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Cold Atmospheric Plasma as a Non-Thermal Oncologic Modality for Skin Cancer: A Systematic Review of Mechanisms and Treatment Efficacy

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ABSTRACT

Introduction: Skin cancer, including melanoma and non-melanoma skin cancers (NMSC), remains a major clinical burden due to recurrence, metastasis, and limited efficacy of conventional treatments. Cold atmospheric plasma (CAP) has emerged as a minimally invasive modality capable of generating reactive oxygen and nitrogen species that selectively induce oxidative stress and cell death in malignant cells. This study aimed to review the current evidence on CAP-based therapy for skin cancer, with emphasis on mechanistic insights, therapeutic efficacy, and synergistic applications.

Materials and Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science for studies published from 2015 to 2025. Relevant search terms included “Plasma Gases”, “Skin Neoplasms”, “Reactive Oxygen Species”, “Reactive Nitrogen Species”, and “Apoptosis”. The inclusion criteria were original and review studies evaluating CAP for melanoma or NMSC, alone or in combination with chemotherapeutics, photodynamic therapy, or photothermal therapy. Exclusion criteria included conference abstracts and studies not focused on skin cancer.

Results and Discussion: The studies reviewed consistently demonstrated that CAP induces oxidative stress-mediated apoptosis, necrosis, and redox disruption in melanoma and NMSC models. CAP enhanced the cytotoxic activity of chemotherapeutic agents and increased the efficacy of photodynamic therapy in superficial tumors. Mechanistic studies confirmed the activation of MAPK and AKT/mTOR suppressive pathways and the induction of immunogenic cell death. Early clinical data, along with the use of dermatologic CAP devices, indicated that CAP is safe. Furthermore, CAP-based combinations have shown superior tumor suppression and potential for dose-reduction of conventional therapies.

Conclusion: CAP represents a promising non-thermal and selective therapeutic option for skin cancer, with notable mechanistic and synergistic advantages. However, further large-scale clinical validation is required to support its integration into multimodal oncologic care.

Keywords: Apoptosis, Plasma gases, Reactive nitrogen species, Reactive oxygen species, Skin neoplasms

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