

PRINCIPLES OF ELECTRIC FIELD APPLICATION IN ELECTROCHEMOTHERAPY

Damijan Miklavcic

University of Ljubljana, Faculty of Electrical Engineering, Trzaska cesta 25, SI-1000 Ljubljana, Slovenia

E-mail: damijan.miklavcic@fe.uni-lj.si

Electrochemotherapy is a combined treatment using electroporation to enhance transmembrane transport of cytotoxic drugs, which have intracellular target, and for which plasma membrane represents a barrier. It is therefore important that two conditions be met: i) the drug is present in the tumor in sufficient concentration, and ii) the whole tumor mass is exposed to sufficiently high electric field (1, 2). The drug is injected either systemically, e.g. intravenously or intratumorally, while the exposure of cells in the tumor to electric is achieved by delivering electric pulses by selecting adequate electrodes and positioning them correctly with respect to the tumor (2, 3).

The membrane of the cell when exposed to sufficiently high electric field will undergo electroporation that will transiently increase its permeability thus allowing increased inflow of molecules that otherwise lack or have hindered transmembrane transport (4). Electric field distribution depends on the geometry and position of the electrodes relative to the tumor (5, 6). For treating metastasis/tumors in the skin selecting appropriate choice of the electrode and placing it seem not to be difficult (1), however when treating deep seated tumors and/or large tumors pretreatment planning (similar to radiotherapy) and image guidance assistance is necessary (7-8). Validated numerical models are essential in achieving best results with electrochemotherapy and developing new approaches (9).

Acknowledgements

This work was in part supported by Slovenian Research agency and

conducted in the scope of LEA EBAM.

References

1. Miklavčič D, Čorović S, Pucihar G, Pavšelj N. Importance of tumour coverage by sufficiently high local electric field for effective electrochemotherapy. *Eur J Cancer* 2006;Suppl 4: 45-51.
2. Miklavčič D, Mali B, Kos B, Heller R, Serša G. Electrochemotherapy: from the drawing board into medical practice. *Biomed Eng Online* 2004;13: 29.
3. Miklavčič D, Snoj M, Županič A, Kos B, Čemažar M, Kropivnik M, Bračko M, Pečnik T, Gadžijev E, Serša G. Towards treatment planning and treatment of deep-seated solid tumors by electrochemotherapy. *Biomed Eng Online* 2010;9: 10.
4. Rems L, Miklavčič D. Tutorial: Electroporation of cells in complex materials and tissue. *J Appl Phys* 2016;119: 201101.
5. Kranjc M, Markelc B, Bajd F, Čemažar M, Serša I, Blagus T, Miklavčič D. In situ monitoring of electric field distribution in mouse tumor during electroporation. *Radiology* 2015;274: 115-123.
6. Miklavčič D, Beravs K, Šemrov D, Čemažar M, Demšar F, Serša G. The importance of electric field distribution for effective *in vivo* electroporation of tissues. *Biophys J* 1998;74: 2152-2158.
7. Pavliha D, Kos B, Županič A, Marčan M, Serša G, Miklavčič D. Patient-specific treatment planning of electrochemotherapy: Procedure design and possible pitfalls. *Bioelectrochemistry* 2012;87: 265-273.
8. Marčan M, Pavliha D, Kos B, Forjanič T, Miklavčič D. Web-based tool for visualization of electric field distribution in deep-seated body structures and planning of

electroporation-based treatments. *Biomed Eng Online* 2015;14(Suppl. 3): S4.

9. Cindrič H, Kos B, Tedesco G, Cadossi M, Gasbarrini A, Miklavčič D. Electrochemotherapy of spinal metastases using transpedicular approach – A numerical feasibility study. *Technol Cancer Res Treat* 2018;17: 1-13.