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Cold Plasma in Modern Oncology: Molecular Mechanisms, Clinical Evidence, and Therapeutic Prospects

Elnaz Balvasi[1*], Behnaz Balvasi[2], Farnaz Shirvani[2], Ghazale Geraily[1,3]

[1]Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Nuclear Engineering, University of Isfahan, Isfahan, Iran
[3]Department of Radiation Oncology, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Introduction: Cold atmospheric plasma (CAP) is a non-thermal approach that selectively targets cancer cells while sparing healthy tissue. CAP generates reactive oxygen and nitrogen species and energetic particles that collectively induce oxidative stress, DNA damage, and immunogenic cell death. These effects enhance apoptosis and activate antitumor immune responses, supporting CAP as a potential adjuvant to radiotherapy, chemotherapy, and immunotherapy.

Materials and Methods: This review summarizes preclinical and clinical evidence on the mechanisms of CAP, its anticancer activity, combination strategies, and clinical feasibility, with emphasis on apoptosis, DNA damage, cell-cycle arrest, and plasma-activated liquids. Relevant studies in plasma medicine and oncology were analyzed.

Results and Discussion: CAP induces apoptosis through mitochondrial disruption and caspase activation and generates DNA breaks while inhibiting major oncogenic pathways such as PI3K/AKT/mTOR and MAPK/ERK. It also enhances tumor responses to radiotherapy and chemotherapy by increasing oxidative stress and reducing drug resistance. Preclinical studies have shown significant tumor suppression with minimal toxicity, while early clinical trials in melanoma, skin, cervical, breast, and head-and-neck cancers demonstrate favorable lesion regression and safety profiles.

Conclusion: CAP is a promising multimodal anticancer strategy with high selectivity. Despite challenges in dosimetry and long-term safety, current evidence supports its integration with conventional therapies. Further clinical validation and device optimization may enable a broader use of CAP in oncology.

Keywords: Cancer therapy, Cold plasma, Plasma-activated liquids, Radiosensitization, Reactive oxygen and nitrogen species

Corresponding Author: Elnaz Balvasi
Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran;
E-mail: balvasielnaz@gmail.com