Importance of saturation power optimization in improving the estimation accuracy of chemical exchange rates with the omega plot: a simulation study

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Introduction: Chemical exchange saturation transfer (CEST) MRI is a sensitive method for measuring chemical exchange rates, which facilitates the quantification of CEST agent concentration [1] and molecular biomarkers (e.g., pH) [2] for investigation of numerous disorders, including acute stroke and tumors [3, 4]. The omega plot has proved accurate in quantifying PARACEST at slow exchanging rates without a priori knowledge of the labile proton ratio and relaxation rate [5]. However, its accuracy in measuring protons at small chemical shifts was found to decrease [6]. Suboptimal saturation powers applied may be one of the potential reasons due to their great impact on the omega plot linearity [5]. In this study, simulations were performed to investigate the importance of saturation power on the omega plot performance for protons with small chemical shifts at varied exchanging rates, from which an optimal range of saturation powers was determined to improve the estimation accuracy of exchange rates.

Methods: In the omega plot, the X-axis intercept provides a direct readout of the exchange rate k_{sw} from the linear plot of $M_{SS}/(M_0 - M_{SS})$ versus $1/\omega_1^2$, where M_{SS} is the steady-state signal at the labile proton frequency, M_0 is the equilibrium magnetization for bulk water, and ω_1 is the saturation power [5]. In this study, continuous-wave CEST MRI was numerically simulated using the Bloch-McConnell equations for a magnetic field strength of 4.7T. Representative relaxation parameters of T_1 and T_2 were 3s and 2s, respectively, for bulk water, and 0.77s and 33ms for the labile proton group. Simulations tested three typical chemical shifts (Δω) of 1.9, 3.5 and 5.0 ppm, and three exchange rates of 25, 50, and 100 s^{-1} with the labile proton to water ratio of 1:2000 and saturation time of 15 s [7, 8]. $M_{SS}/(M_0 - M_{SS})$ as a function of $1/\omega_1^2$ was compared between the desired omega plot and the simulated results, between which the relative difference percentage smaller than 5% was identified with respective saturation powers regarded as optimal for the exchange rate estimation. Exchange rates estimated from the optimal and entire saturation powers were denoted as k_{sw}^{opt} and k_{sw}^{full}, respectively.

Results: The desired omega plot and the simulated results of protons at varied chemical shifts and exchange rates were illustrated in Fig. 1. Briefly, strong saturation powers (i.e., small $1/\omega_1^2$) tended to deviate the omega plot upward from the simulated results, while weak saturation powers (i.e., large $1/\omega_1^2$) likely tilted the omega plot downward. The omega plot exhibited good consistency with the simulated results at intermediate saturation powers (shadow) where estimation accuracy of exchange rates was substantially improved compared to that estimated from the entire range of saturation powers. The optimal saturation power for labile protons with larger chemical shift or faster exchange rates were observed to be stronger than that for protons with smaller chemical shifts or slower exchange rates. Z-spectrums of protons with 3.5 ppm chemical shift and 50 s^{-1} exchange rate saturated with different powers were shown in Fig. 2, where attenuated CEST contrast and non-negligible spillover effect was respectively exhibited for insufficient (blue) and too strong (red) saturation powers compared to that of the optimal ones (shadow).

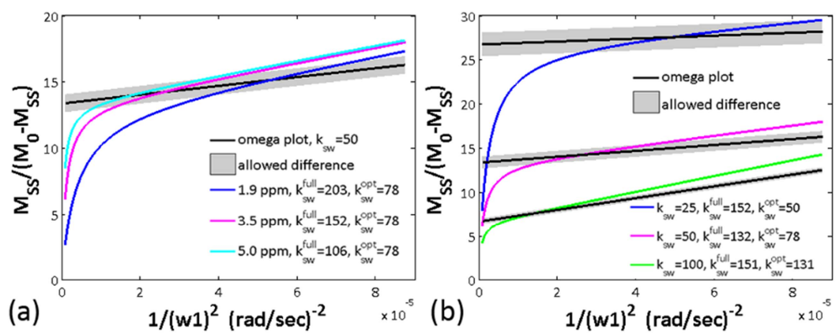

Fig. 1 Comparisons of the omega plot with the simulated results at varied (a) chemical shifts and (b) exchange rates (with unit of s^{-1}).

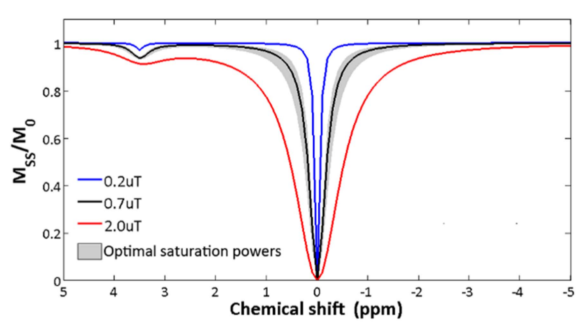

Fig. 2 Z-spectrums under different saturation powers.

Discussion and Conclusion: The omega plot is a facile method to quantify exchange rates. However, its estimation accuracy is found to degrade especially for protons at small chemical shifts where the model assumptions tends to be violated under certain saturation powers [5]. In this study, optimal saturation powers were identified by examining the consistency between the desired omega plot and the simulated results. The optimal saturation powers were observed to be associated with chemical shifts and exchange rates, due to the different competence with the spillover effects for complete saturation [7]. Simulation results showed substantially improved estimation accuracy of exchange rates with optimized saturation powers compared to those fitted from a wide range of saturation powers as conventionally adopted [6]. Note that the estimation accuracy could be further improved with stricter allowed difference between the omega plot and simulated results. The current study confirmed the crucial influence of saturation powers on omega plot performance for protons at small chemical shifts, and demonstrated the importance of saturation power optimization in improving the estimation accuracy of chemical exchange rates.

References: [1] Sun et al., JMR 2010; [2] Liu et al., Mol Imaging 2012; [3] Zhou et al., Nature Medicine 2011; [4] Tietze et al., NMR Biomed 2014; [5] Dixon et al., MRM 2010; [6] Randtke et al., MRM 2014; [7] Sun et al., JMR 2005; [8] Sun et al., MRM 2011.