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Atmospheric-pressure plasma sources: Prospective tools for plasma medicine*

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Abstract: Plasma-based treatment of chronic wounds or skin diseases as well as tissue engineering or tumor treatment is an extremely promising field. First practical studies are promising, and plasma medicine as an independent medical field is emerging worldwide. While during the last years the basics of sterilizing effects of plasmas were well studied, concepts of tailor-made plasma sources which meet the technical requirements of medical instrumentation are still less developed. Indeed, studies on the verification of selective antiseptic effects of plasmas are required, but the development of advanced plasma sources for biomedical applications and a profound knowledge of their physics, chemistry, and parameters must be contributed by physical research. Considering atmospheric-pressure plasma sources, the determination of discharge development and plasma parameters is a great challenge, due to the high complexity and limited diagnostic approaches. This contribution gives an overview on plasma sources for therapeutic applications in plasma medicine. Selected specific plasma sources that are used for the investigation of various biological effects are presented and discussed. Furthermore, the needs, prospects, and approaches for its characterization from the fundamental plasma physical point of view will be discussed.

Keywords: atmospheric-pressure plasma; barrier discharge; biomedical applications; decontamination; plasma jet; plasma medicine; sterilization; temperature; (V)UV-radiation.

INTRODUCTION

Recently, a new area for the application of plasma source operating at atmospheric pressures has emerged: biomedical applications [1–5]. During the last decade, the basics of sterilizing effects of plasmas were well studied [6–12]. Recently, therapeutic applications are of great concern. Existing plasma surgical technologies such as coagulation [13] or ablation [14,15] are mainly based on lethal plasma effects on living systems. But there is an additional huge potential of low-temperature plasmas for selective, at least partially nonlethal, possibly stimulating plasma effects on living cells and tissue [4,16–18]. For example, the plasma-based treatment of chronic wounds can enable a selective antimicrobial (antiseptic) activity without damaging the surrounding tissue, combined with a controlled stimulation of tissue regeneration. Other promising fields are tissue engineering, treatment of skin diseases, tumor treatment based on specific induction of apoptotic processes, or dental applications [18–22]. First practical applications are very promising, and a rapid growth of the new field of plasma medicine can be ex-

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pected. The emergence of plasma medicine as an independent medical field is comparable to the development of laser medicine years ago.

Therapeutic application of plasmas is not only a task for medicine; it is a challenge for plasma physics as well. Therapeutic applications of plasmas dictate the working in open air atmospheres and thus at atmospheric pressures. Adjusted plasma sources for different applications are required, and the proposed selectivity of plasma action implies a thoughtful control of the performance parameters of the plasma sources. This regards the treatment efficiency but also the potential risks connected with the direct plasma application at or in the human body. In particular, there are three tasks to fulfil:

1. the characterization of special biologic effects, e.g., antimicrobial efficiency, cell manipulation, or blood coagulation, including the estimation of specific adverse or toxic side effects in the close cell and tissue environment;
2. the assessment of risk factors such as gas temperature, power transfer from the plasma, UV radiation, radicals, electromagnetic fields as well as the generation of toxic gases and its release into the adjacencies which could be dangerous for patients or therapists; and
3. the profound understanding and knowledge of processes and physical plasma parameters in order to provide optimal tools for the achievement of specific effects.

To achieve selected effects and avoid certain risks, the plasmas must contain certain components in well-defined densities, and it is necessary to know how to control them by external operation parameters. Contrary nonthermal plasmas at atmospheric pressures are still a challenge for plasma diagnostic. Usually they are small-scale (due to the Paschen law with the pressure × distance scaling), constricted or filamentary (i.e., consisting of distinct microdischarges due to the streamer-breakdown process) and transient (due to high collision rates and quenching). Especially on open air an input of nitrogen, oxygen, and water, implying complex plasma chemistry, must be expected. A great deal of effort combining experimental investigation and modeling will be necessary to provide the required knowledge of plasma sources for therapeutic applications.

This contribution intends to give an overview of plasma sources for therapeutic applications in plasma medicine, confined to that one developed and used by INP Greifswald and its network partners in various projects. Therefore, this contribution does not demand completeness, since many other teams worldwide are working on this issue. Overviews on this can be found elsewhere [2,23–25]. After a general introduction in Section 2, selected specific plasma sources that are used for the investigation of various biological effects are presented in Section 3. The general "macroscopic" plasma characterization is demonstrated exemplary. The last section will discuss the needs, prospects, and approaches for the characterization of plasmas for biomedical applications from the fundamental plasma physical point of view.

OVERVIEW ON PLASMA SOURCES FOR THERAPEUTIC APPLICATIONS

Therapeutic applications require cold, nonthermal plasmas operating at atmospheric pressure. Three types of plasma sources are applicable for this issue, namely, barrier discharges (BDs), plasma jets, and corona discharges. So far, activities were focused on the first two types, which are schematically shown in Fig. 1.

