Modified Look-Locker Inversion Recovery (MOLLI) for High-Resolution $T_1$ Mapping of the Heart

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A novel pulse sequence scheme is presented that allows the measurement and mapping of myocardial $T_1$ in vivo on a 1.5 Tesla MR system within a single breath-hold. Two major modifications of conventional Look-Locker (LL) imaging are introduced: 1) selective data acquisition, and 2) merging of data from multiple LL experiments into one data set. Each modified LL inversion recovery (MOLLI) study consisted of three successive LL inversion recovery (IR) experiments with different inversion times. We acquired images in late diastole using a single-shot steady-state free-precession (SSFP) technique, combined with sensitivity encoding to achieve a data acquisition window of <200 ms duration. We calculated $T_1$ using signal intensities from regions of interest and pixel by pixel. $T_1$ accuracy at different heart rates derived from simulated ECG signals was tested in phantoms. $T_1$ estimates showed small systematic error for $T_1$ values from 191 to 1196 ms. In vivo $T_1$ mapping was performed in two healthy volunteers and in one patient with acute myocardial infarction before and after administration of Gd-DTPA. $T_1$ values for myocardium and noncardiac structures were in good agreement with values available from the literature. The region of infarction was clearly visualized. MOLLI provides high-resolution $T_1$ maps of human myocardium in native and post-contrast situations within a single breath-hold. Magn Reson Med 52:141–146, 2004. © 2004 Wiley-Liss, Inc.

Key words: spin-lattice relaxation time; Look-Locker; heart; myocardium

Despite recent technological advances, in vivo $T_1$ quantification of the myocardium with modern magnetic resonance (MR) systems remains a challenge because of severe time constraints due to cardiac and respiratory motion. While myocardial $T_1$ is shorter and therefore relatively easier to measure at low field strengths, it has a value of ~1000 ms at a field strength of 1.5 T, exceeding the duration of the cardiac cycle (~600–1200 ms) in most subjects (1,2). Since standard inversion recovery (IR) measurements require a relaxation period of four to five times $T_1$ to allow for full magnetization recovery after each 180° pulse (3), only four to five such single-point IR experiments can be performed within one breath-hold (ca. 20 s). To achieve accurate $T_1$ estimates from a three-parameter curve-fitting procedure, as is commonly employed, data from at least six to 10 time points should be available (4). The multivpoint approach, as first described by Look and Locker (5), samples the relaxation curve multiple times after an initial preparation pulse (6). This technique has been shown theoretically to be highly efficient (7), and has been widely used for $T_1$ measurements of the brain (8–11). It is not suitable for pixel-by-pixel $T_1$ mapping of the heart because data acquisition is performed continuously throughout the cardiac cycle without regard for cardiac motion, which means that $T_1$ values can only be derived for regions of interest (ROIs) that must be defined manually for every frame (1). The resultant $T_1$ values may consequently be subject to inaccuracy caused by misregistration effects.

In this work we present a pulse sequence scheme that allows for accurate in vivo $T_1$ measurements and $T_1$ mapping of myocardium with high spatial resolution and within a single breath-hold. To overcome the limitations of the conventional LL approach for cardiac applications, we propose a modified LL IR scheme (MOLLI), which introduces two principles to the standard LL sequence: 1) selective data acquisition at a given time of the cardiac cycle over successive heartbeats, and (2) merging of image sets from multiple LL experiments with varying inversion times (TIs) into one data set. While selective data acquisition effectively decreases the number of images acquired in each LL experiment to one per heartbeat, the use of multiple LL experiments with different TIs increases the number of samples of the relaxation curve to a value that is sufficiently high for accurate $T_1$ estimation. The IR preparation pulse is used to yield the maximum dynamic range of the signal. A balanced steady-state free precession (SSFP) readout is chosen over conventional gradient-echo (GE) readout because of its higher signal-to-noise ratio (SNR) and lower tendency to modulate the relaxation curve (12). To minimize artifacts from cardiac motion, the image data acquisition window is restricted to <200 ms in end-diastole by the use of sensitivity encoding (SENSE) (13) with a reduction factor of 2. We investigated the accuracy of $T_1$ measurements with MOLLI using gel phantoms for a wide range of heart rates derived from simulated electrocardiogram (ECG) signals. $T_1$ maps and the $T_1$ values derived from in vivo experiments in two healthy volunteers and one patient with acute myocardial infarction are presented.

