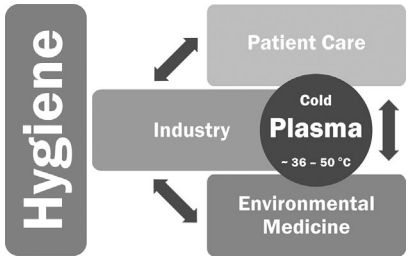
Cold Physical Plasmas in the Field of Hygiene—Relevance, Significance, and Future Applications

Axel Kramer,[†] Sander Bekeschus,*[†] Rutger Matthes, Claudia Bender, Matthias B. Stope, Matthias Napp, Olaf Lademann, Jürgen Lademann, Klaus-Dieter Weltmann, Frieder Schauer

Cold physical plasmas ignited a technological spark in industry, biotechnology, and medicine. Especially the field of hygiene benefited of the plasma's exceptional activity against pathogenic microorganisms. Together with plasma-based surface functionalization, these qualities are highly relevant in a variety of processes in health care, such as the decontamination or sterilization of medical devices, food, packaging materials, waste water, or indoor air. In medicine, plasma has proven to show promising antiseptic results on skin and mucosal membranes in infection-related diseases in dermatology and dentistry. This comprehensive review will discuss the current applications of cold plasma in the fields of hygiene, and will provide a promising outlook on many applications yet to come.



A. Kramer, C. Bender
Institute for Hygiene and Environmental Medicine, University Medicine Greifswald, Walther-Rathenau-Str. 49a, 17485, Greifswald, Germany
S. Bekeschus, R. Matthes, K.-D. Weltmann
Leibniz-Institute for Plasma Science and Technology (INP Greifswald), ZIK plasmatis, Felix-Hausdorff-Str. 2, 17489, Greifswald, Germany
E-mail: sander.bekeschus@inp-greifswald.de
R. Matthes
Center for Dental, Oral, and Maxillofacial Surgery, University Medicine Greifswald, Walther-Rathenau-Str. 42a, 17489, Greifswald, Germany
M. B. Stope
Department of Urology, University Medicine Greifswald, Sauerbruchstr., 17475, Greifswald, Germany
M. Napp
Department of Trauma and Reconstructive Surgery, University Medicine Greifswald, Sauerbruchstr., 17475, Greifswald, Germany
O. Lademann
Department of Anesthesiology and Intensive Therapy, University Medicine Rostock, Schillingallee 35, 18057, Rostock, Germany
J. Lademann
Department of Dermatology, Venereology, and Allergology, Charité University Medicine Berlin, Charitéplatz 1, 10117, Berlin, Germany
F. Schauer
Department of Applied Microbiology, Ernst-Moritz-Arndt University of Greifswald, Friedrich-Ludwig-Jahn-Str. 15, 17489, Greifswald, Germany

[†]These authors contributed equally to this work as first authors.

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1. Introduction

The use of cold plasma (from here on termed "plasma" implying a low-temperature gas discharge, exclusively) technology in the field of hygiene is indicated if one of the following objectives is required: antimicrobial and/or anti-biofilm activity, and skin tolerance or preservation of material properties that are otherwise sensitive to chemicals and/or heat. In case of the latter, plasma is particularly promising where the use of chemical substances is limited. This is the case if such substances leave behind remnant components on the surface or if the chemically active ingredient cannot sufficiently penetrate the target in question. Similarly, some materials do not withstand the chemical reactivity, or the costs for chemical disinfection are higher than compared to the application of plasma. A vast group of studies successfully demonstrated the activity of plasma against microorganisms in vitro in suspension,[1–3] on agar,[4–6] in biofilms,[7–10] on the skin,[11–13] and on the eye.[14] Plasmas can inactivate microorganisms regardless of their multidrug resistance.[15–17] Moreover, the inactivation of bacteriophages and viruses by plasma has been demonstrated.[18–20] Plasma-treated solutions exhibit microbicidal effects as well.[21–23] Up to now, no development of microorganisms resistant to the plasma's cytotoxicity was observed. Plasmas also improve bio-active surfaces and thus increase the tissue-compatibility of implant materials.[24–26] Moreover, plasmas induce metabolic modification in microorganisms which may be useful to improve biodegradation or to increase the production of specific metabolites.[27] We here provide a comprehensive overview of plasma applications, and several important topics will be discussed considering the latest studies involving plasmas in hygiene-related fields of medicine, health care, and biotechnology.

