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Review Article

Expanded Tentacles of Cold Plasma Energy in Dentistry – Review

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Abstract

The atmospheric cold plasma is a non-thermal processing method. This technique becomes a subject of high interest for a wide variety of technological use, medical and dental treatment modalities. This review article on plasma therapy in dentistry is intended to provide with a summary of the current status of this emerging technology, its scope, and its broad interdisciplinary approach. States of matter are liquids, solids, and gases. But a fourth category of matter has been discovered called plasma that's actually the most unusual and the most abundant. It has a plenty of uses in dentistry. It could become a new and painless way to prepare cavities for restoration with improved longevity. Also, it is capable of bacterial inactivation and non-inflammatory tissue modification, which makes it an attractive tool for the treatment of dental caries and for composite restorations. Plasma can also be used for tooth whitening. This review focuses on plasma basics, mean of production, mechanism of its effects upon dental tissues and its wide range dental applications. Lastly but not leastly the review confirmed that no harmful by-products are generated by this technology.

Keywords: *Plasma; Types of Plasma; Cold Atmospheric Plasma (CAP); Applications of Plasma in Dentistry*

Introduction

A plasma is a hot ionized gas consisting of approximately equal numbers of positively charged ions and negatively charged electrons. The characteristics of plasmas are significantly different from those of ordinary neutral gases so that plasmas are considered a distinct fourth state of matter. The fourth state of matter was identified in 1879 by the British physicist Sir William Crookes. The term plasma, coined by Irving Langmuir in 1929, refers to the fourth state of matter (after the solid, liquid and gas forms) (Figure 1) [1,2].

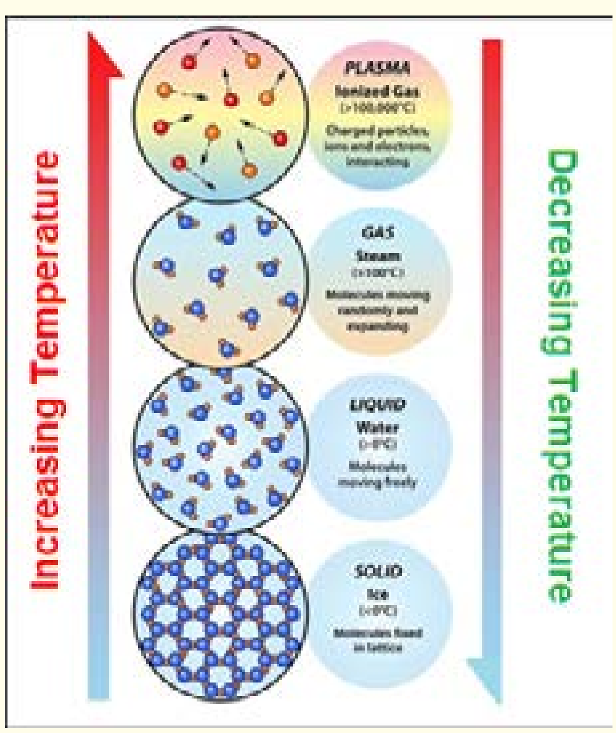

Figure 1: *Four states of matter.*

Although biomedical application of plasma technology has become very popular in various fields today, it is not clear when it was first used in the field of dentistry. It is partly because the plasma has been nearly everywhere and has been related to nearly everything in reality, thus we do not readily recognize it. Perhaps the first application of plasma in dentistry occurred in the manufacturing process of dental instruments or the disinfection of them. Nevertheless, Eva Stoffels is believed to introduce the first investigation with the view of a possible therapeutic and thus medical question for dentistry [3,4].

As in medicine, the dental applications of physical plasma can be mainly subdivided into two principal approaches: one is the use of plasma technology for the treatment of surfaces, materials or devices to realize specific qualities for subsequent special applications including disinfection, and the other is the direct plasma application on or in the human body for therapeutic purposes; however, clear-cut classifications are sometimes impossible because of overlaps. In addition, the use of plasma for medical purposes could be divided according to its temperature and the air pressure at which it is generated [5].

