A new, 3D GRE based CEST imaging method for clinical application and verification with gagCEST in articular cartilage

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Introduction:

Chemical Exchange Saturation Transfer (CEST) is a versatile contrast enhancement mechanism for MR imaging [1,2]. The CEST effect depends on the molecular group that provides the exchanging proton(s). One application of the CEST contrast is cartilage vitality imaging, where the CEST contrast is generated by protons of glykosaminoglykans (gagCEST [3]). However, CEST imaging has not yet found application in clinical routine mainly because of the long scan times necessary to obtain a reliable CEST contrast in multi-slice examinations. In this study, we present a versatile CEST imaging method that provides consistent contrast in 3D scans within clinically acceptable measurement times. Its application is demonstrated in a gagCEST examination of the knee of a patient with osteoarthritis.

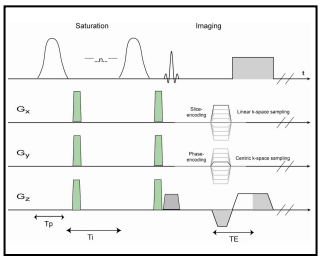

Fig. 1: Schematic illustration of the pulse sequence. It is divided into a saturation part where n saturation pulses are applied followed by an imaging part which acquires part of a 3D volume.

Materials & Methods:

MR imaging: Experiments were performed on a Magnetom Trio (Siemens Healthcare, Erlangen, Germany) with B_0 = 3 T. For articular cartilage imaging a Tx/Rx 8-channel knee coil was used. The saturation scheme consisted of 5 Gaussian-shaped RF pulses with duration of 99 ms and an inter-pulse delay of 100 ms followed by spoiler gradients. Imaging was based on a 3D RF-spoiled gradient echo (GRE) sequence with centric k-space reordering (Fig. 1). Higher order shimming was employed. 14 3D FLASH data sets were acquired - one without saturation (S_0), and 13 data sets with saturation at different frequencies between –2.5 ppm and 2.5 ppm offset from the water resonance. The total acquisition time for all 3D data sets was 11:30 min (matrix: 192x192x35, FOV: 150x150x100 mm^3). Additionally, proton-density weighted FLASH and T_2-weighted double-echo steady-state (DESS) images were obtained to examine cartilage density and intra-articular effusion, respectively.

Data analysis: The magnetization transfer ratio MTR = $1 - S_{Sat}/S_0$ (S_{Sat} being the water signal after saturation) as well as the MTR asymmetry parameter $MTR_{asym}(\delta) = [S_{Sat}(-\delta) - S_{Sat}(+\delta)]/S_0$ were calculated pixel-by-pixel for each slice. The z-spectrum was fitted through all offsets with a cubic spline to determine the position of the minimum signal intensity where the actual water resonance frequency was expected. Subsequently, z-spectra were linearly interpolated to a higher number of points and their minima were shifted to the center frequency along the direction of the offset frequency axis to correct for B_0 inhomogeneities. For pixels in regions with dominant fat signal, z-spectra were not shifted because the signal minimum was found at the fat resonance frequency ($-CH_2-$) as protons resonate ca. -3.3 ppm offset from the water peak. Using the shift values, an offset frequency map was calculated. Data analysis was performed using custom-written code in Matlab 7 (The Mathworks, Natick, MA, USA).

Results and Discussion:

Figure 2 shows MR images of a patient with high-grade chondromalacia of the knee joint after 2x2 cm^2 autologous chondrocyte transplantation (ACT) in the lateral part of the femoral condyle. The transplanted fragment is highlighted in Fig 2a. The MTR_{asym} image shows a signal enhancement at δ = 2 ppm (MTR_{asym} = 4.7 %) within the transplanted region and within joint effusion fluid (Fig 2c). The remaining normal-appearing hyaline cartilage presents with low CEST signal (0.3%). In a healthy volunteer, MTR_{asym} in hyaline cartilage increases from 0.5 to 2 ppm where it reaches maximum values of 5-7 % (Fig. 3c). Even though effusion fluids give rise to CEST signal due to their chemical composition, one can distinguish fluid CEST signal from cartilage CEST signal based on the shape of z-spectra. In general, z-spectra from fluids are narrower than those from tissue. This phenomenon is known from CEST images of the brain, where z-spectra from CSF are narrower than those from normal brain tissue. The probable reason is the higher relative water content in fluids which generates a more intense and more pronounced water peak compared to the signal from tissue leading to a sharper and deeper minimum in the z-spectrum. Hence, the signal increase within the transplanted region is attributed rather to post-operative fluid accumulation than to reasons of transplant vitality.

