

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/317090193>

## Nonthermal Plasma in Dentistry: An Update

Article · May 2017

DOI: 10.4103/jispcd.JISPCD\_29\_17

---

CITATIONS

4

---

READS

232

4 authors, including:



Ranjan Rajeev

KIIT University

25 PUBLICATIONS 25 CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:



Non thermal atmospheric pressure plasma jet for Oral cancer treatment [View project](#)



Co- relation of Periodontal disease and Neurodegenerative diseases. [View project](#)

## Nonthermal Plasma in Dentistry: An Update

Rajeev Ranjan, P. V. Krishnamraju, Thatapudi Shankar,<sup>1</sup> Snigdha Gowd<sup>2</sup>

Department of Periodontics and Oral Implantology, Kalinga Institute of Dental Sciences, KIIT University, <sup>1</sup>Department of Prosthodontics, Kalinga Institute of Dental Sciences, KIIT University, <sup>2</sup>Department of Orthodontics and Dentofacial Orthopedics, Kalinga Institute of Dental Sciences, KIIT University, Patia, Bhubaneswar, Odisha, India

Received : 20-01-17.

Accepted : 30-03-17.

Published : 22-05-17.

### INTRODUCTION

Matter is usually composed of liquids, solids, and gases. A fourth component of matter has been brought to notice that has been named plasma. Sir William Crookes, a British Physicist, discovered plasma in 1879 and Irving Langmuir named it in 1929.<sup>[1]</sup> It is the most unusual and most abundant state of matter. It constitutes approximately 99% of the visible universe. Due to the use of constant energy by stripping electrons, plasmas are naturally energetic. They can exist in a wide range of temperatures without changing state, unlike ordinary matter. For example, the Northern lights are cold as ice while the center of a distant star is extremely hot. Plasma such as gas particles do not have definitive shape. However, the presence of electric and magnetic field shape it into a malleable structure.<sup>[2]</sup> The various ways of creating plasmas include radiofrequency, high voltage DC or AC, microwave frequencies, etc.

On the basis of relative temperatures of the ions, neutrals, and electrons, plasmas are categorized as “thermal” or “nonthermal.” Electrons and heavy particles of thermal plasma remains in thermal balance with each other. The electrons of nonthermal plasma (NTP) are hotter

### ABSTRACT

The recent enormous progress in understanding of plasma physics and development of plasma jet has attracted focus on the application of plasma in medicine and dentistry. Active plasma ions, electrons, and photons have the ability to activate and control various biochemical procedures. Nonthermal plasma (NTP) is widely used for various therapeutic applications in health care. Particularly in dentistry, NTP holds big potential such as for bacterial inactivation, efficient sterilization, and treatment of dental caries. This review intends to provide information on potential NTP applications in dentistry.

**KEYWORDS:** Bacterial inactivation, dental caries, nonthermal plasma, sterilization

whereas ions and neutrals remain at room temperature. Recently, NTP source with <40°C temperature at the point of application have been presented that offer the possibility to treat human beings.<sup>[3]</sup>

Cold atmospheric plasma (CAP) is also known as NTP because of the presence of electrons and heavy particles at a very high temperature and room temperature. The temperature at the point of application is less than 104°F.

Plasma needle, dielectric barrier discharge, plasma pencil, etc. are being used for the production of NTP. Wide applications of CAP in dentistry and oncology have been reported in recent literature considering its ability to kill cancer cells and deactivate various pathogenic microorganisms.<sup>[4]</sup>

Recent literature have shown the applications of CAP for sterilization of medical and dental equipment, packaging

**Address for correspondence:** Dr. Rajeev Ranjan,

Department of Periodontics and Oral Implantology, Kalinga Institute of Dental Sciences, Campus 5, KIIT University, Bhubaneswar, Odisha - 751024, India.  
E-mail: ranjan.rajeev\_84@yahoo.com

### Access this article online

#### Quick Response Code:



**Website:** www.jispcd.org

**DOI:** 10.4103/jispcd.JISPCD\_29\_17

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**How to cite this article:** Ranjan R, Krishnamraju PV, Shankar T, Gowd S. Nonthermal plasma in dentistry: An update. J Int Soc Prevent Communit Dent 2017;7:71-5.

of food in food industry, blood coagulation, promotion of wound healing, etc.<sup>[5-12]</sup> In dentistry, CAP has opened a new painless way to prepare tooth cavities prior to restoration. It can be an effective tool for the treatment of dental caries and for composite restorations due to its properties of deactivation of pathogenic bacteria and modification of noninflammatory tissue. Furthermore, dental applications of CAP are disinfection of root canal, sterilization of dental instruments and equipment, removal of plaque, tooth whitening (bleaching), and increasing bond strength at the interface of dentin and composite.