Born in Gotha, Germany, 1946, Axel Kramer is the Chair of Institute of Hygiene at the University of Greifswald since 1990. He is also Foreign member of the Union of Scientists in Bulgaria since 2002, and since 2009 he is an invited Professor of the Postgraduate School at Tokyo Healthcare University. His research priorities include hospital hygiene, biocompatibility of medical devices, and plasma medicine. His electoral functions include: 1994–1998 vice dean of the Medical Faculty in Greifswald, 1990–2010 president of the German Society of Hospital Hygiene, Vice President of Austrian Society of Hospital Hygiene since 2012, member of the Commission of Hospital Hygiene and Infection control at the Robert Koch-Institute Berlin since 1993.

Born in Berlin, Germany, Sander Bekeschus studied human biology with a major in immunology at the University of Greifswald. He also received his Ph.D. in immunology at the University of Greifswald where he worked in a joint project at the Leibniz-Institute for Plasma Science and Technology (INP Greifswald). Sander's research focuses on deciphering the responses of cells of the innate and adaptive immune system following exposure to cold plasma. Currently, Sander is pursuing a group leader position at the INP Greifswald within the plasmatis project where he and his team study possible roles of cold plasmas in oncological therapies.

Rutger Matthes, born in Zittau, Germany, 1981, studied human biology at the University Greifswald. He received his Ph.D. at the Institute of Hygiene and Environmental Medicine at the same university, 2013. His research is focused to investigations about the antimicrobial effects of cold plasma, especially in biofilms, and about the cell adhesion on plasma-prepared implant material. Currently, he is an employee of the Leibniz-Institute for Plasma Science and Technology (INP Greifswald) and University Greifswald at the Unit of Periodontology. His research aims at finding new options to prevent and to therapy peri-implantitis.

*For a full set of author biographies please see the Supporting Information online.

2. Decontamination of Surfaces and Liquids

2.1. Sterilization

With the use of plasmas, sterilization (i.e., reduction of at least 10^6 log bacteria) can be achieved.[28] Such an innovative technology was strongly needed for the sterilization of new polymeric and heat-sensitive medical products (MPs) and its application was thoroughly reviewed previously.[29–32] The first sterilization device (Sterrad) was commercialized in 1993[33] and was thereafter successfully introduced in health care services as well as in industrial sterilization. The process involves the application of a hydrogen peroxide (HPO) gas (50 °C) under low pressure (6–10 Torr) combined with the ignition of plasma by using high-frequency electromagnetic fields.[34] In addition to bacterial inactivation,[35] the gas also shows a virucidal activity and partially inactivates prions if combined with alkaline cleaning agents.[36] The low relative humidity (5%) required during the sterilization process facilitates the use of this technology for disinfecting moisture sensitive MPs. The prerequisites for a successful sterilization procedure of a given MP is its need to be clean, dry, and in hydrophobic packaging. Furthermore, its surface needs to be readily accessible because complex and hollow surfaces do not allow a uniform penetration of the active components.[37] Contaminations with blood or salt also reduce the

sterilization efficacy and additional cleaning is needed prior to the application of the process.[38] Finally, the efficiency is limited with metals being present in or at the MPs. An analogous sterilization device is the peracetic acid plasma-based sterilizer (Plazlyte) but its sterilization efficiency[39] and by-products[40] were found to be only partially satisfactory. In both devices, the toxic gas is the central component in the sterilization process whereas the plasma seems to rather decompose any chemical remnants of the gas that would otherwise remain on the sterilized item.[41] Recent efforts to increase the plasma activity by using the afterglow of an N_2 or Ar-N_2 plasma resulted in the required 6 log reduction of initial inoculum only after exceedingly long exposure times.[42–44] Although the efficacy of the HPO gas alone could not be enhanced any further, recent studies point to synergistic effects of plasma ions with nitrogen.[45] This underlines the high innovation potential of plasma in sterilization technology.

