Comparing single-shot Look Locker T1 mapping and dynamic 3D T1-weighted gradient echo imaging for free breathing quantitative DCE-MRI in a rat liver tumor model at 1.5 T

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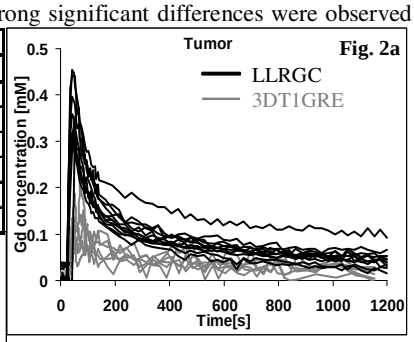
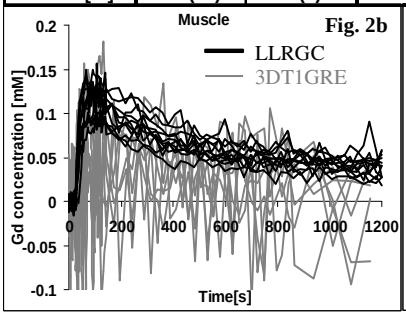
Introduction: Dynamic 3D T1-weighted gradient echo (3DT1GRE) imaging sequences are broadly used in dynamic contrast enhanced (DCE) MRI studies investigating tumor viability (i.e. perfusion, permeability and angiogenesis) [1]. These methods however, are prone to displacement errors, motion and flow artefacts and complex retrospective correction algorithms are needed to allow for a reliable conversion from MR signal to R1 [2]. By dynamically mapping the T1 (1/R1) values directly, motion sensitivity could be greatly reduced. However, such T1 mapping methods must provide sufficient temporal resolution of only a few seconds. A 2D single-shot Look-Locker T_1 mapping technique (LLRGC) applying golden angle radial sampling in combination with a contrast enhancing k-space filter has recently been proposed for this purpose [3]. The present study aims at comparing this dynamic 2D T1 mapping technique (LLRGC) with the standard 3DT1wGRE method for non-triggered and free breathing DCE-MRI experiments in a rat liver tumor model. To allow for transition of this technique to human hepatic cancer studies all experiments were performed on a 1.5 T clinical MR system (1.5T Achieva, Philips Medical Systems, Best, The Netherlands) using a 4-channel wrist array coil.

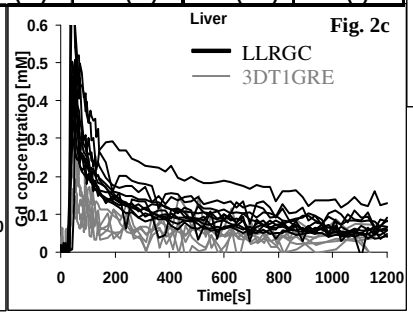
Methods: Experiments, approved by the local ethics committee, were performed in a rat model of unifocal hepatocellular carcinoma (HCC). 12 days after tumor cell implantation into the right lateral liver lobe 11 and 6 tumour bearing rats were imaged with the LLRGC or 3DT1GRE techniques, respectively. Following a survey scan, a multi-slice T_2-weighted TSE sequence was applied for tumor detection. Then, dynamic imaging was performed every 6s during the first 3 minutes and every 24s until 20 minutes within an axial slice (or slice package) covering liver, tumor and back muscles. Gd-DTPA was bolus-injected (≤ 1s) after 60s. For the LLRGC method, after non-selective adiabatic inversion, 225 radial profiles (TR/TE=11.6/5.2ms, flip angle=10°) were acquired during the first 2.6s of the inversion recovery cycle. From these data, 22 T1-weighted images (Δ=2mm, FOV=80x80mm^2, matrix=100x100) were reconstructed by k-space filtering (see [3]), from which the T_1 map was computed applying a three-parameter non-linear least-square fit using $A+B\cdot\exp(-T_R/T_1^*)$ and the correction formula $T_1=T_1^*\cdot(A/B-1)$ [4]. For the 3DT1GRE method, T_{10} values were first determined prior contrast injection according to [2]. Dynamic imaging of an axial package containing 10 slices of 1.2mm (FOV=80x60mm^2, matrix=100x100, TR/TE=9.6/4.7ms, flip angle= 20°) was performed. To minimize errors due to flip angle inaccuracies and for comparison, T1 maps were calculated according to [5] only for the central slice. T_1-time curves were converted to concentration [C_{Gd}]-time curves assuming the fast exchange limit regime $(R_1=R_{10}+r_1\cdot C_{Gd})$ [6] and a Gd-DTPA relaxivity of r_1=4.1mM^{-1}. Pharmacokinetic modelling was performed using an one-compartment model based on the Kety-Schmidt equation [7]. For this purpose, a population based AIF was determined from high temporal resolution dynamic CT data of 11 rats (using Gd-DTPA as contrast agent) applying the model described by Parker et al. [8]. T_{10}, K^{trans}, v_e, delay T_d in arrival of AIF to tissue, renal clearance rate r_c and summed relative squared residuals (SRSR) (to provide values for the goodness of fit) were compared for muscle, liver and tumor tissue for both DCE-MRI methods.

