

Cold atmospheric plasma-future of dentistry

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Abstract: Plasma is known as 'fourth state of matter'. Plasma is two types: thermal and non-thermal or cold atmospheric plasma. Electrons and heavy particles (neutral and ions) present at the same temperature in Thermal plasma. Cold Atmospheric Plasma (CAP) is said to be non-thermal because it has electron at a hotter temperature than the heavy particles that are at room temperature. This review demonstrates different application of plasma in dentistry like effect of plasma on dental implant, dental cavity decontamination, sterilization, root canal disinfection, tooth whitening, polymerization etc.

Keyword: thermal plasma, non thermal plasma, cold atmospheric plasma, dentistry

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I. Introduction

The matter has four state- solid, liquid, gas, and last one is plasma. Plasma is a cloud of proton, neutron and electron. Plasma is closely resembled to gas than any other state because constant contact with each other is not present. Plasma act differently from gas and due to this reason scientists call it as collective behaviour. Plasma can flow like a liquid and it contains area that is like clumps of atom. Plasma is two types - thermal and non thermal plasma. In thermal plasma electron and heavy particles are in thermal equilibrium with each other. In non thermal plasma heavy particles stay at low and electrons in high temperature. Cold atmospheric plasma (CAP) is a type of non thermal plasma and it is special type plasma because temperature is less than 10⁴ °F at point of application.

Various methods are used to produce CAP like Atmospheric plasma pressure jet, Dielectric Barrier discharge, plasma jet pencil and plasma jet needle. The gases which are used for formation of CAP are helium, nitrogen, argon, heliox (mixture of oxygen and helium) and air. CAP has the power to cause deactivation of microorganism, death of cancer cell, detachment of cells. For this reason researchers try to find the effectiveness of CAP in dentistry.

History of plasma:

Plasma (Ancient Greek πλάσμα) means mouldable substance¹. Sir William Crookes first identified plasma in 1879 in Crookes tube and he described plasma as radiant matter². Sir J.J. Thomson in 1897 identified the nature of cathode ray (electron beam)³. Irving Langmuir first coined the term plasma⁴ and he described that like blood plasma which carries red and white corpuscles, plasma an electrified fluid carry electron and ion. The Siemens Company in the late 1850 used plasma discharge to produce ozone. Although biomedical application of plasma is very popular in different field but first application of plasma in dentistry is not clear. Probably first plasma is used during manufacturing of dental instrument or disinfecting them. Bol'shakov *et al.* in 2004 published the effects of radio frequency oxygen plasma on bacteria. Jiang in 2009 developed plasma probe for endodontic canal disinfection.

Method of generation of CAP:

Plasma can be produced by radio frequency, high voltage alternating current (AC) or direct current (DC), microwave frequencies. Medically used plasma device contain syringe and needle. Needle act as an electrode and connected to high voltage direct current (amplitudes of up to 10 kV, repetition rate of up to 10 kHz, and pulse width variable from 200 ns to DC) through ballast resistor (R) 60 - kΩ and capacitor (C) 50 - pF. Due to presence of resistor and capacitor discharged current is limited in safety range. If R is small and C is large chance of feeling shock⁵. Syringe diameter is 6 mm, needle diameter is 200μm and length is 3 cm. When working gas like He/O₂ (20 %) with 0.4 L/min flow rate is injected into hollow syringe and high voltage DC is applied to needle, homogenous plasma is formed⁶.

