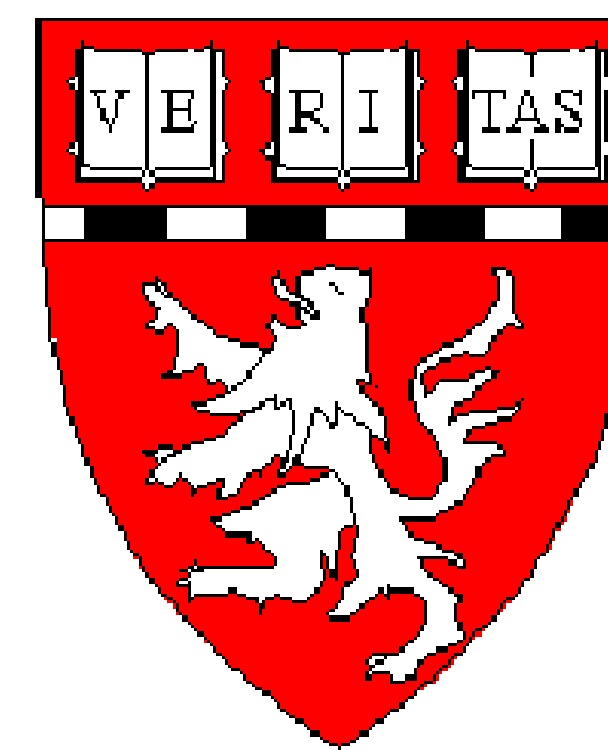




Water and Fat Suppressed Proton Projection MRI (WASPI) Study on Bone Specimens after Proton-Deuteron Exchange



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Introduction

Bone matrix, the organic fraction of bone consisting largely of protein (mostly collagen) and significant water, is a complex material in which water and protein exist in a wide range of motional states, with water undergoing molecular exchange between compartments and some protein protons (hydroxyls, amides, amines, etc.) undergoing chemical exchange with water. Our recent study [1] showed that the Water- And fat-Suppressed Projection Image (WASPI) proton signal of bone matrix is uncorrelated with the bone water content (defined as that water removable by heating under specified conditions in a vacuum oven) but is highly correlated with two independent and widely used chemical measurements of the protein content, which is exactly what one desires if the intent is to measure bone matrix density. Deuterium exchange has been widely used to classify the chemical and motional states of hydrogen in tendon [2] and bone [3, 4]. In this study we use deuterium exchange to identify the source of proton signal in WASPI.

Materials and Methods

Cortical Bone Specimens: 10mm x 5mm x 1.5mm, cut from the midshaft cortices of bovine femora, containing very little fat.

Exchanged Bone Samples: A group of cortical bone specimens immersed in 99% deuterium oxide for up to 15 days, with periodic replacement of the D₂O.

Heated Bone Samples: A group of cortical bone specimens heated at 110 °C for 48 hours in air.

Single Pulse NMR Spectroscopy: Performed with long recycle delay to measure the water content in bone samples by deuterium exchange for up to 11 hours.

WASPI: Performed on exchanged bone samples after various D₂O immersion times and on the heated group before and after heating. A 20% PEO/PMMA blend calibration phantom was imaged alongside the bone specimens as a reference to calculate the measured bone matrix intensity.

NMR and MRI experiments were carried out with a Bruker 4.7T system.

WASPI on Proton-Deuteron Exchanged Bone Samples

Table 1. T₁ correction factors for WASPI image with various proton-deuteron exchange time. Bone matrix T₁ increased with the exchange time. An equilibrium was reached after 5 days of exchange. β is the flip angle.

Exchange time	0	10 min	30 min	1 hr	2.5 hr	7 hr	11 hr	24 Hr	3 days	5 days	7.5 days	15 days
T ₁ (s)	3.18	4.81	4.95	6.58	7.20	7.40	7.46	7.29	7.90	10.5	10.7	10.6
β(degree)	13.7	13.6	13.6	13.7	13.0	12.4	12.1	12.2	12.4	13.0	12.1	12.5
TR(s)	0.15	0.15	0.15	0.15	0.15	0.15	0.40	0.40	0.40	0.50	0.50	0.50
Correction factor F	6.71	8.02	8.13	9.43	9.85	9.96	6.70	6.63	6.75	6.79	6.99	6.90

Table 2. WASPI intensity and exchanged proton content of bone specimens vs. exchange time. During the first hour of exchange, the WASPI intensity was constant, while 50% of the total exchangeable proton content was removed from the specimen by this time. Continued exchange results in slowly decreasing WASPI intensity, possibly involving exchangeable collagen protons [4]. WASPI intensity stabilizes when all exchangeable protons are removed from the sample.

