Tumor Electric Field Distribution Studies using Various Electrode Configurations

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***Abstract*—Electrochemotherapy, the process of applying electric pulses to facilitate drug transport into cells, is an emerging method in molecular medicine and a promising technique for cancer treatment. Pulse parameters and electrode geometry are dominant factors in this process. The goal of this paper is to demonstrate effects of various electrode configurations and pulse characteristics on the homogeneity of electric field distribution of tumor tissues and develop the best suited electrode model for the treatment of large tumors. Maxwell V13, software by Ansoft Corporation is used for 2-dimensional and 3-dimensional modeling of tissues and electrodes. External parallel plate electrodes and internal needle electrodes are compared and analyzed. A multi-needle electrode array model is developed for large and deep tumors. Real life tissue size is modeled and electrode dimensions are taken from published literature. A constant field of 1200V/cm is applied and electric field and energy distribution is obtained for various electrode configurations. Results show that internal electrodes result in an extra 10% reduction in field and are more effective and multi-needle electrode arrays are effective for large tumors. These results will help improve electrochemotherapy techniques for clinical cancer applications that are not receptive to conventional therapies.**

I. INTRODUCTION

Cancer is a group of diseases characterized by uncontrollable growth and spread of abnormal cells and when the spread is not controlled, it can lead to death. According to the American Cancer Society there were approximately 1.5 million cases of cancer estimated in 2010 in the US [1], a third of which resulted in death. Many powerful and promising drugs that have been developed to treat cancer have not been effective because of low efficiency, safety and side effects [2]. This necessitates novel alternate cancer treatment methods. Electroporation is a technique by which high intensity, short duration pulses are applied to temporarily open up pores in the membrane of cells to allow transport of therapeutic materials including drugs, antibodies and genes [3-5]. This technique was first investigated in the late eighties and early nineties where high amplitude exponential and square pulses were used to improve the efficacy of *bleomycin*, an antitumor

drug [6-8]. Since then there is a lot of work published on electrode configurations, dimensions and voltage values suitable for electroporation [9]. Clinical trials on a number of patients have shown that the treatment is highly efficient and has a lot of advantages over traditional therapies [10].

In order to electroporate cells and tissues, it is important to understand the electric field distribution that occurs within body tissue. Finite element analysis is an efficient tool that can be used to study electric, magnetic field distributions and stresses in materials when subjected to an external stimulus. Previous studies have indicated differences in electric field magnitude and homogeneity for parallel plate and needle electrodes for specific external voltages applied [11]. The present work aims at creating 2 and 3-dimensional finite element models and studying the effect of applied voltages in tissues for a number of electrode configurations, such as parallel plane electrodes, and two and multi-needle electrode arrays. These various electrode configurations are compared for different tissue models and electric field distributions are analyzed.

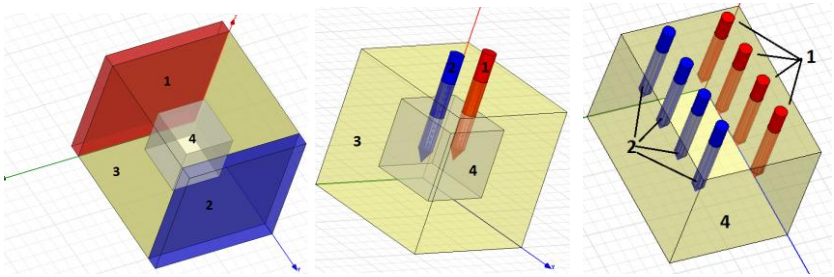
II. SIMULATION

A. Software

Maxwell 13, software by Ansoft Corporation [12] which utilizes finite element analysis was found to be suitable for our research and is used to model tissues and electrodes and run simulations.

