

Cellular MRI to Differentiate Glioma from Radiation Necrosis Using Sensitized Splenocytes

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There is evidence of an accumulation of primed dendritic and sensitized T-cells at the site of glioma, suggesting an initiation of immunity. If intracranial glioma initiates an immunogenic reaction, there should be differential migration and incorporation of magnetically labeled sensitized splenocytes (T-cells) into glioma, but not in radiation necrotic areas. The purpose of this study was to differentiate glioma (9L) from radiation necrosis using ferumoxides-protamine sulfate (FePro) labeled sensitized splenocytes. Labeled rat splenocytes were injected intravenously in rats bearing an intracranial gliosarcoma (9L) or radiation necrosis. Cells were injected 11 days after tumor implantation or irradiation and MRI was obtained 3 days after the injection of cells (day 14). Multi-echo T2-W, T2*-W and 3D gradient echo MRI were obtained by a 7 Tesla MR system. Following *in vivo* MRI, rats were euthanized, perfused, and the brains were collected. Randomly selected rat brains were also underwent *ex vivo* high resolution MRI. Collected whole brains were further fixed and snapped frozen for sectioning. Sections were stained for blood vessels using FITC labeled lectin. Prussian blue staining was performed to detect the iron positive cells. Distribution of blood vessels and pattern of neovascularization at the site of radiation were compared with that of implanted tumor and surrounding brain. Both *in vivo* and *ex vivo* MRI showed low signal intensity areas at the margin of the tumors in rats injected with labeled cells. Iron positive cells were present at the corresponding sites of low signal intensities seen on MRI. There was no definite low signal intensity area indicating accumulated iron positive cells seen at the site of radiation injury and Prussian blue staining also did not show any iron positive cells. By targeting immunogenic reaction, it is possible to differentiate glioma from radiation necrosis using magnetically labeled sensitized splenocytes (or T-cells) and MRI.