Fuzzy Digital Topology and Geometry and Their Applications to Medical Imaging

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Abstract. The primary end-goal of most medical imaging research program is to collect information about function and physiology of internal human organs or tissues through a variety of *in vivo* or *ex vivo* imaging techniques. Often, medical imaging techniques suffer from limited spatial and temporal resolution, noise, background-inhomogeneity, and other artifacts leading to fuzzy representations of target objects in acquired images. Digital topology and geometry play important roles in medical image processing either by expanding the scope of target information or by providing a strong theoretical foundation to a process enhancing its stability, fidelity, and efficiency. The notions of digital topology and geometry are often intertwined in medical imaging applications and sometime it is difficult to draw a dividing line between them. This paper presents recent advancements and overviews of theory and computation of several fuzzy digital topologic and geometric approaches and describe their applications to medical imaging. More specifically, this paper discusses topics related to three-dimensional simple points, local topological parameters, fuzzy skeletonization, characterization of local structures, and their applications to research and clinical studies.

Keywords: Fuzzy subset, digital imaging, topology, geometry, distance transform, simple point, skeletonization, topological classification, medical imaging.

1 Introduction

The primary end-goal of most medical imaging research program is to collect information about function and physiology of internal human organs or tissues through a variety of *in vivo* or *ex vivo* imaging techniques [1]. Often, medical imaging techniques suffer from limited spatial and temporal resolution, noise, background-inhomogeneity, and other artifacts leading to fuzzy representations of target objects in acquired images. Digital topology and geometry [2-7] play important roles in medical image processing either by expanding the scope of target information or by providing a strong theoretical foundation to a process enhancing its stability, fidelity, and efficiency. The notions of digital topology and geometry are often intertwined in medical imaging applications and sometime it is difficult to draw a dividing line between them. The term “digital topology” loosely refers to the use of mathematical topological properties and features such as

connectedness and boundary in computer vision, graphics and image processing. Digital topology has been studied since the late 1960's, when it was introduced by Rosenfeld, whose early articles [2, 3, 8-10] played a major role in establishing the field. It has provided the theoretical foundations for important image processing operations such as object counting, thinning, boundary detection and contour filling etc. During early 1970s, the subject of digital geometry was brought into light when the challenges of defining a digital straight line or straightness of a digital line were introduced. Subsequently, researcher investigated other areas of digital geometry, including curvature, corners, arc length, perimeter, surface area, convexity, convex hull, distance transform etc.

Digital topology and geometry have been applied in medical imaging to solve different important task. For example, component labeling and border tracking have been applied in medical image visualization, manipulation, and analysis [11]. Digital connectivity and minimum cost path has been widely used in medical image segmentation [12-15]. Digital topology has been applied to characterize local structure, e.g., classification of plates and rods in a trabecular bone imaging. Topology has also been used for correction of anatomic structures [16] segmented in acquired images in the presence of noise, partial voluming, and other artifacts. Skeletonization [17-19] has been used to solve several medical imaging purposes, including, representation of anatomic structure, path planning, feature extraction, disease identification etc. This paper presents recent advancements and overviews of theory and computation of several fuzzy digital topologic and geometric approaches and describe their applications to medical imaging. More specifically, this paper discusses topics related to three-dimensional simple points [6, 20, 21], local topological parameters [7], fuzzy skeletonization [19], characterization of local structures [7, 22-25], and their applications to medical research and clinical studies.

