Measurement Precision of Contrast Agent with R2* (Magnitude) and Quantitative Susceptibility Mapping (Phase)

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Purpose: Apparent transverse relaxation rate R_2* and magnetic susceptibility χ [1-2] are distinct measurable parameters that can be used to quantify paramagnetic and superparamagnetic contrast agents. R_2* mapping requires several echoes times in a gradient-echo scan and is based on the analysis of signal amplitude decrease. Quantitative Susceptibility Mapping (QSM) [3-4] uses magnetic field mapping, which can be extracted from the phase data of an identical multi-echo dataset. Here, phantom experiments are performed to compare the measurement precision of contrast agent concentration with R_2* and susceptibility methods.

Methods: Phantoms with two types of contrast agents were realized, Gd-DOTA (Dotarem; Guerbet, France) and superparamagnetic iron oxide nanoparticles (NP) (Endorem; Guerbet, France), especially used for their transverse relaxation effects. Twelve centimeter long, 13 mm diameter cylindrical tubes were filled with solutions of various contrast agent concentrations and were immersed in a cylindrical container filled with water. Gd concentrations ranged from 2.5 mM to 20 mM and NP concentrations ranged from 25 µM to 200 µM. Gd and NP phantoms were imaged at 1.5T (Achieva, Philips, The Netherlands). The tubes were placed aligned with the main magnetic field in an 8-channel head coil. A multi-echo gradient echo sequence with the following parameters was applied: $TR/TE_1/\Delta TE$ = 641/1.79/2.45 ms, 15º flip angle, 32 echoes, FOV = 192 mm, 1.5 mm in plane voxel size, 5 mm thickness slices and a 1.3 kHz bandwidth-per-pixel. These parameters provided proton-density contrast for the first echo so that subsequent processing had no influence from longitudinal relaxation. T_2* reconstruction was performed on the fly and frequency shifts (in Hz) were reconstructed using a weighted linear least squares method of phase over echoes [3]. Susceptibility was assumed to be 3 times the normalized frequency shifts, as it should be for a cylinder aligned with B_0. Regions-of-interest were drawn over the tubes to determine mean and standard deviations of R_2* and susceptibility field effects. Standard deviations were converted into concentration error and compared.

Results: A molar relaxivity r_2* = 5.96 $s^{-1}mM^{-1}$ and a molar susceptibility χ_m = 363 $ppm.M^{-1}$ (corresponding to a molar effect on frequency of 7.7 $Hz.mM^{-1}$) were measured for Gd (Fig.1). The effects were comparable with a slightly lower amplitude effect than phase effect for Gd. A molar relaxivity r_2* = 200.8 $s^{-1}mM^{-1}$ and a molar susceptibility χ_m = 3216 $ppm.M^{-1}$ (corresponding to a molar effect on frequency of 68.4 $Hz.mM^{-1}$) were measured for NP (Fig.2). Amplitude effects were higher than phase effects for NP.
When converted to concentration using these calibration slopes, standard deviation increased with concentration both for amplitude-derived and phase-derived methods (Fig.1d and 2d). Qualitatively on images amplitude-derived concentration are noisier than phase-derived concentration. While amplitude-derived precision varied from 0.5 to 2.5 mM for Gd, and from 8 to 25 µM for NP, phase-derived concentration varied from 0.02 to 0.5 mM for Gd, and from 1.5 to 7 µM for NP. Regardless on the contrast agent used, phase-based concentration measurement was between 5 and 25 times more precise for Gd, and between 3.5 and 5 times for NP. From these data, precision limit for this setup was estimated to be 10 µM and 1.5 µM for phase-derived concentration for Gd and NP, respectively.

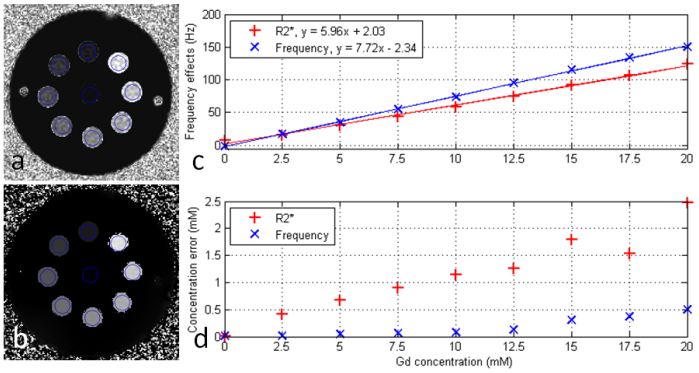

Fig.1: Amplitude-derived (a) and phase-derived (b) concentration maps for Gd phantom. Measured R_2* and frequency shift (c) both linearly increase with concentration. Their associated concentration standard deviations (d) also show an increase with concentration. Amplitude and phase-based contrast had similar frequency effects. Phase-based quantification had a smaller error.

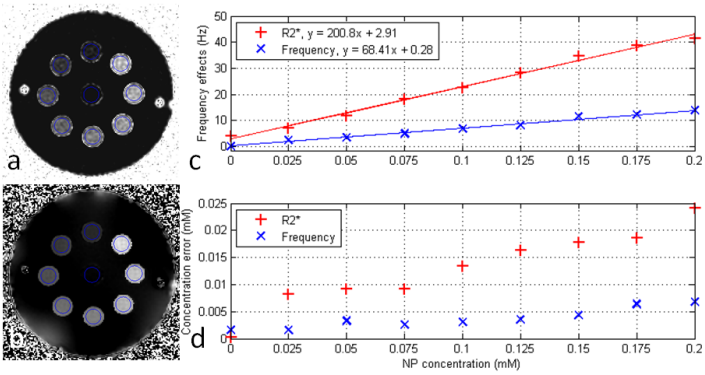

Fig.2: Amplitude-derived (a) and phase-derived (b) concentration maps for NP phantom. Measured R_2* and frequency shift (c) are both linearly increasing with concentration. Their associated concentration standard deviations (d) also show an increase with concentration. Phase-based contrast showed a smaller frequency effect and smaller error.

Discussion and conclusion: We have experimentally shown on a clinical system with standard imaging parameters and setup that, in the ideal case of cylinders oriented along the main field, phase-derived concentration (susceptibility) was between 3.5 and 25 times more precise than amplitude-based (apparent transverse relaxation) measures. These results suggest that QSM may be more precise than R_2* mapping to detect and quantify contrast agents. Complementary studies are needed to estimate the effective precision after QSM reconstruction, in particular the shape factor is expected to impair the precision [2]. As susceptibility is also a major contributor to transverse relaxation rate [1], a combination of phase and magnitude in gradient-echo scans would ideally yield enhanced quantification and detection for molecular MRI involving paramagnetic and superparamagnetic contrast agents.

References: **1.** Haacke, Magnetic Resonance Imaging, Wiley-Liss, 1999. **2.** de Rochefort *et al.*, Med Phys 2008. **3.** de Rochefort *et al.*, MRM 2010. **4.** Shmueli *et al.*, MRM 2009.