Variable Echo Time Imaging and Signal Characteristics of 1-M Gadobutrol Contrast Agent at 1.5 and 3T

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Introduction: Gadobutrol (Gd-Bt, Schering, Germany) contrast agent provides 1-M, Gd concentration which should enhance bolus in CE-MRA compared to standard 0.5-M agents. Improved image quality with Gd-Bt was already observed in peripheral MRA [1]. However applications have been reported for which Gd-Bt didn't result in relevant improvement compared to 0.5 M Gadolinium (Gd) contrast agents [2]. In order to explore the reasons of this counter-performance, the influence of the contrast agent concentration on signal intensity was analyzed for various Gd-Bt concentrations in temperature controlled water and human blood plasma at 1.5T and 3T. The steady state signal intensity (SI) of rf-spoiled gradient echo (GRE) imaging with short echo and repetition times (TE, TR << T2) can be described in terms of T1, T2* and spin density (ρ) of the tissue as well as the sequence parameters TE, TR and flip angle:

$$SI \propto \rho \frac{\left(1-e^{-TR/T_1}\right)\sin(\alpha)e^{-TE/T_2^*}}{\left(1-\cos(\alpha)e^{-TR/T_1}\right)} \quad (1)$$

Injection of Gd-Bt results in T1, T2 and T2* shortening. While T1 shortening result in signal enhancement for T1-weighted CE-MRA, T2/T2* shortening which becomes predominant at high concentrations, results in signal loss. In order to compensate for this, typical CE-MRA techniques are highly optimized and utilize the minimum possible TE. In the presented method, shorter echo times were achieved by the application of an adaptive bandwidth approach. Data were acquired using a high bandwidth and thus shorter TE in central k-space, which largely determines the contrast in the final image, while a lower bandwidth was used in peripheral k-space to enhance readout SNR.

	Water at room temperature			Water 37°C			Human Plasma 37°C		
Relaxation times [ms]	T_1	T_2		T_1	T_2		T_1	T_2	
1.5 T	2683 ± 15	1230 ± 34		4259 ± 91	1689 ± 43		2555 ± 19	675 ± 10	
3 T	2591 ± 45	959 ± 27		4420 ± 103	1388 ± 58		3070 ± 15	452 ± 5	
Relaxivities [L mmol-1 s-1]	r_1	r_2	r_2^*	r_1	r_2	r_2^*	r_1	r_2	r_2^*
1.5 T	4.7 ± 0.2	5.5 ± 0.3	5.5 ± 0.3	3.3 ± 0.2	3.6 ± 0.2	3.9 ± 0.2	4.5 ± 0.2	5.5 ± 0.4	5.8 ± 0.3
3 T	4.7 ± 0.2	5.8 ± 0.3	5.5 ± 0.3	3.3 ± 0.2	3.8 ± 0.2	4.4 ± 0.3	4.1 ± 0.2	5.4 ± 0.5	6.5 ± 0.4
Number of samples (r_i fit)									
1.5 T	6	6	8	6	9	8	5	8	7
3 T	6	7	8	6	9	8	5	7	7
r^2 (r_i fit)									
1.5 T	0.9988	0.9988	0.9997	0.9987	0.9922	0.9963	0.9952	0.9787	0.9945
3 T	0.9987	0.9998	0.9621	0.9980	0.9969	0.9814	0.9930	0.9936	0.9959

Table 1: Relaxation times and Gd-Bt relaxivities for water and human plasma at 1.5T and 3T.

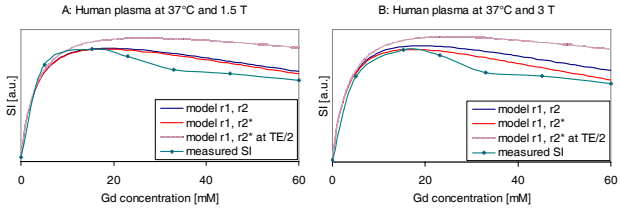

Fig. 1: GRE signal variation as a function of Gd-BT concentration for human plasma at 37°C at 1.5 T (left, TR=4.3ms, TE=1.5ms) and 3 T (right, TR=4.3ms, TE=1.6m). Simulated signal characteristics demonstrate good agreement between the measured data for both models based on R1 and R2 or R1 and R2*. Additional simulation results for reduced echo time (TE/2) indicate the potential for signal enhancement, particularly for high Gd-Bt concentration.

