

L. Qin · H.K. Genant
J.F. Griffith · K.S. Leung
(Editors)

Advanced Bioimaging Technologies in Assessment of the Quality of Bone and Scaffold Materials

Techniques and Applications

With 333 Figures and 44 Tables

 Springer

Ling Qin

Professor of Department of Orthopaedics and Traumatology,
The Chinese University of Hong Kong, Hong Kong SAR, China
e-mail: lingqin@cuhk.edu.hk

Harry K. Genant

Professor Emeritus, University of California, San Francisco,
Chairman Emeritus; Board of Directors, Synarc, Inc
e-mail: harry.genant@radiology.ucsf.ucsf

James F. Griffith

Department of Radiology and Organ Imaging,
The Chinese University of Hong Kong, Hong Kong SAR, China
e-mail: Griffith@ruby.med.cuhk.edu.hk

Kwok Sui Leung

Professor of Department of Orthopaedics & Traumatology,
The Chinese University of Hong Kong, Hong Kong SAR, China
e-mail: ksleung@cuhk.edu.hk

Library of Congress Control Number: 2007929499

ISBN 978-3-540-45454-0 Springer Berlin Heidelberg New York

This work is subject to copyright. All rights reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable for prosecution under the German Copyright Law.

Springer is a part of Springer Science+Business Media

springer.com

© Springer-Verlag Berlin Heidelberg 2007

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Product liability: The publishers cannot guarantee the accuracy of any information about dosage and application contained in this book. In every individual case the user must check such information by consulting the relevant literature.

Editor: Dr. Ute Heilmann, Heidelberg, Germany

Desk Editor: Wilma McHugh, Heidelberg, Germany

Cover design: eStudio, Calamar, Spain

Typesetting and production: LE-TeX Jelonek, Schmidt & Vöckler GbR, Leipzig, Germany

Printed on acid-free paper 21/3180/YL - 5 4 3 2 1 0

Calibration of Micro-CT Data for Quantifying Bone Mineral and Biomaterial Density and Microarchitecture

Bruno Koller (✉) and Andres Laib

Scanco Medical AG, Bassersdorf, Switzerland
e-mail: bkoller@scanco.ch

Abstract

With the awareness of the importance of the bone architecture to the overall stability of bone, micro-CT has become the gold standard for 3D static histomorphometry in bone research over the past 10 years. Nevertheless, bone densitometry is still the method of choice in the clinical environment. It is, however, anticipated that only a combination of the two methods, densitometry and morphometry, will improve the diagnosis and treatment of patients. This chapter introduces the calibration of micro-CT for quantification of bone mineral and material density at both organ and tissue levels and its impact in bone and mineral research based on bone biopsy. This approach may also be widely applied to measure the density of other appreciated materials.

A Need for Quantification of Bone Material Density

Our early micro-CT mainly provided measurements of structural or microarchitectural features of bone and related materials to supplement our pQCT (Densiscan), which measured volumetric bone mineral density (BMD) at organ level (Lai et al. 2005a,b). As the demands on quantification of bone material density at tissue level became increasingly high (Gong et al. 2005; Lai et al. 2005b), consequently we added densitometric features to our micro-CT device, and developed the XtremeCT, a new pQCT densitometry system that assesses bone microarchitecture (Fig. 1).

Micro-CT and XtremeCT Features

For both high-resolution micro-CT and Xtreme CT systems, the techniques and procedures are more or less identical and consist of the following features: Firstly, both systems must have a very good stability over many years. This is achieved with self-calibration and control of the signal before each measurement. Quality-control (QC) phantoms are provided to control the stability of the systems.

