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Alternating electric fields (TTF) for treating glioblastomas: a modelling study on efficacy

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Abstract:
Tumor Treating Fields (TTF) were recently approved by the US FDA for the treatment of recurrent glioblastoma multiforme (GBM). They are thought to act by disrupting spindle microtubule arrangement and interfering with cytokinesis through the orientation of polar macromolecules in the direction of impressed alternating electric fields. The magnitude and direction of the electric field in the tumor are crucial factors of treatment efficacy.
For this computational study we used a realistic head model previously constructed from MRI data to calculate the electric field distribution in the brain. MRIs with a voxel size of 1x1x1 mm3 were segmented into five different tissue types: scalp, skull, cerebrospinal fluid, gray matter, and white matter. Additionally a virtual lesion was included to simulate the presence of a tumor. Electrode arrays which are commonly used for TTF delivery were placed on the scalp, i.e., the placement, shape and size, current density and configuration of the electrode arrays mimicked as closely as possible a commercial device. The electric field was calculated using the finite element method. Our previous calculations predicted that the electric field magnitude exceeded 1 V/cm over large areas of the brain for the two electrode array configuration in use. Based upon in vitro experiments this value should be sufficiently high to arrest cell proliferation. Even so, a higher clinical efficacy of TTF was expected in view of the in-vitro results. Also, a large variability in the treatment response among patients has been observed in all TTF studies. We also observed that the electric field is not uniform as it is affected by the distribution of tissue types, the location and orientation of interfaces between them, and their individual electrical properties.
Differences in the electric field distribution produced by varying the position and size of the tumor and the placement of the electrodes might explain some of the observed variability in response among GBM patients. By calculating the detailed electric field distribution within the realistic head model for varying tumor properties and changing electrode setups, we believe to contribute to further advance our understanding of the mechanisms of action of TTF therapy. As a next step towards personalized TTF therapy, a significant efficacy development will likely depend on patient specific adaptation of the treatment plan.
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