Microscopic Magnetic Resonance Imaging (μMRI) Assessment of Trabecular Micro-Architecture in Non-Osteoporotic Post-Menopausal Women With and Without Fracture

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Purpose: The current clinical standard for osteoporosis diagnosis is bone mineral density (BMD) measurements obtained using dual-energy x-ray absorptiometry (DXA) [1]. However, this diagnostic approach fails to account for other factors such as trabecular micro-architecture which can influence bone strength and hence fracture risk [2]. Microscopic magnetic resonance imaging (μMRI) has been used as a noninvasive method to assess trabecular micro-architecture. Various studies have been shown that μMRI parameters are superior to BMD for distinguishing between osteoporotic women with and without fracture [3-5]. However, no previous study has investigated the ability of μMRI to assess fracture risk in individuals without a DXA-based diagnosis of osteoporosis. Thus, this study was performed to compare μMRI parameters between postmenopausal women with and without fracture who have normal or osteopenic BMD.

Methods: Thirty-six post-menopausal Caucasian women 50 years of age and older with normal or osteopenic BMD (T-scores better than -2.5 at the lumbar spine, proximal femur, and one-third radius on DXA) were included in the study. Eighteen women had a history of low-energy fracture, while 18 women had no history of fracture and served as an age, race, and ultra-distal radius BMD-matched control group. DEXA was performed on all women to measure BMD of the lumbar spine, proximal femur, one-third radius, and ultra-distal radius, while a routine blood chemistry panel was obtained to demonstrate absence of systemic conditions indicative of bone disease. A three-dimensional fast large-angle spin-echo (FLASE) sequence was performed through the non-dominant wrist of all women using the same 1.5T scanner (Signa HDx, GE Healthcare, Waukeshaw, WI) and a specially designed elliptical birdcage coil (Insight MRI, Worcester, MA) [6]. The FLASE sequence was acquired using the following image parameters: TR/TE of 80ms/10ms, 140^{o} flip angle, 7.0 cm x 5.3 cm field of view, 512 x 384 matrix, 0.4 mm slice thickness, one excitation, 137 μm x 137 μm x 400 μm voxel size, and 12.3 minute scan time (Figure 1A). Image analysis was performed by an experienced research technologist from MicroMRI, Inc. (Langhorne, PA) using a previously described semi-automated virtual bone biopsy system [7]. A bone volume fraction mapping technique was used to generate noiseless parametric images of the distal radius where each voxel represented the trabecular bone volume fraction [8]. The average trabecular thickness on the bone volume fraction maps was measured using a fuzzy distance transform algorithm [9]. The bone volume fraction maps then underwent subvoxel processing, binarization, and skeletonization to produce a three-dimensional model of the trabecular network consisting of surfaces and curves which represented the lower-dimensional counterparts of plates and struts respectively (Figure 1B) [10,11]. Digital topological analysis was performed to measure surface-to-curve ratio and erosion index. Wilcoxon signed rank tests were used to compare differences in demographic variables, laboratory values, BMD measurements, and μMRI parameters between post-menopausal women with and without fracture.

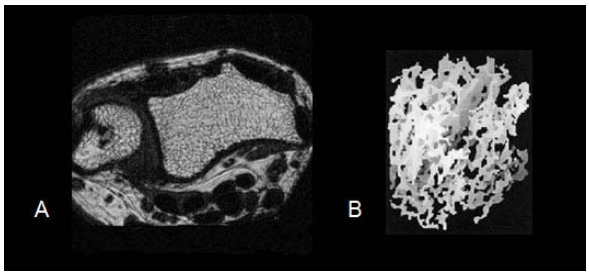

Figure 1: (A) FLASE image of the distal radius with 137 μm x 137 μm x 400 μm voxel size. (B) Three-dimensional model of trabecular micro-architecture obtained using a semi-automated virtual bone biopsy system .

Results: There was no significant difference in post-menopausal women with and without fracture in age (p=0.13), height (p=0.60), weight (p=0.68), body mass index (p=0.26), laboratory values (p=0.15-0.99), lumbar spine BMD (p=0.21), proximal femur BMD (p=0.19), one-third radius BMD (p=0.47), and ultra-distal radius BMD (p=0.90). However, post-menopausal women with fracture had significantly lower (p<0.05) trabecular bone volume fraction and surface-to-curve ratio and significantly higher (p<0.05) erosion index than post-menopausal women without fracture. There was no significant difference (p=0.80) between post-menopausal women with and without fracture in trabecular thickness (Table 1).

Table 1: μMRI parameters in post-menopausal women with and without fracture

μMRI Parameter	Fracture Group	Non-Fracture Group	Difference Between Groups
Trabecular Bone Volume Fraction	9.3% +/- 1.1%	10.2% +/- 0.9%	p<0.001
Trabecular Thickness	85.5μm +/- 8.0μm	85.7μm +/- 6.3 μm	p=0.80
Surface-to-Curve Ratio	5.1 +/- 1.0	5.9 +/- 1.0	p=0.04
Erosion Index	1.4 +/- 1.0	1.2 +/- 1.0	P=0.03

Conclusions: Post-menopausal women with normal or osteopenic BMD who had a history of low energy fracture had significantly different (p<0.05) μMRI parameters than an age, race, and ultra-distal radius BMD-matched control group of postmenopausal women with no history of fracture. Our study suggests that μMRI can be used to identify individuals without a DXA-based diagnosis of osteoporosis who have a heretofore-unappreciated elevated fracture risk. In the future, μMRI may potentially enhance targeting of fracture prevention therapy to include individuals with normal or osteopenic BMD who have impaired trabecular micro-architecture.

References: [1] Hans P, et al. J Clin Densitom. 9:15, 2006. [2] Kleerekoper M, et al. Calcif Tissue Int. 37:594, 1985. [3] Majumdar S, et al. J Bone Miner Res. 12:111, 1997. [4] Link T, et al. J Bone Miner Res. 13:1175, 1998. [5] Wehrli F, et al. J Bone Miner Res. 16:1520, 2001. [6] Techawiboonwong A, et al. J Magn Reson Imaging. 22:647, 2005. [7] Wehrli F, et al. J Magn Reson Imaging. 25:390, 2007. [8] Hwang S, et al. Int J Imaging Syst Technol. 10:186, 1999. [9] Sara P, et al. IEEE Trans Med Imaging. 23:53, 2004. [10] Hwang S, et al. Magn Reson Med. 47:948, 2002. [11] Gomberg B, et al. IEEE Trans Med Imaging. 19:166, 2000. [12] Gomberg B, et al. Adv Exp Med Biol. 496:57, 2001.

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