Results: Table 1 shows the comparison of T_{10}, K^{trans}, v_e, T_d, r_c and SRSR (listed as mean (stddev)) between the techniques for the three tissues of interest. No significant difference was detected for T_{10}, T_d, and r_c. In contrast, strong significant differences were observed for K^{trans}, v_e, and SRSR ($p<0.001$). K^{trans} and v_e values of all tissues derived by 3DT1GRE are significantly lower compared to LLGC. Values reported in literature for rat muscle and HCC are within range of K^{trans} and v_e derived by LLRGC [9-11]. To our knowledge, no such data are available for rat liver. Fig.2a, b, c display all acquired Gd-DTPA concentration time curves (black: LLRGC, grey: 3DT1GRE). Although the onset of bolus arrival is detected simultaneously (similar T_d), peak concentration values for all tissues as detected by 3DT1GRE are below expected concentrations for a double dose Gd-DTPA bolus injection. Nevertheless, time curves for both methods merge after approx. 600-800s producing similar renal clearance rates. The high levels of noise and motion artefacts for back muscle in the 3DT1GRE method prevent reliable pharmacokinetic modelling and comparison for this tissue (SRSR of 205%).

Table 1	Tumor		Liver		Muscle	
Parameters	3DT1GRE	LLRGC	3DT1GRE	LLRGC	3DT1GRE	LLRGC
T10 [ms]	1048 (150)	1073 (75)	468 (102)	519 (46)	956 (316)	918 (40)
Td [s]	-2.38 (4.5)	-1.5 (1.9)	-1.75 (2.6)	2.88 (1.9)	0.5 (6.4)	0.75 (2.1)
Ktrans [min-1]	0.10 (0.05)	0.48 (0.09)	0.22 (0.07)	0.78 (0.21)	0.04 (0.02)	0.10 (0.02)
Ve [%]	7.75 (2.2)	18.37 (2.6)	10.07 (3.8)	22.66 (3.1)	5.6 (1.6)	11.96 (1.8)
rc [min-1]	0.07 (0.03)	0.07 (0.01)	0.06 (0.1)	0.07 (0.2)	0.06 (0.04)	0.06 (0.01)
SRSR [%]	31 (16)	9 (3)	44 (25)	20 (11)	205 (132)	6 (2)







Discussion: The LLRGC method allows for robust detection of Gd-DTPA concentration time curves of hepatic tumor, liver and muscle tissue in anaesthetized free breathing rats by means of DCE-MRI. Calculated K^{trans} and v_e values for tumor and muscle tissue correlate with data from literature. In contrast, K^{trans} and v_e values are strongly underestimated when applying the 3DT1GRE method in this setup. This phenomenon is much likely caused by the artificially high noise level, i.e. motion artefacts, within the pre-contrast image data reducing the detectable difference in MR signal after CA injection. Otherwise, both methods provided similar native T_{10} values, bolus delay times and renal clearance rates. The LLRGC enables quantitative and free breathing DCE-MRI of orthotopic HCC tumor models in rats on a clinical 1.5T MR system.

References: [1] O'Connor JPB et al. BJC, 96, 2007; [2] Cheng HM et al. MRM, 55, 2007; [3] Winkelmann S. et al. IEEE, 26(1), 2007; [4] Deichmann R. & Haase A. JMR, 96, 1992; [5] Li K et al. JMRI, 12, 2000; [6] Landis CS et al. MRM, 44, 2000; [7] Tofts et al. JMRI, 10, 1999 ; [8] Parker GJM et al. MRM, 56, 2006; [9] Yankeelov TE et al. MRM, 57, 2007; [10] Chalmers CR et al. GUT 55, 2006 ; [11] van Laarhoven H et al. JMRI, 18, 2003