Treatment of Liquid Covered Wounds by Dielectric Barrier Discharges *

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Abstract: The treatment of wounds by atmospheric pressure plasmas (APPs) typically proceeds through a liquid layer covering exposed cells. In this paper, we discuss results from a computational investigation of the treatment of liquid covered wounds by filamentary dielectric barrier discharges (DBDs) wherein the blood serum contains blood platelets. Irregularly shaped platelets in the blood-serum may intensify local electric fields launched into the liquid by the DBD filaments. The production and diffusion of reactive oxygen species (ROS) into the blood serum, to the blood platelets and to the underlying cells are also discussed. The studies are performed using a computer model which solves for charged particle, neutral and photon fluxes while solving Poisson’s equation, and resolving spatial scales on reactor-to-cellular levels.

Keywords: Plasma medicine, dielectric barrier discharge

1. Introduction

Non-equilibrium, atmospheric pressure plasma treatment of living tissue is being used in a variety of processes collectively called plasma medicine [1,2]. These processes typically involve direct contact of a non-equilibrium plasma with biological cells resulting in sterilization and producing therapeutic effects. One favored type of plasmas applicator is the floating electrode dielectric barrier discharge (DBD) where the tissue being treated acts as the unpowered electrode. The therapeutic and sterilizing effects of plasmas, and those produced by DBDs in particular, may be attributed to several processes - production of fluxes of radicals and charged species onto cell surfaces, production of energetic fluxes of ions and photons impinging onto wounds and tissue surfaces, and generation of surface and intracellular electric fields. For example, NO which is produced in DBDs sustained in air is known to promote and regulate wound healing [3]. Similarly produced ozone inhibits the growth of cancerous cells [4] and ions speed blood coagulation. Electric fields of sufficient magnitude can initiate electroporation [5].

The treatment of wounds by atmospheric pressure plasmas typically proceeds through a liquid layer covering exposed cells. Plasma activated processes in the blood serum likely catalyze natural wound healing steps that were otherwise hindered. One possible mechanism is the activation of blood platelets by reactive oxygen species and electric fields. Platelets are irregularly-shaped anuclear cell fragments 2-3 μm in size in blood serum. They release a multitude of growth factors and signaling agents that trigger clotting. This process may be accelerated by electric fields produced by filaments in a dielectric barrier discharge. In this paper, we discuss results of a numerical investigation of DBD treatment of liquid covered wounds.

2. Model and Geometry

The model used in the investigation, is nonPDPSIM. The gas phase reaction mechanism and algorithms are the same as those described in Ref. [5] and so will be only briefly described here. nonPDPSIM is a 2-dimensional simulation in which Poisson’s equation for the electric potential, and transport equations for charged and neutral species are solved. The electron temperature, $T_e$, is obtained by solving an electron energy conservation equation with transport and rate coefficients coming from local solutions of Boltzmann's equation. Radiation transport and photoionization are included by implementing a Green’s function propagator.

In DBDs generated in direct contact with tissue, the device typically contains the powered electrode while the tissue is the counter electrode. The model geometry, shown in Fig. 1, is based on the experiments of Fridman et al. [6]. A DBD is positioned a few mm above a thumb having a curved surface with respect to the plasma applicator. The top boundary of the computational domain is the powered metal electrode of the DBD. The electrode is covered by a dielectric 0.8 mm thick having dielectric constant $\varepsilon/\varepsilon_0 = 4$. The other bounding surfaces of the computational domain are grounded.


The skin of the thumb consists of a thin outer layer, the epidermis and an inner layer, the dermis. We resolved the cellular structure in a small patch approximately 100 $\mu$m wide and 80 $\mu$m deep, as shown in Fig. 1. This patch was located at the site at which a plasma filament strikes the skin. Four layers of cells are resolved in the epidermis. Cellular structures are represented as lossy dielectrics with conductivities and permittivities appropriate for biological tissue. The values we used here were measured using dielectric spectroscopy [7]. Typical values for $\varepsilon/\varepsilon_0$ for the plasma membrane of mammalian cells are about 6, and $\sigma$ is about $10^{-7}$ S/cm. For the cytoplasm, $\varepsilon$ is between 30 and that of water, 80, and $\sigma$ is typically one-fifth that of seawater, 0.005 S/cm. The wound is represented as a small slice in the skin to the dermis. This cut was then filled with blood-serum liquid with varied conductivities and $\varepsilon/\varepsilon_0$. The numerical grid uses an unstructured mesh with triangular elements and refinement regions to resolve the details of the plasma filaments, cell interior and nuclei. To initiate the discharge, seed electron were injected from the upper dielectric surface.

The gas mixture is humid air with a reduced reaction mechanism that captures the majority of the major reaction pathways. (See, for example, Ref. [5]). Penetration of gas phase plasma species into the blood serum includes neutral and charged species. Radicals interact with the serum constituents and the underlying tissue. In our model, blood serum is computationally treated as a liquid-density plasma, approximated as water with dielectric constant $\varepsilon/\varepsilon_0=80$. For demonstration purposes, we artificially changed $\varepsilon/\varepsilon_0$ of the liquid in some cases. For liquid water $H_2O_l$ modified cross sections as for gaseous water $H_2O$ were used. Radicals $O$, $OH$, $NO$, ions $N_2^+$, $O_2^+$, and electrons are allowed to diffuse through gas-serum interface. The reaction mechanism for blood-serum includes, in particular, solvation of electrons, clustering of negative ions, proton hopping and reactions of solvated radicals with cells walls resulting in products such as liquid-dissolved $CO_l$.

