Relaxation along Fictitious Field (RAFF) Contrast in Bovine Articular Cartilage

T. Liimatainen[1], M. Nissi[2,3], M. T. Nieminen[4,5], S. Michaeli[6], M. Garwood[6], and O. Gröhn[7]

[1]Department of Biotechnology and Molecular Medicine, University of Kuopio, Kuopio, Finland, [2]Department of Physics, University of Kuopio, Kuopio, Finland, [3]Department of Clinical Radiology, Kuopio University Hospital, Kuopio, Finland, [4]Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland, [5]Department of Medical Technology, University of Oulu, Oulu, Finland, [6]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, United States, [7]Department of Neurobiology, University of Kuopio, Kuopio, Finland

Introduction. Measurement of the physicochemical properties or the content of the proteoglycans in cartilage is desirable, since it would help diagnosis and monitoring of osteoarthritis. Proteoglycan macromolecules contain exchangeable protons in –OH and –NH chemical groups and comprise 4-7% of articular cartilage wet weight. Especially, the –OH groups are in the measurable exchange region for rotating frame methods, such as $T_{1\rho}$ and relaxation along a fictitious field (RAFF), which is based on *sine* and *cosine* amplitude and frequency modulation functions operating in sub-adiabatic regime. The aim of the study was to optimize the RAFF method to detect proton exchange between water and proteoglycan –OH groups. We demonstrate contrast using RAFF and optimized versions of the RAFF method and compare the results with conventional continuous wave (CW) $T_{1\rho}$ in bovine articular cartilage.

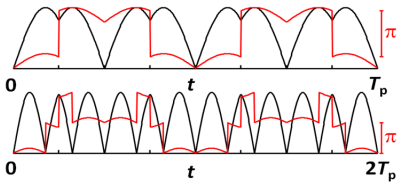

Fig. 1 Amplitude (black) and phase (red) modulations of RAFF [1] (top) and optimized RAFF (bottom).

Materials and methods. Dipolar interactions between identical spins combined with exchange between two spin populations with difference in chemical shifts were simulated using Bloch-McConnell equations to obtain the evolution of MR signal with RAFF. The amplitude and phase modulated RF pulse shapes of RAFF and optimized RAFF with pulse time durations of T_p=4.53 ms and T_p=9.05 ms, respectively, were used (**Fig. 1**) [1]. The pulse train time duration was incremented up to a maximum of 144 ms. Continuous wave (CW) $T_{1\rho}$ was simulated for comparison with RAFF. The rotational correlation time τ_{cw} =10^{-12} s and population P_w=0.93 for the free water pool, τ_{cp} =10^{-8} s and P_p=0.07 for the proteoglycan pool [2], and 1 ppm chemical shift between resonances [3] were used. Full-thickness cartilage disks with subchondral bone (dia.=8.5mm, n=3) were prepared from bovine patellae and immersed in phosphate buffered saline (PBS) containing enzyme inhibitors. Frozen samples were thawed and equilibrated in PBS before the measurements at 9.4T using 19 mm quadrature volume transceiver. After scout imaging, 19.2-by-19.2 mm^2, 1 mm thick slice was selected and 0, 18, 36, 54 ms RAFF or optimized RAFF pulse train with $\omega_1^{max}/(2\pi)$=625 Hz was applied prior to the fast spin echo imaging readout (TR= 5 s, effective TE = 9.2 ms, and matrix size 256·128). $T_{1\rho}$ was measured using adiabatic CW pulses with pulse power matched to rms power of RAFF pulses (375 Hz). Contrast-to-noise-ratio was $CNR_{AB}=|S_A-S_B|/std$, where noise was the std of the relaxation rate constants from ROI in deep cartilage. Statistical significance (p) between the CNRs of $T_{1\rho}$ and RAFF was evaluated using two tailed Student's T-test.

