MTC free APT and rNOE-CEST Images of Human Brain at 7T

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Target audience: Investigators interested in Chemical Exchange Saturation Transfer (CEST) based imaging methodologies such as Amide Proton Transfer (APT) and Nuclear Overhauser Enhancement (NOE) imaging. [1]

Purpose: When investigating CEST based contrasts an asymmetry analysis is usually performed to remove the direct water saturation and the conventional magnetization transfer contrast (MTC). In vivo, such a method is prone to inaccuracy since CEST contrasts occur on both sides of the water, *e.g.* APT and chemical exchange relayed NOE (rNOE).[1] In addition, the conventional MTC that arises from semi-solid macromolecules is asymmetric with respect to the water resonance.[2] In this work, we use the recently developed Variable Delay Multi-Pulse (VDMP)-CEST[1,3] approach to remove the conventional MTC based on its unique exchange rate, hence yielding MTC-free APT and rNOE-CEST images.

Method: The VDMP-CEST pulse sequence consists of a train of RF pulses with a certain inter-pulse delay (mixing time). When varying the inter-pulse delay, the saturation efficiency of protons with different exchange rates differs, which can be seen from the simulated CEST signal using Bloch equations modified to take into account the chemical exchange process and T1-relaxation (Fig. 1). The MTC signal obtained with zero mixing time is equal to that acquired with a mixing time of about 70 ms, which is referred as $\tau_{null\text{-}MTC}$. Therefore, the conventional MTC contribution can be removed by subtracting the two images, while residual APT and rNOE-CEST signals remain. Hence the VDMP saturation can serve as an MTC filter.

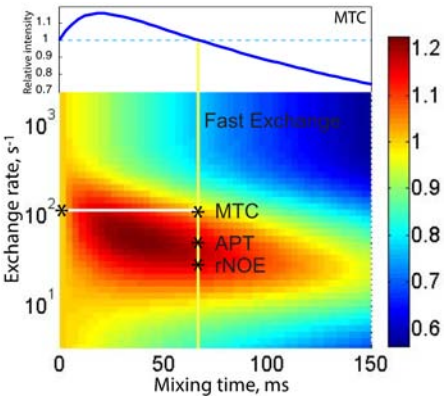

Fig. 1: Bottom: 2D plot of magnetization transfer signal intensities as a function of mixing time for different exchange rates. For clarity, all intensities were normalized to the first data point. The simulation was performed assuming 16 saturation pulses; each with a duration of 10 ms and B1 of 2.18 μT. Top: a projection of MTC signal intensity ($k_{sw} \approx 100$ Hz) change as a function of mixing time.

Human brain images were acquired using a 7T Philips scanner. For the VDMP preparation, 16 single-lobe sinc-gauss pulses, each with 20 ms duration and power of 3.4 μT were used. 8 inter-pulse delays ranging from 0 to 140 ms were tested to find the optimal suppression of MTC, which was verified by looking at signal intensities outside the chemical shift range for mobile protons, i.e. > 5-10 ppm from water. The images were acquired using a single-shot turbo gradient echo with TR (between each echo)/TE/FA = 5 ms/1.48 ms/30°. A single slice with 6 mm thickness across a FOV of 230×230mm^2 with 3×3 mm^2 in plane resolution was acquired. The frequency of the saturation pulse was swept from -20 to 20 ppm at a step size of 1 ppm, except in the range of -4 to 4 ppm, where a 0.5 ppm step size was used. The experiment time for each image was 4.2 s. The maximum SAR for pulse interval 0 ms was 24%.

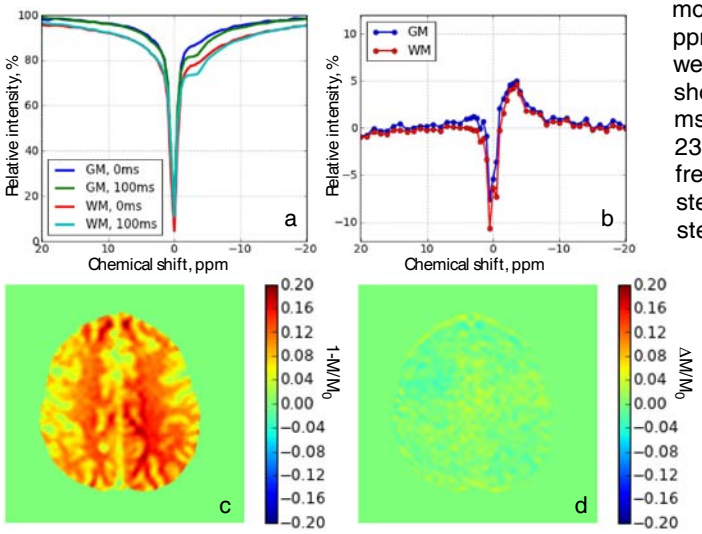

Fig. 2: (a) VDMP-CEST Z-spectra at two mixing times in gray matter (GM) and white matter (WM). (b) The difference spectra for WM and GM. (c) MTC image at 5 ppm. (d) Residual MTC image at 5 ppm after subtraction.

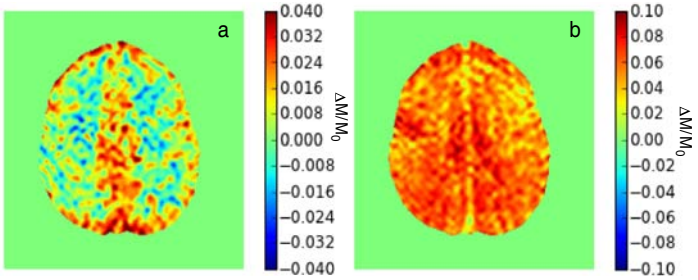

Fig. 3: MTC free APT (a) and rNOE-CEST (b) images.

Results and Discussion: Fig. 2a shows typical Z-spectra, acquired with mixing times 0 and 100 ms in gray and white matter, respectively. It can be seen that MTC signal using 100 ms mixing times has the same signal intensity as using 0 ms. When subtracted, the residual MTC is minimal as can be seen clearly by the difference spectra at offsets >10 ppm and <-10 ppm (Fig. 2b) despite that the MTC is different in gray and white matter. Meanwhile, the APT and rNOE contrasts are well preserved and similar to the observations in a previous study.[1] Examining the CEST images it is evident that even though the MTC image at 5 ppm (Fig. 2c) shows strong gray and white matter contrast, the residual MTC after subtraction is negligible (Fig. 2d). With such clean MTC and water direct saturation (DS) background removal, the APT map (Fig. 3a) shows hyperintensity in the gray matter, consistent with higher concentrations of cellular proteins in these voxels. The rNOE map (Fig. 3b) shows iso-intensity indicating that mobile macromolecules with aliphatic groups contribute in both gray and white matter.

Conclusion: The presented results show that it is possible to obtain MTC-free APT and rNOE images using the VDMP saturation scheme, which could be very useful in assessing differences in mobile protein content in disease applications.

References: [1]. Jones C.K. *et al.* Neuroimage, 2013; 15, 114. [2] Hua J. *et al.* MRM, 2007, 58, 786. [3]. Xu J. *et al.* MRM, DOI: 10.1002/mrm.24850. **Funding Support:** NIH grants P50CA103175, P41 EB015909 and RO1 EB015032.