Inference in Tumour-Immunotherapy Dynamics

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What We're Studying

- Brain-tumour scans (gliomas) taken after surgery.
- Each patient has 4 MRI scans over time, so we can watch the tumour grow or shrink.

Table 1: Scanning statistics of the filtered cohort ($n = 59$).

	Mean	Std. dev.	Range
Number of scans / patient	4.0	0.0	4–4
Inter-scan interval† (a.y.[2])	1.38	0.55	0–3

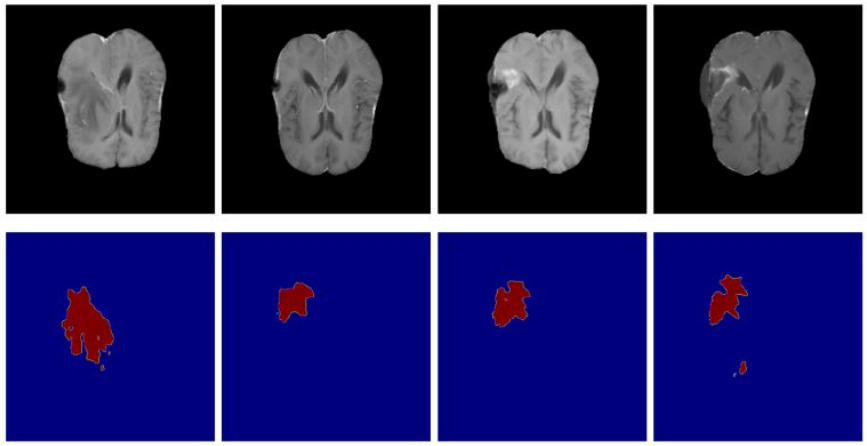


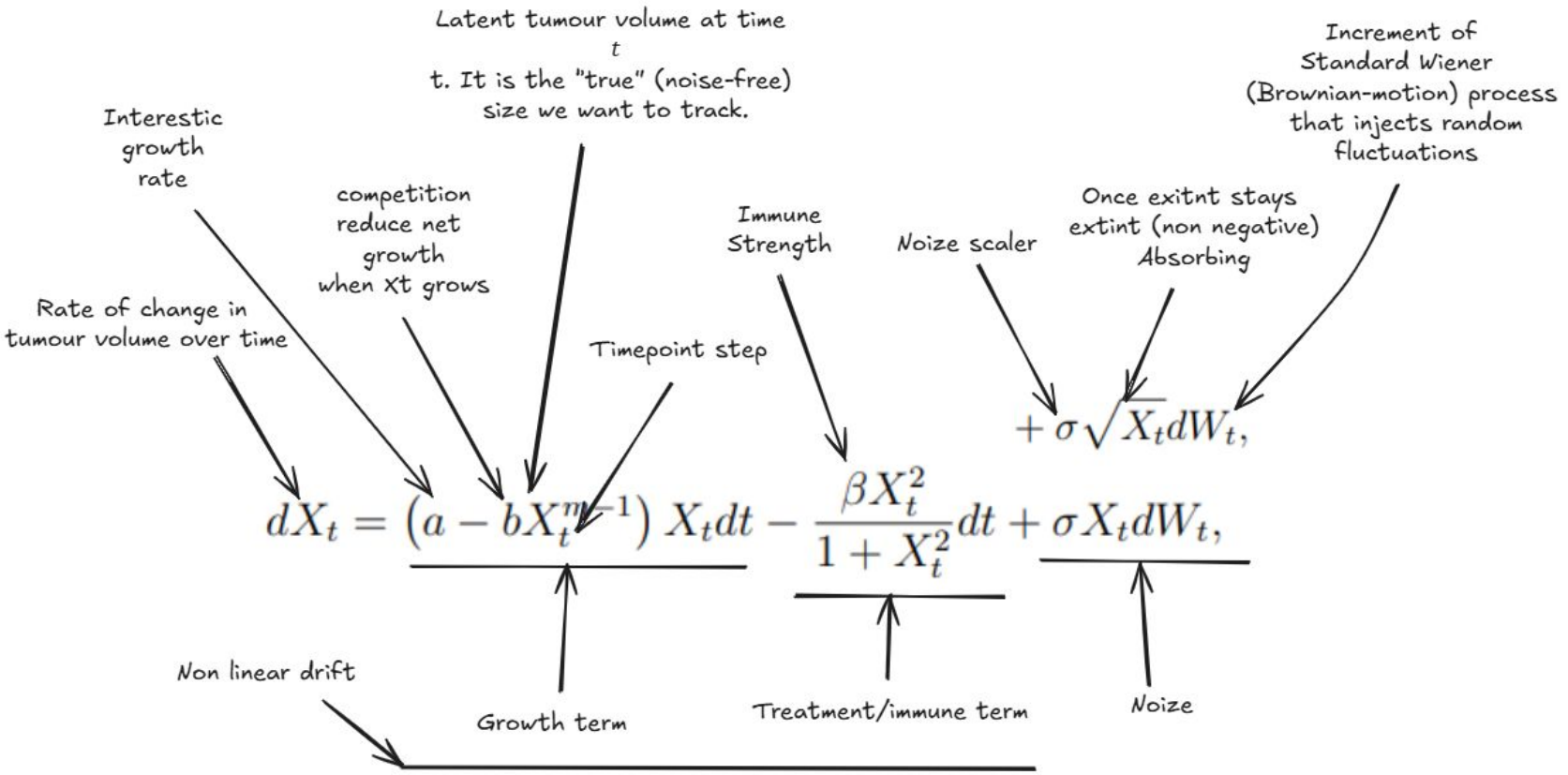
Figure 1: Plot of the scanned images for Patient006 with the masks under.

```python
def _vol(mask_path: str):
    n = nib.load(mask_path)
    return (n.get_fdata() > 0).sum() * np.prod(n.header.get_zooms()) / 1e3  # mm³→mL
```