### 3. Dynamics of Dielectric Barrier Discharges Over the Wound

Filaments were launched from the dielectric directly over the liquid filled wound. The skin is initially uncharged and the DBD voltage is -40 kV. Plasma properties after the streamer intersects with the wound covered with blood serum with dielectric constant $\varepsilon/\varepsilon_0=8$ and 80 are shown in Fig. 2. The dielectric properties of the liquid in the wound affect the filament dynamics. For low permittivity liquids,
the dynamics of the plasma are relatively unaffected by the wound. The plasma is symmetric and concentrated at the top of the wound where the view angle to the plasma is largest. Higher permittivity liquids expel electric field lines from the wound. As a result, the filament partially avoids the wound. Upon intersecting the skin, the plasma filaments charge the surface, producing lateral electric fields which spread the filament over the tissue to many times its diameter. Electron densities reach $10^{15}$ cm$^{-3}$, increasing near the surface.

4. Wet Wound: Fields and Platelets

Plasmas have been shown to speed wound healing though the mechanism that is not yet clear. One possibility is that plasmas in contact with blood serum activates platelets. Platelets are irregularly-shaped anuclear cell fragments 2-3 µm in size in blood serum. The platelets release signal agents which are important to the wound healing process. Release of the signal agents can be stimulated with electric fields. The typical electric fields delivered through blood serum to underlying cells are 50-100 kV/cm, and though to be large enough to produce this stimulation. Irregularly shaped platelets intensify local electric fields within blood-serum and cells.

In the case of wet wound there is no direct penetration of plasma into the wound. Plasma produced species can only diffuse into the wound. High dielectric constant blood-serum partially screens electric fields out of the wound for conditions for which electric fields are high inside dry wound. Electric fields and induced positive charges for a wound filled with blood-serum with and without the platelets are shown in Fig. 3 when the plasma filament touches the wound surface. Without platelets, plasma potential is moderately transferred towards the bottom of the wound. The electric fields in blood-serum with platelets are locally enhanced or depleted depending on the platelets orientation. The largest potential drop across a cell structure and, as a result, the highest electric field occurs in the cells membranes as they are the most resistive. Electric fields in cell cytoplasm are of the same order as in...
the blood-serum. For the same applied voltage, intracellular charges are slightly higher for blood with platelets, probably reflecting local field enhancement. Electric fields induced in blood platelets scale with applied voltage, though peak fields are transient due to the charging of the capacitance of the fluid.

5. Long term diffusion
While plasma effects blood-serum by virtue of being a region of high dielectric permittivity, diffusion of plasma produced radicals through the serum can affect the cell membranes. Electrons, radicals, negative ions and complex ions penetrate the upper layer of blood serum. The solvation time for these particles are short (a few nanoseconds). Once solvated, these species slowly diffuse to the wound bottom. The diffusion process is shown in Fig.4 where dissolved oxygen radicals are plotted as a function of time. (O atoms from the plasma continue to diffuse into the wound.) For purposes of demonstration, we hypothesized a reaction of the dissolved oxygen with organic surfaces in contact with the liquid – platelets and cell membranes. Reaction of dissolved oxygen with cells and platelets were said to produce a generic COL product which then diffuses to fill the wound, also shown in Fig. 4. For this particular shallow wound typical diffusion times are of the order of a few milliseconds.

6. Filaments “See” the Wound
The interaction of filaments with wounds is synergistic. The electrical properties of the wound (e.g., dry or filled with liquid) can dramatically influence the filament even far from the wound. Extreme spatial variation in permittivity may result in “avoidance” of small wounds, as shown above. In this section, we compare wounds of different sizes filled with liquids having different dielectric constant. For typical filament dimensions of 0.5 mm, we consider small (< 0.5 mm), medium (~0.5 mm) and large (> 0.5 mm) wounds. Electric potentials and field lines in the absence of plasma are shown in Fig. 5 for the medium wound with $\varepsilon /\varepsilon_0=5$ and 27. Potentials and electric field lines are perturbed far from the wound depending on the permittivity of wound liquid. The electron density is shown in Fig. 5 for wounds of different size and liquid permittivity. For small wounds the plasma is not significantly perturbed with slightly slower propagation of filament and lower electron density with higher $\varepsilon /\varepsilon_0$. For medium wounds, uniform treatment occurs for low $\varepsilon /\varepsilon_0$ along with noticeable slowing of filament and plasma nonuniformity for high $\varepsilon /\varepsilon_0$. For large wounds further slowing of the filament occurs with a reduction in electron density. With the radius of the filament smaller than the wound the filament is “confined” within the wound.

* This work was supported by Department of Energy Office of Fusion Energy Science

References