### NONTHERMAL ATMOSPHERIC PLASMA

NTP has also been used in the modification of surface characteristics of biomaterials. It is distinguished by a low degree of ionization, low temperature at the point of application, and low atmospheric pressure. NTP is produced by transformation of a compound into a gas. Later, ionization of gas particle takes place by application of energy in the form of laser light, heat, radiation, or electric current.<sup>[13]</sup>

Presence of electromagnetic field supply energy to sustain plasma state. Electrons get accelerated by the presence of an electromagnetic field at a very faster rate than heavy ions. These accelerated electrons are comparatively less effective in transferring energy to heat their surrounding environment than heavy ions.<sup>[14]</sup> Accelerated electrons results into ionization of particles, radiation, and creation of reactive species. Common gas sources used for the production of plasma are argon, hydrogen, oxygen, or nitrogen. In material science, NTP is used in the modification of surface characteristics and properties of materials. Hardness, wetting ability, resistance to chemical corrosion, etc. can be modified by the use of NTP.<sup>[15]</sup>

Electric safety of dielectric barrier discharge (DBD)-type plasma device and pulsed power plasma device is attained by limiting current flow.<sup>[16]</sup> This limitation of current flow is achieved by preventing current-to-transit arcing and use of a pulsed signal.<sup>[16]</sup> Considering the stability and safety of microwave-derived plasma, it is commonly used for biomedical applications. Laroussi *et al.* introduced a miniature jet that they called plasma pencil. The plasma pencil has been used in the treatment of *Escherichia coli*, leukemia cells, and *Porphyromonas gingivalis*.<sup>[17]</sup>

### DENTISTRY AND PLASMA

Sterilization is done by removing all pathogenic and nonpathogenic microorganisms. Efficacy of plasma devices in killing bacteria is better than conventional

nonthermal methods, viz. UV sterilization. This efficacy of plasma devices are determined by gas composition and type of bacterial strain.<sup>[18,19]</sup> Plasma devices lead to generation of various radicals, which results into bacterial deactivation and decontamination. However, because it works at room temperature, it does not result into destruction of living tissues. NTP effectively treats and sterilizes irregular tooth surfaces, which results into decontamination of tooth cavities prior to restoration without drilling.<sup>[20]</sup> Recently, small and easy to use plasma jet device has been developed which can produce NTP inside the root canal. Moreover, NTP has also been used in the management of oral candidiasis, linear gingival erythema, and angular stomatitis.<sup>[21]</sup> NTP treatment enhances the performance, longevity, and durability of composite restoration by enhancing bonding strength at the interface of dentin and composite by approximately 60%. Plasma is also used in bleaching of the teeth by using direct current (DC) plasma jet and hydrogen peroxide.

### APPLICATION IN TREATMENT OF DENTAL DISEASES

#### STERILIZATION BY ERADICATION BY BACTERIA

The plethora of plasma components such as, reactive oxygen species (ROS), electromagnetic fields, and ions and electrons is related to the mechanism of plasma sterilization. Other than the point of contact, plasma can also affect the area around it. Now a days, plasma sterilization has become common and widely used in dentistry.<sup>[7]</sup> The utilization of NTP for decontamination of surgical instruments is limited. Whittaker *et al.* has suggested that use of plasma gas cleaning may be very effective in decreasing the absolute amount of proteinaceous substances from pulp that may be transferred between the patients when endodontic instruments and files are used.<sup>[22]</sup> Li *et al.* indicated that plasma sterilization overcomes the limitations of traditional sterilization methods. It has become a novel method of sterilization by providing the advantages of safety, thoroughness, fastness, and low temperature.<sup>[23]</sup> Sung *et al.* evaluated the effectiveness of NTP device for sterilization of various instruments and equipment made of metals, rubbers, and plastics.<sup>[24]</sup> It was found that NTP device was highly efficacious in deactivation of both *Bacillus subtilis* and *E. coli* and was more potent in killing of *E. coli* than the UV sterilizer.

