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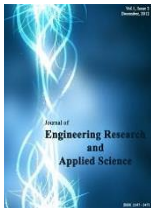

Medical applications of plasma technology

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Abstract
The use of plasma technology is a new field of study that combines life sciences and clinical medicine. The medical application of the physical plazma can be basically examined in two parts. These applications involve the indirect use of plasma-based or plasma-assisted techniques and the direct interaction of the plasma with living tissue. Plasma medicine basically explores the use of plasma technology in the treatment of living cells, tissues and organs. Efforts to use plasma technology for medical purposes, either directly or in the human body, have been intensified. In the fields of cancer therapy, endoscopy, dentistry and dermatology, plasma technology is used for medical purposes. Although the area of plasma medicine is very new and in the developmental stage, it has a great economic potential. Medical authorities need a based on the potential prediction of the plasma source to determine whether the plasma source is suitable for medical applications or biological experiments.The main purpose of this study is to give information about the applications of plasmatic medicine, the determination of the suitability of plasma source for medical applications and the possible interaction mechanisms between plasma and living cells. In addition, the basic principles of plasma technology and its theoretical background are given in detail, and the potential and feasibility of using this technology in medicine has been discussed and summarized.

Keywords: Plasma medicine, non-thermal plasmas, medical application, plasma sources.

1. Introduction

Physical plasmas are induced ionized gases containing atoms, ions and molecules at different concentrations. The ionosphere, polar lights, lightning, sun and all stars are examples of natural plasma. In laboratory conditions, plasma can be obtained by applying electrical energy such as heat energy, chemical energy and nuclear energy to the substance, or by bombarding the substance with particles such as electrons, photons, etc. Plasmas produced in this way are used to produce faster, cheaper and higher quality products in the field of industrial engineering due to the production of high temperatures and different energetic particles [1], [2].

Plasmas can be classified with different plasma parameters such as weakly ionized plasmas and high ionized plasmas, or low pressure plasmas and high pressure plasmas However, the most general classification is based on whether the temperatures of the particles in the plasma are in thermal equilibrium [2-4]. Plasma in which all the particles in the plasma are at the same temperature is called as thermal plasmas and is used in applications where high temperatures are required. The sun, stars and arc discharges are examples of thermally stable plasmas.

Plasmas that can have their electrons at very high energies while other particles at low temperatures are called as nonthermal plasmas. Since the neutral particles of these plasmas do not produce a heat effect at low temperatures, they have significant advantages in heat sensitive applications. Ionosphere from natural plasmas and many gas discharges from laboratory plasmas are examples of non- equilibrium plasmas [3-5]. Most of the energy is preserved as the industries that use plasma energy greatly increase the efficiency of energy consumption. Due to many important advantages, plasmas are widely used in the industry. In Figure 1 were shown the industrial application areas of plasma technology [4].

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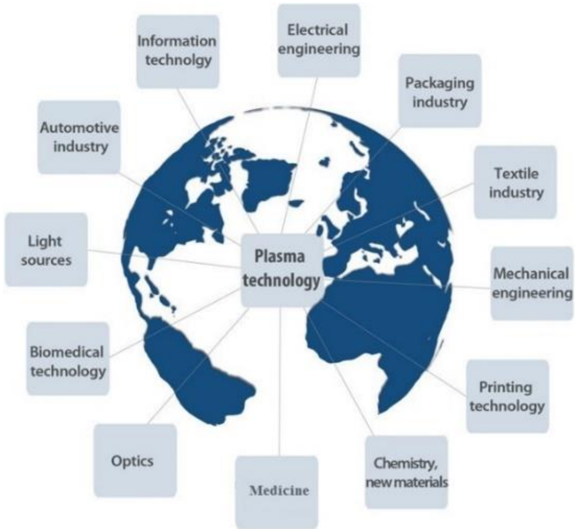

Figure 1. Industrial applications of plasma technology.

Plasma medicine is a new field that combines plasma physics, life sciences and clinical medicine. Plasma technology is widely used in cancer treatment, endoscopy, dentistry and dermatology. It uses physical plasma for medical uses [1]. The plasma source used for plasma medicine is usually cold (non-thermal) plasmas. Cold plasmas are used for various bio-medical applications [3-6].

2. Plasma Resources

Plasma sources used in plasma medicine are non-thermal (cold) plasma sources that are operated at atmospheric pressure. The resources used in plasma medicine are generally divided into two parts.

