ECG-gated Cardiac MRI in Mice on a Clinical 3.0T MR Scanner

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Introduction: Transgenic manipulations in mice are increasingly used to probe genetic and physiological aspects of human cardiovascular physiology. Cardiac magnetic resonance imaging (MRI) in humans is recognized as a robust and accurate method for in vivo assessment of cardiac morphology and function. However, due to the small size and fast rate, cardiac MRI in mice is usually performed on high-field (4.7 – 9.4 T) animal scanners significantly limiting the opportunity for cardiac MRI research in mice [1]. Nevertheless, successful cardiac MRI of mice on a clinical 1.5T system has been reported with the help of a home-built amplifier to enable ECG-gating, demonstrating the potential for conducting research on clinical systems [2, 3]. In this study we demonstrate the feasibility of performing cardiac MRI in mice with a clinical 3.0T system without the need for an amplifier to detect the R-wave for ECG-gating.

Methods and Materials: MRI was performed in eleven mice (C57Bl/6, 8~10w, 26~30g) using a GE clinical 3.0T scanner. The mouse was anesthetized with pentobarbital sodium at 40 µg/g body weight. An intraperitoneal injection line was implanted and extended outside of the scanner so that pentobarbital sodium could be administered to achieve a desired value of heart rate without having to reposition the mouse. The mouse was placed in a supine position with their paws taped to a home-built table, and the table was placed at the center of a quadrature wrist coil (Mayo Clinic BC-10 Coil). Two leads from the standard clinical ECG probe were attached to 2 home-made needle electrodes (~25 gauge). The needle was connected with a bench of thin copper wires, and the other side of the wires was connected to a snap-connector electrode which could be easily clipped on by the lead of the standard clinical ECG probe. To receive ECG signals, one needle was inserted subcutaneously into the right foreleg and the other needle into the left hindleg. The accuracy of correctly detecting the R-wave was nearly 100% for low heart rate (<300 beats/min) and greater than 95% for high heart rate (>400 beats/min). After identifying long-axis and short-axis orientations of the heart, an ECG-triggered fast cine SPGR pulse sequence was used to acquire cardiac images with the following imaging parameters: TR/TE=16.2/7 ms, flip angle 35°, FOV 5.0 cm, slice thickness 1.0 mm, NEX 4, matrix size 256×192, and view per segment 2 or 4. The resulting in-plane resolution was 195x260 μm^2. Seven or eight contiguous short-axis slices perpendicular to the long axis were acquired to cover the left ventricle (LV) from base to apex. After the MRI, the mouse was killed, and its LV was dissected and weighed. *Data analysis*: All cardiac cine images were post-processed with GE ReportCard software. End-diastolic and end-systolic frames were selected according to maximal and minimal ventricular volume of the left-ventricular cavity. The epicardial and endocardial borders of each slice were manually delineated (Fig. 1). The wall area for each slice was then computed from the difference between the epicardial area and the endocardial area. The product of slice wall area with the slice thickness yielded the slice wall volume. Finally, a summation of slice wall volume over all slices yielded the LV wall volume. Myocardial mass was computed by multiplying the LV wall volume with the specific gravity of myocardium, 1.055 g/cm^3. LV volume, stroke volume, ejection fraction, and cardiac output were computed accordingly.

Results and Discussion: Four mice had multiple cardiac scans for a variety of heart rates ranged from 90 to 495 beats/min. One mouse had four cardiac scans at the following four heart rates of 152, 242, 376, and 495 beats/min (Fig. 1). The success of these multiple cardiac scans demonstrated that, for a large range of heart rates, performing cardiac MRI of mice on a clinical 3.0T scanner is feasible. The eleven mice had a total of 23 cardiac scans, providing a total of 23 dataset for the LV myocardial mass estimation using MRI. Fig. 2 shows the scatter plot of the MRI estimated LV myocardial mass versus postmortem LV mass. Correlation between postmortem LV mass and MRI estimated LV myocardial mass was very good, with $LV_{postmortem} = 1.05 \times LV_{MRI} - 13.24$ mg (R^2=0.66 and p<0.001) for the systole and $LV_{postmortem} = 1.05 \times LV_{MRI} - 13.80$ mg (R^2=0.74 and p<0.001) for the diastole, respectively, indicating a good agreement between MRI and postmortem determination. It also showed that the MRI estimated mass was almost the same for both the systole and diastole, indicating the accuracy of the method used for the LV myocardium mass estimation. In conclusion, to the best of our knowledge, this is the first cardiac MRI study of mice using a clinical 3.0T scanner without amplification ECG signal for detecting the R-wave. The methods we have developed and validated should facilitate the study of transgenic mice serially without the necessity for sacrifice after interventions thus allowing assessment of the effect of single or multiple experimental conditions within a single animal over time.

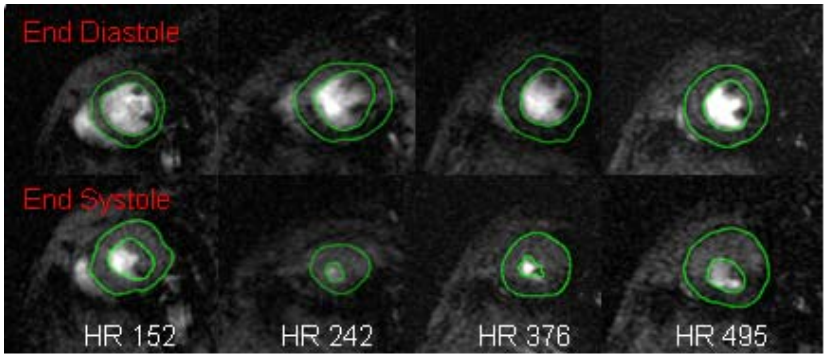

Fig. 1 illustrates the delineation of epicardial and endocardial borders of the LV of a mouse at four different heart rates (HR): 152, 242, 376, and 495 beats/min. Top row: end diastole; Bottom row: end systole.

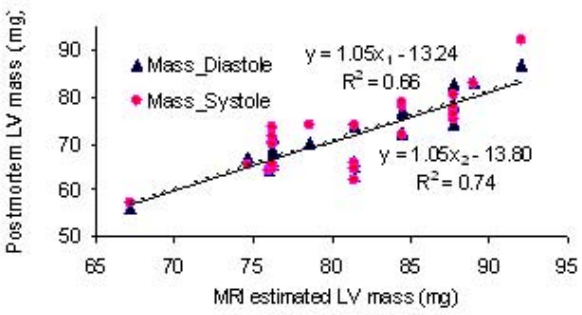

Fig. 2 shows the linear regression of LV mass estimated by MRI and postmortem LV mass. Dash line: systole; Solid line: diastole.

References: 1. Vallee, J, *et al*, MAGMA, **17**: 149-156, 2004. 2. Franco, F, *et al*, Am. J. Physiol., **274**: H679-H683, 1998. 3. Shohet, R, *et al*, Proc Natl Acad Sci USA, **101**: 2088-2093, 2004.