Computational Analysis of Electrical Stimulation Devices to Promote Wound Healing

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ABSTRACT

Electric stimulation (ES) therapy involves the use of low-energy, static, or time-varying electric and magnetic fields and associated electrical currents to stimulate a therapeutic physiological response that accelerates wound healing in human tissue. In this presentation, we discuss this therapy and demonstrate the use of 3D computational models to predict the electric field and current density patterns induced in human tissue by voltage activated electrodes on the skin surface. The analysis takes into account electrode configurations, transient voltage waveforms and all relevant tissues including their frequency dependent electrical properties. The models provide insight into ES therapy and enable the rational design of novel ES devices.

Keywords: Wound healing, electrical simulation therapy, capacitively coupled electrical stimulation wound healing, medical devices, human tissue model, modeling of electrical stimulation wound healing.

1 INTRODUCTION

The treatment of wounds is a fundamental and major challenge in health care. Chronic wounds (e.g. diabetic) are particularly problematic and pervasive, afflicting approximately 6 million patients in the US alone at an annual cost of 20-25 billion dollars. While various methods and have been developed over many decades to treat chronic wounds, a need exists for portable and noninvasive devices that will accelerate wound healing while providing enhanced patient mobility for improved quality of life. Electrical stimulation (ES) methods are among the most promising and versatile therapies for promoting wound healing in a point-of-care format [1]. In this presentation we use mutiphysics computational models to investigate a well-established and effective ES therapy. A simplified structure of human tissue layers is shown in Figure 2. The thickness of these layers varies from person to person. Undamaged skin has an electrical potential of 30-100mV between its upper most layer, the stratum corneum, and the rest of the epidermis. When the tissue is injured, the stratum corneum physically breaks and this potential is disrupted [2]. The ES treatment strategy involves the use of voltage-pulsed capacitively coupled (CC) electrodes placed on the surface of the body, around or on the wound to drive current through it as shown in **Fig. 1** [3]. In this therapy an electric field is generated within tissue that stimulates a multitude of biological processes that collectively promote wound healing. In this presentation we discuss ES therapy and demonstrate 3D computational models that predict ES performance metrics including the electromagnetic field induced within human tissue taking into account different tissue layers and their individual frequency-dependent electrical properties [4]. These models are implemented using the COMSOL Multiphysics 5.2a program (www.comsol.com) and enable the rational design of novel ES wound healing technology.

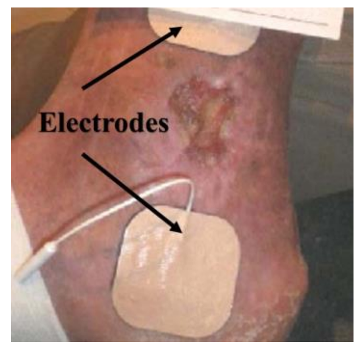

Fig. 1: Capacitively coupled ES wound healing therapy.

2 WOUND HEALING

The different layers of tissue just beneath the skin are shown in Figure 2. The thickness of these layers vary from person to person, and throughout the body on an indiviual. Many healthy tissues produce electrical potentials via the directional transport of ions. Injured tissues also generate significant electric fields and associated currents, which are required for a healthy healing process. One can accelerate the healing process by assisting this dynamic electrical activity. The wound healing process, which occurs in three stages: (a) inflammatory phase (2-5 days), (b) proliferative phase (3- 20 days), and (c) remodeling phase (9 days – 18 months). ES therapy stimulates many beneficial physiological effects during each stage of healing. In the inflammatory phase, ES therapy acts to increase the blood flow, reduce edema and promote phagocytosis. In the

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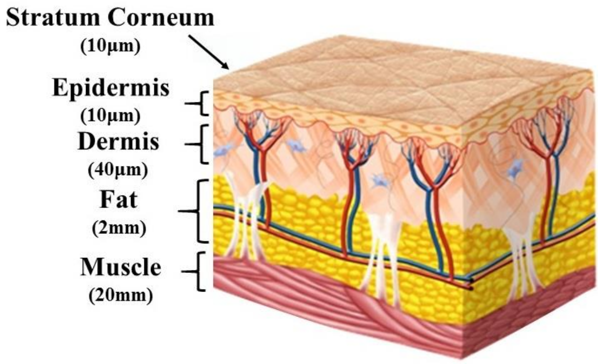

Fig. 2: Tissue layers considered in ES therapy modelling.

proliferative phase, it causes protein synthesis and stimulates fibroblast and wound contraction. In the remodeling phase, keratinocytes are stimulated for reproduction and migration. A wide range of cell types, i.e. lymphocytes [5], fibroblasts [6-8], macrophages [9], keratinocytes[10] respond to ES during the healing process [1, 11, 12].

