Comparative Anti-Tumor Mechanisms of Direct Cold Atmospheric Plasma and Plasma-Activated Liquids

Fereshteh Abbasvandi

ATMP Department, Breast Cancer Research Center, Motamed Cancer Research Institute, ACECR, Tehran, Iran

OPEN ACCESS

Citation:
Abbasvandi F. Comparative Anti-Tumor Mechanisms of Direct Cold Atmospheric Plasma and Plasma-Activated Liquids. *Iran Biomed J.* Supplementary (2-2026): 39.

ABSTRACT

Introduction: Cold atmospheric plasma (CAP) has emerged as a promising non-thermal anticancer strategy due to its ability to generate diverse reactive oxygen and nitrogen species (RONS). These species disrupt redox homeostasis, induce oxidative stress, and selectively damage malignant cells. CAP can be applied through two main approaches—direct plasma exposure and indirect treatment using plasma-activated liquids—each offering distinct therapeutic characteristics.

Materials and Methods: Direct CAP involves exposing the surfaced of tumors to the plasma plume, delivering high concentrations of both short- and long-lived reactive species. This method enables immediate biochemical interactions with cellular membranes and intracellular targets. In contrast, indirect CAP utilizes liquids enriched with stable RONS, such as hydrogen peroxide, nitrites, and nitrates. These substances retain their activity during storage and can diffuse into deeper tissues after administration.

Results and Discussion: The application of direct CAP rapidly compromises membrane integrity, induces mitochondrial dysfunction, and causes DNA damage, leading to the activation of intrinsic apoptotic pathways. It also influences downstream processes, including cell-cycle arrest, autophagy, and immunogenic cell death, making it particularly effective for treating superficial tumors in controlled experimental settings. On the other hand, indirect CAP demonstrates potent cytotoxicity by inducing sustained oxidative stress, reducing metastatic signaling, and overcoming chemoresistance, including in aggressive cancers such as triple-negative breast cancer. Its lower intensity may offer a more favorable safety profile for clinical use.

Conclusion: Both CAP modalities exert strong anticancer effects driven by RONS-mediated oxidative stress; however, their operational differences make them suitable for distinct therapeutic contexts. Future work should focus on optimizing treatment parameters, standardizing device outputs, and integrating CAP with established oncological therapies to enhance clinical translation.

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