Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1−8, 2013

1094-6950/■:1−8/$36.00
http://dx.doi.org/10.1016/j.jocd.2013.09.014

Original Article

Comparison of Short-Term In Vivo Precision of Bone Density and Microarchitecture at the Distal Radius and Tibia Between Postmenopausal Women and Young Adults

Chantal E. Kawalilak,[1] James D. Johnston,[2] Wojciech P. Olszynski,[3] David A. Leswick,[4] and Saija A. Kontulainen[1]*

[1]College of Kinesiology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; [2]Department of Mechanical Engineering, College of Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; [3]Osteoporosis Centre, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; and [4]Department of Medical Imaging, College of Medicine, University of Saskatchewan and Saskatoon Health Region, Saskatoon, Saskatchewan, Canada

Abstract

The purpose was to assess whether precision of bone properties derived via the use of high-resolution peripheral quantitative computed tomography (HR-pQCT) differs between postmenopausal women and young adults. Using HR-pQCT, we scanned the distal radius and tibia at 2 time points in 34 postmenopausal women (74 ± 7 years) and 30 young adults (mean age ± SD: 27 ± 9 years). Standard protocols were used to acquire bone area, density, and microarchitectural properties. We calculated coefficients of variation (CV; percentage CV and percentage CV of the root mean square) and 95% limits of agreement (95% LOA) to assess precision errors. The 95% LOA is the magnitude of individual change needed to be observed to ensure that a real change has occurred. Multiple Mann-Whitney *U*-tests (with the use of Bonferroni correction for multiple comparisons) were used to compare percentage CV between the 2 groups. Significance was set to $p < 0.004$. All standard outcome variables were not significantly different between the groups. The 95% LOA confirmed that the measurement bias between the groups did not differ. These results suggest that short-term precision errors in HR-pQCT−derived bone outcomes are similar between postmenopausal women and young adults.

Key Words: Coefficient of variation; distal radius and tibia; HR-pQCT; microarchitecture; reproducibility.

Introduction

Osteoporosis is a multifactorial disease characterized by low bone mass and the deterioration of bone microarchitecture resulting in bone fragility and a subsequent increase in propensity to fracture *(1)*. Dual-energy x-ray absorptiometry (DXA) is used for assessing areal bone mineral density (aBMD, mg/cm^2) to diagnose osteoporosis *(2,3)*. However, the majority of fragility fractures occur in women whose DXA-derived aBMD and related T-scores are greater than the osteoporosis diagnostic threshold *(4−6)*. Some of these fractures are unrelated to aBMD and are likely the result of deterioration of bone microarchitecture and bone strength, which planar 2-dimensional DXA measures cannot detect. This premise is supported by evidence from women with equal DXA-derived aBMD at the ultradistal radius but substantially different bone microarchitectural properties and strength estimates acquired by the use of high-resolution peripheral quantitative computed tomography (HR-pQCT) *(7)*. Microarchitectural properties at distal bone sites are able to differentiate postmenopausal women who have had a fragility fracture from their nonfracture counterparts *(8−15)*. Therefore, the use of in vivo 3-dimensional high-resolution imaging

Received 06/04/13; Revised 08/31/13; Accepted 09/11/13.
*Address correspondence to: Chantal E. Kawalilak, MSc, College of Kinesiology, University of Saskatchewan, 87 Campus Drive, Saskatoon, SK, Canada S7N 5B2. E-mail: chantal.kawalilak@usask.ca

techniques may improve the diagnosis of osteoporosis and assessment of fracture risk, as well as offer a monitoring tool for microarchitectural deterioration in postmenopausal women.

Measurement reproducibility is essential to reliably monitor bone microarchitectural changes over time, to study changes caused by drug therapy or intervention, and to compare differences between groups of people *(16,17)*. HR-pQCT precision errors in vivo, in terms of percentage coefficient of variation of the root mean square ($CV\%_{RMS}$), have been reported to vary between 0.1% and 5% for selected standard outcomes variables in cortical and trabecular compartments at the distal radius and tibia *(18–20)*. However, the majority of precision studies in vivo using HR-pQCT have been completed with young and middle-aged adults *(18,20)*. It has been suggested that precision errors derived from young adults may underestimate errors in older adults, including clinically relevant postmenopausal women *(21,22)*. For example, older adults may have more difficulty remaining still during scanning (e.g., tremors), and optimum positioning may be difficult to achieve because of a reduced range of motion. In addition, age-related deterioration in bone microarchitecture may challenge the repeatability in HR-pQCT analysis.

