Applying variable RF-power CEST (vCEST) to detect exchangeable hydroxyl protons in the presence of MT at 3 Tesla

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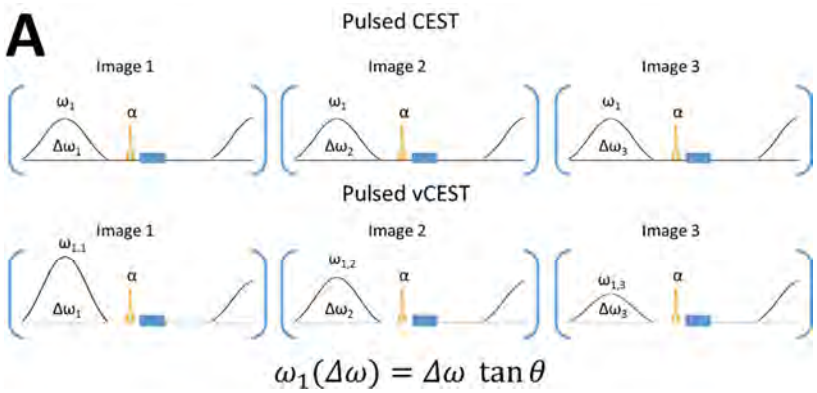
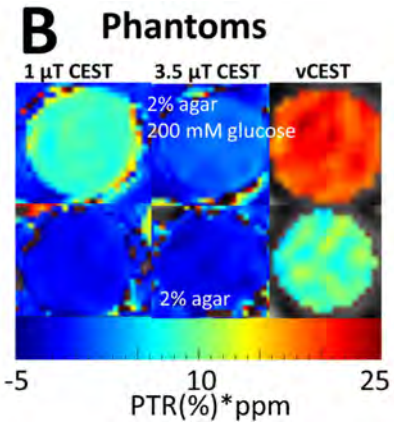
Purpose: Several quantitative MRI techniques are promising for measuring cartilage health and early osteoarthritic changes. One such method is gagCEST, a standard CEST sequence using MTR asymmetry near 1ppm as a surrogate measure of glycosaminoglycan (GAG) concentration. However, the hydroxyl protons of interest have intermediate to fast exchange rate and therefore difficult to measure on 3 T scanners, though there is some success at 7T [**1**]. Novel approaches using spin-lock or combining spin-lock and CEST [**2**] have shown promise in isolating these moieties, however they have not been shown to work at clinical field strengths. We therefore present a new technique using a variable pre-saturation RF power CEST (vCEST) sequence and apply it to imaging knee cartilage at 3T.

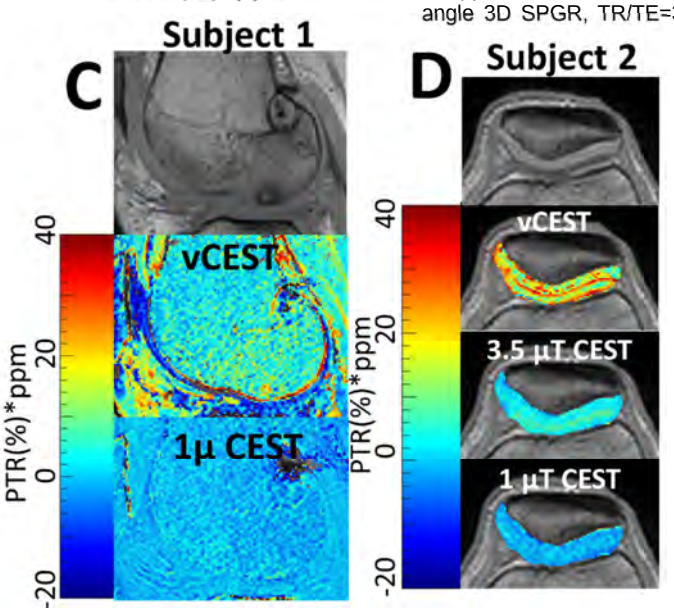
Methods: Theory. Figure A shows the pulsed CEST 3D SPGR vs. the pulsed vCEST. In vCEST the RF pre-saturation power varies linearly with the offset frequency. The effective B_1 angle, θ, is chosen as a constant. In our sequence, we use 1μT/1ppm. This has the effect of flattening the direct water saturation contribution to the z-spectra. With T1 and T2 maps, the constant contribution of DWS can be calculated.



