3rd URSI AT-AP-RASC, Gran Canaria, 29 May – 3 June 2022

Numerical dosimetry of the neuroprotective effect of PEMFs through a semi-specific modeling: comparison between an active and a placebo patient.

Micol Colella*(1), Sara Fontana(1), Noemi Dolciotti(1), Simona Salati(2), Stefania Setti(2), Ruggero Cadossi(2), Francesca Apollonio (1), and Micaela Liberti(1),
(1) Sapienza University of Rome, Italy; e-mail: micol.colella@uniroma1.it
(2) IGEA Biophysics Laboratory, Carpi, Italy;

The application of low intensity and low frequency pulsed electro-magnetic fields (LF-PEMFs) may represent a neuroprotective approach for the treatment of acute (i.e., within 48 hours from the insult) ischemic strokes [1]. Several in-vivo and in-vitro studies have suggested the interaction between the low frequency and low energy (1 mT - 3.5 mT) PEMFs with the A_{2a} and A_3 adenosine receptors, that are involved in the human body's anti-inflammatory and immune responses to events such as ischemic stroke [2]. Consequently, an open-label, study was carried out to evaluate PEMFs safety and tolerability on 6 patients with acute ischemic stroke [3]. A preliminary dosimetric analysis on the aforementioned study assessed a novel approach that employs semi-specific modeling of the patient's head [3]. Furthermore, with this new dosimetric methodology it was possible to build a dose-response curve in a fast and reliable mode, opening the way for the use of a similar approach to other "electroceutical" applications. Such previous results laid the groundwork for the I-NIC project: a multicentric, randomized, placebo-controlled, double-blind study, in which approximately 124 patients are under recruitment with the aim to clarify the effectiveness of the PEMFs therapy [4]. In this study, we present the dosimetric results on one active and one placebo patient recruited for the I-NIC study, with the aim to compare the different trend of the two dose-response curves. The methodological procedure to conduct the dosimetry and attain the dose-response curves followed the one assessed in [3] and is here briefly recalled. For each patient, the semi-specific model is built in the Sim4Life environment (ZTM Zurich MedTech AG) by precisely placing the 3D model of the ischemic lesion at the time of the insult (i.e. pre-) inside a detailed generic head model. The first one is obtained from each patient's MRI scans, whereas the second one is the Virtual Population 84-year-old male model Glenn (ViP, V.3). Finally, the stimulating coil is reproduced in the simulation environment with a single turn rectangular wire with no thickness, placed close to the head, with the ischemic volume centered along the coil axis. A 3D model of the ischemic lesion at the 45 days follow-up is obtained as well (i.e. post-) to correlate the B-field intensities with the evolution of the lesion. Only the pre-treatment ischemic model is considered in the dosimetric problem of PEMFs stimulation which was solved with the FEM quasi-static solver in Sim4Life. To quantify the ischemic volume progression after the PEMFs treatment, B-field values (B_{thr}) in a range from 1 mT to 2 mT were selected and the amount of pre-treatment volume (V_{pre}) exposed to a $B \geq B_{thr}$, as well as the corresponding post-treatment volume (V_{post}) were evaluated for each patient. The ratio V_{post}/V_{pre} was computed with respect to B_{thr} to attain the dose-response curve. Results showed that the volume ratio in one representative placebo patient ranges from 122% up to 150% at 2 mT. Conversely, in one representative active patient, the ratio is always under 100%, addressing a possible reduction of the post-treatment lesion, and its curve decreases for higher B_{thr} values. Such result may suggest the absence of a correlation between the volumetric evolution of the ischemia with the values of magnetic field in placebo patients, and the presence of a descending trend of the dose-response curve in the active patients. Once that the patients' recruitment will be completed, it will be possible to clarify the effectiveness of the PEMFs treatment.

1. Capone F, et al., Pulsed Electromagnetic Fields: A Novel Attractive Therapeutic Opportunity for Neuroprotection After Acute Cerebral Ischemia. Neuromodulation. 2021 Sep 4. doi: 10.1111/ner.13489. Epub ahead of print. PMID: 34480781..

2. V. Varani et al., "Adenosine receptors as a biological pathway for the anti-inflammatory and beneficial effects of low frequency low energy pulsed electromagnetic fields," *Mediat. Inflamm.*, 2017.

3. Colella et. al. Patient Semi-specific Computational Modeling of Electromagnetic Stimulation Applied to Neuroprotective Treatments in Acute Ischemic Stroke, Sci.Rep. 10, 2945 (2020).

4. ClinicalTrials.gov, Campus Bio-Medico National Library of Medicine (US), Identifier NCT02767778, Low-frequency Pulsed Electromagnetic Fields (ELF-MF) as Treatment for Acute Ischemic Stroke (I-NIC).