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Cold atmospheric pressure air plasma jet for medical applications

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By flowing atmospheric pressure air through a direct current powered microhollow cathode discharge, we were able to generate a 2 cm long plasma jet. With increasing flow rate, the flow becomes turbulent and temperatures of the jet are reduced to values close to room temperature. Utilizing the jet, yeast grown on agar can be eradicated with a treatment of only a few seconds. Conversely, animal studies show no skin damage even with exposures ten times longer than needed for pathogen extermination. This cold plasma jet provides an effective mode of treatment for yeast infections of the skin. © *2008 American Institute of Physics*. [DOI: 10.1063/1.2940325]

In recent years, several devices have been presented that were able to generate a cold plasma plume at atmospheric pressure in air. Different designs have been investigated for their ability to treat heat sensitive surfaces and for prospective use in medical applications. Stoeffels *et al.*[1] developed a device generating a plasma which extends to about 1 mm around a needle electrode. A plasma plume of about $1-2$ cm length can be obtained in a design by Foest *et al.*[2] Another arrangement, with a 5 cm long plasma jet was recently presented by Laroussi and Lu.[3] Shin *et al.*[4] developed a plasma needle of $2-5$ cm length, while Cheng *et al.*[5] presented a $1-2$ cm long plasma jet with a temperature of $20-30$ °C. Another arrangement, generating a 6.5 cm long plume and notably operated in nitrogen, was presented by Hong and Uhm.[6] Another nitrogen operated device that generates a $1-2$ cm plasma jet was described by Dudek *et al.*[7] Other plasma torches have also been developed for plasma processing and decontamination of surfaces or semiconductor manufacturing applications at atmospheric pressure. However, these are generally running at temperatures too high to be considered for use on human tissue or any material with low melting point.[8–14]

All but one of the above plasma sources are either operated with radio frequency high voltages of several kilohertz up to several megahertz, or pulsed high voltages applied with repetition rates in the kilohertz range. Only in the configuration of Dudek *et al.* is a direct current applied to generate the plasma. Moreover, with the exceptions of Hong and Uhm's arrangement[6] and the setup used by Dudek *et al.*[7] the operation with a noble gas is required to ensure the stability of the plasma at high pressure. In all these units air is only incorporated from the jet's periphery, accounting for the air admixture to be only a few percent. The biological efficacy of the plasma flow is usually attributed to reactive species such as hydroxyl groups and atomic oxygen, and the use of atmospheric air rather than noble gas greatly enhances their generation. In addition, the operation with ambient air considerably reduces the complexity of the system. However, for direct current operation in atmospheric pressure air, glow discharges are prone to filamentation and will eventually transition into an arc.[15] A way to overcome that problem is using microdischarge geometries. By confining the glow discharge in a hollow cathode geometry with dimensions on the order of 1 mm, a stable discharge can be generated by means of a dc high voltage source.[16–18] This confinement allows the sustainment of a high pressure air dc glow discharge with gas temperatures in the range of 2000 K[19] but electron energies estimated in excess of 10 eV.[18,20]

We were successful in generating a plasma (afterglow) jet in this microhollow cathode geometry by operating it at atmospheric pressure with and into ambient air by utilizing the concept of microhollow cathode discharges.[21] The setup is shown in Fig. 1. A discharge channel through an insulator with a thickness of about $0.2-0.5$ mm and a diameter of $0.2-0.8$ mm separates anode and cathode. A hole with the same diameter in the cathode opens the discharge to ambient air. Air or any other operating gas is ejected from the anode side through the discharge canal. When a dc voltage of $1.5-2.5$ kV is applied between anode and cathode (depending on the thickness of the insulator separating the electrodes), breakdown is initiated in the gap between the electrodes. Subsequently, a glow discharge is sustained at voltages of $400-600$ V with the current limited to 20 mA by a ballast resistor of 51 kΩ. (The current can be decreased, for example, by increasing the value of the ballast resistor. A stable discharge can be sustained for currents as low as
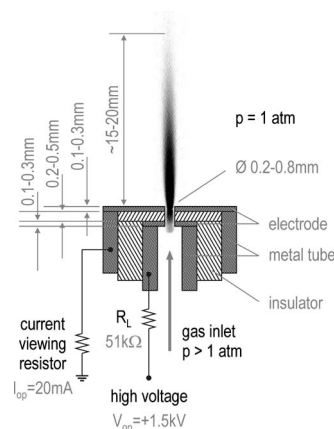

