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Original research article

Non-thermal atmospheric pressure dielectric barrier discharge plasma source construction and investigation on the effect of grid on wound healing application

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ABSTRACT

Non-thermal atmospheric pressure plasma sources are already known as an attractive devices for therapeutic applications including wound healing. The purpose of this investigation was to construct a portable device for skin wound healing. A planar atmospheric pressure Dielectric Barrier Discharge (DBD) plasma device was constructed. The effect of using mesh grid with DBD device was investigated for uniformity treatment of skin wounds. Reactive Nitrogen and Oxygen species were observed in the optical emission spectrum. The experiments were performed in two phases, using the DBD plasma device with/without mesh grid. In each phase, the comparison was performed between the naturally healed wounds and stimulated wounds treated daily (5 days) for 30 s. The reduction of wound area, morphological changes in wounds and tissue histological parameters were analysed. The wounds treated with DBD device with mesh grid were healed faster than the control wounds and the wounds treated with DBD device without mesh grid became more inflamed and they burned as well as the wound area were increased until 8th day of wounding. It is concluded that the DBD device with mesh grid has the ability of wound healing uniformly and without grid, the electrical shock imposed to the mice body prevents natural healing.

1. Introduction

Plasma medicine is a multidisciplinary branch of modern science and technology. It embraces physics (required to develop novel plasma discharges relevant for medical applications), medicine (to apply the technology for not only in vitro but also in vivo testing), and last but not least biology (to understand the complicated biochemical processes involved in plasma interaction with living tissues) [1].

The non-thermal atmospheric pressure plasma sources are the recent technologies in medical treatments. There are three types of these sources which are used in medical treatment application: 1) **Direct plasma**, which uses the skin (or other tissue) as an electrode, so that the produced current has to pass through the body. The most widely used technology is the ‘dielectric barrier discharge’ (DBD) plasma source. 2) **Indirect plasma**, which is produced between two electrodes and then is transported to the area of application entrained in a gas flow. Different devices exist: from very narrow ‘plasma needles’ to larger ‘plasma torches’. 3) **Hybrid plasma**, which is the combination of the production technique of (1) with the (essentially) current-free property of (2). This is also called ‘barrier coronal discharge (BCD)'. This is achieved by introducing a grounded wire mesh electrode, which has much smaller electrical resistance than the skin, so practically all the current passes through the wire mesh [2].

Dielectric Barrier discharges (DBDs) produce highly non-equilibrium plasma in a controllable way at atmospheric pressure, and moderate gas temperature. They provide the effective generation of atoms, radicals and excited species by energetic electrons [3]. Besides providing these species, plasma also delivers electric fields. A related and likely important effect in the plasma treatment of wounds is the generation of intra-wound electric fields [4]. Many researches have been emphasized on the importance of electric field in non- thermal atmospheric pressure plasmas and their biological effects [5–8].

Decisive advantage of the DBDs for the wide field of applications is the non-thermal plasma conditions at low gas temperatures and elevated (typically atmospheric) pressure. DBDs provide high-energy electrons which are able to generate atoms, radicals and excited particles. These discharges demonstrate a great flexibility with respect to their geometrical shape, working gas mixture composition and operational parameters (e.g. input power, frequency of feeding voltage, pressure, and gas flow) [9,10].

The use of plasma which is generated by discharge is widely applied in surface treatment of semiconductor, formation of thin films, ozone

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generation, biomedical applications, etc. Stability achievement of glow discharge at atmospheric pressure depends on the feed gas, the dielectric barrier material, the structure of discharge electrode, the pulsed supply frequency, the gap spacing and the humidity of the gas. Using special kinds of electrode material and configuration, homogeneous glow discharges can be established at atmospheric pressure [11]. Okazaki et al. [12] reported that homogeneous discharge can be obtained with any gases at atmospheric pressure using wire mesh as electrodes behind the dielectric barriers. This result also has been confirmed by Trunec et al. [13]. Also, it has been found that fine mesh electrodes produce more stable glow than coarse mesh electrodes. The stability and uniformity of plasma used for treatment of living tissue is very important, so the effect of using mesh grid with plasma device in treatment application was investigated in this research.

The vacuum equipment and gas storage system need to be removed using air as the working gas at atmospheric pressure. This allows for the building of small and low cost plasma sources.

