Workshop "Plasmas in Medicine"

PLASMA SOURCES FOR MEDICAL APPLICATIONS – OPPORTUNITIES, CHALLENGES AND RESPONSIBILITIES

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Due to the growing interest in using low temperature atmospheric pressure plasma sources for medical applications, Plasma Medicine is currently emerging worldwide as a new independent field of scientific research. Whereas today's commercially available plasma surgical technologies such as argon plasma coagulation (APC) or ablation are mainly based on lethal plasma effects on living systems, the newly emerging therapeutic applications will be based on selective, at least partially non-lethal, possibly stimulating plasma effects on living cells and tissue. The results of first practical studies have been interpreted to be very promising and reveal a huge potential for the application of low temperature atmospheric pressure plasma in fields such as tissue engineering, healing of chronic wounds, treatment of skin diseases, tumor treatment based on specific induction of apoptotic processes, inhibition of biofilm formation and direct action on biofilms or treatment of dental diseases.

Several reviews have appeared recently that focus on the exciting applications, but do not pay proper tribute to the importance of addressing the many underlying basic science questions. According to this, much basic research still needs to be conducted to minimize risk and to provide a scientific fundament for new plasma-based medical therapies. It is almost needless to mention that a therapeutic application of low temperature plasma is not only a demanding task for medicine, but also for plasma physics. The development of suitable and reliable plasma sources for the different therapies and an in-depth knowledge of their physics, chemistry and parameters must be contributed by physical research.

Today, concepts of tailor-made plasma sources which meet the technical requirements for medical devices are still insufficiently developed. The proposed selectivity of plasma action implies an accurate control of the performance parameters of the plasma sources regarding the treatment efficiency as well as potential risks connected with the direct application of plasma at or in the human body. In this context, plasma sources are mostly characterized with regard to special biological effects, e.g. antimicrobial efficiency, cell manipulation or blood coagulation, to evaluate potential therapeutic benefits and specific adverse or toxic side effects in the close cell and tissue environment. But it is also essential to perform a comprehensive assessment of the general risk factors to clarify minimum standards for plasma sources for medical applications and for comparison of different sources. From the present point of view such risk factors are plasma temperature, thermal load, UV radiation, electromagnetic fields, radicals and the generation of toxic gases. The mix of these parameters has to be adapted individually for each application.

Therapeutic applications require low temperature plasmas operating at atmospheric pressure which are meanwhile available in many different designs and configurations. Regarding the manageability in everyday medical life, atmospheric pressure plasma jets (APPJ)

and dielectric barrier discharges (DBD) are of special interest. But the determination of discharge development and plasma parameters is a huge challenge, due the high complexity and limited diagnostic approaches – the plasmas are usually small scale, constricted or filamentary, and transient. Furthermore, working on open air atmospheres, an input of nitrogen, oxygen and water implying complex plasma chemistry must be expected. Therefore, a great deal of effort combining experimental investigation and modeling will be necessary to provide the required knowledge on plasma sources for therapeutic applications.

This contribution intends to give an overview on plasma sources for therapeutic applications and will discuss needs, prospects and approaches for the characterization of plasmas from the fundamental plasma physical point of view. It is confined to the plasma sources developed and used by INP Greifswald and its network partners in various projects. The general "macroscopic" plasma characterization is demonstrated exemplary.

After a general introduction, selected specific plasma sources which are used for the investigation of various biological effects are presented. A comprehensive risk-benefit assessment was realized in the *Campus PlasmaMed* [1] using several in vitro and semi-in vivo models: 2D cell cultures; 3D epidermis model; fresh enucleated beef cattle eye; HET-CAM test (Hen's Egg Test Chorionallantoic Membrane). Clear advantages of different atmospheric pressure sources are demonstrated: significant higher antiseptic effects; promotion of blood circulation and angiogenesis; wound tissue tolerance; no decrease of antioxidative potential in human tissue; effective inactivation of biofilms. Present studies in the *Campus PlasmaMed* are focused on verification of a selective antiseptic effect of various plasma sources, i.e. the inactivation of infectious micro-organisms on living tissue without damaging side effects.

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