ULTRASHORT T2* RELAXOMETRY USING CONVENTIONAL MULTIPLE GRADIENT ECHO SAMPLING WITH S0 FITTING: VALIDATION WITH QUANTITATIVE UTE (QUTE) IMAGING

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Introduction- The increasing interest in high field MR as well as in (super-)paramagnetic contrast agents (iron oxide or holmium based) pose new challenges to quantitative MR imaging. Both interests are associated with increased R_2^* relaxation rates leading to fast signal decay. Gradient echo times of conventional multiple gradient echo (MGE) sampling strategies are often too long to adequately sample such fast signal decays. Hardware limitations (minimal echo time and echo spacing) thus make T_2^* based quantification of ultrashort T_2^* components difficult. To handle this challenge, we propose a post-processing methodology, based on the incorporation of S_0 (S at t=0ms) in the fitting algorithm, which is applicable to any type of conventional multiple gradient echo sampling of FID (MGEFID) strategy used for T_2^* relaxometry. Once the value of S_0 is determined, only one more data point above the noise level is needed to perform submillisecond T_2^* relaxometry. In the study presented here, the feasibility of the S_0-fitting algorithm is investigated by comparing it to quantitative UTE (QUTE), an acquisition method that has recently been proposed to image and quantify sub-millisecond T_2^* species[1,2]. To achieve this goal, paramagnetic particles (holmium-loaded microspheres (HoMS)), are introduced into gels and ex vivo rabbit livers. The resultant ultrashort T_2^* components are subsequently assessed with both methods in a quantitative and qualitative way.

Methods- ***HoMS Phantom*****:** For quantitative imaging an agarose gel (2%) HoMS dilution series with HoMS concentrations ranging from 4 to 15 mg/ml was created, providing a wide range of R_2* values[3]. $MnCl_2.4H_2O$ was added to the native gel to increase the baseline R_2* value ($R_2{}^*_{gel}$=45 s^{-1}) to match liver tissue. ***Ex vivo rabbit liver:*** Qualitative MR imaging was done after administration of 50 mg HoMS to the hepatic artery of an excised rabbit liver. ***MRI:*** MRI was performed on a 3T whole body scanner (Achieva, Philips Medical Systems, The Netherlands). T_2^* relaxometry was done using MGEFID and QUTE. MGEFID was performed in a 3D acquisition mode (cartesian sampling), using a FOV=120x120x37 mm^3; matrix=160x160x37; and $TR/TE_1/\Delta TE/\alpha$ = 35ms/1.57ms/2.3ms/25°. Eight echoes were acquired using flyback gradients so as to keep the readout gradient polarity constant. Total scan time was 3min37s. QUTE was performed by varying the minimal echo time in successive UTE scans in an interleaved manner, allowing sampling of fast decaying signals. QUTE was performed using isotropic 3D radial sampling scheme with a FOV=120^3 mm^3; matrix=160^3; and $TR/\Delta TE/\alpha$ = 16ms/2.3ms/8°. Five echoes were acquired after each excitation. Six interleaves were applied with a minimal TE, respectively, 0.08, 0.15, 0.3, 0.6, 1.2 and 1.8ms. Scan time of each interleave was 7min42s, leading to a total scan time of 46min12s. ***Post-processing:*** T_2^* relaxometry was performed using a mono-exponential weighted least squares (WLS). Data with an SNR<3 were excluded from analysis to prevent the influence of Rician distributed noise at low SNR. HoMS relaxivity (r_2^*) was determined from the calibration curves. ***S_0-fitting:*** S_0 fitting was applied to MGEFID data. Mono-exponential signal behavior and homogeneous signal intensity (S_0) in the tissue of interest were assumed when applying the S_0-fitting algorithm. S_0 maps were generated with the conventional WLS fitting algorithm. The average value of S_0 of the tissue of interest was determined from the S_0 map in a manually selected ROI which did not contain any contrast agent on visual inspection. This value was used as the first data point (S at t=0ms) of the tissue of interest in the mono- exponential WLS fitting algorithm.

Results- R_2^* maps of the HoMS gel phantom are presented in Figures 1a and 2a. For both methods, relaxation rates up to 2000 s^{-1} were determined and the HoMS r_2^* relaxivity appeared to be comparable for pixelwise (Fig. 1b within error bars, 2b) as well as for ROI based analysis (Fig. 1d, 2d) (r_2^*=166-169 $s^{-1}mg^{-1}ml$). The R_2^* map from MGEFID with S_0 fitting shows a higher variance compared to the QUTE R_2^* map, specifically at high HoMS concentrations, which can be attributed to the lower number of data points available for fitting. The linear relationship between the log (signal) vs HoMS concentration shown by the densely sampled interleaved QUTE data (Fig. 2c) confirms the mono-exponential signal decay that was assumed for MGEFID with S_0 fitting (Fig. 1c). The homogeneity of S_0 in a segment of the liver without HoMS is shown in Fig. 3a. R_2^* maps of ex vivo rabbit liver with HoMS (Fig.3) show an excellent agreement between R_2^* values as determined with MGEFID with S_0 fitting and QUTE. Conventional MGEFID without S_0 fitting was unable to determine R_2^*>500 s^{-1}, whereas MGEFID with S_0 fitting detected R_2^* values up to 1000 s^{-1} within the liver (Fig.3b-c).

