

## 4D Mouse Cardiac Isotropic Black-Blood Imaging for Phenotyping

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**Introduction** Congenital heart diseases usually involve structural defects in some part of the heart. Numerous mouse knockout models have been developed to study the genetic origins of these defects. The defects developed by these mice can be either structural or functional and can be in any one of the four chambers or great vessels. MRI is promising as a phenotyping tool. The standard multi-slice cardiac cine MRI protocols for mice are usually based on thick slices (typically 1mm thick) which can not capture atrial structures, and require careful oblique positioning for comparability. This study presents an isotropic cine black-blood MRI protocol with a voxel size of  $(0.2\text{mm})^3$ . Since SSFP/TrueFISP methods are more difficult to implement in high-field microscopy<sup>1</sup>, black blood was used for enhanced tissue-blood contrast for segmentation purposes. 4D isotropic imaging can provide both structural and functional information for all four chambers, and provides easy scan comparability. The effectiveness of this method is demonstrated on a mutant mouse from which 2 transcription factors (IRX4, IRX5)<sup>2,3</sup> involved in cardiac development have been knocked out.

**Methods** Black-blood multi slice mouse cine MRI was recently reported<sup>1</sup>. To extend this method for 3d isotropic acquisition, a MOTSA<sup>4</sup> technique was used with 5 coronal slabs to cover the heart volume. Mice were anesthetized with a mixture of 1.2%-1.6% isoflurane and oxygen. ECG monitoring and gating was performed with a commercial system (SA Instruments Inc.). MOTSA slab thickness was set to 1.6mm, and was encoded with a FOV of 48mm x 24mm x 2.4mm and a matrix size of 240x120x12. The distance between slab centers was 1.2mm, so that only the 6 center slices were used from each slab. 10 temporal phases were acquired with a TR/TE of 14ms/2ms. Excitation flip angle was 10 degrees. The scan was repeated 4 times for signal averaging. Total scan time was 3-4 hours.

**Results** Figure 1 shows long and short axis views of a wild type mouse at beginning (top) and end (bottom) of systole. All slices were extracted from the same measurement using Amira software (ZIB, Mercury Computer Systems, Berlin) for oblique sectioning. The top panel of Fig. 2 shows a segmentation of the 4 chambers at beginning (left) and end (right) of systole based on the same data set. The segmentation was done manually using Amira software. The same information for the mutant mouse (IRX4<sup>-/-</sup>, IRX5<sup>-/-</sup>) is shown in the lower panel of Fig. 2. The enlargement of the right ventricle and left atrium is clearly noticeable in the mutant as well as a change in the location of the papillary muscle.

**Discussion** The mouse cardiac imaging environment differs from the human one in several factors. These include a much shorter cardiac cycle (130-170ms for the anesthetized mouse) longer scan time possibilities (up to 3-4 hours for anesthetized mice) and consequently less sensitivity to respiration. In that context, this study demonstrates how to perform 4D cardiac imaging which is optimized for segmentation and phenotyping analysis. Although the segmentation presented here was performed manually, we expect to implement semi-automatic segmentation with further improvements in image contrast gained through refinement of the double-inversion MOTSA technique and/or use of exogenous contrast agents.

## References

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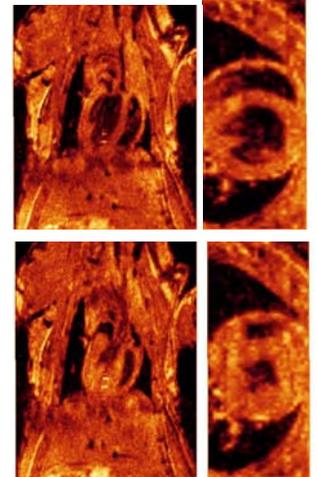
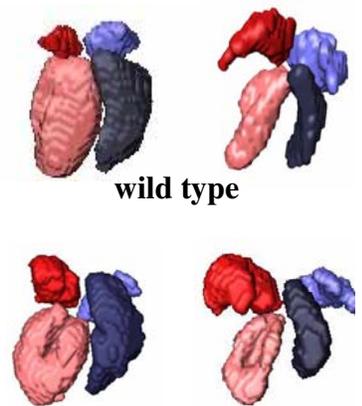


Fig. 1



wild type

mutant

Fig. 2