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Randomized Trial of Linear Accelerator Generated Mini Beam Radiation Treatment: The Final Report and Future Possibilities

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Abstract

Objectives:

The main challenge in treating malignant brain neoplasms lies in eradicating the tumor while minimizing treatment-related damage. Long term treatment-related morbidity regularly accompanies tumor control, and has significant impact on quality of life of cancer survivors. Spatially fractionated radiation has the potential to achieve both cure and to avoid dreaded long term sequelae. We have created a new clinical device which produces mini-beams on a linear accelerator, providing a new type of treatment called mini-beam radiation therapy (MBRT). The objective of this study was to compare the treatment outcomes of MBRT versus standard radiation treatment (SRT), to evaluate the tumor response and the treatment-related changes in the normal brain.

Methods:

Pet dogs with de novo brain tumors were accrued for treatment. Dogs were randomized between standard fractionated stereotactic (9 Gy/3 fractions) radiation treatment vs. a single fraction of MBRT (26 Gy mean dose). Dogs were monitored after treatment for clinical assessment and imaging. When the dogs were euthanized, a veterinary pathologist assessed the radiation changes and tumor response. All brain specimens were evaluated by one neuropathologist for identifying radiation related changes. Hematopathologist evaluated the specimens for cellular infiltrates. All these specimens were also subjected to synchrotron micrography to identify cellular damage at elemental level.

Results:

We accrued 16 dogs, 8 dogs in each arm. In the MBRT arm, 71% of dogs achieved complete pathological remission. Radiation-related changes were all confined to the target region. Structural damage was not observed in the beam path outside of the target region. In contrast, none of the dogs in the control group achieved remission and treatment-related damage was more extensive. Therapeutic superiority was observed with MBRT, including both tumor control and the normal structural preservation. The MBRT findings are suggestive of an immune-related mechanism which is absent in standard treatment.

Conclusion(s):

The first ever randomized study of MBRT of canine brain tumor has clearly shown the ability to achieve the goals of remission and reduced long term radiation toxicity. The results augur potential for conducting human studies with MBRT.