B. Model

A three dimensional electrostatic model that replicates real life situations, for example, a tissue with a tumor, tumor alone, etc. are created, along with electrodes. Fig. 1 shows the various models developed in this research. These models represent a tumor [4] within a normal tissue [3] with a positive [1] and ground [2] electrode for application of external voltage. The electrodes used are parallel plate (Fig. 1a); a pair of needle electrodes (Fig. 1b) and multi-needle electrode array (8 needle electrodes - Fig. 1c). Fig. 1c represents a large tumor with multi-needle electrodes, without the normal tissue around it, as in cases 1a and b.



(a) (b) (c)

Fig. 1. 3D model of positive (1) and negative (2) electrodes, tissue (3) and tumor(4). 1(a) is a model set up with parallel plate electrodes, 1(b) is a model set up with needle electrodes and 1(c) is a set up with multi-electrode array for larger tumors.

The needle electrodes have a 4 mm gap between them and there is a 2 mm gap between each other in the same row, in the case of multi-needle electrode array. A voltage of 480V is applied to obtain 1200V/cm [4] as in human clinical trails is applied at the positive electrode and the negative electrode is grounded.

Parameters of electrodes, tissue and tumor are given in Table 1 and dimensions of model components are listed in Table 2. Dimensions are estimated close to real values and properties of tissue and tumor are as per from previous literature [13, 14].

TABLE 1: MODEL PARAMETERS

No.	Name	Material	Properties	Source
1	Positive Electrode	Perfect conductor	-	480V
2	Negative Electrode	Perfect Conductor	-	0V
3	Tissue	Tissue	$E_r = 200$, $\sigma = 0.4$ S/m	-
4	Tumor	Tumor	$E_r = 1000$, $\sigma = 2$	-

TABLE 2: DIMENSIONS OF MODEL COMPONENTS

Model Component	Length *Breadth (mm*mm)	Height (mm)	Diameter (mm)
Parallel plate electrode	10 * 1	10	-
Needle electrode	-	7	1
Tissue	10*10	10	-
Tumor	5*5	5	-
Large Tumor	14*10	10	-

III. RESULTS AND DISCUSSION

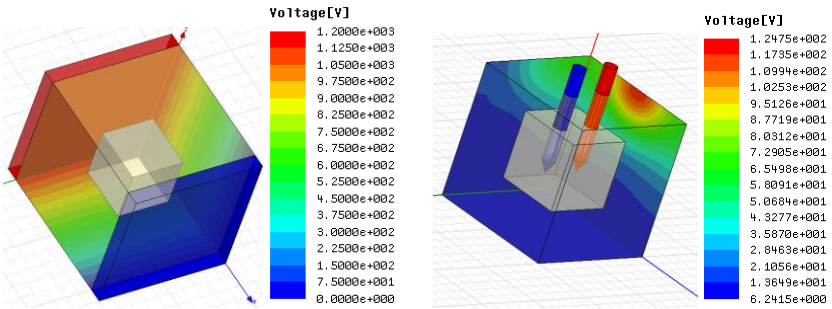
A. Parallel Plate Electrodes versus Needle Electrodes

Figs. 2-4 show the voltage, electric field and energy distribution of parallel plate and needle electrodes respectively. Fig. 2 shows the voltage distribution of the tumor using parallel pate (a) and 2 needle electrodes geometry (b). Parallel plates are placed externally, on two sides of the normal tissue and needle electrodes are inserted internally, within the tumor in the tissue. The voltage is evenly distributed between the positive and negative electrodes in case of parallel plate electrodes where as needle electrodes result in uneven distribution of voltage in the entire tissue area. The voltage is maximum in the region near the electrodes and reduces drastically as the distance from electrodes increase. Hence the position where needles are placed is important when inserted inside the tumor and tissue area.

