Quantification of Spatial Structure of Human Proximal Tibial Bone Biopsies Using 3D Measures of Complexity.

Peter Saparin¹, Wolfgang Gowin¹, Alexei Zaikin², Jesper S. Thomsen³, Steffen Prohaska⁴, Hans-Christian Hege⁴, Jürgen Kurths²

¹Center of Muscle and Bone Research, Dept. of Radiology, University Hospital B. Franklin, Free University Berlin, Germany
²Center for Dynamics of Complex Systems, Institute of Physics, University of Potsdam, Germany
³Department of Cell Biology, Institute of Anatomy, University of Aarhus, Denmark
⁴Zuse Institute Berlin (ZIB), Scientific Visualization Department, Berlin, Germany

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 have further extended this approach to assess 3D bone architecture. In order to justify the technique the measures of complexity of the bone architecture were compared with the results of traditional 2D bone histomorphometry.

The biopsies were taken from 30 human bone specimens at the medial side of the proximal tibial metaphysis 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 embedded in methyl methacrylate and scanned with micro-CT scanner (µCT 40) at Scanco Medical AG, Switzerland, using a voxel size of 20 µm. After the biopsies were micro-CT scanned, they were sectioned, stained, mounted, and evaluated by traditional 2D histomorphometric techniques. Sixteen 10-µm-thick sections grouped in 8 disector pairs were cut from the central 2 mm of the biopsies. The sections were digitized by the use of a flatbed image scanner with an integrated transparency scanning unit. Static histomorphometry was performed by custom-made software.

The first step of our technique is symbol-encoding of the dataset which preserves the robust and crucial information about the original topological 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. At this point in time we have developed the following measures for 3D bone architecture: 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, changed 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 decided 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 resulted in changes of the structural measures less than
3%, whereas a shift in the opposite direction produced changes > 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.

Our newly developed algorithms and measures were directly compared to the results of
standard histomorphometric evaluation. The comparison between the 2D and 3D BV/TV
estimations resulted in an excellent correlation ($r=0.95$). 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 the traditional histomorphometric measures. Our preliminary results
indicate 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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