#### DENTAL CARIES

Raymond *et al.* deliberated the interactions of NTP with dental tissue using a plasma needle.<sup>[25]</sup> Cleaning and disinfection of the infected tissue in a dental cavity or in a root canal can be performed using mechanical or laser techniques. However, with both approaches, heating and

destruction of healthy tissue can occur. A plasma needle is an efficient source of various radicals, which helps in bacterial decontamination. Because it operates at room temperature, it does not cause bulk destruction of the tissue. The conclusion of this study was that plasma treatment is actually a prominent tissue-saving technique that allows irregular structures and narrow channels within the diseased tooth to be cleaned. Short-lived chemical species in the gas phase produced by the plasma needle can interact on a tooth's surface and can dissolve into a liquid. Dissimilar to the liquid rinses with bactericidal ingredients that stay in the mouth after the procedure, the plasma needle produces bactericidal agents locally, which can reach the inside of the cavity and fissure spaces.<sup>[26]</sup>

Yang *et al.* introduced nonthermal argon plasma brush which is highly efficacious in the deactivation and decontamination of *L. acidophilus* and *Streptococcus mutans*.<sup>[27]</sup> The authors revealed that approximately 100% of bacterial decontamination was achieved within 15 s for *S. mutans* and within 5 min for *L. acidophilus*.

### ADHESIVE RESTORATIONS

Dong *et al.* examined the effect of NTP on composite restoration. He found that application of plasma modifies the dentin surface and increases dentin/adhesive interfacial bonding.<sup>[28]</sup> Ritts *et al.* also assessed the effect of NTP brush on composite restoration.<sup>[29]</sup> It was found that NTP can alter the surface characteristics of dentin, which results into increased bonding between dentin and adhesive restorations. Yavirach *et al.* in his study found that plasma treatment of fiber-reinforced composite and resin composite have more tensile shear bond than traditional core build up.<sup>[30]</sup>

### BIOFILMS

Biofilms formed over the tooth surface lead to dental caries, gingival and periodontal diseases, and oral mucositis. These biofilms can also affect dental implant by causing peri-mucositis and peri-implantitis. NTP has the ability to destroy biofilm matrix without causing any damage to the oral tissue.<sup>[31]</sup> Koban *et al.* in his *in-vitro* study found that NTP is more efficient in killing of bacteria present in the dental biofilm than chlorhexidine.<sup>[32]</sup> NTP is also effective in the decontamination of biofilms present either on root canals or on dental slices. Jiang *et al.* in his *in-vitro* study used a plasma plume to disinfect the root canal of extracted human teeth at room temperature.<sup>[33]</sup> The authors got better results with plasma in disinfection of root canal than control.

### ROOT CANAL DISINFECTION

NTP containing He/O<sub>2</sub> (20%) gas have shown rotational and vibrational temperature of approximately 300 K and

2700 K, respectively. At this temperature, approximately 10 mA of current discharge occurs. Plasma produced at this level can completely kill *Enterococcus faecalis* which is responsible for failure of root canal treatment. Pan *et al.* in his *in-vitro* study checked the feasibility of NTP for disinfection of root canal. Authors suggested that NTP has a high rate of killing of pathogenic microorganisms present in the root canal.<sup>[34]</sup>

### TOOTH WHITENING

NTP have also been used in teeth bleaching. Lee *et al.* in his study used NTP for teeth bleaching and demonstrated that this effect is due to the release of OH radicals and removal of surface proteins. The authors found that NTP in combination with hydrogen peroxide were able to remove stains from extracted teeth.<sup>[35]</sup> Direct current plasma jet along with hydrogen peroxide can also be used for tooth whitening.<sup>[36]</sup> Removal of intrinsic stains are always a big concern during teeth bleaching.<sup>[37,38]</sup>