Fig. 3 shows a comparison of the electric field for the above geometry, but using both tumor within tissue model and tissue alone model to illustrate the difference between the nomral and malignant tissues. The electric field inside the tumor and normal tissues is homogenous in the case of parallel plate electrode configuration and is highly non-uniform for needle electrode configuration. The magnitude of electric field is one order (10 times) less for needle electrodes than parallel plate electrodes. This could be due to the fact that the electrodes are placed directly on the tumor tissues which has different electric properties than the normal tissue [15]. Previous studies at an Ireland hospital [11]

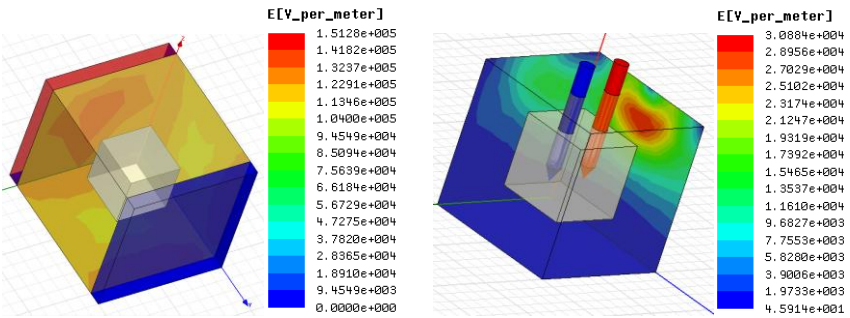
on 2-dimensional models also show similar electric field trends as shown in Fig 5. The electric field in the region around needles was found to be 25% less than that of parallel plate electrodes inside a tumor. This correlates very well with our research and shows that directly electroporating tumor tissues results in a different phenomenon than applying parallel plates over the surrounding tissue and skin. Also, on comparing tumor tissue (Figs 3a, b) with a normal tissue (Figs. 3c, d), it can be seen that the electric field is lower when there is a tumor in the tissue than a normal real life situation, which is a normal tissue. With parallel plate electrodes there is a 5% reduction in electric field where as in case of needle electrodes there is 15% reduction. This shows that needle electrodes inserted into the tumor region would be more effective. This difference exists because of the change in electrical properties (resistivity, conductivity, permitivity) of the tissue when affected with cancer.

The energy distribution (Fig. 4) reveals that energy is 2 orders (100 times) of magnitude higher in the tumor than in the surrounding tissue in the case of needle electrodes compared to parallel plate configuration, since the electric field is lower in the tumor than on the normal tissue. The energy is non-homogenous in the case of needle electrodes where as it is uniform in case of parallel plate electrodes.

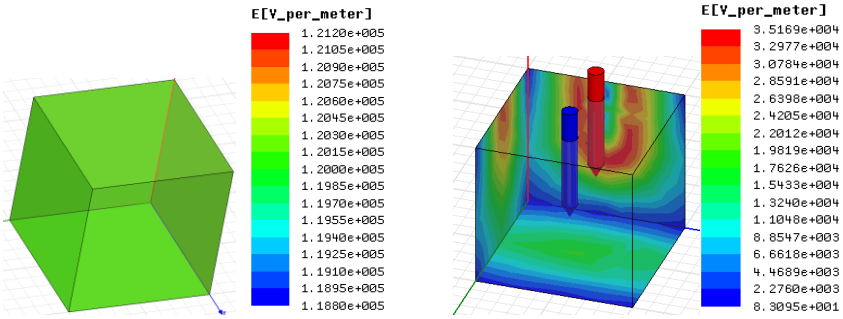


(a) (b)

Fig. 2. Voltage distribution of tumor within tissue with parallel plate (a) and needle (b) electrodes

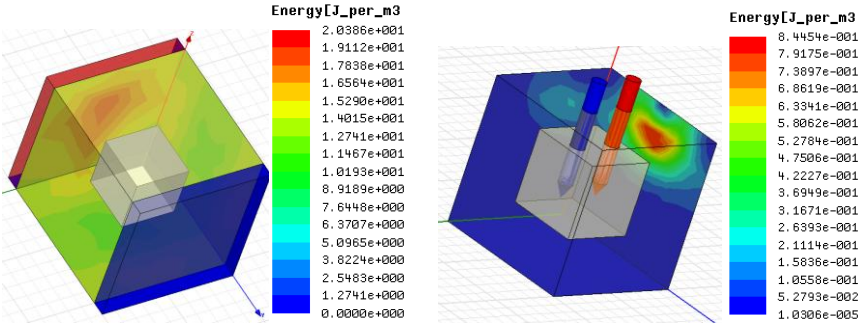


(a) (b)



