Quantitative Bone Matrix Density Measured by Water and Fat Suppressed Proton Projection MRI (WASPI) Using a Polymer Phantom

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Introduction

One of the most important parameters distinguishing osteoporosis from osteomalacia is the degree of bone mineralization (DM), which can be closely defined as the ratio of bone mineral density (BMD) divided by bone matrix density. Presently, the most commonly used bone densitometry method in osteoporosis patients is dual energy X-ray absorptiometry (DXA), which cannot distinguish osteoporosis (low BMD, low bone matrix density, normal DM) from osteomalacia (low BMD, normal bone matrix density, low DM). Therefore, accurate differential diagnosis between osteoporosis and osteomalacia requires information on both BMD and bone matrix density. Indeed, defective mineralization has been commonly discovered in patients who underwent bone biopsies to find an explanation for antiosteoporotic treatment failure. Previously, we had demonstrated that quantitative BMD could be obtained by solid state ^{31}P magnetic resonance imaging (^{31}P SMRI) (1) and solid bone matrix could be visualized by water and fat suppressed proton projection MRI (^{1}H WASPI) (2). In this study, we developed a polymer blend phantom with NMR properties similar to those of solid bone matrix for the quantitative WASPI measurement of bone matrix density.

Materials and Methods

20% Poly(ethylene oxide) (PEO)/80% Poly(methyl methacrylate) (PMMA) blends were prepared by solvent casting from a chloroform solution. Clear and transparent blend film samples were obtained and ground into powder under liquid nitrogen. A fine uniform polymer powder was obtained by sieving through a 200-mesh screen. Cylindrical pellets of the polymer blend powder diluted with silicon dioxide (Fisher Scientific, 40-100 mesh) were made under high pressure (2000-4000 lb) in a hydraulic press and used as an MRI calibration phantom. The polymer phantom densities were 1.17, 0.80, 0.56, and 0.40 g cm^{-3}.

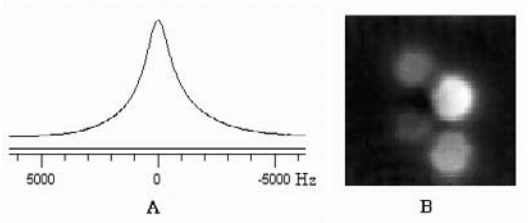

Figure 1. Proton spectrum (A) and SMRI image (B) of the 20%PEO/PMMA blend phantoms. The diameters of the cylindrical phantoms are 0.52cm and thickness is 0.2-0.25cm.

Bovine bone specimens of 1.5cm (L) × 1.5cm (W) × 0.2cm (thick) were cut from the midshaft cortices of fresh bovine femora from a local slaughterhouse. Bone marrow was extracted from the same bovine cortical bone as reference for water and fat suppression in WASPI experiments. Volumes of bone specimens were measured by the water displacement method.

Four-month-old virgin female NIHRNU rats (Charles River Laboratories, Charlestown, MA) were used in this study. Following sacrifice the femurs were disarticulated from the hip and knee for MRI scanning.

Solid state MRI and WASPI data were acquired and processed according to the previous description (1, 2) with a Bruker 4.7T 33cm scanner equipped with a 400mT/m gradient system (Bruker Biospin, Billerica, MA, USA). The ^{1}H larmor frequency was 200.13 MHz.

MRI density values of bone specimens and phantoms were calculated by summing all the pixel values above a threshold value in a rectangular volume of the 3D image containing each object to be analyzed and dividing by that volume.

After MRI, gravimetric analyses (2) were performed on the same bone specimens to obtain bone matrix density for comparison.