BDs are characterized by the presence of at least one isolating layer in the discharge gap [26,27]. The classical configuration is the so-called volume BD (VBD), where one or two electrodes with an isolating layer form the discharge gap. The VBD enables direct treatment of the object to be treated, i.e., the object with stray capacity is the second electrode. Since the local current is limited by the capacity of the discharge configuration, a painless treatment is possible. Special configurations of the BD are the so-called surface discharge and the coplanar discharge. In a surface barrier discharge (SBD), both electrodes are in direct contact with the isolator. In this geometry, the plasma is formed around the electrodes on the isolator surface. In the case of the coplanar discharge, both electrodes are embedded in the

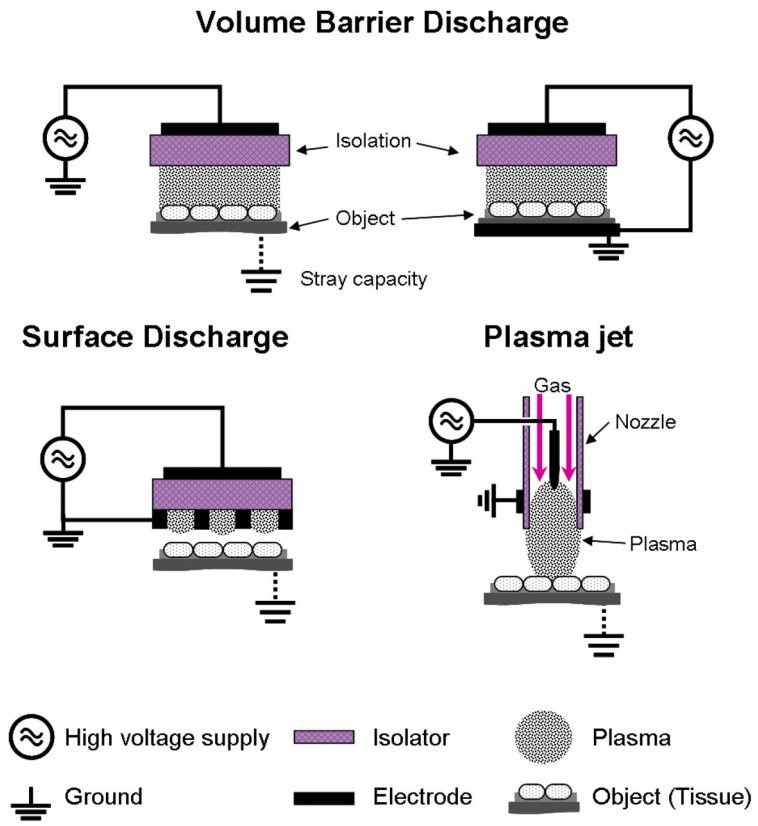

Fig. 1 Plasma sources suitable for therapeutic applications: BDs and plasma jets.

dielectric and the plasma is generated at the isolator surface, too. The same principle can be miniaturized in order to build up microplasma arrays [28–30]. All discharge types enable indirect treatment of wounds, skin area, or other objects, because they are not a distinct part of the discharge configuration.

Plasma jets consist of a gas nozzle applied with one or two electrodes. The plasma is generated inside the nozzle and transported to the object to be treated by a gas flow. There are numerous plasma jets available and described in literature [25]. They mainly differ in electrode configuration, type of gas, and frequency of applied voltage. In general, one must distinguish between remote plasma jets (i.e., the plasma is potential free and consists of relaxing and recombining active species from inside the nozzle) and active plasma jets (i.e., the expanding plasma contains free and high energetic electrons). In the latter case, the substrate must be considered as a second or third electrode, i.e., the plasma is not potential free. Plasma jets enable direct and indirect treatment. Especially from the point of practical manageability, atmospheric-pressure plasma jets (APPJs) are of special interest for medical applications. Their tool-like, small size, and light-weight plasma generation unit allows fast and almost arbitrary three-dimensional movement. They allow small-spot treatments, even of small-sized objects, as well as large-scale treatments by moving the jet over the selected area by applying several nozzles in an array.

SELECTED EXAMPLES OF PLASMA SOURCES

Atmospheric-pressure plasma jets

One of the first plasma jets used for biological decontamination was the so-called APPJ in helium by Selwyn et al. [31,32]. The so-called plasma needle was used for a broad range of biomedical applica-

tions, including tissue treatment, cell manipulation, and dental applications [19,33–39] by Stoffels et al. Another plasma jet which is recently used for numerous biomedical investigation is the APPJ (kINPen® 09) which is shown in Fig. 2. Recently, the device has got the CE marking, i.e., it fulfills the EU consumer safety, health or environmental requirements. It consists of a hand-held unit (dimensions: length = 170 mm, diameter = 20 mm, weight = 170 g) for the generation of a plasma jet at atmospheric pressure, a DC power supply (system power: 8 W at 220 V, 50/60 Hz), and a gas supply unit. The principal scheme of the plasma source is shown in the right part of Fig. 2. In the center of a quartz capillary (inner diameter 1.6 mm) a pin-type electrode (1 mm diameter) is mounted. In the continuous working mode, a high-frequency (HF) voltage (1.1 MHz, 2–6 kV_{pp}) is coupled to the pin-type electrode. The plasma is generated from the top of the centered electrode and expands to the surrounding air outside the nozzle. The whole system works with all rare gases (especially argon) with gas flow rates between 5 and 10 slm. Small admixtures (≤1 %) of molecular gases to the feed gas are possible. At maximal input DC power of 3.5 W to the hand-held unit, the ignited plasma jet has a length of up to 12 mm. Recent investigations have demonstrated that these types of jets are active plasmas, which operate in their "own" argon atmosphere. The use of N_2 and air is also possible by exchanging the nozzle of the device. An important advantage of plasma jets is its ability to penetrate into small structures with high aspect ratios [40], which is demonstrated in the top part of Fig. 3. This feature makes them interesting for the treatment of bodily parts with complex geometries and cavities, e.g., in operative dentistry. Furthermore, plasma jets can be arranged in arrays to adapt on special geometries [12]. In the bottom part of Fig. 3, plasma modules with ring-like mounted plasma jets for the outer treatment of cylindrical objects (e.g., wires, fibers, or catheters) are given as examples. A detailed characterization of the macroscopic parameters of the plasma jet and profound analysis of the main risk factors is given elsewhere [40–42]. Here, only the main facts shall be repeated.