Exchange time	0	10 min	30 min	1 hr	2.5 hr	7 hr	11 hr	24 Hr	3 days	5 days	7.5 days	15 days
Exchanged proton fraction (¹ H spect)	0.00	0.23	0.39	0.50	0.69	1.00	1.00					
WASPI Intensity	1.00	1.01	1.00	0.94	0.60	0.47	0.42	0.40	0.40	0.39	0.39	0.39

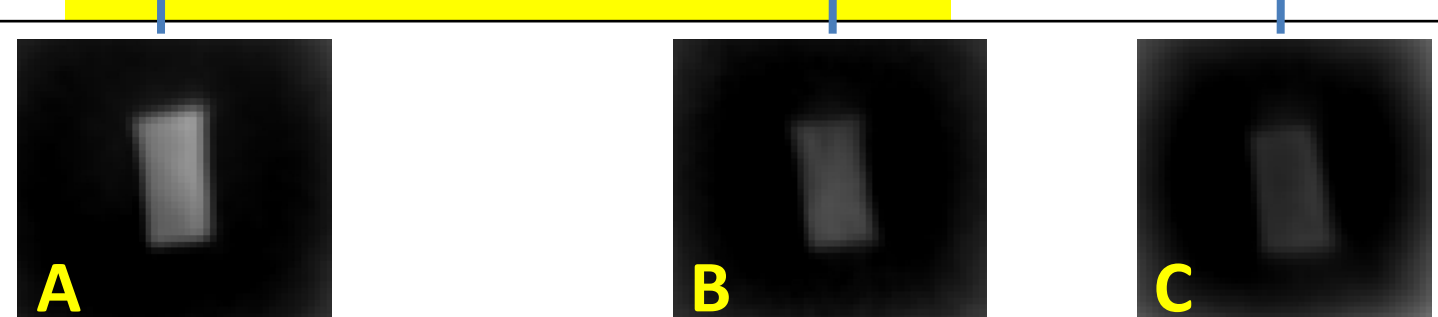


Fig. 1. WASPI images of bone specimens taken before exchange (A), 1hr (B) and 7 hr (C) after exchange.

WASPI on Heated Bone Samples

	Before heating	After heating at 110 °C
T ₁ (s)	3.18	4.24
WASPI Intensity	1.00	0.56
T ₁ corrected		

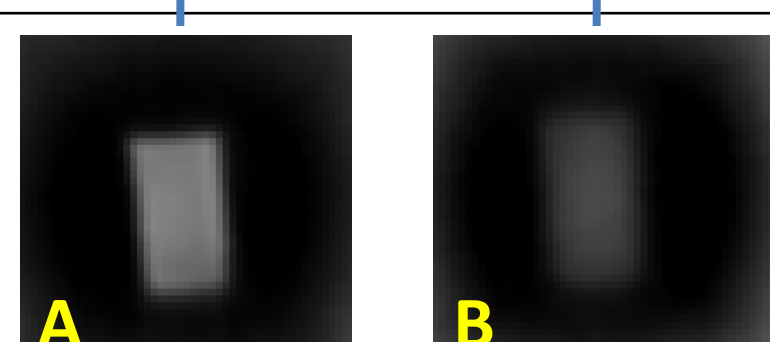


Table 3. WASPI intensity and T₁ of bone matrix before and after heating. T₁ of solid bone matrix increased after heating, the effect of which was corrected in the WASPI images. T₂ of matrix decreased, the effect of which was not taken into account. T₂ corrections are being developed.

Fig. 2. Images of WASPI of bone samples taken (A) before and (B) after heating.