2 Definitions and Notations

Most medical imaging techniques acquire scan data in a three-dimensional rectangular grid. A three dimensional (3-D) rectangular grid may be constructed by dividing the 3-D continuous space $\mathbb{R}^3$ into rectangular parallelepipeds with three orthogonal families each of equally spaced parallel planes. The set of the centers of these rectangular parallelepipeds generates a rectangular grid and it is not difficult to see that, under a proper coordinate system, these points constitute the set $\mathbb{Z}^3$ where $\mathbb{Z}$ is the set of all integers. Each upright rectangular parallelepiped centered at a point in $\mathbb{Z}^3$ is referred to as a voxel or as a point. Two voxels are said to be 26-adjacent if the two share at least a vertex. Two voxels are said to be 18-adjacent if the two share at least an edge. Two voxels are said to be 6-adjacent if the two share a 2-D face. A κ -adjacency, where $\kappa \in \{6, 18, 26\}$, is defined in a way such that each point is κ -adjacent to exactly κ other points in the respective grid. A κ -path π is a nonempty sequence of points where every two successive points are κ -adjacent. Now consider

$\mathcal{S} \subset \mathbb{Z}^3$. Two points $x, y \in \mathcal{S}$ is said to be κ -connected in $\mathcal{S}$ if there exists a κ -path from x to y that is contained by $\mathcal{S}$. A κ -component of $\mathcal{S}$ is a maximal subset of $\mathcal{S}$ where every two points is κ -connected in $\mathcal{S}$; $\mathcal{S}$ is said to be κ -connected if it has just one κ -component, or if $\mathcal{S}$ is an empty set. The set of 26-neighbors of a voxel p together with the voxel p forms a $3 \times 3 \times 3$ neighborhood and it is denoted by $N_{26}(p)$; $N_{26}^*(p)$ denotes the set of all voxels of $N_{26}(p)$ excluding the central voxel p . The other neighborhoods, namely, $N_6(p)$, $N_6^*(p)$, $N_{18}(p)$, and $N_{18}^*(p)$ are defined similarly.

Following Kong and Rosenfeld [4], a binary digital image or an object in a rectangular grind may be represented as a quadruple $\mathcal{B} = (\mathbb{Z}^3, \alpha, \beta, B)$, where the first element $\mathbb{Z}^3$ defines the 3-D image space; the two parameters α and β denote the adjacency relations used for object and background voxels, respectively; here 26- and 6-adjacencies are used for object background voxels, respectively. Similarly, a fuzzy digital image or fuzzy object may be denoted as $\mathcal{O} = (\mathbb{Z}^3, \alpha, \beta, \mu_{\mathcal{O}})$ where $\mu_{\mathcal{O}}: \mathbb{Z}^3 \rightarrow [0, 1]$ is the membership function of the target fuzzy object. The support $\mathcal{O}$ of the fuzzy object $\mathcal{O}$ is the set of all points with nonzero membership values, i.e., $\mathcal{O} = \{p \mid p \in \mathbb{Z}^3 \wedge \mu_{\mathcal{O}}(p) > 0\}$. In a fuzzy digital image, the adjacency relation α is used for voxels inside the support of the object while β is used for the voxels inside the background $\bar{\mathcal{O}} = \mathbb{Z}^3 - \mathcal{O}$.

3 Fuzzy Distance Transform

Distance transform [26-28] is a local depth measure inside an object and we call it “fuzzy distance transform” when the object representation is fuzzy. Fuzzy distance transform [29] accounts for both partial voxel occupancy and spatial heterogeneity of an object distribution. The length of a link $\langle p, q \rangle$ is calculated as $\frac{1}{2}(\mu_{\mathcal{O}}(p) + \mu_{\mathcal{O}}(q)) \|p - q\|$, where, $\|\cdot\|$ denotes any Euclidean L2 norm. The length of a path $\pi = \langle p_1, p_2, \dots, p_l \rangle$ in a fuzzy object $\mathcal{O}$, denoted by $\Pi_{\mathcal{O}}(\pi)$, is defined as the sum of lengths of all links along the path, i.e.,

$$\Pi_{\mathcal{O}}(\pi) = \sum_{i=1}^{l-1} \frac{1}{2}(\mu_{\mathcal{O}}(p_i) + \mu_{\mathcal{O}}(p_{i+1})) \|p_i - p_{i+1}\|. \quad (1)$$

