Dual-Mode Optical-MR Microscopy with Uniplanar Gradient Coils

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Introduction Magnetic resonance microscopy offers unique complementary information to optical microscopy in basic biological and clinical applications. The intrinsically lower resolution of MRI motivates the development of a dual-mode instrument that can tie the internal cell movements of an opaque embryo to the large amount of collected data regarding the external cell motions, as is the case for common amphibian embryo models of early vertebrate development ranging from frog to axolotl. The integration of optical microscopes with MR imaging hardware has become increasingly popular but gradient hardware designs are rarely designed specifically to complement optical imaging. We present here a dual-mode optical-MR microscope based on a uniplanar three-axis water-cooled gradient set integrated with an MR-compatible CCD microscope for applications in developmental biology and embryology.

Methods The uniplanar magnetic field gradient set consisted of a water-cooled three-axis gradient coil module capable of maximum gradient strengths in excess of 1T/m at high duty cycles (1) The gradient module is supported within a frame that doubles as the microscope stage (Figure 1). A single-turn planar RF coil was used for RF transmission and reception. A commercial optical microscope (Monozoom 7, Leica) and MR-compatible CCD camera (MiniVid MV10-U) were adapted for use in high magnetic with white-light LED illumination. Sample temperature was controlled via thermostatic control of the cooling water. A cluster of approximately stage 10 *Xenopus laevis* embryos was prepared according to protocols approved by the Institutional Animal Care and Use Committee (1). Demonstration optical-MR imaging of this cluster was performed within a 7 Tesla 310 mm horizontal bore magnet equipped with a Bruker Biospec Avance console. Volumetric multiple gradient echo images were acquired with the following parameters: TR/TE/Flip = 300/1.5-13/Variable, 6 echos, 128 x 128 x 48 matrix, 75 x 75 x 75 micron voxel (within target volume), total imaging time/volume = 30m43s. Optical images with a field of view of approximately 10mm and a sampling matrix of 1280 x 1024 were acquired every 5 minutes. MRI images were geometrically corrected using the modeled gradient field for each axis as described in (1).

Results and Discussion Xenopus embryos developed normally during the experimental run at a mean temperature of approximately 22°C as measured by a stage-mounted thermocouple. SNR in the MR images was improved by averaging all six gradient echoes acquired with the multiple echo sequence and the application of a 1 voxel FWHM Gaussian spatial filter. Internal fluid spaces and bulk cell movements during gastrulation and neurulation could be visualized effectively by MRI and tied directly to external morphological features imaged in visible light. Optical imaging was unaffected by the 7 Tesla magnetic field, though a small amount of structured noise was detected in the MR images and isolated to the CCD camera sampling. Some condensation was observed on the Petri dish lid that obscured part of the optical imaging field during this experiment. Future prototypes will address this by creating an aperture in the lid over the optical focus.

Conclusions Dual-mode optical-MR imaging of live developing embryos with adequate environmental control is readily achieved using a high performance uniplanar gradient-RF assembly and MR-compatible optical hardware. Applications include

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References (1) Demyanenko et al. A uniplanar three-axis gradient set for in vivo magnetic resonance microscopy. J Magn Reson (2009) vol. 200 (1) pp. 38-48

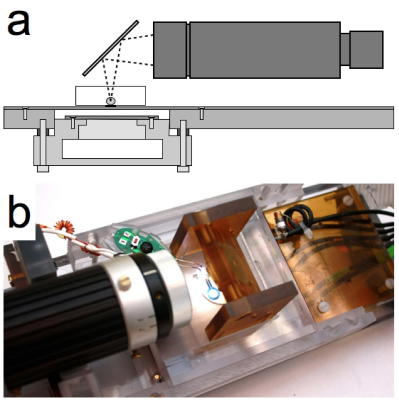

Figure 1: (a) Schematic of the optical microscope and mirror assembly mounted above the uniplanar gradient module. (b) Working prototype optical-MR microscope.

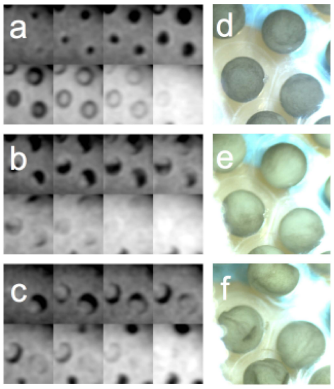

Figure 2: Example time frames of Xenopus lavis development from simultaneous 3D MRI (a-c) and visible light imaging (d-f) at (a,d) 1 hour (b,e) 9 hours and (c,f) 17 hours.