Treatment planning for electrochemotherapy and irreversible electroporation: optimization of voltage and electrode position C1

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Duration of the experiments: 60 min
Max. number of participants: 4
Location: Laboratory of Biocybernetics
Level: Basic

PREREQUISITES

No specific knowledge is required for this laboratory exercise.

THEORETICAL BACKGROUND

Electrochemotherapy 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. The pulses induce electric fields inside the tissue, thereby increasing cell membrane permeability in tissue (electropermeabilization) to otherwise nonpermeant chemotherapeutics. Electrochemotherapy requires the electric field inside the tumor to be higher than the threshold value needed for reversible electropermabilization (E_{rev}) and lower than the threshold for irreversible electropermeabilization (E_{irrev}) in healthy tissue. Treatment planning methods should guarantee that the whole tumor is electropermeabilized, while the damage to healthy tissue is kept to a minimum. It is not necessary that the whole tumor is electropermeabilized by one pulse or pulse sequence - sometimes a combination of several pulse sequences or a combination of different electrodes is required.

The aim of this laboratory practice is to learn how to use optimization techniques to achieve suitable electric field distribution for electrochemotherapy experimental planning and treatment planning.

EXPERIMENT

A finite element based numerical modeling program package COMSOL Multiphysics version 3.5a (COMSOL AB, Stockholm, Sweden) will be used to optimize voltage between the electrodes and position of the electrodes on a simple 2D model of a spheroid 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 ($E_{tumor} > E_{irrev} = 900$ V/cm),
- the damage to healthy tissue ($E_{healthy} > E_{irrev} = 900$ V/cm) 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 % $E_{tumor} > E_{rev}$ and less than 0.1

% $E_{healthy} > E_{irrev}$. After we have finished the treatment planning, we will compare the obtained results to the results of a treatment planning algorithm, which uses the same objective functions and is based on the genetic algorithm optimization method.
Finally, we will use the non-linear model with electric conductivity dependent on the local electric field distribution to investigate the influence of conductivity changes on the treatment plan. This is implemented by changing the electric conductivity in areas, where electric field exceeds the electroporation threshold in several discrete steps.

Protocol: Build the 2-d model by following the lecturer's instructions and take into account your tissue-specific electric properties. Solve the model and evaluate the initial solution. In case, 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. Repeat the process, until the quality of your solution reaches the set goals. Compare the results with others, who have used different tissue properties. Load the non-linear model file provided and compare results with the linear model, then adjust the voltage for the non-linear model until you achieve comparable results to the linear model.

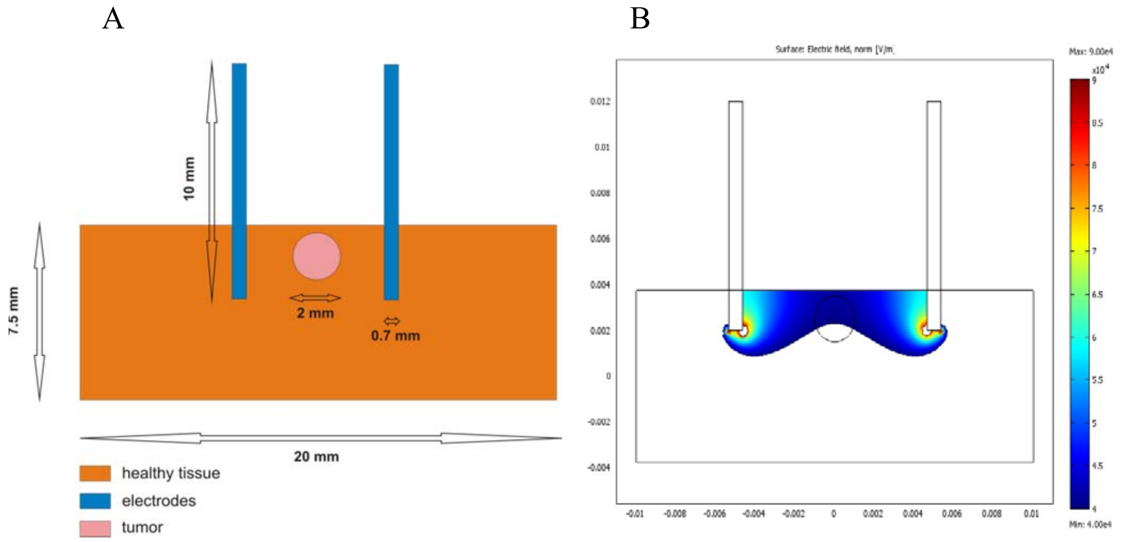

Figure 1: (A) Simple 2D model of tumor and needle electrodes in healthy tissue; (B) electric field over reversible threshold inside the healthy tissue and the tumor.

FURTHER READING:

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NOTES & RESULTS

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