A New Quantitative Approach for Measuring Changes of 3D Structures in Trabecular Bone

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September 15, 2005

Abstract

A novel approach which is based on 3D complexity measures was developed in order to quantify the spatial geometrical properties of trabecular bone. These non-destructive measures are able to evaluate different aspects of the organization and complexity of the architecture of trabecular bone, such as complexity of its surface, node complexity, or trabecular bone surface curvature. Their application to 3D μCT images of human proximal tibiae of various osteoporotic stages illustrates the abilities of these measures. The outcome of the bone architecture evaluation by

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the complexity measures was compared with and validated by the results provided by traditional 2D static histomorphometry. Finally, it can be concluded that this new approach, which was originally designed for quantification of microgravity induced bone loss can be directly applied for diagnosing pathological changes in bone structure in patients as well as to monitor the progress of medical treatment regimens.

1   Introduction

Bone architecture always tends to adapt to the current loading conditions. However, in patients suffering from osteopenia or osteoporosis or in astronauts, the bone density and structure may change so dramatic that the bone will lose a significant amount of its load bearing ability resulting in an increased fracture risk. The structural changes of trabecular bone have received increasing attention in the last years as the loss of bone density cannot explain all variation in bone strength. Moreover, the rapid progress in high resolution 3D Micro-Computed Tomography (μCT) imaging facilitates the investigation of the micro-architecture of bone in a non-destructive manner.

The standard method for assessing the micro-architecture of trabecular bone is histomorphometry, which was developed for 2D histological sections. Recently, some of the traditional 2D histomorphometric methods have been extended for analysis of 3D data[3, 4]. A new approach for quantifying the 3D complexity of trabecular bone networks has been developed using measures of complexity based on symbolic dynamics [8].

In the present study we develop a series of new measures of complexity for quantification of 3D structures. We use 3D geometrical properties like the local ratio of bone volume to bone surface and the local configurations of the bone voxels. We apply these measures to 3D μCT images of human proximal tibiae in order to investigate differences in trabecular bone structure at different stages of osteoporosis. In order to validate our findings, the results are compared with

those obtained by use of traditional 2D static histomorphometry.

2 Measures of Complexity

In order to quantify a geometrical shape we utilize that different 3D objects of the same volume have different surface areas, depending on their geometrical shape. For example, a long cylinder (length is much larger than radius) has a larger surface than a cube of the same volume, and a sphere of the same volume have the smallest possible surface.

Based on the relationship between surface and shape, we therefore introduce a series of measures using the local bone surface and local bone volume. Surface and volume of the trabecular bone are locally estimated in a small cubic box of size s, which moves through the entire 3D bone image. An iso-surface algorithm is applied for estimation of the surface and volume [6]. The iso-surface is constructed by use of the marching cubes algorithm [5]. A marching cube (MC) consists of eight neighbouring voxels (Fig. 1). If two neighbouring voxels of this MC are below and above a predefined threshold separating bone and marrow (i.e. one bone and one marrow voxel), the iso-surface will lie between these two voxels. In such MCs the iso-surface is then formed by a set of triangles, and the surface estimation is the sum of the areas of these triangles. The estimation of the bone volume is based on an extension of the MC algorithm. The bone volume within the MC is filled with tetrahedrons in such a way, that the resulting surface equals the iso-surface, which is formed by the triangles (Fig. 1). The sum of the volumes of these tetrahedrons is the estimated bone volume found in the MC and yields more exact results than the estimation by the commonly used voxel counting.

[Figure 1 about here.]

We now introduce the ratio between the local bone surface S_{bone} and the minimal surface possible for the same local bone volume V_{bone}, which is the surface

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of a sphere S_{sphere}. We call this ratio the *shape index*. As the local bone volume V_{bone} depends on the size of the moving box s, the normalized local bone volume $\hat{V}_{\text{bone}} = V_{\text{bone}}/s^3$ is used ($\hat{V}$ corresponds to the local bone volume fraction BV/TV_{loc}). The shape index

$$\sigma_{\text{loc}} = \frac{S_{\text{bone}}}{S_{\text{sphere}}} \quad \text{with} \quad S_{\text{sphere}} = \sqrt[3]{36\pi \hat{V}_{\text{bone}}^2} \tag{1}$$

distinguishes between shapes whose surface differ for the same volume, like e.g. plates and long cylinders. The value of this index should be larger than one, as the surface of a sphere is the smallest possible. However, the object could be cut by the faces of the moving box. These interfaces are not included in the surface calculation of the structure, resulting in a smaller surface. In severe cases this effect can lead to surface areas that are smaller than that of the reference sphere. However, this is only the case for concave structures. Therefore, values smaller than one indicates concave structures, whereas values larger than one indicates convex structures.