Indeed, plasma generation can be realized at low, atmospheric and high air pressure and their temperature could be different. While thermal plasmas are natural phenomena, non-thermal plasmas are artificially made of, of which composition and temperature are adjustable. Today, non-thermal plasmas are utilized from in the appliances of daily life like energy-saving lamps, flat panel displays to for industrial purposes, such as polymer pretreatment, surface finishing, waste and air pollution management [6].

Non-thermal atmospheric pressure plasma (NTAPP), which is sometimes called cold atmospheric plasma (CAD) or low-temperature atmospheric pressure plasma, has the unique advantage of extending plasma treatment to living tissue. Therefore, all the studies regarding direct applications used this type of plasma even though the individual settings varied. In addition, some of the surface treatments also made use of NTAPP in the form of chairside applications. Various types of plasma devices, such as nanosecond pulsed plasma pencils [7], radio-frequency plasma needles [8], direct-current plasma brushes [9], and plasma jets [10] have been developed for non-thermal atmospheric pressure plasma generation. The common challenge for generating these plasmas is the inhibition of the glow to arc transition at one atmosphere. Different types of discharges have used different schemes to achieve this [11]. This opens up new horizons in the field of dentistry with the size of the device becoming small enough to hold by hand.

In this respect, the present review reports the mechanism of action of Non-thermal atmospheric pressure plasma (NTAPP), which is sometimes called cold atmospheric plasma (CAD) or low-temperature atmospheric pressure plasma, current usage in dentistry. This because it gained considerable attention and will be discussed in great detail in this current review.

Plasma production and mechanism of action

Previously, plasma was used in medicine in relation to heat and thermal treatments for sterilization and to control bleeding. Electrocautery is one of the uses of thermal plasma, but it can result in the charring of tissue [12]. Non-thermal plasma (Figure 2) is a novel technique with selective action no damage to the surrounding tissue [13].

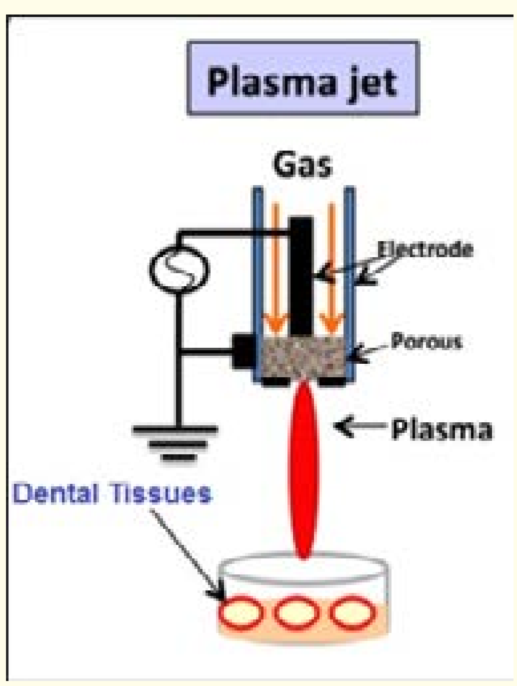

Figure 2: *Diagrammatic representation depicts dielectric plasma discharge and plasma jet.*

Plasma is a collection of stripped particles. When electrons are stripped from atoms and molecules, those particles change state and become plasma. Plasmas are naturally energetic because stripping electrons takes constant energy. If the energy dissipates, the electrons reattach and the plasma particles become a gas once again (Figure 3) [14].

