Frequency Mapping without Phase Wraps

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Introduction: Quantitative susceptibility techniques rely on measuring the magnetic field across a sample. The resonance frequency in each voxel correlates with the local field, which is affected by the main field, static field inhomogeneities, and the magnetic susceptibility of the tissues in and around the voxel (1). To the best of our knowledge, all of the groups measuring magnetic susceptibility utilize phase maps, based on the evolution of the transverse magnetization during a gradient echo sequence (2-6). These phase maps can be converted to frequency (f) images using $f = \varphi/(2\pi * TE)$, where φ is the phase and TE is the echo time (7).

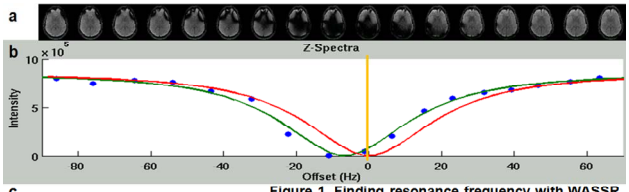

Figure 1. Finding resonance frequency with WASSR. (a) The images acquired at each offset frequency. (b) The signal intensity in each voxel (•) is fit to a (c) Lorentzian curve (--), then the curve is shifted (--) to zero (|). The difference between minimum of the green and red lines show the shift in resonance frequency per voxel, which can be displayed as an f_0 map (Fig. 2d).

While GRE imaging is fast and available on all human scanners, the method has a few disadvantages. Importantly, phase evolution over a relatively long echo time (TE ~ 40ms at 3T) is necessary to visualize the frequency contrast between gray and white matter structures. Such phase images acquired at long TEs will have low SNR. In addition, phase wrap artifacts are found at the interfaces of structures with very different susceptibilities (e.g., around the sinuses). Whole-brain frequency images without phase wraps can be obtained using the WAter Saturation Shift Referencing method (WASSR), in which direct saturation of water is measured as a function of frequency to map the resonance frequency per voxel.(8-9) Application of a low-power RF saturation pulse for a short time over a sweepwidth of offset frequencies is used to create a "direct saturation spectrum" per voxel. This direct saturation spectrum shows the signal intensity as a function of applied frequency, with a Lorentzian lineshape that is not affected by inhomogeneous line broadening (11). The minimum of each direct saturation spectrum occurs at the resonance frequency in each voxel; therefore, fitting this signal curve to a Lorentzian (12) allows the determination of the water frequency per voxel with respect to the scanner reference frequency. The WASSR method can pinpoint the resonance frequency in each voxel by using the magnitude signal and is therefore devoid of phase wrap artifacts. Also, a short TE can be used, which may avoid image artifacts when using echo planar imaging. Here, we show that WASSR produces comparable frequency maps to the frequency maps derived from the typical single-echo GRE.

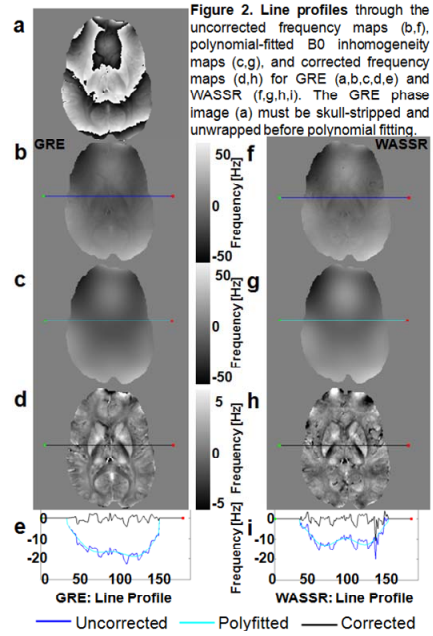

Figure 2. Line profiles through the uncorrected frequency maps (b,f), polynomial-fitted B0 inhomogeneity maps (c,g), and corrected frequency maps (d,h) for GRE (a,b,c,d,e) and WASSR (f,g,h,i). The GRE phase image (a) must be skull-stripped and unwrapped before polynomial fitting.