ES therapies span a wide range of electrode configurations and operating parameters, e.g. voltage waveforms and current levels etc. In some therapies certain electrodes are placed on healthy tissue and others over the wound. In other therapies, all electrodes are placed on healthy tissue surrounding the wound. The latter approach eliminates issues arising from electrodes being in direct contact with the wound. In terms of an electrical response, the upper most layer of the skin, i.e. (stratum corneum ~10 µm thick) offers the most electrical resistance. The equivalent impedance of tissue can be characterized using standard patch electrodes, measuring the current through and voltage across the electrodes, and then solving the corresponding circuit equations to back calculate the equivalent impedance [13]. The equivalent impedance circuit for human body tissue is shown in **Fig. 3**. At higher

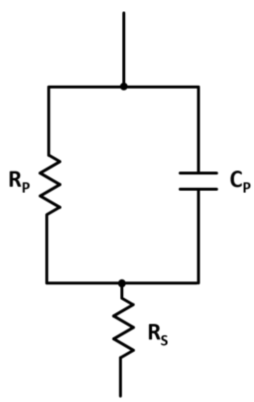

Fig. 3: Equivalent impedance of human body tissue

frequencies the capacitance is short circuited and effective resistance is the series resistance R_s. At lower frequencies the parallel resistance and capacitance also effect the overall impedance.

3 COMPUTATIONAL MODELS

We developed 3D ES models of wound healing using the COMSOL multiphysics software (www.comsol.com). These models include all relevant tissue layers with thicknesses as described by Kuhn [14]. Each tissue layer has distinct eletrical conductivity and permittivity that are frequency dependent. A representative plot of these properties is shown in **Fig. 4**. We programmed the tissue properties for each tissue type into COMSOL, based on data in the IT IS foundation [4] database.

A diagram of the 3D computational model is shown in **Fig. 5**. The COMSOL AC/DC module is used to solve the following equations throughout the computational domain. Current Conservation:

$$\boldsymbol{E} = -\nabla V \tag{1}$$

$$J = (\sigma + j\omega\varepsilon_o\varepsilon_r)E \tag{2}$$

and

$$\nabla \cdot \boldsymbol{J} = 0 \tag{3}$$

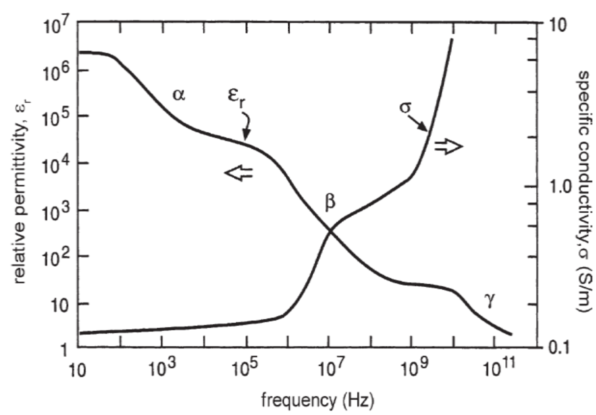

Fig. 4: Representative frequency-dependent electrical properties of tissue, relative permitivity ε_r and conductivity σ.

where ω is the angular frequency of the voltage pulse. It is important to note that for arbitrary, non-sinusoidal voltage waveforms, we decompose the waveform into its Fourier series components (harmonics), solve for the response of each harmonic separately, and then determine the total response via superposition of the harmonic solutions with appropriate spectral weightings.

