Susceptibility Weighted MRI of Ferumoxytol at 3T and 7T in Human Brain

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Introduction

Susceptibility weighted imaging (SWI) is used routinely at clinical field strengths because of its high sensitivity to venous vasculature, blood products, and tissue iron content. This sensitivity is due to the magnetic susceptibility information in the phase images which are used to mask the magnitude images [1]. These susceptibility effects increase with the main magnetic field strength. Recent work [2] has focused on optimization of SWI at 7T, focusing primarily on echo time (TE) and voxel geometries, although it did not address the effects of contrast agents or consider modifying the application of the phase mask.

The recent availability of Ultrasmall Superparamagnetic Iron-Oxide (USPIO; FeO) contrast agents (Ferumoxytol, AMAG Pharmaceuticals, Inc) gives another way to potentially increase the sensitivity of SWI and allow even smaller blood vessels and tissue pathology to be imaged. This contrast agent has a half life in the blood of ~14 hours, and because of its high molecular weight it does not cross the blood-brain-barrier (BBB) soon after injection even in leaky tumors, as opposed to traditional gadolinium based contrast agents. This work investigates the combination of SWI and FeO contrast agents in the study of brain tumors at 3T and 7T.

Methods

Eleven subjects provided informed consent before participating in this study. Data were acquired at 3T (Trio a Tim System, Siemens) using a 12-channel phased array head coil and at 7T (MAGNETOM 7T, Siemens) using an 8-channel phased array head coil (Rapid Biomedical, Wurzburg, Germany). SWI parameters at 3T were TE20/TR30/FA15°, $(0.6\text{mm})^2$x2mm and at 7T were TE12/TR26/FA15°, $(0.5\text{mm})^2$x1.5mm voxels, iPAT2, 5min scan time. Images were acquired before contrast injection, 20 minutes after injection of 0.1 mmol/kg gadoteridol (ProHance, Bracco Diagnostics, Inc), 20 minutes after injection of 0.6 mg/kg FeO, 20 minutes after 4 mg/kg FeO, and 24 hours following 4 mg/kg FeO.

The standard SWI algorithm iteratively applies the phase mask four times to enhance the contrast in the magnitude images. The effect of varying the number of iterations on image quality was investigated offline using Matlab (Mathworks, Natick, MA).

Results and Discussion

Figure 1 shows a comparison of the SWI minimum intensity projections (mIPs) over eight slices at 3T and 7T following FeO injection. Figure 2 shows the SWI mIPs before and after gadoteridol and FeO injections.

The overall sensitivity of SWI was found to be higher at 7T as can be seen in Fig.1. Extremely small blood vessels are more visible in the 7T images. Fig. 2A-B shows that small vessels become more conspicuous after gadoteridol injection, and even more so following FeO injection (Fig. 2C) which gives a remarkable small vessel conspicuity that increases with FeO dose (Fig. 2D). The effects of FeO are still very strong after 24 hours post 4 mg/kg FeO (Fig 2E), and at a higher level than 20 minutes after the 0.6mg/kg FeO injection (Fig 2C) . It is noteworthy that the post-FeO data from 3T (Fig 1A) had greater SWI contrast than the pre-contrast data from 7T (Fig 2A), which demonstrates that FeO may be a relatively simple but powerful way to increase sensitivity for small vessel imaging at clinical field strengths.

Varying the number of iterations of the phase mask had the effect of reducing the "blooming" of the larger vascular structures at the expense of decreased sensitivity to visualize extremely small vessels. It appears that letting this parameter be variable within the image viewing user interface may be warranted in cases of large magnetic susceptibility effects as seen with FeO at 7T.

One of the primary reasons to use mIP images in SWI is to increase the signal-to-noise ratio (SNR), as the SNR in the single-slice SWI images is fairly low at the resolution needed for SWI at clinical field strengths. However, because of the higher SNR at 7T this was no longer a limitation and we were able to easily inspect the base SWI images. Of course, this SNR could be traded for higher resolution.

Other have shown [3] that SWI offers complementary or better information than post-Gd T_1 weighted imaging in detecting boundaries, blood products, and venous vessels. Tumors may take up FeO slowly, so at a time shortly after FeO administration SWI is useful primarily to improve visualization of cerebral vasculature. The very small rate constant of FeO transfer across blood vessels makes FeO potentially useful for differentiating blood pool products from the tumor vasculature, even in the presence of blood vessels that are very leaky to traditional Gd-based contrast agents.

In conclusion, the increased magnetic susceptibility effects, high SNR, and low specific absorption rate (SAR) make SWI an attractive clinical application at 7T. The use of FeO contrast agents at both 3T and 7T is another powerful tool that warrants further optimization.

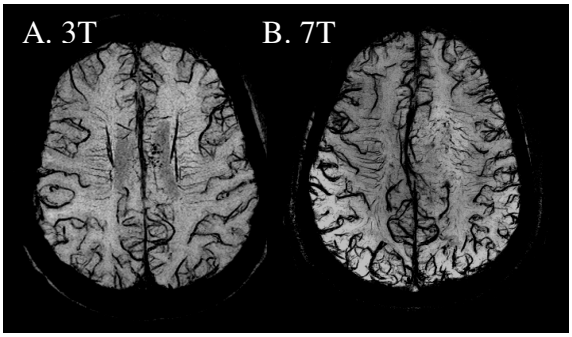

Figure 1. A comparison of SWI at 3T (A) and 7T (B) post 4 mg/kg FeO.

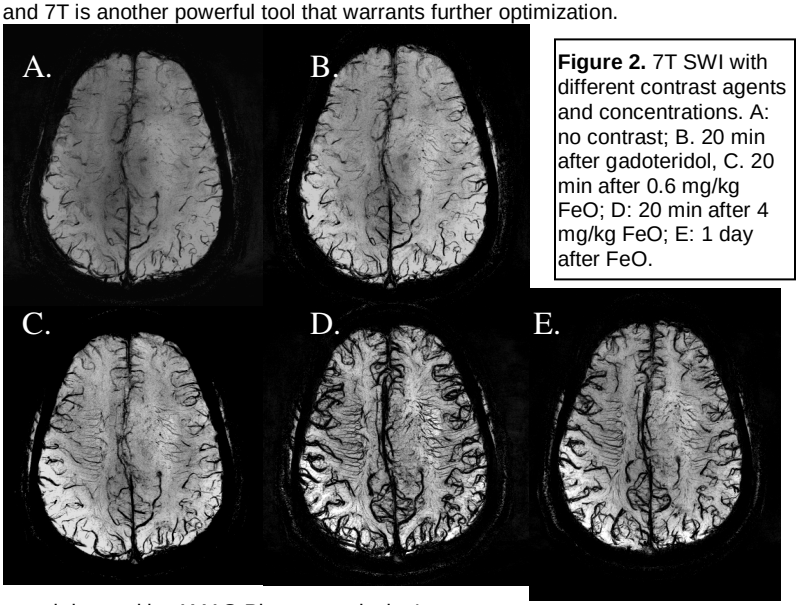

Figure 2. 7T SWI with different contrast agents and concentrations. A: no contrast; B. 20 min after gadoteridol, C. 20 min after 0.6 mg/kg FeO; D: 20 min after 4 mg/kg FeO; E: 1 day after FeO.

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References [1] Haacke et al., MRM 52:612-618 (2004). [2] Deistung et al., MRM 60:1155-1168 (2008) [3] Sehgal et al., JMRI 22:439-450 (2005).