Randomized trial of Linear accelerator generated mini beam radiation treatment- The Final Report and Future possibilities.

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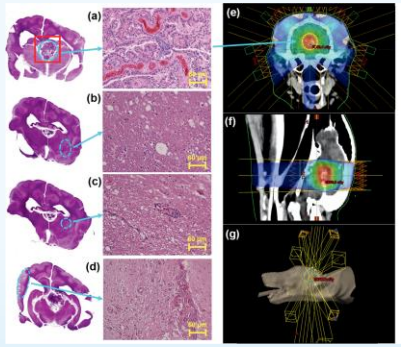


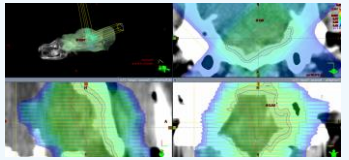
Static field IMRT showing extensive damage to surrounding brain parenchyma

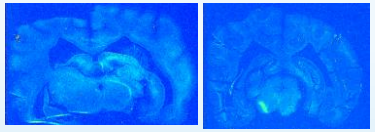
Objectives: The main challenge in treating malignant brain neoplasms lies in eradicating the tumor while minimizing treatment related damage. Long term treatment-related morbidity always accompanies tumor control which has significant impact on quality of life of the patient who has survived the cancer. 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, to provide 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

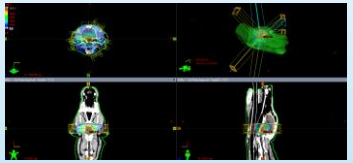
Results: We accrued 16 dogs, 8 dogs in each arm. In the MBRT arm, 71% dogs achieved complete pathological remission. The radiation-related changes were all confined to the target region. Structural damage was not observed in the beam path outside of the target region. In contrast, none of the dogs in control group achieved remission and the 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: The first ever randomized study of MBRT of canine brain tumor has clearly shown the ability to achieve this goal. The results augur potential for conducting human studies with MBRT.

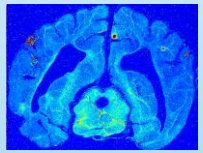


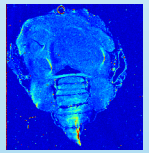


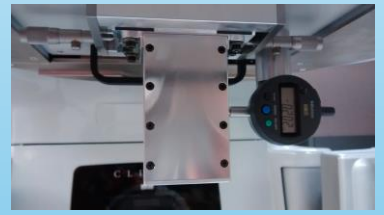
MBRT treated Brain not showing any damage on Synchrotron micrography



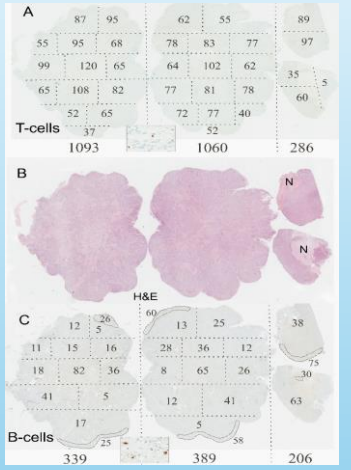
Synchrotron micrography of Brain treated with IMRT showing extensive hemorrhagic changes in brain.





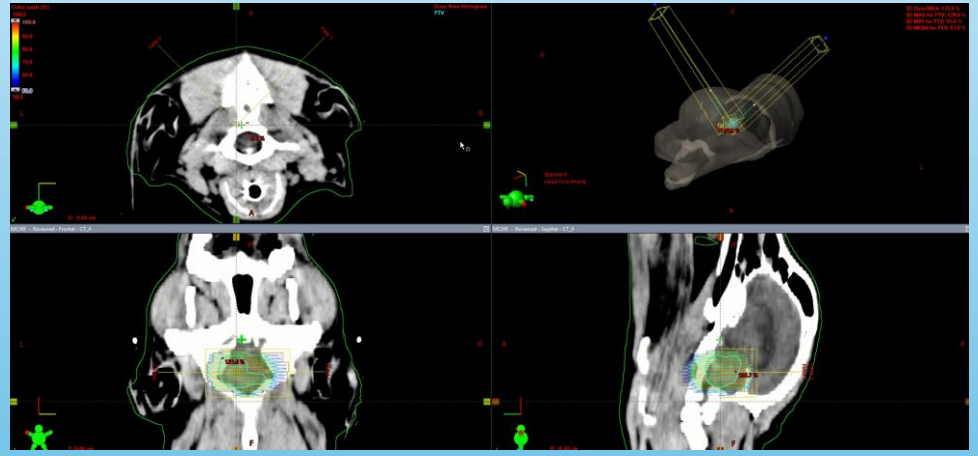


Mini Beam Collimator mounted on a Linear Accelerator



MBRT treated brain tumor showing Tumor infiltrating T lymphocytes (TILs) suggesting immune modulation and surveillance induced by MBRT would have major impact on tumor control

MBRT treated brain tumor showing Tumor infiltrating B lymphocytes (TILBs)



MBRT delivery clearly showing the low entrance and exit dose. It also shows how beamlets are dove tailed with each other showing VPDR is maintained through the target region.

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