‘ALEXANDRU IOAN CUZA’ UNIVERSITY OF IAȘI
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# STUDY OF INTERACTION PROCESSES BETWEEN LOW TEMPERATURE PLASMAS AND ORGANIC MATERIALS OF BIOMEDICAL INTEREST

**- Thesis abstract -**

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# Acnowledgements

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For a period of eight months (May-December 2011) I received a scholarship for doctoral research training, funded by [grant POSDRU/88/1.5/S/47646], at Leibniz Institute for Plasma Science and Technology (INP Greifswald ), under the guidance of Prof. Dr. K.-D. Weltmann (INP director) and Prof. Dr. Th. von Woedtke (Plasma Experimental Medicine Program Manager).

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This doctoral thesis has been developed over a periode of three years (1 October 2009 - 30 September 2012). The thesis manuscript was performed in the Laboratory of Plasma Physics, Faculty of Physics, Alexandru Ioan Cuza University of Iasi, Romania and in the Laboratory of Plasma Sources, Leibniz Institute for Plasma Science and Technology-INP in Greifswald, Germany.

This thesis, entiteled 'Study of the interaction of low temperature plasmas with organic materials biomedical interest', consists of 5 chapters followed by general conclusions, an appendix, a list of publications, list of tables, list of figures and references. The first chapter is documentary, presenting plasma sources used in the biomedical field and general processes that can occur at the interface between electrical discharges in gases at atmospheric pressure and various solid or liquid media. The next two chapters (2-3) present electrical, optical and spectroscopic diagnostics of plasma sources used experimentally by the author. Chapters 4 and 5 present the interaction between plasmas, characterized in previous chapters, and some materials of biomedical interest. Chapters 2-5 contain original contributions of the author, followed by a chapter relating to the findings of the studies undertaken. The thesis also includes an appendix that contains information on epithelial tissue, skin lesions, skin regeneration and oxidative stress. Scientific documentation of the thesis is reflected by the 131 references, representing relevant literature titles.

The objectives of this thesis are to characterize in terms of electrical, optical and spectroscopic diagnosis the low temperature 'plasma jet' source at atmospheric pressure, and the interaction processes of these types of discharges with the surface of some organic materials of biomedical interest.

The thesis begins with '**Electrical discharges in gases at atmospheric pressure**' chapter as a brief introduction stating the employment work of the thesis in the interdisciplinary subject 'Plasma – Medicine'. Most used plasma jet sources at atmospheric pressure and electrode configuration parameters are presented. This chapter is mainely devoted to atmospheric pressure plasma sources that can be found in the literature and those already on the market (such as: 'Plason', 'Plasma Needle', 'MicroPlaSter', 'Plasma Pencil', 'FE-DBD', 'kINPen', 'hairlINePlasma' or '2 D multi jet'). After that the most important physico-chemical processes occurring at the interface plasma-solid / liquid media follows. General processes such as activation and functionalization, etching, crosslinking, polymerization in plasma decontamination and sterilization are presented.

In Chapter 2 '**Plasma electrical characterization**' are presented classical methods of electrical characterization of atmospheric pressure plasmas investigated using visualization and measurement method on discharge voltage and discharge electric current. In this way were determined the discharge power consumption and the amount of electric charge transported.

Experimentally were investigated two plasma jet gas discharges at atmospheric pressure: a dielectric barrier discharge (DBD) and a resistive barrier discharge (RBD).

For the case of DBD plasma source three electrode discharge arrangements were used, namely:

* Two electrodes: the power electrode wrapped on the dielectric quart tube and the earthed electrode, metal foil coated with dielectric disposed at a distance 'd' before discharge tube, DBD-1;

* One power electrode wrapped on the discharge quartz tube, DBD-2;

* Two electrodes: the earthed and power electrodes are wrapped on the quartz tube, DBD-3.

In the experiments a step pulsed voltage waveform was applied between the discharge electrodes with amplitude of 4-8 kV and 2 kHz repetition rate for DBD-1, DBD-2 and DBD-3 plasma sources. For the RBD plasma source a sinus type voltage waveform, with amplitudes of 1.8-5.2 $kV_{pp}$ and 18 kHz repetition rate was applied between dircharge electrodes.

In order to follow the influence of the nature of the introduced additional electrode, the DBD-3 plasma jet was used. The counterelectrode (aluminum tape, glass, human finger) was positioned at a distance of 1 cm of the discharge tube and the oscillograms of the temporal evolution of intensities of the applied voltage and discharge current were aquired.

