The Non-Linearity of CEST and MT Signal Combination

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1. Introduction Chemical exchange saturation transfer (CEST) contrast in biological tissue is normally composed of CEST contrast and magnetization transfer (MT) effect. The asymmetric MT interference from semi-solid macromolecular protons complicates the issue of quantitative CEST measurements.[1,2] Several methods were proposed to eliminate intrinsic MT effect through post-imaging mathematical processing or novel sequence design[3-5]. However, the signal-merging algorithm of CEST contrast and MT interference remains unclear, which may be linear or nonlinear. In this study we performed both numerical simulation and phantom experiments to verify the linear assumption of CEST and MT effects.

2. Methods The Z-spectrum was modeled as a combination of CEST effect from Creatine molecule, MT effect from agar gel, and direct saturation effect of water molecule (W). [5] Therefore, the observable Z-spectra of water, Creatine aqueous solution, gel, and Creatine gel solution are assumed as linear combinations as follows: $Z_{water}= S_0-W$, $Z_{Cre(aq)}=S_0-W-CEST$, $Z_{gel}=S_0-W-MT$, and $Z_{Cre(gel)}=S_0-W-MT-CEST$, respectively, where S_0 represents the unsaturated signal intensity. By definition, The CEST and MT effect can be separated by subtraction of observed Z-spectra : $CEST= Z_{water} - Z_{Cre(aq)}$, $MT= Z_{water} - Z_{gel}$. Under the linear assumption, the simultaneous *CEST&MT* effect equals to $Z_{water} - Z_{Cre(gel)}$, which is speculated to be identical to the sum of CEST and MT effect. Therefore, we use simulation and phantom study to verify this equality.

Simulation: A three-pool model refer to Desmond et al.'s work was used for computer simulation of CEST Z-spectrum. Seven Bloch equations were involved in describing the interactions between bulk water, CEST and MT pool. Matlab function *ode45* was used to solve the seven equations with the relative tolerance value of 10^{-6}. Six seconds continuous wave (CW) saturation process was carried out with simulation parameters: power=1μT, f_{sw}=0.4, f_{mw}=0.025, k_{sw}=100, k_{mw}=48, $T1_w$=3s, $T2_w$=1s, $T1_s$=2.85s, $T2_s$=41ms, $T1_m$=1s, $T2_m$=15μs, where f_{sw} and f_{mw} represents the magnetization ratio of solute to water and MT to water, respectively. *Phantom:* As shown in Fig. 1, a triple phantom was prepared by pure water, 50mM Creatine in water and in 3% agarose solution, which were filled into three 6mL class tubes and put into a 50mL centrifuge tube with 3% agarose in the outer compartment. Imaging experiments were all performed on a 4.7T Bruker Biospec 47/40 spectrometer with a volume coil for both transmission and reception. The central frequency was carefully adjusted and Fastmap shimming was used to minimize field inhomogeneity. Single-shot spin-echo EPI was employed for signal acquisition followed by 1.25μT, 4s CW irradiation. Imaging parameters were: FOV=4.5x4.5cm, matrix size=64x64, slice thickness=5mm, TE=50ms, TR=11.5s. The off-resonance frequencies of CW RF were swept between ±600Hz of water frequency with a step of 100 Hz. Z-spectra and MTR_{asym} were evaluated using self-written MATLAB scripts.

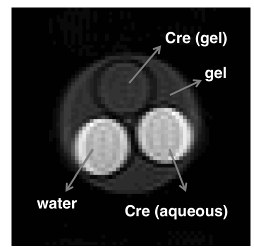

Fig. 1 Phantom image.

3. Results Fig. 2(a) shows the simulated Z-spectra of pure water (Z_{water}), Creatine aqueous solution ($Z_{Cre(aq)}$), gel (Z_{gel}), and Creatine gel solution ($Z_{Cre(gel)}$). As mentioned previously, the effect of CEST, MT, simultaneous CEST&MT, and linear adding CEST+MT can be demonstrated as Fig. 2(b). The calculation revealed that the linear addition of CEST and MT signal (CEST+MT, green dash line) was profoundly higher than the simultaneous CEST&MT effect (black solid line). This numerical simulation revealed that mathematical linear combination fail to describe the correlation of CEST and MT effect. In the phantom experiment, the measured Z-spectra demonstrated a consistent result with numerical simulation, as shown in Fig. 1(c).

4. Discussions In the presence of MT effect from pool of macro-molecules, the linear added CEST contrast was shown to be overestimated approximately 25% than the realistic simultaneous CEST&MT effect. This gap is speculated that MT pool would catch a portion of free bulk water and decrease the CEST signal during chemical exchange process. As a result, it is incorrect to eliminate MT effect through simple linear model calculation. The calculation of asymmetric of MT ratio could be further hampered under the linear assumption. We should be cautious dealing with the signal combination algorithm since the interactions between CEST pool and MT pool may be complicate. Factors such as relative magnetization ratio of MT and CEST, power of saturation period, pH value and T1/T2 are possible to affect the interaction. Comprehensive study of CEST and MT relationship is needed for reducing the asymmetric MT effect, which is one of the important steps for quantitative analysis of CEST contrast.

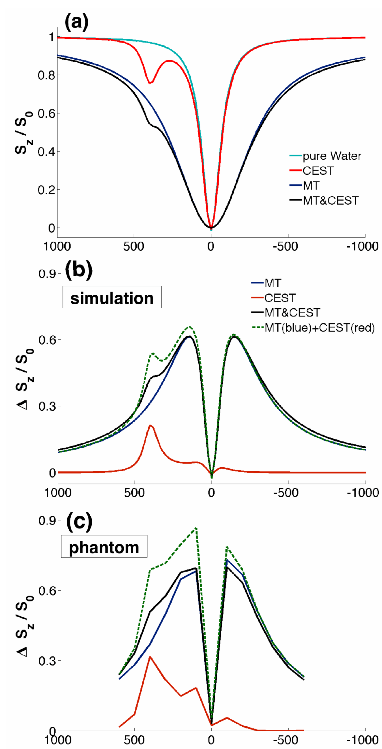

Fig. 2 (a) Simulated Z-spectrum and, (b) Z-spectrum signal after calculation. The linear adding signal was higher than simultaneous CEST&MT. (c) Phantom experiment suggested same result.

References

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