Phantoms. Two 15ml falcon tubes were filled with 2% agar solution to provide macromolecular MT signal. Added to one tube was 200 mM glucose that was mixed just before the solution could cool and harden.



In vivo. Through IRB approval, 2 subjects with previous ACL tears, one with a recent injury and one with an older reconstruction, were recruited. **Imaging.** Phantoms and humans were imaged in a 3T Achieva (Philips, Cleveland) with a 2-channel transmit body coil. An 8-channel receive head coil was used to image phantoms and an 8-channel knee coil for humans. Phantoms were submerged in water and the following pulse sequences were used for parameter mapping: T1 map (IR-TSE, 10 inversion times = 50 – 3000ms); T2 map (multi-echo TSE, T=40 – 20*40 ms); B0 map (WASSR, 3D SPGR with 50 ms/0.1 μT sinc-gauss pre-saturation pulse, 66 frequency offsets from -1 to +1ppm); B1 map (dual TR 25/100ms 3D SPGR); CEST (3D SPGR with 100ms/1μT and 3.5μT sinc-gauss pulse, 49 offsets from -5 to 5 ppm and one S0 image at -100kHz); vCEST(3D SPGR with 100 ms sinc-gauss pulse, RF amplitude varying by 1μT/1ppm with 0.25μT at 0ppm, 49 offsets from -5 to 5 ppm and one S0 image at -100kHz). Human imaging: T1 map (multi-flip angle 3D SPGR, TR/TE=33/2.7ms, angles=3.2,13,17.6°, FOV 150x150x8mm, voxel size 1x1x2mm); T2 map (multi-echo TSE, T=12 – 12*30 ms, FOV 150x150x8, voxel size 1x1x1.75); B0 map (WASSR, 3D SPGR with 75 ms/0.25 μT sinc-gauss pre-saturation pulse, 33 frequency offsets from -1 to +1ppm); CEST (3D SPGR with 75ms/1μT and 3.5μT sinc-gauss pulse, 33 offsets from -4 to 4 ppm and one S0 image at -100kHz); vCEST(3D SPGR with 75 ms sinc-gauss pulse, RF amplitude varying by 1μT/1ppm with 0.25μT at 0ppm, 33 offsets from -4 to 4 ppm and one S0 image at -100kHz). **Image processing.** Both 1μT and 3.5μT CEST data were analyzed using WASSR B0 correction [**3**] and computing the asymmetry (PTR_{CEST}). The vCEST data was analyzed by computing the flattened DWS using measured T1, T2, B0 and B1 maps as inputs to a one-pool model. The measured z-spectrum was subtracted from the computed DWS creating a difference spectrum (PTR_{vCEST}). Voxel maps were made by measuring the AUC around the hydroxyl (0.75-1.75ppm) chemical shift.



Results: In the phantoms, 3.5μT CEST could not detect the hydroxyl signal in the glucose/agar mixture (**Figure B middle**), however, 1μT CEST and vCEST both performed well showing higher PTR in the glucose solution (**Figure B left and right**). In the knees, 1μT CEST was insufficient to provide any asymmetry (**Figures C, D bottom**), however, 3.5μT CEST seems to show some cartilage features (**Figure D middle**). The vCEST mapping resulted in finer detail of the cartilage (**Figure C, D top color plots**).

Discussion: For a high concentration solute in agar, 1μT is enough power to observe the signal, but when going to higher power, the MT and DWS drown the CEST effect. In vivo, the solute concentrations will be much lower and 1μT is not enough input power, though higher power will again produce more MT and DWS. The vCEST scheme addresses both concerns: the input power is low near 0ppm, which reduces the MT at the solute resonance, and the increasing power at higher offsets provide enough power to drive the solute resonance while flattening the DWS contribution. In our two test subjects, no cartilage lesions are observed. However, because of the detailed CEST signal from cartilage, it may be possible to detect depletion of GAG and early osteoarthritic changes with this technique.

Conclusion: We have shown that the vCEST sequence is feasible in vivo and can provide contrast from hydroxyl moieties at 3 T.

References: 1. Singh A, Reddy R, et al. 2012. MRM 68:588-594. **2**. Kogan F, Reddy R, et al. 2012. MRM 68:107-119. **3.** Kim M, van Zijl P, et al. 2009 MRM 61:1441-1450.