Osteoporosis	2	10	23	49
Left Total Femur	50–59,9	60–69,9	70–79,9	80-up
% Normal	72	64	27	10
% Osteopenia	26	29	55	47
% Osteoporosis	2	7	19	43

Conclusions: Our data is not very different from data in European and North American data and our results should alert epidemiologists, decision makers and public health authorities to take the necessary steps for preventing measures in the older population of Brazil.

P212SU. OSTEOPOROSIS RISK FACTORS, VERTEBRAL FRACTURE PREVALENCE AND THEIR INFLUENCE ON QUALITY OF LIFE IN ELDERLY WOMEN LIVING IN A LOCAL NURSING HOME

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This study was designed in order to investigate osteoporosis risk factors, vertebral fracture prevalence and their influence on quality of life in elderly women living in a local nursing home.

Fifty women living in Bursa Nursing Home with a mean age of 79.1 ± 7.7 years, were included in the study. All patients were interviewed for osteoporosis risk factors using a questionnaire, and evaluated by Nottingham Health Profile (NHP). Bone mineral density (BMD) was measured by DEXA and lateral lumbosacral x-rays were taken. Serum Ca, PTH, calcitonin, calcitriol and 24 hour urinary Ca levels were measured. Vertebral fractures were assessed using a semiquantitative method. Subjects with and without fractures were then compared according to osteoporosis risk factors NHP, BMD, and laboratory parameters. Young elderly ($age \leq 74$) and old elderly ($age \geq 75$)subjects were further compared in terms of vertebral fracture prevalence, NHP and BMD.

Vertebral fractures were present in 80% of the subjects. Lumbar BMD was found to be lower in those with fractures. Covered clothing style, inadequate sun exposure, sedantary life style were found to be significantly higher in subjects with vertebral fracture. Hip BMD of subjects with grade 3 fracture was found to be significantly lower than those with grade 1 or 2 fractures. Body mass index was positively correlated with lumbar and hip BMD; age was negatively correlated with hip BMD and NHP pain, physical activity, fatigue, emotional reactions subscales; NHP physical activity score was significantly higher in the old elderly group.

This study demonstrated a high vertebral fracture prevalence in elderly women living in a local nursing home. Certain risk factors

such as covered clothing style, inadequate sun exposure and sedantary life style were associated with a high prevalence of vertebral fractures. Quality of life was found to be influenced only by increasing age. We believe that these findings may provide an insight for larger epidemiological studies as well as contribute to osteoporosis prevention and treatment efforts in this high risk population.

P213MO. BMD IN MEN: WHICH NORMATIVE DATA?

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Objectives: Controversy surrounds which normative data should be used to estimate osteoporosis prevalence in men. Prevalence estimates may vary significantly when different normative standards are applied. Our goal was to determine to which extent different normative sets of data could impact the prevalence of osteoporosis in men.

Material and methods: Five normative data sets (NHANES female norms, local female norms, Hologic densitometer manufacturer female norms, NHANES male norms, Hologic male norms) were used to estimate the prevalence of osteoporosis by World Health Organization diagnostic criteria in a study population of 321 consecutive men aged 20 to 91 (mean 59.3 years) referred to an outpatient osteoporosis center between January 1996 and December 1998.

Results: Statistically significant variations were seen in osteoporosis prevalence measured at three anatomical sites. The greatest relative variation was seen for the total femur, where osteoporosis prevalence ranged from 5.6 percent (NHANES and Hologic female norms) to 12.5 percent (NHANES male norms). The least relative variation was seen at the lumbar spine, where prevalence ranged from 15.6 percent (Hologic female norms) to 27.1 percent (local female norms). When considering osteoporosis at any site, prevalence was lowest (20.3 percent) based on Hologic female norms and highest (32.7 percent) based on local female norms.

Conclusion: Interpretation of prevalence data should include an assessment of how normative standards influence reporting of the population at high risk of fracture.

P214SA. EVALUATION OF THE OSTEOPOROSIS SELF-ASSESSMENT TOOL (OST) AS A SCREENING TEST FOR OSTEOPOROSIS AND OSTEOPENIA IN MEN

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Background: Several indices have been developed to screen women with a high risk of having low bone mineral density, who should benefit of BMD testing. No risk indice has been developed for men so far. The Osteoporosis Self-Assessment Tool (OST), the simplest indice to calculate, might be suitable for ageing men.

Objective: To evaluate the accuracy of OST as a screening tool, predicting osteopenia and osteoporosis risk in a male population.

Methods: 183 men who presented spontaneously at the multiple risk detection campaign organized by the Province of Liège (Belgium) in June 2003. We have collected anthropometrical data and performed a BMD testing in 161 subjects using DEXA technology (Hologic, QDR 1000+). The ability of OST to identify men with osteopenia (T-score ≤ -1.0) or osteoporosis (T-score ≤ -2.5) was evaluated.

Results: The mean age of the sample was 59.4 ($\pm$ 5.8) years. The prevalence of osteoporosis was 9.25% at the femoral neck and 1.25% at the total hip. The prevalence of osteopenia was 30% at the femoral neck and 8% at the total hip. BMD measures were inversely correlated with the values of OST, $r = -0.38$ ($p < 0.005$) and -0.35 ($p < 0.005$) respectively for the femoral neck and the total hip. The area under the ROC curve (AUC) was 0.737 for the femoral neck and 0.760 for the total hip, close to the values observed in women. For the cut-off value of < 4.7 , the sensitivity of OST in identifying men at risk of osteopenia ranged from 75.0% for the femoral neck to 84.6% at the total hip. The specificity of OST was 58.4% for the femoral neck and 51.4% for the total hip. Conclusions: The performance of OST among this sample of men was acceptable. In the future, we need a bigger sample to validate the cut-off value for OST. We conclude that the fitted OST risk indice could be an effective and efficient tool to identify increased risk men for BMD testing.

P215SU. EVALUATION OF PREVALENCE OF OSTEOPOROSIS AND OSTEOPENIA IN MEN PRESENTING AT A MULTIPLE RISK DETECTION CAMPAIGN

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Objectives To describe the risk for osteopenia and osteoporosis in a population of men between 50 and 75 years old who presented at an age related multiple risk detection campaign.

Population and methods The Province of Liège has organized a multiple risk detection campaign for men aged 50 to 70. The participants were randomly selected from a database containing 100000 men. From the 1300 subjects who received an invitation, 183 presented for the multiple risk screening. The tests consisted, in a prostate cancer screening, an andropause screening, a physical performance tests and osteporosis screening. The subjects were also asked to perform a One Minute Risk Test (OMRT).

The osteoporosis screening was performed by DEXA (Hologic, QDR 1000+) at the total hip site and at the femoral neck. 162 subjects had a BMD performed. Correlations with the OMRT and the Osteoporosis Self-Assessment Tool were calculated.

Results The general characteristics of the population are as follows: mean age was 59.4 ($\pm$ 5.8) years, mean Total hip BMD was 1.007 ($\pm$ 0.170) g/cm^2, mean T-score at the hip was -0.172 ($\pm$ 1.128), mean femoral neck BMD was 0.821 ($\pm$ 0.130) g/cm^2, mean T-score at the femoral neck was 0.145 ($\pm$ 0.951). The mean OMRT score was 5.536 ($\pm$ 2.616).

The overall prevalence of osteoporosis was 9.25 % at the femoral neck and 1.25 % at the hip site. The prevalence of osteopenia was 30 % at the femoral neck and 8 % at the hip site.

Conclusion The prevalence of osteoporosis in the selected population appears to be lower than expected. As a result, systematic screening for osteoporosis using DEXA is not recommended in this age range. However, BMD measures inversely correlated with the OST, $r = -0.38$ for the femoral neck and -0.35 for the total hip.

OST is a very simple instrument which would be more suitable to use in such a screening campaign. Indeed it is easy to administer at low cost and resource investment and would give a good preliminary assessment of the osteoporosis risk in such a population.

P216MO. FRACTURE INCIDENCE AFTER FRAGILITY FRACTURES ADMITTED TO THE HOSPITAL

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Aims: To determine the incidence of new clinical fractures in patients admitted to the hospital because of a recent clinical fracture.

Method: We analysed all patients aged over 50 years with a fragility fracture who were treated in our hospital from January to September 2001. Data were collected from questionnaires sent to patients and research in the hospital database for patients who did

not respond or who had died since the fracture. The incidence of new fractures in a two-year follow up period was calculated.

Results: A total of 545 patients were treated, 8 were lost in follow up. 416 were alive and received a questionnaire. 121 Patients had died at the time of the investigation. The response rate of living patients was 81% (337 patients). The number of patients with a new fracture in this group was 52 (12.5%). The new fracture incidence was 10.7% in the group that had died (13 patients).

New fractures were grouped accordingly: upper extremity, lower extremity, wrist, hip, spine and other fractures.

There were 53 patients with recurrent fractures in 389 women (13.6%) and 12 patients with recurrent fractures in 148 men (8.1%).

Conclusions: Overall new fracture incidence during a 2-year period follow-up was 12.1%. These data indicate the need for prevention of new fractures in this high-risk group.

Table 1 Number of patients with incident fractures during follow up and location of fractures.

Location	*Baseline fractures*	*Follow up fractures*
Upper extremity	36	28
Lower extremity	24	32
Spine	4	13
Other	7	3
Hip	11	9
Wrist	19	10

P217SA. TREATMENT OF PATIENTS WITH PREVIOUS OSTEOPOROTIC FRACTURE FREQUENTLY OVERLOOKED IN HOSPITAL MEDICAL WARDS

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Background: Elderly patients with a past history of minimal trauma fracture have a significantly increased risk of further fracture. Current treatments for osteoporosis have been shown to reduce fractures in this high risk group.

Aims: To determine the prevalence of previous osteoporotic fracture in elderly female patients admitted to a general medical ward in a university affiliated, major teaching hospital, and to determine the rates of osteoporosis treatment, either prior to admission or initiated during the admission, in those patients with a fracture history.

Methods: Data were collected by chart review and brief interview of consecutive female admissions, aged 70 and over, to a general medical ward, in particular looking for documented evidence of previous minimal trauma fracture in the hospital chart. Other information, such as medication usage, history of falls and use of gait aid, was also collected.

Results: Over a 6 month period, data on 443 elderly female patients (mean age 83.1) was obtained. The prevalence of previous osteoporotic fracture was 40% with 11% having a history of hip fracture. Only 31% of patients with documented osteoporotic fracture were receiving any form of preventive treatment for future fracture, with supplemental calcium being the most commonly used medication. Anti-resorptive treatment with bisphosphonate or raloxifene was used in only 13% of these patients (6% of hip fracture patients).

Conclusions: Elderly female patients in a general medical ward have a high prevalence of previous osteoporotic fracture, but less than 1/3 are receiving any form of preventative treatment and less than 1/7 are receiving anti-resorptive agents. These patients are regularly reviewed by specialist physicians during their hospital stay, and so there is scope for substantial improvement in the management of this high risk group in order to try and prevent future fractures.

P218SU. RELATIONSHIP BETWEEN HEEL BONE ULTRASOUND, GRIP STRENGTH, AND INTAKE OF DAIRY PRODUCTS IN A POPULATION OF ELDERLY SWISS WOMEN: THE SEMOF STUDY

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Aims: In elderly postmenopausal women, fracture risk is multifactorial. Bone mineral density (BMD) of the hip and bone ultrasound (QUS) of the heel both predict hip fracture risk. Many independent risk factors for hip fractures have been identified in addition to BMD and QUS, i.e. age, weight, fracture after age 50, maternal hip fracture after age 50, smoking, use of arms to stand from chair, speed of gait, neuromuscular or visual impairments. Low grip strength has been considered as a major predictor for very low BMD. The effects of dairy products on BMD and fracture risk have been also demonstrated. But there is no data about the relationship between heel QUS and grip strength and intake of dairy products.

Methods: As a part of the multicenter SEMOF study, 4309 elderly Swiss women aged 75 ± 3 yrs (SD) have been assessed by heel QUS (Achilles+ BUA, GE Lunar). In addition, age, weight, intake of dairy products (proteins), chair test (3 trails), grip strength (Jamar hydraulic dynamometer), fracture history, were assessed. Chair test and fracture history have been considered as discontinuous variables, the other as continuous. The aim of this study was to assess the relationship between these variables, and heel QUS BUA (by ANOVA), the latter being a predictor of hip fracture risk.

Results: In this multivariate model age, weight, grip strength, dairy products intakes, chair test, and fracture history globally explained 20% of the variability of BUA ($p < 0.0001$).

Variable	Coefficient	SE	p-value
Constant (dB/MHz)	109.15	3.94	< 0.001
Age (years)	−0.41	0.05	< 0.001
Weight (kg)	+0.25	0.01	< 0.001
Grip strength (kPa)	+0.34	0.03	< 0.001
Dairy proteins (g/d)	+0.04	0.01	< 0.01
Chair test (missed)	−1.36	0.53	< 0.01
Fracture history (positive)	−2.80	0.28	< 0.001

Conclusion: In this population of elderly Swiss women, adjusted for age, weight, and fracture history, grip strength, intake of dairy proteins, and chair test were independent predictors of bone health, as measured by heel QUS BUA.

P219MO. REFERRAL PATTERNS TO A DEXA SCANNING SERVICE: FIVE YEAR FOLLOW-UP DATA

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Introduction: DEXA is the gold standard technique for the diagnosis of osteoporosis. The technique is becoming more widely available in Ireland. We run a referral-based DEXA service with access open to both inpatients and outpatients.

Methods: We present data from a longitudinal study performed over a five-year period (1998 to 2003). The DEXA database (Filemaker Pro 5.5) at the CAAU was interrogated to specifically assess referral patterns for this diagnostic test. All scans were performed by one of two specialist nurses on either a Lunar DPX 1Q or GE Lunar Prodigy machine. Referrals are taken from primary care or secondary care doctors.

Results: The results of 6579 successive, initial DEXA scans were analysed. Outpatient referrals accounted for 6184 (94%) of all referrals. 1975 (43%) of referrals come from male GPs and 2618 (57%) of referrals from female GPs(ratio of male to female GPs 2:1 in Limerick). Urban Limerick accounted for 3855 (70%) of Limerick referrals whilst rural Limerick accounted for 1599 (30%). Women accounted for 5987 (91%) of total referrals. 1513 (23%) and 2523 (38%) scans produced diagnoses of osteoporosis and osteopaenia respectively. The age profiles of scanned patients shows that most are between the ages of 46 and 65 years (57.1%).

The point prevalence rate of osteoporosis amongst public patients was twice as high as private patients (33% vs. 15%). The highest referring specialties, among secondary care consultants were Obstetrics and Gynaecology and Medicine for the Elderly.

Conclusion: More than 60% of those scanned had significant reductions in bone mineral density. Far fewer men are referred for DEXA than one would predict based on the known prevalence of the disease in men. There is gender bias in referral for DEXA, in terms of both patient and doctor. Urban Limerick is disproportionately represented. There is some evidence that self-selection for DEXA scanning takes place and may be influenced by socioeconomic status. The highest number of scans according to age-range corresponds to the group most at risk for vertebral fracture. Considerable education is needed to raise the awareness of osteoporosis diagnosis amongst specialties that are high steroid users.

P220SA. AN EDUCATIONAL INTERVENTION PROGRAMME IMPROVES THE UNDER-RECOGNITION OF VERTEBRAL FRACTURES AMONG GENERAL INTERNIST RESIDENTS

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Background: Vertebral fractures (VFx) are strong predictors of subsequent fracture risk, but they are largely under-recognized. As a consequence, spinal osteoporosis remains very often undertreated. In order to evaluate the impact of an educational intervention programme on the resident's recognition of VFx of patients hospitalized in the general internal medicine services, we prospectively evaluated VFX on collected X-rays routinely obtained upon patients hospitalization.

Methods: In an initial phase of 3.5-month-duration, we analyzed lateral spinal or chest X-rays of 405 consecutive inpatients ≥60 years. X-ray films were reviewed by two independent and trained physicians as investigators and VFx detected and graded according to Genant's semiquantitative method (SQ1,2,3). The results were compared with the radiologist's report as well as with the resident's discharge summary. In a second phase of 2-month-duration, all internists, but not radiologists, were actively educated to diagnose VFx using a broad range of lectures, posters and flyers. 284 inpatients were included and the percentage of VFx diagnosed was re-evaluated.

Results: Patient's characteristics: Phase 1: 405 patients included; 54% men, 46% women mean age ± SD: 76 ± 9; range: 60–97 yrs. Phase 2: 284 patients included; 56% men, 44% women; mean age ± SD: 76 ± 8; range: 60–100 yrs. Detection of patients with prevalent VFx by both investigators, internists and radiologists in Phases 1 and 2 was as follows (Table)

	PHASE 1			PHASE 2		
	Invest.	Intern.	Radiol.	Invest.	Intern.	Radiol.
Patients with VFx SQ 1+2+3	**n=88 (100%)**	**n=17 (19%)**	**n=26 (29%)**	**n=54 (100%)**	**n=20[#] (37%)**	**n=11 (20%)**
Patients with VFx SQ 2+3	**n=59 (100%)**	**n=13 (20%)**	**n=23* (39%)**	**n=41 (100%)**	**n=20[##] (49%)**	**n=10** (24%)**

*p=0.05 (vs. Intern.) ; **p=0.02 (vs. Intern.);
[#]p=0.02 (vs. Intern. in Phase 1); [##]p=0.005 (vs. Intern. in Phase 1)

Conclusions: Our results of this prospective survey do, at first, confirm the large under-recognition of VFx in hospitalized patients, even with moderate/severe VFx. Our educational programme did significantly improve the VFx detection by the residents as compared to the absence of any change among radiologists who did not benefit from the programme. This study demonstrates the need for and efficacy of such an in-hospital educational campaign and should be broadly implemented in order to improve both the detection of VFx and the therapy of osteoporosis.

P221SU. BONE MINERAL DENSITY IN ASIAN INDIAN WOMEN: IMPLICATIONS FOR DIAGNOSIS OF OSTEOPOROSIS

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Background: Genetics and ethnicity are the two most important determinants of bone mineral density (BMD), thereby necessitating the need for separate reference databases for different ethnic groups. We sought to establish the first BMD reference database for Asian Indian women so that appropriate comparisons can be made in evaluating individuals of Asian Indian origin for osteoporosis.

Methods: 401 apparently healthy women between the ages of 20–59 years from Lucknow, India, were recruited both to develop a reference database in order to calculate ethnic-specific T-scores and to determine age related bone loss. BMD was measured at the lumbar spine, hip, and non-dominant forearm by Hologic 4500 dual energy x-ray absorptiometry. Height, weight, BMI, age at menarche and menopause, and the estimated dietary calcium intake were determined in all subjects.

Results: BMD in Asian Indians was significantly lower than that of U.S. white women at all relevant measurement sites and across all age groups studied. There was the expected age-related decline in BMD. In the 75 women aged 20–29 years, the peak adult BMD reference group, BMD was 0.927 ± 0.097 g/cm^2 at the lumbar spine (L1–L4), 0.767 ± 0.090 g/cm^2 at the femoral neck, 0.839 ± 0.095 g/cm^2 at the total hip, and 0.590 ± 0.050 g/cm^2 at the forearm (distal 1/3 radius). When compared with U.S. white women, peak adult BMD was 10.6% lower at the left femoral neck and total hip; 11.8% lower at the lumbar spine; and 35% lower at the distal forearm. Dietary intake of calcium in Asian Indians in this reference group was 556.3 ± 253.2 mg/d.

Conclusions: At all measurement sites, BMD was significantly lower in Asian Indian women, as compared to U.S. white women, although the lower BMI, calcium intake, and vitamin D nutrition might explain some or most of this difference. Nevertheless, until the BMD-fracture relationship is established in this ethnic group, we recommend the use of the peak adult BMD from this study to calculate T-scores for Asian Indian women.

P222MO. RISK FACTORS FOR AND FREQUENCY OF OSTEOPOROTIC FRACTURES IN URBAN POPULATION OF ANTALYA

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Aims: The aim of this study is to determine possible risk factors for osteoporosis and frequency of osteoporotic fractures in Turkish urban citizens.

Methods: This cross sectional study was carried out in urban population of Antalya (508 840 inhabitants). By random cluster sampling 3173 individuals aged 16 and over were interviewed face to face. The individuals were subjected to a structured interview comprising questions on risk factors for osteoporosis. In postmenopausal women, information was obtained on decreased body height, hunchbacks and fractures. All statistical calculations (chi-square and logistic regression analysis) were carried out by SPSS version 9.05 for Windows.

Results: 1536 men and 1637 women were evaluated. Mean age was 37,7 ± 14,6 years. Of subjects, 655 (20,6%) were aged 50 or over, 234 (14,3%) women were postmenopausal (61 (26%) premature menopause). Mean birth number was 2,9 ± 1,9. The frequencies of the following variables showed significant difference between men and women (respectively): no walking 13% vs 18,2%, no exercise 65,2% vs 72%, low sun exposure 91,3% vs 68,4%, intake of tea 94,4% vs 92,7%, smoking 53,8% vs 24,3% ($p < 0,001$). History of any fracture was significantly higher in men (24,1% vs 13,4% $p < 0,001$)). In postmenopausal women there were 22 osteoporotic fractures (2 hip, 13 wrist, 4 vertebral and 3 rib). History of decreased body height, hunchbacks and use of medications for osteoporosis were found in 59, 41 and 42 postmenopausal women, respectively. 32 women had family history of osteoporosis. History of decreased body height, hunchbacks and wrist fractures were significantly higher in women with premature menopause ($p < 0,01$, $p < 0,01$ and $p < 0,05$, respectively). In multiple logistic regression analysis, calcium intake (based on consumption of dairy products) (OR: 0,052, 95% CI:0,03-0,87), tea

intake (OR:0,084, 95% CI:0,01-0,54) and premature menopause (OR: 13,191, 95% CI:1,88-92,56) were found to be significant determinants for wrist fractures.

Conclusions: In adult population of Antalya, despite its Mediterranean climate, sun exposure is still lower in women. Sporting activites were also lower in women. In postmenopausal women we found 22 osteoporotic fractures. Low calcium and tea intake and premature menopause were significant determinants for wrist fractures.

P223SA. SEVERE VITAMIN D DEFICIENCY AMONG PAKISTANI LIVING IN DENMARK

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Severe vitamin D deficiency leads to rickets in children and to osteomalacia in adults, muscle weakness and, through a decreased intestinal calcium absorption, probably also osteoporosis in the elderly. The best measurement of vitamin D status is serum 25-hydroxy vitamin D (S-25OHD). There is no international consensus on cut-off levels for vitamin D deficiency and vitamin D insufficiency. Here severe deficiency is defined as S-25OHD <10 nmol/l, deficiency as <25 nmol/l, and insufficiency as <50 nmol/l.

The aim of this study was to determine the vitamin D status in an immigrant group in Europe. The subjects were adolescent girls, women and men with Pakistani origin (immigrants or descendants) living in Denmark (55°N). This study includes baseline data from a one-year blinded placebo-controlled intervention study with two doses of vitamin D aiming at assessing the dose necessary to replenish vitamin D status and determining the effect on bone mass.

The table shows the median and percentile values of the S-25OHD concentrations. It also shows the percentages of the subjects who have S-25OHD concentrations below 10, 25, and 50 nmol/l, respectively. More than 4/5 of the girls and women are vitamin D deficient and more than 2/5 have severe deficiency. About 2/3 of the men have vitamin D deficiency and 1/8 have severe deficiency. Nearly all have vitamin D insufficiency.

	Girls	Women	Men
Number of subjects (*n*)	37	116	96
Age (years)[a]	12.2 (10.1–14.7)	36.2 (18.1–52.7)	38.7 (17.9–63.5)
Weight (kg)[b]	46.9 (9.5)	68.0 (14.2)	78.9 (10.9)
Height (cm)[b]	153.3 (6.6)	157.6 (5.4)	172.4 (7.5)
BMI (kg/m^2)[b]	19.9 (3.5)	27.4 (5.7)	26.6 (3.4)
S-PTH (pmol/l)[a]	3.9 (1.8–29.7)	3.6 (1.7–13.6)	3.3 (1.5–13.6)
S-TAP (U/l)[a]	508 (156–1346)	140 (55–290)	153 (84–331)
S-ionized calcium (mmol/l)[a]	1.29 (1.14–1.42)	1.25 (1.12–1.40)	1.26 (1.18–1.43)
U-calcium (mmol/l) [a]	1.74 (0.37–12.01)	1.38 (0.28–7.32)	1.95 (0.30–7.16)
S-25OHD (nmol/l) [a c d]	10.9 (1.8–51.2)	12.1 (2.3–61.2)	21.1 (3.0–62.7)
Percentile 5	1.9	4.0	7.2
Percentile 10	3.3	4.8	9.1
Percentile 25	5.2	8.0	14.8
Percentile 75	19.7	20.2	27.9
Percentile 90	32.7	31.8	35.4
Percentile 95	50.8	41.0	53.0
S-25OHD < 10 nmol/l	46%	40%	13%
S-25OHD < 25 nmol/l	81%	84%	64%
S-25OHD < 50 nmol/l	95%	97%	95%

[a]Median (range) [b]Mean (SD) [c]Analysed by HPLC [d]Significant difference ($P < 0.0001$).
BMI: body mass index, S-PTH: serum parathyroid hormone, S-TAP: serum total alkaline phosphatase, S-25OHD: serum 25-hydroxy vitamin D.
Morning blood samples were taken after an overnight fast, from January to October.

In conclusion, an alarming number of the Pakistani immigrants living in Denmark have severe vitamin D deficiency with possible serious consequences for the muscle function and the bone health.

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P224SU. POSTMENOPAUSAL BONE LOSS AT THE FOREARM: THE NORD-TRØNDELAG HEALTH STUDY, (HUNT-STUDY) NORWAY

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Aims: The purpose of this study was to estimate the postmenopausal bone loss at the forearm.

Methods: As part of a multipurpose population-based health study in the county of Nord-Trøndelag during 1995-97 (the HUNT study), a 30% random sample (N = 2136) of all women aged 50–59 years was invited for forearm bone densitometry (SXA technology). The measurements were performed at distal radius and ulna (10–20% trabecular bone) and ultradistal radius (50–70% trabecular bone). 82% of the women attended and they were invited to a follow-up study including a second bone mineral measurement (BMD) in 2001. Among the women with two BMD measurements (N = 1376) a study population with postmenopausal women (>1 year since menopause, YSM) reporting no history of hormone therapy was selected (N = 511). Average time between baseline and follow-up measurement was 4.6 years (sd = 0.5 year). The baseline and follow-up BMD measurements were analysed in a multiple regression model with age, weight (kg), change in weight (kg), height, YSM and seasonal effect as explaining factors.

Results: In cross-sectional analyses, YSM and weight were significantly associated to BMD at both sites. The BMD changed −3.2 mg/cm^2 (sd = 0.6 mg/cm^2) per one year increase in YSM corresponding to −0.7% at distal site and −0.9% at ultradistal site. In longitudinal analyses, the annual bone loss was 5.5 mg/cm^2 (sd = 1.8 mg/cm^2) and 6.0 mg/cm^2 (sd = 1.9 mg/cm^2) at distal and ultradistal site, respectively, corresponding to 1.2% at distal site and 1.7% at ultradistal site. The bone loss was negatively associated to baseline weight (0.3 mg/cm^2, sd = 0.07 mg/cm^2) at both sites. Further, the ultradistal bone loss was negatively associated to YSM (0.5 mg/cm^2, sd = 0.2) and to weight gain (2.5 mg/cm^2, sd = 0.5 mg/cm^2). At ultradistal site, there was a reduction in bone loss along with reduced baseline level of BMD, which was not found at distal site.

Conclusions: Bone loss is significantly associated with body weight at baseline. At ultradistal site the bone loss is reduced by weight gain and number of years since menopause. The longitudinal change in BMD is larger than the cross-sectional bone loss both at distal and ultradistal site.

P225MO. HIGH PREVALENCE OF VITAMIN D DEFICIENCY AND SECONDARY HYPERPARATHYROIDISM IN AN ELDERLY POPULATION IN THE CITY OF SÃO PAULO, BRAZIL

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Osteoporotic fractures, mainly at the hip are events of high morbi-mortality in elderly population. European and American studies show correlation between these fractures, vitamin D deficiency and secondary hyperparathyroidism. In Brazil, a sunny country, vitamin D deficiency was never thought to be a common problem. We evaluated 422 patients: 180 (122 women and 58 men) living in nursery homes for at least 6 months (group A) with a median age of 76 years old(yo) (60–100yo), and 242 patients (168 women and 74 men) who live in their own houses (group B) with median age of 79yo (61–93yo). A third group (C) of young healthy volunteers (median 32yo) was used as control. We excluded recent bedfast patients or those with renal or hepatic insufficiency.

Fasting blood samples were collected for intact-PTH (normal range (NR): 10–70 pg/ml), 25-hydroxivitamin-D3 (25OHD) (NR: 16–74 ng/ml) and ionized calcium (Cai) (NR: 1.20–1.40 mM). All patients had a quantitative calcaneus ultrasound measurement (USQ-Sahara, Hologic). The data are presented as mean ± standard deviation. Statistics analyses: Mann-Whitney test and Spearman correlation. A $p < 0.05$ was considered significant.

The mean values of 25OHD were 15.2 ± 0.96ng/ml for groups A, 18.9 ± 0.8ng/ml for group B and 37.8 ± 13.7ng/ml for group C. 25OHD was below the normal range in 54% of the patients of group A and in 35.5% of the patients of group B but in none of group C. The PTH levels were higher at group A (99.6 ± 5.9 pg/ml) than B (88.4 ± 3.8 pg/ml) and C (46.1 ± 19.3pg/ml). The median of Cai also differ between the three groups (A = 1.29 ± 0.004 mM; B = 1.25 ± 0.04mM; and C = 1.20 ± 0.05mM. Elevated Cai (> 1.40 mmol/l) associated to high levels of PTH was observed in 7 cases (4%) of group A and 6 cases (2.7%) of group B. The Broad Ultrasound Attenuation were lower in group A compared to group B ($p < 0.0001$), and showed a positive correlation with 25OHD ($r = 0.12$; $p = 0.05$) when both groups were analyzed together.

This study showed a high prevalence of vitamin D deficiency and secondary hyperparathyroidism in this studied population and it was more severe in patients living in nursery homes.

According to this study, São Paulo elderly population should be advised to intake vitamin D.

P226SA. DISTRIBUTION AND CORRELATES OF SERUM VITAMIN D LEVELS IN A SAMPLE OF HIP FRACTURE PATIENTS

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Aims: To assess the distribution and correlates of serum 25,OH vitamin D levels in 392 women and men with hip fractures.

Methods: 25,OH vitamin D levels were measured among 312 enrolled from 392 screened subjects from 50 clinical centers worldwide who had undergone surgical repair of a hip fracture in the preceding 90 days. Male and female subjects at least 50 years old were part of the HORIZON RFT trial, a randomized, placebo-controlled, double-blind trial testing the efficacy of a yearly intravenous bisphosphonate, zoledronic acid, in preventing new clinical fractures in patients with recent hip fracture repair. At screening or randomization, demographic data, and laboratory values for calcium, phosphorous, and creatinine were determined.

Results: Among patients screened, levels of 25,OH vitamin D were low (median = 14.7 ng/mL, IQR = 21.65,7.60), and 51% were at or below the clinically meaningful threshold of 15 ng/mL. Further, level of 25,OH vitamin D was slightly lower in those who were screen failures (13.85 ng/mL vs. 15.05 ng/mL, $p = 0.31$, by Wilcoxon rank sum test). Among those enrolled and randomized, in bivariate analyses by Spearman correlation, level of 25,OH vitamin D was related to male sex ($p = 0.04$), but not to age, race, body mass index (BMI), home as place of residence, screening calcium level, alkaline phosphatase, or creatinine. In multivariate models predicting levels less than 15 ng/mL, higher calcium and creatinine levels were significantly related to low levels of vitamin D (OR = 0.74 (95% CI = 0.54,0.99), 0.96 (95% CI = 0.93,0.99) respectively).

Conclusions: In 312 of 1714 eventual subjects with recent hip fracture enrolled in an ongoing clinical trial, 51% of subjects had insufficient 25,OH vitamin D concentrations. Low vitamin D has important implications for healing and repair of fracture, and, possibly, in preventing subsequent fractures. Physicians should be encouraged to check and monitor levels of vitamin D as well as to treat for vitamin D deficiency in patients experiencing a low trauma hip fracture. This trial will provide important information on the potential additional benefits of an active treatment, zoledronic acid, among this patient population, in whom vitamin D deficiency has been corrected.

P227SU. OSTEOPOROSIS AND EFFECTS ON QUALITY OF LIFE

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Aim: To determine if there is any association between functional status, quality of life and osteoporosis in elderly patients.

Method: Total number of 1247 patients over 64 years old were admitted to Hacettepe University Geriatric Medicine outpatient clinic between February 2002 and July 2003. Osteoporosis diagnosis were made by measuring bone mineral density of every patient. Functional status and quality of life of all patients were evaluated by means of geriatric evaluation scales such as Daily Life Activities Scale, Instrumental Daily Life Activities Scale, Geriatric Depression Scale (GDS), Mini Mental State Examination Test (MMSE) and Mini-Nutritional Status Scale.

Results: 783 female and 464 male patients were examined according to quality of life and osteoporosis. 176 (24.5%) of all osteoporotic cases got a score of less than 24 in MMSE test whereas only 11 (8.7%) patients with normal bone density got a score of < 24 ($p < 0.001$). Mini-Nutritional Status Scale scores did not differ between osteoporosis, osteopenia and normal groups ($p = 0.061$). Daily Life Activities Scale and Instrumental Daily Life Activities Scale scores were not found to be associated with osteoporosis ($p = 0.076$ and 0.755 respectively). 237 (33%) of the osteoporotic patients, 29.5% of osteopenic, 20.6% of normal patients got a score of > 5 in GDS. This difference was statistically significant in favor of osteoporosis ($p = 0.018$). When male and female patients were examined separately, the significant difference in MMSE scores was not found in male patients. In females, 29.8% of the osteoporotic cases got low score in spite of only 13.3% of normal cases geting low MMSE scores ($p = 0.002$). In comparison of osteoporosis and Daily Life Activities Scale, Instrumental Daily Life Activities Scale, Mini-Nutritional Status Scale according to gender no significant difference was found.

Conclusion: Our study showed there was not any significant correlation between Daily Life Activities Scale, Instrumental Daily Life Activities Scale and Mini-Nutritional Status Scale, while there was a statistical relation between MMSE and GDS scores and osteoporosis. Osteoporotic patients should be evaluated with quality of life tests spesific for osteoporosis.

P228MO. WRIST FRACTURE MEDICAL IMPACT

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Aims: To analyse fracture features and medical decisions related to wrist fracture (WF).

Methods: From a database of 30,000 women who had undergone a bone mineral density (BMD) assessment of lumbar spine and femoral neck, we extracted a population of 1,229 postmenopausal (PM) women with WF and did a retrospective, cross-sectional study.

From this latter group, we only analysed the ones who referred having fallen from their height (n = 1,151). A physician, specially trained, asked each and every one of them about her demographic characteristics, fracture-related factors and post-fracture medical indications (validated questionnaire/data referred by the patient).

W.H.O. criterion for osteoporosis (OP) was applied on the region with the lowest T-score value

Results: Demographic characteristics (mean values): Age: 71 years (R: 51–101); Menoage: 47 years (R: 22–55); Height: 154.3 cm (R: 127–174); Weight: 67.38 kg (R: 34.7–103); BMI: 28.31 (R: 14–44.7). Age at the moment of WF: 62 years

HRT use:n = 192 (16.68%).

Preventive Measures:Dairy Products: 552 (48.82%) daily; 428 (38.05%) sometimes; 171 (15.8%) never/Solar Exposure: 235 (20.31%) daily; 660 (57.34%) sometimes; 256 (22.32%) never/Physical Activity: 611 (53.51%) daily; 431 (37.61%) sometimes; 109 (9.47%) never

Other osteoporotic fractures: n = 126 (10.94%) Height loss: n = 529 (45.96%); average loss = 4 cm

Maternal background related to OP: Height loss: n = 475 (41.26%); Hip fracture: n = 123 (10.68 %)

Place where she fell/fractured:Outdoors, n = 775 (63%)

Post-fracture medical indications: BMD referred by the physician in n = 324 (28.14%). Diagnosis: OP n = 137 (11.9%); osteopenia n = 111 (9.64%); normal n = 57 (4.95%); unknown n = 19 (1.65%).

Drug Treatment: n = 695 (60.38%) had taken a drug. From this group, 438 (63.03%) received treatment without a BMD study[Calcium n = 181(41.32%); Bisphosphonates and Calcium n = 155 (35.38%)] and 257 (36.97%) received treatment with a BMD study [Calcium n = 63(24.51%); Bisphosphonates and Calcium n = 135 (52.52%)]

Current BMD: diagnosis: OP n = 529 (45.96 %); osteopenia n = 522 (45.35%); normal n = 90 (7.81%).

Conclusions: A BMD study after they had fractured was indicated to only 28% of the women.

Drug treatment was NOT indicated to 40% of the women (with and without previous BMD assessment). This suggests that WF is NOT considered an osteoporotic event.

P229SA. CROSS-SECTIONAL STUDY OF BONE MINERAL DENSITY IN JIA PATIENTS IN EARLY ADULTHOOD

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Aims: To ascertain lumbar and femoral bone mineral densities (BMD) in patients with juvenile idiopathic arthritis (JIA) in early adulthood.

Methods: BMD was measured at the lumbar spine (L2-L4) and at the proximal femur by dual energy x-ray absorptiometry (DEXA).

Patients, who initially had been diagnosed JIA at the Rheumatism Foundation Hospital during the years 1976–95, were called for a check-up. 116 patients (83 women and 33 men), 21 to 25 years of age, were re-examined in 2002. The mean age of the patients was 7.8 SD 4.5 years at the disease onset. The median interval from disease onset to the re-examination was 16 (range 6–23) years. The patients were divided into three subgroups: oligoarthritis (N = 74), extended oligoarthritis (N = 15) and polyarthritis (N = 27).

Results: Only patients in the extended oligoarthritis subgroup had decreased mean BMD values in the lumbar spine (T-score −0.73, 95%CI: −1.49 to 0.03,). Patients in the extended oligoarthritis and polyarthritis subgroups were found to have low BMD values in the femoral neck, (T-score −0.33, 95%CI: −0.71 to 0.06, and −0.60, 95%CI: −1.12 to −0.08, respectively). A BMI-adjusted difference was found only at the femoral neck between the three subgroups (Figure). Three patients of 116, 2.6%, (95%CI: 0.5 to 7.4) were diagnosed to suffer from osteoporosis, (T-score ÿ≤ −2.5).

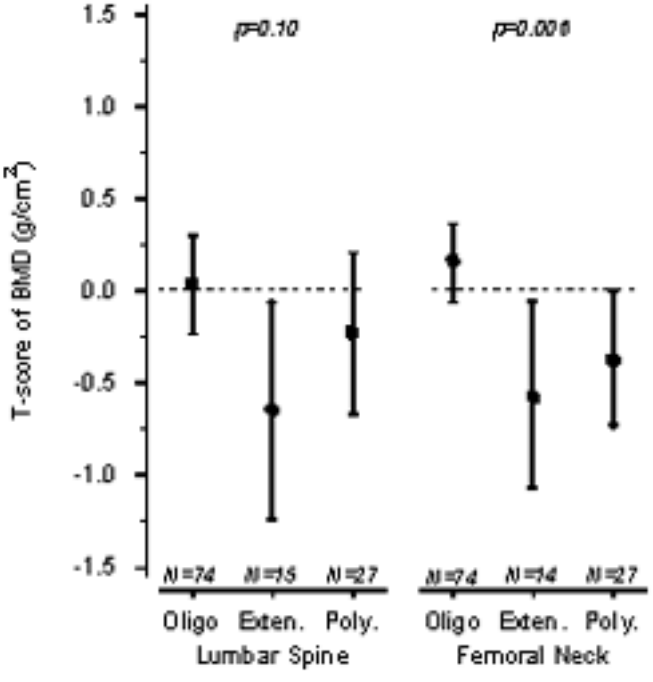

Fig. 1 BMD (T-score) in the lumbar spine and femoral neck of the JIA subgroups

Conclusions: Central bone mineral densities seem to be decreased among adult patients with JIA. The extended oligoarthritis and polyarthritis subgroups seem to thrive worse than the oligoarthritis subgroup. This may have clinical relevance among those patients in later life.

P230SU. AWARENESS, KNOWLEDGE, RISK FACTORS AND CURRENT TREATMENT OF OSTEOPOROSIS IN A BRAZILIAN COHORT OF ELDERLY SUBJECTS

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Aims: To determine differences between the two cohorts and detect differences between men and women as well.

Patients and methods: We evaluated awareness, knowledge, risk factors and current treatment of osteoporosis in 54 consecutive seniors attending an educational/social program for elderly people and 56 elderly subjects living in a nursing home, in São Paulo, Brazil. Subjects included were 90 women and 20 men, with an average age of 76 years. All participants answered an interviewer-administered questionnaire regarding osteoporosis awareness, risk factors and treatment.

Results: Most of the subjects from the nursing home (44%) had finished high school, while the majority of seniors attending the educational program (55.5%) had not completed elementary school. 96% of all subjects were aware of osteoporosis and 49% gave the correct definition. In spite of the different educational backgrounds, awareness of osteoporosis and its correct definition were not different between the two groups, neither between men and women. Television, friends and physicians were identified as the main source of information, especially among women. Most of the subjects (78% and 79%, respectively) were aware that osteoporosis could affect men and that diet was important. In all, 80% knew that osteoporosis could be prevented, and this was less in the nursing home group ($p < 0.001$). Women believed that they could get osteoporosis more than men ($p < 0.001$). Besides old age and estrogen deficiency associated with menopause, the most prevalent risk factors included familial history of fractures (FHF)(19%), past smoking (30%) and previous fractures (13%). FHF and previous fractures were both more common among seniors attending educational program than between subjects from a nursing home ($p < 0.05$) and among women compared to men ($p < 0.05$). Only 25% of the subjects were using specific treatment for osteoporosis and were taking calcium supplements. Our results demonstrate a high level of awareness and accurate definition of osteoporosis in a Brazilian cohort of elderly people.

Conclusions: The study shows that educational programs can provide specific information for elderly people that might influence the management of osteoporosis. Specific therapy and prevention measures for osteoporosis were inappropriately low for this group of subjects at high risk of osteoporosis.

P231MO. STRUCTURAL-FUNCTIONAL STATE OF BONE TISSUE IN SPORTSWOMEN OF HIGH PROFICIENCY: DATA ULTRASOUND DENSITOMETRY

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Modern sports medicine is particularly interested in solving problems connected with ''sportswomen's triad'' arousing out of great physical loading and incorporating disorders in nutritional habits, secondary amenorrhea and structural-functional disorders of bone tissue (osteopenia, osteoporosis). To study state of bone tissue in sportswomen of high profi-ciency, 45 girls aged 12–16 years old (I gr.) continually going in for sports games (handball, volleyball) and 15 girls aged 12–17 years old (mean age 14,1 ± 0,4 years; height 1,45 ± 0,15 m; weight – 35,6 ± 1,3 kg; BMJ 24,7 ± 0,7) members of Ukrainian national team practising gymnastics (II gr.). Control group (CG) was made up by healthy girls

Data	All group	45–49 years	50–54 years	55–59 years	60–64 years	65–70 years
SOS, m/s	1541.3 ± 29.1**a**	1547.5 ± 27.0 **a**	1554.3 ± 30.0**a**	1544.4 ± 29.3**a,b**	1534.7 ± 22.2**a,b,c**	1520.5 ± 28.5**a,b,c**
BUA, dB/MG	106.5 ± 11.0**a**	107.6 ± 10.8**a**	110.5 ± 10.4**a**	106.9 ± 10.1**a,b**	104.9 ± 10.5**a,b,c**	101.1 ± 13.0**a,b,c**
Stiffnes, %	82.6 ± 13.7**a**	84.9 ± 12.8**a**	88.7 ± 14.0**a**	83.8 ± 12.8**a,b**	76.9 ± 11.1**a,b,c**	73.2 ± 14.8**a,b,c**

Notes: $p < 0.05$ (**â**– compared with women aged 40–44 years in premenopausal period, **â**- compared with women aged 50–54 years in postmenopausal period, **c**- compared with women aged 55–59 years in postmenopausal period).

standardized for age, not going in for sports. To assess structural-functional state of bone tissue ;Achilles + ; ultrasound densitometr was used (Lunar Corp.). Speed of ultrasound spreading (SOS, m/s), broadband ultrasound attenuation (BUA, dB/MHz) and Stiffness Index (SI, %) were determined. Analysis of the obtained results has shown that Stiffness Index of bone tissue in girls of I st gr was significantly higher than that of CG irrespective of the age (fig.). Indexes of structural-functional state of bone tissue in gymnasts were considerably higher than those of CG (SOS: 1611 ± 28 m/sec ; by 2,1%; BUA: 108,7 ± 1,6 dB/MHz ; by 5,6%; SI: 107,1 ± 3,by 3% 11; by 14,3%). It means that their bone tissue stiffness was higher compared to representatives of Ukrainian population of the same age. Sports connected with great achievements witnesses many young sportswomen (gymnasts, in particular) having late menarche, arrested sexual development possibly promoting osteopenia and osteoporosis in future. Gymnasts of high proficiency may have hormonal disorders annihilated by constant physical loading leading to in-crease in number and size of trabecular and improve stiffness of bone tissue. Thus, our studies have revealed positive influence of intensive physical leading on structural-functional state of bone tissue in sportswomen of high proficiency.

P232SA. OSTEOPOROSIS IN TURKISH ELDERLY MEN

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Introduction: Although osteoporosis is less frequent in men than women, morbidity and mortality due to osteoporotic fractures are more in men than women. Geriatrists should not only focus on female osteoporosis, but also on men.

Aim: The objective of this study is to determine the frequency of osteoporosis in male patients who were admitted to our Geriatric division, to compare the frequency of osteoporosis between men and women and to examine the related factors.

Method: Total number of 464 male patients over 64 years old were admitted to our outpatient clinic between February 2002 and July 2003. Bone mineral density (BMD), serum 25OH-vitamin D and intact parathyroid hormone (iPTH) levels were calculated in every patient. Calcium intake, history of any fracture, smoking and alcohol habits, have been questioned. Statistical analysis were made by chi-square method.

Results: In examined 464 male patients, 213 osteoporosis case were determined. None of the subjects were on steroid medication, and the other causes of secondary osteoporosis were excluded. 213 (45.9%) of male patients had osteoporosis, 170 (36.6%) had osteopenia. When examining osteoporotic men, serum 25OH-vitamin D levels were low in 8 (1.7%) patients, iPTH levels were high 29 (6.3%) patients. 380 (81.9%) of them had no or low intake of calcium. In statistical analysis, the relation between smoking, alcohol consumption, history of fracture and osteoporosis and osteopenia was not significant. Whereas the finding that osteoporosis is more frequent in men who made no exercise was statistically significant, the relation between smoking and osteoporosis was not. 4.2% of osteoporotic men had body mass index (BMI) of greater than 30 and 22% of BMI greater than 30 had osteoporosis. The negative correlation between osteoporosis and BMI was statistically significant. Serum 25OH-vitamin D and iPTH levels were not different between patients who had osteoporosis diagnosis and those who had not.

Discussion: Osteoporosis incidence in men increases with advanced age. To prevent the morbidity and mortality resulting from osteoporotic fractures, we should be aware of this reality and take precautions on time. In geriatric age group, male patients should also undergo BMD measures once every two years.

P233SU. OSTEOPOROSIS IN A GROUP OF TURKISH GERIATRIC WOMEN

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Introduction: Prevalence of osteoporosis and risk of fragility fractures may vary between countries according to social, cultural and economic factors. In Turkey limited exposure to sunshine, increased prevalence of obesity among women may affect osteoporosis prevalence.

Aim: To determine the frequency of osteoporosis in patients older than 64 years of age who were admitted to our outpatient clinic, to examine the related factors and to help forming our national data.

Method: Total number of 783 female patients who were admitted to Geriatrics Unit and whose bone mineral density (BMD) have been determined between February 2002 and July 2003 were enrolled in this retrospective study. Calcium intake, history of any fracture, smoking and alcohol habits, physical activity, education status have been questioned. Their serum 25OH-vitamin D and intact parathyroid hormone (iPTH) levels were obtained.

Results: In examined 783 female patients with mean age of 71.34, 507 osteoporosis cases with mean age of 71.82 were determined. It was observed that 507 (64.8%) of them had osteoporosis, 232 (29.6%) had osteopenia. 325 (64.1%) of osteoporotic women had no or low calcium intake, 81.1% never smoked, 97.2% had no alcohol consumption. 17.7% of the osteoporotic women had a BMI greater than 30 and among obese women (BMI > 30) 58.8% had osteoporosis, 30.7% had osteopenia. 71.5% of illiterate women had osteoporosis diagnosis and 36% of the osteoporotic women were found to be illeterate. The negative correlation between education status and osteoporosis was statistically significant ($p = 0.017$). Serum 25OH-vitamin D levels were low in 20 (10.2%) of osteoporotic women, iPTH levels were high in 50 (25.5%) of them. 25OH-vitamin D levels were normal in all of the patients in normal group. Nevertheless, relation between 25OH-vitamin D, iPTH and osteoporosis was not significant.

Discussion: Although it is known that body weight is negatively correlated with osteoporosis, interestingly 17.7% of our patients with osteoporosis had BMI greater than 30. To prevent the morbidity and mortality resulting from osteoporotic fractures, we should be aware of this fact and take precautions on time.

P234MO. RISK OF FRACTURE IN PATIENTS WITH AND WITHOUT HYPERTENSION IN THE NORTH OF PORTUGAL

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Backgrounds: Many studies have examined the relationship between presence of hypertension (HT) and bone density. However, fewer studies have examined the risk of fracture in hypertensive patients.

Aims: The aim of our study was to evaluate the incidence of hip and vertebral fractures in patients with and without HT admitted to a central hospital in the North of Portugal between 1989 and 2002.

Materials and Methods: We retrospectively analysed data from all patients aged 25 years or older who satisfied the International Classification of Diseases (9th version) criteria for HT, hip and vertebral fractures. Discharge summaries were obtained for all subjects with hip and vertebral fractures who had been admitted to the hospital between January 1989 and December 2002. Results are expressed as means ± SD or percentages. Statistical analysis was performed with Student's t-test, Chi^2 test or Fisher exact test. P values <0.05 were used to indicate statistical significance.

Results: A total of 644884 admissions were registered during the studied period. There were 38112 admissions with a diagnosis of

fractures without HT and 1300 admissions with a diagnosis of fractures and HT. Hypertensive patients [42.5% men (M) and 57.5% women (W)] were significantly older than normotensive patients (48.4% M and 51.6% W) (73.6 ± 2.6 vs 43.6 ± 3.7 years, $p < 0.001$). The duration of hospitalisation was significantly higher in hypertensive than in normotensive patients (21.4 ± 6.9 vs 12.1 ± 2.6 days, $p < 0.001$). There were no significant differences in the incidence of vertebral fractures in hypertensive and normotensive patients (0.5% vs 0.4%, p = NS). The incidence of hip fractures was significantly higher in hypertensive than in normotensive patients (29.2% vs 12.1%, $p < 0.001$).

Conclusions: This study indicates that HT is a risk factor for hip fractures, suggesting that fracture prevention efforts should be a consideration in the treatment of hypertensive patients.

P235SA. EXAMINATION OF THE EFFECT OF DIETARY HABITS ON BONE MINERAL DENSITY IN HEALTHY MEN AGED 15 TO 49 YEARS LIVING IN THE CITY OF DEBRECEN.

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Introduction: Diet is known to be one of the most important predictors of bone mineral density, the aim of the present study is to characterize the dietary habits and examine its effects on bone mineral density (BMD) in a healthy male population aged 15–49 years.

Patients and Methods: The local population based register was used to select a population based random sample. Subjects with history of non-traumatic fracture, a longer than 3 month history of chronic disease affecting bone metabolism were excluded. A modified version of the WHO osteoporosis questionnaire was used to interview the participants about daily dietary calcium, protein, carbohydrate, fat and energy intake. BMD was measured at the L2-L4 lumbar spine and the femur using the Lunar DPX-L DEXA densitometer.

Results: A total of 177 (average age 39.9 ± 8.7 years) men were enrolled in the study. It was not possible to estimate peak bone mass due to the marked fluctuation in mean BMD across the 5-year age-bands (15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49 years). The mean spine BMD was lowest in the oldest age-band. Mean femoral neck and trochanter BMD was highest between 25–29 years and gradually decreased with age, the lowest values being seen in the 35–39 years age-band. There was significant correlation between L2-L4 BMD and daily dietary calcium ($r = 0.273$, $p<0.001$) and protein ($r = 0.163$, $p = 0.030$) intake; femur neck BMD and daily dietary calcium ($r = 0.271$, $p<0.001$), protein ($r = 0.228$, $p = 0.002$), fat ($r = 0.188$, $p = 0.012$), and energy ($r = 0.172$, $p = 0.022$) intake.

Conclusion: Our findings suggest that among the dietary components examined the daily dietary calcium, protein, fat and energy intake correlated significantly with femur neck BMD and only the daily dietary calcium and protein intake correlated with lumbar spine BMD. The knowledge of dietary components best responsible for a healthy bone mass may help formulate adequate diet oriented preventive strategies in those between 15–49 years of age as such reduce the burden of osteoporosis later in life.

P236SU. BASIC AWARENESS ON OSTEOPOROSIS AND THE RISK FACTORS FOR THE DISEASE AMONG COVERED WOMEN

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Objective: This study was designed to evaluate the basic awareness level among covered women above 40 years of age, and to find out the risk factors for osteoporosis and osteopenia in them.

Design: 517 covered women, who live in Istanbul, Turkey, were included in the study. Questionnaires were applied by interviewers and the bone mineral density (BMD) measurements were done with DXL (Calscan).

Results: The mean age of 517 women was 49.5 ± 7.4 years. Mean height, bodyweight and body mass index were; 154 ± 5.3 cm; 77.7 ± 12.5 kg; and 32.8 ± 5.2 kg/m^2, respectively. Education and socioeconomical levels were low in these women.

Most of the women (59.8%) heard the name of the disease (OP), and the majority (60.6%) learned it from their friends, 12.3% from the doctors, and 7.3 from the media. However, only 6.2% had enough information about OP.

The most common concomitant diseases in this study group were hypertension (18.3%), gastric ulcer (9%), rheumatoid arthritis and osteoarthritis (6.1%), and diabetes mellitus (4.7%). Continued drug use among our study population is relatively high: 30.2%. The ratio of birth control pill use was 23.2%, and 18.8% were given hormone replacement therapy (HRT) after their menopause. The ratio of women who had hysterectomy and/or oopherectomy was very high (16%). The ratio of women, who had history of one fracture, was 11.4%. Only 6.8% regularly perform exercises. Physical activity levels of these women both between 15–25 years of ages, and 25–50 years age were higher.

There was a significant relation between the bone mineral densities and physical activity level ($p < 0.05$). No significant relation was found between BMD's and performance of regular exercises, concomitant drug, birth control pill, and HRT uses, and smoking status.

Osteoporotic patients had a significantly higher rate of history of fractures ($p < 0.05$). The ratio of fractures among covered women who were osteoporotic were common around wrist/forearm. Hip fractures were rare.

Conclusion: Covering can effect vitamin D synthesis and calcium absorption. Education and socioeconomic level among covered women was lower. Peer education is important for informing these women about OP. There is a relation between physical activity level and osteoporosis among covered women.

P237MO. PREVALENCE OF OSTEOPENIA (MILD, MODERATE, SEVERE) AND OSTEOPOROSIS IN 4000 ARGENTINE POSTMENOPAUSAL WOMEN

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Aims: To analyse the prevalence of densitometric diagnoses in ambulatory postmenopausal women and its relation with demographic characteristics.

Methods: Descriptive, cross-sectional study. From a database of 25,510 women who participated in a free osteoporosis detection campaign with BMD assessment and answered a questionnaire, a computer software selected at random 4,000 patients (1,000 for each age decile = 50–59, 60–69, 70–79 and ^{3}80). Diagnoses: Based on the region (lumbar spine /femoral neck) with lowest T-score value (WHO criteria). Osteopenia was classified in mild (T-score −1.0 to −1.49), moderate (T-score −1.5 to −1.99) and severe (T-score −2.0 to −2.49).

Results: Demographic Characteristics (mean/SD): Age: 69.41 ± 9.94 years, Menoage: 19.62 ± 10.55 years, Body Mass Index: 28.06 ± 4.5, Weight: 66.99 ± 11.26 kg. and Height: 1.54 ± 0.06 cm. Densitometric Diagnoses (table 1)

Table 1.

Prevalence in % (n)

Age decile	*50–60*	*60–70*	*70–80*	*80–99*	*Total*
Osteoporosis	*20.8 (208)*	*33.3 (333)*	*40.2 (402)*	*45.6 (456)*	***34.97 (1399)***
Osteopenia	*52.6 (526)*	*51.5 (515)*	*51.4 (514)*	*48.8 (488)*	***51.05 (2043)***
Normal	*26.6 (266)*	*15.2 (152)*	*8.4 (84)*	*5.6 (56)*	***13.98 (558)***

Osteopenia classification: severe 19.32%; moderate 17.75%; and mild 14%.

The prevalence of fractures in severe Osteopenia was not different from Osteoporosis ($p = 0.103$) This was also seen in BMI (28 vs 26), Menoage (16 vs 22), and Age (66 vs 71).

Conclusions: 1) The prevalence of Osteoporosis is similar to the one defined in other international studies. 2) We deemed important

to classify Osteopenia in groups, because fracture risk is higher in Severe Osteopenia. 3) Following the guidelines of previous consensus, BMD measured in only one region, does NOT allow to diagnose Osteoporosis in 19.15% of the women <65 years'old and in 27.51% of the women ^{3} 65 years'old.

P238SA. VALIDATION OF A QUESTIONNAIRE ABOUT RISK FACTORS FOR THE DIAGNOSIS OF OSTEOPOROSIS

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We evaluated in a previous study the predictive value of risk factors related to osteoporosis in a population of 785 women designing a score for diagnostic purposes (score OPAR, osteoporosis Argentina). The aim of the present study is to validate the OPAR score.

Patients and methods: Score was built, including body mass index, age, early onset menopause, history of atraumatic previous fractures, concomitant diseases and chronic use of glucocorticoids.

502 postmenopausal women were included. DEXA (Lunar DPX alpha) measurements were determined in all of them (lumbar spine LS, and proximal femur PF).Statistical analysis was performed by multiple logistic regression to evaluate the association of risk factors as predictors of low bone mineral density values according to T score (WHO classification 1994). OPAR score ranged from 0 to 9 points according to the number and type answers to the risk factors – based questionnaire.

Results: 138 out of the 502 women (27.49%) presented osteoporosis (T score below −2.5 in LS or PF). OPAR score correlated with the diagnosis of osteoporosis (e.g. OPAR 3.5 to 4 = probability of OP 45.5%, OPAR 4.5 or greater than 4.5 = probability of OP is 65.7%)

Area under curve (AUC) was 0.7318.

For practical purposes we propose a cut-off value (cut-off value = 3 points; sensitivity = 63%, specificity = 71.7 %, positive predictive value 45.79% and negative predictive value 83.65%).

We conclude that OPAR is a useful score to focus bone mineral density measurements requests based on risk factors for osteoporosis. After applying OPAR score one out of two women had osteoporosis according to the WHO criteria. This score might be used for general practitioners as a useful tool to identify women to measure bone mineral density in a cost-effective fashion.

P239SU. THE INFLUENCE OF BODY COMPOSITION ON BONE MINERAL DENSITY OF BRAZILIAN WOMEN

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Bone mineral density (BMD) is under the influence of body composition (BC), mainly fat and lean mass, and also it depends on race. Considering that Brazilian people is composed of a wide variety of races, including black, white and mestizos, we studied the influence of BC in BMD of Brazilian women, according to the status of menopause and race. 160 women (90 white and 72 nonwhite) from 20-79 years old were studied. Dual energy x-ray absorptiometry was used to measure the total BMD (TBMD), lumbar spine BMD(LBMD), femur BMD (FBMD), fat mass (FM)and lean mass (LM).

Variables were evaluated as descriptive patterns using mean, standard deviation, median, minimum and maximun values. For the comparison of means of TBMD, regional BMDs and measures of body composition according to status of menopause and race, analysis of variance to one factor was used. For multiple comparisons we used Tukey-HSD test. To compare the difference of means between the variables of white and nonwhite women, the Student t-test was used. The homogeneity of variance was evaluated by Lavene test and the adherence to normal curve by Kolmogorov Smirnov test. Correlation among variables was estimated utilizing the coefficient of Pearson correlation. Multiple regression analysis was carried out to verify the effect of altogether significative correlation found. We concluded: 1) there were no significant differences when we compare the means of LBMD and FBMD between the 162 white and nonwhite women, 2) the mean of TBMD in nonwhite premenopausal women was higher than the mean of white women in the same group, 3) in white premenopausal women the body mass index was the greatest determinant of BMD on all studied regions, 4) in nonwhite premenopausal women lean mass was the greatest determinant on TBMD and on LBMD, while on FBMD it was the age, 5) fat mass was an important determinant of BMD in white postmenopausal women on all studied regions, 6)in nonwhite postmenopausal women lean mass was the significant determinant on TBMD and regional BMDs.

P240MO. FEEFING PATTERNS OF ADOLESCENTS ATTENDING PUBLIC TEACHING CENTERS IN URUGUAY

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Objective: To analyze the behavior and feeding habits of adolescents attending teaching centers in Uruguay.

Methodology: the sample included 3,000 adolescents representative of the various areas in the country and the various socioeconomic levels, attending first and third year high school. This is an exploratory descriptive study. The data were taken through a self-administered questionnaire presented by a nutritionist in each group of adolescents.

Results: The results show that 25% of adolescents do no drink milk daily, being calcium intake insufficient in 44% of the cases studied (assuming that 60% come from dairy sources). The average consumption of calcium for Montevideo was 928.46 with a SD of 550.07, while for the interior of the country it was 974.21 with a SD of 614.14 mg. There is a mild tendency to reduce dairy product consumption as age increases, with lower consumption in third year students versus first year students. Seventy five per cent of the adolescents have breakfast every day.

Fifty per cent report no physical activity outside the curricular activity (2 hours a week). As a counterpart, 42% devote from 2 to 4 hours in sedentary activities as watching TV and 32% devote more than 4 hours a day. Ninety per cent report a great interest on issues related to nutrition and 60% express that they receive their information on food from their families, followed by 30% who state they receive them from their teachers.

Conclusions: We conclude that dairy product consumption is low in the adolescents attending high school. Designing and implementing programs promoting a healthy lifestyle, especially increasing dairy product consumption and physical activity is a priority. These programs must include the adolescents' educators and families, and it is essential to evaluate them after they are implemented.

P241SA. COMPARISON OF VERTEBRAL FRACTURE PREVALENCE AND OSTEOPOROSIS RISK FACTORS BETWEEN COMMUNITY DWELLING OSTEOPOROSIS PATIENTS AND NURSING HOME RESIDENTS

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This study was designed in order to compare community dwelling osteoporosis patients and nursing home residents according to vertebral fracture prevalence and osteoporosis risk factors.

Study population consisted of 56 women aged 70–80 years. First group consisted of 32 osteoporosis patients who were being followed up in a university outpatient clinic and the second group consisted of 24 women living in Bursa Nursing Home. All patients were interviewed for osteoporosis risk factors using a questionnaire, bone mineral density (BMD) was measured by DEXA and lateral lumbosacral x-rays were taken. Serum Ca, PTH, calcitonin, calcitriol and 24 hour urinary Ca levels were measured. Vertebral

fractures were assessed using a semiquantitative method. The two study groups were compared according to vertebral fracture prevalence, osteoporosis risk factors, BMD and laboratory parameters.

The study groups were similar in terms of mean age (Group1: 74.3 ± 3.2, Group2: 75.2 ± 3.1 years) and body mass index (Group1: 27.8 ± 4.7, Group2: 27.8 ± 6.6 kg/m^2), while nursing home residents had a longer postmenopausal duration (Group1 27.4 ± 8.0, Group2: 33.3 ± 9.5 years, p = 0.014). Although vertebral fracture prevalence was found to be lower in the first group (65.6% vs 79.2%), this difference was not statistically significant. Number of fractures was also similar in both groups. Significantly more subjects in the second group had at least one hormonal risk factor such as nulliparity, early menopause and surgical menopause (p = 0.002). BMD measurements were similar in both groups except femur neck BMD which was significantly lower in the second group (Group1: 0.613 ± 0.119, Group2: 0.523 ± 0.139 g/cm^2, p = 0.017). Laboratory parameters were also similar in both groups except 24 hour urinary Ca excretion which was found to be significantly lower in the second group (p = 0.021).

In conclusion, no significant difference in vertebral fracture prevalence was found between community dwelling osteporosis patients and nursing home residents. Low femur neck BMD in nursing home residents might play a role in hip fracture risk but did not correlate with vertebral fracture prevalence in this study population.

P242SU. QUALITY OF LIFE IN POSTMENOPAUSAL OSTEOPOROSIS

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The aim of this study was to determine the impact of osteoporosis on the quality of life in a group of postmenopausal women.

Thirty females with osteoporosis, 30 females with osteopenia and 30 healthy control subjects; all age-matched were included to the study. Demographic data, lumbar spine and femoral neck bone mineral density (BMD) were collected. Quality of life questionnaire of the European Foundation for Osteoporosis (QUALEFFO) was used to assess health-related quality of life.

The mean age of the subjects was 58.1 ± 8.32 years. There was 9 patients with non-traumatic lumbar and/or femoral fracture history. The mean scores of pain and physical activity domains of QUALEFFO were significantly higher in the osteoporotic group than in the osteopenic females and control subjects (pain: 56.8 ± 21.1 vs 42.9 ± 20.2 vs 36.1 ± 21.9 ; physical activity: 47.2 ± 16.7 vs 36.7 ± 12.5 vs 331.7 ± 17.9, respectively). The scores of psychosocial domains were also higher in the osteoporotic females than in other subjects but the difference did not reach to significance. Women who experienced a fracture had significantly higher total QUALEFFO scores, indicating lower quality of life, compared with non-fractured females (48.8 ± 15.2 vs 31.6 ± 11.3, respectively). The BMD levels were similar betweeen the females with and without fractures.

In conclusion, osteoporotic females have a reduced quality of life, especially related with fractures. The negative impact of osteoporosis on quality of life, seems to be more related to physical subgroups rather than psychosocial domains.

P243MO. SIFRAR – AN ORIGINAL SCORE TO ASSESS RISK OF PREVALENT VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN: PRELIMINARY RESULTS

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Aims: To design a score with clinical and densitometric parameters in order to be able to predict the prevalence of vertebral fractures in postmenopausal women.

Methods: Data was obtained from a database with multiple clinical and densitometric parameters collected during an Osteoporosis Detection Campaign. SIFRAR score was calculated according to: Menoage: (year of test minus last menstrual year) divided by 10; Hip T-score multiplied by 1 or Spine T-score multiplied by 2 turning T-score into a positive value (Lower T-score was selected from both); Height loss obtained from the difference between the current height and the calculated maximal height (expressed as an absolute value); History of vertebral fractures: 6 points; Previous non-vertebral fractures: 1 point; Self-reported osteoporosis diagnosis: 1 point; Maternal history of hip fracture: 1 point; Maternal history of vertebral fracture: 1 point; Body Mass Index: 0 (>26); 1 (25-26); 2 (23-24); 3 (21-22); 4 (<20); Self-reported health status: 2 (bad); 1 (regular); 0 (good). SIFRAR was calculated on 4,345 women whose maximal height was calculated either from the knee height or the refered maximal height or the arm span. For these preliminary results 829 patients, with maximal height calculated from the knee height and with a score over 7, were selected. A dorsolumbar spine radiography was performed on this sample and reviewed by trained physicians.

Results:Demographics: Mean Age: 69.88 ±6.28; Mean BMI: 27.04 ±3.64; Mean Menoage: 22.58 ±7.92.The prevalence of vertebral fractures in our sample was 15.92%, with a proportional increase related to the score. The sample distribution and the prevalence of fractures are shown on Table 1.

SIFRAR	Subjects n (%)	Subjects with Prevalent Vertebral Fracture n (%)
<9–≥7	466 (56.22 %)	41 (8.79 %)
≥9	363 (43.78 %)	91 (25.06 %)
TOTAL	829 (100%)	132 (15.92 %)

Conclusions:We consider this score a useful tool which would allow to identify those women to whom a spinal radiography assessment should be recommended. A SIFRAR score over 9 would identify postmenopausal women at high risk of prevalent vertebral fractures.

P244SA. EPIDEMIOLOGICAL MULTICENTER STUDY ON OSTEOPOROSIS: THE EDMUSTO STUDY

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Aims: Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures. Although osteoporosis is a worldwide problem that affects every population and occurs in all geographic areas studied thus far, the incidence differs among different populations and ethnic groups –greatest in whites and Asians and least in blacks. In this study, what we aimed to accomplish was the comparative analysis of bone mineral density measurements of postmenopausal women from 3 different countries. This preliminary report summarizes the early data from Turkey, Iran and Poland.

Methods: The study comprised 679 postmenopausal women; 472 from Turkey, 104 from Iran and 103 from Poland. Demographical data –including age, age at menopause, body weight, height, etc.- daily calcium intake and physical activity levels of the individuals were recorded. Bone mineral density measurements were performed using dual energy x-ray absorptiometry. Statistical analysis was done by using Statistical Package for Social Sciences. Results: The mean ages at menopause were respectively 45.85 ± 6.20, 47.60 ± 3.75, 47.30 ± 5.30 and the difference between the countries was found to be statistically significant (p = 0.009).

Daily calcium intake levels were different among the countries ($p = 0.00$). Physical activity levels of the 3 countries were also found to be different ($p = 0.00$). Bone mineral density measurements of the lumbar vertebrae (L1-L4) and of the femur (total) were different among the countries ($p = 0.00$, $p = 0.00$) whereas of the femoral neck were similar ($p = 0.59$). When all the data from the 3 countries were analyzed together, bone mineral density measurements were found to differ with different daily calcium intake ($p = 0.09$) and physical activity levels ($p = 0.00$).

Conclusions: Overall, although the bone mineral density measurements seem to differ among various populations; daily calcium intake and physical activity levels, indisputably, play an important role in every patient.

P245SU. THE INFLUENCE OF BODY CONSTITUTION ON METACARPAL INDEX, POROSITY INDEX AND BONE MINERAL DENSITY MEASURED VIA DIGITAL X-RAY RADIOGRAMMETRY

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Aims: To investigate the association between different body constitution characteristics and osteodensitometric parameters measured by Digital Radiogrammetry (DXR).

Patients and Methods: In a prospective study 45 healthy persons underwent analysis of bone mineral density (BMD), porosity index (PI) and metacarpal index (MCI) by DXR. Radiographs were scanned into the system which automatically defined regions of interest (ROI) around the narrowest bone parts of metacarpals II-IV. There was no operator activity required nor possibility to influence size or location of the ROI. Cortical thickness of the metacarpals was estimated. Based on the mean bone volume per area and the estimated porosity of the cortical bone (which is separately given in arbitrary units ranging from 1 to 19), the osteodensitometric parameters were computed. Data of height, weight and body mass index (BMI) were acquired and the study group was subdivided into individuals with underweight ($BMI < 25$, $n = 9$), normal weight (BMI 20–25, $n = 20$) and overweight ($BMI > 25$, $n = 16$).

Results: The total group revealed a significant correlation between DXR-BMD and height ($R = 0.73$, $p = 0.00$) as well as weight ($R = 0.54$, $p = 0.00$). Whereas in all subgroups a significant correlation between DXR-BMD and height could be demonstrated, association regarding weight showed a significant correlation for the underweight ($R = 0.79$, $p < 0.05$) and normal weight group ($R = 0.57$, $p < 0.05$), however not for overweight individuals. Only a significant association could be verified between BMI and BMD in the total group and subgroup of underweight individuals.

Equal results were verified for MCI. Only the subgroup of underweight individuals showed a significant correlation between PI and weight ($R = -0.75$, $p < 0.05$) versus height ($R = 0.74$, $p < 0.05$).

Conclusions: DXR related parameters reveal a closed association between height, whereas BMI and weight show no significant results in individuals with increased body weight (i.e., fat mass). Otherwise DXR-PI may point at an increased porosity of cortical bone tissue depend on weight and height in underweight patients.

P246MO. THE PERCENTAGE OF RISK FACTORS FOR WOMEN IN SERBIA WITH LOWER BONE MINERAL DENSITY

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Aim: The aim of this study was to determine the percentage of risk factors for Serbian women with low bone mineral density.

Methods: In the period from April 2002 to October 2003 we took 690 women from all Serbian regions with an average age of 58 years. The bone mineral density (BMD) of all women was measured by DEXA Lunar 2000 at standard region of lumbal spine and hip. During the examination we filled a questionnaire which included questions about the defined risk factors. From this study we excluded all patients with a history of disease or use medicines which have influence on bone metabolism.

Results: Out of 690 examinated women, 237 of them (34.34%) had BMD at osteopenia level, and 453 of them (65.66%) had BMD at osteoporosis level.

Results shown in table 1. 104 (64.99%) women in the group with osteopenia had two or more risk factors, and 354 (78.16%) women in group with osteoporosis, which is statistically significantly higher $p = 0.000$.

Table 1. The perecent of risk factors

Risk faktors	Osteopenia	Osteoporosis
Early menopause before the age of 45	78 (32,91%)	141 (31,13%)
Consuming more than 4 cups of coffee a day	93 (39,24%)	138 (30,46%)
Inadequate intake of calcium	54 (22,78%)	114 (25,17%)
Smoking more than 20 cig/day	111 (46,84%)	153 (33,71%)
Higher BMI	174 (73,42%)	231 (50,99%)
Lower BMI	9 (3,08%)	21 (4,64%)
Physical inactivity	150 (63,29%)	354 (78,15%)
History of previous fractures	81 (34,18%)	252 (63,29%)
one fracture	57 (70,37%)	174 (69,05%)
2 or more fractures	24 (29,63%)	78 (30,95%)
Family inclination towards osteoporosis-fractures	63 (26,58%)	l95 (43,05%)

Conclusion: These results showed that physical inactivity and higher BMI are the most common risk factors in both groups of patients. We did not manage to explain the relation between low BMD and high values of BMI, except that there is a correlation between physical inactivity and BMI. One third of women with osteopenia and one half of women with osteoporosis had previous fractures. In the group of women with osteopenia, postmenopausal osteoporosis was dominant, while the family anamnesis about fractures and osteoporosis was a significant risk factor in the group of patients of osteoporosis. A great number of fractures at women with osteopenia points to the need of early application of antisteoptotic therapy with bisphosphonate in osteopenia treatment, especially for women with two or more risk factors.

P247SA. STRATEGIES FOR THE PREVENTION OF OSTEOPOROSIS IN SCHOOL CHILDREN: "A BREAKABLE AUNT"

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Objective: Campaign for the prevention of osteoporosis in schoolchildren.

Methods: The surveys on risk factors for presenting osteoporosis show that low dairy consumption, sedentarism, cola drinks, and other factors such as low exposure to sun and smoking are among the main factors in the Uruguayan population in general.

A data base on osteoporosis was produced to support the basic information that Roy Berocay, a well-known child story writer in our country, used to create his character.

Aunt Genevieve is an old aunt who presents a significant bone frailty; she has presented several fractures, and in several occasions she does exactly the opposite one is supposed to do to preserve a good bone health.

This book is distributed at public and private schools with a flier in which our society offers basic information on this condition for the teacher.