Because this index is computed for every position of the small box moving through the studied object, we get a distribution of the shape indices over the entire object $p(\sigma_{\text{loc}})$. Based on this distribution, we define the *averaged shape index* as:

$$A_\sigma = \langle \sigma_{\text{loc}} \rangle_{\text{VOI}}, \tag{2}$$

which is the average over all σ_{loc} in the volume of interest (VOI), and the *shape index entropy* as:

$$I_\sigma = -\sum p(\sigma_{\text{loc}}) \log p(\sigma_{\text{loc}}), \tag{3}$$

which is the entropy of the distribution $p(\sigma_{\text{loc}})$ in the VOI. A_σ measures the mean shape of the structures and I_σ measures the variety of the occurring shapes.

Next, we define the *shape complexity* as the conditional entropy of the joint distribution $p(\sigma_{\text{loc}}, V_{\text{loc}})$ with respect to a given bone volume:

$$C_\sigma = -\sum p(\sigma_{\text{loc}}, \hat{V}_{\text{loc}}) \log \frac{p(\sigma_{\text{loc}}, V_{\text{loc}})}{p(\hat{V}_{\text{loc}})}. \tag{4}$$

It quantifies the variety of different shapes for a given bone volume.

As already mentioned, a marching cube (MC) is formed by eight neighbouring voxels, arranged in the shape of a cube. Depending on the positions of the bone voxels in such MCs, there are 256 possible configurations; neglecting rotational and inversion symmetry, there are only 15 fundamental MC cases [5]. However, we will only consider rotational symmetry and ignore inversion. The inversion is not acceptable when analyzing trabecular bone architecture as it is important to distinguish between the inverted pairs of convex and concave MCs such as, for example, seven bone voxels and one marrow voxel versus one bone voxel and seven marrow voxels (which corresponds to the same fundamental MC case). Hence, we will deal with 21 unique MC cases, where such cases are separated [6].

A particular marching cube case corresponds to a specific bone surface configuration and, the distribution of the MC cases is therefore related to the complexity of the object's surface. The number of tetrahedrons in one MC – that were introduced to estimate the bone volume – also corresponds to the complexity of the surface. Thus, these MC cases can be used to define new 3D measures of complexity.

Using the unique marching cube configurations we define a new structural measure by introducing the *marching cubes entropy index*:

$$I_{\mathrm{MC}} = - \sum_{\mathrm{MC}} p(\mathrm{MC}) \log \mathrm{p}(\mathrm{MC}), \tag{5}$$

which is the Shannon entropy of the distribution of the marching cubes cases obtained from the entire VOI. This measure quantifies the complexity of the surface of the trabecular architecture.

3 Materials

These newly introduced measures are used for the assessment of the structural changes that are associated with bone loss. The changes in trabecular bone

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architecture of human proximal tibiae during development of osteoporosis is studied.

Cylindrical biopsies with a diameter of 7 mm were drilled from 29 human proximal tibia specimens 17 mm below the tibial plateau [10]. These trabecular bone biopsies were scanned with a Scanco μCT40 scanner at Scanco Medical AG, Switzerland, with a voxel size of 20 μm.

Standardized volumes of interest (VOI) were applied to the μCT images for quantification of the 3D architecture. These standardized VOIs were located 5 mm below the cortical shell and were 10 mm long. The structural measures of complexity are then computed for these VOIs. In order to validate the developed measures the results of the purposed 3D data evaluation were compared against traditional 2D bone histomorphometry [9, 10].

4 Results

Applying the introduced measures of complexity to the VOIs of the 3D μCT images, we evaluate the micro-architecture of the trabecular bone of 25 proximal tibial biopsies of different osteoporotic stages. The size of the moving box used to calculate local properties was chosen as $20 \times 20 \times 20$ voxels^3.