Work in Progress: In Vivo WASPI and ³¹P SMRI of Human Wrists with Clinical Scanners

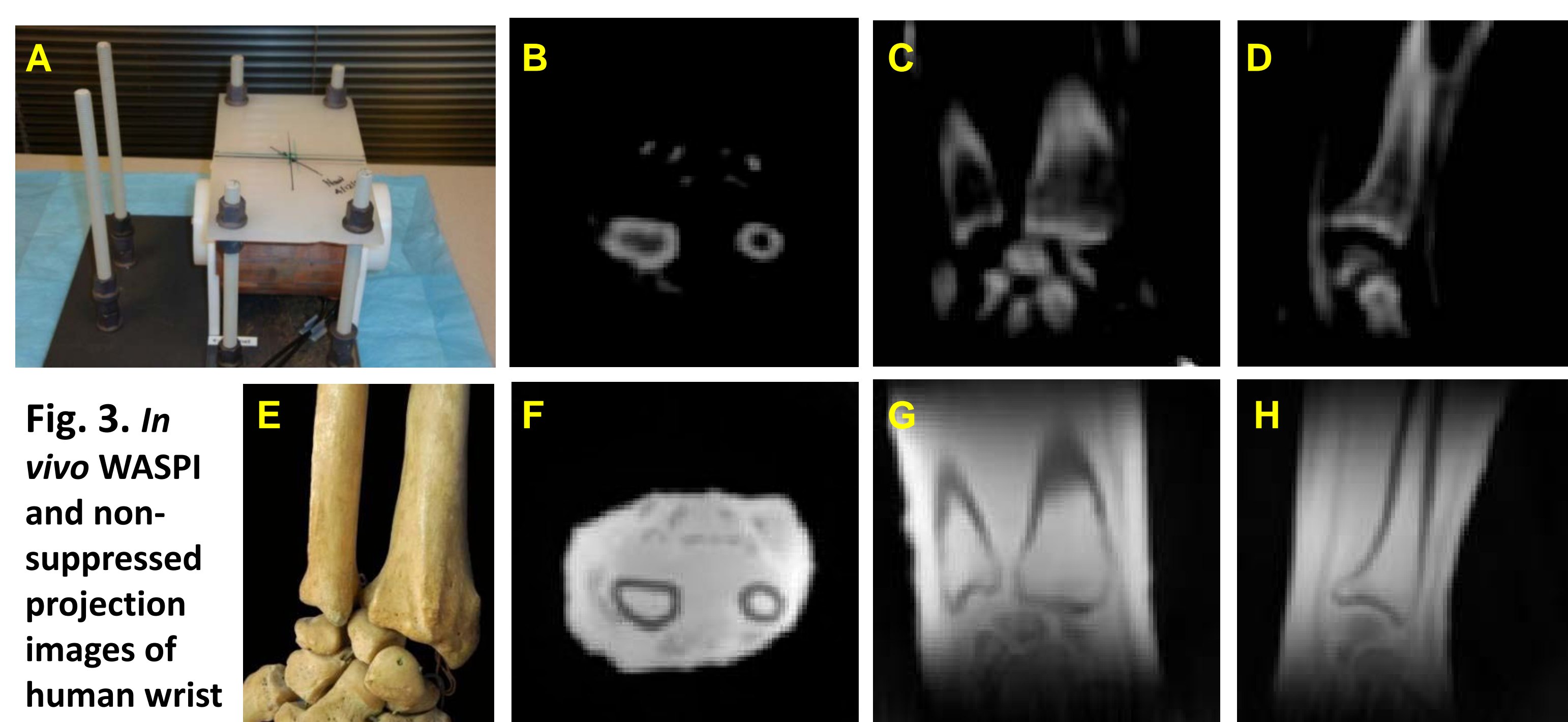


Fig. 3. In vivo WASPI and non-suppressed projection images of human wrist

A. A T/R human wrist coil built on a Teflon tube, photographed with a polyethylene phantom inside it. B-D. In vivo WASPI of the left wrist of a 57-yr-old volunteer. F-H, Corresponding slices from the non-suppressed projection MRI. E. Illustration of human wrist bones.