We first contacted the senior authorities of primary school in our country, and we managed to get funding for publication from the national dairy industry. After getting that support we started distributing the material, following a meeting with teachers from

several schools. This material was later on integrated into the teaching activities at schools, and was disseminated to parents.

Results:There has been an excellent acceptance at all school-teaching levels. Lectures on the book were organized at teaching centers, stating that next year it will be distributed and the material will be worked out.Television programs discussing health topics also gave us space to present educational material for prevention.
Conclusions: Health prevention has succeeded in calling upon many sectors involved in health, teaching and the mass media around a topic that is highly sensitive as bone health in children. Dissemination results are favorable throughout the country. Rheumatologists and teachers have been working jointly in the implementation of the strategies for the prevention of osteoporosis.

P248SU. OSTEOPOROSIS AND RHEUMATOID ARTHRITIS INCIDENCE OF FRACTURES

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It is well known that patients with RA are at a higher risk of presenting fractures due to osteoporosis. This led to the study of a population of patients with RA, the incidente of fractures in that population, and their bone mass, to assess their relation with the stage of the disease and the therapies received, especially Glucocorticosteroids.
Material and Methods Ninety patients with RA (as per ACR criteria) were selected. They were all worked out with densitometry using the dual Dexa method, regardless of their functional class, their time of onset and therapy received. The prospective protocol developed (2002 – 2003) included the following:

- Personal data
  - Age of onset of the RA, time since onset, radiological degree, extraarticular manifestations (Nodules, Vasculitis, Pleuropulmonar Involvement, etc), presence of comorbidity, gastrointestinal manifestations
  - (gastritis, ulcera), glandular diseases: (diabetes, thyroid disease), cardiac disease
  - Hypertension
  - Gyneco-obstetric history, age at menopause, hormone replacement therapy
  - History of joint replacements
  - Presence of fractures, time elapsed at the time of protocolization
  - Clinical laboratory: rheumatoid factor and acute phase reactants
  - CDM using the Dexa method
  - Bone resorption or formation markers
  - Treatments administered: NSAIDs, Corticosteroids
  - prednisone equivalent doses
  - 5mg Methotrexate, Leflunomide, Sulfazalacine, Azathioprina, Hydroxyclhoroquine dosaging and time since the patient has been on the medication
  - Calcium vitamin D, Biphosphonates, other medications, time and doses received

Results: Average age of patients at the time of protocolization was 57 years, with a frank female prevalence Mean age of onset of the disease was 49 years.-22 % presented subcutaneous nodules, 11 % vasculitis, 25 % other complications. 52 % didn't present extra-articular complications Bone Densitometry confirmed osteoporosis in 52%, osteopenia in 22% and normal bone mineral density in 26%.- 11% presented fractures: vertebral, wrist, CF, shoulder, elbow

Conclusions: 80 % of the patients with RA have a reduced bone mineral density, 11% presented fractures as a complication of their osteoporosis.-We highlight the importance of an early diagnosis of this comorbidity and an early therapy, tending to reduce the incidence of fractures.

P249MO. BIALYSTOK OSTEOPOROSIS STUDY (BOS): BMD AND FRACTURES

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Hip T-score –2.5 and below is a WHO diagnostic threshold of osteoporosis. It arises a question, at what BMD fragility fractures occur, which are a main feature of this disease. We tried to answer this question on the basis of BOS and comparison of its data with others (1,2). To asses relations between number and frequency of fractures and BMD, 1005 women aged 46–89, mean 59.3 ± 9.4, filled in the questionnaire concerning known fracture and osteoporosis risk factors and 727 of them have had their bone mass density (BMD) examined by Hologic QDR4500SL in L1-L4 vertebra of spine, neck and total hip. Distribution of age in BOS cohort and whole Polish population is similar.
T-score below –2.5 were observed in 18.4% of women if measured in the spine, in 14.8% if in neck and 2.4% if in total hip. 222 out of 727 (30.5%) have experienced fractures in the past, 53% of them were Colles ones, 9.4% of the ribs, 2.3% of the hip, 3.6% of the vertebra, and 31.5% of others. Mean neck T-score of women with previous fracture were –1.6 (vs –0.96 of that without fracture), and L1-L4 T-score –1.5 (vs –0.99 respectively). 50.0 % of fractures occurred in women with BMD between neck T-score –1.0 and –2.5, and 26.7 % within normal values and only 24.3% within osteoporotic one. Neck T-score of women with previous fracture is the lower the more advanced age, but segment of women with neck T-score below –2.5 is most numerous in the age of 65–74 as well as one year fracture risk increases with age, but absolute number of fractures in BOS cohort is highest in women aged 45–64. Very similar phenomenon, namely, more numerous fractures at the range of osteopenic and normal bone mass has been described by others (1,2).

References:
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2. Wainwright SA et al.: J Bone Miner Res 2001, 16:1077/S155.

P250SA. SKELETAL STATUS IN EASTERN SLOVAKIA MALES ASSESSED BY DXA AND QUANTITATIVE ULTRASOUND

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There are only a few reports of bone mineral density status in males in Slovakia. The aim of the study was to assess the occurrence of osteopenia and osteoporosis in males, analyse the cause of osteoporosis and to interpret obtained results.

In the study we examined a total of 1681 males, mean age 51.2 years, from East Slovakia ironworks involved in regular preventive medical check-up. In 1602 males bone status was measured by quantitative ultrasound (Sahara, Hologic) and in a subgroup of 519 males BMD was assessed by DXA at lumbar spine and hip (Hologic 4500 A). In males examined by DXA osteopenia was found in 53% and osteoporosis in 8.3% of subjects, in 6.7% in lumbar spine and in 1.5% in hip. In subjects examined by QUS, osteopenia was found in 28% and osteoporosis only in 3.4% of males. In males with osteoporosis the cause of decreased BMD was further analysed. 62.3% of males were classified as idiopathic osteoporosis and 37.7% as secondary osteoporosis. In 69% hepatopathia was found as a most frequent cause of secondary osteoporosis and in 31% of them ethyltoxic aetiology was assessed. Endocrine disorder was found in 1%, drugs causing osteoporosis in 1.5 %, rheumatic diseases in 3.4%, gastrointestinal diseases in 3%, nefropathia in 17% and diabetes mellitus in 5% of males.

In our nonselected group of relatively young males involved in preventive medical check-up osteoporosis was found in quite high proportion, comparing with overall estimated prevalence of osteoporosis in European population. Hepatopathia was surprisingly found the most common cause of secondary osteoporosis among the males in our study. Measurement of lumbar spine by DXA

seems to be the most sensitive method to detect the low BMD and risk of fractures in our group of males subjects. If QUS is used in skeletal status evaluation we do not recommend to use T score −2.5 SD (osteoporosis threshold assessed and used in DXA) for fracture risk stratification. T score less than −1 SD, found in 32% males, represent already the high risk group in terms of fracture risk.

P251SU. BONE MINERAL DENSITY REFERENCE VALUES IN MALES AND FEMALES 10 TO 21 YEARS OF AGE IN VENEZUELAN SUBJECTS

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Bone mineral density reference values for Latin American populations are scarce. However, comparison for diagnosis of low bone mineral density in adults requires normal reference values of 20-40 years old control population. In contrast, in young individuals, matched by sex and age. The aim of this study is to show BMD values in normal young Venezuelan males and females subjects between ages 10 and 21. 191 healthy subjects with at least one Venezuelan progenitor, ages between 10 and 21, without any systemic disease of drug use which affects bone metabolism were recruited for bone mineral density assessment. None of the subjects were under heavy physical therapy or training nor had previous fracture. BMD was measured by DEXA (LUNAR DPX. Variation Coefficient: 1.5%) at femoral neck and lumbar spine (L1-L4). Subjects were divided into two groups: 89 males and 102 females. BMD results are presented in the 2 tables as follow.

Table 1 Reference Values

Males. Age	Femoral Neck Mean value (SD)	Troch Mean value (SD)	L1–L4 Mean value (SD)
10–11	0.867 ± 0.13	0.755 ± 0.09	0.779 ± 0.11
12–13	0.956 ± 0.11	0.830 ± 0.08	0.846 ± 0.11
14–15	1.032 ± 0.18	0.911 ± 0.16	0.986 ± 0.16
16–17	1.086 ± 0.10	0.913 ± 0.10	1.103 ± 0.16
18–19	1.135 ± 0.10	0.845 ± 0.04	1.243 ± 0.05
20–21	0.956 ± 0.11	0.752 ± 0.12	1.092 ± 0.03

Females. Age	Femoral Neck Mean value (SD)	Troch Mean value (SD)	L1–L4 Mean value (SD)
10–11	0.754 ± 0.15	0.655 ± 0.11	0.815 ± 0.10
12–13	0.913 ± 0.11	0.782 ± 0.11	0.981 ± 0.14
14–15	0.965 ± 0.12	0.775 ± 0.10	1.037 ± 0.13
16–17	0.995 ± 0.07	0.816 ± 0.07	1.094 ± 0.11
18–19	1.001 ± 0.11	0.759 ± 0.08	1.116 ± 0.07
20–21	0.959 ± 0.11	0.785 ± 0.11	1.156 ± 0.13

This study presents normal reference BMD values for young Venezuelan males and females subjects, 10–21 years of age, obtained with Lunar densitometer.

P252MO. EFFECT OF VERTEBRAL FRACTURE ON QUALITY OF LIFE

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Aim: To investigate the effect of vertebral fractures on quality of life in postmenopausal women.

Method: 41 postmenopausal women referred for osteoporosis screening were included in the study.They were classified into two groups as those having osteopenia (Group I) or osteoporosis (t score ≤−2.5)(Group II). Patients were further investigated by lateral spine radiographs with respect to vertebral fracture defined as 25 percent height loss compared to the neighbouring vertebra. SF 36,QUALEFFO 41 and NHP were the questionnaires used to evaluate life quality.

Results: The mean age of the 11 patients in Group I was significantly ($p \leq 0.05$) greater than those in Group II. Age at menopause, height and weight were not significantly different between the groups. 16 patients had vertebral fractures and the number of fractures was 25. 84% of them were compression type fractures. Energy subgroup of SF 36 was significantly lower in Group II than in Group I (37.3 ± 16 vs 48.2 ± 11, $p \leq 0.05$). Only physical activity subgroup of the NHP was significantly different between the two groups. On the other hand, there was not any significant difference between the two groups and between the patients with and without vertebral fractures with respect to life quality. Number of fractures was significantly correlated ($r = 0.31$) with the home activities subgroup of QUALLEFFO 41 and physical activity subgroup of NHP ($r = 0.32$).

P253SA. OSTEOPOROSIS IN THE URUGUAYAN POPULATION

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The prevalence of osteoporosis in Uruguay affects approximately 5% of the population. For this reason, the Uruguayan Society of Rheumatology and the Department of Basic Nutrition of the School of Nutrition of UDELAR have conducted some studies with the objective of identifying and describing the main risk factors for the disease.

Methods: A study was conducted from June to August, 1999, on a sample of 3,503 adult patients attending the office. They filled a questionnaire with questions on the educational level, life style, food consumption and elements of the personal and family medical history.

While 67% of the women fell into the risk group, only 16% of the men did. The threshold for susceptibility risk to present Osteoporosis was present in 59.1% of the total sample, being remarkably higher for women (67.1%) than for men (16.8%).

Another study was performed in 256 adult women attending to the clinic in Montevideo and the south of the country in the 2000 – 2001 period. The questionnaire included aspects related to food, lifestyles, current and usual weight records and personal and family history. The women in the study had lived more in the city and did less exercise < they had a lower educational level, a lower BMI and lower body weight. The urban conditions of Uruguayan women was found to be associated with OP in a most particular way, being the risk higher in those women who change from rural life to city life.

Finally a descriptive study was carried out on a sample of 1,300 adolescents attending high school. Twenty five per cent do not consume milk daily. There is an insufficient intake of calcium in 44% of the population (assuming that 60% come from dairy products). Fifty per cent do not practice sports apart from the physical activity in high school. Twenty one per cent declared having suffered some fracture.

Conclusions: The studies conducted clearly show the lifestyle and consumption habits as risk factors that are present and might be conditioning the early occurrence of osteoporosis with its serious consequences.

P254SU. MUNICIPALITIES' LEVEL HEALTH EDUCATION FOR OSTEOPOROSIS IN JAPAN

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Aim: In Japan health education for osteoporosis is very important because one of the causes of it is low intake of calcium. Osteoporosis is one of the targets of Healthy Japan 21, which is a health promotion framework in Japan. Main carrier of this education is municipalities. We surveyed their health education programs and their cooperation with other organizations.

Subjects and Method: A questionnaire asking their health education programs for osteoporosis was sent to all municipalities in Japan. Their cooperation with other organizations for health education was also inquired.

Results: 1530 out of 3246 municipalities replied to the questionnaire. There are three types of health education. They were lectures, courses and individual education. 20.0% of municipalities had lectures, 36.8% of them had courses and 33.0% had individual education. Lectures were held 3.7 times a year and courses were held 2.5 times a year. In courses 22.8% of municipalities carried out close examination of osteoporosis. Targets of individual education were mainly selected by the results of screening tests. Courses were considered as the most popular method in the near future

Municipalities had little cooperation with hospitals, public health centers, schools and NGO/NPO.

Discussion: Three types of education are as follows:

1) Lecture: An invited physician talks about osteoporosis including its prevention to the audience. A lecture is independent from another.
2) Course: Participants attend a pre-determined number of learning session about prevention of osteoporosis.
3) Individual Education: Public health nurses or physicians give suggestions of prevention of osteoporosis to participants personally.

Cooperation with other organizations for health education is insufficient. To make more useful health education for osteoporosis, not only developing their programs but also cooperating with other organization are necessary.

Conclusion: To diffuse information of osteoporosis, new strategies for health education and cooperation with other organization should be developed.

P255MO. RELATIONSHIP AMONG THREE INDICATORS OF BONE QUALITY IN THE OSTEOPOROSIS RESEARCH ON PANORAMIC RADIOGRAPHIC

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The more precocious it is the identification of compatible signs with low bone quality, indicative of osteoporosis presence or of other systemic diseases, the earlier treatment may begin, and consequently, the larger possibilities of cure or of the limitation of the damages. The study of bone trabeculae and the mandible cortex may suggest precocious signs of that disease, mainly by the dentist that makes everyday use of the panoramic x-rays.

Aims: Thus, it is intended to evaluate the interrelation of three discriminating aspects of the bone quality, in panoramic x-rays, correlating them with measures of bone mineral density (BMD) of DEXA.

Methods: The thickness of the cortex and trabecular mandibular pattern of 58 panoramic x-rays of women and its respective examinations of BMD had been examined and correlated.

Results: The results showed significance in level of 5% for the correlations among the factors of fractal dimension (FD), percentage of black pixels (ET) and connectivity (TMP/DTP) and significant correlation at level of 1% for the morphologic classification of the cortex (CC) and thickness of the inferior cortex of the jaw (IC) to each other, and for DF and ET. There was also significant correlation in relation to MBD and IC and CC. There was no significant correlation between the parameters analyzed (DF, ET and TMP/DTP) in the evaluation of the morpho-digital standard of trabecular bone in digitalized panoramic radiographic images and the measures of bone mineral density (BMD), for the DEXA.

Conclusions: Therefore, it can be concluded that it is possible to refer to patients for restricted exam with the purpose of researching low mineral bone mass, for the analyses of the inferior cortical of the jaw and of the morphologic trabecular pattern.

P256SA. THE GROWING INCIDENCE OF PROXIMAL FEMORAL FRACTURES IN SLOVENIA

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Background: The Bone and Joint Decade (BJD) project intends to correct dramatically underestimated musculo-skeletal diseases, obtained in last decades all around the world. Elderly crisis forces national governments and medical policy makers to admit decided measures

Methods: The National Action Network (NAN) Slovenia identified 5 main fields of interests, one of them focussed on fragility fractures in the elderly. The National Health Institute analysis showed an overwhelming fragility fracture burden to the national medical budget. An estimate of 20% ratio of people elderly than 65 is expected to the year 2020. In the year 1994, 1370 proximal femoral fractures were operated in 12 regional hospitals of Slovenia while 2590 were operated in 2002. The increase of incidence is significant!

Measures: The following agreed measures of NAN Slovenia were accepted:

- Public educational measures with warnings about unhealthy habits, alcohol intake, cigarette smoking, physical inactivity, etc., proper vitamin D and calcium intake, etc.
- Encouraging the activities of patient oriented societies.
- Correct and comparable data collection on osteoporotic fractures is essential for planning and for convincing decision makers and health authorities.
- Identification of persons at high risk by DEXA measurement in early postmenopausal period reimbursed by the Slovenian Health Insurance Institute.
- Prevalence, treatment, outcome, prevention, rehabilitation and costs of proximal femoral fracture in South East Europe (SEE) Countries should be accumulated.
- At the time fragility fracture is identified, the appropriate treatment of osteoporosis must be introduced. Orthopaedic trauma surgeons must be aware of the treatment of this principle disease.

P257SU. ASSOCIATION OF RISK FACTORS FOR OSTEOPOROSIS AND BONE PERIPHERIC DENSITOMETRY IN WOMEN AND MEN OF MEXICO CITY

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Osteoporosis is a public health problem. In Mexico this problem is aggravated by, inappropriate lifestyle habits and malnutrition.

Objective: To evaluate the relationship among the bone mineral density (BMD) and risk factors for osteoporosis (RFO).

Methods: It was observational and retrospective study. We included 1153 patients with RFO questionnaire and peripherical densitometry. BMD was measured with DEXA of the calcaneus (Lunar). BMD was considered normal when it was found within 1SD of the young adult mean, medium when it was between −1 and −1.8 SD, and low when it was below −1.8 SD. The RF were correlated with these 3 categories of BMD. They were integrated into 9 groups according to BMD and RFO. Group 1 is defined by normal bone mass and no RF and group 9 by low bone mass (BMD T score > −1.8 SD) and more than 5 RF.

Results: The 1153 patients: 119 men (mean age 49 + /−14 yrs) and 1034 women (mean age 44.84 + /−12.34 yrs) The FR associated to

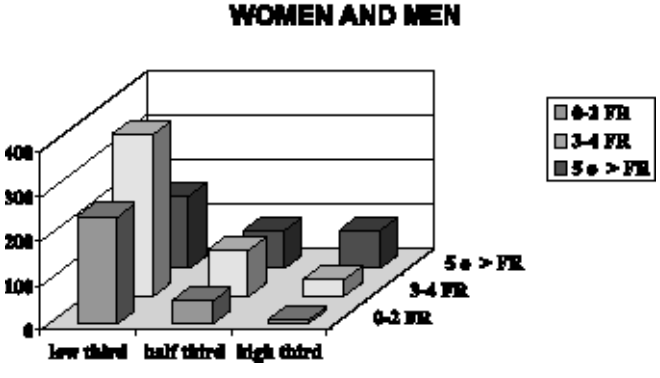

Fig. 1 RISK GROUP

loss BMD: family antecedent of hip fracture. 165 women (15.9%), 25 men (21%), a low calcium intake, 651 women (62.9%), 51 men(42.8%), alcoholism 16 women (1.5%) and 3 men (2.5%), low physical activity, 627 women (60%) and 64 men (53%), appetite suppressant 244 women (23.6%) and 11 men (9.2%), soda consumption, 189 women (18.2%) and 32 men (26.8%), age > 50 yrs women 343 (33.2%), men 52 (43.7%) all between 7–9 the risk group.

Conclusions: We find more protective factors than of risk, concluding that the prevalence of RF for osteoporosis in Mexican women and men is low compared with other countries, but the RF that affects the BMD is not isolated, but results from the combination of inappropriate lifestyle habits, malnutrition and chronic-degenerative diseases.

P258MO. CORTICOSTEROID INDUCED OSTEOPOROSIS: A SURVEY OF PHYSICIAN ATTITUDES IN NEW DELHI, INDIA

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Aims: Osteoporosis is a growing but neglected health problem in India. The level of awareness is low even amongst health care professionals. This survey was carried out to ascertain physician attitudes towards corticosteroid induced osteoporosis (CIO).

Methods: One hundred and five self-administered questionnaires were distributed to doctors (60 working at a tertiary care teaching hospital and 55 family physicians) in New Delhi. The semi-structured questionnaire included 10 questions pertaining to need, frequency and modality of screening employed for CIO, and advice about prevention and treatment.

Results: A total of 80 questionnaires were returned (response rate 76%). While 98% of the doctors working in the tertiary care setting felt that CIO is an important issue, only 60% of family physicians thought so. However, only 40% of these doctors routinely screened patients on long-term corticosteroids for osteoporosis. Advice regarding exercise and calcium rich diet was given by 45% doctors while 87% prescribed calcium and vitamin D supplements and 35% used alendronate in patients on long-term corticosteroids.

Conclusions: Awareness about CIO is low amongst family physicians in India. Routine screening for CIO is not a common practice even amongst physicians aware about this disease. Calcium and vitamin D supplements are the most common preventive strategies employed.

P259SA. PREVALENCE OF OSTEOPOROSIS AND DETERMINANTS OF BONE MINERAL DENSITY IN KUWAITI MEN AGED 50 YEARS OR OLDER

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The present study was aimed at investigating the prevalence of osteoporosis among Kuwaiti males aged 50 years or older and to examine certain determinants of bone mineral density.

172 volunteer Kuwaiti men aged ≥50 years with no risk factors for osteoporosis were evaluated with a questionnaire that included demographic data, complete medical and drug history, smoking habits, daily caffeine consumption and current physical exercise. Each subject underwent anthropometric measures (height, weight) and calculated body mass index (BMI). Bone mineral density (BMD) was measured at the lumbar spine, femoral neck and total hip by dual energy x-ray absorptiometry.

The prevalence of osteoporosis was 1.2%(lumbar spine), 1.2% (femoral neck) and 0.6% (total hip). Osteopenia was detected in 14.5%, 33.1% and 9.3% in spine, femoral neck and total hip, respectively.

Univariate and age and weight adjusted linear regression analysis were used to evaluate the association between the independent variables and BMD.

The determinants of BMD in our study were identified as age, weight and BMI. Common medical conditions (hypertension, type 2 Diabetes Mellitus) and lifestyle factors such as caffeine consumption, current physical exercise and smoking habits did not have any impact on BMD.

We concluded that the prevalence of osteoporosis among Kuwaiti men aged ≥50 year is quite low, however further studies to establish the normative data of BMD in Kuwaiti population are needed. Age, low weight and low BMI were independent risk factors for low BMD in men after the age of 50 years.

P260SU. BONE MINERAL DENSITY IN WOMEN AGED 75 YEARS OR OLDER

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Most of bone mineral density (BMD) studies emphasizes post-menopausal osteoporosis diagnosis and treatment. In this context, the aim of this study was to investigate the bone mineral density status in a group of white women aged 75 years and over. 241 patients were selected from a reference center in bone densitometry in Paraíba, Brasil, and three groups were formed according to the age: 75–79; 80–84 and over 84 years. Then, the age, weight, height, body mass index (BMI) and BMD in lumbar spine (LS) and femoral neck (FN) were analyzed by SPSS ($p < 0,05$). The study was approved by the ethical committee on human research (CEP/HULW), and all the women provided written informed consent. According to the data, the prevalence of osteoporosis and osteopenia was 63,1%/26,5% at LS and 53,9%/38,6% at FN. The analysis between LS and FN showed 42,3% concordance for osteoporosis, 14,1% for osteopenia and 2,9% for the normal status. The main discordant results were between osteoporotic LS and osteopenia FN (19,1%) while the minor was between osteoporotic LS and normal FN (1,7%). It was observed that the correlation and regression analysis were positive between BMD and BMI but were not significant between BMD and age in the three groups. Almost all data showed different levels of bone loss, mainly with osteoporosis status in LS and FN in all groups. The advanced of the age raise the bone mass decrease, predisposing to an increased risk of fracture. However, it was observed that the BMI is a predictor to BMD, predisposing to a decreased risk of fracture. Osteoporosis is an epidemic public healthy problem in the world, needing actions to prevent and treat, in order to get a better healthy quality mainly to the elderly women.

P261MO. BONE MINERAL DENSITY AND FRACTURE IN BELGRADE POPULATION

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Objective: We examined 527 women aged 20–79 (48.54 ± 12.36) and 126 man aged 20–77 (50.22 ± 15.83) from urban part of

Table 1 Results

Decade	Age	Sex	No of pts	Osteoporosis	Osteopenia	Fracture
I	20–29	F	42	0	6 (14,3%)	0
		M	21	0	3 (14,3%)	0
II	30–39	F	63	1 (1,6%)	10 (15,9%)	0
		M	10	0	2 (20%)	0
III	40–49	F	186	5 (2,7%)	37 (18,9%)	23 (12,4%)
		M	27	2 (7,1%)	14 (51,9%)	4 (14,8%)
IV	50–59	F	131	12 (9,2%)	55 (42%)	26 (19,9%)
		M	22	3 (13,7%)	3 (13,6%)	1 (4,6%)
V	60–69	F	81	22 (27,2%)	28 (34,6%)	27 (33,3%)
		M	28	4 (14,3%)	9 (32,1%)	3 (10,7%)
VI	70–79	F	24	8 (33,3%)	5 (20,8%)	5 (20,8%)
		M	18	3 (16,7%)	4 (22,2%)	3 (16,7%)
TOTAL	20–79	F	527	48 (9,1%)	141 (26,8%)	81 (15,4%
		M	126	12 (9,5%)	35 (27,8%)	11 (8,7%)

Belgrade, randomly selected from population register to establish bone mineral density (BMD) and frequency of fracture.

Methods: BMD of spine was measured by dual-energy x–ray absorptiometry (DEXA), using a Lunar DPX-L device. Women and men were stratified per decade of age. Results are on table. Out of 81 women with fracture, 31 (38.27%) had normal BMD, osteoporosis was found in 16 (19.8%) and osteopenia in 34 (42%). Out of 11 men with fracture 4 (36.4%) had normal BMD, osteoporosis was found in 3 (27.3%) and osteopenia in 4 (36.4%).

Conclusion: Our study confirmed previous findings of other authors that for development of fracture, beside low BMD, the other factors are important.

P262SA. CLINICAL AND DENSITOMETRIC FINDINGS IN MALE LOW BONE DENSITY VENEZUELAN PATIENTS

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Male Osteoporosis is an underestimated condition. The aim of this study is to define the clinical and densitometric findings of male patients with low bone density.

We reviewed 150 clinical records of male patients with low bone density. Age, height, weight, psychosocial habits, risks factors, cause of osteoporosis or osteopenia, associated clinical conditions, medical treatments, initial BMD and bone markers were analyzed.

Age was 60.6 years. In the first visit back pain was present in 46.4% of the patients, polyarticular pain in 24.1%, bone fractures in 9.8%, neck pain in 5.4% and lower extremities paresis in 3.6%. Only 10.7 % came for a preventive visit. History of rheumatic diseases were present in 29.4%, hypertension 21.7%, neoplastic disease 19.4%, sexual dysfunction 15.3%, renal stones 10.5% and gastric peptic disease 4.2%. Bone fractures in 20.6%, vertebral fractures in 10.6%, hip fractures in 3.3%. 66.6% had unique and 33.4% multiple fractures. Risk factors for osteoporosis were: sedentary habits in 52.4% of the patients, smoking 33.6%, low calcium intake 74.1%, and alcoholic habits 12.6%. The initial BMD values were: femoral neck 0.759 g/cm^2 ± 0.32, T score -2.11 ± 0.93; lumbar spine 1.012 g/cm^2 ± 0.17, T score -1.83 ± 1.45. Osteopenia was present in 48.7% and osteoporosis in 51.3%. The initial values of bone biochemical markers were: TRAP 9.4 ± 3.23 IU/l, urine NTx 83.78 ± 64.14 nmBCE/mmcrea, Alkaline Phosphatase 45.64 ± 18.26 IU/l. Regarding bone turnover 29% were low and 71% were high bone turnover. Causes of Osteoporosis were: idiopathic 48.7%, induced by steroids (SIO) 19.5%, hypogonadism 14.2%, alcoholism 8%, others causes 9.8%. There are not significant differences between different causes of osteoporosis, regarding BMD, bone biochemical markers, age, weight, height and BMI. Significant correlation was present between TRAP, NTX and AP.

In conclusion our data show similarities with other published data. We found that male osteoporosis is associated with other chronic diseases frequently polymedicated. The three principal causes are idiopathic, SIO and secondary to hypogonadism. The vast majorities are sedentary, has a low calcium intake and shows high bone turnover.

P263SU. THE PREVALENCE OF RHEUMATIC DISEASES IN RURAL EGYPT

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Aims: Epidemiological studies of rheumatic diseases in the community have shown variable prevalence rates between Western and Oriental (Asian and African) populations, and between urban and rural areas. Since there are no published studies of rheumatic diseases prevalence in Egypt, this study was conducted to estimate the prevalence of rheumatic diseases in a rural area in Egypt.

Methods: The study was conducted in Makosa village of Al-Minia governorate in Southern Egypt in 4 phases. Of the whole adult population (15 years and older) of the village comprising 5208 individuals, 88 (1.7%) declined to participate in the study and 5120 subjects (98.7%, 2562 female and 2558 male) were screened by a preliminary WHO-ILAR-COPCORD questionnaire inquiring about pain, swelling, stiffness or tenderness in the bones, joints, and muscles in the last 7 days. Those who answered positively were administered a more detailed questionnaire and invited for examination and laboratory and radiological investigations as required. A rheumatologist administered the 2 questionnaires face-to-face and carried out examinations to ensure reliability and validity of data collection. Consequently, rheumatic cases were classified into specific diagnostic categories according to appropriate criteria.

Results: A total of 857 people answered positively to the screening questionnaire and accepted clinical examination either at clinic or at home. Only 829 (16.2%) individuals had rheumatic diseases after examination and investigations, including 526 females (20.5% prevalence) and 303 males (11.8% prevalence). The prevalence of specific rheumatic disorders was as follows, osteoarthritis 8.5%, spinal disorders 6.4%, soft tissue rheumatism 6.6%, fibromyalgia 1.3%, rheumatoid arthritis 0.29%, systemic lupus erythematosus 0.05%, ankylosing spondylitis 0.09%, Reiter's syndrome 0.04%, undifferentiated spondyloarthropathy 0.02%, pseudogout 0.08%, and dysplasias 0.02%. Among patients with rheumatic diseases, the knee was involved in 55.9%, the back in 30.3%, the neck in 12.9%, the hands in 10.9%, while the elbows, feet and shoulders were afflicted in less than 10% each. It is of concern that a significant proportion of rheumatic diseases have remained undiagnosed in the community.

Conclusion: The prevalence of rheumatic diseases in rural Egypt is 16.2%. Knee and back pain, resulting mostly from joint degeneration, caused the greatest burden of disease.

P264MO. ANKLE FRACTURES IN WOMEN AND OSTEOPOROTIC FRACTURE?

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Ankle fractures in the elderly are common but only few research we find in the literature about this problem in the women over 50 years old. An observational study of 50 women oldest than 50 years was performed among Merida, Venezuela, resident during 5 years. We studied postmenopausal women ages 50-79 years (mean age 59.8 ± 7.7years) with displaced ankle fractures. All the patients were independent in the house and the community. Only 2.0% from an geriatric hospital. The risk factors was smoking in 14.0%, arterial hypertension in 22%, parity between 2 to 5 42.1%, nuliparity 7,9%, Body Mass Index 21.5 kg/m^2.Fracture due to moderate trauma in 80.0% (slide), outside of house in 98.0% of them. Weber B2 Type predominate(54.0%) and 68.0% of surgical procedure in accordance with AO/ASIF principle was performed and the results were good and excellent in 92.0% of cases by the modified Olerud and Molander scoring system. In conclusion ankle fractures is a typical osteoporotic fracture.

P265SA. RISK FACTORS FOR OSTEOPOROSIS IN 446 WOMEN ABOVE 40 YEARS OF VASSOURAS CITY, RIO DE JANEIRO STATE, BRAZIL

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Aim: Analysis of the risk factors to Osteoporosis directly related with lifestyle(poor absorption of the calcium, smoking, non-practice of the physical exercises)in women above 40 years old.

Methods: Between september and december of 2002, interwies were realized with 492 women above 40 years in Vassouras city-countryside of Rio de Janeiro state, Brazil(representing 10% of the feminine population of the city above 40 years).Through the performing of the questionaries by these women from different social classes and areas of the city. They were inquired about the lifestyle

aspects that could come to influence in the loss of the bone mass like regular practice of physical exercises, absorption of the foods rich in calcium and smoking. The women that had a daily calcium absorption < 1000mg/day were considered in the risk group of Osteoporosis – also smokers and sedentaries.

Results: Fourty six women were eliminated in this study because they had a previous diagnosis of Osteoporosis. From 446 interwiees, 401(89,9%) had a daily calcium absorption < 1000mg and only 45(10,1%) presented a daily absorption > 1000mg; 138 (30,9%) were smokers and 267(59,9%)didn't have regular practice of physical exercises –86 women (19,3%) were simultaneously in the tree factors.

Conclusion: According to National Research Council (USA), when the women estrogenus levels begin to decrease, the daily calcium dose becomes to 1000 mg. The regular practice of physical exercises influences the bone and it has been one of the most effective mode to combat the decline of the bone mass as well as the drop out the smoking.

P266SU. ASSESSMENT OF MODIFIABLE OSTEOPOROSIS RISK FACTORS IN PORTUGUESE HEALTHY INDIVIDUALS

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Aims: To assess and characterise habits and behaviours of healthy male and female individuals that represent modifiable risk factors for osteoporosis (OP); to detect differences between genders and young/elder subjects regarding these habits.

Methods: We have performed a transversal study with 188 healthy subjects of both genders and, according to their age, divided in 2 groups: age between 18–29 years (peak bone mass) and 50 years (fast reabsorption). We have applied a questionnaire to characterise physical activity, calcium, protein and salt intake, alcohol, cigars and coffee consumption.

Results: (Table 1) Men are taller and heavier than women. Young persons were taller and weight increased with age. Alcohol consumption rose with age and was superior in males. Young persons preferred beer and elderly persons preferred wine. Alcohol regular consumption in men more than 50 was very high (71,4%). On the contrary, smoking was greater among young females and the majority of men more than 50 years had stopped smoking. Calcium intake was high in all groups.

Table 1

	A Group Women 18–29y	B Group Men 18–29y	C Group Women > 50y	D Group Men > 50y
Subjects (n)	65	32	56	35
Mean age ± SD	21,1 ± 1,9	20,8 ± 2,0	59,1 ± 6,4	64,6 ± 8,6
Weight	56,6 ± 8,3	70,9 ± 7,9	68,4 ± 14,1	75,5 ± 12,1
Height	165,4 ± 5,1	178,7 ± 6	158 ± 6,7	168,2 ± 5,4
Alcoholic habits	6,2% (100% beer)	31,3% (70% beer)	8,9% (100% wine)	71,4% (96% wine)
Smoke	15,4% (0% stopped)	9,4% (33% stopped)	12,5% (57% stopped)	45,7% (87% stopped)
Calcium intake	92,3%	87,5%	75%	74,3%
Physical activity	35,4%	56,3%	5,4%	14,3%

Conclusion: We registered differences between individual's gender and age regarding modifiable OP risk factors. Awareness campaigns that can contribute to OP prevention should be adapted to the targeted populations. Knowing specific habits and behaviours of different groups is essential for their success.

P267MO. RISK OF OSTEOPOROSIS IN A VENEZUELAN POPULATION ACCORDING TO EPIDEMIOLOGICAL VARIABLES

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Objective: To determine the osteoporosis frequency in the Venezuelan population according to a epidemiologic survey of risk factors and to evaluate the impact of these factors in the population.

Methods: During a two years period (2001–2003) 12,965 patients of both sexes, ages between 20 and 90 years were evaluated under a densitometric study, and a self applied survey on modifiable and non-modifiable factors of risk for osteoporosis. The collected data was analyzed by descriptive measures of linear regression and test of fisher.

Results: From the studied variables; calcium ingestion, tobacco and steroids use, exercise and precocious menopause were the factors of higher impact for the presence or absence of osteoporosis. From all the patients diagnosed with osteoporosis, 50% did not consume calcium, 70% of women with osteoporosis smoked and 62% consumed steroids at least during 30 consecutive days, 60.4% did not exercise and 70% had precocious menopause. Alcohol ingestion and the digestive problems did not have a high significance in our study.

Conclusions: The prevention of modifiable risk factors is one of the elements of great relevance in the occurrence of female osteoporosis. It is not clear the risk prevention, except the tobacco consumption in men.

P268SA. IDENTIFICATION OF RISK FACTORS OF OSTEOPOROSIS IN TURKISH MEN

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Aims: To identify the risk factors of osteoporosis(OP) in Turkish healthy men

Methods: 150 men with age 30-80 years are included in the study. Secondary causes of OP were accepted as the exclusion criteria. Patients were evaluated according to bone densitometer (DEXA)parameters, Body Mass Index(BMI), routine biochemical analysis, biochemical markers of OP, estrodiol, free testesterone, PTH, FSH, LH, PRL, cortisole and EVOS assessment questionnaire, and food score.

Statistical analysis: Oneway, Mann-Whitney U TEST, Spearman and Pearson were used.

Results: Current BMI index and BMI of age 25, age, current health status and ability to run were found to be correlated with all DEXA parameters. The difference between current height and height at 25 years, deoxypyridolidine, FSH, LH, cortisole, free-testesterone, activity, ability to stand at least 30 minutes, ability to wash hair at the basin, ability to reach something which is located on the upper shelves and ability to carry an object of 10 kg 10 meters were found to be correlated with the DEXA parameters of the hip region.

Conclusion: Daily activities of life and muscle strength should be categorized as risk factors which could be modified while it is not to possible to modify some risk factors such as age. Althugh it is well known that genetic factors are very important for the development of OP, it is mandatory to arrange the environmental factors taking into consideration that genetic and environmental factors both work together in the development of OP.

P269SU. STUDY OF THE FACTORS OF RISK OF OSTEOPOROSIS IN A POPULATION WHO ARE BETWEEN 50 AND 80 YEARS OLD

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Aims: To evaluate the effectiveness of the valuation of the factors of risk with the real prevalence of osteoporosis in a population who are between 50 and 80 years old three or more factors of the osteoporosis risk.

Methods: The study was made in urban and rural areas of Mallorca Island. Of the 2000 surveys, all made by doctors, 1949 were selected and 51 of them were discarded because of not bring complete or well filled up. To the 1949 patients with three or more factors of risk selected, a densitometry of column and hip was made to the 1949 to inquire out the relation between the factors of risk and the potential index of prevalence of the patology.

Results: Of the individuals selected for the study, 93% of the men and 95% of the women make physical activity in a regular way (1 hour three days a week), mainly in it has bipedestation. Around 80% of the reviewed population has an ingestion superior to 1000 mg

of calcium, and only 8% of men and 4% of women have hull calcic ingestion. Out of 1949 densitometries of column and hip made, 614 (31.5%) present alterations, 461 have osteopemia (Z score −1 to −2.5 SD) and 153 osteoporosis (Z score > −2.5 SD).Of the total detected osteoporosis, 86% came up in women, but 14% in men. Osteopemia follows a similar pattern with 80% and 20% respectively.

Conclusions: Of the made study, a series of points can be concluded, that can be the starting point for other investigation works and that in essence are the following ones:

1. 31.5% of the population who are over 50 in our community present alterations of the bone mineral density and some type of structural deficiency in the bone.

2. 82% of the found alterations of the bone mineral density in this study had not been diagnosed previously. Only 18% had previous diagnosis.

3. The precocious diagnosis of the osteoporosis can reduce in an important way the high sanitary costs of this disease.

P270MO. CONTRIBUTION TO THE SCREENING OF BONE MINERAL DENSITY THROUGH THE CALCANEO OSTEOSONOMETRY METHOD IN WOMEN OLDER THAN 45 YEARS OLD IN THE PÉROLA BYINGTON HOSPITAL

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Objective: Screen the index of bone loss using the technique of calcaneo osteosonometry in women older than 45 years old.

Material and Methods: Retrospective transversal study, with 1017 patients, older than 45 years old, asymptomatic that came to the ambulatory of gynecology between May and November 2003. The patients were all submitted to a consultation to solve the symptoms and after verbal allowance were submitted to calcaneo osteosonometry with the device SONOST 2000, the test lasted about 15 minutes and was performed by the same technician. The T score coefficient was used (young adult) until –1 DP for normal, from –1 through –2,5 DP for osteopenia, and less than –2,5 DP for osteoporosis based on the European curve.

Results: The results found in 1017 patients were white 60%, followed by black 39% and asiatic(45–91). The prevalence of osteoporosis was 4.86%, osteopenia 34.2% and normal 60.94%.

Conclusion: The prevalence of osteoporosis in this study was inferior of the one found in literature, so it is necessary for more studies to confirm this data.

P271SA. IMPACT OF RISK FACTORS FOR OSTEOPOROSIS IN A REGIONAL MEXICAN POPULATION: LOW RATE USE OF HORMONAL REPLACEMENT THERAPY

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Osteoporosis (OP) has a high impact worldwide. The risk factors have been of great use in discriminating people susceptible to the disease.

Objective: The detection of the principle risk factors for osteoporosis in post-menopause Mexican women using a scrutiny questionnaire.

Methods: 2091 post-menopause women completed the "scrutiny questionnaire for detecting post-menopause women with osteoporosis" (Albrand and cols, 1998), which evaluates variables that correspond to risk factors, giving everyone of them certain punctuation according to the answers. If the final punctuation (FP): 4 or more points were considered a risk of osteoporosis and an osseous densitometry was carried out: a) of the forearm with a peripheral X-ray PIXI LUNAR densitometer, b) of the phalanges of the not dominant hand with the metric Bone density system, Alara, Inc. The 1994 world health organization criteria for osteoporosis were used.

Results: According to the scrutiny questionnaire the following prevalances of the risk factors were obtained (table). Of the 2091 women that participated, 469 (23.77%) had a FP = 0 > then 4. Both densitometries were carried out in forthy women. The densitometry resulted in 287 with OP (89% without HRT), 155 with osteopenia (67% without HRT), 59 with a normal osea mineral density (47% without HRT) and 2 with a high dmo (both without HRT).

VARIABLE	FP = 4	FP = 5	FP = 6	FP = 7	FP = 8	FP = 9	FP = 10	TOTAL
More then 10 yrs of menopause	158	115	65	38	25	3	2	406
Non use of estrogens (HRT)	172	117	65	30	25	32	2	422
Fractures after 45 years of age	68	46	36	22	15	3	2	192
Weight of 60 kg or less	54	37	24	23	18	3	2	161
Use of corticosteroids	19	13	7	3	4	1	0	47
Presence of a disease	27	18	10	7	3	0	1	66

*hyperthyroidism, intestinal mal-absorption syndrome, Cushing Syndrome, hyperparathyroidism, chronic renal failure.

Conclusions: We found that the most frequent risk factor is the absence of the use of hormonal replacement therapy. This result is different from those obtained in other countries.

P272SU. BONE DENSITY STATUS IN TURKISH WOMEN AND COMPARISON WITH JAPANESE WOMEN

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The aim of this study was to present BMD status of Turkish women and to compare with Japanese population. This study was performed in 339 healthy Turkish women prospectively ranged in the ages from 20 to 79 years. Bone mineral density (BMD) measurements were performed by Lunar Dual Photon X-Ray Absorbtiometry (DPX) at two sites. These were the spine (anteroposterior) and proximal femur. Lunar DPX densitometry measurements were performed in 19 different centers from different regions of Turkey. In the Turkish females there was a linear correlation between BMD and both weight and BMI especially in the older ages. Spinal peak bone density (PBD) was reached in the 30–39 years age group whereas femoral PMD was reached earlier in the 20–29 years age group in Turkish women. The major decrease in BMD was observed after 50 years related to menopause at all measurement sites. There was also a decreasing trend in BMD values at all sites related to age. BMD values in Turkish and Japanese women were found to be similar at the lumbar spine in the 3rd, 4th and 5th decades, whereas lumbar BMDs in the 6th, 7th, 8th decades were higher in Turkish females. Likewise femoral BMDs were found to be higher in Turkish women in all age groups in comparison with Japanese.

P273MO. RISK FACTORS FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN EXAMINED IN PÉROLA BYINGTON HOSPITAL

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Objective: Identify the factors possibly associated with osteoporosis.

Material and Methods: It is a retrospective transversal study that included 49 women of the endocrine gynecological ambulatory, with osteoporosis diagnosed by osteosonometry of the calcaneo with the result of the T score less or equal –2,5PD (based on the European curve). The study occurred in the period from May to November 2003.

The patients after routine consultation answered a specific questionnaire that identified risk factors to the development of osteoporosis such as weight (BMI), high, age, race, the use of some medicine, alcohol, tobacco, hypertension, etc. In the sequence they were submitted to osteosonometry using the device SONOST 2000, each procedure lasted about 15 minuts and were all realized by the same technician.

\Results: The results from the 49 patients as epidemiological data we had that the majority were white women 68%, followed by black with 30%, and Asiatic with 2%. The median age was 61 years old (45–83), the median time since menopause was 15.4 years (2–36), the medium body mass index (BMI) was 29.40 (17–44). About the risk factors we could verify the presence of blood hypertension in 57.1%, familiar history of osteoporosis in 8.2%, postmenopausal state in 88%, diabetes in 18.4% and use of tobacco in 16.3%.

Conclusions: We can conclude that the factors more frequently associated to osteoporosis were postmenopausal state, age and white race.

P274SA. CLINICAL AND EPIDEMIOLOGICAL FEATURES BETWEEN OSTEOPOROTIC PATIENTS

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Objective: To know clinical and epidemiological features of our patients.

Material and Methods: We evaluated clinical history of patients with diagnosis of osteoporosis, established with DEXA studies, who attended Cayetano Heredia Hospital, Piura, Peru during 2001.

Results: Of 124 patients, 95.2% (118) were women, mean age was 67.0 +/−10.0, 23.4% were menopaused before age 40. 16.1% had previous osteoporotic fracture. Comorbities were: hypertension (25.8%), diabetes (16.9%), rheumatoid arthritis(10.4%), hypothyroidism (4.8%) and aAsthma (4%). BMD mean T at vertebral and hip level were −3.18 +/−0.98 and −2.37 +/−0.89 respectively. Results showed:Treatment with Alendronate had 89.5 %, HRT 50 % and both 49.1%.

BMD	With fracture	Without fracture	p
Hip	−2.9 DS 1.1	−2.2 DS 0.7	0.007
	With Diabetes	Without Diabetes	
L1-L4	−2.6 DS 1.1	−3.3 DS 0.9	0.011

The treatment's recuperation in BMD at L1–L4 and hip level were 4.8% +/−3.6 and 3.3 +/−2.7 respectively.

Conclusions: One out of six had severe osteoporosis. There were differences in BMD between patients with fracture and diabetes. Recuperation of BMD was better at vertebral level.

P275SU. POSSIBLE ROLE OF FIBROBLAST GROWTH FACTOR 23 (FGF23) IN THE PATHOGENESIS OF OSTEODYSTROPHY IN END STAGE KIDNEY DISEASE AND RENAL TRANSPLANTATION

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FGF23 is a recently discovered hormone regulating renal and intestinal PO4 transport. FGF23 excess is a cause of osteomalacia. Since ROD is associated with mineralization defects we questioned whether FGF23 was a factor in ESKD associated defective mineralization. Therefore, we examined serum levels of FGF23 in 20 patients with an age of 36.5 ± 12 years, subjected to bone biopsy prior to and within the first six months of a renal transplant. Pre-transplant biopsies showed increased osteoid volume and thickness, osteoblast surface, as well as resorption and osteoclast surfaces. Serum FGF23 was markedly elevated in ESKD patients on hemodialysis (2115 pg/ml) prior to renal transplantation. At this time, FGF23 levels correlated with osteoid surface ($R = -0.993$, $p < 0.01$) and volume ($R = -0.690$, $P < 0.05$). Since we have shown that post-transplant osteoporosis is related to osteoblast apoptosis and hypophosphatemia in the early post-transplant period, and FG23 is a candidate we analyzed FG23 levels in two groups of patients subjected to bone biopsy within the first six months post transplant − those with and those without osteoblast apoptosis post-transplant. High pre-transplant FG23 levels were predictive of post-transplant osteoblast apoptosis and correlated with changes in osteoblast surface and mineral apposition. Thus, pre-transplant FGF23 levels were higher in patients with post-transplant osteoblast apoptosis (3296 ± 373 vs. 1138 ± 1462, $p < 0.05$) and correlated negatively with post-transplant osteoblast surface ($R = -0.533$, $p < 0.05$). After transplantation, FGF23 decreased to normal levels in patients with or without osteoblast apoptosis (34.9 ± 21.8 vs. 119 ± 241, $p = NS$), but no correlation was found between FGF23 and post-transplant hypophosphatemia. We conclude that FG23 accumulates in ESKD and is associated with decreased osteoid accumulation and decreased mineral apposition. High levels of FG23 also appear to be a factor in determining post-transplant decreased osteoblast function contributed in part by increased rates of osteoblast apoptosis.

P276MO. PREVALENCE AND CORRELATES OF VERTEBRAL FRACTURES IN ADULTS WITH CYSTIC FIBROSIS

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Introduction: Osteoporosis associated with Cystic Fibrosis (CF) is becoming increasingly important as the life expectancy of patients continues to increase.

Methods: We studied 191 adults with CF (18–50 years old; 100 men, 91 women). Total body, lumbar spine, and total proximal femur bone mineral density (BMD) were measured by DXA and lateral spinal radiographs were taken for assessment of vertebral fractures. A range of anthropometric, clinical and biochemical variables were evaluated as potential correlates.

Results: T score values at the lumbar spine lower than −2.5 SD were observed in 27.3% and 11.2% of male and female patients, respectively. These proportions fell to 14% and 9.9% for total hip and 10.4% and 12.1% for total body, in men and women respectively. Vertebral deformities were identified in 26.7% of the patients with a slightly higher prevalence in males (32%) than in females (21%, $p = 0.058$). Multiple vertebral deformities were observed in 12% and 7.7% of men and women, respectively. BMD values were significantly related to body weight, FEV1, age of puberty and occasionally to cumulative steroid dose in both genders. BMD values were also significantly related with serum albumin, IgG and cholinesterase. Serum estradiol levels were found below the normal range in 23% of the women and 27% of the men, and was significantly related to femur BMD values in both women and men. Significantly lower serum estradiol and free testosterone levels were observed in men with vertebral fractures. Serum osteocalcin was below the normal range in 36% and urinary deoxypyridinoline above the normal range in 51% of the patients.

Conclusions: Osteoporosis is a common complication of CF, being related to disease progression and apparently due to both excess bone resorption and inadequate bone formation. Estradiol deficiency may have a significant role in the pathogenesis in both genders. Vertebral fracture prevalence is high and greater than expected from prevalent BMD values.

P277SA. EFFECTS OF 4-YEAR TREATMENT WITH ONCE-WEEKLY CLODRONATE ON PREVENTION OF CORTICOSTEROID- INDUCED BONE LOSS AND FRACTURES IN PATIENTS WITH ARTHRITIS

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The aim of this placebo-controlled study was to determine whether once weekly clodronate (Difosfonal) could prevent osteoporosis in patients with arthritis at the start of corticosteroid therapy. 163 patients, 18–90 years of age, with rheumatoid or psoriatic arthritis, were randomly assigned to receive either clodronate (100 mg im/week) plus calcium and vitamin D (1000 mg and 800 IU, respectively) or calcium and vitamin D alone. Patients had started therapy with prednisone or its equivalent within the previous 100 days and had bone mineral density

≤2.5 SD below mean young normal values at the lumbar spine or femoral neck. The primary outcome was the difference between the two treatment groups at months 12, 14, 23 and 48 in the mean percentage change from baseline in bone mineral density of the lumbar spine, femur and total body. Secondary measurements included changes in the stiffness index evaluated by ultrasound measurements and the rate of new vertebral fractures. The bone density and stiffness did not change significantly in the clodronate plus clacium and vitamin D group, whereas it declined significantly in the calcium and vitamin D group. Depending on the skeletal regions evaluated, 85–98% of patients treated with clodronate had a densitometric change lower than the lowest significant densitometric difference. 100% of patients treated with calcium plus vitamin D had a densitometric decrease greater than lowest sigificant difference. The relative risk of vertebral fractures and multiple vertebral fractures in the clodronate goup compared to the calcium plus vitamin D group was 0.63 (0.35–0.98, 95% CI) and 0.25 (0.15–0.91, 95% CI), respectively. We concluded that pulsatory administration of im clodronate once weekly is a safe therapy for preventing corticosteroid induced osteoporosis in patients with arthritis.

P278SU. RATE OF BONE LOSS IN MULTIPLE SCLEROSIS PATIENTS TREATED WITH GLUCOCORTICOIDS IS BEST EXPLAINED BY PHYSICAL PERFORMANCE

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The aim of this study was to evaluate the relative contribution of physical inactivity, glucocorticoid (GC) treatment, and other factors, to rate of bone loss (RBL) in patients with multiple sclerosis (MS).

Patients and Methods: The study population involved 156 females (mean ± SD, age, 44 ± 9 years, weight, 64 ± 11 kg, height, 166 ± 6 cm, duration of MS 13 ± 8 years) and 34 males (age, 43 ± 11 years, weight, 75 ± 11 kg, height, 178 ± 7 cm, duration of MS, 14 ± 6 years). The average dose of GC was 7.1 ± 2.7 mg/d. The patients were not treated with antiresorptive drugs, they received the daily recommended dose of calcium and vitamin D. Motor function of the patients was evaluated using the Kurtzke scale (KEDDS) useful in measuring the ability to walk that is decisive for normal remodeling of bone. BMD was measured (Delphi A, Hologic, MA) at the lumbar spine and proximal femur (total and neck), at baseline and after 2 ± 0.9 years. Serum aminoterminal propeptide of type I collagen, osteocalcin, and type 1 collagen cross linked C telopeptide (CTX) were measured at the baseline.

Results: BMD≥−1 T-score was found in 18% of the patients (KEDDS, 3.8 ± 1.5, RBL at the total femur, −1.8 ± 2.1%/year). BMD T-score of −1 to −2.5, was found in 52 % of the patients (KEDDS, 4.4 ± 1.7, RBL, −1.8 ± 2.3%/year). BMD≤2.5 T-score, was found in 30% of the patients (KEDDS, 5.5 ± 1.4, RBL, −3.4 ± 4%/year). In the multiple regression analysis, the rate of bone loss was related to the KEDDS ($p \leq 0.001$). The other variables, age, weight, height, sex hormone deficiency, baseline BMD, smoking, duration of MS, duration of GC treatment and the average and cumulative dose of GC, did not enter the equation. The rate of bone loss could also be predicted by serum CTX ($p < 0.01$).

Conclusion: In adults with MS treated with low dose GC, immobilization was the main determinant of the rate of bone loss.

P279MO. BONE MINERAL DENSITY AND SERUM LEVELS OF 25 OH VITAMIN D IN CHRONIC USERS OF ANTIEPILEPTIC DRUGS

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Aims: The aim of this cross sectional study was to evaluate bone mineral density (BMD) and serum levels of 25-hydroxy vitamin D (25OHD) in a group of patients taking anti epileptic drugs (AED) for a seizure disorder.

Methods: Between May 2001 and January 2003, we evaluated 58 patients (40 women/18 men), [34.4 + 6 years old (25–47)] living in Curitiba, who were on anti seizure therapy for 2–38 years. The group was matched by age, gender, and bone mass index to 29 healthy subjects (20 women/9 men); 34.2 + 5.9 years old). Medical history and physical exam were performed on all subjects with particular information sought about fractures and risks factors for osteoporosis. Blood samples were collected for total serum calcium, albumin, phosphorus, creatinine, total alkaline phosphatase (AP), and liver function tests. Bone mineral density (BMD) of the lumbar spine, femur and forearm was determined by dual energy x-ray absorptiometry (Hologic QDR 1000). Between February and April 2003, other blood samples were collected to measure 25OHD, intact PTH and calcium.

Results: Fifteen patients had a fracture history all of which occurred during a seizure. The BMD of the lumbar spine (0.975 + 0.13 g/cm^2 vs. 1.058 + 0.1 g/cm^2, $p < 0.03$) and of the total femur (0.930 + 0.1 g/cm^2 vs. 0.988 + 0.12 g/cm^2, $p < 0.02$) was lower in patients than in controls. 63.5% of patients and 24.1 % of controls had a T-score < −1.0 at least one site. The AED users had higher AP and lower 25OHD ($p < 0.02$). No correlations between BMD and 25OHD were found. The use of phenytoin was correlated with a greater incidence of fractures (RR: 2.38).

Conclusions: We conclude that patients on chronic use of AED have alterations at the bone metabolism characterized in this study by lower BMD of the lumbar spine and total femur and lower serum concentrations of 25OHD and more fractures.

P280SA. RISK FACTORS FOR BONE LOSS IN WOMEN WITH EARLY, ACTIVE RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY IN THE COBRA TRIAL

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Rheumatoid arthritis (RA) is associated with an increased risk for fractures. The degree of bone loss early in the disease process is still a matter of debate. In a double blind randomised trial during one year, patients with early, active RA were treated with sulfasalazine (n = 79) or a combination of sulfasalazine, methotrexate and prednisolone (60 mg/d in week 1 tapered to 7.5 mg maintenance dose in week 7) during 6 months, followed by sulfasalazine alone for 6 months (n = 76). All had supplements of calcium (500 mg/day) and, if baseline serum levels of 25(OH)D3 were low, with vitamin D (400 IU/day). Bone mineral density (BMD) was measured by dual X-ray absorptiometry, and bone resorptionby collagen-1 telepopeptide (CTX-1) in urine by Elisa.

At baseline, BMD in spine and hip was lower in postmenopausal women, and inversely related to CTX1. CTX1 was related to CRP ($r = 0.312$, $p < 0.01$). After one year, bone loss was found in the spine [mean and 95% confidence intervals (C.I.): −0.8% (−1.7, 0.2)] and hip [−1.8% (−3.0, −0.8)]. In a univariate analysis, bone loss after 12 months was dependent on baseline CRP (−2.5% in spine and −2.9% in the hip in women with CRP > 50, versus −0.4% and −0.7% in women with CRP < 50, respectively) and on menopausal status (−2.5% in spine and −3.3% in hip in postmenopausal women, versus 0.2% and −0.2%, respectively in premenopausal women), but not on baseline joint damage, HAQ-score, treatment group, rheumatoid factor and radiographic progression of joint damage. In a multiple regression analysis including these factors, only menopausal status was significantly associated with bone loss in the spine and hip. Postmenopausal women had a higher baseline CRP, osteocalcin and CTX1 as compared to premenopausal women.

We conclude that in women with early active RA, generalised bone loss (in the spine) and periarticular bone loss (in the hip) are mainly determined by menopausal status and are related to bone

resorption and inflammation. These results indicate a role for estrogens in the occurrence of bone loss and inflammation in early RA.

P281SU. LONGITUDINAL ASSESSMENT OF HAND AND AXIAL BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS: A COMPARISON OF BONE MINERAL DENSITY CHANGES IN EARLY VERSUS LATE DISEASE

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Background: Measurement of hand bone mineral density (BMD) using dual X-ray absorptiometry (DXA) is an accurate, reproducible, and sensitive method to quantify hand BMD in patients with rheumatoid arthritis (RA).

Objective: This study proposed to assess hand and axial BMD in RA and to compare BMD changes in patients with early versus late disease followed for one-year.

Methods: One-hundred patients with RA (11M, 89F, mean-age 49, mean-disease duration 7.4 years) were included into the study. Patients who were under treatment of high dose or pulse steroids, or had diseases other than RA which influence bone mass were excluded. Patients were assigned into two groups: early RA ($n = 32$, with a disease duration less than 3 years) and late RA ($n = 68$, more than 3 years). In longitudinal assessment patients currently receiving treatments for osteoporosis other than vit-D and/or calcium supplementation were excluded. Patients' hand (bilateral), spine and femur BMD were measured by DXA at entry and after 12-months. The short-term precision for hand BMD was 0.8 % coefficient of variation.

Results: Patients with late RA had significantly lower right and left hand BMD than patients with early RA. There was not a significant difference between right and left hand BMD in both groups. In early RA group right hand BMD correlated with BMD at spine and hip ($r = 0.64$-0.73, $p = 0.0001$) and negatively correlated with disease duration ($r = -0.46$, $p = 0.008$). In late RA group right hand BMD correlated with BMD at spine and hip ($r = 0.58$–0.73, $p = 0.0001$) and negatively correlated with age ($r = -0.37$, $p = 0.002$) and ESR ($r = -0.44$, $p = 0.0001$). Thirty-five patients (13 early RA, 22 late RA) completed one-year follow-up. The percent loss of BMD in right and left hand, spine, femur neck and trochanter in early RA patients were −3.9, −3.4, −1.8, −0.8, and −5.3, respectively. The percent loss of BMD in right and left hand, spine, femur neck, Ward's and trochanter in late RA patients were −2.2, −3.4, −0.8, −3.8, −2.6, and −5.6, respectively.

Conclusion: RA causes bone loss which is more prominent in hands of patients with early disease. Longitudinal assessment of hand BMD is potentially helpful predicting disease progression in RA.

P282MO. RISK FACTORS ASSOCIATED TO LOW-IMPACT FRACTURES IN MEN WITH ANKYLOSING SPONDYLITIS

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Ankylosing spondylitis (AS) is associated to low bone mineral density (BMD). Whether low bone mass in these patients leads to increased fracture rate is still not clear. The purpose of this study was to investigate risk factors associated to low-impact fracture in men with AS.

PATIENTS AND METHODS: 86 men were enrolled in this cross-sectional study (41 healthy controls). Clinical risk factors were evaluated by a questionnaire that included details about aspects of lifestyle, diet, drug use and previous fracture. All the subjects performed spine and femur BMD (DPX-L, Lunar) and heel QUS (Achilles +, Lunar) measurements. Lateral thoracic and lumbar radiographs were taken to check for the presence of vertebral fractures, according to the Genant method.

Results: AS patients were younger, thinner and shorter than healthy controls (HC). The mean age, weight and height were 42.6 ± 10.5 vs. 38.3 ± 10 years, 71.8 ± 8.5 vs. 67 ± 17 kg, and 1.68 ± 0.07 vs. 1.64 ± 0.08 m, respectively (HC vs. AS). Vertebral deformity (grade II and III) was identified in 21 AS patients and 12 HC ($p < 0.05$). Spine and femur BMD and QUS measurements were not different between AS patients and healthy controls. The mean spine BMD and stiffness index were 1.172 ± 0.01 vs. 1.187 ± 0.02 g/cm^2 and 96 ± 17 vs. 91 ± 19, respectively (HC vs. AS) (NS). After adjustments for age, the most relevant risk factors to discriminate AS patients with low-impact fractures from healthy non-fracture controls were prolonged immobilization, current smoking, poor perception of the global health, corticoid use and previous fracture. Patients with AS had more appendicular and axial fractures than healthy controls even though BMD and heel QUS measurements were similar between the two groups. In conclusion, the clinical risk factors for fractures were more important than bone mass measurements to discriminate AS patients with low-impact fracture from healthy non-fracture controls. Interestingly, AS patients presented fractures even with BMD and QUS values higher than that observed in the population in general.

P283SA. EFFECTS OF ANTIVIRAL DRUGS FOR CHRONIC HEPATITIS C IN BONE TURNOVER AND BONE DENSITY

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Hepatitis Cvirus infection is considered a worldwide pandemia. Nowadays, HCV infection accounts for most patients indicated for liver transplantation, and osteoporotic fractures are frequent after transplantation. Combined therapy with Ribavirin with Interferon (Ifn) induces a sustained virological response in about half of the patients, but these drugs have been related to bone loss in a cross-sectional study.

AIM, PATIENTS AND METHODS: In order to investigate the longitudinal effect of therapy on bone turnover and bone density, thirty-one patients with chronic active hepatitis C were started on Ribavirin plus Interferon-alfa2b for one year. Twelve of them were males 34 to 58 yrs and 19 females 27 to 61 yrs, of whom 5 had regular menses, 5 were on estrogen replacement for menopause and 9 did not receive hormones for menopause. Fasting serum bone specific alkaline phosphatase (BSAP), and urinary N-terminal telopeptide of type 1 collagen (NTx) were measured at baseline, 3 and 6 months on therapy. Bone density was evaluated by DEX Lunar Corp. at lumbar spine (LS) and femoral neck (FN) at baseline and twelve months. Anova for repeated measures, paired and unpaired t tests were used.

Results: There was a significant decrease in urinary NTx at 3 and 6 months (54.9 +/−44.6 to 39.8 +/−53.5 and then to 31.3 +/−22.1 mBCE/mMCr, $p < 0.005$). Serum BSAP did not change during treatment. Before starting antiviral drugs, 9 patients (7 females and 3 males) had osteopenia at LS and 9 patients (7 females and 2 males) had osteopenia at FN. Further 3 females had osteoporosis at LS. In the sixteen patients re-evaluated after 1 year, BMD increased in six and decreased in four, and bone loss was more evident at FN. When the whole group was considered, variations of bone mass were not significant, but women lost more bone than men ($p = 0.016$). There was a trend for correlation between delta-6 months NTx and delta-12 months BMD at FN (r −0.447 p 0.0824).

Our results suggest that antiviral treatment decreases bone turnover but other factors related to hepatitis C probably justify the heterogeneous response of bone mineral density.

P284SU. BONE DENSITY IN ANKYLOSING SPONDYLITIS ASSESSED BY DUAL ENERGY X-RAY ABSORPTIOMETRY AND QUANTITATIVE ULTRASOUND: THE RELATIONSHIP OF BONE MINERAL DENSITY WITH FUNCTIONAL AND DISABILITY STATUS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease involving the sacroiliac joints and axial skeleton and is typically associated with sclerotic changes and syndesmophytes in the spine. Patients with AS usually have difficulties in

activities of daily living and disabling nature of the disease is usually depends on musculoskeletal restrictions.

Objective: This study proposed to investigate bone mineral density (BMD) in AS by using both dual X-ray absorptiometry (DXA) and quantitative ultrasound (QUS) and to assess relationship between BMD and patients' functional and disability status.

Methods: Forty-two patients with AS (age 33.2,disease duration 8.9 years) were included into the study. BMD of the AP lumbar spine and femoral neck, Wards and trochanter was measured using DXA in all patients and broadband ultrasound attenuation (BUA), speed of sound (SOS) were measured at the calcaneus using an Hologic Sahara bone sonometer in seventeen of the patients without talalgia. Daugados Functional Index (DFI), and Articular Index (DAI), Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), Leeds Disability Index (LDI) were used to estimate disease activity, functional and disability status.

Results: According to the L2-L4 t scores, 28.6% of patients had osteoporosis, 33.3% osteopenia, and 38.1% had normal BMD. Femoral neck, Wards and trochanter BMD negatively correlated with BASFI ($r = -0.38$, $r = -0.39$, $r = -0.44$, $p \leq 0.01$ respectively) and LDI ($r = -0.33$, $r = -0.36$, $r = -0.30$, $p \leq 0.05$ respectively) whereas L2-L4 BMD had no significant correlation. BUA and SOS significantly correlated with femoral neck, Wards and trochanter ($n = 17$, $r = 0.50$ to 0.60) but not significantly correlated with L2-L4 BMD. BUA and SOS did not significantly correlated with functional or disability indices. BASDAI correlated negatively with only femural neck (r:−0.31, $p \leq 0.05$) and trochanter ($r = -0.41$, $p \leq 0.01$) BMD.

Conclusion: These results indicate close relationship between functional and disability status and BMD in AS. DXA measurement of femoral neck, Wards' or trochanter BMD may be much more predictive for functional or disability status in AS rather than AP spine measurements. Nevertheless QUS measurements predict bone density in AS, this technique fails to detect patients' functional or disability status.

P285MO. THE EFFECT OF LOW DOSE METHOTREXATE ON BONE DENSITY IN PSORIATIC ARTHRITIS PATIENTS

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OBJECTIVE: The use of high dose methotrexate (MTX) has been linked with bone loss. However, it is not clear whether longterm low dose MTX used in the treatment of psoriatic arthritis is associated with bone loss. We compared the effect of low dose MTX on bone density in prospectively recruited patients with psoriatic arthritis (PsA).

Methods: 50 PsA men taking MTX were compared to 50 controls with PsA and not taking MTX. In all patients, evaluation was made of disease duration, inflammation indices (erythrocyte sedimentation rate, C-reactive protein), functional indices (Steinbrocker scale), and the Health Assessment Questionnaire (HAQ). Bone mineral density (BMD) of the lumbar spine, trochanter, and femoral neck was measured using Lunar dual energy x-ray absorptiometry. Student t tests were used to detect differences in bone density (using T scores) of the MTX group versus controls. Analysis of covariance was used to examine for confounders including disease duration, disease activity and age.

Results: BMD of the femoral neck and trochanter did not differ significantly between the MTX treated groups and controls when analyzed by T scores.

The mean difference between the MTX group and controls of the femoral neck was 0.060 (95% CI 0.15). The absolute BMD of the lumbar spine (L2-L4) did not differ significantly between the group and the controls.

Conclusion: The study suggests that low dose of MTX does not have a negative effect on bone density. Osteoporosis was related to the indices of inflammation but not with disease duration. There was a correlation with HAQ score.

P286SA. BONE MINERAL DENSITY IN FEMALE PATIENTS WITH EATING DISORDER

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Aims: To determine predictive factors for bone mineral density (BMD) loss and fractures in females with eating disorder and to identify any possible benefit of estrogen therapy on bones in the subgroup of patients with amenorrhea.

Methods: The cross-sectional study involved 62 consecutive female patients with eating disorder (30 with anorexia nervosa – restrictive type (AN-R), 16 with anorexia nervosa – bulimic type (AN-B) and 16 with bulimia nervosa – purging type (BN-P)). Characteristics: mean age 26.3 years (SD 6.1), mean duration of the disease 8.7 years (SD 6.3), mean BMI 15.9 (SD 1.8). The studied outcomes were BMD and Z-score of the spine and of the hip, and presence of bone fractures. Several potential predictors were assessed: weight, BMI, years of disease, disease onset before menarche, duration of amenorrhea, estrogen therapy, smoking, alcohol consumption, use of laxatives, vomiting, binge eating and vegetarian diet.

Results: In the multivariate analyses (linear and logistic regression), weight and BMI were found to be the only statistically significant independent predictors of both spine and hip BMD and Z-score ($p < 0.01$). The model for predicting presence of fractures was not statistically significant. Bivariate analyses confirmed just some of the expected relations (positive impact of weight and BMI; negative impact of years of disease, duration of amenorrhea and disease onset before menarche). Most importantly, no impact of estrogen therapy was found, regardless of its type (HRT or contraceptives). Finally, the differences between types of eating disorder were tested, controlling for BMI and duration of amenorrhea/disease onset before menarche. Except for hip Z-score, significant differences were found between the three groups ($p < 0.05$), whereby the patients with BN-P had the highest and AN-R patients had the lowest average values.

Conclusions: Treatment of eating disorder (e.g. weight gain) seems to be crucial for preserving bones of female patients, as weight and BMI were the most important predictors of BMD and Z-score in our group, whereby no benefit of the estrogen therapy was proven. Unfortunately, there were too few fractures in our group for any reliable conclusions regarding this outcome.

P287SU. PARATHYROID FUNCTION AND MARKER OF BONE RESORPTION IN HEMODIALYSIS (HD) PATIENTS, THEIR DYNAMICS ON ALFACALCIDOL THERAPY

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The most common type of renal bone disease is renal osteodystrophy, and its severity is closely related to levels of intact PTH.

Objective: Investigate interrelations between PTH and beta-crossLaps levels in HD patients, estimation effectiveness of alfacalcidol treatment. 224 patients in age from 18–70 were investigated. Intact PTH was measured by IRMA in baseline, 3, 6, 12 months. Beta-crossLaps were measured by Elecsys Systems 2010 modular analytics.

Secondary hyperparathyroidism (SHPT) was diagnosed in PTH level above 260 pg/ml. Optimal levels of PTH (130–260 pg/ml) were revealed in 27% (60 patients). 28% (62 patients) showed PTH levels less 130 pg/ml. SHPT was determined in 102 patients: mild (PTH 260–400 pg/ml) in 30%, moderate (PTH 400–800) in 36%, severe (PTH > 800 pg/ml) in 34% patients. β-crossLaps levels were increased in all patients. T-score was ranged from 4.7–25 in accordance PTH groups (mild, moderate and severe SPHT). There was significant positive correlation between β-crossLaps and PTH levels ($r = 0.844$). Patients with SPHT were treated with alfacalcidol (Alpha D3-Teva) 3 times/week. In 90% patients PTH fell by more than 50%: from 327 to 163 pg/ml in 84% patients with mild SHPT (mean dose alfacalcidol was 1.5 mcg/week); from 589 to 200 pg/ml in 90% patients with moderate SHPT (mean dose alfacalcidol was

2.0 mcg/week); from 1352 to 596 pg/ml in 96% patients with severe SHPT (mean dose alfacalcidol was 2.5 mcg/week). Dynamic of β-crossLaps levels on alfacalcidol therapy was estimated in 36 patients. There was revealed decrease of beta-crossLaps on 38.2%.

Conclusion: SHPT was determined in 45.5% patients in HD. The positive correlation was showed between beta-crossLaps and PTH. Moderate doses of alfacalcidol are effective in the majority HD patients to maintain optimal level of PTH. Patients with mild and moderate SHPT are more susceptible to suppression by alfacalcidol than those patients with severe SHPT at the onset of treatment.

P288MO. 25 HYDROXY-VITAMIN D LEVELS (25OHD) IN A HEALTHY YOUNG POPULATION IN THE CITY OF SÃO PAULO AND ITS CORRELATION WITH OCCUPATIONAL ASPECTS AND CALCIUM METABOLIC PARAMETERS

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Aim: The serum level of 25OHD is accepted as a good index of vitamin D storage. In literature there is a discussion about the normal levels of 25OHD. Sex, age, occupation, lifestyle, ethnical group and latitude can influence 25OHD levels. The objective of this study was to establish the normal levels of 25OHD in a healthy young population living in São Paulo, at the age of their peak of bone mass, and correlate these levels with others parameters.

Methods: 99 healthy young subjects (men = 40 and women = 59; median age 25.0 ± 2.8 years old,range: 17 to 33) were requested to participate in the study. Twenty subjects were medical students, 52 were residents in a School Hospital and the other 28 worked in plants. Fasting blood samples were collected for 25OHD (RIA Nichols Institute), ionized calcium, total calcium, intact PTH, albumin, osteocalcin, alcaline phosphatase, phosphorus, creatinine and glucose. Pearson correlation, linear regression, and Wilcoxon Signed Rank tests were used in statistical analysis and $P < 0.05$ was considered to be significant. All values were expressed by Mean ± Standard Deviation.

Results: The level of 25OHD in the studied population was 31.5 ± 13.6 ng/mL (range: 10–56). Men had higher levels than women (34.1 ± 15.4 and 29.9 ± 12.1 ng/ml, respectively, $P < 0.05$). We found a significant correlation of 25OHD with osteocalcin ($R = 0.29$) and creatinine ($R = 0.43$),but not with ionized Ca, total Ca or PTH levels. According to the occupational distribution, the lowest 25 OHD values were among the residents (26.6 ± 10.4 ng/ml, range: 10–54), compared to the students (36.5 ± 17.0 ng/ml, range: 11–86) and workers (37.9 ± 13.0 ng/ml, range: 14–64).

Conclusions: The normal range for 25OHD in this young healthy population was 37.3 ± 14.7 ng/ml(range: 11–86), excluding the residents. Even in this healthy young population we found significant differences in 25OHD levels considering gender and occupational aspects. The residents usually have a heavy schedule and no time to stay outdoors. The 25OHD concentrations correlated with osteocalcin levels, probably reflecting some systemic effect on bone metabolism.