Between any two points $p, q \in \mathbb{Z}^3$, infinitely many paths may exist; let $\mathcal{P}(p, q)$ denote the set of all paths from p to q . A path $\pi_{p,q} \in \mathcal{P}(p, q)$ is one of the shortest paths from p to q in $\mathcal{O}$, if and only if, $\Pi_{\mathcal{O}}(\pi_{p,q}) \leq \Pi_{\mathcal{O}}(\pi)$ for all $\pi \in \mathcal{P}(p, q)$. It may be noted that the shortest path between two points $p, q \in \mathbb{Z}^3$ may not be unique. The fuzzy distance from $p \in \mathbb{Z}^3$ to $q \in \mathbb{Z}^3$ in an object $\mathcal{O}$, denoted by $\omega_{\mathcal{O}}(p, q)$, is the length of one of the shortest paths from p to q , i.e.,

$$\omega_{\mathcal{O}}(p, q) = \min_{\pi \in \mathcal{P}(p, q)} \Pi_{\mathcal{O}}(\pi). \quad (2)$$

It has been shown in [29] that fuzzy distance satisfies the metric properties in both continuous as well as discrete spaces in any dimension. The fuzzy distance transform or FDT of an object $\mathcal{O}$ is represented as an image $\{(p, \Omega_{\mathcal{O}}(p)) | p \in \mathbb{Z}^3\}$, where $\Omega_{\mathcal{O}}: \mathbb{Z}^3 \rightarrow \mathbb{R}^+$ denotes the fuzzy distance transform value at a given point; $\mathbb{R}^+$ is the set of positive real numbers including zero. $\Omega_{\mathcal{O}}(p)$ is defined as the fuzzy distance between p and its nearest points in $\bar{\mathcal{O}}(\mathcal{O}) = \mathbb{Z}^3 - \mathcal{O}(\mathcal{O})$. In other words,:

$$\Omega_{\mathcal{O}}(p) = \min_{q \in \bar{\mathcal{O}}(\mathcal{O})} \omega_{\mathcal{O}}(p, q). \quad (3)$$

4 Simple Point and Topology Preservation

Saha et al. [6, 20, 21] conceived the concise characterization of 3-D simple points and presented it in the following four-condition format. A voxel or a point p is a (26,6) simple point if and only if it satisfies the following four conditions

Condition Saha 1: p has a white (background) 6-neighbor.

Condition Saha 2: p has a black (object) 26-neighbor.

Condition Saha 3: The set of black 26-neighbors of p is 26-connected.

Condition Saha 4: The set of white 6-neighbors of p is 6-connected in the set of its white 18-neighbors.

The above characterization of 3-D simple point was first documented in a technical report [20] published at the Indian Statistical Institute, February, 1991 which was communicated to Malandain [30] and a seminar talk [31] on the same topic was presented in June of 1991 at the INRIA, Sophia Antipolis Cedex, France. However, as claimed by Malandain [32], he failed to read the technical report and rediscovered the

same result which was presented as follows [33] – a voxel or a point p is a (26,6) 3-D simple point if and only if it satisfies the following two conditions.

Condition MB 1: $N^*(p)$ has exactly one 26-component of black points.

Condition MB 2: The number of 6-components of white points in $N_{18}^*(p)$ that intersect with $N_6^*(p)$ is exactly one.

It is straight forward that Condition MB 1 is equivalent to Conditions Saha 1 and 3 while Condition MB 2 is equivalent to Conditions Saha 2 and 4 which was later acknowledged by Bertrand and Malandain [34]. In fact, the four conditions used in Saha *et al.*'s 3-D simple point characterization define the four different types of topological violations which occur when a non-simple voxel/point is deleted. Condition Saha 1 ensures that no cavity is created by deletion of a point while Condition Saha 2 confirms that no isolated point is deleted. Condition Saha 3 is used to ensure that, after the deletion of a point p , its neighboring points remains connected. Finally, Condition Saha 4 guarantees that the deletion of a point does not create a tunnel in its neighborhood. The following two theorems by Saha *et al.* [6, 20, 21] are crucial to solve the fundamental challenges of 3-D simple point characterization.