mask file → count 1 s → multiply by voxel size (n.header.get_zooms()) → divide by 1 000 → tumour volume in ml

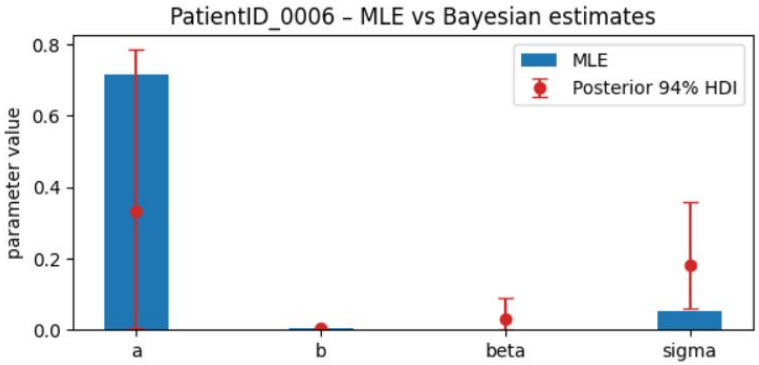
What We're Trying to Do

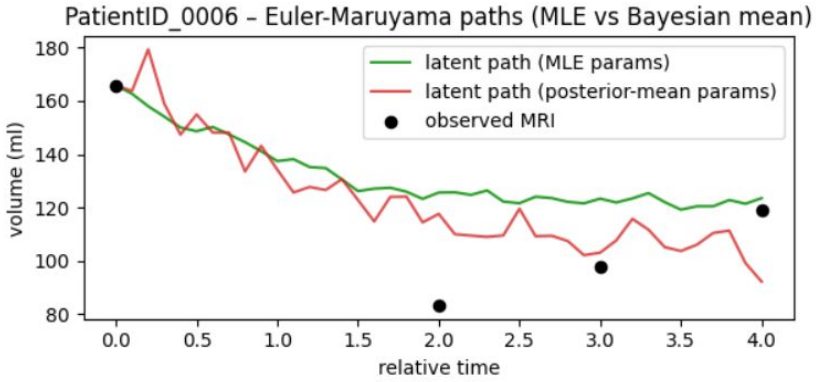
- Build a mathematical "weather forecast" for tumours.
- Instead of temperature and wind, our model predicts how big the tumour will be at future check-ups.



