MR microscopy in studying the development of the chick inner ear

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Introduction: The intricate labyrinth of the inner ear develops from a cyst-like structure known as the otocyst. Characterizing the morphogenesis from the otocyst to the fully developed inner ear has been shown to be vitally important to our comprehension of and strategies for managing congenital hearing loss[1]. However, two major obstacles stand in the way of a truly longitudinal, in-vivo phenotyping MR imaging study. The small scale of the embryonic inner ear and the inherent in-vivo motion of the embryo limits protocols to high spatial and high temporal resolution methods respectively[2]. However, the nature of MR image acquisition necessitates that one must be sacrificed for the other. This study investigates the feasibility of visualizing development through embryological time points using MR microscopy as a non-invasive and non-terminal imaging modality.

Materials & Methods: In ovo proton images were acquired on a Bruker 7T BioSpec 30/70 scanner using an in-house designed single loop coil, 44 mm in diameter. 3D fast spin echo (RARE) and steady state (FISP) imaging sequences were utilized in order to investigate the spatial and temporal resolution limits respectively. T2-weighted RARE imaging consisted of TR/TE=1500/100 ms and a nearly isotropic resolution of 100 microns. T2/T1-weighted FISP protocols consisted of TR/TE=4/2 ms and an isotropic resolution of 200 microns. The high spatial resolution images were obtained using deceased in ovo embryos at varying embryonic stages (E4,7,10,14-18,20,21) to simulate a longitudinal study (Figure 1). A single embryo (E18) was imaged to examine range of motion at high temporal resolution in vivo (Figure 2).

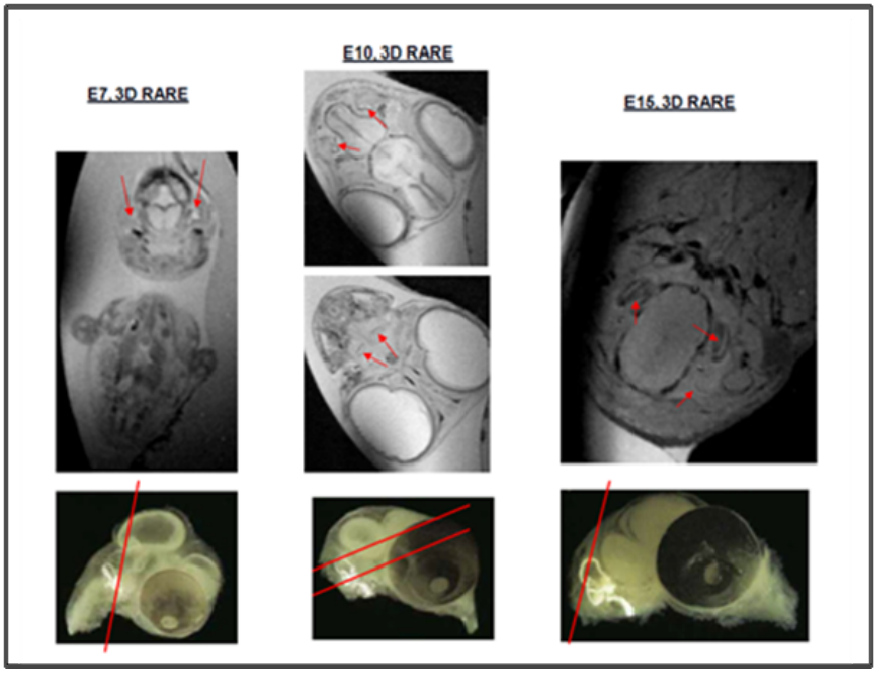
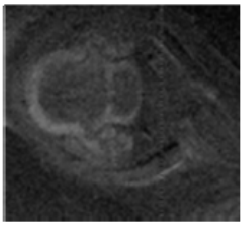


Figure 1 (*left*): Top row (left to right): Representative high resolution, T2 weighted MR images (3D-RARE) of deceased chick embryos at E7,10 and 21. The red arrows indicate the inner ear. Bottom row: Photographs of fixed check embryos at embryonic day 7, 10 and 21.The red lines show approximate slice orientation of the MR images shown above. **Figure 2 (*below*)**: (a) Alive embryo, 2D steady state imaging sequence (FISP); Scan Time = 5 sec. (b) Deceased, 3D steady state (FISP) imaging sequence, Scan Time = 2 min. 22 sec.



(a) (b)

Results & Discussion: Microstructures become resolvable as early as E7 using RARE imaging. As maturation progresses, many identifiable inner ear structures are clearly visible, including the ampulla, sacculus, lagena, cochlear duct, and the lateral, posterior and superior semicircular canals. In vivo FISP imaging, though more susceptible to motion artifact and reduced spatial resolution, was able to resolve the inner ear structures faster than the rate of gross motion. The feasibility of performing a longitudinal study of inner ear development in the chick embryo has been demonstrated. RARE imaging is not optimal for in vivo imaging due to motion sensitivity during the long TRs necessary. FISP imaging is adequate for in vivo studies, but will likely benefit from motion reduction via sedation or other means.

References: 1. Wu DK, et al, Development.125, 11-20, (1998). 2.Morris HD et al, ENC Conference Abstract., 2007