The axial temperature profile of the plasma jet revealed plasma jet temperatures between 63 and 46 °C, dependent on power input and axial distance from the capillary nozzle if the device is operated with continuous high voltage and at a constant argon gas flow of 5 slm. The variable length of the visible plasma jet increases with the power input. At the tip of the visible plasma jet, temperatures have been measured more or less constant around 48 °C.

In order to make the APPJ applicable for therapeutic applications, it is operated in a burst mode, i.e., a constant period of HF voltage supply (plasma on) is followed by a break period (plasma off). By

Fig. 2 Atmospheric-pressure plasma jet (APPJ; INP Greifswald, Germany) for experimental biomedical applications (left: CE approved device; right: schematic set-up) [40].

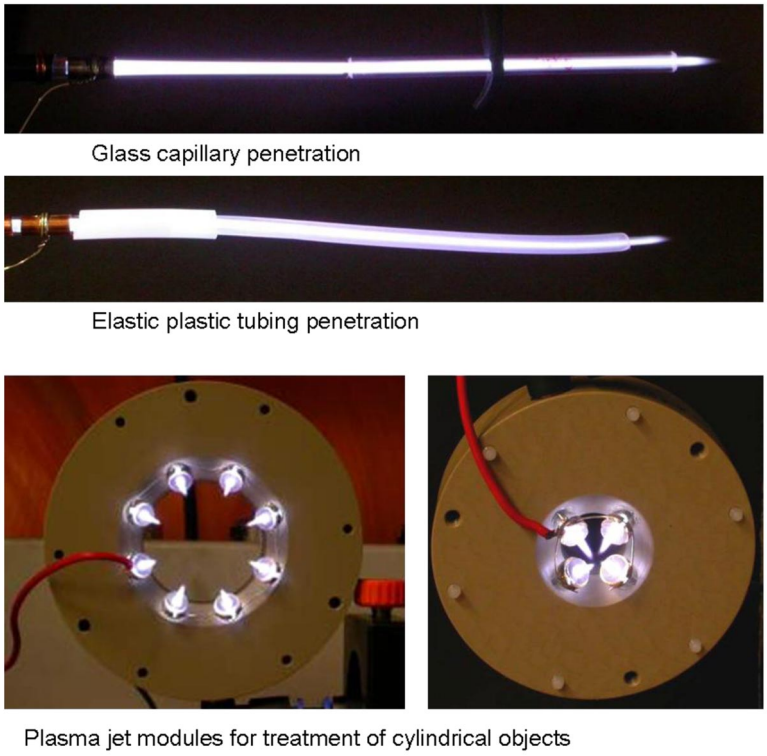

Fig. 3 Demonstration of plasma jet penetration into narrow cavities (top) and modularization for treatment of objects with complex geometries [12].

variation of the burst-to-burst interval, the temperature of the gas can be kept below 30 °C over the full length and, consequently, remains below the biological tolerance threshold. Axial power transfer profiles from the plasma jet indicate that the thermal output from the plasma jet onto the substrate decreases very strongly with increasing axial distance. At the visible tip of the plasma jet, there was found a relatively constant thermal power transfer between 145 and 160 mW, being only slightly dependent on input power. Temperature and thermal output measurements indicate more or less constant energetic conditions at the visible tip of the plasma jet. Therefore, the visible tip of the plasma jet can be used to adjust a general treatment distance.

Radiation emitted from the plasma contains molecular bands of OH-radical and lines of excited argon atoms between 500 and 1000 nm. In the UV-A region between 350 and 400 nm, bands of nitrogen emission have been measured because of increasing mixing of the feed gas argon with the surrounding ambient air. There was no detectable emission in the UV-C range between 200 and 280 nm. The plasma jet emits significant amount of VUV radiation, mainly the 2nd continuum of the argon excimer Ar_2^* between 120 and 135 nm. Since the plasma jet is operated in its own argon atmosphere, considerable amount of VUV radiation can reach the object to be treated [43]. The irradiance in the 260–360 nm UV range was about 5 mW/cm^2 at minimal distance of 5 mm and maximum power of 6 W. With increasing distance from the capillary outlet, drastic reduction of irradiance was detected reaching values between 1 and 2 mW/cm^2. Thus, UV-caused problematic side effects of the plasma jet can be avoided in principle. The absolute VUV radiance of the APPJ reaches maximum values of 2.2 mW mm^{-2} sr^{-1}.