MATERIALS AND METHODS

Pulse Sequence Scheme

The MOLLI pulse sequence scheme is illustrated in Fig. 1. Three successive ECG-triggered LL experiments (LL1, LL2, and LL3) were carried out with three, three, and five single-shot readouts, respectively. Undisturbed magnetization recovery was allowed for at least 4 s between each LL ex-
experiment, with variation dependent on the subjects’ heart rate, and the reconstruction and preparation time of the MR scanner. In each of the three LL experiments, the first single-shot readout was performed at TI (LL1 = 100 ms, LL2 = 200 ms, and LL3 = 350 ms) after a non-slice-selective adiabatic 180° pulse and at delay time TD after the previous R-wave. Subsequent images were acquired at time TD after every R-wave, until the final number of images for each LL experiment was acquired. Data acquisition consisted of a single-slice, single-shot, balanced SSFP pulse sequence (balanced turbo-field echo (BTFE)) combined with SENSE with a reduction factor of 2, number of lines of k-space (TFE factor) = 49, dummy acquisitions = 13, partial Fourier acquisition, flip angle = 50°, repetition time (TR) = 3.9 ms, echo time (TE) = 1.95 ms, field of view (FOV) = 380×342 mm, matrix = 240×151, measured pixel size = 1.58×2.26 mm, slice thickness = 8 mm, and acquisition window = 191.1 ms.

Phantom Studies

The MR studies were performed on a 1.5 T Gyroscan Intera CV MR system (Philips, Best, The Netherlands) with Master gradients (30 mT/m, 150 T/m/s). Seven agarose gel phantoms doped with different amounts of gadolinium-EDTA were studied. After a SENSE reference scan was acquired, two series of MOLLI experiments were performed with a five-element cardiac phased-array coil at “heart rates” of 40–100 beats per min (bpm), which were derived from user-defined simulated ECG signals. The first of these two sets was performed in ascending order, and the second set was performed in descending order of heart rate. Reference values of $T_1$ were established following the MOLLI experiments by means of a standard multipoint IR spin-echo technique (TI = 50–10000 ms) with a birdcage head coil.

$T_1$ Calculations

Images were sorted according to their accumulative time from inversion (t), which is given by

$$t = TI + (n - 1)RR,$$  \( \text{[1]} \)

where N = image number within the LL experiment, and RR = heartbeat interval. Three-parameter nonlinear curve fitting (14) using a Levenberg-Marquardt algorithm was performed for

$$y = A - B \exp(-t/T_1^*),$$  \( \text{[2]} \)

for corresponding ROIs (Origin 7; OriginLab Corp., Northampton, MA) and for corresponding pixels (customized $T_1$ mapping software written in IDL 6.0; RSI UK Ltd., Berkshire, UK). In Eq. [2], y denotes signal intensity, and $T_1^*$ corresponds to the apparent, modified $T_1$ in an LL experiment. We assigned signal polarity for the magnitude images using the approach described by Nekolla et al. (15). This involves the creation of multiple data sets: the first set has all points on the curve assigned as positive values, the second set has the first point of the curve assigned as negative, the third set has the first two points of the curve assigned as negative, and so on. From these sets, the one with the best quality of fit, as defined by the lowest value of chi-square, is selected.

$T_1$ was calculated from the resulting parameters $T_1^*$, A, and B by applying the equation

$$T_1 = T_1^* ((B/A) - 1),$$  \( \text{[3]} \)

as used for studies with conventional LL techniques (16).

To calculate the standard deviation (SD) of the combined estimation error of $T_1$, we added the errors of the three fitting parameters in quadrature.

In Vivo Studies

The study was approved by the local ethics committee, and written informed consent was obtained from all of the subjects. In vivo experiments were performed in the same manner as the phantom studies in two healthy volunteers in mid-cavity short-axis slices before and 10 min after intravenous application of 0.15 mmol/kg gadolinium-DTPA (Magnevist; Schering AG, Berlin, Germany). All of
the MOLLI studies were performed in single breath-holds. One patient with acute anteroseptal myocardial infarction (day 5, peak creatine kinase = 613 U/l, nonreperfused) underwent the same protocol (except for FOV = 410 × 369 mm, and pixel size = 1.71 × 2.44 mm) plus subsequent conventional delayed-enhancement imaging in the same slice (IR-prepared GE, TR = 4.5 ms, TE = 1.8 ms, TI = 260 ms, and the same geometric parameters as for the MOLLI images). Details regarding the subjects are given in Table 1. Quantitative $T_1$ maps were calculated in the same manner as for the phantom studies except that instead of using Eq. [1], we extracted the accumulative time from inversion directly from the headers of the images’ DICOM files as recorded by the MR system. Mean $T_1$ values were obtained for ROIs placed on the $T_1$ maps in normal myocardium, infarcted myocardium (in the patient with myocardial infarction), left ventricular (LV) blood pool, skeletal muscle, and liver with the use of a commercial software package (Mass 5.0; Medis, Leiden, The Netherlands).

