Quantification of Changes in Spatial Structure of Human Bone Biopsies Using 3D Measures of Complexity.

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The aim of the study was to assess the 3D structural composition and deterioration of human bone tissue in osteoporosis using 3D datasets of human tibia bone biopsies acquired by a micro-CT scanner. We applied symbolic dynamics and measures of complexity to assess quantitatively the structural composition of bone tissue in 3D. Originally, these methods were developed and successfully applied for quantification of 2D bone structure from CT-images [1, 2]. Now we apply this approach to assess 3D bone architecture. In order to justify the technique the measures of complexity of the bone architecture ware compared with the results of traditional bone histomorphometry.

The biopsies were taken from 30 human bone specimes at the medial side 17 mm distal of the tibia plateau which is a bone harvesting site for surgeons. All biopsies had a diameter of 7 mm; their length varied between 2 and 4 cm. The biopsy cylinders were embedding in methylmetacrylate. The biopsies were scanned with micro-CT scanner (μCT 40) at Scanco Medical AG, Switzerland, using a voxel size of 20 μm.

The first step of our technique is symbol-encoding of the dataset which preserves the robust and crucial information about the original structure but dramatically decreases the amount of information to be processed to quantify its structural organization. The 3D image was encoded using an alphabet of only three different symbols B, M, S representing respectively the internal voxels of the bone, the bone marrow, and the boundary-voxel between: the bone surface.

At the final stage of our procedure, the special arrangement of symbols is quantified by a set of measures of complexity. We have developed the following measures for 3D bone biopsies at this point in time: Normalized entropy of the geometrical location of bone tissue, special Structure Complexity Index SCI3D, Index of a Global Ensemble IGE, Surface Complexity Index, Surface IGE, and a complexity index of local bone volume to total volume ratio (BV/TV) distribution. In addition, we calculate the BV/TV ratio directly from a given volume of interest (VOI) of a biopsy.

We found, due to the variation in the length of the biopsies, that structural information varies greatly depending on the location within a biopsy. The biopsies were split into 5 mm long fragments starting below the cortical bone. Each segment was quantified by the proposed measures providing the dependence on the position. We found that within the length of 2.5 cm the measures, including BV/TV, change in an interval of 31-82%. Thus, the need for a standardized VOI arose: not only a volume, but also the position of an analyzed part must be standardized in order to produce comparable results. We concluded to use a VOI of 1 cm length where the upper edge is located 5 mm below the cortical bone. A shift of the VOI in the direction towards the cortical bone results in changes of the structural measures less than 3%, whereas a shift in the opposite direction would produce errors > 6%.

Preliminary results of the 3D evaluation show that the complexity of the bone structure decreases during bone loss. This is confirmed by two independent approaches: entropy of geometrical locations, as well as SCI of local BV/TV distribution and symbol-based SCI3D. It is also found that beyond a certain amount of bone material loss, the probabilities of symbols representing the internal bone voxels and the surface voxels decrease at different rates, thus capturing the difference in bone architecture.

Newly developed algorithms and measures were directly compared to the results of histomorphometric evaluation. The embedded and μ-CT scanned tibia biopsies were sectioned, stained, mounted, and evaluated by traditional 2D histomorphometry techniques. Sixteen 10-μm-thick sections grouped in 8 disector pairs were cut from the central 2 mm of the biopsies in order to obtain as large sections as possible. The sections were digitized by using a flatbed image scanner. Static histomorphometry was performed by custom made software. The comparison between the 2D and 3D BV/TV estimations resulted in excellent correlations (r=0.95). This is an indication that our work was performed with utmost care, although the sectioning causes artifacts.

Finally, we compared the rank-order correlation between newly developed 3D measures of structural complexity and histomorphometric measures. Our preliminary results indicates strong (r=0.6-0.8) correlation between some structural parameters of histomorphometry like trabecular thickness, trabecular separation, connectivity density and the complexity measures SCI3D, IGE, SCI based on local BV/TV ratio distribution. This confirms the appropriateness of the developed 3D approach to quantify the architecture of bone. The correlation between the other parameters is found to be moderate to weak, thus suggesting that the different approaches quantify and emphasize different aspects of bone organization.

We conclude that the proposed technique is able to quantify the structural loss of the bone tissue and may help to diagnose and to monitor changes in bone structure of patients on Earth as well as of the space-flying personnel.

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