

## **Wound healing improvement in large animals using an indirect helium plasma treatment**

Emilio Martines, Paola Brun, Roberto Cavazzana, Luigi Cordaro, Matteo Zuin, Tiziana Martinello, Chiara Gomiero, Anna Perazzi, Luca Melotti, Lisa Maccatrozzo, Marco Patruno, Ilaria Iacopetti  
*CLINICAL PLASMA MEDICINE* **17-18** N. UNSP 100095 (2020);

<https://doi.org/10.1016/j.cpme.2020.100095>

Abstract:

### *Background*

To optimize wound healing, the use of low-temperature atmospheric pressure plasma (ionized gas) has been proposed as an innovative therapeutic method for treating extensive and chronic wound. The aim of this study was to evaluate the specific effects of an indirect helium plasma treatment in a sheep surgical wound model based on clinical, histopathological and molecular analyses. This study was part of a larger study aimed at assessing five different wound healing improvement methods.

### *Methods*

Six sheep were used in this study. Six square wounds were performed on the back of each sheep. Five of the lesions were used to analyze the effect of five different treatments, one of which was the plasma treatment. The sixth lesions was used as control. A 2-min plasma treatment was daily performed, using a radiofrequency helium plasma source for indirect treatments, until complete wound healing was obtained. Biopsies were performed at two and six weeks. The plasma effects were tested through clinical evaluation, histopathological and immunohistological evaluation, real time PCR analysis, bacteriological evaluation and intracellular ROS evaluation.

### *Results*

Wound closure time for the plasma-treated wounds was quicker than that of the control group. Plasma treatment drastically reduced the bacterial load in the wounds. A strong increase in intracellular ROS was observed. After six weeks, the inflammatory process was significantly reduced in the plasma-treated case with respect to the control. The plasma treatment was found to lead to an anticipated induction of blood vessel formation, as detected through mRNA expression of VEGF. The high Ki67-positivity at two weeks indicated a strong stimulation of cell proliferation induced by the plasma treatment. The expression of the hair keratine (hKER) at six weeks indicated that the plasma was promoting hair regrowth. The plasma treatment induced an increased rate of reformation of cutaneous adnexa at six weeks.

### *Conclusions*

The obtained results suggest that the plasma action, at the used dose, induces an increase in cell proliferation, a reduction of inflammation, a reduction of the bacterial load, a stimulation of blood vessel formation, and an improvement in the formation of cutaneous adnexa with a positive consequence on hair regrowth.