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Sodium imaging of the human knee using soft inversion recovery fluid attenuation

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ABSTRACT

Sodium signal strength in MRI is low when compared with ^{1}H. Thus, image voxel volumes must be relatively large in order to produce a sufficient signal-to-noise ratio (SNR). The measurement of sodium in cartilage is hindered by conflation with signal from the adjacent fluid spaces. Inversion recovery can be used to null signal from fluid, but reduces SNR. The purpose of this work was to optimize inversion recovery sodium MRI to enhance cartilage SNR while nulling fluid. Sodium relaxation was first measured for knee cartilage ($T_1 = 21 \pm 1$ ms, $T_{2\,fast}^* = 0.8 \pm 0.2$ ms, $T_{2\,slow}^* = 19.7 \pm 0.5$ ms) and fluid ($T_1 = 48 \pm 3$ ms, $T_2^* = 47 \pm 4$ ms) in nine healthy subjects at 4.7 T. The rapid relaxation of cartilage in relation to fluid permits the use of a lengthened inversion pulse to preferentially invert the fluid components. Simulations of inversion pulse length were performed to yield a cartilage SNR enhancing combination of parameters that nulled fluid. The simulations were validated in a phantom and then invivo. B_0 inhomogeneity was measured and the effect of off-resonance during the soft inversion pulse was assessed with simulation. Soft inversion recovery yielded twice the SNR and much improved sodium images of cartilage in human knee with little confounding signal from fluid.

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1. Introduction

Osteoarthritis (OA) is a degenerative disease affecting articular cartilage in an estimated 3 million Canadians [1] and 40 million Americans [2]. Approximately 40% of people over 70 years of age experience symptoms of OA, and by 2020 OA is expected to be the fourth leading cause of disability [3]; it is currently the most common cause of joint replacement [4]. Early detection of the disease and proactive lifestyle change is the current non-surgical strategy for delaying disability due to OA [5]. Unfortunately, early-stage OA is difficult to detect non-invasively [6,7] and standard soft tissue imaging modalities, such as ultrasound and proton magnetic resonance imaging (MRI), are unreliable for early detection [8]. Although gadolinium-based contrast agents with MRI have shown some promise in the evaluation of cartilage health [9], it is a screening procedure that requires the injection of a contrast agent followed by 30 min of exercise before imaging and is not completely benign.

One biochemical marker indicating structural change in early osteoarthritis is a reduction in the concentration of proteoglycan molecules in the collagen matrix [6]. These proteoglycan molecules attract sodium ions and as a result the concentration of sodium

ions in cartilage is linked to the proteoglycan content [10,11]. Sodium (^{23}Na) MRI is capable of detecting in vivo sodium in cartilage of human knee [10,12–14] and thus may be a valid tool for detecting OA in the early stages [15–17] or even to follow cartilage repair [18–20]. ^{23}Na-MRI of the human knee is technically challenging due to the rapid T_2 relaxation of sodium nuclei and the markedly low signal strength from sodium. The low signal is due to both a low natural abundance ([^{23}Na-cartilage] ~ 250–300 mM [15]) and a reduced gyromagnetic ratio when compared to hydrogen. In order to acquire sufficient sodium signal in human knee cartilage, short echo times and large voxel sizes are necessary. Although 2D or 3D Cartesian techniques [13,15,21–24], native to most clinical scanners, have been used in the past for practical reasons, they are not optimal due to their long echo times (2–4 ms). Scan times can be prohibitively long when using a Cartesian acquisition (∼22 min), even with the SNR benefits of 7 T [25–27]. Acquisition methods that start at the center of k-space permit shorter echo times and are better suited for sodium imaging. Straight radial acquisitions are an improvement [28–30] but they inefficiently over-sample the center of k-space; whereas 3D cones [31] or twisted projection imaging (TPI) acquisitions offer a number of advantages. TPI imaging has been shown to improve image quality with either long repetition time implementations [14,16,32] or steady state sequences (to yield greater SNR) [33]. Even at the improved SNR and resolution ($0.8 \times 0.8 \times 4$ mm^3 in 9 min at 4.7 T) obtained using TPI and a steady state acquisition [33], it can be

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difficult to differentiate the cartilage from surrounding sodium compartments such as the synovial fluid and blood.

Similar to proton FLAIR, inversion recovery can be a fluid suppression technique that exploits the longer relaxation parameters of sodium in fluid (versus cartilage) and has been previously shown to minimize sodium fluid signal in the knee at 7 T. This was done, first using a 2D gradient echo single slice acquisition with a rectangular inversion pulse, showing proof of principle [34], then using a 3D radial acquisition with full knee coverage in healthy controls [35]. Its utility was demonstrated in patients who had undergone a knee cartilage restoration procedure [18] and in those with osteoarthritis [17]. The former experiments suggested the use of an adiabatic pulse to ensure inversion even in the presence of B_1 and B_0 inhomogeneities. However, adiabatic pulses are constrained by power absorption limitations (specific absorption rate – SAR) particularly at high field [35]. Inversion recovery techniques eliminate the fluid signal, but at the expense of some of the cartilage signal, necessitating even larger voxel sizes than standard sodium imaging. A study in the brain where sodium signal was suppressed in cerebrospinal fluid showed that additional SNR in brain tissue could be achieved by using a longer 'soft' inversion pulse [36]. By taking advantage of its reduced power and, more importantly, the more rapid T_1 and T_2^* decay that occurs in brain tissue relative to fluid *during* the soft inversion pulse, an increase in signal-to-noise ratio of 85% was shown at 4.7 T in the human brain by using a 10 ms over a 1 ms inversion pulse. This methodology, SIRFLA (soft inversion recovery with fluid attenuation), has not yet been applied to cartilage. Optimizing the sequence parameters via simulation requires knowledge of the T_1 and T_2^* relaxation times of sodium in cartilage and the surrounding fluids. The relaxation parameters for sodium have been characterized in healthy human cartilage in vivo for other field strengths such as 3 T by triple-quantum methods [21,32] and 7 T using conventional methods [30], and for a single subject at 4.7 T [33].

