Variable delay pulse train for fast CEST and NOE-CEST MRI

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Target audience: Investigators interested in CEST imaging and its application to disease.

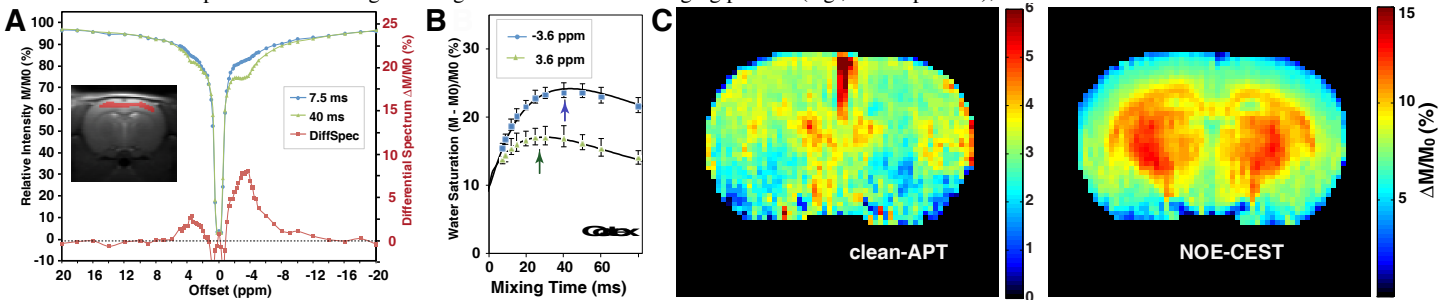
Purpose: Conventional CEST experiments are generally performed by acquiring images as a function of irradiation frequency (Z-spectrum), and then performing asymmetry analysis by subtracting signal intensities of images acquired at positive offset frequencies from signal intensities of images acquired at negative offset frequencies relative to the water signal. However, asymmetry analysis is problematic because the conventional semi-solid magnetization transfer contrast (MTC) is often not symmetric about the water signal. Consequently, the CEST signal may include significant effects from MTC. The CEST signals from amide/amine and aliphatic protons from mobile proteins and tissue metabolites also get mixed in this procedure. We propose a method named variable delay pulsed (VDP) CEST, for obtaining predominantly exchange-based saturation transfer contrast. The new technique is based on a pulsed RF irradiation scheme with the delay (mixing time) between the RF pulses varied between two (or more) separate acquisitions (1, 2). The irradiation frequency is kept at the same frequency of interest and uses the same B1 strength. The CEST image is obtained by subtracting the CEST images recorded at two different mixing times, for instance the minimum mixing time and a longer mixing time at which slower transfer processes such as nuclear Overhauser enhancements (NOEs) are more visible. Effects from direct water saturation (DS), MTC, and very fast exchanging protons will be strongly reduced or removed by the subtraction, while predominantly slower CEST effects such as amide proton transfer (APT) and NOE-relayed CEST contrast are preserved.

Methods: Experiments were performed on three adult male wister rats weighting 280 to 320g. The rats were anesthetized by 5% isoflurane in a 75%/25% air/oxygen mixture followed by 2% to 2.5% isoflurane during the MRI scans. The MRI experiments were conducted on a horizontal 11.7T scanner (Bruker BioSpin). Transmission was achieved using a 72 mm quadrature volume resonator and detection with a 15 mm planar surface coil. Pulsed CEST images (2-4) were acquired using a FSE readout with TR=6 s, TE=4 ms, slice thickness 1 mm, and 64×64 matrix were used (FOV 1.8×1.8 cm^2). The VDP CEST sequence implemented in this work is similar to the conventional pulsed CEST/MT sequence with a CYCLOPS (CYClically Ordered Phase Sequence) type phase cycle for the saturation pulses. The phase cycle and gradients applied for each pulse destroy any residual transverse magnetization that may form stimulated echoes and interfere with the CEST signals. 32 Gaussian shaped RF pulses (180 degree flip angle) with 6.9 ms pulse width (bandwidth 200 Hz, peak power 4 μT) were used for saturation in the VDP CEST for MRI on rats.

Results and Discussion: Typical VDP-CEST Z-spectra from a ROI in the cortex of rat brain are plotted in Fig. A. Z-spectra with minimum mixing time (7.5 ms) and longer mixing time (40 ms) are shown. The difference spectrum (DiffSpec) obtained by subtracting these two Z-spectra is magnified by 4 times for clarity (red scale on right hand side). It can be seen that the MTC could be well suppressed despite using 32 low power saturation pulses as evidenced by the difference spectra at offsets >8 ppm and <-8ppm, which show intensities close to zero. Two strong composite peaks centered at ±3.6 ppm are visible, which are assigned to slowly exchanging amide protons and signals from NOE-relayed aliphatic protons of mobile proteins, respectively. Due to the abundance of aliphatic protons in brain tissue, the aliphatic peak is far stronger than amide peak. Fig. B shows a so-called saturation buildup curve, in which the water saturation level at offsets ±3.6 ppm is plotted as a function of interpulse delay time (mixing time) in VDP CEST. Similar to the QUEST technique, the buildup curve may used to extract the magnetization exchange rates of the CEST and NOE-relayed CEST signals.

The clean-APT (i.e. without DS and NOE contamination and strongly reduced MTC) and NOE-CEST (3.6 ppm) difference images of a rat brain are presented in Fig. C. Here, one extra M0 image was recorded to compensate the signal to noise inhomogeneity across the rat brain due to the usage of surface coil. Both clean-APT and NOE-CEST of the muscle were significantly lower than the values of the rat brain and no skull contrast was seen. The clean-APT image show different contrast from NOE-CEST, which indicates that the slowly transferring amide and aliphatic proton groups can be separated out from total magnetization transfer signal under the current experimental conditions. Therefore, VDP-CEST is specific technique, and can target at different proton species in contrast to conventional MTC.

Conclusion: VDP CEST is a promising technique for obtaining APT and NOE-CEST rapidly. Only two images at the same offset frequency are recorded, and thus CEST images can be averaged to increase the signal to noise ratio (SNR). Another significant advantage of current technique is that APT and NOE-CEST effect can be separated from background signals such as fast exchanging protons (e.g., amine protons), direct saturation and conventional MTC.



References:

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