The contribution of nuclear magnetization to the phase contrast in the 3D SPGR measurement

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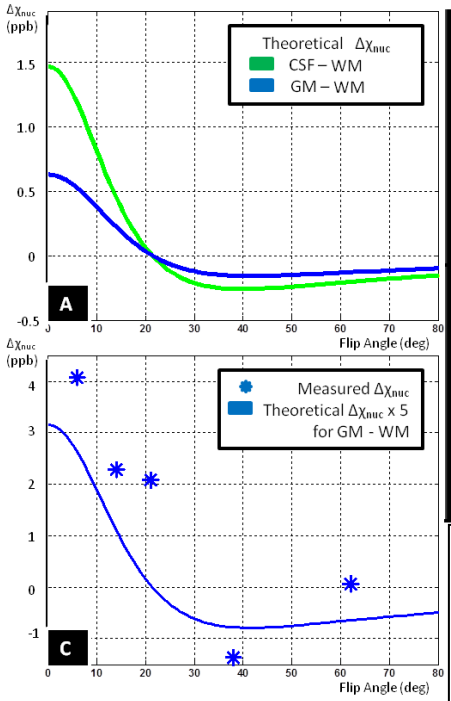
Introduction

Recent studies indicate that phase images acquired with a 3D spoiled gradient echo (SPGR) sequence provide excellent contrast and exceptional sensitivity to small variations in tissue magnetic susceptibilities [**1**]. Susceptibility variations of 16 ppb (parts per billion) and -1.6 ppb have been reported between gray matter (GM) white matter (WM) and between WM and cerebrospinal fluid (CSF) respectively [**1**]). The dominant susceptibility mechanism is generated by the magnetic moment of electron orbitals [**2**] in diamagnetic (e.g. myelin, lipids) and paramagnetic (e.g. ferritin) molecules [**1**]. Nevertheless, tissue nuclear magnetization can generate a paramagnetic susceptibility on the order of 4 ppb [**2**]. In this study we investigate the contribution of the steady state longitudinal nuclear magnetization to the frequency shifts between brain tissues in the 3D SPGR experiment and its dependence on sequence parameters.

Methods

Simulation: The steady state longitudinal magnetization in 3D SPGR depends on **sequence parameters** (repetition time **TR** and flip angle **α**) and **tissue properties** (proton density ρ_0 and relaxation time constant T_1): $M_{ss} = \rho_0\gamma^2\hbar^2B_0(4kT)^{-1}[1- e^{-TR/T1}]/[1-\cos(\alpha)\, e^{-TR/T1}]$. Consequently, the nuclear magnetization induced susceptibility difference between tissues A and B is: $\Delta\chi^{AB}_{nuc} = \chi^{A}_{nuc} - \chi^{B}_{nuc} = \mu_0(M^{A}_{ss} - M^{B}_{ss})/B_0$. Using literature values for ρ_0 and T_1 of brain tissues [**3-4**] we calculated the flip angle (FA) dependence of $\Delta\chi^{AB}_{nuc}$ between different tissue types for an experiment with TR=150ms (**Fig. 1A**).

Human Data: Two healthy volunteers were scanned on a 3T scanner using a 3D SPGR sequence with TE/TR = 38/150 ms, 1x1x1.5 mm^3 resolution and FA = 6˚, 14˚, 21˚, 38˚, and 60˚. Phase images acquired at each FA were high pass filtered to remove the effect of background susceptibilities [5] and local tissue susceptibility differences were quantified using ROI averages (**Fig. 1B**) adjacent to GM/WM and CSF/WM interfaces $\Delta\chi^{AB} = (\Delta\varphi^{A}-\Delta\varphi^{B})/(\gamma B_0 TE)$. Since only the nuclear resonance is affected by the RF pulse, changes in $\Delta\chi^{AB}$ vs FA reflect frequency shifts induced by nuclear susceptibility differences between tissues ($\Delta\chi^{AB}_{nuc}$). Finally, the measured $\Delta\chi^{AB}$ was fitted with a curve and referenced with respect the theoretical zero-crossing at 21˚ (**Fig. 1A**) to remove the susceptibility contribution due to molecular electron orbitals (**Fig. 1C**).