P289SA. FACTORS INVOLVED IN OSTEOPOROSIS IN YOUNG MALE PATIENTS WITH CHRONIC VIRUS C HEPATITIS

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Objective: Evaluation of factors involved in bone loss in men with chronic C hepatitis.

Patients and Methods: Bone mineral density (BMD) was obtained by DEXA, Expert-Lunar Corp., at lumbar spine (LS) and proximal femur (FN), in 74 patients with viral C hepatitis confirmed by positive anti-HCV. According to liver biopsy and/or biochemical tests, patients were classified as: non-cirrhotic (Ncir = 38) and cirrhotic (Cir = 37). Twenty-one of Cir patients are waiting for liver transplantation. Serum bone-specific alkalin phosphatase (BALP), insulin growth factor-1 (IGF-1), testosterone (T), and urinary N-telopeptide of type 1 collagen (NTX) were evaluated. Unpaired t test was utilized to compare the groups.

Results: No difference was found concerning age (NCir 48.9 +/−9.8 and Cir 52.1 +/−11.2 years). We found osteoporosis (T score < −2.5) at LS in 3 NCir and 6 Cir patients, but mean BMD at LS did not differ between groups: Ncir = 1.198 +/−0.182 and Cir 1.184 +/−0.214 g/cm^2, $p = 0.7$. At femoral neck, 1 NCir and 4 Cir patients had osteoporosis, and FN BMD was significantly lower in Cir (0.971 +/−0.172 g/cm^2) vs NCir (1.045 +/−0.154 g/cm^2) $p = 0.043$. Serum IGF1 (median and quartiles) was also lower in Cir = 21.2 ng/mL(8.5–36.7) than Ncir = 91ng/mL (57–111.8), $p = 0.0001$. Serum T (median and quartiles) was 480.5 pg/dL (374–565.5) in Cir and 613.3 pg/dL (507–766.5) in Ncir, $p = 0.067$. No difference was found between groups in BALP and NTx, but these markers of bone turnover were above normal in about 30% of all patients.

Conclusions: We detected low bone mass in young male patients with virus C hepatitis, as 12.1% of them showed osteoporosis at LS and 6.7% had osteoporosis at FN. Bone density at FN and serum IGF1 were lower in cirrhotic patients, who also tended to have lower serum Testosterone. These alterations in anabolic hormones and in bone turnover probably have a negative influence in skeletal homeostasis. We thus suggest that all patients with chronic hepatitis C should be screened for bone density and treated with anti-resorptives and/or anabolic drugs in order to prevent osteoporosis and fractures after liver transplantation.

P290SU. THE SPECTRUM OF RENAL BONE DISEASE IN CHRONIC KIDNEY DISEASE (CKD) STAGES 3 TO 5: POSSIBLE CONTRIBUTION OF OSTEOPOROSIS

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The term renal osteodystrophy (ROD) includes high bone turnover, low turnover and mixed lesions. However, little attention has been paid to the possible contribution of osteoporosis to the bone lesions of CKD, particularly in the increasing population of aging patients. The present study was designed to examine the spectrum of ROD in patients with moderate (stage 3) and severe (stage 4) decrease in GFR compared with kidney failure on dialysis (stage 5). Forty patients (18 female and 22 male), with a mean age of 54 13 years and GFR of 25.8 12.5 ml/min (CKD stages 3 and 4) were compared with 53 patients with kidney failure on dialysis. All patients were subjected to bone biopsy for histomorphometric analysis. As shown in the table, in CKD stages 3 and 4 the prevalence of OP accounted for 25% of the patients and was the second type of bone disease after 2nd HPT. In 12.5% of the patients bone histology was normal. In contrast, in CKD stage 5, 2nd HPT

Bone alterations in CKD

Diagnosis	CKD Stage 3–4, N (%)	CKD Stage 5, N (%)
2nd Hyperparathyroidism (2nd HPT)	12 (30)	24 (45.3)
Mixed Bone Disease (MBD)	6 (15)	15 (28.4)
Adynamic bone disease (ABD)	7 (17.5)	11 (20.7)
Osteomalacia (OM)	0	2 (3.7)
Osteoporosis (OP)	10 (25)	1 (1.9)
Normal bone histology (NB)	5 (12.5)	0
Total	40 (100)	53 (100)

was the most prevalent form of ROD, followed by MBD, ABD and osteomalacia, whereas OP was observed in only one patient. CKD patients stages 3 and 4 with OP had lower serum creatinine (2.60.9 mg/dl vs. 4.11.3 in 2nd HPT, and 5.01.7 in MBD, $p < 0.01$) and tend to be older (61.411 years). Six out of these 10 patients were postmenopausal women In addition, OP patients had lower serum PTH levels (71.3.148.3 pg/ml) compared with all other type of ROD, except ABD. In conclusion, osteoporosis is frequent in CKD, particularly in older postmenopausal women with moderate to severe decrease in GFR. It is possible that the severity of the typical alterations of ROD may mask the possible contribution of osteoporosis in this process.

P291MO. BONE MINERAL DENSITY EVALUATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Inflammatory Bowel Disease (IBD) is a potential cause of secondary osteoporosis.

Aim: The aim of this cross sectional study was to evaluate the bone mineral density (BMD) in a group of patients with IBD and correlate the results with disease activity index and other clinical characteristics.

Methods: Between May and October 2003, 90 patients consecutively seen at the Gastroenterology Clinic of the Federal University of Parana were selected and 76 completed the evaluation. They were divided into two groups, regarding their diagnosis, 39 (21 men, 18 women, mean age: 32.1 ± 8.8 ys) had Crohn disease (CD) and 37 (12 men, 25 women, mean age: 35.9 ± 8.5 ys) had ulcerative colitis (UC). They were compared with 40 healthy subjects (16 men, 24 women, mean age: 34.1 ± 7.1 ys) matched by gender, race and age. Postmenopausal women and subjects with other diseases known to cause osteoporosis were excluded. Medical history was performed in all patients with emphasis on risk factors to osteoporosis and use of glucocorticoids. BMD of lumbar spine and hip was performed by DEXA (Hologic QDR 1000/W).

Results: The groups were homogeneous in all the epidemiologic aspects. BMD of IBD patients was lower than the control group at lumbar spine and total hip ($p < 0.004$ and $p < 0.004$ respectively). No difference was found at BMD between UC and CD patients. Body mass index (BMI) of the IBD group was negatively correlated to the BMD ($p = 0{,}01$). No other correlation between BMD and variables analyzed were found.

Conclusion: Low BMD was found in IBD patients. Among the analyzed variables, only the BMI had a significant correlation with BMD, while the use of corticosteroids, disease activity index, previous surgery and physical activity, did not had any correlation with BMD in these groups of patients.

P292SA. LONG TERM EFFECTS OF GROWTH HORMONE REPLACEMENT THERAPY ON BONE METABOLISM IN PATIENTS WITH GROWTH HORMONE DEFICIENCY WITH SPECIAL RESPECT TO GENDER

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Aims: The effects of growth hormone replacement therapy on bone mineral density and on bone metabolism were investigated with special respect to gender.

Methods: 20 patients (11 men, 9 women, mean age: 43 years) with growth hormone deficiency were involved in the study. Parameters of bone metabolism and bone mineral density of the lumbar spine, the left femoral neck and the forearm were checked prior to and at 3, 6, 12, 18, 24 and 36 months after the start of treatment.

Results: Serum calcium (seCa) increased only after 3 and 6 months; alkaline phosphatase (AP) increased until the first year; phosphate (seP) remained elevated until 18 months. The changes of seCa, AP and seP were more pronounced in males than in females ($p = 0.001$, 0.04, and 0.05, respectively). PTH decreased in both sexes until the first year, then increased, and finally exceeded the baseline level. Before the study, osteoporosis was found in 2 men and 1 woman, osteopenia in 3 men and 4 women. The lumbar and femoral BMD increased first after 12 months of treatment, and further improvement was seen until the end of the study (lumbar: 1.019 ± 0.12 vs 0.941 ± 0.13 g/cm^2, $p < 0.001$; femoral: 0.886 ± 0.12 vs 0.836 ± 0.11 g/cm^2, $p = 0.01$). The radial BMD started to improve after 3 years (0.664 ± 0.1 vs 0.602 ± 0.1 g/cm^2, $p = 0.01$). Although the lumbar BMD and T-scores were increased in both sexes, this effect was greater in males than in females ($p < 0.05$). The femoral and radial BMD and T-scores were increased only in male patients ($p < 0.01$).

Conclusions: GH replacement therapy has temporary effects on bone metabolism: a significant but transient increase in seCa, seP and AP levels and a biphasic change in PTH values could be observed. The beneficial effect of GH treatment on the BMD appeared only after 12 months of treatment but, in spite of the above temporary changes, continuously improved further until the end of the study. The results indicate that generally more marked improvement can be obtained in males than in females during replacement therapy.

P293SU. BONE LOSS IN THE EARLY AND PROLONGED POSTTRANSPLANTATION PERIOD FOR LIVER TRANSPLANTATION

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Objective: To evaluate the bone density, bone turnover, gonadal function after the liver transplantation in the both of the early and prolonged period.

Method and Patients: In the early period (first 3 months) 42 patients aged 19–69 years and in the prolonged period (after 1st year) 37 patients aged 25–72 years without treatment of osteoporosis, a total 79 patients after liver transplantation were evaluated. All patients were on treatment with immunosuppressive agent such as tacrolimus or cyclocporine and on prednisolone. Measurements of lumbar spine and proximal femur and total body BMD were performed by dual x-ray absorptiometry. Biochemical markers of bone resorption and bone formation with serum calcium and phosphorus, urinary calcium and gonadal hormones, growth hormone, thyroid function tests, parathyroid hormone, testosterone and spine radiographs were evaluated on the same times.

Results: In the early period of the posttransplantation, mean T scores for bone mineral density (BMD) decreased by –2.22 (−6.33-0.21)at the lumbar spine and by –2.79 (−7.39—0.42) at the femur total. At one year of posttransplantation mean T scores for BMD were –1.98 (−3.69–0.03) at the lumbar spine and –1.25 (−2.87–0.07) at the femur total. In the both of the period, urine deoxypyridinoline as a marker of bone resorption was increased in all patients. In the prolonged period, osteocalcine as a marker of bone formation was significantly higher than in early period ($p < 0.05$). 14 patients in early period, 24 patients in prolonged period had high values for PTH. In the both of group, the women had low values of gonadal hormones, the men had low values of testosterone. In the 6 patients who were clinically confirmed had a history of vertebral fracture following transplantation.

Conclusion: Our results demonstrates a high prevalence of bone loss which occur during the first months in patients with liver transplantation. Morever, these results suggest that the risk of fracture is considerably increased in patients who did not receive treatment for osteoporosis after transplantation.

P294MO. BONE MASS IN HIV INFECTED CHILDREN

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Aims: To evaluate the ocurrence of osteopenia in children infected with human immunodeficiency virus (HIV).

Methods: 27 patients with vertical HIV infection aged 7.3 ± 3.8 years (14 male) were measured by bone mineral density (BMD), serum calcium, serum alkaline phosphatase, serum phosphorous, calciuria, CD4 and CD8 lymphocyte counts and HIV RNA copy numbers. Clinical variables included sex, age, weigth, heigth and clinical categories. All patients were receiving antiretroviral therapy. BMD were performed at lumbar spine (L1-L4) and expressed in deviation standard score (SDS) by age and sex. Weigth and heigth was referred to NCHS standards and expressed in SDS. Simple linear regression was used to analise correlations between variables and the U-Mann-Whitney to compare groups.

Results: BMD average was normal (−0.74 ± 1.08 SDS). However we verified that 40.7% of the patients had osteopenia (BMD < −1 SDS). When comparing data from osteopenic patients (n = 11) with non-osteopenic patients (n = 16), we observed that weigth (SDS) from osteopenic group was lower than that from non-osteopenic (−1.29 ± 0.66 vs 0.66 ± 1.10; $p < 0.05$), as well as CD4 lymphocyte count (576.4 ± 300.0 vs 925.1 ± 761.4 count/microliter; $p < 0.05$). BMD correlated positively with weigth ($R = 0.37$; $p < 0.05$), CD4 lymphocyte count ($R = 0.43$; $p = 0.02$) and CD8 lymphocyte count ($R = 0.53$; $p = 0.003$); and negatively with age ($R = -0.55$; $p = 0.008$).

Conclusions: Osteopenia occurs in children with vertical HIV infection. Osteopenia was related to lower weigth and lower CD4 lymphocyte count. Our results suggest that duration of HIV infection affects bone mineral acquisition as well as the degree of immunological supression. HIV infection during childhood may predispone to a reduced peak bone mass.

P295SA. SEASONAL VARIATION ON PLASMA LEVELS OF 25 HYDROXY-VITAMIN D (25OHD) IN A HEALTHY ELDERLY POPULATION FROM BRAZIL

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Aim: The major source of vitamin D comes from its synthesis in the skin by sunlight ultraviolet rays. Aging, skin pigmentation and sun screens can interfere in this production. Seasonal variation of plasma concentrations and vitamin D deficiency is widely described in extreme latitudes, but there aren't consistent data about these levels in Brazil. The objective of this study is to investigate this variation in a elderly population in São Paulo, located in a subtropical region (23°34′).

Methods: One hundred one healthy subjects (men = 46 and women = 55, mean 67.5 ± 5.3 years old, range: 55–83) participants in a fitness program for the elderly were requested to participated in this study. Fasting blood samples were collected in August (end of the winter) and in December beginning of the summer) and analyzed for serum 25OHD (RIA Nichols Institute;normal range: 9.2–45.2 ng/ml). We excluded from analyses 6 subjects taking vitamin D supplements. Paired Student's t-test and Wilcoxon Signed Rank Test were used, and $P < 0.05$ was considered significant. Values were expressed by Mean ± Standard Deviation.

Results: We included in the analysis 95 subjects. The 25OHD at the end of winter was 30.8 ± 11.7 ng/ml and significantly increased at the beginning of summer (36.6 ± 12.7 ng/ml). According to gender, the increment was significant only in men (32.6 ± 12.1 to 43.4 ± 12.4 ng/ml), but not in women (29.1 ± 11.2 to 29.7 ± 8.6 ng/ml). There was no difference in 25OHD levels between ethnical groups (Caucasian, Japanese, Afro-Brazilian, and Brazilian-natives). A significant increase on 25OHD levels in summer was only seen in the Caucasian (31.4 ± 11.4 to 37 ± 14.1 ng/ml) and Japanese (31.4 ± 14.5 to 37.7 ± 9.9 ng/ml). In the other groups we did not find any difference between seasons.

Conclusion: There was a seasonal variation on the 25OHD levels in this healthy elderly studied group. The values were lower after winter and higher in summer. This significant increment in summer was due exclusively to the men. In the same way, subjects with darker skin were not able to increase the synthesis of 25OHD in summer. These data suggest that women and people with more pigmented skin are at higher risk of vitamin D deficiency, even in a sunny country like Brazil.

P296SU. PREVALENCE OF OSTEOPOROTIC VERTEBRAL FRACTURES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Aims: To study the prevalence of osteoporotic fractures and associated risk factors in patients with Crohn's disease (CD) and ulcerative colitis (UC).

Patients and methods: This analysis included 43 patients consecutively evaluated at the São Paulo Hospital, São Paulo Federal University, São Paulo, Brazil. Potential risk factors associated with fractures were assessed by a validated questionnaire (EVOS – European Vertebral Osteoporosis Study). All patients had bone mineral density (BMD) measurements done by dual energy x-ray absorptiometry at the lumbar spine and proximal right femur (DPX, Lunar). Quantitative ultrasound of the calcaneus (Achilles +, Lunar) was also performed in all patients. All patients were screened with spine x-ray and the prevalence of vertebral fractures was determined by Genant's method. Non-vertebral fractures were recorded from hospital records and interviews with the patients.

Results: Forty-three patients (24 women and 19 men, mean age 39.3 years, range 20.5–58.3 years) were enrolled in this study. 49% of the patients had CD and 51, 2% had UC. Osteoporosis was observed in 11.4% of our sample (9.1% in CD patients and 13.6% in patients with UC), while osteopenia was diagnosed in most of the patients (72.7% and 40.9% in CD and UC patients, respectively). The prevalence of vertebral fractures in this population was 43.2% (43.7% and 42.8 in CD and UC patients, respectively). Half of the patients in the fracture group were female. After adjustments for age and clinical variables, broadband ultrasound attenuation (BUA) values were significantly lower in patients with fractures as compared to those without. In all other subgroup analyses, no statistically significant differences were found between patients with and without fractures.

P297MO. PREVALENCE OF OSTEOPOROSIS AND FRACTURES IN CHINESE PATIENTS CHRONICALLY TREATED WITH GLUCOCORTICOIDS

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Aims: A cross-sectional study was conducted to measure the bone mineral density and fracture prevalence in patients with autoimmune diseases treated with glucocorticoids in a regional hospital in Hong Kong.

Methods: 118 Chinese patients who have been put on chronic glucocorticoid therapy were asked to fill in an osteoporosis risk factors questionnaire and undergo a DEXA (Lunar) examination of lumbar spine and proximal femur to measure bone mineral density. Radiological examination of spine was done to detect any vertebral fractures. 82.2% (n = 97) were female. 43% (n = 42) were post-menopausal without estrogen replacement. Primary diagnoses included systemic lupus erythematosus (n = 75), glomerulonephritis (n = 22), rheumatoid arthritis (n = 6), and others including mixed connective tissue disease, fibrosing alveolitis and dermatomyositis (n = 15). The mean age was 42.4 ± 11.8 years. The mean body weight and height were 56.0 ± 9.8 kg and 157.5 ± 7.3 cm. The mean

duration of glucocorticoid treatment was 111 ± 81 months. Current daily dose of prednisolone was 9.0 ± 6.1 mg/d and mean cumulative dose was 34.9 ± 27.4 g.

Results: The mean BMD of lumbar spine (L2-4) was 1.031 ± 0.133 g/cm^2 at T-score of −0.85 SD and Z-score of −0.72 SD. The mean femoral neck BMD was 0.800 ± 0.137 g/cm^2 at T-score of −0.91 and Z-score of −0.45. One-Sample T-test showed Z-score was statistically different from zero at the lumbar spine and femoral neck ($p < 0.001$). 13.6% (n = 16) of the patients had T-score less than −2.5 either at lumbar spine or at femoral neck. 11.9% (n = 14) had history of fractures. 4.2% (n = 5) had radiological evidence of vertebral fractures. 25% (9/42) of postmenopausal female on chronic glucocorticoid therapy and 3.6% (2/55) of premenopausal female experienced fractures. 14.3% (3/21) of male had fractures. Those who fractured had statistically significant lower T-score of −1.600 at lumbar spine compared to a mean T-score of −0.749 for those who did not fracture.

Conclusions: Prevalence of osteoporosis and fractures were respectively 13.6% and 11.9% in patients on chronic steroid therapy. Post-menopausal female and male were at a higher risk for fracture. Those who have low lumber spine BMD at T-score < −1.5 should be considered for prophylactic therapy against fractures.

P298SA. IS BEHCET'S DISEASE RISK FOR OSTEOPOROSIS?

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Behcet's disease is a complex, multisystemic, chronic inflammatory disorder characterized clinically by recurrent oral ulcerations, genital ulcerations and uveitis. The etiology and pathogenesis of this syndrome remain obscure. However, some factors are suspected, including immunological abnormalities, genetic propensity, and. infectious precipitants, Considering the chronicity and unclear etiology of the disease, In this study we aimed that is Behcet's disease a risk for lower bone mineral density (BMD).

This study was carried out on sixty patients (24 males and 36 females, mean age 35.65 ± 7.93 years) diagnosed accorging to the International Study Group Criteria with Behcet's disease and 24 sex- and age-matched healthy controls (8 males and 16 females, mean age 33.587 ± 6.47 years). Postmenopausal women with Behcet's disease and patients receiving oral corticosteroid and other drugs which caused of osteoporosis were excluded from the study. The mean disease duration was 7.23 ± 6.14 years. BMD was measured with dual x-ray absorptiometry at the lumbar spine and left femur. The mean Z scores of the patient and control groups were −0.77 ± 1.06 and −0.20 ± 0.84 at the lumbar spine, respectively, and −0.58 ± 0.89 and −0.50 ± 0.69 at the left femur, respectively. The mean BMD values of the patients and control groups were 0.917 ± 0.278 and 1.033 ± 0.313 at the lumbar spine, respectively, and 0.843 ± 0.147 and 0.847 ± 0.194 at the left femur, respectively. There was significant differences in BMD values and Z scores of lumbar spine ($p < 0.05$). No significant differences in BMD values and Z scores of the left femur were detected in the groups ($p > 0.05$). Disease duration did not influence bone mineral density, and age had a positive correlation with bone mineral density in patients with Behcet's disease.

In conclusion, our study confirms that bone mineral density in Behcet's disease was lower than in healthy subjects at the lumbar spine Behcets disease can be risk for osteoporosis.

P299SU. OSTEOPOROSIS IN SPINAL CORD INJURED PATIENTS

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Osteoporosis is a potential problem which increases morbidity of the spinal cord injured patients. The purpose of this study was to investigate the possible risk factors and the characteristics of osteoporosis in spinal cord injured patients. Ninety three spinal cord injured patients were investigated and compared with 30 control subjects. The patient group was evaluated with respect to level and severity of injury, ambulation capacity, duration of sun exposure, drug intake, nutrition and endocrinal pathologies. Also the fractures present in the history of the patients were recorded. The bone mineral density (BMD) measurements of lumbar spine, hip (femoral neck, Ward's triangle and trochanter) and total body (arms, legs and total) of the two groups were obtained using dual energy x-ray absorbtiometry. T-test, one way ANOVA test, regression analysis were used as statistical analysis.

The BMD values at leg, femoral neck, trochanter and Ward's triangle were statistically lower in the patient group compared with the control group whereas the BMD values at the arm were significantly higher in the patient group. No statistical difference was detected at lumbar and total BMD values. Eleven (11.5%) of the patients reported fractures with minor trauma. There was no significant difference related with severity and level of the injury, ambulation, smoking and nutritional habits (calcium intake, cafeine). When the patients were grouped according to drug consumption related with osteoporosis, interestingly the BMD values of the patients using these drugs were statistically higher.

Osteoporosis after SCI constitutes a potential problem in the rehabilitation of these patients. The clinical importance of the osteoporosis lies in the increased risk of fractures which worsens the quality of life of these patients. During the rehabilitation period diagnosis and management of osteoporosis should be considered. Further studies investigating the risk factors of osteoporosis in spinal cord injured patients are needed.

P300MO. INFLUENCE OF CORTICOSTEROID THERAPY ON BIOCHEMICAL, DENSITOMETRIC AND HISTOMORPHOMETRIC BONE PARAMETERS IN POSTMENOPAUSAL WOMEN

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Aims: We investigated the influence of longterm corticosteroid therapy on bone mineral density, biochemical markers and histomorphometric parameters of bone turnover in postmenopausal women.

Methods: Bone mineral density (BMD; DXA, QDR Hologic 4500A) at lumbar spine (LS) and femoral neck (FN), biochemical markers of bone turnover (serum osteocalcin – OC, urinary excretion of pyridinolin – PYD and desoxypyridinolin – DPD) and bone histomorphometric parameters from iliac crest biopsy were determined in 42 postmenopausal women without previous bisphosphonate or fluoride therapy. 25 patients (group A, mean 62.6 y) had primary osteoporosis. 17 patients (group B, mean 63.0 y) had longterm corticosteroid treatment (for at least one year, cumulative doses > 4 g of prednison-equivalent) due to inflammatory rheumatic disease (13), COPD (2) or chronic inflammatory liver disease (2).

Results: In patients with longterm corticosteroid therapy (group B) we found a significantly lower BMD at FN (0.58 ± 0.08 vs 0.65 ± 0.09 g/cm^2, $p = 0.03$) despite a comparable BMD at LS (0.72 ± 0.18 vs 0.73 ± 0.12), a significantly lower osteocalcin level (5.8 ± 2.9 vs 8.1 ± 2.4 ng/ml, $p = 0.02$, reference value 8.5 ± 3.5) as marker of reduced bone formation, an elevated PYD-level (79.5 ± 42 vs 54.7 ± 30 nmol/mmol Krea, $p = 0.06$, ref. 40 ± 10) as marker of increased bone and additional cartilage resorption (predominantly inflammatory rheumatic diseases) as well as a comparably elevated DPD-level (21.3 ± 9.0 vs 20.8 ± 8.2 nmol/mmol Krea, n.s., ref. 10 ± 3.5) as marker of increased bone resorption in both groups. Bone histomorphometry showed a tendency towards a lower bone formation rate under corticosteroids (0.058 ± 0.029 vs 0.081 ± 0.084 μm^2/μm^{2}xd, n.s.) and comparable osteoid and erosion surfaces
(OS: 11.9 ± 10 vs 9.8 ± 8.1%, n.s., ES: 15.5 ± 13 vs 14.3 ± 6.0%, n.s.).

Conclusions: Postmenopausal women with osteoporosis tend to increased bone resorption relatively independent of longterm corticosteroid therapy, but there seems to be an additional inhibitory effect of corticosteroids on bone formation.

P301SA. CHRONIC DEPRESSION AS RISK FACTOR FOR OSTEOPOROSIS

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WHO ranked depression as one of the most urgent health problems worldwide. Once believed to be essentially an adult disorder, depression is increasingly diagnosed in younger populations and the incidence shows permanent rise. Hormonal, immunologic and habitual features of this illness have some somatic influences and between the others it can alter metabolism of bone cells. The aim of our study was estimation of influences of depression, its duration, heaviness and treatment on bone mineral density (BMD).

We investigated BMD of lumbar spine and hip (measured by DEXA method on LUNAR DPX-IQ) in 23 premenopausal women with at least two years course of established diagnosis of chronic recurrent major depression (F33 according to ICD-10 and DSM-IV criteria). Results were compared with 22 healthy premenopausal controls. Both groups were statistically identical toward ages of life and menarche, numbers of pregnancies and deliveries as well as smoking habit and body mass index. No one woman from investigated as well as control group had any other known risk for osteoporosis or was treated for it.

On lumbar spine we established osteodensitometric diagnosis of osteoporosis in 9 (39%) and of osteopenia in 5 (21%) women with depression while in control group no one has osteoporosis and only 4 (18%) has osteopenia. BMD was significantly lower in depression group (1.051 ± 0.135 vs. 1.235 ± 0.043 g/cm^2). Measuring of BMD on the hip showed that 8 depression patients (35%) have osteoporosis and 5 (22%) have osteopenia. In the control group no one has osteoporosis and 3 (14%) has osteopenia. BMD was also significantly lower 0.968 ± 0.159 vs. 1.212 ± 0.078 g/cm^2. Duration of depression and its heaviness (expressed as number of recidivism and through Hamilton Depression Scale) indicates strong correlation with BMD decrease while treatment had no any influence.

Our results indicate that chronic depressions especially those with long and heavy course may represent a new not well-recognized risk factor for osteoporosis.

P302SU. THE EVALUATION OF DENSITOMETRICAL FINDINGS IN DIABETES MELLITUS TYPE 2 PATIENTS: OUR EXPERIENCES

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AIM: To determine correlation between glycemic control and osteoporosis in diabetes mellitus type 2 patients (DM type 2).

Methods: The subjects were divided into one group consisting of 60 DM type 2 patients and control group made up of 27 non-diabetic subjects randomized according to their age and gender.

The bone mineral density was measured by DXA densitometry at the lumbar spine and in the hip-neck region. Osteoporosis was defined as T-score: normal ($T > -1.0$), osteopenia ($-1.0 < T < -2.5$) and osteoporosis ($T > -2.5$ SD).

Results: Distribution of results in DM type 2 patients suggest that osteopenia is most frequent among male participants (60%), with more than half the total number of instances located at the lumbar spine (55.56%); female osteopenia on the other hand, was mostly found at the neck of the hip. The most frequent finding in women (51.87%) were cases of osteoporosis, with over two-thirds of such cases being found within the lumbar spine.

The densitometrical result of normal was almost equally divided between patients above and below the age of 60 years in both groups of participans (OR = 1.07 vs. OR = 0.94) but osteopenia was more frequent within older patients in both groups (OR = 6). Osteoporosis was more common among older diabetic women than among controls (OR = 2.6).

There was no significantly established correlation between body mass index (BMI) and densitometrical results neither within diabetic patients ($p = 0.631$) nor controls ($p = 0.343$).

Elevated values of glycosylated haemoglobin (HbA_1C) ≥6.5% were found in 80.95% of diabetic patients, with 30.95% of them displaying severely elevated levels (≥11.5%). Osteoporosis was the most frequent finding (47.6%) in diabetic women with elevated HbA_1C. According to the results, significant positive correlation was established between HbA_1C and alternation of bone mineral density in all DM type 2 patients ($r = 0.52$, $p \leq 0.05$).

However, greater risk of osteoporotic fractures was established in diabetic patients (RR = 1.36) and especially in diabetic women (RR = 1.75).

Conclusion: Badly controlled glycemia is an important factor, and accelerates the reduction of bone mineral density according to age, gender and obesity but also independently of those factors. This is our preliminary exploration which will be continued with a larger number of participants.

P303MO. OSTEOPOROSIS SECONDARY TO SYSTEMIC MASTOCYTOSIS IMPROVES WITH BISPHOSPHONATES

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Aim: Mastocytosis comprises a heterogeneous group of disorders of mast cell proliferation. Skeletal symptoms are the presenting clinical manifestation in 5% of patients and are present in up to 75% of all patients. This report aims to highlight effective treatment of osteoporosis associated with systemic mastocytosis (SM) with bisphosphonates.

Methods: We report six patients with osteoporosis secondary to SM who were treated with bisphosphonates. Hologic bone mineral densities (BMD) of the lumbar spine and hip were recorded at baseline and following intervention.

Results: The mean age of subjects was 58 years (range 40–70 years), mean duration of SM was 8 years (range 3–13 years) and mean duration of treatment with a bisphosphonate was 8 years (range 1–13 years). An increase in BMD was seen in 5 out of the 6 patients at the lumbar spine (the 6th patient had fractured all lumbar vertebrae). BMD at the hip increased in 3 patients and stabilised in the remainder. No further fractures occurred during the study period. Recalcitrant bone pain improved in all subjects following bisphosphonate treatment.

Conclusion: The aetiology of osteoporosis associated with SM is multifactorial. Mast cells uncouple bone formation and resorption with the balance in favour of bone loss. Mast cells secrete tryptase which activates peripheral blood mononuclear cells resulting in the synthesis and release of tumour necrosis factor alpha and interleukin –6 (IL-6). The degree of osteoporosis and the severity of symptoms correlate with IL-6 levels. Heparin also produced by mast cells has resorptive and collagenolytic effects.

Although rare, osteoporosis secondary to SM is associated with significant morbidity. We recommend serial BMD estimation and bisphosphonate therapy. Furthermore, bisphosphonates have an analgesic role in refractory bone pain in SM.

P304SA. BONE MINERAL DENSITY EVALUATION AFTER PARATHYROIDECTOMY IN PRIMARY HYPERPARATHYROIDISM

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Primary hyperparathyroidism (PHP) is a hypercalcemic disorder due to excessive secretion of parathyroid hormone (PTH) from one or more parathyroid glands. PHP has been associated with bone loss, but traditional bone involvement such as osteitis fibrosa has become uncommon, and PHP is increasingly being detected during the asymptomatic phase. The need for parathyroidectomy has been questioned in such patients because there may be no disease progression in the absence of surgery. In order to evaluate the parathyroidectomy impact on bone disease

in PHP patients, we studied in a prospective way bone density in PHP patients who underwent parathyroidectomy between June 2000 to June 2003. There were 24 patients, 16 females and 8 males, aged 12–80 years (mean 52 years). The diagnosis was confirmed by high total and/or ionized calcium levels and high levels of PTH. The mean total calcium was 11.7 mg/dl (range 9.6–15.8), mean ionized calcium was 1.57 mmol/l (range 1.34–2.08) and mean PTH was 391.6 pg/ml (range 90–2500). Histopathological diagnosis was: adenoma in 19 patients, double-adenoma in 1, hyperplasia in 3 and carcinoma in 1 patient. In 13 patients bone density was available in post-operative follow-up of 13 months (range 2–30 months). Among these patients, 69.2% (9 patients) and 61.5% (8 patients) presented with an increase in bone mineral density (BMD) higher than 3% at lumbar spine and femoral neck respectively. Bone mineral density (BMD) analysis showed an increase of 4% on average at lumbar spine and an increase of 3.14% in femoral neck. Taking into account patients age, BMD analysis showed a remarkable increase in younger ones, as expected. Among younger patients (mean 35.4 years), BMD increased 5.1% and 5.6% at lumbar spine and femoral neck respectively, while in older ones (mean 68.4 years) BMD increased only 2.1% and 2.8% at same regions.

Conclusion: there is a considerable impact of parathyroidectomy in BMD in PHP patients. This trend was remarkable among younger ones, regardless of small number of our series. Findings suggest that surgical approach in PHP patients might be of interest mainly in younger patients, in whom remarkable improvement of bone status was seen.

P305SU. PROGNOSTIC FACTORS OF BONE MINERAL DENSITY IN SYSTEMIC SCLEROSIS

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Objective: To analyse the results of bone densitometry in a group of patients with systemic sclerosis (SSc), evaluating the prognostic factors associated to a low bone mineral density (BMD).

Methods: Cross-sectional study analysing 74 female SSc patients, aged 22 to 51 years, who performed a bone densitometry using dual x-ray absorptiometry. BMD values (lumbar spine, femoral neck, Ward and trochanter) were compared according to hormonal status (fertile and postmenopausal), SSc clinical variant (limited and diffuse), race and the previous use of corticosteroids and cyclophosphamide. These results were compared with 64 fertile and 60 postmenopausal healthy women; it was used ANOVA for comparing the SSc patients with the control group, excluding the influence of age, age at menopause and body mass index (BMI).

Results: Thirty-four SSc patients presented normal densitometric values, 26 presented osteopenia and 14 densitometric osteoporosis. In the SSc group, there was a low BMD associated to menopause in the four densitometric sites, predominating in patients with more than 10 years of menopause in lumbar spine, femoral neck and Ward triangle. No statistical association was found between BMD values and SSc clinical variants, race and previous use of corticosteroids and cyclophosphamide. BMD values in the four studied sites were significantly lower in the SSc fertile group compared to the fertile controls, and this statistical significance persisted in femoral neck, Ward triangle and trochanter after ANOVA for rank correction for age and BMI. The densitometric values in all the studied sites were also significantly lower in the SSc postmenopausal group compared to the postmenopausal controls, but when corrected for BMI values, there was only a statistical trend related to femoral neck.

Conclusion: In the present study, a low BMD and densitometric osteoporosis in SSc patients were associated to menopause, independent of the SSc clinical variants, race and previous use of corticosteroids and cyclophosphamide. When compared to a control group, it was observed a low BMD in the fertile SSc group, after correction for age and BMI.

P307SA. BONE MINERAL DENSITY IN LONG-TERM SURVIVORS OF HIGHLY-MALIGNANT OSTEOSARCOMA

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This study presents evidence of the long-term effects on bone mineral density (BMD) in long-term survivors of highly-malignant osteosarcoma treated with the chemotherapy protocols of the German-Swiss-Austrian Osteosarcoma Study Group (COSS) which includes high-dose methotrexate. Forty-eight subjects (mean age: 31 ± 4.2 years, mean follow-up: 16 ± 2.2 years) participated in the study. BMD of lumbar spine and proximal femur of the non-operated side were measured by dual energy X-ray absorptiometry. A questionnaire was administered to determine personal and life style factors as well as patients' medical history and medication. In the sample, ten patients were osteoporotic, twenty one osteopenic, and seventeen normal according to WHO definition. Eighteen patients reported bone fractures after receiving chemotherapy. The sample had statistically significantly lower BMD levels for all sites measured. In conclusion, long-term survivors of highly-malignant osteosarcoma treated with one of the COSS protocols showed lower BMD values that are statistically as well as medically significant.

P308SU. PERIARTICULAR BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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The hand is the principal site of inflammation in rheumatoid arthritis. Periarticular osteoporosis is an early finding in the hands of patients with rheumatoid arthritis, due to release of bone resorbing cytokines from the inflamed synovium, increased vascularity and immobility of affected joints. In clinical practice, rheumatologist and radiologist refer to periarticular osteoporosis that is visible on plan radiographs. Recently, dual x ray absorptiometry (DEXA) has been used to measure global bone mineral density (BMD) of hand. Only few studies used DEXA to more detailed measurements of periarticular BMD. The aim of this study was to examined the global and periarticular BMD of hand in patients with established RA and compare its with healthy controls.

Fourteen female patients with RA and 30 healthy female were recruited. Bone mineral density was measured at the no dominant hand using Lunar DPX-IQ densitometer. Periarticular BMD was measured at 12 predetermined regions of interest (ROIs) from the second and third fingers.

Mean global hand BMD was significantly ($p < 0.05$) lower in patients with RA (table 1.) Patients with RA also had significantly ($p < 0.05$) lower BMD at each of the ROIs.Periarticular osteoporosis was related to the DAS28 and grip strength, but not to duration of disease.

Table 1 Results

	Patients with RA	Healthy controls
No	40	30
Age	56 15	57 9
Mean global BMD of hand (g/cm^2)	0c .382 0.046	0.395 0.039

In conclusion, hand BMD measurement using DEXA may be a useful routine clinical measure of disease activity and severity.

P309MO. INDIUM-111 OCTREOTIDE SCINTIGRAPHY AS A DIAGNOSTIC TOOL IN ONCOGENIC OSTEOMALACIA

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Aims: Acquired, adult-presenting hypophosphatemic osteomalacia, a rare form of bone mineral loss is either idiopathic or associated with tumours. These usually small mesenchymal tumours are often benign and difficult to find. As the most recent evidence suggests, osteomalacia-inducing tumours can express somatostatin receptors. This raises the possibility that radiolabeled octreotide scintigraphy may be used in their localization. Our aim was to locate such tumours by scintigraphy.

Methods: Here we present a case of hypophoshatemic osteomalacia of possibly oncogenic origin. A 60-year-old man was examined for chronic lower extremity pain that had not been relieved by nonsteroidal anti-inflammatory drugs. The serum calcium level was normal, but phosphate values were low and serum alkaline phosphatase activity was elevated. A bone scan revealed multiple foci of activity. Causes of hyperparathyroid disease were ruled out and a possibility of oncogenic osteomalacia was raised. However, conventional methods (x-ray, CT, MRI, ultrasound) were unable to find a tumour. Osteomalacia was diagnosed and vitamin D3 therapy was started. Nevertheless, within a few months the disease got worse and fractures of the left hip and ribs occurred. Only 1,25 dihydroxycolecalciferol therapy and phosphate supplementation was able to prevent the patients from further deterioration. For further examination, Indium-111 octreotide scintigraphy was applied.

Results: Indium-111 octreotide scintigraphy located a small (approx. 2 cm diameter) solid somatostatin receptor expressing tumour right below the liver. A second CT scan, although it was negative at the onset of the disease, also revealed a tumour at the same location.

Conclusion: Our results suggest that Indium-111 octreotide scintigraphy can be a suitable diagnostic tool to locate osteomalacia-inducing tumours even if conventional methods fail. Further studies on a large number of patients are necessary to address this important issue because removal of the tumour is usually curative in oncogenic osteomalacia.

P310MO. RISK FACTORS FOR REDUCED BONE DENSITY IN HAEMODIALYSIS PATIENTS

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We report a prospective study examining the prevalance of reduced bone mineral density (BMD) and its association with a wide range of factors, in a heterogenous group of 97 chronic haemodialysis patients. Femoral neck and lumbar BMD were measured by dual energy x-ray absorptiometry (DEXA) Osteopenia was defined as greater than standart deviation (SD) less than the mean of peak bone mass (T score < -1) osteoporosis was defined as gerater than 2.5 SDs less than the mean of peak bone mass (T score < -2.5) Stepwise multiple linear regression analysis was used to identify risk factors associated with low bone mass.

The patients were 50.5 ± 4.2 years of age and 48% were men; the patients had received dialytic therapy for 6.7 ± 2.5 years (3–192 months). BMD was reduced in dialysis patients in both sexes in comparison with the healthy subjects. There was significant correlation between BMD and the serum b 2 microglobulin, parathyroid hormone (PTH), magnesium, kreatinin, ferritin, alkaline phosphatase and osteocalcin levels. We found that osteopenia in 39.1% patients, osteoporosis in 43.7% patients. Significant relationship was found among hemodialysis duration and osteopeni/osteoporosis. The BMD had significant association with age, female gender, age at menarche, weekly heparin dose, daily physical activity.

Secondary hyperparathyroidism, a dynamic bone disease and osteomalacia, the main bone problems in chronic renal failure, may all be responsible for a reduction in BMD. This can result in an increased fracture risk. When considering bone disease among patients with end stage renal disease, physicians should also consider osteoporosis and impact of race on BMD.

P311SU. BONE MINERAL DENSITY IN PATIENTS USING COUMADINS

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Coumadins are known to impair the vitamin K metabolism. This inhibitory effect affects bone mineralization mediated by osteocalcin, a protein related to vitamin K activity. Therefore, it has been proposed that chronic oral anticoagulation produces osteoporosis. Data avaible is controversial.

Aims: To evaluate the bone mineral density (BMD) of a group of anticoagulated patients against a healthy population.

Methods: 62 consecutive patients from the external offices of an Haematology Service were included. 34 were currently receiving coumadins since 3 years ago or more (cases), 28 had never received oral anticoagulation (controls). All patients receiving corticosteroids, diuretics,anticonvulsivantes, hormones or bone related drugs were excluded. Femoral neck (FM) and lumbar spine (LS) BMD were measured by DEXA (Hologic Delphi).

Results: The media age of cases was 61 years old (30–70) and for control was 59 years old (42–69). FN BMD of cases was 0.837 g/cm^2 while in controls was 0.828 g/cm^2 (p 0.72); T-score of FN was -0.652 vs. -0.75, respectively (p 0.62). LS BMD of cases was 0.975 g/cm^2 and controls showed LS BMD 1.015 g/cm^2 (p 0.42): T-scores were -0.55 and -0.66 respectively (p 0.66).

Conclusions: BMD was not diminished in a population treated with oral anticoagulants for several years and chronic oral anticoagulation would not be a cause for secondary osteoporosis.

P312MO. EARLY BONE LESION DETECTION WITH MAGNETIC RESONANCE IN DIAGNOSTICS OF RHEUMATOID ARTHRITIS

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Objective: To assess the possibilities of magnetic resonance (MR) in the early diagnostics of bone changes in rheumatoid arthritis (RA).

Material and method: 16 patients (13 women and 4 men) with polyarthralgia and clinical signs of rheumatoid polyarthritis were examined with magnetic resonance. For all the patient the conventional x-ray of both hands in two projections were performed, as well as clinical laboratorical analyses. MR examination was carried out, using GE 1.0 T Signa Horizon LX Highspeed system with the examination of head with reel and the carpal part of the hands, including the wrist joint and metacarpal bone and the joints of proximal parts of phalanxes in accordance with a standardised MR examination protocol, including into the series of examinations also administrations of intravenous contrast substance Gd-DTPA.

Results: 3 patients were diagnosed uneven thickening of the synovium around the metacarpophanalngeal joint of the first finger, 7 patients – in the joint of the wrist – radiocarpal, ulnocarpal, intercarpal bone joints, 4 patients had the aforementioned changes in symmetrical locations. 7 patients were diagnosed with inflammatory type changes in the flexor and extensor tendon sheaths. 10 patients were diagnosed minor erosions up till 1 cm in diameter, os lunatum – 4, os scphoideum – 5, os triquertum – 6, os trapezium – 2 . 1 patient was not diagnosed any changes in the wrist bones and joints.

Conclusions: MR is a highly sensitive method for visualising inflammatory type changes in the hand joints – bones and synovium and is a perspective method for using MR for radiological diagnostics of RA for the prognostication of the course of the disease and the assessment of pharmacotherapy. This aloud prevents developing of peripheral osteoporosis and bone lesions. MR findings in cases of RA are not specific, therefore precise diagnostics of RA call for correlation with clinical laboratorical data.

P313SA. PROGNOSTIC FACTORS OF LOW BONE MINERAL DENSITY IN ANKYLOSING SPONDYLITIS

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Objective: Ankylosing spondylitis (AS) is a disease characterised by a low bone mineral density (BMD) in the early stages of the disease. It was studied the epidemiologic features associated to BMD in a series of AS patients.

Methods: The authors studied the BMD values in 83 male AS patients, analysing the importance of race, disease duration and HLA-B27 in the determination of BMD; there was also a comparison between 27 AS patients and a control healthy group of 27 individuals paired by age, race and body mass index (BMI).

Results: African-Brazilian AS patients presented a higher BMD in Ward ($p = 0.028$) and trochanter ($p = 0.019$). Patients with less than 10 years of disease duration presented a significantly higher BMD in femoral neck ($p = 0.031$), Ward ($p = 0.021$) and trochanter ($p = 0.049$). HLA-B27 positive patients had a lower BMD at the lumbar spine ($p = 0.036$) than HLA-B27 negative patients. Age at onset, positive family history and previous use of methotrexate did not represent a significant statistical factor in the studied patients. Comparing 27 AS patients with 27 age, race and weight-paired controls, it was observed a significant lower BMD in lumbar spine ($p = 0.009$) and femoral neck ($p = 0.006$) in the AS patients.

Conclusion: Race, disease duration and HLA-B27 represented prognostic factors of BMD values in the present series of AS patients.

P314SU. BONE MINERAL DENSITY IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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OBJECTIVE: To determine the bone mineral density (BMD) status of our Paediatric Systemic Lupus Erythematosus (PSLE) population and to compare the frequency of osteoporosis in patients with active disease requiring high dose corticosteroids with that requiring low dose of corticosteroids

Methods: Medical reports of all children diagnosed as Systemic Lupus Erythematosus at our hospital, between 1990 and 2003, were reviewed, including clinical data, disease activity, dose and duration of corticosteroid therapy. BMD measurements of the lumbar spine (L1-L4) were performed using dual x-ray absorptiometry (DEXA). Z scores were calculated from the BMD data for comparison with normative data.

Results: A total of 30 patients were assessed: 20 requiring high dose of corticosteroid therapy 10 requiring low dose corticosteroid therapy Baseline BMD measurements and Z scores demonstrated osteoporosis in the majority of patients requiring high dose of corticosteroids (18 of the 20) and only in half (5) of the 10 patients requiring low dose of corticosteroids.

Conclusion: Osteoporosis is common in patients with active disease requiring high dose corticosteroids. Treatment must be considered in order to prevent osteoporosis complications but it is necessary to study the beneficial/risks effects of osteoporotic treatments in children.

P315MO. OSTEOPOROSIS IN PATIENTS WITH TERMINAL STAGE OF CHRONIC RENAL INSUFFICIENCY

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Osteoporosis is common associated disease in patients with end stage of chronic renal failure.

We studied the prevalence of osteoporosis in patients with end stage renal failure treated with chemodialysis three times a week. The patients were examined to determinate the bone mineral density (BMD) measured by DXA on dominant and non dominant forearm via DTX-200 Osteometer-Denmark. Also we noticed the level of alkaline phosphatase (ALP) and parathormon (PTH).

The mean age of patients on chemodialysis (19 male and 12 female) was 53.74 ± 11.94, and the mean of duration of chemodialysis was 4.82 ± 4.2 years. 7 of 12 females (mean age 49.8 ± 11.98) were in postmenopausal period (45.3 ± 7.0 years of menopausal age). The mean BMD (g/cm^2) of values for dominant forearm were 0.367 ± 0.103, T score -3.65 ± 1.7SD, and 0.369 ± 0.108, Tscore -3.34 ± 1.7 SD for non dominant side. We found significantly ($p < 0.001$) positive correlation between the BMD values, independent of applied side of arterio-venous shunt. The levels of ALP (441.09 ± 344.2) and PTH (32.15 ± 32.02 pmol/l) were significantly higher than in control group of healthy donors ($p < 0.001$). The obtained results showed significant correlation between ALP and PTH ($r = 0.77$, $p < 0.001$) and between biochemical parameters and BMD, as well as between duration of chemodialysis and loss of BMD ($r = -0.62$, $p < 001$), but we didn't find correlation between duration of chemodialysis and ALP i PTH. Only in 8 (mean od duration of chemodialysis were 2.56 ± 1.39) of 31 cases we didn't find osteoporosis (3 of them were in referent ranges of BMD, ALP and PTH, 5 in osteopenia but in 3 of those cases ALP and PTH were elevated). In other wise in 38.7% of patients ALP were in referent or border line values, and BMD were in osteoporosis.

So, we obtained osteoporosis in 23 of 31 (74%) investigated chemodialysis patients. Secondary hyperparathyroidism (47%) was one of causes of osteoporosis in patients with end-stage renal failure. These results seem to provide evidence that BMD measured by DXA on forearm is a good early predictor of osteoporosis in patients with terminal stage of chronic renal failure who require renal replacement therapy.

P316SA. IS FIBROMYALGIA IN MEN ASSOCIATED TO LOW BONE MINERAL DENSITY OR OSTEOPOROTIC FRACTURES ?

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The relationship between low bone mineral density (BMD) and osteoporosis in patients with fibromyalgia is still controversial. Our main aim was to investigate the association between BMD and quantitative ultrasound (QUS) measurements and low-impact fractures in male patients with fibromyalgia (FM) compared to male healthy controls.

Patients and Methods: Forty men with FM, according to American College of Rheumatology Criteria for FM, were enrolled in this study. Forty-two ethnically matched healthy men were used as controls. Risk factors for osteoporosis and fractures were evaluated by a questionnaire that included details concerning aspects of diet, lifestyle, hormonal factors, previous fracture and drug use. Spine and femural BMD (DPX-L, Lunar) and heel QUS (Achilles +, Lunar) measurements were performed in all patients. Patients suspected to have secondary osteoporosis were excluded. Lateral thoracic and lumbar radiographs were taken to survey for the presence of vertebral fractures. Genant method was used to identify and classify vertebral deformities in these patients.

Results: FM patients were younger than healthy controls (42.1 ± 10.9 and 47 ± 12 years, respectively; $p = 0.05$). The groups were matched to height (1.68 ± 0.8 vs. 1.68 ± 0.7 m) and weight (71.7 ± 8.4 vs. 74.7 ± 12.3 kg). Spine and femural BMD and QUS measurements were not different between FM patients and healthy controls (spine BMD: 1.174 ± 0.2 vs. 1.187 ± 0.2 g/cm^2, femur BMD 1.012 ± 0.1 vs. 1.025 ± 0.2 g/cm^2 ; stiffness index: 96 ± 17 vs. 95 ± 14 , respectively). Surprisingly, 11 healthy controls had vertebral deformities (graded II or III) compared to only 3 FM patients ($p = 0.01$).

In conclusion, fibromyalgia in men is not associated to low bone mass or osteoporotic fractures.

P317SU. RISEDRONATE THERAPY OF SECONDARY OSTEOPOROSIS IN OSTEOCHONDRODYSPLASIA

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Introduction: Secondary osteoporosis is a common feature in osteochondrodysplasia. Some types of this heterogeneous group of diseases are characterized by platyspondylia and should be considered as differential diagnosis in cases of generalized vertebral deformities. There are only few reports on osteological therapy in these rare hereditary diseases.

Case report: Spinal x-ray of a 42-year-old woman with dwarfism (1.32 m) showed generalized platyspondylia. Bone mineral density at lumbar spine (BMD-LS, DXA, Hologic QDR4500A) corresponded with osteoporosis (T-score –3.5). Most osteological serum parameters were normal (calcium, phosphate, iPTH, 25-OH-vitamin-D, bone alkaline phosphatase, osteocalcin), in contrast to a distinctly elevated excretion of collagen-crosslinks: PYD 121 (ref. 30–50), DPD 19.2 nmol/mmol Crea (ref. 6.5–13.5). Iliac crest biopsy with histomorphometry revealed a high-turnover osteoporosis. Monitoring under therapy with risedronate (Actonel®) 5 mg/d: Excretion of collagen-crosslinks (PYD 44, DPD 9.8 nmol/mmol Crea) had normalized after 3 months. BMD-LS increased by 4.6% per year. An increase in bone volume (BV/TV from 13.2 to 18.6%) and a decrease in parameters of bone formation and resorption was found by histomorphometry after 2 years of treatment.

Discussion:

1. Most cases of osteochondrodysplasias are caused by mutations of collagen-genes or of the fibroblast growth receptor 3. The superficial manifestation at the spinal column in our patient was primarily suggestive of Dysplasia spondyloepiphysarea tarda. As differential diagnosis, an osteochondrodysplasia due to mucopolysaccharidosis IV A (M. Morquio A, characterized by mutations in the N-acetylgalactosamin-6-sulphatase-gene – GALNS) had to be considered. Urine search tests for MPS-IV were negative, but activity of galactose-6-sulphate-sulphatase in leucocytes was markedly reduced. Molecular genetic examinations revealed a mutation in GALNS-gene, thus making M. Morquio probable. A causal treatment is not available.

2. There are no reports on the effectiveness of bisphosphonates in the treatment of osteochondrodysplasias. After 3 months of therapy, risedronate caused a distinct reduction in the excretion of collagen-crosslinks in our patient. After 2 years, densitometry showed a marked increase in BMD-LS. Moreover, bone volume had increased and bone turnover had normalized according to histomorphometry.

Conclusion: Bisphosphonates seem to be effective drugs in the treatment of osteochondrodysplasia such as MPS-IV and should be considered in early disease.

P318MO. ORAL BIPHOSPHONATES IN OSTEOPOROTIC LONG-TERM SURVIVORS OF HIGHLY-MALIGNANT OSTEOSARCOMA

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Two thirds of long-term survivors of highly-malignant osteosarcoma treated with chemotherapy protocols including high-dose methotrexate (MTX) have low bone mineral density (BMD) and one third report about fractures after completion of chemotherapy. Ten patients with BMD < 2.5 STD (6 male, 4 female; mean age: 33 ± 1.4 years) participated in this study. Patients received risedronate orally once daily (5 mg) or weekly (35 mg) plus a calcium / vitamin D combination daily. BMD of lumbar spine (LS) and proximal femur of the non-operated side (PF) were measured by dual energy X-ray absorptiometry at twelve months after beginning of the treatment (mean time after chemotherapy at beginning of oral biphosphonate treatment: 13.8 ± 2.3 years). After one year of oral bisphosphonate treatment BMD increased at a mean by 2.28 % in the LS, whereas in the PF no changes were seen. No fracture occurred during the study time. In conclusion, it was shown that even in long-term survivors of highly-malignant osteosarcoma treated with chemotherapy protocols including MTX increases in BMD values are possible.

P319SA. INTERMITTENT REGIMEN OF SALMON CALCITONIN IN THE TREATMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS (GIO)

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The aim of this study was to investigate effectiveness of intermittent treatment of salmon calcitonin in GIO and usefulness of bone turnover biochemical markers for assessment of response to calcitonin therapy.

Methods: 15 postmenopausal women with GIO (age 55 ± 8.2 years) received nasal spray of salmon calcitonin (Miacalcic, Novartis) in dosage 200 IU/day intermittently for 12 months. Control group consisted of 10 postmenopausal women with GIO did not receive any treatment for study period. BMD was measured by DEXA at baseline and after 12 months. Serum osteocalcin, total alkaline phosphatase (AP), cross-laps, parathyroid hormone, calcium, magnesium and inorganic phosphorus were measured at baseline and after 3 months.

Results: There was a significant increase ($p < 0.05$ vs baseline) in BMD of lumbar spine in 3%, total proximal femur in 4%, femoral neck in 3.4% and trochanter in 4.3% and no significant change in distal forearm BMD in treated patients. We found a decrease in total magnesium from 0.81 ± 0.05 to 0.75 ± 0.04 mmol/l ($p < 0.01$), ionized magnesium from 0.58 ± 0.04 to 0.54 ± 0.03 mmol/l ($p < 0.001$), osteocalcin from 28 ± 19 to 24 ± 18 ng/ml ($p < 0.001$) and cross-laps from 0.53 ± 0.33 to 0.45 ± 0.30 ng/ml ($p < 0.05$) in treated women. There were a decrease in osteocalcin from 30 ± 19 to 25 ± 19 ng/ml ($p < 0.01$) and cross-laps from 0.51 ± 0.29 to 0.40 ± 0.26 ng/ml ($p < 0.05$), and an increase in AP from 98 ± 24 to 106 ± 27 U/l ($p < 0.05$) in responders to calcitonin treatment by spinal BMD ($n = 9$). There were no any significant changes in biochemical picture in non-responders.

Conclusions: These results demonstrated that intermittent treatment of salmon calcitonin increases BMD in axial and peripheral skeleton and decreases bone remodeling in patients with GIO. Osteocalcin, cross-laps and AP are sensitive biochemical markers for early monitoring of efficacy of intermittent salmon calcitonin therapy.

P320SU. SOCIO-ECONOMIC ASPECTS OF OSTEOPOROSIS IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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A retrospective study was carried out on 77 subjects investigated in the clinic for hyperparathyroidism(HPT) for a 7-year interval (1996–2002). Primary HPT(PHPT) was proved in 31 subjects(40.26%), secondary HPT(SHPT) – in 16 subjects (20.78%) with chronic renal failure, functional SHPT in cases with postmenopausal osteoporosis, senile osteoporosis and vitamin D-resistant or deficient states was found in 16 subjects (20.78%), paraneoplastic syndrome in 1 (1.3%), and in 13 subjects (16.88%) the diagnosis was overthrown. PHPT is more common in the females: 24 (77.42%) in our group. 16 (66.66%) of them were postmenopausal and preserved menstrual cycle was observed in 8 (33.34%) of them. 7 (22.58%) of the PHPT subjects were male. The first signs and symptoms that raised suspicion for PHPT were: 1) Bone pain in 17 subjects (54.84%), 2) Nephrolithiasis in 12 subjects (38.71%), 3) Hypercalcemia in 2 subjects (6.45%). The lack of officially regulated, unlimited free screening for Ca/P metabolism abnormalities was the reason only two of the subjects in the current study were investigated for PHPT after these cheap and widely available tests. The vast majority of the subjects were

admitted to the clinic for investigation at an advanced stage of the disease; in two of them the nephrocalcinosis had already led to chronic renal failure and all patients with bone involvement had very low bone mineral density (85.7% of the female subjects had high fracture risk, 2 male subjects were with osteopenia and 2 others with osteoporosis).

Currently subjects with PHPT can be diagnosed through: 1) Thyroid ultrasound and an accidental finding of enlarged parathyroid glands(cost 8 Euro); 2) Bone mineral density measurement and additional investigation of the causes of osteoporosis by clinical chemistry and hormonal assays (cost 13–50 Euros); 3) Investigation of the subjects undergoing lithotripcy (cost 160 Euro). These procedures are available only for patients who can afford them.

Conclusion: Health authorities must with no delay introduce free, unrestricted clinical chemistry screening for Ca/P metabolism abnormalities to permit the early and economically efficient diagnosis of this disorder which is rather frequent after the menopause.

P321MO. NOTTINGHAM HEALTH PROFILE IN WITH POSTMENOPAUSAL OSTEOPOROSIS

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Osteoporosis is a metabolic bone disease characterized by loss of bone density and increase susceptibility to fracture. It affects large numbers of individuals worldwide, especially postmenopausal women. Pain, activity loss, fractures from osteoporosis makes daily life difficult. The aim of study is to assess pain and quality of life in patients with osteoporosis. 80 postmenopausal women were included to the study. 45 postmenopausal women were osteoporotic, 35 postmenopausal women were normal, according to BMD measurements. Notthingham Health Profile-1(NHP-1) quality of life measurement scale was applied to each individual, and 6 scores (pain, physical activity, energy level, sleep, social isolation and emotional reaction)were evaluated.

There was no statistically significant difference between two groups in quality of life messured by NSP-1 ($P > 0.05$), except pain, physical activity scores. NHP-1 may be reliably used in postmenopausal osteoporosis. Because it is easy to apply and it can evaluate the clinical consequences like pain, together with emotional parameters of the osteoporosis.

P322SA. AGE PECULIARITIES OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS AT RHEUMATOID ARTHRITIS

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On the basis of complex investigations of structural and functional state of bone tissue in 215 patients with rheumatoid arthritis, that protractedly received systemic glucocorticoid therapy (for more than 6 months), the age peculiarities of forming osteoporosis were determined.

Methods: It was established that age is an important determinant of bone loss and glucocorticoid-induced osteoporosis. Structural and functional state of bone tissue was investigated by ultrasound densitometry methods [ultrasound densitometry «Achilles+» Lunar Corp., Madison, USA, 1995) and echoosteometry (ultrasound device «Echoosteometry» EOM-01c)].

Results: It was established that systemic glucocorticoid therapy causes impetuous bone loss with osteoporosis forming, that was diagnosed in 50.67% of patients. The most significant changes of structural and functional state of bone tissue under the influence of glucocorticoids were discovered among junior patients (20–44 years) – osteoporosis was diagnosed in 45.2% of this age group. The highest percentage of osteoporosis (68.12%) was discovered among senior patients (60–74 years). Systemic glucocorticoid therapy provokes profound changes of qualitative indices of ultrasound densitometry and spongy bone tissue.

Conclusions: Glucocorticoid induced osteoporosis is a relevant clinical feature of rheumatoid arthritis. It is necessary to allow for it at assigning glucocorticoids to senior patients (60–74 years).

P323SU. THERAPEUTIC ACTIVITY OF BISPHOSPHONATES IN PATIENTS WITH PROSTATIC CANCER

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Bone metastases are frequent occurences in prostate cancer.The impact of bone metastasis in prostate cancer is remarkably prominent due to the following factor: together with breast and pulmonary carcinoma bone metastasis from prostate carcinoma account for more than 80% af all bone metastatic involvement. Bone metastatic pain is a symptom of the disease onset in 10 to 20% of patients. Patients with hormone-refractory metastatic prostate cancer are particularly prone to incapacitating progressive bone disease. Prostate cancer bone metastasis characteristically appear on radiographs as area of increased bone density, suggesting excessive bone formation by osteoblasts as the predominant reaction to metastatic tumor. Hormonal therapy has since become the focus of the management of advanced prostate cancer as is widespread use of early as well as adjuvant hormone therapy. One of the drowbacks of long-term androgen deprivation is the bone loss and the risk of osteoporotic fractures. Osteoporosis is often more severe than in postmenopausal women and the mortality after osteoporotic hip fracture in men is higher mortality then in aged matched women. Futhermore in men with prostate cancer those with fragility hip fracture have a higher mortality than those without fracture, independently from bone metastatic disease. Antineoplastic treatment options are limited especially for those who are ederly and may have additional complicating medical conditions. Bisphosphonates have been shown to be effective in reducing bone complications in with osteolytic metastases as well as osteoblastic metastases, given the substantial osteoclastic activity in this type of metastasis. An emerging rationale for the use of bisphosphonates in prostate cancer is the reduction of the fracture risk and the prevention of bone loss.

Parenteral clodronate (Difosfonal) had proven to be effective in reducing symptomatic bone progression-free survival and severe bone complications and recent data of randomized controlled trial with clodronate suggests that starting bisphosphonates earlier in the metastatic state may give better results.

P324MO. EFFECTS OF HYALURONAN ON BONE RESORPTION AND BONE MINERAL DENSITY IN A RAT MODEL OF ESTROGEN DEFICIENCY-INDUCED OSTEOPENIA

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Objective: Hyaluronan (or hyaluronic acid, HA) is an essential component of extracellular matrices. HA of appropriate molecular weight and concentration can induce osteoblast differentiation and bone formation *in vitro*. The aim of our study was to evaluate the effects of HA of different molecular weights on ovariectomy (OVX) induced bone loss in rats.

Methods: Adult female Sprague Dawley rats (270 ± 10 g) were subjected to bilateral ovariectomy or sham surgical procedure. Fifty animals were divided into 5 groups: sham-operated (SHAM); OVX controls; OVX rats treated with: HA of molecular weight of 0.75 MDa in the dose of 1 mg/kg/d; with HA of molecular weight of 1.62 MDa in the dose of both 0.5 mg/kg/d and 1 mg/kg/d. HA was applied orally once a day for the period of 8 weeks after ovariectomy. Body weight, urinary pyridinoline (Pyr), deoxypyridinoline (Dpyr) corrected to urinary creatinine, serum nitrite/nitrate concentrations, whole-body and the femoral bone mineral density (BMD) were measured.

Results: HA treatment had no effect on body weight gain in OVX rats. Excretion of urinary Pyr and Dpyr significantly increased in OVX rats compared to SHAM controls. The higher molecular weight HA (1.62 MDa) significantly reduced urinary Pyr and Dpyr concentrations measured on day 28 after ovariectomy ($p < 0.001$). Serum concentrations of NO metabolites, nitrite/nitrate significantly decreased in OVX rats in comparison with SHAM

controls ($p < 0.001$). HA of both molecular weights (0.75 MDa and 1.62 MDa) significantly enhanced serum nitrite/nitrate concentrations in OVX rats, exceeding the levels measured for SHAM controls. The higher molecular weight HA reduced both whole-body and femoral BMD loss in OVX rats in a dose-dependent manner.

Conclusion: Our study represents the first report suggesting that orally applied high molecular weight HA (1.62 MDa) inhibits bone resorption and provides a protective effect on bone density in ovariectomized rats.

P325SA. LOW DOSE ESTRADIOL CONTINUOULSY COMBINED WITH TRIMEGESTONE EFFECTIVELY PROTECTS AGAINST BONE LOSS IN POSTMENOPAUSAL OSTEOPENIC WOMEN

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Aim: To determine the efficacy of a novel low-dose hormone replacement therapy for the prevention of postmenopausal bone loss in osteopenic women.

Design: This was a multicenter, double-blind, randomized, placebo-controlled clinical trial including 360 healthy postmenopausal women with osteopenia (bone mineral density (BMD) at the lumbar spine between 1.0 to −2.5 SD below young normal mean). Women were allocated to receive treatment with either 1 mg 17beta-estradiol continuously combined with 0.125 mg trimegestone ($n = 179$) or placebo ($n = 181$) for 2 years. All participants received calcium and vitamin D supplementation throughout the study. Efficacy parameters were BMD at the lumbar spine, total hip, femoral neck and serum markers of bone formation (osteocalcin, bone-specific alkaline phosphatase) and resorption (serum CTx and urinary CTx) measured at regular intervals.

Results: Seventy percent of women completed the trial. BMD increased significantly in the active treatment group at all sites measured (spine: 6.3%, total hip: 3.9%, femoral neck: 3.8%, all $p < 0.001$). The corresponding changes in serum and urinary CTx were 52 and 54%, whereas the changes in OC and BSAP were 40 and 33%, respectively ($p < 0.05$). Seventy-five percent of women had amenorrhea from the first cycle, and 5% withdrew prematurely due to drug-related adverse event (mastalgia, metrorrhagia).

Conclusion: This novel low-dose estrogen plus progestin therapy provides an effective and safe prevention of postmenopausal bone loss in osteopenic women.

P326SU. EFFECTIVE DOSES OF IBANDRONATE DO NOT INFLUENCE THE 3-YEAR PROGRESSION OF AORTIC CALCIFICATION IN ELDERLY OSTEOPOROTIC WOMEN

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Aim: Recent animal experiments demonstrated an anticalcifying effect of aminobisphosphonates, which might have implications for plaque instability and risk for thromboembolic complications. The aim of the present study was to assess the influence of clinical doses of intravenous or oral ibandronate on the 3-year progression of aortic calcification (AC) in elderly women to test whether these experimental observations are applicable for clinical settings.

Methods: Participants were 473 elderly osteoporotic women, who were randomized to receive treatment with either oral (2.5 mg daily or 20 mg intermittent) or intravenous (0.5 mg or 1.0 mg every 3 months) ibandronate. Bone mineral density (BMD) was measured at the lumbar spine and the total hip using dual-energy X-ray absorptiometry (DEXA) on a yearly basis. Aortic calcification was visualized on lateral lumbar radiographs on a yearly basis and the severity was graded by a validated scoring system.

Results: At baseline, there was a significant inverse correlation between the severity of AC and BMD at the hip ($r = -0.151$, $p = 0.003$), but not at the lumbar spine. This association was independent of age, BMI, and smoking habits. The two oral doses and the 1.0 mg iv dose evoked statistically significant increases in both hip and spine BMD compared with placebo, whereas the 0.5 mg was significant only at the hip ($p < 0.05$). Neither the yearly rate of progression nor the 3-year change of AC was significantly different between the ibandronate and placebo-treated groups ($p > 0.05$). Furthermore, there was no statistically significant correlation between the 3-year change in hip or spine BMD and the simultaneous change in AC.

Conclusion: The present study demonstrates that clinical doses of ibandronate have no influence on the 3-year progression of AC in osteoporotic elderly women indicating that previous experimental results are not applicable to the doses of ibandronate used in clinical settings. Ibandronate is safe to be used for the long-term treatment of osteoporosis.

P327MO. THE PHARMACOLOGICAL TREATMENT OF OSTEOPOROSIS IN CLINICAL PRACTICE (“TOP STUDY”)

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Aims: Gather information from Italian clinical practice regarding: 1) influence of risk factors, bone mass measurement and specialization background of the prescriber on pharmacological treatment threshold and treatment choice; 2) compliance; 3) primary motivation for discontinuing or modifying drug dosage; 4) influence of concomitant medications.

Methods: The study included women of any age who were prescribed a pharmacologic therapy for osteoporosis and returned for a follow-up visit after at least 12 months or for adverse events. 141 centers throughout Italy were involved.

Results: Information was obtained from 10,189 women aged 64 ±9 SD years; 61% of the patients were taking at least one drug for concomitant disease and 30% took two or more drugs. The most frequent concomitant medications were antihypertensives (29%), NSAIDs (13%), drugs for gastrointestinal disease (11%) and statins (8%).

74% of the patients had recognized risk factors; mainly reduced physical activity (37%), low body weight (27%), early menopause (21%) and smoking (13%).

Only 53% and 37% of the patients had BMD values ≤ −2.5 SD at the spine and hip respectively; 48%–64% of the patients had Z score values ≥ −1.

23% of the patients with previous osteoporotic vertebral or hip fractures were not on therapy with drugs that had evidence of efficacy (estrogens, raloxifene, alendronate and risedronate).

Alendronate was the most frequently prescribed drug by most specialists, but Gynecologists and General Practitioners prescribed mostly estrogens or intramuscular clodronate, respectively.

25% of the patients discontinued therapy before the second year: 17% within the first year and 10% within six months. The medication most frequently interrupted within six months was weekly intramuscular clodronate (24%) or daily oral alendronate (17%).

Only 71% of the patients took the drug according to the indications of the manufacturer. Once weekly alendronate had the best global compliance. The main motivations for discontinuing or failing to observe the dosage instructions were in order of frequence: the appearance of drug related side effects, insufficient motivation to treatment, fear of side effects, cost, inconvenient modality of administration, lacking documentation of beneficial effects on bone density or laboratory tests.

P328SA. DAILY AND WEEKLY ALENDRONATE COMPLIANCE: A SOUTH AMERICAN EXPERIENCE

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The therapeutic efficiency of a given anti-osteoporotic treatment can be assessed by the NNT (number of patients to be treated) to prevent one fracture. The NNT at clinical practice may vary from the one calculated in clinical trials due to low rates of adherence, early withdrawals, or frequent mistakes with the administration procedures. Furthermore, there are also geographic reasons linked to health education, and pharmacoeconomic aspects which may greatly influence the therapeutic efficiency. Therefore, regional compliance studies are needed in order to identify local factors affecting therapeutics outcomes. The ECMO I and II multi-center studies are educational programs aimed to improve adherence to prescriptions and compliance to daily administration of alendronate 10 mg (MARVIL® 10) or weekly of 70 mg (Marvil® 70). Both formulations have proved in vitro and in vivo equivalence with the reference compound. A total of 4,917 patients with primary osteoporosis diagnosed either by DXA (WHO criteria) or by the existence of a low energy fracture (mainly spine crush) were included in both studies. The sample includes a great variety of sanitary, economic, and technical conditions that will allow the further clustering of data and the observation of particular factors affecting compliance. Adherence was monitored through an independent telephone network. Of the patients evaluated treated either daily (n = 1875), or weekly (n = 2552) with alendronate, 5.5% and 4.0% never bought the medication; 15.4 and 13.2 abandoned during the first 6 month. The main reasons to quit in half of them was the cost of the medication (14 USD monthly), adverse reactions and personal reasons (educational reasons?) were other relevant factors. Initial adherence and compliance rate proved to be high with both schedules (over 80%/6 months) showing that upper gastrointestinal discomfort is not the major problem in compliance. Being tolerability acceptable and using bio-equivalent formulations, economy and education appears as the factors challenging an NNT comparable to the one of clinical trials.

P329SU. CLINICAL AND ECONOMIC IMPACT OF COMPLIANCE WITH OSTEOPOROSIS MEDICATION

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Drug therapy for osteoporosis has been shown in trials to reduce fracture risk by up to 40%. This benefit is obtained only if women consistently take medication for a year or more. We studied the impact of compliance to treatment on health and economic outcomes in a real-world setting.

Data on demographics, prescription drug dispensing, physician services and hospitalizations were obtained from the Protocare Sciences databases for women with osteoporosis who were dispensed an osteoporosis medication between 1997 and 2002. A validated computer algorithm was used to reconstruct each subject's pattern of osteoporosis medication use. Subjects were considered "highly" compliant over a given period if the medication dispensed covered at least 80% of that interval. Fracture occurrences, hospitalization rates and general medical costs were derived from hospitalization and medical service records. The impact of compliance on fracture rates was analyzed with proportional hazards regression, with compliance defined as a time-dependent variable, and controlling for other risk factors. Hospitalization rates were analyzed with a Poisson regression model and (log-transformed) costs were analyzed using linear regression, controlling for history of hospitalizations as an indicator for severity.

38,120 women suffering from osteoporosis were identified with an average follow-up of 1.6 years. Almost 74% did not have medication available to cover at least 80% of the time they were followed. The overall fracture rate was 6.2% per year. High compliance decreased the fracture rate by 14% (95% CI 8% to 20%), controlling for other known risk factors. High compliance lowers the risk of all-cause hospitalization by about 27%, whereas a history of hospitalization was associated with a threefold increase in risk (RR = 3.13) regardless of the compliance level. Average monthly costs for all medical services – including hospitalization and physician service costs – were higher among low compliers: 600 USD vs. 340 USD/month ($P < 0.0001$, controlling for severity).

Conclusions: The desired goal of keeping patients with osteoporosis on chronic treatment is not being achieved adequately in actual practice and the social and economic implications of this behavior are substantial. Until compliance is improved we will continue to fail in meeting an important public health goal.

P330MO. VITAMIN D SUPPLEMENTATION IN OLDER SUBJECTS

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Vitamin D status in the elderly has been universally found to be deficient. Current theory suggests part of the bone loss of aging may be due to secondary hyperparathyroidism from D insufficiency. The level of 25 OH Vitamin D (25 OHD) where PTH start to rise has been suggested to be about 60 nmol/l.

Aims: The object of this study was to describe the vitamin D status in our elderly population, show what levels of 25 OHD produced maximum reduction in PTH level and what level of oral supplementation was needed to achieve that level in most people.

Methods: The study population consisted of a convenience sample of 150 older subjects, 50 men and 100 women, (mean age 73.2 ± 14 S.D.). As well as clients with spinal osteoporosis, we included those (n = 33) with a history of hip fracture and frail older people attending the Geriatric Day Hospital for rehabilitation with a variety of disorders. A history of vitamin D supplementation was taken, including vitamin D in multivitamin preparation. Blood was drawn for measurement of PTH, 25 OHD, BUN and creatinine. Subjects were included if on a stable dose of vitamin D for over three months and excluded if BUN and Creatinine were abnormal.