2.2. Reprocessing of Medical Products

Plasma-assisted decontamination is a promising option for MPs that are subject to preparative processes prior to their use. Plasmas can penetrate into small cavities which may be suitable to decontaminate endoscopes that are otherwise difficult to recycle. With the introduction of small and portable plasmas jets, these devices can easily be re-located (e.g., in surgical units) to decontaminate any surface in need (such as surgical equipment).[46] Moreover, many cleaning systems for contact lenses are not satisfactory,[47] and plasma treatment may be an alternative to safely decontaminate these MPs.[48] A benefit of plasma technology is also seen in implantology. Implants may receive plasma treatment prior to surgical insertion in order to functionalize the implant's surface for improved autologous cell attachment and to inactivate any bacteria introduced during the surgical procedure. This may be of particular importance in orthopedic surgery where infections with antibiotic-resistant bacteria occur frequently.[49] Likewise, plasma may be beneficial in infection-related surgical revisions in situ where the implant and its surrounding tissue need therapeutic attention. Plasma retains the desired characteristics of particularly sensitive materials and may be, therefore, beneficial in such applications.[50] For example, the antimicrobial activity of poly lactic-co-glycolic acid embedded in protein structures is not compromised after exposure to plasma.[51]

2.3. Plasma Applications in Food Hygiene and Packaging Materials

The production of food involves an ever increasing share of technologies in order to stay up to date with the latest inventions, regulatory laws, ecological standards, changes in global supply and trade, and the customers' demand for high-quality products. Physical methods for food decontamination, such as gamma and beta radiation, ultrasonic irradiation, high hydrostatic pressure, or pulsed electrical fields as well as chemical methods, for example, ozonation or ethylene oxide, have their limitations. Among them are health risks, huge financial investments, or product quality impairment, to name a few. Accordingly, plasma has been considered to be an alternative option circumventing these pitfalls. After treatment, no substances released by plasma remain on the food. At the same time, essential food characteristics remain untouched. Plasmas are also active against microorganisms that are sometimes pathogenic or putrefy food as has been shown in fish, meat, poultry, cheese, fruits, vegetables, seeds, eggs, dried nuts, dried milk, and spores in spices.[52–60] Also, an inactivation of *Escherichia coli*, *Salmonella spp.*, *Vibrio parahaemolyticus*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Bacillus cereus*, and foodborne viruses in different foods could be demonstrated.[61–66] For food decontamination, the guidelines of the US Food and Drug Administration require a 5 log bacterial reduction. Depending on the type of microorganism, plasmas achieved this condition within a few seconds to 30 min of treatment time.[67] Surfaces in the foods manufacturing process including packaging materials[68–70] or bottles[71–73] can also be decontaminated with plasma. A high voltage dielectric barrier discharge (DBD) reduced biofilm-resident *Pseudomonas aeruginosa* by 5.4 log within 60 s and completely within 300 s of exposure time.[74] This highly effective plasma source generates a variety of potential applications in the food industry. Plasmas not only decontaminate surfaces but liquids as well.[75–77] In the manufacturing process, plasmas can also remove allergens from surfaces[78] and reduce enzymatic activities on food that otherwise impact the food's sensorial or nutritional quality.[79] Nonetheless, key limitations for plasma treatment of food may be the variety and complexity of the equipment necessary and the largely unexplored impact of plasma on the sensory and nutritional quality of treated foods.[80]

2.4. Anti-Mold Activity and Antifungal Effects

Penicillium and *Aspergillus* species as well as other molds (*Cladosporium* and *Neurospora* species) can be inactivated by plasma.[81,82] As such, plasma may be an alternative to biocides for treating wood or fighting indoor molds, especially if chemical decontamination compromises material properties.[83] The efficacy of plasma against fungi was shown for airborne spores[84] and aerosols[85] as well as the decontamination of surfaces of several materials, such as cotton and textile fibers,[86,87] nuts,[88] pistachios,[89] red

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pepper powder,[90] strawberries,[91] and brown rice cereal bars.[92] Decontamination was also demonstrated for seed surfaces of grain and legumes with plant pathogenic molds[93–95] and for plant disease treatment.[96] Additionally, molds and yeasts in meat and fish products can be inactivated.[97,98] The use of plasma is advantageous as it readily spreads into small cavities, evenly dissipating its reactive species content over the surface exposed. In this way, plasma was used for the elimination of biofilms and the inactivation of cells from pathogenic *Candida* species[99–106] and other yeasts[107–109] as well as dermatophytes.[110]

