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 medullablastoma tumor model using T2-weighted and DCE MRI.

Methods

Mouse Model: D283med (ATCC) human medulloblastoma cells ($1x10^6$) 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 (6×10^4 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 mm^2, 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^o) 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) mm^3. 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. (Fig.1) 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.

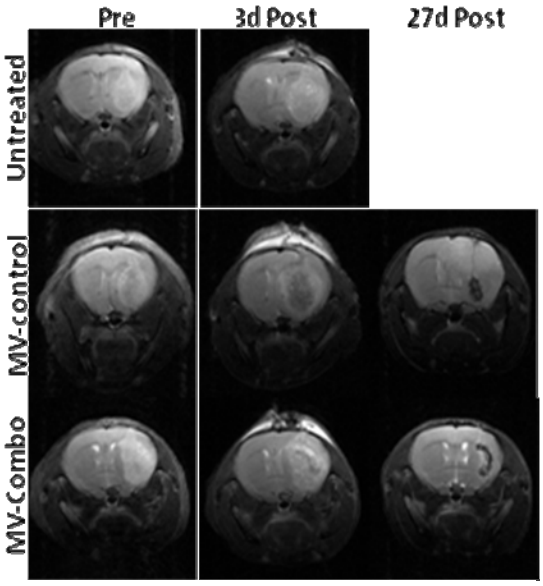

Figure 1.T2-weighted images medulloblastoma

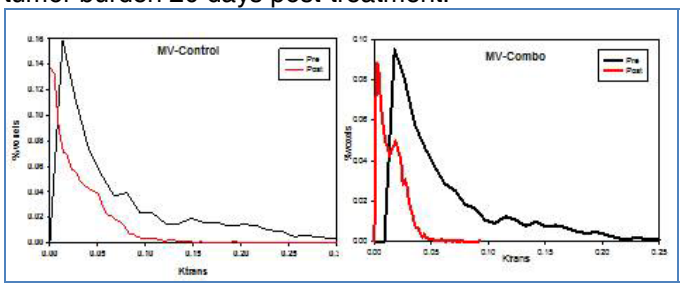

Figure 2. Histogram plots K^{trans}

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