II. Method of production

- 1. Direct barrier discharge (DBD):** First DBD experiment was conducted by Siemens in 1857. This technique is used during sterilization of living objects, angiogenesis, surface treatment, excimer formation and inactivation of bacteria⁷. Dielectric covering two flat metal electrodes is present in DBD. One is high voltage and another is grounded electrode. Gas passing between electrodes is ionized and plasma is formed. High voltage alternative current is required and power consumption is 10-100 W⁸. Variation in electrode is present, like dielectric material cover only one electrode instead of two and cylindrical electrode is present instead of flat. Floating electrode DBD (Fe - DBD) was developed by Fridman et al⁹. It consists one high voltage and another one is active electrode like, human skin and organ. The power electrode should be placed close (< 3 mm) to second electrode to produce plasma. DBD also used on melanoma skin cancer, endothelial cell and deactivation of *Bacillus stratosphericus*¹⁰.
- 2. Atmospheric plasma pressure jet (APPJ):** It consists two electrodes through which mixture of gas (Helium, oxygen and other gas) flow at high rate. Radio frequency (RF) power (50-100 W) at 13.56 MHz is applied on discharge creating central (cathode) electrode and outer electrode (anode) is grounded. Cathode is made of tungsten or stainless steel with 1 mm diameter. The application of APPJ is inactivation of bacteria. Koinuma et al. In 1992 developed the earliest radiofrequency cold plasma¹¹.
- 3. Plasma needle:** Stoffels et al. in 2002 developed miniature atmospheric plasma needle¹² and in 2004 new version was created¹³. The new version plasma needle consists of 0.3 mm diameter metal stand with a sharpened tip perspex tube. Due to high thermal conductivity helium is most frequently used. Microplasma is created when RF power at 13.05 MHz ranging between 10 mW and several watts is applied. Small area in dentistry can be treated by microplasma^{14, 15}. It can be used to deactivate *E.coli*¹⁶.
- 4. Plasma pencil:** Laroussi et al. developed plasma pencil¹⁷. It consists two electrodes with same diameter and the diameter is 2.5 mm. Between two electrodes 0.3 - 1 cm gap is present and thin copper ring attached to dielectric disk. High voltage submicrosecond pulses are applied between electrodes to create plasma, while gas is injected through electrode hole. When discharge is created plasma pulme is launched through the hole of outer electrode. Due to low temperature (290 K) plasma pulme (length up to 5 cm) can be touched safely. Plasma pencil has been used for *P. gingivalis*, *E. coli*, leukemia treatment¹⁸.

Application of CAP

- 1. Sterilization:** Plasma sterilization efficacy is influenced by gas composition, bacterial stain and driving frequency. It is more effective than ultra violet (UV) ray sterilization^{19, 20}. The plasma sterilization mechanism is related to abundance plasma component like oxygen, electrons and ions, electromagnetic field and UV²¹. Plasma is effective on contact area not only contact point. Plasma sterilization recently has been used for dental disease treatment. Whittaker et al. has indicated that use of plasma is effective in reducing protenaceous material which transferred between patients during filing²². Yang Hong Li et al. stated that plasma sterilization may become novel method for sterilization due to low temperature, thoroughness, roughness and safety²³. Su-Jin Sung et al. evaluated sterilizing effect of atmospheric pressure non thermal air plasma device. This device was effective in killing both *E. coli* and *B. subtilis*. It is more effective in killing of *E. coli* than UV sterilization²⁴.

Bacteria that can be inactivated by plasmas include^{25, 26}

Sl. no	Group	Species
1.	Streptococci	<i>Streptococcus mutans</i> , <i>Streptococcus sobrinus</i> , <i>Streptococcus parasanguis</i> , <i>Streptococcus mitis</i> 1, <i>Streptococcus oralis</i> , <i>Streptococcus intermedius</i> , <i>Streptococcus vestibularis</i> , <i>Streptococcus mitis</i> 2, <i>Streptococcus gordonii</i> , <i>Streptococcus sanguis</i> , <i>Streptococcus anginosus</i>
2.	Lactobacilli and Bifidobacter	<i>Lactobacillus fermentum</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus acidophilus</i> , <i>Lactobacillus rhamnosus</i> , <i>Bifidobacterium dentium</i>
3.	Actinomyces	<i>Actinomyces israelii</i> , <i>Actinomycesgerencseriae</i> , <i>Actinomycesnaeslundii</i> , <i>Actinomycesodontolyticus</i> , <i>Rothiadentocariosa</i>
4.	Microaerophiles	<i>Actinobacillusactinomycetemcomitans</i> , <i>Eikenellacorrodens</i>
5.	Aerobes	<i>Neisseria mucosa</i> , <i>Haemophilusparainfluenzae</i>
6.	Anaerobes 1	<i>Fusobacterium nucleatumssnucleatum</i> , <i>Campylobacter rectus</i> , <i>Veillonellaparvula</i> , <i>Capnocytophagagingivalis</i> , <i>Peptostreptococcusasaccharolyticus</i> , <i>Gemellamorbilloorum</i> , <i>Prevotellamelaninogenica</i> , <i>Leptotrichiabuccalis</i> , <i>Eubacteriumsabarreum</i> , <i>Corynebacterium matruchotii</i> , <i>Prevotellanigrescens/intermedia</i>
7.	Anaerobes 2	<i>Porphyromonasgingivalis</i> , <i>Selenomonasnoxia</i> , <i>Micromonas micros</i>