Results: Baseline 25 OHD levels in our population showed 12.6% to be deficient (<25 nmol/l), 54% to be between 25 and 60 nmol/l (insufficient) and 33% over 60 nmol/l. Including people on supplementation, it was apparent that PTH levels reached the lowest plateau at 25 OHD levels of between 80–100 nmol/l. To achieve this level in most older people, a supplement of at least 1000 IU per day is required. It was found that even on a dose of 1000 IU/day for over three months only 83% of subjects achieved levels over 80 nmol/l and only 52% over 100 nmol/l.

Conclusions: We conclude that in order to maximize the reduction in bone loss due to a degree of secondary hyperparathyroidism, in elderly subjects, a daily supplement of 1000 IU is required for most and more may be required for some subjects.

P331SA. THE COST-EFFECTIVENESS OF CALCIUM AND VITAMIN D SUPPLEMENTATION IN WOMEN WITH LOW DIETARY INTAKE OF THESE NUTRIENTS AND AT RISK OF OSTEOPOROSIS

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Aims: The objective of this study was to evaluate for England and Wales the cost-effectiveness of supplementing calcium and vitamin D in women with low dietary intakes of those nutrients given age, T-score and prior fracture criteria.

Method: A systematic review was undertaken of randomized controlled trials which measured the efficacy of calcium and

vitamin D supplementation in such women in preventing fractures. Data were found regarding efficacy at the hip and non-vertebral sites. As no data were found relating to vertebral fractures, the efficacy seen for all non-vertebral fractures was used as a proxy.

These data were used to simulate the experience of hypothetical patients in a mathematical model populated by evidence from reviews of utilities, costs, and epidemiological data. Fractures were simulated at the hip, vertebra, wrist and proximal humerus. Analysis was undertaken at 50, 60, 70 and 80 years for women who had suffered a prior fracture, and at 70 and 80 years for women without a prior fracture.

Data were recorded on the incremental costs and incremental quality adjusted life years (QALY) associated with calcium and vitamin D supplementation compared with no treatment, allowing cost per QALY ratios to be calculated.

Results: The T-Score threshold at which treatment was cost-effective was estimated assuming that a cost per QALY ratio below £30,000 denoted cost-effectiveness. This threshold was −1.00SD in women with previous fractures aged 70 years and over – essentially all women in this category, given the typical T-Scores at these ages. However, at ages 50 and 60 years the thresholds were −3.50SD and −2.75SD respectively, significantly lower than the respective average T-Score. For women without a prior fracture the thresholds were −1.00SD at age 80 years and −1.50 at age 70 years, again lower than the average T-Score at these ages.

Conclusions: Our work has shown that supplementation of calcium and vitamin D is cost-effective in all women aged 70 years or greater with low intakes of these nutrients, regardless of a measured T-Score or prior fracture history. However, treatment is only cost-effectiveness in younger women following a prior fracture and with confirmed low T-Scores.

P332SU. CONTRASTING EFFECTS OF TERIPARATIDE AND ALENDRONATE ON BONE TURNOVER ASSESSED BY BONE HISTOMORPHOMETRIC PARAMETERS IN WOMEN WITH OSTEOPOROSIS

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Aim: We conducted a prospective randomized double blind study in postmenopausal women with osteoporosis to contrast the effects of teriparatide 20 μg/d (TPTD) and alendronate 10 mg/d (ALN) on bone remodeling at the tissue level, as assessed by bone histomorphometry.

Methods: Patients were randomly assigned to receive either teriparatide (n = 102) or alendronate (n = 101) for 18 months. Biochemical markers of bone turnover and areal and volumetric bone mineral density were measured in all patients. Bone biopsies suitable for histomorphometric analysis were obtained in separate subsets of patients at 6 months (TPTD, n = 8; ALN, n = 9) and 18 months of treatment (TPTD, n = 8; ALN, n = 7).

Results: Histomorphometric indices of bone remodeling were significantly greater in the teriparatide group than in the alendronate group at both time points (table, mean ± SD). In trabecular bone, histomorphometric indices reflecting bone formation and activation frequency were generally greater at 6 months than at 18 months in the teriparatide group, while the same indices remained suppressed at both time points in the alendronate group. In the teriparatide group, the peak in histomorphometric bone formation indices coincided with peak levels for biochemical markers of bone formation (N-terminal propeptide of type I collagen, C-terminal propeptide of type I collagen, and bone specific alkaline phosphatase). Bone resorption, as reflected by erosion surface, although generally greater in teriparatide compared with alendronate, did not reach the magnitude of treatment differences attained in formation indices. The extent of resorption remained relatively constant over time in both groups.

Bone Envelope Histomorphometric Index	6 months		18 months	
	TPTD	ALN	TPTD	ALN
Trabecular				
Osteoid Surface (%BS)	17.26** ± 7.94	6.83 ± 5.17	12.63* ± 6.64	5.29 ± 3.04
Eroded Surface (%BS)	3.08 ± 2.03	2.17 ± 1.35	3.89 ± 2.30	2.59 ± 1.28
Mineralized Surface (%BS)	8.10** ± 4.42	0.22 ± 0.29	4.40** ± 2.90	0.38 ± 0.31
Bone formation rate (μm/d)	0.062* ± 0.036	0.002 ± 0.002	0.030* ± 0.022	0.003 ± 0.002
Activation frequency (#/yr)	0.99** ± 0.56	0.02 ± 0.03	0.46** ± 0.32	0.04 ± 0.03
Endocortical				
Eroded Surface (%BS)	5.60* ± 3.83	2.79 ± 1.29	5.62 ± 4.58	4.06 ± 3.51
Mineralized Surface (%BS)	18.73** ± 10.38	0.44 ± 0.95	9.69** ± 6.73	1.02 ± 1.40
Bone formation rate (μm/d)	0.098* ± 0.053	0.007 ± 0.008	0.064* ± 0.049	0.009 ± 0.007

*P < 0.05; **P < 0.01 (TPTD vs. ALN using two-sided exact test).
%BS = percentage of bone surface.

Conclusion: Bone formation was greater at 6 months compared with 18 months in the teriparatide-treated group. The values at both time points were significantly greater than that observed with alendronate therapy, confirming the opposite mechanism of action of the two treatments. Furthermore, these results reveal the sustained, positive formation-resorption balance achieved by teriparatide compared with alendronate.

P333MO. GROWTH HORMONE RECEPTOR-INDEPENDENT REGULATORY ACTIONS OF TESTOSTERONE ON SKELETAL HOMEOSTASIS DURING PUBERTY IN MALE MICE

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Growth hormone (GH) and androgens are both known to affect skeletal growth during puberty. The aim of the present study was to evaluate a possible interaction between GH and androgen action and, particularly, whether the ability of androgens to stimulate skeletal modeling requires the presence of a functional GH receptor (GHR). To this end, we evaluated the effects of testosterone (T) replacement (1.5 μg T daily via subcutaneous silastic implants) in orchidectomized (orch) male mice with disrupted GHR (GHRKO) and corresponding wild-type mice (WT) during late puberty (6–10 weeks). Results are expressed as % gain or loss compared to orch and analyzed via two-factor ANOVA. Both in GHRKO and WT, T enhanced recruitment of osteoblasts at the outer site of the femur and increased periosteal bone formation rates by 94% and 81% in GHRKO and WT, respectively, as measured by dynamic histomorphometry on femoral cross-sections. This increase of periosteal bone formation was associated with statistically similar increases in body weight (+26% and +14%, resp.) and lean body mass (+24% and +13%, resp.) in GHRKO and WT. At the inner site of the femur however, T reduced bone turnover at the endocortical (bone formation rates −51% and −56% in GHRKO and WT, resp.) and trabecular sites (osteoid perimeter −59% and −39%, resp.). This decrease in bone turnover was reflected by a significant reduction in serum osteocalcin in both models (−28% and −41%, resp.). In line with these findings, T significantly increased trabecular bone volume in GHRKO as well as WT. In these models, T did not affect femoral length and serum IGF-I. The end result of T action on appendicular skeleton was a similar thickening of the cortex and maintenance of trabecular bone in GHRKO and WT. We conclude that, in the context of the mice models studied, T action during puberty on trabecular and cortical bone is independent of GHR activation. These findings support the concept that T action on skeletal modeling does not involve activation of the GH axis.

P334SA. RAPID PAIN RELIEF AND REMISSION OF STERNOCOSTOCLAVICULAR HYPEROSTOSIS (SCCH) AFTER INTRAVENOUS IBANDRONATE THERAPY

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Aims: Sternocostoclavicular hyperostosis (SCCH) is a rare, localised disturbance of bone metabolism that is extremely painful and leads to significant deterioration in QoL. It is often diagnosed late or remains undiagnosed. The aetiology of SCCH is unknown. The condition flares up sporadically, causing pain and swelling in the sternoclavicular region with considerable impairment of shoulder girdle movement. The pain is frequently resistant to standard analgesic therapy. Typical X-ray signs are hyperostosis in the medial third of the clavicula, the anterior insertion of the first rib and the manubrium. Reduction of localised high bone turnover with bisphosphonates may improve outcome in this condition.

Methods: Three women, aged 40, 55 and 68 years, with 5–15 year histories of severe localised and therapy resistant pain had consulted numerous doctors and hospitals without definitive help or relief. Biopsies in two patients produced no clear diagnosis beyond 'an analgesic-resistant local inflammatory process'. Our diagnosis of SCCH was based on typical localization, X-ray findings and high uptake at bone scanning. Pain, measured on a 10-point visual analogue scale (VAS), averaged 9.7 before treatment. Erythrocyte sedimentation rate, and in one case alkaline phosphatase levels, were slightly elevated, but no typical laboratory pattern emerged. All three women had systemic osteopenia or osteoporosis. We treated patients with initial infusions of 4mg ibandronate followed by 2 mg i.v. ibandronate injections every 3 months for up to 1 year, with daily calcium and vitamin D supplementation throughout the study and follow-up.

Results: Pain relief was rapid and persistent: average VAS pain scores were 4.7 after 2 weeks, 1.7 after 3 months and 0.3 after 12 months. Bone scans after 3 months showed significant decreases in tracer uptake and area of involved bones. X-rays after 12 months showed structural improvements. Mean BMD increased by 9.1% at the lumbar spine and 7.0% at the femoral neck after 1 year. Follow up to month 24 revealed no symptoms of recurrent disease.

Conclusions: Treatment with i.v. ibandronate injections for SCCH was successful in terms of pain relief, improvement in QoL and disease remission in this condition of localised increased bone turnover of unknown aetiology.

P335SU. CHLORIDE CHANNEL INHIBITION PREVENTS BONE RESORPTION IN OVARIECTOMIZED RATS WITHOUT CHANGING BONE FORMATION

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Chloride channel activity (ClCN7) is essential for osteoclastic acidification of the resorption lacunae and thereby for dissolution of the inorganic phase of bone. Consequently, inhibition of the osteoclastic chloride channel should prevent bone resorption. Accordingly, we have tested chloride channel inhibitors on bone turnover. Most interesting, we found that bone resorption could be inhibited without affecting bone formation in vivo. This study indicates that chloride channel inhibitors are highly promising for treatment of osteoporosis.

The chloride channel inhibitor, NS3736 (1-[4-Bromo-2-(1H-tetrazol-5-yl)-phenyl]-3-(4-chloro-3-trifluoromethyl-phenyl)-urea), blocked osteoclastic acidification and resorption in vitro with an IC50 value of 30 microM. When tested in the rat ovariectomy model for osteoporosis, daily treatment with 30 mg/kg p.o. restored bone resorption to control levels as measured by CTX and protected bone strength and bone mineral density by approximately 50% 6 weeks post-surgery. Most interestingly, bone formation assessed by osteocalcin, mineral apposition rate and mineralized surface index was not inhibited.

Analysis of chloride channels in human osteoclasts revealed that ClC-7 and CLIC1 were highly expressed. Furthermore, by electrophysiology we detected a volume activated anion channel on human osteoclasts. Screening 50 different human tissues showed a broad expression for CLIC1 and a restricted immunoreactivity for ClC-7, appearing mainly in osteoclasts, ovaries, appendix and Purkinje cells. This highly selective distribution predicts that inhibition of ClC-7 should target specifically osteoclasts in vivo. We suggest that NS3736 is inhibiting ClC-7, leading to a bone specific effect in vivo.

In conclusion, we show for the first time that chloride channel inhibitors can be used for prevention of ovariectomy-induced bone loss without impeding bone formation. We speculate that the coupling of bone resorption to bone formation is linked to the acidification of the resorption lacunae, thereby enabling compounds that directly interfere with this process to be able to positive impinge on this process resulting in a net gain of bone mass and strength.

P336MO. ALENDRONATE THERAPY OF PEDIATRIC PATIENTS WITH OSTEOGENESIS IMPERFECTA

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Osteogenesis imperfecta (OI) is a rare crippling disorder leading to fractures and bone deformities. Previously employed therapy with calcitonin, calcium and vitamin D resulted in minimal increase in bone mineral density (BMD) and did not reduce the incidence of fractures. As there have been reports on promising effect of pamidronate treatment in children with OI, we intitiated therapy with another bisphosphonate, alendronate, in a group of children with OI.

Parental and patient consent was obtained prior to this treatment. We observed 30 children with OI, mean age 13.7 years. Alendronate was administered orally for one year: children aged 4–10 years received 5 mg/day, children above 10 years of age were given 10 mg/day. Prior to the onset of therapy, spinal BMD Z-score (measured by DXA) was below −2.1 in all children and all patients had more than 2 fractures/year. After one year of therapy, we observed significant increase in spinal BMD (+14.5%, $p < 0.05$). After another 2 years of therapy, there was yet further increase in spinal BMD (+6.3%). The changes in BMD were related to the mobility status of the patients, as immobilized patients had a less apparent increase in BMD. The interpretation of BMD measurements in hip and forearm was not possible due to multiple bone deformities. The values of bone markers (S-osteocalcin, S-procollagen III, U-deoxypyridinoline crosslinks) decreased significantly ($p < 0.05$) after one year of therapy. In the following 2 years there were no further significant changes in these parameters with the exception of U-deoxypyridinoline. In the course of the first year of alendronate therapy we observed just one fracture in the entire group, this as a result of a skiing accident in a patient with OI type Sillence I. We did not observe any adverse effect of alendronate therapy regarding gastrointestinal tract or biochemical changes. The x-rays of long bones did not reveal any negative effect of alendronate on metaphysis or growth cartilage. In conclusion, alendronate seems to be a safe and effective drug in pediatric patients with OI.

P337SA. RISEDRONATE REDUCES FRACTURE RISK IN OSTEOPOROTIC WOMEN OVER 80 YEARS OF AGE: IMPLICATIONS FOR THE USE OF ANTIRESORPTIVE AGENTS IN THE OLDEST

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In persons over 80 years of age (the "oldest old"), there is no published evidence that antiresorptive agents lead to greater reductions in fracture risk than calcium and vitamin D alone. The risedronate database includes almost 1400 individuals over 80 years of age with confirmed osteoporosis. The aim of this study was to determine the efficacy of risedronate in reducing vertebral fracture risk in women 80 years of age or older with osteoporosis.

We performed a pooled analysis of data from three randomized, double-blind, controlled, 3-year fracture endpoint trials conducted from November 1993 to April 1998 (HIP, VERT-MN, and VERT-NA) conducted in Europe, North America, and Australasia. Patients included were those with documented osteoporosis (a femoral neck BMD T-score < −2.5SD and/or at least one prevalent vertebral fracture) 80 years of age or older. Patients received placebo (n = 688) or risedronate 5 mg/day (n = 704) for up to 3 years. All patients received 1000 mg/d calcium and, if baseline levels were low, up to 500 IU/d vitamin D. Vertebral radiographs were taken at baseline and at yearly intervals to determine prevalent and incident vertebral fractures.

At baseline, the mean femoral neck T-score was −3.05 SD, and 84% of the patients had at least one prevalent vertebral fracture. After 1 year, the risk of new vertebral fractures in the risedronate group was reduced by 81% compared with placebo (95% confidence interval [CI], 60%–91%; P < .001). The number of women who needed to be treated to prevent one new vertebral fracture after 1 year was 12. This early onset of efficacy was consistent across the clinical programs. Risedronate continued to show antifracture efficacy over 3 years. Risedronate was well tolerated, with a safety profile comparable to placebo.

We conclude that antiresorptive treatment provides an antifracture benefit in addition to that afforded by calcium and vitamin D in women 80 years of age or older with documented osteoporosis. These findings provide the first evidence that, even in the oldest old, reducing bone resorption rate remains an effective treatment strategy for osteoporosis.

P0338SU. INFLUENCE OF CONVENTIONAL AND HIGH DOSES OF ESTROGEN ON THE DEGREE OF MINERALISATION OF BONE TISSUE: A QUANTITATIVE MICRORADIOGRAPHIC ANALYSIS IN POST-MENOPAUSAL WOMEN

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The beneficial skeletal effects of menopausal estrogen replacement therapy (HRT) are well documented and are believed to be mediated predominantly by inhibition of osteoclastic bone resorption. The role of secondary mineralization of bone in the preservation of bone quality is also well established in postmenopausal women treated with bisphosphonates or SERMs. The aim of the present study was to investigate the effect of conventional and high dose estrogen on the degree of mineralization of bone (DMB).

Transiliac bone biopsies were obtained from 20 patients before and after 24 months (18 to 38 months) treatment with conventional HRT, and from 19 patients who had received high doses of estradiol (implant 100 mg every 3–6 months for at least 14 years). Bone samples were embedded in LR White Resin. Thick sections were ground to a uniform thickness of 100 µm and then microradiographed with an aluminum step-wedge. DMB was measured in compact, cancellous and total bone and expressed as g mineral/cm^3 of bone (mean ± SEM).

Values obtained in patients before HRT were lower than those reported in premenopausal women and similar to those reported for postmenopausal women with untreated osteoporosis. After conventional HRT, the increase in DMB in total bone was 4.4 ± 1.9% when compared to pre-treatment values (4.1 ± 2.1% in compact bone, 4.5 ± 2.3% in cancellous bone); these differences were not significant. In women who had received high dose estradiol therapy, DMB in total bone was 6.9 ± 1.9% higher than in untreated women (8.6 ± 2.1% in compact bone, 6.5 ± 2.1% in cancellous bone); these differences are statistically significant (p < = 0.03). After high dose therapy the greatest change was noted in cortical bone as previously reported by histomorphometry. The increases of DMB were due to a shift of the curves towards high DMB with a decrease of the low DMB values, but without changes in the heterogeneity of the distributions (preservation of the quality of mineralization).

Our results demonstrate that estrogen therapy is associated with an increased degree of mineralization of bone (prolongation of secondary mineralization) similar to that observed with other antiresorptive agents. However, it was about 2-fold lower than that observed after alendronate therapy(10 mg/day/3 years).

P0339MO. RISK ASSESSMENT FOR OSTEOPOROTIC FRACTURE IN INSTITUTIONALISED RESIDENTS IN COMPARISON TO A COMMUNITY DWELLING POPULATION: THE UK NATIONAL OSTEOPOROSIS SOCIETY (NOS), OSTEOPOROSIS NURSE INITIATIVE (ONI) PROGRAMME

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Aims: Identifying people at high risk of fracture has the potential for cost-effective targeting of fracture prevention measures. In 2001 the UK National Osteoporosis Society launched a primary care programme [ONI], with the aim of identifying older subjects at increased risk of fracture via a structured audit programme. This subsequent analysis aimed to determine osteoporotic fracture risk in institutionalized residents in comparison to community-dwellers.

Methods: Five specialist nurses across the UK used a modified, validated fracture risk assessment tool (Black et al, Osteoporosis Int 2001) on women aged over 75 years identified from general practice databases. The variables considered were: age, previous fragility fracture, maternal hip fracture, weight < 57 kg, inability to rise from a chair without using arms, and current smoker. Resulting scores were converted in each subject to give a low, moderate or high risk status for fracture. Falls history (previous year) was recorded.

Results: The mean age of the overall population (n = 14955) was 81 years (SD = 5). Proportion of subjects classified as high, moderate and low fracture risk were 30%, 59% and 11% respectively. 374 subjects [mean age 88 (SD = 6) were identified as nursing or care home residents. In these institutionalized subjects the proportion classified as high, moderate and low fracture risk (compared to community-dwelling age-matched controls) were 79% (vs 63%), 20% (vs 35%), and 1% (vs 2%) respectively [ChiSquare = 24.5, df = 2, p < 0.001]. Inability to rise from a chair without using arms was significantly different between the institutionalized and age-matched community controls [87% vs 63%; ChiSquare = 54.0, p < 0.001], and there was a tendency towards a difference in previous fracture history [40% vs 34% respectively; ChiSquare = 2.8, p < 0.1]. There were no significant differences in the other assessment tool risk factors. Institutionalized residents were more likely to be recurrent fallers than controls [29% vs 21%; ChiSquare = 5.6, p = 0.018].

Conclusions: Institutionalised residents demonstrate a higher fracture risk profile than community-dwelling subjects. The former group therefore should be particularly targeted for fracture risk identification and subsequent prevention measures including calcium and vitamin D, hip protectors and fall prevention. The next 2 year phase of the UK ONI project will concentrate on this high risk group.

P340SA. HYPOPHOSPHATEMIC RICKETS

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Aims: Review of the literature of rare x-linked or autosomal dominant perhaps acquired hypophosphatemic rickets and compared the literature of the disease with experiences obtained during 3 years disease history of a 2.5 year-old girl at time of diagnosis.

Methods: Analysis of the family and own history of the patient and diagnostic (laboratory data, x-ray, ultrasound) and differencial diagnostic investigations. Treatment and its effects have been followed for 3 years.

Results: The family history did not reveal any individual with bone disease, but the mother had a body height and serum phosphate level below the average. From the age of 6 months, lower extremity of the patient had become extremely curved. Her body

height was below 3rd percentile (−2 cm) at 2.5 years of age. Serious hip and leg deformity, generalized signs of rickets, hypophosphatemia and slight hyperphosphaturia were observed. As an effect of the treatment (phosphate: 45–47 mg/kg b.w. and 1-α-(OH)D3: 38–46 ng/kg b.w.) applied for 3 years the rickets healed and a normal growth velocity (8 cm/year) has been attained. Her stature height is presently at 10th percentile at 5.5 years of age.

Conclusions: Although hypophosphatemic rickets was diagnosed relatively late in a child with serious clinical manifestations, we were able to demonstrate good results with adequate therapy recommended in the literature. Following this treatment while assuring biochemical balance in order to avoid complications, there is hope not only for further improvement of the bone disease, but also for an acceptable body height at adulthood.

P341SU. PRECLINICAL EVIDENCE FOR THE INTERMITTENT ADMINISTRATION OF IBANDRONATE IN OSTEOPOROSIS

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Aims: Although oral bisphosphonates are the current mainstay of treatment for postmenopausal osteoporosis, they must be given daily or weekly and in accordance with complex dosing recommendations. Simplified regimens with extended between-dose intervals may improve patient acceptability and convenience, potentially enhancing long-term adherence to treatment and therapeutic outcomes. Ibandronate is a potent nitrogen-containing bisphosphonate (Table). The efficacy, safety and potential for intermittent dosing with ibandronate has been extensively evaluated in animal models of osteoporosis.

Methods: The ibandronate preclinical development programme closely followed the World Health Organization's recommendations for the use of animal models of osteoporosis. Aged ovariectomised rats, growing intact rats, adult ovariohysterectomised beagle dogs, minipig models of glucocorticoid-induced bone loss and ovariectomised cynomolgus monkeys were used to evaluate the effect of ibandronate on bone mass, architecture, strength and quality. The effect of dose and dose scheduling on bone mass and architecture was also explored.

Results: In the studied animal models, subcutaneously or intravenously administered ibandronate dose-dependently reduced bone turnover and increased bone mineral density, while maintaining bone architecture, strength and quality (Table). No adverse effect on bone mineralisation was detected (Table). Studies of the effect of dose and dose scheduling on efficacy parameters demonstrated that intermittent administration of ibandronate produces similar benefits to continuous dosing (Table). Collectively, these data indicate that the efficacy of ibandronate is determined primarily by the total administered dose within a given time period, and not dosing frequency.

Table 1 Summary of the key pharmacological properties of ibandronate in various animal models

Property	Animal model
Potency 2–500 times > earlier bisphosphonates (clodronate, pamidronate, alendronate and risedronate)	Retinoid-stimulated TPTX rat
Inhibits bone resorption	Growing intact rat; OHX beagle dog; growing intact rat; Nx rat; unloaded rat
Increases or prevents bone mass and density	Growing intact rat; intact rat; OVX monkey; OHX beagle dog; CIO minipigs
Prevents deterioration of bone architecture	OHX beagle dog; OVX monkey, aged OVX rat
Preserves bone strength Maintains or restores bone quality	Intact rat; OVX monkey OHX beagle dog; aged OVX rat; OVX monkey; intact rat; CIO minipigs
No adverse effect on bone mineralisation	Growing intact rat; OHX beagle dog
Prevents increase in erosion depth	OHX beagle dog
Efficacy with intermittent dosing	OHX beagle dog; aged OVX rat; OVX monkey; intact rat; CIO minipigs; Nx rat; unloaded rat
Efficacy determined primarily by cumulative dose	OHX beagle dog; aged OVX rat; growing intact rat

TPTX: thyroparathyroidectomised
OHX: ovariohysterectomised
OVX: ovariectomised
Nx: nephrectomised
CIO: corticoid-induced bone loss

Conclusions: The efficacy of ibandronate when administered either continuously or intermittently has been demonstrated in an extensive preclinical development programme. Subsequent clinical investigations have proven the efficacy and safety of ibandronate when administered intermittently. Ibandronate is currently the only bisphosphonate to have prospectively demonstrated fracture efficacy when given with an extended between-dose interval of >2 months.

P342MO. DOSE-RELATED EFFECTS OF NOCTURNAL BONE REMODELLING PROCESSES BY SUBCUTANEOUS GLP-2 IN POSTMENOPAUSAL WOMEN

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The gastrointestinal hormone, glucagon like peptide-2 (GLP-2) has been suggested as a key regulator of the postprandial reduction of bone resorption. Bone resorption when assessed with biochemical markers such as CTX has been shown to exhibit a significant circadian variation. This circadian variation is nearly eliminated upon fasting and induced by nutritional intake. We have shown that the acute postprandial reduction of bone resorption coincides with the release of GLP-2 from the intestine and thus GLP-2 could be involved in an entero-osseous axis, which coordinates bone resorption in response to nutrient intake. In accordance, we have located the GLP-2 receptor on osteoclasts and show that *in vitro* GLP-2 exposure to osteoclasts leads to a 50% reduction in bone resorption.

Given that nocturnal increase in bone resorption reflects the highest activity level of the osteoclasts, we speculate that a reduction of bone resorption during the night could have an overall positive influence on the bone health.

We conducted a bedtime study in healthy postmenopausal women with parenteral administration of GLP-2 at 10 p.m. The objective was to study the effect of GLP-2 injection on nocturnal bone turnover processes. A total of 45 women were included and randomly assigned to treatment with either placebo (saline), 1600 μg GLP-2 or 800 μg GLP-2 twice (administered 3 hours apart). The principal part of the study lasted for 24 hours. On the day of treatment the women were instructed to report in the morning after fasting from 10 p.m. the evening before. At 9 a.m., noon and 6 p.m. participants were served regular fixed meals. In between meals, participants were fasting, but allowed to drink water.

We found a dose-related reduction of s-CTX after injection of GLP-2 ($p < 0.05$) and osteocalcin levels were increased as compared to placebo ($P = 0.07$), suggestive of a stimulative effect on bone formation. An area under the curve (AUC_{0-10h}) analysis for s-CTX and osteocalcin after GLP-2 injection confirmed the dose related effects on the bone turnover.

In conclusion, these observations suggested that GLP-2 might be useful as a pharmacological agent for the regulation of bone turnover processes.

P343SA. RISEDRONATE SODIUM FOR POSTMENOPAUSAL OSTEOPOROSIS: A SWISS POST AUTHORIZATION SURVEY IN PRIVATE MEDICAL PRACTICE

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Aims: In everyday practice the safety and efficacy of drugs may substantially differ from the results obtained in double-blind controlled trials. In this post authorization survey (PAS), the use of risedronate sodium for the prevention and treatment of osteoporosis in postmenopausal women was analyzed under routine medical practice.

Methods: Private practice physicians were asked to document the clinical status of postmenopausal women prior to initiation of therapy with risedronate 5 mg daily and the subsequent 6 months of treatment. To monitor the persistence and compliance, disposable, single-use devices for measurement of urinary crosslinked N-telopeptides (NTX), a marker for bone resorption, were used. The physician's assessments of efficacy and tolerability and adverse drug reactions (ADRs), defined as adverse events that in the physician's opinion have a causal relationship to risedronate, were documented. Descriptive statistical analyses of these data are presented below.

Results: Between August 2001 and January 2003, 105 physicians documented treatment of 352 patients with a mean age of 69 years. At treatment initiation, 49% of patients had a kyphosis and 67% demonstrated height loss. 84% had at least one clinical risk factor for osteoporosis and 40.6% had 3 or more risk factors for osteoporosis. 34% of the patients had a prevalent vertebral fracture. NTX measurements were performed at baseline and at 3 and 6 months of treatment in 97 patients. After 3 and 6 months the median urinary NTX was decreased by 35%. Physicians assessed therapy success as very good or good for 69.2% of the patients. 1.4% of the patients assessed the therapy success as poor. The tolerability of risedronate was assessed as very good or good by 77.0% of the patients. 10.2% of the patients experienced an ADR. The incidence and nature of ADRs were similar to those seen in pivotal clinical trials.

Conclusions: The results of this PAS confirm the good safety and tolerability profile as well as the anti-resorptive benefit of risedronate treatment in a large group of osteoporotic postmenopausal women in a routine medical practice.

P344SU. TERIPARATIDE MITIGATED THE CASCADE OF RISK FOR VERTEBRAL FRACTURE IMPARTED BY INCREASING SPINAL DEFORMITY INDEX

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The Fracture Prevention Trial was a double-blind study of 1,637 postmenopausal women with osteoporosis randomized to receive placebo or teriparatide [rhPTH (1-34)] 20 (TPTD20, commercially available) or 40 mcg/day. Patients were treated for a median 19 months. The primary findings from this trial have been published (Neer NEJM 2001). The spinal deformity index (SDI) incorporates the number and severity of prevalent vertebral fractures, two critical determinants of future fracture risk in women with osteoporosis.

Aims: To assess TPTD20 vertebral fracture efficacy as measured by increases from baseline in SDI score in Fracture Prevention Trial patients with increasing baseline SDI scores.

Methods: Patients had spinal radiographs at baseline and study endpoint assessed using a visual semiquantitative technique (Genant JBMR 1993). For each radiograph, fractured vertebrae were assigned scores of 1, 2, or 3 for mild, moderate, or severe fractures, respectively, and the SDI was calculated by summing these scores. The proportion of patients having increases in baseline-to-endpoint SDI scores of >1, >2, and >3 units were analyzed using a logistic regression model that included therapy and baseline SDI as predictor variables.

Results: With increasing baseline SDI score, placebo-treated patients had a marked increase in the risk of SDI scores worsening by >1, >2, and >3 units during the trial. However, this risk cascade was mitigated in TPTD20-treated patients (Fig. 1).

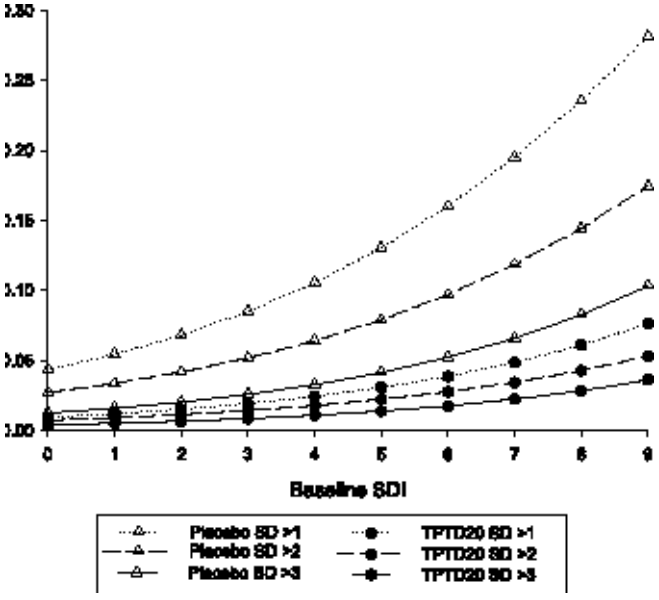

Fig. 1 Probability of SDI change by baseline SDI

Conclusions: The results observed in the placebo group confirm that SDI scores provide important prognostic information. Specifically, with increasing baseline SDI score, there was a cascade of risk for new or worsening vertebral fractures, as measured by the increase in SDI score. With TPTD20 treatment, this cascade of risk for future vertebral fracture was mitigated. These findings provide evidence that TPTD20 alters the natural history of the progression of osteoporosis.

P345MO. STRONTIUM DIRECTLY STIMULATES OSTEOCLAST APOPTOSIS

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Strontium ranelate reduces the risk of vertebral and non-vertebral fracture in women with postmenopausal osteoporosis by inducing a decrease in bone resorption and an increase in bone formation. As strontium ($Sr2+$) is a bone-seeking agent, high concentrations of $Sr2+$ are likely to occur in the sub-osteoclastic compartment and in the vicinity of the cells during bone resorption. High concentrations of extracellular calcium ($Cao2+$) are known to downregulate osteoclastic bone resorption, at least partly by inducing osteoclast (OC) apoptosis. The objective of the present study was to specify the role played by extracellular Sr ($Sro2+$) concentrations on bone resorption and OCs activities. Using 10-days old rabbit purified OCs, the effects of $Sro2+$ alone (1.8–24 mM) or in combination with $Cao2+$ (1.8–20 mM) were assessed on bone resorbing activity by measurement of area of pits. OCs were seeded on bovine bone slices and adherent cells cultured in the presence of $Sro2+$ for 48 h. Apoptosis of isolated OCs was assessed by Hoechst staining, and confirmed by DNA scales electrophoresis.

$Sro2+$ inhibited osteoclastic bone resorption from 12 mM (−25%, $p < 0.05$) to 24 mM (−50%, $p < 0.01$), and $Sro2+$ dose-dependently stimulated OC apoptosis. Independently, $Sro2+$ and $Cao2+$, around 20 mM, induced a similar rate of OC apoptosis (approx. 50%). Tested together, $Sro2+$ and $Cao2+$ have additional effects on bone resorption as well as on mature OC apoptosis. The use of specific inhibitors of intracellular $Ca2+$ signaling pathway (U73122, Caffeine, 2APB and SKF-96365) indicates that the transduction pathways involved in Sr- and Ca-induced OC apoptosis are different but cumulative.

Our data strongly suggest that exposure of OCs to an increasing amount of Sro2+ is responsible for a decrease in the bone resorption process mediated, at least in part, by the induction of OC apoptosis. Although, Sro2+ and Cao2+ both stimulate a G protein-coupled receptor, which could be the calcium-sensing receptor, they have differential intracellular effects which independently trigger OC apoptosis and could act in a cooperative manner. These results support the mechanism of reduced bone resorption observed in various in vivo and in vitro experiments with strontium ranelate.

P346SA. CATABOLIC BONE RESPONSE TO GH AND ATTENUATED BUT MAINTAINED ANABOLIC RESPONSE TO PTH(1–34) IN RATS FED A LOW PROTEIN DIET

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Stimulators of bone formation can improve bone structure and strength, being thereby particularly suitable for the management of patient with severe osteoporosis. Protein undernutrition frequently occurs in elderly probably contributing to the pathogenesis of osteoporosis. Whether protein intake could influence the response to bone anabolic agents is unknown. To address this issue, six-month old female rats were fed isocaloric diets containing 2.5% (low Protein) or 15% (normal Protein) casein for 2 weeks. Then, bGH (0.5 or 2.5 mg/kg BW) or its solvent were given subcutaneously to rats on either diet twice daily for 4 weeks. In a second series of experiment using the same experimental design, PTH(1–34) (5 or 40 μg/kg BW) or its solvent were given in rats fed the two diets. Proximal tibia bone mineral density (BMD) and ultimate strength were measured. bGH treatment dose-dependently decreased BMD ($-5.1\% \pm 2.$ 5 and $-10.7\% \pm 1.8$*, with 0.5 or 2.5 mg/kg BW of bGH) and bone strength ($-20.1\% \pm 4.9$* and $-44.0\% \pm 5.6$*) in rats fed a low protein diet. No significant effects were observed in rats fed the normal protein diet after this short period of treatment. PTH(1–34) treatment dose-dependently increased BMD ($+10.0\% \pm 2.2$* and $+21.5\% \pm 2.2$*, with 5 or 40 μg/kg BW of PTH(1–34)) and ultimate strength ($+55.3\%$ ± 14.3* and $+96.5\% \pm 16.1$*) in rats fed the normal protein diet. In rats fed a low protein diet, BMD and ultimate strength were $+4.1\% \pm 2.0$ and $+11.0\% \pm 2.7$*, and $+4.2\% \pm 8.4$ and $+43.8\% \pm 13.0$*, respectively. Thus to achieve the same effect on BMD or strength a dose 8 times higher of PTH(1–34) was required in rats fed an isocaloric low protein diet. GH treatment resulted in a negative bone balance when protein intake was reduced. In contrast PTH(1–34) induced a positive bone balance but at a higher dose than in rats with the normal protein diet. These results indicate that protein isocaloric restriction could markedly influence response to anabolic agents, emphasizing thus the major importance of dietary protein intake in the bone response to GH or PTH administration.

P347SU. STRONTIUM RANELATE DOSE-DEPENDENTLY INCREASES BONE STRENGTH AND INTRINSIC BONE QUALITY IN INTACT FEMALE RATS

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Recent clinical studies have demonstrated that strontium ranelate reduces the risk of vertebral and non-vertebral fracture in postmenopausal osteoporotic women. In the present study, we investigated the long-term effects of strontium ranelate on bone strength in intact female rats at the level of L4 lumbar vertebra. Four groups of 30 rats (seven-week old at treatment initiation) were fed ad libitum a diet containing strontium ranelate at a daily dose of 0 (control), 225, 450 or 900 mg/kg/day, for 104 weeks. From the load deflection curve, obtained by compression of the vertebral body, maximal load, stiffness, yield point, total energy (E), and elastic and plastic energy were measured.

Strontium ranelate treatment dose-dependently increased maximal load (up to $+20\%$ at 900 mg/kg/d, $p < 0.05$) and yield point (up to $+13\%$, ns) without affecting stiffness, indicating no mineralization defect, thus suggesting an improvement of the bone quality. This was confirmed by the increase of energy to failure (up to $+54.5\%$, $p < 0.05$) achieved with strontium ranelate treatment at 900 mg/kg/d, which was essentially due to a significant increase in plastic energy ($+136\%$, $p < 0.01$), with an increase in elastic energy ($+26\%$, NS). These results strongly suggest that bone formed under strontium ranelate treatment is able to withstand greater deformation before fracture while possessing similar elastic properties to normal bone. Such modifications observed under strontium ranelate treatment are in agreement with an improvement of intrinsic bone quality leading to greater bone resistance.

P348MO. LONG TERM TREATMENT OF OVARIECTOMIZED RATS WITH BLACK COHOSH: SITE SPECIFIC EFFECTS AND CALCIUM BALANCE

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Black cohosh (Actea (=Cimicifuga) racemosa) is a herbal remedy traditionally used to treat symptoms of peri- and postmenopause. Its efficacy in alleviating hot flushes, night sweats and somatic climacteric complaints has been proven in clinical studies which, however, took at the most few months. For monitoring significant osteoprotective effects in humans, such a short duration of treatment has proven insufficient, even though short-term animal studies have been able to demonstrate a positive influence of black cohosh on metabolic bone parameters [Nisslein and Freudenstein 2003. J Bone Miner Metab 21(6) 370–6].

We therefore performed a study, where adult female Sprague Dawley rats (20 animals per group) were ovariectomized (ovx) and the subsequently established imbalance of bone metabolism was monitored via urinary crosslink measurements. Intervention therapy with an isopropanolic black cohosh extract (60 or 300 mg herbal drug/kg b.w./d) was started in two treatment groups, whereas raloxifene-treated animals (3 mg/kg b.w.) served as positive controls and placebo-treated ovx- or sham-operated animals served as two negative control groups. Treatments lasted for 10 months and besides crosslink measurements, urinary calcium excretion was continuously monitored. At the end of the study, femoral bone density and fracture resistance at the femoral head and lumbar vertebral site were measured.

As expected, ovx-induced alterations in bone metabolism were rapidly evident in all monitored parameters, and corroborated later in necropsy findings of reduced bone density and fracture resistance. Raloxifene significantly antagonized ovx-induced osteoporosis as evident in parameters of bone strength and urinalysis. Black cohosh also proved effective against ovx-induced bone resorption: Levels of urinary crosslinks were significantly reduced compared to untreated ovx-controls. Effects on bone density and fracture resistance were however more pronounced at peripheral bones than at the spine. Interestingly, in black cohosh treated animals, the observed reduction in calcium excretion was dose-dependent. After treatment with high-dose black cohosh, calcium levels were even below pre-ovx values.

We observed no adverse events in high-dose long-term treated rats and therefore we consider the isopropanolic extract of black cohosh, as contained in Remifemin®, as a safe alternative for menopausal women with a positive influence on bone metabolism and calcium balance.

P349SA. STRONTIUM RANELATE REDUCES THE RISK OF VERTEBRAL AND NON-VERTEBRAL FRACTURES IN CAUCASIAN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS

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Strontium ranelate, a new orally active anti-osteoporotic agent, has been reported to have a dual action on bone metabolism, simultaneously increasing bone formation and decreasing bone resorption. A large phase 3 program including 2 multinational, double blind, placebo controlled studies has been performed. In both studies, patients were randomly assigned to receive strontium ranelate 2g/day or placebo for 3 years associated to calcium and vitaminD supplementation according to the patient's status.

The SOTI study (Spinal Osteoporosis Therapeutic Intervention) focused on vertebral anti-fracture efficacy of strontium ranelate, in 1649 post menopausal women with osteoporosis [age: 69.7(7.3) years; Lumbar Bone Mineral Density (BMD Tscore: −3.6(1.3); mean(SD)], 87.5% having at least one prevalent vertebral fracture (2.2 per patient), has demonstrated a rapid and sustained vertebral anti-fracture efficacy of strontium ranelate in the intent-to-treat population, with a relative risk reduction of vertebral fracture of 49% ($p < 0.001$) the first year of treatment and 41% ($p < 0.001$) over 3 years. At 3 years lumbar BMD in strontium ranelate group increased by 14.4% as compared to placebo ($p < 0.001$) and femoral neck BMD by 8.3% ($p < 0.001$).

The TROPOS study (Treatment Of Peripheral OSteoporosis) investigated the efficacy of strontium ranelate on non-vertebral fractures in 5091 women with post-menopausal osteoporosis [age: 76.8(5) years, Femoral Neck BMD T-score −3.1(0.6), 36.8% had at least one prevalent non-vertebral fracture]. In the intent-to-treat population, the risk for experiencing a new non-vertebral fracture during the 3 years was reduced by 16% (RR = 0.84 95%CI [0.702;0.995], p = 0.04, adjusted cox model on pre-defined influential covariates age, BMI, FN BMD and country). 41% reduction of the hip fracture risk (RR = 0.59; 95%CI [0.37;0.95], p = 0.03) was also achieved in patients having taken strontium ranelate for at least 18 months.

At 3 years femoral neck BMD in strontium ranelate group increased by 8.2% as compared to placebo ($p < 0.001$) and lumbar BMD by 14.7% ($p < 0.001$).

In both studies strontium ranelate had a good bone and general safety profile.

The present data support the efficacy of strontium ranelate in reducing the risk of vertebral and non vertebral fracture in postmenopausal women with osteoporosis, representing a new candidate in the treatment of postmenopausal osteoporosis.

P350SU. RALOXIFENE TREATMENT IMPROVES THE STRUCTURAL GEOMETRY OF THE HIP: RESULTS FROM THE MULTIPLE OUTCOMES OF RALOXIFENE EVALUATION (MORE) TRIAL

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Aims: Raloxifene treatment increases lumbar spine and femoral neck BMD and reduces the risk of vertebral fractures. In this study our objective was to determine the effect of raloxifene treatment on the structural geometry of the proximal femur. A subset of postmenopausal women with osteoporosis (n = 1903, mean age 67 ± 7 y) enrolled in the MORE trial was randomized to raloxifene 60mg/d (n = 632, RLX60), raloxifene 120 mg/d (n = 648, RLX120) or placebo (n = 623).

Methods: Study participants received hip DXA scans at baseline and 1, 2 and 3 year time points. The DXA scans were analyzed with a Hip Structure Analysis (HSA) program that measured BMD and geometric properties of the proximal femur traversing regions of the femoral neck, intertrochanter and proximal femoral shaft. Mean response to treatment (area under curve of the repeated measurements) was calculated as a summary measure and used a dependent variable in analysis of covariance with the baseline value as a covariate.

Results: Mean differences following three-year treatment with raloxifene, compared to placebo, are presented in the table below. Following treatment with raloxifene, BMD increased and the buckling ratio (an index of structural instability) decreased at all regions, compared to placebo. The cross sectional area and bending strength (section modulus) increased at the narrow-neck and intertrochanter for both RLX60 and RLX120, but femoral shaft strength showed significant improvement only in the RLX120 group, compared to placebo. There were no differences in bone outer diameter between groups, suggesting the rate of periosteal apposition following raloxifene treatment cannot be detected by the HSA technique.

Mean Percent Change from Placebo

*p < 0.002	Femoral Neck		Intertrochanteric		Femoral Shaft	
	RLX60	RLX120	RLX60	RLX120	RLX60	RLX120
BMD	2.2 %*	2.2 %*	1.7 %*	1.9 %*	1.1 %*	1.4 %*
Cross Sectional Area	2.2 %*	2.3 %*	1.7 %*	1.8 %*	0.7 %	1.5 %*
Outer Diameter	0.0 %	0.1 %	0.0 %	0.0 %	−0.5 %	0.0 %
Section modulus	2.1 %*	2.2 %*	1.3 %*	1.7 %*	−0.1 %	1.1 %*
Buckling ratio	−2.5 %*	−2.4 %*	−2.3 %*	−2.1 %*	−1.6 %*	−1.4 %*

Conclusions: Raloxifene treatment improves indices of mechanical strength and stability at all regions of the proximal femur with no apparent dose effect except at the femoral shaft where fragility fractures are rare.

P351MO. EFFECTS OF ALENDRONATE (ALN) ON THE "ELASTIC" (PRE-YIELD) AND "PLASTIC" (POST-YIELD) BEHAVIOR OF CORTICAL BONE IN OVARIECTOMIZED (OX) RATS.

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Effects of bisphosphonates on bone mineralization and strength are not necessarily correlative. To analyze ALN effects on bone strength, forty 3-month old rats were OX and given immediately 0 (OX-C, n = 13), 5 (OX-5, n = 13) or 25 ug/kg sc (OX-25, n = 14) 2/wk for 6 months, keeping further 15 as sham controls. Their femurs were scanned by pQCT and tested in bending.

Despite not affecting bone mineralization (cortical vBMD) and cross-sectional diaphyseal geometry (diameters, moment of inertia −MI-), OX impaired the intrinsic stiffness of cortical tissue (elastic modulus, E) and the structural stiffness of femur shafts (load/deformation ratio), and reduced yield and fracture loads (Wy, Wf). The post-yield fraction of Wf (Wp = Wf −Wy) was significantly enhanced by OX, perhaps because of the naturally inverse relationship between the tissue's ability to prevent crack generation (impaired) and progress (improved). Effects of ALN were dose-dependent. The highest ALN dose prevented all negative effects of OX and improved Wf over sham values. No changes in Wy were observed in treated rats (no effect on crack generation). However, Wp (bone toughness) was enhanced in a similar proportion than it was in OX rats. The naturally negative "distribution/quality" curves (correlations between cortical architecture, MI and intrinsic stiffness, E) shifted to the "anti-anabolic" region (lower-left) in the graphs for OX rats and to the "anti-catabolic" region (upper-right) for ALN-treated rats with respect to sham controls. This would indicate negative or positive interactions of OX and ALN, respectively, with the feed-back control of bone architecture as a function of bone stiffness and mechanical usage of the skeleton (bone mechanostat theory).

In agreement with previous observations in intact rats treated with Olpadronate, lack of effects on bone mineralization and geometry in this study suggests that both OX and ALN treatment would have improved Wp (and additionally ALN would have improved Wf) by affecting some microstructural determinant(s) of bone material's stiffness and toughness (creeping factors)

independently of bone mineralization. These novel effects of bisphosphonates may explain the striking dissociation observed between induced improvements in BMD and fracture incidence in large studies with postmenopausal osteoporotic women.

P352SA. SPATIAL DISTRIBUTION OF CORTICAL BMD DID NOT COMPROMISE THE BENEFICIAL EFFECTS OF TERIPARATIDE ON RADIUS GEOMETRY IN POSTMENOPAUSAL OSTEOPOROTIC WOMEN

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We had previously reported that, relative to placebo, teriparatide-treated patients had significantly higher axial (Ix) and polar (Ip) moments of inertia at distal radius,suggesting an improvement in bone strength and resistance to fractures. However, bone strength is not only determined by geometry, but also by bone material properties. Using bone mineral content (BMC) and density (BMD) as surrogates for bone material quality we had attempted to show that for any level of BMC or BMD, teriparatide-treated patients had better distribution of bone, as represented by Ix and Ip. This analysis assumed a homogenous distribution of cortical BMD in the bone cross-section. However, teriparatide may increase bone porosity and newly formed bone may include incompletely mineralized bone with lower BMD.

We assess here the influence of BMD distribution at the cross-sectional area on the estimation of cortical bone architecture at distal radius.

pQCT scans were performed in 72 postmenopausal osteoporotic women after a median 18 months of treatment with teriparatide at doses of either 20 (n = 29) or 40 (n = 21) ug or placebo (n = 22), using a Stratec 960 pQCT machine at a site corresponding to 15% the length of the ulna from the distal radius end. The density-weighted cortical area axial (Ixw) and polar (Ipw) moments of inertia were calculated by correcting the area of each pixel by the ratio of the individual pixel density and the average density of the cortex. Using this approach, incompletely mineralized or high-porosity bone areas contribute less to the moments of inertia values.

Cortical BMD was not significantly lower in the teriparatide-treated patients as compared with placebo (886.9 ± 103.5 vs. 904.5 ± 118.4 mg/ccm). Ix and Ip values were significantly higher in the teriparatide-treated patients as compared with the placebo group (Ix 789.4 ± 238.9 vs. 654.7 ± 145.8 mm4, $p = 0.008$; Ip 2986.4 ± 800.7 vs. 2716.1 ± 728.7 mm4, $p = 0.016$). After corrected for BMD, Ixw and Ipw were still significantly higher in the treatment group as compared with placebo (Ixw 1071.4 ± 346.8 vs. 892.5 ± 215.9, $p = 0.010$; Ipw 3265.9 ± 1050.7 vs. 2850.6 ± 756.2 mm4, $p = 0.005$).

These results suggest that the putative effects of teriparatide on cortical BMD do not prevent the improvements in cortical bone architecture associated with teriparatide treatment.

P353SU. BONE LOSS PREVENTION AFTER TOTAL HIP ARTHROPLASTY: EFFECT OF INTRAMUSCULAR CLODRONATE. ITALIAN MULTICENTER STUDY

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One of most common cause of prosthetic failure after total hip arthroplasty is acute periprosthetic bone loss. Aim of this study was to evaluate the effectiveness of a pharmacological prophylaxis for this process. Primary outcome was the effect of intramuscular clodronate (Difosfonal) on early periprosthetic bone mineral density (BMD) after 1 year in N = 100 patients undergoing total hip arthroplasty. Secondary outcomes were the evaluation of biochemical bone turnover markers and radiological and clinical evaluations.A significant reduction in bone loss in clodronate treated group, compared with placebo group (calcium 1000 mg plus vitamin D 800UI), was seen either in proximal femur and in the pelvis.A significant suppression of all biochemical bone turnover markers, compared with placebo, was associated with clodronate prophylaxis. No clodronate inducted interference was seen regarding the symptoms improvement or radiological outcomes; no significant adverse events were associated with clodronate treatment. The study suggests that clodronate may be effective and safe in preventing bone loss after total hip arthroplasty; more studies regarding this issue will be helpful to determine a large scale efficacy of this prophylaxis in patients undergoing total hip arthroplasty.

P354MO. PATIENT COMPLIANCE AND PREFERENCE OF ALENDRONATE'S ONCE WEEKLY ADMINISTRATION IN COMPARISON WITH ALL DAILY TREATMENTS FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

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It is widely accepted that compliance in drug therapy is very important in chronic diseases. In addition to that, the end therapeutic result appears to be closely connected to the good or bad compliance of the patient during treatment. However compliance studies in Osteoporosis (OP) are very rare event in the international litterature although OP is a chronic disease.

In order to examine the patients compliance under different treatment regimens an open label, randomized, crossover 12 months study has been performed at 98 Rheuma or Endocrino centers all over Greece. 1180 patients (mean age 61.3 years) were treated for 6 ms with Alendronate 10 mg/d (52.2%), Raloxifen 60 mg/d (27.3%) and Risedronate 5 mg (20.5%) and then replaced the above drugs with Alendronate 70 Once Weekly (OW) for another six months.

After experiencing both regimens, a questionnaire was administered which addressed compliance, preference, convenience and willingness to take the regimens long term. Results were evaluated using Chi square and Gart's test.

After the analysis of the results, the overall compliance during daily treatment was 73.4% and during OW treatment 95.6%. In addition 95.1% of the patients preferred the OW regimen while the 98.2% of them found that OW regimen was more convenient and the 98.3% chose the OW regimen as the one that they would be more willing to use in long term. All the results were statistically significant ($p < 0{,}001$ for each of them) and consistent across the subgroups (eg, the drug used during the first 6 months).

In conclusion this study demonstrates that the patient's compliance is much better with the Alendronate OW dosing regimen than with all other tested regimen methods. In addition to that, the study shows that the patients preferred this regimen from all others daily OP treatments.

P355SA. EFFECTS OF INTERMITTENT MONTHLY I.V. ADMINISTRATION OF CLODRONATE ON BONE MINERAL DENSITY IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS: A TWO-YEAR FOLLOW-UP STUDY

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Gastrointestinal (GI) intolerance represents the main adverse effect of long term oral aminobisphosphonate therapy in osteoporosis. This makes patients reclutant to undergo or continue oral treatment. We carried out this study to evaluate the two-year effects of an intermittent monthly i.v. infusion of clodronate (Difosfonal), 600 mg in 500 ml of saline, on bone mineral density (BMD) in 50 osteoporotic postmenopausal women (T-score ≤ -2.5 at the lumbar spine L2–L4) who were intolerant to oral administration of aminobisphosphonates. Clodronate-treated patients received oral supplementation of calcium (600mg) plus vitamin D3(400 IU) every day for 2 years. A control group of 21 osteoporotic women only received oral supplementation of

calcium and vitamin D3 at the same dose and for the same length of time. The control group showed a progressive but not statistically significant percent decrease in both spine (−1.4%) and total hip (−1.2%) BMD over the 2-year follow up. In contrast, in the group treated with clodronate spine BMD significantly rose at the first yearly check-up (L2–L4, Mean ± SE: 3.0 ± 0.5; p≤0.001 vs baseline) and a further but not statistically significant increase was seen after the second year of treatment (+0.32%). The increase in BMD at the total hip was not statistically significant during the first and second year of treatment, being 1.0% and 0.91% respectively. In 19 women treated with clodronate, serum CTX levels was significantly suppressed after 6 months (−30.2%; p≤0.05 vs baseline) with no subsequent change at the second year of the study. In the clodronate group the treatment was withdrawn in 2 women for hypotension during the infusion (n = 1) and for urtical skin reaction (n = 1). Two patients in the clodronate group and 2 subjects in the placebo group did not conclude the study for GI intolerance to calcium supplementation. These results indicate that monthly i.v. clodronate administration is an alternative safe treatment that may provide clinically relevant benefits to skeletal bone density in osteoporotic postmenopausal women, improving patient compliance to long-term therapy with bisphosphonate.

P356SU. A MULTI-CENTERED, RANDOMIZED, DOUBLE-BLIND PLACEBO CONTROLLED STUDY OF RISEDRONATE ON BONE MINERAL DENSITY AND BONE TURNOVER MARKERS IN OSTEOPOROTIC CHINESE WOMEN

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Risedronate has been shown to be effective in preventing fractures in Caucasian women. To assess the efficacy and tolerability of Risedronate 5 mg/d versus placebo in Chinese postmenopausal women, we studied 65 osteoporotic women with BMD T score ≤2.5 at the spine. BMD at L1-4 lumbar spine, femoral neck and total hip region, serum osteocalin and urine N-telopeptide were assessed at 3 monthly intervals. No difference in BMD and bone turnover markers was observed at baseline between the 2 groups. Risedronate significantly increased BMD at 3 months [lumbar spine 3.5% ($p < 0.0001$), femoral neck 1.9% ($p < 0.02$), total hip 2.7% ($p < 0.0001$)], and 12 months [lumbar spine 6.2% ($p < 0.0001$), femoral neck 1.9% ($p < 0.02$), total hip 2.7% ($p < 0.0001$)], whereas no difference in BMD was seen in the placebo group. Risedronate significantly decreased osteocalcin by means of 2.9% and 11.4% and N-telopeptide by means of 31.7% and 40.1% at 3 and 6 month respectively from placebo. Significant differences were already observed at the lumbar spine BMD and urinary N-telopeptide at month 3 between the 2 treatment groups. The change in NTx at 3 months correlated to the change in BMD at 12 months. In conclusion, as similar to Caucasian women, early efficacy of Risedronate on BMD and bone turnover markers is seen in postmenopausal osteoporotic Asian women.

P357MO. CALCIUM SUPPLEMENTATION FAILS TO REDUCE BONE TURNOVER IN ELDERLY WOMEN WITH OSTEOPOROSIS OR OSTEOPENIA WITH VITAMIN D INSUFFICIENCY

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Introduction: The effect of short term calcium supplementation by a clinical nutriment on bone turnover was studied in elderly women with normal or decreased calcidiol serum level.

Methods: Eighty eight postmenopausal women (60–75 years) were enrolled in the study to investigate the effect of 1120 mg calcium and 208 IU vitamin D in a complex composition (Fortimel®, Nutricia) on bone turnover after 4 weeks treatment. All women suffered from osteopenia or osteoporosis detected by bone densitometry. Serum parathyroid hormone levels and bone turnover markers (serum β-CrossLaps, osteocalcin, alkaline phosphatase) were determined before and after the treatment. Moreover, calcidiol serum level was also measured at the beginning of the study. A questionnare was used to define gastrointestinal side effects and urinary calcium/creatinine ratio was calculated to estimate the risk of kidney stone development.

Results: The serum level of β-CrossLaps was elevated (526.97 ± 29.26 pg/ml) before the study and reduced during the treatment (485.58 ± 28.27 pg/ml, $p = 0.03$). Both of the serum osteocalcin (28.58 ± 1.37 vs. 27.03 ± 1.36 ng/ml, $p = 0.025$) and alkaline phosphatase (200.46 ± 8.72 vs. 186.94 ± 11.64 U/l, $p = 0.033$) decreased. The serum 25-OH vitamin D3 was below 30 ng/ml in 20 patients before the treatment. A correlation ($r = 0.508$, $p < 0.001$) between the decreasing of bone formation and the decreasing of bone resorption was found only in patients with nomal serum 25-OH vitamin D3 concentration (≥30 ng/ml). However, the bone turnover did not decreased in patients with calcidiol deficincy. Urinary calcium/creatinine ratio remained unchanged during the treatment, but two patients suffered from constipation and one of them had diarrhea due to the calcium supplementation.

Conclusion: Calcium supplementation in a complex clinical nutriment proved to be able to decrease bone turnover, even after a short treatment period of not more than 4 weeks. However, this treatment was ineffective in patients with vitamin D deficiency suggesting the importance of serum calcidiol measurement before calcium supplementation. Calcium in complex with other nutrients did not increase the risk of renal stone developments and hardly caused gastrointestinal problems.

P358SA. ACUTE NEPHROTOXICITY OF THREE INTRAVENOUS BISPHOSPHONATES IN THE RAT

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Aims: Several bisphosphonates have been associated with acute renal toxicity, particularly when high doses are administered by rapid intravenous (i.v.) infusion. The present study, conducted in rats, compares the experimental acute nephrotoxicity of three i.v. bisphosphonates: the highly-potent, nitrogen-containing bisphosphonates ibandronate and zoledronate and the less potent, non-nitrogen-containing bisphosphonate, clodronate.

Methods: The female rats used in the various studies were aged 6, 11 or 34 weeks and weighed 110–319g. Ibandronate and zoledronate were given as a single i.v. dose over a range of 1–20 mg/kg and 1–10 mg/kg, respectively. Clodronate was administered as two intraperitoneal (i.p.) injections of 200 mg/kg on a single day. Clinical biochemistry and kidney histopathology were performed on the first and fourth day after dosing.

Results: Tubular degenerative changes were evident (by histology) only on the fourth day after dosing with 1–20 mg/kg i.v. ibandronate, 3–10 mg/kg i.v. zoledronate, or 200 mg/kg i.p. twice-daily clodronate. These findings were similar in the younger and older animals. Characteristically, the changes comprised degeneration and single cell necrosis of the proximal convoluted tubules (PCT). The lesions induced by ibandronate and clodronate were locally restricted to the S1 and S2 segments of the PCT while, with higher doses of zoledronate, the S3 segments and distal tubules were also affected. The dose-effect relationship was stronger for zoledronate than for ibandronate: the ratio between the lowest lethal dose and the minimally nephrotoxic dose was 25 for ibandronate, but only 3.3 for zoledronate. Clinical biochemistry and urinalysis parameters such as serum creatinine and urea,

urinary volume, and urinary excretion of enzymes and protein, did not reliably indicate the kidney damage observed histopathologically.

Conclusions: The renal toxicity caused by high doses of bisphosphonates differs qualitatively in the lesions formed and quantitatively in the dose-effect relationship. Our findings show that clinical monitoring of renal safety cannot reliably exclude the presence of early-stage tubular damage. With long-term treatment, such subclinical changes may accumulate to clinically relevant levels with zoledronate, but not with ibandronate (see Pfister T, et al. Toxicology 2003;191:159–67).

P359SU. SUCCESSFUL PREDICTION OF BIOMARKER RESPONSE TO ORAL MONTHLY IBANDRONATE

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Aims: Ibandronate is a potent nitrogen-containing bisphosphonate with proven fracture efficacy in postmenopausal osteoporosis (PMO) with extended dosing intervals. An ongoing clinical development programme is evaluating novel intermittent oral and i.v. (injection) ibandronate regimens. A modelling and simulation project was initiated to identify regimens likely to provide substantial clinical efficacy.

Methods: Using data from prior studies of continuously and intermittently administered oral and i.v. ibandronate (involving >700 patients), a pharmacostatistical model was developed, which was capable of describing the time course of uCTX change (a biomarker of pharmacodynamic response) with ibandronate.[1] The model was validated by retrospectively simulating the outcomes of prior studies of oral and i.v. ibandronate. To assist the selection of dose regimens for clinical evaluation in the phase I, dose-ranging, Monthly Oral Pilot Study (MOPS), the uCTX response with several oral monthly ibandronate regimens was simulated. Simulations were replicated 100 times (per individual) in 250 'virtual' patients.

Results: The predicted time course of residual uCTX suppression (i.e. one month after dosing) with 100 mg and 150 mg oral monthly ibandronate is depicted below. Using the model, the following oral monthly doses were identified for clinical evaluation in MOPS: 50 mg, 100 mg, and 150 mg. The recently reported clinical findings from MOPS confirm that the 100 mg and 150 mg doses, given once-monthly for three cycles, provide significant efficacy (as assessed by changes in uCTX).

Conclusion: The utility of a pharmacostatistical model in the clinical development of a bisphosphonate in PMO was verified. A multinational study (Monthly Oral iBandronate In LadiEs: MOBILE) is ongoing to establish the long-term (1 and 2 year) efficacy and safety of 100 mg and 150 mg oral monthly ibandronate regimens in PMO.

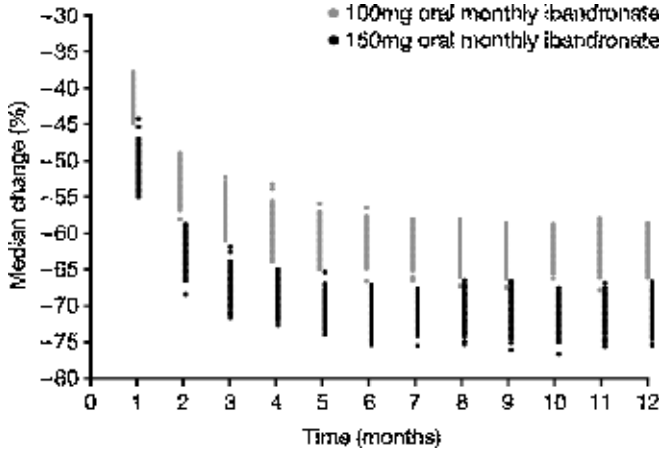

Fig. 1 Simulated residual uCTX suppression with 100 mg and 150 mg oral monthly ibandronate over 1 year

1. Gieschke R, et al. Osteoporos Int 2002;13(Suppl. 3):S23 (Abstract P36).

P360MO. EFFECT OF ORAL VITAMIN D2 YEARLY BOLUS ON HIP FRACTURE RISK IN ELDERLY WOMEN: A COMMUNITY PRIMARY PREVENTION STUDY

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Background: Vitamin D deficiency is a well recognized risk for hip fracture. Both vitamin D insufficiency and hip fracture are so frequent in the elderly that a population-wide preventive intervention is warranted.

Methods: This is a community study including approximately 50000 women of ≥65 years of age registered at one of the health districts of the Veneto region in Italy. Hip fracture incidence (ca. 460 events per year) was evaluated over 4 years from 1999 to 2002. An oral bolus of 400.000 IU vitamin D2 was offered to all women aged ≥65 during the winters 2000–2001 and 2001–2002. There were no exclusion criteria. 45% and 47% of eligible women had the vitamin D bolus in 2000–2001 and 2001–2002, respectively. The patients with incident hip fracture were identified as soon as referred to the hospitals of the health district and interviewed on their participation to the vitamin D preventive program.

Results: The proportion of women who had the vitamin D intervention declined with advancing age from 50–55% in women aged 60–70 years to 22–26% in those aged ≥90 years. The two year intervention on the community decreased the incidence of fracture from 1.51% to 1.41% (−10%, $p = 0.050$) in comparison to the previous two years. The age-adjusted relative risk of hip fracture during 2001 and 2002 in women who had the vitamin D intervention relative to control women decreased by 17% ($p = 0.056$) and by 25% ($p = 0.005$) respectively. The risk reduction was considerably greater in the cohort aged ≥75 years. 25-OH vitamin D concentrations in the 120 women in whom it was measured rose significantly by 9 ng/ml over 4 months since dosing.

Conclusions: Despite several obvious limitations linked to its nature, this study sufficiently documents that yearly vitamin D bolus supplement given as primary prevention to elderly women, decreases the incidence of hip fracture. For its high safety, feasibility and cost-effectiveness this primary intervention has impressive generalisability potentials.

P361SA. EFFECT OF YOGA EDUCATION ON QUALITY OF LIFE IN POSTMENOPAUSAL OSTEOPOROSIS

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Osteoporotic vertebra and hip fractures are a major cause of dysfunction, disability, mortality and loss of life quality in our growing and ageing population. In the premenopausal period exercises prevent rapid bone loss due to estrogen deficiency and increase muscle strength, mobility and flexibility thereby decreasing risk of falls and fractures. Yoga exercises, which have been an inseperable part of the Eastern culture for hundreds of years, are now being used in the field of osteoporosis rehabilitation. Yoga has a positive effect on balance, posture, flexibility,and life quality by its effects on balance, stretching, relaxation and strengthening. The aim of this study was to evaluate the effect of yoga exercises in postmenopausal osteoporotic women on balance and life quality and to compare the result with a classic osteoporosis exercise program. Twenty-six postmenopausal osteoporotic women over 55 years of age were included in the study. A neuromuscular test battery and the QUALEFFO as life quality index were used for assessment of balance and life quality. The

results showed that yoga education has a positive effect on pain, physical functions, social functions, general health perception and balance. As a conclusion yoga appears to be an alternative modality for the rehabilitation of osteoporotic subjects.

P362SU. EFFECTS OF EXERCISE AND NUTRITION ON BALANCE AND RISK OF FALLING IN ELDERLY PEOPLE WITH DECREASED BONE MINERAL DENSITY

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Aims: A pilot study was set up at the Centre for Prevention and Treatment of Osteoporosis at the University of Zurich. It is aimed at determining if the risk of falling can be influenced by exercise and nutrition in a population of elderly people diagnosed with severe osteopenia or osteoporosis.

Methods: The study was designed as a randomized controlled prospective trial of 12-month duration with an initial 3-month intervention program aimed at testing the combined effects of exercise with protein and calcium/vitamin D supplementation as opposed to calcium/vitamin D supplementation alone. A total of 22 female patients, aged 72.2 ± 7.1 SD yrs, BMI: 23.2 ± 2.8 SD kg/m^2 presenting with severe osteopenia or osteoporosis $\pm$ fractures were included after they gave their written informed consent. Primary outcome is risk of falling (Berg Balance Test), whereas secondary outcomes include muscle strength, postural sway, aerobic capacity, activity level and general health assessed upon entry, then at month 3, 6, 9 and 12 respectively. In addition, spine and hip BMD as well as WBC including bone, fat and lean mass are measured at baseline and after 12 months by DEXA (Hologic QDR 4500 Elite). Various biological parameters, including serum Vit. D and IGF-1 levels are measured initially and after 12 months.

Results: At the end of the first 3-months, the intervention group presented with a significant decrease in the risk of falling (−7%), a significant increased muscle strength (+22%) and aerobic capacity (+39%) as compared to the control group. These results were maintained by month 6. The BMD, WBC and biological parameters results will be provided at the end of the study by month 12.

Conclusions: These initial results are promising and clearly do reflect a better body balance and a decreased risk of falling in the intervention group. The initial assessment of total hip and femoral neck BMD, WBC fat mass, lean mass, serum Vit. D and IGF1 are in agreement with previous published work in elderly severe osteopenic or osteoporotic women. Overall data and conclusion will be presented at the congress.

P363MO. UNCOUPLING BONE TURNOVER WITH STRONTIUM RANELATE, A PROMISING AGENT FOR THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Aim: Traditional antiresorptive agents such as hormone replacement therapy, selective-estrogen receptor modulators, and bisphosponates inhibit bone resorption but also bone formation (coupling) leading to considerable limitations in terms of increasing bone mass and thus curing osteoporosis. Ongoing reseach targets the identification of drug-candidates that can provide inhibition of bone resorption with favorable or no effect on bone formation (uncoupling). The aim of the present study was to investigate the simultaneous effect of strontium ranelate on biomarkers of bone formation and resorption assessed in samples collected from a 3-year fracture study (SOTI) on a large number of osteoporotic women.

Design: Study participants were 1649 postmenoausal women with osteoporosis. Women were randomly selected to receive treatment with either 2 g/day strontium ranelate or placebo for 3 years. All women received treatment with calcium and vitamin D. Efficacy parameters were the changes in biochemical markers of bone resorption (serum C-telopeptide of colagen type 1, s-CTX) and bone formation (bone-specific alkaline phosphatase, BSAP; serum osteocalcin, s-OC).

Results: Strontium ranelate evoked moderate but sustained decrease in s-CTX (15%) and simultaneous increase in s-OC and BSAP (10%).

These changes in bone turnover translate to a sustained positive calcium balance corresponding to ~50 mg per day. This positive calcium balance kept over a 3-year treatment period may theoretically result in a ~10% increase in bone mineral content of the skeletal system contributing to decreased risk for osteoporotic fractures.

Conclusion: The moderate, but sustained and lasting uncoupling of bone formation from bone resorption makes strontium ranelate a promising agent for the treatment of postenopausal osteoporosis. Further studies are required to better understand the mechanisms of action of this drug-candidate.

P364SA. IN VIVO AND IN VITRO BIOEQUIVALENCE OF TWO FORMULATIONS CONTAINING ALENDRONATE

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Alendronate formulations are effectively administered to prevent new fractures due to osteoporosis. In many countries generic versions have been authorised in order to lower the cost of therapy and enhance compliance rates, but equivalency with the reference compound is unknown. As the absorption of alendronate is extremely low, and the digestive side effects can be associated to formulations (the pill effect), it is of importance to describe the equivalence of any available alendronate formulation.

Marvil® tablets (Alend/ro® in some countries), contain alendronate 10 and 70 mg, obtained by an independent method. The crystals of its hydrated molecule are quite identified (Vega et al, Acta Cryst 1996,C52:2198–2201), and the product has been tested in experimental assays and its formulations used in clinical studies. Data have been published by independent institutions. We hereby report in vitro and in vivo equivalence tests performed under GLP and GCP norms. Reference formulations were purchased in USA. In vitro dissolution assays show quick, complete and comparable dissolution rates with both formulations. These studies are being further confirmed by an international audit assay. Two clinical bioequivalence studies with either 10 and 70 mg tablets were performed at the Buenos Aires Italian Hospital and FLENI MRC unit respectively, following a double blind, randomised, parallel, cross-over design, including 12 and 24 healthy subjects. Urine samples were obtained at intervals of 6 hour each, during 24 hours and submitted to analysis at the University of Leiden (The Netherlands). The absorption rate of the four tested formulations was found between 0.5 and 0.7%, with great inter-individual variability, as expected, within the range of the reference compound ($p < 0.05$, beta power > 0.80). In conclusion, Marvil® formulations are comparable to the alendronate formulations commercialized in USA.

P365SU. BACK PAIN RISK IS REDUCED IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS TREATED WITH TERIPARATIDE AS COMPARED WITH ALENDRONATE: RESULTS FROM TWO DOUBLE-BLINDED COMPARATOR TRIALS

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Compared to placebo, teriparatide 20 and 40 mcg/d (TPTD20 and TPTD40) treated postmenopausal women with osteoporosis had significantly reduced risk of back pain, moderate or severe back pain, and severe back pain (Neer NEJM 2001, Genant ASBMR 2003).

Aims: To compare the incidence of back pain occurring in postmenopausal women treated with teriparatide or with alendronate.

Methods: Two double-blind trials compared oral alendronate 10 mg/d (ALN10) plus placebo injection with oral placebo plus teriparatide injection in postmenopausal women with osteoporosis. Patient inclusion and exclusion criteria were similar in the trials. Back pain data were collected during adverse event monitoring. In study A, women were randomized to TPTD20 or ALN10 for 18 months. In study B, women were randomized to TPTD40 or ALN10 for a median 14 months and women completing this trial were enrolled in a follow-up study.

Results: In each trial, baseline demographics in the two groups were similar. Compared with ALN10, women treated with TPTD20 had reduced risk of back pain (P = 0.051), moderate or severe back pain (P = 0.003), and severe back pain (P = 0.04), with relative risk reductions of 27%, 44%, and 52%, respectively (Table, I). Women treated with TPTD40 had reduced risk of back pain (P = 0.012) and moderate or severe back pain (P = 0.016), with relative risk reductions of 71% and 80%, respectively, versus ALN10 (Table, II). During the trial plus 18 months of follow-up, women in the TPTD40 group had reduced risk of back pain (P = 0.015), and moderate or severe back pain (P = 0.016), with relative risk reductions of 66% and 80%, respectively, versus the ALN10 group (Table, III).

