Optimization of RF saturation to minimize B_0 inhomogeneity effects in pulsed amide proton transfer imaging

R. Scheidegger[1,2], E. Vinogradov[1,3], and D. C. Alsop[1,3]

[1]Radiology, Beth Israel Deaconess Medical Center, Boston, MA, United States, [2]Health Sciences and Technology, Harvard-MIT, Cambridge, MA, United States, [3]Radiology, Harvard Medical School, Boston, MA, United States

Introduction

Chemical exchange saturation transfer[1] (CEST) of the amide protons present on the backbone of proteins and peptides – dubbed amide proton transfer imaging - has shown promise as an indicator of tissue pH[2] and as a marker for brain tumors[3]. In order to maximize the CEST contrast, RF irradiation power must be optimized to maximize saturation of amide protons resonating at 3.5ppm, while minimizing direct water saturation. Because the applied RF frequency is very close to the free water frequency, strong direct saturation effects are unavoidable and vary quickly with the center frequency of the water line. Thus, APT imaging is strongly dependent on B_0 homogeneity and is prone to severe susceptibility artifacts. The goal of this abstract was to optimize the RF irradiation scheme in order to minimize the APT dependence on B_0. By using pulsed-RF saturation, the pulse profile, pulse width and interpulse delay can be varied to modulate the frequency selectivity of the irradiation. This allows maximizing the CEST contrast while decreasing RF spillover. In addition, we introduce a new magnetization transfer ratio (MTR) parameter based on a three-way subtraction and show it further decreases the dependence of APT on B_0 homogeneity compared to traditional MTR asymmetry analysis.

Methods

The APT contrast was modeled using the Bloch equations for a two-pool exchange model[4]. Numerical simulations were performed in Matlab, with amide proton content M_{0s}=1:1000 M_{0w}, longitudinal relaxation times T_{1w}=1.5s, T_{1s}=0.77s, transverse relaxation times T_{2w}=60ms, T_{2s}=33ms and chemical exchange rate from amide group to free water k_{sw}=30Hz. The RF pulse train consisted of 800 inversion pulses with either Gaussian, Hanning or Blackman profile. Pulse width (pw) was varied from 3ms to 30ms and interpulse delay (τ_d) from 1ms to 100ms. B_0 inhomogeneity (ΔB_0) was varied from -2ppm to 2ppm. APT MRI contrast was quantified by the magnetization transfer ratio asymmetry parameter: $MTR_{asym}(3.5ppm) = [S_{sat}(-3.5ppm) - S_{sat}(+3.5ppm)] / S_0$. In addition, a new Saturation with Frequency Alternating RF Irradiation (SAFARI) was evaluated where RF pulses are applied alternating between positive and negative offset (S_{sat} (±3.5ppm). Using this approach the APT MRI contrast was quantified by: $MTR_{SAFARI} = [\ S_{sat}(+3.5ppm) + S_{sat}(-3.5ppm) - 2\ S_{sat}(\pm\text{-}3.5ppm)] / S_0$. Because the water line is symmetric applying single frequency irradiation at 3.5ppm should be identical to alternating irradiation at frequencies –3.5ppm and +3.5ppm with the same total power. The amide protons however will experience full saturation at 3.5ppm, no saturation at -3.5ppm and saturation at half the power with SAFARI. As a result MTR_{SAFARI} will be zero for direct water saturation effects, but will retain APT contrast.

Results and discussion

1) Pulse shape: To minimize errors due to B0 inhomogeneity we want an RF pulse shape with frequency selectivity approximating a rectangular pulse with bandwidth = 2.5ppm. This pulse would saturate the amide protons in the presence of $\Delta B_0 \leq$ 1ppm, without saturating the water line up to ΔB_0 = 2ppm. All three pulses examined had very similar frequency profile for a given pulse width, but the Blackman pulse had decreased sidelobes compared to the Hanning pulse. Fig 1a,c show the amide proton contrast obtained when off resonance Blackman pulses are applied. For MTR_{asym} (Fig. 1a), 15ms pulses achieve 50% effect at ±1ppm, however, they do not suppress the signal well outside the desired range. MTR_{SAFARI} (Fig. 1c) shows improved selectivity compared to MTR_{asym} and 10ms to 15ms pulses yields the desired frequency selectivity

