

### **Echocardiographic assessment of normal embryonic and fetal mouse heart development**

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**Background** - The identification of several genetic mutations involved in congenital heart disease has led to the generation of specific genetically mutated mouse models to study normal and abnormal cardiac development. Up till now studies in embryos / fetuses of these models mainly focused on the cardiac morphology and the availability of functional i.e. hemodynamic data is limited. In this study we assessed the morphological and hemodynamic parameters of normal developing mouse embryos / fetuses by using a high-frequency ultrasound system.

**Methods** - A timed breeding program was initiated with a wildtype mouse line. All recordings were performed in sedated (Isoflurane 1.5%) pregnant mice under stable vital parameters (heart rate, respiratory rate and body temperature). Trans-abdominal echocardiographic assessments were performed in individual embryonic hearts at 12.5 days post conception (dpc), which were also assessed at early and late fetal stages of development, 14.5 and 17.5dpc respectively (n=105).

**Results** – At the three stages assessed we could clearly visualize the individual compartments of the embryonic / fetal hearts: the left and right atria and ventricles and the developing inter-ventricular septum. Furthermore, at 14.5 and 17.5dpc the aorta and pulmonary artery were identified. Between 12.5 and 17.5dpc the embryonic / fetal heart rate increased significantly from  $125 \pm 9.5$  to  $219 \pm 8.3$  beats per minute. Reliable echo-Doppler recordings were made in the common atrioventricular canal and outflow tract (12.5dpc) and across the developing mitral, tricuspid, pulmonary and aortic valves orifices (14.5 and 17.5dpc). Furthermore, M-mode recordings (short/long axis) were made of the developing ventricles in order to calculate the shortening fractions (SF%) and diameters of the ventricular walls and inter-ventricular septum.

**Conclusion** - High-frequency echocardiography is a promising and useful imaging modality for structural as well as hemodynamic analysis of embryonic / fetal mouse hearts at subsequent stages of development. The implementation of this technique in embryos and fetuses of genetically mutated mouse models will provide important new data to unravel the etiology of congenital heart diseases. Furthermore, these data will help in the detection of human congenital heart disease at early stages of pregnancy.

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