Bone 54 (2013) 133–140

Contents lists available at SciVerse ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

Computational identification and quantification of trabecular microarchitecture classes by 3-D texture analysis-based clustering ☆

Alexander Valentinitsch [a,c,*], Janina M. Patsch [a,c], Andrew J. Burghardt [c], Thomas M. Link [c], Sharmila Majumdar [c], Lukas Fischer [a], Claudia Schueller-Weidekamm [b], Heinrich Resch [d], Franz Kainberger [a,b], Georg Langs [a]

[a] Computational Image Analysis and Radiology Lab, Department of Radiology, Medical University of Vienna, Vienna, Austria
[b] Division of Musculoskeletal Radiology and Neuroradiology, Department of Radiology, Medical University of Vienna, Vienna, Austria
[c] Musculoskeletal Quantitative Imaging Research Group, Department of Radiology & Biomedical Imaging, University of California San Francisco, San Francisco, CA, USA
[d] Medical Department II, St. Vincent Hospital Vienna, Vienna, Austria

ARTICLE INFO

Article history:
Received 13 June 2012
Revised 20 December 2012
Accepted 22 December 2012
Available online 10 January 2013

Edited by: Harry Genant

Keywords:
HR-pQCT
3D-Texture analysis
Unsupervised clustering
Trabecular microarchitecture classes

ABSTRACT

High resolution peripheral quantitative computed tomography (HR-pQCT) permits the non-invasive assessment of cortical and trabecular bone density, geometry, and microarchitecture. Although researchers have developed various post-processing algorithms to quantify HR-pQCT image properties, few of these techniques capture image features beyond global structure-based metrics. While 3D-texture analysis is a key approach in computer vision, it has been utilized only infrequently in HR-pQCT research. Motivated by high isotropic spatial resolution and the information density provided by HR-pQCT scans, we have developed and evaluated a post-processing algorithm that quantifies microarchitecture characteristics via texture features in HR-pQCT scans. During a training phase in which clustering was applied to texture features extracted from each voxel of trabecular bone, three distinct clusters, or *trabecular microarchitecture classes* (*TMACs*) were identified. These TMACs represent trabecular bone regions with common texture characteristics. The TMACs were then used to automatically segment the voxels of new data into three regions corresponding to the trained cluster features. Regional trabecular bone texture was described by the histogram of relative trabecular bone volume covered by each cluster. We evaluated the intra-scanner and inter-scanner reproducibility by assessing the precision errors (PE), intra class correlation coefficients (ICC) and Dice coefficients (DC) of the method on 14 ultradistal radius samples scanned on two HR-pQCT systems. DC showed good reproducibility in intra-scanner set-up with a mean of 0.870 ± 0.027 (no unit). Even in the inter-scanner set-up the ICC showed high reproducibility, ranging from 0.814 to 0.964. In a preliminary clinical test application, the TMAC histograms appear to be a good indicator, when differentiating between postmenopausal women with ($n = 18$) and without ($n = 18$) prevalent fragility fractures. In conclusion, we could demonstrate that 3D-texture analysis and feature clustering seems to be a promising new HR-pQCT post-processing tool with good reproducibility, even between two different scanners.

Introduction

Osteoporosis is a metabolic bone disease characterized by bone loss resulting in high fracture susceptibility due to reduced bone mass, bone density, and bone quality. Bone quality refers to surrogate parameters such as bone microarchitecture, turnover, damage accumulation, and mineralization, that contribute to bone strength and fracture risk independently of bone mass [1]. In the last two decades, high-resolution magnetic resonance imaging (HR-MRI) and high-resolution peripheral quantitative computed tomography (HR-pQCT) have emerged as non-invasive research techniques that allow the quantification of bone microarchitecture without bone biopsy [2]. The non-invasive investigation of bone microarchitecture has provided substantial insights to gender-, age- [3–5] and compartment-specific bone morphology, in health, various forms of osteoporosis [6–8], and

Abbreviations: HR-pQCT, High-resolution peripheral quantitative computed tomography; MUW, Medical University of Vienna; UCSF, University of California, San Francisco; Tb.ROI, Trabecular region of interest; TMAC, Trabecular microarchitecture class; DC, Dice coefficient; GLCM, Gray level co-occurrence matrix; PMMA, Polymethylmethacrylate; GMM, Gaussian mixture model; PE, Precision error; ICC, Intraclass correlation coefficient.