2. **Implant modification help in osteointegration:** Modification focus upon interaction of implant to body fluid which help in bone healing. Plasma increases surface roughness and wettability which help in cell adhesion^{27, 28}. Chair side application of non thermal atmospheric pressure plasma (NTAPP) prior to placement of implant is recently reported^{29, 30}, which help in reducing contact angle and supporting spread of osteoblastic cell. One of the advantages of using plasma is that no residue present after plasma treatment. Some physiochemical characteristics were changed like, surface free energy, functional hydroxyl groups, component of hydrocarbone³¹.
3. **Intraoral disease:** Candida albicans causes denture stomatitis, angular stomatitis, median rhomboid glossitis and gingival erythema. Koban et al. and Yamazaki et al. reported that plasma jet can cure the disease caused by C.albicans^{32, 33}.
4. **Oncology:** It has been reported that CAP induces necrosis, cell detachment, apoptosis and deterioration of tumour cells by disrupting 's' phase of cell division³⁴. Effective result of CAP was obtained from in vivo and in vitro study in oncology. However more study need for proper technique and implementation.
5. **Dental caries:** plasma can decontaminate dental cavity without drilling. It is very useful to treat child patients. Eva Stoffels, suggested the use of plasma needle on the basis of the ability of plasma to kill E.coli³⁵. Goree et al. reported that non atmospheric plasma can kill S.mutans³⁶. Plasma causes bacterial decontamination in room temperature with the help of free radicals. Plasma does not cause bulk tissue destruction. Laser or mechanical technique also decontaminate dental cavity but they produce heat and cause healthy tissue destruction.
6. **Root canal disinfection:** Lu et al. used a plasma jet device which could generate plasma inside root canal. Plasma causes disinfection of the canal without feeling pain. The root canal system has complicated structures like, isthmus, deltas, ramifications, particular dentinal tubules and irregularities. It has been suggested that bacteria can enter dentinal tubules as deep as 500-1000 μm ³⁷. When Helium/oxygen (20%) is used as plasma, vibrational and rotational temperatures of the plasma are about 2700 K, 300 K respectively and current is about 10 mA then effective destruction of E. faecalis is found. Yinglong et al performed an in-vitro study and found that twelve minutes exposure of non thermal plasma for three weeks completely kill E. Faecalis³⁸.
7. **Tooth whitening:** Lee et al. found that CAP can bleach tooth surface by increasing production of hydroxyl ions and removing surface proteins³⁹. Lee et al. also suggested that the plasma combined with hydrogen peroxide removed stain from extracted teeth which was stained due to either coffee or wine⁴⁰. Park et al. suggested that low frequency plasma along with hydrogen peroxide removed intrinsic stain of teeth. Kim et al. produced liquid plasma by using RF driven gas-liquid hybrid plasma System. This study was done by placing the RF plasma jet and immersing the target tooth in deionized water. After treating the tooth for 8 min color changes were observed. The OH radicals were suggested the main causative factors for bleaching⁴¹. Nam et al. used forty extracted human molar teeth with intact crowns. The forty teeth were randomly divided into four groups (n=10) and were treated with Carbamide peroxide + Plasma Arc Lamp (PAC), Carbamide peroxide + CAP, Carbamide peroxide + diode laser, or Carbamide Peroxide alone (control). They described CAP as most effective bleaching agent⁴². Claiborne D et al. treated extracted human teeth by plasma plume. They observed a significant increase in whitening of the teeth after exposure to CAP + 36% hydrogen peroxide gel, compared with only 36% hydrogen peroxide⁴³. Jamali et al. found that prolonged plasma treatment without bleaching removed small amount of blue-stain but the combination of plasma treatment and bleaching removed most of the blue-stain⁴⁴.
8. **Biofilms:** Biofilms develop on tooth and any other hard surface in oral cavity .They cause caries, periodontal diseases and can also lead to inflammation around dental implants. Rupf et al. suggested that the combination treatment of plasma with a non-abrasive air/water spray is effective for the elimination of biofilms from dental implants⁵¹. Koban et al. found *in vitro study* that the treatment of of *S.mutans* composing dental biofilms with non-thermal plasma was more effective than the treatment with chlorhexidine⁵². Jiang et al. developed a plasma plume to disinfect root canals from extracted human teeth at room temperature⁵³. Schaudinn et al. eliminated biofilms from root canals of extracted teeth by using a plasma needle⁵⁴.
9. **Polymerization:** Plasmas can also help in polymerization⁴⁵. Plasma exposure causes high cross-linking and high degrees of polymerization⁴⁶. Plasma arc curing units for curing composite resin are popular due to

their short curing time in comparison to conventional units^{47,48}. Plasma polymerization characteristics are reported to be less than optimal⁴⁹. Recently, effective polymerization of self-etch adhesives was done by the non-thermal plasma brush⁵⁰.

