Journal of Clinical Densitometry, vol. 10, no. 1, 86−92, 2007

1094-6950/07/10:86−92/$32.00
DOI: 10.1016/j.jocd.2006.07.007

Original Article

Analyzing Cortical Bone Cross-Sectional Geometry by Peripheral QCT: Comparison With Bone Histomorphometry

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Abstract

A distinct advantage of peripheral quantitative computed tomography (pQCT) is its ability to assess bone strength by measuring cross-sectional geometry and density of cortical bone. For accurate determination of cortical bone cross-sectional area (CoA), it is important to select the appropriate analysis mode and thresholds. No study has assessed which analysis protocol best represents tibial bone geometry—as determined by histomorphometry. We measured bone geometry from 16 human cadaver tibiae (mean age 74 [SD 6] yr) with pQCT (XCT 2000) at the 25% site, measured proximally from the distal tibia plafond. We conducted histomorphometry at the same site as the criterion standard. Scans were analyzed using modes and thresholds recommended by the manufacturer (Norland Stratec Medizintechnic GmbH, Pforzheim, Germany). We also investigated agreement of two additional thresholds (calculated by half-maximum height and inflection point methods) to define the endosteal border of cortical bone. Compared to the criterion, the smallest error (−1.0%, $p = 0.002$) in total cross-sectional area (ToA) was obtained using Contour mode 3 with an outer threshold of 169 mg/cm^3. The smallest error (0.1%, NS) in CoA was obtained with Separation mode 4 (outer threshold 200 mg/cm^3, inner threshold 670 mg/cm^3). CoA was overestimated by 5−7% ($p < 0.001$) from the criterion when an inner threshold of 480 mg/cm^3 was used in combination with any of the recommended outer thresholds. pQCT measurements of bone geometry in vitro vary to some extent between modes and thresholds selected. The effect of variation in bone geometry measurements on the predictive ability of bone strength indices derived from CoA needs to be assessed.

Key Words: pQCT; histomorphometry; bone geometry; cortical bone area; accuracy.

Introduction

Designed for their function, long bones are light, stiff, and adapted to resist loads applied during locomotion *(1)*. In the long bone diaphysis, these requirements are met by positioning the mineralized cortex away from the neutral axis of the bone—a geometric feature that confers lightness and strength to the structure *(1,2)*. A distinct advantage of peripheral quantitative computed tomography (pQCT) is its ability to assess bone strength by measuring both bone cross-sectional geometry and tissue density *(3)*. These parameters can be obtained for both cortical and trabecular compartments by selecting a specific analysis protocol. The cortical bone compartment is then used to calculate bone strength indices, such as the strength−strain index (SSI) *(4,5)*.

The most commonly used pQCT models (XCT-960/2000/3000, Norland Stratec Medizintechnic GmbH, Pforzheim, Germany) measure bone cross-sectional geometry (i.e., total [ToA, mm^2] and cortical bone cross-sectional areas [CoA, mm^2]) precisely *(6−11)*. However, to determine ToA and CoA, the XCT software *(4,5)* provides the user with a wide range of modes and thresholds from which to choose from. To date, there is little evidence regarding the modes and

Received 03/27/06; Revised 07/12/06; Accepted 07/12/06.
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thresholds that best represent human long bone geometry *(6,12–14)*. As indices of bone strength (cross-sectional moment of inertia, section modulus, and SSI) are dependent on measurement of CoA, it is fundamentally important to have both accurate and precise representation of the cortical bone compartment.

Therefore, our objective was to compare a histomorphometry criterion with selected pQCT modes and thresholds of bone geometry in the human tibia.

Methods

Cadaver Specimens

We obtained 16 human cadaver tibiae (7 pairs, 2 singles) from the Vancouver General Hospital and Health Sciences Donation Service. The mean age of 5 female and 4 male donors was 74 yr (SD 6 yr). All specimens were fresh frozen at −20°C and thawed initially for imaging procedures and histomorphometry. The study was approved by the Clinical Ethics Review Board at the University of British Columbia.

pQCT Scan Acquisition

First, we acquired a 30-mm planar scout view over the ankle joint. The reference line was placed between the distal tibial cartilage and subchondral bone (Fig. 1A); a single 2.3-mm slice at the 25% site of the tibial length (measured proximal to the reference line) using the Norland/Stratec XCT 2000 (Stratec Medizintechnik GmbH, Pforzheim, Germany; Fig. 1B). We used an in-plane pixel size of 0.20 × 0.20 mm and a scan speed of 10 mm/s. All measurements were made by one trained technician.

