Robust Simultaneous ΔR2 and ΔR2* Estimation for Vessel Size Imaging

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Introduction

The analysis of the microvasculature of a tumor is of high interest in oncology research, both for diagnosis and therapy monitoring. Tropez [1] and Kiselev [2] have shown that the mean vessel size within an imaging voxel in MR images can be estimated from the local change of the reversible (ΔR2*) and irreversible (ΔR2) relaxation rates, induced by the application of an iron-oxide based blood-pool agent. However, the range of available SPIO contrast agents still limits the application of the vessel size imaging (VSI) in translational research. The fast wash-out characteristics demand the *rapid* and *simultaneous* quantification of ΔR2* and ΔR2 [3]. Lately, much effort has been put on the development of sequences for fast and simultaneous measurement of R2 and R2*, mostly utilizing (turbo-) spin-echo or GRASE sequences [4,5]. However, little focus [6] has been put on the adequate processing of the measured data. We present a new MR sequence with a dedicated post-processing algorithm to achieve accurate ΔR2* and ΔR2 maps that are insensitive to large scale B0 and B1 field inhomogeneities as well as slice imperfections. The approach has been evaluated in phantom and animal experiments.

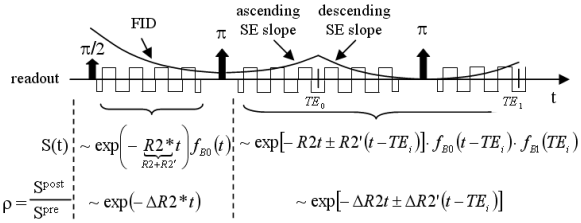

Fig. 1. *Turbo spin-echo sequence with multiple gradient echoes to sample the FID and the slopes of one or more spin echoes. The change in the relaxation rates is directly fitted from the ratio of the signal pre and post contrast agent injection.*

Methods

As shown in Fig 1, the approach makes use of a turbo-spin-echo TSE sequence with N_{FID} and N_{GE} gradient-echoes to sample the FID and the ascending and descending slopes of N_{SE} spin echoes. An overall theoretic signal model of mono-exponential decays is fitted pixel-wise to the *ratio* $\rho(t)= S^{post}(t)/S^{pre}(t)$ of the signals pre and post contrast agent injection. The basic assumption behind that approach is that static B0 and B1 inhomogeneities as well as the effect of slice imperfections to the flip angle profile can be described as multiplicative functions f_{B0} and f_{B1} and thus factor out by division of the two signals (Fig. 1). A non-linear least square (Levenberg-Marquardt) algorithm is utilized to obtain the unknowns ρ(0), ΔR2* and ΔR2. The ratio data are weighted according to their expected variance, which is derived from the error propagation function of ρ(t). This is essential to avoid unstable or excessive ratio values, when dividing by small values S^{pre} in regions of noise or at late echo times. All imaging was performed on a 1.5T clinical whole body scanner (Philips Achieva, The Netherlands). Phantom Experiment: The phantom contained 3 samples surrounded by water and filled with different concentrations of an SPIO contrast agent (Resovist, Bayer Schering, Germany). In each of four injections, the R2 and R2* of all samples were increased by $10.3s^{-1}$ each by adding SPIOs (FOV 210mm, 3 slices à 5mm, multi-slice excitation, N_{SE}=3, N_{GE}=25, N_{FID}=9, matrix = 224x224, TE_{SE0}=40ms, 2:22min incl. preparation). Animal experiment: ΔR2*, ΔR2, and vessel size maps of a tumor (breast carcinoma, SKBR3), implanted 21 days prior to the experiment, were obtained twice after two injections of 200 µl/body weight of an USPIO contrast agent (Supravist, Bayer Schering AG) to evaluate the reproducibility of the approach. Scan parameters: FOV 60mm, 4 slices à 1mm, multi-slice excitation, NSA=2, simultaneous scan: N_{SE}=2, N_{GE}=15, N_{FID}=3, matrix = 128x105, NSA=2, TE_{SE0}=57ms, 3:30min incl. prep. The results were all compared with the maps generated with multi-spin-echo (N_{SE}=20, 8min) as well as multi-gradient-echo (N_{GE}=11, 4min) reference scans of the same spatial resolution. The comparison with subsequent reference measurements is possible due to the long blood cycle time of the contrast agent in use [7]. In preceding measurements, the diffusion constant and vessel volume fraction were determined to be $0.8\mu m^2ms^{-1}$ and 2.3%, respectively.

