A Multi-echo Length and Offset VARied Saturation (Me-LOVARS) CEST Method

Xiaolei Song1,2, Jiadi Xu1,2, Shuli Xia3, Nibhny N. Yadav1,2, Bachchu Lal1, Jeff W.M. Bulke1,2, John Laterra1, Peter C.M. van Zijl1,2, and Michael T. McMahon1,2

1 Division of MR Research, The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University, Baltimore, Maryland, United States, 2 F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, United States, 3 Department of Neuro-Oncology, Kennedy Krieger Institute, Baltimore, MD, United States

Target Audience: Researchers who are interested in CEST/APT imaging, MR pulse sequences and oncological imaging.

Conventional CEST: Readout only after the whole preparation

[Diagram showing RF, Saturation Prep., TR, EPI, FID signal, Reco. Image, Avg. 3.3-3.9 ppm, CEST contrast (Aptw), MTR asym, APT maps, Amide (-NH), Amines (-NH2)].

Purpose: CEST imaging allows the detection of low concentration solute based on multiple proton-exchange events occurring during the long preparative saturation pulse (or pulse train), with promising applications in oncological imaging. The CEST contrast builds up with saturation length (t sat), which can be used for estimating exchange rate (kex)2,3 and improving contrast maps2. In addition, the optimal t sat for maximum contrast varies with kex or saturation field strength (B1) changes, especially in vivo with different levels of interference from conventional magnetization transfer contrast (MTC) and direct saturation (DS). Currently, CEST studies collecting saturation data as a function of saturation frequency (Z-spectra) with one pre-determined t sat in the interest of minimizing scan time. Here we present an efficient CEST imaging method, named Multi-echo Length and Offset VARied Saturation (Me-LOVARS), which allows acquiring a series of Z-spectra at multiple t sat values, without extra scan time cost.

Methods: Me-LOVARS sequence: Employing the idea of Look-Locker fast TI mapping technique 2, the Me-LOVARS method divides the long saturation pulse (T sat) into 3 blocks, each with a length of 1/3T sat (0.5-1sec.), and in between inserts a low flip-angle (FA = α) fast gradient echo read-out sequence (here EPI), followed by a flip back pulse (FA = -α) for retaining the longitudinal magnetization.

Acquisition: Images were acquired on SCID/NCR mice (n=3) bearing intracranial xenografts derived from human glioblastoma neurospheres (HSR-GBM1A) on a Bruker BioSpec 11.7T scanner, with a 72mm volume coil as transmitter and a 4-channel phased array surface coil receiver. MR parameters were: 3 sat. pulses for Me-LOVARS with each length of 0.8sec. (1/3T sat), B1=1.8-2.2uT, 4 segment EPI (7.85ms per segment), α=25°, TR/TE=16.5s/15.5s, matrix size = 96x64, saturation offsets at [+4.8, +4.2, +3.9, +3.6, +3.3, +3.0, +2.7, +2.4, +2.1, +1.5, +0.9, 0]ppm. Conventional CEST images with single EPI readout (t sat = 2.4 sec.) were also acquired using the same parameters.

Post-processing: Voxel-by-voxel Z-spectra B0 correction was performed through interpolating the original data to every 0.1ppm using a piecewise polynomial fitting, with B0 values from WASSR 5. CEST contrast was quantified by MTR asym = (S asym - S contr)/S contr. To increase the CNR, the contrast maps for amide (-NH, APT weighted) and amine (-NH2) freq. were obtained by averaging MTR asym from 3.3 to 3.9 ppm, and from 2.6 to 3ppm, respectively.

Results and Discussion: Based on Bloch simulations and experiments, an optimized FA of 25° was chosen for imaging mice brains at 11.7T. In contrast to conventional CEST with image readout only after the whole saturation prep. (Fig.a), Me-LOVARS collects multiple readouts during the preparation, which yields contrast build-up information without penalty in scan time (Fig.b). ME-LOVARS obtains 3 APTw images with varied saturation lengths (1/3t sat, 2/3t sat and t sat), but using the same time as the conventional CEST single EPI readout (44 sec. per image without acceleration), with the last image (APTw(t sat)) similar to conventional single EPI readout. As a result, the B0-corrected APT maps (Avg. MTR asym from 3.3 to 3.9 ppm) of the 3 sat lengths also show similar contrast between tumor and contralateral control tissue (~6.5%) compared to that using conventional EPI readout. The amine contrast maps (Avg. MTR asym from 2.6 to 3 ppm), however, shows a more obvious build-up (2%) from 1/3 t sat to 2/3 t sat. This is expected because these protons exchange faster. Fig.c shows the build-up of the avg. MTR asym curves for 2 mice with ROIs of the tumor core (red) and contralateral control tissue (blue), with different build-up for amide and amine frequencies. Note that the larger standard deviation of MTR asym for control tissue is partially due to different B1 between mice, which affects asymmetric MTC and Nuclear Overhauser Effect (NOE).

Conclusion: Me-LOVARS method allows efficient collection of additional CEST data with multiple t sat’s, for enhancing contrast or improving quantification of exchange.

Figures: Comparison between conventional CEST (a) and Me-LOVARS (b), with (c) showing the build-up of avg. MTR asym curves from 2 mice acquired by Me-LOVARS.


Acknowledgement: NIH grant R01 EB012590, EB015031, EB015032.