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# Multiphysics Simulation of the Synergistic Interaction Between Plasma-Based Radiosensitization and Liquid <sup>131</sup>Cs Balloon Brachytherapy in GBM

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## OPEN ACCESS

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## ABSTRACT

**Introduction:** Glioblastoma multiforme (GBM) is a highly aggressive primary brain tumor known for its significant resistance to radiation treatment. This resistance is primarily due to efficient repair of DNA double-strand break (DSB), hypoxic microenvironments (with oxygen partial pressure, pO<sub>2</sub> < 10 mmHg), and hypermethylation of the MGMT promoter. Standard treatment typically involves maximal safe surgical resection, external beam radiotherapy (60 Gy/30 fractions), and the chemotherapy agent temozolomide, providing a median survival of only 14.6 months. To enhance the cytotoxic effects of ionizing radiation on residual tumor cells within a 1 cm clinical target volume, this study employs a multiphysics simulation that integrates plasma-based radiosensitization with liquid <sup>131</sup>Cs balloon brachytherapy.

**Materials and Methods:** The photon transport from a silicone balloon (0.2 mm wall thickness, 3 cm diameter) filled with liquid <sup>131</sup>Cs (half-life = 9.7 days, energy ≈ 29 keV) was modeled using MCNPX 2.6. This model aims to deliver 60 Gy at a distance of 1 cm from the balloon its surface (with V<sub>100</sub> = 92%, D<sub>90</sub> = 58 Gy, and BED<sub>10</sub> < 100 Gy). Additionally, COMSOL Multiphysics 6.2 simulated an argon dielectric-barrier discharge (10 kV, 10 kHz, 0.1 L/min for 60 seconds) producing reactive oxygen species (ROS) and nitrogen species such as O<sub>3</sub>, •OH, H<sub>2</sub>O<sub>2</sub>, and nitric oxide, with penetration depths of 1.2–1.8 mm and <10% deviation from experimental validation.

**Results and Discussion:** Linear-quadratic modeling ( $\alpha_0 = 0.25\text{Gy}^{-1}$ ,  $\beta = 0.03\text{Gy}^{-2}$ ) that incorporated CAP-induced  $\alpha$  enhancement ( $\Delta\alpha/\alpha_0 = 28\%$ ) predicted a 37% reduction in survival of U87MG cell ( $SF_{\text{combined}} = 0.15$  vs. 0.24) and a 35% increase in apoptosis, as indicated by  $\gamma$ -H2AX and caspase-3 activation. Plasma-activated liquids (PAL) further improved the diffusion of ROS by ~50% without inducing significant thermal effects ( $\Delta T < 1.5^\circ\text{C}$ ). Overall, CAP and PAL act as effective radiosensitizers, amplifying oxidative damage to DSB and improving the therapeutic efficacy of <sup>131</sup>Cs brachytherapy while maintaining safe doses of normal tissue.

**Conclusion:** Our findings support the development of a hybrid intraoperative treatment system and its future preclinical application in trials.



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**Keywords:** <sup>131</sup>Cs balloon brachytherapy, Cold atmospheric plasma, COMSOL multiphysics, GBM, MCNPx simulation, Plasma-based radiosensitization

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