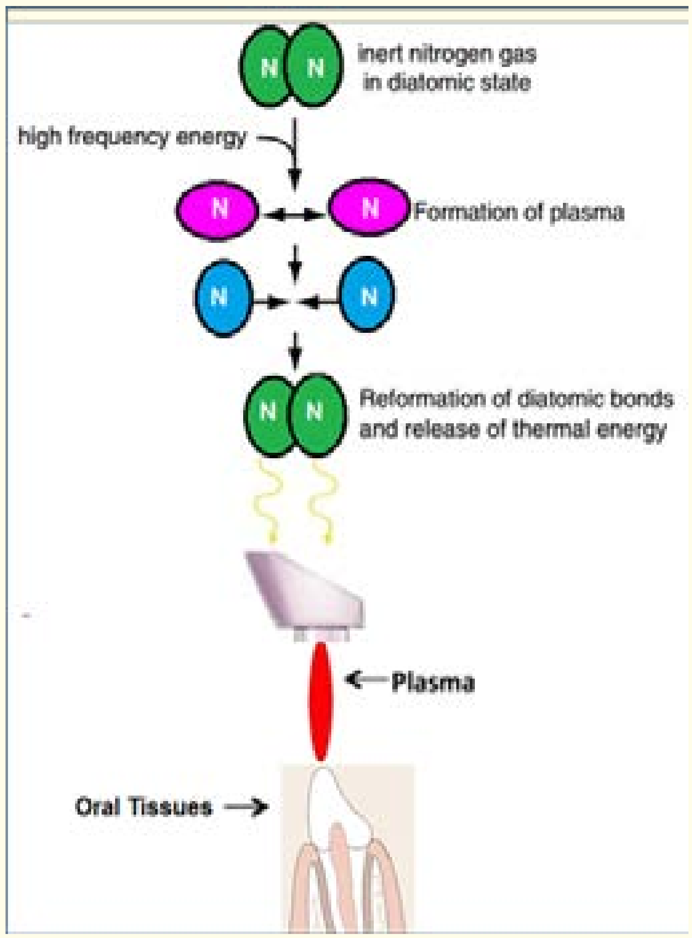

Figure 3: *Mechanism of plasma production.*

Non-thermal plasma consists of partially ionized gases (helium, argon, oxygen, nitrogen may be used) with free electrons, generated at a low temperature (less than 40^0C). The use of plasma has recently expanded in the fields of medicine and dentistry [1].

The mechanism of action of plasma is based on release of free radicals and reactive species (e.g., reactive oxygen and nitrogen species, i.e., ROS and RNS) [15].

These radicals control the cell redox signaling pathway and can be used for sterilization and wound healing and apoptosis of cancer cells, but their high concentration can have adverse effects on the cells. It has been found that non-thermal plasma can produce significant amounts of ozone [16,17]. This generated ozone in aqueous media further generates biologically active ROS and RNS. Plasma jets are ionized local gas flows, generated under normal pressure by means of microwaves, high frequency or pulsed direct current in so-called plasma-jet sources using noble gases. Reactive oxygen species are produced through an admixture of chemically active gases (O_2, N_2 and others), which are able to react with biological material or tissues [18]. Furthermore, UV irradiation, ions and electrons are emitted in the plasma discharges, which also interact with biological material or tissues [19,20].

Plasma is used in dentistry either for surface treatment or direct applications. Modification of dental implant surface, enhancing of adhesive qualities, enhancing of polymerization, surface coating and plasma cleaning are examples for surface treatment. Microbicidal activities, decontamination, root canal disinfection and tooth bleaching are examples for direct applications with other miscellaneous ones. Non-thermal atmospheric pressure plasma was of particular focus since it is gaining considerable attention due to the possibility for its use in living tissues [21].

Dental Application of Plasma

Surface treatment

Modification of the implant surface to improve osseointegration

The effect of plasma on titanium surfaces indicated that this treatment is capable of improving cell adhesion by changing surface roughness and wettability, which decreases after plasma exposure [22,23]. Recently, a chairside operating NTAPP immediately prior to implant placement was also reported [24,25], which stated that plasma treatment reduced the contact angle and supported the spread of osteoblastic cells. One of the advantages of plasma treatment is that it leaves no residues after treatment. Plasma treatment of zirconia implants, which is increasing as an alternative to the conventional titanium implant due to its superior esthetic properties [26]. Plasma treatment of zirconia implant increased its hydrophilicity and enhanced osseointegration in *in vitro* as well as *in viv*o experiments [27,28].

It is demonstrated that nonthermal atmospheric pressure plasma (NTAPP) treatment could improve the hydrophilicity of the titanium surface, contributing to enhancement and maintenance of the biological activity and interactions between blood proteins and osteoblastic cells until 4 weeks. These changes could thus increase early osseointegration between titanium implants and surrounding bone and reduce healing time, allowing patients to return to their normal lifestyles more quickly [29].

