Bayesian Modeling to Predict Tumor Biological Parameters for Personalized Radiotherapy

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ABSTRACT

Purpose: Infer patient-specific tumor-biology parameters, with uncertainty, from sparse tumor-volume data.

Methods: A logistic-growth model with linear-quadratic cell-kill term was fit in a Bayesian framework (NUTS/MCMC) to three tumor volumes per patient using population-based priors, estimating growth rate (ρ), radiosensitivity (α), carrying capacity (K), and initial burden (N_0). The pipeline was validated *in silico* on five synthetic patients with hidden ground truth.

Results: All fits converged. Posteriors were much tighter than priors, and every hidden true value fell within its 94% credible interval. α and N_0 were most sharply identified, K well constrained for high-burden tumors, and ρ the least.

Conclusion: As a proof of concept, the framework recovers patient-specific parameters with calibrated uncertainty from as few as three volumes. Real-patient validation and time-varying parameters are next.

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INTRODUCTION

- Radiation therapy (RT) is used in more than 50% of the patient's receiving treatment for cancer.
- Despite the standardized protocols for imaging, staging and treatment, clinical outcomes are highly variable at the individual patient level.
- Quantifying intrinsic heterogeneity in treatment response should be a prerequisite for any rational scheme of adaptive RT.
- Various tumor modeling approaches are being studied that can infer patient specific biological parameters to adapt RT according to each patient.

METHODS AND MATERIALS

- A Bayesian calibration model based on the current literature was constructed to predict three biological parameters: (i) Proliferation rate 'ρ' (ii) Radiosensitivity 'α', (iii) Carrying capacity 'K'
- Five in silico patients with distinct biological parameters were created, hidden from the model.
- The mathematical foundation is based on a logistic growth model coupled with a linear-quadratic (LQ) term to account for killing by radiation.
- The priors were based on historical population data.
- Posteriors were sampled with the No-U-Turn Sampler (6 chains × 1,000 tuning + 3,000 draws; target acceptance was 0.95)

Patient	ρ (1/day)	K (cells)	α (Gy^{-1})	β = α/10 (Gy^{-2})	N_0 (cells)
P1	0.05	7.0×10^{10}	0.090	0.0090	2.0×10^{10}
P2	0.09	9.0×10^{10}	0.075	0.0075	3.5×10^{10}
P3	0.13	1.1×10^{11}	0.060	0.0060	4.6×10^{10}
P4	0.17	1.3×10^{11}	0.045	0.0045	6.0×10^{10}
P5	0.21	1.5×10^{11}	0.030	0.0030	8.0×10^{10}

Table 1. Ground-truth parameters (hidden from the model).

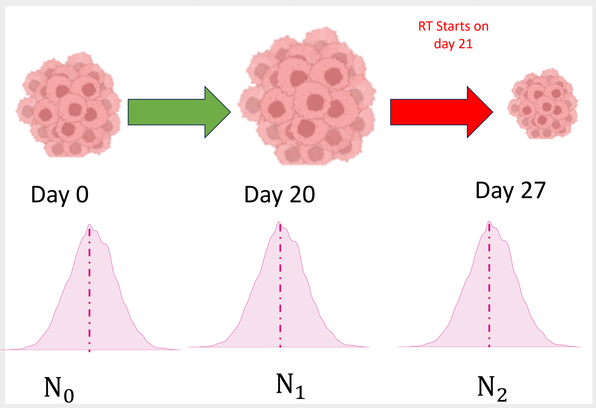

Fig 1. Observation schedule: volumes at days 0, 20, 27

Key Assumptions

- Tumor-biology parameters (ρ, K, α) were assumed to stay constant throughout treatment.
- No repopulation, reoxygenation, or emerging radio-resistance factor were modelled.
- No separate chemotherapy factor was modelled.
- A fixed $\frac{\alpha}{\beta}$ ratio = 10 Gy was used.

Mathematical Model

$$S = \exp\left(-\alpha d - \beta d^2\right),$$

$$N_{k+1} = \begin{cases} S \cdot N_{k+1}^{(\text{grow})}, & t_k \in \mathcal{F}, \\ N_{k+1}^{(\text{grow})}, & t_k \notin \mathcal{F}. \end{cases}$$

$$N_{k+1} = N_k + \rho N_k \left(1 - \frac{N_k}{K}\right) \Delta t.$$

RESULTS

- Posteriors were substantially tighter than the priors.
- The hidden ground-truth values fell inside their posterior credible intervals for every patient.

