Cold Atmospheric Plasma in Oral Health and Plasma Medicine: A Survey

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Abstract

Cold Atmospheric Plasma (CAP) is a non-thermal ionized gas capable of generating Reactive Oxygen and Nitrogen Species (RONS), which are pivotal in its antimicrobial and therapeutic applications. This survey examines CAP's dual role in oral health and plasma medicine, highlighting its efficacy in pathogen reduction and wound healing. CAP's ability to modulate oxidative stress through selective RONS generation offers promising therapeutic avenues, particularly in cancer therapy and regenerative medicine. Recent advancements in CAP technology, such as low-cost Atmospheric Pressure Plasma Jet (APPJ) devices, enhance its applicability across medical contexts. These innovations are supported by the integration of sensors and electronics, facilitating accessible plasma studies. However, challenges remain in standardizing protocols, optimizing CAP parameters, and understanding RONS interactions with biological systems. Continued research and interdisciplinary collaboration are crucial to overcoming these obstacles, ensuring CAP's safe and effective application in diverse medical fields. As plasma medicine progresses, CAP is positioned to revolutionize therapeutic interventions, providing novel solutions for microbial infections and oxidative stress-related conditions.

1 Introduction

1.1 Overview of Cold Atmospheric Plasma (CAP)

Cold Atmospheric Plasma (CAP) is a non-thermal plasma generated by applying energy to a gas, resulting in reactive species that effectively inactivate viruses and microorganisms. Operating at room temperature, CAP is particularly suitable for sensitive environments such as oral health and plasma medicine [1]. Its unique ability to generate Reactive Oxygen and Nitrogen Species (RONS) is critical for its antimicrobial effectiveness and therapeutic potential [2]. The adaptability of CAP allows it to conform to complex shapes, enhancing its medical applicability [3].

In oral health, CAP serves as a promising tool for pathogen reduction and healing promotion, providing a novel alternative to traditional antimicrobial methods that often face resistance issues [4]. Its role in plasma medicine extends to modulating oxidative stress in biological tissues, thus improving therapeutic outcomes [5]. The development of low-cost, flexible atmospheric pressure plasma jet (APPJ) devices has further expanded CAP's potential in medical applications, demonstrating good antimicrobial efficiency while adhering to safety regulations [6]. Additionally, CAP effectively manages complexity and enhances performance in various applications, including oral health [7].

Integrating low-cost sensors and circuits into CAP systems can enhance accessibility and educational efforts in plasma science [8]. CAP's capacity to sterilize sensitive materials, as evidenced by its applications in mask decontamination, underscores its versatility in medical contexts [9]. The multidisciplinary nature of plasma medicine, as discussed in this survey, emphasizes CAP's applicability in treating wounds and cancer, showcasing its broad therapeutic potential [10]. Optimizing CAP technology for efficiency parallels advancements in neural networks, suggesting promising avenues for future research [11].

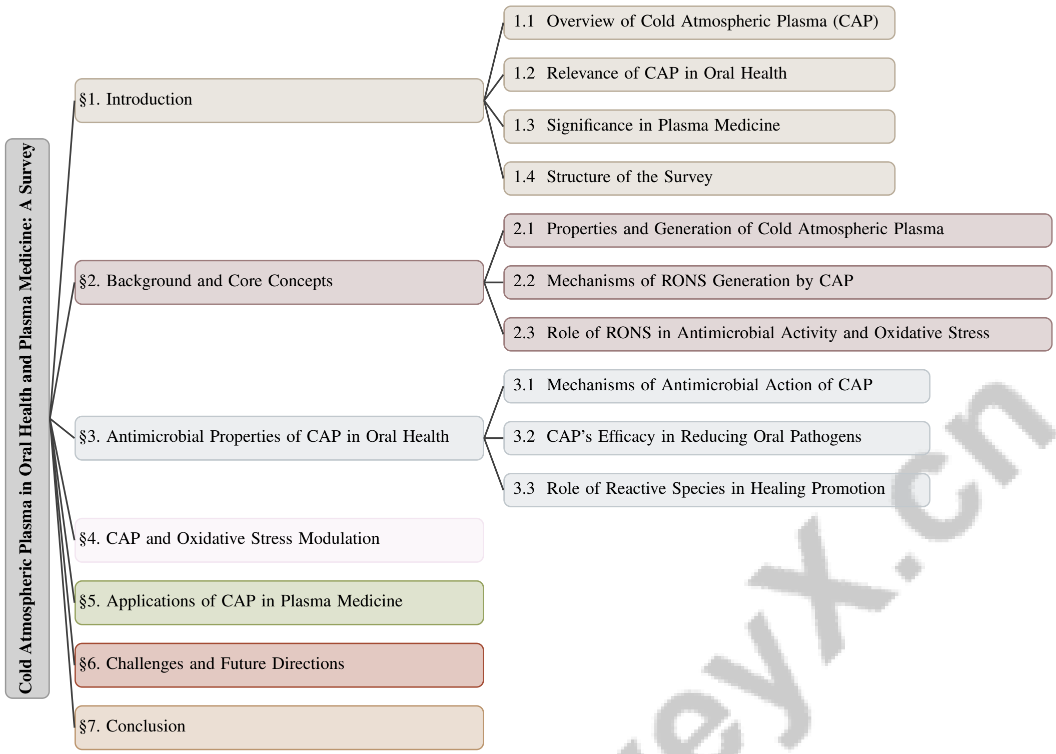

Figure 1: chapter structure

1.2 Relevance of CAP in Oral Health

CAP has gained considerable attention in oral health due to its multifaceted benefits, particularly in microbial inactivation and tissue regeneration [5]. Its ability to generate RONS at room temperature enables effective targeting of a wide range of oral pathogens while preserving healthy tissues, addressing challenges such as antibiotic resistance [12].

Beyond its antimicrobial properties, CAP significantly promotes tissue regeneration, enhancing oral wound healing. Studies have demonstrated CAP's efficacy in reducing dependence on conventional treatments, thereby improving patient outcomes [13]. This application aligns with a broader trend of integrating advanced plasma technologies in biomedical fields, including cancer treatment and tissue repair [12].

However, a comprehensive understanding of Low Temperature Plasmas and their applications remains limited, hindering innovation in healthcare industries [1]. Further research could unlock new possibilities for CAP in oral health, improving its efficacy and safety. Additionally, sustainable applications of CAP, such as its potential in inactivating viruses in irrigation systems, highlight its versatility for broader environmental and health-related uses [14].

1.3 Significance in Plasma Medicine

CAP plays a transformative role in plasma medicine, offering innovative solutions across various medical applications. Its ability to generate RONS at room temperature is crucial for modulating oxidative stress in biological tissues, leading to enhanced therapeutic outcomes. This property is particularly significant in treating chronic wounds, where CAP's antimicrobial and anti-inflammatory effects facilitate accelerated healing [4].

CAP's potential extends to oncology, where its application in cancer therapy is gaining traction. By inducing oxidative stress selectively in cancer cells, CAP promotes apoptosis while sparing healthy cells, positioning it as a valuable adjunct or alternative to conventional treatments [7].

Furthermore, CAP is effective for sterilization, decontaminating medical equipment and surfaces without causing thermal damage [9]. This capability is vital for infection control, especially in

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hospital settings where preventing nosocomial infections is critical [10]. The development of low-cost and flexible CAP devices enhances accessibility and applicability across various medical contexts, from in-home care to remote facilities.

Integrating CAP into plasma medicine aligns with the trend toward precision medicine, tailoring treatments to individual patient needs. Continued exploration of CAP's mechanisms and its interactions with biological systems is essential for optimizing its therapeutic efficacy and safety [1]. As research advances, CAP's potential to revolutionize medical treatments through its unique properties and broad applicability becomes increasingly evident, underscoring the need for interdisciplinary collaboration in this emerging field [8].

