Modeling MT Effect of Bound Water Pool and its use in Correction of CEST Contrast for MT Asymmetry

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INTRODUCTION

MRI of magnetization transfer (MT) effect (1), exhibited by water protons bound to solid like macromolecules, has been used to explore macromolecular environment of tissue under consideration. The magnitude of the MT effects is described by the so called MT ratio (MTR), in which MTR is equal to the ratio of water signal intensities with (S) and without (S_0) off-resonance irradiation. The z-spectra (1-4) of tissue, having bound water pool, are slightly asymmetric around the water resonance frequency (3, 4), with the center of the z-spectrum shifted slightly upfield (lower frequency) from the water signal. The amount of MT asymmetry (MTasy) is intrinsic parameter of tissue and can provide more insight into tissue environment. Independent observation of MT effect is not possible due to direct saturation (DS) of free water pool during z-spectra acquisition, and it appears as if the center of the z-spectrum is always assigned to free water spectrum. The MTasy interferes with chemical exchange transfer technique (CEST) contrast computation and usually underestimates or completely suppresses true CEST contrast. Potential applications of CEST technique is hampered by MTasy. Removal of MTasy contribution from CEST contrast is crucial before its application to explore *in-vivo* tissue environment and bio-chemical changes related to disease conditions. Studies have been carried out to model MT effect along with direct saturation using a two (5) and three pool model (CEST). However, reported model cannot separate pure MT effect required for MTasy removal from direct saturation and is computationally complex. Here a simple procedure is presented to model pure MT effect using a few frequencies data of z-spectra with negligible contribution of DS. This procedure is validated using numerical simulations of Bloch-McConnell equations (6) and *in-vivo* brain data. Current method is also tested for B_0 and B_1 in-homogeneities.

MATERIALS AND METHODS

Theory: Both DS of free protons and MT effect from saturated bound water protons contribute to z-spectra data. Basic strategy of current procedure is to choose a frequency ranges $\pm(F_2\text{-}F_1)$ at which DS is < 1% and MT effect is > 5% to model MT effect contributions to z-spectra using polynomial of degree 6. This polynomial is used for estimating entire MT data at [[$-F_2$, to F_2]] ppm. For example we used F_1=20ppm, F_2=50ppm for brain data obtained using a saturation pulse train with Hanning windowed rectangular pulses lasting for 1s with a peak B1 of 250Hz.

Simulations: Numerical simulations of Bloch-McConnell equations (6) with two (free & bound water) and three pool (free water, bound water and CEST (3ppm)), are used to model z-spectra with physiological parameters. The simulations were carried out with the same saturation pulse train as experiments. The bound water pool central frequency was manually shifted by -3ppm for generating data for testing accuracy of the current method. The parameters used in simulations were: T_{1w}=2s, T_{2w}=0.6s, T_{1m}=1s, T_{2m}=10µs, [M_a]=67M and 73M, [M_b]=13M and 8M. The simulations were also used to check the sensitivity of the current method to B_0 and B_1 in-homogeneities.

In-vivo Data: Three human volunteers were scanned for brain z-spectra data on 7T MRI scanner. The study was conducted under an approved Institutional Review Board protocol of the University of Pennsylvania. Here flash readout was used for acquiring magnetization prepared by saturation pulse. The z-spectra's with different saturation pulse amplitude (B_1=100Hz, 150Hz, 250Hz) were acquired.

MTasy Correction: Before CEST contrast computation, modeled MT effect was subtracted from CEST data.

***CEST contrast computation*:** The data was corrected for B_0 and B_1 in-homogeneities, using B_0 and B_1 maps and neighborhood frequency data, before CEST contrast computation. Contrast is computed using equation, *CEST=100*[S(-ppm) – S(+ppm)]/S(-ppm)*. Normalization by –ve ppm instead of S_0 is essential for CEST in order to minimize contribution from DS and MT effect.

RESULTS AND DISCUSSIONS

The z-spectra generated using simulations, modeled MT and extracted DS curve for B_1=250Hz, 1s and B_1=100Hz, 3s are shown in Fig.1A and 1B respectively. For demonstration of proposed method in *in-vivo* situation, brain z-spectra with B_1=250Hz and 2s duration are used. In Fig.2, z-spectra, modeled MT and extracted DS curve from cingulated gyrus (CG) region of *in-vivo* human brain is shown. Fig.3 shows CEST asymmetry (CESTasy) curves from CG and corpus callosum (CC)

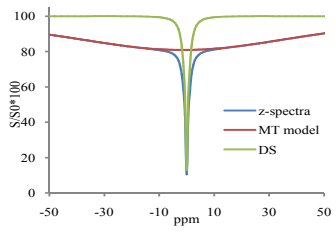

Fig.1A: z-spectra (blue) using simulations, modeled MT (red) and extracted DS curve (green), B_1=250Hz, 1s

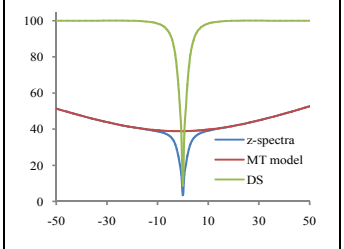

Fig.1B: z-spectra (blue) using simulations, modeled MT (red) and extracted DS curve (green), B_1=100Hz, 3s

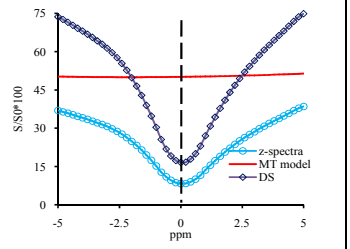

Fig.2: Z-spectra, MT model and extracted DS curves from brain tissues (CG)

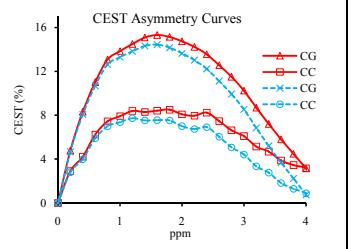

Fig.3: CESTasy curves without (dotted line) and with (solid line) MTasy correction from human brain.

without (dotted line) and with (solid line) MT asymmetry correction. MTasy correction increases the CEST contrast observed. CESTasy curves from white matter (WM) regions of brain (example, CC) showed higher differences between without and with MTasy correction compared to gray matter (GM) regions (example, CG). This is in consistence with high MT effect in WM tissues compared to GM. Differences become larger at higher frequencies. In CG estimated center of MTasy was -2.2ppm and in CC -2.8ppm, which is in agreement with previously reported shift. Current procedure for modeling MT from z-spectra is insensitive to small field in-homogeneities. However, computation of CEST contrast requires B_0 and B_1 correction. Other functions like Lorentzian may also be used in place of polynomial fitting and for optimization; further studies are being carried out. In conclusion, current procedure can model pure MT effect; can be used to remove MTasy contribution in CEST contrast; is simple and robust. Further studies for optimization of this procedure are in progress.

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