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Abstract

Is Immune Modulation Possible with Radiation Treatment? - Report of a Randomized Phase III Study Irradiating Canine De-Novo Brain Tumors

Vijayananda Kundapur [1], Monique Mayer [2], Andrew Alexander [3], Narinder Sidhu [4], Victor Zherebitskiy [5], Roland Auer [6]

1. Radiation Oncology, Saskatoon Cancer Center 2. Small Animal Clinic/ Veterinary Radiation Oncology, Western College of Veterinary Medicine, Gainesville, USA 3. Physicist, Saskatoon Cancer Centre, Saskatoon, CAN 4. Medical Physics, BC Cancer Agency, British Columbia, CAN 5. Nuropathology, Univerisity of Saskatchewan, Saskatoon, CAN 6. Nuropathology, University of Saskatchewan, Saskatoon, CAN

Corresponding author: Vijayananda Kundapur, vijayananda.kundapur@saskcancer.ca

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Objectives: Tumors in brain are currently treated with conventional radiation therapy techniques with poor tumor control but are associated with considerable side effects. Synchrotron generated micro-beam radiation therapy (SMBRT) has shown promising results in preserving brain architecture; however physical characteristics of SMBRT limit its use. We have successfully implemented a new clinical device for use on linear accelerator in clinical use, which produces fine beams of radiation called mini-beams (MBRT) of 1000 um size using 6 MV photons. The objective of this study was to test if MBRT can emulate the SMBRT biological effects using spontaneous brain tumors in dogs.

Methods: Pet dogs with de-novo brain tumors were accrued for treatment across the country. Dogs were randomized between standard Stereotactic (9 Gy x 3 fractions) radiation treatment (SRT) Vs single fraction MBRT (26 Gy to mean dose). Dogs were followed for clinical assessment and MRI. Whenever dogs were euthanized, a veterinary pathologist assessed the radiation changes and tumor response.

Results: Between 2013 and 2017, we accrued 16 dogs (8 on SRT and 8 on MBRT arm and range of follow up 1.5 - 50 months SRT group Vs 3 - 36 months with MBRT group). SRT treated dogs follow-up scans and postmortem evaluation showed residual tumor in all of them. In contrast, > 50% dogs have pathological complete response in MBRT treated dogs. All these dogs have shown lymphocyte infiltration in the target area which was not seen in control group. There were definite treatment-related changes seen in both arms of treatment, however changes were more pronounced in SRT group.

Conclusions: Results show MBRT has a superior therapeutic ratio with excellent tumor control and fewer long term pathologically correlated toxicities. Post mortem evaluation shows the possibility of immune response as noted with lymphocyte infiltration. This might pave way for a new modality of radiation treatment, which would require a phase I human studies.

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