**RESULTS**

**Phantom Studies**

Figure 2 gives signal intensity curves (with restored signs) for the seven gel phantoms at a simulated heart rate of 80 bpm. Table 2 gives the reference values for $T_1$ of the gel phantoms, as well as the results for the first series of MOLLI studies at heart rates of 40–100 bpm. Figure 3 shows the percentage error in $T_1$ estimation at different heart rates as compared to reference values. The duration of the breath-hold MOLLI data acquisitions ranged from 14.7 to 23 s. There was a systematic underestimation of $T_1$, with maximum error of −10.0% (mean ± SD: −6.8 ± 2.1%) for $T_1$ values from 191 to 1196 ms, and with maximum error of −22% for $T_1 = 60$ ms. Underestimation was more pronounced for lower heart rates and for very high or very low values of $T_1$. Series 2 (varying of heart rate in descending order; results not shown) produced the same pattern of measurement error as series 1, confirming the initial results (maximum error of series 2: −10.1%, mean ± SD: −5.8 ± 2.9%, Pearson’s correlation for $T_1$ values of series 1 vs. series 2: $r = 0.999$, $P < 0.001$, $N = 49$).

**In Vivo Studies**

Pre- and postcontrast $T_1$ maps are shown in Fig. 4 for the two volunteers, and in Fig. 5 for the patient with acute myocardial infarction. The duration of the MOLLI studies ranged from 15.1 to 18.2 s. There was a clear delineation of the LV wall and the papillary muscles in all three cases. Table 3 summarizes the $T_1$ values (± SD) derived from ROIs for different tissues. $T_1$ values for the myocardium, LV blood pool, skeletal muscle, and liver were in good agreement with corresponding values available from the literature (1,2,17,18). In the patient, the area of infarction showed a markedly increased $T_1$ value as compared to...

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**Table 2**

<table>
<thead>
<tr>
<th>Heart rate (bpm)</th>
<th>60</th>
<th>191</th>
<th>470</th>
<th>763</th>
<th>929</th>
<th>1014</th>
<th>1196</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>50 ± 0.6</td>
<td>176 ± 0.8</td>
<td>455 ± 4.3</td>
<td>707 ± 8.8</td>
<td>850 ± 8.6</td>
<td>915 ± 9.6</td>
<td>1076 ± 10.1</td>
</tr>
<tr>
<td></td>
<td>50 ± 0.6</td>
<td>176 ± 0.8</td>
<td>455 ± 5.5</td>
<td>710 ± 10.1</td>
<td>859 ± 10.3</td>
<td>927 ± 11.3</td>
<td>1093 ± 12.8</td>
</tr>
<tr>
<td>60</td>
<td>47 ± 0.8</td>
<td>177 ± 1.1</td>
<td>452 ± 5.8</td>
<td>701 ± 10.2</td>
<td>850 ± 10.3</td>
<td>917 ± 11.4</td>
<td>1085 ± 12.4</td>
</tr>
<tr>
<td>70</td>
<td>48 ± 0.6</td>
<td>177 ± 1.3</td>
<td>456 ± 6.6</td>
<td>714 ± 11.5</td>
<td>863 ± 12.0</td>
<td>932 ± 13.5</td>
<td>1098 ± 15.2</td>
</tr>
<tr>
<td>80</td>
<td>47 ± 0.7</td>
<td>178 ± 1.5</td>
<td>453 ± 6.4</td>
<td>705 ± 11.3</td>
<td>857 ± 11.6</td>
<td>925 ± 13.0</td>
<td>1091 ± 15.0</td>
</tr>
<tr>
<td>90</td>
<td>48 ± 0.7</td>
<td>178 ± 1.7</td>
<td>457 ± 6.9</td>
<td>722 ± 12.1</td>
<td>873 ± 12.7</td>
<td>941 ± 14.7</td>
<td>1116 ± 17.4</td>
</tr>
<tr>
<td>100</td>
<td>48 ± 0.6</td>
<td>179 ± 1.9</td>
<td>461 ± 7.3</td>
<td>726 ± 13.4</td>
<td>880 ± 14.3</td>
<td>951 ± 16.7</td>
<td>1125 ± 20.1</td>
</tr>
<tr>
<td>Mean</td>
<td>48.1 ± 1.3</td>
<td>177.4 ± 1.1</td>
<td>455.7 ± 2.8</td>
<td>712.2 ± 9.1</td>
<td>861.9 ± 11.2</td>
<td>929.7 ± 13.0</td>
<td>1097.8 ± 17.3</td>
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</table>
remote myocardium (1360 ± 104 vs. 948 ± 67 ms, respectively) except for the subendocardial region at the center (1106 ± 72 ms). After the application of contrast medium, $T_1$ in the outer layer of the infarcted area was 37.4% lower than $T_1$ in remote myocardium (281 ± 44 vs. 449 ± 35 ms), corresponding to prolonged wash-out of contrast medium in the necrotic area that was visualized as “delayed enhancement” in the IR-prepared GE image. The center of the infarcted area exhibited a $T_1$ relaxation time that was higher than that of remote myocardium (511 ± 114 vs. 449 ± 35 ms, respectively) and presented as a “hypoenhanced core” on the IR-prepared GE image.

