A Rodent Model of Post-Treatment Radiographic Imaging Changes - So-called "Pseudoprogression"

Randy L. Jensen MD

Department of Neurosurgery, Huntsman Cancer Institute, University of Utah

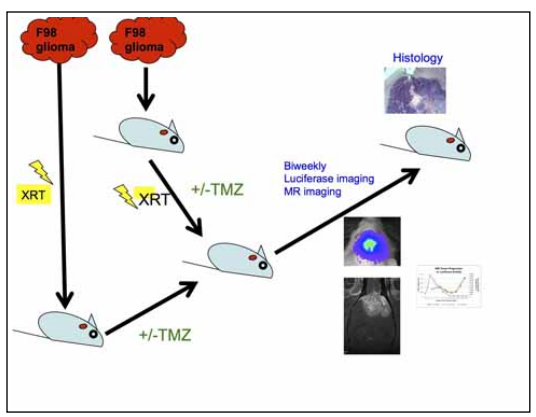
Introduction

The lack of a definitive imaging modality to distinguish post-treatment radiographic imaging changes (PTRIC), including pseudoprogression and radiation necrosis, from true tumor progression presents a major unmet clinical need in the management of GBM patients. At present there are no animal models of PTRIC

Methods

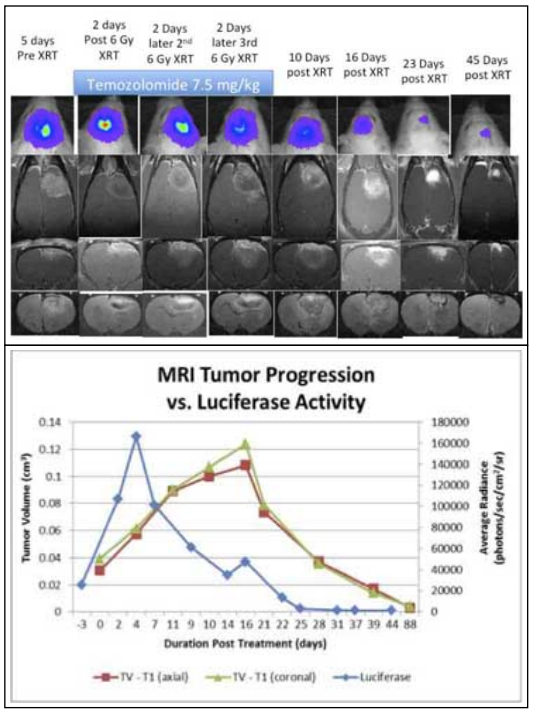
We developed a rodent model of PTRIC by intracranially implanting rats with either preirradiated (2-10 Gy) or nonirradiated glioma cells transfected with a constitutively active luciferase reporter. The rats were treated with or without temozolomide (TMZ) chemotherapy and rats implanted with nonirradiated cells were treated with focused tumor irradiation (2-10 Gy) to the implanted tumor cells and surrounding brain. Cell growth was monitored by bioluminescence imaging of the luciferase reporter and brain MRI measurement of tumor growth. Tumor histology was confirmed by light microscopy and immunohistochemistry.

Experimental plan



Tumor "cure"

6 Gy XRT X3, TMZ (7.5 mg/kg)

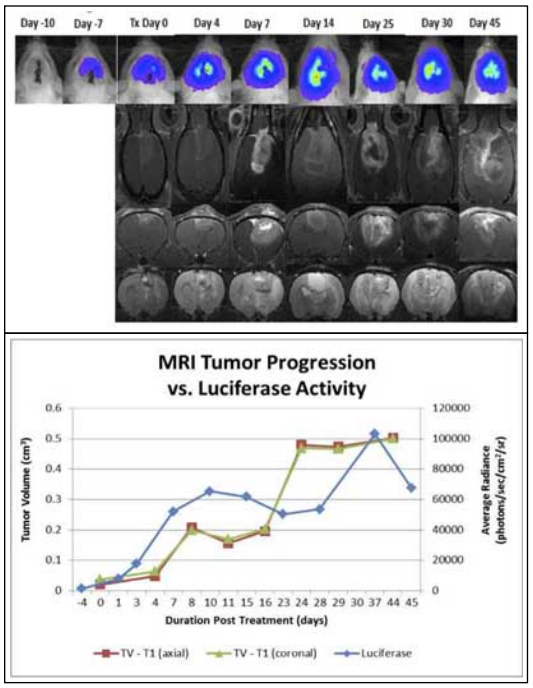


Results

Animals implanted with irradiated cells did not produce PTRIC even when co-treated with TMZ. Rats considered to have tumor progression demonstrated steadily increasing luciferase activity coupled with increasing gadolinium-enhanced tumor volume and were found in animals receiving radiation doses less than 2Gy X3 without TMZ chemotherapy. Conversely, pseudoprogression was manifest by decreasing luciferase activity with increasing gadolinium volume over time found in tumors treated with 2Gy X3 and concurrent TMZ. Tumor histology was correlated with luciferase activity.

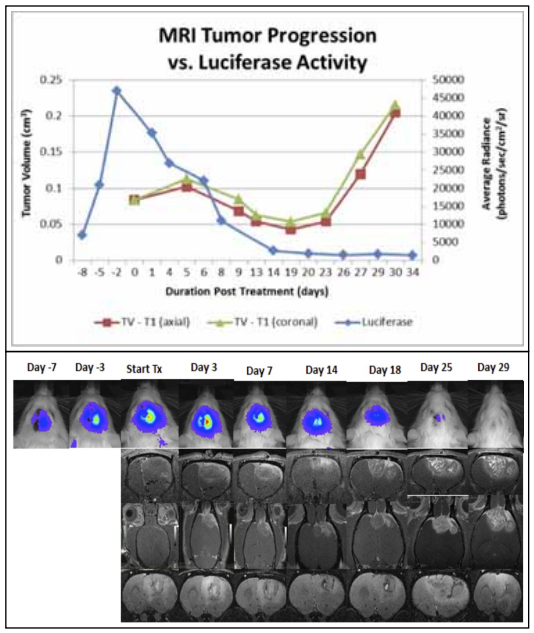
Tumor progression model

3Gy X3, DMSO X6



Pseudoprogression model

3 Gy X3, 7.5 mg/kg TMZ X6



Conclusions

Our preliminary data suggests a potential model of pseudoprogression and/or radiation necrosis. This model needs to be further characterized with advanced imaging techniques including perfusion MR and multitracer PET imaging. We plan to use this model for future molecular and cellular studies to understand the cause and potential exploitation of these effects for better patient care.