Correlation of Brain Iron with Susceptibility: Comparison of Gradient Echo and WASSR Acquisition at 3 Tesla

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Introduction: Quantitative Susceptibility Mapping (QSM) methods rely on measuring the local resonance frequency per voxel. This local field is affected by the main field, background field gradient inhomogeneities, and the magnetic susceptibility of the tissues in and around the voxel.[1] Previous works have measured magnetic susceptibility by utilizing phase maps generated from gradient echo (GRE) images.[2-6] However, such maps contain phase wrap discontinuities (shown in Fig. 1 "3D GRE Phase"), especially at longer echo times (TEs) and in positions further from the magnet center, which complicate data interpretation.

Whole-brain frequency maps without phase wraps can be obtained using the WAter Saturation Shift Referencing (WASSR) method, in which the resonance frequency per voxel is characterized by directly saturating water with a radiofrequency (RF) prepulse across a range of offset frequencies.[7-9] With a low RF pulse power and short duration, such saturation causes a Lorentzian absorption lineshape that is not affected by inhomogeneous line broadening.[10,11] When plotting the saturated signal intensity as a function of RF offset frequency with respect to the scanner reference frequency, the point of minimum signal of the Lorentzian occurs at the resonance frequency for each voxel. This raw resonance frequency map can be converted to a magnetic susceptibility map.

Figure 1: Processing quantitative susceptibility maps from GRE and WASSR at 3T

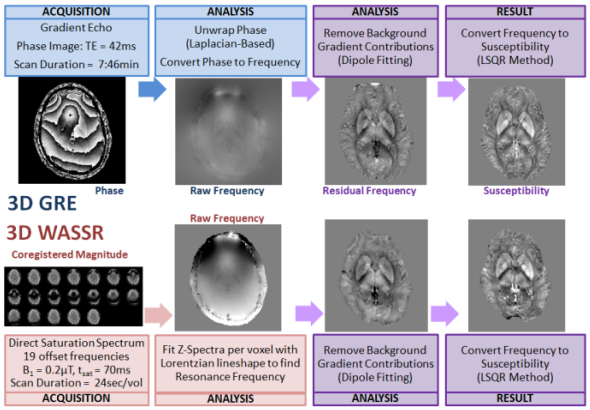
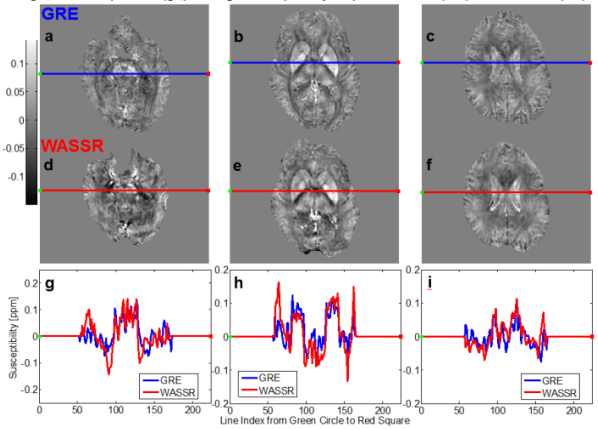


Figure 2: Line profiles (g-i) through susceptibility maps from GRE (a-c) and WASSR (d-f)

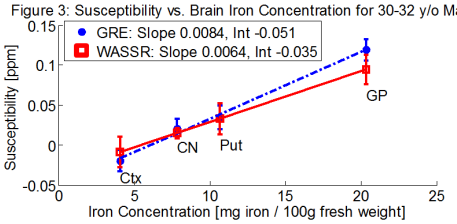


Subjects and Methods: Five healthy male volunteers (30-32 years old) were studied after IRB approval and written informed consent, using a 3T Philips system with dual-channel body-coil excitation and 32-channel head coil receive. Phase images were acquired at TE=42ms from a 3D gradient echo sequence (SENSE 2x1x2, TR=70ms, $\alpha=20^{o}$, Scan Duration=7:46min). WASSR images were acquired with a 3D gradient-echo multi-shot EPI readout (EPI factor=33, TR=150ms, TE= 22ms, $\alpha=20^{o}$, Volume Acquisition Time=24sec, Scan Duration=8:01min) with a direct saturation sinc-gauss prepulse (B_1=0.2μT, t_{sat}=70ms) at 19 offset frequencies between +/-120Hz, along with a volume acquired with no applied saturation. For both scans, the acquired resolution was 1.2mm^3 isotropic, covering the whole brain (100 slices). Using MATLAB, GRE images were unwrapped with a Laplacian-based method[12], then divided by 2π*TE to obtain a raw frequency map. WASSR images were coregistered to the no-saturation volume, and the magnitude signal at each offset frequency was fitted per voxel to a Lorentzian lineshape, resulting in maps of the resonance frequency. Raw resonance frequency maps from GRE and WASSR were independently processed to remove background field gradients with dipole fitting[13] and to convert the corrected frequency maps to magnetic susceptibility with the LSQR method, with stopping criteria calibrated from one volunteer who was scanned at multiple orientations.[3,5]