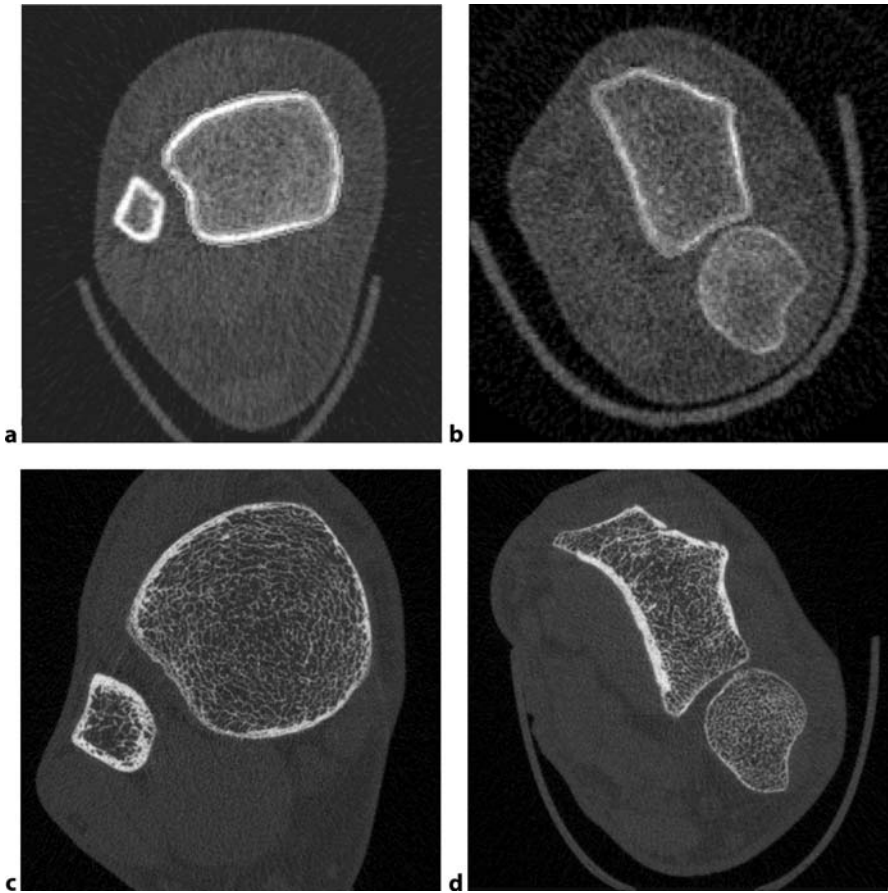


Figure 1. Human tibia (a) and radius (b) scanned at 300μm voxel size by pQCT (Densiscan) compared with human tibia (c) and radius (d) scanned at 82 with XtremeCT

Secondly, due to the polychromatic beam of X-ray sources, the beam-hardening artifact has to be addressed very carefully. The beam hardening effect leads to a dependence of the density readout from the object size. Densities, therefore, may vary between smaller and larger people or smaller and larger biopsies just because of their size. This artifact is eliminated by filtering the primary beam and by applying a correction function to the measured signal. By applying special beam-hardening correction curves that are adapted to scanning bone, the cupping artifact can be avoided, and the gray-scale image values are homogeneous throughout the region of interest (Fig. 2).

Thirdly, CT systems can measure the absorption of the X-rays, but not directly the density of the material; however, assuming a proper beam-hardening correction, the density is linearly correlated to the absorption (within our energy range); therefore, we can measure reference materials of known density and then apply a conversion function to the bone measurements.

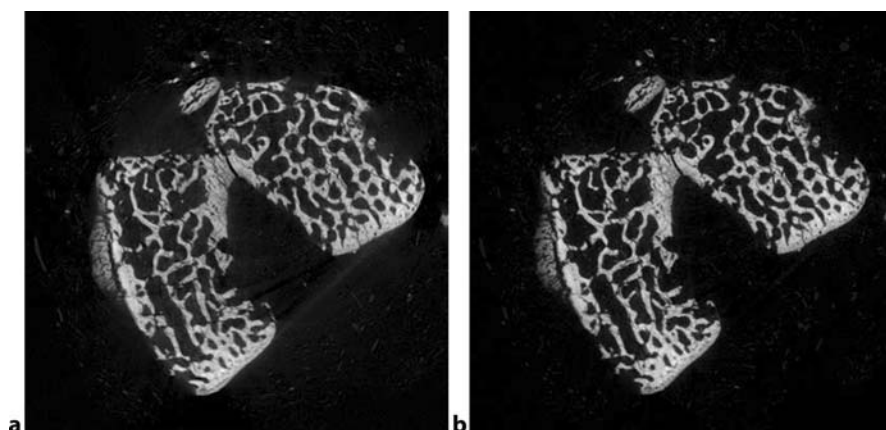


Figure 2. Dry excised distal rat femur. **a** Without specialized beam-hardening correction. **b** With beam-hardening correction for bone

Evaluation of Bone Mineral Density at Organ and Tissue Level

For the purpose of BMD measurement, we designed reference phantoms made of five different hydroxyapatite (HA) densities for the whole line of our micro-CT scanners (Fig. 3), which only vary in size for the different instruments; therefore, we are able to cross-calibrate all our systems. The whole procedure of density calibration can also be applied to different materials and reference phantoms, so users can build their own calibration sets, e. g., for Al, Mg, or scaffold scanning. Since all our systems are calibrated, they provide true volumetric BMD for both patients and bone specimens.

