

Plasma/target interactions in biomedical applications of cold atmospheric pressure plasmas: Implications for “dose” regulation in treatments

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INTRODUCTION: The last decade has seen an impressive increase of the research dedicated to the biological applications of low temperature atmospheric pressure plasmas. Medical applications are tacking an increasing place underlined by many clinical trials. They now concern numerous domains, including blood coagulation, dental care, skin decontamination and hygiene, wound and ulcer treatment, dermatology, cancer treatment. Biological applications are also now extended to agriculture and, more recently, to cosmetic. Despite the huge number of *in vitro* and *in vivo* experiments, there are still numerous challenges to overcome linked to the nature of the encountered target (biological tissues and materials, organs and their direct environment, liquids) that have a direct effect on the produced plasma itself and on the generated species. That must therefore be taken into account in the applied treatments and complicates the definition of a "plasma dose" expected by many.

RESULTS: The extremely strong coupling between the plasma characteristics and those of the target (e.g. ref. [1, 2]), plays a very important role in the results observed during treatments. A variation in the chemical or physical characteristics of the target will involve significant differences in the gas flow, the local temperature, or the induced electric field, resulting *de facto* in variations in the production of the reactive species. It also concerns the transposition of the results between the *in vitro* and the *in vivo* experiments that are carried out under extremely different conditions, especially concerning the equivalent electric circuit of the reactor / plasma / biological target assembly. These problems directly affect the identification of the processes involved and currently limit the possibility of a definition of a "dose" in plasma treatments. In addition, a study recently reported in [3] led to think over non-sustainable tumor response. The loss of effectiveness under long-term plasma treatment of cancer tissue opens questions

about plasma application and protocol. It must be considered that the treated area is morphologically and chemically changing over the time, from activated surrounding to more normal tissues that are less humid and bacteriologically cleaner. This aspect is of particular importance for the development of efficient systems and protocols for any plasma therapeutic approaches. It induce a in real-time in situ control of plasma production and at longer term a protocol adaptation taking into account the biological target evolution.

DISCUSSION & CONCLUSIONS: After a presentation of the context, we will focus on the different problems linked to the plasma/target interaction, including treatments of tissues and liquids. We will discuss the induced changes in gas flow and plasma characteristics, as well as changes induced in microenvironment of living targets and their implication on the definition of a “plasma dose” for general use in plasma medicine. We will emphasize on the fact that plasma diagnostics must be performed in real treatment conditions. We will also tackle the main issues and challenges linked to the control of the multimodal action of non-equilibrium cold plasmas on living organisms.

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