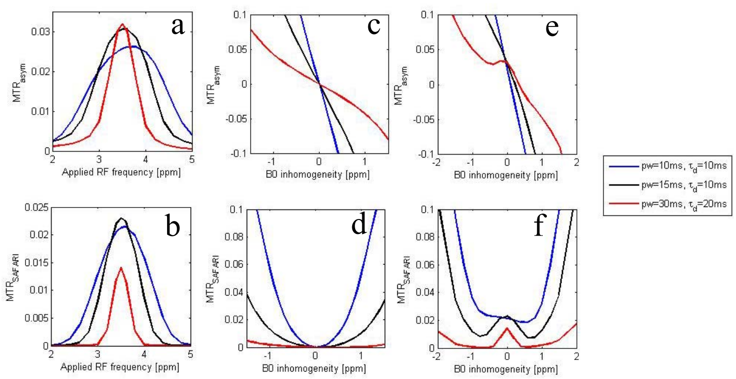

Fig. 1: Top: MTR_{asym} , bottom: MTR_{SAFARI} for a,b) ΔB_0=0, k_{sw}=30Hz, 2ppm<ω_{RF} <5ppm; c,d) k_{sw}=0 , -1.5ppm<ΔB_0<1.5ppm, ω_{RF} =3.5ppm; e,f) k_{sw}=30Hz and -2ppm<ΔB_0<2ppm, ω_{RF} =3.5ppm.

2) Interpulse delay: To optimize the CEST contrast direct water saturation must be minimized while achieving efficient amide saturation (Fig 2). For a given pw water saturation can be decreased by increasing τ_d, however, τ_d must remain on the order of ~1/k_{sw} to saturate the amide protons. Fig. 2a,b show MTR_{asym} and MTR_{SAFARI} for varying pulse widths and interpulse delays. MTR_{asym} was maximized for 30ms pulses with τ_d =1ms while MTR_{SAFARI} was maximized for 15ms pulses with τ_d =1ms. Note that in practice τ_d must be at least 2/3 of pw, which still gives close to maximum contrast for 15ms and 30ms pulses.

3) Saturation scheme. In order to minimize the errors due to asymmetric water saturation in the presence of ΔB_0 MTR_{asym} and MTR_{SAFARI} must be zero in the absence of chemical exchange (Fig. 1c,d) MTR_{asym} increases quickly as B_0 homogeneity deteriorates (Fig. 1c). MTR_{SAFARI} is much more stable and remains zero with up to ±1ppm inhomogeneity for 30ms pulses (Fig. 1d). Including chemical exchange, Fig. 1e,f show the competing effect between increased MTR parameters due to asymmetric water saturation in the presence of inhomogeneity and decreased amide proton saturation due to off-resonance labeling. For MTR_{asym}, 30ms pulses retain CEST contrast the best but direct water saturation still dominates, and the CEST effect is no longer detectable for ΔB_0 greater than a few tenths of a ppm. In contrast, MTR_{SAFARI} has almost no error due to direct water saturation for ΔB_0 < 1ppm and the CEST contrast is dominated by the ability of the RF pulse to maintain efficient amide proton saturation. This is optimum for the 10ms Blackman pulse.

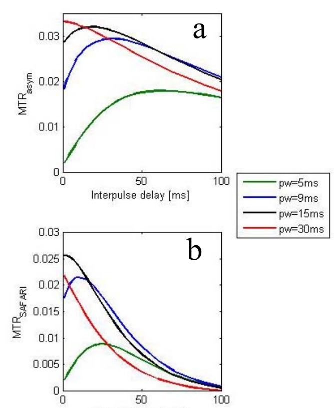

Fig. 2: Optimization of MTR_{asym} (a) and MTR_{SAFARI} (b) as a function of τ_d and pw.

In summary, MTR_{asym} is maximized with Blackman pulses (pw=30ms, τ_d =20ms) while withstanding B_0 inhomogeneity below ±0.3ppm. MTR_{SAFARI} is maximized with Blackman pulses (pw=10ms, τ_d =10ms) while withstanding B_0 inhomogeneity below ±1ppm.

References: (1) Ward et al JMR 2000;143:79-87. (2) Zhou et al. Nat Med 2003; 9:1085-1090. (3) Jones et al MRM 2006;56:585-592. (4) Woessner et al. MRM 2005;53:790-799.