The DXA densitometry is limited to areal BMD measurement. This means one cannot distinguish between different parts or regions within the bone. Calibrated mi-

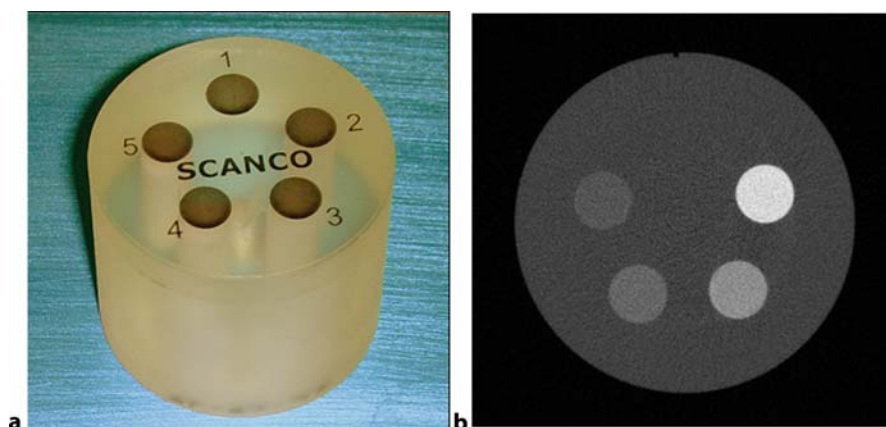


Figure 3. Quality control and density calibration phantom (**a**) and its CT scan (**b**)

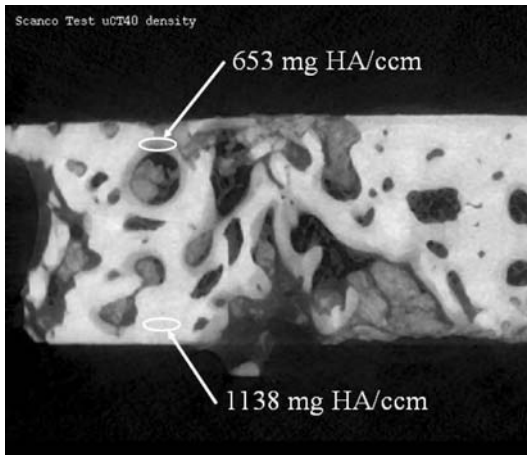


Figure 4. Local changes in BMD within a bone sample

crotomography now offers true volumetric densitometry for apparent density (bone and marrow space) within different regions of the specimen. In addition to the apparent density, we can also measure the material density within the cortex and trabecular bone at organ level and even local changes of bone matrix density at tissue level, i. e., within a single trabecula.

For material density measurements, it is very important to have a very high resolution, as otherwise partial-volume effects may affect the results. For this reason, the outermost layer is excluded from analysis for achieving precise results. This is shown by measuring different bone specimens using micro-CT and then ash. An example of local changes within a bone sample is illustrated in Fig. 4.

Evaluation of Structural Parameters

Once the object is scanned and segmented, the whole 3D structure can be visualized. In contrast to traditional 2D histomorphometry, the trabecular bone structure can now also be quantified in 3D, and therefore one does not have to rely on any model assumptions about the shape of bone anymore (no plate model assumption).

By filling the trabeculae with overlapping maximal spheres (Hildebrand and Rüegsegger 1997a,b) the local thickness of the bone at each place can be calculated as the diameter of the biggest sphere that fits inside the bone at this place. The mean value of all local thickness values then gives trabecular thickness (Tb.Th). Since this calculation is done for every point of bone, histograms of local thickness values can also be plotted. Applying the same technique to the marrow space, trabecular separation Tb.Sp is calculated, and the histogram of local separations can be given. From the histogram, the homogeneity of the trabecular network can now be quantified as the standard distribution of Tb.Sp: Tb.Sp.SD is large for networks that are less regular and contain large “holes” (Laib et al. 2002).

