Title: Implanted Electrode Design and Optimization for the Treatment of Primary Brain Tumors

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Structured Abstract:

Introduction: Gliomas are the most common malignant primary brain tumors, with glioblastoma multiforme (GBM) being the deadliest of all. Diffuse intrinsic pontine glioma (DIPG) is a tumor located on the brainstem which occurs in children, with typical survival of less than a year after diagnosis. For most high grade tumors such as GBM, the treatment strategy is to use a combination of chemo and radiation therapy, after surgical tumor removal, to treat the cancer cells that remain. For DIPG, surgical removal is not possible due to the location of the tumor, so radiation therapy is the main treatment option. It was recently shown that applying alternating electric fields of intermediate frequency (200 kHz, 1-3 V/cm) to the brain have the potentials to slow down the progression of cancer, through inhibition of cell division [1],[2]. The clinical application of this method uses external electrode arrays placed on the scalp, where an electric field is applied for a minimum of 18 hours per day. These external arrays fail to reach tumors located on the brainstem, which leads to the hypothesis that implanting electrodes directly in the tumor could give the desired results. An internal placement, like deep brain stimulation (DBS) to treat neurological disorders, would allow patients with brainstem tumors to receive tumor treating fields therapy. Computational studies on the electric field distribution for external electrode arrays [3] have quantified the field within the brain, but this has yet to be investigated for implanted electrodes, and is necessary for finding the optimal electrode configuration.

Methods: In this study, finite element method was employed using COMSOL Multiphysics (v. 5.2a) to solve for the electric field from different implanted electrode configurations in a spherical tumor model. Material properties for the tumor, surrounding white matter and electrodes were defined, including the dielectric and conductivity values for each material. The separation distance of electrodes was then optimized for tumor coverage using a parametric sweep for a range of distances.

Results: Starting with the current design of DBS electrodes, the ideal electrode contact configurations and locations were determined for 2, 3, 4, and 5 electrode models. Next, the separation of the electrodes was optimized for tumor coverage over a 1 V/cm electric field.

Discussion: Computer simulations of the electric field are a crucial step in designing electrodes to best treat these high grade primary brain tumors. Implanted electrodes could be especially useful for treating tumors located on the brainstem such as DIPG, where surgical tumor removal is not possible. In the future, electrode design will be further optimized with additional parameters, and patient specific tumor models will be incorporated in the optimization.

[1] Gutin et al., Am. Soc. Clin. Oncol., 2012
[2] Xu et al., Anticancer Research, 36:71-80, 2016
[3] Lok et al., Cancer Medicine, 6(6):1286-1300, 2017