High-resolution MRI analysis of breast cancer xenografts on the CAM @ 11.7T

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Introduction: The chick chorioallantoic membrane (CAM) model has been successfully used to study angiogenesis, cancer progression and its pharmacological treatment, pharmacokinetics, and properties of novel nanomaterials[1]. Magnetic resonance imaging (MRI) is an attractive technique for non-invasive imaging and longitudinal monitoring of physiological processes and tumor growth. This study proposes an age-adapted cooling regime for immobilization of the chick embryo, enabling high-resolution MRI of the embryo and the CAM tumor xenografts, which was evaluated for tumor growth and morphology.

Methods and Materials: 44 chick embryos were enrolled in this study. The novel immobilization and high-resolution imaging protocol was optimized in 29 embryos and its application to tumor growth monitoring evaluated in 15 embryos after xenotransplantation of human MDA-MB-231 breast cancer cells on the CAM.

Imaging was performed at an 11.7T small animal MRI system (Bruker BioSpec). Data was received with a 60mm quadrature volume TR resonator. Tumor volumes were monitored from d4 to d9 after grafting applying a high-resolution T2-weighted multislice rapid acquisition with relaxation enhancement (RARE) sequence: TR/TE = 4320/45ms, resolution = 77×91µm^2, slice thickness = 0.5mm, interslice distance = 0.5mm. 30 slices were acquired for whole embryo coverage. The acquisition time was 35 minutes for a single scan. Immobilization of the embryo was achieved by cooling at 4°C before imaging, with cooling times adapted to development age. At d9 after cancer cell grafting, the solid tumor tissues were collected and compared with the MRI derived data.

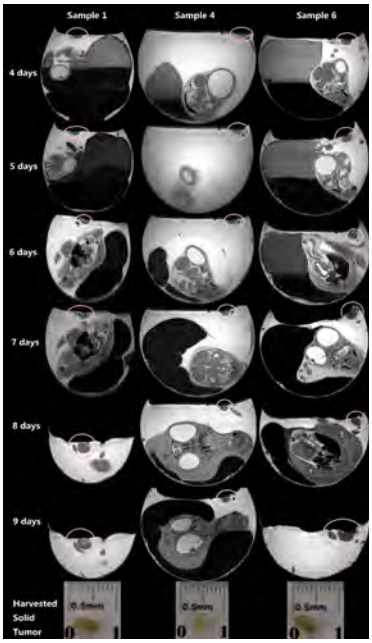

Fig. 1: Longitudinal high-resolution MRI images of breast cancer xenografts (circles) grown in ovo

Results: With the adaptive cooling regime, motion artifacts could be completely avoided for up to 90 minutes scan time, enabling high-resolution in ovo imaging. Excellent anatomical details could be obtained in the embryo as well as in the grafted tumors (Fig.1). Tumor volumes could be quantified and monitored over time (Fig.2). The histological analysis reveals the shape and structure of the tumor as seen with MRI (Fig.3). With MRI as well as with histological analysis two different tumor components (open / closed arrow) and a large vessel can be clearly appreciated.

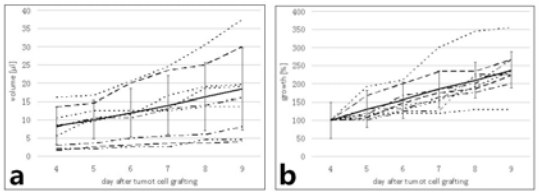

Figure 2: Volumes (a) and relative growth (b) of the breast cancer xenografts in a CAM model as analyzed by MRI.

Discussion and Conclusion: The obtained results proof the feasibility of high-resolution MRI for longitudinal tumor and organ growth monitoring. The suggested method is promising for future applications such as testing tailored and/or targeted treatment strategies, the longitudinal monitoring of tumor development, the analysis of therapeutic efficacies of drugs, or the assessment of pharmacokinetics. The method provides an alternative to animal experimentation.

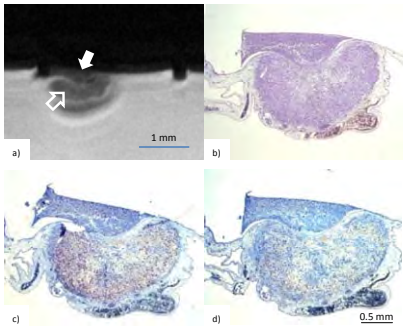

Figure 3: Correlation of immunohistological analysis of tumor xenografts on CAM and MRI.

References: [1] Bain MM, et al. JMRI. 2007;26:198–201