- Dielectric Barrier Discharge (DBD)
- Atmospheric Pressure Plasma Jets (APPJ)

A. Dielectric Barrier Discharge (DBD)

Dielectric Barrier Discharge (DBD) is cold plasma source that limit current using a dielectric containing one or two electrons. Conventional DBD include two planar electrodes coated with at least one dielectric material, and the electrodes are separated by a small gap called the discharge gap. In Figure 2 were shown the structure of the DBD device

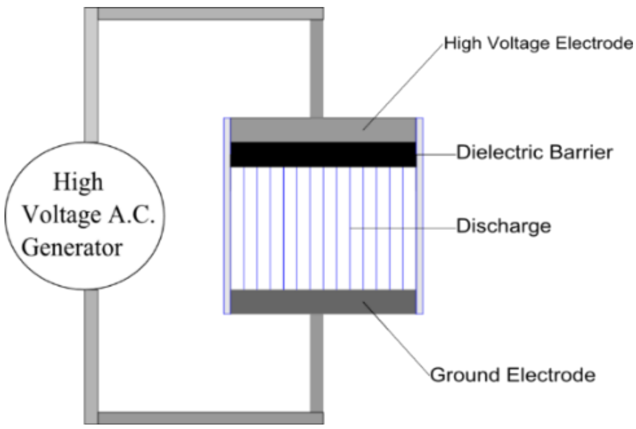

Figure 2. Typical construction of DBD device.

Dielectric barrier discharges are usually induced by high AC voltages with frequencies in the kHz range. For medical application of DBDs, the human body can serve as one of two electrodes, a system capable of designing plasma sources consisting of only one electrode coated with a dielectric. DBDs are used for medical applications such as bacterial inactivation, treatment of skin diseases and wounds, tumor treatment and skin surface disinfection [6-8]. The electrical diagram of the DBD device were shown in Figure 3

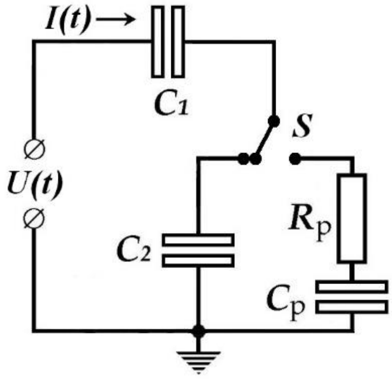

Figure 3. Electric diagram of DBD device.

In Equation (2.1), C_1 is the dielectric capacitance and C_2 is the capacitance of the air gap. The current of the circuit is expressed by Equation (2.2).

$$C_s = \frac{C_1 C_2}{C1 + C2} \quad (2.1)$$

$$I(t) = C_s \frac{dU}{dt} \quad (2.2)$$

The Equation (2.3) represents the I-V characteristic of DBD in a most general form. In Equation (2.4) U_p is drop in potential on plasma, ΔU is the constant near-electrode drop in potential.

$$I(t) = \frac{1}{R_p}\left[U_g(t) - \frac{\exp(-t/_{R_p C_p})}{R_p C_p}\left(\int_0^t U_g(t_1)\exp(t_1/_{R_p C_p})\, dt_1 + C_{int}\right)\right] \quad (2.3)$$

$$U_g = U_p + \Delta U \quad (2.4)$$

B. Atmospheric Pressure Plasma Jets (APPJ)

Atmospheric Pressure Plasma Jets (APPJ) is a plasma source that uses a gas stream to deliver reactive species produced in the plasma to the tissue or sample. The gas used is usually mixed with helium or argon, sometimes with a small amount of O2, H2O or N2 to increase the production of chemically reactive atoms and molecules. The use of noble gases keeps temperatures low and makes it easy to produce a constant discharge [9].

There is a wide variety of APPJ designs used in the experiments. Many APPJs use a dielectric to limit current, as in DBD. APPJs that use dielectrics to limit current usually consist of a high voltage electrode wound from the outside and a tub made of quartz or alumina. APPJs that do not use a dielectric to limit current use a high-voltage pin electrode at the center of the quartz tube. In all of these designs, APPJs generate ionizing waves that start in the jet and emit to mix with the ambient air.

In Figure 4, a schematic diagram of a plasma jet consisting of a needle-type electrode centered in quartz receptacles with an inner diameter of 1.6 mm and an outer diameter of 4 mm were shown [9]-[11].

Direct contact of the plazma with the tissue or sample can cause larger amounts of reagent species, lysed species, and photons to be sent to the sample. The designs that do not use a dielectric to confine the current flow from two planar electrodes with gas flow between them. Most devices of this type produce thin (mm diameter) plasma jets on which larger surfaces can be treated. Low temperature plasma jets are used in a variety of biomedical applications, such as inactivation of bacteria and killing of cancer cells [9], [10].

