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Technical note

Mapping of left ventricle wall thickness in mice using 11.7-T magnetic resonance imaging

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ABSTRACT

Background: The left ventricle (LV) wall thickness is an important and routinely measured cardiologic parameter. Here we introduce three-dimensional (3D) mapping of LV wall thickness and function using a self-gated magnetic resonance (MR) sequence for ultra-high-field 11.7-T MR cine imaging of mouse hearts.
Methods and results: Six male C57BL/6-j mice were subjected to 11.7-T MR imaging (MRI). Three standard views—short axis, long axis four-chamber, and long axis two-chamber—and eight consecutive short axis scans from the apex to base were performed for each mouse. The resulting 11 self-gated cine images were used for fast low-angle shot analysis with a navigator echo over an observation period of approximately 35 min. The right ventricle (RV) and LV were identified in the short axis and four-chamber views. On 3D color-coded maps, the interventricular septum wall (diastole: 0.94 ± 0.05 mm, systole: 1.20 ± 0.09 mm) and LV free wall (diastole: 1.07 ± 0.15 mm, systole: 1.79 ± 0.11 mm) thicknesses were measured.
Conclusion: This 3D wall thickness mapping technique can be used to observe regional wall thickness at the end-diastole and end-systole. Self-gated cine imaging based on ultra-high-field MRI can be used to accurately and easily measure cardiac function and wall thickness in normal mouse hearts. As in the preclinical study, this versatile and simple method will be clinically useful for the high-field-MRI evaluation of cardiac function and wall thickness.

1. Introduction

One challenge associated with cardiac magnetic resonance imaging (MRI) of small rodents is the need for adjustments to sequence acquisition parameters to compensate for high heart and respiratory rates. Shorter cardiac cycles and similar blood flow velocities of mice and rats, relative to those of humans [1], cause losses of blood magnetic resonance (MR) signals, leading to reduced blood and heart tissue contrast at certain stages of the cardiac cycle. In rodents, a high-resolution electrocardiogram (ECG) and respiratory-gated cine cardiac high-field MRI have been used to quantify cardiac function [2–5]. This cine MRI protocol, which is similar to human cardiac MRI, generates a stack of two-dimensional (2D) slices with a thickness of <1.0 mm along the main cardiac axis to achieve full cardiac coverage. Subsequently, ventricular volume segmentation at the end-diastole and end-systole is used to evaluate cardiac function. This method has been successfully used to evaluate rodent models of heart disease [2–4].

Measurement of the left ventricle (LV) wall thickness by MRI, computed tomography, and echocardiography is an important step in a routine cardiologic analysis as the LV wall thickness is a prognostic marker of hypertrophic cardiomyopathy [6,7]. Previous reports have compared MRI-based measurements to those obtained using echocardiography and cineangiography [8,9] as well as the accuracy, reliability, and time-saving potential of automated methods compared with manual quantitative methods for assessing segmental LV function and wall thickness [10]. As a result, various LV functional analysis methods, including real-time, high spatial resolution, high temporal resolution, and four-dimensional mapping, have been proposed [11–13].

Recent approaches to LV measurement are based on self-gated MR sequences in the absence of external monitoring devices (e.g., ECG

Abbreviations: bpm, beats per minutes; ECG, electrocardiogram; EDV, end-diastolic volume; ESV, end-systolic volume; FA, flip angle; FLASH, fast low-angle shots; FOV, field of view; LV, left ventricle; MRI, magnetic resonance imaging; NEX, number of excitation; RF, radiofrequency; ROI, regions of interest; RV, right ventricle; SD, standard deviation; SV, stroke volume; SNR, signal-to-noise-ratio; 2D, two-dimensional; 3D, three-dimensional; TE, echo time; TR, repetition time.

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and respiratory monitoring units) [14,15]. These imaging sequences, which involve prospectively triggered techniques, are based on the acquisition of a navigator signal with every k-space line, followed by the sorting of data according to their origins in the cardiac and respiratory cycles [16]. Self-gated techniques are both useful and robust for cardiac imaging evaluations of mice disease models [17,18]. Currently, high-field MRI evaluations of cardiac disease models have been introduced for many research purposes, such as evaluations of transgenic mice [19,20], tracking of transplanted cells [21], and monitoring of stem cell therapy responses [22,23]. Accordingly, a similarly versatile and simple high-field MRI-based method has been sought for the evaluation of heart function and wall thickness in mice.

The present study proposes the use of a three-dimensional (3D) mapping method for LV wall thickness evaluation. This method involves self-gating and conventional prospectively triggered MR sequences for the cine imaging of entire mice hearts using ultra-high-field 11.7-T MRI.

2. Methods

2.1. Animal preparation

This study was approved by the Animal Welfare Committee of our institution. Six 20-week-old male C57BL/6-j mice (n = 6; mean body weight, 29.2 ± 3.2 g; Japan SLC, Hamamatsu, Japan) were allowed to rest for 1 week before the experiment. The animals had free access to food and water and were housed under standard laboratory conditions (22–23 °C room temperature, ~50% humidity, 12/12-h light/dark cycle).

