Unambiguous Localization of Contrast Agents via B_0-Field-Cycling

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Introduction: Recently a novel MRI contrast mechanism taking advantage of relaxivity dispersion has been presented [1]. The new approach combines conventional MRI with Fast Field Cycling methods to distinguish between tissue with and without contrast agent. The main idea is to place an offset field generator inside a (clinical) MR scanner to acquire images at different magnetic field strengths. Its contrast mechanism exploits the fact that contrast agents with significant relaxation dispersion (*dR/dB*) [2] can be switched in strength by field cycling. Therefore the method allows unambiguous localization of the contrast agent even if no prescan data without contrast agent is available for comparison like e.g. in long term studies. However previous algorithms used with the inversion as magnetization preparation faced problems if more than one different relaxation rates (at B_0) are present in the sample – an unavoidable fact for in vivo measurements.
In this work we present a setup and a modified analysis algorithm which eliminates these limitations. Our method acquires two scans at field strengths $B_0 \pm \Delta B$ and combines them into a new image. Its resulting intensity distribution scales with relaxivity dispersion such that signal from the contrast agent is enhanced and pure tissue signal strongly suppressed.

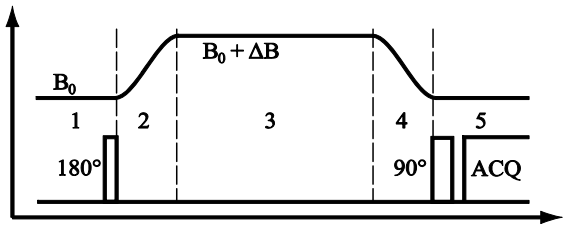

Fig. 1: Scheme of experiment with phases: polarization (1), ramp (2), evolution time at $B_0 \pm \Delta B$ (3), ramp (4) and acquisition (5).

Methods: Clinical MR scanners are not capable of sending and receiving RF fields at frequencies much different from the Larmor frequency given by B_0. Therefore the presented experiments need to switch fields between a magnetization preparation and data acquisition. Fig. 1 shows the different phases of the experiment: polarization and inversion at B_0 (1), field ramp to $B_0 \pm \Delta B$ (2), evolution time at $B_0 \pm \Delta B$ (3), field ramp to B_0 (4) and 90° pulse with acquisition (5). It can be shown [3] that the magnetization at beginning of acquisition is proportional to a magnetization relaxed at $B_0 \pm \Delta B$ for the duration of the cycled field (phase 3), independently of the waveforms of the field ramps.
The switchable field is realized by a home build solenoid coil achieving an offset field of ±80mT and is driven by a home build bipolar power source. The coil is placed in the isocentre of a clinical scanner and holds a birdcage resonator for RF sending and receiving. Switching times are <4ms for ramp up and <2ms for ramp down.
Main goal of the analysis algorithm is to extract relaxivity dispersion in the images and reject as much spin density, T_1 or T_2 weighted information as possible. The resulting contrast is found by subtracting two normalized scans at $B_0 \pm \Delta B$, but previous algorithms encountered problems with an inversion as magnetization preparation due to the new equilibrium magnetizations at $B_0 \pm \Delta B$ such that undesired signal contributions appeared.
A first change is implemented by using a dynamic normalization. It accounts for a magnetization vector starting with magnitude M_0 and relaxing towards magnitude $M_0 (1 \pm \Delta B / B_0)$.
Nevertheless there is still an undesired signal arising from different relaxation rates in the sample at B_0. Assuming a sample with two regions: one containing a contrast agent with a large relaxation rate and the other holding pure tissue with a small relaxation rate. To eliminate signal from the pure tissue the normalization needs to match the behavior of the magnetization in the region. Processing the contrast agent with the same normalization will feature – besides the intended signal – an undesired signal as this region has relaxed much faster towards the new equilibrium magnetizations such that the normalization is not appropriate. The resulting unwanted contribution could be eliminated by choosing a different normalization, but every change will override the suppression of pure tissue signal. This implies that biological samples with a full range of relaxation rates yield undesired signals for all but one of the relaxation rates making an unambiguous localization of the contrast agent impossible.
To overcome the problem a second change has been implemented: The images are separated into homogeneous regions with just small differences in relaxation rates. These regions can be normalized independently with the local relaxation rate at B_0. Hence all regions are treated with the optimal normalization and do not feature any unwanted contributions. The resulting intensity is a pure function of relaxation dispersion coming from the contrast agent and does not contain any background.

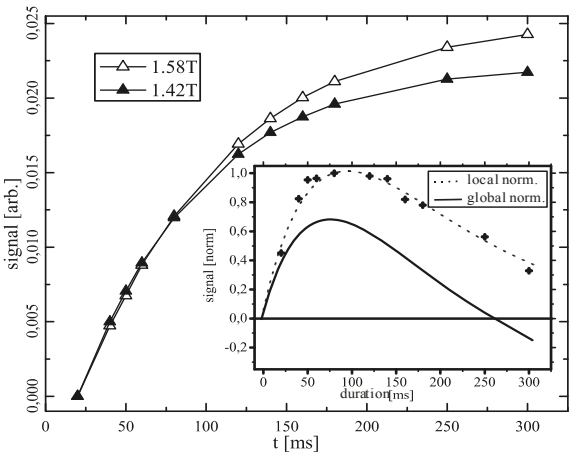

Fig. 2: Relaxation curves measured at 1.42T (▲) and 1.58T (Δ) with different relaxation rates and different equilibrium magnetizations, the inset shows the calculated relaxivity dispersion intensity with global (solid) and local normalization (dotted) and processed data (points). Values for Vasovist (0.66mM/l) in PBS with 4.5% RSA.

Results: We measured a sample containing Vasovist (0.66mM/l) in phosphate-buffered saline (PBS) with rabbit serum albumin (RSA) at 4.5% weight to volume. Fig. 2 shows relaxation curves at 1.42T (▲) and 1.58T (Δ) for the contrast agent. The different equilibrium magnetizations are clearly visible. If looking closely the crossing of the two curves at 80ms indicates the different relaxation rates. Relaxation dispersion is determined to be $-(18.8 \pm 1.9)\ s^{-1}mMol^{-1}T^{-1}$ at 1.5T.
From these values we calculated the theoretical intensity for the contrast agent as function of field duration at $B_0 \pm \Delta B$ (phase 3) for applying a global or local normalization to suppress signal from PBS and RSA. These curves are shown in the inset of Fig. 2 as solid or dotted line respectively. Using a global normalization yields a smaller signal due to the undesired contributions and runs into negative values when these are dominant. In contrary local normalization yields higher, pure positive signal. We processed our data with a local normalization and superposed the data points. They match well the theoretical curve for local normalization and indicate that the data yields the desired pure positive relaxivity dispersion curve.

Conclusion: We have demonstrated a setup for imaging in a clinical scanner between 1.42T and 1.58T. With its help we quantified a contrast agent with high relaxivity dispersion and used our modiefied analysis algorithm to gain a pure relaxation signal which allows us to unambiguously identify contrast agents. The measured results match well the theoretical calculations and encourage that future work can be carried out on biological samples. To further improve the analysis we will implement a fast relaxivity prescan at 1.5T prior to the experiment. It will produce a relaxivity map of the imaging region such that normalization can be carried out on a voxel by voxel basis. In this case the modified analysis algorithm can be applied to arbitrary inhomogeneous samples.

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