Enhancing adhesive qualities

Use of plasma in composite restorations

The CAP plasma generates reactive species that arrive on the surface of the composite resulting in both microstructural and surface chemistry modifications that improve adhesive bonding. Plasma treatment increases bonding strength at the dentin/composite interface by roughly 60%, and thus significantly improves composite performance, durability, and longevity [30]. When utilized correctly and efficiently, non-thermal plasma is a gentle method that can be used to change the surface characteristics of the top layer of polymeric surfaces, such as collagen fibrils on the dentin surfaces, and thus enhance the surface for various types of adhesives used in composite restoration [31].

Conventional adhesive systems employed several methods to improve wettability, to elevate the surface energy and to increase the roughness through techniques involving etch-and-rinse, acid primers, Hydroxyethylmethacrylate (HEMA) primers and laser irradiation [32-35].

In the same respect, plasma treatment has been introduced as an alternative or additional procedure, especially in the bonding of ceramic restorations, which is more difficult to achieve. Generally, the etching of feldspathic ceramic with hydrofluoric acid and coating with a silane coupling agent has been recommended as a reliable protocol [36,37]. However, because the procedure is complicated and requires toxic chemicals, other ceramic bonding techniques such as silica coating have been introduced [38,39]. As an alternative for adhesion enhancement in dental ceramic bonding, atmospheric pressure plasma treatment has been suggested [40]. It enhances adhesion by producing carboxyl groups on the ceramic surface and improves the surface hydrophilicity as a result [41].

The nonreactive surface of zirconia, sometimes described as “ceramic steel”, presents a consistent issue of poor adhesion strength to other substrates [42]. Silane treatment used for silica-based substrates is not applicable [43]. In addition, zirconia itself is known to be hydrophobic and possesses very low surface concentrations of OH groups [44]. For this more complicated bonding, several other methods have been proposed [45,46]. Plasma treatment was also tested and the results showed that a significant increase in the microtensile bond strength to zirconia surfaces was observed when non-thermal plasma was applied alone or in combination with resin. According to the XPS results, an increase of elemental O and a decrease of elemental C was detected on the zirconia surface after non-thermal plasma application [47]. Another attempt using plasma fluorination was reported, which is expected to increase hydroxylation at the surface, making it more reactive, thus allowing for covalent bonding between the zirconia surface and resin cement [48]. One report demonstrated that the high polarity was obtained on zirconia and titanium surface after NTAPP application [49].

For enamel, dentin and composite, it is. reported that a super-hydrophilic surface could be easily obtained by plasma brush treatment without affecting the bulk properties regardless of the original hydrophilicity [50].

Non-thermal plasma treatment was associated with stronger bonding of the conventional resin cement to fiber posts [51].

A study showed that the shear bond strength (SBS) between zirconia and resin cement was improved when NTAPP treatment was applied to colored zirconia. In particular, colored zirconia with molybdenum showed a higher SBS compared to other zirconia types before and after processing with NTAPP [52].

By delivering reactive species, including ions, radicals, and UV photons, NTAPs have exhibited various biological and chemical effects critical to dental bonding. Significant increase in surface hydrophilicity/wettability is furnished on dental surfaces, including enamel, dentin, and resin/composite, reflecting plasma’s capability to etch/ablate and introduce functional groups to surfaces by bombardment of reactive species. Plasma-induced polymerization has been confirmed, with monomer conversion superior to traditional light curing. Enhanced penetration of adhesives has been seen on NTAP-treated dental surfaces resulting in better hybrid layer and longer resin tags. NTAP has also been found to induce chemical grafting of HEMA to dentin collagen, signifying additional bonding mechanism between adhesive and collagen besides pure mechanical interlocking [53].

Enhancing polymerization

Plasmas also induce polymerization of polymers. Polymers synthesized by plasma exposure demonstrated high cross-linking and high degrees of polymerization [54]. For composite resin, plasma arc curing units (Figure 4) are popular because of their short curing time in comparison to conventional units [55,56]. However, their polymerization characteristics are reported to be less than optimal [57].

Figure 4: *Plasma light curing unit.*

Recently, the non-thermal plasma brush was reported to be effective in the polymerization of self-etch adhesives with no negative effects of water on the degree of conversion of plasma cured samples [58].

Surface coating

Variation in surface texture or nanoscale topography features can affect the cell response for a titanium implant [23]. Plasma spraying, which used to be one of most popular coating techniques for implants, can be considered as one type of plasma treatment that increases osseointegration, but it has been reported to have problems such as delamination [59]. The coating on the fiber post-surface using glow discharge Was reported to increase the tensile-shear bond strength between the post and composite [60-62]. Several microcomposite and ceramic materials were coated with plasma-assisted thin film coatings and the potential for reduction of bacterial adhesion exhibited some promise [61].