1.4 Structure of the Survey

This survey on Cold Atmospheric Plasma (CAP) in oral health and plasma medicine is structured to comprehensively examine the topic, beginning with an introduction that contextualizes CAP's relevance and applications. The survey is organized into several key sections, each focusing on specific aspects of CAP and its implications.

The initial section provides an overview of CAP, emphasizing its properties and significance in oral health and plasma medicine. This is followed by a detailed exploration of core concepts, including CAP's properties, generation methods, and the mechanisms through which it produces RONS.

Subsequent sections investigate CAP's antimicrobial properties in oral health, detailing its efficacy in reducing pathogens and promoting healing [4]. The survey then discusses CAP's modulation of oxidative stress, highlighting the dual role of RONS in promoting and mitigating oxidative stress and the therapeutic implications of these processes.

The broader applications of CAP in plasma medicine are examined next, focusing on its roles in cancer therapy, wound healing, and other medical fields. This includes an analysis of innovative CAP devices and techniques that enhance its applicability across diverse medical contexts.

The survey concludes with a discussion of challenges and future directions in CAP research, identifying biological and clinical challenges, the need for optimization of CAP parameters, and potential research directions [1]. This comprehensive structure ensures a thorough understanding of CAP's potential and ongoing research efforts to harness its benefits in oral health and plasma medicine.The following sections are organized as shown in Figure 1.

2 Background and Core Concepts

2.1 Properties and Generation of Cold Atmospheric Plasma

Cold Atmospheric Plasma (CAP) is distinguished by its non-thermal nature, operating at room temperature to produce reactive oxygen and nitrogen species (RONS) crucial for antimicrobial and therapeutic uses [5]. The plasma sheath plays a pivotal role in managing electrical coupling and mass transport at the plasma-liquid interface, highlighting CAP's distinctive properties [15]. However, the complex interactions between plasma and biological tissues present challenges for the safe clinical implementation of CAP technology [10].

CAP can be generated through various methods, with Atmospheric Pressure Plasma Jet (APPJ) devices being a key approach. These devices employ a dielectric barrier discharge reactor powered by a portable supply, ensuring adherence to medical safety standards while maintaining low temperatures suitable for sensitive tissues [6]. An innovative method involves using a flexible aerogel matrix between electrodes, forming a morphing multi-jet plasma source that adapts to complex surface topographies, enhancing treatment applicability for irregularly shaped biological tissues [16]. Additionally, the use of helium as a working gas in APPJ methods, along with electric field vector mapping, optimizes plasma interaction with target surfaces [17].

CAP technology's adaptability is akin to the Dynamic Dimensionality Reduction Algorithm (DDRA), which optimizes system properties for specific applications while preserving essential features [7]. This adaptability is crucial for tailoring CAP properties to meet diverse medical needs, from wound healing to oncology [18].

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CAP's multifunctional potential spans multiple fields, with ongoing research addressing limitations and expanding its medical and industrial applications. Recent studies underscore CAP's role in enhancing tissue regeneration, boosting immune responses, and serving as an antibiotic alternative. For example, integrating aluminum foam in CAP treatments increases the delivery efficiency of reactive species while minimizing clinical damage. Advances in plasma source design, such as flexible dielectric barrier discharge systems, are paving the way for more effective plasma treatments in contexts like wound healing and cancer therapy. Continued research efforts are essential for unlocking CAP technology's full capabilities across diverse applications [12, 16, 18, 19].

2.2 Mechanisms of RONS Generation by CAP

Cold Atmospheric Plasma (CAP) generates Reactive Oxygen and Nitrogen Species (RONS) through complex interactions between ionized gas molecules and their environment, crucial for applications in plasma medicine and antimicrobial treatments [20]. RONS generation is primarily driven by energy transfer during CAP interactions with substrates or biological tissues, leading to the ionization and excitation of gas molecules [1]. This ionization facilitates the production of reactive species that induce oxidative stress and modulate physiological processes, establishing CAP as a versatile tool in medical therapies [21].

The choice of plasma-forming gas significantly affects RONS generation. For instance, using CO_2 as a plasma-forming gas in plasma-activated water (PAW) selectively generates reactive oxygen species (ROS) while minimizing reactive nitrogen species (RNS), allowing for tailored chemical compositions for specific treatments [2]. This selectivity is crucial for optimizing therapeutic effects, particularly in plasma medicine, where precise modulation of RONS is essential for effective outcomes.

Atmospheric Pressure Plasma Jets (APPJ) are particularly adept at generating RONS in various liquids relevant to plasma medicine, combining features of dielectric barrier discharge (DBD) and CAP jets for treating large areas and non-flat surfaces. The use of helium as a working gas enhances the thermal and reactive properties of plasma, optimizing interactions with target surfaces and biological tissues [22].

CAP's interaction with microbial cells generates RONS that effectively inactivate microorganisms, further enhanced by specific gas combinations that facilitate reactive species generation, thereby improving CAP's efficacy in microbial inactivation [9, 6]. The generation of RONS by CAP is crucial for its multifunctional potential, enabling applications in plasma medicine, including cancer therapies through selective apoptosis induction in tumor cells, as well as sterilization and wound healing. The ability of CAP to produce a delicate mix of RONS in various liquids enhances therapeutic efficacy, while ongoing research aims to optimize concentrations and delivery methods for maximum clinical effectiveness [23, 24, 25, 3, 20]. A comprehensive understanding of these mechanisms is vital for optimizing CAP's efficacy and safety in medical and industrial contexts, paving the way for innovative treatments and technologies.

2.3 Role of RONS in Antimicrobial Activity and Oxidative Stress

Reactive Oxygen and Nitrogen Species (RONS) generated by Cold Atmospheric Plasma (CAP) are pivotal for its antimicrobial activity and modulation of oxidative stress, which are crucial for therapeutic applications. The antimicrobial efficacy of CAP largely stems from the selective generation of reactive oxygen species (ROS) in plasma-activated water (PAW), enhancing its ability to inactivate pathogens while avoiding adverse effects associated with reactive nitrogen species (RNS), such as low pH [2]. This selective generation of ROS is vital for optimizing CAP's antimicrobial properties, offering a potent alternative to traditional treatments [26].

Beyond antimicrobial activity, RONS are central to oxidative stress modulation. Oxidative stress arises from an imbalance between oxidants, such as RONS, and antioxidants, leading to potential molecular damage and associated diseases. This imbalance is a core issue in plasma medicine, where CAP's therapeutic potential is harnessed to modulate oxidative stress in various medical contexts, including cancer treatment [20].

RONS influence cellular processes through complex interactions with signaling pathways. For instance, ROS can activate or inhibit the NFB pathway, illustrating the intricate relationship between oxidative stress and cellular signaling [27]. Such interactions are essential for understanding how CAP can modulate physiological responses, particularly in inflammation and immune responses.

Furthermore, the relationship between RONS and mitochondrial function is critical for understanding their impact on muscle function and regeneration. The interplay between mitochondrial activity and RONS underscores their influence on cellular metabolism and tissue repair processes [21]. This highlights CAP's potential to enhance regenerative medicine applications by modulating oxidative stress and promoting tissue healing.

The role of RONS in antimicrobial activity and oxidative stress modulation is central to CAP's multifunctional potential. By leveraging the selective generation of reactive species, CAP provides innovative solutions for managing microbial infections and oxidative stress-related pathologies, paving the way for advancements in plasma medicine and therapeutic interventions [28].