I. Study A

	ALN10 N = 101		TPTD20 N = 102		Relative Risk (P-value)
	n	%	n	%	
Back Pain	39	38.6	26	25.5	.73 (0.051)
Moderate or Severe Back Pain	33	32.6	15	14.7	.56 (0.003)
Severe Back Pain	12	11.9	4	3.9	.48 (0.04)

II. Study B

	ALN10 N = 73		TPTD40 N = 73		
	n	%	n	%	
Back Pain	14	19.2	4	5.5	.29 (0.012)
Moderate or Severe Back Pain	10	13.7	2	2.7	.20 (0.016)
Severe Back Pain	2	2.7	1	1.4	.52 (NS)

III. Study B + 18 Months Follow-up

	ALN10 N = 53		TPTD40 N = 52		
	n	%	n	%	
Back Pain	15	28.3	5	9.6	.34 (0.015)
Moderate or Severe Back Pain	10	18.9	2	3.9	.20 (0.016)
Severe Back Pain	3	5.7	1	1.9	.33 (NS)

Conclusions: In two clinical trials, women randomized to teriparatide had substantially reduced risk of back pain compared with women randomized to alendronate.

P366MO. HORIZON-PIVOTAL FRACTURE TRIAL: UNIQUE DESIGN OF A RANDOMIZED, PLACEBO-CONTROLLED TRIAL TO EXAMINE THE EFFECT OF ANNUAL INFUSION OF ZOLEDRONIC ACID (5 MG) ON HIP AND SPINE FRACTURE REDUCTION

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A single infusion of zoledronic acid has been shown to increase bone mineral density (BMD) at the spine by approximately 5% and decrease bone resorption by about 50% at 12 months compared with placebo. However, the potential to reduce fracture risk is not known. To evaluate the effect of once-yearly zoledronic acid on modifying fracture risk, we are conducting a 3-year, randomized, placebo-controlled trial known as HORIZON-PFT.

7764 women between the ages of 65 and 89 years were recruited from 230 clinical centers in 27 countries, representing a diverse population with respect to socioeconomic, racial and cultural background. Major inclusion criteria were: a femoral neck BMD t-score less than or equal to −2.5, or between −1.5 and −2.5 in the presence of at least one vertebral deformity. Participants were randomized to placebo or zoledronic acid (5 mg delivered in 100 ml volume, 15 minute infusion). Study medication is administered annually, and participants are followed for 3 years. All participants receive 1000 to 1500 mg of elemental calcium plus 400 to 1200 IU of vitamin D per day (minimum background therapy). Co-primary endpoints are hip fractures and new vertebral fractures. Secondary efficacy endpoints include: non-vertebral fractures; change in BMD by DXA; changes in biochemical markers of bone metabolism; and changes in bone density and size by QCT. Safety endpoints include evaluation of adverse events, assessment of bone histology by histomorphometry, and post-dose monitoring for acute changes in renal lab values.

An innovation in this trial is that women who were taking non-bisphosphonate medications for osteoporosis, including HT, SERMS, and calcitonin (''usual care''), were allowed to participate. For the co-primary endpoints, the effect of the study medication on hip fractures will be tested in all women, whereas the effect on vertebral fractures will be tested in the subset (6113) who at baseline were not taking ''usual care'' medication. The study was designed under the expectation that about 58% of participants would be taking ''usual care'' medications, but in fact only 21% were actually enrolled into this subset.

P367SA. OSTEOPOROSIS IN GENERAL PRACTICE

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An informative research regarding general practice was carried out nearby GPs consulting rooms during first semester of 2003, in order to verify if an adequate diagnosis of osteoporosis is usually performed and wich are the consequent therapies. A fully privacy respectful questionnaire, including 14 questions, was submitted to 30,000 GPs all over national territory. An high percentage of duly filled forms was collected; data suggest that osteoporosis is still underestimated, probably due to the patients low perception of the disease. In a chronic pathology, an effective treatment, safe and allowing a good compliance should be useful, but not any bisphosphonate is able to warrant all these characteristics.

P368SU. INFLUENCE OF REGULAR EXERCISE ON BONE MINERAL DENSITY IN ELDERLY WOMEN

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Osteoporosis is a disease in which the density and quality of bone are reduced, leading to weakness of the skeleton and increased risk of fracture. Bone mineral density (BMD) measurements are effective in assessing fracture risk, confirming a diagnosis of osteoporosis and monitoring the effect of treatment.

Non-medical therapy, such as a healthy diet and exercise, has been shown to have a beneficial effect on bone.

Physical activity during childhood and adolescence is positively related to bone density but effects in postmenopausal women are modest. Elderly people who have experienced some bone loss may benefit from a program of weight-bearing and endurance exercises.

The aim of this study was to assess the effect of regular, long term and supervized exercise program on bone mineral density in elderly women.

Seventy-six women with postmenopausal osteoporosis (mean age 60 ± 10 yrs) were enrolled in the study. Control group was consisted from 22 postmenopausal osteoporotic women. No significant diferences existed between exercise and control group for

age, years since menopause, body mass index or height ($p > 0.05$). The exercise regimen involved aerobic exercises, strength training and stretching exercises. We used some equipment such as ankle-wrist weights, dumbbells, and theraband for strengthening local sites. Supervised exercises were performed once a week at the hospital and than patients continued regularly exercise at home 3 times a week for one year.

A Hologic Delphi-W dual x-ray absorbtiometry was used to assess BMD of the lumbar spine and total hip.

Differences between the 0 and 12 months in the groups were estimated using paired t tests. Differences between the two groups were estimated using unpaired t tests .

In the exercise group there was a significant increase in % BMD change between 0 and 12 months in the femoral neck, and T score was increased significantly in the same region ($p < 0.05$). In comparison, percentage BMD change and T score were also significant in the exercise group ($p < 0.05$).

Our results suggested that, regular, supervized exercises have a positive effect on BMD, especially in the femaral neck in the elderly osteoporotic women.

P369MO. THE EFFECT OF KYPHOSIS ON CARDIOPULMONARY EXERCISE TEST AND EXERCISE TOLERANCE IN PATIENTS WITH SEVERE OSTEOPOROSIS: PRELIMINARY RESULTS

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Background: Loss of bone in osteoporosis (OP) can lead to gradual compression or wedging of the vertebrae and narrowing of the intervertebral discs. With resultant increase in the kyphotic curve.

Aim: To evaluate the effects of the deformation of the thoracic cage on cardiopulmonary exercise test parameters and aerobic capacity in patients with OP.

Methods: 34 patients with OP were consented to participate in the study. The patients were divided into two groups according to time since the diagnosis of OP. Group I was newly diagnosed (less than one year) and the group II was diagnosed late (more than six years). Anteroposterior and lateral radiographs of the thoracic and lumbar spine and dual energy x-ray densitometry were obtained in all patients. The number and severity of vertebral deformity were measured by using the Kleerekoper and Gennant index in spine radiographs. The degree of dorsal kyphosis was measured by using the Cobb technique.

Pulmonary function was spirometrically assessed, cardiopulmonary exercise test was performed with a treadmill by using breath by breath analysis of oxygen consumption.

Results: Mean time since diagnosis of OP was 11.1 months in group I and 80.1 months in group II. Mean age was 56.2 years and 55.8 years respectively. When compared with group I, there was a slight decrease in some of the cardiopulmonary exercise test and exercise tolerance in group II.

Conclusion: When compared with newly diagnosed patients, longer duration of OP might produce a slight respiratory dysfunction and a decline in exercise tolerance in women. Therefore active prevention or treatment of OP is needed to retard the development of vertebral deformity and such cardiopulmonary dysfunctions.

P370SA. BONE TURNOVER RESPONSE AND BONE MINERAL DENSITY CHANGES AFTER 1 YEAR TREATMENT WITH RISEDRONATE 35MG WEEKLY IN VENEZUELAN TYPE I POSTMENOPAUSAL OSTEOPOROTIC WOMEN

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Suppression of bone remodeling and increase of Bone Mineral Density (BMD) are two targets of osteoporosis treatment. The aims of this study are to show changes in bone turnover and BMD after one year treatment with Risedronate in a group of Venezuelan postmenopausal osteoporotic women.

117 postmenopausal women with type I Osteoporosis received 35 mg/weekly of Risedronate on fasting state during one year. All received Calcium Citrate 650 mg/d plus 400 IU vitamin D. BMD was assessed by DEXA (LUNAR Prodigy, VC: 1.5%), Biochemical markers of bone turnover were measured as follow: NTx Osteomark, Ostex, Seattle, USA. Tartrate Resistant Acid Phosphatase, TRAP: Hydrolysis of paranitrophenyl phosphate at 4.8 pH. Total Alkaline Phosphatase, TAP: Labtest, Roy modified.

Mean age was 63 ± 8.39 (30–86), age of menopause was 47 ± 5.79 (25–58). BMD at femoral neck increased from 0.749 ± 0.1 to 0.759 ± 1 ($p < 0.05$). At lumbar spine from 0.869 ± 0.1 to 0.883 ± 0.1 ($p < 0.05$). T score decreased from -1.941 to -1.925 p = NS at femoral neck and at lumbar spine from -2.74 to -2.57 ($p < 0.0001$); percent changes in BMD were $+3.4\%$ at femoral neck and $+4.9\%$ at lumbar spine. Variation of bone markers at initial, six and twelve months were NTx $122 \pm 80 \pm 39$ and 64 ± 50 nmol/BCE/mmol/creat ($p < 0.001$ initial vs 6 and 12 months), percent changes were -52% at 6 months and -47% at 12 months, TAP 46 ± 12, 30 ± 13, 36 ± 10 IU/l ($p < 0.0001$ initial vs 6 and 12 month), Percent changes were -34% at 6 months and -22% at 12 months. TRAP, 8 ± 3, 7 ± 2, 7 ± 3 IU/l ($p < 0.001$ initial vs 6 month and $p < 0.06$ initial versus 12 month) Percent changes were -13% at 6 months and at year.

In conclusion, the use of 35 mg/week of Risedronate during one year decreased bone markers significantly; NTx 47%, TAP 22% and TRAP 13%. BMD increased significantly, $+3.4\%$ at femoral neck and $+4.9\%$ at lumbar spine.

P371SU. BONE MARKERS AND BONE MINERAL DENSITY AFTER TWO YEARS TREATMENT WITH ALFACALCIDOL IN HIGH REMODELING POSTMENOPAUSAL WOMEN WITH LOW MINERAL DENSITY

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Vitamin D metabolites have been used for osteoporosis treatment. Main actions on bone are: mineralization, stimulation of osteoblast and diminish resortion. However, available information about action of alfacalcidol on resorption markers in a prospective double-blind, placebo control trial are scarce.

92 postmenopauseal women with low BMD (T-score between SD-1 and SD-3 at L2-L4 or femoral neck) and high turnover: N-telopeptide (NTx), Tartrate Resistant Acid Phosphatase (TRAP) or Total Alkaline Phosphatase (TAP) 1 SD or more above the premenopausal mean were randomized in a double-blind, placebo control, twelve months trial 1 μg/day with alfacalcidol. The variation rate was NTx -28%, TRAP -23%, AP -16%, BMD remained stable in both groups. A twelve months extension, as an open label study, was offered to patients on alfacalcidol. Out of the 45 patients on alfacalcidol 18 agreed to follow the extension protocol. At 24 months there was significant reduction in alkaline phosphatase (-31.25%), no significant changes were observed in NTx (-22.6%) and TRAP (-16%), BMD remained stable, but there was a tendency to decrease.

Conclusion: Alfacalcidol, at 1 μg/day in patients with low BMD and high turnover maintained BMD and suppressed bone remodeling during the first year. After switching to 0.5 μg/day for a second year resorption bone markers like NTx and TRAP tend to rise while bone formation and TAP remain suppressed. BMD showed a tendency to decrease during the second year of the trial.

	Initial	12 months	24 months
Serum Ca	9.25 ± 0.51	9.05 ± 5.55	9.34 ± 0.40
AP (IU/L)	48.63 ± 15.37	40.80 ± 10.4**	33.30 ± 6.3***
TRAP (IU/L)	9.92 ± 2.9	7.58 ± 2.35***	8.33 ± 0.28
NTx (BCE/Creat)	128.72 ± 67.28	92.97 ± 55.78*	99.53 ± 41.5
L2-L4 grs/cm^2	0951 ± 0.09	0.95 ± 0.12	0.877 ± 0.06
Fem neck grs/cm^2	0.793 ± 0.9	0.790 ± 55.78	0.773 ± 0.05

*** = $p < 0.001$ ** = $p < 0.01$ * = $p < 0.05$ vs initial

P372MO. A COMPARATIVE STUDY BETWEEN INTERMITTENT CYCLICAL AND CONTINUOUS ALENDRONATE IN THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Aims: To compare the efficacy of intermittent cyclical and continuous alendronate in the treatment of postmenopausal osteoporosis.

Patients and Method: 30 postmenapousal women were enrolled in the study. The patients were randomized into two treatment groups. The first group was given 10 mg daily alendronate with calcium 500 mg/d and Vitamin D3 300.000 IU/M, the second group was given cyclical intermittent 10 mg daily alendronate for 2 months, followed by 2 months of drug-free period with calcium 500 mg/d and Vitamin D3 300.000 IU/M for one year. Measurements of lumbar spine and proximal femur BMD were performed at baseline and at 12th month by dual x-ray absorptiometry. Biochemical markers of bone resorption and formation, serum calcium and phosphorus, urinary calcium and serum alkaline phosphatase levels were evaluated at same time intervals. Radiographs of the thoracic and lumbar spine were taken at baseline and at 12th month.

Results: There were no statistically significant differences in the baseline mean BMD and T scores between two groups. At the end of the study, the group receiving intermittent alendronate showed statistically significant increases in T scores of the femoral neck ($p < 0.05$). In the group receiving alendronate 10 mg continuously, T scores of the lumbar spine and femoral neck significantly increased from baseline ($p < 0.05$). However, the improvement in the lumbar spine BMD was found in favour of patients receiving alendronate 10 mg continuously ($p < 0.05$). Compared to baseline, no significant difference was found in the markers of bone resorption and formation in both treatment groups ($p < 0.05$).

Conclusions: With regard to our results, 10 mg continuously administration of alendronate may be better than intermittent administration in patients with postmenopausal osteoporosis.

P373SA. BRAZILIAN EXPERIENCE WITH RALOXIFENE AND ALENDRONATE: COMPLIANCE AND PATIENTS' CLINICAL FEATURES

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Choose is a prospective observational 12 month-study designed to evaluate patient satisfaction and compliance related with raloxifene or alendronate in a natural setting. In Brazil, 32 physicians were involved in the study that included 247 postmenopausal women over 60 years old with either osteopenia or osteoporosis. Raloxifene was prescribed for 181 women and alendronate was prescribed for 95 women (10 mg/d or 70 mg weekly, 23% and 77%, respectively). The median chronological age for raloxifene group was 69.0, and 71.3 years for the alendronate group ($p = 0.011$). The time since menopause onset was 19.8 + 8.2 (median + SD) and 22.5 + 9.8 years for raloxifene and alendronate groups, respectively ($p = 0.016$). HRT was the most frequent prior treatment in the raloxifene or alendronate groups (38% and 13% of women, respectively, $p < 0.001$). DEXA result was the most frequent clinical criteria to prescribe an anti-resorptive treatment in both groups. 13% of women in the raloxifene group and 24% in the alendronate group had a previous osteoporotic fracture ($p < 0.001$) at baseline. 22% of the raloxifene patients and 20% of alendronate patients abandoned treatment after 12 months of treatment (N.S.). Patient satisfaction, evaluated by a visual analog scale, was not statistically different between groups before and after 12 months of treatment (mean = 89.1 cm for raloxifene and 79.6 for alendronate, N.S.). Thus, raloxifene was prescribed for younger postmenopausal women with shorter time since menopause than for those alendronate was prescribed. Besides, raloxifene was more commonly prescribed than alendronate after HRT, although a great number of patients with prevalent osteoporotic fractures were on alendronate. Raloxifene and alendronate treatments had the same discontinuation rate and both treatments were well tolerated by women with osteoporoses although the majority of the patients on alendronate were on weekly dose. In conclusion, patients profile for raloxifene and alendronate were different, but discontinuation rate were not different in an observational Brazilian study.

P374SU. DRUG-DRUG INTERACTIONS ARE UNLIKELY WITH IBANDRONATE

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Aims: Many patients treated with ibandronate, whether for osteoporosis or metastatic bone disease, will be receiving concomitant medications. It is therefore important to investigate the potential of ibandronate for drug-drug interactions.

Methods: Ibandronate has been the subject of extensive pharmacological and pharmacokinetic examination in both animals and human subjects. In-vitro and in-vivo preclincal studies have explored renal excretion, protein binding and effects on cytochrome P450 (CYP) activity. Pharmacokinetic studies in human volunteers and patients have provided further data on the possibility of interactions with concomitant drugs.

Results and Discussion: In rats, high doses of classical inhibitors of either anionic or cationic renal transport systems did not affect the renal clearance of ibandronate or the glomerular filtration rate. These results indicate that ibandronate is not secreted by either anionic or cationic renal transport systems and therefore would be unlikely to interact with drugs excreted by these systems. Protein binding, a factor known to influence drug-drug interactions, at the range of concentrations of ibandronate found in vivo in human serum is relatively low (86%). In-vivo studies in rats indicate that ibandronate does not induce CYP activity in the liver. In human liver microsomes in vitro, ibandronate at concentrations of up to at least 100 μM (360 μg/ml) showed no affinity for any of the main human liver CYP isoenzymes (1A2, 2A6, 2C9, 2C19, 2D6, 2D1 or 3A4). These findings suggest that ibandronate is unlikely to produce drug-drug interactions through inhibition of CYP activity. No, or only minor, clinically irrelevant pharmacokinetic changes were observed when ibandronate was taken concomitantly with hormone replacement therapy, tamoxifen, or melphalan and prednisolone. These drugs are frequently taken by postmenopausal women, women with breast cancer, and patients with multiple myeloma, respectively. A minor increase in the AUC (20%) of ibandronate in combination with ranitidine was attributable to an increase in gastric pH and was not considered clinically relevant.

Conclusions: Preclinical findings demonstrate that ibandronate has negligible effects on renal excretion, or CYP activity, and shows relatively low protein binding. These data are consistent with those from human pharmacokinetic studies indicating that ibandronate is unlikely to produce drug-drug interactions.

P375MO. INTERMITTENT INTRAVENOUS IBANDRONATE INJECTIONS: RENAL SAFETY PROFILE

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Aims: Intravenous (i.v.) administration of several bisphosphonates, including alendronate and zoledronate, may cause acute renal toxicity. Consequently, current bisphosphonates must be given as i.v. infusions. However, these are inconvenient and frequently may result in thrombotic and infectious complications. In addition, they cannot be used in primary care. I.v. dosing of bisphosphonates by injection could provide a simpler, more convenient, alternative. Ibandronate is a nitrogen-containing bisphosphonate with one of the highest potencies of all bisphosphonates. This, together with its good tolerability, allows administration as an i.v. injection in regimens with extended between-dose intervals. Various preclinical and clinical studies have investigated the effects of intermittent i.v. ibandronate injections on renal function.

Methods: In a preclinical study in rats, minimally nephrotoxic doses of ibandronate (1 mg/kg) or zoledronate (1 or 3 mg/kg) were given as an i.v. injection either intermittently once every 3 weeks for 25 weeks or as a single dose. In initial clinical studies, i.v. ibandronate was administered at a high dose of 6 mg over a decreasing infusion time (60–15 minutes) or at a dose of 3 mg over 1–2 minutes. In subsequent placebo-controlled studies involving approximately 3,500 women with postmenopausal osteoporosis, i.v. ibandronate (dose range 0.25 mg–2 mg) injections (15–30 seconds) were given once every 3 months for up to 3 years.

Results: In the preclinical study, intermittent i.v. ibandronate injections did not produce cumulative subclinical renal damage (as shown by histopathology, serum biochemistry and urinalysis). This was in marked contrast to findings with intermittent i.v. zoledronate, which showed a cumulative pattern of subclinical renal damage that could not be detected by monitoring of standard renal safety lab parameters. In the various clinical studies, no renal toxicity (as assessed by serum biochemistry, urinalysis and adverse event reporting) has been observed with ibandronate.

Conclusions: The potency and excellent tolerability of ibandronate allows dosing by i.v. injection in regimens with extended between-dose intervals. The findings of the studies discussed herein highlight the good renal safety of these regimens. I.v. injections avoid the inconvenience and complications of i.v. infusion and offer a convenient alternative to oral dosing that can be given in primary care.

P376SA. TREATMENT OF OVARIECTOMIZED RATS WITH STRONTIUM RANELATE IMPROVES BONE STRENGTH AND BONE QUALITY

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The efficacy of strontium ranelate (SR), a new compound which has shown anti-fracture activity in postmenopausal osteoporosis, was assessed on ovariectomy-induced bone loss using mechanical strength testing of the lumbar vertebra. Six-month old Sprague-Dawley rats were either ovariectomized (OVX) or received sham (SHAM) surgeries. Beginning 1 day post-ovariectomy, 3 groups of OVX rats were treated daily for 52 weeks with 125, 250, or 625 mg/kg of SR and one received vehicle. Vehicle-treated OVX and SHAM animals served as controls. After 12 months treatment, bone loss in the OVX rats was substantiated by a 12.7% lower lumbar spine BMD compared to SHAM ($P < 0.01$). Furthermore, in 3rd lumbar vertebra (LV3), OVX rats had 49.0% lower cancellous bone volume (BV/TV), a 36.3% decrease in trabecular number (Tb.N) and a 107.7% increase in trabecular spacing (Tb.Sp; $P < 0.01$ for all parameters). The changes in bone mass and architecture led to declines of 31.9%, 33.3% and 34.9% in the maximum load (load necessary to break the bone), stiffness (bone elasticity) and ultimate strength (maximum stress the bone can sustain) of the 5th lumbar vertebra (LV5; $P < 0.01$ for each parameter). SR treatment of OVX rats dose-dependently increased the mechanical properties of LV5 with maximum load, energy to failure and ultimate strength increased up to 24.7%, 74.5% and 26.4% with 625mg/kg/d ($P < 0.01$). At this dose, the values for biomechanical parameters in OVX animals were nearly equivalent to those in SHAM animals. These changes occurred without any modification of bone stiffness. Furthermore, bone histomorphometry also showed positive, dose-dependent effects of SR on LV3 with increases in BV/TV and Tb.N (39.6% and 28.0%; $P < 0.05$), and decrease in Tb.Sp (30.8%; $P < 0.01$). However, as the improvements in bone mass and architecture were intermediate between SHAM and OVX values, the magnitude of improvement in mechanical strength can also be explained by an improvement in bone quality synergistic with SR's effects on bone architecture. In conclusion, these results indicate that treatment with SR in OVX rats improves bone strength and quality and support SR efficacy and safety as an anti-osteoporotic therapy.

P377SU. CONTINUOUS COMBINATION OF 17BETA-ESTRADIOL WITH DROSPIRENONE FOR THE PREVENTION OF POSTEMENOPAUSAL BONE LOSS

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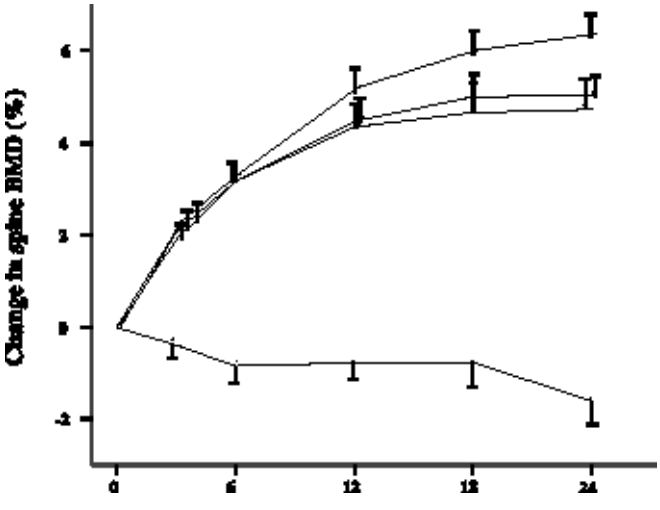
Aims: To evaluate the safety and efficacy of 17beta-estradiol continuously combined with drospirenone, a novel progesterone, for the prevention of postmenopausal osteoporosis.

Methods: This was a single-center, randomized, double-blind, placebo-controlled clinical trial. Participants were 240 healthy postmenopausal women aged 45–65 years, who received treatment with 1 mg 17beta-estradiol combined with either with 1, 2 or 3 mg drospirenone daily. Efficacy parameters were the changes in bone markers (bone formation: osteocalcin, bone resorption: serum and urinary CTx), bone mineral density (BMD) at the lumbar spine, hip, and total body.

Results: A total of 180 women (75%) completed the 2-year treatment period. Bone markers decreased significantly from baseline (serum osteocalcin 52%, serum and urinary CTx 67% and 75%, respectively). BMD at the lumbar spine, hip, and total body increased by 7, 4 and 3%, respectively, in all hormone-treated groups compared with placebo (all $p < 0.001$). Total cholesterol and LDL-C decreased by 8% and 13%, respectively (both $p < 0.001$). Triglyceride and HDL-C remained unchanged. No significant dose-related effects were found on any of the study parameters. Endometrium thickness (ET) increased by 1.2 mm only in the 1 mg drospirenone group ($p < 0.01$ versus placebo).

Conclusion: The combination of 17-beta estradiol with drospirenone provides an effective medication for the prevention of postmenopausal bone loss in both the spine and the hip. The ideal combination seems to be the 17beta-estradiol + 2 mg drospirenone.



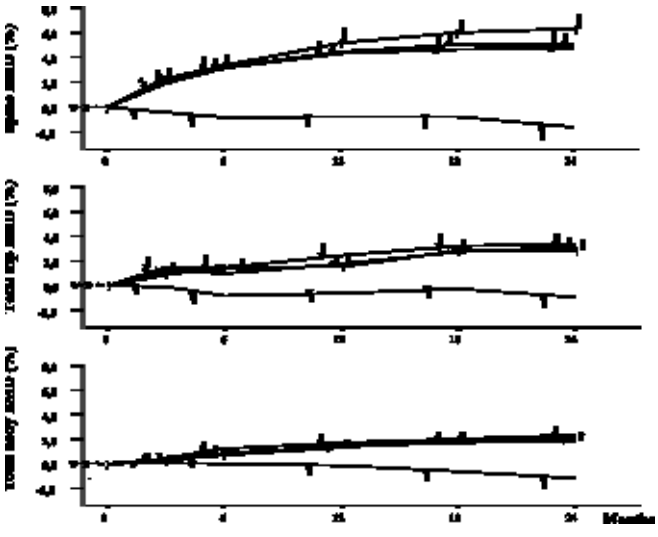


Fig. 1 Changes in spine BMD

P378MO. EFFECTS OF HORMONE REPLACEMENT THERAPY (HRT) AND SELECTIVE ESTROGEN RECEPTOR MODULATORS (SERM) ON CARTILAGE DEGRADATION IN POSTMENOPAUSAL WOMEN

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Aim: The aim of our study was to investigate the effects of HRT and SERMs on cartilage turnover assessed by urinary CTX-II, a marker of type II collagen degradation, in postmenopausal women.

Methods: The effects of HRT were assessed in a study of 531 postmenopausal women; 58–94 years (mean 68 years) from the OFELY cohort. Lateral spine and fixed flexion radiographs of the knees were scored for narrowing and osteophytes by the methods of Lane and Altman, respectively. Clinical examination of the hands osteoarthritis (OA) was performed in all women. The effects of the SERMs raloxifene and levormeloxifene on CTX-II were investigated in 234 postmenopausal women participating in two randomized placebo controlled studies.

Results In the OFELY cohort, the prevalence of lumbar spine disc degeneration, knee and clinical hand OA was respectively of 65%, 32% and 56%. Spine, knee and hand OA contributed independently of each other to increased CTX-II levels ($p = 0.0014$, 0.003 and 0.004, respectively). In women without OA, CTX-II was not associated with HRT.

After adjustment for age and BMI, OA patients on current HRT had CTX-II levels 30% ($p < 0.0001$) lower than never users, with values similar to non OA women. Past users had CTX-II levels similar to never users. After 6 months of treatment with raloxifene at doses of 30, 60 or 120 mg/d, CTX-II decreased by 35% and by 50% in women receiving levormeloxifene at doses of 1.25 to 20 mg/d ($p < 0.001$ vs placebo) with no significant dose dependent effect with raloxifene.

Urinary CTX-II levels (ng/mmol Cr)			
Spine and/or knee and/or hand OA (n = 443)			Non OA (n = 88)
HRT use			
Current (n = 116)	Never (n = 283)	Past (n = 44)	
169 ± 100*	243 ± 123†	281 ± 109†	163 ± 82

* $p < 0.0001$ vs Never and Past users; † $p < 0.0001$ vs Non OA

Conclusion: HRT and treatment with SERMs are associated with decreased type II collagen degradation in postmenopausal women, with a more pronounced effect in those with OA characterized by increased cartilage turnover. The potential structure modifying effects of HRT and SERMs in postmenopausal women with OA should be further investigated.

P379SA. OSTEOPOROSIS DELAYS FRACTURE HEALING: RESULTS FROM AN ANIMAL STUDY OF OSTEOPOROSIS

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Aim: Osteoporosis does not only cause fractures – it also influences fracture treatment. The surgical treatment is affected twofold: by reduction of the fixation strength in weak bone and by a delay in fracture healing. However, clinical and experimental studies concerning the influence of osteoporosis on fracture healing are inconsistent. The aim of this study therefore was to evaluate the healing of a long bone defect using an established sheep model of osteoporosis.

Methods: Osteoporosis was induced in seven Swiss mountain sheep using a combination protocol of ovariectomy, low calcium diet, movement restriction and highdose steroids. The induction was terminated 1 month prior to operation to avoid any influence on fracture healing. A standardized mid-shaft tibial osteotomy was performed and stabilized using a custom-made external fixator for 8 weeks. In vivo bending stiffness was measured in weekly intervals, callus area, density and osteoporosis status at 0, 4 and 8 weeks. Bending and torsional stiffness were measured ex vivo. Another 7 sheep with mid-shaft tibial osteotomy served as a control.

Results: The increase of in vivo bending stiffness was delayed by 2 weeks in osteoporotic sheep ($\alpha < 0.05$) and stiffness did not reach initial values after 8 weeks. Torsional stiffness at 8 weeks was reduced 33% and bending stiffness 21% as compared to the control group. Callus density as well as callus area were significantly reduced ($\alpha < 0.05$) in the osteoporotic group (callus density −16% at 4 weeks, −23% at 8 weeks, callus area −29% at 4 weeks, −21 % at 8 weeks). Bending stiffness correlated with callus density at 8 weeks ($r = 0.76$) and torsional stiffness with callus area ($r = 0.60$). Cancellous bone density recovery was linear at a rate of 3.4% in the osteoporotic sheep.

Conclusions: Osteoporosis seems to retard callus formation and maturation, thus influencing fracture healing. These findings should be taken into account during operative and conservative fracture treatment when healing time is critical. Adequate osteoporosis treatment should supplement surgical intervention when density is below normal.

P380SU. SAFETY AND EFFICACY OF THE USE OF ZOLEDRONIC ACID (ZA) IN CHILDREN WITH OSTEOGENESIS IMPERFECTA (OI) TYPE III AND IV: PRELIMINARY DATA

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OI is a genetic disease characterized by bone fragility and increased fracture risk. Treatment with pamidronate has shown to be safe and efficient to reduce fractures and improve the life quality in OI. Zometa™ (ZA) is the most powerful bisphosphonate available and has a faster time of infusion than pamidronate. This makes a great difference mainly for children. Its efficacy and safety in children with OI, however, has not yet been tested.

Aim: To verify the safety and efficacy of ZA during one year treatment in children with OI type III or IV.

Methods: Nine children were selected to participate in a research protocol to receive ZA at a dose of 0.4 ± 0.08 mg/kg/year in a 30 min i.v. infusion every three or four months. Five patients have finished one year of treatment and the remaining, still under treatment, have received at least one infusion. Before each infusion,

blood was collected for total and ionized calcium, alkaline phosphatase, phosphate, CTx and osteocalcin in serum, intact PTH, renal and hepatic function and hemogram. Bone mineral density (BMD) at lumbar spine and total body were measured at the baseline and at the end of the study.

Results: Out of 9 patients (7 boys, 2 girls), 5 had type IV and 4 type III. The average age was 5.1 ± 2.8 (from 1.6–9.4). The adverse events were: fever (9), nausea (5) and vomiting (2) during the 24 hours following the first infusion. Except for one patient with anemia at baseline, all had normal laboratory parameters at baseline and there were no significant changes before each infusion until the end of the study. From baseline to the end of treatment, spine BMD increased significantly (0.310 ± 0.073 to 0.462 ± 0.019 mg/cm^2, respectively, $p < 0.016$) and total body BMD almost reached significance (0.672 ± 0.126 to 0.758 ± 0.064 mg/cm^2, $p < 0.059$).

Conclusion: ZA demonstrated to be safe and efficient in increasing BMD in this group of children with OI. Due to its fast procedure, it is more convenient for children. However, a ZA effect on fracture risk still has to be proved, so it can be a new option in the treatment of OI.

P381MO. BIOMECHANICAL EFFECTS OF RECOMBINANT HUMAN GROWTH HORMONE (RHGH) ON BONES AND MUSCLES OF OVARIECTOMIZED (OX) RATS

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Doses of 150 IU/kg/d were given during 3 months to 3-month old rats, either intact of OX. At the end of the study their diaphyses were scanned by pQCT and tested in bending. The fresh gastrocnemius muscles were weighed.

OX reduced bone tissue mineralization and stiffness. A significant enhancement of bone growth in width improved significantly the diaphyseal architecture (cross-sectional moment of inertia, CSMI). This geometric improvement overcompensated the negative impact of the OX-induced impairment on bone material mineralization and stiffness, thus the diaphyseal strength was increased. The assayed dose of rhGh was little effective in intact rats. However, it prevented the OX-induced impairment in bone tissue mineralization (not stiffness) and improved additively the OX-enhanced geometric variables. These effects of OX and rhGH were correlative with additive increases in muscle mass. Simple regression analyses showed that the impact of the muscular improvement was more evident on bone architecture than it was on bone strength.

The positive OX and rhGH effects on cortical bone mass and architecture seemed to have derived from the induction of an "anabolic" shift of the bone mechanostat threshold for triggering bone modeling during growth, with a positive biomechanical impact on the diaphyses (larger CSMI and fracture load than controls). The apparent incongruence between the repercussion of the additive improvement in muscle mass induced by OX and rhGH on bone geometry (larger impact) and strength (lower impact) can be explained by the impairment in bone material stiffness induced by OX and not prevented by rhGH (perhaps because rhGH did not act on the microstructure of the mineralized tissue). Based on original arguments, these evidences support the possible ability of rhGH to improve human postmenopausal osteopenias with a relatively large impairment in cortical bone mass and/or distribution. However, the actual benefit of the positive rhGH effects on bone mass and architecture in any species would remain uncertain as long as the nature of rhGH effects on the OX-impaired bone material stiffness is unknown. In addition, these results are interesting because they defy the prevailing view that the remaining bone tissue in metabolic osteopenias is normal.

P382SA. NEW INSIGHTS ON OLPADRONATE EFFECTS ON BONE MATERIAL AND STRUCTURAL PROPERTIES RELATED TO STRENGTH.

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Doses of 45–90 mg/kg/d of OPD (IG-8801, Gador SA, Buenos Aires, carcinogenicity dose-range finding study) were orally given during 3 months to 20 male and 24 female rats 4–5-sem old (7 & 9 controls). The cortical vBMD, cross-sectional perimeters (PM), area (CSA) and moment of inertia (MI) of femur diaphyses and their structural stiffness (load/deformation ratio) and strength during the successive "elastic", reversible (pre-yield, no microcracks) and "plastic", irreversible (post-yield, microcrack accumulation) deformation periods were determined by pQCT and bending tests. The pre-yield stiffness of cortical tissue (elastic modulus, E) and a Bone Strength Index, BSI = vBMD * MI (which can predict ultimate strength but does not capture any microstructural indicator of cortical tissue) were calculated from those data.

No effects on growth were observed. Treatment improved significantly CSA and MI by increasing both endosteal and periosteal PMs, more evidently in male than female rats, with no effects on cortical vBMD and E. As a result, mild increases in diaphyseal stiffness and strength at yield (only significant in males) were observed. Diaphyseal ultimate strength was substantially enhanced (males, +38%, $p < 0.001$; females, +17%, $p < 0.01$) chiefly because of a large increase in the post-yield fraction of ultimate load (bone "toughness"; males, +300%, $p < 0.001$; females, +80%, $p < 0.05$). The BSI failed to predict ultimate load in treated animals.

The positive effects of the assayed OPD doses on pre-yield bone behavior would reflect an anabolic improvement in diaphyseal geometry induced independently of bone material's mineralization and elastic stiffness (i.e., beyond the homeostatic control of bone structure as predicted by bone mechanostat theory). The large effects on bones' post-yield behavior and ultimate strength should be assigned to changes in some "creeping" factors not determined in the study, affecting crack progress within cortical tissue ("plastic" deformation period, bone toughness) previously to fracture. Failure of BSI to predict ultimate strength suggests that the observed bone strengthening would have been determined chiefly through changes in some mineralization-unrelated, microstructural factors in this study. These results point out some novel bisphosphonate effects on bone strength and mechanism of fracture with no apparent involvement of bone mineralization.

P383SU. ADDITIONAL EFFECTS OF GROWTH HORMONE ON BONE TURNOVER AND BONE DENSITY IN PATIENTS WITH IDIOPATHIC OSTEOPOROSIS MAINTAINED ON ALENDRONATE

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Idiopathic osteoporosis (IO) is a rare condition usually related to osteoblastic dysfunction and decreased IGF-1 concentration both in serum and bone. Clinical presentation and bone turnover are heterogeneous, and both anti-resorptive as well as anabolic drugs have been used. In GH-deficient patients, treatment with recombinant human growth hormone (hGH) induces a transitory increase in bone turnover, which delays the increment in bone density.

Aim: To evaluate the additional effects of hGH on bone density and turnover in patients with IO receiving alendronate (ALN).

Patients and Methods: Eight patients, 3 men (20–42yrs) and 5 women (30–49yrs) with IO, that were on chronic alendronate 70 mg/week, also received recombinant human (hGH) 2.0 IU/day for one year. All patients were calcium and vitamin replete. Fasting morning serum and urine samples were obtained at baseline and along treatment for determination of insulin growth factor 1 (IGF1) and urinary N-telopeptide of type 1 colagen (NTx). Lumbar spine and femoral neck bone mineral density were determined by DEX, Expert-Lunar Corp.at baseline and 1 year.

Results: hGH was well tolerated. Serum IGF1 remained above baseline values, but within upper third of normal range during all treatment ($p = 0.0003$). Urinary NTx significantly increased at 45 days ($p = 0.0336$), but returned to baseline values at 1 year (13.8 ± 6.8 to 24.1 ± 11.5 and then to 14.7 ± 11.3 nMBCE/mMCr,

respectively), p = 0.02. Compared to previous year with ALN alone, hGH promoted a beneficial effect on lumbar spine bone density in 2/3 of the patients, but the effects at FN were heterogeneous.

Conclusions: ALN did not prevent the increase in bone turnover usually seen in the first six months of hGH therapy, but the association of both drugs optimized the positive response of bone density.

P384MO. TRICKERY, DECEPTION AND ECONOMIC EVALUATIONS: IS THERE MORE HARM THAN GOOD?

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Background:The use of economic evaluations, and in particular decision analytic modeling studies, has increased dramatically over the past decade. There is good reason for this increase as decision makers need information on both costs and effects in order to decide which programs, drugs or services to provide. However, it is common to see very different results and conclusions from two separate evaluations of the same disease and interventions. Reasons for these differences lie in part because of different data sources or assumptions made by the investigators. However, these differences also reflect alternatives in general approach, assumptions made, or how results are presented. Since there is a potential for investigator bias and misrepresentation that may interfere with a fair assessment of cost-effectiveness, users of these analyses should be armed with the tools to critically appraise cost-effectiveness studies.

Aims: The purpose of this presentation is to present some common methodological issues in economic appraisal that users should be aware of in order to decided how useful is the information presented and what impact these issues might have on the overall results.

Methods: Using a practical example of a cost-effectiveness model developed for postmenopausal osteoporosis in Canada, we test the importance on the results achieved of using various data sources, analysis techniques and assumptions typically made by authors of cost-effectiveness modeling studies. In particular, we explore the impact of using different data sources, omitting certain health states or adverse events and including/excluding selective comparators from the analysis.

Results: The findings from this analysis show that the results and conclusions drawn from the results are heavily influenced by the data sources used, the health states/conditions included in the analysis and the treatment comparators considered for the analysis.

Conclusions: The results from this study shed some light on why cost-effectiveness results vary so much from one study to another. Users of cost-effectiveness studies should be aware of the potential for bias and misrepresentation in these studies. In light of the findings from this study, increasing scrutiny should be devoted into who conducted the analysis, the funding source for the study and any potential conflicts of interest.

P385SA. THE SECONDARY PREVENTION OF OSTEOPOROSIS IN PATIENTS ATTENDING FRACTURE CLINIC

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Aim: Identification and management of osteoporosis and falls will prevent fractures. However, the majority of patients remain undiscovered until they present with their first fracture. Our aim was to investigate whether attendance to fracture clinic was utilized for prevention of further fractures.

Method: A retrospective study was conducted of 107 people who had attended fracture clinic during the period January 2003 to October 2003. Clinic records were checked for whether investigation and management for osteoporosis and falls was suggested.

Results: Out of 107 patients, the age ranged from 50 to 94yrs, with an average age of 68. The majority of patients were female 71 (66.4%), consultants and junior staff saw 53.3% and 46.7% of patients respectively. 22 Colles fractures were identified, 1 vertebral fracture and 8 neck of femurs, the rest were miscellaneous fractures. 14 (13.1%) of the patients had a previously documented fracture. The majority of fractures were caused by falls 77 (72.0%), however 45 of these falls were of an undetermined nature. Of these, 3 (6.7%) were referred for further investigation into the cause of the fall. In total, 2 (1.9%) patients were referred for investigation into osteoporosis. Not one patient was started on treatment, neither was it suggested to the GP or the patient. No patients bone mineral density was known. 91 (85.0%) of patients are currently not receiving any treatment for possible osteoporosis. Out of those on treatment, 3 (2.8%) were on calcium alone, 9 (8.4%) were on calcium and vitamin D, and 4 (3.8%) were on a combination of calcium, vitamin D and bisphosphonate.

Conclusion: We are currently not adequately investigating or treating people with possible osteoporosis and falls in fracture clinic. Screening of patients in fracture clinic provides an opportunity to identify those who may benefit from treatment of osteoporosis and prevention of further falls.

P386SU. BONE FORMATION ACTIVITIES BY NOVEL SYNTHETIC BONE ANABOLIC PEPTIDES

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Many therapeutic agents have been developed for the prevention of osteoporosis, but PTH 1–34 is the first anabolic agent to be approved. Although it has been met with great enthusiasm, there is still a need for other anabolic agents. Here we report the initial findings of novel synthetic peptides (AC-130 series) on bone metabolism in vitro.

Matrix proteins thought to be involved in the bone formation and/or mineralization process often contain characteristic sequence motifs. Many of these proteins contain regions of acidic residues as well as the modified amino acid, phosphoserine (Pse). Based on this concept, we synthesized a series of small peptides containing Gly, Ser, and Pse and evaluated their activities on bone metabolism in vitro.

To assess effects on bone formation, peptides were evaluated in a standard neonatal mouse calvaia assay. After 7 days in culture, several analogs demonstrated an increase in osteoblast number (up to ~60.7% compared to vehicle) and a corresponding increase in bone thickness (up to ~56.9 % compared to vehicle). A more detailed dose response study for the 93002-G analogue was performed using the same assay. In this study, a maximal effect on osteoblast activity and bone formation occurred at doses between 10–100 ng/ml. Higher doses (up to 100 ug/ml) were tested and were found to be less effective. Furthermore, when compared to the peptide backbone containing no Pse groups, the peptide containing Pse was more potent by roughly one order of magnitude.

Various analogs were also evaluated for effects on osteoclast formation and bone resorption in vitro. None of the analogs tested showed any effect on either 1,25 vitamin D induced osteoclast formation or on PTHrP induced bone resorption.

In summary, we have identified a series of unique peptides that preferentially stimulate bone formation in vitro. We also conclude that the presence of Pse groups is important in the biological activity of these compounds. Preliminary data indicate that such compounds may also be orally available due to their small size and lack of any known proteolytic sites. Additional studies are underway to assess the activities of these peptides in vivo.

P387MO. ORAL MONTHLY IBANDRONATE IS WELL TOLERATED AND EFFICACIOUS IN POSTMENOPAUSAL WOMEN: RESULTS FROM THE MONTHLY ORAL PILOT STUDY (MOPS)

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Aims: Women receiving bisphosphonate therapy for postmenopausal osteoporosis prefer, and are therefore more likely to comply with, less frequent dosing schedules. A once-monthly regimen could enhance therapeutic outcome by optimally combining convenience and effectiveness. Ibandronate, a potent, nitrogen-containing bisphosphonate with proven antifracture efficacy when given with extended between-dose intervals, is in clinical development as a once-monthly oral formulation. The Monthly Oral Pilot Study (MOPS) is a randomized, double-blind, dose-finding, phase I study exploring the tolerability, pharmacokinetics and pharmacodynamics of this formulation in postmenopausal women.

Methods: A total of 144 postmenopausal women (aged 55–80 years; time since menopause ≥3 years) were randomized to 3 months' treatment with one of four oral monthly regimens: placebo, 50 mg, 100 mg, or 150 mg ibandronate. Calcium and vitamin D supplements were withheld to ensure detection of all treatment-related effects. To isolate the effects of dose from those of first-time treatment, the 50 mg arm was divided after the first treatment cycle, with women receiving either 50 mg or 100 mg ibandronate for the last two cycles.

Results: The safety profile of once-monthly ibandronate was similar to placebo. Adverse events (AEs) were typical of the bisphosphonate class and mostly mild to moderate in intensity. There were no reports of serious AEs or unexpected safety issues. Systemic exposure (AUC and Cmax) to ibandronate increased in a dose-related manner. Dose-dependent suppression of biochemical markers of bone resorption was also observed: serum CTX and urinary CTX/creatinine levels changed by −12.3% and −5.5%, respectively, in the placebo group and −56.7% and −54.1%, respectively, in the 150 mg group, relative to baseline after 3 months (i.e. 30 days after final dose).

Conclusions: At the studied doses, once-monthly oral ibandronate was well tolerated and highly effective in suppressing bone turnover. These findings demonstrate the significant potential of oral monthly ibandronate in the management of postmenopausal bone loss. Further evaluation of the efficacy and tolerability of once-monthly ibandronate in postmenopausal women with osteoporosis is under-way in a large, randomised, controlled trial (Monthly Oral iBandronate In LadiEs: MOBILE).

P388SA. THE RIGOROUS FRACTURE DIAGNOSIS METHODOLOGY USED IN THE PIVOTAL PHASE III STUDY SUPPORTS THE ANTIFRACTURE EFFICACY OF ORAL DAILY AND INTERMITTENT IBANDRONATE

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Aims: The BONE study (oral iBandronate Osteoporosis vertebral fracture trial in North America and Europe) reported a significant reduction in the risk of new vertebral fractures with oral daily and intermittent ibandronate (62% and 50%, respectively). The study was performed in 73 centres in Europe and North America. Standardization of X-ray technique and reproducibility of fracture diagnosis are important to the robustness of results of clinical trials in osteoporosis, especially when numerous centres are involved. A process of cross-validating fracture diagnoses was developed for BONE to ensure consistency of diagnosis between centres and enhance the high-quality protocol.

Methods: X-rays were read and diagnoses made at single centres in Europe and North America. Prevalent and new incident fractures were established by morphometric criteria and required qualitative confirmation, including differential diagnosis of deformation, by an experienced radiologist. To improve and assess homogeneity of diagnoses between centres, the European centre reviewed all North American films (qualitative assessment only), blind to initial North American diagnoses. The North American centre reassessed films in light of the European readings before submitting final diagnoses.

Results: For incident vertebral fractures, agreement between diagnoses by morphometric and qualitative methods was excellent: there were only two discrepancies in final diagnosis of 995 film sets reviewed by both centres (kappa coefficient: 0.97; 95% CI, 0.91, 1.0). Agreement between the European and North American centres on final morphometric diagnoses was also excellent: there were discrepancies in four patients (kappa coefficient: 0.94; 95% CI, 0.88, 1.0), resulting in a potential difference of two fractures in the trial results. Prevalent fractures were diagnosed from single baseline X-rays, rather than the series available for new fractures, making diagnosis more complex. Because of differences in deformation aetiology (e.g. degenerative, traumatic, etc), 21% (359/1715) of prevalent fractures identified by morphometric analysis did not meet qualitative criteria for osteoporotic fracture (kappa coefficient: 0.87; 95% CI 0.85, 0.88). Nevertheless, agreement between centres on final diagnoses of prevalent osteoporotic fractures was achieved in all but six patients (8%).

Conclusion: The excellent consistency of fracture diagnosis between centres offers robust support for the methodology used in BONE and associated outcomes.

P389SU. UNDERESTIMATED MUSCULOSKELETAL ADVERSE EFFECTS OF ORAL TREATMENT WITH ONCE WEEKLY ALENDRONATE 70 MG AND RISEDRONATE 35 MG: INCLUDING POSSIBILITIES FOR THEIR PREVENTION

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Aims: Intravenous applications of nitrogen containing bisphosphonates are associated with acute phase reactions including generalized myalgia, arthralgia and bone pain. The aim of the study was to examine if similar effects might occur also in oral treatment regimens.

Methods: Consecutive patients with oral alendronate (ALN) or risedronate (RSN), given daily (d) or once weekly (ow), were examined and followed up. Any musculoskeletal adverse effects occurring during the first month of treatment were registered and analyzed according to causality, severity and impact on further drug intake.

Results: 612 patients (mean age 68.2 +/−9.7 yrs; 527 females, 85 males) with ALN or RSN treatment were analyzed. Treatment was initialized with: ALN 10d (n = 273), ALN 70ow (n = 134), RSN 5d (n = 177), and RSN 35ow (n = 28) respectively. Severe musculoskeletal adverse effects (leading to treatment discontinuation) were reported in 34 cases: 27 in ALN 70ow (27/134 = 20.1%) and 7 in RSN 35ow (7/28 = 25.0%) with no statistically significant difference between these groups. No cases were reported for d treatment regimens. None of 302 patients initially treated with a bisphosphonate reported any musculoskeletal adverse effect when later switching to ow administration (218 pat. to ALN 70ow and 84 pat. to RSN 35ow). 27/34 patients (80%) with significant musculoskeletal adverse events after newly given ow bisphosphonate agreed to a reexposure starting with d dosage for 14 days and switching then back to the ow regimen. No reappearance of musculoskeletal adverse events was reported in those cases.

Conclusions: Musculoskeletal adverse effects of oral nitrogen containing bisphosphonates given ow are an underestimated fact in clinical practice. They seem to occur just if first bisphosphonate treatment is started with the ow regimen (higher single dose). This can be avoided by initialising the treatment with the d dose for about 14 days before switching to the generally more convenient ow regimen.

P390MO. OUTCOME IN PATIENTS WITH OSTEOPOROTIC FEMORAL NECK FRACTURES DEPENDS ON THE TREATMENT USED

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Hip fractures among the elderly are related to a high degree of mortality and disability. The views of the treatment methods of elderly patients with femoral neck fractures are opposing. In the

4-year period the General and Teaching Hospital Celje admitted 164 patients older than 65 years for treatment due to a dislocated femoral neck fracture (Garden 3,4). The patients were divided into two groups according to the fracture management approach. 52 patients were treated for dislocated femoral neck fracture through internal fixation with three screws (Group A). 81 patients were treated for dislocated femoral neck fracture through cemented bipolar prosthesis (Group B). The one-year survivability was examined and compared between the two groups. A multivariant analysis was used to examine the impact on the final outcome of the treatment and one- year survivability.

A good treatment outcome was reported in 44% elderly managed with osteosynthesis and in 66% patients treated with prosthesis. A cumulative one-year survivability rate was 64.6% in patients treated with osteosynthesis while in patients treated with prosthesis the rate was 75.7%. The pre-fracture medical condition (3.88 odds ratio), treatment approach (0.33 odds ratio) and clinical rehabilitation efficiency (0.07 odds ratio) had a statistically significant impact on the functional one-year post-fracture result. The age of the patients (0.30 odds ratio) and hospital rehabilitation efficiency (2.89 odds ratio) had a significant impact on the post-fracture survivability.

The authors claim that a primary cemented bipolar prosthesis is the treatment choice for elderly with dislocated femoral neck fracture.

P391SA. LONGER TERM EFFECTIVENESS OUTCOMES OF NONCOMPLIANCE AND NONPERSISTENCE WITH DAILY REGIMEN BISPHOSPHONATE THERAPY IN PATIENTS WITH OSTEOPOROSIS TREATED IN TERTIARY SPECIALIST CARE

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Background: Bisphosphonate (BP) therapies for osteoporosis (OP) must be taken longer-term to provide full benefits. Patient non-compliance and non-persistence with chronic therapies are costly.

Methods: We studied patients with OP treated with daily BP regimens in routine clinical care by tertiary care specialists collaborating in a systematic prospective observational clinical data collection program. We report follow-up rates in the program and inconsistent use of BP therapy, either early discontinuation of BP or self-report of taking BP less than 80% of the time over the follow-up interval. We compared longer-term clinical outcomes between patient groups who reported inconsistent and consistent use of BP therapy: change in BMD (analysis of covariance) and incidence of fracture (Poisson regression).

Results: From 1990 to 2002, 4,405 patients with OP (t-score < -2.5) (mean age 64 (SD = 12), 86% female) were treated with BP. Cumulative follow-up rates in the program after 1, 2, and 3 years were 78%, 63% and 52%. Complete data for analysis of longer-term clinical outcomes were available for 1,041 patients (23.6%). This subset excludes patients who did not return for follow-up and is considered significantly enriched for patients who adhere to therapeutic advice rather than representative of the average patient population. In consistent BP users (n = 920, 88%), lumbar spine BMD increased significantly from baseline after 1, 2 and 3 years: 3.3% (95% CI: 0.6%, 6.1%), 4.9% (2.2%, 7.7%) and 6.5% (3.7%, 9.3%). In inconsistent BP users (n = 121, 12%), no significant improvement occurred until a modest gain of 3.2% (0.03%, 6.3%) in Year 3, with a significant difference trend in the BMD increase ($p = 0.002$). The differences in BMD increase between consistent and inconsistent users after 1, 2 and 3 years were significant at 1.4% (0.5%, 2.3%), 2.4% (1.2%, 3.6%) and 3.3% (1.5%, 5.2%). There was a trend of a 27% greater 10-year fracture risk in inconsistent compared to consistent BP users (adjusted relative risk 1.27 (0.9, 1.8), $p = 0.18$).

Conclusions: This study demonstrates that patients who use BP inconsistently do not attain the proven clinical benefits of BP therapy.

P392SU. STRONTIUM IS A FULL AGONIST OF THE EXTRACELLULAR CALCIUM-SENSING RECEPTOR (CAR) TRANSFECTED IN HUMAN EMBRYONIC KIDNEY CELLS

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Strontium ranelate has been shown to be effective in reducing fracture risk in women with postmenopausal osteoporosis but its cellular mechanism of action has not yet been fully elucidated. Extracellular strontium ($Sr2+o$), similarly to extracellular calcium ($Ca2+o$), could exert its actions, in part, via the extracellular calcium-sensing receptor (CaR), as the atomic and ionic structures of strontium and calcium are close. The goal of this study was to evaluate whether $Sr2+o$ directly activates the CaR by assessing changes in intracellular transduction pathways and biological responses namely, elevations in the cytosolic calcium concentration ($Ca2+i$), accumulation of inositol phosphates (IPs), activation of mitogen-activated protein kinase (MAPK) and stimulation of the activity of a non-selective cation channel (NCC). These pathways were tested in CaR-transfected or non-transfected (control) HEK293 cells. Raising the level of $Ca2+o$ (0.1–10 mM) produced a dose-dependent activation of the CaR in CaR-transfected HEK293 cells as assessed by increases in $Ca2+i$, enhanced accumulation of IPs, activation of MAPK, and increased activity of the NCC. $Sr2+o$ (0.1–10 mM) also dose-dependently activates the CaR in CaR-transfected HEK293 cells as assessed by the same four parameters. $Sr2+o$ efficacy is similar to that of $Ca2+o$ for activation of the NCC and MAPK, and about 30% lower for stimulating increases in $Ca2+i$ and accumulation of IPs. Neither $Sr2+o$ nor $Ca2+o$ had any effect on these four parameters in non-transfected cells. The results obtained in this study show that $Sr2+o$ is a full agonist of the CaR. Thus $Sr2+o$ could exert some of its actions in vivo via the CaR receptor.

P393MO. THE COMPARISON OF EFFECTIVENESS OF HORMONE REPLACEMENT THERAPY (HRT) IN PREVENTION OF GLUCOCORTICOID-INDUCED AND POSTMENOPAUSAL OSTEOPOROSIS

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The aim of this study was to investigate effectiveness and tolerability of HRT in perimenopausal women receiving oral glucocorticoids (GC).

Methods: HRT (estradiol 2 mg, dydrogesterone 10 mg) was cyclically prescribed in two study groups for 6 months. Group 1 consisted of 19 perimenopausal women constantly treated with oral GC (16.0 ± 9.5 mg/day) for at least 1 year (age 51.3 ± 4.5 yrs), group 2 comprised 17 perimenopausal women never received GC (age 51.9 ± 2.8 yrs). BMD and biochemical data were measured at baseline and after 6 months.

Climacteric symptoms were assessed at baseline and in 1, 3 and 6 months.

Results: We found a significant decrease in serum calcium from 2.6 ± 0.13 to 2.4 ± 0.2 mmol/l ($p = 0.04$) in group 1 and from

2.5 ± 0.11 to 2.3 ± 0.07 mmol/l ($p = 0.02$) in group 2 and in serum alkaline phosphatase from 195 ± 49 to 145 ± 47 IU/l ($p = 0.001$) in group 1 and from 168 ± 22 to 135 ± 45 IU/l ($p = 0.03$) in group 2. There was an increase in spine BMD ($+3.0\%$, $p = 0.0004$ and $+1.8\%$, $p = 0.04$ accordingly) and in Ward's triangle BMD ($+4.5\%$, $p = 0.0001$ and $+3.9\%$, $p = 0.03$ accordingly). Climacteric symptoms significantly improved in both groups in the first month and speed of regression was not dependent on daily GC dose but on symptom severity. There was a decrease in serum low-density lipoproteins cholesterol from 2.8 ± 1.0 to 2.6 ± 1.1 mmol/l ($p = 0.02$) and an increase in serum high density lipoproteins cholesterol from 1.9 ± 0.81 to 2.3 ± 0.56 mmol/l ($p = 0.005$) in group 1, and there was no significant change in blood lipids in group 2. Tolerability of HRT was satisfactory in both groups.

Conclusions: These results demonstrated an equal efficacy of HRT in preventing of postmenopausal and glucocorticoid-induced osteoporosis and in treating of climacteric symptoms in perimenopausal women which were treated or not treated with oral GC. Atheroprotective effect of HRT was seen only in women received oral GC.

P394SA. PROSPECTIVE CONTROLLED STUDY OF TREATMENT OF PAINFUL OSTEOPOROTIC VERTEBRAL FRACTURES BY KYPHOPLASTY

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Evidence based treatment with calcium, vitamin D3, bisphopshonates, raloxifene and parathyroid hormone does not solve the clinically severe complications of osteoporosis: pain and impaired mobility of patients with vertebral fractures. This study evaluates pain, mobility, number of new vertebral fractures and healthcare utilisation by kyphoplastic stabilization and augmentation of vertebral fractures. 60 patients with primary osteoporosis and painful vertebral fractures were included in this cohort study. 40 patients were treated with kyphoplasty while 20 served as controls. The groups were analysed prior to treatment and 3 and 6 months later. Outcomes assessed were pain, mobility, radiomorphometric changes, new vertebral fractures and healthcare contacts after 6 months follow up. All patients received medical treatment with 1g calcium, 1000 IE vitamin D3, standard dose of oral bisphosphonate, required pain medication and physical therapy. After 6 months comparing the kyphoplasty group to the controls we observed significant improvements in the radiomorphological changes, in pain and mobility scores and a decrease in the number of healthcare contacts. In additon there were fewer new vertebral fractures after kyphoplasty compared to the controls. In conclusion, kyphoplasty appears to be a valuable addendum to classical pharmacological treatment of patients with painful osteoporotic vertebral fractures.

P395SU. BISPHOSPHONATE THERAPY IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN ON LONG-TERM HORMONE REPLACEMENT THERAPY

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Hormone replacement therapy (HRT) is a well recognized preventive therapy in osteoporotic women. However, in women in whom HRT is unable to restore normal bone mineral density (BMD) values, an adjunctive therapy must be considered.

Here we report the results of a randomized controlled study on women on HRT for ge 3 years with subnormal spine BMD (T score at least le −2.5 below peak of bone mass).

Thirty-six patients were randomized to receive for two years either 50 mg intravenous (IV) neridronate bimonthly and 500 mg calcium plus 400 U vitamin D supplements daily (n. 18) or calcium vitamin D supplements alone (control group, n. 18). Treatment was continued over 2 years with an additional 2 years follow-up of calcium-vitamin D supplements alone in both groups. All patients continued HRT.

Neridronate was well tolerated with the appearance of typical clinical signs of an acute phase reaction in 5 of the patients and only after the first infusion.

In the control group no significant changes in BMD or bone markers were observed over the four years of observation. In the neridronate group BMD rose progressively at the spine up to $4.2\% \pm 4.3\%$ (SD) and at the femoral neck up to $4.7\% \pm 5.4\%$ (SD) at the end of the second year. In the succeeding 2 year follow-up these gains were fully maintained at both skeletal sites. Serum bone alkaline phosphatase (bone AP) and serum type I collagen C-telopeptide (sCTX) significantly decreased within 2 months in the neridronate group by 16% and 14% respectively. Both bone markers returned almost to baseline values 2 years after treatment discontinuation. No significant changes were observed in the control group.

This study shows that in patients on long-term HRT the administration of bisphosphonate may be associated with additional clinically relevant increases in BMD.

P396MO. PATIENT'S SATISFACTION ASSOCIATED WITH RALOXIFENE OR ALENDRONATE DURING A BRAZILIAN OBSERVATIONAL STUDY

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Choose, a Brazilian prospective observational 12 month-study, was designed to evaluate patient satisfaction and compliance related with raloxifene or alendronate. In Brazil, 32 physicians were involved in the study that included 247 postmenopausal women over 60 years old with either osteopenia or osteoporosis. Raloxifene was prescribed for 181 women and alendronate (10 mg/d or 70 mg weekly, 23% and 77%, respectively) was prescribed for 95 women. The median chronological age for raloxifene group was 69.0, and 71.3 years for the alendronate group ($p = 0.011$). Patient satisfaction, evaluated by a visual analog scale, was not statistically different between groups before and after 12 months of treatment (mean = 89.1 cm for raloxifene and 79.6 for alendronate, N.S.). Treatment satisfaction was also evaluated by a 10-item questionnaire at basal and after 6 and 12 months of therapy. Raloxifene was felt to be swallowed easier ($p = 0.008$), to be taken easier ($p = 0.000$), and was not associated with specific time to be taken ($p = 0.000$). EQ5D questionnaire was also completed at basal, after 6 and 12 months of treatment by patients of both groups. That questionnaire evaluated mobility, self-care ability, ability to usual activities, presence of pain or discomfort, and presence of anxiety or depression. There was no statistically significant difference between groups in evaluated by EQ5D questionnaire. In conclusion, patient satisfaction assessed by a 10-item questionnaire was greater with raloxifene than with alendronate after 12 months of treatment as evaluated by a Brazilian observation study. There were no significant differences in patient satisfaction assessed by visual analog scale nor by EQ5D questionnaire.

P397SA. ORAL IBANDRONATE PROVIDES SIGNIFICANT ANTIFRACTURE EFFICACY IN WOMEN WITH LOW BONE MASS

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Aim: The BONE (oral iBandronate Osteoporosis vertebral fracture trial in North America and Europe) study demonstrated the efficacy and safety of oral ibandronate when administered daily or with a between-dose interval of >2 months in postmenopausal women (aged 55–80 years; TSM ≥5 years) with osteoporosis (1–4 prevalent vertebral fractures, BMD T-score ≤−2.0 in ≥1 vertebra). After 3 years, oral daily and intermittent ibandronate reduced the risk of new vertebral fractures by 62% (95% CI: 41, 75; p = 0.0001) and 50% (95% CI: 26, 66; p = 0.0006), respectively. A prospective analysis examined the consistency of the ibandronate effect in osteoporotic women with low bone mass as defined by the World Health Organization (WHO): spinal BMD T-score < −2.5.

Methods: A total of 2,946 women were randomised to placebo, oral daily (2.5mg) or intermittent (20mg every other day for 12 doses every 3 months) ibandronate. All participants received daily calcium (500mg) and vitamin D (400IU). A predefined analysis investigated the effect of ibandronate in women with lumbar spine BMD T-score < −2.5.

Results: Of the patients with a BMD T-score < −2.5, 5% and 7% in the daily (n = 575) and intermittent ibandronate arms (n = 558), respectively, sustained new vertebral fractures relative to 13% receiving placebo (n = 587), after 3 years. This translates to relative-risk reductions of 59% (95% CI: 34, 74; p = 0.0002) and 43% (95% CI: 13, 63; p = 0.0092), respectively. These findings were consistent with the overall study results (Fig. 1). Oral daily and intermittent ibandronate also produced significant increases in spinal and hip BMD, regardless of baseline BMD T-scores.

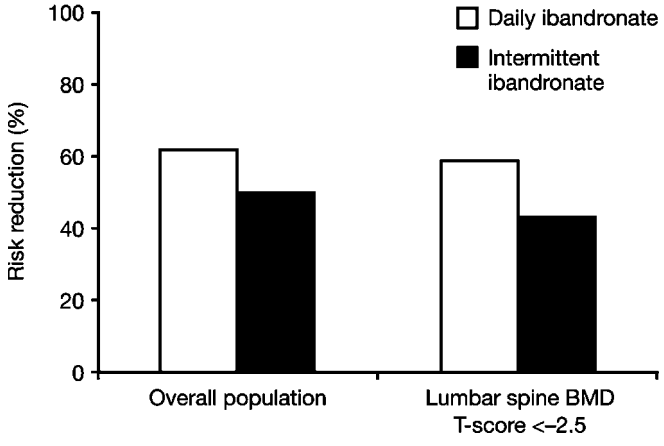

Fig. 1 Reduction invertebral fracture risk with oral ibandronate in the overall population and in women with a lumbar spine BMD T-score < −2.5

Conclusions: Consistent with the overall study population, oral daily and intermittent ibandronate produced robust anti-fracture efficacy in patients with a baseline BMD T-score of <−2.5 (WHO definition of osteoporosis). These findings indicate that ibandronate will provide a feasible alternative to current bisphosphonates in a wide spectrum of osteoporosis patients.

P398SU. A SINGLE DOSE OF ZOLEDRONIC ACID PREVENTS THE BONE LOSS INDUCED BY CALCIUM DEPRIVATION IN THE C57BL MOUSE

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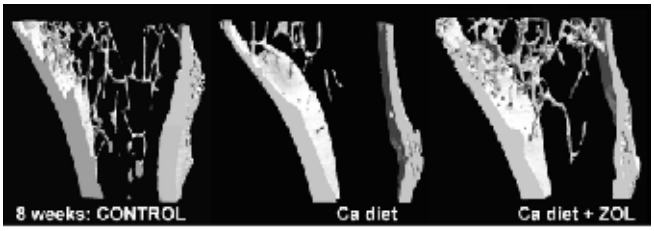
Aims: In adult humans, a low calcium diet induces secondary hyperparathyroidism that is responsible for high bone turnover and osteoporosis. In animals, a low calcium diet induces: a significant increase in bone remodeling markers, an increase in osteoclast number, and a reduction in the bone mineral density. Histomorphometric studies have confirmed that both trabecular and cortical bone are altered in animals fed a low calcium diet. Recently, a single annual zoledronic acid (ZOL) infusion was reported to be as efficient as daily oral dose of bisphosphonate in the treatment of osteoporotic patients. We have evaluated the potential preventive effects of a single dose of ZOL on the rapid deleterious consequences of low dietary calcium in a murine model. ZOL dosage was calculated to mimic the annual dose used in humans.



Bone volume	Week 0	Week 2	Week 4	Week 8
Controls	7.8±1.3	7.5±1.3	7.9±1.4	8.8 ±1.0
Ca diet		6.3±1.5	4.8±0.8	4.5 ±1.0
Ca diet + ZOL		9.6±3.9	10.9±1.7	10.9 ±1.3

Methods: 10 groups of nine C57BL mice (6–10 weeks old) were given laboratory food (either standard or calcium deprived), and water ad libitum (either tap or distilled). ZOL+ animals received at Day 0, a single injection of ZOL in the tail vein (120 μg/kg, sc) and were fed with a low calcium diet; animals used as control or fed with a low calcium diet received a single saline injection by the same route. Animals were euthanasied at 0, 2, 4 and 8 weeks and the effect of calcium deficiency with/without ZOL was quantified by x-ray microcomputed tomography of the tibia metaphysis.

Results and conclusion: Calcium diet induced a rapid trabecular bone loss with reduced Tb.N and increase in Tb.Sp. ZOL+ animals had an increased bone volume and preserved Tb.N. The effect of a single ZOL injection was evidenced on the modeling and remodeling areas and was maintained during all the duration of the study.

P399SU. NASAL CALCITONIN AND ALENDRONATE THERAPY HAVE DIFFERENT EFFECTS ON MARKERS OF BONE METABOLISM IN ELDERLY PATIENTS

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Bone metabolism can be evaluated through the use of markers of bone resorption and bone formation. These measures may help to evaluate patients at risk of osteoporotic fracture and may be useful in monitoring some osteoporosis therapies. The large day-to-day variability in results often limits their clinical usefulness for individual patient care. Although markers response to alendronate and calcitonin therapy has been reported in younger women, there are fewer data reported in the elderly.

We investigated 20 elderly women (average 77.3 + 5.5 years, 66 to 87 years) with spine, total hip or femoral neck T-score < −2.2 randomly assigned to therapy with either nasal spray calcitonin 200 IU daily (n = 10) or alendronate 10 mg daily (n = 10) in a single blind trial. Bone markers (urine NTx/creatinine and serum BSAP) were determined at baseline, 3 months, 6 months, and 9 months from fasting morning specimens. Mean baseline NTx was elevated at 60.9 mmol/mmol creatinine (range 5–65, premenopausal mean = 35 mmol/mmol creatinine) and BSAP was 20.9 + 5.6 mmol/l. At no time was there significant change in either NTx or BSAP in women

on CT therapy. ALN-treated patients showed suppression of NTx by 66% + 9 ($p = 0.01$) at the 3-month time-point with continued suppression at 6 months (60% + 20 ($p = 0.02$)) and 9 months (61% + 28; $p = 0.01$). ALN suppressed BSAP by 19% + 14 ($p = .09$), 20% + 18 ($p = .03$), and 16% + 30 ($p = .09$) at 3, 6, and 9 months respectively. Significant differences were seen between the marker response on CT and ALN at all time-points for NTx and at all but the 9 month time-point for BSAP. We have shown that bone markers continue elevated in women long after menopause and that the response of bone markers to antiresorbtive therapy in elderly women is similar to that seen in younger women. Bone markers, particularly resorbtion markers, may be useful to follow patients on ALN therapy but would be of no use in following CT therapy.

P400SA. CONTRALATERAL BMD MEASUREMENTS PREDICT BONE QUALITY OF THE HUMERAL HEAD BETTER THAN IPSILATERAL DISTAL MEASUREMENTS OF THE SAME BONE

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Aim: Bone mineral density (BMD) is not only an important variable to estimate fracture risk but may also be essential for decisions with respect to optimal fracture treatment. Bone densitometry is best performed site-specific on the same bone. However, in case of a sustained fracture, BMD measurement at a fracture site is subjected to inaccuracies. Promising alternatives for estimation of bone quality are measurements at the same contralateral or at a different ipsilateral location. Aim of this study was to evaluate which of these locations should be used in order to estimate bone quality at a fracture site of the proximal humerus.

Methods: 41 pairs of fresh frozen human cadaver humeri (age 75.5 ± 13.6 years) were used. For every bone, cancellous BMD values were obtained by peripheral Quantitative Computed Tomography (pQCT) (Densiscan 1000, Scanco Medical, CH) at the proximal, metaphyseal and at the distal, metaphyseal area. Correlations between BMD values of the ipsi- and contralateral sides were computed.

Results: Mean cancellous BMD of the proximal humerus was significantly lower (by 53%, $p < 0.001$) than that of the distal humerus. Correlations between intra-individual distal and proximal BMD were moderate for both left ($R^2 = 0.37$, $p < 0.01$) and right humeri ($R^2 = 0.40$, $p < 0.01$) (Fig. 1). BMD comparison between left and right humeri revealed high correlations for the distal ($R^2 = 0.90$, $p < 0.01$) and the proximal location ($R^2 = 0.74$, $p < 0.01$).

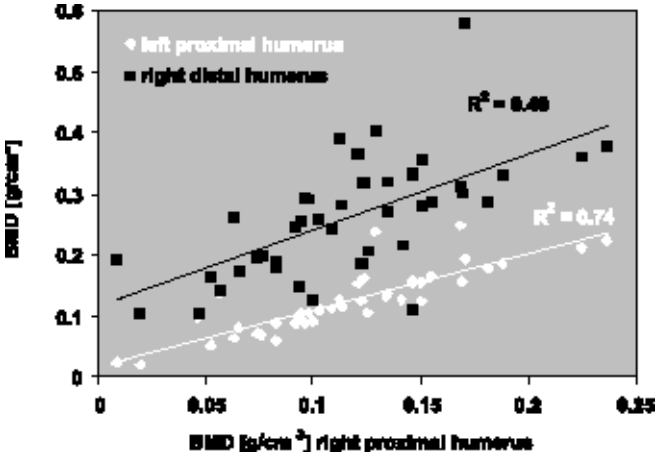

Fig. 1 Correlation between BMD values of the ipsi- and contralateral sides of the right proximal humerus

Conclusions: High correlations between contralateral BMD values may be the result of similar biomechanical loading conditions. Although a relationship between proximal and distal bone quality of the same bone was found, the coefficient of determination was only moderate. Thus, if bone quality at the humeral head has to be considered for the choice of an appropriate fracture treatment, bone quality at the fracture site is better predicted by BMD measurement at the contralateral rather than the ipsilateral distal side.

P401SU. DIFFERENTIAL EXPRESSION IN BONE OF RATS: MODEL FOR OSTEOPOROSIS AFTER USING A CHINESE HERB RECIPE

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Aim: Chinese herb recipe Jian Gu Chong Ji is proved to have a positive effect on osteoporosis by previous clinical and laboratory research. To explore the possible target of this recipe, we examined the differentially expressed genes after Jian Gu Chong Ji was applied.

Method: 63 female SD rats were randomly distributed into four groups: three are ovariectomized and fed with Jian Gu Chong Ji, estrogen or water respectively and the fourth is sham ovariectomized and fed with water. After 14 weeks feeding, bone mineral density (BMD) of the femur, lumbar spine and total body was measured by DXA. Total RNA from the femur was extracted and samples of each group were pooled to be applied in differential display RT-PCR. The differentially expressed fragments were cloned and sequenced. Semiquantitative RT-PCR was used to confirmed the results.