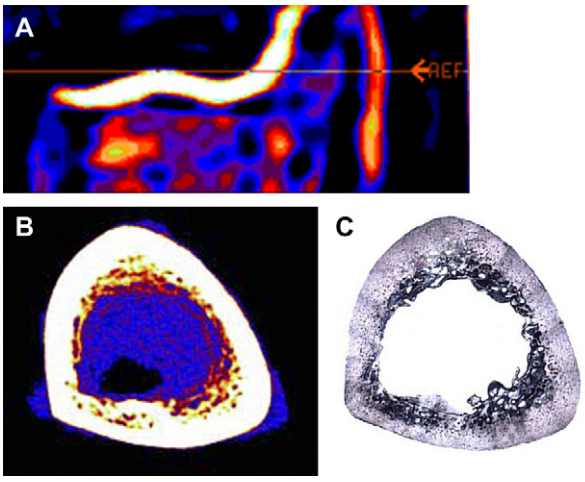

Fig. 1. (**A**) Scout view of the distal tibia and the reference line; (**B**) pQCT scan at the 25% site; and (**C**) its associated histomorphometric image.

pQCT Scan Analysis

Norland/Stratec XCT 5.50 software was used for all analyses *(4,5)*. To obtain ToA_{pQCT} (mm^2), we used Contour modes 1 and 3 with three manufacturer recommended outer thresholds (169, 200, and 280 mg/cm^3) to separate the soft tissue from the outer edge of bone *(4,5)*. We selected the modes that allow the operator to set the threshold. The algorithm in Contour mode 1 separates the soft tissue from the periosteal border by excluding voxels with density lower than the user-defined threshold *(5)*. Contour mode 3 performs an iterative contour detection procedure. Based on the user-defined threshold the algorithm finds the first voxel of the outer bone edge. This first voxel is then compared to a set of its neighboring voxels and in a certain manner those voxels are proofed to determine the bone edge *(5)*.

To obtain CoA_{pQCT} (mm^2), we used Separation mode 4 because only this mode allows the operator to define both an outer and an inner threshold to determine cortical borders *(5)*. CoA measurements by QCT were shown to be most accurate when periosteal (outer) and endosteal (inner) borders were defined at separate thresholds *(15)*. The three outer thresholds (169, 200, and 280 mg/cm^3) were used in combination with four inner thresholds—(1) Manufacturer 1 (MANUFR 1): 710 mg/cm^3; (2) Manufacturer 2 (MANUFR 2): 480 mg/cm^3; (3) calculated half-maximum height (HMH); and (4) inflection point density. We describe the calculation of the HMH and inflection point density below.

Half-Maximum Height

We calculated an operator-dependent inner threshold, based on the determination of HMH *(16)* for each pQCT scan using the XCT 5.50 ''Profile'' function (Fig. 2). From the system generated bone profile we extended a line from the superior to the inferior border of the region of interest. From this line, a single investigator (DL) manually identified the maximum density of the cortex and the minimum density at the endosteal border for each specimen. HMH was determined as the average density of these maximum and minimum densities. We used the mean of HMH densities across all specimens as the inner density threshold to determine CoA.

Inflection Point

We also defined an operator-independent inner threshold (inflection point) to minimize any investigator bias that may be present in the HMH threshold estimation. The inflection point thresholds were calculated from the concentric peel (Concpeel) function *(5)*. The pQCT Concpeel function calculates the average density of tissue in concentrically peeled rings commencing at the center of mass and progressing to the periosteal surface. The software provides a graph of the bone mineral density distribution within the bone cross section (Fig. 3). We defined cortical bone from this Concpeel function by calculating the greatest increase in bone mineral density between the rings. The greatest change in bone mineral density with respect to ring number occurs where the derivative of the bone mineral density vs ring number function