Plasma cleaning

In contrast to the conventional methods of cleaning such as the use of solvents or aggressive chemicals, plasma cleaning leaves no residue, and, when optimized, typically generates only CO_2, H_2O, and N_2 as gaseous waste. Gas plasma treatment has the potential advantages of lack of toxic residue effects, reduced turnover time, and applicability for sterilization of heat- and moisture-sensitive instruments [62,63].

Its effectiveness has led to its use as a decontamination method from chemical and biological warfare agents or from spores [64,65]. Dental treatment can frequently induce cross-contamination between dental patients and dentists through instruments and materials as well as between impression materials and dental technicians [66-68]. Contaminated endodontic files exposed for a short period to low-pressure oxygen–argon plasma showed a reduction in the absolute amount of proteinaceous materials [69].

Atmospheric pressure non-thermal air plasma treatment of diamond burs and silicone impression materials lead to significant reduction for both Escherichia coli and Bacillus subtilis after treatment with [70]. Plasma devices have shown to kill a higher proportion of bacteria than UV sterilization [71]. Hydroxyl radicals generated by plasma along with other free radicals destroy membrane lipids in bacteria cell membrane and thereby deactivate the bacteria [70,72]. Stomatitis caused by *Candida albicans* can be cured by plasma jets [71,73].

Effects of CAP on malignant cells

The conventional therapies for cancerous diseases are based on removal of the tumor, chemotherapy and/or radiation. Nevertheless, some cancers remain hard to eradicate. *In-vitro* and *in-vivo* studies have been performed on the efficacy of CAP at killing cancer cells. The results of the pilot studies performed by several research groups confirmed that treatment with low-temperature plasma is able to induce several modes of cell death including apoptosis and necrosis. They also noticed decreased cell migration and induction of senescence in cancer cells [74]. Regarding the mechanism of the Atmospheric Pressure Plasma therapy on cancer cells, the hypothesis is that the ROS (reactive oxygen species) plays the main role. ROS are well known to be harmful to cells inducing apoptosis, senescence, or cell cycle arrest. It is proposed that ROS is the mechanism through which CAP induces apoptosis [75].

Miscellaneous

In addition to the disinfective role of plasma cleaning on elastomeric impression materials, plasma treatment was reported to increase the surface wettability [76]. The wettability of impression materials is an important requirement for the accurate reproduction of intraoral structures, since it is directly related to the quality of die stone casts, and, therefore, the castability of prostheses [77]. The surface properties of several set elastomeric impression materials contaminated with saliva were inspected after plasma cleaning and exhibited a general increase in the critical surface tension and an improvement in the castability of all materials was also noted [78,79]. Denture stomatitis is brought about by the adhesion of *Candida albicans* to the denture surface [80]; plasma treatment reduces this adhesion [81,82].

As a polymerization technique of glass fiber to improve mechanics, plasma was investigated and showed some promise in increasing the flexural strength of the denture base resin [83]. Another important medical application is argon-plasma coagulation [84]. Plasmas can also be used to give hydrophilic properties to surfaces [85].

Direct plasma application

Microbicidal activities

Methods for the decontamination and conditioning of intraoral surfaces are of great interest in the field of dentistry. Cold plasmas are of particular interest, as heat damage to dental pulp must be prevented [86]. The removal of carious dentin has been suggested as an alternative to conventional drilling [3,4]. The sterilization effect was suggested to be due to reactive oxygen species [75].

The decontamination of implant surfaces represents a basic procedure in the management of peri-implant diseases [87], but remains a challenge. Recently the use of NTAPP has been suggested for the removal of biofilms in general [88], and for the treatment of both peri-implant mucositis and peri-implantitis in particular [89-91].

The mechanisms are due to the generation of reactive species such as oxygen, nitrogen or nitrogen oxide radicals [92,93], and the etching effect of the plasma on biofilms during the chemical process of oxidation [94].

