COMPARISON OF SELF GATED CARDIAC MRI WITH ECHOCARDIOGRAPHY FOR DETERMINATION OF LEFT VENTRICULAR FUNCTION IN RODENT MODELS OF HYPERTROPHY

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Introduction: The stroke-prone spontaneously hypertensive rat (SHRSP) is an excellent experimental model of essential hypertension. In addition, this strain demonstrates left ventricular hypertrophy. In humans, echocardiography and MRI are used as quick, non-invasive and accurate procedures for measuring cardiac parameters including left ventricular mass (LVM) and dimensions, as well as the assessment of blood velocity through the large vessels and heart. Until recently, the application of these techniques in animal research has been impeded by technology difficulties, expense and the problem of imaging a small, rapidly moving object such as the rodent heart. Previously, our group identified quantitative trait loci (QTL) for left ventricular mass index (LVMI) on rat chromosome 14 in an F2 cross between SHRSP and WKY [1]. The aim of this project was to demonstrate the validity of echocardiography and self gated cardiac MRI as high fidelity, high throughput techniques for characterising cardiac differences in mass and function in 16 week old SHRSP, normotensive Wistar Kyoto (WKY) rats and the congenic strain SP.WKYGla14a.

Methods: Transthoracic echocardiography and MRI were performed on lightly anesthetized rats (1.25% to 1.5% isoflurane in 1.5Litres/minO_2). Left parasternal and left apical echocardiographic 2-D and 1-D images were obtained using an Acuson Sequoia C512 ultrasound system using a 15 MHz linear array frequency transducer at an image depth of 2 cm. Pulse wave Doppler imaging was acquired from the apical view using pulsed wave (15 MHz linear array transducer) and continuous wave (8.5 MHz phase array transducer) with the sample volume placed at the tip of the mitral valve to obtain mitral valve inflow velocities. The magnetic resonance imaging experiments were performed on a 7T Bruker Biospec system (Bruker Biospec, Karlsruhe, Germany), with a 20mm diameter surface coil for image acquisition. A modified Flash sequence was used for retrospective CINE MR with an oblique saturation slice navigator echo, covering the pulmonary veins and inferior vena cava. The navigator signal is retrospectively used to determine cardiac and respiratory cycles, allowing the MRI k-space data to be reorganized and reconstructed retrospectively, producing cardiac images that are free of motion artifacts. This ability to produce cardiac MRI images without the need for ECG or respiration sensors allows for non-invasive multislice imaging of cardiac function (Fig 1). Echocardiographic analysis was carried out using Axius quantification and vector velocity imaging (VVI) software and MRI analysis was completed using Image J software (http://rsbweb.nih.gov/ij/).

Figure 1. Short axis slice of a rat heart during diastole (left) and systole (right). Both epicardial and endocardial borders were manually delineated for calculation of LV mass and volume.

Results: Echocardiogaphic and MRI evaluation of LVM was validated by *post mortem* weighing of excised left ventricle plus septum. An excellent correlation was found between gravimetric LVM and both echocardiographic measured LVM (r^2 = 0.90, n=22) and MRI measured LVM (r^2 = 0.79, n=22) (Figure 1). LVM Index was significantly increased in SHRSP compared to WKY (2.2 vs 2.86 g/kg; * indicates P<0.001) as assessed by MRI however, LVM Index was significantly lower in the SP.WKYGla14a when compared to SHRSP rats (2.6 vs 2.86 g/kg; # indicates P<0.05) (Figure 2). No significant change in Ejection Fraction was observed between the strains. Echocardiographic 2-D VVI analysis showed reduced systolic and diastolic myocardial deformation in SHRSP (P<0. 003, P<0. 001 respectively) versus age matched WKY.

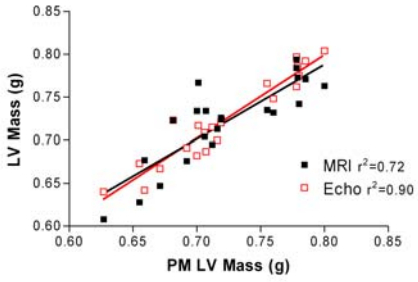

Figure 2. Correlation between MRI and echocardiography estimated LV Mass with Post Mortem LV mass values

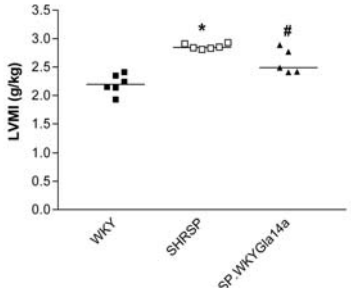

Figure 3. MRI estimated LVM Index in WKY, SHRSP and SP.WKYGla14a rats. All data shown are mean ± S.D. * indicates P<0.001 compared to WKY and # indicates P<0.05 compared to SHRSP.

Conclusions: Echocardiography and self gated MRI have been used as complimentary non-invasive methods to assess LVM and cardiac function in rats. Both MRI and echocardiography demonstrated a quantitative trait loci (QTL) for LVM Index on rat chromosome 14 in the congenic strain SP.WKYGla14a. A good correlation between *post mortem* LVM with both imaging techniques demonstrate that echocardiography and MRI are invaluable high fidelity modalities for use of LVM quantification and cardiac function in small rodents.

References

[1] Clark JS et al. (1996) Quantitative trait loci in genetically hypertensive rats. Possible sex specificity. Hypertension 28(5): 898-906.