Electromagnetic stimulation applied to neuroprotective treatments in acute ischemic stroke

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Several in-vivo and in-vitro studies demonstrated that exposures to low frequency and low energy PEMFs (1-3.5 mT) induced an upregulation of adenosine receptors that play a key role in the protection against ischemic demage [1,2]. Such preclinical results, allowed to hypothesize that LF-PEMFs could be an alternative neuroprotective approach for ischemic stroke. To move towards demonstrating this hypothesis, an open label, one arm, dose-escalation, exploratory study was carried out, in order to evaluate the safety and tolerability of PEMFs in patients affected by acute ischemic stroke [3]. The study consisted of a 5-days intervention phase and a 12-months follow-up phase. Within 48 hours from the stroke onset, three enrolled patients underwent a 120 minutes PEMFs treatment, daily for 5 consecutive days. Clinical follow up lasted 12 months and brain MRI was performed before and one month after the treatment. Results from this study demonstrated the safety and tolerability of the PEMFs and opened the way to the on-going randomized, placebo-controlled, double-blind study [4] that foresees roughly 124 patients and will clarify whether PEMFs could represent a potential approach to neuroprotection. In this work we investigate the possibility to identify a dose-response curve when looking at the potential beneficial effects, the model adopted is semispecific [5]. The novelty of semi-specific approach is to represent the ischemic volume of each patient inserted in the correct position inside a standard human head model. This leads to a faster and reliable procedure suitable for the analysis of a large sample of patients. In our work, the 3D model of the ischemic lesion was obtained segmenting the MRI scans of each patient. The segmentation masks contained geometrical information of the lesion and were imported and processed in Sim4Life in order to generate the corresponding surface-based model. To build the semi-specific head model, the ischemic lesion was accurately placed inside the head of human body model Duke (ViP, v1), to match real position inside the patient. Geometry of the stimulator was reproduced in the simulation environment with a single turn rectangular coil with no thickness. The coil was placed close to the head, with the ischemic volume centered along the coil axis. In this way we obtained three different configurations corresponding to the three different patients herein studied. For each patient, models of the ischemia before (pre-) and one month after (post-) treatment were obtained. Pre-treatment ischemic model was included in the dosimetric study, as it simulates the lesion treated with the PEMFs stimulation. While post-treatment one was considered only during post processing to evaluate and quantify variations of the geometry, with the aim to obtain a correlation between intensity of the electromagnetic quantities (B and J) and changes in ischemic volume and geometry and thus building a dose response curve. Results showed a smaller area of post treatment regions with respect to pre-treatment ones when intensity of B field is greater than 1.5 mT, thus when the distance from the vertices of the coil is less than 25 mm. A more quantitative analysis was conducted evaluating the ratio between post-treatment and pre-treatment volumes as a function of $|\mathbf{B}|$ and $|\mathbf{J}|$ thresholds. Results showed an overall reduction of the ischemic volume in the three patients considered and that the higher is the intensity of exposure, the less is the percentage of remaining volume. Thus, with this methodology it's possible to build a dose-response curve for biophysical stimulations in a fast and reliable way. These results are the bases for the on-going randomized, double-blind, placebo effect study. Once the on-going study has clarified the effectiveness of the therapy, we expect to apply this same methodology to the given wider sample.

References

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