Methods: All measurements were performed at 1.5T and 3T (Magnetom Sonata and Trio, Siemens, Germany) MR systems. Signal characteristics were evaluated using phantoms based on distilled water and human blood plasma at room and body temperature (active temperature regulation). T1, T2 and T2* were determined for each individual sample using a series of turbo spin echo (TSE), spin echo (SE), and gradient echo measurements with 59 inversion times, 44 echo times and 12 echo times, respectively. Based on the estimated T1, T2 and T2* at different Gd-Bt concentrations, relaxivities R1, R2 and R2* were obtained by exploiting the linear relationship between concentration induced changes in relaxation time $T_i(c)$ and relaxivity R_i:

$$\left(\frac{1}{T_i(c)}-\frac{1}{T_i(0)}\right)=R_i\cdot c\,,\quad i=1,2,2^* \quad (2)$$

where $T_i(0)$ is the relaxation time of the solvent and c represents the Gd concentration.
Variable bandwidth results are presented for identical protocols at 1.5 T and 3 T (TR/TE = 4.7 / 2.4 ms, bandwidth = 390 Hz/Px, flip angle = 15°). The readout bandwidth was linearly adjusted within [BW_{min}, BW_{max}] depending on the phase encoding step (ky) and resulted in linearly varying TE (VTE sequence). Measurements were performed using multiple bandwidth ratios ($BWR=BW_{max}/BW_{min}$).

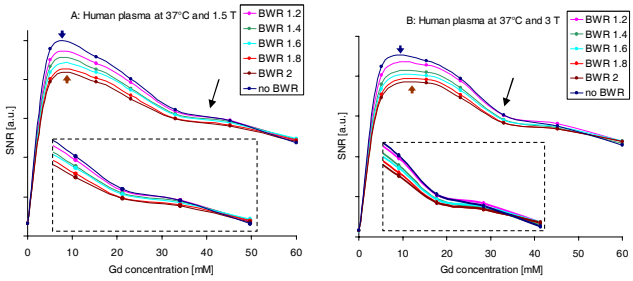

Fig. 2: SNR versus Gd-Bt concentration in plasma for various BWR at 1.5T (left) and 3T (right). The long black arrow indicates when the original sequence SNR (BWR 1.0) is being surpassed by the variable bandwidth approach. The small arrows indicate the shift of the peak SNR to higher concentrations if BWR is increased from 1.0 (no BWR) to 2.0.

Results: Measured relaxation times (T_i) and Gd-Bt relaxivities (R_i) are in accordance with published results [3] and are listed in Table 1 for water and human plasma. As expected, significant T1-lengthening as well as T2 shortening for increased field strength was found for all solvents. From Fig. 1, it is evident that numerical calculations based on the estimated relaxivities (Table 1 and eq. 1) could successfully be used to simulate GRE signal characteristics. No substantial discrepancies between SI simulations based on R2 and R2* were observed and both models exhibit good agreement with the measured data. An additional simulation at TE/2 represents the optimal contrast agent concentration (max signal) shift toward higher concentrations as a consequence of echo time reduction.
Results of human plasma VTE measurements with constant TR are summarized in Fig. 2 and 3. It is evident that an increase in BWR results in SNR loss predominantly for small contrast agent concentrations. However, due to the reduced T2 and T2* effects for BWR>1, SNR loss is less severe at high concentrations. More noticeably, SNR can even be improved as indicated by the crossing (long black arrow) of the SNR curves near 40 mmol/l. Finally, the inherent VTE-GRE trade-off between peak SNR loss and SNR gain at the high Gd-Bt concentration is represented in Fig. 3.

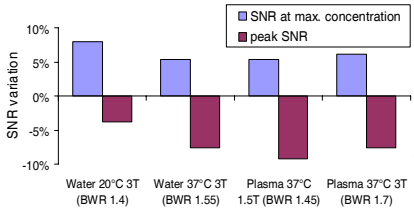

Fig. 3: Relative SNR variations at constant TR. Relative SNR variations at maximum concentrations are represented for the BWR resulting in the highest SNR gain and with the corresponding peak loss.

Discussion: MR-signal properties were explored for several experimental settings and concentrations of Gd-Bt in water and human plasma for 1.5T and 3T. Numerical simulations based on experimentally obtained relaxivities provide a useful tool to model GRE signal characteristics and were in good agreement with measured signal intensities. Although T2 and T2* effects lead to signal loss for high concentrations, the associated decay as a function of Gd-Bt concentration is relatively flat and introduces only moderate losses for realistic concentration. Surprisingly, even for human plasma, we measured similar R2* in comparison to R2 and did not observe a relevant decrease in SI at higher concentrations due to T2* shortening in water or human plasma. Nevertheless, stronger T2* effect may be expected for blood such that R2* increase and potential signal loss at high contrast agent concentration may be more important for in-vivo applications.
A variable TE approach based on adaptive bandwidth adjustment was implemented and evaluated. Measurements for different bandwidth-ratios i.e. shorter echo time in central k-space, revealed enhanced SNR at high contrast agent concentrations. Results indicating the potential of VTE for imaging with increased SNR at high contrast agent concentrations. However, peak SNR was generally reduced resulting in sub-optimal performance at lower contrast agent concentrations. Further studies are thus needed to determine the optimal trade-off between BWR and peak SNR penalty in an in-vivo setting with realistic concentrations and bolus transit times.

References: [1] Goyen M, et al. Top Magn Reson Imaging 2001;12(5):327-335. [2] Fink C, Puderbach M, et al. J Magn Reson Imaging 2005;22(2):286-290.
[3] Rohrer et al, Invest Radiol 2005; 40(11):715-724.