Vertebral bone marrow fat content measured by MRI associated with lower bone mineral density: a human cadaver study

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Target audience: Diagnostic radiologists

Purpose: Adiposity is known to increase with age; however, recent studies have indicated that a shift in stem cell lineage allocation toward adipogenesis and away from osteoblastogenesis may contribute to age-related bone loss[1]. Clinical studies using different methods including magnetic resonance spectroscopy (MRS), to assess marrow fat have found a negative correlation with bone mineral density (BMD) and a positive correlation with prevalent vertebral fracture[2]. However, no validation data on the relationship between marrow fat obtained by a clinically available fat-quantification method and BMD in an in vitro study are currently available. Therefore, the present cadaveric study was conducted in order to validate the relationships among vertebral marrow fat, BMD, and bone strength.

Methods: Fresh human L1, L2, and L3 vertebral bodies were obtained from 10 adult cadavers (age range, 72–90 years). The vertebrae were scanned by 3-T MRI (Ingenia; Philips Healthcare) and 64-section MDCT (VCT; GE Healthcare). Each vertebra was scanned with a bone mineral reference phantom to obtain tissue BMD (tBMD) by MDCT. The MR imaging protocol included a sagittal, coronal, axial T1-weighted fast spin echo sequence to prescribe the spectral acquisition box. Single-voxel MRS was acquired in vertebral bodies using a stimulated-echo acquisition mode (STEAM) sequence (TR, 2000 ms; TE, 9.5), each with 128 signal averages (NSA), bandwidth ± 1000 Hz, and 1028 data points. Spectral data were obtained from the central 10-mm-thick voxel (2×1.5×1 cm^3). After phase, baseline, and frequency shift correction, the following 2 peaks were fitted using SpectroView software (Philips Healthcare): the water peak at 4.67 ppm and the fat peak at 1.3 ppm (the bulk CH_2 methylene protons). From the area under each peak, the bone marrow fat (FF by ^{1}H MRS) was defined as fat/(fat + water) × 100%. Axial images for a six-echo mDIXON with T2* corrections and a multi-peak model for fat were obtained using the parameters for the 3D fast gradient echo mDIXON sequence (flip angle, 3°; slice thickness, 2.5 mm; matrix, 128×143; NSA, 1; FOV, 200×175mm; TR/ΔTE=12/1.25 ms). The mDIXON fat fraction (FF by mDIXON) was expressed as fat/(fat + water) × 100%, and it was obtained pixel by pixel from the same central area of 2×1.5 cm^2 as that of ^{1}H MRS in the central four slices (i.e., 10 mm thickness) using mDIXON-Quant software (Philips Healthcare).

Scanning parameters for MDCT were 120 kVp, 750 mA, and 64×0.625 collimation, resulting in a voxel size of 200×200×160 μm^3. Finite element modeling (FEM) and microstructural analysis were performed using a 3D image analysis system (RATOC System Engineering). Failure load and trabecular microstructural parameters including trabecular thickness (Tb.Th) and degree of anisotropy (DA) were calculated.

Pearson's correlation coefficients between FF by mDixon and ^{1}H MRS were calculated. The relationships among tBMD, trabecular indices, and FF by mDixon and 1H MRS were evaluated using Spearman's correlation coefficient (ρ).

Figure 1. Pearson's correlation coefficients between FF by mDixon and 1H MRS (a) and relationships between tBMD and FF by mDixon (b) and ^{1}H MRS (c).

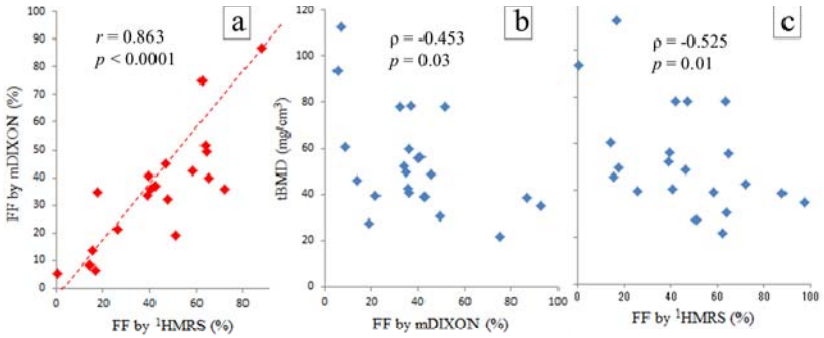


Table 1. Correlation coefficients for fat fractions, tissue BMD, and trabecular indices.

