Differentiation of Fe^{2+} and Fe^{3+} with iron-sensitive MRI

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Introduction

Background: In MRI, the presence of iron in a sample or in tissue can be detected by relaxation-based methods or by susceptibility-sensitive tech- niques. [1] Both approaches have been used for an (at least approximately) quantitative measurement of tissue iron concentrations. A wide range of slopes describing the linear dependence of, e. g., relaxation rates and iron concentrations in brain tissue have been published (see Table 5 in ref. 1 for a review).

Problem: These dependencies for iron-induced relaxation changes were determined in most cases without considering the differences between the relaxivities of the ferric (Fe^{3+}) and ferrous (Fe^{2+}) form of stored iron. [2,3]

Purpose: The purpose of the present study is to demonstrate the different behaviors of ferric and ferrous iron ions in MRI and to suggest a technique to differentiate quantitatively between both forms of iron in tissue.

Methods

MR imaging: A phantom consisting of tubes with different concentrations (0.1, 0.3, 1.0, 3.0, and 10 mmol/L) of ferrous and ferric chloride solutions was examined on a 3-Tesla whole-body MRI system. A multi-echo gradient-echo sequence (TE=10, 20, 30, ..., 80 ms) was used for both T_2^* and quantitative susceptibility measurements.

Evaluation: T_2^* was determined with non-linear exponential fits based on the mean signal of regions of interest. The susceptibilities, χ, of the test tubes were calculated (separately for the acquisitions with TE=10, 20, and 30 ms) by simultaneously fitting the magnetic field of cylindrical tubes to the acquired phase data after removal of background fields and phase unwrapping with the SHARP algorithm. [4,5] To employ the different behaviors of ferrous and ferric chloride solutions for sample differentiation, we determined the ratio of the relaxation rate changes

$$\Delta R_2^*(c_{Fe}) = 1/T_2^*(c_{Fe}) - 1/T_2^*(c_{Fe} = 0)$$

and the susceptibility changes

$$\Delta\chi(c_{Fe}) = \chi(c_{Fe}) - \chi(c_{Fe} = 0)$$

for all concentrations.

Results

The dependences of the susceptibility, $\Delta\chi$, and the relaxation rates, ΔR_2^* on the iron concentration are shown in Fig. 1. While the susceptibility changes are comparable for ferrous and ferric chloride (about 0.075 ppm/(mmol/L), Fig. 1A), the relaxivity of ferrous chloride (about 0.5 s^{-1}/(mmol/L), Fig. 1B) is approximately one order of magnitude smaller than that of ferric chloride (about 12 s^{-1}/(mmol/L)). The ratio $\Delta R_2^*/\Delta\chi$ is greater than 50 s^{-1}/ppm for all samples with ferric solution and lower than 20 s^{-1}/ppm for all samples with ferrous solution (with the exception of the sample with 0.3 mmol/L ferrous chloride, which might have been prepared with too low ferrous concentration).

Discussion

Our results illustrate substantial differences between the relaxivities of ferrous and ferric chloride solutions. These differences have been analyzed earlier in the context of Fricke gels for radiation dosimetry and are due to the different correlation times of the dipolar interactions between the iron ions and the water protons. [2,3] On the other hand, both forms of iron influence the susceptibility of the sample very similarly, which is explained by the fact that only the additional magnetic field due to the paramagnetism of the iron ions is observed (and the magnetic moments of ferrous and ferric ions are very similar). These different mechanisms can be exploited by determining the ratio $\Delta R_2^*/\Delta\chi$, which provides a good differentiation between both form of iron ions. Thus, the change of iron concentration (independent of the oxidation state) can be determined quantitatively based on susceptibility differences and, simultaneously, ferric and ferrous iron ions can be differentiated based on MR relaxometry.

Conclusions

Ferrous and ferric chloride show markedly different relaxation behaviors in MRI, but similar influences on the susceptibility. These properties can be used to differentiate ferrous and ferric samples in our phantom. Future work is required to investigate if this approach is also feasible for measurements of (changes of) Fe^{2+} and Fe^{3+} concentrations in biological tissue in vivo.

References

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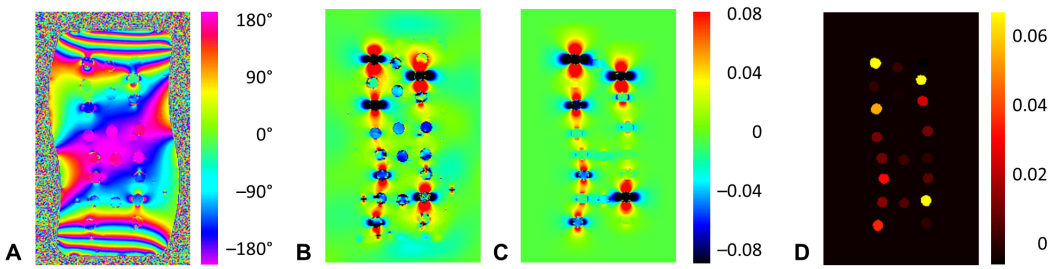

Fig. 1: Complex image phase (**A**), internal magnetic field perturbations (IMP, ppm) determined with the SHARP algorithm (**B**), dipole fit to IMP (ppm) (**C**), and magnetic susceptibility differences (ppm) (**D**).

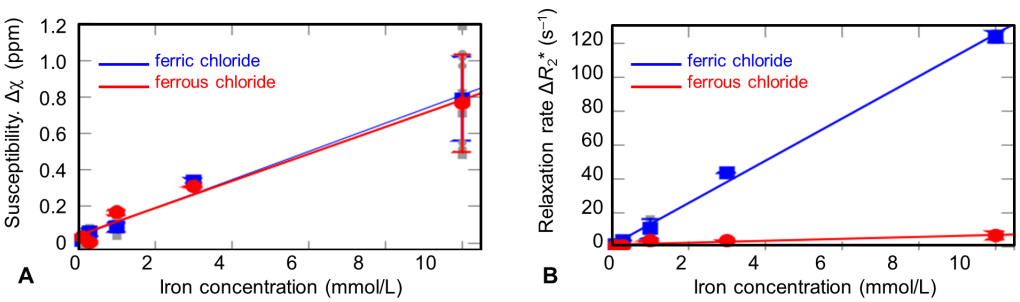

Fig. 2: Change of (**A**) magnetic susceptibility, $\Delta\chi$, and (**B**) relaxation rate, ΔR_2^*, depending on the concentration of ferric (blue) and ferrous (red) iron ions.

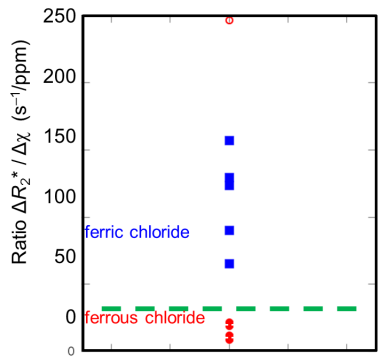

Fig. 3: Ratio ΔR_2^* / $\Delta\chi$ of relaxation rate and susceptibility changes. Suggested threshold for differentiation is dashed at 30 s^{-1}/ppm.

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