The purpose of this work was to improve fluid-suppressed sodium imaging of cartilage in the human knee by using soft inversion recovery. This was accomplished by first measuring T_1 and T_2^* relaxation times for cartilage and fluid in the human knee at 4.7 T, and then simulating various combinations of inversion pulse length and repetition time while keeping specific absorption rate (SAR) and scan time constant. Validation of this approach and the simulations was performed on a saline/agar phantom. Off-resonance was simulated to determine its effect on the resulting sodium signal. The predicted optimal parameters were used to compare SIRFLA to hard IR for fluid-suppressed sodium MRI of healthy human knee.

2. Materials and methods

Sodium images were acquired on a Varian Inova 4.7 T whole body scanner (Walnut Creek, CA) with a 53 MHz 12 rung custom home-built birdcage knee coil (diameter 17.8 cm, leg length 10 cm) positioned concentrically within a wider 200 MHz proton birdcage coil to enable subsequent anatomical scans without subject repositioning (diameter 19.2 cm, leg length 12 cm).

2.1. Phantom and subjects

A phantom was constructed for validation of the inversion recovery simulations. The phantom consisted of two concentric hollow glass spheres. The outer sphere (98 mm diameter) was filled with 5% agar (Invitrogen) containing 500 mM NaCl, and the inner sphere was filled with 500 mM NaCl in water (58 mm diameter).

Nine healthy subjects (age: 29 ± 2 years, age range: 25–34 years, weight: 151 ± 26 lb, weight range: 110–190 lb, 3 females, 6 males) were scanned to determine cartilage relaxation times and B_0 homogeneity. Optimal inversion recovery parameters obtained from simulation were tested on four healthy subjects (age: 27 ± 3 years, age range: 25–32 years, weight: 130 ± 23 lb, weight range: 110–150 lb, 2 females, 2 males). All volunteers freely gave written informed consent prior to participation in this study as required by the Health Research Ethics Board at the University of Alberta.

2.2. Sodium image acquisition

Manual shimming of the entire volume was performed by adjusting X, Y, Z, and Z^2. MRI was acquired using a 3D twisted projection imaging (TPI) sequence with anisotropic k-space acquisition and sampling density weighted apodization [37]. Projection set design (including the generation of gradient and refocusing files), image reconstruction, and data analysis were all performed using custom software programmed in Matlab. The TPI acquisition consisted of 3000 projections with 260 points per projection and a dwell time of 0.05 ms. Each projection had a twist (p) of 0.172 and a read out length of 12.95 ms. Effective TE was 0.186 ms, calculated as the delay between the center of the RF excitation pulse to the start of data acquisition. The field of view was $12 \times 12 \times 12$ cm^3, and the nominal acquisition resolution was 1.5×1.5 mm^2 in-plane and 6 mm out of plane (13.5 mm^3 voxels). The data was gridded on a Cartesian matrix of size $256 \times 256 \times 256$. Note that these k-space acquisition parameters were kept constant for all the TPI measurements of relaxation, fluid attenuation, or steady state acquisition.

2.3. Determination of relaxation times

The T_1 relaxation times were determined for femoral–tibial cartilage, patellar–femoral cartilage, fluid, and popliteal blood in subjects (as well as the agar and saline in the phantom) using an inversion recovery (IR) sequence and TPI acquisition. Inversion times of TI = 3, 7, 15, 25, 40 and 70 ms were acquired with the TR adjusted to ensure a recovery time of 150 ms between excitation and inversion. The width of the inversion pulse (P_{inv}) was 1.0 ms. Total scan time for all six inversion times was 45 min. T_1 was calculated by a mono-exponential least-squares regression fit to the average signal obtained in each ROI for each inversion time.

In a separate session, the $T_{2\,slow}^*$ and $T_{2\,fast}^*$ relaxation time maps were determined via biexponential fits for cartilage and fluid in vivo, as well as the agar and saline in the phantom using a 90° excitation pulse followed by a series of increasing delays (TE = 0.21, 0.30, 1.20, 2.20, 4.20, 10.20, and 40.2 ms) prior to image acquisition and TR = 150 ms. Total scan time for all seven echo times was 48 min.

The $T_{2\,fast}^*$ and $T_{2\,slow}^*$ relaxation constants were determined by either mono-exponential least squares regression fits to the average signal intensity obtained in each ROI for each echo time for the fluids, or bi-exponential least squares regression fits to the average signal for tissue or agar. For the bi-exponential fit, the relative signal contributions of the fast and slow relaxation were also determined.

2.4. Sodium simulation and IR pulse sequence timings

The evolution of the sodium signal was simulated, as has been shown previously [38–41], to determine the inversion recovery parameters that maximized SNR efficiency from sodium in cartilage while suppressing signal from fluid in the knee. The duration of a rectangular inversion pulse (P_{inv}) was varied from 1 to 30 ms in