Bone Mineral and Matrix Densities Measured by Solid-State 1H and 31P MRI

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Introduction: Osteoporosis and osteomalacia are distinct bone disorders that both manifest as reduced apparent bone mineral density (BMD), and are indistinguishable by in vivo densitometric techniques. Osteoporosis involves both bone matrix and mineral loss, while osteomalacia involves mineral deficiency only. The differentiating factor is bone mineralization [1]: mineral per volume of bone matrix. MRI of bone is made difficult by unfavorable magnetic relaxation properties, but advances in solid-state ^{31}P and ^{1}H MRI have led to the possibility of quantitative measurement of bone mineral ^{31}P and collagen-bound water ^{1}H densities, respectively [2-4]. The objective of this work was to quantify relative bone mineral ^{31}P and matrix-bound water ^{1}H densities on a clinical MRI scanner to infer bone mineralization in specimens from human donors.

Theory: Water ^{1}H NMR signal in bone at 3T occurs in two compartments: long T_2 > 1 ms, corresponding to free water in pores ('pore water'); and short T_2 ~ 300-400 µs, corresponding to motionally restricted water bound to bone matrix collagen ('bound water') [5]. Bone matrix density is proportional to bound water and inversely proportional to pore water [6]. Adiabatic RF pulses saturate bound water protons (longitudinal magnetization M_z ~ 0) while partially inverting pore water protons (M_z < 0). After an inversion time delay (TI), pore water M_z will be nulled (M_z ~ 0) and bound water M_z will have recovered (M_z > 0) due to partial longitudinal (T_1) recovery. Imaging can then be performed, yielding an image predominantly of bound water.

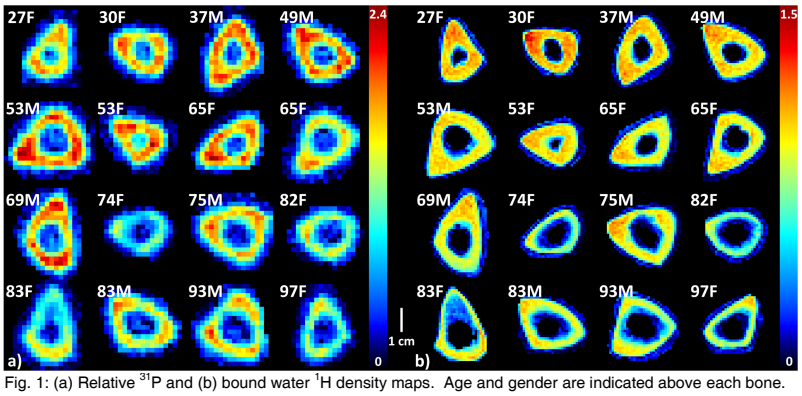

Fig. 1: (a) Relative ^{31}P and (b) bound water ^{1}H density maps. Age and gender are indicated above each bone.

Methods:

Specimens: Tibial cortical bone specimens, 36 mm long, were taken from 16 human donors (27-97 y/o, NDRI). Donors with bone-demineralizing disorders were excluded. Each bone was scanned with suitable ^{31}P and ^{1}H reference intensity phantoms.

Hardware: MRI scanning (^{1}H at 3T, ^{31}P at 7T) was performed on Magnetom whole-body MRI scanners (Siemens, Erlangen, Germany). A custom RF coil was used (7T ^{31}P: 120.3 MHz, 3T ^{1}H: 123.3 MHz). Three fiducial markers of trioctyl phosphate ($C_{24}H_{51}O_4P$) were affixed to the coil for registration of an RF field map, acquired on a water phantom at 3T.

MRI: ^{31}P relaxation times were measured in each specimen. Each bone was imaged using ^{31}P zero echo time imaging with pointwise encoding time reduction with radial acquisition [7] (^{31}P ZTE, res=2 mm^3 isotropic, flip angle=5°, gradient=36.7 mT/m, TR=20 ms, NEx=100, 5000 half-projections, PETRA radius=5 points, scan time 3h3m) and ^{1}H Single Adiabatic Inversion Recovery Rapid ZTE-PETRA (^{1}H SIR-rZTE, res=1 mm^3 isotropic, gradient=18.3 mT/m, TR=300 ms, inversion pulse BW=5 kHz, duration=5 ms, TI=100 ms, 7 readouts/excitation, flip angle=24-40°, 10000 half-projections, PETRA radius=4 points, scan time 26m45s).