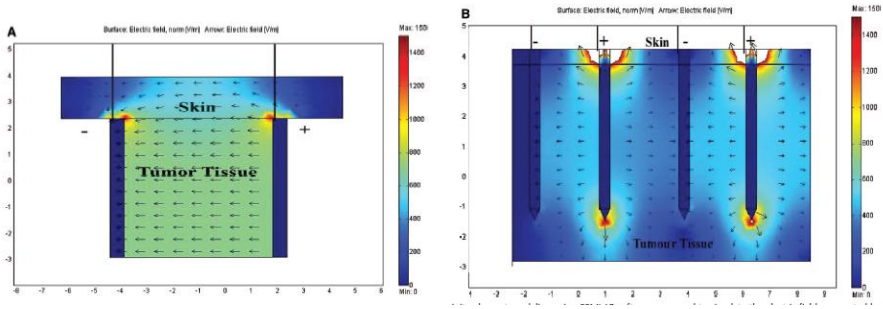
(c) (d)

Fig. 3. Electric Field Distribution of tumor within tissue with parallel plate (a) and needle (b) electrodes and normal tissue with parallel plate (c) and needle (d) electrodes



(a) (b)

Fig. 4. Energy Distribution of tumor within tissue with parallel plate (a) and needle (b) electrodes



(a) (b)

Fig. 5. Electric Field Intensityof tumor tissue with parallel plate (a) and needle (b) electrodes [11]

B. Multi-needle Electrode Array

Tumors can vary in size depending on the type of the tumor and the stage of the cancer. Clinical trials on patients have revealed that tumors can be less than 3mm or even greater than 30mm in size [10]. For large tumors, if a single pair of needle electrodes with 4mm gap is used, the tumors would have to be treated multiple times at different locations in

order to cover the entire area. This would not only be more time-consuming, but the drug effect may also reduce (the pulses have to be applied within a few minutes of the drug injection) and also the patients have to be sedated for longer durations. Thus, it is desirable to have a large multi-needle electrode array which would produce the same effect in a larger area with a fewer attempts than it is being practiced currently. Another serendipity of using large needle array is the advantange that the electric field in this case is stronger and more uniform with multiple needle electrodes than a single pair of electrodes.

Fig. 6 shows the 2D electric field distribution in the tumor using multi-needle electrodes, with arrays of 4 (a), 8 (b), and 16 electrodes (c). The electric field is evenly distributed between the positve and negative column of electrodes in case of the 4 electrode array and it is the same in the case of 8 and 16 electrodes also. The magnitude of electric field is $1.1*10^5$ V/m (1100V/cm, close to the desired value of 1200V/cm) in the tumor region between electrodes in case of 4 needle electrodes. Similar values are obtained for the 8 and16 electrode arrays too.

