Stimulation of wound healing by helium atmospheric pressure plasma treatment

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Abstract
New experiments using atmospheric pressure plasma have found large application in treatment of living cells or tissues, wound healing, cancerous cell apoptosis, blood coagulation on wounds, bone tissue modification, sterilization and decontamination. In this study an atmospheric pressure plasma jet generated using a cylindrical dielectric-barrier discharge was applied for treatment of burned wounds on Wistar rats’ skin. The low temperature plasma jet works in helium and is driven by high voltage pulses. Oxygen and nitrogen based impurities are identified in the jet by emission spectroscopy. This paper analyses the natural epithelization of the rats’ skin wounds and two methods of assisted epithelization, a classical one using polyurethane wound dressing and a new one using daily atmospheric pressure plasma treatment of wounds. Systemic and local medical data, such as haematological, biochemical and histological parameters, were monitored during entire period of study. Increased oxidative stress was observed for plasma treated wound. This result can be related to the presence in the plasma volume of active species, such as O and OH radicals. Both methods, wound dressing and plasma-assisted epithelization, provided positive medical results related to the recovery process of burned wounds. The dynamics of the skin regeneration process was modified: the epidermis re-epitelization was accelerated, while the recovery of superficial dermis was slowed down.

1. Introduction

In the recent period, new experiments using atmospheric pressure plasma have found large application in treatment of living cells and tissues. All of them create a new field at the frontier between plasma science and technology and (bio)medicine, mainly known as Plasma Medicine. Nowadays major interest concerns the plasma jet discharges at atmospheric pressure. The variety of the atmospheric pressure plasma jet can be characterized using parameters such as working gas, repetition frequency of the applied voltage pulse and the electrode configuration. Due to its simplicity and versatility, atmospheric pressure plasma jet is applied in the treatment of different types of biopolymers or bio-composites and even micro-organisms or living tissue. Atmospheric plasma jets can be generated in various gaseous environments, using both dc and ac excitation. Regarding the ac excitation, a broad range of working frequencies is reported, from a few kHz to radiofrequency (RF) and microwaves. Depending on jet configuration and electrical excitation, plasma characteristics may differ significantly [1]. Currently two main explanations for the plasma propagation in air exist. Some authors [2, 3] suggest a streamer model based on photoionization to explain the effect, and others [4] argue that the dielectric-barrier discharge (DBD) forms a hypersonic plasma bullet train due to an ionization wave. A common geometry of atmospheric pressure plasma jet is the one using a coaxial DBD configuration, with one or two electrodes wrapped around a quartz tube. The discharge is driven by a few kHz repetition rate pulsed voltage in a helium gas flow through the tube. This experimental arrangement has attracted the interest of many researchers, due to the plasma jet length which is suitable for a variety of potential applications, from localized thin-film depositions to biomedical processes [5]. It is well known
fibres recovery was observed in the superficial dermis (the appearance is similar to that at day 14) associated with mononuclear inflammatory infiltrate; plasma-treated lesions, PTW, presented corrugated and thick epidermis, with a sinuous basement membrane and well represented spinous and corneum layers; the dermis beneath still remained hyalinated with collagen fibres condensed and poor monocytic infiltrate.

Keratinocyte activity is clearly accelerated both by planimetric measurements and histologic aspect of the epidermis. The fibrocyte response is obviously increased as can be seen in figure 13(c), and the superficial dermis is clearly condensed with lower affinity for the collagen stain compared with the surrounding normal dermis. Overall, we can conclude that direct plasma treatment of wounds or only plasma activation of wound dressings, modify the dynamics of the skin regeneration process. The epidermis re-epitelization was accelerated, while the recovery of superficial dermis was slowed down.

4. Conclusions

Optical emission spectroscopy is a quick and powerful technique for monitoring of the active species present in plasma, most importantly OH, N$_2$, N$_2^+$ and O. Optical emission spectroscopy was applied in order to determine the rotational and vibrational temperatures of the studied plasma. The rotational temperature, $T_{rot}$, was estimated around 540 K. The vibrational temperature, $T_{vib}$, was found to be between 2600 and 3500 K. The axial and radial emission profiles can also provide a measurement of the plasma active size. We also found a ‘plasma bullet’-like behaviour of our discharge, proved by time-resolved fast photography. We have achieved accelerated re-epitelization in the plasma-jet-treated skin lesions. The overall analysis of hematologic, biochemical and histological parameters showed positive correlation until day 14. At day 21, although haematology and biochemistry showed normal values compared with the control, the histological images showed abnormal epidermis and subjacent dermis regeneration under direct plasma irradiation. Good results were obtained for the polyurethane wound dressing compared with the untreated group. It was pointed out that under direct plasma irradiation the inflammation parameters remained at low levels while local oxidative stress was increased. Also the keratinocyte and the fibrocyte response seemed to be quite accelerated. Re-epitelization is just a part of the skin regeneration process, which recruits cellular and humoral components, with the aid of epidermal and dermal interaction via signal molecules. We found an increased oxidative stress induced inside the plasma-treated living tissue, that can be related to the presence of plasma-active species, such as O and OH radicals. Regarding the biological effects, it was found that both direct plasma treatment of wounds or only plasma activation of wound dressings modifies the dynamics of the skin regeneration process. The epidermis re-epitelization was accelerated, while the recovery of superficial dermis was slowed down.

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