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

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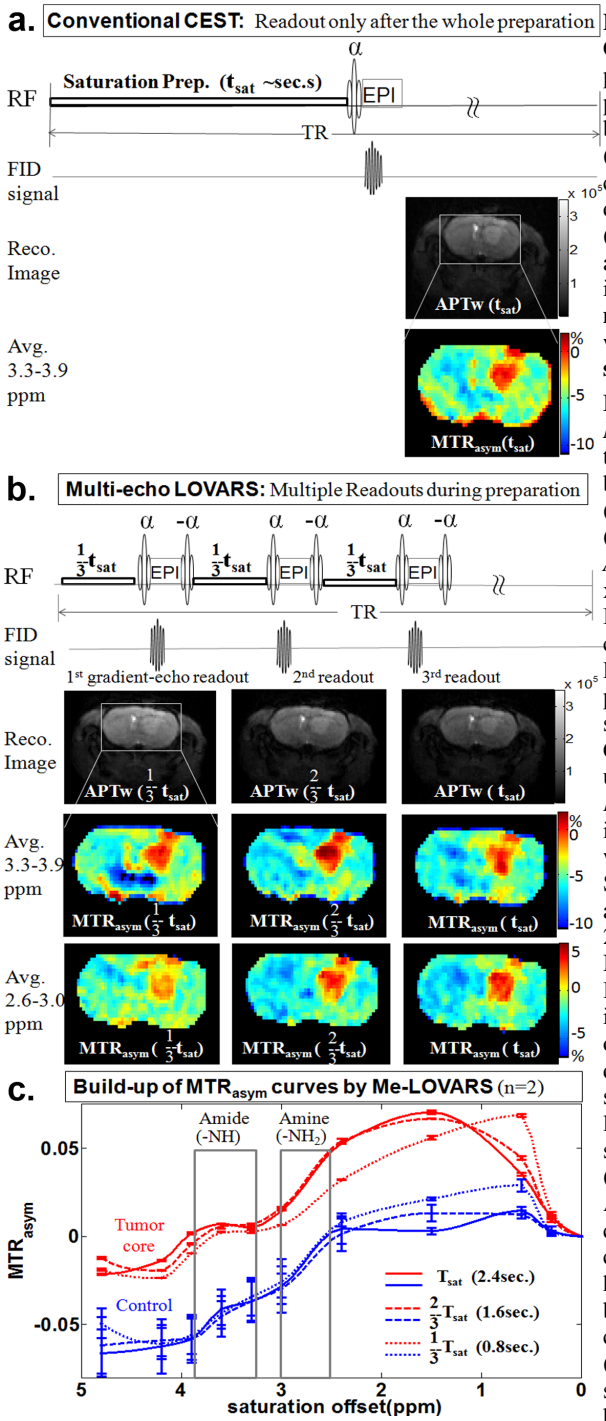
Target Audience: Researchers who are interested in CEST/APT imaging, MR pulse sequences and oncological imaging.



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.

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[1]. The CEST contrast builds up with saturation length (t_{sat}), which can be used for estimating exchange rate (k_{ex})[2,3] and improving contrast maps[4]. In addition, the optimal t_{sat} for maximum contrast varies with k_{ex} or saturation field strength (B_1) 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 T1 mapping technique[5], 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.($1/3T_{sat}$), B_1=1.8-2.2uT, 4 segment EPI (7.85ms per segment), α=25°, TR/TE=5s/5.27ms, FOV=16.5x15.5x1mm, matrix size = 96x64, saturation offsets at [±4.8, ±4.2, ±3.9, ±3.6, ±3.3, ±3, ±2.4, ±1.5, ±0.6, ±0.3, 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[6]. CEST contrast was quantified by $MTR_{asym} = (S_{-\Delta\omega} - S_{+\Delta\omega})/S_0$.To increase the CNR, the contrast maps for amide (-NH, APT weighted) and amine ($-NH_2$) freq. were obtained by averaging MTR_{asym} from 3.3 to 3.9ppm, 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 B_0-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 B_1 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. Further *in-vivo* mice studies are on-going using this build-up information to differentiate tumor types/grades[8].

References [1]Zhou, et al. Nat Med 2011,17; [2]McMahon, et al. MRM. 2006, 55; [3]Sun, et al MRM, 2012, 67 [4]Song,et al. MRM 2012, 68; [5]Gowland, et al. MRI, 1993, 30; [6]Kim, et al RM 2009, 61; [7]Togao, et al Proc. ISMRM 2012, #744. **Acknowledgement** NIH grant R01 EB012590, EB015031, EB015032.