A New Algorithm for Cortical Bone Segmentation with Its Validation and Applications to In Vivo Imaging

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Abstract. Cortical bone supports and protects our skeletal functions and it plays an important in determining bone strength and fracture risks. Cortical bone segmentation is needed for quantitative analyses and the task is nontrivial for *in vivo* multi-row detector CT (MD-CT) imaging due to limited resolution and partial volume effects. An automated cortical bone segmentation algorithm for *in vivo* MD-CT imaging of distal tibia is presented. It utilizes larger contextual and topologic information of the bone using a modified fuzzy distance transform and connectivity analyses. An accuracy of 95.1% in terms of volume of agreement with true segmentations and a repeat MD-CT scan intra-class correlation of 98.2% were observed in a cadaveric study. An *in vivo* study involving 45 age-similar and height-matched pairs of male and female volunteers has shown that, on an average, male subjects have 16.3% thicker cortex and 4.7% increased porosity as compared to females.

Keywords: Osteoporosis, cortical bone, segmentation, CT imaging, fuzzy distance transform, connectivity.

1 Introduction

Cortical bone is one of the two types of osseous tissue that forms the cortex of individual bones and facilitates supporting and protecting their functions. Adult bone diseases, especially osteoporosis, lead to increased risk of fracture associated with substantial morbidity, mortality, and financial costs [1]. Although, osteoporosis is clinically defined by low bone mineral density (BMD), currently, much interest exists in the study of other factors affecting bone strength including cortical and trabecular bone micro- and macro-architecture [2]. Several studies have reported that volumetric and structural changes in cortical bone are important in assessing bone strength and discriminating between healthy individuals and patients with osteoporotic fractures [3,4]. Fracture risk, one of the serious consequences of osteoporosis, is also influenced by alterations in bone morphology, such as the distribution of bone mass between cortical and trabecular bone, cortical thickness and porosity [5,6]. Cortical bone loss and periosteal new bone formation are also used for therapeutic evaluation of

osteoarthritis [7]. Over the last few decades, several studies have been conducted to better understand the role of cortical bone properties in determining the status of bone health and treatment effects [8,9]. Also, research studies have established the relationships between cortical bone porosity and bone biomechanical strength [10]. These results and observations in several clinical and research studies demonstrate the importance of cortical bone parameters in understanding overall bone quality.

Most of the previous cortical bone segmentation algorithms were dedicated for micro-CT [7,11] or high resolution peripheral quantitative CT (HR-pQCT) [3,8,9,12] imaging. In this paper, we present a new cortical bone segmentation algorithm for *in vivo* multi-row detector CT (MD-CT) imaging. Major benefits of MD-CT imaging include – (1) faster acquisition, i.e., less chance of motion artifacts, (2) wider clinical access and better patient comfort, and (3) large field of view, i.e., reduced positioning error and application of post-image registration methods to improve serial reproducibility. Cortical bone segmentation for *in vivo* MD-CT imaging meets several major challenges, including limited image resolution and partial volume effects. These challenges are further intensified by non-uniformity of cortical bone thickness and presence of holes inside cortical bones. Also, the presence of thick trabeculae near cortical bone region usually causes morphological opening based algorithms to fail. These challenges of MD-CT based cortical bone segmentation are met by utilizing larger contextual and topological information of the bone through a modified fuzzy distance transform (FDT) [13] and connectivity analyses [14]. The algorithm finds the periosteum and endosteum boundaries of the target bone under a simple topo-morphologic model without using ad hoc assumptions and parameters. Accuracy, reproducibility, and effectiveness of the method have been evaluated.

2 Methods

The overall method is completed in two steps – (1) bone alignment and ROI detection and (2) cortical bone segmented over the ROI in the reoriented image. These steps are accomplished using a modified version of fuzzy distance transform and connectivity analysis.