It is experimentally observed that, if the discharge works with 2 electrodes maximum value of the first current pulse appears at 3.5 µs with amplitude of 3.06 mA and the second current pulse appears at 28.8 µs with amplitude of 0.6 mA.

In Chapter 3 '**Plasma optical and spectroscopic characterization**' optical and spectroscopic diagnostic techniques used in this paper are presented. Using optical emission spectroscopy were identified atomic and molecular species generated in the plasma. By this technique were determined the energetic characteristics of the discharge through rotational and vibrational temperatures of single molecules. Plasma sources under investigation were: DBD-1, DBD-2, DBD-3 and RBD. The studied plasma jet discharges optical emission spectra (250-850 nm) reveals working gas lines, He, and impurities lines / bands: $N_2$, $N^+_2$, OH, O [1-4]. Experimentally a redistribution of spectral lines / bands intensities according to studied plasma sources was observed.

In subsections '**Rotational temperatures**' and '**Vibrational temperatures**' the methods for determining the rotational ($T_r$) and vibrational ($T_v$) temperature of molecular ions or molecules of nitrogen are presented. $T_r$ values were determined as 560 K and 470 K (± 30 K) for DBD-1and DBD-2/3 plasma sources. Also the $T_v$ value in the electrode gap were determined as ranging between 3500 and 2600 K (± 50 K). Because discharges DBD-1, respectively DBD DBD-2-3 are non-equilibrium plasmas the discharge gas temperature estimation is sometimes overestimated.

In subsection '**Atmospheric pressure electrical discharge fast photography**' fast photography technique of studied discharges is presented. Using this technique we can reveal discharge formation and spatial development stages. Thus, using an ultra fast (ICCD) was recorded plasma emitted radiation of DBD-1, DBD-2, DBD-3 DBD and RBD sources with an exposure of 50 ns [1, 5]. From acquired ultra fast images a 'plasma bullet' behavior is observed for all the studied discharge sources.

Information on the geometric and kinetic characteristics of plasma formation was obtained from processed ICCD images. These experimental results are presented in section '**Plasma jet dimensions and velocities**'. For DBD-1 plasma source, the plasma velocity varies between 10 and 30 * $10^4$m / s in the direction of gas flow. For DBD-2 configuration, the plasma velocity ranges between 0.1 and 14 * $10^4$m / s. In the case of RBD plasma source velocity values were determined to be between 0.3 and 15 * $10^3$m / s [1]. Plasma structure diameter values for DBD-1, DBD-2, DBD-3 and RBD sources were determined as having values between 0.1 and 9.0 mm and the corresponding areas between 0.03 and 23.15 $mm^2$.

Chapter 4 '**Plasma jet - biological material interaction**' is dedicated to plasma interaction with biological material.

'**Plasma-human living tissue interface'** section presents studies on the lifetime of the discharge DBD-3 in contact with human finger skin. Applied voltage and discharge current intensity values were recorded between plasma electrodes. Optical emission spectrum of the jet discharge reveals He excited species and bands / lines of OH, $N_2$, $N^+_2$ and O. Note that in case of using a counter electrode that corresponding bands of nitrogen species emitted by plasma grow in intensity at the expense of He and O lines.

For a better understanding of plasma dynamics in the vicinity of studied living tissue (finger) surface fast photography technique was performed. Experiments aimed DBD-3 plasma source in He in two cases: with a dielectric (quartz disk) or human finger as counter electrode. After plasma expansion outside the discharge tube in air the existence of a plasma structure, donut-shaped, was highlighted in ICCD images. If the plasma jet is concentrated on a counter electrode, plasma structure spreads on its surface till extinction.

In subchapter '**Plasma-animal living tissue interface**' studies on electrical and spectral behavior of the DBD-3 jet discharge in contact with three types of animal tissue (dead) surfaces were performed. As in the previous study (plasma- living tissue interaction, human finger) electrical and optical methods of plasma diagnostics at the interface with animal tissue (adipose, epithelial, muscle of porcine origin) were used.

During experimental studies differences between current-voltage waveforms depending on the animal tissue nature were observed. Differences were also observed in the emission spectra and the photomultiplier curves. An important aspect in terms of applicability in bio-medicine is that NO emission bands appear in the emission spectra of the plasma source, only the treated tissue interface. However the photomultiplier signals have amplitudes and durations smaller than in the plasma-living tissue interaction studies.

Chapter 5 of the thesis '**Plasma jet - microorganisms / epithelial tissue interaction**' is devoted to application of plasma jets for sterilization, inactivation of microorganisms and to living tissue treatments.