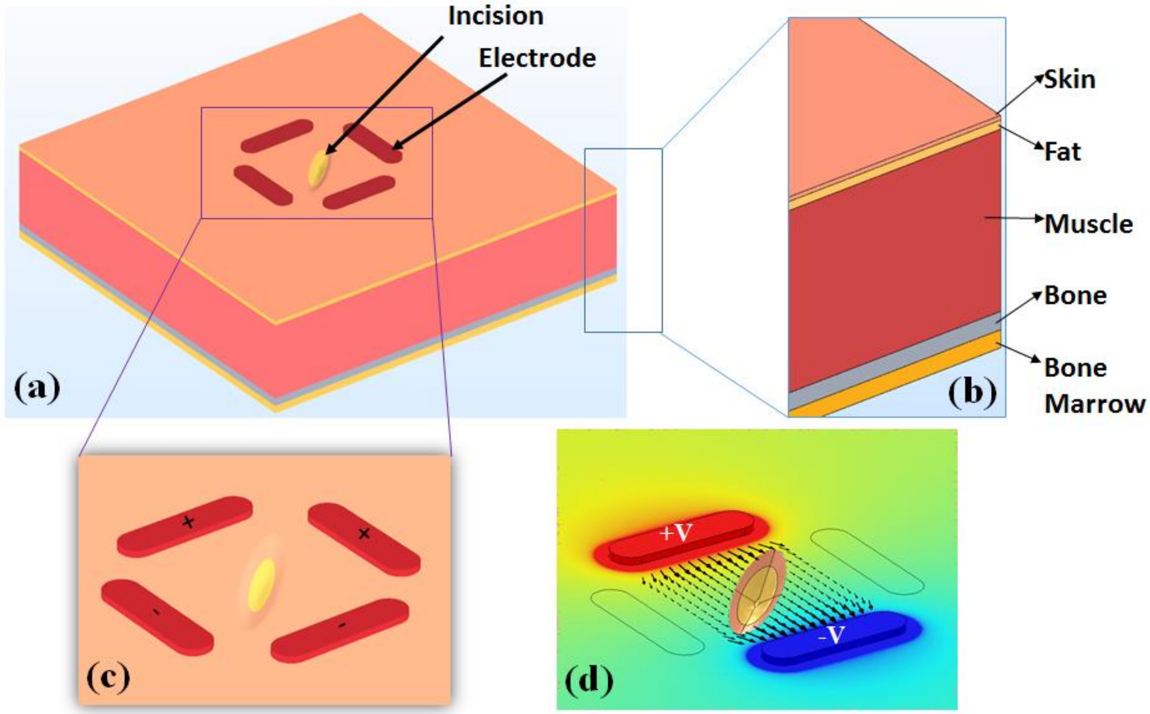

Fig. 5: Capacitively coupled (CC) electrode wound healing therapy: (a) human tissue model and 4-electrode ES configuration, (b) layers of the human tissue, (c) magnified view of 4-electrode configuration, and (d) current density distribution around wound with opposing electrodes activated.

Fig. 5 shows an ES therapy simulation in which four electrodes are configured on the suface of the skin surrounding an incision-like wound. The tissue layers in the model are shown in **Fig. 5b**. The induced current density around and through the wound due to two activated and opposing electrodes is shown in **Fig. 5d**. A similar analysis for all four electrodes activated is shown in **Fig. 6.** In this case, a significant potion of the current flows away from the wound rather than around and through it. A cutaway view of the current density inside the tissue with all for electrodes actiuvated is shown in **Fig. 7**. We developed similar models to predict the impedance of various portions of human anatomical structures. Measured data was available for the impedance as a function of frequency between two gel Ag/AgCl electrodes spaced 30 mm apart center-to-center on a forearm. A comparison of predicted and measured resistance values for this case is shown in **Fig. 8**.

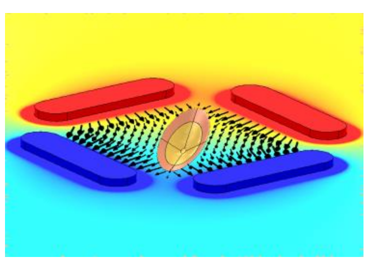

Fig. 6: ES current density (log scale) distribution with four electrodes activated.

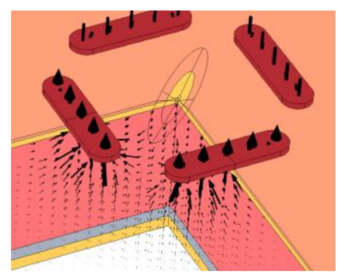

Fig. 7: Cutaway view of current density inside tissue with four electrodes activated.

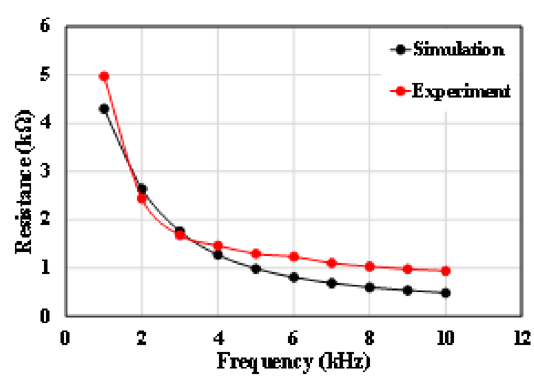

Fig. 8: Comparison of predicted and measured resistance values as a function of frequency.

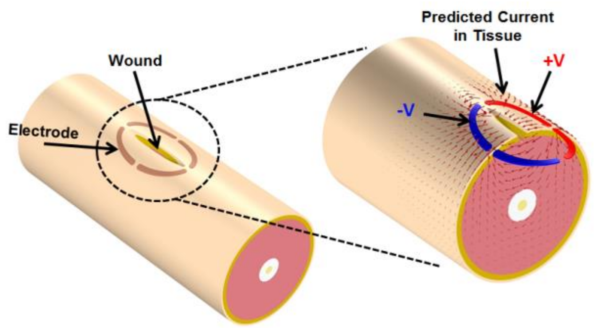

Fig. 9: ES model of voltage activated electrodes around an incicion and induced current density within an anatomical forearm.

Figure 9 shows still another 3D model of ES therapy applied to a model of human forearm alternated between the two electrode pairs. Predicted current density vectors pass into the wound region.

4 CONCLUSION

Electrical stimulation is a proven therapy to accelerate tissue healing and holds great potential for the treatment of various chronic wounds. Moreover, ES therapy lends itself to point-of-care treatment via the development of compact and portable electrical drive circuitry. However, rigorous models that predict ES induced field and current distributions within tissue are lacking, but are needed for the rational design of ES systems. There are several challenges in developing such models, e.g. they need to account for electrode properties and configurations, different drive voltage signals and importantly, the frequency dependent electrical properties of all relevant tissues. In this presentation we have demonstrated the development of rigorous 3D ES simulation models using commercial software COMSOL Multiphysics 5.2a. Such models should be of use in the design and optimization of new ES therapy technology.

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