☆ Funding: NIH RC1 AR058405; NIH R01 AR060700; NIH RO1 AG17762; Austrian Science Fund (FWF) Erwin-Schrödinger Grant J-3079; Philips Clinical Research; EU FP7 KHRESMOI.

* Corresponding author at: Computational Image Analysis and Radiology Lab, Department of Radiology, Medical University of Vienna, Währinger Gürtel 18–20, A-1090 Wien, Austria. Fax: +43 1 40 400 4898.

E-mail addresses: alexander.valentinitsch@meduniwien.ac.at (A. Valentinitsch), janina.patsch@ucsf.edu (J.M. Patsch), andrew.burghardt@ucsf.edu (A.J. Burghardt), thomas.link@ucsf.edu (T.M. Link), sharmila.majumdar@ucsf.edu (S. Majumdar), lukas.a.fischer@meduniwien.ac.at (L. Fischer), claudia.schueller-weidekamm@meduniwien.ac.at (C. Schueller-Weidekamm), heinrich.resch@bhs.at (H. Resch), franz.kainberger@meduniwien.ac.at (F. Kainberger), georg.langs@meduniwien.ac.at (G. Langs).

8756-3282/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bone.2012.12.047

other metabolic bone diseases [9]. In particular, HR-pQCT has been used to identify novel discriminative characteristics between patients with prevalent osteoporotic fractures and non-fracture controls that exhibit almost similar areal bone mineral density (aBMD) by dual-energy X-ray-absorptiometry (DXA) [6,10].

Along with the increasing use of HR-pQCT in clinical research, novel image processing techniques have been developed [4,11–14]. Fixed quadrant models have been used to identify regional variations in bone microarchitecture [14] and to capture subtle treatment effects that remained undetected by global standard evaluations [15]. In contrast to this method, which subdivides scan regions into quadrants, three-dimensional (3D) texture analysis of HR-pQCT data is able to recognize morphological pattern groups without the definition of preset geometric regions of interest. 3D texture analysis therefore has the potential to contribute unique quantitative information on the spatial distribution of bone mass that is not captured by assessment of bone density or structure metrics. Two-dimensional (2D) texture analysis has been previously applied to conventional radiographs and CT scans and has been able to distinguish patients with prevalent osteoporotic fractures from non-fracture controls [16,17]. In bone research, fractal analysis has been the most widely used texture-analysis technique [18,19] and has shown a strong relationship with histomorphometry and measures of bone strength [20,21]. In radiographs of the spine, the proximal femur and the calcaneus, fractal analysis yielded good discrimination between patients with and without prevalent fragility fractures [22,23]. Another texture-based quantification method is the trabecular bone score (TBS) which is applied to DXA-derived projection images of the spine and relates to some extent to μCT-based microstructure measures [24–26]. Recently, Bachetta et al. [27] applied 2D texture analysis to radial and tibial radiographs and found significant associations with trabecular microarchitecture assessed by HR-pQCT. Fouque-Aubert et al. [28] used a similar approach to correlate 2D texture of hand radiographs with local 3D bone microstructure in patients with rheumatoid arthritis. To our knowledge, 3D texture analysis, which can deliver more spatial image information than 2D techniques, has not been applied to HR-pQCT scans. Therefore, contributions of our study include 1) the introduction of a novel post-processing technique of HR-pQCT data based on 3D-texture-analysis and clustering, 2) the validation of our technique by assessment of single-site, short-term, and cross-site reproducibility in cadaveric specimens, and 3) a preliminary application of the technique to a small set of HR-pQCT scans of postmenopausal women with and without fragility fractures.

