Rapid T1 Mapping of Mouse Myocardium with Saturation Recovery Look-Locker Method

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Introduction

Recently, there is a growing interest in using dynamic contrast-enhanced MRI to assess cardiac functions [1]. Because of the linear relationship between R_1 ($R_1=1/T_1$) and the concentration of contrast agent [1], a rapid and accurate cardiac T_1 mapping method is desired. Look-Locker pulse sequence has been used for robust and relatively fast *in vivo* T_1 measurement [2]. However, it generally requires a repetition time (TR) that is 5 times the T_1 for complete relaxation of longitudinal magnetization (M_z) in each repetition. Though turbo gradient echo, segmentation and parallel imaging techniques have been used to shorten the imaging time [3], these techniques may not be applicable in mouse hearts because of the extremely fast heart rate (400~600 bpm). In the current study, we aimed to develop a saturation recovery Look-Locker (SRLL) method for rapid cardiac T_1 acquisition in mouse.

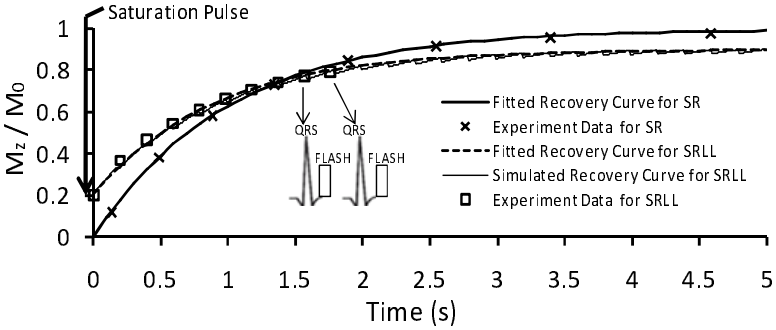

Figure 1. A schematic diagram of saturation recovery Look-Locker (SRLL) method. Experimentally measured data points and the corresponding fitted curves are for T_1 of 100 μM $MnCl_2$ solution. Multi-point spin echo saturation recovery (SR) is performed to obtain the reference T_1. SRLL fitted T_1 is used to simulate the evolution of M_z with perturbation of FLASH acquisitions.

Methods

SRLL Protocol A schematic diagram of one k-space line acquisition with the SRLL method is shown in Fig.1. To eliminate the requirement of long TR, an ECG-triggered saturation pulse is applied at the beginning of each acquisition cycle, followed by 10 sequential FLASH acquisitions separated by interval τ. For *in vivo* studies, acquisition of FLASH images was triggered by ECG every two heart beats.

Phantoms and Animals For in vitro validation, 10 μM and 100 μM $MnCl_2$ solutions were sealed in 1 mL centrifuge tubes as phantoms with moderate T_1 (~2.3 s) and short T_1 (0.8 s) values. For *in vivo* studies, 4 month old C57BL/6J mice (body weight, 30.5±0.1 g) were used. The animals were anesthetized with 1% isoflurane. Heart rate was maintained at around 500 bpm with 0.8–1.8% isoflurane. A 120 mM $MnCl_2$ solution was intraperitoneally injected at a rate of 0.2 mL/hr for 25 minutes.

MRI Study The MRI study was performed on a horizontal 9.4T Bruker scanner (Bruker Biospec, Germany) with a 35 mm inner diameter volume coil that transmits and receives at ^1H frequency. ECG and respiratory signal was monitored by a physiological monitoring system (SA Instruments, Billerica, MA). Imaging parameters are shown in Table 1. Equilibrium magnetization (M_0) images were acquired by using the same imaging parameters except for long TR (10 s). Multi-point spin-echo saturation recovery (SR) or inversion-recovery Look-Locker (LL) methods [2] were used for the purpose of validation.

Table 1. Imaging parameters for phantom and in vivo T_1 mapping.

