Chemical Exchange Saturation Transfer (CEST) Imaging with Double Angles and Varying Duty Cycles

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Target Audience: Investigators who are interested in chemical exchange saturation transfer (CEST) imaging.

Purpose: CEST has emerged as a novel imaging contrast with the capability of detecting metabolites in biological tissues. Conventional CEST contrast is obtained by calculating the magnetization transfer ratio asymmetry (MTR_{asym}). In *in vivo* studies, the measured CEST contrast is influenced by the MT asymmetry of the macromolecular proton pool and nuclear overhauser enhancement (NOE). This work describes the development of a new metric, named magnetization transfer ratio with double angle and varying duty cycles ($MTR_{double,vdc}$), based on pulsed-CEST and previously developed chemical exchange rotation transfer[1,2]. A π pulse train at a high duty cycle (dc) (83.8% in this work) is used to maximize exchange effects; while a 2π pulse train at a low dc (20.95% in this work) is used to minimize such effects. The MT and direct saturation effects are approximately the same, so the difference in the label signals provides a contrast that is primarily from chemical exchange. The equivalency of this approach to an ideal continuous-wave (CW) experiment is demonstrated.

Methods: Numerical simulations: A three-pool model of tissue protons containing macromolecular, free water and amide protons with a chemical exchange rate of 50 Hz was adopted. To investigate the dependence of pulsed-CEST on irradiation flip angle (iFA) and dc, iFA was varied between 120° and 900°, stepped by 30°, and dc was varied between 20.95% and 83.8% at five levels. The average saturation power was set at 0.6 μT. To demonstrate the proportionality of $MTR_{double,vdc}$ vs. MTR_{asym}(CW), model system parameters were varied systematically within broad ranges. The dependence of the ratio on average irradiation power and B_1^+ field inhomogeneities was also simulated. A four-pool tissue model with MT asymmetry and NOE included was also simulated.

Data acquisition: All data were acquired on a 9.4T Agilent MRI scanner. All data were acquired with a spin-echo echo-planer-imaging sequence. A creatine/agar phantom served as a three-pool model with no MT asymmetry. The *in vivo* data were acquired from male Fischer 344 rats. Pulsed- (2π with dc of 20.95%, π with dc of 83.8%) and CW-CEST data were collected at average power of 1 uT. B_0 maps were determined using the WASSR method[3].

Data processing: All data were corrected with B_0 maps on a pixel-wise basis and interpolated to steps of 1 Hz in RF offsets.

Results and Discussion:

Fig. 1 shows the simulated reference and label signals of pulsed-CEST vs. iFA and dc. The signals of a CW sequence at the same average irradiation power were also plotted. It can be seen that the difference between the signals using a π pulse at a high dc and 2π pulse at a low dc will provide the maximum CEST contrast, and their signals at the negative offsets are approximately the same. The ratio of $MTR_{double,vdc}$ vs. MTR_{asym}(CW) is ~60% for all simulated parameter ranges, and at non-optimal powers. In the phantom, the obtained ratio was generally in agreement with the simulations. Fig. 2 shows $MTR_{double,vdc}$ and MTR_{asym}(CW) from a ROI defined in the gray matter in the rat brain *in vivo*. It can be seen that with the presence of MT asymmetry and NOE, the measured MTR_{asym}(CW) values are negative. However, $MTR_{double,vdc}$ always yields positive contrast. Representative amide, amine, and two NOE contrast maps are shown in Fig 3.

Conclusion: The new metric, $MTR_{double,vdc}$, takes the advantage of the dependence of pulsed-CEST label signal vs. iFA and dc, while the MT and spillover effects are generally only a function of average irradiation power. The approach enhances the contrast in CERT (previously acquired at constant dc[1]), eliminates the possible contamination from neighboring exchanging sites seen in three-offset fitting methods[4], and does not have the strong model dependence seen in lineshape fitting methods[5,6]. Numerical simulations indicate that this contrast is approximately proportional to what the CW contrast would be in ideal conditions for a wide range of model parameters, indicating that this approach could also be potentially extended to analytical approaches for quantitative CEST imaging. The measured $MTR_{double,vdc}$ in phantoms and rat brain in vivo demonstrate the feasibility of this approach in practical imaging. For imaging metabolites at low frequency offsets, such as creatine-CEST and glycol-CEST, or to obtain contrast at higher average irradiation powers, the $MTR_{double,vdc}$ approach may be more challenging. Another challenge lies if B_1^+ field inhomogeneities are significant, because they cause strong oscillations around the π pulse.

References: 1. Zu, MRM 2011. 2. Zu, MRM 2013. 3. Kim, MRM, 2009. 4. Jin MRM 2013. 5. Zaiss, JMR, 2011. 6. Scheidegger, Neuroimage 2014.

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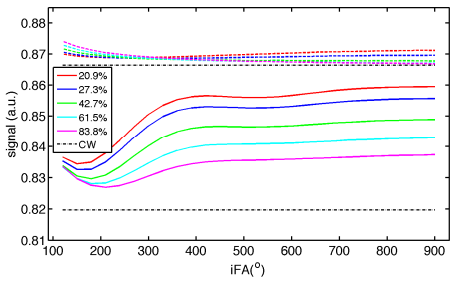

Fig. 1 The simulated pulsed-CEST label signal vs. iFA and DC for an APT model.

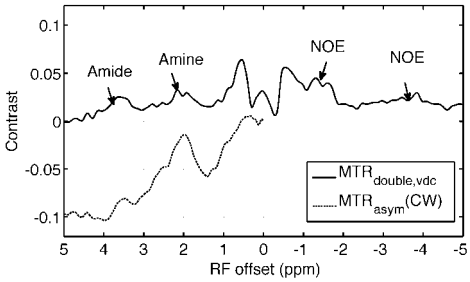

Fig. 2. The $MTR_{double,vdc}$ and MTR_{aysm}(CW) in gray matter of a rat brain.

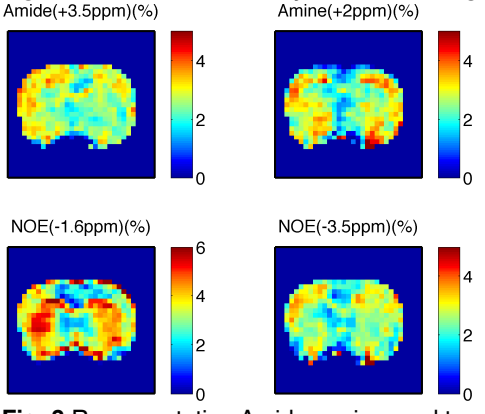

Fig. 3 Representative Amide, amine, and two NOE contrast maps obtained from the $MTR_{double,vdc}$ approach.