Enhancement of endogenous CEST effects by optimizing pre-saturation pulse train properties

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Introduction

Amide proton transfer (APT), a sub-type of chemical exchange saturation transfer (CEST), uses the chemical exchange between amide and bulk water protons in cells to create a contrast in MR imaging [1-2]. Parameters which influence the transfer rate can be obtained from analysis of the z-spectra. The commonly employed theory [3] is based on assumption of continuous wave (cw) RF pre-saturation which is restricted in clinical MRI systems. Moreover, pulse trains with equivalent power as cw saturation [4] are expected to reach the maximum effect with long saturation (sat) pulses. In this study the asymmetry effect is optimized by pulse length t_p and interpulse delay t_d especially for pulse trains of Gaussian pulses. The investigation shows an optimum for pulse lengths in the range of 10 ms depending on B_1 and frequency offset of the proton pool of interest.

Theory

For comparison of pulsed irradiation to cw irradiation, Gaussian pulses with a cw equivalent power deposit during pre-sat are calculated by

$$f(t,t_0) = B_{1,\max} \cdot \exp\left(\frac{-(t-t_0)^2}{(2\sigma^2)}\right), \qquad B_{1,\max} = \frac{\sqrt{t_p + t_d}}{\sqrt{\sqrt{\pi}\sigma}} \cdot B_1, \qquad \sigma = \frac{t_p}{6}$$

Which are concatenated to a pulse train of n pulses with the effective sat time $t_s = n \cdot (t_p + t_d)$.

After saturation and acquisition of the z-spectrum signal S, the asymmetry is calculated by $MTR_{asym} = (S(-\Delta\omega) - S(\Delta\omega))/S_0$. In the pulsed case MTR_{asym} is altered by time dependent spillover effect, influences of spoiling, spectral RF distribution and relaxation effects during interpulse delays. So, the available MTR_{asym} can be optimized by choice of duty cycle and pulse number n, which, for constant t_s, imply t_p and t_d.

Table 1: simulation parameters

Pool	Water	CEST
M_0	*1*	*0.002*
T_1	*450 ms*	*1000 ms*
T_2	*220 ms*	*15 ms*
offset	*0 ppm*	*1.9 ppm*
k	*0.25 Hz*	*125 Hz*

Materials & Methods

The time dependent 2-pool-Bloch-McConnell equations with transfer terms were solved by common numeric solutions [5] discretised in time domain. In simulations with Gaussian pulse trains with a cw equivalent power of B_1=2μT and a constant saturation time t_s=300 ms the duty cycle $t_p/(t_d+t_p)$ was varied from 50-100% and n was varied from 1 to 60 pulses with spoiling after each pulse. The asymmetry of z-spectra simulated with the parameters of table 1 at B_0=3 T was calculated.

Phantom experiments with 50 mM creatine dissolved in phosphate buffered saline at pH=7.4 were performed on a clinical tomograph (Magnetom Trio; Siemens Healthcare, Erlangen, Germany) with B_0 of 3T using a standard 32 channel head coil. Signal was acquired with a 3D RF-spoiled gradient echo (GRE) sequence with Gaussian-shaped pre-sat pulses (B_1: 2 μT, t_s=300 ms, duty cycle 50%) before each acquisition of 19 data points of each z-spectrum. Spoiler gradients in all 3 directions were applied after each sat pulse. Matlab 7 (The Mathworks, Natick, MA, USA) was used for data analysis.

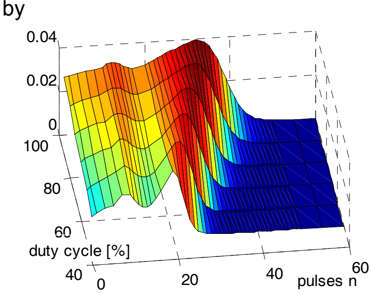

Figure 1: simulated MTR_{asym}(1.9 ppm, 2 μT) over duty cycle and pulse number n

Results & Discussion

Figure 1 shows simulated MTR_{asym}(1.9 ppm) as a function of duty cycle and number of pulses n. A high duty cycle enhances MTR_{asym} in all cases. The dependence on the pulse number n is surprising: The cw analogue case (n=1 and duty cycle of 100%) does not yield optimal MTR_{asym}. Instead, for duty cycle of 100% maximum MTR_{asym} is found at n=32. For duty cycle 50% there is a maximum at n=20 where t_p = t_d = 7.5 ms. In addition, there is a smaller lobe at n=9 where t_p = t_d =16.7 ms. The bump in MTR_{asym} follows a line of constant t_p=8.5 ms demonstrating the relationship between this parameter and the saturation bandwidth $\sigma_{RF}=1/t_p\approx 1$ ppm of a Gaussian pulse and shows the range of influence of "pulsed spillover". The delay t_d seems to cause only effects of relaxation. Figure 2 shows the distorted z-spectra which result from short pulses: for n=15 the direct saturation minimum vanishes and there are side lobes in the z-spectrum that weaken the asymmetry (Fig. 3). For n=19 the side lobes show to produce lower spillover near the CEST resonance and therefore the asymmetry increases. Differences between simulation and measurement are attributed to different relaxation parameters, but also B_1 and spoiling inhomogeneities in the experiments. Due to the formation of the side lobes, the optimization strongly depends on the absolute value of B_1 and the offset of the CEST pool of interest. The same useful substructures showed up in z-spectra of egg white measurements with *in-vivo*-like properties (no data shown).

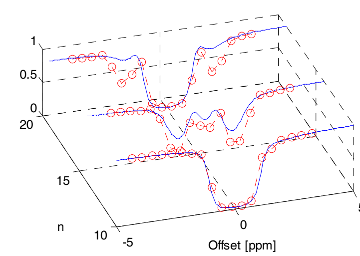

Figure 2: meas. (circles) and simulated (solid) z-spectra (B_1=2μT)

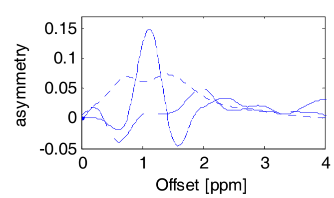

Figure 3: measured asymmetry (spline interpolation) for n=19 (solid), n=15 (dashed) and n=10 (dotted)

Conclusion

CEST employing Gaussian pulsed saturation can be optimized by using the explicit time dependency of Bloch-McConnell equations. Simulations enables prediction of optimal pulse lengths (order of ms) in contrast to single cw-like pulses. In excess of cw spillover effect, a pulsed spillover effect was found to dilute MTR_{asym} within $\Delta\omega\approx 1/t_p$. The proposed Gaussian pulse schemes are feasible in clinical MRI scanners and promise optimized and selectively enhanced detection of labile protons localized in small metabolites and their transfer properties *in vivo*.

References

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