Investigating the potential of low concentrations of iron-oxide contrast agents at low magnetic field strengths for the purpose of MR guided interventions

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Synopsis

Iron-oxide contrast agents might prove valuable in endovascular interventions at low-field MRI because their relaxivities are more favorable at lower field strengths, but still maintaining and generating positive contrast. Differences between a range concentrations of a gadolinium-based and a super paramagnetic iron-oxide (SPIO) contrast agent were compared both in simulations and experimentally on 0.25T using three different MR sequences. Optimal contrast for all sequences was found around 0.15mM for the SPIO agent and for concentrations higher than 7.0mM for the gadolinium agent. The use of low concentration SPIOs therefore is more beneficial for imaging at low magnetic field strengths than gadolinium-based contrast agents.

Purpose

Low-field MRI can be an interesting route for performing endovascular interventions due to its open configuration and different relaxation mechanisms of contrast materials, which have different relaxation characteristics depending on the magnetic field strength they are used in. At low field strength (<1T), some contrast materials that normally exhibit negative contrast have been shown to generate positive contrast at very low concentrations.[1] This might be a very interesting route to improve SNR at these low fields while also minimizing contrast agent administration. The used SPIO contrast agent has an additional advantage of an intravascular half-life of more than 15 hours, versus ~1 hour of gadolinium-based contrast agents, which can possibly eliminate the need for bolus injections during an intervention.[2] Sequences that can be useful during such interventions are regular spin echo sequences for anatomical reference, spoiled gradient echo T_1 sequences for angiographic purposes, and balanced steady-state free precession for real-time dynamic imaging. This research tries to find the optimal contrast agent and corresponding concentration range for endovascular interventions on low-field MRI.

Methods

The gadolinium-based contrast agent gadoterate acid (Gd-DOTA, Dotarem®, Guerbet, Roissy CdG, France) and super-paramagnetic iron oxide (SPIO) ferumoxytol (Feraheme, AMAG Pharmaceuticals, Waltham, MA, USA) were analyzed in this research. T_1 and T_2 of demi-water and r_1 and r_2 values of Dotarem and Feraheme were measured with a Bruker Minispec NMR (0.47T), and these values were used to calculate the final T_1 and T_2 based on a concentration range of 0-20mM.[3] From these concentration ranges the optimal concentration in terms of signal intensity were determined on a spin echo (SE), spoiled gradient echo (SGE), and balanced steady-state free precession (bSSFP) sequence with maximized T_1-weighing. Signal equations for these sequences are well known in literature. The range of parameters used in the simulations are depicted in Figure 1.

Experiments were performed on a 0.25T low-field MRI (G-scan Brio, Esaote, Italy) with concentrations Dotarem and Feraheme based on best outcomes of the previously mentioned simulations. The signals were normalized based on the signal of demi-water without contrast agent. The main outcome is the ratio of increase in signal intensity with respect to the starting situation with no contrast material added and the best concentration that goes along with this.

Results

We calculated relaxivity values of Feraheme (Fe) of r_1 = 102 mM^{-1} s^{-1} and r_2 = 228.7 mM^{-1} s^{-1} with R-squared values of 0.95 and 0.99. For Dotarem (Gd) this was r_1 = 3.25 mM^{-1} s^{-1} and r_2 = 3.93 mM^{-1} s^{-1} with R-squared values of 0.99 and 1.0. Figure 2 shows the signal intensity curves for respectively a spin echo, spoiled gradient echo, and balanced steady-state free precession sequence of the Fe- and Gd-based contrast agents on 0.47T and 1.5T. The bSSFP sequence showed for Dotarem a small peak, and for Feraheme a decrease in signal intensity. Figure 3 shows the experimental results on a 0.25T MRI with these maximum concentrations compared to demi-water of the SE and SGE sequences. Figure 4 shows normalized signal measurements on these scans compared to the simulated sequences.

Discussion

The range of concentrations was much lower for the SPIO contrast agent than for the gadolinium based contrast agent without a large decrease in signal enhancement. Since the simulations are based on a 0.47T NMR results, the experimental 0.25T MRI results may be underestimated.The simulations show that low-field MRI is beneficial for all tested sequences over 1.5T for Feraheme, but not for gadolinium. The experimental MRI resultsshowed equal mutual relationships between different concentrations of Dotarem and Feraheme, but the scaling was not equal with the simulatedsequences. We confirmed that low concentrations of Feraheme (<0.30 mM) lead to similar signal enhancement as moderate concentrations of Dotarem (7 mM).

Conclusion

The use of iron-oxides is more beneficial for imaging at low magnetic field strengths than gadolinium-based contrast agents. The increase in signal is much higher at much lower concentrations.

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References

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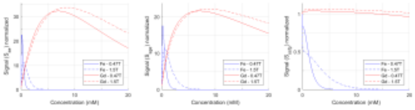
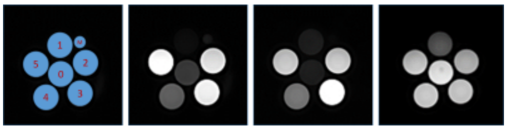
Figures

	SE	SGE	BSSFP
TR (ms)	50	26	10
TE (ms)	18	10	5
FA (°)	90	40	60
Slice thickness (mm)	10	10	10
Num. acquisitions	1	1	3
Acq. res. (mm x mm)	0.78x0.78	0.78x0.78	0.98x0.98

MR parameters of the investigated sequences.



Simulated signal of an SE sequence (left), SGE sequence (middle), and bSSFP sequence (right). The optimal concentration for signal increase was lower for Feraheme than Dotarem, and the normalized signal increase was higher on lower field strength for Feraheme, but not for Dotarem.



Left: numbering of the samples, with 0 = reference (demi-water), 1 = 1.2mM Fe, 2 = 0.3mM Fe, 3 = 0.15mM Fe, 4 = 14mM Gd, 5 = 7mM Gd. ‘M’ indicates a marker for orientation. Middle left: SE sequence results. Middle right: SGE sequence results. Right: bSSFP sequence results.

		SPIN ECHO		SPOILED GRADIENT ECHO		BSSFP	
	Sample	*Simulated*	*Measured*	*Simulated*	*Measured*	*Simulated*	*Measured*
1.	**Reference**	1	1	1	1	1	1
1.	**1.2 mM Fe**	0.6	0.3	2.4	0.9	0.5	0.4
1.	**0.3 mM Fe**	17.8	3.9	15.5	5.1	0.8	0.8
1.	**0.15 mM Fe**	22.6	4.2	17.5	6.8	0.8	0.9
1.	**14 mM Gd**	25.0	1.7	18.9	3.0	1.0	0.9
1.	**7 mM Gd**	32.3	4.6	21.6	5.0	1.0	0.8

Signal intensity normalized with respect to the reference (demi-water) sample (=value 1) of the simulated sequences versus the measured signals.