Signal Characteristic of a 1-molar Contrast Agent at 1.5 and 3T and Improvements with a Variable TE GRE Sequence

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Introduction: Gadobutrol (Gd-Bt; Gadovist®, Schering AG, Berlin, Germany) is a contrast agent based on Gadolinium (Gd). It provides a doubled Gd concentration of 1 M which should enhance bolus sharpness and reduce injection volume in CE-MRA. Improved image quality was already observed with this new contrast agent in MRA [1], however applications have been reported for which Gd-Bt didn't result in relevant improvement compared to 0.5 M Gadolinium contrast agents [2]. In order to explore the reasons of this counter-performance, the influence of the contrast agent concentration on signal intensity (SI) has been analyzed for various Gd concentrations in water at 1.5 and 3 T. Particular attention has been given to the assessment of the influence of increased T2/T2* effects at high concentrations. Following those considerations, variable TE pulse sequences are proposed in order to enhance SNR for high contrast agent concentration in CE-MRA. In particular, initial results of a modified rf-spoiled gradient echo (GRE) pulse sequence with variable bandwidth are presented.

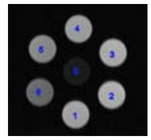

Fig. 1 Phantom (GRE)

Tab. 1 Measured relaxivities

	r_1 [L mmol^{-1} s^{-1}]	r_2 [L mmol^{-1} s^{-1}]
1.5 T	3.4 (3.0-3.9) [1]	7.31 (7.27-7.36) [1]
3 T	4.7 (4.0-5.6) [1]	7.1 (5.8-9.4) [1]

[1] 95% confidence interval

$$SI \propto \rho\left(1-e^{-TR/T1}\right)\sin(\alpha)e^{-TE/T2*}\left(1-\cos(\alpha)e^{-TR/T1}\right)^{-1} \quad (1)$$

Theory: The well known GRE steady state SI equation (1) depends on T1, T2* and spin density (ρ) of the tissue as well as on the sequence parameters TE, TR, α . Application of Gd-Bt results in shortened T1, T2 and hence T2*. While T1 shortening is beneficial and can result in dramatic signal enhancement for T1-weighted CE-MRA, T2/T2* shortening which becomes predominant at high concentrations, results in signal loss. T1 and T2-shortening can be estimated from relaxivities, however T2* is more complex and also depends on the setup and molecular environment. Using (1) and neglecting T2* effect, the relationship between TE and Gd-Bt concentration and SI can be evaluated from relaxivities: reducing TE enhances SI and higher concentrations benefit even more form shorter TE [3]. Consequently, TE is normally pushed to its minimum limit introduced by maximum gradient strength, slew rate and bandwidth-SNR considerations. We suggest going beyond the TE limit by adjusting TE in relation to the k-space position (variable TE approach). Assuming a k-space independent readout noise distribution, the readout bandwidth was adjusted for each phase encoding step in order to optimize the bandwidth vs SNR compromise. A higher bandwidth and thus shorter TE were used in central k-space where the image energy is the biggest while lower bandwidth in peripheral k-space was used to enhance readout SNR.

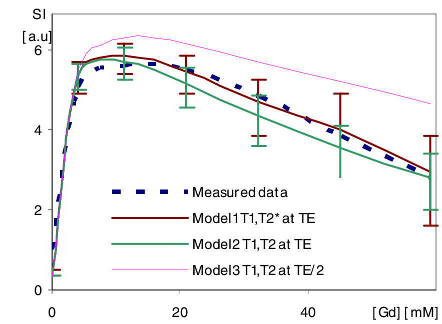

Fig. 2 SI vs. [Gd] in water; simulations and measurements. Error bars are derived from the 95% confidence intervals on T1, T2 and T2*. Measured SI is normalized with respect to the mean SI of Model1. Model3 assumes all parameters but TE identical.

Methods: A phantom composed of seven tubes with different concentrations of Gd-Bt in water has been designed ([Gd] = 0…59.0 mM, Fig. 1). Highest concentrations of this phantom were chosen so that to exceed peak contrast agent concentration in aorta for standard CE-MRA [4] while remaining within limits that may be physiologically acceptable. The phantom was imaged at room temperature at 1.5T and 3T (Magnetom Sonata and Trio systems, Siemens, Erlangen, Germany). T1 relaxation times were measured using an inversion recovery spin echo sequence with varying TI at constant TE and TR (27-49 measurements with exponential TI progression). T2 relaxation times were determined using a spin echo sequence with various TE at constant TR (26-40 measurements with exponential TE progression). T2* relaxation times were assessed using a gradient echo sequence with various TE at constant TR and α (10-24 measurements). The relaxation times were experimentally determined by fitting relaxations models to measured SI [5] and used to simulate SI which were compared with measurements of an rf-spoiled gradient echo sequence on a 8-channel head coil under a variety of sequence parameters (TR 3.53….10 ms, TE 1.51…4.8 ms, α 5…70°). Multiple acquisitions were performed in order to reach steady state (typically 8 measurements). Simulations were executed with one set of parameters based on T1, T2 and another set using T1 and T2*. In order to verify the feasibility of an adaptive bandwidth approach, an rf-spoiled gradient echo sequence has been modified. The readout bandwidth was linearly adapted to the line position in the k-space domain. Hence the TE was linearly varying while TR remained constant. The bandwidth ratio (BWR) was defined as the ratio between the bandwidth in outermost k-space and the bandwidth in central k-space. This sequence has been evaluated at 3 T and 20°C.

