H-FIRE

Tumor chemoresistance and its proximity to critical structures make glioblastoma a prime theoretical candidate for nonthermal ablation with irreversible electroporation (IRE) and high-frequency IRE (H-FIRE). IRE and H-FIRE are treatment modalities that utilize pulsed electric fields to permeabilize the cell membrane. Once the electric field magnitude exceeds a tissue-specific lethal threshold, cell death occurs. Benefits of IRE and H-FIRE therapy include, but are not limited to, the elimination of cytotoxic effects, sharp delineation from treated tissue and spared tissue, a nonthermal mechanism of ablation, and sparing of nerves and major blood vessels. Preclinical studies have confirmed the safety and efficacy of IRE and H-FIRE within their experimental scope [1].

The lethal electric field (LEF) thresholds for three typical cerebral cells, including a malignant glioblastoma cell line and two cell lines from the healthy blood-brain barrier (BBB), treated by H-FIRE or IRE protocols were investigated in an in vitro 3D cell model. A conventional IRE protocol and three novel H-FIRE protocols (1-3-1, 0.5-1-0.5, and 1-1-1) were used to treat the cerebral cells in both 3D single-cell and two-cell models. The electrical conductivity of the 3D cell model under different electric field strengths were characterized with the measurement of electrochemical impedance spectroscopy. Based on this measurement, a numerical electrothermal model of electroporation was built for the determination of the LEF threshold with different protocols and temperature monitoring. Cell viability was assessed by fluorescence staining 6 hours after the treatment. The result showed no thermal lethal effect on cells when these protocols were used. The LEF threshold for glioblastoma cells was significantly lower than that of the healthy BBB cells. These results suggest the possibility of selective ablation of human cerebral glioblastoma by IRE and H-FIRE treatments with no injury or reversible injury to healthy cells, and the potential use of IRE for transient disruption of the BBB to allow chemotherapy to reach the tumor [2].

1)
Lorenzo MF, Arena CB, Davalos RV. Maximizing Local Access to Therapeutic Deliveries in Glioblastoma. Part III: Irreversible Electroporation and High-Frequency Irreversible Electroporation for the Eradication of Glioblastoma. In: De Vleeschouwer S, editor. Glioblastoma [Internet]. Brisbane (AU): Codon Publications; 2017 Sep 27. Chapter 19. PMID: 29251858.

2)
Shu T, Ding L, Fang Z, Shuangquan Y, Chen L, Moser M, Zhang WJC, Qin Z, Zhang B. Lethal Electric Field Thresholds for Cerebral Cells with IRE and H-FIRE Protocols: An In Vitro 3D Cell Model Study. J Biomech Eng. 2022 Apr 21. doi: 10.1115/1.4054381. Epub ahead of print. PMID: 35445240.