Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–12, 2017

1094-6950/■:1–12/$36.00
http://dx.doi.org/10.1016/j.jocd.2017.02.002

Original Article

Measuring Marrow Density and Area Using Peripheral Quantitative Computed Tomography at the Tibia: Precision in Young and Older Adults and Individuals With Spinal Cord Injury

Jenna C. Gibbs,[*,1] *Zachary M. Brown,*[1] *Andy K. O. Wong,*[2,3,4] *B. Catharine Craven,*[1,5,6] *Jonathan D. Adachi,*[7] *and Lora M. Giangregorio*[1,5,8]

[1]*Department of Kinesiology, University of Waterloo, Waterloo, ON, Canada;* [2]*Joint Department of Medical Imaging, Toronto General Research Institute, University Health Network, Toronto, ON, Canada;* [3]*Centre of Excellence in Skeletal Health Assessment, Toronto General Research Institute, University Health Network, Toronto, ON, Canada;* [4]*Arthritis Program, Toronto General Research Institute, University Health Network, Toronto, ON, Canada;* [5]*Lyndhurst Centre, Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada;* [6]*Department of Medicine, University of Toronto, Toronto, ON, Canada;* [7]*Department of Medicine, McMaster University, Hamilton, ON, Canada; and* [8]*Schlegel Research Institute for Aging, University of Waterloo, Waterloo, ON, Canada*

Abstract

The objective of this study was to compare the test-retest precision error for peripheral quantitative computed tomography (pQCT)-derived marrow density and marrow area segmentation at the tibia using 3 software packages. A secondary analysis of pQCT data in young adults (n = 18, mean ± standard deviation 25.4 ± 3.2 yr), older adults (n = 47, 71.8 ± 8.2 yr), and individuals with spinal cord injury (C1–T12 American Spinal Injury Association Impairment Scale, classes A–C; n = 19, 43.5 ± 8.6 yr) was conducted. Repeat scans of the tibial shaft (66%) were performed using pQCT (Stratec XCT2000). Test-retest precision errors (root mean square standard deviation and root mean square coefficient of variation [RMSCV%]) for marrow density (mg/cm^3) and marrow area (mm^2) were reported for the watershed-guided manual segmentation method (SliceOmatic version 4.3 [Sliceo-WS]) and the 2 threshold-based edge detection methods (Stratec version 6.0 [Stratec-TB] and BoneJ version 1.3.14 [BoneJ-TB]). Bland-Altman plots and 95% limits of agreement were computed to evaluate test-retest discrepancies within and between methods of analysis and subgroups. RMSCV% for marrow density segmentation was >5% for all methods across subgroups (Stratec-TB: 12.2%–28.5%, BoneJ-TB: 14.5%–25.2%, and Sliceo-WS: 10.9%–23.0%). RMSCV% for marrow area segmentation was within 5% for all methods across subgroups (Stratec-TB: 1.9%–4.4%, BoneJ-TB: 2.6%–5.1%, and Sliceo-WS: 2.4%–4.5%), except using BoneJ-TB in older adults. Intermethod discrepancies in marrow density appeared to be present across the range of marrow density values and did not differ by subgroup. Intermethod discrepancies varied to a greater extent for marrow area and were found to be more frequently at mid- to higher-range values for those with spinal cord injury. Precision error for pQCT-derived marrow density segmentation exceeded 5% for all methods of analysis across a range of bone mineral densities and fat infiltration, whereas precision error for marrow area segmentation ranged from 2% to 5%. Further investigation is necessary to determine alternative acquisition and analysis methods for pQCT-derived marrow segmentation.

Key Words: Aging; marrow fat adiposity; peripheral quantitative computed tomography; precision; spinal cord injury.

Received 11/25/16; Revised 01/25/17; Accepted 02/13/17.
*Address correspondence to: Jenna C. Gibbs, PhD, Department of Kinesiology, University of Waterloo, 200 University Avenue West—BMH 1014, Waterloo, ON N2L 3G1 Canada. E-mail: jenna.gibbs@uwaterloo.ca

Introduction

Bone marrow adiposity develops when fat cells accumulate between the trabeculae of cancellous bone and within the diaphysis of long bone. Bone marrow adipocytes and osteoblasts share the same precursor, known as mesenchymal stem cells *(1)*, and therefore interact with one another to regulate growth, regeneration, and repair in the bone marrow space. Excessive bone marrow adiposity has been shown to negatively influence areal bone mineral density (aBMD) *(2,3)* and bone microarchitecture *(4–6)*, and to potentially contribute to an increased risk of osteoporosis and fragility fracture *(2,7)*. Age-related bone loss has been linked to preferential differentiation of mesenchymal stem cells to adipocytes over osteoblasts, possibly leading to higher marrow adiposity and lower bone strength *(8,9)*. Marrow fat accumulation has also been observed following immobilization or bed rest *(10,11)*, suggesting that bone-fat interactions may promote accelerated bone resorption and aBMD loss in conditions of neurological impairment-related paralysis, such as spinal cord injury (SCI) *(12)*. To study the impact of marrow adiposity on bone strength and fracture risk, standardized, noninvasive methods for the measurement of marrow adiposity must be established, including determining the precision of marrow segmentation across a wide range of bone and fat properties.