Root canal disinfection in endodontic treatment

Root canal disinfection can be considered as a special type of decontamination. However, it is separately mentioned as a single topic in this review because of its importance in the endodontic procedures for successful outcome and difficult nature of eradicating the root canal micro-organisms due to its biological and geometrical characteristics. It has been reported that bacteria can enter dentinal tubules as deep as 500 - 1000 μm [95].

Using NTAPP alone because it is as a gas phase has a capability of reaching deep into the complex canal. Therefore, there is a unique advantage of direct contact with bacteria when using NTAPP, which is compulsory but impossible with conventional methods [96,97]. Plasma-jet device, which could generate plasma inside the root canal is used for root canal decontamination. The plasma could be touched by bare hands and directed manually by a user to place it into root canal for disinfection without causing any painful sensation. Plasma can efficiently kill Enterococcus faecalis in several minutes [98,99].

Wound healing after laser and plasma treatment

Photo-bio modulation is known to occur due to changes in the mitochondrial activity within cells as an after-effect of plasma treatment (as plasma also generates various Reactive oxygen species (ROS) and reactive nitrogen species, (RNS) species). in turn causing increased mitochondrial respiration [100].

As a result of plasma treatment, there is alteration in the cell/plasma membrane with induction of intracellular reactive oxygen/nitrogen radicals. Low dose of plasma is effective for proliferation, migration and repair of damaged cells/DNA, but at high doses can cause cell cycle arrest or apoptosis. Plasma can also have positive effect on the angiogenesis and cell proliferation. It is reported the formation of new micro vessels after plasma treatment. The effect can lead to modification of cell adhesion molecules which in turn affects the cell matrix interaction, and hence initiate faster wound healing [101].

Tooth bleaching has become a popular esthetic service in dentistry. Hydrogen peroxide (H2O2) is a widely used bleaching material that is effective and safe [102]. In-office bleaching systems usually use a 30 - 44% H_2O_2 bleaching gel and a high-intensity light source [103,104]. The light source may enhance bleaching by heating the H_2O_2 and consequently accelerating bleaching, but this mechanism has yet to be confirmed. The application of light may or may not significantly improve the efficacy of the bleaching system [105]. Plasma treatment was suggested to be complementary to the conventional method because it provides effective bleaching without thermal damage [106,107]. Atmospheric pressure plasma can be used in place of light sources for teeth bleaching by increasing the production of OH radicals and the removal of surface proteins. Tooth whitening can also be achieved using a DC plasma jet and hydrogen peroxide. Intrinsic stains are a serious factor in tooth discoloration [105,108]. The temperature remained under 80°F throughout plasma teeth whitening which is below the thermal threat for vital tooth bleaching [109]. The tooth bleaching method using atmospheric pressure plasma shows reasonable promise of becoming practical in the future.

Plasma arc welding [110]

Tungsten Inert Gas (TIG) Welding and Plasma Arc Welding (PAW) are techniques in which a union is obtained by heating materials by an arc established between a non-consumable tungsten electrode and the part to be welded (Figure 5).

Figure 5: *Ceramic torch, with tungsten electrode, positioned over the sample.*

The electrode and the area to be welded are protected by using an inert gas, usually argon or a mixture of inert gases (argon and helium). The basic equipment consists of a power supply, a torch with a tungsten electrode, a shielding gas source, and an opening system for the arc. The main difference between TIG and plasma welding is the use of a constrictor torch that concentrates the electric arc in plasma welding (Figure 6). Filler metal can be used or not.

Figure 6: *Plasma welding machine for Dentistry.*

Advantages

- High quality welds of excellent finishing, particularly in small joints;
- The thickness of the joint allows for welding in any position, e.g. repairing removable partial prosthesis;
- Excellent control of the weld pool, i.e. the region being welded;
- Expending less time;
- Can be done directly on the working model (no need to investment model);
- The equipment is affordable compared to that of laser welding;
- Allows welding in regions near the resins and porcelains;
- Allows welding with the frameworks in close contact or with minimal space for
- welding, using filler metal.

Disadvantages

- The electric arc welding processes, such as TIG and plasma welding, are characterized by the imposition of a large amount of heat to achieve fusion of the base and filler material, which causes important microstructure transformations. These transformations occur in a region called the HAZ (Heat Affected Zone), which is a base metal region whose structure or properties were changed by temperature variation during welding.