3 Antimicrobial Properties of CAP in Oral Health

The pursuit of novel antimicrobial strategies in oral health has spotlighted Cold Atmospheric Plasma (CAP) as a promising candidate. CAP's distinctive capability to generate reactive species allows it to effectively target and neutralize a range of pathogens. As illustrated in Figure 2, this figure delineates the antimicrobial properties of CAP, detailing its mechanisms of action and efficacy in reducing oral pathogens while promoting healing. It highlights CAP's effectiveness through the generation of reactive oxygen and nitrogen species (RONS), device versatility, and its potential in reducing microbial load. Furthermore, the figure underscores the integration of machine learning in predicting CAP's effects and identifies critical research gaps for further exploration. This section delves into the mechanisms of CAP's antimicrobial action, emphasizing the roles of RONS in combating oral pathogens, thus underscoring its potential as a transformative tool in dental practices for enhanced oral health outcomes.

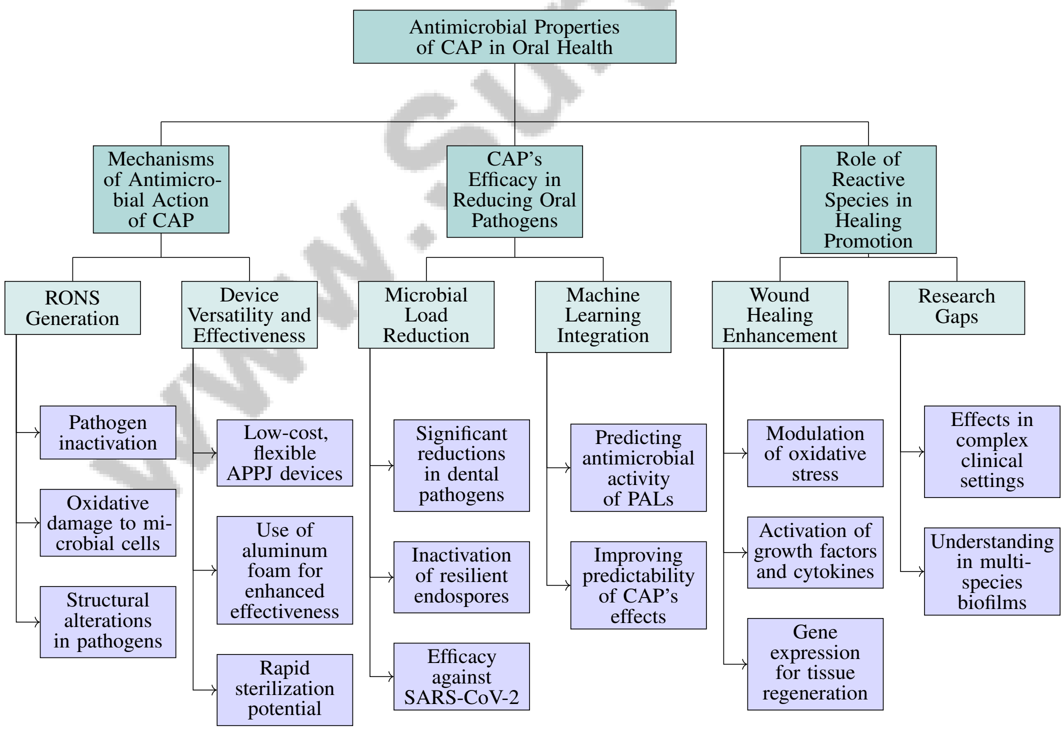

Figure 2: This figure illustrates the antimicrobial properties of Cold Atmospheric Plasma (CAP) in oral health, detailing its mechanisms of action, efficacy in reducing oral pathogens, and role in healing promotion. It highlights CAP's effectiveness through RONS generation, device versatility, and potential in microbial load reduction. Additionally, it emphasizes the integration of machine learning in predicting CAP's effects and identifies research gaps for further exploration.

3.1 Mechanisms of Antimicrobial Action of CAP

Cold Atmospheric Plasma (CAP) demonstrates antimicrobial efficacy primarily through RONS generation, which is crucial for pathogen inactivation. Atmospheric Pressure Plasma Jets (APPJ) enhance CAP's antimicrobial properties by producing high RONS concentrations in various liquid media, facilitating selective microbial targeting [20]. The utilization of CO_2 plasma to generate plasma-activated water (PAW) further amplifies antimicrobial effects by selectively producing reactive oxygen species (ROS) [2].

CAP's antimicrobial action involves direct RONS interactions with microbial cell components, inducing oxidative damage and structural alterations that deactivate pathogens. Studies have shown CAP's rapid inactivation of dental pathogens, achieving significant microbial reductions [29]. Additionally, CAP influences inflammation modulation, growth factor stimulation, and bacterial load reduction, especially in wound healing contexts [30].

The versatility of CAP devices, such as low-cost, flexible APPJ, is evidenced by biological assays measuring microbial inhibition and cell viability [6]. CAP afterglow treatment can achieve over a 6-log reduction for *E. coli* in a short time, highlighting its rapid sterilization potential [9]. Incorporating aluminum foam in CAP systems enhances effectiveness by absorbing high-voltage sparks and minimizing tissue damage while allowing effective reactive species penetration [18].

This is illustrated in Figure 3, which depicts the primary mechanisms and applications of Cold Atmospheric Plasma (CAP) in antimicrobial contexts, highlighting RONS generation, specific applications in dental and wound healing, and innovative device designs. CAP's antimicrobial action is rooted in its ability to generate and deliver reactive species that interact with and inactivate pathogens. The integration of diverse mechanisms within CAP positions it as a promising tool for microbial infection control, with applications in clinical settings for sterilization and infection management, as well as in food safety for produce decontamination. CAP's ability to inactivate bacteria and spores while preserving heat-sensitive materials suggests it as a viable alternative to traditional antimicrobial methods, particularly for sterilizing delicate surfaces. Further research is essential to optimize CAP's efficacy across various microbial species and treatment conditions [12, 29, 4, 9, 31].

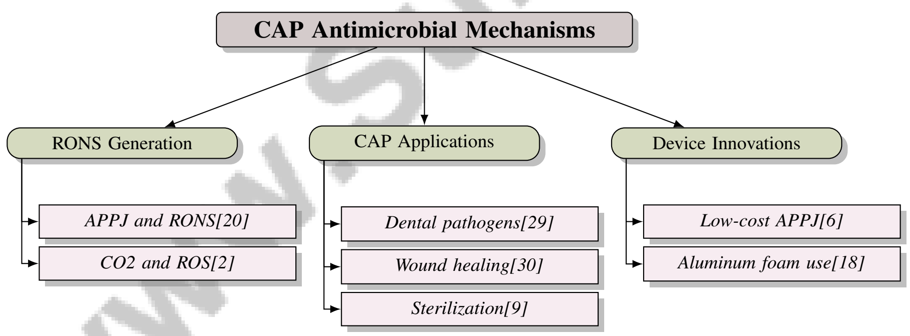

Figure 3: This figure illustrates the primary mechanisms and applications of Cold Atmospheric Plasma (CAP) in antimicrobial contexts, highlighting RONS generation, specific applications in dental and wound healing, and innovative device designs.

3.2 CAP's Efficacy in Reducing Oral Pathogens

Cold Atmospheric Plasma (CAP) has demonstrated significant efficacy in reducing oral pathogens, offering a novel strategy for managing microbial load in dental practices. Extensive research on CAP's antimicrobial effects against common dental pathogens such as *Streptococcus mutans*, *Enterococcus faecalis*, and *Candida albicans* has reported substantial microbial reductions [29]. These findings emphasize CAP's potential as an effective tool for controlling oral infections and reducing reliance on traditional antimicrobial treatments, which face challenges like antibiotic resistance.