3. Plasma-Based Surface Modification and Their Functionalization

In technical processes, plasmas have been an indispensable tool for material processing.[111] Depending on the desired properties, the plasma process can be adjusted for different purposes. First, cell adhesion and growth on surfaces can be promoted by: i) enhancing the hydrophilic character, roughness, and/or texture; ii) functionalizing the surface with grafted polar groups or with coatings embedding polar groups; or iii) by functionalizing the surface with chemical groups for immobilizing, for example, peptides or sugar molecules that mimic the extracellular matrix.[112] Plasma treatment of surfaces of polyvinyl chloride and silicone rubber led to the improvement of surface hydrophilicity and wettability.[113] By applying positively charged nanoscale polymer layers on implants and using plasma techniques, the adhesion and growth of bone cells is promoted.[114,115] Second, the adhesion of biomolecules or prokaryotic and eukaryotic cells can be discouraged by increasing the chemical inertia, for example, by antifouling coatings using polyethylene oxide (PEO)-like compositions or by grafting fluorinated groups at the surface of the substrate.[116–118] This was recently also achieved using atmospheric pressure plasma.[119] The resulting hydrophobicity prevents the attachment of dirt and pathogens, and promotes their removal.[120–122] This functionalization of the surface allows adapting the surface tension for controlling the adhesion or repulsion of substances, cells, or microorganisms.[123–125] Third, plasma processes at low or atmospheric pressure can facilitate the deposition of composite coatings with hydrophilic matrices embedding bioactive or microbicidal molecules.[126–128] For example, an allylamine plasma polymer film can immobilize silver nanoparticles or titanium–copper layers on surfaces.[129–132] These plasma coatings can be applied to many types of materials, thereby generating vast opportunities to develop, for instance, antimicrobial implants or antiseptic wound dressings and surgical sutures. The antimicrobial efficacy of an oxygen-plasma-treated surface was retained for 16 days, and a titanium dioxide film is being discussed as the effective agent.[133] After surgical insertion of titanium implants, these coatings may prevent biofilm formation. Plasma may, therefore, be advantageous for the initial biointegration of implants.[134] Similarly, plasma-induced surface modification of heat-polymerized acrylic resin can also prevent an early adherence of *Candida albicans*, which may be beneficial in dental applications.[135]

4. Plasmas in Environmental Technologies

4.1. Air Decontamination, Air Purification, and Odor Removal

Plasmas are suitable to complement air cleaning processes. After treatment of contaminated air with plasma, an inactivation of bacteria,[136] fungi,[85] and viruses[137] was demonstrated. High voltage static electricity plasma was found to be suitable to clean exhaust air and kill bacteria from air-condition systems.[138] In particular, the plasma's ozonation seems to be responsible for the inactivation of bacteria and fungi, which fosters the use of plasmas in purification procedures of ambient air.[139,140] Plasma was also demonstrated to rapidly inactivate allergens.[78] The detoxification of air pollution caused by volatile organic compounds (VOCs, such as TCE, TCA, toluene, and xylene), acid and greenhouse gases (such as SO_x, NO_x, HCl, CO_x, N_xO_y, and PFCs), or ozone depletion substances (Freon or Halon) may be assisted by plasma.[141–144] Generally, a number of pollutants are present in waste air, and plasma decomposes different hazardous air pollutants at the same time.[145–149] Plasma removes toxic particles in shipping diesel engine exhaust gases,[150] including NO_x.[151–153] The exploitation of plasma to treat the gaseous effluents released by waste management plants also was recently demonstrated.[154] Several volatile organic compounds cause odor nuisances and these odorous substances can be removed using plasma treatment.[155–157] For example, the elimination of organic sulfur compounds, such as carbon disulfide (CS_2) in air was achieved recently.[158] Furthermore, malodorants from waste air of water treatment plants, pesticide factories, sludge treatment plants (with simultaneous sludge stabilization), food waste sludge, and pigsty were reduced by plasmas.[159–164] Several reviews are available comparing different air cleaning technologies and discussing their limitations, especially with respect to the generation of undesirable by-products.[165–167] To avoid some of these limitations, combinations of plasma treatment with other technologies (e.g., heterogeneous catalysis, photocatalysis, and absorption techniques) were shown to be promising.[168–180] In general, such hybrid systems were more efficient with regard to VOC decomposition than approaches utilizing plasma alone. Recently, the Plasma-Norm process was introduced. Herein, particles and dust are