Result: The femur and lumbar spine BMD of Jian Gu Chong Ji group was higher than that of the ovariectomized group fed with water ($P = 0.002$, 0.001, respectively). We found out 10 differentially expressed gene fragments. After cloning, sequencing and BLAST searching, nine of them matched with highly homologous sequences in Genbank. Among them two were known proteins: hyaluronan-mediated motility receptor (RHAMM) and ATPase, Na + /K + transporting beta 3 polypeptide (ATP1b3). Semiquantitative RT-PCR showed that RHAMM was downregulated by Jian Gu Chong Ji while ATP1b3 was upregulated.

Conclusion: The effect on osteoporosis by Jian Gu Chong Ji might be partly contributed to the regulation of RHAMM and ATP1b3.

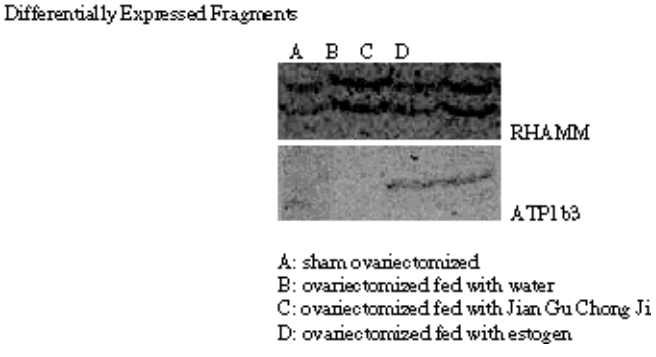

Fig. 1 Differentially Expressed Fragments

P402MO. MODELING THE COST-EFFECTIVENESS OF OSTEOPOROSIS TREATMENTS THE IMPACT OF PATIENT COMPLIANCE

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Aims: Economic evaluations based on modeling are routinely used to compare alternative osteoporosis treatment strategies to support decision-makers in decisions on drug therapies. A major concern in osteoporosis treatment is that therapy benefits may be

lower in due to non-compliance. However, economic consequences of non-compliance are seldom included in economic modeling. The objective with this study was to build a computer simulation model explicitly including the impact of patient compliance with osteoporosis treatments, and estimate the potential cost-effectiveness of different drug alternatives that differ in compliance compared to no treatment applied to a US setting.

Methods: An individual state transition model was built to reflect different compliance patterns during drug intervention. The model takes a life-time perspective: all female patients are followed from treatment start to age of 100 years or death taking into account yearly changing risks of hip, vertebral or wrist fractures, or to remain in a certain health status without any fracture or to die. Women (T-score = −2.5 and a previous vertebral fracture) start treatment with 70 years of age. The model considers effects of morbidity and mortality during the first year after fracture as well as long-term effects of fractures beyond that first year. During the intervention period which is modeled to be 5 years long, yearly changing probabilities of discontinuation of the comparative drug treatment is simulated. The model was populated with US data. Fracture risk reductions as well as yearly drug costs are assumed to be identical. The cost-effectiveness was estimated for different assumptions about the rates of compliance with osteoporosis treatments. Discount rate for costs and effects is 3%.

Results: A therapy offering full compliance and a therapy not offering full compliance was both found to be cost-effective compared to no treatment. When comparing the therapy alternatives the treatment offering full compliance was associated with higher effects (QALYs) and lower average lifetime fracture costs.

Conclusions: The results indicate that an osteoporosis drug which guarantees a full year patient compliance might have potential gains with regard to cost-effectiveness and potential decrease of osteoporosis-related fracture risk.

P403SA. THE COST-EFFECTIVENESS OF BISPHOSPHONATES, RALOXIFENE AND HORMONE REPLACEMENT THERAPY IN WOMEN WITH ESTABLISHED OSTEOPOROSIS AND REPLETE OF CALCIUM AND VITAMIN D

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Aims: This paper evaluates, within a UK setting, the cost-effectiveness of bisphosphonates, raloxifene, and HRT in women with established osteoporosis and replete of calcium and vitamin D.

Methods: A mathematical model, constructed to simulate the experience of hypothetical patients, was populated by evidence from a systematic review of randomised controlled trials of clinical efficacy, and reviews of utilities, costs, and epidemiological data. Adverse events included were hip, vertebral, wrist and proximal humerus fractures, and breast cancer and coronary heart disease (CHD). Analyses were conducted for women aged 50, 60, 70 and 80 years at the threshold of osteoporosis (T-score = −2.5SD) with a prior fracture and for women with double this fracture risk, due to a lower T-Score or other risk factors.

Results: The main outcome measure for each intervention was the cost per quality adjusted life year (QALY) gained compared with no treatment. In patients at greatest risk of osteoporotic fracture, alendronate and risedronate had superior cost-effectiveness results. In younger women with a T-Score of −2.5SD raloxifene appeared the most cost-effective intervention, although this was due to the assumed beneficial effects on breast cancer. HRT was estimated to be harmful to women aged 60 or older due to the assumed adverse effect on breast cancer and on CHD. Etidronate was always inferior to alendronate and risedronate. Cost-effectiveness results are presented in the table assuming double the fracture risk compared with women at the threshold of osteoporosis.

Conclusions: It was most cost-effective to treat women with established osteoporosis aged 70 years or older with alendronate or risedronate. For women aged 50 or 60 years, the first-line intervention was dependant on the absolute fracture risk, at the threshold of osteoporosis the most cost-effective intervention was raloxifene, where this risk was doubled, the most cost-effective interventions became alendronate or risedronate.

Incremental costs and QALYs of each intervention compared to no treatment for 100 women with established osteoporosis and T-Scores of −2.5 SD assuming that the expected risks of fracture are doubled.

	Age 50 years Mean Cost per QALY (£000) (95% CI)	Age 60 years Mean Cost per QALY (£000) (95% CI)	Age 70 years Mean Cost per QALY (£000) (95% CI)	Age 80 years Mean Cost per QALY (£000) (95% CI)
Alendronate	25 (18 – 50)	16 (10 – 41)	D-ing (D-ing – 14)	D-ing (D-ing – 3)
Etidronate	45 (35 – 70)	41 (32 – 65)	12 (9 – 20)	17 (11 – 32)
Risedronate	26 (19 – 42)	19 (12 – 37)	2 (D-ing – 13)	D-ing (D-ing – D-ing)
Raloxifene	29 (24 – 41)	20 (16 – 29)	22 (17 – 32)	17 (12 – 26)
HRT	34 (14 – D-ed)	D-ed (12 – D-ed)	10 (D-ing – D-ed)	38 (D-ing – D-ed)

P404SU. OUR EXPERIENCES WITH BALLOON KYPHOPLASTY IN THE TREATMENT OF OSTEOPOROTIC VERTREBRAL COMPRESSION FRACTURES (VCF)

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Aims: To look for pain relief and correction of spinal deformity after balloon-kyphoplasty. In addition to this we were interested in new fractures nearby the operated segments.

Methods: All together 85 vertebrae were treated in 54 patients (48 women, 6 man, age 72 years). These 85 vertebrae were divided into 49 with acute fractures (AF, operation shorter than four weeks after fracture) and 20 subacute fractures (SAF, four to eight weeks). From this, 54 patients had 11 adequate trauma, 15 had a non-adequate accident and 28 had spontaneous fractures. For pain estimation we used the VAS-scale, for measurement of kyphosis angle we used lateral x-ray of the spine.

Results: AF-group (n = 49) showed an improved kyphosis angle of 11.5 grad postoperative and 10.7 grad after four weeks. In the SAF-group we could see an improvement of 1.8/1.7 grad. Looking to the pain-score the AF showed the following VAS values: 8.8 preoperative, 4.1 postoperative and 3.2 after four weeks. SAF showed: 8.3, 4.7 and 4.2. In no case had we seen any disturbance in wound heeling. Leakage of cement occured in 12 cases (14% of 85), there was only one case with radiculopathy (1.2% from 85 vertebras, 1.85% from 54 patients).

Conclusions: 1. Fresh osteoporotic vertebral fractures can be well restored within the first 4 weeks after fracture. 2. Subacute fractures do not allow good improvement of the kyphosis angle. 3. In both cases, good pain relief is possible. 4. The complications happened within the first month of using of this method (i.e. within the learning phase). Therefore, good training is necessary. 5. In some cases new fractures happened in the vertebrae nearby the operated segment. 6. Our two years experience showed that endangered adjacent segments should be treated also. 7. Balloon-kyphoplasty is a very safe therapy option in the treatment of acute vertrebral fracture. 8. Furthermore, osteoporotic patients with fractures must also be treated with changes in nutritional behaviour, movement therapy, evidenced based medical therapy (modern bisphosphonates, SERMs, parathormone, calcium and vitamin D), as well as psychological care.

P405MO. DIAGNOSIS AND TREATEMENT OF OSTEOPOROSIS: FREQUENCY IN A RIO DE JANEIRO OSTEOPOROSIS CENTER

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Aims: Osteoporosis is a common disease charachterized by a decrease in bone mineral density with an increase in fracture risk. It is nowadays a worldwide public health problem with increasing costs. The purpose of this study is to evaluate the rate of osteopenia and osteoporosis in patients examined in a Osteoporosis Diagnostic Center in Rio de Janeiro and the use of pharmachological therapy in these patients.

Methods: The results of 2270 subjects underwent to a bone density tests in a period of 90 days. The authors studied the distribution of rate about sex, age, diagnosis, skeletal sites and treatment used. In data analysis the Chi square test was used. In comparison of the proportion between treatment and diagnosis, the Z test of normal curve was used.

Results: We observed that the average age of the subjects was 59 ± 10.9 years. 2237 were females and 33 were males. The results showed that 46.9% had osteopenia and 19.4% had osteoporosis (figure). Among those patients with osteopenia 55.1% were using some pharmachological therapy and among those with osteoporosis only 59,6% were being treated: 7.3% were in use of alendronate, 4.2% in use of raloxifene and 48.1% in use of TRH, Calcium with Vitamin D or Calcium alone (figure).

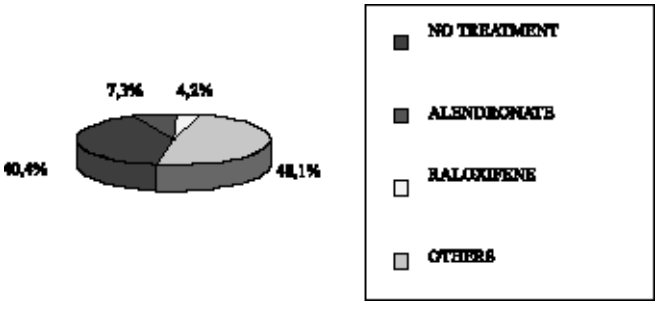

Fig. 1 Percentual distribution related to the treatment of the patients with Osteoporosis

Conclusions: The authors concluded that despite the correct use of bone density test and the diagnosis, a large number of patients with osteopenia and osteoporosis are not being properly treated.

P406SA. THE EFFECT OF DIFFERENT BISPHOSPHONATE TREATMENT IN PAGET'S DISEASE OF BONE

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Objective: To asses the usefulness of quantitative bone scintigraphy (QBS) in the monitoring of bisphosphonate treated patients and to evaluate the relationship between biochemical marker of bone turnover and bone scan indices of disease activity.

Methods: We investigated one year efficacy of three different bisphosphonates in 71 patients with Paget's disease. Patients received infusion pamidronate 30 mg/d for 6 days (39 patients), oral tiludronate 300 mg/d for 90 days (25 patients) and oral alendronate 10 mg/d for 12 months (7 patients). Serum samples were obtained from 71 patients with Paget's disease to determine the levels of total serum alkaline phosphatase (total AP). QBS was performed in every patient and the results were expressed as a ratio, obtained by comparing isotope uptake at an effected and an uneffected control site. Reduction in bone pain was assessed using a pain scale. Efficacy and side effects were monitored for a follow up period of up to one year.

Results: Total AP levels decreased significantly after pamidronate ($p < 0.001$) and tiludronate treatment ($p < 0.001$) respectively. QBS ratio changed significantly after pamidronate ($p < 0.001$) and tiludronate treatment, $p < 0.001$) respectively. The pain scale score decreased significantly in all cases. The side effects were the following: fever at five cases, bone pain at three cases and stomach-ache at two cases.

Conclusion: The treatment with iv pamidronate, oral tiludronate and oral alendronate results decreased pain, total AP levels and QBS ratio.

P407SU. DOES INJECTABLE BIOMATERIAL RESTORE BONE MASS AND ARCHITECTURE IN A RAT MODEL OF OSTEOPOROSIS (ORCHIDECTOMY AND DISUSE)?

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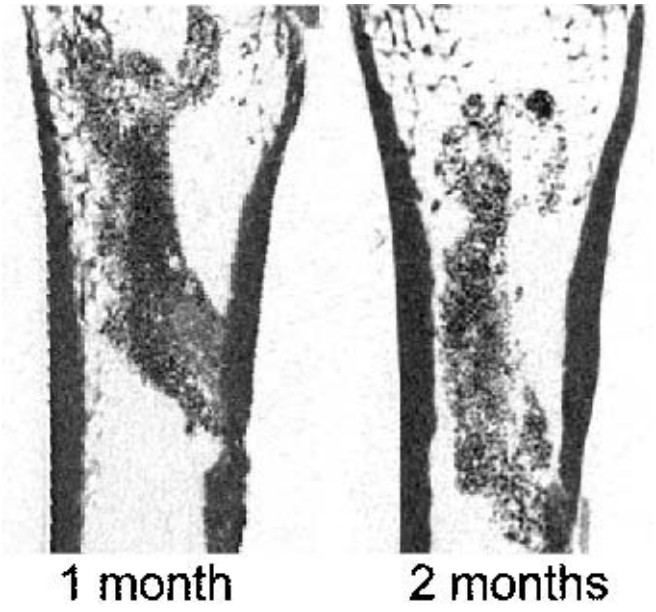
Aims: The use of osteoconductive biomaterials is often required in osteoporotic patients who need orthopaedics or maxillo-facial surgery. The purpose of this study was to use an injectable bone substitute (IBS-1) in a rat model of osteoporosis obtained by combining orchidectomy (ORX) and disuse. The effects of ORX, localized paralysis by botulinum toxin (BTX) and prevention by IBS-1 were investigated.

Methods: 52 aged male rats were randomised into 4 groups: SHAM operated; ORX-BTX (right hindlimb). One month after surgery, ORX-BTX rats had a bone marrow ablation (ORX-BTX-ABL) combined with injection with IBS-1 (ORX-BTX-ABL-IBS-1). Animals were studied 1 and 2 months after IBS-1 injection. BV/TV and Structure Modeling Index (SMI) were measured by X-ray microcomputed tomography in the secondary spongiosa. Histomorphometry was performed on the femur to measure osteoid, osteoclast activity and cell repartition.

Results: BV/TV was decreased 2 months after ORX-BTX; ORX and BTX effects were cumulative on bone loss since significant differences were observed between left and right limb. ABL had no effect on bone volume compared with ORX-BTX results. The combined volume of bone and material (B + Mat)V/TV was elevated at 1 month but returned at normal level on the 2nd month. SMI increased significantly in ORX-BTX (confirming an increased conversion of plates into pillars) and in ORX-BTX-IBS due to the remanence of biomaterial. Histomorphometry showed marked osseous formation apposed onto the biomaterial granules but bone had a woven texture. A dramatic increase in the number of non-osteoclastic TRAcP positive cells was found in the implanted area.

Conclusion: Our findings suggest that IBS-1 and newly formed bone are resorbed after a restoration period in this model of osteoporosis. Biomaterial trials must be conducted with long-term implantation periods in aged and osteoporotic animals to determine their potent ability to permanently restore trabecular microarchitecture.



P408MO. COMPARISON OF THE EFFECTS OF ALFACALCIDOL-ALENDRONATE-CALCIUM AND VITAMIN D-ALENDRONATE-CALCIUM TREATMENTS IN POSTMENOPAUSAL OSTEOPOROSIS

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Aims: To compare the efficacy of alfacalcidol with alendronate-calcium and Vit-D with alendronate-calcium in the treatment of women with postmenopausal osteoporosis.

Patients and Method: 72 patients with postmenopausal osteoporosis were randomly treated with either alendronate 10 mg daily, calcium and alfacalcidol (Group 1, n = 33) or alendronate 10 mg daily, calcium and Vit-D (Group 2, n = 39) for one year. Biochemical markers of bone resorption and bone formation with serum calcium and phosphorus, urinary calcium and serum alkaline phosphatase were performed at baseline and at 12th month. Bone mineral density (BMD) of lumbar spine, femur neck and total femur was measured by dual x-ray absorptiometry (DEXA) at the initial assessment and after 12 months of treatment.

Results: In the baseline measurements, there were no differences between age, body weight and length variables, whereas body mass index (BMI) in group 1 was greater than group 2 (25.23 versus 27.18, $p < 0.05$). At the end of one year, compared to baseline, both T scores and BMD in the lumbar spine, femur neck and total femur increased significantly in patients receiving alfacalcidol ($p < 0.05$). T scores of lumbar spine, femur neck, total femur and BMD of total femur increased significantly in patients receiving Vit-D after one year ($p < 0.05$). There were no significant differences in BMD and T scores between both groups.

Conclusions: These results indicate that both Vit-D and alfacalcidol were effective in the management of postmenopausal osteoporosis when combined with alendronate and calcium. The two treatment groups did not differ with respect to increases in the T scores and BMD.

P409SA. STRONTIUM RANELATE REDUCES THE RISK OF VERTEBRAL FRACTURES IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN WITHOUT PREVALENT VERTEBRAL FRACTURE

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Strontium ranelate is a new anti-osteoporotic agent having demonstrated its efficacy on both vertebral and non vertebral fractures: Two large phase III randomized, double blind, placebo controlled clinical trials, SOTI (1649 patients with prevalent vertebral fracture and low lumbar BMD) and TROPOS (5091 patients aged above 70 years and low femoral neck BMD) were conducted to assess the efficacy of strontium ranelate in reducing the risk of osteoporotic fractures in postmenopausal osteoporotic women. It has been shown that strontium ranelate significantly reduces the risk of vertebral fracture (SOTI study) and non vertebral fractures including hip fractures (TROPOS study).

A pre-planned meta analysis was performed on the pooled data from SOTI and TROPOS trials. Among the whole population of these studies, 2605 osteoporotic postmenopausal women without prevalent vertebral fracture (VF) were included and received strontium ranelate 2 g/day orally (n = 1285) or placebo (n = 1320) plus a Calcium/Vitamin D supplementation in both groups during 3 years. Vertebral X-rays were performed yearly (semi-quantitative assessment).

No statistical differences between groups were detected for main baseline characteristics: mean age (SD): 75(5) years; time since menopause: 26(7) years; mean(SD) Lumbar T-score: −2.70(1.53); mean(SD), Femoral Neck T-score: −2.97(0.56).

A significant reduction in the incidence of patients experiencing a VF was demonstrated in the intent-to-treat population over 3 years with a reduction of the relative risk by 48 % (95%CI [0.40; 0.67], $p < 0.001$). 87 patients in strontium ranelate group and 161 patients in placebo experienced a vertebral fracture during the study.

Strontium ranelate has already demonstrated its efficacy in reducing the risk of VF (41%) in patients with prevalent VF in SOTI study. The present analysis confirms its antifracture efficacy (reduction of the risk of 48%) in postmenopausal osteoporotic women without prevalent VF. Strontium ranelate is well-tolerated.

Strontium ranelate is a new anti-osteoporotic agent effective in reducing the risk of vertebral fracture in post-menopausal women with or without prevalent vertebral fracture.

P410SU. FRACTURE PREVENTION STRATEGIES ON A GERIATRIC UNIT: A SURVEY OF PATIENT KNOWLEDGE/ATTITUDES AND RESOURCE KIT DEVELOPMENT

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Aims: Osteoporosis in the older person is a leading cause of loss of independance. Despite emerging new therapies, suboptimal management is still an issue in patients discharged from acute care following fractures. The objective of this project was to develop an algorithm for the management of older persons with an acute fracture, to prepare a Patient Resource Kit and a fracture-specific medical discharge summary that is provided to family physicians on discharge from an acute setting for continuity of care.

Methods: Interviews using standardized questionnaires were conducted with ten patients admitted with a fracture. Subsequently, a focus group was held to further assess patient needs and review relevence of different materials. A chart review was performed using a standard format to assess the interventions performed during the hospital stay and the management offered. Discussions were also held with the interdisciplinary team members, including: the physiotherapist, occupational therapist, dietician, social worker, pharmacist and nursing staff. This poster will present the process of needs assessment, resource development and evaluation.

Results: Based on the above needs assessment the following was developed:

1) A Patient Resource Kit on Fracture Prevention was developed and subsequently evaluated using a telephone follow up. The kit contains five sections that cover topics: general information on osteoporosis-including local resources, calcium/Vitamin D supplements and osteoporosis treatments, exercise therapy, home safety and hip protectors.
2) An algorithm for the interdisciplinary management of an older person with an acute fracture (attached).
3) A Medical Discharge Summary form for the family physician who will provide ongoing care in the community, containing information relevant to fracture prevention.

Conclusions: A needs assessment conducted with patients and program staff can assist in developing resources that are patient specific and relevant to the care of those with fracture risk and raise the awareness of osteoporosis.

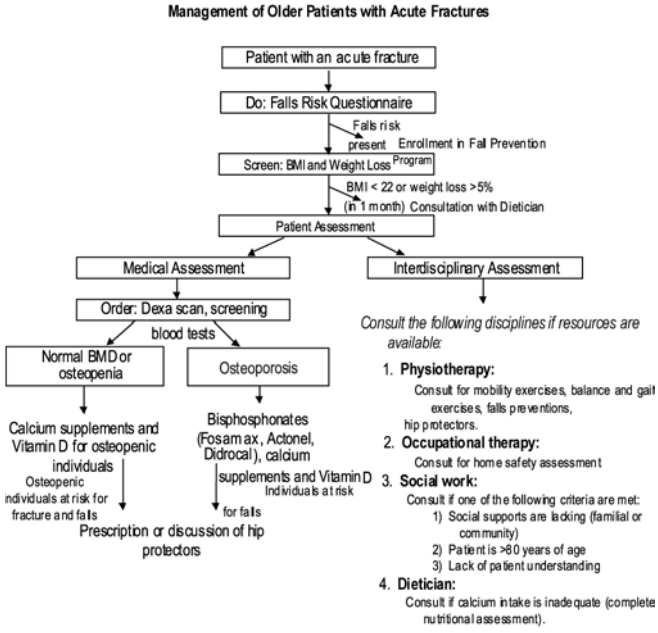

Fig. 1 Fracture Prevention in the Older Person Algorithm

P411MO. POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS ARE COMPLIANT AND SATISFIED WITH DAILY RALOXIFENE TREATMENT: RESULTS FROM A SIX-MONTH AUSTRIAN OBSERVATIONAL STUDY

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Aims: In this study our objective was to assess the treatment compliance and satisfaction of postmenopausal women with osteoporosis treated with raloxifene 60 mg/d for six months.

Methods: 2846 postmenopausal women diagnosed with osteoporosis (t-score < 2.5 SD below the young adult mean or at least 1 vertebral fracture), were treated with raloxifene and monitored for a period of 6 months. Overall patient health and reasons for switching from another osteoporosis treatment were evaluated at baseline. Patient compliance and satisfaction with treatment (assessed by physicians) and adverse events were evaluated at 6 to 8 weeks and 6 months. Following 6 months of treatment, each study participant completed an overall treatment satisfaction questionnaire.

Results: The mean age of the women enrolled in the study was 68 years (SD ± 9.04), and 70% of the women were 55 to 75 years of age. Fifty percent of the patients (n = 1423) had not received treatment for osteoporosis prior to the start of the study, and the second half of the study population was switched from another osteoporosis therapy to raloxifene due to intolerability (73%) or dissatisfaction with efficacy (26%). After 6 months of raloxifene treatment, physicians rated raloxifene tolerability to be ''very good'' or ''good'' in 92% of patients. During the 6 month observation period, 25 adverse events and 3 serious adverse events were reported. Only 4 adverse events were related to raloxifene treatment and none were serious. 75% of the patients were compliant with daily raloxifene treatment, 17% took raloxifene almost every day and 2% forgot to take raloxifene more frequently. Compliance information could not be obtained for 3% of the patients. Drug discontinuation was seen in 3 % of the patients due to various reasons. After 6 months, 90% of the physicians evaluated patient satisfaction with raloxifene treatment as ''very satisfied'' or ''satisfied''. Patient self-assessment revealed a treatment satisfaction of 73%.

Conclusions: This Austrian observational study confirms that raloxifene treatment is well tolerated, resulting in high treatment compliance and overall patient satisfaction.

P412SA. EFFECT OF VARIOUS TYPES OF INULIN AND OLIGOFRUCTOSE FROM CHICORY ON BONE

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Addition of non-digestible oligosaccharides to the diet of rats may increase intestinal calcium absorption. The role of inulin (IN) and oligofructose (OF) from chicory on BMD acquisition was assessed in growing rats. Thirty-nine Whistar male rats, aged 6 weeks and weighing on average 162 g were fed with AO4 diet containing 0.6% phosphorus and 1% calcium. They were divided into 3 groups: Group 1: usual diet = controls (C). Group 2 received OF with a degree of polymerization (DP) between 2 and 20. Group 3 received IN with DP between 2 and 60 (average DP of minimum 8). Dosages of soluble fibres from IN, OF in diet amounted to 5%. Treatment duration was 3 months, when the rats were sacrificed. Whole body BMC (WBBMC) was measured by DXA (QDR-1000W, Hologic Inc., Bedford, MA) at the start and after 3 months. pQCT (research XCT, Norland, Fort Atkinson, WI) of vertebral body of L3 (VBBMD), of left mid-femur and of left tibia was used to measure BMD after sacrifice. The weight gain was a little greater after 3 months in group 2. WBBMC increased significantly in group 2 as compared to other groups (287% in group 2, vs. 272; and 265% in C and group 3, respectively). pQCT measurements showed a VBBMD, trabecular BMD and cortical + subcortical BMD of L3 significantly higher in group 3 (648, 262 and 963 g/cm3, vs. 616, 233, 929 and 642, 258, 956 g/cm3 in C and group 2, respectively). The BMD of total mid-femur was also the highest in group 3 (1002 vs. 985 and 977 g/cm3 in group 2 and C, respectively). At mid-tibia and metaphyseal proximal region, BMD was also higher in group 3 (1048, 625 vs. 1006, 567 and 1012, 589 g/cm3 in group C and 2, respectively).

In conclusion, a significant effect of IN OF feeding was observed particularly on BMD of peripheral bones in growing rats, which should encourage to test these natural products in humans in order to maximize bone acquisition.

Work supported by a grant of Cosucra Group, Warcoing, Belgium.

P413SU. ASSESSMENT OF VITAMIN K AND CALCIUM INTAKES AMONG PATIENTS USING ORAL ANTICOAGULANTS

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Because of the presence of vitamin K-dependent proteins in bone, there has been an interest in determining whether vitamin K nutritional status or warfarin anticoagulation therapy have an effect on bone metabolism.

Aims: The aim of the study was to assess the dietary vitamin K and calcium intakes of a group selected from an outpatient anticoagulation clinic.

Methods: 115 patients of the Anticoagulation Clinic of the Botucatu Medical School (UNESP) were enrolled in the study. A food frequency questionnaire was applied in order to know the usual intake of vitamin K and calcium. Dietary information was converted to vitamin K and calcium with the computer software: Programa de Apoio à Nutrição. The results were expressed by the calculation of the median and 10 and 90 percentiles values.

Results: The median intake of vitamin K was 120 mcg/day (range 7.4–829; P10: 50 mcg/day and P90: 290 mcg/day), and the median of usual intake of calcium was 642 mg/day (range 176 to 1761 mg/day; P10: 307 mg/day and P90: 1177 mg/day).

Conclusion: Besides the already established role of calcium it appears that vitamin K has also a important role to play in bone metabolism. Vitamin K and calcium intakes of the group were lower than the recommended and may not be able to maintain normal bone health.

P414MO. TIBOLONE IN TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS: EXPERIMENTAL AND CLINICAL DATA

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Tibolone was proven to prevent bone loss in postmenopausal women and relieve climacteric symptoms as effectively as estrogen without stimulating endometrium and breast. The aim of this research was to study biomechanic, biochemical and osteometric bone data of rats belonging to two age groups (6 months and 18 months old) after surgical bilateral oophorectomy and tibolone (Livial®) therapy. We studied structural-functional state of bone mass, climacteric symptoms of postmenopausal women with and without Livial therapy. Experiments showed bilateral oophorectomy to reduce biomechanic characteristics of bone (bone destruction and bone strength indices) and osteometric indices, as well as to change the biochemical bone properties. Six-week Livial therapy improves biomechanic, biochemical and osteometric bone data of rats in both groups. Clinical research revealed structural-functional state of bone and climacteric symptoms of women after natural menopause (duration of postmenopausal period made up 3–5 years) after Livial therapy. Structural-functional state of bone was determined by ultrasound densitometer, Achilles + (Lunar Corp., Madison, WI). Speed of ultrasound spreading (SOS, m/s), broadband ultrasound attenuation (BUA, dB/MHz) and Stiffness index of bone tissue (SI, %) were calculated, and acuteness of climacteric symptoms was determined by Kupperman scale. It was established that one-year Livial therapy of postmenopausal women removed climacteric symptoms, improved structural-functional state of bone mass (increased the Stiffness index ($p < 0.05$). This research has not shown any side effect attached to tibolone application. Therapy by Livial is effective in correction of structural-functional disturbances and treatment of postmenopausal osteoporosis and its complications.

P415SA. USE OF CLODRONATE IN THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS: EVALUATION OF THE COMPLIANCE

Ragusa O L F, Grua D; Rosiello P; ASL6; Phys Med and Rehab, Venaria Reale, Turin, Italy

Aims: The primary aim of this study was to assess the compliance of clodronate therapy in postmenopausal osteoporotic women. The compliance is very important for the adherence to the full rehabilitative project, that includes also the restore of the osteometabolic omeostasis and education programs. Injective therapy with clodronate (1 fl 100 mg once weekly) should improve the compliance more than the oral one. Secondary to verify the antalgic effectiveness of clodronate. Finally to check the effectiveness of clodronate in improving the bone mineral density at 18 months in patients with postmenopausal osteoporosis.

Methods: We selected, during the first 6 months of 2001 and the 2002, 251 women with postmenopausal OP, 55–65 years old. The first step was to determine the risk-score through anamnesis, particularly the nutritional and activity status with a questionnaire. Then the patients undergo a clinic evaluation with postural examination. We measured the main biochemical bone markers and the BMD with spinal DXA at baseline. The pain was measured with the visuoanalogyc scale. We assessed also the Activity Daily Living and identified the ICF itmes. The clinical follow up was every six months. We stressed the message about the importance of modify their lifestyle and of carry on continously the treatment. Moreover we monitored at 6–12–18 months the markers of bone resorption. At 18 months the patients undergo an examination with DXA.

Results: We had only 3 drop outs, caused by the appearance of other pathologies. At the follow up at 6, 12, 18 months we found a decrease of 50 percent in the markers, as usually happens with the bisphosphonates. At 18 months there was an increase of BMD (5–6% from baseline). Several ICF items were modified.

Conclusions: The planning of follow up every 6 months reduces significantly the drop out: only 3 subjects stopped the treatment, because their new pathology needed others pharmacological therapies. The increased adherence to the osteoporosis program improved the acceptance of the therapy.

Moreover we found, by evaluating a questionnaire compiled by the women, that the weekly parenteral way choosed was very important to reach the total adherence to rehabilitation project.

P416SU. LOW INTENSITY PULSED ULTRASOUND APPLIED TO BONE OF OSTEOPENIC RATS

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Osteoporosis is a bone disease characterized by low bone mass and consequent deterioration of bone architecture, which increases the bone fragility and the risk of fracture. The decrease of bone mass is caused by an increase of bone resorption, thus disturbing the balance between osteoblasts and osteoclasts. Osteoporosis prevalence is large in older population, usually in postmenopausal women and systemic diseases, as occurs after a spinal cord injury. Thus, treatment to prevent or to stabilize osteoporosis is rather important; in particular for spinal cord injured patients since bone mineral content (BMC) decreases quickly.

According to bone biomechanics, ultrasound is capable of stimulating bone formation due to promotion of local bone micro-deformations, as the natural mechanical incentive. Its efficiency in accelerating the healing of fresh fractures, delayed healing and nonunions has already been confirmed through previous works. However there are no studies which investigated the effect of low intensity ultrasound in cases of osteoporosis without fractures.

In this study, the action of low intensity pulsed ultrasound for 20 min/day, during 20 days was analyzed, in an attempt to revert bone loss in the proximal femur of osteopenic rats. Although the quantitative results of BMC demonstrated no significant difference among the groups ($p > 0.05$), the histological investigations have shown the occurrence of recent bone formation not observed in the non-treated group. Moreover, the treated femur presented less microarchitectural deterioration than the non-treated group, analyzed by scanning electron microscopy. These results suggest that the low intensity ultrasound can interfere in a positive way on osteoporosis.

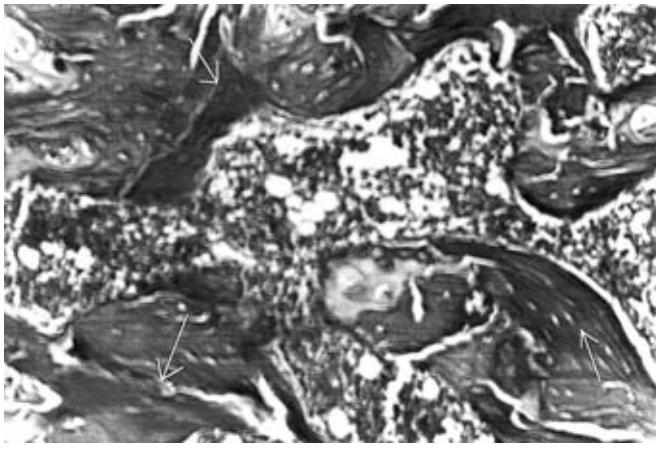

Fig. 1 Longitudinal sections of the proximal femur of treated group; arrows indicate recent bone formation. Masson Trichrome stain, x160

Acknowledgements: The State of São Paulo Foundation for Research (FAPESP).

Carvalho DCL, Cliquet Jr A et al. Non-pharmacological treatments in the stimulation of osteogenesis. Journal of Public Health 36: 647–654, 2002.

P417MO. CALCITONIN AND ALENDRONATE COMBINED THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Aim: Rheumatoid Arthritis (RA) is an autoimmune disorder of unknown etiology characterized by symmetric, erosive synovitis and in some cases, extraarticular involvement. Localized and generalized osteoporosis is one of the extraarticular manifestations of RA. In this study we evaluated the effects of Calcitonin and Alendronate therapy either alone or in combined manner in patients with RA.

Method: Eighty patients with RA were included to the study. All the patients were using methotrexate 10 mg/week and prednisone 7.5 mg/day. Randomly dividing the patients in to four groups, the first group consisting of 20 patients were given alendronate 70 mg/week, second group consisting of 21 patients were given 200 IU/day calcitonin nasal spray and the third group consisting of 15 patients were given combined therapy of 70 mg/week alendronate and 200 IU/day calcitonin nasal spray. 24 patients in the fourth group or the control group were given none of the above mentioned antiresorptive agents and all the patients in these groups were also using 600 mg calcium and 400 IU vitamin D. The DEXA bone mineral density (BMD) of lumbar, hip and forearm regions and laboratory investigations of all the patients were performed before and at the 12th month of the therapy.

Result: At the end of 12th month, only the combined therapy group displayed statistically significant decreases of alkaline phosphatase levels which points out that the high bone turnover seen in RA patients can only be normalized by the combination therapy of these two potent antiresorptive agents. At the end of first year, the combined therapy group showed statistically significant increases at the lumbar and hip regions where as at the forearm regions they stabilised the BMD value.

Conclusion: We recommend the use of calcitonin and alendronate combined therapy especially for the severe active cases of RA but further prospective studies consisting of larger patient populations were needed to confirm the additive effects of this combined therapy on the fracture risk in these patients.

P418SA. STRONTIUM CONCENTRATIONS IN BONE, WHOLE BLOOD AND URINE FROM OSTEOPOROTIC SUBJECTS WITH PROXIMAL FEMUR FRACTURES

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Aims: The purpose of this work was to show the correlation between [Sr] in samples of different types (bone, blood and urine) from osteoporotic patients who had undergone surgery due to proximal femur fracture.

Material and methods: This study involved 25 patients, 17 female and 8 male, with age ranking from 47–89 years old (67.6 ± 12.3 years), all of them with hip fractures. For the determination of Sr in bone digest blood and urine a Perkin-Elmer model 41000 ATOMIC ABSORPTION SPECTROMETER equipped with nitrous oxide/acetylene flame was used. Statistical evaluation: Statistical Analysis System (SAS) software operated under UNIX using ANOVA and Pearson correlation and paired t-Student tests for a confidence level of 95% ($p = 0.05$).

Results: Women were older than men (70.9/65.1). Sr concentration in bone and blood was higher in the female group but its elimination is higher in the male group. According to the age, the Sr concentration in bone (28.00 ± 7 μg/g) has a highly positive correlation (IC = 96%) with the blood content (25.17 ± 6.28 μg/l) and less marked of them (IC = 32%) with urine (87.43 ± 18.94 μg/l). Sr in the three samples has an inverse relationship with age, and urine is the most representative (62% vs 38%) and 35% bone and blood, in a respective way.

Conclusions: Sr in blood, urine and bones had an inverse correlation with age. It is probably due to the narrow age range of the subjects selected for this study. There is a highly positive statistical correlation between [Sr] in bones and blood assuring the homeostatic condition thus the determination of Sr in blood could be useful for diagnosis purposes. The behavior of Sr in urine might be related with the decreased renal function in old people. Extending this study to a more numerous elderly population and sampling urine over a 24 h period might be useful to: a) investigate the interactions of Sr with other elements like Ca; b) get a better insight into the renal clearance in osteoporotic subjects. It, is possible white blood Sr modification with osteoporotic treatment in prospective study.

P419SU. STRONTIUM RANELATE TREATMENT PREVENTS OVARIECTOMY INDUCED BONE LOSS IN RATS BY MAINTAINING THE BONE FORMATION AT A HIGH LEVEL

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Strontium Ranelate is a new active compound in postmenopausal osteoporosis. Static and dynamic bone histomorphometry assessed its effects in prevention of ovariectomy-induced bone loss. Six-month old Sprague-Dawley rats were either ovariectomized (OVX) or received sham (SHAM) surgeries. One day after ovariectomy, 3 OVX groups were treated daily for 52 weeks with 125, 250, or 625 mg/kg of strontium ranelate and one received vehicle. Vehicle-treated OVX and SHAM animals served as controls. Regarding the control groups after 1-year treatment, a 72% reduction in cancellous bone volume (BV/TV) in OVX vs. SHAM ($p < 0.01$) was noted in the proximal tibia. The reduced BV/TV was related to a 70% decrease in trabecular number (Tb.N) and a 394% increase in trabecular spacing (Tb.Sp;both $p < 0.01$). Similar findings were observed in the lumbar vertebra: decreases of 49% and 36% in BV/TV and Tb.N, respectively and a 108% increase in Tb.Sp ($p < 0.01$ for all parameters). Significant increases in bone formation were also observed at these two sites, confirming the presence of high-turnover bone loss in the OVX controls. At the proximal tibia, strontium ranelate treatment showed positive, dose-dependent effects on all parameters compared to OVX: increased BV/TV (116%) and Tb.N (64%) and decreased Tb.Sp (53%) in rats treated with 625 mg/kg/d of strontium ranelate ($p < 0.01$ for all parameters). In this treated group, trabecular thickness (Tb.Th) was increased by 23%. In vertebrae, strontium ranelate at the dose of 625 mg/kg/d increased BV/TV by 40% ($p < 0.05$) and Tb.N by 28% ($p < 0.05$), increased Tb.Th by 12% and decreased Tb.Sp by 31% ($p < 0.01$), respectively, in comparison with OVX. In the proximal tibia as in lumbar vertebrae, bone structure improvements appeared to be a consequence of strontium ranelate's effects on bone formation as the bone formation rates (BFR/BS) in strontium ranelate treated animals were equivalent to those observed in OVX. Finally, the absence of any mineralization defect under strontium ranelate treatment was confirmed as no modification of the osteoid tissue and of the mineral apposition rate was noted.

These results indicate that strontium ranelate treatment prevents OVX-induced bone loss via a pathway that stimulates bone formation at a high level when bone resorption is decreased.

P420MO. STRONTIUM RANELATE TREATMENT PRESERVES BONE CRYSTAL CHARACTERISTICS AND BONE MINERAL REACTIVITY

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This work determined the effects of strontium ranelate on the characteristics of bone mineral crystals, ionic exchanges at the mineral level and dissolution properties of bone apatite. Female Cynomolgus monkeys were treated with 0, 200, 500, 1250 mg/kg/d of strontium ranelate for 52 weeks, 4 were sacrificed at the end of treatment, and 2 after a 10-week reversibility period. On powdered samples of the humeral diaphysis, metaphysis and epiphysis, the Ca, Sr, P, Mg, and CO3 ions contents (chemical measurements), crystals size (X-ray diffraction) and fine structural characteristics (FTIR spectroscopy) were determined. Diaphysis powdered samples underwent an exchange test (in a solution of Ca(NO3)2 for 30 min) or a dissolution test (in acetate, 0.1 M, pH 5, for 60 min at 37 °C). Powders were analysed before and after these tests by the techniques previously described. Release of ions in the acidic buffer during dissolution, was determined by chemical measurements and Ca release with a Ca-selective electrode.

Strontium ranelate treatment induced a dose-related increase in the bone Sr content with no modification of the stoichiometry, crystal size and nonapatitic environments. Sr uptake as well as its release was observed preferentially in the epiphysis and metaphysis. This can be due to higher surface contact with body fluids for the epiphysis and metaphysis than for the diaphysis and/or to differences in turnover rate and crystals characteristics in these locations. The exchange test demonstrated a slight constant exchange rate of 9–12% Sr in diaphysis crystals, independent of the treatment dose and bone Sr content. This indicated that easily exchangeable Sr from bone was located in labile hydrated nonapatitic environments on crystal surface. Strontium ranelate treatment had no effect on the bone dissolution rate, or on the amounts of Ca, Mg and P ions released in the buffer. The amount of Sr ions released was dependent on the bone Sr content.

These data demonstrate the strontium ranelate safety at bone apatite crystal level and the preservation of the apatite reactivity, based on the absence of changes on exchange and dissolution properties after long-term treatment using a dose up to 40 times the human therapeutic dose of 2 g/day.‘

P421SA. OSTEOPLASTY OF VERTEBRAL COMPRESSION FRACTURES: A RETROSPECTIVE ANALYSIS IN OSTEOPOROTIC PATIENTS

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Study design: Retrospective review of 50 patients with osteoporosis and vertebral compression fractures (VCFs) treated with percutaneous osteoplasty (PO) and percutaneous vertebroplasty (PV).

Objective: To evaluate clinical effect of PO and PV patients with VCFs due to osteoporosis

Summary of Background Data: Osteoporotic patients with VCFs have a long time recovery period and patients develop time-related clinical complications (e.g.: prolonged bed rest or medication side-effects). Osteoplasty and vertebroplasty improve outcome in short and long-term follow-up.

Material and Methods: 50 patients (age between 65 and 101 years old) had a total of 80 VCFs. Patients failed to improve after short-time conservative treatment (at least 2 weeks). All patients had primary osteoporosis VCFs. Surgical treatment was done under general anesthesia. Transpedicular vertebroplasty with bilateral approach was done in 15 VCFs (T12) and unilateral extrapedicular osteoplasty in 65 VCFs. Osteoplasty and vertebroplasty were done using low-pressure injection devices for cement delivery (AOM Interpore, Irvine, CA, USA). The majority of VCFs in osteoporosis occurred at lumbar and lower thoracic spine. Patients were evaluated with Visual Analogic Scale (VAS), Oswestry Disability Index Score (ODIS) and Prolo Functional Outcome Scale (PFOS) at 6, 12 and 24 months follow-up. All patients had MR examinations with STIR technique (except one with a previous history of cerebral aneurysm surgery).

Results: Vertebroplasty and osteoplasty were statically significant in VAS, OSDI and PFOS. There was no infection. Complications with neurological compromise requiring surgical decompression occurred in 2 patients (failure to recognize posterior cortical wall rupture). 2 patients had axial loading fractures related to the adjacent level treated.

Conclusion: PO and PV have a positive clinical effect in osteoporotic patients. Early treatment reduce pain and morbidity related with VCFs. Low-pressure injection systems had fewer complication rate and further prospective trials are needed to asses the role of prophylactic treatment in high-risk patients.

P422SU. LOW-INTENSITY PULSED ULTRASOUND EFFECTS ON A BONE MODEL OF OVARIECTOMIZED FEMALE RATS

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Aim: To analyse low-intensity pulsed ultrasound effects on a ovarectomized (OVX) female rats bone model through flexion-compression test.

Methods: Female Wistar rats were dividid in three groups (OVX group, intact group that did not suffer any kind of intervention and treated group where animals were both OVX and exposed to ultrasound). In the treated group, the ultrasound exposition was initiated on the first day after the surgery, and it was extended for nine weeks, six days per week, during twenty minutes per day. Through the flexion-compression test, carried out on the femur’s proximal extremity, the maximum limit was evaluated.

Results: The maximum limit deformation wasn’t altered in these different groups, (Intact 125.2 ± 20.3; OVX 106.4 ± 11.2; treated 122.9 ± 14.9.Though, the maximum limit load average in the ovariectomized group was significantly lower when compared to the intact and treated groups (Intact 0.51 ± 0.13; OVX 0.51 ± 0.07; treated 0.47 ± 0.08), and between the intact and treated groups, the average wasn’t statistically different, suggesting that despite of the treated group was submitted to ovariectomy, the average value of the maximum limit load was similar to the intact group by the ultrasound influence.

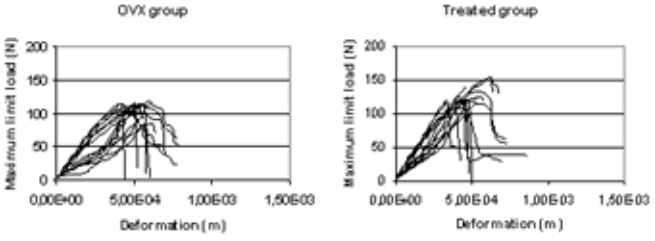

Fig. 1 Diagram load versus deformation OVX group and treated group

Conclusion: There is possibility of the bone loss of bone mass caused the maximum limit load decreasing and the low-intensity pulsed ultrasound stimilation on femurs of ovariectomized female rats contributed to the preservation of this mechanical parameter.

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P423MO. EFFECTS OF 6-MONTHS VIBRATION LOADING AND RESISTANCE TRAINING ON MUSCLE STRENGTH AND HIP DENSITY IN POSTMENOPAUSAL WOMEN: A COMPARATIVE TRIAL

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High-frequency mechanical strain stimulates bone strength in different animal models. However, randomized controlled data on the safety and efficacy of vibration loading on the human skeleton are lacking. The aim of this randomised controlled trial was to assess the musculoskeletal effects of high-frequency loading by means of whole-body vibration in postmenopausal women.

Seventy volunteers (age, 58–74 years) were randomly assigned to a whole-body vibration training group (WBV, n = 25), a resistance training group (RES, n = 22), or a control group (CON, n = 23). The WBV-group and the RES-group trained three times weekly during 24 weeks. The WBV-group performed static and dynamic knee-extensor exercises on a vibration platform (35–40 Hz, 2.28-5.09 g), mechanically loading the bone and evoking reflexive muscle contractions. The RES-group trained knee-extensors by dynamic leg press and leg extension exercises, increasing from low (20RM) to high (8RM) resistance. The CON-group did not participate in any training. Hip bone density was measured using DXA at baseline and after the 6-month intervention. Isometric and dynamic strength were measured by means of a motor-driven dynamometer. Data were analyzed by means of repeated measures ANOVA.

As expected, muscle strength and hip BMD remained unchanged in the CON group (not shown). WBV training improved isometric and dynamic muscle strength (+15% and +16% from baseline, respectively, $p < 0.01$). Similar increases in muscle strength were observed in the RES group (not shown). WBV also significantly increased BMD of the hip (+0.93%, $p < 0.05$), whereas no change in hip BMD was observed in the RES group (−0.60%, NS). Compared to the RES and CON groups, the 6-month vibration intervention resulted in a significant net benefit in total-hip BMD (+1.51% and %1.53%, respectively, $p < 0.01$). Serum markers of bone turnover did not change in any of the groups (not shown). No vibration-related side effects were observed.

These findings suggest that WBV training may be a feasible and effective way to modify well-recognized risk factors for falls and fractures in older women, and support the need for further human studies.

P424SU. CALCITONIN AND ALENDRONATE COMBINED THERAPY IN OSTEOPOROSIS

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Aim: Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture risk. Several inhibitors of bone resorption have been shown to increase skeletal mass and in this study we evaluated the results of the combination therapy of two antiresorptive agents in postmenopausal osteoporotic patients.

Method: 57 patients were included in the study. After randomly dividing these patients into three groups, first group consisting of 21 patients were given 200 IU/d Calcitonin nasal spray (CT), the second group consisting of 20 patients were given Alendronate 10 mg/d (ALN) and the third group consisting of 16 patients were given 200 IU/d Calcitonin nasal spray and Alendronate 10 mg/d (COM). All the patients were given daily 600 mg calcium and 400 IU vitamin D3 supplements. Bone mineral density (BMD), bone spesific alkaline phosphatase (AP), osteocalcin (OC) levels were determined before and at the 6th month of treatment.

Results: At the 6th month of therapy CT group displayed 1.76% increase in BMD and 9.3% and 11.6% decreases in AP and OC levels. Also ALN group displayed 6% increase in BMD and 36.1% and 60% decreases in AP and OC levels respectively. On the other hand COM group showed 7.04% increase in BMD and 42.2% and 62.5% decreases in AP and OC levels.

Conclusion: The results of this study reveals that the combination therapy of two antiresorptive agents that were inhibiting osteoclastic activity by different mechanisms may have additive effect on bone remodeling. But the results of this preliminary study needs to be confirmed by larger populaton based prospective studies.

P425SU. NOVEL IBANDRONATE REGIMENS IN POSTMENOPAUSAL OSTEOPOROSIS: DESIGN OF THE DOSING INTRAVENOUS ADMINISTRATION (DIVA) STUDY

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Aims: In postmenopausal osteoporosis (PMO) management, bisphosphonate administration by intermittent intravenous (i.v.) injection offers advantages over both oral and i.v. infusion dosing. Recent studies support the clinical potential of i.v. ibandronate injections with extended between-dose intervals. Notably, in a recent phase II/III study, i.v. ibandronate injections (2 mg), administered once every 3 months, produced changes in BMD and markers of bone turnover similar to those observed with oral nitrogen-containing bisphosphonates of proven fracture efficacy, including daily and intermittent ibandronate. A randomised, double-blind, parallel-group, multicentre study (Dosing Intra-Venous Administration: DIVA), is ongoing to further assess the influence of dose and dosing interval on the efficacy and safety of i.v. ibandronate injections in postmenopausal osteoporosis.

Methods: DIVA is a non-inferiority study using the proven oral daily ibandronate regimen as active control. A total of 1,395 women (aged 55–80 years, time since menopause ≥ 5 years) with osteoporosis (lumbar spine BMD T-score < −2.5 and ≥ −5.0) were randomised into one of four groups in a 2:1:2:1 ratio: Group A: 2 mg q 2 mo i.v. ibandronate and oral daily placebo; Group B: 2.5 mg oral daily ibandronate and i.v. placebo q 2 mo; Group C: 3 mg q 3 mo i.v. ibandronate and oral daily placebo; Group D: 2.5 mg oral daily ibandronate and i.v. placebo q 3 mo. Data from Groups B and D will be pooled for the efficacy analyses. Patients are receiving 24 months of ibandronate plus daily calcium (500 mg) and vitamin D (400IU). The primary efficacy endpoint is relative change from baseline in lumbar spine BMD after 1 year. Secondary efficacy endpoints include BMD at other sites and biochemical markers of bone turnover. Adverse events are monitored. ECGs and bone biopsies for histomorphometric analyses are being carried out in a subset of patients.

Results and Conclusions: Non-inferiority analysis is an accepted and widely used methodology for demonstrating therapeutic equivalence of regimens. In the DIVA study, antifracture efficacy will be concluded if the i.v. injection regimens show non-inferiority to the proven oral daily regimen for lumbar spine BMD change. Intermittent i.v. ibandronate injections are expected to provide a complementary therapeutic modality to oral dosing in PMO.

P426MO. EFFECT OF ESTRADIOL PLUS NORETISTERONE ACETATE ON BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

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Aim: To evaluate the effect of estradiol plus noretisterone acetate on bone mineral density in women in postmenopausal women.

Methods: 99 patients had been studied in observational non-randomized prospective study at Women's Health Reference Center, São Paulo, Brazil, divided into two groups. Group 1: 54 patients were treated with 2 mg of estradiol plus 1 mg norteisterone acetate for 12 months. Group 2: 45 patients were not treated for 12 months (Control group). Basal and final bone mineral density had been evaluated by DEXA of lumbar spine and femoral neck. Results: Group 1: Basal lumbar spine was 1.040 g/cm^2 and after 12 months was 1.072 g/cm^2 (Increase 3.1%). Basal femoral neck was 1.105 g/cm^2 and after 12 months was 1.125 g/cm^2 (Increase 1.9%). Group 2: Basal lumbar spine was 1.077 g/cm^2 and after 12 months was 1.067 g/cm^2 (Decrease 0.9%). Basal femoral neck was 1.118 g/cm^2 and after 12 months was 1.110 g/cm^2 (Decrease 0.7%).

Conclusion: Estradiol plus noretisterone acetate can reduce the risk of rip in postmenopausal women.

P427SA. DMARDS TREATMENT AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To investigate the influence of DMARDs treatment on bone mineral density (BMD) and in patients (pts) with rheumatoid arthritis (RA).

Methods: 109 active RA pts (97 women and 12 men) with mean age 55.6, mean disease duration 14.7, mean number of previous DMARDs 3.6 were included in this study. All patients were taking a DMARDs during of 1 year observation: Methotrexate (MTX) in 35%, Sulfasalazine (SF) in 9%, a intramuscular gold salts (IMG) in 10%, a steroids in 13%, combination of a DMARD and steroids in 26% cases. 51 pts (46.7%) were taking a steroids as the only medication and as in combination with a DMARD. BMD at lumbar spine (L1–L4), at the left hip (femoral neck and Ward's triangle) and at the right forearm was measured with DEXA. BMD was assessed at baseline and after 1 year of DMARDs treatment.

Results: At baseline an osteoporosis at L1–L4 was found in 18.6% pts, osteopenia – in 28.8% pts, at the femoral neck – in 19.5% and 29.6%, Ward's triangle – in 33.1% and 33.9%, respectively. BMD was not changed in 1 year observation. IMG were significantly delayed an osteoporosis progression at all sites, but higher at femoral neck and Ward's triangle in comparison with MTX ($p < 0.001$ and $p < 0.001$), SF ($p < 0.003$ and $p < 0.0003$), steroids ($p < 0.04$ and $p < 0.002$) and its combination with DMARD ($p < 0.001$ and 0.001), respectively. A steroids were significantly more decreased BMD at femoral neck ($p < 0.03$). However, a combination of DMARD and steroids were not negatively influenced on BMD at any site.

Conclusion: DMARDs treatment was delayed the rate of BMD loss, an IMG have demonstrated more substantial effect. A steroids in combination with a DMARD can achieve a positive influence on disease activity and bone mass. An efficacy of DMARDs treatment is a strong reserved factor of osteoporosis.

P428SU. PATIENT EDUCATION PRACTICES AMONG BONE DENSITOMETRY TECHNOLOGISTS

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Aims: The Osteoporosis Counseling Survey (OCS) was administered to ionizing bone densitometry technologists to assess their knowledge about osteoporosis, beliefs about the disease, attitudes towards osteoporosis preventive care, and bone health promotion counseling habits. The descriptive study was conducted to analyze predictors for osteoporosis prevention patient education. Increasing counseling maximizes the potential for health benefits from medical care for patients at risk.
Methods: The sample consisted of 158 bone densitometry equipment operators in Arkansas and 417 radiologic technologists (RTs) registered by the American Registry of Radiologic Technologists (ARRT) with advanced certification in bone density (RTBDs). The study subjects performing bone density exams in Arkansas were health professionals such as nurses and RTs. Although no RTs registered by the ARRT in bone densitometry (RTBDs) were employed in Arkansas, 14 responders in Arkansas were clinical densitometry technologists (CDTs) certified by the International Society for Clinical Densitometry (ISCD).
Results: Response rates were 52% from the Arkansas sample and 60% from the national RTBD sample, for 58% overall. Although the responders reported counseling a majority of their patients about osteoporosis prevention (mean 82% + 3.6), they appeared to define patient counseling in different ways. BD certified providers were more likely than non-certified providers to have higher internal motivation and perceptions of fewer barriers to health counseling. Providers with high internal motivation and low personal barriers were more likely to counsel their patients than providers with low personal interest and greater concerns related to having inadequate knowledge, time, confidence, or encouragement to engage in counseling. Knowledge, beliefs, and attitudes accounted for 25% of the variation in the regression model, while another 16% of the variation related to the age of the provider, certification in BD, and employment where patients were assessed for their health behaviors related to osteoporosis.
Conclusions: Recommendations for increasing bone health promotion during densitometry exams include increasing equipment operator motivation to provide health education through sensitivity training, promoting models for clinical integration of preventive services, and creating educational opportunities to strengthen counseling skills. Future studies should more clearly define health counseling or incorporate measures for counseling to increase reporting accuracy.

P429MO. BISPHOSPHONATES ANTALGIC ACTIVITY IN RECENT VERTEBRAL FRACTURE: A CLODRONATE VS NERIDRONATE COMPARISON

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Fractures are the most common and dangerous osteoporosis involvement. A vertebral breakdown, by stimulating one or more algogenic structure, will decrease the motility of involved skeletal sections, compress intervertebral discs and/or cause interapophysary distractions, responsible of a further myoceptive stimulation. Paravertebral muscles splinting brings about lumbar stiffness and antalgic postures; during vertebral pain several physiopathologic mechanisms cause asymmetric effects that worsen pelvis motility and posture. These are the pathogenetic conditions that cause an alteration of either static or dynamic postural balancing of foot rest during lumbar pain. Pressure on feet and length of the step will change due to an antalgic action and a lower pressure will be applied on the foot in the painful site. Objective of this study is to evaluate if lumbar or sacral pain is able to cause an alteration of foot rest and if pain improvement is related with a walk and foot rest modification. The previously known Clodronate (Difosfonal) antalgic activity was compared to Neridronate (Nerixia) one. 16 women (mean age 72 years) with recent dorsal or lumbar pain due to a vertebral fracture were enrolled in the study. In any patient with radiologic diagnosis of vertebral fracture, the following evaluations at T0 (baseline), T1 (15 days), and T2 (40 days), were performed, clinical examination, subjective evaluation of pain on visual analogic scale, podometric examination of static foot rest and walk dynamics, performed with "DINATTO 2,5" machine. The patients were randomized to receive 300 mg/die i.v. of Clodronate in 250 cc of physiological saline during first 10 days and then 100 mg i.m. of Clodronate any 3 days up to day 30 (CLD group), or 100 mg i.v. of Neridronate in 250 cc of physiological saline at days 1 and 30 (NER group). The study suggests that only Clodronate performs a double therapeutic action; in patients with vertebral fracture, Clodronate supplies an anti-osteoporotic action, by reducing bone resorption and a basic antalgic action, improving the highly painful symptomatology and allowing a reduction in NSAID intake.

P430SA. STRONTIUM RANELATE REDUCES THE RISK OF VERTEBRAL FRACTURES IN POSTEMENOPAUSAL WOMEN WITH OSTEOPENIA

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Strontium ranelate 2 g/day is an orally active anti-osteoporotic agent which reduces over 3 years the risk of vertebral fractures by 41%, non-vertebral fractures by 16% and hip fractures by 41% in postmenopausal women with osteoporosis based on results of a phase III program including 2 international randomised, double blind, placebo controlled clinical studies: SOTI (1649 patients with low lumbar BMD and having at least one prevalent vertebral fracture) and TROPOS (5091 patients with low femoral neck BMD).

An analysis was performed on the pooled data from SOTI and TROPOS studies. Amongst the whole population, 409 patients with lumbar and/or femoral neck T-score between −1 and −2.5 and both T-scores > −2.5, with or without prevalent fractures were included and received strontium ranelate 2 g/d orally or placebo for 3 years, associated to calcium and vitamin D supplementation according to the patient's status. Vertebral X-rays were performed yearly.

No relevant differences between groups were detected for the main baseline characteristics: mean(SD) age: 73(6) years; time since menopause: 25(8) years; mean(SD) Lumbar T-score: −1.20(1.15); mean(SD) Femoral Neck T-score: −2.06(0.44).
In the intent-to-treat population, strontium ranelate was associated with a 62% reduction in the relative risk of vertebral fracture over 3 years (as assessed through semi-quantitative method by a central reading centre) (RR = 0.38, 95%CI[0.21;0.70], p = 0.001). Amongst the 409 described patients, 43% of patients presented an osteopenia according to their BMD values (described above) and had no prevalent fracture. In this subgroup, strontium ranelate reduced the risk of vertebral fracture by 72% over 3 years (RR = 0.28; 95% CI [0.07; 0.99]) (p = 0.045).

We infer that strontium ranelate, a new anti-osteoporotic agent, reduces the risk of vertebral fractures in women with osteopenic range of BMD by 62% and in women with osteopenia without any prevalent fracture by 72%.

P431SU. THE HORIZON-TOP TRIALS PROGRAM: A RANDOMIZED, DOUBLE-BLIND COMPARISON OF ZOLEDRONIC ACID AND RISEDRONATE IN THE TREATMENT OF PAGET'S DISEASE OF BONE

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Bisphosphonates are the mainstay for the treatment of Paget's disease of bone (PDB). The ongoing **H**ealth **O**utcomes and **R**educed **I**ncidence with **Z**oledronic Acid **O**nce Yearly – **T**reatment **O**f **P**aget's (HORIZON-TOP) program was designed to demonstrate non-inferiority of zoledronic acid (ZA; a potent third generation, N-containing bisphosphonate) to risedronate (RIS) for the treatment of PDB. HORIZON-TOP is the largest program to date in PDB and comprises two similarly designed, international, multi-center, randomized, double-blind trials. 357 patients were randomized to either one ZA 5 mg i.v. infusion (15 minutes) and 2 months daily oral placebo, or one i.v. placebo infusion and 2 months daily oral RIS 30 mg, and followed for 6 months. The primary endpoint is the proportion of patients achieving a therapeutic response, defined as a reduction of at least 75% from baseline in serum alkaline phosphatase (sALP) excess or sALP normalization at the end of six months. The secondary efficacy endpoints are reductions in serum C-telopeptide and urine alpha C-telopeptide levels and reductions in pain severity and interference as measured by the Brief Pain Inventory. Additional exploratory efficacy parameters are propeptide of N-terminal type I collagen, physical and mental quality of life and gait speed. Safety evaluations include the monitoring of clinical and laboratory adverse events. Following the 6-month trial period, responders (patients who achieve the primary endpoint) were offered the opportunity to enter an extension observation period, during which the sALP level is monitored every 6 months until it returns to within 20% of the baseline value. Therefore, the potential for rapid and sustained remission in PDB with ZA will be evaluated by serial monitoring of biochemical markers of bone turnover. Patient follow-up will continue until offset of effect is observed. Furthermore, this trial will provide an opportunity to assess the acceptability and convenience of i.v. bisphosphonate administration to patients, compared with oral dosing.

P432MO. KYPHOPLASTY IN THE TREATMENT AND PREVENTION OF COMPRESSION VERTEBRAL FRACTURES

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In the management of osteoporotic vertebral fractures Kyphhoplasty is presently able to solve the spinal deformation and the painful symptomatology and it can also prevent further bone loss and fracture, but the increased risk of this complication is not well evaluated. From November 2002 to November 2003 we have treated 78 patients with vertebral compression fractures (VCF) due to osteoporosis, in 25 cases there were present two or more vertebral body fractures. All the patients underwent percutaneous treatment with Kyphoplasty in a period ranging from 30–180 days after VCF. In 46 patients treated early (30–60 days after VCF) we have not found new fractures at the follow up, on the other side in 32 patients treated after more than 90 days from VCF, we have noted a new vertebral fracture at the short-term follow up (1–3 months) in 12 of them. All the new fractures are present in a lower level of the column with respect to prior treatment; 8 of them have had two or more vertebral fractures. In these cases we have proceeded to a new Kyphoplasty and no other VCF were found at this time.

The presence of one or more vertebral fractures increase risk of sustaining a vertebral fracture by 5 fold per year and the early treatment is basic in the prevention of further VCF.

Kyphoplasty is in our experience a valid treatment option both to solve the vertebral fracture and to prevent new VCF.

P433SA. A FIVE-YEAR ALENDRONATE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS IN PATIENTS WITH IMPAIRED FASTING GLUCOSE

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Background and Aims: While osteoporosis can nowadays be effectively treated, it is important that osteoporosis treatment regimen does not worsen patients concomitant diseases. The aim of this study was to monitor in patients with impaired fasting glucose (IFG: serum levels of fasting glucose ≥6.1 and ≤6.9 mmol/l) that are treated for postmenopausal osteoporosis both bone mineral density (BMD) and levels of blood glucose and HbA1c.

Material and Methods: Eleven women with postmenopausal osteoporosis (T-score below −2.5 SD) and IFG were enrolled in a five-year prospective study. Patients age was 59 to 74 years old (mean: 65 years) and 8 to 25 years (mean: 16 years) after the menopause. They were treated with alendronate (10 mg/d during the first four years, 70 mg/w during the fifth year) in combination with 500-mg/d elemental calcium. During the five-year follow-up, the BMD in the lumbar spine (L1–L4) and left hip was measured in all patients using dual energy X-ray densitometry (Hologic QDR 2000+). The serum levels of glucose, HbA1c, Ca, alkaline phosphatase (ALP) and creatinine were measured every 6 months. All patients were treated for IFG only with diabetic diet.

Results: In 5 years, BMD increased on average by 8.1 % (range 0.2–9.6 %) in the lumbar spine (L1–L4) and by 4.8 % (range 0.5–8.7 %) in the left hip. Levels of Ca, ALP and creatinine were within normal limits during the treatment, and no clinical side effects were observed during the study. Serum levels of fasting glucose showed no statistically significant changes during the alendronate treatment, with an average value of 6.3 mmol/l (range 6.1–6.6 mmol/l) in the beginning of the treatment and 6.5 mmol/l (range 6.4–6.8 mmol/l) after 5 years of the treatment. Similarly, the average level

of HbA1c was 6.5 % (range 6.2–6.6 %) at the start of the treatment and 6.7 % (range 6.2–6.8 %) after 5 years of the treatment.

Conclusions: Results of our study indicate that osteoporosis can be effectively treated in patients with IFG for up to five years, while maintaining (with little variation) serum levels of fasting glucose and HbA1c.

P434SU. EFFICACY OF INTRAMUSCULAR CLODRONATE (DIFOSFONAL) IN PATIENTS WITH COLLES' FRACTURE

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The recent literature underlined the efficacy of the bisphosphonates on mineralisation of bone. However only clodronate has a considerable antalgic effect without any interference on callus repair after Colles' fracture. In a randomized and prospective study we studied 40 postmenopausal women whether 12 weeks treated with clodronate 100 mg/d i.m. for the first week and that 100 mg i.m./weekly (clodronate group) or calcium 1000 mg and 880 UI vitamin D3 (placebo group). Treatment was given for 12 weeks. The bone mineral density (BMD) of the forearm was measured with DEXA (Hologic 1000W) at 1, 3, 6 and 12 months after the fracture. The efficacy of intramuscular clodronate on mineralisation of fracture callus in this study was substantial, the BMD having increased by 23% after 3 months of clodronate treated. The intramuscular clodronate was usually well tolerated. In conclusion the pharmacologic features of the intramuscular clodronate offer new opportunities to the treatment for the mineralisation of callus after Colles' frecture. Intramuscular clodronate was proved to have a peculiar and fast activity on bone pain.

P435MO. ANTALGIC EFFICACY OF THE BISPHOSPHONATES IN VERTEBRAL FRACTURES OF RECENT ONSET

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The effectiveness of the bisphosphonates in increasing bone mass and in reducing the risk of fractures in patients suffering from osteoporosis has been widely documented in the literature. The same cannot absolutely be said as regards their possible antalgic effectiveness. The authors therefore assess the reduction in pain in osteoporotic patients suffering from vertebral fracture on recent onset, treated with 3 different bisphosphonates (clodronate, alendronate, risedronate). Apart from the traditional visual analogic scale, foot support static analysis and step dynamics were employed using a computerized objective method. The results obtained confirmed that i.m. clodronate (Difosfonal) leads to a marked reduction in pain symptomatology, unlike alendronate and risedronate. It can be stated that clodronate presents noteworthy antalgic activity compared to alendronate and risedronate, reducing the extremely intense and frequent pain symptomatology in the most feared complication of osteoporosis.

P436SA. THE EFFECTIVENESS OF ALENDRONATE, RISEDRONATE AND CALCITONIN TREATMENT IN POSTMENOPAUSAL OSTEOPOROSIS

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The aim study was to investigate the efficacy of alendronate, risedronate and calcitonin in the treatment of postmenopausal osteoporosis

Fifty four patients with postmenopausal osteoporosis were randomly assigned into equal 3 treatment groups. First group received 10 mg/day alendronate, second group were treated with 5mg/day risedronate, three group received 200 IU/day calcitonin. All groups received a daily supplement of 1000 mg calcium. Treatment regimens were applied for 12 months. Dual energy X-ray absorptiometry (DXA) was used for the measurement of bone mineral density (BMD) of the lumbar spine and left hip before and after the study period.

In the first group, a significant increases in lumbar spine (L1-L4) and left hip (total) BMD was detected in patients with postmenopausal osteoporosis at the end of first year ($p < 0.03$, $p < 0.001$ respectively). A significant increase both regions determined in the second group at the end of first year ($p < 0.001$, $p < 0.01$ respectively). In the three group, a significant increases in both sites was observed in the patients at the end of first year ($p < 0.05$, $p < 0.01$ respectively).

This study clearly demonstrates the efficacy of alendronate, risedronate and calcitonin in preventing the bone loss related to postmenopausal osteoporosis.

P437SU. TWO YEARS EXPERIENCE IN THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS WITH ALFACALCIDOL

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Postmenopausal osteoporosis is characterised by an increased resorption of trabecular bone mainly due to a higher responsiveness of osteoblastes to parathormone (PTH) action, a consequence of estrogen deficit. Increased resorption results in reduced secretion of PTH, reduced renal activation of the 25-OH-cholecalciferol in 1.25 (OH_2D_3 and a reduction of the absorption of intestinal calcium. Treatment with alfacalcidol is physiological; it has been shown to be effective in increasing intestinal absorption of calcium and reducing the loss of bone mass.

Aims: To determine the efficacy of alfacalcidol (Alpha D_3®) on bone mass.

Method: 1465 patients had bone densitometry performed using DXR-BMD (Pronosco-X-posure System). From among these 1018 were in postmenopause: inclusion criteria were healthy women with osteopenia: 391 patients (T score: −1 to −2.4) and osteoporotic women: 165 patients (T-score lower than −2.5). The other 462 women were represented by the control group. The treatment: the group with osteopenia received 0.5 μg alfacalcidol/day, and the group with osteoporosis 1 μg alfacalcidol/day. After 12 and 24 months all patients ware evaluated for change in BMD.

Results: In the group with osteopenia the BMD increased by 3.4% and 2.3% after one and two year respectively. In the group with osteoporosis, BMD increased by 1.8% and 2.4% after one and two years respectively. The decreased of BMD in control group was between 1.8% and 3.4% in the first year and second year respectively.

Conclusions: Alfacalcidol confirmed the abolishment of the loss of bone mass in our study, and also increased the bone mass density significantly compared with the control group.

P438MO. ORAL IBANDRONATE PRODUCES SIGNIFICANT ANTI-FRACTURE EFFICACY WHEN ADMINISTERED LESS FREQUENTLY THAN CURRENT BISPHOSPHONATES

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Aims: Patients taking current oral bisphosphonates must follow stringent dosing guidelines every day or week. This may cause inconvenience, thereby reducing therapeutic compliance and resulting in suboptimal clinical outcomes. Ibandronate is a potent nitrogen-containing bisphosphonate that has been designed to address unmet needs in osteoporosis management, namely dosing simplicity, leading to greater dosing convenience. A multinational, phase III study recently examined the efficacy and tolerability of an intermittent ibandronate regimen given with an extended between-dose interval of >2 months (oral iBandronate Osteoporosis vertebral fracture trial in North America and Europe: BONE).

Methods: In this study, postmenopausal women (aged 55–80 years, ≥ 5 years postmenopause) with osteoporosis (BMD T-score ≤ −2.0 at the lumbar spine in ≥1 vertebra [L1-L4], 1-4 prevalent vertebral fractures [T4–L4]) were randomised to receive placebo (n = 982) or oral intermittent ibandronate (20mg every other day

for 12 doses every 3 months; n = 982) or oral daily (2.5mg; n = 982) ibandronate for 3 years. All participants received daily calcium (500 mg) and vitamin D (400IU) supplementation.

Results: After 3 years, oral intermittent ibandronate significantly increased lumbar spine and total hip BMD (5.7% and 2.9%, respectively; $p < 0.0001$ for both sites versus baseline), significantly decreased biochemical markers of bone resorption ($p < 0.0001$) and formation ($p < 0.0001$), significantly decreased height loss ($p = 0.0144$) and significantly reduced the risk of new vertebral fractures (by 50%; $p = 0.0006$), relative to placebo. This is the first time that a bisphosphonate has prospectively demonstrated antifracture efficacy in a regimen with a dosing interval > 2 months, in the overall population of a well-designed trial. Oral intermittent ibandronate was well tolerated, with an incidence of adverse events similar to placebo. This is notable as: one third of patients had pre-existing upper GI disorders; patients received a cumulative ibandronate dose of 240 mg in just 24 days.

Conclusions: The robust findings from this study demonstrate that ibandronate is highly effective when given in less frequent regimens than once weekly. As a result, a large trial has been initiated to investigate a simple, once monthly oral ibandronate regimen, which is predicted to enhance patient management in postmenopausal osteoporosis by optimising dosing convenience and consequently improving treatment adherence.

P439SA. USE IN HCV-HIV-INFECTED WITH BONE MASS LOSS OF CALCITONIN AND ALENDRONATE

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Introduction: Hepatitis C virus (HCV) is an RNA virus is a major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Owing to shared routes of transmission, HCV and human immunodeficiency virus (HIV) coinfection are common, affecting approximately one-third of all HIV-infected persons. Low bone mineral density may be yet another common adverse effect of protease inhibitor combination therapy.

Objective: Determining if the combined use of calcitonin and alendronate influences on bone mass loss.

Material and method: We studied for 6 months 21 women who were 44 to 64 years old at base line, were within 2 and 11 years of menopause, and had a bone mineral density at the lumbar spine between 145 mg/cc and 50 mg/cc measured by the QBMAP system with a spiral CT Picker PQ-S densitometer at L2, L3, L4 and L5. Of all the women, 10 were assigned to 10 mg of alendronate, 800 IU of vitamin D3 and 1 g of calcium carbonate supplementation. 11 were treated with 10 mg of alendronate, 200 IU of intranasal calcitonin, 800 IU of vitamin D3 and 1 g of calcium carbonate supplementation. The SPSS programme was used for statiscal analysis.