Besides (V)UV and heat radiation, the plasma jet provides a mixture of charged and non-charged reactive species, above all reactive oxygen species (ROS) and reactive nitrogen species (RNS) and other

toxic gases. Maximum concentrations of ozone between 0.10 and 0.13 ppm have been measured in the close proximity of the plasma jet. More afar, ozone gas concentration did not exceed concentrations of 0.10 ppm. No measurable concentrations of nitrogen dioxide were found around the operating plasma jet.

Bactericidal activity of the plasma jet with different performance parameters are demonstrated in Fig. 4 [41]. Therefore, 50 µl of an overnight-grown liquid culture of *Eschericha coli* NTCC 10538 have been plated onto CASO agar plates containing phosphate buffer. 1 h after preparation, a circular area of 2.8 cm in diameter has been treated by the APPJ (power 3 W; argon gas flow 2 slm) for 45 s one or two times, respectively. The APPJ was moved following meandric pattern, and the agar surface was fixed in that way, that the tip of the visible plasma jet touched the agar surface. After plasma treatment, the agar plates have been cultivated for at least 18 h at 35 °C. As shown in Fig. 4, a circular contaminated area of about 6.2 cm^2 resulted in significant reduction of colony-forming units (CFUs) compared to the non-treated area. Nearly the same result was found by treating the same area but using the burst mode with a burst-to-burst interval of 100 µs. However, after a single burst-mode treatment, minor bacteria inactivation was found, whereas treating three times resulted in a complete decontamination of the treated area. Consequently, the burst-mode performance of the plasma jet can reduce the temperature load of the target without loss of biological, in this case, antimicrobial activity.

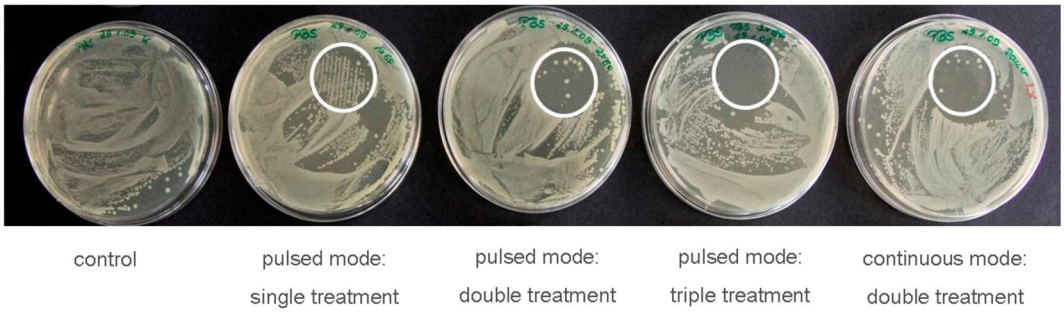

Fig. 4 Results of antibacterial treatment of *E. coli* on agar using different APPJ working modes as well as different treatment times [40].

SBDs for indirect application

SBDs and coplanar (barrier) discharges are useful for indirect treatment of surfaces and other objects, since the complete electrode design can be incorporated in a single component [44,45]. The plasma device can be brought in closed contact to the object to be treated (distance electrode and object about 0.5 mm and more). The object is not a part of the electrode arrangement and thus is not influencing the discharge by its stray capacitances. However, it is unclear which plasma species are able to reach the object. In molecular gases at atmospheric pressure, collisional quenching is a significant loss process and transient species react with the background gas very fast. However, significant antimicrobial effects by indirect plasma treatment using SBDs have been investigated [46].

To investigate the effects of indirect plasma treatment for biomedical issues, the following discharge devices based on SBDs have been developed. Circuit boards consisting of epoxy-glass fiber bulk material are very useful for the set-up of SBD electrodes. With a thickness of 1.5 mm and a breakthrough voltage of at least 40 kV/cm, it is suited as barrier material [46,47] while different electrode shapes can be realized by conventional etching of the copper film (35 µm thickness). An electrode made of a circuit board (size 10 × 16 cm) used for the treatment of test strips is shown in Fig. 5, top. The line-like electrode on the top of the dielectric material consists of 0.6-mm-wide lines 4 mm apart from each other. This is the high-voltage part of the electrode system. At the back side, the grounded electrode is