filtered first. Secondly, microorganisms and odor molecules trapped are subsequently decomposed by plasma.[181] Non-reacting compounds are absorbed in a carbon-based filter storage which is constantly regenerated by the plasma. End products are oxygen, water, and CO_2.[182]

4.2. Waste Water Purification and Degradation of Environmental Micropollutants

Conventional water treatment processes are limited in removing all substances and pollutants.[183] Consequently, remaining micropollutants are evident in the aquatic environments, for example, rivers, lakes, and ground water. Plasma technology is a promising tool to degrade such pollutants in effluents of wastewater treatment plants.[184] Plasma discharges were shown to effectively eliminate phenols, anilines, and naphthols,[185–187] halogenated substances,[188–192] pesticides,[193] cyanides[194] and organic micropollutants,[195] antibiotics,[196] and other pharmaceutical compounds[197] including drugs.[198,199] In combination with an acidification of the water, spreading of pathogenic and drug-resistant bacteria through waste water can be combated via generation of plasma-derived reactive oxygen and reactive nitrogen species.[200] Microwave plasmas depollute herbicides and other toxins in waste water and contribute to the degradation of dyes and organic compounds.[201] In general, the application of plasma seems suitable for the purification of dye-polluted wastewater from textile industry.[202–204] High-voltage pulsed plasma decomposes unwanted substances in waste water of the food industry.[205] This avoids pollution with chlorides and secondary reaction products, such as trihalomethanes. Moreover, the efficacy of plasma for the elimination of pollutants in water is markedly enhanced using combined techniques including, for example, titanium dioxide (TiO_2) as photocatalyst,[206] ozonation, hydrogen peroxide,[207] and adsorption[208] or precipitation processes.[209] With regard to energy efficiency, reactors can differ up to five orders of magnitude from each other[210] which should be considered for environmental reasons prior to any commercialization.

4.3. Applications in Other Biotechnological Processes

Plasma can be used in the brewery industry for inactivating yeasts[211] as well as for the abatement of organic pollutants and the bio-decontamination of brewery effluents.[212] Plasma treatment was also effective in soil decontamination. Plasma eliminated hazardous compounds, such as pathogenic bacteria and toxic substances, to improve soil bioremediation processes,[213–215] and to recover soil properties or fertility.[216] In agriculture, plasma was used for the treatment of seeds to achieve an inactivation of fungal pathogens[217] and to increase the germination rate or growth of seedlings.[94,218] In general, an amplified yield of cells (biomass) or a stimulated production of specific metabolites (e.g., alcohols, triterpenes, ergosterol, polysaccharides, or hydrogen) can be induced using plasma treatment. This was also elegantly shown for plasma-derived oxygen radicals specifically enhancing the growth rate of *Saccharomyces cerevisiae*.[219] This applies to both prokaryotic[220–222] and eukaryotic cells.[223] These effects may be based on mutations[224] or a plasma-stimulated cellular metabolism and growth. As such, plasmas may spur biodegradation processes for the treatment of waste water or the removal of solid waste by microorganisms. The plasma-assisted penetration of biomolecules through biological membranes may present an additional tool in biotechnology[27] and even medicine. For example, plasma treatment in combination with 2-deoxy-D-glucose, a glycolytic inhibitor, synergistically induced cell death in cancer cells.[225] Another technological application of plasma might be the specific modulation of plant metabolites in medical plants.[226]

