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Treatment planning for electrochemotherapy and irreversible electroporation: optimization of voltage and electrode position

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Duration of the experiments: 90 min
Max. number of participants: 6
Location: Laboratory of Biocybernetics
Level: Basic

PREREQUISITES

No specific knowledge is required for this laboratory exercise.

The aim of this laboratory practice is to learn how to use numerical modelling techniques to achieve suitable electric field distribution for successful electroporation-based treatments.

THEORETICAL BACKGROUND

Electrochemotherapy (ECT) is an efficient local treatment of cutaneous and subcutaneous tumors, which combines the delivery of nonpermeant, cytotoxic chemotherapeutics (e.g. bleomycin, cisplatin) and short high-voltage electric pulses [1, 2]. The pulses induce electric fields inside the tissue, thereby increasing cell membrane permeability in tissue (electropermeabilization) to otherwise nonpermeant chemotherapeutics. ECT requires the electric field inside the tumor to be higher than the threshold value needed for reversible electroporation (E_{rev}) while irreversible electroporation (E_{irrev}) in nearby critical structures should be limited [3]. For irreversible electroporation (IRE), the electric field in the entire target volume needs to be above the irreversible electroporation threshold [4]. It is not necessary to electroporate the entire target volume by a single pulse or pulse sequence - sometimes a combination of several pulse sequences or a combination of different electrodes is required [5].

EXPERIMENT

A finite element based numerical modeling program package COMSOL Multiphysics version 5.4 (COMSOL AB, Stockholm, Sweden) will be used to optimize voltage between the electrodes and position of the electrodes on a simple 3D model of a spherical subcutaneous tumor and surrounding tissue (Figure 1a). Electrode positions and the applied voltage should be chosen, so that the following objectives are fulfilled:

- For electrochemotherapy: the tumor is permeabilized ($E_{tumor} > E_{rev} = 400\ V/cm$),
- For irreversible electroporation: the tumor is permeabilized above the irreversible threshold ($E_{tumor} > E_{irrev} = 600\ V/cm$),
- the damage to healthy tissue is kept to a minimum.

We will calculate the electric field distribution in the model after each change of the electrode placement or voltage. The final goal of this exercise is to achieve 100 % $E_{tumor} > E_{rev}$ (or 100 % $E_{tumor} > E_{irr}$ when planning for IRE) and minimize E_{irr} in healthy tissue.

Protocol:

1.) Build the 3-d model by following the lecturer's instructions and take into account your tissue-specific electric properties.
2.) Solve the model and evaluate the initial solution.
3.) In the case that the initial solution is inappropriate (see e.g., Figure 1b), try to improve on the solution by changing electrode positions and voltage between the electrodes. Calculate the electric field distribution in the model after changing the electrode positions or voltage and then determine the coverage of tumor tissue with $E_{tumor} > (E_{rev}$ or $E_{irrev})$ and determine damage to healthy tissue due to irreversible electroporation.
4.) Repeat the process, until the quality of your solution reaches the set goals. Compare the results with others who have used different tissue properties
5.) . Use a parametric study to find the lowest voltage which achieves the objective for the selected electrode geometry.
6.) Change conductivity model to electric field-dependent conductivity σ=σ(**E**) [6].
7.) Repeat the parametric study and compare with previous results.

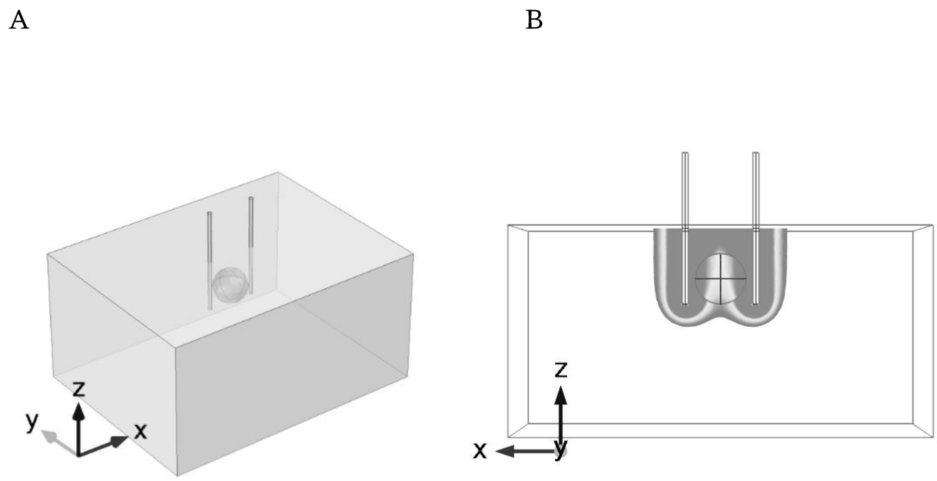

Figure 1: (A) Simple 3D model of tumor and needle electrodes in healthy tissue; (B) electric field over reversible threshold inside the healthy tissue while the tumor is not electroporated.

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NOTES & RESULTS