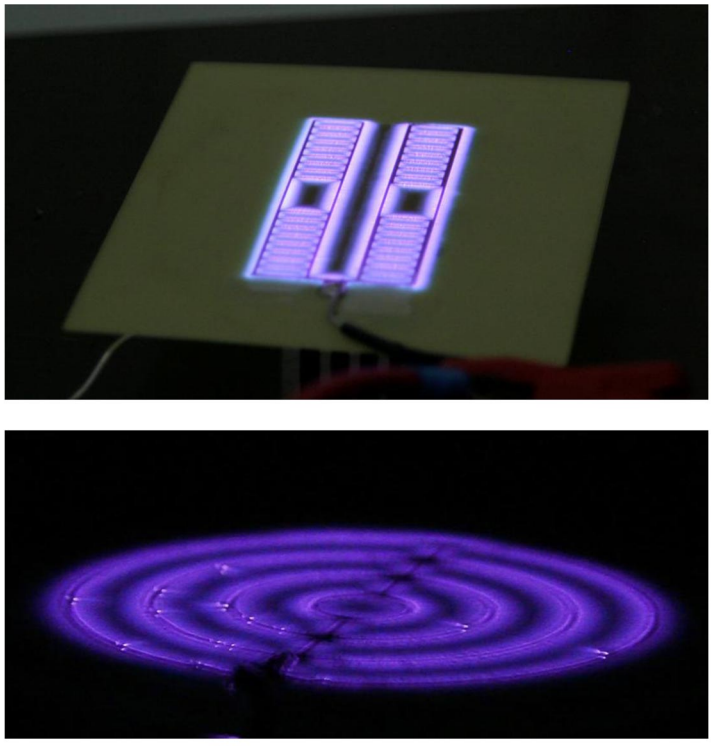

Fig. 5 Various surface discharge electrodes made of circuit board materials for indirect plasma treatment of test strips, liquid samples, cell samples, etc. [46,48].

directly situated beneath the line-like part and has the same outside dimensions. This electrode had no structure and was extended. To get a controllable environment, the electrode arrangement can be placed in a gas-tight chamber. The reduction of microorganisms placed on test strips (polyethylene, plate size 33×8 mm^2) by plasma have been tested using spores of *Bacillus atrophaeus*. The test strips were placed on spacers above the structured electrode.

For the treatment of liquids, the set-up shown in Fig. 5, bottom, was used. In this arrangement, the high-voltage surface electrode array had a line-like structure consisting of four concentric rings (0.75-mm wide). The diameter of the outer ring was 35 mm, distances between the ring-shaped electrodes were 3 mm each. On the other side of the dielectric, a 35-mm-diameter round nonstructured flat copper surface served as grounded electrode. This electrode array was mounted by a special construction into the upper shell of a petri dish (diameter 60 mm) in that way that the distance between the high-voltage electrode surface and the surface of the liquid sample in the lower shell of the petri dish can be adjusted between 2 and 5 mm [48].

The plasma of the SBD can be intensified and controlled by various gas atmospheres. If the gas is injected via the electrode configuration, it will pass the plasma zone more or less completely. Configurations and examples of the realization of such approach are shown in Fig. 6. The carrier gas is injected via the perforated ground electrode. Directly on the perforated electrode, a single electrode or an array of electrodes, which are surrounded by isolating layer, are mounted. The direct gas injection enables the generation of nonthermal plasma which can be moved over an object in closed contact. To drive the plasma in such configurations, any ac or pulsed high voltage with appropriate amplitude and power can be used. To characterize BDs, the measure of the dissipated energy per pulse or cycle of the high voltage and thus the dissipated power is a standard method [49,50]. Therefore, the applied voltage must be measured with a high-voltage probe connected to an oscilloscope. Furthermore, either a shunt

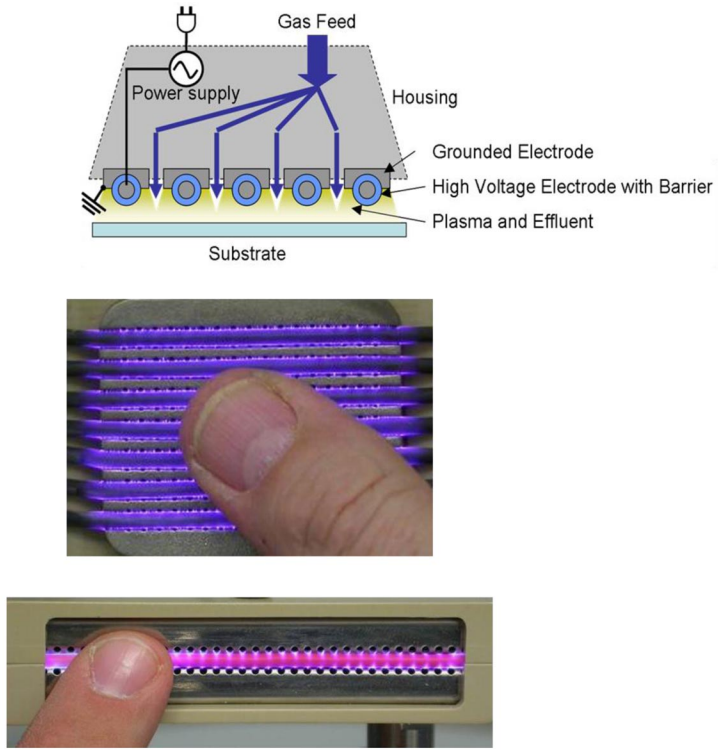

Fig. 6 SBD electrodes with direct carrier gas support for generating mobile contact plasma.

