Rapid Quantification of Arterial Input Function and Myocardial T1 Changes in Mice during Contrast Agent Injection

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Introduction

Dynamic contrast enhanced MRI (DCE-MRI) has been used increasingly in cardiovascular MR (CMR) (1). The time course of contrast agent accumulation in myocardium and blood is required for quantitative analysis. A common practice is to obtain contrast agent concentration from the signal intensity of T_1-weighted gradient-echo images. However, this approach is subject to multiple artifacts (1). More accurate quantification can be obtained from T_1 measurements because of the linear relationship between R_1 and the contrast agent concentration (2). Previously, we developed an ECG-triggered saturation recovery Look-Locker (SRLL) method that allowed T_1 mapping of mouse myocardium in 3 min (3). However, the longer T_1 value of the blood may require a longer imaging time. This leads to inadequate temporal resolution to track the dynamics of contrast agent in rapid circulating blood in mice. In the current study, we aimed to develop and evaluate a modified SRLL (MSRLL) method with improved temporal resolution for T_1 quantification of both blood and myocardium in DCE-MRI experiments.

Methods

MRI Protocol The MRI study was performed on a horizontal 7T Bruker scanner (Bruker Biospin Co. Billerica, MA). The ECG-trigger SRLL pulse sequence was described previously (3). Briefly, a 90˚ RF pulse was applied at the beginning of each phase encoding step, followed by a series of ECG-triggered FLASH acquisitions to track the longitudinal recovery process. In the current study, three nonselective 90˚ RF pulses were applied using a 18 cm long volume coil to achieve whole body saturation. To improve the temporal resolution of T_1 mapping, 32 phase encoding lines in the low spatial frequency range were acquired during the injection and washout periods. The images were expanded to a larger matrix size (128x64) offline with the high spatial frequency lines from the images acquired at baseline (Fig. 1). Such acquisition scheme effectively halved the imaging time.

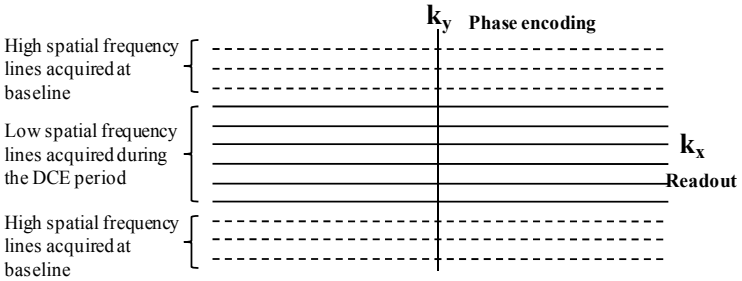

Figure 1. The expansion scheme of undersampled images acquired during the DCE period.

Phantom Study A water-filled 2cm diameter and 8 cm long phantom was imaged using SRLL and MSRLL methods, respectively. The following imaging parameters were used: TE, 1.7 ms; TR, 3.5 s; number of FLASH images, 16; flip angle, 10˚; slice thickness, 1.5 mm; number of averages, 1; FOV, 3x3 cm^2. The equilibrium magnetization was measured at baseline with a TR of 5 s and a matrix size of 128x64.

Animal Preparation and MEMRI Protocol Four month old C57BL/6J mice (n = 5) were used. Animals were prepared as previously described (3). Heart rate was maintained at around 480 bpm with 0.8–2% isoflurane. To demonstrate the utility of MSRLL in DCE-MRI experiment, a 126 mM $MnCl_2$ solution was injected via tail vein at a dose of 14 nmol/min/g (body weight) for 30 min, followed by a 30 min washout period. ECG and respiratory signal was monitored by a physiological monitoring system (SA Instruments, Billerica, MA). 11~14 FLASH images were acquired at end-diastole, rendering a TR of ~3.5 s. Other imaging parameters were the same as for phantom study. Baseline T_1 was measured with both large (128x64) and undersampled (128x32) matrix sizes. During the injection and washout periods, images were acquired with undersampling in phase encoding direction for high temporal resolution (<2 min).

