

DDIF: A novel contrast for MRI of trabecular bone

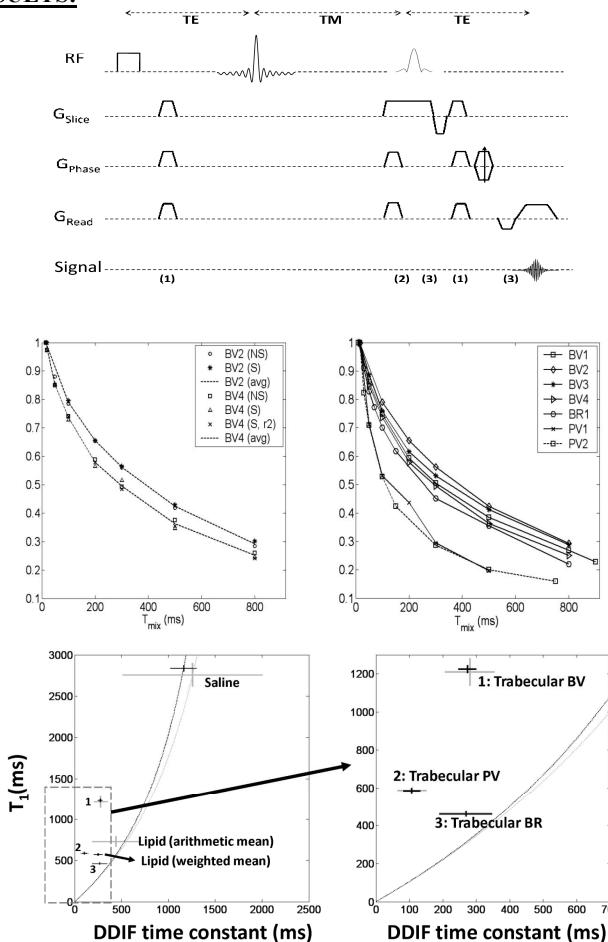
D. Mintzopoulos¹, J. L. Ackerman¹, and Y-Q. Song²

¹Martinos Center, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, United States, ²Schlumberger-Doll Research, Cambridge, MA, United States

INTRODUCTION: Fragility fracture is a serious and costly public health issue [1] and improved methods for screening, diagnosis and treatment monitoring of metabolic bone disease are needed. In particular, there is strong interest in non-invasive, clinically applicable MRI methods to study trabecular bone structure *in vivo* [2, 3]. We employed a novel method, DDIF (Decay due to Diffusion in the Internal Field), to study (*ex vivo*) intact animal trabecular bone specimens of varying trabecular structure and porosity, containing marrow and blood, close to *in vivo* physiological conditions. The DDIF contrast is related to the surface-to-volume ratio of the porous structure of bones. DDIF has been studied for marrow-free trabecular bone [4, 5], but not in intact trabecular specimens containing marrow and surrounded by soft tissue. Bone marrow is comprised of slowly diffusing large lipid molecules (adipocytic, yellow, marrow) and fast diffusing watery haematopoietic red marrow containing iron-carrying haemoglobin. The two components differ in diffusion and relaxation time constants [6]. Water is by far the most diffusible molecule, and the dominant source of DDIF contrast. However, the reduction of water diffusion constant and of T_1 in marrow compared to bulk water may reduce the DDIF contrast and make it harder to measure it experimentally. We examined the feasibility of DDIF in realistic bone specimens, in view of *in vivo* application to humans.

MATERIALS AND METHODS: *Animal Bone Samples:* Fresh animal bone specimens were acquired locally. Samples were maintained at body temperature during scanning. **Imaging:** Imaging was performed in a 4.7 T, 33 cm horizontal bore magnet (Oxford Instruments) with a Bruker BioSpin Avance console, a Bruker gradient system capable of 40 G/cm, and a Bruker volume coil of 7 cm inner diameter and 10 cm active length.

RESULTS:



DDIF imaging pulse sequence. Only the stimulated echo is imaged. The magnetization lies in the transverse plane during encoding time TE and is “stored” along the z -axis during mixing time TM . Gradient lobes (“2”) between the 2nd and 3rd pulses dephase unwanted coherence pathways. A gradient (“1”) dephases the FID produced by the third pulse, and is repeated between the 1st and 2nd RF pulses in order to balance the coherence pathway for the stimulated echo. The measured DDIF rate is $R_{DDIF}^{measured} = (1/T_1) + R_{DDIF}^{seg} + R_{DDIF}^{internal}$, where $R_{DDIF}^{internal}$ is the DDIF decay rate due to the internal field and R_{DDIF}^{seg} is the extra decay rate induced by the sequence (externally applied gradients), $R_{DDIF}^{seg} = \gamma^2(\sum_i G_i^2) t_G^2 D$; The bias was $(1/R_{DDIF}^{seg}) \approx 6.8s$ for water ($D \approx 2.5 \times 10^{-5} \text{ cm}^2/\text{s}$).

Reproducibility and variability of trabecular specimen measurements. **Left:** Two bovine vertebra trabecular specimens (BV2, BV4). NS = non-selective pulse, S = water-selective pulse. (S, r2, \times) denotes replicate measurement of BV4(S) acquired three days later to examine the repeatability and robustness of the DDIF measurements. Dotted lines: averages of each of the two data sets (no fitting). **Right:** DDIF curves (water-selective imaging, S) from four bovine vertebrae specimens (BV1 – BV4), a bovine rib specimen (BR1), and porcine vertebrae specimens (PV1, PV2) (data not fitted). BV specimens have low lipid content and hard-pulse (NS) data do not differ appreciably from water-selective (S) data. PV specimens are markedly different. All curves normalized to highest signal intensity.

Measured DDIF time constant and relaxation time T_1 . **Left:** data are separable when plotted in a two dimensional space. Group averages: trabecular bovine vertebra (BV, #1), trabecular porcine vertebra (PV, #2), and trabecular bovine rib (BR, #3). **Right:** magnification of boxed area (only trabecular group averages shown). Arithmetic averages in lighter gray; weighted averages in black. The boundary line (absence of DDIF effect) separating the region with significant DDIF effect from the unphysical region to the right [$R_{DDIF} > (1/T_1)$], is referenced on the saline. The rate due to the pulse sequence is $R_{DDIF}^{seg} = R_{DDIF}^{(saline)} - (1/T_1)^{(saline)}$. Lipids do not exhibit significant DDIF effect and lie very close to the boundary line. Trabecular bone data are all in the left region, indicating significant DDIF effect.

CONCLUSION: DDIF (Decay due to Diffusion in the Internal Field) is an MRI method providing a novel diffusion contrast. The DDIF contrast is related to the surface-to-volume ratio of the porous structure of bones. We employed DDIF to study fresh bone specimens containing blood and marrow under *ex vivo* conditions closely resembling *in vivo* physiological conditions, and we observed significant DDIF effect on trabecular bone samples, while the DDIF effect was considerably smaller for soft tissue outside the bone and for lipids. Our data indicate that it may be possible to characterize specimens of different porosity. These results indicate that DDIF imaging is possible in spite of the reduction of T_1 and diffusion coefficient in bone marrow, and suggest that the application of DDIF *in vivo* is possible for improving bone characterization.

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