Results and Discussion: Figure 1 shows the main processing steps for QSM with GRE versus WASSR. Figure 2 displays line profiles through susceptibility maps generated from both methods. Figure 3 plots the susceptibilities for four gray matter regions as a function of average non-heme iron concentration, based on an age-dependent fit of histology-based brain iron extracted from 81 subjects aged 30-100 years old.[14] The results show a comparable linear correlation between brain iron and susceptibility measurements with GRE and WASSR.

GRE imaging is fast and available on all human scanners, but has a few disadvantages. Firstly, phase images come with phase wraps, which complicate data interpretation at the interfaces of structures with very different susceptibilities (e.g., near the sinuses). Secondly, phase contrast relies on the use of fairly long TEs (depending on field strength) to visualize gray and white matter structures, resulting in images with lower signal-to-noise ratio (SNR) and longer imaging times at lower fields. Thirdly, the 3D GRE volume is acquired over a relatively long time (Scan Duration ~ 8min at 3T); if the subject moves at any point during the acquisition, the entire scan is distorted. Fourthly, rapid GRE scanning often heats the magnet bore components, thereby changing the magnet frequency according to Curie's Law, which may drift several Hz over the total scan time. The WASSR method uses the magnitude signal (with no phase wraps), a shorter TE (with more signal, ~20ms at 3T), and EPI acquisition (~20-30sec per volume). If the subject moves while one volume is acquired at a particular RF offset frequency, that volume may be discarded without drastically affecting the entire experiment, because the other volumes may still be fit to a Lorentzian lineshape. Also, a frequency correction based on the individual scans can be applied to determine field drift. The contrast-to-noise ratio (CNR) and SNR of susceptibility maps from WASSR depend mainly on sampling rate; more volumes acquired at closely-spaced RF offset frequencies will result in a more clearly-defined susceptibility map. GRE imaging is especially conducive at higher magnetic fields, which induce larger frequency shifts, at shorter TE. However, at lower fields with lower frequency shifts, GRE is limited by spatial SNR, longer echo times required for phase contrast, and resulting longer scan times. In WASSR, the sweepwidth needed to cover the distribution of frequency shifts across the brain is proportional to the field in Hz, but the same in ppm, allowing the same number of RF offset frequencies to be acquired at each field, and resulting in susceptibility maps that will be comparable between fields.

Figure 3: Susceptibility vs. Brain Iron Concentration for 30-32 y/o Males



Conclusion: WASSR is somewhat slower than GRE MRI, but should be advantageous for low-field imaging with subjects that are likely to move (e.g., children), or across areas with large susceptibility differences that would produce many phase wraps. Because iron content affects the susceptibility in a particular tissue, GRE and WASSR have the potential to characterize neurodegenerative diseases in which brain iron is expected to change (e.g., Alzheimer's Disease).

References: [1]. Reichenbach, et al. JMRI 1997, 7:266. [2] Duyn, et al. PNAS 2007, 104:11796. [3] Wharton, et al. NeuroImage 2010, 53:515. [4] Liu. MRM 2010, 63:1471. [5] Liu, et al. NMR Biomed 2011, 24:1129. [6] Schweser, et al. NeuroImage 2011, 54:2789. [7] Kim, et al. MRM 2009, 61:1441. [8] Smith, et al. MRM 2009, 62:384. [9] Lim, et al. ISMRM 2010, #4531. [10] Mulkern et al. Med Phys 1993 20:5. [11] Liu, et al. CMMI 2010 5:162. [12] Li, et al. NeuroImage, 2011, 55:1645. [13] de Rochefort, et al. MRM, 2008, 63:1003. [14] Hallgren, et al. JNeurochem, 1958, 3:41. **Funding**: NIH-P41RR15241