First section '**Plasma assisted microorganism inactivation**' study focuses on the effect of inactivation of Escherichia coli and Pseudomonas aeruginosa under DBD plasma action. For both types of bacteria a linear dependence between the growth inhibition zone diameter and plasma exposure time (range 25-100 s) was found. The inhibitory effect was attributed to reactive plasma species: $N_2$, $N^+_2$, O and $O_3$ even [4].

In section '**Stimulated regeneration of wounded epithelial tissue - animal model**' experimental results are presented related to stimulation of healing of wounded (acid burned) epithelial tissue (skin) by means of atmospheric pressure plasma jet (DBD-1) treatments.

Experiments were performed on Wistar rats, following a protocol developed by Dr. C. Grigoraş. 3 groups of healthy Wistar rats were used divided as follows: CG = control group; UTW = rats with burns of the skin that healed naturally, PTW = rats with skin burns plasma jet treated plasma.

To study plasma induced reepitelization a model of burning Wistar rat skin was used. After making the wounds PTW group have undergone treatments in DBD-1 discharge. Plasma treatment duration was 40 s for each lesion for 21 days.

After performing plasma treatment of injuries, biological samples were taken on days 3, 8, 14 and 21 for biochemical and histology tests [3, 6].

After conducting biochemical tests it was observed that plasma treated samples (PTW) in the first few days (3-8) have slightly higher values of studied parameters than those of control samples (CG,) thereafter for day 14 and 21 approaching normal. This fact, for PTW samples, can be attributed to reactive oxygen species from the plasma. Also, increased levels of oxidative stress in these samples can result in a local decontamination and stimulate healthy cells.

Histology tests provided information on the behavior of skin components from the plasma treatment and spontaneously regenerated samples. In these tests an acceleration of epithelization of damaged areas was found for plasma treated wounds. For a complete reepitelizare the required recovery time decreases approximately by half (3 weeks) for plasma treated lesions unlike untreated areas.

At the end of the thesis manuscript are outlined the main **Conclusions** drawn out from chapters 2-5:

1) Based on measurements of atmospheric pressure DBD discharge electrical parameters and taking into account plasma geometry the following plasma parameters were calculated: the discharge electric currents (1-2 mA), the plasma voltage amplitude (4-8 kV) and the electrical power transferred to the discharge (15-20 W). An electrical method for estimating the average plasma velocity was also presented.

2) In this study the influence of counter electrode nature (solid / liquid conductor / insulator) on the intensity of discharge current was investigated. Were used as counter electrodes aluminum tape, glass slides, distilled water solution, buffer solution, saline and living tissue (human finger). Experimentally a shift and an increase in the duration of the jet discharge current pulse by counter electrode type were observed.

3) Plasma active species have been identified in this type of discharge: OH, $N_2$, $N^+_2$, O emission by optical spectroscopy. After determining the rotational and vibrational characteristic temperature values we concluded that plasma jet is a cold discharge. This is revealed by rotational temperature, $T_r$ 560 K (± 30 K) for DBD-1 source, respectively Tr 470 K (± 30 K) for DBD-2 source. Vibrational temperature ($T_v$) of nitrogen molecules values for the two configurations used are between 3500 K (± 50 K), near high-voltage electrode, and 2600 K (± 50 K) at 10 mm from the discharge tube. These values are close to those reported in the literature for this type of plasma.

4) High speed photography was used to capture the spatial - temporal evolution of jet discharge. We observed a maximum value for the propagation velocity of the plasma jet of 30 * $10^4$ m / s for DBD-1 and 14 * $10^4$m / s for DBD-2 for primary discharge current. For the secondary discharge current velocity values of 7 * $10^4$m / s for DBD-1 and 4 * $10^4$m / s for DBD-2 were determined. In the case of RBD source values for the

propagation velocity of the plasma jet are between 0.3 and 15 * $10^3$m / s Also three regions of the propagation velocity of the plasma jet were identified: a region of acceleration, constant speed region and a region of deceleration, with different spatial distributions, depending on the configuration of the discharge electrodes.

5) Plasma dynamics in the vicinity of living tissue (finger) was studied using electrical, optical and spectroscopic diagnostics methods in order to simulate plasma-living organism interaction. Using fast photography was highlighted that there is a plasma formations in the immediate vicinity of the finger. Both spatial dimensions and life time in the vicinity of finger surface were determined. Duration of interaction values were determined to be between 10-16 μs and plasma-surface interaction sizes were found to range from 0.8 to 2.4 mm.

6) In order to monitor plasma-tissue (dead) animal interaction, studies have been conducted on the life time of plasma structure in the vicinity of animal tissue surface. Plasma dynamics in the vicinity of dead animal tissue (adipose, epithelial or muscle) was studied using electrical and spectroscopic methods. An important aspect of applicative point of view is that NO molecular emission bands appear only at plasma-animal tissue interface.