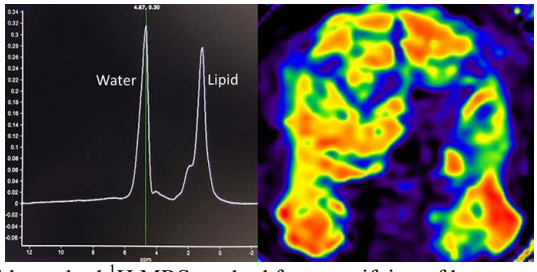
		FF by mDIXON		FF by 1H MRS	
	Parameter	ρ	p	ρ	p
tBMD (mg/cm^3)		-0.453	0.03	-0.525	0.01
Morphology	BV/TV (%)	-0.416	0.06	-0.335	0.15
	Tb.N (/mm^3)	-0.289	0.20	-0.202	0.39
	Tb.Th (μm)	-0.548	0.01	-0.476	0.03
	Tb.S (μm)	0.176	0.45	0.061	0.80
	Structure model index	0.464	0.03	0.390	0.09
	Euler's number	0.477	0.03	0.423	0.06
	DA	0.496	0.02	0.643	<0.01
Mechanics	Failure load (N)	-0.368	0.10	-0.602	<0.01

Results: Fat fractions were 38.3% (standard deviation (SD), 24.1%) by mDIXON and 46.0% (SD, 26.5%) by ^{1}H MRS. Values of FF assessed with mDIXON correlated with those from ^{1}H MRS (Figure 1a, Figure 2, $r = 0.863$, $p < 0.0001$). Fat fractions were negatively associated with MDCT-derived tBMD (Figure 1b and 1c, ρ = -0.453, $p = 0.03$ for mDIXON; ρ = -0.525, p = 0.01 for ^{1}H MRS).

MDCT/FEM-derived failure load was negatively associated with FF by ^{1}H MRS (ρ = -0.466, $p = 0.04$), but not with FF by mDIXON.

Among the MDCT-derived trabecular indices, Tb.Th and DA were significantly associated with FFs by both of mDIXON and ^{1}H MRS. The structure model index and Euler's number were significantly associated only with FF by mDIXON.

Figure 2. Representative bone marrow spectrum with individual peaks for lipid and water after fitting (Left) and the axial fat fraction image of L2 obtained by mDIXON (Right).



Discussion: The present findings demonstrate that the mDixon correlats well with the gold standard ^{1}H MRS method for quantifying of bone marrow fat content. This finding is consistent with previous reports on liver and pancreas[3]. The present data suggest that the mDIXON can be used in clinical applications as an alternative to the more time-consuming ^{1}H MRS. However, mDIXON yielded consistently lower fat values when compared to ^{1}H MRS. This could be due to systematic underestimation by the current algorithm of mDIXON-Quant software. In this study, higher marrow fat was associated with lower tBMD in the cadaveric spine. This result is concordant with a previous report[4] that compared trabecular BMD and FF by ^{1}H MRS. Our study demonstrated that this relationship can also be assessed by the clinically relevant mDIXON technique. The present findings confirm an earlier report that showed MDCT-derived compressive strength of the spine was negatively associated with FF by ^{1}H MRS (5). In the present study, compressive strength was not significantly related with FF by mDIXON. This may currently limit the use of mDixon when aiming at detection of subtle change of bone strength in the spine.

Conclusion: Fat fraction by mDIXON correlated well with that of ^{1}H MRS for quantification of bone marrow. Fat fraction by mDixon was underestimated compared to ^{1}H MRS. There was a negative correlation between marrow fat and tissue BMD. This relationship can also be assessed by the mDIXON technique. Further study is needed to assess the feasibility of using mDIXON for quantification of vertebral marrow fat in vivo.

References: (1) Moerman EJ, et al. Aging Cell. 2004;3:379–389. (2) Sheu Y, Cauley JA. Curr Osteopor Rep. 2011;9:67–75. (3). Livingstone RS, et al. Magn Reson Mater Phy (2014) 27:397–405. (4) Schwartz et al. J Clin Endocrinol Metab. 2013;98:2294-2300.