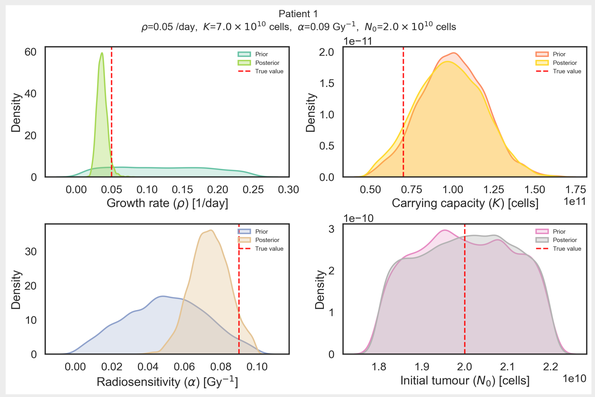

Fig 2. Prior vs posterior for patient 1

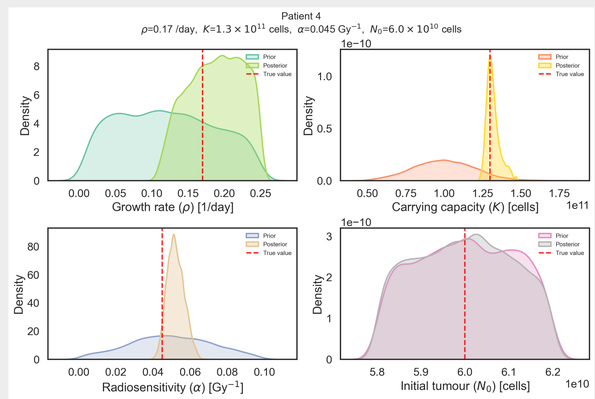

Fig 3. Prior vs posterior for patient 4

Discussion

- All 20/20 true parameter values fell within their 94% highest density interval.
- Identifiability was found to be parameter dependent.
- N_0 and α are sharply constrained.
- K was well constrained for higher-burden tumors that approach saturation within the observation window.
- The ρ was the least identifiable, its posterior remained comparatively broad, reflecting a partial ρ–K degeneracy.
- Adding one more scan would most improve ρ.
- Synthetic data came from the same logistic + LQ model, so this validates parameter recovery, not structural model adequacy.
- Model mismatch against real tumor dynamics remains untested.

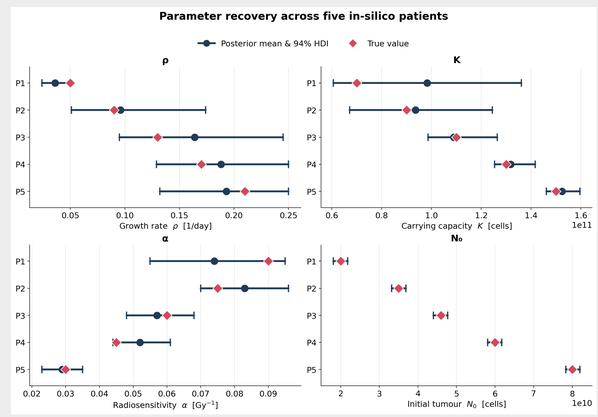

Fig 4. Forest plot for all patients

CONCLUSIONS

- These results motivate the next step i.e. validation against real longitudinal patient data.
- The model should be extended to allow time-varying parameters during treatment.
- This model treats the whole tumor as a single number, future work should resolve individual tumor sub-regions.
- Such a framework could support uncertainty-aware, personalized prediction of tumor response.

REFERENCES

1. Chaudhuri A, Pash G, Hormuth II DA, Lorenzo G, Kapteyn M, Wu C, Lima EABF, Yankeelov TE and Willcox K (2023) Predictive digital twin for optimizing patient-specific radiotherapy regimens under uncertainty in high-grade gliomas. Front. Artif. Intell. 6:1222612. doi: 10.3389/frai.2023.1222612