MD-CT images may be represented on a three-dimensional (3-D) rectangular grid Z^3 using a function $f_{CT}: Z^3 \rightarrow [\min_{CT}, \max_{CT}]$. Each grid point $p \in Z^3$ is referred to as a *voxel* whose size is defined by image resolution. Here, 26-adjacency is used for bone voxels, while 6-adjacency is used for marrow voxels. The cortical bone segmentation algorithm presented here utilizes the fuzzy distance transform (FDT) [13] and connectivity [14]. A *fuzzy digital* or simply a *fuzzy object* $\mathcal{O}$ is essentially a fuzzy subset $\{(p, f_{\mathcal{O}}(p)) \mid p \in Z^3\}$ of Z^3 where $f_{\mathcal{O}}$ is the membership function. For any voxel p within the support $O = \{p \mid p \in Z^3 \wedge f_{\mathcal{O}}(p) > 0\}$ of a fuzzy object $\mathcal{O}$, FDT computes the distance of p from the background $B = Z^3 - \mathcal{O}$ in the presence of material inhomogeneity and partial voxel volume. The first step of FDT computation is to initialize a zero FDT value in B and a large value in $\mathcal{O}$. The second step is an iterative propagation of FDT such that

$$FDT_{\mathcal{O}}(p) = \min_{q \in N(p)} FDT(q) + \frac{1}{2}(f_{\mathcal{O}}(p) + f_{\mathcal{O}}(q))|p - q|, \quad (1)$$

where $N(p)$ is the set of adjacent voxels of p including p itself. Here, a simple yet effective variation of FDT algorithm is introduced that may be useful in several applications. Let us define three sets – (1) L : set of voxels initialized with a large value, i.e., the set of voxels where FDT value is unknown during initialization, (2) U : set of voxels initialized with non-large values, i.e., the set of voxels where FDT value is known at the time of initialization, and (3) V : the set of voxels where no path propagation is allowed, i.e., outside the region of interest. Note that the initial values over U may be non-zero and non-uniform.

Fuzzy connectivity [14] $\mu_{FC}: Z^3 \times Z^3 \rightarrow Z$ between two voxels on a grey-scale image defines the connectivity of the strongest path between the two voxels where the strength of connectivity of a path is the smallest grey value on the path. Often, a fuzzy connected object is defined as an image $FC: Z^3 \rightarrow Z$ using a set S of seeds voxels where $FC(p) = \max_{s \in S} \mu_{FC}(p, s)$.

2.1 Bone Alignment and ROI Detection

The purpose of this module is to ensure that cortical bone measures are computed from the same anatomic location in individuals' bones and it is accomplished by producing axial cylindrical regions of interest (ROIs) at matching tibial sites. This module begins with conversion of CT image values into bone mineral density (BMD) values using a calibration phantom. All subsequent operations are applied on the BMD image. The next step is to generate a filled-in bone shape (Fig. 1(b)) that separates the tibial region from other bones and soft tissues. First, a simple thresholding at 1,233mg/cc is applied on the BMD image to isolate the bone region from marrow, cortical pores, and the space outside the tibia. The BMD threshold value was selected as the average of threshold values manually selected by three users on five randomly selected *in vivo* MD-CT data sets. Each user was asked to select a threshold value that isolates bone from marrow. The same BMD threshold value was used for all experiments presented in this paper. Let S_{bone} denote the set of bone voxels and let $S_{\text{non bone}}$ denote the set of non-bone voxels, including marrow, cortical pores, and the space outside the tibia. The filled-in bone shape is computed in the following four steps:

- Step 1:** Computation of distance transform DT_{bone} from S_{bone} ; thus, at any image voxel $p \in Z^3$, $DT_{\text{bone}}(p)$ indicates the distance of p from S_{bone} .
- Step 2:** Computation of fuzzy connectivity $FC_{\text{morpho}}: Z^3 \rightarrow Z$ on DT_{bone} with a seed S preset at a distant background voxel, e.g., the corner voxels of the image space. Marrow voxels inside the tibia are expected to be disconnected from the background, so ideally FC_{morpho} values at marrow voxels should be zero. Often, the cortex contains small leaks and fuzzy connectivity paths may sneak through those leaks. However, since such leaks are small holes on the cortex, $DT_{\text{bone}}(p)$ values at these leaks are small and any path through such holes are small in value. Therefore, FC_{morpho} at marrow voxels are always small because a path from the background to marrow has to pass through one of the leaks on the cortex.