The proton resonance line width and T₁ of bone matrix were ~1.5-2 kHz and 1.8 s at 3T, respectively. The cortical bone was not visible (dark) in the conventional (non-suppressed) images, but clearly visible in the WASPI images with SNR ~45 and trabecular bone in the distal radius with SNR ~10. The spatial resolution was ~2.4 mm and the total acquisition time was 18 min, which can be shortened to 12 min with 2.5 mm resolution). The soft tissue (marrow and muscle) signals were suppressed (dark). It is striking how the WASPI images resemble plain film x-ray radiographs, with soft tissue dark and solid bone bright, but the sources of WASPI and x-ray signals are quite different. The WASPI signal arises from solid bone matrix. The x-ray signal arises predominantly from the mineral content. Although these constituents have similar spatial distributions in bone, the distributions are not identical, which makes WASPI useful for measuring matrix density, and in combination with mineral density information yields the extent of mineralization. This study was recently reported in a paper [5] (J Magn Reson Imaging 2010 April issue; 31: 954-963).

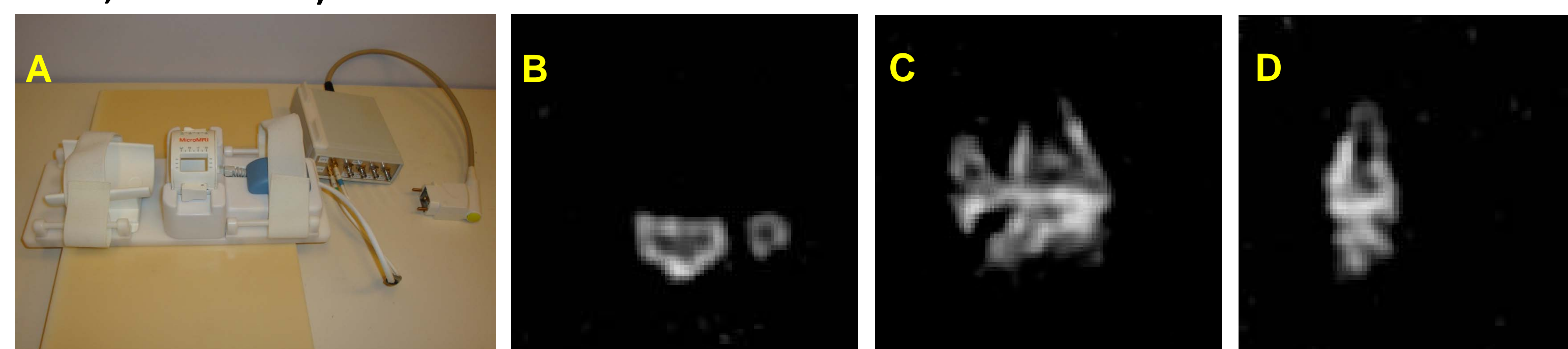


Fig. 4. In vivo ³¹P Solid State MRI of human wrist.

The intrinsic receiver dead time of the ³¹P channel of a Siemens 3T Trio scanner is about 185 μs. Therefore, a frequency converter was developed to circumvent this excessive dead time by utilizing the proton channel of the scanner (receiver dead time: 10 μs), to observe the short T₂ ³¹P MR signal from bone mineral.

A T/R coil specially designed for the human wrist was utilized to produce a strong B₁ field (10°, 10 μs) and a passive T/R switch was developed to help shorten the receiver dead time (A).

The ³¹P resonance line width and T₁ of human bone mineral were measured in vivo to be 2-2.5 kHz and ~17 s at 3T, respectively. ³¹P SMR images of the wrist of a 41 yr old volunteer (B: transverse, C: coronal, D: sagittal) were obtained in 37 min, showing only bone mineral with a spatial resolution of 3 mm in all three dimensions.

Conclusions

The proton-deuteron exchange experiments show that protons in soft tissue (exchanged within 1 hr) do not contribute to WASPI images; a large portion of the WASPI signal is from a proton pool of bone collagen and other macromolecules which cannot be exchanged with deuterons; another portion of the WASPI signal is from a proton pool of motionally restricted bone water, bound water in bone matrix, or bone collagen, which are exchangeable between 1 hr and 5 days. These two proton pools give rise to the WASPI signal, which can therefore be justifiably assigned to solid bone matrix.

These advances in implementing WASPI and ³¹P SMRI in clinical scanners demonstrate that ³¹P SMRI/WASPI measurement of bone mineral density and matrix density of human wrist in vivo is feasible.

References

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Acknowledgement

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