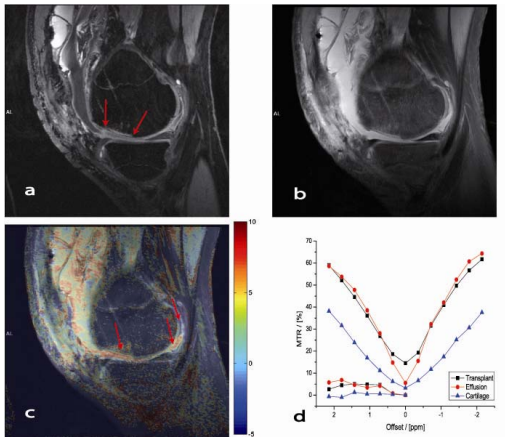

Fig. 2: (a) T_2-DESS, (b) proton-density weighted, and (c) MTR_{asym} image superimposed on a morphologic image of a patient with high-grade chondromalacia after ACT. Arrows indicate ROIs with z-spectra and MTR_{asym} shown in (d). From left to right: transplant, joint effusion, and normal-appearing cartilage.

B_0 inhomogeneities in the knee cartilage were found to vary between –0.6 ppm and +0.6 ppm on average. This requires B_0 correction techniques to produce reliable CEST images. Therefore, we sampled complete z-spectra instead of acquiring two images at opposing offset frequencies. Thus MTR_{asym} images could still be reconstructed after B_0 correction and shifting points to nominally different offset frequencies. The maximum CEST signal is obtained at ~2 ppm in healthy cartilage corresponding to the resonance of the hydroxyl protons of glykosaminoglykans at δ=1.9 ppm [4]. In contrast, the –OH signal at 0.9 ppm cannot be obtained reliably, possibly due to direct saturation effects as a result of the spectral proximity to the water signal. Scan time could still be reduced by decreasing the number points of the z-spectrum. In the knee, however, retrospective B_0 correction requires a large saturation bandwidth to enable reliable CEST images.

Conclusion:

With the proposed technique it is possible to obtain reliable CEST signal intensities from a 3D volume in various tissues within clinically acceptable scan times. Articular cartilage vitality can be monitored by determination of glykosaminoglykan content using CEST imaging and distinguished from joint effusion.

References:

[1] Sun PZ *et al*. Magn. Reson. Med. 2008; 59 1175-82
[2] Zhou J *et al*. Magn. Reson. Med. 2008; 60; 842-49
[3] Ling W *et al*. PNAS 2008;105(7); 2260-70
[4] Ling W *et al*. NMR Biomed 2008; 21; 289-95

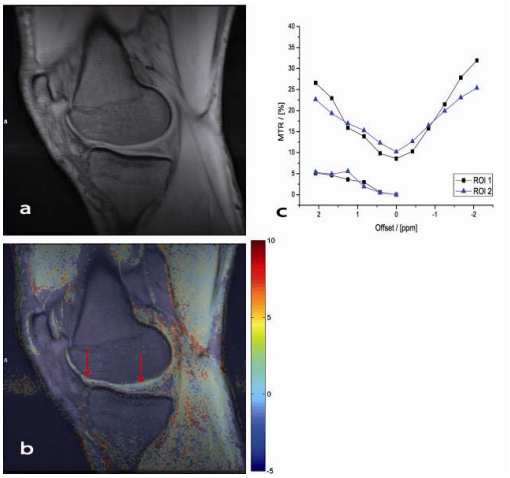

Fig. 3: (a) Proton-density weighted, and (b) MTR_{asym} image superimposed on a morphologic image of the knee of a healthy volunteer. (c) z-spectra and MTR_{asym} from cartilage ROIs marked in (b).