	Age	Porosity	pQCT	pQCT/BVF	^{31}P T_1	r^{31}PD	r^{31}PD/BVF	rBWD	rBWD/BVF
RDR	2.5x10^{-3}	9.9x10^{-7}	0.09	0.18	0.33*	0.50**	0.62***	8.6x10^{-3}	0.02
rBWD/BVF	0.59***	0.40*	0.41*	0.04	0.21	0.59**	0.51**	0.94***	
rBWD	0.70***	0.63***	0.50**	0.01	0.19	0.59**	0.45**		
r^{31}PD/BVF	0.26*	0.15	0.36*	0.17	0.47**	0.96***			
r^{31}PD	0.39*	0.32*	0.46**	0.11	0.45**				
^{31}P T_1	0.02	0.09	0.51**	0.45**					
pQCT/BVF	4.2x10^{-3}	0.02	0.39*						
pQCT	0.29*	0.48**							
Porosity	0.54**								

Table 1: Correlation matrix of R^2 values (*p<0.05, **p<0.005, ***p<0.0005). RDR, relative density ratio; rBWD, relative bound water density; r^{31}PD, relative ^{31}P density; BVF, bone volume fraction = 1-porosity.

Density Quantification: Bones, reference intensities, and fiducial markers were masked and thresholded. Images were corrected for transmit and receive B_1 inhomogeneity and differences in relaxation times between bone and reference. Relative ^{31}P and bound water ^{1}H densities in bone were expressed relative to the reference intensity using Eq. 1, where f_{xy} and f_z describe the response of transverse and longitudinal magnetization to a square pulse [8].

pQCT: A 2D image was acquired at the center of each bone with 0.4x0.4x2.3-mm^3 resolution using a Stratec XCT 2000 scanner (Orthometrix, White Plains, NY). BMD was quantified using the scanner software's in vivo tibial measurement protocol.

µCT: A 3D image of each bone was acquired with 9-µm^3 isotropic resolution using a Bruker µCT scanner (Bruker, Kontich, Belgium), segmented, and binarized. Porosity was quantified as the ratio of pore volume to total volume, both excluding the endosteal cavity.

Analysis: Correlations were examined by regression calculated using least squares.

$$S(\vec{r}) \propto \rho(\vec{r}) \frac{1-\exp\left(-TR/T_1\right)}{1-f_z(\vec{r})\exp\left(-TR/T_1\right)} f_{xy}(\vec{r}) \exp\left(-TE/T_2^*\right) \hat{B}_1(\vec{r})$$

Equation 1: Steady-state signal equation for ZTE. Terms f_{xy} and f_z depend on T_2 and RF pulse duration and amplitude. The signal equation is more complex for the multiple-readout SIR-rZTE sequence.

Results: Maps of relative ^{31}P and bound water ^{1}H densities are shown in Fig. 1. Both densities correlate negatively with age and porosity, and positively with pQCT density. The relative densities correlate with each other (R^2 = 0.59, p < 0.001), and their ratio, which represents bone mineralization, is not correlated with age, pQCT density, or porosity. R^2 values of other correlations are shown in Table 1.

Discussion and Conclusions: MRI and pQCT cannot resolve individual pores, so an age-related increase in porosity manifests as a decrease in apparent density as long as the mineralization is invariant. Bone mineralization can be inferred from pQCT BMD by dividing by (1-porosity); this was uncorrelated with age, indicating full mineralization. Consistent with this observation, both MRI-based densities correlate with pQCT density and porosity. Further studies in demineralized bones will test the ability of this MRI-based method to distinguish osteoporotic- from osteomalacic-type disruptions of bone homeostasis.

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