In-utero imaging of the early mouse embryo

P. Parasoglou[1,2], C. A. Berrios-Otero[1,2], B. J. Nieman[3], and D. H. Turnbull[1,2]
[1]Skirball Institute of Biomolecular Medicine, New York University School of Medicine, New York, New York, United States, [2]Department of Radiology, New York University School of Medicine, New York, New York, United States, [3]Mouse Imaging Centre, The Hospital for Sick Children, Toronto, Ontario, Canada

Introduction

The mouse is the primary system for studying mammalian development. The study of embryonic and fetal development is an application well suited to the non-invasive nature of magnetic resonance imaging (MRI). However, significant technical challenges associated with *in-utero* imaging in animals as small as mice, mostly related to maternal and embryonic motion have resulted in a limited number of previous studies [1,2,3,4]. Vascular development in particular involves the formation of highly complex three-dimensional (3D) system of interconnected blood vessels, hence requires the acquisition of high-resolution (typically 120 μm or higher) 3D images. This can lead to long acquisition times in order to achieve acceptable signal to noise ratio (SNR), which has limited *in-utero* MRI to the latest gestational stages (embryonic day E17.5) [5]. In this work we report the acquisition of high-resolution 3D images of the vasculature of embryos from embryonic day E10.5, without the use of a contrast agent. Being able to image embryos from this early stage will allow longitudinal studies from the onset of the cardiovascular and nervous system development.

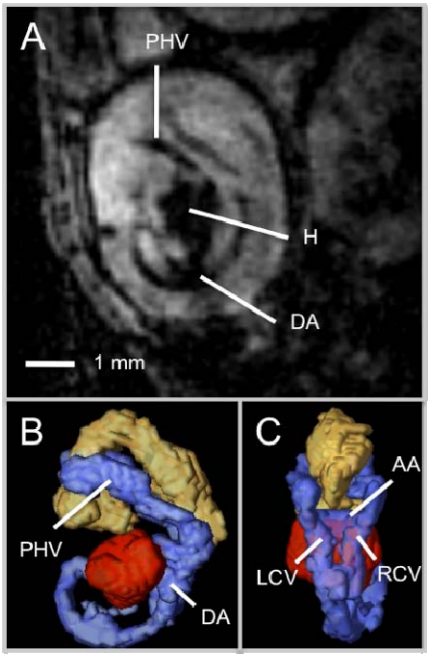

Fig.1 A) Oblique mid-sagittal view from a 3D image of an embryo at embryonic day E10.5. B-C) 3D segmentation of the heart (red), vasculature (blue) and neural tube (yellow). Labels: Heart (H), dorsal aorta (DA), primary head veins (PHV), left and right carotid veins (LCV and RCV), aortic arch (AA).

Method

A modified 3D gradient echo was employed that includes the acquisition of self-gated signals that can be used as traces of physiological motion (i.e. respiration/ cardiac motion), which can reduce motion artifacts by post-processing [4]. Embryo displacements were corrected by co-registering and averaging sequentially acquired low SNR volumes. Mice were anesthetized with isofluorine and imaged *in-vivo* using a 7.0T magnet with a Bruker Biospin Avance II console. A quadrature surface coil (Bruker Biospin MRI) was used for receive and a volume resonator (72-mm inner diameter quadrature resonator; Bruker Biospin MRI) for transmit. The acquired images had isotropic resolution of 100 μm, a field of view of 0.94 x 1.20 x 0.80 cm and image parameters TE/TR = 25 / 50 ms with a 20 degree flip angle. Eight 3D averages were acquired in 64 min. Semi-automatic segmentation of embryonic vasculature and significant anatomical structures were performed using Amira software (Mercury Computer Systems, inc).

Results

Mouse embryos were imaged *in-utero* between E10.5 and E17.5. In Fig.1 an example of a high-resolution image of an E10.5 embryo is shown, demonstrating the neural tube, the heart and several early-forming blood vessels.

Conclusions

Until now *in-utero* MRI studies of the mouse have been limited to the latest stages of gestation limiting its use for longitudinal studies of embryonic development. To our knowledge this is the first time high resolution 3D images have been acquired at this early stage, showing the exciting possibility of performing longitudinal studies of embryonic development at stages close to the onset of neurogenesis and embryonic cardiac activity.

Acknowledgements

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