  These changes generate a complex region of stresses and deformations, leading to results that are not always desired, including material distortion, residual stresses, generation of fragile microstructures, grain grow, cracks, fissures, and changes in mechanical, physical, and chemical properties, among others;
- Insufficient weld penetration in butt type joints;

- The presence of porosities in the region of the union that is due to the inclusion of argon gas, which is necessary to maintain the inert atmosphere during the welding procedure and thus minimize interaction with air elements. These bubbles and crashes act as initiators of fractures and points of stress concentration, and can lead to the failure of welded structures in a short period of time.

Conclusively tungsten inert gas welding, one form of plasma arc, is reported to produce better results than brazing or laser welding [110].

Miscellaneous

Koban., *et al*. reported an interesting direct application of NTAPP, which reduced the contact angle of untreated dentin surface and caused a superior spreading of osteoblasts on the dentin. These results may be utilized to optimize periodontal regeneration in the future [111]. The interaction of NTAPP with the human periodontal ligament mesenchymal stem cells demonstrated that NTAPP inhibited the migration of the cells and induced some detachment, without affecting their viability [112].

Plasma in dental cavities

Yang., *et al*. introduced and conducted a study on low-temperature atmospheric argon plasma brush for effectively deactivating *Streptococcus mutans* and *Lactobacillus acidophilus*. He concluded that about 100% bacterial elimination was achieved within 15 seconds for *Streptococcus mutans* and in 5 minutes for *Lactobacillus acidophilu*s. Also, in comparison to lasers, plasmas can access small irregular cavities and fissure spaces [110,113]. Non-thermal atmospheric plasma brush was used for bacterial disinfection, which is necessary in dental restorations to prevent secondary caries. Plasma is an efficient source of various radicals, which are capable of bacterial decontamination, and operates at room temperature and thus, does not cause bulk destruction of the tissue [4,114].

Safety measures for the cold plasma energy in dentistry

Plasma is a rich source of radicals and other active species. As it is already know that free radicals have earned a bad name in biology and medicine because of their capability of causing severe cell damage, especially the ROS. The ROS family comprises radicals like oxygen (O), hydroxide (OH) and hydroperoxyl group (HO_2), peroxide anions like oxygen ions (O¡2) and hydroxide ions (HO¡2), ozone and hydrogen peroxide. When the ROS level in body fluids becomes too high, various types of damage occur, known under a common name of oxidative stress. It is believed that oxidative stress bears at least partial responsibility for diseases like arteriosclerosis, cancer and respiratory problems. Moreover, high concentrations of oxygen radicals accelerate ageing of cells and tissues. On the cellular level, several effects leading to cell injury have been identified: lipid peroxidation, DNA damage and protein oxidation [80,115].

On the other hand, free radicals have various important functions in the body. For example, macrophages generate ROS to destroy the invading bacteria, and endothelial cells (inner artery wall) produce nitric oxide (NO) to regulate the artery dilation. Plasmas are often very complex mixtures; in fact, they owe their specific properties to the synergy of various components: charged particles (electrons, positive and negative ions), metastables, re-vibrationally excited molecules, active radicals and (UV) photons [116]. Therefore, it is a great challenge for the experimentalist to characterize the plasma and to tailor its properties to achieve desired benefits.

Conclusion

The literature on plasma sterilization has been growing substantially in the recent past. Based on the above evidence, we can conclude that CAP has a bright future in dentistry due to its multiple applications in various treatments. Plasma dental treatments are basically painless, drill-less making it patient friendly especially in children and under-served communities, where education and familiarity with the dentist's chair are, by definition, limited. Also, due to its versatile applications it can be used in almost all the branches of dentistry. However, more studies need to be performed regarding the mechanism of action. Therefore, with further research plasma technology can become a valuable tool in dentistry.

The costs associated with the use of plasma devices are much lower than those of laser devices, making it plasma devices much more suitable for surgical purposes. In comparison to a laser treatment, where delayed wound healing and rare post-treatment discomfort can arise, the use of plasma has shown no such deleterious effects during or after treatment. Research is being done to include more plasma devices for dental treatment and sterilization procedures [117].

Conflict of Interest and Source of Funding

This was a self-funded work with no conflicts of interest.

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