5. Plasma Medicine

5.1. Wound Care

The field of plasma medicine possesses a high innovation potential[227–229] and the treatment of chronic wounds with plasma is particularly promising as numerous studies have suggested in vitro and in vivo.[230–238] In addition to the plasma's antiseptic activity,[239–241] some cells are eliminated by plasma-induced apoptosis,[242–244] and the proliferation and migration of fibroblasts and keratinocytes as well as angiogenesis is promoted.[245–248] Mild inflammatory stimuli in, for example, immune cells[249–251] and skin cells,[252–256] may help the chronic wound to transit from stagnation into the phase of acute inflammation, to subsequently mediate wound healing. As plasma is also active against biofilms and antibiotic-resistant bacteria, it may support wound contracture[257] after successful decolonization as recently demonstrated.[258] Similar studies confirmed an antiseptic action of plasma in vivo without delaying the healing response.[259] In domestic animals, considerable therapeutic success was achieved in chronic wounds while decreasing the pronounced exudation.[260] An activity of plasma against relevant veterinary dermatophytes was found as well.[261] Plasma treatment is indicated if a combination of antiseptic and wound healing-promoting effects is desired, for example, in chronic wounds, otitis media, pyotraumatic dermatitis, or dermatophytosis. However, the lack of long-lasting antimicrobial effects of plasma has to be considered. This may be compensated by the concomitant use of antiseptics that confer retentive antibacterial properties.[260] To further

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enhance skin or wound treatment, plasma may be used to selectively increase the penetration of drugs[262] or drug-coated nanocapsules[263] into the tissue.

5.2. Hand Decontamination

Hand decontamination was proposed as a promising option for the use of plasma.[264–266] It was reported to decontaminate the physiological and artificial (*Staphylococcus epidermidis* and *Micrococcus luteus*) skin flora.[267] Yet, and from a health care management perspective, there are practical pitfalls. In a 1000-beds hospital, at least 700 hand sanitizers are required. For cost reasons, the use of plasma in clinics would, therefore, be restricted to selected areas or groups of people although recently a hand sanitizer for less than US$100 was presented.[268] Compared to alcohol-based hand sanitizer, a benefit of plasma is the lack of alcohol resorption to the skin.[269–271] In an intensive therapy department, however, hand sanitation is carried out up to 200 times during a work shift. This would lead to a substantial skin exposition if plasma was to be used. Thus, further clarification is needed whether repeated exposure to plasma may compromise the skin's physiology or health because an unreserved safety of plasma applications is a prerequisite before a regular clinical use can be envisaged. A similar risk assessment needs to be carried out for plasma-activated liquids (PAL) which may also be used for hand decontamination. Compared to a direct plasma application, any immediate effect of short-lived reactive components, UV radiation, electrical fields, and temperature is excluded or minimized in PAL per se. As such, PAL may serve as a valuable alternative to direct plasma treatment regimens.

5.3. Preoperative Skin Antisepsis

Preoperative skin antisepsis plays a vital role in the prevention of surgical site infections (SSI). Antiseptic measures prevent the carryover of skin-resident flora to deeper layers of the skin during surgical skin incision.[272] This flora mainly populates the stratum corneum and the distal portions of hair follicles and sebaceous ducts. About one-fifth of the skin flora resides at a depth of more than 0.3 mm.[273] In particular, surgical interventions with a high risk of SSI by the skin-resident bacteria, such as shoulder surgery or hip replacements, are in need of complementary antiseptic measures.[274–276] Alcohol-based skin antiseptics do not completely eliminate the skin-resident micro-flora, especially in deeper layers of the skin or in small cavities.[277] By contrast, plasma and/or its reactive components also seem to be able to penetrate small cavities, such as hair follicles[278,279] which may qualify plasma to be considered as an adjunct antiseptic measure in surgery.

5.4. Decolonization of MRSA

A complete decolonization of multidrug-resistant pathogens is only successful if all reservoirs are decolonized simultaneously. Therefore, modern anti-MRSA concepts comprise the use of antiseptics in the vestibule of the nose (the primary habitat of MRSA) and of antiseptic mouth rinse and body wash at the same time. If wounds or the eye are colonized, these must be included in the decolonization procedure.[280] It was previously suggested that the direct treatment with plasma may be an alternative for the use of antiseptics.[281,282] This is, however, improbable for two reasons. First, it is a technical challenge to decontaminate the total body area with plasma within a reasonable time frame. Even if this issue was to be solved, this procedure would present a strong total exposure to plasma with yet unknown immediate or long-term risks. Second, plasma effects are not lasting, possibly leading to a re-colonization unless literally all pathogens were eliminated. Also, plasma triggers oxidative stress responses[283] which may regulate protective mechanisms against reactive species in bacteria.[284,285] However, in vitro pathogens have not been observed to develop any resistance against two different plasma sources[286,287] which is in contrast the case for certain antibiotics. This active mechanism of action would qualify plasma for adjunct and combinatory antiseptic therapies. Another interesting option could provide the treatment with PAL in combination with direct plasma exposure but this needs further research and evaluation of long-term risks. At present, only in vitro studies are available for the plasma-based inactivation of MRSA, and success rates of MRSA decolonization in infected patients cannot be fully estimated based on these data.

