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A MULTICOMPARTMENT PHENOTYPE-STRUCTURED MODEL OF TUMOR RESPONSE TO HYPOXIA AND RADIOTHERAPY

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ABSTRACT

Recent studies have highlighted the critical role of tumor–microenvironment interactions in shaping therapy outcomes. Hypoxia, in particular, acts as a key environmental stressor, fostering more aggressive phenotypes and affecting radiotherapy efficacy in two main ways. On one hand, hypoxia-adapted cells exhibit high resistance to environmental stresses, allowing them to survive in poorly oxygenated regions where ionizing radiation is less effective. On the other hand, their slower proliferation rates make them less vulnerable to treatments that primarily target dividing cells.

This work presents a continuous mathematical model to investigate how hypoxia drives the evolutionary dynamics of cancer cells and impacts radiotherapy. Building on [1], the model employs a phenotype-structured population framework and is formulated as a system of coupled nonlinear integro-differential equations, incorporating a second compartment to account for non-proliferating cells arising from radiation-induced damage, enabling a more realistic representation of tumor response.

The model integrates oxygen spatial heterogeneity and phenotypic traits to assess alternative radiotherapy schedules beyond the standard of care. Preliminary simulations suggest that exploiting tumor reoxygenation through adaptive treatment timing can substantially improve therapeutic outcomes and inform future clinical trial design.

REFERENCES

[1] Chiari G, Fiandaca G, and Delitala ME: *Hypoxia-related radiotherapy resistance in tumors: treatment efficacy investigation in an eco-evolutionary perspective.*, Front. Appl. Math. Stat. (2023).