Simultaneous Quantification of the Arterial Input Function and Myocardial T1 in Small Animals using Saturation Recovery Look-Locker

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Introduction

There is an increasing use of dynamic contrast enhanced MRI (DCE-MRI) in pre-clinical studies using small animals. To perform quantitative DCE-MRI analysis, the concentrations of the contrast agent in both blood and tissue of interest need to be sampled at high spatial and temporal resolution. Such requirement is technically demanding in cardiac studies, especially for the estimation of contrast agent concentration in blood, also known as the arterial input function (AIF). Among the currently available methods, direct blood sampling is invasive and can only be performed at low sampling rate because of the small blood volume (~2 ml in mouse). Estimation using T_1-weighted imaging is noninvasive, but susceptible to field inhomogeneity. Alternatively, direct measurement of the blood T_1 changes offers accurate estimation of the AIF. However, such approach is limited by the long imaging time. Recently, we developed an ECG-triggered saturation recovery Look-Locker (SRLL) method which allowed T_1 mapping of mouse myocardium in <3 min [1]. In the current study, we evaluated the utility of this method in simultaneous quantification of AIF and myocardial T_1 in a two-dose manganese-enhanced MRI (MEMRI) experiment.

Methods

Measurement of AIF requires whole body saturation of the circulating blood. A water phantom was used to establish the effective saturation region. Four month old C57BL/6J mice were then used for *in vivo* validation in a two-dose MEMRI study. The MRI study was performed on a horizontal 7T animal scanner (Bruker Biospin, Billerica, MA). Whole-body saturation was evaluated using two volume coils (Bruker, Billerica MA) that were normally used for imaging of rats and mice, respectively. A 3-cm surface coil (Bruker, Billerica MA) was placed closely to the imaging subject as the receiver for optimized SNR. $MnCl_2$ solution was infused via tail vein for 30 min at a rate of 7 (n = 6) and 14 nmol/min/g body weight (BW) (n = 8), respectively. Myocardium and blood T_1 was measured using the SRLL pulse sequence with a temporal resolution of <3 min [1]. T_1 maps were acquired continuously before, during, and after Mn^{2+} infusion using the following imaging parameters: TE, 1.7 ms; nominal TR, 2.5 s; number of FLASH images, 9~12; flip angle, 10°; slice thickness, 1.5 mm; number of averages, 1; FOV, 3x3 cm^2; matrix size, 128x128/64 (Baseline/during DCE acquisition). Parametric R_1 ($1/T_1$) maps were generated offline using an in-house developed Matlab software [1].

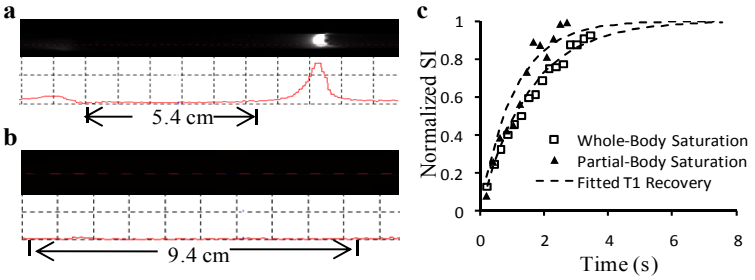

Figure 1. (a)&(b) Signal intensity profile along the long axis of the cylindrical water phantom. Partial-body and whole-body saturation was achieved by the mouse coil and rat coil with length of 7.8 and 18 cm, respectively. **(c)** Normalized signal intensity (SI) evolution of the left ventricular blood after saturation preparation in mouse.

Mn^{2+} concentration was measured in a separate experiment using atomic absorption spectroscopy (AAS). Since the relaxivity coefficient linking R_1 changes and Mn^{2+} concentration is relatively constant, consistent ratios of Mn^{2+} concentration and R_1 change between the two dose groups were expected to indirectly validate the SRLL measurement. Therefore, same Mn^{2+} infusion protocol was adopted. Blood withdrawal and heart extraction was performed at baseline, end of infusion and washout period for both dose groups, respectively (n = 2 for each subgroup). The extracted samples were then burnt into ashes and dissolved in 20% nitric acid before being measured on an atomic absorption spectrophotometer (Buck Scientific, East Norwalk, CT).

