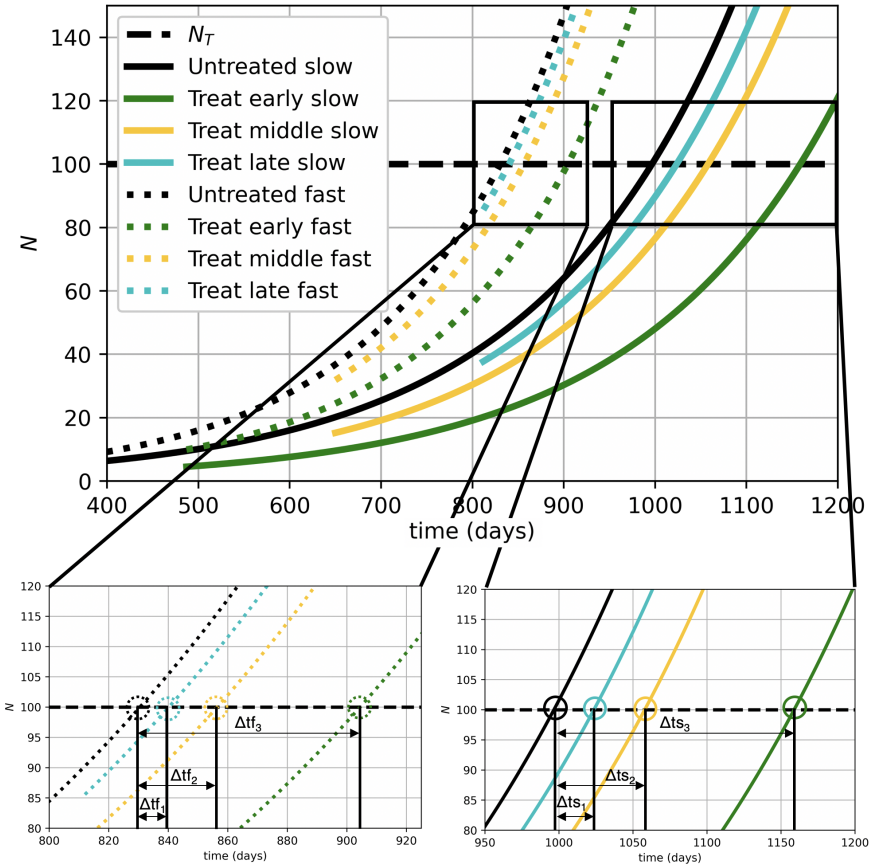
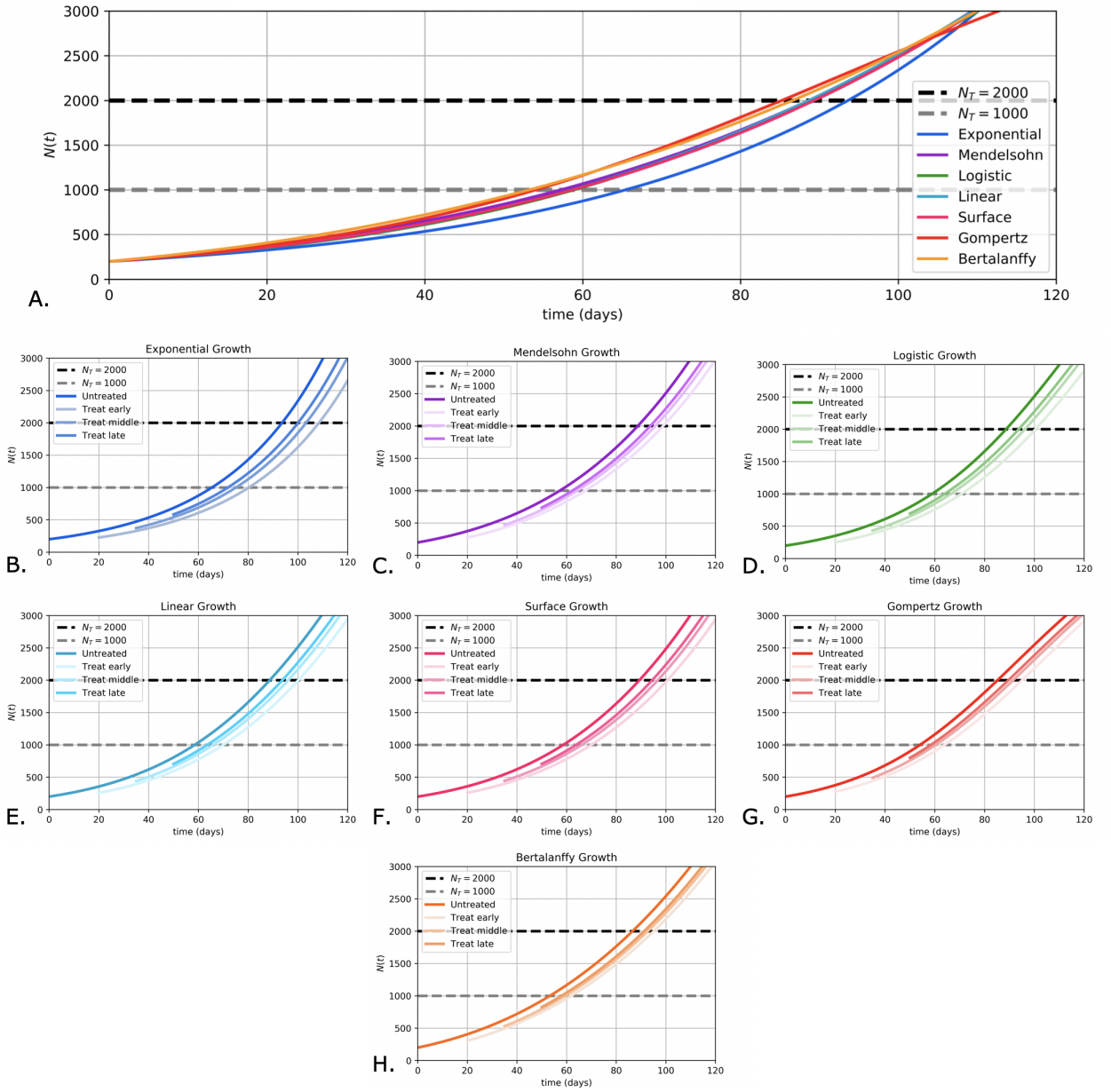
Supplementary Information



