



August 12, 2018

Ronald Myers, PhD Staff Science Editor JoVE One Alewife Center, Suite 200 Cambridge, MA 02140 Tel: 617-945-9051

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RE: JoVE manuscript submission

Dear Dr. Myers:

We would like to submit our work, entitled "Tumor Treating Fields Therapy: Cell Biology, Electric Field Modeling, and Clinical Application" to JOVE Medicine Section for consideration for publication. This work has not been and is not being considered for publication elsewhere. We believe that our submission is well suited for the JoVE format. All authors have agreed submission of this manuscript.

As you may know already, Tumor Treating Fields are low frequency alternating electric fields that are approved by the FDA for the treatment of patients with newly diagnosed and recurrent glioblastomas. However, the anti-cancer mechanism behind this technology is not well understood. An earlier publication by Omar et al. in J. Vis. Exp. e51638 (2014) described the application of the transducer arrays performed using a plastic model of a human head and the first generation NovoTTF-100A System. In our manuscript, we provided a comprehensive discussion of several scientific domains that are relevant for our understanding of this technology, including electric field effects on cancer cell biology, physics of electromagnetism and MRI-guided computational modeling. We also included videos of blebbing of cells during mitosis. Most importantly, we will demonstrate in a patient head the application of the transducer arrays (including nuances that are pertinent to skull defects and surgical scars on the scalp), the operation of the second generation Optune System, and the identification of various pitfalls in the process that may result in complications.

We also would like to submit here a list of three potential reviewers. They are:

Dr. Rimas V. Lukas (Rimas.Lukas@nm.org) at Northwestern University Feinberg School of Medicine

Dr. Jay-Jiguang Zhu (Jay. Jiguang. Zhu@uth.tmc.edu) at the University of Texas Medical School at Houston

Dr. Suyash Mohan (<u>Suyash.Mohan@uphs.upenn.edu</u>) at the University of Pennsylvania School of Medicine

We look forward to hearing from you.

Sincerely yours,

Eric T Wong, MD Associate Professor of Neurology Harvard Medical School

Director, Brain Tumor Center & Neuro-Oncology Unit Beth Israel Deaconess Medical Center

Director, Neuro-Oncology Fellowship Program Beth Israel Deaconess Medical Center

Member, Neuro-Oncology Protocol Committee Dana Farber/Harvard Cancer Center