Results

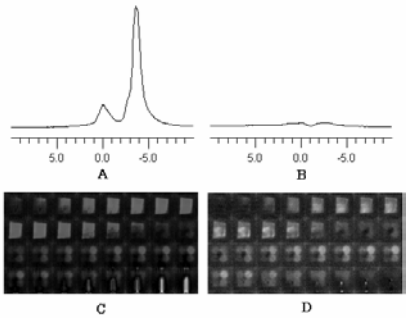

Figure 2. Proton spectra, SMRI and WASPI images of a piece of bovine cortical bone, 4 polymer phantoms and a tube of bone marrow. A. Single pulse ^{1}H spectrum. Water and fat peaks were at 0.00 and -3.50ppm, respectively. B. Water and fat suppressed spectrum. C. Non-suppressed SMRI. D. WASPI images.

1) The observable WASPI ^{1}H MRI signal of bone arises from solid matrix, which is dominated by collagen fibrils and other immobile intracellular and extracellular molecules such as tightly bound water. The signal of fluid constituents, primarily molecularly mobile water and lipid were largely suppressed. The line widths of WASPI ^{1}H NMR signals are in the range of several thousand Hz, corresponding to T_2^*s on the order of 100μs. Therefore, the calibration phantom must have a single T_2^* which is comparable to that of solid bone matrix. As shown in figure 1A, the polymer phantoms have a single ^{1}H NMR peak, corresponding to a single T_2^*, and the line width is around 2000Hz, corresponding to the T_2^*s on the order of 100μs. The SMRI images of the polymer phantoms also show the linearity of the MRI intensities with different phantom densities (figure 1B).

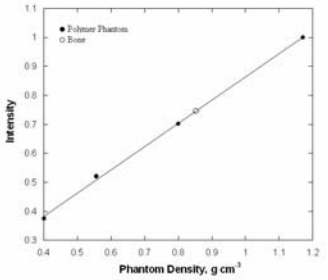

Figure 3. Calibration curve relating known phantom densities to the measured MRI signal intensity of the bovine cortical bone.

2) Figure 2A shows the proton spectrum of a piece of bovine cortical bone, four polymer phantoms and a tube of fresh bovine bone marrow held in a 1.5cm diameter sample holder. The receiver dead time was 100 μs, largely eliminating the solid signals. The water and fat peaks were at 0.00 and -3.50ppm respectively. Figure 2B shows the water and fat suppressed spectrum of same sample acquired with the WASPI sequence without projection gradient, in which water and fat peaks were suppressed to the baseline. Figure 2C and D show the SMRI and WASPI images of the samples. The signal of bone marrow was suppressed in the WASPI images.

3) Figure 3 shows the linear least squares fit of the phantom calibration data, and the MRI-derived bone matrix density result. The bone matrix density determined by MRI and gravimetric analysis are listed in table 1. The ratio of MRI density/Gravimetric density is 0.86 and 0.83 for bovine and rat bone specimens respectively.

Table 1. Bone matrix density determined by MRI and gravimetric analysis

	Bovine Cortical	Rat femur
MRI bone matrix density, g cm^{-3}	0.726	1.190
Gravimetric Analysis, g cm^{-3}	0.842	1.44
Conversion Factor (MRI/Gravimetry)	0.86	0.83

Discussion

The preliminary data in this study shows that bone matrix density values measured by MRI and gravimetric methods are linearly correlated. The conversion factor is about 0.8, and varies by only 3.6% between the two bone specimens. Though a larger sample size will be needed to obtain a statistically sound factor, this study demonstrated that using a polymer blend phantom to quantitatively measure bone matrix density is feasible, and should be applicable to humans when implemented on clinical scanners. The polymer blend, although designed to have solid state MR properties similar to those of bone matrix while having long term stability and no susceptibility to bacterial spoilage or water loss, is chemically very different from bone matrix. Therefore there is no expectation that the conversion factor be equal to unity. As long as the conversion factor is constant, the measurement of bone matrix density by WASPI can be accomplished.

References

1. Wu Y, Ackerman JL, Chesler DA, Li J, Neer RM, Wang J, Glimcher MJ. Calcif Tissue Int 1998, 62:512-8.
2. Wu Y, Ackerman JL, Chesler DA, Graham L, Wang Y, Glimcher MJ. Magn Reson Med 2003, 50:59-68.