Theorem 1. If point p has at a white 6-neighbor, the number of tunnels $\eta(p)$ in $N_{26}^*(p)$ is one less than the number of 6-components of white points in $N_{18}^*(p)$ that intersect with $N_6^*(p)$, or, zero otherwise.

Theorem 2. The number of cavities in $N_{26}^*(p)$ is one when all 6-neighbors of p is black (object) and zero otherwise.

The above two theorems define the following local topological numbers proposed by Saha *et al.* [6, 7, 20, 21] that relate to different topological entities in the local neighborhood of a voxel/point characterizing its topological properties.

$\xi(p)$: The number of objects components in $N_{26}^*(p)$

$\eta(p)$: The number of tunnels in $N_{26}^*(p)$

$\delta(p)$: The number of cavities $N_{26}^*(p)$

Bertrand and Malandain [34, 35] have advocated the following topological numbers.

$T_{26}(p)$: The number of 26-components of black points in $N_{26}^*(p)$

$T_6(p)$: The number of 6-components of white points in $N_{18}^+(p)$ that intersect with $N_6^+(p)$

Although, the number $T_6(p)$ is inspired by Theorems 1 and 2, it fails to distinguish between the two different topological situations – creation of a tunnel versus creation of a cavity.

5 Fuzzy Skeletonization

Blum's pioneering work on grassfire transform [36] led to the notion of skeletonization that converts a volumetric object into a union of surfaces and curves. The process is defined using fire propagation on a grass field, where the field resembles an object. The fire is simultaneously set at all boundary points and it propagates inwardly at a uniform speed. The skeleton is defined as the set of quench points where two or more fire fronts meet. However, the notion of skeletonization for fuzzy objects has not yet been defined. To define a fuzzy skeletonization process, we suggest modifying the Blum's grassfire transform for a fuzzy object where the membership function is interpreted as local material density so that the speed of grassfire at a given point is inversely proportional to its material density. Following this notion, it can be shown that fuzzy distance transform (FDT) [29] value at a point p is proportional to the time when the fire front reaches p . Therefore, during the fuzzy grassfire propagation, the speed of a fire front at a point equates to the inverse of local material density and this equality is violated only at quench points where the propagation process is interrupted. Thus, a voxel $p \in Z^3$, where Z is the set of integers and Z^3 represents a rectangular image grid, is a fuzzy quench voxel in a fuzzy digital object $\mathcal{O}$ if the following inequality holds for every neighbor q of p

$$FDT(q) - FDT(p) < \frac{1}{2}(\mu_{\mathcal{O}}(p) + \mu_{\mathcal{O}}(q))|p - q|. \quad (4)$$

Saha and Wehrli [37] introduced the above definition of fuzzy quench voxel which was further studied by Svensson [38] where she referred to it as the center of fuzzy maximal ball (CFMB). Also, it may be noted that the definition of fuzzy quench voxel is equivalent to that of center of maximal ball (CMB) [39] for binary digital objects. Two types of quench points may form –surface- and curve-quench points (Figure 1). A surface quench point is formed when two opposite fire fronts meet while a curve quench point is formed when fire fronts meet from all directions on a plane. In a digital space, surface-quench voxel is formed when two opposite fire fronts meet along x-, y- or z-direction and a curve-quench voxel is formed when fire fronts meet from all eight directions in xy-, yz-, or zx-planes.

Fig. 1. Illustration of independent fire fronts meeting at surface- (a) and curve-like (b) quench voxels

During the process of fuzzy skeletonization, voxels are removed in the increasing order of their FDT values. The overall fuzzy skeletonization process is summarized in the following. Here, $\mathcal{O} = \{p | \mu_{\mathcal{O}}(p) > 0\}$ denotes the support of the fuzzy object $\mathcal{O}$.