Step 3: Selection of a threshold value thr on FC_{morpho} that barely disconnects marrow voxels from S ; let $S_{\text{non tibia}}$ be the non-tibia region obtained by thresholding FC_{morpho} at thr .

Step 4: Computation of $DT_{\text{non tibia}}$ from $S_{\text{non tibia}}$ and select the filled-in tibia as the region generated by thresholding $DT_{\text{non tibia}}$ at thr .

This filled-in bone is used to reorient the tibia to determine the matching ROIs in the individual's bone. First, a rough estimate of the distal tibial end plateau location is performed, which is located just above the first image slice containing a 2-D cavity in the filled in bone while tracing slices from proximal to distal (Fig. 1(c)). Image slices above 8% of tibial length from the end plateau are used to compute the tibial axis; also, a 40% peel is applied to this region to make it thinner and easier to determine the axis; see Fig. 1(c). The axis of tibia is computed as the best-fit line to this region. The bone is reoriented to align its axis with the image z-axis (Fig. 1(d)). Finally, the image is interpolated at 150 micron isotropic voxel and the distal tibial end plateau is relocated using the same logic as before. Four adjacent axial cylindrical ROIs, each covering 2% of the tibial length, are located at 8%, 10%, 12% and 14% proximal to the distal endplate as shown in Fig. 1(d). All cortical bone segmentation and analyses were applied over this axial cylindrical ROI covering 8% of the tibial length. The length of tibia is acquired during the MD-CT scout scan.

Fig. 1. Illustration of the process of bone filling, alignment, and ROI selection. (a) An original MD-CT image slice. (b) Filled-in bone. (c) Initial location of distal tibial end plateau (white dot) and the shaded region used for bone alignment. (d) Final ROI covering 8-16% of tibia. Although, the process is applied in 3-D, 2-D illustrations are used for convenience.

2.2 Cortical Bone Segmentation Algorithm

This step is conducted on reoriented and interpolated images. Let S_{tibia} denote the set of voxels falling inside the filled-in reoriented tibia within the target axial cylindrical ROI (Fig. 2(a)) and let f_{BMD} denote the BMD map. Also, let $S_{\text{bone}} \subset S_{\text{tibia}}$ denote the set of bone voxels while $S_{\text{non bone}} = S_{\text{tibia}} - S_{\text{bone}}$ be the set marrow and cortical pore voxels within the tibia (Fig. 2(c)). Let $S_{\text{periosteum}}$ denote the set of voxels 26-adjacent to S_{tibia} ; thus, the set of voxels $S_{\text{periosteum}}$ (Fig. 2(c)) wraps around

the ROI used for cortical bone analyses. The set of voxels outside $S_{\text{tibia}} \cup S_{\text{periosteum}}$, denoted by $S_{\text{background}}$, are excluded. Non-bone voxels $S_{\text{non bone}} \subset S_{\text{tibia}}$ inside the tibia are further classified into confident marrow (green) and possible cortical pore (blue) voxels; let S_{marrow} and S_{pore} denote these two sets. The set S_{marrow} is defined as the largest 6-component of $S_{\text{non bone}}$ and $S_{\text{pore}} = S_{\text{non bone}} - S_{\text{marrow}}$. It is quite straight-forward and easy to get S_{tibia} , S_{bone} , $S_{\text{periosteum}}$ and S_{marrow} on the image using thresholding and a region growing algorithm.