In dental settings, reducing microbial load is critical for infection prevention and oral health promotion. CAP applications have been staged to demonstrate significant microbial load reductions [26]. Studies report notable log reductions in microbial populations, including the inactivation of resilient endospores like *Bacillus atrophaeus* [4].

CAP's versatility extends to viral agents; for instance, it effectively inactivated SARS-CoV-2 by modifying its proteins, thereby preventing transmission and showcasing its potential in managing viral threats in dental environments [32]. The development of low-cost, flexible APPJ devices further enhances CAP's efficacy against various bacteria and fungi, underscoring its broad-spectrum antimicrobial activity [6].

Moreover, integrating machine learning techniques to predict the antimicrobial activity of plasma-activated liquids (PALs) has achieved significant accuracy, laying a foundation for future research in plasma medicine and improving the predictability of CAP's effects [33]. This advancement could lead to more targeted and efficient CAP treatments, reinforcing its role in oral health applications.

The growing body of research confirms that CAP effectively reduces oral pathogens primarily through RONS generation, positioning it as a compelling alternative or complementary option to traditional antimicrobial treatments in dental care. A systematic review of 55 in-vitro studies indicates that CAP's antimicrobial efficacy varies based on factors such as pathogen type, gas composition, and treatment duration, with a time-dependent increase in effectiveness. This positions CAP as a promising candidate for future clinical applications, pending further investigation into its use in multi-species biofilm models and randomized clinical trials [12, 29, 34]. Continued exploration of CAP's mechanisms and optimization of its application parameters are essential for fully realizing its potential in enhancing oral health outcomes.

3.3 Role of Reactive Species in Healing Promotion

Reactive species generated by Cold Atmospheric Plasma (CAP) significantly enhance healing processes in oral health by influencing cellular activities and modulating the wound environment. CAP's ability to produce RONS at room temperature allows interaction with biological tissues without thermal damage, making it ideal for promoting wound healing [35]. For example, microplasma array technology effectively patterns reactive features onto surfaces like polystyrene, influencing cellular processes and enhancing tissue regeneration [35].

CAP's contribution to healing is multifaceted, involving modulation of oxidative stress and stimulation of cellular signaling pathways crucial for tissue repair. The reactive species generated by CAP can activate growth factors and cytokines, promoting cell proliferation and migration, essential steps in the wound healing cascade [29]. CAP also enhances the expression of genes associated with tissue regeneration, further supporting its role in oral health [35].

Despite CAP's promising potential in promoting healing, key gaps remain in understanding its effects, particularly in complex clinical settings and multi-species biofilms [29]. Addressing these gaps through further research is critical for optimizing CAP's application in oral health, ensuring efficacy and safety in promoting healing processes. Exploring CAP's mechanisms in clinical environments will provide valuable insights into its therapeutic potential and pave the way for innovative treatments in regenerative medicine.

4 CAP and Oxidative Stress Modulation

4.1 Dual Role of RONS in Oxidative Stress Modulation

Cold Atmospheric Plasma (CAP) generates Reactive Oxygen and Nitrogen Species (RONS) that play a pivotal role in modulating oxidative stress, exhibiting both beneficial and harmful effects based on their concentration and type. At lower concentrations, RONS facilitate apoptosis in cancer cells, selectively inducing oxidative stress to target tumor cells while preserving normal tissues, a process crucial for oncological applications [36, 37, 2]. However, excessive RONS can cause oxidative distress, disrupting healing and regeneration [38].

As illustrated in Figure 4, the dual role of RONS in modulating oxidative stress is highlighted, showcasing their beneficial effects, such as cancer cell apoptosis, alongside their harmful effects, including oxidative distress. This figure also emphasizes technological advances in selective ROS generation and the application of machine learning in plasma medicine. The impact of RONS varies with cell type and microenvironment, necessitating a nuanced understanding of their interactions with cellular components and signaling pathways like NFB [27, 28]. The absence of nitrogen species in CO_2 plasma enhances selective ROS generation, improving antimicrobial properties and managing oxidative stress [2]. Machine learning techniques predicting the microbial inactivation efficacy of plasma-activated liquids (PALs) have further refined plasma treatment parameters [33]. The complexity of RONS in oxidative stress modulation underscores the need for ongoing research to harness their therapeutic potential, balancing cellular damage with protective mechanisms across various biological contexts [39, 38, 25]. By focusing on selective reactive species generation, CAP offers innovative solutions for managing oxidative stress-related pathologies, advancing plasma medicine and therapeutic interventions.

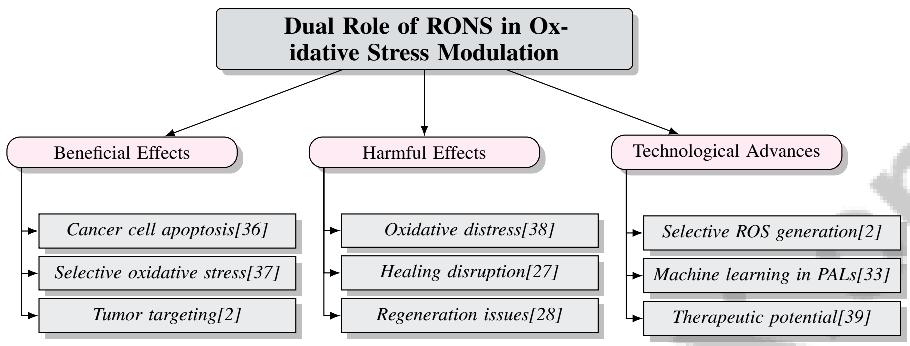

Figure 4: This figure illustrates the dual role of Reactive Oxygen and Nitrogen Species (RONS) in modulating oxidative stress, highlighting both beneficial effects, such as cancer cell apoptosis, and harmful effects, like oxidative distress. It also outlines technological advances in selective ROS generation and machine learning applications in plasma medicine.

4.2 Therapeutic Implications of Oxidative Stress Modulation

Modulating oxidative stress through CAP presents substantial therapeutic potential, particularly through RONS-mediated apoptosis in cancer cells, facilitating tumor reduction while preserving healthy tissues [40]. CAP's adaptability to various surface shapes, as demonstrated by morphing plasma sources, enhances its application across diverse medical contexts by allowing uniform treatment over larger areas [16]. The dynamic dimensionality reduction algorithm (DDRA) provides insights into CAP's modulation of oxidative stress and promotion of healing processes, which is crucial for optimizing therapeutic outcomes [7]. CAP's ability to modulate oxidative stress pathways, such as the JNK/cytochrome c/caspase-9/caspase-3 pathway, underscores its potential in inducing programmed cell death or pyroptosis, enhancing treatment efficacy [7]. Beyond oncology, CAP maintains material integrity during treatments, such as enhancing mask permeability without compromising breathing resistance, relevant in medical contexts where preserving material properties is critical [9]. CAP's modulation of oxidative stress holds significant therapeutic promise across various fields, including wound healing and cancer treatment. CAP selectively targets cancer cells by elevating intracellular ROS levels, leading to cell death, particularly in cells with compromised antioxidant defenses. Integrating CAP with external factors like vitamin C and static magnetic fields has improved treatment efficacy, highlighting oxidative stress modulation's role in advancing therapeutic interventions [41, 34, 39, 38]. Continued exploration of CAP's mechanisms and optimization of application parameters is essential for realizing its full potential in plasma medicine, paving the way for innovative treatments and improved patient outcomes.

