A Multi-parametric Multi-echo Saturation (MMS) method enabling CEST fingerprinting

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Target Audience: Researchers, radiologists interested in CEST/MT/APT imaging.

Purpose: CEST contrast varies as a function of saturation power (B_1) and length (t_{sat}), offering opportunities for generating the CEST 'fingerprint' for various agents with exchangeable protons of different exchange rates. Based on our multi-echo Length and Offset Varied Saturation (MeLOVARS) methods[1,2], we developed a hybrid MeLOVARS sequence enabling acquisition of multiple readouts weighted with multi-parametric saturation. This allows modulation of CEST with both B_1 and t_{sat}, with the goal of improving CEST specificity for different exchanging species.

Methods: A CEST agent, 5-Amino salicylic acid, featuring an intramolecular-bond shifted hydrogen (IM-SHY)[3] with offset $\Delta\omega$ of 8.5 ppm was dissolved in PBS (20mM). Samples at pH values 6.9 and 7.2 in 5mm NMR tubes were imaged on a Bruker Biospec 17.6 T vertical-bore scanner at 310K, using a 15mm volume coil as trans/receiver. Fast CEST acquisition was performed using a hybrid MeLOVARS sequences (**Fig.1d**) containing 8 modules with saturation pulses of 0.5 sec. in length with B_1^{low} = 3.6 uT (Module 1, 3, 5, 7) and B_1^{high} = 7.2 uT (Module 2,4,6,8), each followed by a single-shot EPI readout. Two regular MeLOVARS sequences of eight modules with either B_1 = 7.2 uT or B_1 = 3.6 uT were also collected for comparison, with all the other parameters same. The image parameters are: TR/TE = 8 s / 5.25 ms, EPI module time = 11ms and Matrix Size = 64x48. Z-spectra were acquired with the saturation offset incremented 0.3 ppm from -9.9 ppm to -6.9 ppm, and from 6.9 ppm to 9.9 ppm.

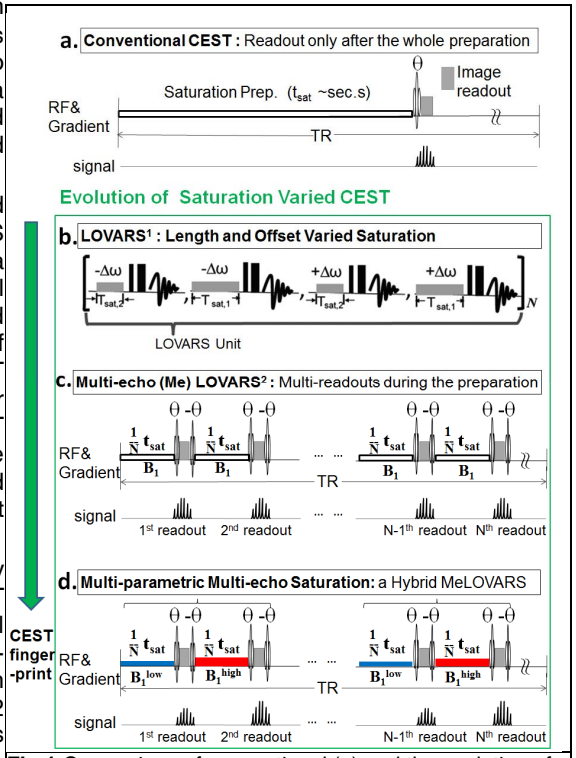

Fig.1 Comparison of conventional (**a**) and the evolution of our saturation-varied CEST schemes, from LOVARS (**b**), MeLOVARS (**c**) to the proposed Multi-parametric Multi-echo saturation (MMS) (**d**), for fast image acquisition of images with interleaved B_1 to modulate CEST contrast.

