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Technological Issues

Use of Relative vs Fixed Offset Distance to Define Region of Interest at the Distal Radius and Tibia in High-Resolution Peripheral Quantitative Computed Tomography

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Abstract

Although the region of interest in high-resolution peripheral quantitative computed tomography, defined based on the manufacturer's protocol for in vivo scanning, provides consistency and is practically convenient, it does not take into account possible variation in morphology in the regions adjacent to the measurement site. This study aimed at compare the morphologic variation in measurements using the standard fixed offset distance to define the distal starting slice against those obtained by using a relative measurement position scaled to the individual bone length at the distal radius and tibia in normal healthy adult subjects. A total of 40 healthy adult subjects (median height, 175.3 cm; range: 150.0–196.0 cm) were included in the study. High-resolution peripheral quantitative computed tomography at the distal radius and tibia was performed in all subjects, the region of interest defined by, first, the standard measurement protocol, where the most distal CT slice was 9.5 mm and 22.5 mm from the end plate of the radius and tibia, respectively, and second, the relative measurement method, where the most distal CT slice was at 4% and 7% of the radial and tibial lengths, respectively. Volumetric densities and microarchitectural parameters were compared between the 2 methods. Measurements of the total and cortical volumetric density and cortical thickness at the radius and tibia and cortical porosity, trabecular volumetric density, and trabecular number at the tibia were significantly different between the 2 methods (all $p < 0.001$). The predicted morphologic variation with varying measurement position was substantial at both the radius (up to 34%) and the tibia (up to 36%). A lack of consideration to height (and in turn the bone lengths) in the standard patient protocol could lead to the introduction of systematic errors in radial and tibial measurements. Although this may not be of particular significance in longitudinal studies in the same individual, it potentially assumes critical importance in cross-sectional studies.

Key Words: HR-pQCT; region of interest; relative measurement method; standard measurement protocol.

Introduction

High-resolution peripheral quantitative computed tomography (HR-pQCT) has paved the way to gain insights into bone compartment–specific geometry and microarchitecture noninvasively. On the basis of the manufacturer's default protocol for in vivo scanning, the region of interest (ROI) is initiated at 9.5 mm and 22.5 mm proximal to the end plate of the distal radius and tibia, respectively. This ROI is ideal because there is a good representation of both trabecular and cortical components. In addition, it is a transition region in terms of the load-carrying roles of the trabeculas and cortex at the radius and tibia with trabecular bone primarily carrying the load at the distal end of the ROI and the cortical bone at the proximal end *(1)*.

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Although the use of fixed offset distances to define the measurement site provides consistency and is practically convenient, it does not take into account the possible variation in the morphology in the regions adjacent to the measurement site. This may not be of particular significance in longitudinal studies in the same individual but is potentially of critical importance in cross-sectional studies. Although matching for height when comparing between patients and normal individuals will partially offset this limitation, it will still not account for subjects with disproportionate short or tall stature or in osteoporotic subjects who have a reduction in height because of a predominant decline in axial length.

In an ex vivo study looking at the site-specific variation of bone microarchitecture in cadaver bones using HR-pQCT, Boyd et al *(2)* found a higher variation at the radius than the tibia in the distal 27.06 mm (330 slices) analyzed on a slice-to-slice basis. Moreover, they reported a variation as high as 19% in morphologic parameters between the proximal and distal measurement sites *(2)*. Using the microdissection and ashing technique, Schlenker et al *(3)* reported a 10%−50% variation in trabecular bone content in the distal 12 cm of the radius with a substantial decline in the distal 2−3 cm, which usually corresponds to the ROI in standard HR-pQCT measurements. Currently, there are no in vivo studies assessing the implications of these morphologic variations when using a fixed offset to define the ROI in both sexes and across a wide range in body height.