5 Applications of CAP in Plasma Medicine

The exploration of Cold Atmospheric Plasma (CAP) has significantly expanded, revealing its diverse applications in various medical fields. Table 3 presents a comprehensive comparison of Cold Atmospheric Plasma (CAP) applications, detailing the mechanisms, therapeutic focus, and innovative features across different medical fields. Table 1 presents a comprehensive summary of the methods and innovations in Cold Atmospheric Plasma (CAP) applications, emphasizing its therapeutic potential in cancer treatment and the development of novel CAP devices and techniques. This section focuses on the utilization of CAP in cancer therapy, elucidating its mechanisms and therapeutic advantages. By examining the interactions between CAP and tumor cells, we can appreciate its potential to transform

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Category	Feature	Method
CAP in Cancer Therapy	Reactive Species Strategies Immunotherapy Enhancement	CAP-DI[42] CAP[19]
Innovative CAP Devices and Techniques	Targeted Reactive Control Integrated Therapeutic Techniques	CAP-DI[40], CAP-W[43] CST[34], PP-CAPJ[44]

Table 1: This table provides an overview of the methods and innovative techniques employed in Cold Atmospheric Plasma (CAP) applications, particularly in cancer therapy and device development. It categorizes the strategies based on their features and methods, highlighting advancements in reactive species strategies, immunotherapy enhancement, targeted reactive control, and integrated therapeutic techniques.

cancer treatment paradigms. The subsequent subsection specifically addresses CAP's role in cancer therapy, detailing its efficacy and the underlying biological processes involved.

5.1 CAP in Cancer Therapy

Cold Atmospheric Plasma (CAP) has emerged as a novel modality in cancer therapy, primarily due to its ability to induce apoptosis and necrosis in tumor cells via reactive oxygen and nitrogen species (RONS) [43]. This approach selectively targets cancer cells while preserving healthy tissues, thus minimizing collateral damage [41]. The selective anticancer properties of CAP are linked to the specific vulnerabilities of cancer cells, which can be assessed through their H_2O_2 consumption and scavenging capabilities [41].

Recent advancements have introduced CAP-activated deionized (DI) water as a medium for delivering reactive species, enhancing therapeutic efficacy beyond direct CAP application [42]. Additionally, the Positive-Pulsed Voltage Cold Atmospheric Plasma Jet (PP-CAPJ) method significantly amplifies the cytotoxic effects of cancer treatments, presenting a promising alternative to traditional therapies [44]. The combination of CAP with other modalities, such as static magnetic fields (SMF) and vitamin C, has been shown to improve control and mortality rates in breast cancer cells, indicating the potential for synergistic effects in combination therapies [34].

CAP also enhances immune responses by improving immune cell function, leading to robust antitumor responses in vivo [19]. This immunomodulatory effect positions CAP as a promising tool in cancer immunotherapy, providing a safe method to boost the body's defenses against tumors.

Comparative studies of atmospheric pressure plasma jet devices, including the plasma gun and plasma Tesla jet, have evaluated their safety and therapeutic efficiency in reducing tumor progression in cholangiocarcinoma [45]. Such studies highlight the necessity of optimizing CAP delivery methods to maximize therapeutic benefits while ensuring patient safety.

The application of CAP in cancer therapy marks a significant advancement in oncology, presenting a viable alternative to conventional treatments. Ongoing research and innovation in CAP technology and delivery methods are essential for realizing its full potential as a non-invasive cancer treatment. Recent findings indicate that CAP can selectively induce cell death in various cancer cell lines through mechanisms involving reactive oxygen species (ROS) and physical factors like electromagnetic emissions. Furthermore, the integration of CAP with agents such as vitamin C and static magnetic fields shows promise in enhancing its efficacy against specific cancer types, paving the way for targeted therapies that leverage CAP's unique properties [12, 37, 41, 7, 34].

5.2 CAP in Wound Healing and Regenerative Medicine

Cold Atmospheric Plasma (CAP) has emerged as a valuable tool in wound healing and regenerative medicine, leveraging its ability to generate reactive oxygen and nitrogen species (RONS) to facilitate tissue repair and regeneration. The clinical application of CAP in wound healing is supported by its safety profile and long-term effects, as highlighted in recent surveys [13]. CAP's non-thermal nature allows for direct application to wounds without thermal damage, making it particularly suitable for chronic wounds and promoting expedited healing. Figure 5 illustrates the application of Cold Atmospheric Plasma in wound healing and regenerative medicine, highlighting its safety profile, innovative methods, and antimicrobial properties.

Innovative applications of CAP in regenerative medicine include discharging CAP in deionized water, which enhances its penetration into tissues and effectiveness in promoting cellular activities vital for tissue repair [43]. This method not only improves the delivery of reactive species but also maximizes the therapeutic effects of CAP, supporting tissue regeneration.

CAP's efficacy in wound healing stems from its ability to modulate the wound environment by reducing microbial load, stimulating growth factor release, and enhancing cell proliferation and migration. These effects are crucial for initiating and sustaining the healing process, especially in cases where traditional treatments have been inadequate. CAP significantly contributes to regenerative medicine by improving the integration and functionality of biomaterials used in tissue engineering and creating an optimal microenvironment conducive to cell proliferation, migration, and differentiation. Its antimicrobial properties also present an alternative to traditional antibiotics, underscoring CAP's potential in advancing therapeutic strategies [41, 12, 18].

The application of CAP in wound healing and regenerative medicine signifies a major advancement in medical treatments, offering a safe and effective alternative to conventional therapies. Continued research into the mechanisms and optimization of CAP application is vital for unlocking its full potential in medical settings. CAP's unique properties, including its ability to enhance cell proliferation, migration, and differentiation, coupled with its antimicrobial effects, position it as a promising alternative in tissue repair and regeneration. Recent studies highlight CAP's use in various biomedical applications, including wound healing, antitumor therapies, and infection control, while innovative delivery systems like aluminum foam and morphing plasma sources are being developed to improve CAP treatment efficacy and safety. By enhancing our understanding of CAP's biochemistry and optimizing its clinical applications, we can pave the way for groundbreaking solutions in regenerative medicine [12, 16, 18].

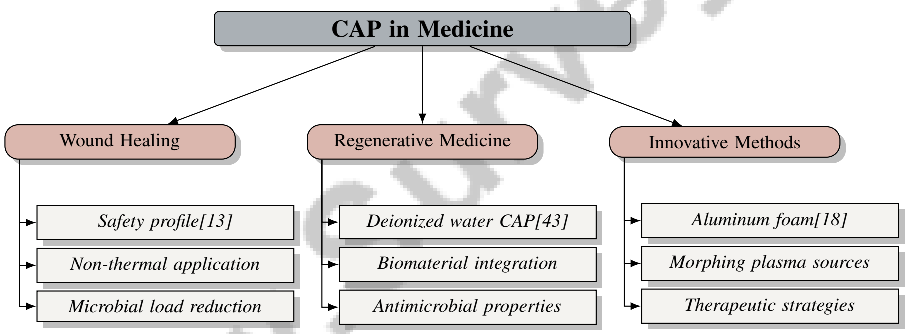

Figure 5: This figure illustrates the application of Cold Atmospheric Plasma (CAP) in wound healing and regenerative medicine, highlighting its safety profile, innovative methods, and antimicrobial properties.

5.3 Innovative CAP Devices and Techniques

Method Name	Technological Advancements	Therapeutic Integration	Controlled Environment
CST[34]	Innovative Devices And Techniques	Cap With Smf	Controlled Laboratory Conditions
CAP-W[43]	-	-	Cap-W
CAP-DI[40]	Innovative Devices And Techniques	Combining Plasma Solutions	Cap Generated Water
PP-CAPJ[44]	Positive-pulsed Voltage	Gold Nanoparticles Combination	Trapezoidal Pulse Shape

Table 2: Comparison of Innovative Cold Atmospheric Plasma (CAP) Methods, highlighting technological advancements, therapeutic integration, and controlled environments. The table presents various CAP techniques, including CST, CAP-W, CAP-DI, and PP-CAPJ, detailing their unique features and contributions to enhanced medical treatments.

