Effects of Cold Plasma on the Survival of Cancer Cells in vitro—A Systematic Review of Recent Experimental Findings

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ABSTRACT

Introduction: Cold atmospheric plasma (CAP) has emerged as a promising non-thermal oncological tool due to its ability to generate reactive oxygen and nitrogen species, UV photons, charged particles, and transient electric fields. These components interact synergistically with cancer cells, inducing oxidative stress, activating cell death pathways, and uncovering tumor-specific vulnerabilities. Recent preclinical studies demonstrate that both direct exposure to CAP and the use of plasma-activated liquids suppress proliferation, enhance apoptosis and ferroptosis, and selectively damage malignant cells while sparing most healthy tissues.

Materials and Methods: CAP triggers the accumulation of reactive oxygen species (ROS), lipid peroxidation, DNA damage, cytochrome c release, and caspase-dependent apoptosis. Also, ferroptosis has been reported to be modulated by iron metabolism and lipid-ROS pathways. The weaker antioxidant defense and altered redox homeostasis in cancer cells contribute to their selective vulnerability to these processes.

Results and Discussion: Our results indicated that both CAP and plasma-activated media reduced cell viability in hepatocellular, breast, cervical, colon, and lung cancer models. CAP modulated the USP49/HDAC3 signaling pathway, activated p53 pathways, and enhanced apoptotic markers. Additionally, the combination of CAP with chemotherapy improved drug sensitivity and overcome chemoresistance. In vivo studies further confirmed reduced tumor volume, decreased microvessel density, and enhanced vascular permeability. Importantly, the safety and feasibility of CAP treatment was affirmed in phase I clinical trials.

Conclusion: Current experimental and translational findings support CAP as a selective, multi-mechanistic, and minimally invasive anticancer strategy. Its ability to induce apoptosis, ferroptosis, and immune-stimulatory responses highlights its potential as an adjunct or standalone therapeutic tool. Future research should focus on device standardization, dose-response optimization, mechanistic modeling, and controlled clinical trials to fully establish CAP as a clinical cancer therapy modality.

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Keywords: Apoptosis, Cold atmospheric plasma, Ferroptosis, Oxidative stress, Plasma-activated medium

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