FIG. 1. Schematic of discharge geometry and electric circuit overlaid an actual negative image of the plasma jet.
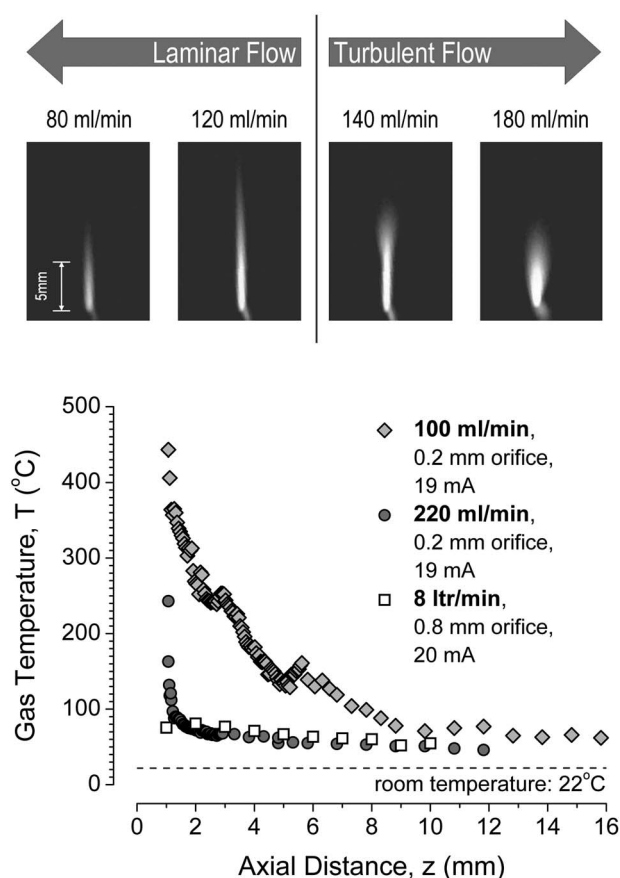
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FIG. 2. The upper section shows images of the expelled afterglow plasma plume, which demonstrate different flow characteristics. For a flow rate of about 140 ml/min the exhaust stream changes from laminar to turbulent. The lower section shows corresponding gas temperatures along the plasma plume. For turbulent flow rate conditions, temperatures decrease to values close to room temperature within a few millimeters.
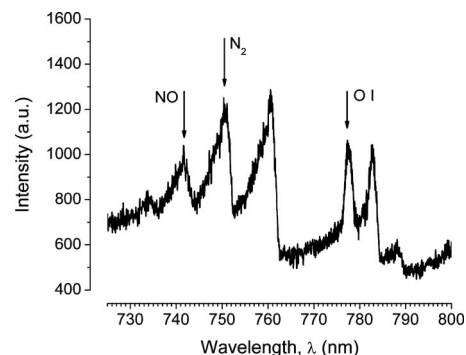

FIG. 3. Emission spectrum close to infrared wavelengths recorded for the operation of the discharge with ambient air, showing lines and bands for reactive species such as atomic oxygen at 777.2 nm and nitric oxide at 742.0 nm.

2 mA.) Accordingly, a power of less than 10 W is dissipated in the plasma while most of the power supplied by the power supply in the current setup is dissipated in the ballast resistor. For use as a handheld device, we placed the microhollow cathode assembly on the end of two metal tubes separated from each other by a third insulating tube, as shown in Fig. 1. For practical use and safety it is easiest to ground the outer tube and apply high voltage to the internal electrode, shielded from accidental contact. The inner tube also serves as the conduit for the gas flow to the discharge. For diameters of the discharge canal of less than 1 mm, the discharge is stable and the discharge current can be controlled by adjusting the applied voltage and gas flow. The gas flow also provides an effective cooling mechanism for the discharge plasma. For flow rates on the order of 8 l/min, this cooling effect allows the use of easily machineable electrode materials such as brass and insulators made from polytetrafluoroethylene or acetal. For these conditions, we could continuously operate the discharge for 3–4 h/day for a week without changes in the electrical discharge parameters.

The temperature in the ejected plasma and afterglow plume depends on current and on the gas flow characteristics. For small flow rates, a laminar flow can be maintained through the orifice, as shown in Fig. 2, corresponding to rather high temperatures close to the nozzle (Fig. 2, lower section). With increasing flow rates the flow eventually becomes turbulent. In this regime, eddies are mixing the hot exhaust stream with cold ambient air, thereby effectively reducing the heavy particle temperature. The flow for our electrode, gas, and discharge conditions remains laminar up to a critical Reynolds number of 100 and becomes turbulent for a numbers exceeding 300. The estimate has to take into account changes of gas viscosity and density with temperature, which are difficult to accurately assess for a change of several hundred degrees in close proximity to the nozzle. In our microhollow cathode geometry (with the flow through an orifice of less than 1 mm), laminar flow conditions for a discharge channel of 0.2 mm correspond to a flow rate of 120 ml/min and for a hole of 0.8 mm, to a ten times higher flow rate. The images presented in Fig. 2 show the transition from laminar to turbulent flow for a discharge channel of 0.2 mm in diameter. The related measurements in Fig. 2 document how the change in flow characteristic affects the change in temperature with distance from the cathode. As seen in the lower section of Fig. 2, for flow rates of 220 ml/min the jet approaches room temperature for distances exceeding 5 mm. Even at distances of 5 mm from the nozzle, gas temperatures do not exceed 55 °C (328 K).

