Title: Applications of Electric Field Optimization Methods for Primary Brain Tumour Treatment with Intratumoral Modulation Therapy

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Structured Abstract:

Introduction: Low intensity, non-ablative electric fields are a new treatment modality for primary brain tumours, with external electrode arrays currently being used in clinical trials to treat Glioblastoma Multiforme (GBM). Intratumoral modulation therapy (IMT) is a developing technology that applies electric fields directly to the tumour volume using implanted electrodes. By using electrodes placed within the tumour volume, IMT could provide a continuous treatment to unresectable tumours located anywhere in the brain, including those located on the brainstem.

Our group has investigated single electrode stimulation both in vitro and in vivo, showing the effectiveness of electric fields on reducing tumour growth for GBM and Diffuse Intrinsic Pontine Gliomas. To treat human tumours, multiple electrodes with optimized stimulation and configurations are required to produce fields large enough to cover the tumour. Using a custom optimization algorithm, we have explored optimal configurations and maximum treatable tumour size for up to 5 electrodes. In addition, we evaluated multiple stimulating contacts per electrode, and applied our algorithm to design an in vitro validation experiment.

Methods: COMSOL Multiphysics (v 5.4) was used to create spherical tumour and electrode geometries with separately programmable electrode contacts, and to solve for the electric field. Our pattern search optimization algorithm was coded in MATLAB, which determines the geometrical configurations and stimulation parameters that maximize the field coverage over time. The algorithm was designed so that it can be applied to any in vitro, in vivo or patient specific human tumour model, for various optimization parameters including number of electrodes, number of contacts, location, input voltage and relative phase shift.

Results: The optimized relative phase shifts of multiple contacts per electrode was found to create electric fields that rotate in three dimensions to encompass the entire tumour volume. For a 2.4 cm diameter tumour, 5 electrode, 3 contact model, the objective function value was improved by 36% when compared to the single contact model. An in vitro experiment was also designed to compare stationary and rotating electric fields. The optimization algorithm was applied to determine the location and stimulation parameters for both a stationary and rotating case such that the field inside a viewing window was a constant 1 V/cm.

Discussion: In this study we have shown the adaptability of our optimization methods to incorporate various models and parameter optimization. The use of multi-contact electrodes increases field shaping abilities to allow for custom optimizations for irregularly shaped tumour volumes. The experiment designed using our optimization methods can now be tested to determine the importance of field direction on cell death.