Specialty area: Quantitative Musculoskeletal Imaging: Structure & Function-Cartilage Structure & Function

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Highlights

- Cartilage contains negatively charged glycosaminoglycan macromolecules (GAG)
- Loss of GAG is an early biomarker for Osteoarthritis
- Sodium MRI and $T_{1\rho}$ MRI are both sensitive to changes in GAG and hence serve as non-invasive biomarkers of OA in humans.

TALK TITLE: Measuring Cartilage Glycosaminoglycan: Sodium & $T_{1\rho}$ MRI

TARGET AUDIENCE: Healthcare professionals and scientists in the field of MSK, imaging, biology, and biomechanics.

OUTCOME/OBJECTIVES: Audience members will be able to identify how sodium MRI and $T_{1\rho}$ MRI serve as MRI biomarkers of cartilage degeneration.

PURPOSE

There is a need for valid biomarkers that are sensitive to early makers of the disease process in OA. In this context, the loss of glycosaminoglycans (GAG) has proven to be the best target for MRI. Conventional MRI permits the direct visualization of cartilage at high resolution and can detect morphologic changes with high levels of accuracy. However, it has not proven either sensitive or specific for the detection of early GAG changes. Consequently, sodium and T1ρ MRI have become the most sensitive and specific methods to detect loss of GAG in cartilage. In the near future, both these methods would provide the necessary differential and non-invasive diagnostic capability during the development of novel treatments methods for OA and eventually help to guide effective treatment.

METHODS

Sodium MRI and $T_{1\rho}$ MRI are distinct manifestations of pulse sequences (1) compared to conventional vendor-supplied pulse sequences. In addition, sodium MRI also requires special hardware modifications in order for the scanner system to transmit and receive a sodium MRI signal.

RESULTS

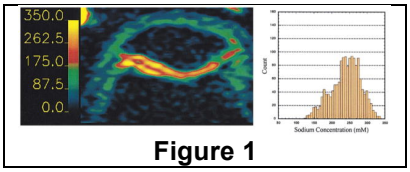

Figure 1

Reddy et al at 4T (2), for the first time, demonstrated the feasibility of acquiring a high-resolution (voxel size of 6.25 µL) 3D data set of sodium images of the knee of healthy human volunteers with excellent SNR (16:1) at 4T. Representative sodium concentration ([Na]) map calculated from sodium MRI of the human patellar cartilage *in vivo* using a surface coil (Figure 1) on a 4T whole body scanner (3). The barscale is [Na] in millimolar. The histogram contains only the pixels from the cartilage on or near the patella. The mean [Na] was 245 mM, i.e. FCD = –165 mM. Recently, the availability of 7T whole body human scanners has reinvigorated the research in sodium MRI of cartilage. *In vivo* sodium MRI of human patellar cartilage (Figure 2) with 3D cones sequence was obtained on a 7T whole body MRI scanner (4). Axial proton MRI of the knee joint obtained from a healthy volunteer. b: Standard-resolution (1.3 × 1.3 × 4.0 mm^3, voxel volume of 6.8 µL) sodium image from the full 3D volume acquired (cartilage SNR = 16). e: High-resolution (1.0 × 1.0 × 2.0 mm^3, voxel volume of 2 µL) sodium image from the full 3D volume acquired (cartilage SNR = 9). c,f: Color-coded sodium image overlaid on corresponding gray-scale anatomic

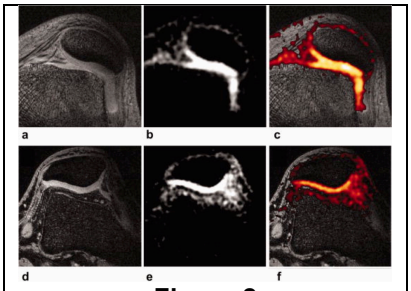

Figure 2

MRI from the first panel. Higher sodium signal is obtained in cartilage due to the presence of GAG. The high-resolution image shows a better delineated cartilage due to a thinner slice and reduced partial volume artifact but with only ~60% of the SNR of the standard resolution image.

$T_{1\rho}$-weighted images and color-coded $T_{1\rho}$ maps (Figure 3) of the human knee joint *in vivo*. Left panel images (A, C, E) are of the patellar cartilage in the axial orientation and right panel images (B, D, F) are femoral and tibial cartilage in a coronal orientation. Images were obtained from a healthy volunteer on a 7T Siemens whole-body MRI scanner. Images A and B are obtained at TSL = 0, with little $T_{1\rho}$ contrast and images C and D were obtained at TSL = 40 ms, with significant $T_{1\rho}$ contrast. Bottom row shows calculated and color-coded $T_{1\rho}$ maps (in ms) of cartilage overlaid on the corresponding anatomical gray-scale images. The arrow in F indicates the medial side femoral cartilage with reduced contrast among different layers due to magic angle effect (5).

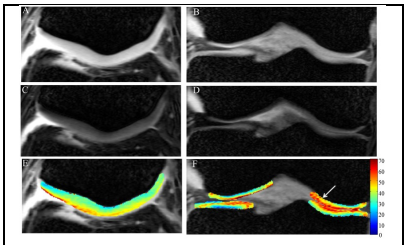

Figure 3

DISCUSSION

Due to the sensitivity of sodium MRI to PG, this method is most valuable clinically in the early diagnosis of OA and in gauging the effectiveness of early treatment methods, such as Disease Modifying Osteoarthritic Drugs (DMOADs), where cartilage is fairly intact. In this context, methods to improvements in SNR of sodium images play a crucial role. Advances in gradient technology (with a gradient strength of >4G/cm) enable one to achieve ultra-short TE (<200μs) that can significantly improve SNR (6). Radiofrequency coil technology (multiple channel capability) and compressed sensing (7) , and tuned pre-amplifiers (8) have further contributed to improved SNR. These advances may potentially make the clinical sodium MRI feasible at 3T scanners, but still with limited SNR. Further, the recent proliferation of 7T whole-body MRI scanners in clinical research centers could have a significant impact on sodium MRI and its potential for clinical use. Clinical research studies using $T_{1\rho}$ conducted so far have been mostly of a demonstration of feasibility kind on a limited number of volunteers. But, future studies, for example on a large group of OA subjects with mild to moderate OA (with a different degree of radiographic OA) and age-matched healthy subjects, would address the issues of accuracy and precision of the measurement, effect of age, disease of severity and longitudinal changes in disease, paving the way for eventual regulatory approval in routine clinical use.

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