The purpose of this study was to compare the morphologic variation in measurements using the standard fixed offset distance to define the initiation of the measurement site and ROI against those obtained by using a relative measurement position scaled to the individual bone length at the distal radius and tibia in normal healthy adult subjects. We hypothesize that there will be a significant disparity in the indices obtained by the 2 methods.

Subjects and Methods

This study included 40 healthy adult subjects and was conducted at the Department of Endocrinology at Odense University Hospital, Odense, Denmark. Subjects were recruited between August 2013 and January 2014 by means of poster advertisements in the university and the university hospital and were included on the basis of their ability to provide informed consent and if their height was between 150 and 190 cm in women and 160−200 cm in men *(4)*. Pregnant women, subjects with known underlying metabolic bone disease, overt endocrine disease, kidney or liver disease, or those on medication known to affect bone metabolism were excluded.

All participants provided verbal and written informed consent. The study was performed according to the guidelines of the Declaration of Helsinki. The study protocol was approved by the Regional Scientific Ethical Committee of Southern Denmark (Ref. IDs S-20130055).

Body height was measured in all participants to the nearest 0.1 cm on a wall-mounted Harpenden Stadiometer (Holtain Ltd., Crymich, UK). Forearm length (radial length) was measured from tip of the elbow to the radial styloid process with the forearm flexed to 90°, and lower leg length (tibial length) was defined from the medial condyle to the medial malleolus with the knee at 90° to the nearest 1 cm using an inch tape. All measurements were performed by one of the authors (VS).

High-Resolution Peripheral Quantitative Computed Tomography

Assessment of volumetric bone mineral density (vBMD) and microarchitecture was performed using an HR-pQCT system (Xtreme CT; Scanco Medical, AG, Brüttisellen, Switzerland) at the nondominant distal radius and distal tibia (the opposite limb in the presence of a previous fracture). The image acquisition, analysis, and validation of the method and the manufacturer's default protocol for in vivo imaging have been described in details previously *(5−8)*. Briefly, in the first fixed offset method, the manufacturer's default protocol was applied for in vivo scanning, where the most distal CT slice was 9.5 mm and 22.5 mm from the end plate of the distal radius and tibia, respectively *(8)*. Each measurement included 110 parallel slices in the axial direction corresponding to 3-dimensional (3D) representation of 9.02-mm-thick cross-sections.

Second, the relative (scaled to the bone length) measurement method was applied, where the most distal CT slice was at 4% of the radial length and 7% of the tibial length from the end plate of the distal radius and tibia, respectively *(8)*. Again, each measurement included 110 parallel slices in the axial direction which corresponded to the 3D representation of 9.02-mm-thick cross-sections. The anatomic landmarks (distal end plate of the radius and tibia) used for defining the most distal CT slice were identical in the standard and relative methods.

The manufacturer's default protocol of initiating measurement at 9.5 mm from the distal end of the radius would result in the start of the measurement site being 5.3% to 3.3% (in radial lengths of 18 cm−29 cm; from unpublished data in our dual-energy X-ray absorptiometry machine) relative to the radial length. Similarly, at the tibia, this would be between 8% and 5% (in tibial lengths ranging from 29 cm to 45 cm). Hence, we have taken 4% and 7% as the arbitrary values at the radius and tibia, respectively. Moreover, there is a good representation of trabecular and cortical bone in these regions of the bones as shown in various studies in children and adolescents *(9,10)*. The values for the initiation of the measurement site corresponding to 4% and 7% of the radial and tibial lengths are listed in Supplementary Table 1.

Structure extraction and morphometric evaluation were done using the standard approach *(8)*, and the following outcome variables were included in our analysis: HR-pQCT−derived vBMD (mg hydroxyapatite/cm^3) for the entire (total vBMD), trabecular (Tb vBMD), and cortical regions (Ct vBMD); trabecular number (Tb.N; mm^{-1}); and trabecular thickness (Tb.Th; mm). Next, the 3D measurements of cortical thickness (Ct.Th; mm) and cortical porosity (Ct.Po; %) were