2.2. MRI

MRI was conducted using an 11.7-T vertical-bore Bruker Avance II imaging system (Bruker Biospin, Ettlingen, Germany) and a volume radiofrequency (RF) coil with an inner diameter of 25 mm for transmission and reception (m2m Imaging Corp., Cleveland, Ohio, USA). All MRI experiments were performed while animals were under general anesthesia induced and maintained by 1–2% isoflurane (Abbott Laboratories, Abbott Park, IL, USA), administered via a mask covering the animals' noses and mouths. Respiratory signals and body temperature were monitored using a physiological monitoring system (SA Instruments, Inc., Stony Brook, NY, USA). Body temperatures were continuously maintained at 36.0 ± 0.5 °C by keeping the animals on circulating water warming pads throughout all experiments.

For imaging, the slice center was set carefully at the heart. First, a three-plane fast low-angle shots (FLASH) sequence was performed to define the slice orientation. Next, three established standard cardiac MRI views (short axis, long axis four-chamber, and long axis two-chamber) were obtained via self-gated cine imaging with a navigator echo. Finally, eight consecutive scans of the short axis from the apex to the base of the heart were performed using the same 2D self-gated cine imaging protocol. These 11 self-gated cine imaging scans were subsequently used for FLASH with a navigator echo (IntraGate, Bruker) and the following parameters: repetition time (TR)/echo time (TE) = 5.0/2.2 ms, flip angle = 10°, field of view (FOV) = 3.20 cm × 3.20 cm, matrix = 256 × 256, slice thickness = 1.0 mm, number of excitation (NEX) = 300, eight concomitant slices covering the whole heart from apex to base, 10 phases per cardiac cycle, expected heart rate = 400 beats per minutes (bpm), expected respiratory rate = 60 bpm, in-plane resolution per pixel = 125 μm, acquisition time = 3 min 14 s per scan, and total acquisition time = approximately 35 min.

2.3. MRI data analysis and statistics

From the short axis images, end-diastolic and end-systolic frames were selected according to maximal and minimal ventricular volumes. In both frames, the epicardial border was first manually outlined and the LV cavity segmented. Respective volumes were calculated as the

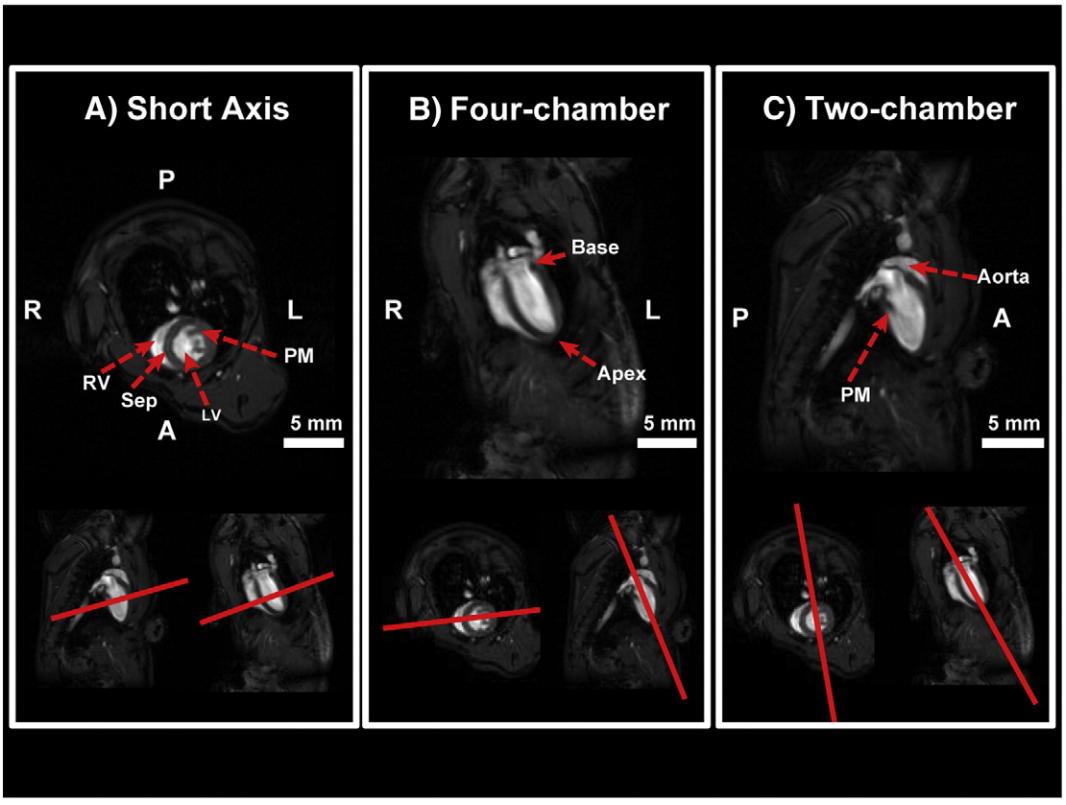

Fig. 1. Examples of typical three-plane images and slice positions in three views. A, Short axis view; B, Four-chamber view; C, Two-chamber view. Red lines represent the slice planes under the other two planes. Red arrows indicate the LV, RV, septum (Sep), papillary muscles (PM), apex, base, and aorta. The white bar represents 5 mm. A: anterior, P: posterior, R: right, L: left. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)