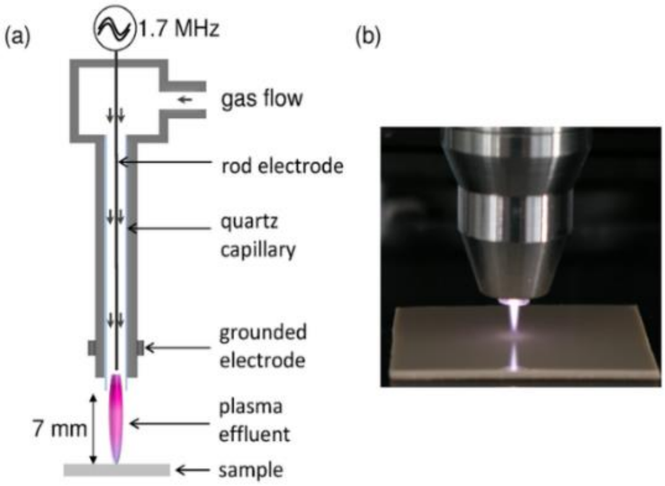

Figure 4. Atmospheric pressure plasma jet (kINPEN08).

3. Using of Plasma Technology in Medicine

The medical application of the physical plazma can be basically examined in two parts [6], [12].

- Indirect use of plasma-based or plasma-assisted techniques
- Direct interaction of the plasma with living tissue.

Plasmas are applied in the treatment of many diseases threatening human health on living cells with different production techniques and different application doses. In Table 1 were shown the areas where plasma technology is used and the treatment methods [12].

Table 1. Using areas of plasma technology in medicine and treatment methods.

	Using Area	**Treatment Method**
1	Pulmonology	Pulmonary inflammation therapy
2	Traumatology and Orthopedics	Bone marrow inflammation and related wound healing
3	Gynecology	Uterine region inflammation and wound healing
4	Dentist	Treatment of gum inflammation, stopping gum bleeding, periodontal application.
5	Oral Surgery	Keloite, phlegmon and abscess treatment and bacterial cleaning
6	Ophthalmology	Corneal injury treatment, burn treatment and bacterial cleaning
7	Ear-Nose-Throat	Nasal inflammation, sinusitis and bacterial cleansing
8	Dermatology	Psoriasis, eczema, cutaneous leishmaniasis, vasculitis, ulcerous area on the skin and bacterial cleansing
9	Gastroenterology	Treatment of erosion in the mouth, duodenum and intestinal exits, Chronic ulcer treatment
10	General Surgery	Stopping the blood, coagulation and seamless integration of the open wound, bacterial sterilization
11	Oncology	Cancer treatment

4. Medical Applications of Cold Plasmas

Nonthermal (cold) and thermal (hot) plasmas have been proven to neutralize and destroy various microorganisms such as bacteria, fungi, viruses, spores and different parasites and pathogens.
In Figure 5, MRSA (Methicillin Resistant Staphylococcus aureus) bacteria exposed to cold plasma at low temperature were given electron microscopy images. In Figure 5a, microscopic images of non-plasma-treated bacteria were given [13]-[15]

As seen in Figure 5, cold plasma, which produces almost no heat effect, completely changes the structure of bacteria. As the application time increases, the bacteria completely disappear. In bacteria, change and death occur due to the synergistic effect produced by cold plasma, such as charged particle effect in cold plasma, radical particle effect and UV effect..

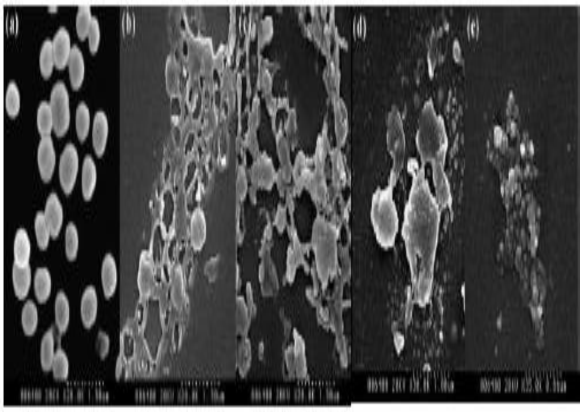

Figure 5. Effect of plasmas on MRSA bacterial cells. a) Plasma-free bacteria b) 1 second c) 2 seconds d) 3 seconds e) 4 seconds electron microscopy images of MRSA bacteria exposed to cold plasma

In Figure 6, Escherichia coli bacteria are observed to be destroyed only by the cold plasma jet system over time [16].

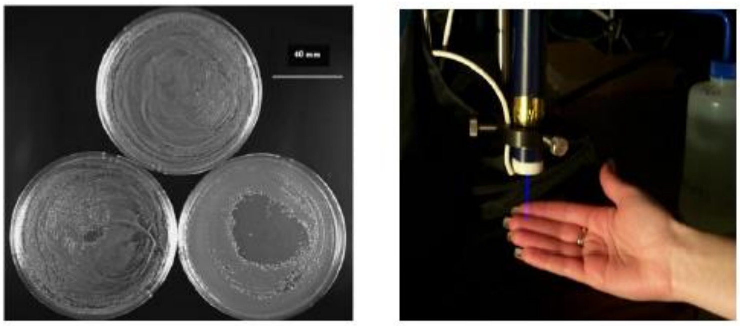

Figure 6. Local destruction of Escherichia coli bacteria in the Petri after 30 s and 120 s.

