Increased CNR in On-Resonance PARACEST Imaging

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Introduction

On-resonance PARACEST (1) uses a short, low power on-resonance 360° Waltz pulse (2). Non-exchanging spins will be rotated a full 360°, whereas exchanging spins will be rotated less than 360° and produce a decrease in the measurable water signal. This technique is appropriate for fast exchanging lanthanide complexes (e.g., Tm) and is sensitive to all offset frequencies. In the presence of significant macromolecular content (e.g., in vivo) the measurable signal is decreased (3) by up to 90% even without PARACEST agents present. This results in a significant decrease in dynamic range of the measurable signal. We propose to use a delay after the Waltz pulse to allow the signal to regrow with T1 to produce a larger signal dynamic range and more accurate PARACEST signal measurements. Intuitively, if there is zero delay then there will be less signal in order to accurately detect changes. If there is a very long delay (> 3T1) then there is negligible PARACEST as there will be no effect from the Waltz pulse. Therefore, there should be a maximal contrast to noise ratio at a given delay post saturation.

Methods

Phantoms of 0, 2, 6 and 10 mM Tm-DOTAM-glycine-lysine (4) in 10% bovine serum albumin were created. T1 and T2 relaxation was measured on a 9.4T vertical bore Varian system using an inversion recovery sequence (TI=0.0125, 0.025, 0.05, 0.1, 0.2, 0.4, 0.8, 1.6, 3.2, 6.4, 12.8, 25.6s) and a multi-echo spin-echo sequence (TE=0.00125, 0.0025, 0.005, 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1.28, 2.56s), respectively. On-resonance PARACEST weighted FLASH images (TR/TE=5/2.2 ms) were acquired with a 6 μT, 240 ms Waltz 16 (2) on-resonance pulse followed by a delay of 0 to 2000 ms post-saturation and pre-imaging. The mean, *m*, and standard deviation, *s*, of the signal intensity was calculated for each phantom. The contrast to noise ratio (CNR) was defined as $(m_0 - m_x)/\sqrt{(s_x/m_x)^2 + (s_0/m_0)^2}$ where x=2, 6 or 10 mM phantom intensity and subscript 0 represents 0 mM phantom intensity. A poly-exponential was fit to the CNR curve and the delay time for maximal CNR was calculated.

Results and Discussion

Intuitively, the signal-to-noise ratio in the contrast image would be low at 0 ms post-saturation delay and the signal difference in the contrast image would be 0 at > 3T1 post-saturation delay. The contrast to noise ratio as a function of post saturation delay is shown in Figure 1 (a, blue curve) for the 10 mM phantom. Each curve was fit to a poly-exponential (black dashed line in Figure 1a) and the maximal CNR was at 241, 441 and 503 ms post saturation delay for the 2, 6 and 10 mM phantoms, respectively (Figure 1b). A globally optimal delay would not be possible in tissue as the T1 would vary for different tissue regions and as the PARACEST concentration changes. A post-saturation delay of 350 ms would be sufficient for a large range of T1 as shown in Figure 1b.

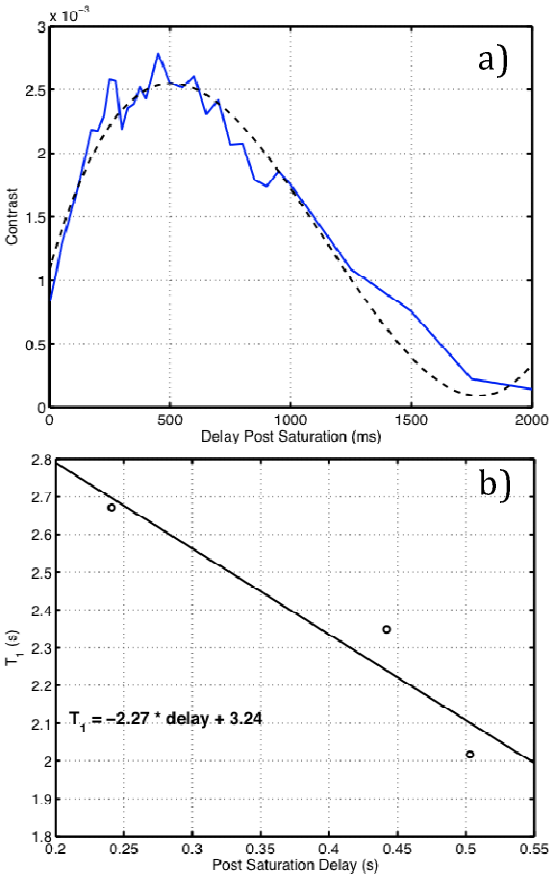

Figure 1: a) Contrast to noise ratio verses post saturation delay for the 10 mM Tm-DOTAM-gly-lys and linear fit of saturation delay versus measured T1 (black dashed line). b) Post saturation delay vs T1 relationship.

Conclusion

Detected signal is very low for on-resonance PARACEST images due to the macromolecules *in vivo*. A delay after the Waltz pulse allows the signal to regrow by T1 and therefore increases the maximal contrast in the PARACEST images. The optimal delay time depends on the T1 of the tissue and contrast agent but a delay around 350 ms would increase contrast to noise ratio for a wide range of biologically relevant T1 values.

References: 1) Vinogradov, et al., JMR, 2005, 2)Levitt, Prog Nucl, Magn Reson Spectrosc, 1986, 3) Vinogradov, et al., MRM, 2007, 4) Suchý et al., Bioorg Med Chem, 2008.