An Improved Empirical Solution for Describing Chemical Exchange Saturation Transfer (CEST) MRI

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Introduction Both numerical simulation and analytical solution have been developed to describe CEST MRI phenomenon, which have aided our ability to quantify and optimize CEST imaging [1,2]. In fact, a concise empirical solution has been proposed which decomposes CEST contrast as a product of the "ideal" contrast, saturation coefficient and spillover factor [3]. However, the empirical solution is only a first order approximation and susceptible to non-negligible errors when describing fast exchange CEST agents with intermediate RF power. While on the other hand, there has been enormous interest of developing PARACEST and LIPOCEST agents of fast exchange [4-7]. Hence, it is necessary to improve the precision of the empirical solution so as to establish the theoretical framework for guiding such efforts.

Theory The proton transfer ratio (PTR) is given as $PTR = k_{ws}/r_{1w} \cdot \alpha \cdot (1-\sigma)$, in which k_{ws} and r_{1w} are the backward chemical exchange and apparent relaxation rates of water, α and σ are the saturation coefficient and spillover factor, respectively [3]. The simplistic empirical solution is essentially a normalized product of solutions for weak and strong RF irradiation pulse. While it approximates the exact solution for cases of very strong and extremely weak RF irradiation, previous empirical solution is prone to errors when describing fast exchangeable protons under intermediate RF powers. Hence, higher order correction terms need to be added to improve its precision. Specifically, the spillover factor was obtained under the assumption that labile protons are fully saturated, which of course is not fulfilled for finite RF powers. In fact, the spillover factor (1-σ) is overestimated and should be modulated by the ratio of unsaturated protons given as $c = 1 - k_{ws}/r_{1w} \cdot (1-\sigma) \cdot (1-\alpha)$, and the corrected PTR (cPTR) is equal to $cPTR = \frac{k_{ws}}{r_{1w}} \cdot \alpha \cdot (1-\sigma) \cdot \left[1 - \frac{k_{ws}}{r_{1w}} \cdot (1-\alpha)\right]$.

Materials and Methods Numerical simulation and data processing routines were written in Matlab (Mathworks, Natick MA) with representative parameters. Specifically, the ratio of labile protons to bulk water was set to be 1:1,000, and longitudinal relaxation times for water and labile protons were 1.5 s and 1 s, with their transverse relaxation times being 1 s and 30ms, respectively. A typical labile proton frequency offset of1,400 Hz (i.e., 3.5ppm at 9.4T) was used, and the RF irradiation power was varied from 0 to 5 μT (i.e., 0 ~200 Hz). For each RF power, the CEST MRI contrast was obtained by taking the difference of normalized MT ratio asymmetry at the reference and label offset (i.e., ±1,400 Hz).

Results and Discussion The empirical solutions and numerical simulation were compared in Fig.1. Specifically, Fig.1a shows the simplistic empirical PTR solution (solid red) as a normalized product of labeling coefficient (α) and spillover factor (1- σ). In contrast, Fig. 1b shows the modulation factor compensated spillover factor c· (1- σ). It is important to note that the compensated spillover factor (solid green) is less than the simplistic solution (dashed green), in particular for weak and intermediate RF powers. It is so because the assumption that labile protons are fully saturated is invalid for finite RF powers, and hence, the CEST MRI is susceptible to less spillover effects than predicted. Fig. 1c compares numerical simulation (green circles), simplistic PTR (solid red) and compensated PTR (solid blue), which indicated that the proposed compensated PTR solution agrees well with numerical simulation, significantly improved from the simplistic solution method. In fact, the difference between empirical solutions and numerical simulation is given in Fig. 1d. The error for simplistic PTR solution (ΔPTR) was 6.5 ± 2.9% (mean ± S.D.) for RF power between 0 and 5 μT, in contrast to 1.1 ± 1.0% found for the proposed compensated PTR solution (ΔcPTR). In summary, our study showed that by taking into account of the second order correction term, the compensated PTR significantly improved the precision of the empirical solution, in excellent agreement with numerical simulation for a wide range of RF power. As such, the proposed formula is suitable to quantify CEST MRI for a wide range of experimental conditions, and may eventually help guide the development of novel and sensitive exogenous CEST agents.

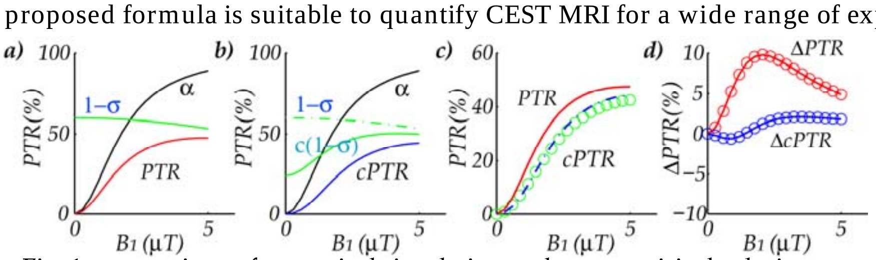

Fig. 1, comparison of numerical simulation and two empirical solutions. a) simplistic empirical solution. b) spillover effect corrected PTR (cPTR). c) cPTR agrees well with numerical simulation, better than PTR. d) cPTR shows significantly reduced error when compared with simplistic PTR.

References

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