		TR (s)	TE (ms)	Flip Angle (degree)	τ (ms)	Data Points	FOV (cm^2)	Matrix Size
Validation SR	Phantom	10	9.5	90	--	8	2.5x2.5	128x128
LL	In vivo	8	1.9	10	220~250	40	2.5x2.5	128x64
SRLL	Phantom	2	1.9	10	195	10	2.5x2.5	128x128
SRLL	In vivo	2.3	1.9	10	220~265	9~11	2.5x2.5	128x64

Multi-point spin echo saturation recovery (SR) and fully relaxed inversion recovery Look-Locker (LL) methods were used as validation studies.

Data Analysis SI of left ventricle (LV) myocardium was normalized to the corresponding M_0 scans so that it is on the scale of 0 to 1. The normalized SI was fitted to a three-parameter equation $SI = M^* + (M(0)-M^*) \times \exp(-t/T_1^*)$ using a Levenberg-Marquardt algorithm in Matlab. M^* is the saturated M_z with perturbation of FLASH acquisitions. M(0) is the M_z immediately after the application of saturation pulse. T_1^* is the effective spin-lattice relaxation constant. T_1 can be calculated as $T_1 = T_1^* / M^*$ [2].

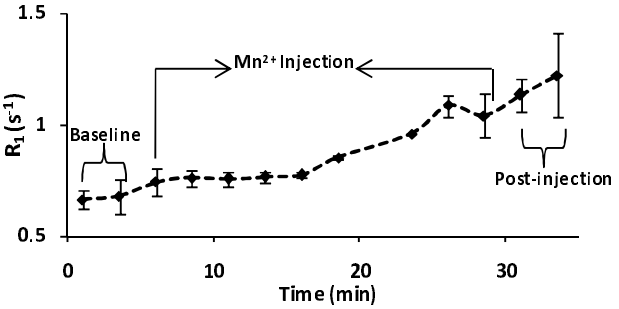

Figure 2. The dynamic change of SRLL measured R_1 values pre-, during and post- 25 minutes of $MnCl_2$ injection.

Results

Acquisition time for in vitro phantom with an interval of 195 ms was 4 min. For *in vivo* studies, average heart rate was 500 bpm, giving rise to an average acquisition time of 2.5 min. For both phantom and *in vivo* studies, there was good agreement in measured T_1 values by SR, LL and SRLL methods (Table 2). Fig.2 shows that during the course of $MnCl_2$ injection, R_1 values in myocardium increased gradually from 0.67±0.05 s^{-1} to 1.18±0.13 s^{-1} in response to a total amount of 0.3 μM/g (body weight) $MnCl_2$ injection.

Table 2. Validation (SR or LL) and SRLL measurements for T_1.

	Phantom (n=2)		In vivo Mouse Myocardium (n=2)	
	10 μM $MnCl_2$	100 μM $MnCl_2$	Baseline	Post-Mn injection
SR-measured T_1 (s)	2.32±0.14	0.83±0.01	--	--
LL-measured T_1 (s)	--	--	1.51±0.16	0.91±0.17
SRLL-measured T_1 (s)	2.32±0.08	0.86±0.02	1.50±0.11	0.86±0.09

Conclusion

Using SRLL method, a temporal resolution of 2.5 minutes for cardiac T_1 mapping in mouse heart was readily achieved without the use of parallel imaging or EPI, which often introduce adverse effect on SNR and require additional hardware and software for small animals. The accuracy of SRLL method is demonstrated by its good agreement with T_1 measurements by SR and LL methods in both phantom and *in vivo* studies. For dynamic contrast-enhanced MRI study using mouse model, the steady increase of R_1 in response to $MnCl_2$ injection was observed, demonstrating the utility of this method in delineating dynamic changes in relaxation rate from *in vivo* MEMRI studies. In summary, this study suggests that SRLL may provide a rapid and robust cardiac T_1 mapping method for use in small animals.

References

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