Potential of hydrogels and liquids in plasma therapy of osteosarcoma

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Abstract: This conference will summarize the findings of our research group regarding the applicability of hydrogels in plasma therapies, in particular in the treatment of osteosarcoma, In particular, the following will be discussed: i. The effects of plasma-treated liquids on bone cancer (Osteosarcoma), together with ii. the development of vehicles based on biocompatible hydrogels for the delivery of plasma-generated reactive oxygen and nitrogen species.

Keywords: osteosarcoma, atmospheric pressure plasma jet, hydrogel, plasma activated media.

1. Introduction

Over the last few years, significant attention has been paid to biomedical applications of Atmospheric Pressure Plasmas (APP) [1,2]. Plasma chemistry leads to the generation of an abundance of reactive species (RONS) which are suspected to play a key role in selective cancer cell death without damaging surrounding healthy tissues. Such effects have also been observed in plasma activated liquids (PAM), opening the door for minimally invasive therapies (Figure 1).

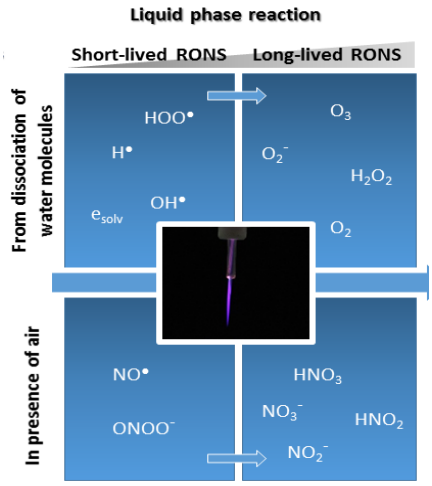

Figure 1. Overview of the short- and long-lived RONS generated in liquid media by APPJ that are most often quantified in literature (Adapted from Khlyustova et al. [4]).

Osteosarcoma (OS) is the most common bone malignant neoplasm primary solid tumor that develops in bone. Although standard chemotherapy has significantly improved long-term survival over the past few decades, the outcome for those patients with metastatic or recurrent OS remains dismally poor and, therefore, novel agents and treatment regimens are urgently required.

2. Materials and methods

Different natural and synthetic hydrogels encompassing different crosslinking methods have been prepared in a range of concentrations have been treated with different APP jets prior to crosslinking. Different APP conditions have been evaluated (ie. time, gas flow, distance to the sample). Quantification of [H_2O_2] and [NO_2^-] has been performed reacting the treated biopolymers with $TiSO_4$ or Amplex Red methods and Griess reagent, respectively. Ringer's saline has been employed as control for the determination of RONS generated by APP. Osteosarcoma cell viability has been evaluated at different timepoints in the treated hydrogels.

3. Results & Discussion

It is our aim to investigate the effects of atmospheric plasma jets in the generation of RONS in liquids of biological interest [3,4], and their efficiency and selectivity in OS treatment will be presented, together with possible mechanisms involved. Moreover, achieving a sustained release of the plasma-generated RONS to the diseased site is highly relevant. Therefore, it is our interest to elucidate the potential of hydrogels to generate and store RONS generated by plasmas. Hydrogels are highly hydrated natural, synthetic or semi-synthetic networks of cross-linked polymer chains whose features such as biocompatibility make them great candidates for the design of advanced biomaterials [5].

We will discuss the use of different hydrogels for plasma treatment and their outcomes; in general, their physic-chemical properties remain unchanged by the plasma treatment.

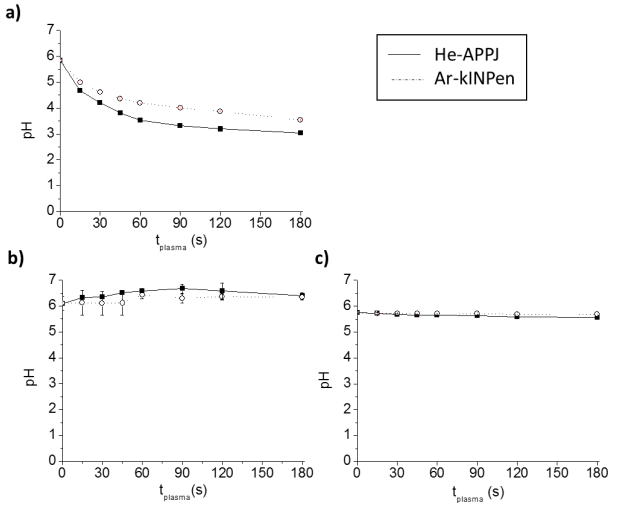

Figure 2. Example of the different evolution of pH with atmospheric pressure plasma jet treatment in a) water, or two different hydrogels before crosslinking: b) alginate or c) gelatin

The capacity of the hydrogels to generate RONS during plasma jet treatment is highly dependent on the chemistry of the polymer solution, but often several-fold higher concentrations can be obtained than in a typical isotonic saline solution. The hydrogels show capacity for release of the RONS.

The biological effects of the treated liquids or hydrogels are investigated in different cell lines and discussed with regard to the different reactive species generated in the PAM (ie. $[H_2O_2]$, $[NO_2^-]$, short-lived RONS).

4. Acknowledgements

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5. References

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