Results

As depicted in Fig. 2, the proposed method yields ΔR2 and ΔR2* values that are in good agreement with the expected values (solid line) independently of the initial and additional SPIO concentrations. Fig. 3 shows part of a T2-weighted baseline image with colored overlays of ΔR2 and ΔR2* obtained with the proposed simultaneous method and the reference scans after the first injection. Despite the high heterogeneity, which hampers the comparison of mean values, the structural appearances of the simultaneously derived maps compare very well with the reference measurements. Fig. 3 also depicts the vessel size maps obtained after the two injections. The quantitative and qualitative similarity of the two maps implies good reproducibility of the proposed method independently of the contrast agent concentration.

Discussion and Conclusion

(Turbo-) spin-echo sequences are known to be very sensitive to the presence of static field inhomogeneities, RF and slice imperfections, hampering accurate estimation of ΔR2 and ΔR2*. With the proposed method, changes in the relaxation rates ΔR2* and ΔR2 are directly determined from the ratio of the signals pre and post contrast agent injection. In that way, the effect of static field inhomogeneities and the effect of RF and slice imperfections cancel out that appear as multiplicative functions to the FID and the spin-echo signal, respectively. The utilization of an overall fit model also enables high resolution imaging with long readout gradients at the expense of the number of gradient echo images, since the redundant R2 and R2* dependence of FID and spin-echo data stabilizes the fit in terms of SNR and accuracy. Further studies need to analyze the impact of diffusion as well as variations of inner voxel susceptibility gradients on the signal ratio. With regard to the sequences described by the GESFIDE [4] or GESSE [6] techniques that utilize only the first spin-echo, the presented approach extends the range of measurable T2 values by using multiple spin echoes. Highly accurate ΔR2 and ΔR2* values have been obtained in phantoms and mice. Our results imply that the proposed method is well suited for application in vessel size imaging. These findings are under further investigation and evaluation in a comprehensive animal study.

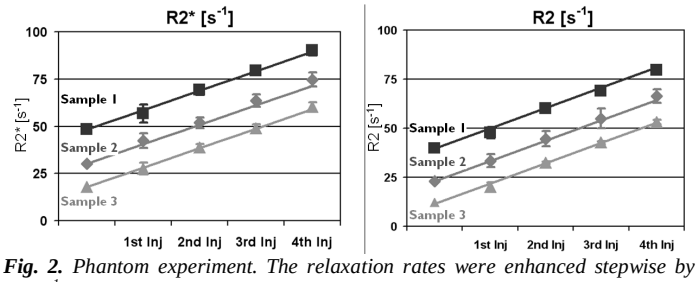

Fig. 2. *Phantom experiment. The relaxation rates were enhanced stepwise by $10.3s^{-1}$ per injection of an SPIO contrast agent diluted in distilled water. The simultaneous determination of ΔR2 and ΔR2* very well matches with the expected values.*

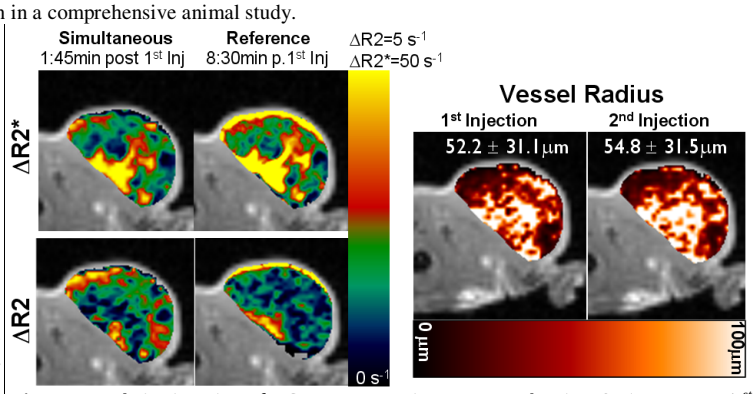

Fig. 3. *Vessel size imaging of a SKBR3 tumor in a mouse. The ΔR2 & ΔR2* maps (1st Inj.) nicely agree with the reference. The similarity of the VS maps after both injections indicates the reproducibility of the approach.*

[1] Tropès et al, MRM 45, pp 397-408, 2001, [2] Kiselev et al, MRM 53, pp 553-563, 2005, [3] Lawaczeck et al, Acta Radiologica 38, pp 584-597, 1997, [4] Ma et al, JMR 111, pp 61-69, 1996, [5] Gmitro et al, MRM 53, pp 1363-1371, 2005, [6] Yablonskiy et al, MRM 37, pp 872-876, 1997, [7] Allkemper et al, Radiology 223, pp 432-438, 2002