CEST and Sodium Imaging of Glycosaminoglycans in-vivo on the 3T: Preliminary Results

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Introduction

Quantitative assessment of Glycosaminoglycans (GAGs) in the clinical environment can assist with assessment, treatment and prognosis of disorders associated with cartilage degradation and loss, such as osteoarthritis or intevertebral disc (IVD) degeneration. Several techniques have been employed to assess the state of the GAG; among them, delayed gadolinium enhanced MRI of cartilage (dGEMRIC, (1)), quantitative $T_{1\rho}$ (2), sodium imaging (3) and gagCEST (4). dGEMRIC has emerged as a gold standard in the assessment of cartilage degeneration. However, the method requires the injection of the exctracellular contrast agent and may not be easily extendable to IVD studies. Other methods rely on the endogenous effects. In particular, sodium imaging employs endogenous ions whose concentration is roughly proportional to FCD (and GAG). At the same time the low sensitivity of sodium imaging and the requirement of specialized hardware hamper its integration into standard clinical protocols. While $T_{1\rho}$ offers sensitivity and relies on endogenous effects, it may not be specific to GAG induced changes.

A gagCEST method, introduced recently, targets predominantly GAG molecules. It is based on the Chemical Exchange Saturation Transfer (CEST) approach in which RF saturation is used to "label" a specific chemical group (5). Subsequent saturation transfer to water results in the reduction of the observed water signal and, hence, allows the detection of small amounts of constituents that are unobservable with standard MRI. In gagCEST, the endogenous -NH and –OH groups present in GAG polysaccharide units are pre-saturated, offering a potential endogenous marker for the determination of GAG in tissue. Hence, gagCEST may provide sensitive and selective tool for GAG assessment. Here we will show preliminary results of implementation of gagCEST and sodium imaging in the clinical environment and correlation between the results obtained using the two methods *in-vivo*.

Materials and Methods

The imaging was performed on the clinical 3T Signa GE scanner (GE, Waukesha, US). For CEST imaging, gradient echo (GRE) sequence with MT preparation was employed. For knee proton imaging a dedicated transmit/receive coil was used. Fast Spin Echo was employed to achieve high resolution T_2 weighted anatomical images: 22x22cm FOV, TR/TE 3000/8.1msec, 256x256 matrix size, 10 mm slice thickness, 1 NEX. For CEST, imaging was performed with: 22x22cm FOV, TR/TE 200/2.9msec, 256x256 matrix size, 10mm slice thickness, 1 NEX. A Fermi shaped RF pulse was used for CEST saturation, with the total length of 50msec, and the effective flip angle of 3250^0 (effective B_1=180Hz). To analyze measurements more quantitatively, we define an asymmetry parameter for a particular off-resonance Δ from the bulk water frequency (5): $MTR_{assym}(\Delta)=I(-\Delta)-I(\Delta)/I(-\Delta)$, where $I(\Delta)$ is the signal intensity measured with the pre-saturation RF frequency of Δ. We will use the abbreviation MTR_{assym} to emphasize that other factors except chemical exchange may contribute to the observed signal asymmetries. For sodium imaging, a home-built quadrature coil was employed. A 3D GRE sequence was used with TR/TE 30/2msec, 32x32cm FOV, 256x256 matrix size, 10mm slice thickness, 24 NEX. Sodium images were post-processed off-line using Matlab software, and a Fermi filter was applied to improve image SNR.

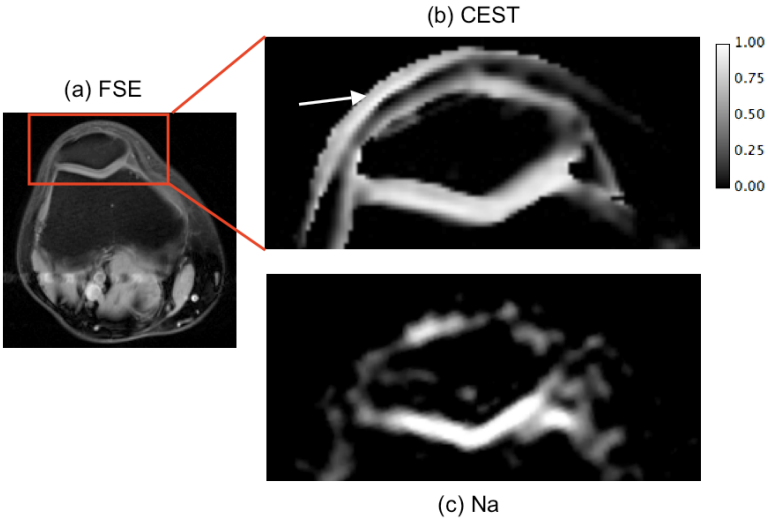

Figure 1 *Images of human knee in-vivo: (a) T_2 weighted image, (b) MTR_{assym}(1ppm) map (c) Na image. The area highlighted by the red rectangle in (a) is zoomed-in on (b)*

Results and Discussion

Fig.1 displays images of a knee joint acquired in the 34 yr old volunteer without known knee problems. Fig.1.a shows T_2 weighted images of the knee. The area marked by the red rectangle in (a) is zoomed-in on (b) and (c). Panel (b) displays a MTR_{assym}(1ppm) map obtained from images acquired with RF saturation at -1ppm and +1ppm. Fig. 1.c shows a corresponding sodium image. The sodium image shows only areas of FCD concentration, i.e. areas containing GAG, and the agreement between the Na image and MTR_{assym} map is quite good. Notice that sodium, as well as MTR_{assym}, was observed outside the articular cartilage area. While the results are preliminary and additional investigation is necessary, these might be GAG containing connective tissue areas. The white arrow at Fig.1.b points at an image artifact around the skin, probably arising from susceptibility mismatch at the tissue-air interface. Such susceptibility differences result in B_0 inhomogeneities leading to artificial asymmetry.

Conclusions

The preliminary results presented here indicate potential for the gagCEST technique to detect GAG and for the high degree of correlation between sodium and CEST imaging. At the same time, additional development is required for the technique to become a reliable method, robust with respect to experimental imperfections. Work is in progress to extend both of the methods to IVD imaging.

References

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