Parameter estimation

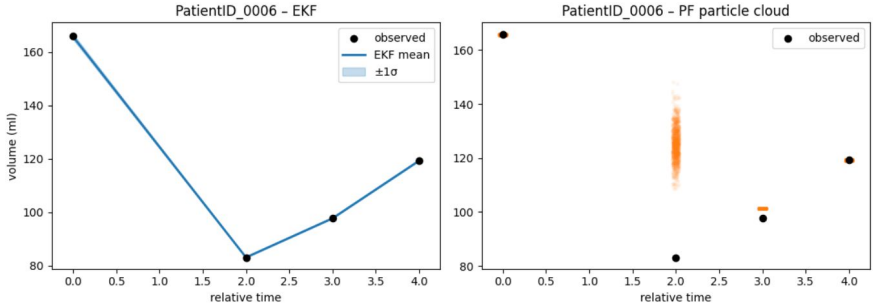
	param	MLE	PostMean	HDI_low	HDI_high
0	a	0.714179	0.332248	0.005928	0.786004
1	b	0.005776	0.003309	0.000574	0.006384
2	beta	0.000011	0.032181	0.000811	0.088400
3	sigma	0.053121	0.181595	0.059046	0.359174

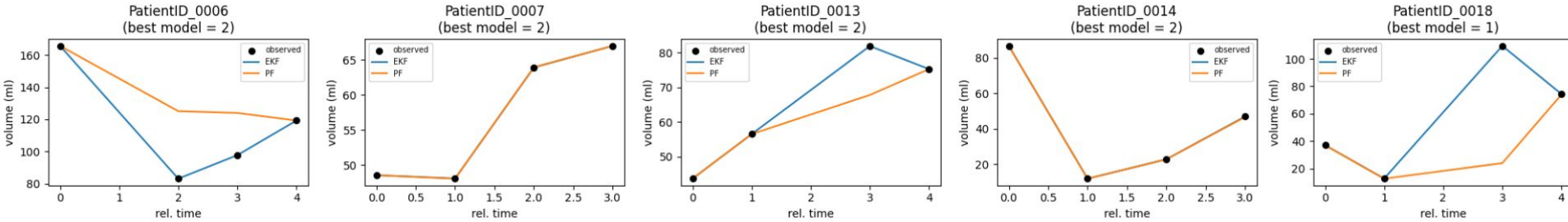




Euler–Maruyama Maximum-Likelihood (frequentist)	Bayesian inference with NUTS (PyMC)
Pick a single “best” set of parameters θ =(a,b,β,σ) that maximises the probability of seeing the MRI data.	Obtain a full posterior distribution p(θ | data) to quantify uncertainty in every parameter.
Minimize the: sum of all densities in all steps (negative log likelihood) using BFGS (estimates hessian matrix * - gradient)	run 4 simulations of MCMC that samples from posterior distribution (each 1000 tunes + 1500 sample drawings)
Pros: quick; gives a single answer for filters. Cons: Ignores parameter uncertainty	Posterior mean/median, credible intervals, pairwise scatter—full uncertainty picture. captures parameter uncertainty; can propagate it to forecasts. Cons: slower; requires convergence checks.

