Improved MRI detection of low concentration paramagnetic contrast agent using steady state fully coherent gradient echo sequences

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Introduction

MRI is emerging as an important molecular imaging tool for the *in vivo* detection of disease markers. MRI, however, suffers from a relatively low sensitivity in comparison with optical or radioactive techniques, such as PET or SPECT ([1]). In this *in vitro* study we show that Balanced-FFE and Rephased-FFE (steady state fully coherent gradient echo sequences, echo as well as FID rephased) offer a marked gain in sensitivity of up to a factor 6 in the detection of low concentrations of contrast agent, when compared to the commonly used T_1-FFE sequence. The increased sensitivity is demonstrated both theoretically and experimentally using a concentration series of Gd-DTPA in $MnCl_2$ doped water.

Materials and Methods

6 Samples ($MnCl_2$ solution (13 mg/l), Ø=22 mm) with increasing Gd-DTPA concentrations, 0/0.04/0.08/0.12/0.16/0.2 mM, were bundled in a head-coil and imaged with a 1.5 T MRI scanner (Philips Medical Systems, Best). The images were made with the following parameters: TR/TE = 4/1.69-2 ms, matrix=128^2, NSA=8 and FOV=14x14 cm^2. Prior to the measurements, the B_0 field was shimmed locally and the scan-preparation parameters were fixed. The Balanced-FFE, Rephased-FFE, and T_1-FFE images were recorded as a function of the flip angle. Calculations ([2]) were performed using the experimentally determined T_2/T_1 ratio of the samples. The reference sample (no Gd-DTPA) had a T_2/T_1 ratio of 215/1406 ms/ms. The relaxivities R_1 and R_2 of the solutions were 4.1 and 5.5 $s^{-1}mM^{-1}$, respectively.

The images of the samples were analyzed by calculating the mean values of the signal to noise ratio (SNR) in a region of interest. For the flip angle, at which the 0.2 mM sample showed the highest enhancement, the SNRs of each sample were subtracted from the SNR of the reference sample. In this way we obtained the contrast to noise ratio (CNR) as a function of concentration. The sensitivity was defined as the change in CNR per mM Gd - DTPA concentration.

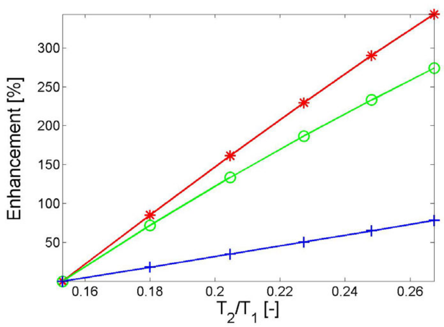

Figure 1. The calculated signal enhancement (reference signal is the reference sample with T_1-FFE) of T_1-FFE (+), Balanced-FFE (O) and Rephased-FFE (*) at theoretical optimum flip angles, with the T_2/T_1 ratios of the 6 samples.

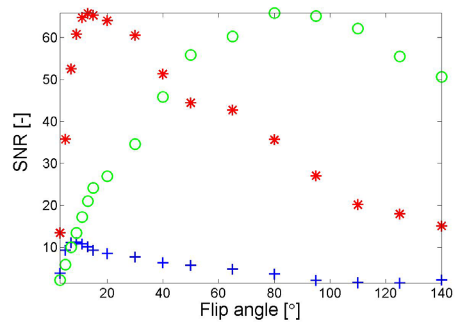

Figure 2. SNR of the reference sample (no Gd-DTPA) as function of the flip angle. Symbols as in figure 1.

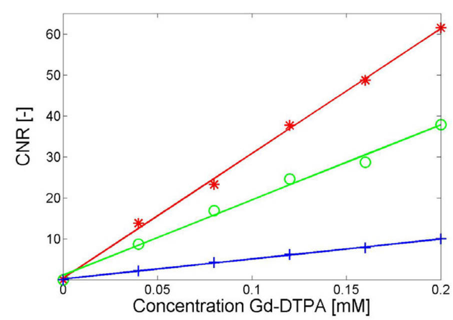

Figure 3. CNR increase relative to [GD-DTPA]=0 as a function of the Gd-DTPA concentration of the 6 samples. Symbols as in figure 1.

Results

Figure 1 shows the calculated signal enhancement for the three sequences as function of the T_2/T_1 ratio. The theoretical optimum flip angles were 9°, 77° and 1° for T_1-FFE, Balanced-FFE and Rephased-FFE, respectively. The graph clearly demonstrates, that for both Balanced-FFE and Rephased-FFE a striking gain in signal enhancement is predicted. In figure 2 the SNR of the reference sample, without Gd-DTPA, for the three sequences is plotted. The shapes are in accordance with the theory ([2]). Figure 3 shows the measured CNR as a function of the Gd-DTPA concentration. Note that the successive points in figure 3 correspond to the T_2/T_1 ratio points in figure 1. The flip angles for the maximum CNR of the three sequences were 15°, 125° and 65° for T_1-FFE, Balanced-FFE and Rephased-FFE, respectively. The sensitivity of these sequences (Fig. 3) is almost constant in the observed range of concentrations. The sensitivities for the Gd-DTPA solutions are 49 mM^{-1} (r^2=0.9984) for T_1-FFE, 184 mM^{-1} (r^2=0.9919) for Balanced-FFE and 305 mM^{-1} (r^2= 0.9982) for Rephased-FFE. As compared to T_1-FFE, Rephased-FFE and Balanced-FFE show a dramatic increase in sensitivity, in agreement with figure 1.

Discussion and conclusions

The signal enhancements predicted by the calculations were in good agreement with the measured signal enhancements, considering the fact that our simple model calculations did not take into account the slice profile and residual B_0 inhomogeneities. All sequences showed excellent linearity of the sensitivity as function of concentration, which is critical for quantification purposes. The Rephased-FFE displays the highest sensitivity, which makes this sequence the most attractive for molecular imaging with MRI. Another advantage of Rephased-FFE is the lower flip angle needed, which allows for very short repetition times, even at high field strengths for which SAR limits become important.

In conclusion, we have shown that steady state fully coherent gradient echo sequences, such as Balanced-FFE and Rephased-FFE, offer a marked gain in sensitivity in the detection of low concentrations of Gd-DTPA as compared to T_1-FFE. These sequences are therefore attractive candidates for the *in vivo* detection of disease markers using targeted contrast agents.

References

1. Aime et al., Biopolymers. 2002;66:419-428.
2. Vlaardingerbroek and den Boer, 'Magnetic Resonance Imaging', third edition, page 224, rephased FFE