The Proton Resonance Enhancement for CEST imaging and Shift Exchange (PRECISE) family of RF pulse shapes

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INTRODUCTION:

One of the challenges of CEST MRI is that it can be an insensitive technique due to the other sources of water signal loss that occur upon application of CEST preparation pulse trains and difference imaging. In general, one approach to increasing the efficiency of magnetization transfer has been to employ optimized pulse shapes. Previously, people have chosen a number of pulse shapes, however, these were not explicitly optimized to maximize CEST. The gradient ascent method of Kuprov, Glaser, and colleagues can be applied to optimize RF pulse design. We have adopted this approach to generate the Proton Resonance Enhancement for CEST imaging and Shift Exchange (PRECISE) family of 100 ms pulses which could be plugged into various CEST pulse sequences, including fast spin echo sand steady state CEST sequences.

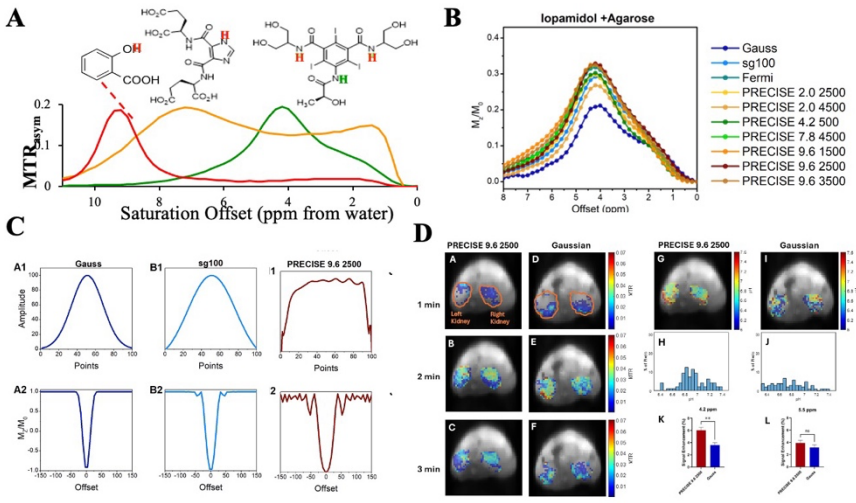
METHODS:

The gradient ascent pulse optimizations were conducted similarly to those described previously by Glaser and colleagues [1]. We used a set of 3 pool Bloch equations assuming a water pool (a), a semi-solid pool (b), and one CEST agent pool (c). The cost function to assess the performance is: $MTR_{asym} = \frac{(M_a^z(-\omega) - M_a^z(+\omega)}{M_a^0}$. Phantoms were prepared using three CEST agents shown in Fig 1A: 1) salicylic acid, 2) I45DC-diGlu and 3) iopamidol. These were either dissolved in PBS at 50 mM or in 1% agarose. *Phantom CEST MRI* data were acquired on a Bruker 11.7 T vertical scanner using the RARE sequence. *In vivo CEST MRI* were acquired on two groups of mice to evaluate either the PRECISE 9.6 2500 pulse or the standard gaussian pulse. The tail vein was cannulated for the administration of iopamidol. The animals were subjected to anesthesia with 0.5%–2% isoflurane during scanning. A single 1.5 mm thick axial slice, centered on both kidneys, was selected for CEST imaging. Dynamic CEST experiments utilized a saturation module comprising 29 RF pulses, each lasting 100 msec with an inter-pulse delay of 1 ms and an amplitude of 4 μT. A total of 234 CEST images were acquired, comprising 10 images at 40 ppm and 112 sets of images at 4.3 and 5.5 ppm. 0.15 mL of iopamidol (0.370 M in saline) was administered over 1 min, 3 minutes after the commencement of CEST data acquisition.

RESULTS:

We optimized pulses for all three agents we planned on evaluating. We first tested the pulses optimized for 9.6 ppm and 7.8 ppm to SA and I45DC-diGlu. For both agents, we observed maximal CEST contrast for the PRECISE 9.6 2500 pulse. We further evaluated our shapes on a 2nd phantom containing iopamidol in agarose and PBS with the agarose results shown in **Fig. 1B**. Here again, the PRECISE 9.6 2500 produced the strongest contrast at 4.2 ppm.

To understand the frequency selectivity of these pulses, we calculated the inversion bandwidth and display these for three pulses in **Fig. 1C**. As expected, the gaussian shape the smallest inversion width, and also a very low side band ripples The PRECISE 9.6 2500 pulse displays smaller side band ripples compared to the other PRECISE shapes, which is a desirable feature. Finally, we decided to evaluate how the PRECISE 9.6 2500 pulse would perform for pH mapping and injected 5 mice per group with iopamidol (**Fig. 1D**). The CEST contrast at 4.2 ppm and 5.5 ppm were calculated to be 5.95 ± 0.97 % and 3.80 ± 0.90 % for the PRECISE 9.6 2500 pulse and 3.49 ± 0.82 % and 3.04 ± 0.87 % for the Gaussian pulse. On performing the Mann-Whitney test, the signal enhancement for the PRECISE 9.6 2500 had a statistically significant difference compared to Gaussian. The pH distribution was bell-shaped, and for PRECISE, 9.6 2500 compared to Gaussian with a lower variance.



CONCLUSION:

We have identified a new shape for 100 msec pulses (PRECISE 9.6 2500) that can be inserted into a wide variety of CEST pulse trains and show this generates improved CEST contrast over 3 standard shapes in both phantoms and live mice.

REFERENCES:

(1) Khaneja,et al..*JMR* **2005**, *172* (2), 296-305.