Recent advancements in Cold Atmospheric Plasma (CAP) technology have led to the development of innovative devices and techniques that enhance its applicability in medical treatments. Table 2 provides a comprehensive comparison of these advancements, illustrating the diverse methodologies and their respective contributions to therapeutic integration and controlled environments. Notably, air CAP employs various electrode patterns to generate reactive oxygen and nitrogen species (RONS) specifically for cancer treatment [46]. This versatile platform targets tumor cells, utilizing the unique properties of RONS to induce oxidative stress and apoptosis selectively in cancerous tissues.

The integration of CAP with synergistic modalities has further expanded its therapeutic potential. For example, combining CAP with static magnetic fields (SMF) and vitamin C has significantly improved treatment efficacy in cancer therapy, enhancing the cytotoxic impact on cancer cells compared to CAP alone [34].

Moreover, the generation of CAP in deionized (DI) water represents a significant advancement in controlling reactive species generation. This method, known as Cold Atmospheric Plasma Discharged in Water (CAP-W), provides a controlled environment that enhances cancer cell targeting, facilitating apoptosis induction and improving therapeutic outcomes [43]. The precise modulation of oxidative stress in this medium is crucial for optimizing CAP's therapeutic effects [40].

Another innovative approach utilizes positive-pulsed voltage to generate CAP jets (CAPJ), which can enhance the delivery of therapeutic agents such as gold nanoparticles to cancer cells, thereby increasing treatment cytotoxicity and efficacy [44].

Advancements in nanomedicine have also led to the development of RONS-responsive polymers, which offer targeted delivery and controlled release of therapeutic agents for biomedical applications [47]. These polymers can be integrated with CAP devices to enhance treatment precision and effectiveness, especially in complex medical scenarios.

These innovations in CAP devices and techniques highlight the potential of CAP to revolutionize medical treatments through enhanced precision, efficacy, and safety. Continued research and development in cold atmospheric plasma (CAP) is essential for fully exploiting its unique properties and diverse applications in modern medicine. CAP, characterized by its partially or fully ionized gas state, has shown promise in antimicrobial treatments, tissue regeneration, and cancer therapies. By deepening our understanding of the interactions between CAP and biological systems, researchers can develop innovative therapeutic interventions that may overcome the limitations of traditional medical approaches, ultimately leading to improved patient outcomes across various medical disciplines [12, 10, 18, 16, 1].

Feature	CAP in Cancer Therapy	CAP in Wound Healing and Regenerative Medicine	Innovative CAP Devices and Techniques
Mechanism	Rons-mediated Apoptosis	Rons For Tissue Repair	Rons Generation
Therapeutic Focus	Cancer Treatment	Wound Healing	Medical Treatments
Innovative Features	Cap-activated DI Water	Non-thermal Application	Cap IN DI Water

Table 3: This table provides a comparative analysis of Cold Atmospheric Plasma (CAP) applications in cancer therapy, wound healing, and regenerative medicine, alongside innovative CAP devices and techniques. It highlights the mechanisms, therapeutic focus, and distinctive features associated with each application, emphasizing the role of reactive oxygen and nitrogen species (RONS) in mediating therapeutic effects.

6 Challenges and Future Directions

6.1 Biological and Clinical Challenges

Cold Atmospheric Plasma (CAP) technology faces significant biological and clinical challenges that must be addressed to optimize its medical application. A major issue is the lack of standardized protocols for assessing the biological effects of Reactive Oxygen and Nitrogen Species (RONS) generated by different plasma sources, complicating therapeutic efficacy evaluations [20]. This inconsistency necessitates comprehensive studies to establish reliable protocols for consistent outcomes. Scalability remains a critical challenge, requiring optimization to enhance therapeutic efficacy across diverse cancer types [42]. Additionally, controlling the concentration and distribution of reactive species in larger tissues poses difficulties [43]. Effective cancer cell eradication must be achieved while maintaining safe temperature thresholds to avoid damage to healthy tissues [44].

As illustrated in Figure 6, which highlights the primary biological and clinical challenges in the application of CAP technology, standardization issues, scalability, and experimental translation barriers are critical areas of concern. Many CAP studies rely on in vitro experiments, which may not accurately reflect in vivo complexities [41], complicating clinical translation. Prolonged plasma treatment can increase material permeability, affecting properties such as those in masks [9], necessitating optimized treatment durations to prevent unintended alterations. Similar to challenges in neural network architectures, optimizing CAP parameters involves trade-offs between model complexity and computational efficiency [11]. Interdisciplinary collaboration is essential to advance CAP applications and realize its full potential in medical treatments.

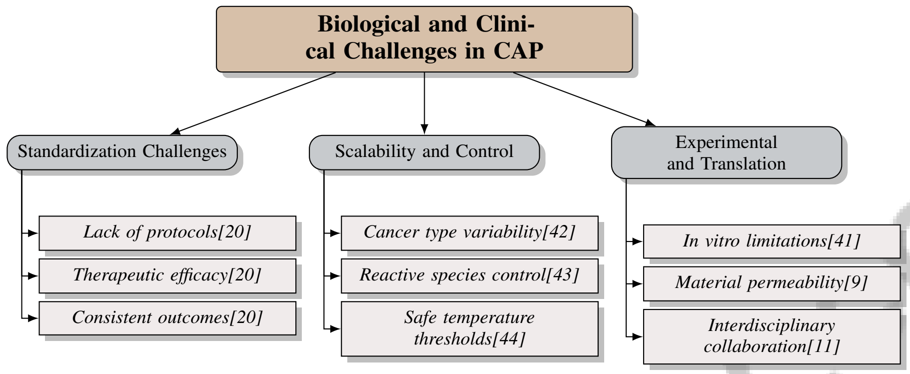

Figure 6: This figure illustrates the primary biological and clinical challenges in the application of Cold Atmospheric Plasma (CAP) technology, highlighting standardization issues, scalability, and experimental translation barriers.

6.2 Optimization of CAP Parameters

Benchmark	Size	Domain	Task Format	Metric
PAL-MI[33]	762	Plasma Medicine	Classification And Regression	ACC, R2
APPJ[45]	1,000	Oncology	Tumor Volume Measurement	tumor volume reduction, dermal toxicity score

Table 4: This table presents a comparative analysis of representative benchmarks utilized in the optimization of CAP parameters. It includes details on the benchmark names, dataset sizes, respective domains, task formats, and evaluation metrics, providing a comprehensive overview of the current state of research in plasma medicine and oncology.

Optimizing CAP parameters is crucial for enhancing efficacy and safety in medical treatments and water decontamination. Table 4 provides a detailed overview of the benchmarks employed in the optimization of CAP parameters, highlighting their relevance in advancing medical treatments and water decontamination technologies. The inconsistent efficacy of CAP in cancer therapy underscores the need for precise control over operational parameters, such as discharge voltage and treatment duration, to achieve uniform results across various cancer cell types [48]. Adapting CAP for different tumor types requires refinement in plasma source designs and treatment protocols. In water treatment, optimizing CAP parameters is necessary for effective targeting of various virus types and scaling technology for practical use [14]. This involves fine-tuning the plasma generation process to maximize pathogen inactivation while minimizing energy consumption. The development of low-cost sensors and circuits offers a promising avenue for facilitating inexpensive plasma experiments and optimizing parameters through real-time monitoring [8].