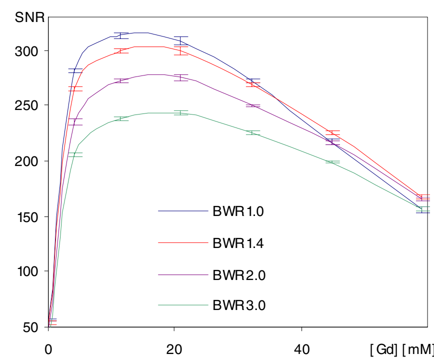

Fig. 3 SNR * vs. [Gd] in water for various BWR.

Results: Due to timing limitations of spin echo sequences, T1 and T2 could not be measured for high concentrations of contrast agent. Thus, T1 and T2 at the lowest concentrations (up to 11.4 mM) were used to determine the relaxivities (Tab. 1) and the relaxation times at all concentrations were extracted from those relaxivities. Considering the long T1 of water, a correction factor was applied to the fitted formula to correct for steady state effects [5]. The measured T2* times were substantially lower than T2 at all concentrations. Fig. 2-3-4 are showing SNR and SI for a FLASH sequence with TR=4.7 ms, TE=2.4 ms and α =15° at 3 T and 20°C, however we obtained comparable results over a wide range of sequence parameters. On Fig. 2, there is no significant discrepancies between SI simulations based on T2 and T2* (solid lines) and both show good agreement with the measured data (dashed line) after mean value normalization. The SI loss at higher concentration as a result of the predominance of T2/T2* effects is verified. An additional simulation (solid purple line) for SI at TE/2 represents the effects of a reduced echo time: increased SI and a peak SI shifted toward higher concentrations thereby minimizing T2/T2* related signal loss. Results from the variable bandwidth technique are depicted in Fig. 3-4. A loss of SNR is observed for high BWR and small concentrations of contrast agent. However, for appropriate BWR, SNR at high concentrations can be improved (note the crossing of the SNR curve at BWR=1.4 with the original SNR curve at around 36 mM in Fig. 3 and the increasing SNR for high concentrations in Fig. 4).

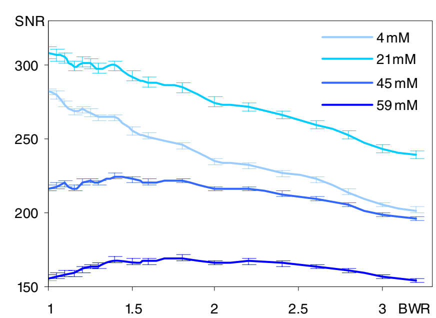

Fig. 4 SNR * vs. BWR for various concentrations.

* Error bars represent 95% confidence interval assuming Gaussian distribution.

Discussion: Although, we measured substantially shortened T2* in comparison to T2, by comparing simulated signal intensities based on measured relaxivities, we did not observe a relevant decrease in SI at higher concentrations due to T2* shortening in water. However, strong T2* effect can be expected in blood or plasma [3] such that T2* shortening and potential signal loss at high contrast agent concentration may be more important for in-vivo applications. The performance of the adaptive bandwidth approach has to be put in regard to the relative long TE of the FLASH sequence used for our implementation. Initial results of variable bandwidth measurements are encouraging and indicate the potential of this method for reducing echo time and consequently enhancing SNR at high contrast agent concentrations. Further studies are thus needed to adapt the approach to a gradient optimized angiography sequence with very short TE and to explore the full potential of the variable bandwidth approach. As reducing TE is shifting the concentration at peak SI toward higher concentrations, we could expect the SNR gain to be shifted as well. Another approach to decrease TE in central k-space could be a variable TE approach (VTE) where the echo time is dependant on the phase encoding step. Depending on the image dimensions, it may allow to substantially decrease TE in the high energy central k-space.

References: [1] Goyen et al, J Magn Reson Im 2001; 14:602-607 [2] Fink et al, J Magn Reson Im 2005; 22:286-290. [3] van Osch et al, Magn Reson Med 2003; 49:1067–1076 [4] Stehling et al, Radiologe 1997 ; 37:501-507 [5] Rohrer et al, Invest Radiol 2005; 40(11):715-724.