The plasma or afterglow jet with a 1−2 cm (visible) length, contains charged particles as well as radicals. Due to recombination and attachment, the electron density rapidly decreases with distance from the nozzle. Negative and positive ions will be found at larger distances from the nozzle due to their lower recombination rate. Excited species and reactive species will survive longest and can interact with materials at a distance of up to a few centimeters, depending on the lifetime of the radicals. To identify reactive species that are generated in the discharge and subsequently expelled with the gas flow, spectra were recorded for emission along the axis of the jet in the range from 200−850 nm with a half-meter spectrometer (Acton Research Spectra Pro 500i). A near infrared section of the spectrum is presented in Fig. 3. It shows, in particular, contributions from atomic oxygen (OI $^5S^0$-^5P, 777.2 nm), as well as emission of some other reactive oxygen compounds.[22,23] These highly reactive species are considered to be the most effective agents in attacking cells or organic material in general.[24–26] In addition to these primary discharge products, high concentrations of ozone are measured as a result of various secondary reactions. With a half-life of several hours or even days (depending on temperature and humidity), this radical is well known as a disinfecting agent. By itself, the generation of ozone as a sec-
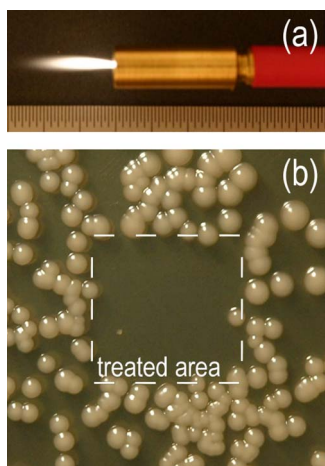
FIG. 4. (Color online) (a) Afterglow plasma jet generated with an air flow rate of 8 l/min. The plume is extending to about 1.5 cm. (b) Yeast inoculated agar plate shown was treated with this afterglow plasma jet across a 1×1 cm^2 area. The exposure at a distance of 1 cm for 90 s completely removed the fungus.

ondary reaction product is indicative of high concentrations of precursor species, such as O, OH$^-$, and NO$^-$. Excited species responsible for the glow can be observed up to a distance of 1.5–2 cm. Above 2 l/min the extent of this luminous plume is virtually independent of the flow rate. In general, this length is indicative of the distance many reactive species can extend into the ambient atmosphere. In measurements with an air ion counter (20 Million Model, Alpha Lab, Inc.) we found that high concentrations of negative and positive air ions can be observed beyond the immediate range of the plasma plume, up to a distance of several centimeters from the nozzle. Previous studies found that these long-lived compounds are very effective bactericidal agents.[27]

In studies on the plasma jet efficacy, we have been focusing on yeast. Yeast infections are known to be notoriously difficult to treat by topical methods. The strain *Candida kefyr* was cultured on agar (Sabouraud's dextrose agar) in a 100 mm petri dish. A 1 cm^2 area of inoculated agar was exposed to the plasma expelled with an air flow rate of about 8 l/min, at a distance of 1 cm from the discharge. Under these conditions, the afterglow plume has a visible length of 1.3 cm and a temperature of 45 °C at the treatment distance. A picture of the microjet is shown in Fig. 4(a). The exposure was controlled by stepper motors, which moved the microjet across an area of 1 cm^2 with a speed of 0.5 mm/s in a crisscrossing pattern in increments of 0.5 mm between passes. Accordingly, the total treatment time was 90 s during which the plasma passed over every point twice. As the image in Fig. 4(b) demonstrates, the fungus is completely removed in the exposed area, whereas a control exposure, i.e., only flowing the air without starting the discharge, has no effect.

Animal studies show that the exposure of healthy skin to the plasma jet, when using the same treatment parameters for the *in vitro* studies, and even a treatment with a ten times higher "dose" (ten identical exposures of 90 s), did not result in any damage. The results were obtained on hairless SKH-1 mice (IACUC approved). Biopsies were taken 1 and 5 days after the treatment to assess damage. The treatment did not inflict any thermal injuries[28,29] and histology on the samples did not show any difference between treated and untreated cells.

In summary, the studies prove that the use of direct current microhollow cathodes discharges to generate an atmospheric pressure air plasma, and turbulent flow used as cooling mechanism, allows us to generate a simple, but effective system for fungal decontamination on sensitive surfaces such as mammalian skin. This "microplasma jet" therefore offers an effective method to treat yeast infections on skin. It is reasonable to assume that similar effect can be obtained on other microbes and possibly even viruses. The major advantage is that healthy cells do not seem to be affected, while pathogens can be eradicated.

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