Enhancing CAP device design is also critical, focusing on gas inlet distribution and electrode configurations to improve jet directionality and treatment uniformity [16], particularly for applications requiring precise targeting of reactive species, ensuring patient safety. Addressing issues such as patient leakage current exceeding safety limits is necessary for compliance with safety standards [6]. The multifaceted challenge of optimizing CAP parameters necessitates concerted research and development efforts. By overcoming existing challenges, researchers can enhance CAP's effectiveness and safety in treatments, facilitating broader implementation in diverse medical fields, including antimicrobial therapies, tissue regeneration, and cancer treatment. Innovative approaches, such as using aluminum foam to optimize reactive species delivery while minimizing tissue damage, further highlight CAP technology's transformative potential in healthcare and environmental contexts [12, 18].

6.3 Future Research Directions

Future research on CAP should focus on optimizing treatment protocols and exploring synergistic effects with other cancer therapies to enhance therapeutic outcomes [19]. Key areas include refining Atmospheric Pressure Plasma Jet (APPJ) devices to reduce leakage currents and investigating alternative working gases to improve efficacy while ensuring safety [6]. Additionally, optimizing treatment times is essential to balance sterilization efficacy with material integrity, particularly in medical and industrial sterilization applications [9].

The development of flexible, porous silica aerogels enabling multiple plasma jets marks a significant advancement in plasma technology for biomedical applications. This design integrates capacitive dielectric barrier discharge (DBD) and cold atmospheric plasma jet (CAPJ) features, allowing effective surface treatment of three-dimensional objects. Utilizing a helium flow subjected to sinusoidal voltage facilitates a two-dimensional plasma jet distribution, extending about 1 cm beyond the active DBD region, promising applications in wound healing and cancer surgery where precise plasma parameter adaptation is crucial [3, 16, 20]. Future research should focus on optimizing these plasma parameters and understanding the underlying mechanisms to improve clinical therapeutic outcomes.

In cancer therapy, integrating CAP with nanoparticles holds potential for enhancing treatment efficacy, necessitating research on nanoparticle formulations and mechanisms behind increased uptake and cytotoxic effects. Furthermore, exploring additional feeding gases and conducting in vivo studies to validate the effectiveness of CAP-activated deionized water are essential steps in advancing CAP's applicability. Incorporating real-time data processing applications into CAP treatments, similar to hybrid models in neural networks, could significantly enhance the accuracy and adaptability of CAP therapies in clinical settings. This integration would allow real-time monitoring of cancer cell responses to CAP, enabling dynamic adjustments in treatment parameters, thus improving therapeutic outcomes and paving the way for adaptive CAP platforms for various medical conditions [12, 18, 48, 13, 33]. Addressing these research directions will refine CAP technology, delivering more effective and safe treatments and promoting broader adoption in diverse medical fields.

7 Conclusion

Cold Atmospheric Plasma (CAP) emerges as a pivotal innovation in oral health and plasma medicine, primarily due to its ability to generate Reactive Oxygen and Nitrogen Species (RONS), which are essential for antimicrobial efficacy and oxidative stress modulation. CAP's effectiveness in diminishing oral pathogens and promoting tissue regeneration positions it as a viable alternative to traditional antimicrobial therapies. In the realm of plasma medicine, CAP's unique ability to selectively induce oxidative stress offers promising therapeutic potentials, particularly in oncology and wound care.

Advancements in CAP technology, including the development of cost-effective Atmospheric Pressure Plasma Jet (APPJ) devices, have significantly enhanced its accessibility and adaptability across various healthcare applications. The integration of affordable sensors and electronic components further supports the practical application of plasma studies, facilitating educational and research opportunities in institutions with limited resources.

Despite these promising developments, several challenges remain in fully harnessing CAP's capabilities. Critical issues include the need for standardized operational protocols, optimization of CAP parameters, and a deeper understanding of the complex interactions between RONS and biological systems. Continued research and interdisciplinary collaboration are vital to addressing these challenges, ensuring the safe and effective application of CAP in diverse medical contexts. As the field of plasma medicine evolves, CAP stands poised to transform therapeutic approaches, offering novel solutions for the management of microbial infections and diseases associated with oxidative stress.

References

[1] Philip Efthimion, Igor Kaganovich, Yevgeny Raitses, M. Keidar, Hyo-Chang Lee, Mikhail Shneider, and R. Car. Critical need for a national initiative in low temperature plasma research, 2020.

[2] Vikas Rathore and Sudhir Kumar Nema. Selective generation of reactive oxygen species in plasma-activated water using co2 plasma. *Journal of Vacuum Science & Technology A*, 41(4), 2023.

[3] Carles Corbella and Sabine Portal. Flexible plasma multi-jet source operated in radial discharge configuration, 2021.

[4] Sandra Moritz, Alisa Schmidt, Joachim Sann, and M. H. Thoma. Surface modifications caused by cold atmospheric plasma sterilization treatment, 2020.

[5] Thomas Von Woedtke, Anke Schmidt, Sander Bekeschus, Kristian Wende, and Klaus-Dieter Weltmann. Plasma medicine: A field of applied redox biology. *In vivo*, 33(4):1011–1026, 2019.

[6] Fellype do Nascimento, Aline da Graça Sampaio, Noala Vicensoto Moreira Milhan, Aline Vidal Lacerda Gontijo, Philipp Mattern, Torsten Gerling, Eric Robert, Cristiane Yumi Koga-Ito, and Konstantin Georgiev Kostov. A low cost, flexible atmospheric pressure plasma jet device with good antimicrobial efficiency, 2024.

[7] Dayun Yan, Qihui Wang, Manish Adhikari, Alisa Malyavko, Li Lin, Denis B. Zolotukhin, Xiaoliang Yao, Megan Kirschner, Jonathan H. Sherman, and Michael Keidar. A new physically triggered cell death via transbarrier contactless cold atmospheric plasma treatment of cancer cells, 2020.

[8] Alessandro N. Vargas, Victor Miller, Ali Mesbah, and Gabriele Neretti. Low-cost sensors and circuits for plasma education: characterizing power and illuminance, 2024.

[9] Alisa Schmidt, Chen-Yon Tobias Tschang, Joachim Sann, and Markus H. Thoma. Cold atmospheric plasma sterilization of ffp3 face masks and long-term material effects, 2021.

[10] Mounir Laroussi. Plasma medicine: A brief introduction, 2021.

[11] Dirk Ellerweg, Achim von Keudell, and Jan Benedikt. The mystery of o and o3 production in the effluent of a he/o2 atmospheric pressure microplasma jet, 2011.

[12] Review.

[13] Rico Rutkowski, Georg Daeschlein, Thomas von Woedtke, Ralf Smeets, Martin Gosau, and Hans-Robert Metelmann. Long-term risk assessment for medical application of cold atmospheric pressure plasma. *Diagnostics*, 10(4):210, 2020.

[14] Arijana Filipić, Gregor Primc, Rok Zaplotnik, Nataša Mehle, Ion Gutierrez-Aguirre, Maja Ravnikar, Miran Mozetič, Jana Žel, and David Dobnik. Cold atmospheric plasma as a novel method for inactivation of potato virus y in water samples. *Food and environmental virology*, 11(3):220–228, 2019.

[15] Patrick Vanraes and Annemie Bogaerts. The essential role of the plasma sheath in plasma–liquid interaction and its applications—a perspective. *Journal of Applied Physics*, 129(22), 2021.

[16] Carles Corbella, Sabine Portal, Li Lin, and Michael Keidar. Towards the fabrication of a morphing plasma source for biomedical applications, 2021.

[17] Sylvain Iséni. Electric field vector mapping of guided ionization waves at atmospheric pressure, 2017.

[18] Zhitong Chen, Richard Obenchain, and Richard E. Wirz. Cold plasma treatment for biomedical applications: using aluminum foam to reduce risk while increasing efficacy, 2023.