5.5. Oral Plasma Applications

Plasma is highly effective against the oral microflora which creates a variety of potential applications in the oral cavity.[288–290] Bacteria penetrates about 500–1000 μm into the dentin canal lumen,[291] hampering the effectivity of conventional chemicals for tooth root canal disinfection. In root canals of extracted teeth, an only 2-log reduction of *Enterococcus faecalis* was achieved after 8 min of plasma treatment. Accordingly, re-colonization occurred, which was completely eliminated after 30 min of plasma treatment.[292] By applying plasma to endodontic root canals, a complete destruction of biofilms on or in the dentin was achieved up to a depth of 1 mm.[293] These results were confirmed on extracted teeth.[294] After treatment of oral biofilms, a plasma jet's antibacterial action was significantly greater if compared to the effects of the antiseptic gold standard chlorhexidine.[295] For a DBD plasma source, exposure times exceeding 5 min were required.[296] Plaque-biofilm was successfully removed as well using plasma.[297,298] Plasma

may be also an option to disinfect dental dentures, effectively reducing the risk of denture-associated stomatitis[299] by combating *Candida glabatra*.[300] Combining plasmas with antibacterial solutions may reveal promising therapeutic options, too. The tooth surface can be rendered hydrophilic after exposure to plasma which enhances osteoblasts adhesion and spreading.[301–303] This may be of benefit in periodontal disease. Plasma treatment can also increase the cohesion between teeth and composite fillings.[304,305] Finally, exposure to plasma improves the tissue compatibility of dental implants and facilitates the immobilization of antimicrobial peptides on their surface. These bio-functional dental implants may become useful in odontology in the near future.[306]

5.6. Inactivation of Parasites

Plasmas are also effective against parasites. The spider mite, a major and worldwide occurring plant pest, and the hop aphid are killed by plasma.[307] An activity of plasma against mites was demonstrated in vitro.[308] As plasma readily penetrates small cavities it may also be an option for the treatment of feline and canine demodicosis. Plasma treatment can be used to kill ticks as well. An irreversible inactivation was revealed after 5 min of plasma treatment.[309] A prerequisite for the application of plasma in clinics is its compatibility with the tissue in question.

5.7. Intraoperative Plasma Application (Plasma Surgery)

Although there has been significant progress of plasma applications in several of biotechnology and medicine, others may be very promising in the future, such as the local, intraoperative plasma treatment. This approach seamlessly combines the features of wound healing promotion, immune stimulation, and antisepsis. Therefore, plasma applications may be highly suitable for accessory use in surgery, especially in the context of molecular scalpel concepts. This could be of particular interest for local excisions of tissue areas which are adjacent to critical organs (e.g., nerves, blood vessels, and gastrointestinal tract) that could be violated by conventional surgical techniques. In a clinical context, such plasma scalpel techniques are expected to minimize tissue violation and the risk of infections. They may also enhance postoperative scar formation as demonstrated recently.[310]

6. Conclusion

Plasma sources for sterilization and microbial decontamination have found their place in medicine, in the food industry, and in air purification technologies. Particularly in the field of waste water treatment, there is an enormous potential for the plasma-assisted elimination of pharmaceutical remainders. With the development of portable and easy-to-handle plasma sources, many opportunities will also arise for their use in medicine. Current medical applications of plasma focus on the treatment of chronic wounds, the surface modification of implant materials, the removal of biofilms on implants in situ, and antiseptic applications in the oral cavity. In the near future, plasmas are expected to become attractive for a variety of other applications in the field hygiene.

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