The key idea of the segmentation algorithm is to compute cortical bone thickness at every voxel on the periosteal boundary as its distance from the endosteum and then delineate the cortex as the set of all voxels whose distance from some periosteal voxel is smaller than or equal to its thickness value. A major challenge is the presence of cortical pores artificially reducing local thickness at nearby periosteal voxels. Such artifacts are detected by identifying sudden recessions in thickness values along periosteum and then linking those with possible pores. Initial thickness values at periosteal voxels are computed as their FDT values from the set of marrow or possible pore voxels, i.e., $S_{\text{marrow}} \cup S_{\text{pore}}$. For FDT computation during this step, zero value is initialized inside $S_{\text{marrow}} \cup S_{\text{pore}}$ while a large value is initialized inside $S_{\text{bone}} \cup S_{\text{periosteum}}$; finally, the set of voxels $S_{\text{background}}$ is excluded from path propagation. However, as it has already been stated, computed thickness values along the periosteal border may contain sudden recession points due to the presence of cortical pores. On a given slice, a periosteal boundary is a digital 4-closed curve, say, $p_0, p_1, \dots, p_{i-1}, p_i, p_{i+1}, \dots, p_{N-1}$. A given voxel p_i on the periosteum is a *recession voxel* if $FDT(p_i)$ is smaller than half of the average FDT value of the voxels $p_{i \pm j \bmod N}$, where $j = L, L+1, \dots, H$. After a recession voxel p_i is detected, the non-bone voxel, say q , nearest to p_i is identified. Finally, if q is a possible pore voxel, i.e., $q \in S_{\text{pore}}$, then the 6-component C_q of S_{pore} containing q is conformed as a cortical pore and $S_{\text{non bone}}$ is reduced to $S_{\text{non bone}} - C_q$ while S_{bone} is augmented to $S_{\text{bone}} \cup C_q$. After all recession voxels are identified and the pores are filled, the FDT for periosteal thickness is recomputed and the process continues until no new recession voxels are found on periosteum. For all experiments presented in the current paper, the process converged in three or fewer iterations.

At every voxel $p \in S_{\text{periosteum}}$, the FDT value computed as above gives the cortical bone thickness at p ; let us denote it as $\tau(p)$. The purpose of the current and final step of cortical bone segmentation is to delineate the cortical bone region. The principle of this step is to find the cortex as the set of all voxels whose distance from some periosteal voxel p is less than its cortical thickness $\tau(p)$. This step is accomplished using a modified FDT computation from the periosteum. Specifically, during this step, at each voxel $p \in S_{\text{periosteum}}$, the FDT value is initialized as $-\tau(p)$, the negative of the cortical bone thickness at p . A large value is initialized at each voxel inside S_{bone} ; finally, all voxels outside $S_{\text{bone}} \cup S_{\text{periosteum}}$ are excluded for path propagation. Let $\rho(p)$ denote the computed FDT value at each voxel inside S_{bone} . The cortical bone region S_{cortex} is delineated as the set of all bone voxels p with a negative FDT value $\rho(p)$ as follow:

$$S_{\text{cortex}} = \{p \mid p \in S_{\text{bone}} \wedge \rho(p) < 0\}. \quad (2)$$

Fig. 2. Results of intermediate steps of the cortical bone segmentation algorithm. (a) ROI volume and an image slice used for illustration. (b) BMD image. (c) Marrow space (green), possible cortical pores (blue), and periosteal surface (red). (d) FDT from marrow space and possible cortical pores. (e) Same as (d) after filling confirmed cortical pores. (f) FDT from periosteal boundary by initializing the negative value of local cortical bone thickness; see text for explanation. (g) Cortical bone segmented as the region with negative FDT values in (f). (h) Segmented trabecular bone region. (i) Overlaid cortical bone region on the CT image.

Finally, the outer layer on cortex $S_{\text{outer cortex}}$ is defined as the set of cortex bone voxels which are 6-adjacent to $S_{\text{periosteum}}$.

2.3 Experimental Methods

The aims of our experiments were – (1) to evaluate the method’s accuracy in terms agreement with gold standard results of cortical bone segmentation, (2) to examine the method’s repeat MD-CT scan reproducibility, and (3) to assess the method’s ability to differentiate cortical bone measures among different groups of people. All experiments were performed at the distal tibia site. To evaluate the method’s reproducibility, three repeat scan MD-CT imaging was performed on human cadaveric ankle specimens. *In vivo* MD-CT imaging scans were performed on volunteers to evaluate the method’s accuracy and efficiency.