Low frequency plasma source along with hydrogen peroxide can be used to remove intrinsic stain, as suggested by Park *et al.*<sup>[39]</sup> Kim *et al.* in 2012 developed a radiofrequency driven gas liquid hybrid plasma system. In this study, de-ionized water was used for tooth bleaching by immersing target tooth in water. Bleached tooth surface was observed after 8 min of immersion for plasma chemical reaction.<sup>[40]</sup> In an *in-vitro* study, Nam *et al.* used a plasma jet for bleaching of tooth. Authors found that NTP was the most effective in tooth bleaching without causing any damage to the tooth than carbamide peroxide alone and a combination of carbamide peroxide and diode laser.<sup>[36]</sup> This result was supported by Claiborne *et al.* in his *in-vitro* study.<sup>[41]</sup> In a study by Zhu *et al.*, results revealed that, compared with conventional teeth bleaching, immediate bond strength of resin-enamel treated by cold plasma was not affected.<sup>[42]</sup>

### DISCUSSION

Plasma remains in gaseous medium and can reach inaccessible areas of tooth surface such as fissures and grooves. The biggest advantage associated with use of NTP is that it kills only pathogenic bacteria present in dental plaque without affecting the surrounding healthy tissues. Because NTP does not lead to increase in temperature at the point of application, it does not causes any thermal damage and pain in patients. NTP equipment was used to kill *E. faecalis* biofilm incubated for 3 weeks. No cultured bacteria were recovered from the agar plate after 12 min of treatment, which indicates that the *E. faecalis* biofilm was destroyed completely.

Unique characteristics of NTP have opened a new era in dental care. It has shown promising results in sterilization, root canal disinfection, blood coagulation,

wound healing, etc. However, because oral diseases are polymicrobial in nature, there is a need of research to evaluate the effect of NTP on each and every pathogens involved in dental plaque formation. Other than this, the fundamental concepts of plasma and its interaction with living tissues should also be investigated more. This will be helpful in finding hidden potential of plasma in dental care.

### LIMITATION

Overall, CAP also has its own advantages and disadvantages. Being a new technology, improvement is required regarding safety of the equipment. It is a highly sensitive technique.

Cost of the NTP device and its maintenance are prime concern at present. Portability of the NTP device is also one of the concern in dental care.<sup>[43]</sup> Recently NTP has been tried in oncology with some promising results. However, there is a need for research to determine the effect of NTP on normal cells in detail.<sup>[44-46]</sup>

### CONCLUSION

Based on the information provided above, we can conclude that NTP has a promising future in dentistry due to its antimicrobial properties. Plasma dental treatments are painless and drill-less, thereby making them patient-friendly, especially in children and underserved communities, where communities, education, and familiarity with the dentist's chair are, by definition, limited. However, more studies need to be made for the clarity in the mechanism of action and its varied application in the dental field.

### FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

### CONFLICTS OF INTEREST

There are no conflicts of interest.