Materials and methods

Samples, HR-pQCT acquisition and standard evaluation

Fourteen human distal radius sections were acquired from a non-profit, NIH-funded American tissue bank (NDRI, Philadelphia, Pennsylvania) and embedded into polymethylmethacrylate (PMMA) to construct structure realistic phantoms at the Department of Radiology of the University of California, San Francisco (UCSF) [29]. The bone specimens were approximately 1-cm thick and were obtained from the anatomical site consistent with the standard in vivo HR-pQCT acquisition protocol (i.e. 9.5 mm proximal to the distal radius endplate). Using XtremeCT (Scanco Medical AG, Brüttisellen, Switzerland), each section was scanned with a nominal isotropic voxel size of 82 μm. The X-ray source potential was 60 kVp with a current of 900 μA. A two-dimensional detector containing 3072×256 CCD elements was used to acquire 750 projections at a 200 ms integration time per projection. To evaluate short-term reproducibility, all specimens were scanned three times, with repositioning performed before each acquisition. For cross-site reproducibility experiments, an additional scan was acquired, after which the embedded samples were shipped to the Medical University of Vienna and scanned using the same imaging protocol. Densitometric and morphometric standard evaluations were performed according to Laib et al. [11]. We calculated trabecular bone volume fraction (BV/TV) from the volumetric BMD of the trabecular compartment (Tb.BMD) using the assumption that compact bone has a matrix mineral density of 1200 mg HA/cm^3. Additionally, trabecular BMD was calculated for a peripheral region adjacent to the cortex (pTb.BMD) and central trabecular region (mTb.BMD) [30]. From the binary image, trabecular number (Tb.N) was measured using the direct 3D distance transform (DT) approach [31,32]. Based on the densitometric BV/TV and direct Tb.N, trabecular thickness (Tb.Th) and trabecular separation (Tb.Sp) were derived using traditional plate model assumptions. Cortical thickness (Ct.Th) was defined as the mean cortical volume divided by outer border surface.

Cortex segmentation and definition of the trabecular region of interest

Cortical and trabecular bone compartments were segmented by an in-house threshold-independent segmentation tool (TIST) [33]. In order to avoid inclusion of the subcortical compartment in our calculations we peeled 8 voxels from the extracted trabecular mask. We refer to the mask volume after peeling (i.e. our defined trabecular region of interest — Tb.ROI) as the *total volume* (*TV*). In this manuscript we report microarchitectural properties of the Tb.ROI based on texture analysis.

Image registration and normalization

In order to assess short-term (i.e. intra-scanner) and cross-site (i.e. inter-scanner) reproducibility, all scan data (USCF and MUW) for each sample were co-registered. We used a standard monomodal intensity-based medical image registration algorithm that minimizes the sum of squared intensity differences (SSD) between the registered volume images [34]. The transformation applied to register was rigid due to our rigid object (i.e. bone). The software was implemented in MATLAB (Mathworks, Natick, MA). To eliminate scanner site detector differences, all images were converted from their original grayscale attenuation values to equivalent hydroxyapatite densities (mgHA/ccm) using a linear relationship derived from a calibration phantom. The calibration phantom contained five different cylinders with varying concentrations of HA-resin (0, 100, 200, 400, 800 mgHA/ccm). The dynamic range of the images was −500 mgHA/ccm to 1500 mgHA/ccm.

Feature extraction of trabecular bone

The three-dimensional gray scale image properties of HR-pQCT volumes were evaluated in order to quantify microarchitectural characteristics in the defined trabecular region of interest (Tb.ROI) (i.e. the peeled trabecular mask). We refer to these characteristics as texture patterns. For each volume unit (voxel) a local texture descriptor was calculated based on the surrounding 15×15×15 voxels. Voxels outside the Tb.ROI were not included in any neighborhood calculations. We used two methods for feature calculation: 1. Three-dimensional gray level co-occurrence matrix (3D GLCM) [35–37], 2. partial derivatives [38].

A GLCM extracts statistical image information regarding the distribution of the differences in intensity values between voxels separated by a certain distance and/or direction. For the 3D GLCM 13 different possible directions were extracted at three different scales defined by the radius of the neighboring voxels (radius: 1, 2, 4 voxels). Linear binning was applied in order to map 12-bit gray-level intensities to 8 gray levels. The calculation resulted in rotation invariant features by averaging over all directions: energy, entropy, correlation, contrast, variance, sum average, inertia, cluster shade, cluster prominence, homogeneity, maximal probability and inverse variance [39].