[19] Fengdong Cheng, Dayun Yan, Jie Chen, Zi Wang, Alex Horkowitz, Michael Keidar, and Eduardo M. Sotomayor. Enhancing innate and adaptive immune systems by cold atmospheric plasma (cap) and its antitumor immunity, 2022.

[20] Anna Khlyustova, Cédric Labay, Zdenko Machala, Maria-Pau Ginebra, and Cristina Canal. Important parameters in plasma jets for the production of rons in liquids for plasma medicine: A brief review. *Frontiers of Chemical Science and Engineering*, 13:238–252, 2019.

[21] Ming-Ming Chen, Yan Li, Shou-Long Deng, Yue Zhao, Zheng-Xing Lian, and Kun Yu. Mitochondrial function and reactive oxygen/nitrogen species in skeletal muscle. *Frontiers in cell and developmental biology*, 10:826981, 2022.

[22] Fellype do Nascimento, Torsten Gerling, and Konstantin Georgiev Kostov. On the gas heating effect of helium atmospheric pressure plasma jet, 2023.

[23] Juan Tornin, Cédric Labay, Francesco Tampieri, Maria-Pau Ginebra, and Cristina Canal. Evaluation of the effects of cold atmospheric plasma and plasma-treated liquids in cancer cell cultures. *Nature Protocols*, 16(6):2826–2850, 2021.

[24] Shihao Tan, Haiwei Zhu, Dawei Liu, Song Zhang, and Hongxiang Chen. Molecular mechanism of cleavage of sars-cov-2 spike protein by plasma generated rons. *Frontiers in Physics*, 12:1357639, 2024.

[25] Georg Bauer, Dominika Sersenová, David B Graves, and Zdenko Machala. Cold atmospheric plasma and plasma-activated medium trigger rons-based tumor cell apoptosis. *Scientific reports*, 9(1):14210, 2019.

[26] Dušan Branỳ, Dana Dvorská, Erika Halašová, and Henrieta Škovierová. Cold atmospheric plasma: A powerful tool for modern medicine. *International journal of molecular sciences*, 21(8):2932, 2020.

[27] Krithika Lingappan. Nf-κb in oxidative stress. *Current opinion in toxicology*, 7:81–86, 2018.

[28] Eloisa Sardella. Generation and control of plasma induced reactive oxygen/nitrogen species in liquids: a route toward selective cell responses.

[29] Gert Jungbauer, Dominick Moser, Steffen Müller, Wolfgang Pfister, Anton Sculean, and Sigrun Eick. The antimicrobial effect of cold atmospheric plasma against dental pathogens—a systematic review of in-vitro studies. *Antibiotics*, 10(2):211, 2021.

[30] Shahriar Mirpour, Sara Fathollah, Parvin Mansouri, Bagher Larijani, Mahmood Ghoranneviss, Mohammadreza Mohajeri Tehrani, and Mohammad Reza Amini. Cold atmospheric plasma as an effective method to treat diabetic foot ulcers: A randomized clinical trial. *Scientific reports*, 10(1):10440, 2020.

[31] Cindy Smet, Estefania Noriega, Frederik Rosier, JL Walsh, VP Valdramidis, and JF Van Impe. Impact of food model (micro) structure on the microbial inactivation efficacy of cold atmospheric plasma. *International Journal of Food Microbiology*, 240:47–56, 2017.

[32] Guiqiang Wang, Dehua Kong, Wei Tang, Jie Fang, and Zhitong Chen. Mechanisms and safety of air plasma inactivated sars-cov-2, 2023.

[33] Mehmet Akif Ozdemir, Gizem Dilara Ozdemir, Merve Gul, Onan Guren, and Utku Kursat Ercan. Machine learning to predict the antimicrobial activity of cold atmospheric plasma-activated liquids, 2022.

[34] R. Mehrabifard, H. Mehdian, K. Hajisharifi, and E. Amini. Improving cold atmospheric pressure plasma efficacy on breast cancer cells control-ability and mortality by using vitamin c and static magnetic field, 2023.

[35] Endre J Szili, James Dedrick, Jun-Seok Oh, James W Bradley, Roderick W Boswell, Christine Charles, Robert D Short, and Sameer A Al-Bataineh. Microplasma array patterning of reactive oxygen and nitrogen species onto polystyrene. *Frontiers in Physics*, 5:1, 2017.

[36] Bhawana Adhikari, Manish Adhikari, Bhagirath Ghimire, Gyungsoon Park, and Eun Ha Choi. Cold atmospheric plasma-activated water irrigation induces defense hormone and gene expression in tomato seedlings. *Scientific reports*, 9(1):16080, 2019.

[37] Dayun Yan, Haitao Cui, Wei Zhu, Niki Nourmohammadi, Julian Milberg, Lijie G Zhang, Jonathan H Sherman, and Michael Keidar. The specific vulnerabilities of cancer cells to the cold atmospheric plasma-stimulated solutions. *Scientific reports*, 7(1):4479, 2017.

[38] Helmut Sies. Oxidative stress: Concept and some practical aspects. *Antioxidants*, 9(9):852, 2020.

[39] Thierry Rabilloud, Mireille Chevallet, Sylvie Luche, and Emmanuelle Leize-Wagner. Oxidative stress response: a proteomic view, 2008.

[40] Zhitong Chen, Li Lin, Xiaoqian Cheng, Eda Gjika, and Michael Keidar. Effects of cold atmospheric plasma generated in deionized water in cell cancer therapy, 2016.

[41] Dayun Yan, Jonathan H. Sherman, Jerome Canady, Barry Trink, and Michael Keidar. The cellular ros-scavenging function, a key factor determining the specific vulnerability of cancer cells to cold atmospheric plasma in vitro, 2017.

[42] Zhitong Chen. Cold atmospheric plasma activated deionized water using helium, argon, and nitrogen as feeding gas for cancer therapy, 2022.

[43] Zhitong Chen, Xiaoqian Cheng, Li Lin, and Michael Keidar. Cold atmospheric plasma discharged in water and its potential use in cancer therapy, 2016.

[44] I. Schweigert, M. Biryukov, A. Polyakova, N. Krychkova, E. Gorbunova, A. Epanchintseva, I. Pyshnaya, Dm. Zakrevsky, E. Milakhina, and O. Koval. Pulsed voltage cold atmospheric plasma jet and gold nanoparticles enhance cytotoxic anticancer effect, 2023.

[45] F. Judée, J. Vaquero, S. Guégan, L. Fouassier, and T. Dufour. Atmospheric pressure plasma jets applied to cancerology: correlating electrical configurations with in vivo toxicity and therapeutic efficiency, 2019.

[46] Fan Bai, Yingjie Lu, Yujie Zhi, Yueye Huang, Long Li, Jiaoxiao Luo, Jamoliddin Razzokov, Olga Koval, Maksudbek Yusupov, Guojun Chen, and Zhitong Chen. Air cold atmospheric plasma with patterns for anaplastic squamous cell carcinoma treatment, 2023.

[47] Michał Sołtan, Dorota Bartusik-Aebisher, and David Aebisher. The potential of oxygen and nitrogen species-regulating drug delivery systems in medicine. *Frontiers in Bioengineering and Biotechnology*, 10:973080, 2022.

[48] Eda Gjika, Sonali Pal-Ghosh, Anna Tang, Megan Kirschner, Gauri Tadvalkar, Jerome Canady, Mary Ann Stepp, and Michael Keidar. Adaptation of operational parameters of cold atmospheric plasma for in vitro treatment of cancer cells. *ACS applied materials & interfaces*, 10(11):9269–9279, 2018.

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