Primary skeletonization

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select voxels  $p \in \mathcal{O}$  in the order of FDT values
if  $p$  is not a fuzzy axial voxel and its deletion pre-
serves 3-D topology and 2D topology on mid-planes
    remove  $p$  from  $\mathcal{O}$ , i.e., set  $\mu_{\mathcal{O}}(p) = 0$ 

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Final skeletonization:

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select voxels  $p \in \mathcal{O}$  in the order of FDT values
if  $p$  is in two-voxel thick structure and its deletion
preserves 3-D topology and 2D topology on mid-planes
    remove  $p$  from  $\mathcal{O}$ , i.e., set  $\mu_{\mathcal{O}}(p) = 0$ 
select voxels  $p \in \mathcal{O}$  in the order of FDT values
if topologic and geometric features of  $p$  fail to agree
and its deletion preserves 3-D topology
    remove  $p$  from  $\mathcal{O}$ , i.e., set  $\mu_{\mathcal{O}}(p) = 0$ 

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This notion of primary and final skeletonization was simultaneously introduced by Saha et al. [18] and Arcelli et al. [39]. Saha et al. described it in 3-D while Arcelli et al. presented the idea in 2-D for a DT-based skeletonization algorithm.

Removal of a voxel $p \in \mathcal{O}$ preserves the topology of $\mathcal{O}$ if and only if p is a (26,6) simple voxel [6] in $\mathcal{O}$. Beside the 3-D topology preservation condition, an additional constrain of 2D topology preservation in all three middle planes of the candidate voxel is subjected to ensure continuity of surface-like structures and to avoid undesired drilling effects as illustrated by Saha et al. [18].

Several new concepts including fuzzy axial voxels, local and global significance factors and two-voxel thick structures are introduced for fuzzy objects are presented by Jin and Saha [19]. Also, a condition defining the disagreement between topological and geometric features of a voxel is provided. Finally, a new noisy skeletal branches pruning algorithm based on global significance factor (GSF) is introduced [19].

Results of application of skeletonization and pruning of two other medical images are presented in Figure 2. For all these examples, the results of skeletonization and pruning are visually encouraging.

Fig. 2. Results of application of fuzzy skeletonization on two anatomic structures fuzzy segmented from acquired images. (a) A part of cerebrospinal fluid segmented from human brain MR imaging. (b) An axial image slice illustrating the fuzziness and noise. (c) Surface rendering of the fuzzy skeleton. (d-f) Same as (a-c) but for micro-CT data of a human tooth.

6 Characterization of Local Structures

In this section, two different approaches of characterizing local structures are presented. Digital topological analysis uniquely determine the topological class of each voxel in a skeletal representation of a 3-D object. On the other hand, in a volumetric representation of an object, the process volumetric topological analysis characterizes individual location on the continuum between a perfect plate and a perfect rod. These two different methods are described in the following.

7 Digital Topological Analysis

Digital topological analysis or DTA was invented by Saha and Chaudhuri [7] and later adopted in the context of trabecular bone image analysis [22, 23, 25]. For the sake of brevity, here, we only describe some basic ideas necessary to understand the developments in the following sections. Let us explain the idea on an object $\mathcal{S}$ that may be represented as a union of finitely many surfaces and curves in a continuous 3-D-space (see Figure 3(a)). It is interesting to note that a point in $\mathcal{S}$ may be classified depending on its local topological property. For example, the removal of a point p_s on

Fig. 3. Illustrations of possible topological classifications. (a) An example in the continuous 3-D space. (b) An example in a digital space.

a surface of $\mathcal{S}$ creates exactly one tunnel in a sufficiently small neighborhood of that point. The removal of a point p_{ss} on a junction of multiple surfaces creates multiple tunnels. It creates exactly two objects on a curve (p_c) and multiple objects at a junction of curves (p_{cc}). At a junction of surface and curve (p_{sc}), it creates multiple objects and exactly one tunnel and so on.

