# Electrochemotherapy treatment planning: optimization of voltage and electrode position C1

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Duration: 45 min
Max. no. of participants: 4
Location: Laboratory of Biocybernetics
Level: Basic

## PREREQUISITES

No specific knowledge is required.

## 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 (electropermeabilization) to otherwise nonpermeant chemotherapeutics. Efficient electrochemotherapy requires the electric field inside the tumor to be higher than the threshold value needed for reversible electropermabilization ($E_{rev}$), while it has to lower than the threshold for irreversible electropermeabilization ($E_{irrev}$) in healthy tissue. Electrochemotherapy 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 distributions in electrochemotherapy experimental planning and treatment planning.

## EXPERIMENT

A finite element based numerical modeling program package COMSOL Multiphysics (COMSOL AB, Stockholm, Sweden) will be used to optimize voltage between the electrodes and position of the electrodes on a prepared simple 2D model of a spheroid subcutaneous tumor and surrounding tissue (Figure 1a). Electrode positions and voltage should be chosen, so that the tumor is permeabilized ($E_{tumor} > E_{rev} = 400\ V/cm$) and the damage to healthy tissue ($E_{healthy} > E_{irrev} = 900\ V/cm$) is kept to a minimum. Two objective functions have already been defined: percentage of reversibly electropermabilized tumor volume ($\%E_{tumor} > E_{rev}$) and percentage of irreversibly electropermeabilized healthy tissue ($\%\ E_{healthy} > E_{irrev}$). Our goal is to achieve 100 % $E_{tumor} > E_{rev}$ and less than 0.05 % $E_{healthy} > E_{irrev}$. 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.

**Protocol:** First you take a look at the provided solution, which is not suitable , as it causes a lot of healthy tissue damage while the whole tumor is actually not permeabilized (Figure 1b). Then you try to improve on the solution by changing electrode positions and voltage between the electrodes. You calculate the electric field distribution in the model after changing the electrode positions or voltage and then calculate both objective functions. You repeat the process, until the quality of your solution reaches the set goals.

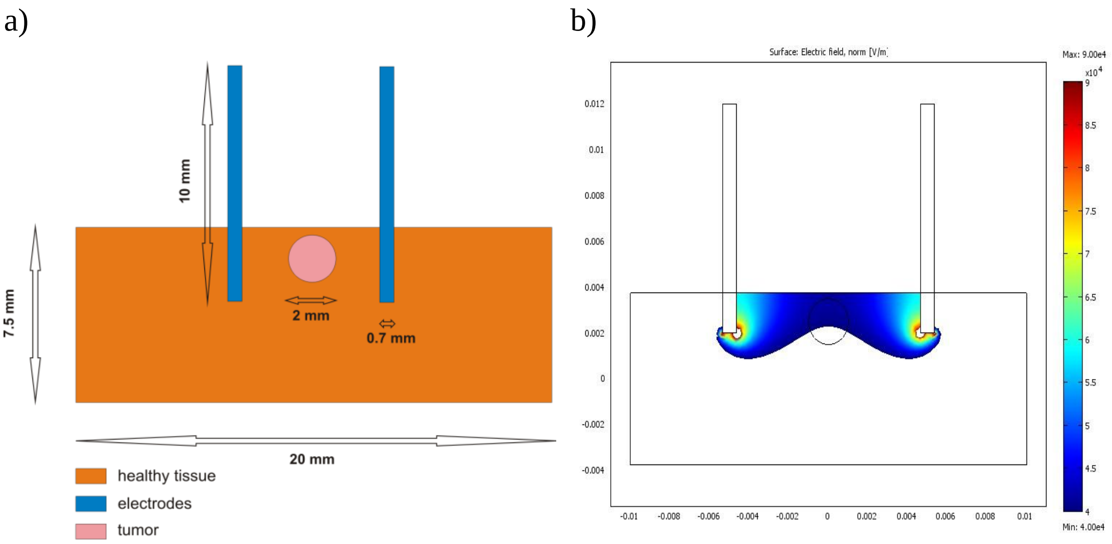


***Figure 1:*** a) Simple 2D model of tumor and needle electrodes in healthy tissue; b) electric field over reversible threshold inside the healthy tissue and the tumor.

## FURTHER READING


1. Miklavčič D, Čorović S, Pucihar G, Pavšelj N. Importance of tumor coverage by sufficiently high local electric field for effective electrochemotherapy. *EJC Supplements*, 4: 45-51, 2006.
2. Čorović S, Županič A, Miklavčič D. Numerical modeling and optimization of electric field distribution in subcutaneous tumor treated with electrochemotherapy using needle electrodes. *IEEE Trans. Plasma Sci.*, 36: 1665-1672, 2008.
3. Županič A, Čorović S, Miklavčič D. Optimization of electrode position and electric pulse amplitude in electrochemotherapy. *Radiol. Oncol.*, 42: 93-101, 2008.
4. Edd JF, Davalos RV. Mathematical modeling of irreversible electroporation for treatment planning, *Technol. Cancer Res. Treat.*, 6: 275-286, 2007.


## NOTES & RESULTS

| Distance between electrodes [mm] | Electrode depth [mm] | Voltage [V] | $E_{tumor}>E_{reversible}$ [%] | $E_{healthy}>E_{irreversible}$ [%] |
|---|---|---|---|---|
| 10 | 1.75 | 450 | 68.7 | 0.16 |
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