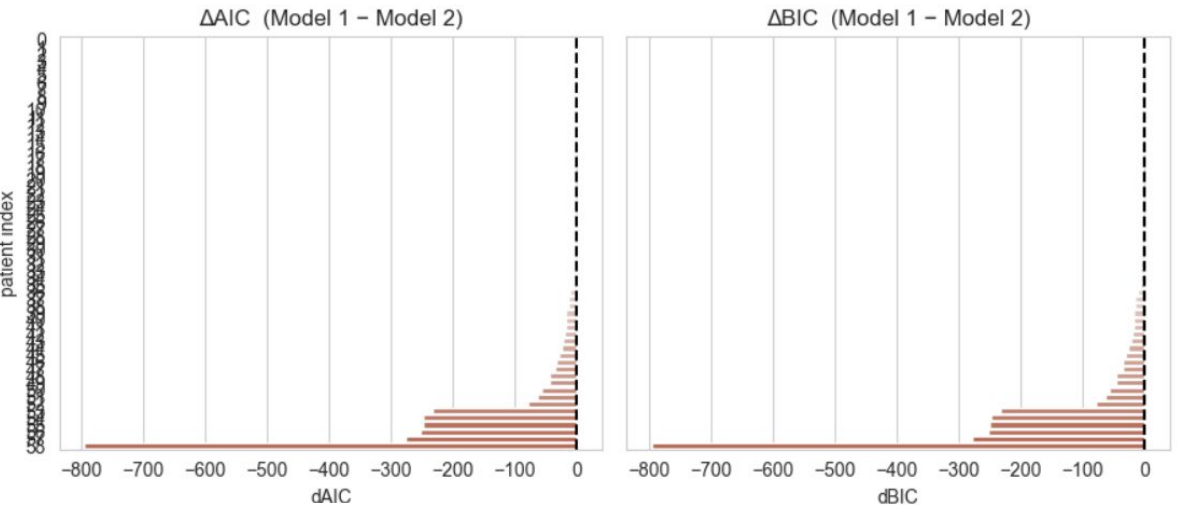
Tracking Hidden State

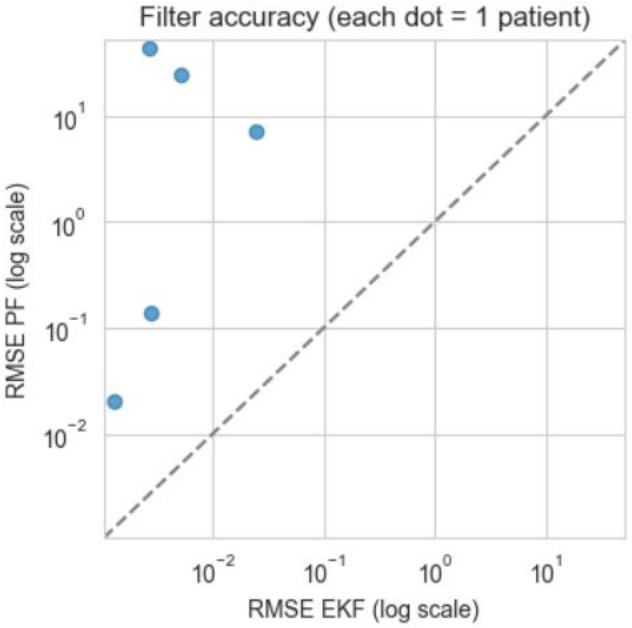


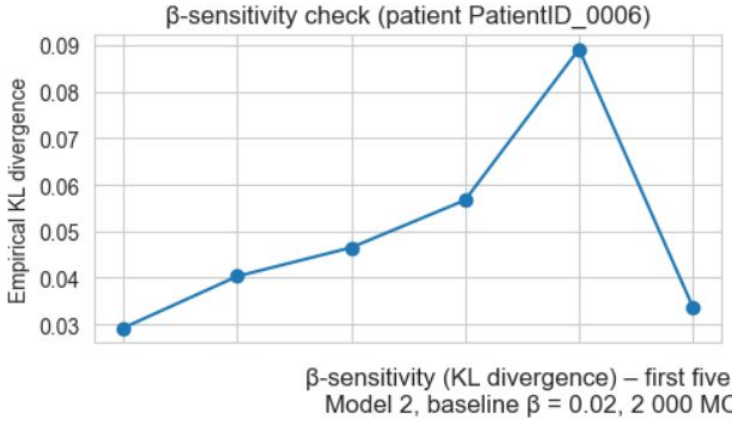


Feature	Extended Kalman Filter (EKF)	Particle Filter (PF)
Core idea	Smooth the noizy points. Linearise the nonlinear model around the current mean, then apply Kalman-filter equations (predict then update).	Just like the EKF, the PF tries to guess the true tumour size at each scan time. Difference: instead of a single mean ± variance, it keeps a cloud of many possible sizes (particles) so it can model very non-Gaussian uncertainty.
State representation	Single mean x^k and variance Pk.	Thousands of particles. Each particle has own path.
Model requirement	Needs first derivative (Jacobian) of drift; assumes Gaussian noise.	Only needs ability to simulate the model forward; no linearisation or Gaussian assumption.
Computation cost (4 scans)	≈ 0.0001 s (microseconds)	≈ 0.001 s (milliseconds) with Np=1000.
Memory	Negligible (a few scalars per step).	O(Np) particles; larger but still small at N=1000.
Accuracy on our data	Higher RMSE in 52 / 59 patients (misses heavy non-linearity).	Lower RMSE in 52 / 59 patients; better at rebounds & near-zero volumes.