Results: Fig.2a shows the 8 CEST MTR_{asym} spectra acquired simultaneously by the hybrid MeLOVARS method for 5-Amino SA of pH=6.9, generating a CEST 'fingerprint' (the upper row), which is also similar morphologically to a real fingerprint. For the frequencies around the peak (8.7ppm here), the MTR_{asym} build-up pattern based on varied saturation B_1 and tsat, shows a more-oscillated pattern for pH 6.9 with a higher exchange rate (~900/s), compared with that for pH7.2 with a lower k_{ex}(~600/s). **Fig.2b** further compared the contrast build-up patterns acquired by the MMS, compared with the conventional MeLOVARS with only 7.2uT or with only 3.6uT. Based on a 2-pool Bloch-equation simulations, we generated the signal ocsillation patterns using MMS for multiple samples with distinct K_{ex} and concentrations. As shown, although their MTR_{asym} values are similar due to contributions from the concentrations (all conc. are 35mM for three curves of lower k_{ex} values), in MMS build-up curves higher k_{ex} (>500/s) shows additional high-frequency oscillations compared to the more-smoothed build-up patterns similar to previous QUEST/QUESP (**Fig.3c**).

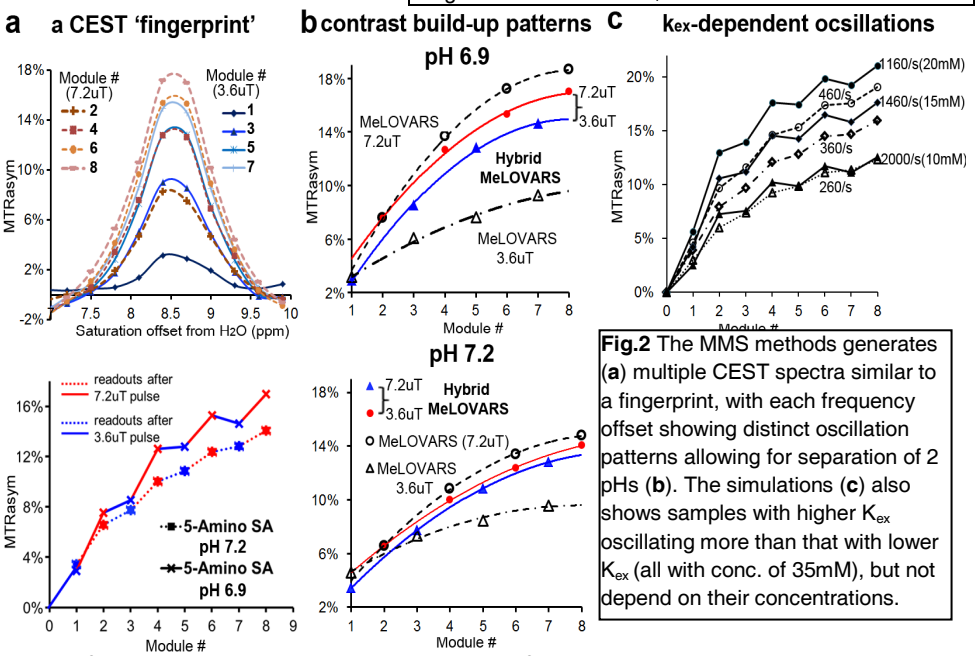

Fig.2 The MMS methods generates (**a**) multiple CEST spectra similar to a fingerprint, with each frequency offset showing distinct oscillation patterns allowing for separation of 2 pHs (**b**). The simulations (**c**) also shows samples with higher K_{ex} oscillating more than that with lower K_{ex} (all with conc. of 35mM), but not depend on their concentrations.

Discussion and Conclusion: Based on the idea of varied saturation CEST, we have developed Multi-parametric Multi-echo Saturation (MMS) method, so called a hybrid MeLOVAS methods, enabling fast acquisition of multi-parametric saturation weighted images. On phantom data, it allows separation of different pH solutions according their addition saturation-modulation patterns. This potentially allows separation of K_{ex} contributions to CEST contrast from the concentration contributions. It also has potentials *in vivo* for increasing the specificity of CEST imaging, with modulation of different sources of saturation contrasts.

References: [1]Song, et al MRM 2012 68(4): 1074. [2]Song, et al Proc. of ISMRM 2013#2545, [3]Yang & Song et al, Angew. Chem. Int. Ed., 2013, 52: 8116. [4]Song& Yang et al Contrast Media Mol Imaging. doi: 10.1002/cmmi.1597