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Validating skullremodeling surgery configuration to enhance TTFields for first recurrence glioblastoma with computational modeling

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Background: Skullremodeling surgery (SR-surgery) entails removing bone in the skull to enhance Tumor Treating Fields therapy in first recurrent glioblastoma. Our phase 1 trial (NCT02893137) tested various SR-surgery configurations (burrholes, skull thinning, and craniectomies) concluding it was safe. Our phase 2 investigator-initiated, randomized, comparative, multi-center trial (NCT04223999) testing efficacy of SR-surgery in combination with TTFields therapy was recently initiated. To standardize the SR-surgery for the phase 2 trial, a configuration with five burrholes was chosen. The burrholes are each 15mm in diameter and placed above the tumor cavity in a cross-diagonal pattern that fits in a 45×45 mm square. This configuration exposes a large area of the skull without forcing the patient to wear protective headgear. This computational study examines the effect of this SR-surgery configuration and the influence of array placement on the electric field strength.
Methods: A computation head model was created using the dataset "almi5" from SimNIBS in which we induced a 2 cm sphere-shaped tumor in the frontal lobe. The TTFields electrode arrays were rotated stepwise every 15° from the forehead to the occipital part corresponding to 0° and 180°respectively, resulting in 13 different positions. These simulations were performed with the SR-surgery configuration imposed on the head model and with an intact skull.
Results: 1) The SR-surgery configuration increased the electric field strength significantly in the peritumor and tumor tissue. 2) The SR-surgery configuration had minimal effect on the healthy white and grey matter tissue. 3) The highest electric field values in the peritumor and tumor tissue were seen when the edge of the arrays of both pairs was placed above or close to the burr-holes and the underlying tumor.
Conclusion: According to our simulation, the chosen SR-surgery configuration significantly increases the effect of TTFields in the peritumor and tumor tissue when electrode arrays are placed near the SR-surgery.
Keywords: recurrent glioblastoma; skullremodeling surgery; TTFields; phase 2 clinical trial; computational study