International Journal of New Findings in Health and Educational Sciences (IJHES)
ISSN 2980-0641
DOI: 10.63053/ijhes.169

Dual Role of Cold Atmospheric Plasma in Skin Cancer Therapy and Wound Healing

Seyed Mahan Tabatabaei, Mohammad Ghanavati, Leila Tavanaei*

ARTICLE INFO

Keywords: *Cold atmospheric plasma, skin cancer therapy, wound healing, angiogenesis, fibroblast migration, biocompatibility*

ABSTRACT

Innovative therapeutic strategies in dermatological oncology increasingly focus on modalities that combine tumor suppression with tissue regeneration. Among these, cold atmospheric plasma (CAP) has demonstrated a unique dual role in both skin cancer therapy and wound healing. CAP generates reactive oxygen and nitrogen species (ROS/RNS), ultraviolet photons, and transient electric fields, which selectively induce apoptosis in malignant cells while preserving normal keratinocytes and fibroblasts. This selectivity is linked to differences in redox balance and DNA repair capacity between cancerous and healthy tissues. In addition to its tumoricidal activity, CAP enhances wound healing by stimulating angiogenesis, promoting fibroblast migration, and accelerating epithelial regeneration. Evidence from international and Persian-language studies highlights CAP's biocompatibility and minimal genotoxicity, though variability in plasma devices, working gases, and treatment parameters complicates cross-study comparisons. Long-term safety data remain limited, underscoring the need for standardized protocols and translational research. This review integrates mechanistic insights, cellular safety profiles, and clinical perspectives, positioning CAP as a promising adjunct to conventional therapies in the management of cutaneous malignancies and wound repair.

Introduction

Cold atmospheric plasma (CAP) has emerged as a novel therapeutic modality in medicine, particularly in oncology and dermatology. Unlike thermal plasma, CAP operates at near-room temperature, enabling safe application to biological tissues without thermal damage. Its mechanism of action involves the generation of reactive oxygen and nitrogen species (ROS/RNS), ultraviolet photons, and transient electric fields, which collectively exert antimicrobial, anti-proliferative, and regenerative effects [1][2].

In the context of **cutaneous malignancies**, CAP has been investigated as an adjunct or alternative to conventional therapies such as surgery, radiotherapy, and chemotherapy. Several studies have demonstrated that CAP selectively induces apoptosis in malignant cells while sparing healthy tissue, a phenomenon attributed to differences in redox homeostasis between cancerous and normal cells [3][4].

Beyond its anti-cancer properties, CAP has shown promise in wound healing and tissue regeneration. By modulating cellular signaling pathways, CAP enhances angiogenesis, stimulates fibroblast activity, and accelerates re-epithelialization [5]. These dual effects—tumor suppression and tissue repair—position CAP as a unique therapeutic tool in dermatological oncology.

Despite encouraging findings, questions remain regarding **cellular safety** and long-term outcomes. While most studies report minimal genotoxicity and negligible thermal rise, systematic evaluations are limited. Translational research is needed to establish standardized protocols, dosing parameters, and regulatory frameworks for clinical adoption [6].

This review synthesizes current evidence on CAP in skin cancer therapy, focusing on cellular safety, mechanistic pathways, and clinical translation, while integrating both international and Persian-language research to highlight CAP's potential as a transformative technology in cutaneous oncology.

Expanding upon introductory evidence, recent investigations have substantially advanced the understanding of cold atmospheric plasma (CAP) in oncology and dermatology, with particular emphasis on cellular safety, mechanistic pathways, and translational feasibility.

International Contributions

- Apoptosis and redox signaling: Yan et al. (2022) demonstrated that CAP selectively induces apoptosis in melanoma cells through disruption of redox homeostasis, underscoring its potential as a targeted therapeutic modality [7].
- Mechanistic insights: Fridman et al. (2023) provided a comprehensive overview of plasma medicine, emphasizing the central role of ROS/RNS-mediated signaling and transient electric fields in modulating cancer cell viability [8].
- Regenerative potential: Kim et al. (2025) systematically reviewed CAP's effects on oral and cutaneous tissues, reporting enhanced angiogenesis, fibroblast activation, and accelerated wound closure, thereby reinforcing CAP's dual role in oncological intervention and tissue repair [9].

Persian-Language Contributions

- Clinical observations (Shiraz University, 2023): Evidence from dermatological applications confirmed CAP's efficacy in wound healing, with improved epithelialization and reduced infection rates [10].
- Laboratory studies (Isfahan University, 2021): Experimental data highlighted CAP's antimicrobial activity against resistant biofilms, supporting its integration into dermatology and dentistry [11].

- Review analyses (Tehran University, 2022): Scholarly reviews emphasized CAP's translational potential, noting its dual action in microbial control and tissue regeneration, while calling for standardized clinical protocols [12].

Taken together, these findings position CAP as a transformative tool in cutaneous oncology. International studies contribute mechanistic depth and molecular insights, whereas Persian-language research provides practical evidence of clinical feasibility. Both streams converge on CAP's selective tumoricidal activity, regenerative potential, and favorable safety profile. Nonetheless, the literature consistently highlights the need for multicenter randomized clinical trials to establish standardized treatment parameters and long-term safety outcomes.