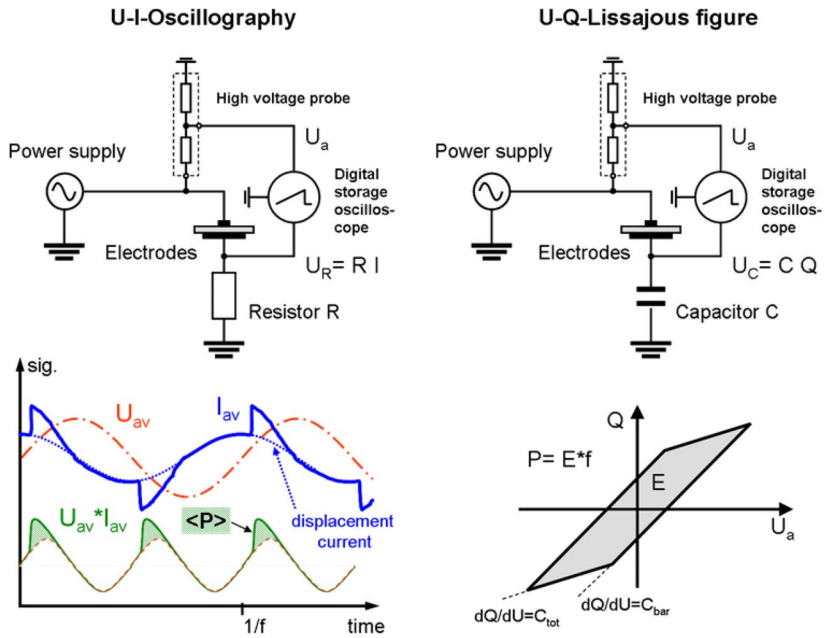

Fig. 7 Methods to determine the dissipated energy and power into a barrier or surface discharge arrangement (U_a – applied voltage; f – frequency of applied voltage; I – current; Q – charge, E – energy per cycle; P – power).

or a capacitor must be implemented between the grounded electrode and the grounding point (see Fig. 7). The voltage measured across the shunt is proportional to the discharge current. Modern oscilloscopes with appropriate band width and sampling rate enable averaging of the current and voltage curves (see Fig. 7, left, bottom). Averaging the product of current and voltage determines the mean power <P>. If the plasma is not ignited, the current will consist of the displacement current (sinusoidal if applied voltage is sinusoidal) and the mean power will be zero. If the plasma is on, the active discharge current will be measured additional to the displacement current and the dissipated power into the discharge is determined. The more precise method is the so-called voltage-charge Lissajous figure (Fig. 7, right), since it is independent of the parameters of the oscilloscope. Furthermore, it is better suited for pulsed applied voltages. The charge dissipated into the plasma is measured via the voltage across the capacitor, which must be larger than the capacities of the electrode configuration. The charge Q is the integral of the current. If applied voltage and charge are plotted in the x–y diagram, a straight line with the slope corresponding to the total capacity of the electrode configuration will be investigated in plasma-off mode. In plasma-on mode, a parallelogram will be generated (see Fig. 7, right, bottom). The area of the U-Q-Lissajous figure is the dissipated energy per cycle of the applied voltage [26,27,49].

An example of application of the Lissajous figure method on surface discharge electrode described above (Fig. 5, top) is shown in Fig. 8. From the Lissajous figure (discharge driven by sinusoidal ac voltage), the electrical parameters, total electrode capacity C_{tot}, and capacity of the dielectric material C_{bar}, can be determined. Using these capacity values and assuming that the gas capacity and the capacity of the dielectric barrier are in series, the capacity of the discharge volume can be estimated to be 112.5 nF for this configuration. The encircled area of this plot obtained by integration is equal to the dissipated energy per period, which is about 3 mJ in this case. Referring to an active discharge area of 12 cm^2 and the used pulse pattern with 250 ms plasma-on time, the maximum power consumption is 650 mW, which is equal to 54 mW/cm^2. Compared to other plasma sources, this value is very small. Therefore, the temperature of the electrode and sample are close to room temperature and did not exceed 30 °C.

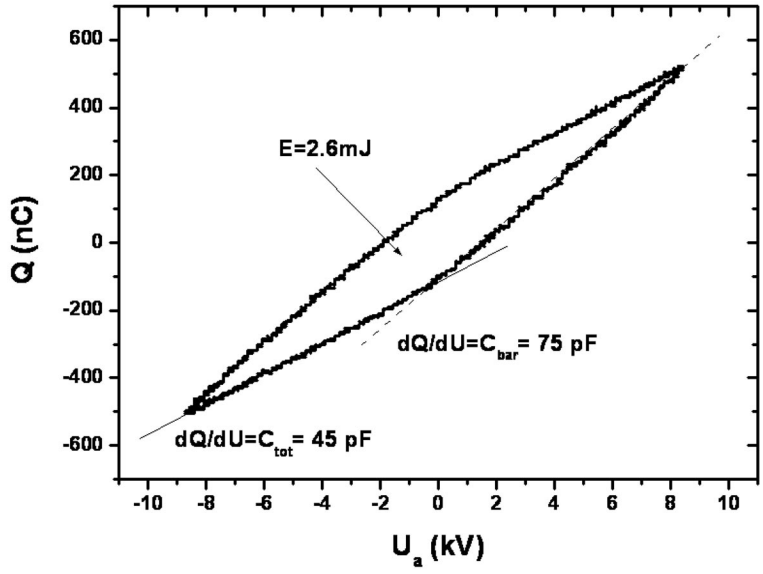

Fig. 8 Dissipated energy and capacities of SBD plasma and electrode, respectively, measured by Lissajous figure [46].