Results: The characteristics of the women recruited for both groups were similar. Mean mineral bone density at the lumbar spine was between 1 and 3 DS below the mean value for 30 years old normal premenopausal women. After a treatment of 12 months no statistically significant difference was found among both groups as for the bone mineral density at the lumbar spine.

Conclusions: It is necessary to carry out a wider and longer study, among

HIV-HCV patients, but it seems that alendronate contribute advantages to decrease bone mass loss, at least, at lumbar spine, without calcitonin. Osteoporosis is a multifactorial disease, maybe its best treatment and prevention is combining several drugs and attitudes. It would be good to test several adjusted doses to decrease side effects. These results can be interesting for HIV-HCV infected, who are prescribed a lot of medication.

P440SU. PULSED SIGNAL THERAPY (PST) FOR THE TREATMENT OF OSTEOPOROSIS

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Aims: Biophysically, it is known that bone possesses electromechanical properties and natural biopotentials essential in bone remodeling. Pioneers, Yasuda, Bassett and others, observed that repair and adaptive remodeling processes, occurred in response to mechanical loading and that such responses could be elicited by an electrical stimulus – an exogenously applied electrical current, including PEMF.

Methods: Recently, science has focused on the biomolecular properties of bone and cartilage, and the similarity of their lineages, such that reconstitution of cartilage has been found to essentially parallel that of bone. BMSCs (bone marrow stromal cells) have been shown to differentiate into osteoblasts, chondrocytes and specialized connective tissue cells, giving rise to skeletal tissues. Additionally, several factors, including growth factors, affect BMSC proliferation rate and osteogenic, and/or chondrogenic, potential, and FGF2 has been shown to maintain BMSCs in an immature state as chondro-osteo-progenitor cells. The latest research findings have identified Cbfa1 as a late transcription factor in both bone and cartilage development.

Results: Biophysically, it has been established that PST® emulates the innate physiological and mechanical stresses evoked, and required, in bone formation. It passively induces fluid flow and ionic displacement, thereby generating a piezoelectric (''streaming potential'') and eventually activating various signaling network paths – as in mechanotransduction. Basically, a specific pulsed signal is carried on an ELF electromagnetic field, and transferred to bone and through adjacent tissue, resulting in reconstitution of the disturbed electrical field, reestablishment of innate regenerative processes, and reactivation of cartilage, bone, and other connective tissue. Following more than 25 years of PST® success in the treatment of connective tissue disorders, a pilot study on postmenopausal women with osteoporosis was initiated. Preliminary results have demonstrated a significantly increasing trend in vBMD (namely, trabecular bone density) post-PST® and an associated decrease in pain. International medical regulatory approval for the treatment of osteoporosis with PST® technology was granted in 2003.

Conclusion: PST® has already been shown to increase collagen levels, and other matrix components in cartilage, such that protocols to investigate PST® anabolic effects in bone, by increasing mRNA expression levels (BMP-2 and BMP-4 by rtPCR, for example), are being developed.

P441MO. EFFICACY OF INTRAMUSCULAR CLODRONATE IN PATIENTS WITH COLLES' FRACTURE

Priano F[1], Versace F[1], Coari GC[2]; [1]Casa di cura ''Villa Montallegro'', Genova, Italy, [2]Casa di cura ''S. Camillo'', Forte dei Marmi, Lucca, Italy

Recent literature underlined the efficacy of bisphosphonates on mineralisation and resorption of bone. However only clodronate has a considerable antalgic effect without any interference on callus repair after Colles' fracture. In a randomized and prospective study of 40 postmenopausal women with Colles' fracture we studied wthether 12 weeks of treatment with intramuscular clodronate (Difosfonal). The patients were randomized into 2 groups: CLD group (100 mg/d of im clodronate for the first week and that 100 mg weekly) and PLC group (1000 mg of calcium and 800 IU of vitamin D3/d). The BMD (bone mineral density) of the forearm bones was measured with DEXA (Hologic 1000 W) 1, 3, 6 and 12 months after the fracture. The pharmacologic features of the intramuscular clodronate offer new opportunities to the treatment for the mineralisation of callus after Colles' fracture, and clodronate was proved to have a peculiar and fast activity on bone pain: a 100 mg/d of im clodronate regimen has shown to remarkably relieve patients from pain in the first week of administration while reducing analgesics consumption to a great extent if compared to the placebo group.

P442SA. INTERDISCIPLINARY APPROACH TO VERTEBROPLASTY AND BALLOON KYPHOPLASTY IN THE TREATMENT OF OSTEOPOROTIC VERTEBRAL COMPRESSION FRACTURES

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Aim: Osteoporotic vertebral compression fractures (VCFs) are associated with a series of clinical consequences leading to

increased morbidity and even mortality. Traditional medical options including bed rest, analgesics and bracing have proven to be insufficient. Furthermore, the problem of osteoporosis is underestimated and often not diagnosed. Therefore, early diagnosis and therapeutic intervention is desirable in order to remobilise patients and prevent further bone loss. Here, vertebroplasty and balloon kyphoplasty may provide immediate pain relief by minimally invasive fracture stabilisation. Due to the complex nature of systemic osteoporosis coupled with the intricate biomechanics of vertebral fractures, patient selection and follow-up should be conducted in a clinical setting which is ideally treated in an interdisciplinary manner by the rheumatologist and spine surgeon.

Method: With vertebroplasty, a needle (usually a bone biopsy needle) is percutaneously introduced into the affected vertebral body via a transpedicular or extrapedicular approach. Bone cement (polymethylmethacrylate) is then injected directly into the vertebral body at moderate to high pressure at low viscosity in order to achieve trabecular filling. Balloon Kyphoplasty, which involves the insertion of an inflatable bone tamp into the fractured vertebral body, is a modification of vertebroplasty that has the potential to reduce kyphosis and restore the normal sagittal alignment of the spine. Balloon Kyphoplasty also increases operative safety, as PMMA is injected at high viscosity and low pressure into the cavity created during balloon inflation.

Results: Biomechanically, both procedures are very efficient in restoring vertebral strength and alleviating spinal pain. However, the sagittal balance of the spine should be taken into account. While vertebroplasty essentially freezes the deformity, balloon kyphoplasty has been found to reduce segmental kyphosis on average by 6–18°.

Conclusion: While patients appear to benefit from this both procedures, neither procedure alone has been shown to prevent further vertebral fractures. Hence, it is of outmost importance to inhibit the vertebral fracture rate in these patients with continued pharmacotherapy and physiotherapy.

P443SU. EFFECT OF SODIC ALENDRONATE ON BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

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Aim: To evaluate the effect of sodic alendronate on bone mineral density in postmenopausal women.

Methods: 35 patients had been studied in observational nonrandomized prospective study at Women's Health Reference Center, São Paulo, Brazil, were treated with 10 mg of sodic alendronate plus 1 mg of calcium carbonate per day for 24 months. Basal and final bone mineral density had been evaluated by DEXA of lumbar spine and femoral neck.

Results: Basal lumbar spine was 0.867 g/cm^2 and after 24 months was 0.914 g/cm^2 (Increase 5.5%). Basal femoral neck was 0.783 g/cm^2 and after 24 months was 0.800 g/cm^2 (Increase 2.2%). No patients evidenced clinical rip during the treatment.

Conclusion: Sodic alendronate can reduce the risk of rip in postmenopausal women.

P444MO. HORMONE THERAPY IN THE TREATMENT OF OSTEOPOROSIS: DILEMMA AT THE BEGINNING OF THE MILLENNIUM

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Estrogens can be utilized to prevent bone loss, which results in osteoporosis. In case of established disease, estrogens can stabilize or even increase the bone mineral density. It is proven that estrogens have a favourable effect in 90-100% of women, independent of age.

In general, estrogens should not be prescribed isolated. Consequently, estrogenprogestative combined hormone therapy is indicated in women who have an uterus. Progesterone protects in an effective way against endometrial cancer. The majority of the women who were hysterectomized can make isolated use of the estrogens in their different form of administration.

Hormone therapy can contribute to prevent postmenopausal osteoporosis, but should not be used as the first choice. It presents as a secondary advantage and offers a certain protection for the bones when it is administered during a short period of time with the intention to reduce climacteric symptoms. When they are reduced or eliminated, other nonhormonal therapies must be considered.

In determined situations, hormone therapy can be appropriate when the menopause begins near the age of 40 years, particularly if the woman presents multiple risk factors for the disease and when osteodensitometry reveals reduction of bone density. It is important to individualize the hormonal treatment in each woman with a rigorous clinical and laboratorial follow-up.

Hormone therapy is beneficial for bone health, but its use implies risks, which must be evaluated. Considering this, the authors analyse the importance of individualized hormone therapy and its therapeutical limits.

P445SA. COMPARISON OF ALENDRONATE AND RISEDRONATE IN THE TREATMENT OF OSTEOPOROSIS IN MEN

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Biphosphonates are widely used in the treatment of osteoporosis in women, however these drugs are also used in the treatment of osteoporosis diagnosed in men.

A group of 36 men with osteoporosis was examined. The patients from Group I were administered alendronate at the dose of 10 mg daily, while the patients from Group II received risedronate at the dose of 5 mg daily, for 12 months. In addition, all the patients obtained calcium and vitamin D in individually calculated doses, based on serum and urine calcium concentrations. Densitometric examination of the hip was performed in all the patients at the beginning of the therapy and after 12 months of treatment.

BMD in the femoral neck increased by 4.7% in Group I ($p < 0.01$), and by 10.1% in Group II ($p < 0.05$) following bisphosphonate treatment vs BMD value before treatment. The observed changes of total hip BMD values and of BMD in other hip subregions were not statistically significant. Dyspeptic symptoms were observed in one patient from Group I, and in two patients from Group II. Those patients continued the therapy with bisphosphonates, combined with specimens protecting gastric mucosa. We did not observe new osteoporotic fractures in those patients.

Both alendronate and risedronate caused an increase of BMD in the femoral neck and their efficacy did not differ in any significant way. Alendronate seemed to be better tolerated by the patients than risedronate.

P446SU. ADIPONECTIN: A PATHOGENIC FACTOR OR A CONFOUNDER OF BONE MASS?

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Methods: Participants were 290 women selected from a population-based cohort to represent various distinct forms of body fat distribution (leanness, central, peripheral, and general adiposity). Central and peripheral (arm + leg) fat mass as well as bone mineral density (BMD) at the hip and spine were estimated with dual energy x-ray absorptiometry. Furthermore, we measured serum adiponectin, estradiol, SHBG and calculated free-estradiol index as estradiol/SHBG.

Results: Women with peripheral adiposity showed the highest (4.95 ± 0.23 μg/ml), whereas women with central adiposity the lowest (3.12 ± 0.20 μg/ml) levels of serum adiponectin ($p < 0.05$). In contrast, women with central adiposity revealed the highest ($1.56 \times 10{-}3$ ng/ml, $n = 48$), whereas women with peripheral

adiposity the lowest ($0.781 \times 10\text{-}3$, $n = 44$) levels of serum free-estradiol ($p < 0.05$), independently of total fat mass. There was a significant inverse correlation between serum free-estradiol and adiponectin even after adjustment for age, BMI, and central fat mass ($r = -0.29$, $p < 0.001$). Free-estradiol was directly correlated with BMD at both measured anatomical sites ($p < 0.001$). Although adiponectin was significant inverse correlate of both spine and hip BMD, these assocations were no longer apparent after ajustment for free-estradiol ($p > 0.05$).

Conclusions: The results suggest that the true mediator of the bone protective effects of visceral fat mass is endogenous free-estradiol, which either directly or indirectly inhibit the secretion of adiponectin. Accordingly, adiponectin seems to be a confounder of BMD. However, further research is required to clarify whether the antiatherogenic effects of adiponectin has any implications for hip BMD.

P447MO. NO EFFECT OF VITAMIN A INTAKE ON BONE MINERAL DENSITY AND FRACTURE RISK IN PERIMENOPAUSAL WOMEN

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Background: In recent studies from Sweden and USA, a high vitamin A intake has been associated with low bone mineral density (BMD) and increased fracture risk. In Sweden and USA, food items such as milk and breakfast cereals are fortified with vitamin A, whereas in Denmark there is no mandatory fortification with vitamin A.

Aim: We investigated relations between vitamin A intake and BMD and fracture risk in a Danish population consuming mostly unfortified food items. Within a population-based cohort study in 2016 perimenopausal women, associations between BMD and vitamin A intake was assessed at baseline and after 5-year follow-up. Moreover, associations between baseline vitamin A intake and 5-year changes in BMD were studied. Finally, fracture risk was assessed in relation to vitamin A intake.

Results: In our cohort, dietary retinol intake (0.53 mg/day) was lower than the intake reported in recent studies form Sweden (0.78 mg/day) and USA (1.66 mg/day). Cross-sectional and longitudinal analyses showed no associations between intake of vitamin A and BMD of the femoral neck or lumbar spine. Neither did BMD differ between those 5% who had the highest- and those 5% who had the lowest vitamin A intake. During the 5-year study period, 163 subjects sustained a fracture (cases). Compared to 978 controls, logistic regression analyses revealed no difference in vitamin A intake.

Conclusion: In a Danish population, average vitamin A intake is lower than in Sweden and USA and not associated with detrimental effects on bone. Further studies should explore whether fortification of food items (as in Sweden and USA) is harmful to bone health.

P448SA. ABOUT ESTROGENS EFFECTS ON MEN: BONE MORPHOLOGY, MINERAL DENSITY AND RESISTANCE INDEX IN TWO ESTROGEN-DEFICIENT MALE ADULTS

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The effects of estrogens on bone tissue in males have not been well established. We had the opportunity to observe several bone parameters in two estrogen deficient men (both were 28 years old). They presented a typical phenotype of a congenital aromatase deficiency. The first patient presented an homozigous mutation of the exon V of the CYP 19 gene from ACG to ACA affecting the splicing of the RNA and associated with an androgen deficiency and a crypthorquidism. He had dolic biotype features in head, mainly due to basal jaw development. Mid-shaft cortical area (Act), cross sectionals moments of inertia (CSMI), volumetric bone mineral density (vBMD) and stress-strain indexes (SSI) of bone resistance to deformations were estimated at different sites (tibia, radio, jaw) by tridimensional tomography (XCT 3000-Stratec, Pforzheim). Structural deformations were clearly observed at mid-shafts Act; over-normal vBMD values were clearly observed at jaws (from 1255-1355 mg/cm^3); threshold analysis showed an irregular distribution of the area with a high bone density (over 700 mg); $SSI_{polar}$and $SSI_{x.axis}$ indexes were apparently normal but CSMIs were variable.

The second patient had a mutation in the exon IV from ATG to AGG, methionine to arginine. But it is an heterozygous mutation of the CYP19 gen. He presented a phenotype of estrogen and aromatase deficiencies. Cephalometrywas over normal value for the race and sex (+3 SD). Specifically, perialveolar, not basals, are preserved. Histomorphometric analysis of transiliac bone biopsy performed after double tetracycline labelling showed a high bone turnover with an active osteoblastic synthesis. The eroded surfaces were 2.7 fold higher than controls, osteoid surfaces and volume were increased by x2.6 and x2.8 respectively. The mineralising surfaces were extended at 21.7 %. There was no mineralization defect. These findings may be explained from different viewpoints, including: 1- Mechanically, bone alterations may correspond to a non-directional modelling and remodelling since born, and cortical changes may be an adaptive mechanism 2- Metabolically, long-term non-hormonal controlled bone turnover may disturb directional modelling and remodelling resulting in deformations. Despite mechanisms, bone quality in these two males without estrogens synthesis is abnormal, although resistance is still acceptable.

P449SU. DO WE HAVE TO REVISE THE PLASMA VALUES OF 25OHD IN NORMAL ELDERLY SUBJECTS?

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The normal plasma level of 25OHD in elderly population is not yet universally accepted. According to the values provided by the kits we use, the lower limit of normal is 25 nmol/L. It is, however, crucial in elderly population to reach appropriate values of 25OHD in order to avoid secondary hyperparathyroidism and its deleterious consequences for skeleton integrity.

We, therefore, looked at the relation between 25OHD levels and the values of iPTH as measured by 3 different assays: intact PTH [IRMA (NV 10-60 pg/ml)], "automated iPTH advantage" (NV 11–74 pg/ml) [comprising for both former assays PTH (1–l84) + (7–84)], bio-iPTH (NV 7–43 pg/ml) in 30 ambulatory postmenopausal females aged 67.7 (6.4 SD) years with an initial 25OHD level lower than 75 nmol/L, prior to and after supplementation with daily vitamin D (880 IU) plus 1 g elemental calcium for 2 months. After therapy, there was no significant change neither in serum calcium nor in creatinine clearance. IPTH values decreased significantly in the 3 dosages. The correlation between assays was the best between bio-iPTH and "automated iPTH" both prior to and after therapy ($r2 = 0.96$ and 0.94, respectively). There was no apparent excessive production of the 7–84 PTH fraction neither before nor after therapy.

The cut-off of 25OHD for a iPTH level just below the upper limit of normal in the 3 kits was between 62.5 and 75.0 nmol/L, thus values significantly higher than those usually considered as normal according to the kits used in clinical practice.

In conclusion, to avoid secondary hyperparathyroidism in elderly population, even ambulatory, the lower limit of plasma 25OHD should be set at least at 62.5 nmol/L instead of 25, which means that the vast majority of elderly patients have too low values, and are exposed to secondary osteoporosis.

This value should ideally be met before any other antiosteoporotic therapy should be considered.

P450MO. HYPERPARATHYROIDISM AND OSTEOPOROSIS IN 735 WOMEN: THE NORDOS STUDY

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Primary hyperparathyroidism (pHPT) is a disorder, which is frequently asymtomatic, and the long-term implications for the bone are not fully known. Vitamin D insufficiency in the elderly is accompanied by elevation of parathyroid hormone (PTH).

The aim of the present study was to examine the relationship between serum calcium, PTH, thyroxin and bone mineral density.

Population and Method: 735 women aged 70 years old from random samples in Göteborg and malmö participated in the study. Fasting blood samples were collected and serum levles of calcium, intact parathyroid hormone (iPTH), Nichols, and free thyroxin were analysed. Bone density was measured with Hologic 4500a. Phantom measurements in hip and lumbar spine showed no significant differences between Göteborg and Malmö.

pHPT was defined as Ca > 2.40 mmol/l and PTH > 65.0 ng/l or Ca > 2.60 mmol/l and PTH > 0.0 ng/l. Age related hyperparathyroidism was defined as Ca > 2.40 mmol/l and PTH > 65 ng/l.

Results: 3.0% (N = 21) had a pHPT and 4.8% (N = 34) had age related hyperparathyroidism. Mean serum calcium in the group with pHPT was 2.53, in the group with age related hyperparathyroidism 2.30 and for the control group 2.35 mmol/l. Cut off levels for upper quartile and quintile limits of serum calcium was 2.38 and 2.40 respectively. Mean PTH in the different groups was 85.3 and 91.9 respectively and in the controls 36.1 ng/l. There was a correlation between PTH and serum calcium ($r = 0.08$, $p < 0.02$). In the group with pHPT 38% had osteoporosis, according to the WHO criteria. In women with age related hyperparathyroidism 56% had osteoporosis compared to the contorl group, 33%, OR2.6 (1.297–5.210). If pHPT was defined as Ca > 2.60 and PTH > 65 there was no relation to decreased BMD or osteoporosis.

Women with hyperparathyroidism had increased prevalence of thyroid disease ($p < 0.03$)

Conclusion: In this study of a representative sample of 70 year old women we found a higher risk for osteoporosis in women with age related hyperparathyroidism but not in those with pHPT. Elderly with age related hyperparathyroidism should be treated with calcium and vitamin D to prevent osteoporosis.

P451SA. THE ANALYSIS OF THE RELATIONSHIP BETWEEN VERTEBRAL FRACTURES, BONE MINERAL DENSITY AND THE TRABECULAR BONE ARCHITECTURE: A STUDY OF PATIENTS WITH BACK PAIN

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It is well known that bone dynamically adapts throughout life to outer forces, such as compression, extending and bending forces by structural adaptation mechanisms and that the mechanical sensitivity of octeocytes is essential in those processes.

Disturbed microarchitecture of trabecular bone leads to vertebral fractures even when flexion, lateral flexion and rotation of the vertebral column occur under physiological axial load.

Aim: Analysis of the relationship between bone trabecular architecture (bone structure) and bone mineral density as well as bone fractures in patients with degenerative changes and back pain.

Methods: 58 patients were measured using DXA and radiography methods. BMD of L3 vertebrea as well as t-score of L3 were assessed using Lunar DPX-plus. Radiographic images of L3 were digitalized using an Arcus II. Black and white mode was selected for further analysis and the histogram of intensity with 8 defined parameters was performed. All statistical analyzes were performed using the STATISTICA 5.0 software. A discriminant function analysis was performed for compute the classification functions and Mahalanobis distance for all groups. The patients were divided according to existence of fracture: with (20 persons) and without (38 persons) vertebral fractures.

Results: Significant differences were found between fractured and non-fractured patients concerning the microarchitecture of analyzed vertebrae. In the fractured group significantly disturbed trabecular bone microarchitecture of L3 was noted. Basing on microarchitecture of L3 it was possible to differentiate studied patients according to number of diagnosed fractures. Moreover, in the fractured group, but not in non-fractured, the significant relation between 8 defined parameters and BMD was found.

Conclusions: It can be concluded that analysis of microarchitecture limited only to L3 using Arcus II system allowed to differ our patients into fractured and non-fractured groups. Moreover, basing on analysis of microarchitecture of L3, it was possible to properly discriminate patients with increased risk of fracture located in other vertebrae. Lack of significant relationship between microarchitecture of L3 analyzed using our system and BMD of L3 assessed in non-fractured group indicates that mechanical competence of bone is related not only to bone mineralization but also to it's structural quality.

P452SU. INFLUENCE OF TESTOSTERONE ON BONE MINERAL DENSITY OF MEN WITH PROLACTINOMA

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Aim: To evaluate the correlation between serum testosterone (T) and bone mineral density (BMD) in 30 men with prolactinoma treated with dopamine agonists (group P) and 24 age-matched control subjects (group C). Mean time since diagnosis of prolactinoma was 48 months.

Methods: BMD was evaluated by dual energy x-ray (DXA) of lumbar spine (LS), femoral neck (FN), trochanter (TR) and total femur (TF). At this time, serum prolactin (PRL), T and SHBG were analyzed and the means of PRL and T were calculated for the period of 12 months previous to DXA.

Results: In group P, the prevalence of osteopenia was 44.4% at LS, 33.3% at FN, 30.8% at TR and 19.2% at TF. In the control group, there were no cases of osteopenia at LS and the prevalence of osteopenia at other regions was 9.1% at FN, 11.1% at TR and 11.1% at TF. Differences between groups P and C were significant at LS ($p = 0.0001$) and FN ($p = 0.043$). BMD was associated with age at LS ($p = 0.003$) and FN ($p = 0.007$). Mean serum T during the previous 12 months and by the time of DXA was below normal range in 43.3% of the patients. Testosterone was negatively associated with mean PRL during the previous 12 months ($p = 0.002$) and by the time of DXA ($p < 0.0001$). TR BMD was negatively associated with mean 12-month PRL levels ($p = 0.047$). Mean 12-month testosterone levels influenced LS ($p = 0.045$), TR ($p = 0.019$) and TF ($p = 0.037$) BMD. By the time of DXA, LS BMD was associated with PRL ($p = 0.012$), T ($p = 0.028$) and free testosterone index ($p = 0.04$). Prevalence of osteopenia was influenced by a positive family history at TR ($p = 0.016$) and TF ($p = 0.01$) and by smoking at FN ($p = 0.012$).

Conclusion: In our study, about half of the male patients treated for prolactinoma maintained low testosterone levels. Our results suggest that hypogonadism accounts for the high frequency of osteopenia in this population.

P453MO. MUSCLE AND BONE VARIABLES INTERRELATE IN NORMAL THORACIC CURVES BUT NOT IN KYPHOTIC PATIENTS: OBSERVATIONS FROM THE THIRD LUMBAR SPINE

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Bone strength and/or stability depends on the macro and microstructure adaptation of a functional part of the skeleton

with daily forces loading the area. Hence regional muscles contribute to the corresponding structure stability. As it is debatable whether exercises benefit deformed spines, as found in osteoporosis, we wanted to know upto which degree of thoracic curve muscle-bone interrelationship is conserved. Accordingly, in conditions where bone variables correlate with muscle variables, exercise should be approachable, but when it does not, it could be useless or harmless. The tomographic variables, at L3 level of 232 women, with different thoracic curve were studied by quantitative computarized tomography (QCT). Volumetric bone mineral density (vDMO), area (A) and bone mineral content (BMC) at total bone, cortical and trabecular sites; regional muscle density and areas at total, anterior (right and left sides) and posterior sites; as well as DMO, z and t scores, were assessed and correlated with anthropomorphometric parameters, including kyphosis angle as an indicator of spine deformation. Patients age (mean and SEM) was 58.6 (0.6) years; height 162.2 (0.4) cm; b.w. 69.8 (0.8) kg, including pre and postmenopausal women, with and without extra-spine fractures, and other features. Kyphosis angle (average Cob angle 42.3 range 26.6–69.2 degrees) was not associated with other fractures showing regionality. Correlation of this indicator with DMO (-0.69; $p < 0.05$), and vDMO cortical (-0.79; $p < 0.05$) vDMO trabecular (-0.65: $p < 0.05$) were significant but modest. Least square curves show that negative linearity of kyphosis angle with density, area and muscular variables is maintained up to 40 degrees of spine deformation. Over such value any relationship is completely lost. Our primary conclusions is that muscle development by exercises could influence spine stability when: 1) loading are locally applied; 2) the deformation is below 40 degrees; and 3)muscle and bone variables should be assessed before prescribing thoracic exercises in mild deformed spines. In conclusion, muscle development helps healthy people only, and/or deformations appear when the bone-muscle interrelationship is broken, suggesting a regional mechanostatic defect.

P454SA. EFFECTS OF RUNNING OR RESISTANCE EXERCISE ON BONE AGING IN MALE RATS

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71 male *Wistar* rats were submitted to different types of physical activity (sedentary control, running exercise and resistance exercise) were employed to study bone mineral density (BMD), biomechanical properties and cortical thickness. The animals were sacrificed at 3, 8 and 18 months of age. The specific training began at 3 months of age after the femur was obtained from the initial control. The running exercise was performed on a running treadmill, three times a week, for 60 min a day, at 16 m/min. The resistance exercise was performed three times a week on an effort board specially designed in our laboratory with a slope at 18 degrees with weights progressively bigger during the whole experiment. The bone density was measured using dual-energy x-ray absorptiometry and the biomechanical properties (strength and stiffness) were measured using universal test equipment *Kratos* Model k5002. The 8-month old rats had significant results in total BMD (0.2365 ± 0.007 g/cm^2) and stiffness (198.80 ± 38.61 kN/mm) in the group trained with running exercise when compared to the control or resistance exercise group ($p < 0.05$ – ANOVA). The 18-month old group had higher and significant results in total BMD (0.2388 ± 0.003 g/cm^2), Strength (154.8 ± 16.9 N) and cortical thickness (559.7 ± 54.9 m) with resistance training when compared with sedentary and running groups ($p < 0.05$). We found that the control and running groups had higher values at 8 months old and a tendency to decrease at 18 months of age. The resistance group inverted this tendency because the best and significant values of bone density, strength and cortical thickness were in the 18-month old rats. The physical activities, specially the resistance exercise, delayed the bone loss and changed the natural tendency of aging, improving the bone quality.

P455SU. A CALCIUM-RAISING MECHANISM LOWERS PTH LEVELS AND BONE TURNOVER WITH PRESERVATION OF BONE MASS INDICES IN INSTITUTIONALIZED ELDERLY AT HIGH RISK OF FRACTURE

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Introduction: Little is known on the relationship between the presence of diabetes mellitus and possible effects on bone metabolism in institutionalized elderly who are at very high risk of fracture.

Patients and methods: We compared 301 female residents with DM with 1398 non-diabetic individuals living in 95 homes for elderly. Patients age was between 70 and 100 years. Exclusion criteria were known malignancies, hypercalcemia and predefined significant impairments of liver- and kidney function. We did quantitative bone ultrasound measurements at the calcaneus, radius and the proximal third phalanx. Biochemical measurements included serum calcium, albumin, creatinine, total alkaline phosphatase, osteocalcin, serum cross laps (sCTX), PTH and vitamin D levels. Patients were prospectively followed for fractures over two years.

Results: Diabetic patients had significantly higher bone mass measurements at the calcaneal- and radial site and also higher readings at the phalanx. All analyses were performed after adjustment for age, BMI and renal function. Whereas non-diabetic residents showed an age-associated decline in bone ultrasound measurements, diabetic patients did not. In diabetic subjects serum PTH, osteocalcin and sCTX levels were significantly lower and protein-normalized serum calcium levels higher when contrasted with non-diabetic patients (see table). A total of 110 prospective hip- and 242 non-vertebral fractures occurred. Incidence rates for non-vertebral fractures were 15% (DM) and 14% (non-DM) and for hip fractures 6% (DM) and 7% (non-DM), respectively, and none of these differences were significantly different.

Table 1 Bone relevant parameters in institutionalized patients with and without diabetes mellitus (DM)

	Z-score calcaneus	Z-score radius	Z-score phalanx	Total ALP (IU/L)	PTH (pg/ml)	OC (ng/ml)	sCTx (ng/ml)	Ca (mmol/l)
NIDDM	0,027**	−0,496 **	−0,655	115	63,9**	30,4**	0,32**	2,38**
Controls	0,465	−0,787	−0,776	120	80,5	39,8	0,39	2,34

**$p < 0.01$ compared to controls

Conclusion: Bone ultrasound measurements were markedly higher in elderly institutionalized residents with DM at all ages. Our data suggest the presence of a calcium-raising mechanism that lowers PTH levels and bone turnover. These beneficial changes in bone metabolism of patients with DM may be offset by a higher propensity of falls since fracture rates were comparable to non-diabetic subjects.

P456MO. RALOXIFENE PREVENTS BONE LOSS IN CASTRATED MALE MICE

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Selective estrogen receptor modulator (SERM) raloxifene was administered to intact and castrated male mice, and its effect on tibial bones and circulatory calcium, phosphate and testosterone were compared with controls and castrated animals.

Raloxifene has estrogen agonist effects on bone but is not feminizing. Adult male strain H mice were used for the experiment and were divided into four groups of 8 animals each. 1) intact, 2) intact fed by raloxifene for 2 months, 3) animals 2 months after castration, 4) castrated mice fed by raloxifene for 2 months. Raloxifene(Evista Eli Lilly) was mixed into the diet at the dose of 0.1 mg/kg/day for 2 months. When animals were killed, blood was withdrawn from the heart and the seminal vesicles and tibia bones were removed. Bone density, ash and mineral content of the tibia were determined. Morphometric measurements were performed directly on the x-rays after maginification with fine caliper.

Raloxifene in a dose used in humans for treatment decreased the weight of seminal vesicles, an organ which is highly sensitive to the androgen effect, decreased the concentration of testosterone, but did not have any negative effect on bone density or mineral content in intact mice. When castrated mice with extraordinary low concentration of testosterone and weight of seminal vesicles were treated with raloxifene, the changes in bone density and bone mineral resulting from castration were not entirely prevented, but increased above the values of intact mice. At the same time cortical bone was lost in orchidectomized mice and this decrease in cortical thickness of femur was completely prevented by raloxifene treatment.

Therapy with estrogen agonist raloxifene in castrated mice supports the hypothesis that estrogens may also have physiological skeletal effects in male mice.

These pilot data support the theoretical usefulness of the raloxifene as a therapeutic regimen for male osteoporosis.

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P457SA. TROCHANTERIC FRACTURE OCCURRENCE ASSOCIATED WITH IMBALANCE BETWEEN SERUM STIMULATORY AND INHIBITORY INSULIN-LIKE GROWTH FACTOR BINDING PROTEINS

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Intertrochanteric fracture occurrence is associated with a more severe degree of osteoporosis than femoral neck fracture. In this study, we addressed the hypothesis that differences in skeletal fragility between the two fracture types might be related to differences in exposure to stimulatory and inhibitory components of the insulin-like growth factor (IGF) system. While IGFBP-5 modulates IGF actions on bone positively, IGFBP-4 has been documented to inhibit IGF actions on bone cells.

We measured circulating concentrations of IGF-I, IGF-II, IGF binding protein IGFBP-4, and IGFBP-5 in 69 women after sustaining a fracture of the proximal femur (50 femoral neck fractures and 19 intertrochanteric fractures, respectively). All patients were sampled within 18 hours, prior to surgery, and protein concentrations were unrelated to the time elapsed after fracture.

Compared to femoral neck fractures, trochanteric fractures were found to be associated with lower trochanteric BMD ($p = 0.01$), a deficit in circulating IGF-II and IGFBP-5 ($p < 0.001$), and an increase in serum levels of the inhibitory IGFBP-4 ($p < 0.001$), even after adjusting for age. No differences were observed in calciotropic hormones or overall rate of bone turnover (not shown). A similar deficit in serum stimulatory components of the IGF system was observed when comparing trochanteric fracture patients with elderly controls (not shown). In age-adjusted analyses on pooled data from both fracture types, trochanteric BMD was associated positively with IGFBP-5 ($p = 0.007$) and negatively with IGFBP-4 ($p = 0.02$).

These findings suggest that, in the context of age-associated osteoporosis of the proximal femur, low trabecular bone density is associated with deficiency of the IGF system. Although limited by its cross-sectional and observational design, this study provides further evidence for a partially different pathophysiology between the two types of hip fractures and supports the hypothesis that activity of the IGF system contributes to the preservation of bone mass in old age.

P458SU. CHRONIC EFFECTS OF ALUMINUM ACCUMULATION ON THE "ELASTIC" (PRE-YIELD) AND "PLASTIC" (POST-YIELD) BEHAVIOR OF RAT CORTICAL BONE

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In order to analyze the effects of Al accumulation on pre- and post-yield behavior of cortical bone, 14 rats aged 90 days received ip doses of 27 mg/d of elemental Al as Al(OH)3 during 26 weeks while other 14 remained as controls. Their femur diaphyses were studied tomographically (pQCT) and tested in bending. The load/deformation curves obtained showed the successive, linearly elastic (Hookean, pre-yield) and nonlinear, "plastic" (non-Hookean, post-yield) deformation periods of bones, separated by the yield point.

No effects on body weight were observed. Aluminemia and bone histological and ash data confirmed Al accumulation. Treatment reduced cortical bone mineralization (volumetric cortical BMD, $p < 0.01$) with a negative impact on the intrinsic stiffness of cortical tissue (Young's elastic modulus, E, $p < 0.05$). Despite the absence of any cortical mass increase (cross-sectional area), an improvement of the spatial distribution of the available cortical tissue (cross-sectional moment of inertia, MI, $p < 0.05$) occurred through a directional modulation of the modeling drifts during growth. Up to the yield point, neither the strength, strain, or structural stiffness (load/deformation ratio) of the diaphyses were affected by treatment. However, Al intoxication reduced significantly the ultimate load, Wmax and the "post-yield" fraction Wp of that load (bone "toughness", $p < 0.01$). A positive correlation between Wmax and Wp for all the studied animals as a whole was observed.

The presumably adaptive response of bone modeling (as assessed by the MI) to the induced impairment of the intrinsic stiffness (E) of bone tissue should have resulted adequate for maintaining a normal structural stiffness (load/deformation ratio) of femur diaphyses according to the bone "mechanostat" theory, but not so to provide a complete neutralization of the impaired diaphyseal strength (Wmax). Although a relative inhibition of bone formation could not be discarded, an Al-induced impairment of bone "toughness" (Wp) should have caused the striking disruption observed between effects on bone stiffness and strength. In addition to describe an unusual finding, these results suggest that the microstructural elements affecting the post-yield behavior of cortical bone in these conditions ("creeping factors") should be further investigated as a novel, promising field in skeletal research.

P459MO. PERSISTENCE OF THE DEFICIT OF BONE MINERAL DENSITY (BMD) IN ADULT SUBJECTS WITH CELIAC DISEASE IN DIETARY TREATMENT

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Low bone mass is common in celiac patients due to reduction of both calcium and vitamin D absorption and to secondary hyperparathyroidism. Although it has been demonstrated that dietary therapy may improve the BMD, normalizing vitamin D and PTH levels, it is still unclear if this is a diet-dependent effect. To clarify the role of diet in these patients, we studied 21 subjects, 15 women and 6 men, (average age 45.7 ± 1.5 y, ranging 33-35), affected by celiac disease, clinically and instrumentally diagnosed. All patients followed a dietary therapy since from the establishment of diagnosis (2.9 ± 0.5 y, range 1–9 y). Lumbar BMD evaluation by DXA technique has been performed and circulating levels of calcium, phosphorous, osteocalcin (Oc), bone alkaline phosphatase (BAP), C-telopeptide (CTX), 25-OH-vitamin D, PTH and 24 h urinary calcium and phosphate excretion have been also evaluated. Twenty-five healthy subjects, sex- and age-matched (15 women and 10 men), represented the population control. In affected patients lumbar BMD exhibited L1–L4 T-score values $= -1.84 \pm 3$): 8 patients (38.1%) were osteoporotic, 6 (28.6%) osteopenic and 7 patients (33.3%) had a normal BMD. 67% of patients showed reduction of BMD. All the patients exhibited normal levels of calcemia, phosphoremia, PTH, 25–OH vitamin D, calciuria and phosphaturia. Among four affected subject, one had low values of 25 OH vitamin D and three exhibited a partial deficit (19%), but a similar percentage was found in the control group. Bone turnover markers resulted

slightly increased (Oc 21.8 ± 2.9 ng/ml; BAP 20.9 ± 1.7 g/l; CTX 4762 ± 650 pmol/l), without statistically significant difference with the control group. A significant correlation was observed between BMD and patients age (r −0.55, $p < 0.05$) and BMD and age at diagnosis of celiac disease (r −0.68, $p < 0.01$). No significant correlation between BMD and duration of the dietary therapy has been observed. In conclusion, 2/3 of patients had low BMD, mostly not attributable to secondary hyperparathyroidism and/or vitamin D deficiency or increase of bone turnover, probably as consequence of celiac disorder. An early diagnosis is important to protect from a persistent skeletal damage. The opportunity to associate diet to drugs acting on bone turnover should be evaluated.

P460SA. INCREASED ACTIVITY OF INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-4 PROTEASE IN TROPHOBLASTIC DISEASE PATIENTS

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Trophoblastic disease is composed of hydatidiform mole, invasive mole and choriocarcinoma. 18–29% of patients with complete mole will develop a persistent trophoblastic tumor while 1–10% of patients with partial mole will develop a trophoblastic tumor. Therefore the early diagnosis and follow up after operation of trophoblastic disease are very important. Recently pregnancy associated plasma protein-A(PAPP-A) was proved to have a same role for IGF binding protein-4(IGFBP-4) protease which shows an increasing function for fetal growth by degradation of IGFBP-4 and increasing IGF in pregnancy serum. We hypothesized that trophoblastic disease which shows placental hyperplasia will also have a IGFBP-4 protease activity and this activity may be used as an early diagnosis and follow up of trophoblastic disease.

Serum samples from 6 non-pregnant, 18 pregnant(5 of 1st trimester, 10 of 2nd trimester, 3 of 3rd trimester), 12 postpartum women and 3 trophoblastic disease patients (2 of complete H-mole patients, 1 of partial H-mole patient) were collected and measrued for β-HCG, IGF, PAPP-A level and IGFBP-4 protease activity by IGF-II ligand blot analysis and electrophoresis method.

Results from in vitro protease assays using recombinant IGFBP-4 revealed that IGFBP-4 proteolysis is determined and significantly increasing during the first(56%) and second trimesters(90%) and reached a plateau by the third trimesters(94%). In the trophoblastic disease, the IGFBP-4 proteolytic activity was 97% which was nearly the same activity of terminal pregnancy. This activity was gradually decreased by 75% after 1 week, 58.7% after 2 weeks, 33% after 3 weeks of operation. The β-HCG was also decreased from 490,400 mIU/mL to 123,822.2 mIU/mL after 1 week, 1,352.3 mIU/mL after 2 weeks, 128.5 mIU/mL after 3 weeks of operation. PAPP-A level was also decreased gradually from 34.87 μg/ml to 25.5 μg/ml after 1 week, 12.0 μg/ml after 2 weeks, 2.7 μg/ml after 3 weeks of operation.

These results demonstrated that IGFBP-4 protease activity was significantly increased during pregnancy and also extremely elevated in the early stage of trophoblastic disease and gradually decreased after removal of molar tissue. Therefore it can be estimated that measuring IGFBP-4 pretease activity may play an important role for early diagnosis and follow up of trophoblastic disease.

P461SU. EFFECTS OF CADMIUM ON MINERAL STATUS AND MECHANICAL PROPERTIES OF RAT BONE

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Bone damage (osteopenia, osteoporosis and/or osteomalacia) belongs to the main effects of chronic exposure to cadmium (Cd). Recently, in a rat model of human exposure (environmental and occupational), we have noted that even low exposure to Cd may lead to disorders in bone mineral status [1, 2]. Skeletal demineralization is one of the main causes of bone deformities and fractures.

The aim of the present study was to investigate the risk of tibia fracture during chronic exposure to Cd.

Tibia samples collected from control and Cd-exposed female rats (1, 5, 50 and 100 mg Cd/L in drinking water as cadmium chloride for 12 months) were subjected to densitometric (Lunar DPX-L) measurements of bone mineral content (BMC) and bone mineral density (BMD), mechanical testing (a three-point bending test; Instron 4301 universal testing machine) and Cd analysis (AAS method, Hitachi).

In all the Cd-exposed rats, a decrease in the tibia BMC and BMD was observed compared to control. The treatment with Cd also resulted in a weakness in the bone strength reflected in a decrease in the yield load and ultimate load. The Cd-induced weakness in the tibia mechanical properties well correlated with disorders in its mineral status and Cd accumulation.

The results show that even low level exposure to Cd, corresponding to human environmental exposure, affects the mineralization of the tibia making the bone more vulnerable to fractures. This study together with our previous findings [1] confirms the hypothesis that Cd may be a risk factor for bone damage at low chronic exposure.

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P462MO. VITAMIN K STATUS IN OSTEOPOROTIC PATIENTS

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Aims: New studies show the important role of vitamin K in bone metabolism. Therefore it was the aim of our study to investigate the vitamin K status and the level of undercarboxylated osteocalcin (uOC) in patients with osteoporosis/osteopenia.

Material und Methods: Samples from 129 patients with osteoporosis/osteopenia were taken (age 68.0 years, 104 women, 25 men). The levels of serum vitamin K (HPLC) and uOC were estimated by ELISA.

Results: (see Table 1) Only 19% of osteoporotic patients show low (subnormal) vitamin K levels regarding the up to date (normal) low limit but half of patients showed increased values of uOC. Patients with severe osteoporosis (with fractures) showed a tendency (not significant) to highest values of uOC. On basis of the shown results half of the osteoporotic patients appear to have a subnormal intake (food and drug) of vitamin K.

	Mittelwert	SD	Minimum	Maximum	N
Vitamin K (ng/l)	421,11	303,60	39,00	1663,00	n = 113
μc-Osteocalcin (ng/ml)	3,30	8,45	0,05	95,00	n = 129

Conclusions: Several investigations show that low BMD and/or a higher fracture risk is associated with a 5–8 times higher concentration of uOC. There is evidence that concentrations of vitamin K, considered as normal levels today are not adequate to guarantee a full carboxylation of osteocalcin. By vitamin K supplementation in pharmacological doses uOC can be significantly reduced. We conclude that adequate vitamin K for keeping sufficient bone metabolism may be much higher than the intake for holding up normal blood coagulation. Under these aspects the actual recommendation for the daily vitamin K support seem to be not of adequate sufficiency.

P463SA. IMPAIRED GLUCOSE TOLERANCE AND BONE MINERAL CONTENT IN OVERWEIGHT LATINO CHILDREN WITH FAMILY HISTORY OF TYPE 2 DIABETES

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Research on the skeletal status of pre-diabetic (type 2) children and the important predictors of bone mass in this population is warranted. We examined the hypothesis that bone mineral content (BMC) and density (BMD) will be lower in children with impaired (IGT) versus normal glucose tolerance (NGT). Body composition, total body BMC and BMD of 185 overweight Latino children (107 boys, 78 girls, 11.9 ± 1.7 years) with family history of type 2 diabetes were measured using dual-energy x-ray absorptiometry (DXA). Blood was sampled and assayed for glucose and insulin during a 2-hour oral glucose tolerance test. Area under the insulin curve (AUC) was used to assess the cumulative insulin response to oral glucose. Insulin sensitivity (SI) and the acute insulin response to glucose (AIR) were also determined by an intravenous glucose tolerance test. Partial correlations controlling for lean mass, age, and Tanner stage revealed an inverse relationship between AIR and both BMC ($r = -0.29$, $p = 0.00$) and BMD ($r = -0.22$, $p = 0.003$). AUC was also inversely related to BMC ($r = -0.28$, $p = 0.00$) and BMD ($r = -0.31$, $p = 0.00$). Fasting ($r = -0.16$, $p = 0.04$) and 2-hour insulin ($r = -0.16$, $p = 0.04$) were inversely related to BMC; the correlations between these variables and BMD were similar. There was no significant difference in bone mineral between IGT ($n = 46$) versus NGT ($n = 138$) children. Stepwise multiple linear regression revealed that 88% of the variance in log-transformed BMC is attributed to lean mass (86%), age (1%), and AIR (1%). Similarly, log-transformed BMD was explained by lean mass (66%), Tanner stage (3%), and AUC (2%) for a total of 71% of the variance. The findings of this study suggest that in overweight children with family history of type 2 diabetes, lean mass is the primary predictor of BMC and BMD, while age, Tanner stage, and the acute and cumulative insulin responses to oral glucose make subtle independent contributions to the total variances. In addition, poor glycemic control does not seem to be detrimental to bone mass in this cross-sectional study of a group of pre-diabetic children.

P464SU. GASTRIC MUCOSA, HELICOBACTER PYLORI INFECTION AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

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Osteoporosis is a result of progressive bone loss and affects 30% of postmenopausal women. Gastrectomy is a risk factor for osteoporosis and the lost of acid gastric secretion could be involved, but disease mechanisms are still not completely understood. Experimental evidences suggest a connection between an ill-defined oxyntic mucosa factor and calcium metabolism (Persson, 1989). Helicobacter pylori (Hp) infection is associated with gastritis, glandular atrophy and endocrine cell abnormalities. We studied the lumbar spine mineral density, and the histophatological changes of gastric mucosa, including Hp infection and endocrine cell density, in postmenopausal women. 50 postmenopausal women, mean age 61.7 ± 7 y, without hormonal replacement therapy were submitted to gastroduodenal endoscopy and bone densitometry (DEXA). WHO criteria for osteoporosis was used. Tissue samples were collected from gastric mucosa for histology, and the study of parietal cells (PC; immunoperoxidase staining), and argyrophil cell (AgrC, Grimelius staining) density in the oxyntic mucosa. The diagnosis of gastric mucosa atrophy was based on PC density in oxyntic mucosa sections. Hp infection was defined by positivity in at least two methods: urease, histology and ^{13}C-urea breath test. Statistical analysis was performed with Student t test and linear regression (level of significance was 0.05). Thirty-two (64%) patients presented active pangastritis, 18 (38%) had predominantly antral gastritis ($n = 7$) or normal gastric mucosa ($n = 11$). The prevalence of Hp infection was 68% (34 patients). The prevalence of lumbar spine osteoporosis was 36% (18 patients). PC density (PC/mm^2) in osteoporotic patients ($n = 18$; 36%) was 948 ± 188, and 804 ± 203 in patients without osteoporosis ($n = 32$; 64%), $p = 0.038$. AgrC density (ArgC/mm^2) was, respectively, 190 ± 101 and 173 ± 66 in patients with and without osteoporosis ($p > 0.05$). Hp was positive in 56% (10/18) of the osteoporotic patients and in 75% (24/32) of those without osteoporosis ($p > 0.05$). As our results show that women with lumbar spine osteoporosis have a better preserved oxyntic gastric mucosa, the connection between bone metabolism and stomach would not be related to the acid secretion or Hp infection, and other factors should be considered, such as the possible participation of a gastric hormone described in experimental studies.

P465MO. ABNORMALITIES OF BONE AND CALCIUM METABOLISM IN ELDERLY PATIENTS WITH DEMENTIA

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While dementia has been supposed as a risk factor for osteoporotic fracture, vertebral fracture was evaluated in addition to ultrasonic measurement of calcaneous bones and determination of biochemical markers.

Subjects (119 females with 79.9 years of age and 43 males with 74.1 years of age) were institutionalized in dementia wards of Aino Hospital and 17 female elderly individuals without dementia with 80.2 years of age were institutionalized at Kohsaiin Hospital. Vertebral fracture was evaluated from lateral view of X-ray film of Th4 to L5. Ultrasonic measurement of calcaneous bones (SOS: speed of sound) was performed by CM-100 (Furuno, Nishinomiya).

Number of subjects with dementia who showed vertebral fracture was 140 among 163 and that in 17 non-dementia subjects were 10 and the incidence of fracture was significantly different ($p = 0.0105$ by Fisher's exact test). SOS was significantly higher in non-dementia female group than in dementia female group. Urinary deoxypyridinoline/creatinine was significantly elevated in female dementia group than in non-dementia female group. Serum bone alkaline phosphatase was significantly lower in dementia female group than in non-dementia female group. Serum 25OHD was 15.8 ± 4.0 ng/ml in dementia female group and that in non-dementia female group was 18.6 ± 4.6 ng/ml, and the difference was not significant. Intact PTH did not show significant difference either.

In conclusion, elderly patients with dementia showed higher incidence of vertebral fracture in addition to low bone mineral density, accelerated bone resorption and reduced bone formation.

P466SA. BONE MINERALIZATION AND DIETARY INTAKE OF SELECTED NUTRITIONAL COMPOUNDS IN SCHOOL AGE CHILDREN

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The aim of the study was to answer the question about the state of bone mineralization in relation to dietary intake of selected nutritional compounds in school children.

Material and methods: The study comprised 253 healthy children aged 9.5–13.5 years, attending schools in Lodz, Poland. Bone mineralization was evaluated by ultrasound examination of the calcaneous with Achilles Solo apparatus. Speed of sound (SOS), broadband ultrasound attenuation (BUA) and automatically calculated Stiffness index were analysed. In all children mean dietary intake of selected nutritional compounds, such as calcium, phosphorus, potassium, natrium, magnesium, vitamin D and protein was assessed by 3-day diet interviews.

Results: Decreased Z-score values of at least one of the ultrasound parameters were observed in 114 (45%) of school children. Mean values of ultrasound parameters were higher in the group of boys as compared to girls. Among the abnormalities in dietary intake of chosen nutritional compounds the most frequent were calcium deficiency in 224 (88.5%) of examined children (mean daily

intake in girls: 57.4% and in boys: 66.5% of reference uptake), low vitamin D intake in all school kids (22.4% of reference intake) and magnesium diet deficiency in about half of the studied group. In all examined persons high natrium consumption was found, and also increased protein intake in 84.2% and phosphorus in 76% of them. In children consuming the lowest amount of calcium (I quartile: below 479 mg/24 h) the mean values of ultrasound parameters were lower than in the group of the highest intake of this microelement (IV quartile: above 836.9 mg/24 h). In the studied group we observed statistically significant, negative correlation between protein intake and absolute values of ultrasound parameters.

Conclusions: Results of the study indicate that calcium and vitamin D deficiency and evaluated consumption of natrium, protein and phosphorus are very common in the diet of school children. These abnormalities may be the reason of the decrease of skeletal mineralization in the developmental age, and lowering of bone mass later in life, which can be connected with the risk of osteoporosis occurrence.

The study was sponsored by the State Committee for Scientific Research grant No. 3P05E13322.

P467SU. LIVER METABOLITE OF VITAMIN D AND INDICES OF CALCIUM-PHOSPHATE METABOLISM IN CHILDREN WITH OSTEOPOROSIS AND OSTEOPENIA

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Low concentration of liver metabolite of vitamin D can indicate the decreased supply of this vitamin. The literature data show that considerable deficiency in supply of vitamin D in the period of intensive growth can cause decreased bone mass.

The aim of this study was the assessment of the liver metabolite of vitamine D concentration and calcium-phosphate metabolism in children with osteopenia (OPn) and osteoporosis (OP).

Patients and methods: The study comprised 107 children aged 5.2–18 years: 43 girls and 64 boys. Among them 58 had OP (24- primary and 34- secundary, mainly caused by long glucocorticoid therapy). In all children 25OHD serum concentration was determined by radiocompetitive method; the concentration of calcium, phosphorus and magnesium by widely accepted methods and PTH by radioimmunometric method. Urine 24 h elimination of calcium and phosphorus ions was also defined.

Results: In 50 children (26 with OP and 24 with OPn) the decreased (< 20 ng/ml) concentration of 25OHD in serum was observed. In biochemical markers of calcium and phosphate metabolism such abnormalities as hypomagnesemia in 28 children (4 with OP and 14 with OPn), hypocalcemia in 15 children (11 with OP and 4 with OPn) and increased urine concentration of calcium in 13 children (adequately 6 and 7) were found. In both groups of children a significant correlation between concentration of 25OHD, bone mineralization and other biochemical markers of calcium-phosphate metabolism was not found. A statistically significant positive correlation between serum concentration of calcium and bone mineral density was observed.

Conclusions: Results of our study show a significant deficiency of vitamin D in children with OP and OPn. Moreover, our observations have an important value for etiopathogenesis and treatment of the decreased bone mineralisation in the period of intensive growth.

The study was sponsored by Medical University of Lodz from resources assigned by the State Committe for Scientific Research grant No. 502–11–831.

P468MO. PROSPECTIVE STUDY OF BONE MASS IN HEALTHY PREMENOPAUSAL WOMEN AND ITS DEPENDENCY ON CORPUS LUTEUM FUNCTION

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In fertile women with long-term amenorrhoea or shortened luteal phase, a decrease in the axial trabecular bone density has been observed. It was found that giving gestagen increased the trabecular and cortical bone density or halted the breakdown process.

Pursuing the question of the influence of endogenous gestagen on the premenopausal loss of bone mass, we performed a two-year prospective study on bone mineral content in the axial skeleton (lumbar vertebra 1) and in the distal radius (trabecular and cortical compartments) in 35 to 45-year old premenopausal women, either non-ovulating or with insufficient luteal phases (n = 21) and compared them to women of the same age with intact ovulatory cycles (n = 18). In addition, the turnover parameters deoxypyridinoline, alkaline osteoblast phosphatase and osteocalcin were measured.

After a two-year observation period, the bone density showed no statistically differing results (trabecular bone axial and peripheral, cortical bone peripheral) between the two groups. In the longitudinal comparison within the groups, no differences between study time 0 and 2 years were found. In addition the bone build-up and breakdown parameters did not demonstrate significant differences, neither between the groups nor within each group during the follow up time of two years.

Either a two-year observation period is not adequate for registering the effects of an endogenous lack of gestagen on bone mass or the length of the luteal phase does not play a significant osteopprotective role as previously assumed.

P469SA. MULTIPLE BONE FRACTURES IN THE EVALUATION OF OSTEOPENIA AND OSTEOPOROSIS RISK IN THE DEVELOPMENTAL AGE

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The aim of this study was to evaluate bone mineralization and chosen indices of calcium-phosphorus metabolism in children with multiple bone fractures.

Patients and methods: The study comprised 48 children, aged 6–17 years, with at least 3 bone fractures in anamnesis; mainly with long bones, but also with vertebral fractures. Most of these fractures were connected with low energy trauma; in 22 patients they repeated during one year. In all children bone mineralization was assessed by dual energy x-ray absorptiometry method in total body and spine programme. Osteoporosis (OP) was diagnosed when besides clinical symptoms Z-score values were below −2.0 and osteopenia (OPn) when ranged from −1.0 to −2.0. In all patients calcium, magnesium and phosphorus concentrations were determined in serum and in diurnal urine collection of these ions. The concentration of parathormone and liver metabolite of vitamin D (25OHD) were also assessed in serum. The results were evaluated individually using available standard norms.

Results: In 10/48 children OP (in 7 primary and in 3 secondary) and in 20/48 OPn (16 and 4, respectively) were diagnosed. The decreased bone mineralization was than observed in 30 children (62.5%). Such biochemical abnormalities as the decrease of 25OHD (below 20 ng/ml) in 21, the decrease of magnesium concentration in serum in 15, and hypercalciuria in 9 of the examined children were observed. The statistically significant, negative correlation between phosphorus diurnal urine elimination and absolute values of bone mineral density in total body and spine programme was assessed.

Conclusions:

1. Decreased skeletal mineralization was observed in more than half (62.5%) of the studied children with multiple bone fractures in anamnesis.
2. The decrease of 25OHD concentration in serum or hypomagneasemia seem to be factors which may be connected with repeated bone fracters.
3. The results of this study indicate that multiple bone fractures can be one of the clinical symptoms of osteopenia and osteoporosis in the developmental age and the condition of risk of osteoporosis in the future.

The study was sponsored by Medical University in Lodz from The State Committee for Scientific Research founds No 50711744.

P470SU. CALCIUM LOSS IN URINE IN THE COURSE OF RHEUMATOID ARTHRITIS

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Aims: To determine if duration of Rheumatoid Arthritis (RA) has an impact of calcium loss in urine.

Methods: 120 adult patients diagnosed with RA were studied (2002–2003). Demographics and laboratory findings were collected. Calcium to creatinine ratio in urine was used to determine calcium loss in urine. Morning sample of urine was evaluated once. Statistical analyses were performed.

Results: 118 patients entered the study: 93 women and 25 men. Their mean age was 58. The mean time of the duration of the disease was 8.4 years. Patients were allocated to 3 groups depending on disease duration. Group 1: patients up do 5 years since the first diagnosis of RA (43 patients, mean duration of the disease 2.7 years), group 2: patients in a period 6-10 years since first diagnosis (35 patients, mean duration of the disease 8.2), and group 3: patients having RA longer than 10 years (40 patients, mean duration of the disease 14.3 years). The mean score of calcium to creatinine ratio was assessed in subgroups. It was 0.36, 0.37 and 0.39 in group 1, 2 and 3, respectively ($p < 0.05$).

Conclusions: In assessed groups, patients with longer history of RA showed to have significant larger loss of calcium in urine than patients with short history. Calcium to creatinine ratio in urine increases in the course of the disease. Basing on the results of the study we consider the duration of the RA as another risk factor of developing of osteoporosis. Further studies on larger group of patients are needed.

Correlation between calcium to creatinine ratio and duration of Rheumatoid Arthritis

P471MO. USEFULNESS OF SELECTED BIOCHEMICAL MARKERS OF BONE METABOLISM IN CHILDREN WITH PRIMARY OSTEOPOROSIS AND OSTEOPENIA

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The aim of the study was to assess biochemical markers of calcium–phosphate metabolism and selected bone turnover markers in children with primary decrease of skeletal mineralisation to establish clinical course of the disturbances.

Patients and methods: The study comprised 50 children, aged 6–18 years, in whom on the basis of clinical, biochemical, radiological and densitometric estimation primary (idiopathic) osteoporosis was diagnosed in 24 and osteopenia in 26 children.

Clinical evaluation included data from the history concerning among others, occurrence of fractures and/or pain complaints, as well as present symptoms the children demonstrated on admission to hospital. All children were subjected to bone densitometry (DEXA method) in total body and spine programme. Osteoporosis was diagnosed with Z-score < -2.0 SD, while osteopenia with Z-score in the range below -1.0 to -2.0 (with other symptoms suggesting these diseases). Secondary causes of bone mass decrease were excluded in all the examined children.

Calcium, phosphorus and magnesium concentrations were determined in serum and their diurnal elimination with urine. The concentration of parathormone (PTH) was determined in serum by radioimmunometric method; liver metabolite of vitamin D (25OHD) by radiocompetitive method and osteocalcin concentration and bone alkaline phosphatase isoenzyme activity with ELISA. In urine elimination of crosslinked N-telopeptides of collagen type I (Ntx) with ELISA.

Results: The most frequently found abnormalities among biochemical bone metabolism markers were increase of osteocalcin (39/50) and decreased concentration of 25OHD in serum (in 30/50 children below 20 ng/ml). Moreover, in 20/50 children increased urine elimination of Ntx was observed.

Conclusions

1. Accelerated bone turnover expressed by the increase of both bone formation as well as resorption markers may be a factor of increased risk of fractures in the investigated group of children.

2. Decreased concentration of liver metabolite of vitamin D in 60% of children points to the necessity of its pharmacological supplementation.

The study was partly sponsored by the State Committee for Scientific Research grant No 3 PO5E 05 624.

P472SA. HYPOMAGNESEMIA IS ASSOCIATED WITH AN INCREASED BONE FRAGILITY IN POST-MENOPAUSAL WOMEN? PRELIMINARY DATA

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Several animal studies show that magnesium deficiency results in decreased bone mineral density, therefore it may be a risk factor for osteoporotic bone fractures.

Aim of our study is to evaluate the percentage of vertebral fractures in postmenopausal women and whether it is associated with redacted level of serum magnesium.

We studied 26 female patients treated with calcium and vitamin D supplementation, mean age 68.92 ± 9.28, mean years since menopause 16.86 ± 8.24, without any other known causes of hypomagnesemia and that did not show any diseases of calcium phosphate metabolism, as assessed by normal serum level of calcium, phosphate and alkaline phosphatase (Ca: 9.18 ± 0.36 mg/dl, P: 3.61 ± 0.58 mg/dl, ALP: 152.22 ± 22.25 mU/ml).

In all patients the presence of vertebral fractures was detected by interpreting lateral spine films, according to a protocol adapted from the semiquantitative technique described by Genant HK (JBMR 1993).

An increased percentage of vertebral fractures was observed in patients with redacted levels of magnesium. The mean value of magnesium in patients with vertebral fracture was 1.78 ± 0.11 mg/dl vs 1.99 ± 0.19 mg/dl in patients without fractures ($p = 0.042$ with student's t-test).

These data show that there is a statistic correlation between low serum levels of magnesium and vertebral fractures, although these are preliminary data in a small population. In order to demonstrate if hypomagnesemia is an independent risk factor for osteoporotic fractures other clinical studies are necessary.

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P473SU. THE VALUE OF PARATHORMONE IN SERA OF PATIENTS WITH OSTEOPENIA AND OSTEOPOROSIS

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Aims: The purpose of this study was to investigate the levels of Parathormone Intact-IRMA in patients presenting with osteopenia and osteoporosis and to evaluate its clinical importance.

Methods: An open clinical randomized study was designed in this research.

Total of 65 patients, with 97% women, were included in this study. The majority of them were in the age range of 50–60 years old. Osteoporosis using T-score method was found in 66% of subjects and 34% had osteopenia. The mean value of body mass index was 24.29 kg/m^2. Immunoradiometric analysis (IRMA method) was used for measuring of parathormone value in sera. The normal range for parathormone level was considered between 10–65 pg/ml. The diagnostic ultrasound procedure of the neck and scintigraphy of parathyroid glands were performed.

Results: The results obtained in this study showed the following: The normal level of I-Parathormone was found in 73.69% of patients, increased level in 15.79% and decreased ones in 10.53% of examined individuals.

No parathyroid gland enlargement was detected on ultrasound and scintigraphy procedure.

Conclusion: The measuring of I-Parathormone is a useful parameter in the evaluation and management of osteoporosis. It is especially important when option of parathormone as therapy for osteoporosis is considered. The mild hyperplasia of the parathyroid glands at cellular level could not be excluded.

P474MO. GHRELIN STIMULATES PROLIFERATION AND INHIBITS APOPTOSIS IN MC3T3-E1 CELLS

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Ghrelin is a 28-amino acid peptide that has recently been discovered in human and rat stomach. Ghrelin strongly stimulates the release of growth hormone and is a natural ligand of the growth hormone secretagogue receptor (GHSR), which belongs to a seven transmembrane receptor family. Previous studies have shown that GHSRs are expressed mainly in the brain and pituitary, but are also detected in a variety of tissues including myocardium, adrenal, and gonads. This study was undertaken to investigate the expression and role of ghrelin and GHSR in osteoblasts using mouse calvarial osteoblast cell line MC3T3-E1. We have identified the expression of both ghrelin and GHSR by RT-PCR analysis of MC3T3-E1 cells. Treatment of these cells with ghrelin from 10^{-11} to 10^{-8} M showed dose-dependent stimulation of proliferation as assessed by MTT assay. [3H]-Thymidine uptake was also increased by 41% after treatment with 10^{-12} M of ghrelin. Moreover, when apoptosis was evaluated using fluorescence microscopy and flow cytometry after cell staining with DAPI or Hoechst 33342, ghrelin treatment suppressed serum deprivation- and TNFalpha-induced apoptosis in this cell line.

We examined the mitogen-activated protein kinase (MAPK) pathway as a possible downstream signaling of ghrelin in the regulation of proliferation and apoptosis. Ghrelin (10^{-9}M) elicited a rapid phosphorylation of Erk1/2 (p42/p44 MAPK) in MC3T3-E1 cells, which was abolished by treatment with MEK inhibitor, PD98059 and U0126. Activation of MAPK pathway by ghrelin was abolished by treatment with PKC inhibitor, staurosporin, suggesting that PKC-MEK cascade is used for ghrelin signaling via its receptor in osteoblasts. Ghrelin treatment has no effect on the differentiation of osteoblasts as assessed by alkaline phosphatase activity and expression of osteocalcin. Taken together, ghrelin stimulates cell growth as well as inhibits apoptosis without apparent effect on differentiation. We suggest ghrelin as a direct mitogen and survival factor of osteoblast.

P475SA. SHORT-TERM EFFECTS OF LEPTIN ON HUMAN OSTEOBLASTS ARE INFLUENCED BY IL-6 AND POTENTIALLY MEDIATED BY BONE MARROW STROMAL CELLS

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The influence of leptin on bone tissue is not clearly defined. A central action on hypothalamus has been proposed but a peripheral effect on bone cells is also suggested. As human osteoblasts express leptin receptor which shares homology with those of cytokines from the IL-6 family, the short-term direct effects of leptin and the influence of IL-6 were investigated in human osteoblasts derived from primary cultures (hOB). Between 10 and 200 ng/ml, leptin significantly ($p < 0.01$) and dose-dependently decreased the hOB proliferation. At higher doses, this effect was not significant. When hOB were simultaneously exposed to leptin 10 ng/ml and IL-6 0.1 ng/ml, their inhibitory effects were amplified: leptin : $-5.2 \pm 2.6\%$; IL-6:$-10.8 \pm 5.9\%$; leptin + IL-6:$-18.3 \pm 9.3\%$ vs controls. But with higher doses of leptin or IL-6, IL-6 tended to reduce the effects of leptin. When hOB were previously exposed to IL-6 before adding leptin, the inhibition of hOB proliferation was always higher than with IL-6 or leptin alone. In contrast, leptin significantly increased alkaline phosphatase activity but this effect tended to decrease with the dose. The presence of IL-6 did not modify or tended to inhibit this effect. A possible indirect effect of leptin through bone marrow stromal cells (hBMS) was also investigated in a model of co-culture between hOB and hBMS cells. After exposure to 200 ng/ml of leptin, hBMS cells induced an increase by 38% of hOB proliferation when compared to hOB cultured in presence of control hBMS. This suggested that leptin-treated hBMS may release factors which secondary acted on hOB. This was confirmed by the stimulatory effect of the conditioned medium of leptin-treated hBMS on hOB proliferation (+21%). In conclusion, leptin between 10 and 200 ng/ml inhibits the hOB proliferation and increases the alkaline phosphase activity suggesting that leptin may favor the osteoblast maturation. These effects are influenced by the presence of IL-6. Leptin may act directly on the human osteoblastic cells but the effects may also depend on the presence of cytokines potentially released by bone marrow stromal cells and present in the microenvironment of the osteoblasts.

P476SU. CALCIUM PLAYS A CENTRAL ROLE IN PARATHYROID HORMONE-STIMULATED RAT INTESTINAL CELLS

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At present , PTH is commonly used in osteoporosis treatment. Although the effects of PTH in bone cells is well characterized, the hormone action in rat intestinal cells is not completely defined. Previous studies demonstrated that in intestinal cells (enterocytes), the hormone increases intracellular Ca2+ levels by promoting an IP3- mediated mobilization of Ca2+ from inner stores and by Ca2+ influx through voltage-dependent Ca2+ channels. PTH also stimulates in these cells the phosphorylation and activation of mitogen-activated protein kinase (MAPK) and the activity of phosphoinositide 3-kinase (PI3K), a lipid kinase which plays an important role in mitogenesis. We also found that PI3K contributes to MAPK phosphorylation by PTH. In the present study we examined whether Ca2+ is upstream mediator of PTH-induced MAPK activation. Immunoblot analysis revealed that removal of external Ca2+ (EGTA 0.5 mM), chelation of intracellular Ca2+ (BAPTA 5 μM), or blockade of L-type Ca2+-channels with verapamil (10 μM) significantly decreased PTH-activation of MAPK. Furthermore, a similar degree of phosphorylation of MAPK was elicited by the Ca2+ mobilizing agent thapsigargin, the Ca2+ ionophore A23187, ionomycin and membrane depolarization with high K+. Inclusion of fluphenazine (50 μM) did not prevent hormone effects on MAPK, ruling out the involvement of calmodulin in this process. We also studied whether Ca2+ is upstream mediator of PTH-induced PI3K activation by assessment of PI3K activity. BAPTA (5 μM) significantly decrease PTH-activation of PI3K and tyrosine phosphorylation of p85,the regulatory subunit of PI3K.

Our results suggest that Ca2+ plays a central role in the signalling pathway leading to PI3K and MAPK activation by PTH in rat intestinal cells. Impairment of PTH activation of both enzymes may result in abnormal proliferation in the duodenum and the source of several diseases.

P477MO. PARTICIPATION OF A PROTEIN PHOSPHATASE IN THE REGULATION OF INTRACELLULAR CALCIUM CONCENTRATION IN OSTEOBLASTS BY OLPADRONATE AND LIDADRONATE

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In previous studies we found that the bisphosphonates (BPs) olpadronate (OPD) and NH_2-olpadronate (lidadronate; LID) are able to regulate, in the short term, cytosolic Ca^{2+} levels ($[Ca^{2+}]_i$) in ROS 17/2.8 rat osteoblastic-like cells. This effect is dependent on prestimulation with the osteotropic agent ATP and due mainly to influx of the cation from the outside through voltage-operated calcium channels (VDCC) and purinergic activation of PLC. In the present work, we evaluated the mechanism by which these BPs modulate the Ca^{2+} response in osteoblasts. By using Fura-2-loaded ROS17/2.8 cells, cytoplasmic Ca^{2+} changes were recorded by fluorimetry. The bisphosphonate-induced rapid changes in $[Ca^{2+}]_i$ were not observed in a Ca^{2+} –free medium or in medium with 1.5 mM Ca^{2+} plus 5 μM nifedipine or 5 μM verapamil, involving extracellular Ca^{2+}influx through VDCC channels in BPs effects. The protein phosphatase inhibitors orthovanadate and sodium fluoride mimicked the purinergic-dependent BPs-induced Ca^{2+} response at low concentrations (1–200 μM) but at higher levels caused a more sustained Ca^{2+}influx blocking the action of BPs. Previous binding assays using [^{3}H]-olpadronate in whole cells showed the presence of a specific, saturable and high affinity binding site for OPD. We now observed that an important proportion of the BPs binder is located in the osteoblast plasma membrane. In addition, like olpadronate and lidadronate, 8 mM p-nitro-phenylphosphate or á-naphthylphosphate (phosphatase substrates), compete for binding to this site, whereas purinergic agonists and antagonists, and both protein phosphatase inhibitors (0.2–8 mM) did not displace [^{3}H]OPD. These results suggest the existence of cell membrane target for bisphosphonates, presumably a protein phosphatase, through which BPs modulate the purinergic Ca^{2+}signaling and in turn trigger a cellular response in osteoblasts.

P478MO. ACTIVATION OF NORMAL HUMAN OSTEOCLASTS BY ACIDOSIS

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Aims: Rodent and avian osteoclasts (OC) are strongly activated to excavate resorption pits when extracellular pH is reduced, and acidification is required for resorption to occur. Systemic acidosis in humans causes bone loss and may play a role in the pathogenesis of osteoporosis. We have now investigated the effects of pH on the function of normal human OC.

Methods: Human OC were generated by culturing peripheral blood mononuclear cells from healthy donors on bovine bone chips ($2–5 \times 10^5$ cells/chip; n = 6–8) for 16d with RANKL (5 ng/ml) and M-CSF (20 ng/ml) in pH 7.42 medium at 5% CO_2. The resulting OC cultures were then acidified with 0-15 mmol/l H^+ and maintained for a further 3d. Acid-base parameters were monitored by blood gas analyser; multinucleated OC and resorption pit areas were assessed 'blind'.

Results: Reducing extracellular pH for the final 3d of culture caused striking, progressive increases in resorption pit formation by human OC, with peak stimulations of 5–6-fold at pH∼6.9–7.0. Numbers of OC (∼100/ bone chip) were not significantly affected by acidification over 3d but were reduced in cultures kept continuously at low pH for 19d. The acid response curve of human OC differed from that of rodent OC, in that it was shifted markedly in the alkaline direction, with ½-maximal activation at pH∼7.3 (as opposed to pH∼7.1 for rodents). Other experiments showed that cathepsin K and tartrate-resistant acid phosphatase were upregulated at pH 7.0 in human OC cultures.

Conclusions: Acid-activation is a fundamental property of all OC studied to date, and extracellular H^+ appears to be the long sought-after 'osteoclast activation factor'. The pH-activation profile of human OC corresponds with that of the H^+-sensing human G-protein-coupled receptors reported present on bone cells (Nature 425:93–8, 2003). Such pH sensors may present an interesting new class of drug targets.

