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Bayesian Calibration and Model Selection for Evaluating Radiotherapy and Immunotherapy in Triple-Negative Breast Cancer

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Breast cancers are classified according to the expression of estrogen, progesterone, and HER2 receptors. In the absence of these biomarkers, the cancer is characterized as triple-negative breast cancer (TNBC), which does not respond to targeted therapies. Therefore, strategies to enhance immunotherapy are required, particularly given that radiotherapy can modulate the tumor microenvironment by increasing immune cell levels [2].

We utilized tumor volume data to develop a calibration and model selection framework for mathematical models based on ordinary differential equations (ODEs), employing a Bayesian approach [3]. The investigations used 4T1 cells as a model for TNBC, which exhibited distinct radiation response profiles (sensitivity and resistance). The experimental design involved 56 mice distributed into six groups: control (sensitive and resistant cells without treatment), radiotherapy (sensitive and resistant cells), immunotherapy (sensitive cells), and a combination of radiotherapy and immunotherapy (sensitive cells). Figure 1 presents the calibration and model selection framework.

The model selected for studying the effects of radiotherapy is described by the following ODE:

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) - N\sum_i \alpha D_i^{rad} e^{-\beta(t-\tau_i-\delta)}, \tag{1}$$

where r denotes the intrinsic tumor growth rate, K is the carrying capacity, α represents the efficiency of radiotherapy in reducing tumor cells, β is the decay rate of radiotherapy efficacy, δ is the delay before the radiotherapy effect begins, and D_i^{rad} is the dose administered at time τ_i, for $i = 0, 1, 2, 3, 4, 5$ days.

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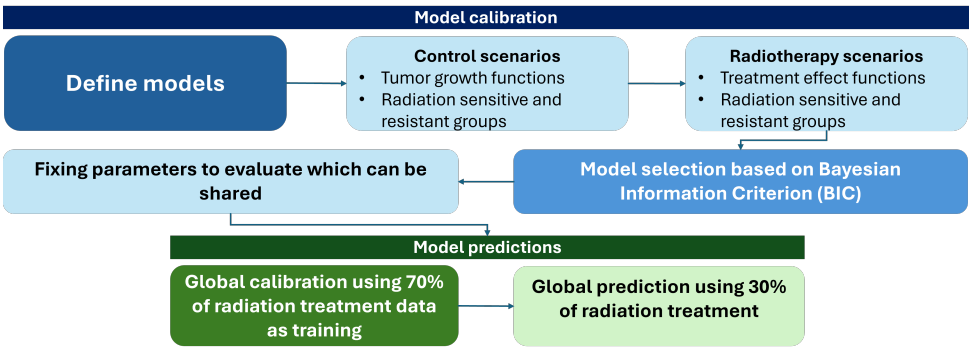

Figure 1: Model calibration and prediction framework, including model definition, calibration with control and radiotherapy data, and selection via the Bayesian Information Criterion. Source: Authors.

The model revealed that radiation-resistant cells grow significantly faster ($r_r = 1.15 \times 10^{-1}$ day^{-1}, about 29.3% higher than r_s), likely due to increased epidermal growth factor receptor (EGFR) expression [1]. Radiation-resistant cells also exhibit enhanced post-treatment repair, as shown by a higher estimated β_r value (about 442% higher than β_s). The next steps involve selecting the effects of immunotherapy, and using the full model to analyze the data with a combination of radiotherapy and immunotherapy.

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