The optical emission in the range from 250 to 450 nm (see ref. [46] for details) is dominated by the molecular bands of the second positive system of nitrogen (between 300 and 400 nm), as already observed for VBDs and SBDs. The emission intensity was found to depend on the relative air humidity and decreases with increasing humidity levels due to quenching processes. This decrease can be explained by lowering the number of microdischarges with rising humidity and thus higher electrical conductivity of the air. For the selected process parameter and gas composition, neither lines from excited OH in the region from 308 to 310 nm nor significant emission below 290 nm were investigated. While there is no emission in the UVC–C range, the antimicrobial effects obtained in this configuration cannot be caused by UV photons.

The power generator for the antimicrobial treatment was a Fourier synthesis pulse generator with maximum output voltage amplitude of 10 kV. The repetition rate of the alternating pulses was 2 kHz. To keep the process in maximum 5 °C above room temperature the plasma was pulsed with 1 Hz with at most 500 ms plasma-on time. These values were also used in [46]. Significant antimicrobial effects were carried out. In particular, a distinct correlation of the reduction of spores on the humidity level of air was found in agreement with punctual studies reported in literature [51]. In dry air, no reduction was found, at 70 % relative humidity all spores were deactivated within a treatment time of 2.5 min. Higher plasma power leads to higher killing rates of the microorganisms. The plasma power can be influenced by, e.g., longer duty cycles, higher working frequencies, changing the properties of the dielectric material, and increasing supply voltage.

Indirect plasma treatment of liquid volumes up to 10 ml leads to significant decontamination of liquids. However, as it was reported by other authors, too, antimicrobial plasma effects were clearly accelerated if liquid pH decreased as a result of plasma treatment. But acidic conditions alone did not result in comparable inactivation of bacteria. Photometric detection of nitrate and nitrite concentrations as well as comparison with liquid treatment by NO gas suggested the conclusion that acidification is mainly a result of the generation of nitric acid induced by RNS like NO from the plasma phase. However, for antimicrobial activity additional action of ROS must be considered. This was supported by the finding of increasing H_2O_2 concentration as a result of indirect SBD plasma treatment but not of NO gas treatment. For further clarification of detailed plasma–liquid interactions leading both to acidification and antimicrobial activity, much more detailed plasma diagnostics as well as liquid analytics have to be done. In particular, the determination of reactive species and stable molecules in the plasma phase is necessary. Furthermore, the corresponding concentrations must correlate with concentrations of species emerging in the liquid phase as a result of plasma treatment. The study of plasma–liquid interactions and subsequent chemical reactions in the liquid phase are necessary to get further insights in plasma interactions with living systems which are mediated to a great extent by plasma interactions with physiologic liquids. Therefore, research in plasma–liquid interactions will become an important field of basic research in plasma medicine, too [48].

Barrier discharges for direct application

Direct application of VBDs for skin and wound treatment has been demonstrated by means of so-called floated electrode BD plasma [2,18,24,52–55] by Friedman et al. This plasma source has demonstrated its ability for living tissue sterilization, blood coagulation, and promotion of apoptotic behavior in melanoma skin cancer cells among others. Here, another novel approach for the direct BD treatment of microbiological samples is presented, the so-called hollow electrode BD (see Fig. 9). The system has been developed for the treatment of samples (dielectric of metallic as in Fig. 9) placed in well microtitre plates. Since well plates are made of dielectric materials they can serve as the barrier in a VBD arrangement. Therefore, well plates are placed on the grounded electrode, which was cooled by a Peltier-element in order to control the temperature of the objects to be treated. Hollow and thin metal tubes serve as high-voltage electrodes and gas injection pipes in one function. Two columns of the well-plate remain untreated for control samples. Different gases can be used, but first studies are focused on argon

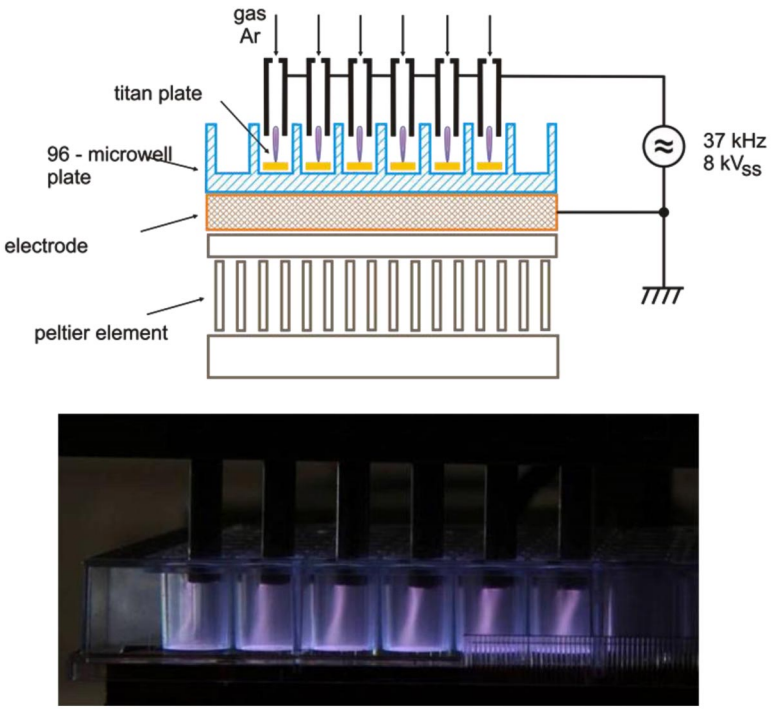

Fig. 9 Hollow electrode VBD for the treatment of samples in microtitre well-plates.