The deadly effect is expected because hot plasmas produce a high heat effect on the bacteria. However, the destructive effect of cold plasmas on bacteria, which produces almost no heat effect as in Fig. 6, is a whole new method. This is very different from chemical methods and sterilization techniques. Cold plasma does not cause any chemical damage to the physical, even when applied directly to humans. For this reason, they are used even in the sterilization of bacteria on human [17], [18].

With cold plasmas, different types of bacteria can be killed in very short application times. Because cold plasmas produce plasma at temperatures as low as room temperature, they do not have the effect of temperature on the bacteria itself or bacteria. For this reason, heat is used as an important method in the sterilization of sensitive environments. In recent years, sterilization of polymer-based medical electronic devices has become extremely important. For example, micro-cameras moving in the human body, or other expensive medical devices, can not be used on another patient without being sterilized after being used in a patient.

There is no toxic waste or radiation effect in sterilization with plasma [15]-[18].

Hot plasmas are less commonly used because they produce heat effects on living organisms. Cold plasmas, mostly at temperatures of 15-30 ° C, have different applications on the live. Different effects on the living tissue of cold plasmas brought with it various applications. Cold Plasmas are used in wound and burn treatment (Figure 7), skin regeneration and acne-stain cleansing (Figure 8), blood coagulation and wound closure (Figure 9) [12], [17].

Figure 7. Wound-burn treatment with cold plasmas.

Figure 8. a) Skin regeneration, b) Stain clearance

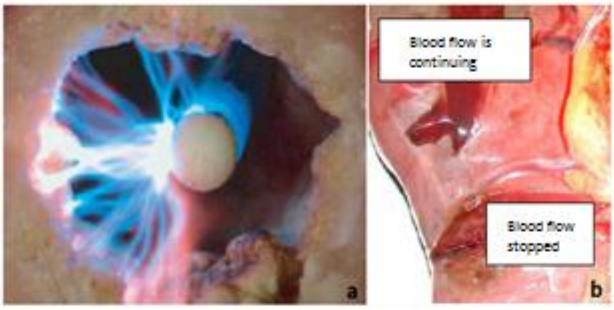

Figure 9. a) Cold plasma application in the body, b) Clotting of the blood and stopping the blood flow.

Cold plasma cells have effects such as cell detachment necrosis and apoptosis according to the administration dose in eukaryotic cells. Each effect has different results depending on the energy and time of application of the cold plasma to the unit surface.
For example, cold plasma application in wound, burn, inflammation treatment optimizes the formation of new cells by killing the cells in the application area. The cause of the formation of necrosis here is mostly the radical particles in the cold plasma and UV rays. Radical particles initiate necrosis with oxidative stress and change in DNA structure rather than UV [12], [14]-[17].
It is observed that cold plasmas activate thrombocytes and increase fibroblast proliferation in blood applications. However, blood clotting occurs because the pH level of the blood changes and the Ca + 2 ions become more liberated. For this reason, the wound is used for healing and for stopping blood flow from open wound [12], [18].
One of the most important applications of cold plasmas in medicine is the treatment of cancer. It has been observed that cold plasmas destroy cancer cells when administered at specific doses on cancer cells. Plasma using cells as an electrode to produce plasma was observed to kill cancer cells without damage to healthy cells when administered to melanoma skin cancer cells at doses of 5 seconds and 1.4 W / cm2. In many different cancer cells, successful results have been obtained at different doses [12], [16]-[18].

5. Conclusion

In this study, a broad overview of the use of non-thermal (cold) atmospheric pressure plasma is presented. Medical applications of cold plazma are in the developmental stages in areas such as corneal infections, blood clotting, cancer treatment, treatment of dental diseases. Although initial results are very promising, it would not be easy to carry cold plasmas to medical practice. The main hurdle here is that the interaction of non-thermal atmospheric pressure plasma with the physical, chemical and biological mechanisms between living cells, tissues and organs can not be precisely determined. It is known that the direct interaction with hot plasma is mainly by heat transfer. But direct interaction in the non-thermal plasma depends on numerous variables such as various charges, electric field, UV, radicals, electronically excited atoms and molecules. Despite all these challenges, the number of researchers interested in plasma medicine is rapidly increasing. It is anticipated that this growth will enable the plazma to become one of the modern technology fields used in the near future.

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