Neuro-Oncology 16:v213–v216, 2014.
doi:10.1093/neuonc/nou278

NEURO-ONCOLOGY

Abstracts

TM-16. INVESTIGATING THE MECHANISMS OF ACTION OF TUMOR TREATING FIELDS: A COMPUTATIONAL MODELING STUDY

Cornelia Wenger[1], Pedro Cavaleiro Miranda[1], Ricardo Salvador[1], and Peter J. Basser[2]; [1]Institute of Biophysics and Biomedical Engineering, Faculty of Science, University of Lisbon, Lisbon, Portugal; [2]Section on Tissue Biophysics and Biomimetics (STBB) Eunice Kennedy Shriver, NICHD, Bethesda, MD, USA

Tumor Treating Fields (TTFields) have been approved by the US FDA for the treatment of recurrent glioblastoma multiforme. This is a non-invasive and regional therapy that entails delivering low-intensity (1-3 V/cm) alternating electric fields of intermediate frequency (~ 200 kHz) to the brain via two perpendicular transducer arrays placed on the patient's scalp. Preclinical studies suggest the mechanism of action of TTFields is anti-mitotic, selectively affecting proliferating cells with no observed impact on quiescent cells. Effects such as prolonged and abnormal mitosis, as well as cell destruction in late cytokinesis, accompanied by rupture of the cell membrane and membrane blebbing are seen in vitro. These experiments also showed that the anti-mitotic effect is tuned to specific frequencies in different cancer cell lines. Additionally considering the specific morphology of proliferating cells, TTFields are thought to act by disrupting microtubule spindle arrangement and interfering with cytokinesis through the orientation of polar macromolecules in the direction of the impressed field. A computational model has been developed to test the influence of alternating fields on single cells during different stages of mitosis and cytokinesis, incorporating the distinct dielectric properties of cancerous glial cells. Simulations using a rounded cell during metaphase revealed that the distribution of the TTFields exhibits a transition region for which the intracellular electric field starts to significantly increase, possibly effecting microtubule spindle alignment. Furthermore models of different stages of cytokinesis predict a well-defined frequency at which dielectrophoretic forces induced in the hourglass shaped dividing cell reach a maximum. Depending on the length of the cleavage furrow this optimal frequency lies between 100 and 250 kHz, which is in agreement with experimentally observed frequencies at which TTFields are most effective in vitro. Additionally this modeling framework allows the study of effects of field strength, membrane properties and cell size.