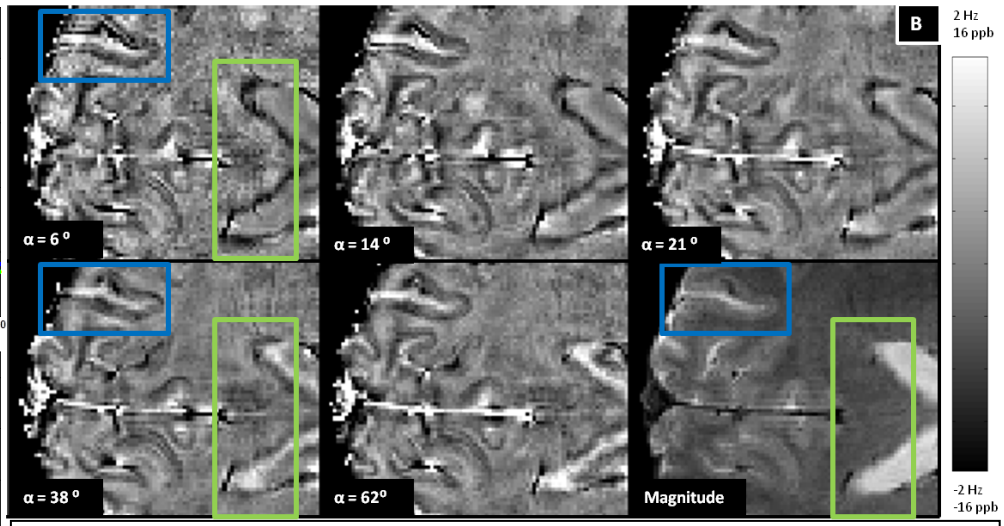


Figure 1: (A) Theoretical nuclear susceptibility induced frequency shift at **GM/WM** and **CSF/WM** as a function of flip angle (FA) – maxima occur for small FA (paramagnetic $\Delta\chi_{nuc}$) and FA = 38˚ (diamagnetic $\Delta\chi_{nuc}$), no $\Delta\chi_{nuc}$ induced frequency shift for FA = 21˚. **(B)** Filtered phase images acquired with different FAs. Variations in nuclear susceptibility induced frequency shifts at **GM/WM** and **CSF/WM** interface are largest for FA = 6˚ and 38˚ (**blue** and **green** box, respectively). **(C)** Nuclear susceptibility induced frequency difference at **GM/WM** interface **(blue box)** estimated from phase images follow the trend predicted by simulations.

Results and Discussion

Our simulation demonstrates that the nuclear susceptibility induced frequency shifts in GM/WM and CSF/WM decrease for FA=0-40˚ over a range of **0.8 ppb** and **1.8 ppb** respectively, followed by a plateau region (**Fig. 1A**). For FA=21˚ tissue variations of steady state nuclear magnetization are minimized and the phase reflects only susceptibility differences due to molecular electron orbitals. The quantitative ROI analysis in healthy volunteers reveals a similar trend: an initial decrease over a range of **4.0 ppb** and **5.4 ppb** was observed for GM/WM (**Fig. 1C**) and CSF/WM respectively, followed by a plateau for larger flip angles. The noise level in the filtered phase images varied between 0.9-1.8 ppb. Discrepancies between the ranges of predicted and observed nuclear susceptibility induced frequency shift variations with FA can be attributed to the non-locality of phase measurements and to the contributions from macromolecular protons with T1 in the 35-350ms range [**6**].

Conclusions

We conclude that depending on sequence parameters, differences in steady state nuclear magnetization between GM/WM and CSF/WM can result in both paramagnetic and diamagnetic frequency shifts within a range of a few parts per billion. It is hoped that our preliminary findings will improve the design of robust 3D SPGR protocols for quantitative mapping of iron [**7**] and myelin [**8,9**] concentrations in brain tissues and will facilitate a more rigorous investigation of the contrast mechanism underlying phase imaging and susceptibility mapping.

References: 1. Duyn et al, PNAS 2007;28:11796, **2**. Schenck, Med Phys 1996;23:815, **3**. Haacke, 1999, **4.** Stanisz et al, MRM 2005;54:507, **5.** Haacke et al, MRM 2005;52:612, **6.** Behar et al, MRM 1994;32:294, **7.** Fukunaga et al, PNAS 2010;107:3034, **8.** Schweser et al, ISMRM 2011;120. **9.** Liu et al., Neuroimage 2011;56:930