4.1 Complexity and bone volume fraction

Firstly, we study the differences of the trabecular bone structure due to bone loss, represented by a decreasing bone volume fraction BV/TV (Fig. 2).

[Figure 2 about here.]

During the bone loss, A_σ increases. Moreover, its values are less than 1.0 for BV/TV values larger than 20%, which suggests that a large number of concave structures exist in the trabecular bone of proximal tibia, especially for dense

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bone. The Spearman's rank correlation coefficient between BV/TV and A_σ is $R = -0.74$, which is significant at the $p = 0.01$ level.

This finding is further corroborated by I_σ and C_σ which reveal similar trends with decreasing BV/TV. C_σ is significantly correlated with BV/TV. From these results we can infer that the deterioration of tibial trabecular bone results in a series of new different trabecular shapes.

In contrast, I_{MC} decreases with decreasing BV/TV. In addition, I_{MC} exhibits a nonlinear relationship to BV/TV. In contrast to the findings of A_σ and C_σ this suggests a reduction in the complexity of the bone surface with decreasing BV/TV.

4.2 Comparison to histomorphometric structural parameters

The histomorphometric measures are commonly used as the "Gold standard" when evaluating the micro-architecture of trabecular bone. Therefore, we compare our newly introduced measures of complexity with the following histomorphometric measures: *Trabecular Bone Pattern factor* TBPf [2], *node terminus ratio* Nd/Tm [1], as well as *trabecular separation* Tb.Sp [7].

[Table 1 about here.]

Table 1 and Figure 3 shows the correlation between the different newly developed measures of complexity and the histomorphometric measures. Clear relationships are revealed between the measures of complexity and the histomorphometric measures. However, some relationships are stronger than other. I_{MC} exhibits the strongest relationship with histomorphometry of all the 3D measures: it is anti-correlated with TBPf and Tb.Sp and correlated with Nd/Tm. The signs of correlations are opposite for all the other 3D measures. I_σ and C_σ reveal a more nonlinear relationship with especially Tb.Sp (Fig. 3A). The Spearman's rank correlation reveals significant correlations between the histomorphometric

measures and A_σ, C_σ and I_{MC}. Since I_σ is not significantly correlated to any of the histomorphometric measures, this measure may contain additional information about the bone structure, which is not included in BV/TV or any of the other histomorphometric measures.

The relationships we found suggest that the proposed new measures of complexity are able to quantify 3D bone architecture. In addition, they contain important information about the trabecular geometry and can be used to describe changes in the spatial structure of trabecular bone.

[Figure 3 about here.]

5 Conclusion

The proposed new structural measures of complexity can be directly computed from 3D images. They contain important information about the 3D structure of trabecular bone and can be successfully used to describe the deterioration of the trabecular bone network that takes place during the development of osteopenia and osteoporosis.