Each image data set was processed through the following cascade of steps – (1) computation of BMD image, (2) bone reorientation, interpolation, and ROI selection, and (3) application of cortical segmentation on the ROI image data. For cadaveric ankle specimens, INTableTM calibration phantom was used to convert the MD-CT Hounsfield numbers into BMD (mg/cm^3) measures while GammamaxTM calibration phantom was used for *in vivo* scans. As described in Section 2.1, four axial cylindrical sections covering 8-16% of tibia were used. Each cylindrical section was further subdivided into four angular sections [8], namely anterior, posterior, medial and lateral, using the reference line joining the center-of-gravities of cross-sections of tibia and fibula; see Fig. 3. Thus, with each of the 4 cylindrical sections being divided into 4 angular regions, altogether 16 ROIs were used for computing cortical bone measures. On each of the sixteen ROIs, cortical thickness and porosity are defined as:

$$\text{cortical thickness} = \frac{|S_{\text{cortex}}|}{|S_{\text{outer surface}}|}, \quad (3)$$

$$\text{porosity} = \frac{\rho_B - (\sum p \in S_{\text{cortex}} \frac{BMD(p)}{|S_{\text{cortex}}|})}{\rho_B - \rho_M}, \quad (4)$$

where ρ_B and ρ_M are the true material density of bone and marrow in mg/cc . Essentially, Equation (4) is derived from the relationship $(1 - \text{porosity}(p)) \times \rho_B + \text{porosity}(p) \times \rho_M = BMD(p)$, where $\text{porosity}(p)$ is porosity at a specific voxel p . Note that $BMD(p)$ is the apparent density at p as observed in the acquired image.

Fifteen fresh-frozen human cadaveric ankle specimens were obtained from nine body donors (age: 55Y to 91Y). Exclusion criteria for this study were evidence of previous fracture or knowledge of bone tumor or bone metastasis. These ankle specimens were collected under the Deeded Bodies Program, The University of Iowa, Iowa City, and were kept frozen until the performance of MD-CT imaging. Forty-five male (M) and forty-five female (F) volunteers of age 18 to 23 years were recruited for the *in vivo* study.

Fig. 3. Illustration of angular ROIs using the reference line joining the center of gravity of tibia with that of fibula. Each angular section covers 90° of angular space.

2.4 MD-CT Imaging

High resolution MD-CT scans of the distal tibia were acquired at the University of Iowa Comprehensive Lung Imaging Center on a 128 slice Somatom Definition Flash scanner (Siemens, Munich, Germany) using the following CT parameters: single tube spiral acquisition at 120kV, 200 effective mAs, pitch factor: 1.0, scan length of 10cm beginning at the distal tibia end-plateau and total effective dose equivalent: 17mrem $\approx$ 20 days of environmental radiation. One AP scout scan of the entire tibia was acquired to locate the field of view (FOV) and to determine tibial length. After scanning each specimen in a helical mode with a 0.4 mm slice thickness, data were reconstructed at 0.2 mm slice thickness using a normal cone beam method with a special U70u kernel achieving high structural resolution. Three repeat MD-CT scans of each distal tibia specimen were acquired after repositioning the specimen on the CT table before each scan. Human subjects were scanned using the exact same CT protocols lying on the CT table in the feet-first supine position.

3 Results

Results of intermediate steps during cortical bone segmentation on an *in vivo* MD-CT image are illustrated in Fig. 2. Final results of cortical bone delineation are visually satisfactory. Quantitative results of experiments are presented next.