### REFERENCES

- Neha S, Manjunath KM. Cold plasma: Northern lights in the dental office: A brief review. *J Int Clin Dent Res Organ* 2016;8:81-3.
- Martin M. From distant stars to dental chairs- Plasmas may promise pain-free and durable restorations. *AGD Impact* 2009;37:46.
- Kong MG, Kroesen G, Morfill G, Nosenko T, Shimizu T, Dijk JV, *et al.* Plasma medicine: An introductory review. *New J Phys* 2009;11:115012.
- Hoffmann C, Berganza C, Zhang J. Cold atmospheric plasma: Methods of production and application in dentistry and oncology. *Med Gas Res* 2013;3:21.
- Deng S, Ruan R, Mok CK, Huang G, Lin X, Chen P, *et al.* Inactivation of *Escherichia coli* on almonds using non thermal plasma. *J Food Sci* 2007;72:62-6.
- Shintani H. Inactivation of bacterial spore, endotoxin, lipid A, normal prion and abnormal prion by exposures to several sorts of gases plasma. *Biocontrol Sci* 2016;21:1-12.
- Mohd Nasir N, Lee BK, Yap SS, Thong KL, Yap SL. Cold plasma inactivation of chronic wound bacteria. *Arch Biochem Biophys* 2016;605:76-85.
- Volotskova O, Dubrovsky L, Keidar M, Bukrinsky M. Cold atmospheric plasma inhibits HIV-1 replication in macrophages by targeting both the virus and the cells. *PLoS One* 2016;11:e0165322.
- Song AY, Oh YA, Roh SH, Kim JH, Min SC. Cold oxygen plasma treatments for the improvement of the physicochemical and biodegradable properties of polylactic acid films for food packaging. *J Food Sci* 2016;81:E86-96.
- Bahrami N, Bayliss D, Chope G, Penson S, Pehinec T, Fisk ID. Cold plasma: A new technology to modify wheat flour functionality. *Food Chem* 2016;202:247-53.
- Smet C, Noriega E, Rosier F, Walsh JL, Valdramidis VP, Van Impe JF. Impact of food model (micro)structure on the microbial inactivation efficacy of cold atmospheric plasma. *Int J Food Microbiol* 2017;240:47-56.
- Shi Q, Song K, Zhou X, Xiong Z, Du T, Lu X, *et al.* Effects of non-equilibrium plasma in the treatment of ligature-induced peri-implantitis. *J Clin Periodontol* 2015;42:478-87.
- Annunziata M, Canullo L, Donnarumma G, Caputo P, Nastri L, Guida L. Bacterial inactivation/sterilization by argon plasma treatment on contaminated titanium implant surfaces: *In vitro* study. *Med Oral Patol Oral Cir Bucal* 2016;21:e118-21.
- Hippler R, Kersten H, Schmidt M, Schoenbach KH. *Low temperature plasma physics: Fundamental aspects and applications* 2008 Weinheim, Germany Wiley-VCH.
- Iza F, Kim GJ, Lee SM, Lee JK, Walsh JL, Zhang YT, *et al.* Microplasmas: Sources, particle kinetics and biomedical applications. *Plasma Process Polym* 2008;5:322-44.
- Sharma A, Pruden A, Zengqi Y, Collins GJ. Bacterial inactivation in open air by the afterglow plume emitted from a grounded hollow slot electrode. *Environ Sci Technol* 2005;39:339-44.
- Laroussi M, Tendero C, Lu X, Alla S, Hynes WL. Inactivation of bacteria by the plasma pencil. *Plasma Processes Polym* 2006;3:470-3.
- Mccullagh C, Robertson J, Bahnemann DW, Robertson P. The application of TiO<sub>2</sub> photocatalysis for disinfection of water contaminated with pathogenic micro-organisms: A review res. *Chem Intermed* 2007;33:359-75.
- Kim GC, Kim GJ, Park SR, Jeon SM, Seo HJ, Iza F, *et al.* Air plasma coupled with antibody-conjugated nanoparticles: A new weapon against cancer. *J Phys D Appl Phys* 2009;42:032005.
- Louroussi M. Low temperature plasma-based sterilization: overview and state-of-the-art. *Plasma Process Polym* 2005;2:391-400.
- Arora V, Nikhil V, Suri NK, Arora P. Cold Atmospheric Plasma (CAP) in Dentistry. *Dentistry* 2014;4:189.
- Whittaker AG, Graham EM, Baxter RL, Jones AC, Richardson PR, Meek G, *et al.* Plasma cleaning of dental instruments. *J Hosp Infect* 2004;56:37-41.
- Yang Hong L, Liu S, Hu T. Application of low-temperature plasma in dental clinical sterilization. *Foreign Med Sci Stomatol* 2013;40:483-5.
- Sung SJ, Huh JB, Yun MJ, Myung B, Chang W, Jeong CM *et al.* Sterilization effect of atmospheric pressure non-thermal air plasma on dental instruments. *J Adv Prosthodont* 2013;5:2-8.
- Sladek REJ, Stoffels E, Walraven R, Tiebeek PJA, Koolhoven RA. Plasma treatment of dental cavities: A feasibility study. *IEEE Trans Plasma Sci* 2004;32:1540-3.