Validation

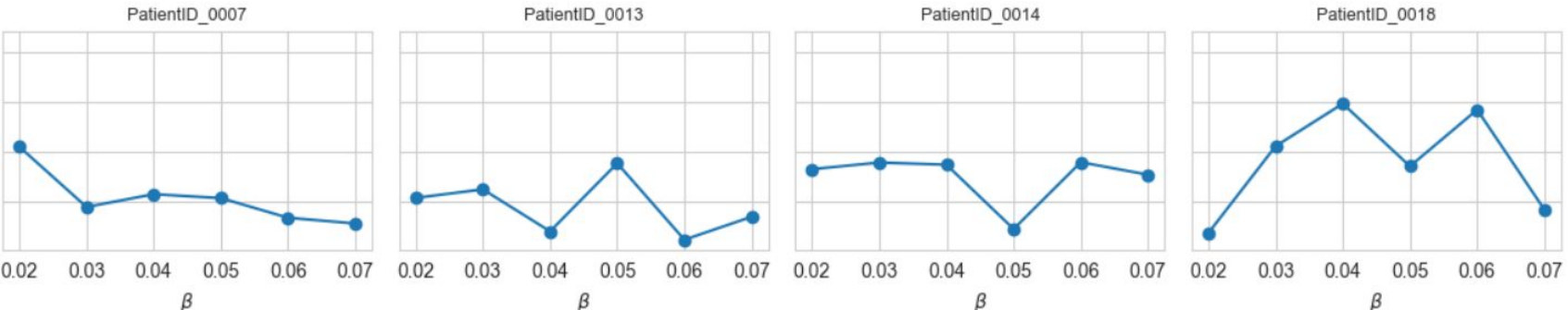






Treatment might be helpful!

β-sensitivity (KL divergence) – first five patients
Model 2, baseline β = 0.02, 2 000 MC paths



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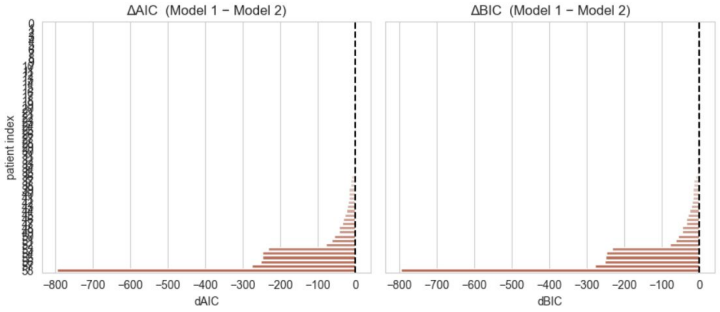
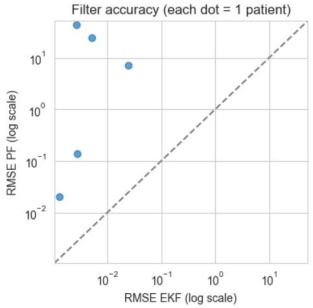
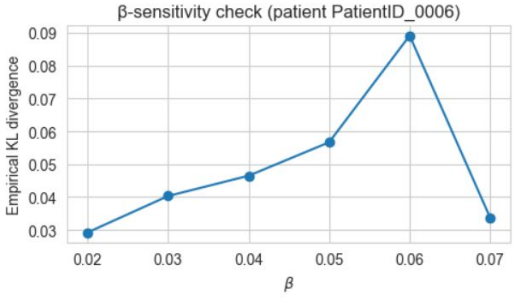