3.1 Accuracy of Cortical Bone Segmentation

The experiment for accuracy evaluation of the method was performed on ten randomly chosen *in vivo* MD-CT ankle images. To examine the accuracy of our cortical bone segmentation, a gold standard segmentation of cortical bone was derived by manually outlining cortical region on twenty slices for each MD-CT image data, among which five consecutive slices were randomly selected from each of the four cylindrical ROI sections. Segmentation of periosteal boundary is straight-forward and may be obtained by simple thresholding and region growing. Therefore, we restrained ourselves from manual delineation of periosteal boundary and considered segmentation results of periosteum as the ground truth. However, on a given image slice, we manually delineated the endosteal boundary and assembled it with the segmented results of periosteal boundary to generate the ground truth for cortical bone mask on the specific image slice. This work is done by an independent expert using the ITK-SNAP software. Let $S_{\text{cortex}}^{\text{true}}$ be the set of voxels falling inside the true cortical bone region and let $S_{\text{cortex}}^{\text{MD-CT}}$ be the computerized segmentation result. Jaccard index is used to characterize the accuracy as follows:

$$\text{accuracy} = \frac{S_{\text{cortex}}^{\text{true}} \cap S_{\text{cortex}}^{\text{MD-CT}}}{S_{\text{cortex}}^{\text{true}} \cup S_{\text{cortex}}^{\text{MD-CT}}} . \quad (5)$$

As observed in experimental results from ten *in vivo* MD-CT data, the method achieves an average accuracy of 95.1% with a standard deviation of 1.0%. Considering the challenges of cortical bone segmentation at relatively low resolution as offered

by MD-CT imaging, the observed accuracy results are encouraging. Also, the Dice's co-efficient for our cortical bone segmentation results is 97.5%, which is significantly better than the value of 90.4% for the same co-efficient as reported in [12].

3.2 Repeat Scan Reproducibility of Cortical Bone Segmentation

For this experiment, three repositioned repeat scan MD-CT images of fifteen cadaveric ankle specimens were used. BMD computation, ROIs selection, and cortical bone segmentation and measurements were performed independently on each repeat scan data. For quantitative assessment of reproducibility of cortical bone segmentation algorithm, repeat scan intra-class correlation (ICC) values were computed for each measure over each ROI from three repeat scan data of the fifteen cadaveric specimens. The observed ICC values for both cortical thickness and porosity measures were high, with the average ICC value for cortical thickness over the sixteen different ROIs being $98.2\% \pm 1.5\%$ (mean $\pm$ std.) and $97.9\% \pm 0.9\%$ (mean $\pm$ std.) for cortical porosity. The observed results of repeat scan reproducibility of cortical bone measures were highly satisfactory, confirming the repeatability of cortical bone segmentation and measures.

3.3 Results of *In Vivo* Study

To evaluate the effectiveness of the method, first, *in vivo* MD-CT data of forty-five male and forty-five female age similar (18Y to 23Y) volunteers were used to form height order-matched pairs by gender. The heights of used data are $180.88 \pm 7.89\text{cm}$ (mean $\pm$ std.) for male, and $165.56 \pm 5.62\text{cm}$ (mean $\pm$ std.) for female, and the R^2 value of linear correlation of matching heights in the groups was 0.972. Cortical bone segmentation and measurement were conducted and a paired t-test was performed for both cortical thickness and porosity measures derived from each of the sixteen ROIs. Quantitative results have shown that male subjects on average had 16.3% thicker cortex and 4.7% increased porosity as compared to females. Results of paired t-test among height matched male and female volunteers showed the difference was statistically significant with p-values less than 0.01 on all sixteen ROIs, for both thickness and porosity.

4 Conclusion

A new cortical bone segmentation algorithm with regional cortical measures has been developed for MD-CT bone imaging at a peripheral site. The algorithm is fully automated and has been applied on cadaveric as well as on *in vivo* MD-CT images of distal tibia. The new cortical bone segmentation algorithm makes effective use of larger contextual and topologic information of the distal tibial bone geometry. In this context, a new variation of fuzzy thickness computation has been introduced and its application to cortical bone segmentation has been demonstrated. Experimental results from ten human and fifteen cadaveric distal tibia MD-CT data have demonstrated that the method is highly accurate and reproducible. Also, *in vivo* data from ninety age similar and height order matched male and female volunteers has shown that male subjects have thicker and more porous cortex at distal tibia as compared to females.

Acknowledgements. This work was supported by the NIH grants R01-AR054439 and R01-DE012101. The authors wish to thank Mr. Jered Sieren for performing MD-CT cadaveric and human bone imaging.

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