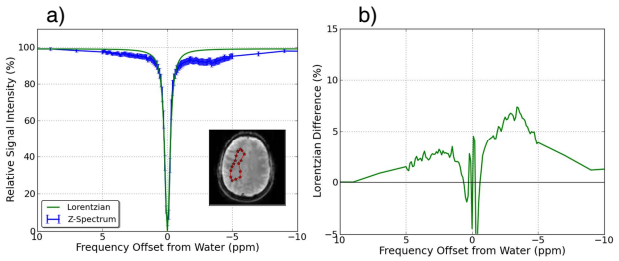
NOE Imaging in the Human Brain at 7T

Craig K Jones[1,2], Alan Huang[1,2], Jiadi Xu[1,2], Richard AE Edden[1,2], Michael Schär[3,4], Jun Hua[1,2], Nikita Oskolkov[1,2], Michael McMahon[1,2], and Peter van Zijl[1,2]

[1]Department of Radiology and Radiological Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, United States, [2]FM Kirby Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, United States, [3]Philips Medical Systems, Highland Heights, OH, United States, [4]Keller Center for Imaging Innovation, Barrow Neurological Institute, Phoenix, AZ, United States

Purpose: CEST is a magnetization transfer (MT) technique to indirectly detect pools of exchangeable protons through the water signal. Low power RF pulses can slowly saturate protons with minimal interference of conventional semi-solid based MT contrast (MTC).[1,2] When doing so, in addition to the usual downfield CEST/APT signals, saturation-transfer signals are revealed upfield from water in the CEST spectrum, which is in the frequency range of non-exchangeable aliphatic and olefinic protons. The visibility of such upfield signals indicates the presence of a transfer mechanism to the water signal, while their finite width indicates that these signals are likely due to mobile solutes. These effects have been attributed to saturation relayed by intramolecular nuclear overhauser enhancements (NOE) in mobile macromolecules to water[3-5] either directly via dipolar transfer[3,5] or relayed via exchangeable protons,[4] in an NOE-relayed exchange process that is the inverse of the well-know exchange-relayed NOEs in high resolution NMR protein studies.[6] Here we mapped the amide proton and NOE transfer effects using low power pulsed saturation with only very small MT contributions and by fitting the Z-spectrum without asymmetry analysis. We also compared the timings of NOE peak (upfield) and amide proton transfer (APT) peak (downfield) buildup.



Methods: Z-spectra were acquired in whole brain and in a protein phantom (Bovine serum albumin, BSA) using a 3D multi-shot gradient-echo (TR/TE/FA = 65ms/7.2ms/12º, EPI factor 7; 40 slices, 3x3x3 mm^3) in six volunteers on a 7T Philips scanner. Saturation pulse: 1μT, 25ms single-lobe sinc-gauss pulse (208º) in each TR.; Z-spectra: 121 offsets frequencies from -40 ppm and 40 ppm with a dense sampling of 0.1 ppm from -5 to 5 ppm. The frequencies were applied in a random order and an unsaturated image was acquired every 5 volumes to correct for potential baseline intensity drift. Three regions of the z-spectra (|f| < 1 ppm, f > 10 ppm and f < -10 ppm) were simultaneously fit to a Lorentzian function to fit out effect of direct water saturation[2]. A Lorentzian difference analysis (LDA) was calculated as the difference between the fitted water Lorentzian and the data. Because we do not use asymmetry analysis we use the terminology clean-APT to indicate amide proton transfer without NOE and direct saturation interference and minimal MTC interference.

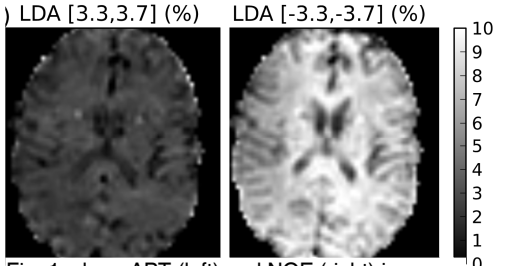


Fig. 1: clean-APT (left) and NOE (right) images.

Results: Fig. 1a shows a drift-corrected z-spectrum with Lorentzian water fit. The LDA is shown in Fig. 1b. The clean-APT range was assigned from 3.3-3.7 ppm and NOE from -3.3 to -3.7 ppm (highest LDA signal). The clean-APT showed minimal contrast between white and gray matter (Fig. 2 left), while the NOE maps have a higher LDA in white matter (Fig. 2, right). Fig. 3 compares the profile of the NOE-relayed spectrum with that of a residual MRS macromolecular spectrum, showing qualitative resemblance, in line with previous water exchange spectra based on the inverse process.[6] The timings of the NOE buildup and clean-APT buildup were studied using a time-dependent pulsed saturation experiment (increasing delay between saturation pulses) in the BSA phantom showing a delayed buildup of the NOE-relayed signals compared to the clean-APT signals (Fig. 4).

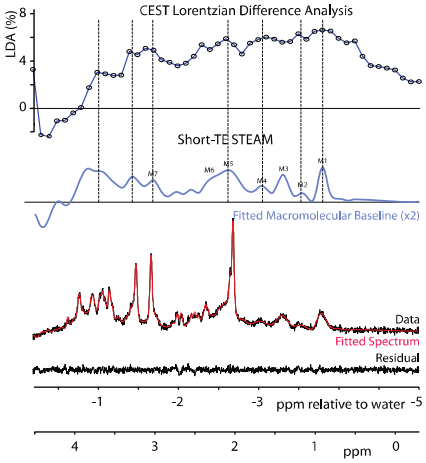


Figure 3: NOE Spectrum compared to MRS macromolecular spectrum.

Discussion: The amide proton transfer and NOE images were created without the need of asymmetry analysis and therefore should better represent exchangeable mechanisms without cross contamination from other exchange resonances. Peaks upfield from water in the Lorentzian difference spectrum appear similar to peaks in a short-TE STEAM MR spectrum and provide corroboration that they are in large part based on mobile macromolecules. The buildup of the NOE-based signal was slower than the clean-APT, further confirming that the upfield signal is related to an exchange relayed mechanism.

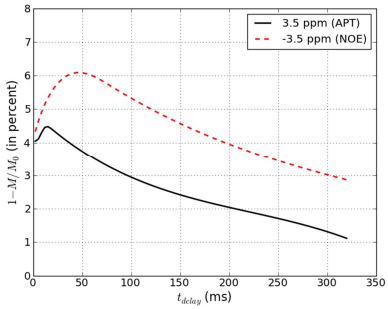


Figure 4: Time dependent saturation buildup of BSA at 3.5ppm (clean-APT) and -3.5ppm (NOE).

Conclusions: At the power level used, the NOE-relayed effects are 2-3 percent units higher in the white matter than the gray matter and therefore may be useful to study diseases that affect the white matter such as multiple sclerosis or cancer. We are currently investigating to which extent residual MTC effects contribute to the upfield signals.

Refs: 1) Desmond & Stanisz MRM 67, 979 (2012); 2) Jones et.al., MRM 67,1579 (2012); 3) Ling et.al. PNAS 105, 2266 (2008); 4) van Zijl & Yadav, MRM 65, 927 (2011); 5) Jin et al, MRM 2012, on-line; 6) van Zijl et al, MRM 49, 440 (2003). Funding: NIH grants R01EB015031, R01EB015032, 1S10 RR028955, P50CA103175 and P41 EB015909