Subjects and Methods: Six healthy male volunteers (27 to 30 years old) were studied after IRB approval and written informed consent. A 3T Philips MR unit was used with body-coil excitation and a 32-channel SENSE head coil for reception. Phase images at an echo time of 42ms were acquired using a 3D multi-echo gradient echo sequence (SENSE = 2x1x2, TR = 70ms, TE_1 = 6ms, ΔTE = 6ms, α = 20°, Scan Duration = 6:59min). The WASSR images were acquired using a 3D gradient-echo multi-shot EPI readout (EPI factor = 33, TR = 147ms, TE = 19ms, α = 20°, Scan Duration = 6:28min) with a direct saturation sinc-gauss prepulse (B_1 = 0.2μT, t_{sat} = 70ms) at 17 offset frequencies linearly spaced between -75 to 75Hz and including a volume with no applied saturation. For both GRE and WASSR scans, resolution was 1.2mm^3 isotropic, covering most of the brain (90 slices). Both sets of images were coregistered to the WASSR volume without a saturation prepulse, using FSL FLIRT rigid body registration and a normalized mutual information algorithm. GRE images were phase unwrapped and divided by 2π*TE to obtain frequency maps. The signal in the WASSR images at each offset frequency was fitted per voxel to a Lorentzian lineshape to obtain maps of the resonance frequency, linewidth, initial magnetization, and baseline noise. The resonance frequency images from both GRE and WASSR were fit to an 8th order polynomial to determine macroscopic B_0 inhomogeneities and large susceptibility distortions. Subtracting this fit from the original resonance frequencies produced a "corrected" frequency map of the local field per voxel.

Results and Discussion: WASSR acquisition and processing are shown in **Fig. 1:** Direct saturation images are acquired as a function of offset frequency (a), and the intensity per voxel (b) is fit to a general Lorentzian lineshape (c) to determine the resonance frequency per voxel. **Fig. 2:** Comparison of GRE and WASSR data sets for one slice. Line profiles show how 8th order polynomial fitting allows subtraction of the slowly varying B_0 inhomogeneities from the resonance frequency maps to determine smaller local frequency shifts. **Fig. 3** shows the mean and standard deviation of the frequency shifts in various regions of interest with respect to CSF. The frequency differences range from 0.5Hz in the internal capsule to 5.3Hz in the corpus callosum to 8.0Hz in the globus pallidus. At 3T, high resolution frequency maps are difficult to acquire due to lower contrast-to-noise ratio (CNR) than at higher fields. The CNR of the WASSR map, however, depends on the sampling accuracy of the Lorentzian, which depends on the sweepwidth of the offset frequencies and the number of points used to cover the brain frequency range. The frequency range increases with field strength (13). This allows a narrower sampling interval for WASSR at lower fields, which may permit the improved measurement of small frequency shifts at lower fields. Because WASSR frequency measurements depend on the saturation prepulse, any readout may be used, which allowed a high EPI factor and rapid acquisition of twenty volumes at a scan time comparable to GRE.

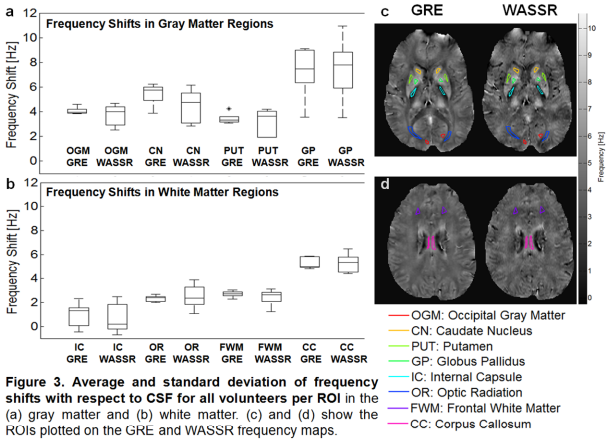

Figure 3. Average and standard deviation of frequency shifts with respect to CSF for all volunteers per ROI in the (a) gray matter and (b) white matter. (c) and (d) show the ROIs plotted on the GRE and WASSR frequency maps.

Conclusion: The WASSR method can produce frequency maps without phase wraps, which might be especially useful at lower fields.

References: [1] Reichenbach JR, et al. JMRI, 1997,7:2; [2] Duyn JH, et al. PNAS, 2007,104(28); [3] Shmueli K, et al. MRM, 2009,62:6; [4] Liu T, et al. MRM, 2009,62:6; [5] Wharton S, Bowtell R. NeuroImage, 2010. [6] Liu C. MRM, 2010,1477. [7] Jezzard P, Balaban RS. MRM, 1995:34. [8] Smith SA, et al. MRM, 2009:62. [9] Kim M, et al. MRM, 2009,61:6; [10] Mulkern RV, Williams ML. Med Phys, 1993:20. [11] Liu G, et al. CMMI, 2010, 5. [12] Yao B, et al. NeuroImage, 2008, 44:4.
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