In a digital space, we identify eight different topological classes of skeletal voxels, namely, isolated, curve interiors, curve edges, surface interiors, surface edges, and curve-curve, surface-curve, and surface-surface junctions (Figure 3(b)). However, the classification in a digital space is not as straightforward as in the case of R^3 . DTA is solved in three sequential steps – (1) determination of local topological type, (2) initial topological classification based on these types and (3) final classification after corrections at different topological junctions. Local topological type [7] provides only a partial classification which is essentially derived from the three local topological parameters $\xi(p)$, $\eta(p)$ and $\delta(p)$ (see Section 4). During the second step, a unique initial classification is achieved by reviewing the local topological type of 26-neighbors of each voxel not uniquely classified during the first step. After initial classification, the process is complete except for some possible corrections at junctions.

Fig. 4. Rod-like versus plate-like networks in 3-D projection μ MRI images of radial TB [22]: (a) highly rod-like (F 74 yrs.), (b) moderately rod-like (F 53 years), (c) predominantly plate-like (M 68 yrs.), (d) highly plate-like (M 60 years). Topological parameters parallel visual assessment of increasing plate-like morphology with the surface-to-curve ratio increasing nearly 20-fold from (a) through (d).

This step is primarily accomplished by analyzing the topology of edge type voxels and the fact that, under a normal circumstance, edge voxels on a surface form a 26-closed curve and this normal topology of edge voxels is perturbed only at junctions. Local topological properties have been used by others researchers to decompose an object into different segments [35, 40].

This method has been widely applied in characterizing trabecular bone micro-architecture at in vivo resolution. Two composite parameters, the surface-to-curve ratio (S/C) and erosion index (EI) were derived from individual topological parameters obtained using digital topological analysis (DTA). EI, for example, was defined as the ratio of the sum of parameters expected to increase upon osteoclastic resorption, divided by the sum of parameters expected to decrease secondary to such processes. Figure 4 illustrates the sensitivity of the topological parameters to bone-loss induced structural changes: the BV/TV value of the four subjects varies by a factor of 2 while the S/C varies by a factor of 20 [22]. In an in vivo MR study [25] involving 79 post menopausal women covering a range of DEXA BMD's, topological entities (surface density, S/C) measured at the distal radius were found to be statistically significant discriminators of patients with vertebral deformities (n=29) from those without deformities. Over the last few years the DTA technique has been applied in several clinical and research studies at the University of Pennsylvania [25, 41] and has also been adopted by several other research groups [42-44].

Fig. 5. Results of intermediate steps during the VTA process. (a) A TB region selected from a μ CT image of a human ankle specimen. (b-d) Color coded (red: pure rod, green: pure plate, yellow: intermediate) voxel display of manifold distance transform (b), manifold scale (c) and surface rendition of VTA (d).

8 Volumetric Topological Analysis

Volumetric topological analysis (VTA) [24] identifies topological entities on the continuum between a perfect plate and a perfect rod in a volumetric BMD representation of a TB network. VTA starts with a fuzzy object $\mathcal{O}$ (e.g., TB) and is completed in five sequential steps (Figure 5) – (1) fuzzy surface skeletonization [19], (2) digital topological analysis (DTA) [7, 23], (3) manifold distance transform (MDT) [24], (4) manifold scale computation [24], and (5) volumetric feature propagation [24]. The output of VTA is a function $VTA: \mathcal{O} \rightarrow R$ where $VTA(p)$ at an object voxel p gives the local object structure width measurement (μm); see Figure 5(d) for interpretation of different measurements on a surface-like volumetric structure. Two trabecular bone measures, namely, mean trabecular bone plate surface-width (SW_{VTA}) and trabecular surface to curve ratio (SCR_{VTA}) are computed using VTA analyses over a target volume of interest. Recently, tensor scale [45, 46] has been used to compute local structure width. Results from a cadaveric validation study on MDCT based trabecular and cortical bone measures demonstrated high repeat scan reproducibility of VTA measures. (Table 1(a)) and strong ability to predict experimental bone strength (Table 1(b), Figure 6).