Results

Figure 1 illustrates the saturation effect from the two coils. The rat coil rendered an effective saturation region of 9.4 cm in length (Fig. 1a), which covered the entire mouse body (~8 cm) with the tail curled on the side of the body. As a result, the error caused by inflow of the unsaturated blood spins was eliminated, rendering a consistent signal recovery curve (Fig. 1b).

Figure 2 shows the R_1 dynamics in the *in vivo* MEMRI experiment. The estimated R_1 values of blood (0.57±0.06 s^{-1}) and myocardium (0.75±0.11 s^{-1}) at baseline were consistent with those reported in literature [2]. Mn^{2+} infusion led to an increase in R_1 in both blood and myocardium. Compared with those of the low Mn^{2+} dose group, the increases of R_1 was 2.2 times greater for both blood (0.38±0.20 s^{-1} vs 0.84±0.28 s^{-1}) and myocardium (0.60±0.30 s^{-1} vs 1.36±0.33 s^{-1}) in the high Mn^{2+} dose group (Fig. 3a). While blood R_1 returned to baseline values at the end of washout period, myocardial R_1 remained high, suggesting Mn^{2+} retention (Fig. 3b&d).

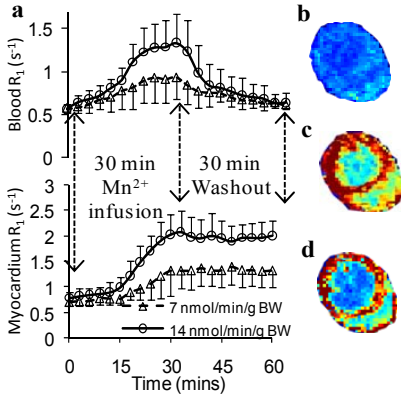

Figure 2. (a) Time courses of blood and myocardium R_1 in response to Mn^{2+} injection; **(b)** – **(d)** R_1 maps acquired at baseline **(b)**, end of 30 min infusion **(c)** and end of 30 min washout period **(d)**.

The absolute Mn^{2+} concentration measured by AAS was consistent with MRI results. Compared with the low dose group, injection of high dose Mn^{2+} solution raised the Mn^{2+} concentration in blood and myocardium by 1.8 and 2.3 times, respectively (Fig. 3c&d). At the end of the washout period, nearly all Mn^{2+} in the blood were cleared out, while the concentration in myocardium remained the same as the end of Mn^{2+} infusion (Fig. 3c&d). These results confirmed the validity of the SRLL method for simultaneous quantification of AIF and myocardial T_1.

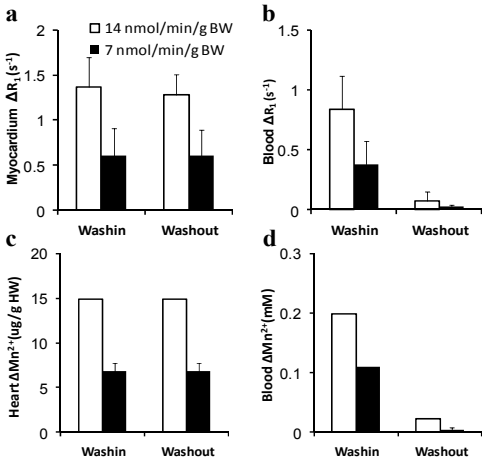

Figure 3. Changes in ΔR_1 and absolute Mn concentration at the end of injection and washout sessions.

Conclusion

Current method can provide rapid quantification of the AIF and myocardial T_1 in small animals (<3 min). The validity was confirmed by a good agreement between the SRLL-measured T_1 changes and the AAS-measured Mn^{2+} concentration. In addition to the application in mouse model, the current method can be easily translated to imaging large mammals and humans using the same principle. Further reduction in acquisition time can be achieved by combining the current method with other fast imaging techniques such as compressed sensing and parallel imaging.

References

1. Li et al. MRM 2010.

2. Waghorn et al, NMR in Biomed 2008.