Acknowledgments

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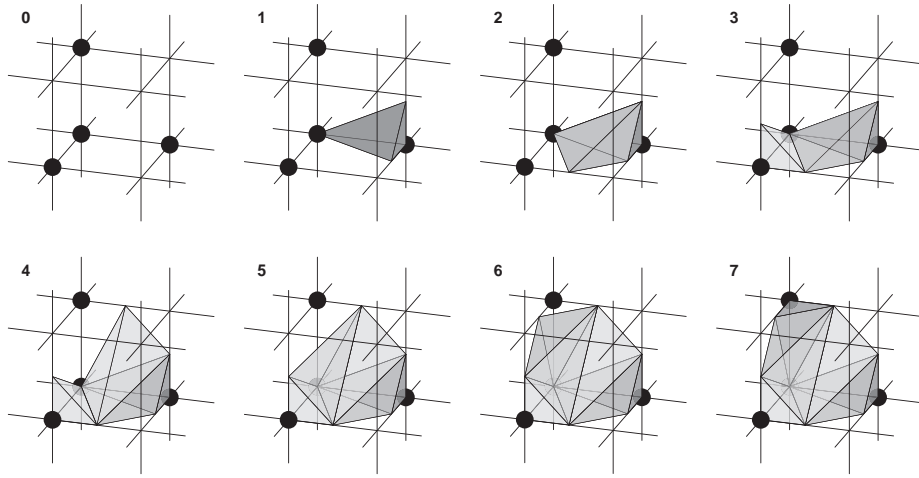
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Figure 1: A marching cube (MC) consists of eight voxels forming the corners of the MC. A piece of surface is constracted as a set of triangles touching the MC edges at such points where the threshold value lies between bone and marrow voxels (panel 7). For volume estimation, the MC is filled with tetrahedrons (panels 1-7).
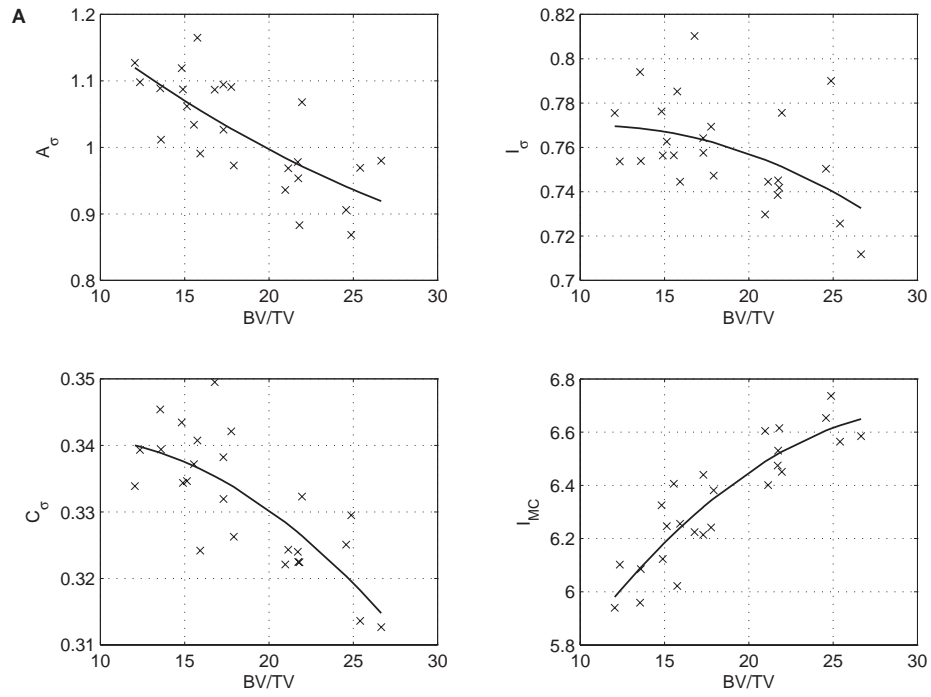
Figure 2: Measures of complexity vs. bone fraction (BV/TV) for the proximal tibia. The continuous line is a polynomial data fit.
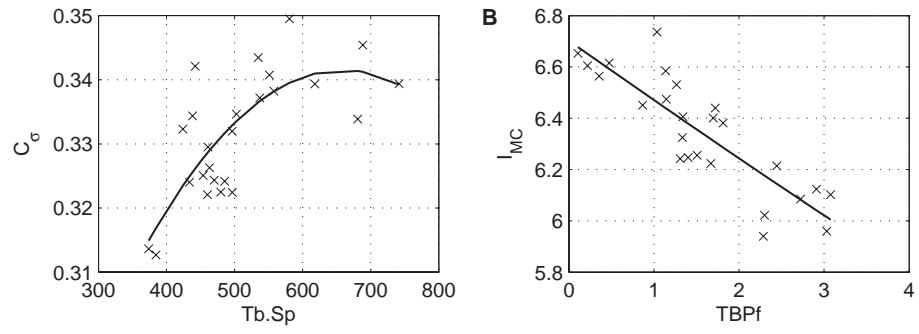
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Figure 3: Measures of complexity vs. bone loss (BV/TV) for proximal tibia. The line is a squared fit to guide the eye.

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Table 1: Spearman's rank correlation coefficients between the measures of complexity and BV/TV, TBPf, Nd/Tm, and Tb.Sp. The values are statistically significant at the $p = 0.01$ level.

	A_σ	I_σ	C_σ	I_{MC}
BV/TV	−0.74		−0.72	0.87
TBPf	0.66		0.63	−0.88
Nd/Tm	−0.68		−0.63	0.68
Tb.Sp	0.50	0.51	0.66	−0.68