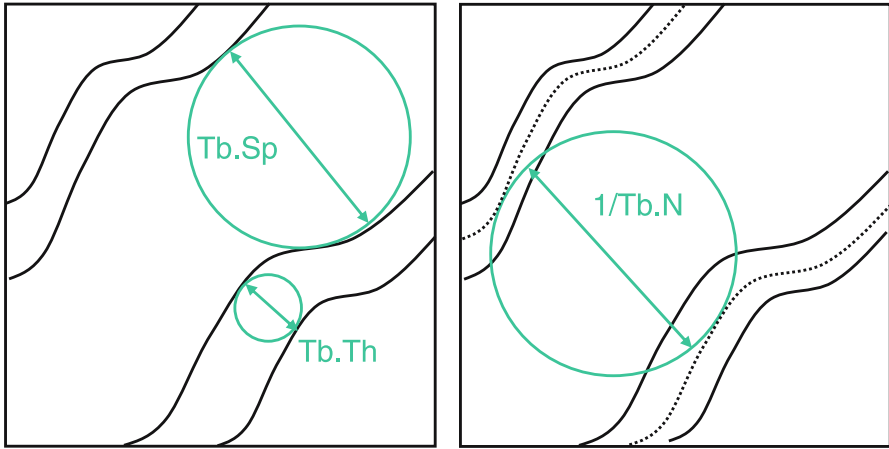


Figure 5. The determination of Tb.Th, Tb.Sp and Tb.N

Trabecular number is usually defined as the number of trabeculae an observer meets per millimeter of flight-path through the bone, averaged over all directions of the flight. By determining the mean distance of the skeletonized structure and inverting this number, Tb.N can now be quantified without model assumptions, e. g., $Tb.N = 3$ trabeculae per millimeter of flight length, i. e., the distance between the midpoints of the trabeculae is 0.333 mm, thus 1 divided by 0.333 mm is the desired Tb.N of 3 [1/mm]; (Fig. 5).

With the method of Odgaard and Gundersen (1993), the topology of the trabeculae can be assessed, and the number of connections and the connectivity density (number of connections divided by total volume) can be calculated based on Euler numbers. When trabecular bone is visualized, it is interesting to note that some bone sites look more plated-like (e. g., human femoral head), whereas other bone sites have distinctly rod-like bone (e. g., human spine). This feature of bone architecture can now be quantified with the structure model index (SMI; Hildebrand and Rüegsegger 1997a,b) with perfectly plate-like bone having an SMI of 0, and perfectly rod-like bone having an SMI of 3. Values of SMI in-between denote a mixture of plate- and rod-like bone, or bone with “rods” with elliptical cross-section.

Triangulating the surface model of bone then allows to also quantify bone surface and assess the potentially active remodeling surface of trabecular bone (Hildebrand and Laib 1999; Lorensen and Cline 1987).

Conclusion

The interests on quantification of bone material density at tissue level in vivo for human became increasingly high in bone and mineral research. The new generation of pQCT, i. e., the XtremeCT is developed, which is able to assess both bone microarchitecture and BMD at both organ and tissue levels.

References

- Gong H, Zhang M, Yeung HY, Qin L (2005) Regional variations in microstructural properties of vertebral trabeculae with ageing. *J Bone Miner Metabol* 23:174–180
- Hildebrand T, Laib A (1999) Direct three-dimensional morphometric analysis of human cancellous bone: microstructural data from spine, femur, iliac crest, and calcaneus. *J Bone Miner Res* 14:1167–1174
- Hildebrand T, Rüegsegger P (1997a) A new method for the model independent assessment of thickness in three-dimensional images. *J Microsc* 185:67–75
- Hildebrand T, Rüegsegger P (1997b) Quantification of bone microarchitecture with the structure model index. *Comput Methods Biomech Biomed Eng* 1:15–23
- Lai YM, Qin L, Hung VWY, Chan KM (2005a) Regional differences in cortical bone mineral density in weight-bearing long bone shaft: a pQCT study. *Bone* 36:467–471
- Lai YM, Qin L, Yeung HY, Lee KM, Chan KM (2005b) Regional differences in trabecular BMD and microarchitecture of weight bearing bone under habitual gait loading: a pQCT and micro-CT study in human subject. *Bone* 37:274–282
- Laib A, Newitt DC, Lu Y, Majumdar S (2002) New model-independent measures of trabecular bone structure applied to in vivo high-resolution MR images. *Osteoporosis Int* 13:130–136
- Lorensen WE, Cline HE (1987) Marching cubes: a high resolution 3D surface construction algorithm. *Comput Graphics* 21:163–169
- Odgaard A, Gundersen HJG (1993) Quantification of connectivity in cancellous bone, with special emphasis on 3-D reconstruction. *Bone* 14:173–182