Discussion & conclusions- S_0 fitting in combination with MGEFID expands the quantifiable R_2^* range up to R_2^*>2000s^{-1} (T_2^*=0.5ms), as compared to conventional MGEFID relaxometry. S_0 fitting does not require adaptations to the scan protocol, leaving the total scan duration unchanged. The r_2^* relaxivity of HoMS as determined with MGEFID with S_0 fitting and QUTE matched very well. QUTE allowed the characterization of very fast decaying signals and demonstrated that homogeneously distributed HoMS in gel exhibit mono-exponential signal decay. Although very suitable for validation studies, the scan time of QUTE is prohibitive for this method to be used in most clinical applications. Furthermore, the UTE technique is not generally available. In conclusion, MGEFID with S_0 fitting, on the other hand, provides a time-efficient alternative to QUTE for R_2^* mapping of a wide range of relaxation rates, that is suitable for in vivo studies, such as the assessment of tissue iron overload diseases (thalassaemia: myocardial or liver iron) as well as the quantification of any T_2^* contrast agent such as HoMS and (U)SPIO's.

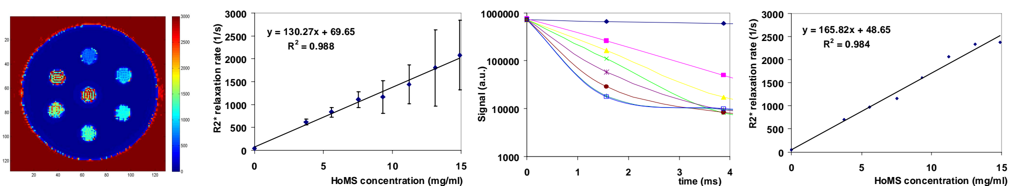

Figure 1. MGEFID with S_0-fitting a) R_2^*map. b) Pixelwise R_2^* analysis. c) MR signal vs time. d) ROI R_2^* analysis

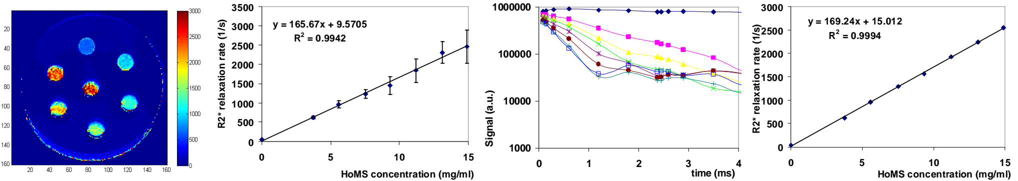

Figure 2. QUTE a) R_2^*map. b) Pixelwise R_2^* analysis. c) MR signal vs time. d) ROI R_2^* analysis

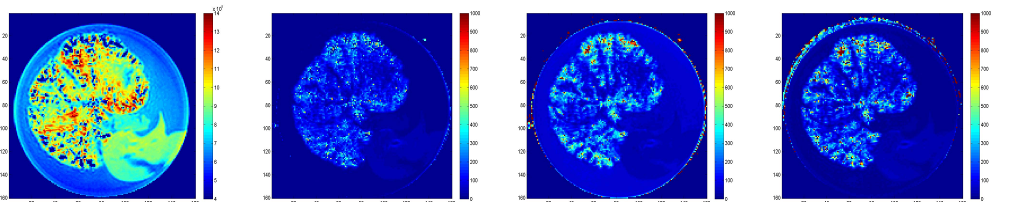

Figure 3.a) S_0 map of ex vivo rabbit liver, showing homogeneous intensity in a liver lobe without HoMS (lower right). R_2^* maps of liver with HoMS as determined with MGEFID without (b) and with (c) S_0 fitting. S0 fitting shows a good correspondence with interleaved QUTE (d), even at R2* > 500 s^{-1}.

References [1]Robson MD, Clin Rad 2004, 59:727-735 [2]Rahmer J, MRM 2006, 55:1075-1082 [3]Seppenwoolde JH, MRM 2005, 53: 767-84