Imaging of embryonic cardiovascular development with high-field MR microscopy

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Introduction

(Ultra) high field MR microscopy has been used for several studies of embryological development ex vivo. However, real time visualization of embryonic development in vivo was always thought to be idealistic, and was for that reason our challenge. Our goal was to follow up embryonic development in vivo with emphasis on heart development and to study possible side effects of the MRI procedure. From an embryological point of view avian models are often used to study heart malformations. Also, with the growing amount of transgenic mouse models, mouse embryological heart development is becoming more common. We therefore imaged avian embryos (quail) inside their egg and correlated in-vivo measurements of embryonic growth with well established ex-vivo tables. After the last MRI experiment embryonic weight and reached end stage of the experimental group was compared with that of a control group. As proof of principle, we also imaged mouse embryos in utero, as a first step towards the study of in vivo mouse heart development.

Materials and methods

Quail: quail embryos were longitudinally studied with MRI to cover all stages of heart development. We chose embryonic days (ED) 3, 5, 7, 9 and 11 out of a total incubation period of 20 days, to be representative for embryonic heart development. Movement of older embryos was minimized by cooling the eggs down to room temperature for 30 minutes.

Mouse: Pregnant mice were anaesthetized with isoflurane and mounted into the imaging probe using a toothbar to ensure their position in a vertical situation .

MRI: Imaging was performed on a vertical Bruker 9.4 T system, with gradients of 1T/m and a 30-mm-diameter birdcage resonator. Multi-slice RARE was used for 10-30 slices of 0.3 mm thickness, with TR/TE=5000/9 ms, RARE factor of 8, FOV=22 mm (quail) or 30 mm (mice), matrix=256, 8 averages and a total scantime of 22 minutes per embryo.

Results

We were able to follow individual quail embryos inside their eggs and to study heart development non-invasively. Examples of transverse slices through the heart of quail embryos during development are depicted in Figure 1. Both experimental embryos and control embryos reached stage 38 after 11 days and there was no statistical difference in their weight. Important structures for congenital malformation like pharyngeal arch arteries, atria, ventricles and the ventricular septum could be observed.

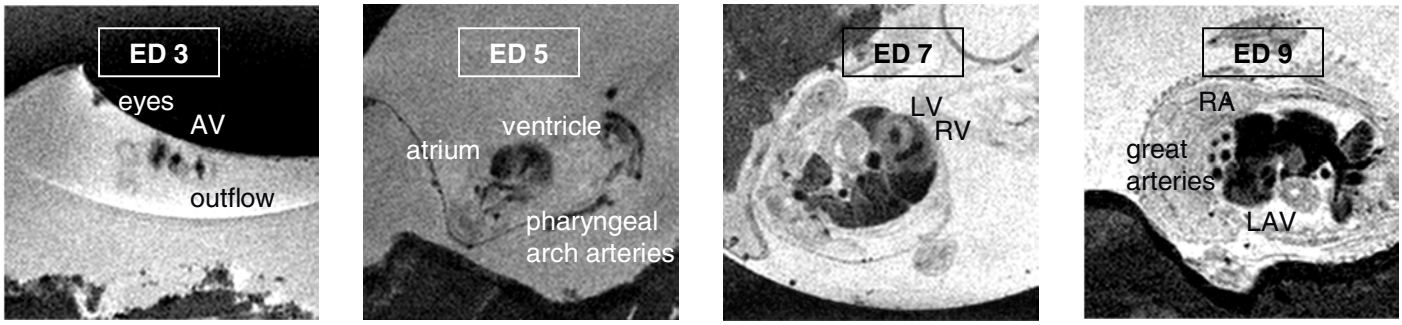

Figure 1: Transverse slices through the embryonic quail heart. In-plane resolution 89 µm. AV, atrioventricular canal; LV, left verntricle; RV, right ventricle; LAV, mitral valve; RA, right atrium.

Conclusions

Heart development can be studied with MR microscopy with a resolution high enough to diagnose a congenital malformation. Even with nowadays state of the art equipment it is possible to visualize living mouse embryos *in utero*. We did not observe harmful effects of MRI on embryonic growth.