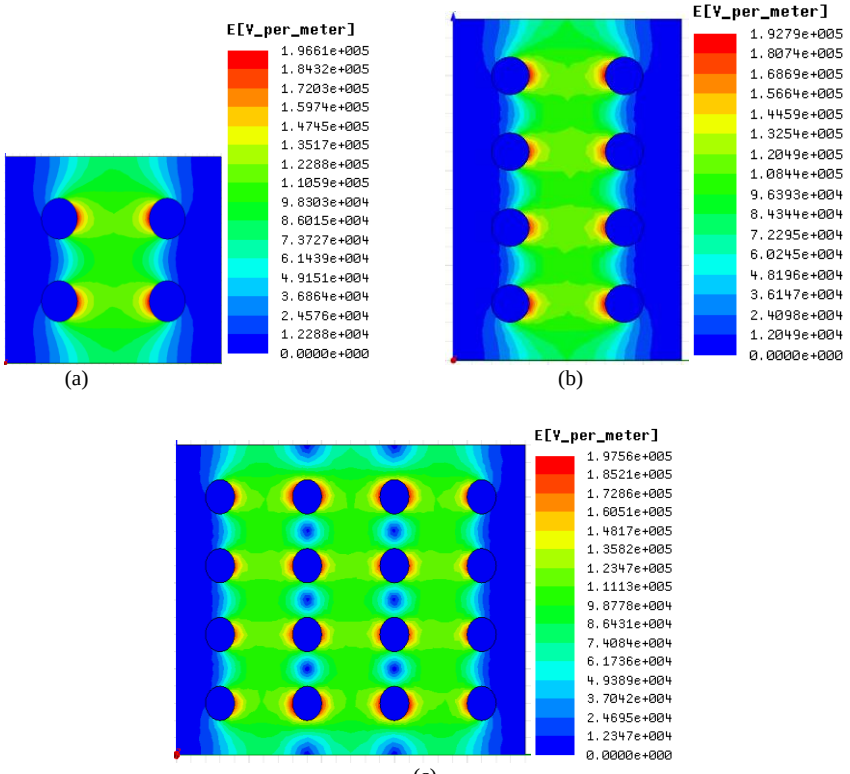
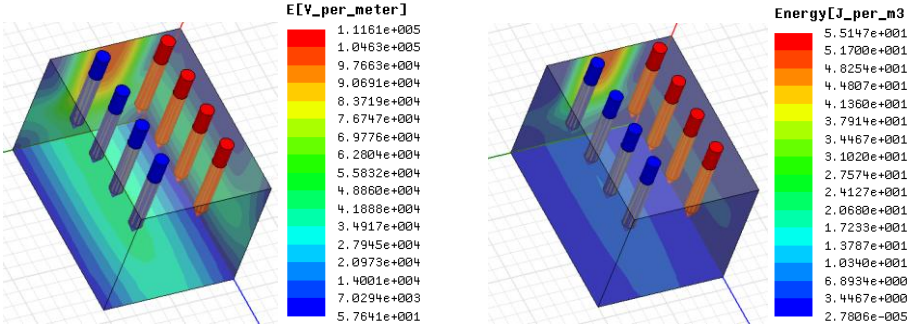


Fig. 6. 2D E-Field Distribution of 4-needle electrode array (a) 8-needle electrode array (b) and 16-needle electrode array (c)

Fig. 7 shows the 3D distribution of the electric field using 8 multi-needle electrode array. The electric field distribution in the 3D model with 8 needle electrode array (Fig. 7a) is similar to the values obtained n 2D. The energy distrution (Fig. 7b) shows a maximum magnitude of 55 J/m^3 of energy in the region between the electrodes. Hence depending on the size of the tumor, multiple electrodes can be arranged side-by-side to form a larger electrode array and produce a uniform field in a large tumor area.



(a) (b)

Fig. 7. 3D E-Field Distribution (a) and Energy Distribution (b) of 8-needle electrode array

IV. Conclusions

The electric field distribution for a tumor model within normal tissues is studied using parallel plate and needle electrodes. Needle electrodes can be inserted right into the region where a tumor is present (intra-tumorally) so that a high field is produced only in the region around it, keeping the surrounding tissue unaffected. Needle electrodes result in 10% increased reduction of electric field which makes it more beneficial than parallel plate electrodes. A pair of needle electrodes results in a highly non-uniform concentrated electric field. Using an array of needle electrodes makes the field uniform and much stronger for large tumor areas. Studies on 4-, 8- and 16-electrode arrays show an even distribution of electric field which is desired. The electric field was found to be a uniform $1.1*10^5$ V/m between the electrodes for all three array configurations. Electroporation is an effective way to target tumor tissues and get rid of them while normal tissues are still unaffected. Modeling and simulation studies show favorable electric field distributions that can be used in the development of electrodes and setting pulse parameters for practical treatment. These results will help improve electrochemotherapy techniques to treat tumors that are not receptive to conventional therapies.

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