**T2-weighted and DCE MRI of Medulloblastoma Mouse Model and Oncolytic Measles Virus**

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**Introduction and Objective**

Medulloblastomas are the most common childhood brain cancer. They account for 15-20% of all pediatric brain tumors. It is a highly invasive tumor with a poor prognosis in a subset of patients. The goal of this study was to monitor the treatment effect of an oncolytic measles virus (MV) in a medulloblastoma tumor model using T2-weighted and DCE MRI.

**Methods**

**Mouse Model:** D283med (ATCC) human medulloblastoma cells ($1 \times 10^6$) were implanted orthotopically in 12 female athymic nu/nu 6-8 week-old mice. Twenty-three days later 4 mice/group were stereotactically treated at the same location with (6×10⁴ pfu) measles virus (MV-control) (Studebaker, NeuroOnc 2012:12(10);1034), a combination MV containing the human endostatin/angiostatin fusion transgene and MV containing the murine endostatin/angiostatin fusion transgene (MV-combo), or with Opti-MEM™ (Life Tech, NY) serum medium (untreated).

**Imaging and Analysis:** T2-weighted imaging was performed 1 day pre- and 3, 7, 13, 20, and 27 days post treatment. DCE-MRI was performed 1 day pre- and 3 days post-treatment. The imaging was performed using a Bruker Biospin 94/30 magnet (Bruker Biospin, MA), a 2.0 cm diameter receive-only mouse brain coil, and a 70 mm diameter linear volume coil. T2-weighted images were collected using a T2-weighted RARE sequence (TR/TE=3500/36ms, RARE factor=8, FOV=20x20 mm², matrix size=256x256, slice thickness=1 mm, navg=1). DCE data were collected using a FLASH sequence (TR/TE=135.8/2.4ms, flip angle=50°) over the same FOV. Several baseline images were collected prior to a bolus of Gd-DTPA injection (0.5 mmol/kg) through a tail vein catheter and for 20 min post-injection. Tumor volume was calculated from manual outlines of the T2-weighted images. A General Kinetic model was used to calculate $K_{trans}$ and $v_e$ for each voxel in the tumor. The arterial input function was calculated from an average of the voxels within an ROI of the superficial temporal vein.

**Results and Discussion**

The mean (s.d.) tumor size pre-treatment was 20.7 (7.8) mm³. Tumor size increased 158% for the control mice and 70% for the MV-treated mice 3 days post treatment. Necrotic regions were observed in T2-weighted images of the MV-treated mice as early as 3 days post-treatment. This corresponded with an increased $v_e$ calculated from the DCE images. A decrease in $K_{trans}$ was observed post-treatment in the MV-treated mice (Fig. 2) as opposed to the untreated mice, however no significant difference in $K_{trans}$ was observed between the MV-combo and MV-control mice. A 64% decrease in tumor size was observed in the MV-treated mice 27-days post treatment and all control mice were dead due to primary tumor burden 20 days post-treatment.

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**Figure 1.** T2-weighted images medulloblastoma

**Figure 2.** Histogram plots $K_{trans}$

This data indicates that MV was successful in reducing the primary tumor, and that no difference in the perfusion properties measured using DCE-MRI were observed in mice treated with MV-combo from that of MV-control.