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Abstract

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Abstract

Objectives: Emerging evidence indicates that low-dose ionizing radiation may modulate brain glucose metabolism without inducing neuronal death. This concept of radiomodulation has also been supported by preclinical studies in mice and pigs, which demonstrate that low-doses of ionizing radiation can alter neuronal network activity. Clinically, low-dose ionizing radiation offers two notable advantages: (1) submillimeter targeting precision (≤ 1 mm), (2) a brief treatment duration (< 30 minutes), and (3) reversibility of non-lesion modulation. Preliminary clinical work by Solvason et al. further supports feasibility: among three patients with treatment resistant depression (TRD) treated using low-dose X-ray irradiation, none exhibited neurofunctional impairment, and two experienced sustained symptomatic improvement lasting over six months. Building upon both preclinical evidence and these early clinical observations, the present study aims to investigate the safety and efficacy of low-dose X-ray radiation directed at the subgenual anterior cingulate cortex (sgACC) in patients with TRD.

Methods: This is a pilot study involving up to 20 participants treated with ZAP-X (ZAP Surgical, San Carlos) TRD stereotactic radiosurgery (SRS). Subjects will be outpatients from the HMH Centers, and the surrounding community who have been diagnosed with a current depressive episode for at least one year duration, as per DSM V-TR criteria, and have had failure to show clinical improvement after at least four different medication trials of adequate duration and dose and/or one course of ECT during the current episode. A medication trial is defined as an adequate dose and duration of one of four classes of psychoactive medications: lithium, anticonvulsant mood stabilizers, atypical antipsychotic mood stabilizers, and/or antidepressant medications. One course of ECT is defined as receiving 12 acute treatments. Although ECT may be an important inclusion criteria, patients may participate in this study without undergoing a previous trial of ECT if clinically appropriate. The sgACC target will be localized at Cg25 using T1-anatomical and diffusion tensor MRI with Quicktome (Omniscient Neurotechnology, Atlanta) brain mapping software. The target will be constructed bilaterally in the right and left hemispheres using Eclipse (Varian Medical Systems, Palo Alto) treatment planning software (TPS). The ZAP-X TPS will then compute an optimal set of beam delivery trajectories in which a dose of 25 Gy is prescribed to the target volume. ZAP-X SRS will be administered to the right and then left hemispheres over two consecutive days.

Results: Preliminary treatment planning results from 3 patients utilized a single isocenter, 5 mm collimator, and gantry path 6 for each target. The average Optic Chiasm D0.035cc = 240 ± 30 cGy, Left Optic Nerve D0.035cc = 110 ± 40 cGy, Right Optic Nerve D0.035cc = 118 ± 6 cGy, Left Eye Dmax = 72 ± 5 cGy, Left Eye Dmax = 74 ± 3 cGy, Left Cochlea D0.035cc = 14.9 ± 1.6 cGy, Right Cochlea D0.035cc = 12.6 ± 1.4 cGy, and Brain - GTV V1200cGy = 0.23 ± 0.04 cc. The average treatment time per target = 24.822 ± 0.017 minutes.

Conclusion(s): Delivery of low-dose X-ray radiation for TRD is feasible using ZAP-X SRS. If successful, TRD SRS will allow for the unique approach of using a non-ablative, non-invasive, non-implanted device to modulate an area of the prefrontal cortex compared to current standard neuromodulation treatments for TRD.