26. Vandana BL. From Distant Stars to Dental Chairs: An Update on Plasma Needle. *Int J Dent Sci Res* 2014;2:19-20.
27. Yang B, Chen J, Yu Q, Li H, Lin M, Mustapha A, *et al.* Oral bacterial deactivation using a low-temperature atmospheric argon plasma brush. *J Dent* 2011;9:48-56.
28. Dong X, Chen M, Wang Y, Yua Q. A Mechanistic study of Plasma Treatment Effects on Demineralized Dentin Surfaces for Improved Adhesive/Dentin Interface Bonding. *Clin Plasma Med* 2014;2:11-6.
29. Ritts AC, Li H, Yu Q, Xu C, Yao X, Hong L, *et al.* Dentin surface treatment using a non-thermal argon plasma brush for interfacial bonding improvement in composite restoration. *Eur J Oral Sci* 2010;118:510-6.
30. Yavirach P, Chaijareenont P, Boonyawan D, Pattamapun K, Tunma S, Takahashi H, *et al.* Effects of plasma treatment on the shear bond strength between fiber reinforced composite posts and resin composite for core build-up. *Dent Mater J* 2009;28:686-92.
31. Delben JA, Zago CE, Tyhovych N, Duarte S, Vergani CE. Effect of atmospheric-pressure cold plasma on pathogenic oral biofilms and *in vitro* reconstituted oral epithelium. *PLoS One* 2016;25:e0155427.
32. Koban I, Holtfreter B, Hu'bnner NO, Matthes R, Sietmann R, Kindel E, *et al.* Antimicrobial efficacy of non-thermal plasma in comparison to chlorhexidine against dental biofilms on titanium discs *in vitro* – Proof of principle experiment. *J Clin Periodontol* 2011;38:956-65.
33. Jiang C, Chen MT, Gorur A, Schaudinn C, Jaramillo DE, Costerton JW, *et al.* Nanosecond pulsed plasma dental probe. *Plasma Processes Polym* 2009;6:479-83.
34. Pan J, Sun K, Liang Y, Sun P, Yang X, Wang J, *et al.* Cold plasma therapy of a tooth root canal infected with enterococcus faecalis biofilms *in vitro*. *J Endod* 2013;39:105-10.
35. Lee HW, Kim GJ, Kim JM, Park JK, Lee JK, Kim GC. Tooth bleaching with non thermal atmospheric pressure plasma. *J Endod* 2009;35:587-91.
36. Nam SH, Lee HW, Cho SH, Lee JK, Jeon YC, Kim GC. High-efficiency tooth bleaching using non-thermal atmospheric pressure plasma with low concentration of hydrogen peroxide. *Journal of Applied Oral Science* 2013;21:265-70.
37. Lee HW, Nam SH, Mohamed AAH, Kim GC, Lee JK. Atmospheric pressure plasma jet composed of three electrodes: Application to tooth bleaching. *Plasma Process Polym* 2010;7:274-80.
38. Sun P, Pan J, Tien Y, Bai N, Wu H, Wang L, *et al.* Tooth whitening with hydrogen peroxide assisted by a direct-current cold atmospheric-pressure air plasma microjet. *IEEE Trans Plasma Sci* 2010;38:1892-6.
39. Park JK, Nam SH, Kwon HC, Mohamed AA, Lee JK, Kim GC. Feasibility of non thermal atmospheric pressure plasma for intracoronal bleaching. *Int Endod J* 2011;44:170-5.
40. Kim MS, Koo IG, Choi MY, Jung JC, Eldali F, Lee JK, *et al.* Correlated electrical and optical studies of hybrid argon gas-water plasmas and their application to tooth whitening. *Plasma Process Polym* 2012;8:339-45.
41. Claiborne D, McCombs G, Lemaster M, Akman MA, Laroussi M. Low temperature atmospheric pressure plasma enhanced tooth whitening: the next-generation technology. *Int J Dent Hyg* 2014;12:108-14.
42. Zhu MM, Wang GM, Sun K, Li YL, Pan J. Bonding strength of resin and tooth enamel after teeth bleaching with cold plasma. *Beijing Da Xue Xue Bao* 2016;48:116-20.
43. Khalil J. Periodontal disease: An overview for medical practitioners. *Lik Sprava* 2008;3:10-21.
44. Kang SU, Seo SJ, Kim YS, Shin YS, Koh YW, Lee CM, *et al.* Comparative effects of non-thermal atmospheric pressure plasma on migration and invasion in oral squamous cell cancer, by gas type. *Yonsei Med J* 2017;58:272-81.
45. Lee JH, Om JY, Kim YH, Kim KM, Choi EH, Kim KN. Selective killing effects of cold atmospheric pressure plasma with NO induced dysfunction of epidermal growth factor receptor in oral squamous cell carcinoma. *PLoS One* 2016;11:e0150279.
46. Chang JW, Kang SU, Shin YS, Seo SJ, Kim YS, Yang SS. Combination of NTP with cetuximab inhibited invasion/migration of cetuximab-resistant OSCC cells: Involvement of NF-κB signaling. *Sci Rep* 2015;5:18208.