10. Use of Plasma in Composite Restorations: Previously it was shown that plasma treatment increased bonding strength at the dentin- composite interface by roughly 60%, and these interface-bonding significantly improved composite performance, longevity and durability. Current clinical practice mainly depends on mechanical bonding rather than chemical bonding. The main culprit for failure of mechanical bonding is smear layer. The etch techniques create a porous surface for adhesive infiltration. Smear layer actually inhibits adhesive diffusion throughout the prepared dentin surface. It causes inadequate bonding which helps in entering bacterial enzymes and degrading the composite-tooth interface⁵⁸. Kong et al., reported the effects of plasma treatment on dental composite restoration. They investigated that atmospheric cold plasma brush (ACPB) treatment can modify the dentin surface and increase the dentin-adhesive interfacial bonding⁵⁹. Chen et. al. suggested that plasma brush treatment resulted super-hydrophilic enamel, dentin surface for composite restoration⁶⁰. Another study reported that interfacial bonding strength of peripheral dentin surface was increased by plasma treatment, while over 100 s of prolonged treatment decreased the interfacial bonding strength⁶¹. However, no improvement was observed in the bonding strength of plasma-treated inner dentin probably due to the variation in composition of dentin⁶².

11. Post and Core: Yavrich et al., studied the plasma treatment effects on the shear bond strength between fibre reinforced composite posts and resin composite. They concluded that plasma treatment increased the tensile-shear bond strength between post and composite⁵⁸. Costa Dantas et al. reported that plasma treatment improved the wettability of the post⁶³. Real improvement in adhesion was not observed after argon plasma treatment but high surface roughness due to ethylenediamine plasma treatment was significantly indicated. Studies have revealed that plasma surface treatment reveals aging effect⁶⁴. Ye et al. observed that non-thermal plasma treatment resulted aging effect of post-surface. They reported that the improvement in bond strength disappeared when the fiber posts were exposed to air for 1 h or longer after being treated with plasma⁶⁵.

12. Miscellaneous: Koban et al. reported that direct application of NTAPP reduced the contact angle of untreated dentin surface and this caused a superior spreading of osteoblasts on the dentin. These results may be utilized for periodontal regeneration in the future⁵⁵. Miletic et al. demonstrated the interaction of NTAPP with the human periodontal ligament mesenchymal stem cells⁵⁶. They reported that NTAPP inhibited the migration of the cells and induced some detachment, without affecting their viability. In addition, the plasma significantly attenuated the cells' proliferation, but promoted their osteogenic differentiation. Pei et al. showed that 25.5 um thick *E. faecalis* biofilm layer was penetrated by NTAPP, which is the deepest up to now⁵⁷.

III. Discussion

Plasma can penetrate into irregular cavities and fissures because it is a gaseous medium. In comparison to laser beams, plasma has many useful advantages in its application to oral tissues. Plasma kills only pathogens in bacterial plaque without damaging the normal tissue. Pain is not present during plasma treatment because it does not cause thermal damage to tissue. Another advantage of plasma treatment is that it does not produce any toxic residues. Considering the all characteristics of plasma like its effect in sterilizing, polymerization, intra oral disease, dental caries, root canal disinfection, dental implant and tooth bleaching, the application of plasma to dental health care is a novel technique. Plasma drug delivery system in the dental tissue is invented as a new possibility in the future⁶⁶. Based on known physical and biological properties of plasma some dental applications are possible, but further investigation is needed to know the principles of how plasma influences cells. We are still far away from dental and medical plasma application. Further study is required to develop a safe, efficient and echo- friendly plasma technology⁶⁷.

IV. Limitations

Due to new technology CAP also has some limitations like, cost of the equipment, marketing, maintenance and availability. Now-a-days, research of the CAP effect on tumor cells is being done and some positive results are reported. The effect on normal cells has to be studied in depth and validation needed for its successful application⁶⁸⁻⁷⁰. Some more research is needed for this technology to be used in a cost effective, efficient and predictable manner in clinical settings.

V. Conclusion

Clear conclusions are not yet drawn about the effects of NTAPP on human and nonhuman cells. Further exploration should be required. The confusion may be due to the beginning era of the novel field of plasma dentistry. The advancement technologies parallel to plasma dentistry will surely overcome this confusion in the near future. More in vivo studies strongly need for the plasma treatment to be used and accepted widely. The user-friendly technique would gain more popularity because manufacturers recently provide hand-held devices proper for the clinic. Further understanding of the cellular and molecular mechanisms involved could also give researchers and clinicians insight into future applications.

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