7) After plasma treatment of in microorganisms we observed an increase in the inhibition zone of colonies of Escherichia coli and Pseudomonas aeruginosa with increasing duration of treatment (20-100 s). Bactericidal effect of DBD discharge is attributed mainely to plasma reactive species.

8) Plasma jet was used to treat burned epithelial areas (wounds) performed on Wistar rat dorsal skin. These lesions were produced using chemical burn technique (sulfuric acid solution). Following plasma jet treatment experimentally was observed accelerated reepitelization of damaged skin compared to those who have been healed naturally. Using a plasma jet 40 s daily treatments the regeneration duration is halved compared to natural healing of skin burned wounds.

**Published articles:**

**1.** T. Gerling, **A. V. Nastuta**, R. Bussiahn, E. Kindel, K.-D. Weltmann, Back and forth directed plasma bullets in a helium atmospheric pressure needle-to-plane discharge with oxygen admixtures, Plasma Sources Sci. Technol., 21(3):034012; JUN 2012, 2 citations, i.f.: 2.521, a.i.s.: 0.843;

**2.** I. Topala, **A. V. Nastuta**, Helium atmospheric pressure plasma jet: diagnostics and application for burned wounds healing, Plasma for Bio-

Decontamination, Medicine and Food Security, Ed. Springer Netherlands, 335-345, ISBN:978-94-007-2852- 3; FEB 2012

**3. A. V. Nastuta**, I. Topala, G. Popa, ICCD imaging of atmospheric pressure plasma jet behavior in different electrode configurations, IEEE Trans. Plasma Sci., 39(11-1):2310-2311, NOV 2011, 1 citation, i.f.: 1.174, a.i.s.: 0.423;

**4. A. V. Nastuta**, I. Topala, C. Grigoras, V. Pohoata, G. Popa, Stimulation of wound healing by helium atmospheric pressure plasma treatment, J. Phys. D: Appl. Phys., 44(10):105204; MAR 2011, 3 citations, i.f.: 2.544, a.i.s.: 0.898;

**5.** C. Grigoras, I. Topala, **A. V. Nastuta**, D. Jitaru, I. Florea, L. Badescu, D. Ungureanu, M. Badescu, N. Dumitrascu, Influence of atmospheric pressure plasma treatment on epithelial regeneration process. Rom. J. Phys., 56(S):54-61; JUN 2011, i.f.: 0.414, a.i.s.: 0;

**6.** A. Poiata, I. Motrescu, **A. V. Nastuta**, D. E. Creanga, G. Popa, Microorganism response to atmospheric pressure helium plasma DBD treatment. J. Electrostat., 68(2):128-131; APR 2010, 3 citations, i.f.: 1.078, a.i.s.: 0.457;

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*Published articles off topic thesis:*

**1.** Crisan D., Dragan N., Raileanu M., Crisan M., Ianculescu A., Luca, D., **Nastuta A.**, Mardare D., Structural study of sol–gel Au/TiO2 films from nanopowders. Appl. Surface Sci., 257(9):4227–4231; FEB 2011, i.f.: 2.103, a.i.s.: 0.549;

**2.** Schrittwieser R., Ionita C., Murawski A., Maszl C., Asandulesa M., **Nastuta A.**, Rusu G., Douat C., Olenici S. B., Vojvodic I., Dobromir M., Luca D., Jaksch S., Scheier P., Cavity-hollow cathode-sputtering source for titanium films. J. Plasma Phys., 76(3-4):655–664; JAN 2010, 1 citation, i.f.: 1.078, a.i.s.: 0.305.

In the period October 2009-September 2012 I attended a total of 13 conferences nationally / internationally: 4 oral presentations and 9 poster presentations.

i.f.= impact factor; a.i.s.= absolute influence score

Selected bibliography :

[1] T. Gerling, A. V. Nastuta, R. Bussiahn, E. Kindel, K.-D. Weltmann. Plasma Sources Sci. Techn., 21(3):034012, 2012.
[2] A. S. Chiper, B. G. Rusu, A. V. Nastuta, G. Popa. IEEE Trans. Plasma Sci., 37(10):2098–2102, 2009.
[3] A. V. Nastuta, I. Topala, C. Grigoras, V. Pohoata, G. Popa. J. Phys D: Appl. Phys., 44(10):105204, 2011.
[4] A. Poiata, I. Motrescu, A. V. Nastuta, D.E. Creanga, G. Popa. J. Electrostat., 68(2):128–131, 2010.
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