Some studies have been done on the effect of non- thermal atmospheric pressure plasma on the wound healing process. Fridman et al. [14,15] studied the use of non-thermal atmospheric pressure plasma discharge for coagulation and sterilization of the surface wounds. They used DBD plasma and observed that this technique would decrease wound healing time and virtually would eliminate wound infection with skin flora. Danil Dobrynin et al. [16] determined the toxic doses of cold plasma treatment of living tissue for both intact and wounded skin. They have shown that plasma treatment is safe for living intact and wounded skin when applied for doses with several times higher than required for the effective inactivation of bacteria on the surface of agar or in liquid. Danil Dobrynin et al. [17] also studied on open wounds contaminated with bacteria which were treated with Floating Electrode (FE)–DBD plasma directly. Their work confirmed the ability of using the cold plasma to inactivate pathogenic organisms in a live animal model. They observed a 3-log reduction of bacteria after one minute exposure with plasma. In vivo skin treatment using two portable plasma devices, direct and an indirect, cold atmospheric plasma treatment was investigated by Li et al. [18]. Their research demonstrated that portable air plasma devices are indeed a potential alternative to alcohol-based disinfectants. Isbary et al. [19] examined the safety and efficiency of cold atmospheric argon plasma to decrease bacterial load as a new medical treatment for chronic wounds in vivo. They concluded that cold atmospheric argon plasma treatment may be a safe and painless new technique to decrease bacterial load independent of the strain for chronic infected wounds. The effect of atmospheric pressure plasma in process of wound healing has been investigated by Shahram Salehi et al. [20] using atmospheric pressure plasma jet for wound treatment. Elizabeth Garcia-Alcantara et al. [21] have been investigated on accelerating mice skin acute wound healing in vivo by combined treatment of Argon and Helium plasma needle. They concluded that acceleration during the wound healing process can be attributed to the formation of reactive species such as NO. Sara Fathollah et al. [22] have investigated on the effects of the atmospheric pressure plasma on wound healing in diabetic rats. Dual effects of atmospheric pressure plasma jet on skin wound healing of mice have been also studied by Gui-Min Xu et al. [23].

In this research, a planar dielectric barrier discharge plasma device has been constructed which works in atmospheric pressure air with sinusoidal power supply. The animal tests have been performed in two phases: with the use of mesh grid (hybrid plasma) and without mesh grid (direct plasma). Then, the effect of planar DBD plasma has been investigated on the wound healing in the skin of Balb/c mice. The emission spectrum of the DBD plasma, wound area reduction and histological parameters have been determined in this work. The purpose of this study was to construct a portable non-thermal plasma device with no need to the vacuum and gas equipment as well as with good uniformity for wound healing. So, the effect of the presence of mesh grid with DBD device on wound healing has been also investigated.

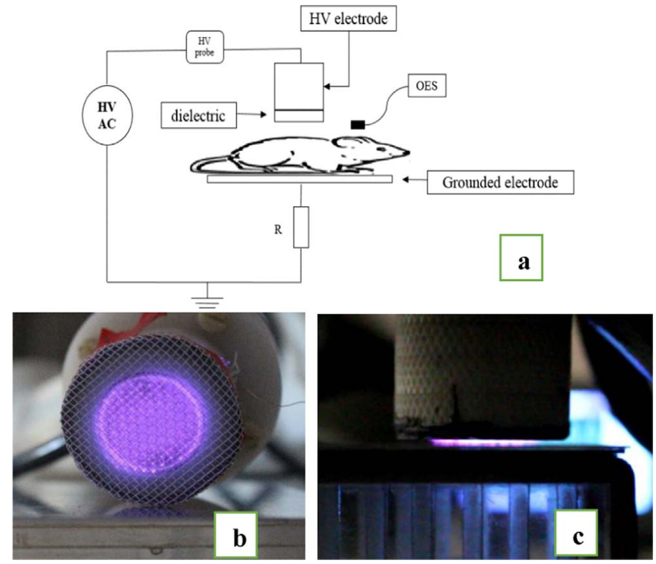

Fig. 1. The experimental setup: a) Schematic diagram of the DBD plasma wound treatment setup, b) DBD plasma device with mesh grid, c) DBD plasma device without mesh grid.

2. Material and method

2.1. Plasma setup and diagnostics

In this research, a planar Dielectric Barrier Discharge was constructed. A schematic diagram of the DBD test setup is shown in Fig. 1a and the DBD plasma device with and without grid are shown in Fig. 1b and c, respectively.

The non-thermal atmospheric pressure DBD plasma device was constructed with the 25.4 mm diameter electrode and was supposed to work in air. The electrode and insulator were made up of copper and polytetrafluoroethylene (Teflon), respectively. The insulating dielectric barrier was made of quartz with 1.8 mm in thickness which was attached to the electrode tightly. The homemade power supply with the ability of producing sinusoidal frequency and voltage was used for producing discharge. This power supply generates sine waves with the output values in the range of 0–30 $kV_{p\text{-}p}$ and the intermediate frequency between 10–12 kHz. The high voltage was applied between the insulated electrode and the surface which must be treated. The mesh grid with the wire diameter of 1 mm and with the aperture of 1.4 mm was used. The mesh grid was grounded.

For measuring the current passing through the plasma, a carbon film resistor with the resistance of 27 Ω was used. The voltage drop across the resistor was measured with the Tektronix P2220 voltage probe. The voltage across the DBD was measured with the wide bandwidth probe, Tektronix P6015A. Signals were observed and recorded by digital phosphor oscilloscope (Tektronix DPO7104, 1 GHz bandwidth). The power of discharge was approximately 26 W for mesh grid device.

The gap distance between dielectric and mice was selected 1 mm for all tests.

The Optical Emission Spectrum within the range of 200–1000 nm was measured with the compact CCD spectrometer (CCS200 with the FWHM spectral accuracy of < 2 nm). The spectra were subtracted from the dark baseline.

2.2. Animal samples

In these work, 6-week old male 24 Balb/c mice with the weight of