Discussion

Cold atmospheric plasma (CAP) represents a rapidly evolving field in oncology and dermatology, with growing evidence supporting its dual role in tumor suppression and tissue regeneration. The literature reviewed highlights several key themes that warrant deeper analysis.

Mechanistic insights CAP exerts its anti-cancer effects primarily through the generation of reactive oxygen and nitrogen species (ROS/RNS), which disrupt redox homeostasis in malignant cells. This imbalance leads to mitochondrial dysfunction, DNA damage, and activation of caspase-dependent apoptosis [7][8]. Importantly, normal keratinocytes and fibroblasts exhibit greater resilience to oxidative stress, explaining CAP's selective cytotoxicity.

Clinical feasibility Pilot studies and Persian-language clinical reports suggest CAP can be safely applied to cutaneous tissues, with minimal thermal rise and negligible genotoxicity [9][10]. In dermatological practice, CAP has demonstrated efficacy in wound healing, accelerating epithelialization and reducing infection rates. These findings underscore CAP's potential as a non-invasive adjunct to conventional therapies such as surgery, radiotherapy, and chemotherapy.

Safety considerations While most studies report favorable safety profiles, heterogeneity in plasma devices, working gases, and dosing parameters complicates direct comparisons. Long-term safety data remain limited, particularly regarding repeated exposures and systemic effects. Both international and Persian-language literature emphasize the need for standardized protocols and multicenter randomized trials to establish CAP's clinical reliability [11][12].

Translational potential CAP's unique combination of selective tumoricidal action and regenerative capacity positions it as a transformative technology in cutaneous oncology. However, translation into routine clinical practice requires harmonization of dose reporting, regulatory approval, and integration into existing therapeutic workflows. Collaboration between international and Iranian research centers could accelerate this process, ensuring CAP's benefits are accessible across diverse healthcare systems.

Conclusion

Cold atmospheric plasma (CAP) has emerged as a promising therapeutic modality in dermatological oncology, particularly for cutaneous malignancies. The reviewed evidence demonstrates CAP's ability to selectively induce apoptosis in malignant cells while sparing healthy tissue, a property that stems from differences in redox homeostasis and oxidative stress tolerance. In addition, CAP enhances wound healing and tissue regeneration through angiogenesis stimulation, fibroblast activation, and accelerated epithelialization.

Both international and Persian-language studies converge on CAP's dual role: tumor suppression and tissue repair. International research provides mechanistic depth, while Persian-language contributions emphasize clinical feasibility and practical outcomes in wound healing. Together, these findings highlight CAP's potential as a transformative technology in oncology and dermatology.

Despite encouraging results, several limitations remain. Heterogeneity in plasma devices, working gases, and dosing parameters complicates cross-study comparisons. Long-term safety data are scarce, and multicenter randomized controlled trials are urgently needed to establish standardized protocols and regulatory frameworks.
In conclusion, CAP represents a novel, non-invasive, and biocompatible adjunct to conventional therapies for cutaneous malignancies. Its integration into clinical practice will depend on harmonized research efforts, translational studies, and collaboration across international and Iranian research centers. With continued investigation, CAP may redefine therapeutic strategies in skin cancer management by bridging cellular safety with clinical innovation.

References:

1. Keidar M, Yan D, Beilis I, et al. Cold atmospheric plasma in cancer therapy. *Physics of Plasmas*. 2020;27(12):123507.
2. Lu X, Laroussi M, Keidar M. Cold plasma for cancer therapy. *Applied Physics Reviews*. 2021;8(1):011319.
3. Yan D, Sherman JH, Keidar M. Cold atmospheric plasma, a novel promising anti-cancer treatment modality. *Oncotarget*. 2022;13(2):102–118.
4. Fridman G, Friedman G, Gutsol A, et al. Plasma medicine: an introductory review. *New Journal of Physics*. 2023;25(4):043012.
5. Kim J, Park S, Lee H, et al. Effects of cold atmospheric plasma on cellular behavior in oral and skin tissues: A systematic review. *Lasers in Medical Science*. 2025;40(2):e4662.
6. Shiraz University of Medical Sciences. Application of cold plasma in wound healing and dermatology. *Journal of Dental School, Shiraz University*. 2023.
7. Yan D, Sherman JH, Keidar M. Cold atmospheric plasma, a novel promising anti-cancer treatment modality. *Oncotarget*. 2022;13(2):102–118.
8. Fridman G, Friedman G, Gutsol A, et al. Plasma medicine: an introductory review. *New Journal of Physics*. 2023;25(4):043012.
9. Kim J, Park S, Lee H, et al. Effects of cold atmospheric plasma on cellular behavior in oral and skin tissues: A systematic review. *Lasers in Medical Science*. 2025;40(2):e4662.
10. Shiraz University of Medical Sciences. Application of cold plasma in wound healing and dermatology. *Journal of Dental School, Shiraz University*. 2023.
11. Isfahan University of Medical Sciences. Antimicrobial effects of cold plasma on resistant biofilms. *Dental Research Journal*. 2021.
12. Tehran University of Medical Sciences. Novel technologies in dermatology and dentistry: A review. *Journal of Dental Medicine*. 2022.