Critical Concentration of Contrast Agents for Quantification of Enhancement: Another reason for Dose Reduction

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Introduction: The importance of dose-minimization in Contrast-Enhanced (CE) MRI techniques has recently been highlighted by recognition of an association between gadolinium-based contrast agents and nephrogenic systemic fibrosis (NSF) in renal failure patients[1]. Recent studies practically verified the possibility of such a minimization without compromising image quality[2]. Dose reduction has yet other advantages to be explored, namely keeping the relation between the image enhancement and contrast agent (CA) concentration in the linear range. This linearity is required for applications such as quantitative perfusion imaging[3] and prediction of contrast agents' dynamics in MR angiography, using the theory of linear time-invariant (LTI) systems[4]. In this study we introduce the concept of "critical" concentration of CA up to which there exists a mostly linear dependence of signal intensity (SI) on concentration of the CA. Using this concept and our simulation we also explain how in lower doses the effect of RF field inhomogeneity is minimized on SI. Finally we present actual data with proper diagnostic value obtained through the tailored protocol.

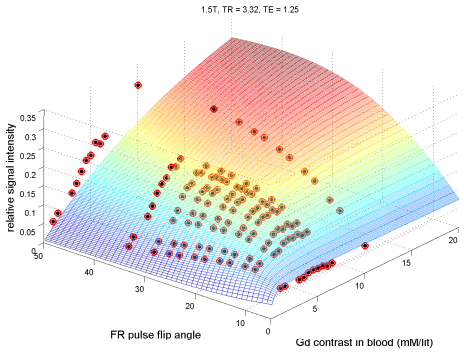

Figure 1. Relative signal intensity from the analytical expression for a range of [Gd] and flip angles (mesh) are in agreement with the experimental measurements on a phantom (dots).

Theory: Contrast agents decrease the relaxation times of the blood and therefore accelerate the recovery of the longitudinal magnetization. Using the relaxivity of gadopentetate dimeglumine (Gd-DTPA) and the related formula, we simulated the effect of CA concentration on the magnetization recovery as well as the corresponding relative SI of the spoiled gradient echo achieved from repetitive RF pulses. Using the concepts of poles and zeroes in calculus we estimated the critical concentration of the CA up to which there exists a mostly linear dependence of SI on concentration of the CA. The approximation is:

$$[Gd]_c = \left(\frac{1}{\cos(\alpha)} - 1\right) \cdot \frac{1}{TR \cdot R_1}$$

where α is the flip angle, TR is the repetition time and R_1 is the longitudinal relaxivity. Figure 2 shows that in the low dose range the SI is a linear function of [Gd] and also it is robust against flip angle deviations between 15 to 30 degrees.

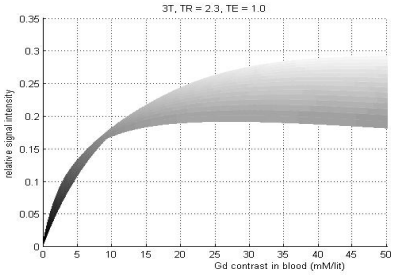

Figure2. Signal intensity vs. [Gd] for a range of flip angles from 15 to 30 degrees. It shows SI is insensitive to flip angle changes when [Gd]< 10 mL/lit.

Experiments: The actual SI for a range of gadolinium concentration ([Gd]) and flip angles were measured using an in-house phantom to examine the accuracy of the formula under non-ideal conditions of the imaging such as RF field inhomogeneity or non-accurate values for relaxivities. We verified a close agreement between the experimental results in non-ideal conditions and the analytical simulation (figure 1). Next, twenty patients (63.5±16.2 years, 9 Males) underwent high spatial resolution (0.7x0.6x0.8 mm) contrast enhanced MRA of the carotids at 3.0T, using a 32 channel system (TIM Trio, Siemens Medical Solutions) and a spoiled gradient echo. Initially, a contrast timing run, with 0.9 sec temporal resolution, was performed with 1.5 ml of Gd-DTPA. For 3D MRA the CA was diluted four folds (approximately equal to 0.06 mM/kg) and administered with an infusion rate of 2cc/s which led to a [Gd] of 3 mM/lit in blood. Flip angle was set between 18 to 25 degrees to ensure the linear and robust relation of SI to [Gd]. Using linearity assumption the SI was estimated for the main injection based on the enhancement obtained in the timing run through a LTI system simulation.

Results: All MR angiograms were scored for image quality on a 4-point scale by two independent expert readers and were scored either excellent (18) or good (2) for overall image quality. For all cases the center of K-Space data, that characterizes the contrast enhancement, was acquired within the "85% peak period" predicted by our simulation for carotids.

Conclusion: Using low-dose contrast agents, below a critical concentration, not only increases the safety measure in clinical practice but also guarantees the linear relation of SI and CA concentration. This linearity is necessary for the quantitative perfusion imaging and prediction of contrast agents' dynamics in MR angiography. The reduced-dose does not compromise the image quality required for clinical diagnosis and, further, in the routine range of flip angles the obtained SI is robust against RF filed inhomogeneity.

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