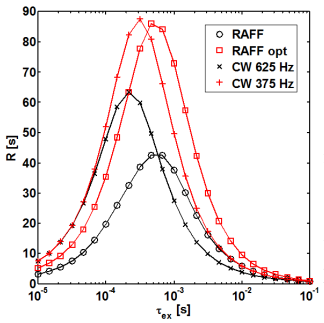

Fig. 2 Simulated RAFF, optimized RAFF and conventional continuous wave $T_{1\rho}$ relaxation rate constants. The power of $T_{1\rho}$ was matched with the rms of the power used for RAFF

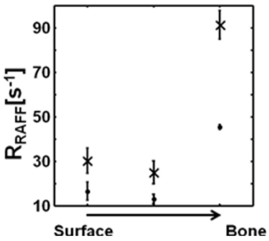

Fig. 3 Relaxation rate constants measured with RAFF (·) and optimized RAFF (x) in cartilage (mean±std, n=3).

Results. Simulations demonstrated up to 2-fold increase in the RAFF relaxation rate constants when the optimized RAFF was used (**Fig. 2**), experimental measurements confirmed this result (**Fig. 3**). The peak in the relaxation rate was obtained with the same exchange correlation time (τ_{ex}) using either RAFF or the optimized RAFF. By equaling the power of the CW pulse with the RAFF rms power, $T_{1\rho}$ showed similar maximum of the relaxation rate constant as optimized RAFF. However, this maximum was shifted towards longer τ_{ex} in RAFF. An enhanced contrast was observed when using optimized RAFF in bovine articular cartilage (**Fig. 3.**). Relaxation measurements with optimized RAFF provided better CNRs between deep and intermediate (3.2±0.6) and between deep and superficial cartilage (2.9±0.3) than $T_{1\rho}$ (1.9±0.8 p=0.01 and 1.70±0.29 p<0.01, respectively).

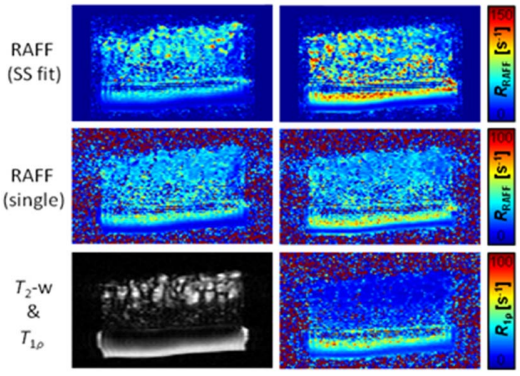

Fig. 4 RAFF and optimized RAFF relaxation rate maps (upper row) calculated taking into account formation of the steady state. RAFF, and optimized RAFF maps generated using monoexponential decay function (second row). T_2-weighted image, and $R_{1\rho}$ ($\gamma B_1/(2\pi)$=375 Hz) relaxation rate map (bottom row).

Discussion and conclusions. RAFF method provided greater CNR between deep and intermediate and between deep and superficial than conventional CW $T_{1\rho}$ corresponding to increasing proteoglycan content towards bone. It is shown that with optimized duration of the *sine/cosine* modulation utilized in RAFF, the sensitivity to the anisochronous exchange, e,g exchange between –OH groups and free water in articular cartilage, is enhanced. With the used settings of B_1, RAFF provided higher CNR between superficial and deep cartilage than $T_{1\rho}$. We demonstrate here for the first time the great potential of RAFF to detect anisochronous exchange in articular cartilage. Furthermore, we show that RAFF provides higher contrast between cartilage layers than conventional spin-lock $T_{1\rho}$, suggesting the rate constant measured with RAFF to be a potential biomarker for cartilage degeneration, possibly also in *in vivo*.

References: [1] Liimatainen et al. Proc. Int. Soc. Magn. Reson. Hawaii, 2008. [2] Mow C et al. Biomaterials 1992;13:67-97. [3] Ling W et al. PNAS 2008:105:2266-2270.