**DISCUSSION**

The MOLLI imaging scheme achieved highly accurate $T_1$ measurements in phantoms of various $T_1$ times, covering the full range of $T_1$ that can be expected in human soft tissues under both native and contrast medium-enhanced conditions. The size of the observed measurement error was comparable to that seen in conventional fast $T_1$ measurement techniques used for brain studies (9–11).

Compared to the $T_1$ mapping technique described by Wacker et al. (2,19) in a study using multishot saturation recovery images, MOLLI images have a higher matrix (240 × 151 vs. 128 × 80) despite their lower acquisition time (191 vs. 230 ms), and hold higher dynamic signal range due to the use of an inversion pulse instead of a saturation pulse. This explains the good results of the in vivo part of this study, in which quantitative $T_1$ maps of mid-ventricular short-axis slices were obtained within single breath-holds in volunteers and in a patient with acute myocardial infarction. The image quality of the $T_1$ maps was high enough for relatively small anatomical structures, such as papillary muscles within the heart or veins in the liver, to be identified.
Table 3

| T1 Values (ms) Obtained From MOLLI T1 Maps Before (Native) and After Administration of Contrast Medium (CM), Derived From Regions-of-Interest for Normal Myocardium, Skeletal Muscle, Liver, and Left Ventricular Blood Pool |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Myocardium                      | Skeletal muscle  | Liver           | Blood           |
| Volunteer 1                    | Native 1076 ± 72                | CM 492 ± 39      | Native 794 ± 109| CM 535 ± 47     | Native 666 ± 64 | CM 347 ± 18     | Native 1551 ± 55 | CM 313 ± 10     |
| Volunteer 2                    | Native 969 ± 84                 | CM 450 ± 40      | Native 769 ± 35 | CM 475 ± 18     | Native 611 ± 23 | CM 333 ± 19     | Native 1544 ± 69 | CM 325 ± 14     |
| Patient                        | Native 948 ± 67                 | CM 449 ± 35      | Native 719 ± 68 | CM 510 ± 40     | Native 591 ± 63 | CM 304 ± 26     | Native 1518 ± 69 | CM 266 ± 14     |

The T1 values derived for normal myocardium and various noncardiac tissues compared favorably to those reported in the literature for measurements at 1.5 T (1,2,17,18). In agreement with reports from low-field systems (20) and from a preliminary high-field study (21), the area of infarction in our patient was visualized on native images as a region of increased T1 times. After the contrast medium was applied, the infarcted region presented as a region with markedly lower T1 times compared to the remote myocardium, corresponding to the “delayed enhancement” phenomenon commonly utilized for viability imaging (22,23). Pre- and postcontrast T1 times were acquired in vivo, both before and after the application of contrast medium, yielding T1 values for a number of different tissues, including myocardium, which agree well with those found in the literature. Signal changes in areas with delayed enhancement were quantified. MOLLI provides a promising tool for the measurement of myocardial T1 times under clinical conditions.

CONCLUSIONS

The agreement of the results from series with ascending and descending heart-rate orders rules out radiofrequency power-induced thermal changes within the phantoms as a cause of the observed heart-rate dependency. Because of its systematic nature, the measurement error could in principle be corrected for mathematically; however, the investigation of such a correction is beyond the scope and design of this study. It could be postulated that a correction for heart rate may increase the reproducibility of myocardial T1 measurements in the general population. Further investigations with a larger number of subjects will be necessary to answer this question.

ACKNOWLEDGMENTS

D.M. would like to thank Dr. Andrew Jackson for his valuable help in developing the analysis software. This study was carried out at the British Heart Foundation (BHF) Cardiac MRI Unit, Leeds, UK. D.M. is supported by a Marie Curie Individual Fellowship by the European Commission.

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