Table 1. (a) Intraclass correlation (ICC) values of MDCT bone measures from three repeat cadaveric scans ($N = 15$). (b) Ability of MDCT TB measures to predict experimental bone strength; r values of linear correlation with TB yield stress. Abbreviations – TB: trabecular bone; Th: thickness; Poro: porosity; vBMD: volumetric BMD; SW: surface-width; NA: Network area; Sp: spacing

TB vBMD	TB SW	TB NA	TB Th	TB Sp
0.996	0.98	0.98	0.95	0.96

(a)

TB vBMD	TB SW	TB NA	TB Th	TB Sp
0.89	0.96	0.94	0.93	0.93

(b)

Results of Human Studies: An MDCT human bone imaging protocol (IRB ID # 201106785) was established at the University of Iowa. The use of ultra-sharp reconstruction kernels overcame the limitation of spatial resolution observed by previous investigators [47]. In a human pilot study [48], ten athletes (6 male), eleven patients (5 male) with cystic fibrosis (CF), 12 patients (6 male) on continuous treatment with a selective serotonin reuptake inhibitor (SSRI) for at least one year (duration: 3.3 ± 3.0 years; fluoxetine-equivalent dose: 36 ± 13 mg/day), and three patients (all female) with clinically confirmed anorexia nervosa (AN) were recruited (18 to 23 years of age for all groups). Age-sex-BMI-similar healthy controls were selected from the Iowa Bone Development Study (IBDS) cohort (42 male/46 female). MDCT scans of the distal

Fig. 6. A leave-one-out experiment demonstrated that MDCT derived TB plate width predicts experimental bone strength with an average error of 14%. The prediction functions for different instances of leave-one-out tests were stable.

tibia and whole body (WB) DXA were acquired. Pairwise comparisons between IBDS controls and participants from the three patient groups revealed that differences in cortical bone in SSRI and AN patients are non-significant, while CF patients demonstrate detectably lower cortical bone (Figure 7). The SSRI, CF and AN groups had compromised TB vBMD and TB microarchitecture which more prominently distinguished them from controls as compared to DXA BMD (Figure 7). The CF and AN groups had significantly higher TB spacing as compared to the SSRI group (Figure 7) indicating possible heterogeneous bone loss (Figure 8(c)) with potentially enhanced

Fig. 7. Average differences of bone measures in athlete, cystic fibrosis, selective serotonin reuptake inhibitor, and anorexia nervosa groups as compared to age-sex-BMI-similar healthy controls from the Iowa Bone Development Study. Age-sex-height matching was used for the anorexia nervosa group.

Fig. 8. Color-coded illustration of TB plate/rod classification for a IBDS female control (a) and an age-similar, sex- and BMI-matched patient on continuous treatment with an SSRI (b), and another age-similar, sex- and BMI-matched patient with confirmed diagnosis of CF (c). The healthy female (a) has more TB plates (green) as compared to the two patient participants. Between the two patients, the CF patient (c) has some signs of heterogeneous bone loss.

risks of fracture. In the athlete group, differences in cortical bone, compared to controls, predominated over differences in TB measures.

Peripheral MDCT imaging, together with advanced processing algorithms, are well-suited for *in vivo* skeletal assessment, capturing differences in volumetric, geometric, and microarchitectural properties of cortical and trabecular bones. Performance of the method needs to be validated against state-of-art HR-pQCT and the preliminary findings from the pilot *in vivo* study require confirmation in a larger sample accounting for various potential confounders.

9 Conclusion

Digital topology and geometry are useful in many real-life medical imaging applications benefitting clinical and research studies. Primarily, digital topology and geometry play three important roles at the level of method design and developments – (1) effective solution of many classical problems in medical imaging, (2) expansion of the scope of target information, and (3) provision of a strong theoretical foundation to a process enhancing its stability, fidelity, and efficiency. Over the last several decades there have been significant advancements in different areas of digital topology and geometry, including, distance analyses, topology preservation, skeletonization, local structure characterization etc. and some of these methods are being routinely applied on human studies. There are several unanswered fundamental questions related to digital topology and geometry which provides more research opportunities in this field.

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