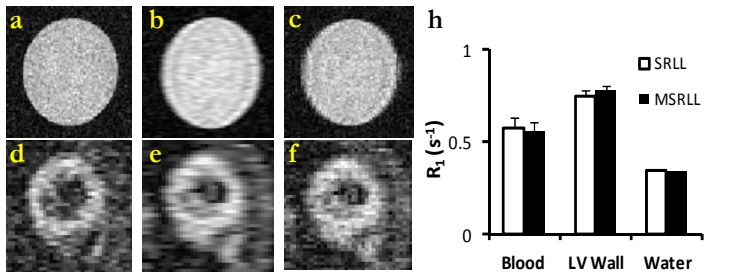

Figure 2. Water phantom and in vivo mouse heart. **(a) & (d)** Images acquired with large matrix size. **(b) & (e)** Images acquired with small matrix size. **(c) & (f)** Composite images of (b)&(e) expanded with high spatial frequency lines from (a)&(d), respectively. **(h)** T_1 values estimated from SRLL and MSRLL methods.

Image Analysis Composite images with a matrix size of 128x64 were generated by expanding the un dersampled images with the high spatial frequency lines from the baseline image (Fig. 1). All images were further zero filled to 128 x 128. Parametric T_1 maps were generated using an in-house developed Matlab software described previously (3).

Statistic Analysis All results were expressed as mean ± SD. Paired student's *t*-test analysis were performed to compare T_1 values estimated using MSRLL method to those using SRLL for both phantom and in vivo studies. $P<0.05$ was considered statistical significant.

Results

Each T_1 map was completed within 2 min using MSRLL method. The composite images exhibited comparable SNR and edge information as the images acquired with twice phase encoding lines (Fig. 2). The accuracy of MSRLL method was demonstrated by its strong agreement in T_1 values measured by SRLL method (Fig. 2h). Further, the estimated T_1 values of both myocardium and blood were consistent with the literature (4). Fig. 3 shows that during the course of $MnCl_2$ injection, R_1 values of blood and myocardium increased from 0.57±0.06 s^{-1} and 0.75±0.03 s^{-1} to 1.39±0.28 s^{-1} and 2.04±0.31 s^{-1}, respectively. During the washout period, blood R_1 decreased rapidly to the baseline level, while myocardial R_1 remained unchanged, suggesting Mn^{2+} retention in the myocardium.

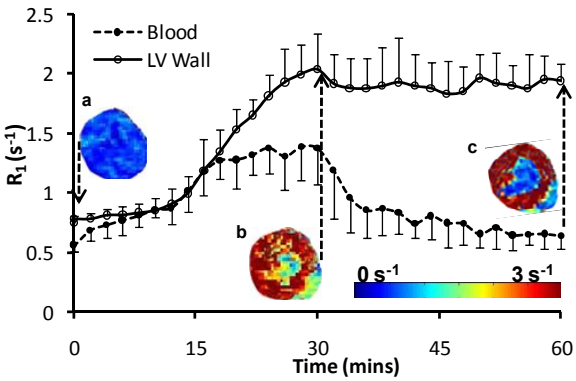

Figure 3. Dynamics of LV and blood R_1 in response to Mn^{2+} injection. **(a) – (c)** R_1 maps acquired at (a) baseline, (b) end of 30 min Mn^{2+} infusion and (c) end of 30 min washout period.

Conclusion

The MSRLL method allows the measurement of both myocardium and blood T_1 in mouse within 2 min. The accuracy was validated in both phantom and *in vivo* studies. The practical utility of this method was demonstrated in a dynamic manganese-enhanced MRI study. In summary, this study suggests that MSRLL may provide a rapid and robust method for simultaneous quantification of the arterial input function and myocardial contrast agent accumulation in DCE-MRI studies.

References

1. Edelman RR. Radiology 2004. **2.** Bokacheva L et al. MRM 2007. **3.** Li W et al. ISMRM Proc. 2009, No.442. **4.** Lu et al. MRM 2004;