Supplementary Fig 1: **Change in OS is modulated by tumor growth rate, intervention timing, and intervention efficacy. Top:** We plot two illustrative exponential growth curves from Equation 1 in black, using a faster (dotted line) and slower (solid line) growth rate, r. The slower growth rate is the same curves shown in Figure 1. At three different time points, we subtract N_c cells from the two curves to simulate an oligometastasis-directed intervention, and the tumor continues to grow at the original rate from the new size. These subsequent tumors then grow and eventually intersect an arbitrary threshold cell (a surrogate for maximum tolerated disease burden) number (N_T - dashed horizontal line). **Bottom:** We plot two expanded windows of the above plot, showing greater detail of the faster (left, dotted) and slower (right, solid) growth curves as they reach N_t. In these plots, we can then determine the change in survival (vertical black lines). The change in this time represents the Δtf and Δts for each intervention in the fast and slow curves, respectively. Notably, the x-axis for the faster (left, dotted) growth curves accounts for fewer days, despite having the same relative length as the x-axis for the slower (right, solid) growth curves. This was necessary in order to annotate the smaller Δtf for the faster growth curves.



Supplementary Fig 2: **A visual representation across seven ODE tumor growth models, demonstrating that earlier intervention creates a larger improvement in OS.** Models were produced using the parameters denoted by Murphy et al., 2016 [1], where the seven models were fit to 14 timepoints of xenograft tumor growth data from Worschech et al [2]. **A.** A comparison of the seven growth curves with no interventions built with various ODE models. **B-H.** Individual plots visually demonstrating the change in OS for three intervention times for all models included in A. The calculation of change in OS, is demonstrated in Figure 1 with the calculation of Δt.

References

[1] Hope Murphy, Hana Jaafari, and Hana M Dobrovolny. Differences in predictions of ode models of tumor growth: a cautionary example. *BMC cancer*, 16(1):1–10, 2016.

[2] Andrea Worschech, Nanhai Chen, A Yu Yong, Qian Zhang, Zoltan Pos, Stephanie Weibel, Viktoria Raab, Marianna Sabatino, Alessandro Monaco, Hui Liu, et al. Systemic treatment of xenografts with vaccinia virus glv-1h68 reveals the immunologic facet of oncolytic therapy. *BMC genomics*, 10(1):301, 2009.