Evidence from one HR-pQCT study suggested comparable precision errors between young adults and older females (minimum cut-off age: 40 years) *(19)*. However, measurements from older female subjects were repeated on the same day *(19)*, which has been shown to enhance the pQCT repeatability *(23)*. Notwithstanding, there is a need for comparison data from older postmenopausal women to confirm whether menopausal status influences precision errors of HR-pQCT–derived bone properties measured at least 24 h apart. Finally, previous HR-pQCT precision studies reported a selection of standard outcome variables. For example, precision of trabecular meta and inner densities are unknown. The objective of our study was to assess whether postmenopausal women could be scanned by the use of HR-pQCT with similar precision to young adults. We hypothesized that postmenopausal women would have greater precision errors (i.e., poorer repeatability) compared with young adults.

Methods

Participants

The first group of was a random subsample of 34 postmenopausal women from the Saskatoon cohort of the Canadian Multicentre Osteoporosis Study (Table 1) *(24)*. Postmenopausal status was assessed with a questionnaire (Table 1). We obtained osteoporosis status based on femoral neck T-scores from the Saskatoon Canadian Multicentre Osteoporosis Study database (Table 1) *(25)* and compared osteoporosis status in our sample with the literature to substantiate that the bone health in our sample was representative to postmenopausal women *(24,26,27)*. The second, comparison group was a convenient sample of 15 female and 15 male volunteers (Table 1). We combined the sexes to form an ''ideal group'' of young adults with optimal bone properties for comparison with the postmenopausal women. There was no effect of sex on precision in young adults (data not shown). Participants' consent was obtained prior to the study. This study was approved by the University of Saskatchewan Biomedical Research Ethics Board.

Table 1
Participant Demographics of Participants With Osteopenia or Osteoporosis

	Postmenopausal	Young adults	
Variables	Females	Males	Females
Age, yr	74 ± 7	25 ± 4	26 ± 8
Height, cm	160.1 ± 5.7	179.5 ± 4.1	166.5 ± 4.6
Weight, kg	72.4 ± 12.9	88.5 ± 4.1	71.4 ± 12.4
Osteopenia, n (%)	20 (63)	–	–
Osteoporosis, n (%)	5 (16)	–	–

Note: Values are mean ± SD or number (n) and percentage (%).

HR-pQCT Imaging

All participants had their nondominant arm and ipsilateral leg immobilized in the manufacturer provided cast before imaging to acquire the correct limb position and to prevent gross participant movement *(28)*. After we positioned the participant's limb comfortably in the scanner, a 2-dimensional anterioposterior scout view scan was used to set the reference line and define the region of interest (Fig. 1). HR-pQCT (XtremeCT; Scanco Medical AG, Brüttisellen, Switzerland) was used to acquire 110 parallel CT slices over a 9.02-mm region of the distal radius and distal tibia (Fig. 1). The radius and tibia regions of interest were 9.5 mm and 22.5 mm, respectively, proximal to the reference line placement (Fig. 1). The field of view was reconstructed over a 1536 × 1536 matrix using an isotropic resolution of 82 μm. The effective dose was <3 μSv and the measurement time was approximately 2.8 minutes for each scan *(28)*.

HR-pQCT Analysis

One trained operator (C.E.K.) scanned, graded, and analyzed all images. The postmenopausal women had follow-up measures a minimum of 1 week (9.9 ± 3.7 d) after the first measurement, whereas the young adults had follow-up measures a minimum time period of 1 day (24.0 ± 4.8 h) from the first scan. All images were grading for quality according to a 5-point scale defined by the manufacturer and reported in a previous publication *(29)*. Upon detection of motion artifacts (e.g., streaking or broken cortices) a repeat scan was performed. Images graded as quality 5 were excluded from the study. At the radius, 4 scans from the older adult group and 1 scan from the young adult group were removed because of excessive movement artifact. We also excluded an additional 2 older adult radius scans due to a skeletal defect noted by the study radiologist (D.A.L.). At the tibia, 2 scans were