as carrier gas. Indeed, such an arrangement cannot be used for the treatment of living objects, except microorganisms on test strips, but enables a treatment under defined conditions with a profound electrical characterization based on the methods described in the previous sub-chapters. This will be a part of future investigations including the biomedical investigations.

THE CHALLENGES FOR PLASMA RESEARCH AND POSSIBLE PROSPECTS

In most gases (e.g., air and argon) and discharge configurations, a BD is filamentary, i.e., the plasmas consist of a number of constricted microdischarges visible as discharge filaments [56,57]. A filamentary character can be investigated for several plasma jet arrangements, too [12]. Microdischarges can be interpreted as tiny plasma reactors that act independently from each other. The coaction of many, more or less identical microdischarges determines the characteristics of the plasma. Experimental and theoretical study of BDs in air and oxygen has a long tradition connected with their wide use in industrial ozone generation [26,57]. The diagnostics of BDs started in the 1930s with electric measurement of the discharge properties by means of oscilloscopes, as described and demonstrated in the previous section. Since it is hard to carry out any experiment on filamentary plasmas, much effort has been devoted to computer simulations describing the microdischarges development. In the 1980s, first measurements of single microdischarges current pulses and of the transferred charge were realized and the application of optical streak cameras allowed first insights in the development of microdischarges in air [44,58]. Numerous integral measurements in different gases using the "classical" emission and absorption spectroscopy enabled the estimation of the molecular temperatures (e.g., of the rotational temperature which is often taken as a measure for the gas temperature) as well as the investigation of excited and metastable species together with the basic elementary processes. The determination of the spectrally and spatiotemporal resolved luminosity from erratically distributed microdischarges succeeded by the

technique of cross-correlation spectroscopy [59]. Many activities focused on the investigation of the Stark effect in BDs and make use of laser-induced fluorescence (LIF) and intensified charge-coupled device (ICCD) camera measurements. Such investigations allowed the estimation of the electron density, the electric field strength as well as of the spatial-temporally resolved detection of atoms (see [57] and references therein as well as [60]).

The diagnostics of plasma jets is a fairly new issue, since they are rather novel types of plasma generation. Due to the fact that many different plasma jets exist, the situation is much more diverse than for BDs. Electrical characterization, short-time photography by means of ICCD cameras and optical emission spectroscopy (down to the VUV region) were intensively used (see [25] and references therein). For selected plasma jet configurations, laser diagnostics (LIF) was used [61]. An important milestone in the investigation of plasma jets was the discovery of so-called plasma bullets [62–66]. I.e., plasma jets in noble gases (helium and argon) turned out to consist of continuous trains of small point-like plasma packets, moving with velocity orders of magnitude larger than the gas flow velocity. Under these conditions, the plasma jet dynamics is mainly controlled by the electrical field, which is not only determined by the electrode configuration. Stray capacitances of the substrate and the periphery can act as additional electrodes. The results on plasma bullets reveal many similarities with so-called streamers, but there are more investigations necessary to enable comprehensive understanding of the nature and parameters of plasma bullets. Although the above-mentioned experimental techniques allow spatially, temporally, and spectrally resolved measurements, the densities of relevant reactive species as well as the local basic plasma parameters have been determined under selected conditions, which are sometimes beyond the situation in a therapeutic application. This regards in particular the gas mixtures and the influence of the treated object on the plasma. Numerous efforts are necessary to provide profound data and description of the plasma itself as well as the interaction with the treated objects. The application of modern diagnostics sometimes requires the abstraction of the practical treatment situation. But if the experiments are performed under well-defined conditions, the results can be projected, thus being helpful to characterize and optimize the process.

CONCLUSIONS

The challenging biomedical applications of plasmas (e.g., in dermatology, dentistry, surgery, cosmetics, etc.) require atmospheric-pressure plasma sources which are meanwhile available in many different designs and configurations. This paper has given numerous examples of plasma sources used by INP Greifswald and network partners, but many other teams worldwide are working on this issue, too. Clearly, there is a need for standard parameters to compare the efficacy of these sources regarding different applications. In this context, experimental conditions—such as the vital environment and microbiological test procedures—have to be documented carefully.

The physicists and engineers have made the first step in the field of plasma medicine, but physicians have (sometime) to take over the lead. The contributions of physicist and engineers will then exceed the supply of advanced plasma sources. Great efforts are necessary to characterize and understand the plasmas (qualitatively and quantitatively), which is a challenge on it's own regarding nonthermal atmospheric-pressure plasma sources.

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