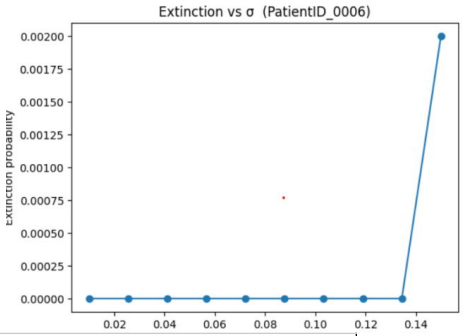


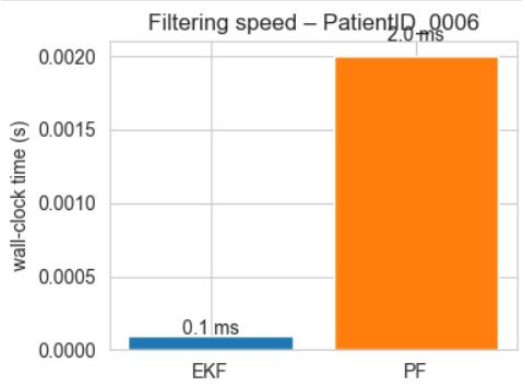


Plot	What it shows	How to read it	Key takeaway
ΔAIC & ΔBIC bars (left-hand pair)	For every patient we subtract the information criterion of Model 2 from Model 1: ΔAIC = AICM1 − AICM2 and same for BIC. Bars are sorted; colour indicates sign (blue ≈ Model 1 better, red ≈ Model 2 better).	The dashed vertical zero line is “no preference.” Bars left of zero → negative Δ → Model 2 preferred; farther left = stronger evidence. Bars right of zero → positive Δ → Model 1 preferred.	Nearly every bar is negative and often very large in magnitude (hundreds), so Model 2 wins decisively for most patients.
RMSE EKF vs PF scatter (bottom left)	Each dot = one patient. Abscissa = EKF RMSE, ordinate = PF RMSE (both log scale). The dashed line is the identity where EKF and PF are equally accurate.	Dots below the dashed line → PF error < EKF error. Distance from the line = relative accuracy gain.	All points fall below the line: PF beats EKF for every patient—sometimes by orders of magnitude—while still being fast enough.
β-sensitivity KL curve (right-hand plot)	For a showcase patient (PatientID 0006) we varied β around its MLE and measured how much the stationary-volume distribution diverges (empirical KL) from the baseline.	The x-axis is the β value tested; y-axis is KL divergence (0 = identical distribution). Higher curve value = bigger shift in long-term tumour size.	Divergence rises steadily until β≈0.06, then drops, suggesting treatment benefit grows up to β≈0.06 and then saturates—increasing β further gives diminishing returns.
Computation cost (4 scans)	≈ 0.0001 s (microseconds)	≈ 0.001 s (milliseconds) with Np=1000.	
Memory	Negligible (a few scalars per step).	O(Np) particles; larger but still small at N=1000.	
Accuracy on our data	Higher RMSE in 52 / 59 patients (misses heavy non-linearity).	Lower RMSE in 52 / 59 patients; better at rebounds & near-zero volumes.	

Comparative analysis

- Higher noize can lead to extinction





Aspect	Observation	Practical meaning for Patient 0006
Dual peaks	• Tiny spike at 0 ml = rare “extinction” paths (absorbing state). • Broad peak at ≈ 120–140 ml = dominant long-run tumour size when extinction does not happen.	Complete self-cure is possible but extremely unlikely; most trajectories settle around 130 ml.
Effect of raising β	• β 0.00 -> 0.05: main peak shifts gradually left -> slightly smaller steady-state volumes. • β ≥ 0.06: peak position stabilises; curves for β 0.06 and 0.08 almost overlap.	Immunotherapy gains taper off beyond β ≈ 0.06 (diminishing returns).
Extinction bar	Height of 0-ml bar changes very little across all β values.	Even strong β does not make spontaneous, permanent remission appreciably more likely under Model 2.
Bottom-line	• Moderate β increase (≤ 0.05) shaves a few ml off equilibrium size. • Further increase (> 0.06) brings minimal additional shrinkage and no boost in cure chance.	For this patient, escalating therapy intensity past β ≈ 0.05 is likely inefficient.