In vivo proton magnetic resonance spectroscopy and magnetic resonance imaging (MRI) can separately quantify the level of adiposity within the bone. Using proton magnetic resonance spectroscopy, lipids can be quantified by fitting acquired spectra to known spectral profiles. Various fat-water subtraction (suppression pulses) or separation (chemical-shift) techniques have been developed using MRI to measure fat fraction. These methods have noninvasively quantified marrow fat content in humans with relative precision (4.5%–5% error *(13)*, 0.9% error [intrarater], and 2.2% error [inter-rater] and intraclass correlation coefficients [ICCs] = 0.78–0.99) *(14,15)*. Peripheral quantitative computed tomography (pQCT) has also been used to analyze marrow adiposity and indices of bone strength at the femur and tibia using a threshold-based edge detection method from the BoneJ software that is run in the National Institutes of Health (NIH) ImageJ *(5,16)*. Rantalainen et al *(5)* found acceptable test-retest precision with repositioning for marrow segmentation using BoneJ in 8 young women (<1% error). However, Rantalainen et al's study did not meet International Society for Clinical Densitometry (ISCD) criteria for precision study sample size requirements (15 subjects when scanned in triplicate or 30 subjects when scanned in duplicate) *(5)*. Although it is appealing to measure marrow properties using technology that is already available to quantify volumetric bone mineral density (vBMD) and bone strength indices, the precision of pQCT-derived marrow measures has not been established using ISCD standards *(17)*.

Estimates of bone, muscle, and fat from pQCT images can be obtained using the manufacturer Stratec software *(18)* or the freely available BoneJ software *(5,19)*, both of which apply threshold-based edge detection algorithms to differentiate between tissue boundaries. However, threshold-based techniques may result in failed or inaccurate marrow segmentation due to poor tissue boundary identification in the presence of fat infiltration and endocortical bone resorption, or from any subtle movement artifact or beam hardening due to an increase in the overlying tissue volume *(20,21)*. Reliable protocols using watershed algorithm-guided manual segmentation from the SliceOmatic software to quantify muscle and fat densities within the leg have been reported (0.6%–4.1% error and ICC > 0.90, respectively) *(18,22)*. The application of the watershed algorithm-guided technique may be advantageous for studies of marrow adiposity in older adults and individuals with SCI to address imprecision due to aBMD loss confounding the segmentation of the endocortical border. However, the precision of pQCT-derived marrow measurement using the watershed-guided manual segmentation method is unknown.

The present study reported the test-retest precision error of pQCT-derived marrow measures in young and older adults and in individuals with SCI using Stratec, BoneJ, and SliceOmatic software packages. We hypothesized that the SliceOmatic watershed algorithm would demonstrate acceptable agreement with threshold-based methods for quantifying marrow density and marrow area at the midtibia in young adults, individuals with SCI, and older adults. A secondary objective was to determine intra- and inter-rater reliability and precision for marrow measures using the SliceOmatic watershed algorithm method.

Methods

Study Design and Sample Selection

Our study was a cross-sectional secondary analysis of pQCT data collected in young adults (18–30 yr, n = 18), adults (18–45 yr) with complete or incomplete SCI (American Spinal Injury Association Impairment Scale—class A, B, or C) for ≥6 mo (n = 47), and older women (≥60 yr, n = 19) *(18,23)*. The selection of these subgroups allowed us to describe marrow characteristics and precision estimates across a wider range of individuals. Young adults were a convenience sample of local community participants *(23)*. Individuals with SCI were recruited from local physiatrists' clinics as part of an investigation of bone structure differences across impairment subgroups with SCI *(23)*. Participants with SCI were excluded if they had bilateral metal implants, prior fracture of the tibia, or metabolic bone diseases known to affect BMD and bone structure *(23)*. Older women were a random sample from the Hamilton cohort of the Canadian Multicentre Osteoporosis Study (CaMos) that studied the association between pQCT and high-resolution pQCT *(18)*. The study received ethics clearance through the University of Waterloo Research Ethics Committee.