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Atmospheric plasma jets for therapeutic applications: issues and challenges

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The action of Low Temperature Non Thermal Plasma has been now widely demonstrated both in vitro and in vivo (on animal models and on human) on a large variety of cell lines, tumor types and diseases. Nevertheless, due to the great variety of plasma components able to play a role, the precise understanding of the process chain leading to the observed effects is far to be reached. It is not easy to isolate or to measure the plasma component individual action or, in contrast, to evaluate the potential benefit or synergy of combined ones. Up to now, many experiments in vitro have been realized with that intention, but the translation to in vivo results is rather complicated, even, in many cases, impossible due to the complex environment of the cells in vivo, including vascularization (then blood flow and oxygenation/physioxia) and the body response (signaling, recruitment, immune system). Generally, the first step of dedicated studies concerns in vitro cell viability or toxicity in culture media with the analysis of both the induced changes in the cells and in the medium. It must be stressed that the used experimental conditions together with the fact to treat cells in multiwell plates outside their incubation chamber may generate cell stress that can affect their behavior and then leading to biased results. Moreover, complex interactions between the plasma itself, the gas flow and the target (liquid, tissue, inert surface) can drastically change the production and the interactions of the reactive and charge species during the treatments. This is particulary true with multijets as will be shown. Last, but not least, the transient electric field generated by the plasma jet can interact with the surrounding environment and potentially acts in synergy, or not, with the other active plasma components.

This presentation will show some of the issues and challenges associated with treatments by a plasma jet (here Plasma Gun and Plasma Multijets), in relation with conditions associated with hypoxic/physioxic environments. We will present results on direct effect of plasma treatment on both the culture medium and cells, including liquid evaporation, oxygen deprivation, extra and intracellular RONS generation, membrane poration, cell depolarization, with the potential role of electric field in the treated and adjacent wells. We will particularly emphasize the importance of cell oxygenation level which is a key factor in the proliferation/ regression of tumors in hypoxic environment. It will be shown that an uncontrolled plasma jet in vitro treatments can lead to drastic changes in the oxygen pressure (and temperature) in cell culture during the experiment with sequences of maxima (leading to normoxia) and minima (potentially leading to strong hypoxia). The latter contrasts with the plasma oxygen pressure and blood flow increases measured in the in vivo conditions. This also means that a great attention must paid in the modeling of interactions of plasma jets with physiological liquid media since the initial concentration of oxygen can be greatly affected.

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