Modulated CEST, using cross-correlation to measure the CEST effect

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Introduction

Chemical Exchange Saturation Transfer (CEST) contrast agents use magnetic transfer to create the contrast. The CEST contrast uses protons that exchange with the water protons. Upon RF saturation of these protons, the water signal intensity is affected. The advantage over common T1 or T2 altering contrast agents is that the contrast can be turned on and off upon saturation. The most commonly used method to determine the CEST contrast is to acquire an image with RF saturation at the CEST resonance frequency and to compare this with a reference image acquired with the RF saturation at the opposite frequency (relative to the water frequency) [1]. Here we introduce a new measuring method which is based on modulating the CEST contrast in a known paradigm and correlate the changes in signal intensity with this modulation. This method is similar to functional MRI. The advantages are that it can be executed real-time and scanning can be stopped when sufficient clustering of correlation has been reached. Furthermore, when there are signal changes during scanning, e.g. caused by motion or flow artefacts or concentration changes of the agent, the correlation method will detect the CEST contrast more reliably than standard averaging would.

Experimental

The method was implemented on a 3.0 T whole body clinical scanner (Achieva dual-quasar, Philips Medical System, Best, The Netherlands). RF saturation was introduced in a time series scan. Saturation pulses were applied at the CEST resonance frequency (on+); for the reference scan this was applied at the opposite frequency (relative to bulk water; on-). The samples contained different concentrations of an Yb-DOTAM-G3 CEST agent [2]. The setup is shown in figure 1. A time series was acquired using low saturation power (1.6 µT). The paradigm was: 1 time on+; 1 time on-, this was repeated 32 times. The clustering of correlation was monitored after 8, 16, 32 and 64 scans. The cross-correlation values were calculated using the real-time fMRI tools available on the scanner. In the same experiment these correlation values were compared to the contrast-to-noise values obtained by averaging. These CNR values were calculated by subtracting the on+ signal intensity from the on- intensity (from modulus images) and divided by the noise value from the surroundings.

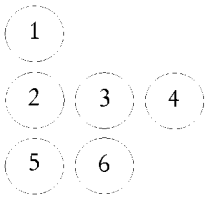


Figure 1:

The concentration of the CEST samples used in the experiment

1: Buffer

2: 1.25 mM

3: 2.5 mM

4: 6.4 mM

5: 9.6 mM

6: 13 mM

The samples were placed in a container with water.

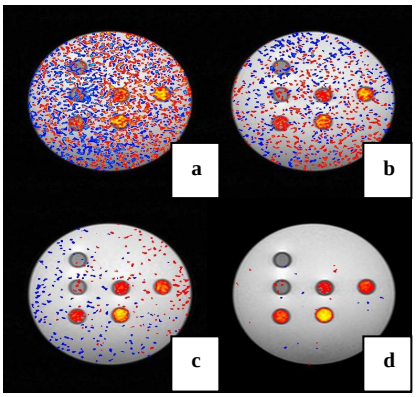
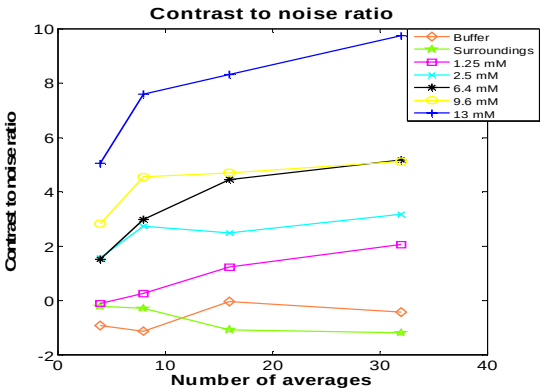


Figure 2: Correlation plot for the samples as shown in figure 1. Colour coding is: Blue: correlation -1; Yellow: correlation 1

Shown in this figure are the correlation maps that were obtained after

8 dynamics (a); 16 dynamics (b); 32 dynamics (c); 64 dynamics (d), respectively



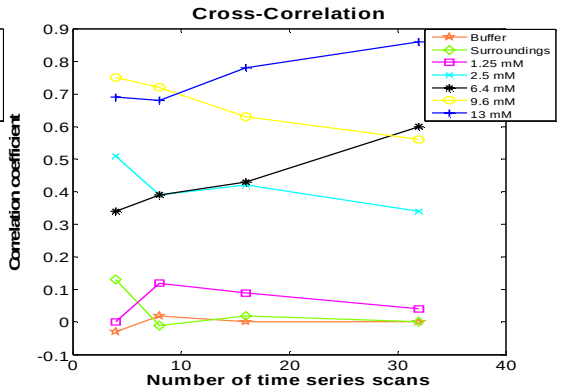


Figure 3: Comparison of the contrast to noise ratio's and the correlation values. The CNR is shown for the CEST effect at 4, 8, 16 and 32 averages, respectively. Similar, the correlation is shown after 4, 8, 16 and 32 dynamics. For stable samples the performance of both methods is comparable.

Results

Figure 2 shows that the correlation map improves as more dynamics are being processed.

The CNR and correlation plots (figure 3) show that for stable phantoms, both methods led to comparable results. For example, when using a threshold for the contrast to noise ratio of 2, this compares to a correlation threshold of 0.3. It is seen that these limits were met for the same concentrations in both methods. The control buffer sample showed no CEST effect above the limits in both types of measurement.

Conclusion

It is found that the correlation method to measure CEST contrast effects is at least as sensitive as averaging. The clustering of correlation can be followed real-time, scanning can be stopped when sufficient correlation is detected, ensuring optimal use of scan time. Furthermore, we expect that the correlation technique is less influenced by time dependent contrast changes than the averaging method. These signal changes can be caused by motion or flow artefacts, as well as dynamic changes of the agent concentration as expected in-vivo.

References

1) Ward et al; A new class of contrast agents for MRI based on proton chemical exchange dependent saturation transfer (CEST). J Magn Reson 2000;143:79–87.

2) Pikkemaat et al; Dendritic PARACEST contrast agents for magnetic resonance imaging. Contrast Media Mol Imaging. 2007 , in press