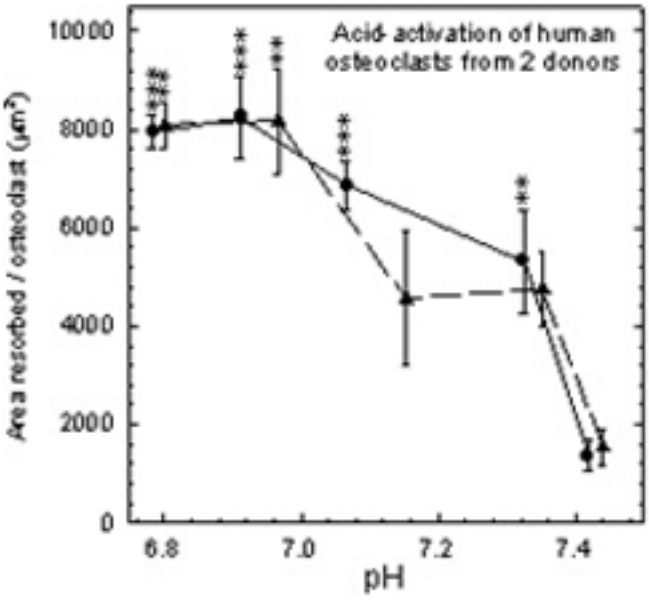

Fig. 1 Acid activation of human osteoclast from two donors

P479SU. BISPHOSPHONATES AFFECT THE GROWTH, DIFFERENTIATION AND CYTOSKELETON OF UMR106 OSTEOBLASTS IN CULTURE

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Bisphosphonates (BP) are analogs of pyrophosphate used in the treatment of bone loss. They act by decreasing osteoclastic resorption, although recent evidence suggests that BP may also act indirectly through osteoblastic functions. We have investigated the effect of three BP; alendronate (from Elea, Argentina), pamidronate and zoledronate (from Novartis, Switzerland) on the proliferation (crystal violet assay), differentiation (alkaline phosphatase [ALP] specific activity), morphological and cytoskeleton alterations (actin, tubulin and focal adhesion kinase [FAK] immunofluorescence staining) of UMR106 rat osteosarcoma-derived cells. After 24 h incubation, 10–4 M pamidronate and zoledronate significantly inhibited cell growth (82–87% basal), while alendronate showed no effect. Longer incubation periods with alendronate (48 h) induced a biphasic effect: low doses of this BP stimulated cell proliferation (ranging from 109–113 % basal, at 10–10 to 10–7 M), while cell growth was inhibited at doses of 10–4 M (74% basal). After 48 h of incubation, pamidronate and zoledronate inhibited UMR106 proliferation (ranging from 59–78% basal, at 10-5 to 10-4 M). A biphasic effect was also observed on osteoblastic differentiation when cells were exposed to alendronate: low doses inhibited ALP specific activity (89% basal at 10–10 M), while high concentrations stimulated it (115% basal for 10–4 M). Pamidronate and zolendronate stimulated osteoblastic differentiation in a dose-dependent manner (ranging from 111–132% basal, 10–10 to 10–5 M). UMR106 cells untreated with BP showed a regular distribution of actin stress fibers and tubulin in the cytoplasm, while fluorescence associated with FAK was mainly concentrated in the nuclei. Cells exposed to 10–4 M BP displayed redistribution of actin, mainly concentrated in the plasma membrane, loss of cytoplasm and intercellular

processes, and a diffuse network of tubulin was also observed. We also assessed the direct effect of BP on the ALP present in an UMR106-Triton X-100 extract. High concentrations (10-5 to 10-4 M) of all three BP were able to inhibit ALP with similar potencies in this in vitro assay (85-50% basal). In conclusion, BP can affect osteblastic growth and differentiation, and induce morphological alterations at high doses. Zoledronate and pamidronate were more potent than alendronate in inhibiting proliferation, enhancing differentiation and inducing cytoskeletal alterations.

P480MO. ENDOTHELIN-1 INDUCES MMP-2 AND MMP-9 SYNTHESIS AND ACTIVATION IN HUMAN OSTEOSARCOMA CELLS.

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Degradation of extracellular matrix (ECM) is an essential step in the invasion of malignant tumor including osteosarcoma. Matrix metalloproteases (MMPs) and endothelin-1 (ET-1) are among the factors contributing to ECM degradation and are a potential target in cancer. This study investigates the effect of ET-1 and its precursor, Big ET-1, on MMP-2 and MMP-9 synthesis and activity in osteosarcoma (MG63) and chondrosarcoma (SW1353) cell lines using Western Blot, zymography, RT-PCR and Northern Blot. The effect of specific inhibitors including those of Nf-kB and furin convertase was also investigated. First, we showed that ET-1 and its two receptors (ETA and ETB) are constitutively expressed in both osteosarcoma and chondrosarcoma cells. Then, we demonstrated that MMP-2 protein expression and enzymatic activity are significantly induced by both ET-1 and Big ET-1 and that the enzymatic activity of MMP-2 is significantly increased when compared to MMP-9. Furthermore, inhibition of IkB-alpha phosphorylation blocked MMP-2 production and activity indicating the involvement of Nf-kB, a ubiquitous trancription factor playing a central role in the differentiation, proliferation and malign transformation process. Similarly, inhibition of Big ET-1 maturation by the furin convertase inhibitor, abrogated MMP-2 synthesis and enzymatic activity. We conclude that increased levels of MMP-2 and MMP-9, two major enzymes which have been associated with the invasive cancer process, can be induced by ET-1 and Big ET-1 in the tumor cells MG63 and SW1353. These findings demonstrate that ET-1 acts as an autocrine mediator in osteosarcoma and chondrosarcoma cells via induction of MMP-2 and MMP-9 synthesis and activity. Thus we could attribute to ET-1 a causal role in the tumor cell growth promotion.

P481SA. CALCITONIN DEFICIENCY IN PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME

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The aim of this study is to evaluate calcitonin secretion stimulated by calcium and pentagastrin in 14 males infected by HIV and suffering from the disease according to the CDC (1987/1993) criteria. They were 33.5 years old (range: 24–53 y), body mass index (BMI) was 20.8 ± 3.3 kg/m^2, 10 healthy men were considered as normal control, aged 34.7 years (range: 25–49 y), BMI 23.8 ± 4.7 kg/m^2. All of them underwent a stimulation test with calcium gluconate (2 mg elemental calcium/kg i.v. during 60 s) followed by a bolus of 0.5 µg/kg pentagastrin (Peptavlon TM, Ayerst, USA) i.v. Sampling times were −10, −5, 0, 2, 5, 10 min. Serum Ct concentration was determined by immunoradiometric assay (IRMA) (CIS, France). Mann Whitney test was used to compare the results between groups, expressed in the table. We concluded that patients suffering from AIDS have decreased secretory reserve of calcitonin and can be considered as calcitonin deficient.

Group	Mean basal Ct# (ng/l)	Peak	Delta (Peak – basal)
NC	2.72 (0.09 – 8.52)	35.73 (29.14 – 103.64)	34.01 (15.24 – 99.58)
AIDS	2.02 (2.02 – 21.8)	12.06 (0 – 224.44)	9.07 (0 – 220.7)
p	0.923	0.017*	0.005*

Values expressed as median (min- max).

P482SU. EFFECTS OF RALOXIFENE, A SELECTIVE ESTROGEN RECEPTOR MODULATOR, ON BONE MINERAL DENSITY AND BONE TURNOVER MARKERS IN ELDERLY MEN

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Background: Men with osteoporosis have been neglected and only a few therapeutic trials have been performed. Several investigations evidence implicate estrogen deficiency as a cause of bone loss in elderly men.

Methods: In a 18 months double-blind trial, we studied the effect of 60 mg of Raloxifene (a selective estrogen receptor modulator [SERM] that has an agonist effect on bone but not feminizing) or placebo, given daily, on bone mineral density and bone turnover markers in 158 men (mean age $\pm$ SD, 79.1 ± 12.4 years) with osteoporosis; 33% had low serum free testosterone concentrations at base line. Men with secondary causes of osteoporosis were excluded. All patients received calcium and vitamin D supplements.

Results: The men who received Raloxifene had a mean ($\pm$SE) increase in bone mineral density of 5.2 ± 0.5% at the lumbar spine, 2.2 ± 0.2% at the femoral neck, 2.74 ± 0.4 at the trochanter and 1.7 ± 0.6% for the total body ($P < 0.001$ for all comparisons with base line). In contrast, men who received placebo had an increase in lumbar spine bone mineral density of 1.1 ± 0.3% ($P < 0.001$ for the comparison with base line) and no significant changes in femoral neck or total body bone mineral density. Mean changes in urinary cross-linked N-telopeptide of type I collagen (NTX) excretion were related directly to the baseline serum estradiol level in the raloxifene group $r = 0.67$; $p = 0.003$) but not in the placebo treated ($r = 0.18$; $p = 0.574$) men ($p = 0.015$).

The incidence of vertebral fractures was lower in the Raloxifene group than in the placebo group (1.2% vs. 6.4%, $P = 0.02$). Men in the placebo group had a 1.9 mm decrease in height, as compared with a decrease of 0.4 mm in the Raloxifene group ($P = 0.02$).

Conclusions: In men with osteoporosis, Raloxifene significantly increases spine, hip, and total body bone mineral density and decreases bone turnover markers in elderly men.

P483MO. REDUCTION OF THE PERIPROSTHETIC BONE REMODELING IN UNCEMENTED FEMORAL HIP IMPLANTS USING CLODRONATE: A PROSPECTIVE STUDY WITH A CONTROL GROUP

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Objectives: To study the effect of Clodronate in periprosthetic bone remodelling around uncemented femoral hip implants in the early phases.

Methods: The authors studied 21 patients operated on uncemented femoral hip implants with proximal hydroxylapatite coatings (ABG®, Stryker Howmedica). The study protocol considered the administration of Difosfonal 100 mg i/m everyday during the 1st week, then 100 mg i/m every week for 6 months and 100 mg i/m every 2 weeks for the next 18 months. The DEXA evaluations were performed since the 15th post-operative day followed by scans at 3, 6, 12 and 24 months. The control group considered 24 patients operated using the same technique and the same implant but without administration of Clodronate.

Results: The results denoted a different behaviour of the periprosthetic bone mineral density (BMD) between the two groups, with a significant decrease of BMD in the study group. The differences were statistically significant for the global periprosthetic density (–3.41% vs –9.75%), the lateral metaphyseal region

(+5.40% vs –6.94%), the medial metaphyseal region (–10.8% vs –32.6% at 2 years). No significant differences were found in the diaphyseal regions.

Conclusions: The results of this prospective study can allow us to conclude that Clodronate is a useful tool to reduce periprosthetic bone resorption around uncemented femoral hip implants in the early phases. However the follow-up time is too short to draw any conclusions about the long-term survival of the implants.

P484SA. EFFECTS OF RALOXIFENE ON BONE DENSITY AND BIOCHEMICAL MARKERS OF BONE REMODELING IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS AND DIABETES

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Raloxifene can treat and prevent new vertebral fractures, increase bone mineral density (BMD), and decrease biochemical markers of bone turnover in postmenopausal women with osteoporosis. This randomized, double-blind 1-yr study assessed the effects of Raloxifene in 260 postmenopausal women with osteoporosis and type 2 Diabetes (femoral neck BMD T-score < –2). Women (aged 70 yr; 5 yr since their last menstrual period) received Raloxifene 60 mg/d or placebo: At baseline, 6 and 12 months, BMD was measured by dual x-ray absorptiometry. The bone turnover markers serum osteocalcin, bone-specific alkaline phosphatase, and urinary N telopeptide corrected for creatinine were measured. All changes in BMD and bone markers at 12 months were different between placebo and the Raloxifene group ($P < 0.05$). On average, lumbar spine BMD increased by 1.3 and 4.3% from baseline with placebo versus Raloxifene group, respectively. The increase in femoral neck BMD in the Raloxifene group (2.9%) was greater 0.8% increases in the placebo group ($P < 0.001$). The changes from baseline to 12 months in bone markers ranged from 6.4 to −13.0% with placebo, −21.7 to −49.1% with Raloxifene. Raloxifene increased lumbar spine and femoral neck BMD, and decreased osteocalcin and N-telopeptide corrected for creatinine. Raloxifene reduced bone turnover more than placebo, resulting in greater BMD increment.

P485SU. INTERRELATIONS BETWEEN LIPID METABOLISM, BONE MARKERS AND MINERAL BONE DENSITY (BMD) IN WOMEN WITH POSTMENOPAUSAL OSTEOPENIA

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The aim of study is revealing connections with bone and lipid metabolism, osteopenia and atherosclerosis.

98 women with moderate osteopenia (T-score in BMD L1-L4 – 2.13) in the age of from 50-75 years, was divided on 3 age groups are surveyed: group 1–34 patients 50-59 years, group 2–35 patients 60-65 years, group 3–29 patients 66-75 years.

Methods: BMD measured on DEXA device Prodidgy (Lunar) and estimated data L1-L4 and femoral neck. Osteocalcin and â-CrossLaps were measured by Elecsys Systems 2010 modular analytics. Lipids: total cholesterol (TC), high density lipids cholesterol (HDL), low density lipids cholesterol (LDL) and triglycerides were measured on biochemical analyzer Hitachi 912.

Results: It has not been found any significant differences between groups BMD, β-CrossLaps and osteocalcin among the following parameters. The carried out correlation analysis has revealed the following features: weak, but significant connection BMD L1-L4 with HDL ($r = 0.35$-0.37) in groups 1 and 2; negative correlation between β-CrossLaps and BMD L1-L4 ($r = -0.39$ in group 1, −0.56 in group 3). Negative connection between β-CrossLaps and HDL also is revealed in the group 1 ($r = -0.45$) and positive correlation of osteocalcin with HDL in group 1 ($r = 0.46$) and in the group 2 ($r = 0.58$).

Conclusion: Thus, dependence between BMD and HDL comes to light during early and average postmenopause, that can specify a protective role for HDL not only during development of atherosclerosis, but also concerning age loss of bone mass. The revealed negative interrelation between HDL and β-CrossLaps – a marker of bone resorption confirms this assumption. Positive correlation between osteocalcin and HDL can indicate interrelations between bone formation with lipid metabolism and common features in development atherosclerosis and osteoporosis.

P486MO. NUMBER NEEDED TO TREAT (NNT) WITH ALENDRONATE, ALPHACALCIDOL, RISEDRONATE AND TIBOLONE TO SUPPRESS SIGNIFICANTLY BONE TURNOVER AND TAKE IT AS A GOOD EARLY TREATMENT RESPONSE

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Significant suppression of bone remodeling is correlated with decrease in fracture risk and could be taken as a sign of early good response. We estimated the number of patients needed to treat with different drugs used in osteoporosis in order to achieve a significant decrease in bone markers in 4 different treatments groups. All women with Type I Osteoporosis, were used for the analysis, 96 received alendronate, 82 alfacalcidol, 92 risedronate and 35 tibolone. Biochemical markers of bone turnover were measured as follows: NTx, Osteomark (Ostex, Seattle, USA). Tartrate Resistant Acid Phosphatase, TRAP: Hydrolysis of paranitrophenyl phosphate at pH4.8. Total Alkaline Phosphatase, TAP: Labtest, Roy modified. Levels of significant change in each case at 6 months treatment were: −15% or more for serum markers TAP and TRAP and −30% or more for urine markers N telopeptide (NTX). Hypothetical placebo groups for each drug were created using the same marker values at initial and 6 months. A significant decrease in markers was taken as probability of a good event. Absolute Benefit Increase (ABI) and Number Needed to Treat (NNT) were calculated according to standard procedures (Glossary, Evidence-Based Medicine, 1998, 3:1–32).

Table 1 NNT and bone markers

	Alkaline Phosphatase		TRAP		NTx	
	NNT	ABI (%)	NNT	ABI (%)	NNT	ABI (%)
Alendronate	1.55	64.48	1.57	63.30	1.15	86.60
Alphacalcidol	2.32	43.04	1.71	58.32	2.27	43.92
Risedronate	2.20	45.30	2.13	46.86	1.5	65.29
Tibolone	1.32	75.73	1.46	68.37	3.12	31.96

Conclusion: NNT with the drugs presented in this study showed high efficiency in suppressing bone remodeling, less than 3 cases and sometimes less than 2 are needed to treat to achieve early good response. Also follow up with each drug should be done by a specific marker, for example alendronate, risedronate and alphacalcidol with telopeptides and tibolone with alkaline phosphatase. This analysis must be carried out with other drugs, clinical settings and different markers.

P487SA. MEASUREMENT OF OSTEOPROTEGERIN AND RANKL IN POSTMENOPAUSAL WOMEN

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Osteoprotegerin and RANKL are important regulators of bone turnover by controlling osteoclast differentiation. RANKL is critical for osteoclast fusion, activation and survival. Osteoprotegerin, the decoy RANKL receptor, inhibits the osteoclast differentiation process. It has been demonstrated that osteoprotegerin concentrations are higher in postmenopausal women with osteoporosis and high bone turnover. In this study, relationship of osteoprotegerin and RANKL with standard bone markers in

serum was investigated in 50 postmenopausal women aged 48–80 years. Osteoporosis of the spine was detected in 28 and of the hip in 5 patients. T-score of the spine and hip was significantly lower in patients receiving antiresorptive therapy($n = 29$). Correlation of hip T-score was significantly positive with menopause duration. Bone resorption marker (Crosslaps serum, Osteometer) correlated positively with total alkaline phosphatase and with hip T-score. No statistically significant relationship was obtained either for osteoprotegerin or RANKL with other bone markers,T-scores for the hip and spine, antiresorptive therapy, age and duration of menopause. Measurement of osteoprotegerin and RANKL did not contribute in this patient sample to better understanding of bone turnover in the postmenopause. Clinical significance of osteoprotegerin and RANKL, in comparison to standard bone markers was not established in this patient sample.

P488SU. BIOMARKER IN REHABILITATION OF OSTEOPOROSIS

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Aims: The intervals of investigations of used bone markers in international studies are three or more months. But our patients are only three weeks in our clinic for rehabilitation of osteoporosis and therefore are the time intervals too long for estimation of the activity of therapy? The aims of the study are: 1) Is a ultra short time monitoring of biomarkers and therapy of osteoporosis useful?, 2) Is it possible from the decrease of resorption markers to prognosticate an increase in bone density?

Methods: We investigated 38 osteoporosis patients (31 women, 7 men) with t-score (Lunar DPX IQ) < -2.5 WHO and estimated the resorption marker beta-CTX in Serum (Elecsys-beta-CrosslapsTM Serum Roche Diagnostics GmbH, Mannheim) and NTX in urine (Ortho Clinical Diagnostics, Neckargemünd). Investigation times: Baseline and two and six weeks after the start of therapy. Used therapy: Basic therapy with calcium und vitamin D (1000/1000) and 1x1 Fosamax 70 mg/week or 1x1 Actonel 5 mg/d or 1x1 Evista 60 mg/d.

Results: 1) Regardless of the used therapy, beta-crosslaps in serum showed after two weeks a decrease of 43.8% and after six weeks of 59.3% to baseline. 2) NTX in urine decrease 27.3% after two weeks and 65.5% after six weeks. 3) In head-to-head comparison of both methods under the same therapy (Fosamax 70mg + calcium vitamin D) the beta-crosslaps in serum showed a decrease of 46.2% and NTX in urine a decrease of 30.7% after two weeks.

Conclusions: The resorption marker beta-CTX in serum and NTX in urine showed an effective reduction of bone resorption already after two weeks. Both markers are useful in the estimation of the therapy effects and the of patients compliance. The marker in serum seems to be more sensitive. We think that after a three weeks rehabilitation procedure from the decrease of the resorption marker can estimated the increase of bone density in the following year. We can answer it exactly when our study is finished after one year with the first control of bone density.

P489MO. CHANGES OF BIOCHEMICAL RESORPTION MARKERS DURING FRACTURE HEALING IN OSTEOPOROSIS: RESULTS OF A PROSPECTIVE STUDY IN PROXIMAL FEMUR FRACTURES

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Aims: The aim of this exlorative study was to evaluate the development of biochemical resorption markers during the fracture healing in patients with osteoporotic fractures of the proximal femur.

Methods: This prospective study included 33 patients with a fracture of the proximal femur, 25 control persons without a fracture and in addition 35 patients with a fracture of the distal forearm. The concentration of the biochemical resorption markers N-terminal telopeptide (NTx), Desoxypyridinoline (D-Pyr) and Pyridinoline (Pyr) were measured in the first urine spot preoperatively and at day 2, 4, 10 and 14 postoperatively. Further the bone mineral density (BMD) of the lumbar spine was determined in all patients with the quantitative computed tomography (qCT) to diagnose osteoporosis.

Results: Among the 33 study patients with a proximal femur fracture were 60% women and 40% men, osteoporosis was diagnosed in 90% of the patients, while only 10% showed a normal bone density. We found a positive correlation between age and BMD in both sexes (female $p = 0.002$; men $p = 0.01$). It was noticed that pertrochanteric fractures were more common with 64% than femoral neck fractures with 36%. Looking at the fracture classification systems a preponderance of high-grade fractures was visible in females with femoral neck fractures.

A statistically significant increase was found in the three measured biochemical resorption markers NTx, D-Pyr and Pyr during the observing period of 14 days of fracture healing ($p < 0.001$). Concerning the biochemical bone markers we found clear trends between the subgroups. The measured resorption markers NTx, D-Pyr and Pyr reflected higher concentrations in patients with osteoporosis, in female patients, in patients who sustained a pertrochanteric femur fracture and after a cemented implantation of the total hip prosthesis.

Conclusion: The biochemical bone resorption markers changed differently depending upon the BMD, sex and fracture type during the first 14 days of fracture healing. Furthermore our data suggest, that the ability of fracture healing is not impaired in osteoporosis.

P490SA. RELATIONSHIP OF BONE MINERAL DENSITY AND BIOCHEMICAL MARKERS OF BONE TURNOVER IN POSTMENOPAUSAL WOMEN

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Bone loss is most rapid in women in the first few years after menopause but continues in the postmenopausal years. The aim of this study was to evaluate the levels of bone markers in 83 postmenopausal women with low bone mineral densities (BMD) in comparison with 10 healthy young women.

We measured the serum levels of bone-specific alkaline phosphatase (BAP) and C-terminal propeptide of type I collagen (CICP) as markers of bone formation and deoxypyridinoline (Dpd) as marker of bone resorption. All markers were determined by monoclonal competitive enzyme immunoassay (EIA, Metra Biosystem). BMD was measured by dual energy x-ray absorptiometry of forearm (DTX-200 Osteometer).

The control group women aged from 27–35 (30.3 ± 3.6) with T score -0.58 ± 0.40. Postmenopausal women aged from 43–83 (67.3 ± 9.11) and menopausal period started from 33–56 (47.8 ± 5.05) years. In elementary group we divided the patients according osteoporosis in 83.2% cases (T score $- 3.46 \pm 0.73$), and osteopenia in 16.8% cases (T score -2.15 ± 0.20). We found compressive vertebral fracture in 33.7% patients using thoracic and lumbal lateral x-rays.

Obtained results showed that BAP (U/l) was significantly higher ($p < 0.01$) in elementary (14.8 ± 4.4) group at whole and osteoporosis (15.7 ± 4.42) patients vs. control group (11.5 ± 1.94). The levels of CICP, Dpd and Dpd/creatinine were not significantly different in any investigated group vs. control group. However, 11 of 69 cases with osteoporosis had elevated levels of CICP (four of them had compressive vertebral fractures). Correlation analyses showed significant negative association between BMD and BAP ($r = -0.307$, $p < 0.01$), Dpd ($r = -0.248$, $p < 0.05$) and CICP ($r = -0.224$, $p < 0.05$) in elementary group, and positive association between BMD and frequencies of fracture ($p < 0.001$) in cases with osteoporosis. Despite of these results we found the correlation between BAP and CICP ($p < 0.001$), while Dpd and Dpd/cre were not correlated with BAP and CICP.

All investigated bone markers showed relation with BMD, but despite found correlation between markers of bone formation (BAP and CICP) we did not find correlation with marker of bone resorption (Dpd), that indicates uncoupled balance between bone formation and bone resorption in patients with low BMD.

P491SU. VALUES OF BONE TURNOVER MARKER IN MEXICAN HEALTHY POSTMENOPAUSAL WOMEN: URINARY N-TELOPETIDE AND URINARY CALCIUM/CREATININE

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A high bone turnover, as assessed by the levels of biochemical markers, may lead to increased skeletal fragility, estrogen deficiency after spontaneous as well as artificial menopause results in an increase in bone remodeling. A sustained increase in bone turnover induces a faster bone loss and therefore an increased risk of osteoporosis, predict the occurrence of osteoporotic fractures, and to monitor the efficacy of treatment, especially anti-resorptive therapies. It has also been suggested that measurement of bone turnover before treatment might be useful for selecting the type of therapy

The purpose of this study was to evaluate the usefulness of urine N- telopeptides (U-NTX) and Ca/Cr in healthy postmenopausal women.

Methods: In this observational and retrospective study, after exclusion of women with bone diseases or treatments, we analyzed the results of 684 healthy postmenopausal women characterized for 1–5 years after cessation of menses. We assessed in all patients bone mineral density (BMD) of the spine and femoral neck regions utilizing DEXA (HOLOGIC) to establish the diagnosis of normal according to WHO criteria. We have measured Ca/Cr and U-NTX levels (ELISA) in a sample from second morning urine.

Results: 684 healthy women 45–60 years were studied. We found values of U-NTX with range of 27–400 nM/mM Cr (mean of 100 and median 80), Ca/Cr values range of 0.01–0.75 (mean 0.17 and median 0.15), in 456 the age menopause was 5 yrs (33%), $97 < 5$ yrs (14%) and 17 with 1 yr (2.4%), the correlation between NTX and age menopausal were significant ($p < 0.01$).

Conclusion: The results showed that N- telopeptides correlate with age of menopause. The biological markers of bone turnover are elevated in 5 years following menopause, this is suggestive of their potential usefulness in the selection of high risk patient in postmenopausal osteoporosis. However, the normal values should be established for all bone markers in large samples of healthy premenopausal women, with normal BMD at the spine and hip measured by DEXA, geographic areas, races have been investigated in prospective studies.

P492MO. CAN BONE MARKERS BE EFFECTIVELY DECREASED IN EARLY PHASE OF CALCITONIN TREATMENT?

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Objective: The purpose of this study was to evaluate efficacy of calcitonin on bone markers in patients with postmenopausal osteoporosis in the early phases of treatment. Design: There were 30 patients with a mean age of 58.2 ± 5.4 years in the treatment group, and 26 patients with a mean age of 58.8 ± 5.2 years in the placebo group in this randomized placebo-controlled study. The patients received 100 IU salmon calcitonin or placebo injections subcutaneously and 1000 mg elementary calcium for 2 weeks. Baseline plasma osteocalcin (OC) and urine deoxypyridinoline (DPD) were measured and repeated after two weeks.

Results: Baseline OC and DPD levels were 8.3 ± 4.8 ng and 7.7 ± 7.2 mM/m in the treatment group while those were 7.8 ± 6.3 ng and 4.8 ± 1.7 mM/m in the placebo group, respectively. Plasma OC and urine DPD levels were 8.5 ± 4.1 ng, 4.3 ± 2.4 mM/m and 8.5 ± 5.1 ng, 6.2 ± 6.8 mM/m at the end of the study in the treatment and placebo group, respectively. Although there was a decrease in urine DPD levels in the treatment group at the end of the second week, the difference was not statistically significant. However, there was no change between plasma OC levels at the baseline and at end of the study in both the treatment and placebo group.

Conclusion: Bone resorption markers such as DPD can decrease even after 2 weeks treatment with subcutaneous calcitonin injection in patients with postmenopausal osteoporosis.

P493SA. EVALUATION OF SERUM SIALIC ACID LEVELS IN POSTMENOPAUSAL PERIOD

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Objective: Sialic acid is one of the small chemicals which are a component of a number of more complex chemical structures in the human body. SA is found in glycoproteins, gangliosides, and glycolipids. The aim of our study was to investigate clinical usefulness of serum levels of sialic acid in postmenopausal period.

Materials and methods: We studied 20 patients with postmenopausal and 20 healthy women subjects. Serum sialic acid levels were determined according to the method of Shamberger.

Results: Serum SA levells were 1.75 ± 0.64 mmol/I for the postmenapausal group, 1.66 ± 0.53 mmol/I for the healthy control group. The SA levels of the patients with postmenopausal period were higher than those of the healthy control group, but no significant difference was found between the patient and control groups ($p > 0.05$).

Conclusion: Our study demonstrated that the serum levels of SA can not be used as a useful and novel marker for evaluating the disease status in the postmenopausal period.

P494SU. SERUM C TELOPEPTIDE (CROSSLAPS) VALUES IN NORMAL DENSITOMETRIC PREMENOPAUSAL WOMEN IN VENEZUELA

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C-telopeptide has been reported as a very specific resorption bone marker. It is a collagen type I degradation product which indicates osteoclastic activity. Its suppression after antiresorptive treatments has been correlated with fracture prevention efficacy. There have been reported regional differences in bone markers around the world, so each laboratory should investigate its own reference range. The aim of this study is to show the normal range of serum C-telopeptide (β CrossLaps) in normal densitometric premenopausal women in Venezuela.

93 premenopausal women with at least one Venezuelan progenitor, age 39 ± 3.5 (32–47), with normal BMD at lumbar spine and femoral neck (LUNAR DPX) and without any systemic disease or drug use which affects bone metabolism were included. None of the women were under heavy physical therapy or training nor had previous fracture. Fast blood samples were taken and frozen at −70°C. C-telopeptide (β CrossLaps) was measured by electrochemiluminescense immunoassay on the Roche Elecsys 1010. All assays were done at the same time. Intra-assay variation 2.6%

BMD values were at lumbar spine 1.2406 ± 0.13 g/cm^2, T-score $+0.34$ and at femoral neck 1.002 ± 0.12 g/cm^2, T-score $+0.19$. Mean CTx values were 0.281 ± 0.134 ng/ml (range: 0.092–0.645), Normal range: (mean ± 1SD): 0.147–0415 ng/ml. Percentile 10–90: 0.126–0.492 ng/ml. Normal reference values reported by Roche for premenopausal women are: 0.299 ± 0.137 ng/ml. Normal range: mean ± 1SD: 0.159–0.439. Significant negative correlation was found between serum CTx and weight ($r = -258$, $p < 0.05$) and not with age or height.

Reference values of C telopeptide (β CrossLaps) in normal densitometric premenopausal Venezuelan women are: mean ± 1SD: 0.281 ± 0.134 ng/ml, range (mean ± 1SD): 0.147–0415 ng/ml. These values are similar to the ones supported by Roche based in follow-up measurements of samples from the OFELY study.

P495MO. SEGREGATION OF THE CODON 404 MUTATION IN EXON 8 OF SEQUESTOSOME 1 GENE IN MEMBERS AFFECTED BY PAGET'S DISEASE OF BONE FROM AN ITALIAN FAMILY

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Paget's disease of bone (PDB) is a metabolic bone disorder affecting up to 3% of Caucasian populations over 55 years of age. Focal and disorganized increase of bone turnover characterizes PDB. Recently, mutations in the gene encoding sequestosome 1 (SQSTM1) have been identified as a common cause of sporadic and familial PDB in French Canadian, British descendent and US patients. Mutations were reported to localize at exons 7 and 8 of the gene, affecting the highly conserved ubiquitin-binding domain (UBA). We originally performed mutational analysis of exon 7 and 8 in 62 PDB Italian patients, identifying one "classical" P392L and two novel mutations, M404V and G425R, at exon 8, the latters consisting, respectively, of A > G and G > A transversion. Recently, we had the opportunity to perform mutational analysis in 20 individuals, 4 affected by PDB and 16 unaffected members from the Italian family of patient exhibiting the M404V mutation. Affected subjects were clinically evaluated both by biochemical and imaging tests. The M404V mutation was found in 8 individuals: 3 with clinically diagnosed polyostotic PDB and 5 "asymptomatic" offspring (age range from 41 to 53 years) of three affected patients. Not mutated individuals did not exhibit any clinical evidence of PDB. Mutation M404V consists of a highly conservative amino acid substitution, and Methionine residue at position 404 is highly conserved among other species, rat and mouse, suggesting an important role in the functionality of the SQSTM1/p62 protein. This familial segregation of M404V mutation with PDB phenotype strongly supports the hypothesis that this mutation is involved in PDB pathogenesis, according to a possible dominant negative mechanism of action. Moreover, its location at exon 8 level confirms the evidence of a clustered mutational area at this level in this disorder, supporting the role of the UBA domain in the biological properties of SQSTM1/p62 protein. Both instrumental and biochemical evaluation of the 5 "asymptomatic carriers" will potentially provide new important acquisitions on the pathogenesis of this metabolic disorder of bone.

P496SA. ESTROGEN RECEPTOR ALPHA AND AROMATASE GENE POLYMORPHISMS: RESPONSE IN BONE MINERAL DENSITY TO HRT IN POSTMENOPAUSAL WOMEN

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Genetic factors regulate BMD and possibly development of osteoporosis. Estrogens play a pivotal role in maintaining bone. The formation of estrogens from C19 steroids is catalyzed by aromatase in women and men. It is known that polymorphism at the human ERalpha and at the aromatase genes are associated with low BMD in postmenopausal women. We evaluated the possibility of interaction between aromatase and ERalpha genotypes with bone mass and we assessed the response in BMD to HRT in postmenopausal women. Subjects consisted of 209 Italian postmenopausal women with a range of age 36–76 years (mean 61.3 + /−8.6). Subjects under HRT received TTS 50 microg/d and nomegestrol acetate 5 mg/d (12 days/month). LS-BMD was measured at the baseline and after 1 year. PvuII and XbaI polymorphism of the ER-alpha was determined by PCR and TTTA repeats by sequence analysis. The capital P and X and the lower-case p and x represent respectively the absence and the presence of the restriction site. For the TTTA repeats polymorphism the subjects were divided on the basis of the mean TTTA repeats: low (< 8) medium (8–10) and high (>10). The genotype distribution for ER-alpha was as follow: XX 42.3%; Xx 43.9%; xx:13.76% (c2 analysis: $p = 0.3$) and PP: 33.3%; Pp:47.09%; pp: 19.53% (c2 analysis: $p = 0.07$) and for the aromatase TTTA repeats was: low: 41%; medium 40% and high:19%. The genotype with a low number TTTA repeats was more frequent in osteoporotic and osteopenic subjects in comparison with normal (42.8 and 39.2% vs.17.86%). Ancova analysis did not show any statistical differences in the LS-BMD of various ER-alpha genotypes ($p = 0.6$), although LS-BMD tended to be lower in subjects with pp and xx genotypes. During HRT an increase of the LS-BMD was present in all the genotypes suggesting a feeble influence of the polymorphism on the hormone response. The same results were observed for the aromatase gene polymorphism. The absence of difference in the LS-BMD in subjects with or without HRT suggests a low influence of the aromatase gene on the HRT response. In conclusion, ER-alpha and aromatase gene polymorphism do not seem to influence the response to HRT.

P497SU. TOMOGRAPHIC AND BIOMECHANICAL ANALYSIS OF MUSCLE-BONE INTERACTIONS IN MICE ARTIFICIALLY SELECTED FOR BODY CONFORMATION

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Antagonistic artificial selection of adult male and female mice with wide variation in body conformation produced animals with light body/long skeleton (CBi/L) or heavy body/short skeleton (CBi/C) from a parental line CBi. On changing the natural proportions between body and skeletal size/shape, this procedure allowed analyzing correlations between the body and gastrocnemius weight and indicators of material, geometric and structural (mechanical) properties of cortical bone of the femur diaphyses (as assessed by pQCT and bending tests at a low strain rate) avoiding the natural, allometric associations which normally blunt the biomechanical interrelationships between muscles and bones.

As expected, the selection procedure altered the natural proportions between gastrocnemius mass, body weight and femur length, and between femur length and diaphyseal cross-sectional properties (moment of inertia, CSMI). The CSMI correlated closer with gastrocnemius weight than it did with body weight. Diaphyseal strength correlated significantly with CSMI, gastrocnemius weight and body weight. Correlation of CSMI with gastrocnemius weight was closer than with body weight and was the only graph describing the studied association as a single (linear) function for all the 3 strains studied as a whole.

Results suggest that 1. muscle mass would not depend alometrically on body weight in any circumstance; 2. the geometric proportions between long-bone length and cross-sectional properties would not be independent determinants of bone structure or strength; 3. muscle development would not depend on bone development; 4. the diaphyseal design would be adapted to muscle ability to directionally deform the skeleton rather than to the weight of the supported biomass; and 5. the biomechanical adaptation of bone strength to customary mechanical usage as allowed by the biochemical and microstructural constitution of the skeleton would be determined more closely by the dynamic influence of muscle contractions than by the static, gravitational load of the body weight. Those relationships, difficult to assess in natural conditions, are crucial for interpreting the biomechanical homeostasis of the skeletal structure and the etiopathogenesis of all osteopenias and osteoporoses. This knowledge could be extrapolatable to the pathogenetic analysis of many human bone-weakening diseases.

P498MO. THE RELATIONSHIP BETWEEN COLI A1 POLYMORPHISMS (SP 1) AND COLI A2 POLYMORPHISMS (ECO R1 AND PUV II) WITH BONE MINERAL DENSITY IN CHINESE MEN AND WOMEN

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Aims: The objectives of this study are to document the frequency of COLI A1 and COLI A2 polymorphisms, as well as their relationship with bone mineral density in Chinese men and women.

Methods: Two groups of Chinese subjects were studied. They were 450 women aged 50–79 years and 233 men aged 70–79 years. The study subjects were recruited through social centers in the district of Shatin, Hong Kong.

Results: In 100 men and women, COLI A1 Sp 1 polymorphism was not found, which was consistent with other previous studies in Asian population. However a significant relationship was observed between COLI A2 Eco R1 and Puv II genotypes among the Chinese men studied. The mean bone mineral density was consistently lower in men of the EE and PP genotype ($p < 0.05$ by ANOVA) than in men of the ee and pp genotypes. However, no association between bone mineral density and the Eco R1 or Puv II genotypes were observed in Chinese women ($p > 0.05$ by ANOVA).

Conclusions: We conclude that COLI A1 Sp 1 binding site is absent in Hong Kong Chinese, while the COLI A2 Eco R1 and Puv II genetic polymorphism may be associated with the bone mineral density of elderly Chinese men.

P499SA. RELATIONSHIP BETWEEN PARATHYROID HORMONE GENE POLYMORPHISM, BONE MINERAL DENSITY, AND BONE RESPONSIVENESS TO HORMONE REPLACEMENT THERAPY IN POSTMENOPAUSAL KOREAN WOMEN

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Aims: To evaluate the relationship between parathyroid hormone (PTH) gene BstBI polymorphism, bone mineral density (BMD) and bone responsiveness to hormone replacement therapy (HRT).

Methods: PTH BstBI polymorphism was determined by restriction fragment length polymorphism (RFLP) in 444 postmenopausal Korean women. Among these women, 309 women received sequential HRT for 1 year. Serum bone alkaline phosphatase, CrossLaps, osteocalcin, calcitonin, and PTH levels were measured by immunoassay and serum calcium and phosphorus levels by atomic absorptiometry. BMD at the lumbar spine and proximal femur was determined by dual energy X–ray absorptiometry before and after HRT of 1 year.

Results: PTH genotype frequencies were 81.1% for BB, 18.0% for Bb, and 1.2% for bb (uppercase letters signifying the absence and lowercase letters the presence of the restriction site). BMD at the femoral neck in women with the bb genotype was higher than that in women with the Bb ($p < 0.01$) or BB ($p < 0.005$) genotype respectively. Similar trends were found in BMD of lumbar spine and Ward's triangle. PTH genotypes were not distributed differently between HRT–responders and HRT–nonresponders (women who lose more than 3% of bone mass per year) and were not related with annual percent change of BMD after HRT. There were no significant differences in levels of calcitonin, PTH, calcium, phosphorus, and bone turnover markers, or their 6 month percentage changes after HRT among PTH genotypes.

Conclusions: PTH BstBI polymorphism is not associated with bone responsiveness to HRT but BMD in Korean women.

P500SU. ASSOCIATION STUDY OF THE ESTROGEN RECEPTOR THYMINE–ADENINE REPEAT POLYMORPHISM WITH THE EFFECTS OF HORMONE THERAPY ON SERUM LIPID AND BONE DENSITY IN POSTMENOPAUSAL WOMEN

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Several biologically plausible mechanisms have been proposed for estrogen–associated changes in lipid and bone metabolism. These effects are thought to be mediated via estrogen receptor (ER). Several polymorphisms in the gene encoding estrogen receptor alpha may modify the effects of hormone–replacement therapy on lipid and bone mineral density in postmenopausal women.

We examined 284 postmenopausal women for thymine–adenine (TA) repeat polymorphism at the ER gene locus and its relationship to lipid and bone density. Their mean age was 52.2 ± 5.0 years. We also investigated the association between ER TA repeat polymorphism and changes in lipid and bone density after 3 months and 1 year of hormone therapy. According to the mean number of TA repeats, the women were divided into two groups: group H, with higher number of repeats ($TA > 16$)($n = 110$); group L, with lower number of repeats ($TA = 16$)($n = 174$). Group L showed significantly increased changes in total and LDL cholesterol levels after 3 month estrogen replacement therapy than in group H (changes in total cholesterol: −8.4 ± 11.3% vs. −4.2 ± 12.5%, $p = 0.019$), (changes in LDL cholesterol: −18.7 ± 18.4% vs −8.8 ± 30.1%, $p = 0.006$). There was no significant relationship between TA repeat polymorphism and changes in HDL cholesterol, triglyceride levels and bone mineral density after 1 year hormone therapy.

These data suggest that ERTA repeat polymorphism may predict the response of lipid profile to estrogen replacement therapy.

P501MO. RELATIONSHIP BETWEEN POLYMORPHISMS OF ESTROGEN RECEPTOR GENE AND SPINE BONE MINERAL DENSITY IN PRE– AND PERIMENOPAUSAL WOMEN FROM A CITY OF ARGENTINA

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Aims: To determine the estrogen receptor (ER) genotypes in pre and perimenopausal women from Córdoba, city located in the central part of Argentina, in relation with their lumbar spine bone mineral density (BMD) and other variables associated to the calcium and phosphorus metabolism .

Methods: Recruitment was achieved through voluntary response to advertisement for a study on genetic markers affecting bone density in healthy pre and perimenopausal women. 98 women, divided in three age groups (21–30, 31–40 and 41–55 years old) were studied. The exclusion criteria included hepatic or renal diseases, malabsorption, hyperparatiroidism, malignity in the last 5 years and use in the last 3 months of estrogen, glucocorticoids or other drugs known to influence on calcium metabolism. Serum calcium and phosphorus were measured by spectrophotometric techniques and PTH–intact molecule was quantitated by IRMA. DNA was isolated from blood, the appropriate segment was amplified by PCR and the ER genotypes were determined by using PvuII and XbaI as restriction enzymes. PP and XX represented homozygotes without the site of restriction, pp and xx homozygotes with the restriction sites and Pp and Xx were the heterozygotes. BMD was measured in lumbar spine using a Nordland dual–energy–X ray absorptiometer.

Results: Values of calcemia, phosphatemia and serum PTH did not show any differences between women from the different groups. The genotype frequencies for the two polymorphic sites of ER were as follows: XX 8.42%, Xx 44.21% and xx 47.36% (for XbaI) and PP 10.52%, Pp 49.47% and pp 40.00%. Spine BMD was significantly lower in the group 21–30 years old as compared to the other two groups (ANOVA $P < 0.05$). In the group 31–40 years old, women with genotype XX had a higher spine BMD than women with either genotype xx or Xx (ANOVA $P = 0.05$).

Conclusions: The data suggest that premenopausal women of this city would reach the bone mass peak in spine after 30 years of age and the genotype XX would be favorable to acquire a better spine BMD.

P502SA. 1,25(OH)2 VITAMIN D INCREASES THE BONE DENSITY OF THE LUMBAR SPINE OF OSTEOPENIC WOMEN IN ASSOCIATION WITH TAQI POLYMORPHISM OF THE GENE FOR VITAMIN D RECEPTOR

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1,25(OH)2 vitamin D has direct anti–resorption and anabolic effects on bone (1). However, the degree of increase in bone mineral density (BMD) differs from case to case when taking this hormone. The aim of the present study was to monitor the changes in the BMD of the lumbar spine and the proximal femur in 35 osteopenic, but otherwise normal women (27 of which were post–menopausal) given the two–year taking of 1,25(OH)2 vitamin D (ROCALTROL, Hoffmann La Roche) in a dosage of 0.5 ug/d, together with calcium (500 mg/d). BMD was measured with the aid of dual x–ray absorptiometry (DXA) before the beginning of treatment and afterwards in the course of the second year of treatment itself. Its growth was expressed in terms of a percentage of the initial value. TaqI polymorphism was determined using a restriction analysis of the PCR product.

Results: There was an increase in BMD of the lumbar spine ($P < 0.001$) and the proximal femur ($P < 0.01$) in the second year of treatment with Rocaltrol. A higher growth of BMD in the lumbar spine was observed in women with a TT genotype than in carriers of allele t (genotypes tt and Tt) ($P < 0.028$, ANCOVA). The response of BMD in the proximal femur was independent of genotype.

Conclusions: The study confirmed that there is a significant increase in BMD of both the parts of the skeleton measured in the second year of treatment with Rocaltrol. In the process, the growth of BMD values in the lumbar spine was dependent on TaqI polymorphism. The results of three–year monitoring will bring a final answer to question as to whether the gene for vitamin D receptor has a predictive significance for the curative effect of 1,25 (OH)2 vitamin D on the osteopenic lumbar spine.

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P503SU. ESTROGEN RECEPTOR ALPHA XBAI POLYMORPHISM, TOXIC ADENOMA, AND THYROID HORMONE–STIMULATED BONE LOSS

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The genetic background of toxic adenoma (TA), and thyroid hormone–stimulated bone loss have not yet been established. In this study, we investigated the possible functional contribution of the estrogen receptor alpha gene (ERa) XbaI, vitamin D receptor gene BsmI and interleukin–1 receptor antagonist protein gene VNTR polymorphisms to the pathogenesis of TA and thyroid hormone–stimulated bone loss. We genotyped 296 F(18–79 years) women: 107 patients with TA, and 189 healthy controls (C). In a subgroup of postmenopausal women (71 TA, 189 C), bone mineral density (BMD) of the lumbar spine, femoral neck and distal radius was measured. The xx allele of ERa was present significant less frequently in TA group compared to the controls. There was no other significant difference in the distribution of genotypes in the study groups. There was no correlation between genotypes and BMD adjusted for age and BMI at any site in the postmenopausal subgroups. Our data suggest that ERa XbaI polymorphism might play a role in the development of toxic adenoma. At the same time, the studied genetic variations do not appear to have an impact on thyroid hormone–related bone loss.

P504MO. COLLAGEN TYPE I GENE ABNORMALITIES AND OSTEOPOROSIS

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Background: The role of collagen gene abnormalities in osteoporosis (OP) has garnered a lot of research attention ever since a type I collagen gene abnormality was demonstrated in patients with osteogenesis imperfecta (OI) in 1984. Subsequently type I collagen genes were cloned, several gene mutations were described and correlated with clinical varieties in different diseases, and most recently, attempts to correct the genetic abnormalities by bone marrow transplantation and gene therapy have been carried out. In this article, the biology and molecular genetics of type I collagen is presented, and the role of type I collagen gene abnormalities in the aetiopathogenesis, clinical expression and treatment of OP is reviewed.

Methods: A Medline search was carried out for publications addressing the biology, genetics and disease related to type I collagen gene abnormalities. Other sources of information included the online human genome database, and the web–based Online Mendelian Inheritance in Man (OMIM).

Results: Type I collagen, the most abundant protein in humans, is inherited by 2 different genes on chromosomes 17 and 7. Over 300 mutations in type I collagen genes resulting in human disease have been described. Mutations in either of the 2 genes are responsible for 90% of cases of OI, a hereditary form of OP, the arthrocalsia and dermatospraxis types of Ehlers–Danlos syndrome (formerly EDS VII), and some cases of idiopathic OP. The type and site of mutation are correlated with the severity of OP, with deletions resulting in milder forms than substitutions, and mutations near the carboxy– terminal resulting in the most severe forms of OP. Bisphosphonates have shown beneficial effects in reducing fractures in all those diseases. Allogenetic bone marrow transplantation (BMT) has been attempted in severe OI, with encouraging results, and gene therapy experiments in animal models have been published.

Conclusion: Collagen type I gene abnormalities are the definitive cause for most cases of hereditary OP, and they have a prominent role in idiopathic OP, together with other known risk factors. Bisphosphonates are the treatment of choice for hereditary forms of OP, while BMT and gene therapy show promising results for severe cases.

P505SA. CALCIUM METABOLISM AND ENDOCRINE FUNCTIONS IN A FAMILY WITH FAMILIAL HYPOCALCIURIC HYPERCALCEMIA

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We report two Hungarian patients with familial hypocalciuric hypercalcaemia (FHH) caused by a mutation of the calcium–sensing receptor (CaSR) at codon 55. The proband and her father were heterozygous for this mutation. Design: We have performed detailed clinical and laboratory assessments of this family to characterize the effects of CaSR mutation on bone turnover and on several endocrine organs expressing CaSR. Interestingly, we could not detect any failure in the function of any tissues – such as bone – we examined, except in serum calcium levels. Both subjects have had normal bone mineral density. To our knowledge, this has been the first report from Eastern and Central Europe showing P55L mutation of the CaSR, as well as the first publication discussing the effect of this mutation on several endocrine systems containing CaSR.

A New Dimension in the Treatment of Postmenopausal Osteoporosis

Sponsor: SERVIER

SY1. PREVENTION OF VERTEBRAL FRACTURES

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The use of strontium ranelate, a bone–seeking compound with a novel mechanism of action, in the prevention of fractures in postmenopausal women with osteoporosis has been investigated in 2 randomized controlled trials, SOTI (Spinal Osteoporosis Therapeutic Intervention) and TROPOS (TReatment Of Peripheral OSteoporosis). Strontium ranelate was given orally at a dose of 2 g daily for 3 years and vertebral fractures were assessed by the semi–quantitative method. The study population in SOTI consisted of 1649 women, mean age 69.7 years, and that in TROPOS of 5091 women with a mean age of 76.8 years. Prior to the study, the calcium and vitamin D status of the patients started to be normalized, and during the study all patients received appropriate calcium and vitamin D supplementation.

In the SOTI study, there was a 41% reduction in the relative risk (RR) of vertebral fracture (RR = 0.59; 95% confidence interval [CI], 0.48–0.73; P < 0.001) over 3 years of treatment. This beneficial effect occurred rapidly, so that after 1 year of treatment, the reduction in the RR was 49% (RR = 0.51; 95% CI, 0.36–0.74; P < 0.001). The proportion of women experiencing a new vertebral fracture in the treatment and control groups was 20.9% and 32.8%, respectively, after 3 years, and 6.4% and 12.2%, respectively, after 1 year. Over 3 years, the risk of developing a new clinical vertebral fracture was also significantly reduced (RR = 0.62; 95% CI, 0.47–0.83; P < 0.001), this reduction being observed from the first year (RR = 0.48; 95% CI, 0.29–0.80; P = 0.003). The beneficial effects of strontium ranelate on vertebral fractures were confirmed in TROPOS with a significant reduction of 45% in patients without prevalent vertebral fracture over 3 years of treatment (RR = 0.55; 95% CI, 0.42–0.72; P < 0.001). In a pooled analysis of SOTI and TROPOS, the RR of new vertebral fracture over 3 years of treatment was reduced by 48% in patients without prevalent vertebral fractures (RR = 0.52; 95% CI, 0.40–0.67; P < 0.001). A significant and similar increase in lumbar spine bone mineral density was seen in both studies in strontium ranelate–treated women after 3 years compared with the control group.

The beneficial effect on vertebral fractures was also seen in patients with osteopenia (femoral or lumbar bone mineral density T–score between −1 and −2.5 and no T–score lower than −2.5) and with or without prevalent vertebral fracture (RR = 0.38; 95% CI, 0.21–0.70; P = 0.001) over 3 years of treatment.

These results demonstrate that strontium ranelate significantly reduces vertebral fractures in postmenopausal women regardless of the severity of osteoporosis and in postmenopausal women with osteopenia.

SY2. PREVENTION OF NONVERTEBRAL FRACTURES

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Strontium ranelate is a new antiosteoporotic agent with a unique mode of action, simultaneously increasing bone formation and decreasing bone resorption. The vertebral antifracture efficacy of strontium ranelate in postmenopausal women with osteoporosis was confirmed in the SOTI (Spinal Osteoporosis Therapeutic Intervention) trial. The TROPOS (TReatment Of Peripheral OSteoporosis) trial aimed to assess the nonvertebral antifracture efficacy of strontium ranelate. Both trials were international, prospective, randomized, double–blind, and placebo–controlled, and strontium ranelate was given orally at a dose of 2 g daily. Normalization of calcium and vitamin D status began prior to inclusion during the run–in study FIRST (Fracture International Run–in for Strontium ranelate Trials), appropriate supplementation being continued throughout the studies.

The study population in TROPOS consisted of 5091 women, mean age 76.8 years, mean femoral neck bone mineral density (BMD) T–score = −3.1, and mean lumbar spine BMD T–score = −2.8, 36.8% of them having at least one prevalent nonvertebral fracture.

In TROPOS, there was a significant reduction in the relative risk (RR) of nonvertebral fracture (RR = 0.84; 95% confidence interval [CI], 0.702–0.995; P = 0.04) over 3 years of treatment. When considering the major nonvertebral sites of osteoporotic fractures, e.g., humerus, pelvis and sacrum, ribs, hip, clavicle, and wrist, a significant decrease in the RR was also observed (RR = 0.81; 95% CI, 0.66–0.98; P = 0.031). Although the study was not designed to demonstrate antifracture efficacy at the hip, a 36% decrease in the RR of hip fracture was shown in patients ≥74 years and with a femoral neck BMD T–score < −3 (RR = 0.64; 95% CI, 0.412–0.997; P = 0.046), over 3 years. Furthermore, a 41% decrease in the RR of hip fracture was shown in patients having taken the drug for at least the first 18 months (RR = 0.59; 95% CI, 0.37–0.95; P = 0.025).

In addition, a significant increase in femoral neck and in lumbar spine BMD was observed with a relative change from baseline to 3 years of + 8.2% and + 14.7% compared with placebo, respectively. Strontium ranelate was well tolerated throughout the study.

These results show that strontium ranelate significantly reduces nonvertebral fracture risk and, more specifically, major osteoporotic nonvertebral fracture and hip fracture risks in postmenopausal women with osteoporosis.

SY3. A NOVEL MODE OF ACTION OPTIMIZING BONE FORMATION AND BONE RESORPTION

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Strontium ranelate has been demonstrated to decrease the risk of fractures in postmenopausal women. Its efficacy in clinical studies is based on its original mode of action, on both bone resorption and formation. Pharmacological studies in animal models showed that strontium ranelate decreases bone resorption but maintains or increases bone formation, resulting in improved bone mass. In the model of ovariectomized (OVX) rats, strontium ranelate prevented the reduction in bone mineral content and the decrease in trabecular bone volume induced by estrogen deficiency (+ 115% in tibia and + 50% in the vertebra in comparison with OVX rats in a 52–week study). In this model of osteopenia, strontium ranelate acted by decreasing bone resorption whereas bone formation was maintained at a high level, as documented by plasma biochemical markers and histomorphometric indices of bone formation. In the model of osteopenia induced by hind limb immobilization in rats, strontium ranelate reduced histomorphometric parameters of bone resorption (osteoclast surface: −16%) and partially limited long bone loss, as assessed by bone mineral content (+ 7.5%), bone volume, and biochemical indices of bone resorption. In normal mice, strontium ranelate increased bone formation and vertebral bone mass (+ 36% and + 59% in males and females, respectively). In normal rats, strontium ranelate also increased the bone trabecular volume (+ 41%) without any alteration of mineralization. The unique mode of action of strontium ranelate both on bone formation and resorption was supported by in vitro studies. In rat calvaria culture systems and rat osteoblastic cell cultures, strontium ranelate enhanced preosteoblastic cell replication and increased collagen synthesis by osteoblasts. Moreover, strontium ranelate decreased bone resorption in organ cultures and decreased the resorbing activity of isolated mouse osteoclasts. The evaluation of bone markers in clinical trials (SOTI and TROPOS) supports the mode of action of strontium ranelate: bone alkaline phosphatase levels increased and C–telopeptide of type I collagen levels decreased in treated patients compared with the placebo group at all time–points. Thus, pharmacological and clinical studies suggest that strontium ranelate optimizes bone resorption and formation resulting in increased bone mass, which may be of great value in the treatment of osteoporosis.

SY4. A NOVEL MODE OF ACTION LEADING TO RENEWED BONE QUALITY

Ammann P; HUGE, Hôpital Cantonal, Genève, Switzerland

Various bone resorption inhibitors have been shown to decrease the risk of osteoporotic fractures. However, there is still a need for agents promoting bone formation by inducing positive uncoupling between bone formation and bone resorption. Strontium ranelate represents a good candidate.

In vitro studies showed that strontium ranelate stimulates bone formation and inhibits bone–resorbing activity. In vivo, strontium ranelate decreased bone resorption whereas bone formation was maintained in ovariectomized rats, preventing trabecular bone loss induced by estrogen deficiency. In intact female rats, strontium ranelate was demonstrated to significantly increase alkaline phosphatase, a marker of bone formation. The dramatic increment in trabecular bone volume and in bone diameter are further elements in favor of an in vivo stimulation of bone formation.

In intact female rats, a 2–year period of exposure to strontium ranelate mixed in the diet did not cause any alteration of bone mineralization as assessed by histomorphometry or bone stiffness evaluation. A dose–dependent increase in bone strength, bone mass, and bone microarchitecture was observed at the level of the vertebral body, which contains a large proportion of trabecular bone, and at the level of the midshaft femur, which mainly contains cortical bone, these results being confirmed in ovariectomized rats. The increment in bone mechanical properties was characterized by an increase in ultimate strength but also by a dramatic improvement in energy to failure, which was essentially due to an increment in plastic energy, without significant influence on elastic energy. These results strongly suggest that bone formed on strontium ranelate treatment is able to withstand greater deformation before fracture while possessing similar elastic properties as normal bone. Such modifications observed on strontium ranelate treatment are in good agreement with an improvement in intrinsic bone quality and also in trabecular bone mass leading to greater bone resistance.

These data indicate that strontium ranelate stimulates bone formation and inhibits bone resorption, and increases bone mass without modification of the bone mineralization process, resulting in bone strength improvement.

SY5. CLINICAL BENEFITS FOR THE PATIENT

Delmas PD; INSERM Unit 403 and Rheumatology Department of Hôpital E.Herriot, Lyon, France

The efficacy and tolerability profile are essential factors in the choice of first–line treatment in a chronic disease such as postmenopausal osteoporosis. Furthermore, quality of life has recently appeared as an important outcome in clinical studies.

Strontium ranelate, 2 g/day orally, a novel antiosteoporotic agent, has been evaluated in more than 6700 patients in 2 large randomized, double–blind, placebo–controlled clinical trials (SOTI [Spinal Osteoporosis Therapeutic Intervention] and TROPOS [TReatment Of Peripheral OSteoporosis]). These studies showed that strontium ranelate reduces the vertebral and nonvertebral fracture risk in postmenopausal osteoporotic women. The reduction in the relative risk of vertebral fracture has also been demonstrated in patients with osteopenia as well as in osteoporotic patients, with or without prevalent fractures.

The Health–Related Quality Of Life (HRQOL) was evaluated in 1240 patients from 11 countries with the QUALIOST® questionnaire (developed by Servier and MAPI for patients with vertebral osteoporosis). The global score was significantly improved in the strontium ranelate group whereas a deterioration was observed in the placebo group ($P = 0.03$). This improved quality of life with strontium ranelate is likely to be related to the significant decrease in the incidence of patients experiencing new vertebral or clinical vertebral fractures, to the reduction in back pain and the smaller decrease in body height as compared to the placebo group, as well as to the good tolerability profile of strontium ranelate, including at the upper gastrointestinal level.

Thus, strontium ranelate is an antiosteoporotic agent that combines efficacy, tolerability, and ease of administration (at bedtime). Taken together, these results illustrate the clinical benefits of strontium ranelate in the treatment of postmenopausal women with osteopenia or osteoporosis, with or without vertebral fractures.

Bone and Healthy Aging: The Spectrum of Risk

Sponsor: PFIZER

SY6. HEALTH BEYOND MENOPAUSE

Utian W

With more women now living well beyond the age of 65, an increasing number of years of a woman's life are spent after the menopause. Because of this, both the acute symptoms and the long–term diseases associated with menopause and aging, such as osteoporosis, cardiovascular disease, breast cancer, urogenital changes, and female sexual dysfunction, will have a major impact on the quality of life of older women and on the health care system. These conditions may be prevented and/or treated if appropriate screening is offered in a timely manner.

As a result of the shift away from the use of estrogen–progestin therapy in postmenopausal women, there is now a growing unmet need for new drugs that can improve the symptoms of the menopause and prevent osteoporosis and cardiovascular disease without increasing breast cancer risk. This presentation will discuss the potential of new therapies to address the varied health care needs of postmenopausal women. It will also describe how the current health care system is failing those women who do not go to their doctors while they are transitioning menopause. As a consequence, these postmenopausal women do not get the appropriate health education, counseling and preventive treatment that could make enormous improvements to their long–term medical outcomes. Fundamental changes need to occur in the way health care providers and third–party payers deliver and pay for health care, and in providing health education, counseling and preventive medicine to all women >50 years of age. Only then can we provide 'healthy aging' to women.

SY7. BONE HEALTH BEYOND MENOPAUSE: ASSESSING WHO IS AT RISK OF DEVELOPING OSTEOPOROSIS

Siris E

Postmenopausal estrogen deficiency is the primary cause of increased bone loss associated with menopause and as a consequence large numbers of postmenopausal women are at risk of developing osteoporosis. The costs of osteoporosis are high, both in terms of the financial cost to society and the individual costs to women who experience the morbidity associated with fractures.

The National Osteoporosis Risk Assessment (NORA) study is an observational registry of postmenopausal women in the United States that started collecting data in 1997. Its database contains peripheral and central measurements of bone mineral density (BMD) in addition to information on risk factors, treatment patterns, and osteoporosis history and fracture data. To date, 200,000 postmenopausal women have joined the registry and provide data and health information on a regular basis. Although diagnostic tools for measuring BMD and effective therapies for treating osteoporosis exist, they are commonly underutilized when treating older female patients. The NORA study has shown that new, less expensive peripheral technologies for measuring low BMD could be used for routine screening of older women and has previously reported the prevalence of osteoporosis in asymptomatic postmenopausal women and the prevalence of low BMD, and the association with risk factors for osteoporosis and fracture incidence.

This presentation will show recent data from the National Osteoporosis Risk Assessment and discuss how postmenopausal osteoporosis should be best managed, both in terms of screening and treatment.

S8. NEXT GENERATION SERMS: ENHANCED TREATMENT FOR OSTEOPOROSIS AND GENERAL MENOPAUSAL HEALTH

Thompson D

Selective estrogen receptor modulators (SERMs) are a diverse class of agents that have emerged as safe and effective treatment alternatives to HRT for patients requiring preventive pharmacotherapy for osteoporosis. They have the potential to offer the physician a major advantage over estrogens in that they exert selective agonist or antagonist effects on a range of estrogen–target tissues. Each SERM has a unique profile of biological activity that is dependent upon three interactive mechanisms: tissue–specific estrogen receptor expression, differential estrogen receptor conformation on ligand binding, and differential expression and binding of cofactor proteins. Together these profiles of SERMs allow differential tissue responses ranging from estrogen antagonist effects in the breast and uterus to agonist effects in bone. This presentation will describe the unique biological properties of the SERM class, present proposed mechanisms of action, and characterize the different tissue activities.

Glucocorticoid/Inflammation–induced Osteoporosis – Pleiotropic Effects of D–Hormone Analogs

Sponsor: TEVA & TEIJIN

SY9. D–HORMONE AND THE IMMUNE SYSTEM

Cantorna MT; The Pennsylvania State University, PA, USA

D–hormone ($1,25(OH)_2D_3$) is an important immune system regulator. $1,25(OH)_2D_3$ has been shown to inhibit the development of autoimmune diseases including experimental inflammatory bowel disease (IBD), rheumatoid arthritis (RA), multiple sclerosis (MS) and type 1 diabetes. Paradoxically other immune mediated diseases (experimental asthma) and immunity to infectious organisms were unaffected by $1,25(OH)_2D_3$ treatment. The effectiveness of $1,25(OH)_2D_3$ treatment of autoimmune diseases comes as a result of the inhibition of the development and function of Th1 cells and the induction of other Th cells including Th2 cells. Interestingly Th2 cells express as much as 64 times more mRNA for VDR than Th1 cells. In addition there are a number of genes which are differentially regulated by $1,25(OH)_2D_3$ in Th2 cells versus Th1 cells. In IBD the $1,25(OH)_2D_3$ mediated mechanism includes the inhibition of three TNFα (TNFα, LPS–induced TNFα, and TNF receptor) related genes in the colon. D–hormone is a selective regulator of the immune system and the outcome of $1,25(OH)_2D_3$ treatment depends on the nature (infectious disease, asthma, autoimmune disease etc.) of the immune response.

SY10. PREVENTION OF BONE LOSS IN HIGH RISK PATIENTS BY D–HORMONE ANALOGS

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Alfacalcidol has been investigated, in high quality randomized controlled trials, for the management of involutional and glucocorticoid–induced osteoporosis. All these trials conclude that alfacalcidol induces a substantial effect on bone loss and fracture rates in osteoporosis and is beneficial in preventing bone loss in glucocorticoid–induced osteoporosis. In patients requiring treatment with high doses of glucocorticoids (up to 46 mg/day), alfacalcidol and calcium significantly prevented bone loss at the level of the lumbar spine. These positive results were obtained without inducing a significant increase in serum or urinary calcium. These results were confirmed with doses of alfacalcidol from 0.25 μg to 1 μg/day, at the level of the lumbar spine, femoral neck and radius, in women aged 32 to 52 years starting steroid treatment for rheumatic disorders or asthma. These results compares favourably with the negative outcomes observed when plain vitamin D (50 000 IU/day + 1000 mg calcium) was investigated in patients with glucocorticoid–induced osteoporosis. In a meta–analysis assessing the effect of D–Hormones in patients with primary or secondary osteoporosis, D–Hormones have shown to prevent spinal bone loss both in postmenopausal and glucocorticoid–induced osteoporosis. D–Hormones were also shown to significantly reduce the overall fracture rates, these effects being predominant in vertebral fracture rates observed in primary osteoporosis. When comparing the effect of D–hormone to those of native vitamin D, D–Hormones appear to exhibit a higher preventive effect on bone loss and fracture rates in patients with primary osteoporosis. When comparing the adjusted global relative risks for fractures when allocated to D–Hormones (risk difference = 10%) or native vitamin D (risk difference = 2%), D–Hormones provided a more marked preventive efficacy against fractures. Lower fracture rates for D–Hormones users were confirmed for spinal and non–spinal fracture rates. In conclusion, D–Hormones have shown significant effect in preventing glucocorticoid–induced bone loss and in reducing fracture rates in postmenopausal osteoporosis. In meta–analyses, their effect has been shown to be more pronounced than the effect of native vitamin D, in primary and secondary osteoporosis.

SY11. ALFACALCIDOL VERSUS PLAIN VITAMIN D IN INFLAMMATION–INDUCED BONE LOSS

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Inflammatory diseases lead to systemic osteoporosis. Causal factors are increased circulating concentrations of inflammatory cytokines such as interleukin 6 (IL–6) and Tumor necrosis factor alpha (TNFalpha), glucocorticoid medication, and reduced physical activity. In addition, disturbances of vitamin D metabolism play an important role for the development of inflammation induced osteoporosis. Therefore, D–hormone analogs offer an important treatment option. 1,25–dihydroxyvitamin D (D–hormone) prevented bone loss in the rat model of inflammation mediated osteopenia (IMO) and in an arthritis model. One explanation is the fact that animals and humans with inflammatory diseases exhibit markedly reduced circulating concentrations of D–hormone, partly the result of inhibition of renal 1–alpha–hydroxylase by TNFalpha. Moreover, the number of vitamin D receptors is reduced by glucocorticoids. Moreover, D–hormone has pleiotropic effects not only on calcium homoeostasis but also on muscle (improving strength), nerve system, and on the immune system. D–hormone inhibits the release of cytokines (IL–1,IL–6, TNFalpha) from macrophages and stimulates osteoprotegerin secretion in vitro and improves arthritis in animal models.

In our own study, 71 patients with rheumatoid arthritis and osteopenia (mean age 65 years) were randomised to receive either vitamin D (1000 IU/day) or the prohormone Alfacalcidol (Alpha D_3® TEVA, 1 μg/day). All patients were supplemented with Calcium 500 mg/day. Blood and urine samples were obtained before, 2 and 4 weeks after treatment. A pain score was also obtained. Muscle power was determined by isokinetic test (leg extension).

Alfacalcidol did not cause hypercalcemia. There was a slight decrease in serum TNF–alpha in patients receiving Alfacalcidol ($p < 0.03$), other cytokines and osteoprotegerin did not change. After 4 weeks, calciuria was increased (mostly within the normal range) in patients receiving Alfacalcidol and slightly in the vitamin D group. Only Alfacalcidol decreased PTH ($p < 0.002$) as well as the urinary bone resorption marker NTX ($p < 0.003$). A significant decrease of pain score occurred only in the Alfacalcidol group ($p < 0.0001$). In patients receiving Alfacalcidol muscle power increased by 58% compared to 18% in patients of the vitamin D group ($p < 0.05$).

Alfacalcidol, but not plain vitamin D, has pleiotropic effects improving bone metabolism and clinical symptoms in patients with rheumatoid arthritis.

SY12. D–HORMONES FOR PREVENTION OF BONE LOSS AFTER ORGAN TRANSPLANTATION

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Active vitamin D metabolites such as 1,25 dihydroxy vitamin D (calcitriol) and 1–α hydroxyvitamin D (alfacalcidol), also called D–Hormones, have been shown to be effective in preventing bone loss in patients starting glucocorticoids, suggesting a role for these agents in transplant osteoporosis. Vitamin D metabolites could reduce post–transplantation bone loss by reversing glucocorticoid–induced decreases in intestinal calcium absorption and mitigating secondary hyperparathyroidism (1), which appears to be a prominent mechanism of post transplant bone loss (2). A potential reduction in immunosuppressive requirements with active vitamin D metabolites (3) is an additional consideration in their use.

In a two year randomised double blind study of 65 patients undergoing cardiac or single lung transplantation, the efficacy of treatment with calcitriol in primary prevention was examined (4). Patients were randomly allocated to receive either placebo or calcitriol (0.5–0.75 mcg/day), the latter for either 12 months or 24 months after transplantation (ie 3 groups). All groups received 600 mg calcium/day. Bone loss at the proximal femur was significantly reduced or prevented at all three sites by treatment with calcitriol for 2 years compared with treatment with calcium alone. Bone loss at 24 months averaged 8.3% for those treated with calcium alone, compared to 5.0% for those treated with calcitriol for 2 years. However treatment with calcitriol for 12 months followed by calcium for 12 months resulted in similar proximal femoral bone loss to that seen in those patients treated with calcium alone for 24 months (7.4%), suggesting prophylaxis with calcitriol needed to be continued beyond 12 months. Over two years, 22 new vertebral fractures/deformities occurred in 4 patients treated with calcium alone compared with one new vertebral fracture in one patient treated with calcitriol. Mild hypercalcemia was not uncommon, but there were no significant differences between groups in serum creatinine after two years. These data suggest calcitriol in doses of 0.5 mcg or greater daily may have a role in reducing bone loss after cardiac or lung transplantation, but treatment needs to be continued beyond one year. A more recent study further supports these findings.

In a two year double blind randomised trial in 149 patients after cardiac transplantation, alendronate 10 mg daily was compared with calcitriol 0.5 mcg daily (5). Rates of bone loss were compared to 27 control subjects concurrently transplanted, but not randomised to therapy. Subjects randomised to alendronate and calcitriol did not experience significant bone loss in contrast to the control group. The change in spinal BMD was +0.3% with alendronate, –0.6% with calcitriol and –3.2% in controls. The change in hip BMD was −1.3% with alendronate, –0.4% with calcitriol and –6.2% in controls. Urinary NTX fell by 34% with alendronate, 26% with calcitriol but were unchanged with controls. New vertebral fractures occurred in 6.8% of subjects treated with alendronate, 3.6% of subjects treated with calcitriol and 13.6% of the control subjects. In the second year after discontinuation of both agents, BMD remained stable despite marked increases in bone turnover in the calcitriol group.

These studies suggest a role for active vitamin D metabolites or D–Hormones in preventing bone loss in patients after transplantation.

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SY13. ALFACALCIDOL VERSUS PLAIN VITAMIN D IN THE TREATMENT OF GLUCOCORTICOID/ INFLAMMATION–INDUCED OSTEOPOROSIS

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The aim of our study was to compare directly plain vitamin D and alfacalcidol in patients with established glucocorticoid–induced osteoporosis (GIOP). 204 patients on long–term glucocorticoid (GC) therapy were included as matched–pairs to receive randomly either 1 µg alfacalcidol (Alpha–D3®, TEVA) plus 500 mg calcium per day (group A, n = 103) or 1000 IU vitamin D3 plus 500 mg calcium (group B, n = 101). Correspondingly the two groups were well matched in terms of mean age, sex ratio, mean height and weight, daily dosage and duration of GC–therapy and the percentages of the underlying diseases (chronic obstructive pulmonary disease, rheumatoid arthritis, polymyalgia rheumatica). The mean bone mineral density (BMD) values at baseline for the two groups were at the lumbar spine of a T–score of −3.26 (alfacalcidol) and −3.25 (vitamin D3) and at the femoral neck −2.81 and −2.84 resp. Rates of prevalent vertebral and non–vertebral fractures were not different between the groups.

During the three year study we observed a median percentage increase of BMD at the lumbar spine of 2.4% in group A compared with a loss of 0.8% in group B ($p < 0{,}0001$). The 3 years rate of patients with at least one new vertebral fracture was 9.7 percent among those assigned to the alfacalcidol group, as compared to 24.8 percent among those assigned to the vitamin D group (Risk Reduction: 0.61; 95% CI 0.24 to 0.81; $p = 0.005$). The 3 years rate of patients with at least one new non–vertebral fracture was 15 percent in the alfacalcidol group, as compared to 25 percent in the vitamin D group (Risk Reduction: 0.41; 95% CI −0.06 to 0.68; $p = 0.081$). In accordance with the observed fracture rates, the alfacalcidol group showed a substantially larger decrease in back pain than the plain vitamin D group ($p < 0{,}0001$). Generally side effects in both groups were mild and only 3 patients in the alfacalcidol group and 2 patients in the vitamin D group had moderate hypercalcemia.

We conclude that alfacalcidol plus calcium is highly superior to plain vitamin D3 plus calcium in the treatment of established GIOP.

SY14. REDUCTION OF FALLS AND FALLERS IN HIGH RISK PATIENTS BY D–HORMONE ANALOGS

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Aims: The number of fallers and falls in elderly can significantly be reduced by treatment with D–hormone analogues. For the activation of calcitriol (D–hormone) renal function is detrimental. We therefore determined the cutoff levels of creatinine clearance (CrCl), used as a marker of renal function, at which D–hormone serum levels declines. Using the data of a double–blind randomized study and the determined cutoff, we analyzed if CrCl is associated with the risk of falls and whether treatment with Alfacalcidol can reduce this risk.

Methods: For 36 weeks randomly 378 community–dwelling elderly men and women received 1μg Alfacalcidol (Alpha–D_3® TEVA) or placebo daily. Incidence and number of falls were regularly assessed with the help of a questionnaire. In multivariate–controlled logistic regression models, we assessed, according to treatment groups and according to a CrCl cutoff at 65 ml/min, the risk to become a faller and the risk of falls. Presented results are from ITT analyses.
Results: In multivariate–controlled analyses D–hormone serum levels were significantly associated with CrCl ($p < 0.0001$) and steadily declined below a CrCl of 65 ml/min. In multivariate controlled analyses parameters associated with low D–hormone serum levels were in order of significance: a CrCl of < 65ml/min ($p = 0.0008$), the use of diuretics ($p = 0.001$) and a diagnosis of adult onset diabetes ($p = 0.003$). In the Placebo group, we observed significantly more fallers in participants with a CrCl of < 65ml/min compared to participants with a CrCl of ≥65ml/min (OR 4.01, 95%CI 1.48–10.98, $p = 0.006$). 36 weeks of treatment with Alfacalcidol was in participants with a CrCl of < 65ml/min, compared to placebo, associated with a significant reduction in the number of fallers (OR 0.26, 95%CI 0.08–0.80, $p = 0.019$), and a significant reduction of number of falls (OR 0.29, 95%CI 0.09–0.88, $p = 0.028$). No clinically relevant hypercalcemia were observed.
Conclusion: A reduced CrCl of < 65ml/min is, similarly to other risk factors (serum–cytokines , glucocorticoid–treatment), significantly associated with low D–hormone and with a significant increased risk of falls. Treatment with Alfacalcidol significantly and safely reduces in a community–dwelling elderly population with a CrCl of < 65ml/min, the low CrCl associated increased number of fallers and the high risk of falls.