Ferumoxytol-enhanced Plural Contrast Imaging of the Human Brain

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Purpose: To exploit the 3D multi-echo GRE sequence coupled with and without the injection of ferumoxytol for plural-contrast clinical neuroimaging at 3T.

Introduction: Ferumoxytol (Feraheme, AMAG Pharmaceuticals, Inc., Cambridge, MA), an FDA-approved ultra-small paramagnetic iron oxide (USPIO) compound, has been used as an "off label" contrast agent to study inflammatory processes, vascular lesions, tumor, or stroke [1-6]. It is retained in the intravascular space early after injection and does not cross an intact blood brain barrier [7-8]. The high magnetic susceptibility of ferumoxytol considerably reduces the T2* and the long intravascular half-life allows high-resolution/high-SNR acquisitions that may be useful to study brain disorders[9]. Particularly in pediatric brain, where patient cooperation can be problematic, we are striving to generate and study multiple image contrasts from a single imaging sequence. The 3D multi-echo gradient-recalled echo (ME-GRE) technique is a particularly good candidate for this, as it allows for the simultaneous generation of naturally co-registered images with various contrasts[10-11]. Here we show preliminary data scanned with a 5:44-minute 3D ME-GRE sequence acquired both pre- and post ferumoxytol, with the subsequent generation of R2* maps, local field maps, Susceptibility-Weighted Imaging (SWI), Time-of-Flight Magnetic Resonance Angiography (TOF), and Quantitative Susceptibility Maps (QSM).

Methods: With IRB approval, pediatric patients were scanned on a 3T GE scanner (MR750, GE Healthcare Systems, Waukesha, WI) equipped with an 8-channel head-coil. In addition to the regular clinical pediatric brain protocol, a flow-compensated 3D GRAPPA-accelerated ME-GRE sequence was scanned both before and after the intravenous injection of a single dose of ferumoxytol (0.1 mL Fe/kg). The following parameters were used: resolution = 0.57x0.86x2.5mm^3, 66 z-partitions, acceleration factor = 2, 8 echoes ranging from TE = 4.3ms – 37.5ms with 4.7ms increments, TR = 40.8ms, scan time = 5:44min. On completion of the scan, the raw data from the scanner were automatically reconstructed using compiled threaded MATLAB (MathWorks Inc., Natick, MA, USA) code, with all images sent to the hospital database (PACS). First, the 8-channel coil data were combined with the complex sum-of-squares. Weighted magnitude images (wMag) were calculated using the echo time of each echo image as a weighting factor. R2* (1/T2*) maps were calculated from mono-exponential fit of echoes. Field maps were generated by first performing a complex fit across echoes[12-14], followed by phase unwrapping using a Laplacian algorithm[15] and projection onto dipole fields[16-18]. QSM images were generated from this field map using the MEDI algorithm[12,16-18]. SWI images were created by generating a phase mask (using a 2D Hanning window), and multiplying this mask 5 times by the weighted-magnitude image[19-20]. TOF images were produced by taking the Maximum Intensity Projection (MIP) over the first echo.

Results: Fig. 1 shows the multiple contrasts acquired on an 11yr old post-surgical male patient using the 0.6x0.9x2mm^3 3D ME-GRE sequence. Both pre- and post-ferumoxytol as well as the difference images are shown. The high spatial resolution and high SNR of the 3D ME-GRE images allows the visualization of fine vascular detail. The blooming effect seen on the field map are blood products at the surgical resection site. The R2* difference maps are proportional to the cerebral blood volume fraction according to the steady-state perfusion theory[21]. The spatial resolution achieved here is however much higher than the one usually obtained using Dynamic Susceptibility Contrast approaches. Since the vasculature was suppressed on the post-ferumoxytol TOF images (likely due to the severe T2* shortening effect), the TOF difference images appear background suppressed – corresponding reasonably well with the regular TOF-MRA (**Fig. 2**).

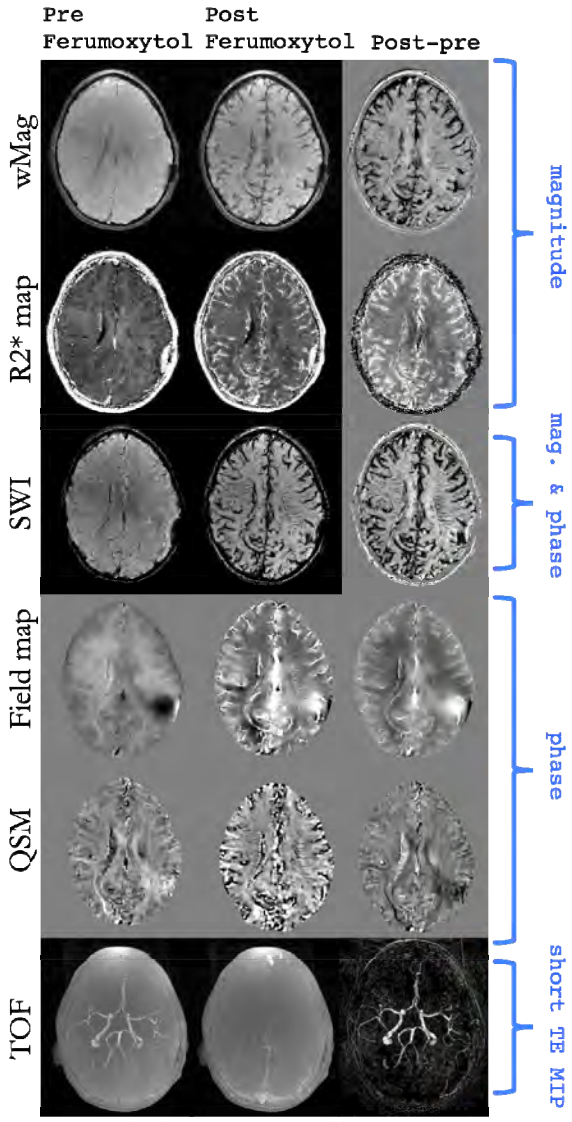

Fig. 1: Plural contrasts generated from one 3D ME-GRE sequence, both pre- and post ferumoxytol. Difference images are shown in the far right column.

Conclusion: Here we show that the use of just one 5:44-minute 3D ME-GRE sequence and subsequent post-processing toolkit has the potential to reveal complementary image features, by providing multiple contrast mechanisms such as R2* maps, Field maps, SWI, QSM, and TOF-MRA. This sequence has the potential to be a surrogate for other single-sequence alternatives in clinical practice. Further work is needed to determine the extent to which these contrasts improve our understanding of normal tissue anatomy as well as changes in tissue in various pathological conditions. This might be particularly adapted to study vascular malformations or lesions with heterogeneous tissue components such as brain tumors.

Fig. 2: Regular TOF-MRA (scan time = 5 mins).

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