

Quantitative mathematical modeling of clinical brain metastasis dynamics in non-small cell lung cancer

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Table S1: Growth kinetics of primary lung tumors

Ref.	All	Adenocarcinoma	Squamous cell carcinoma	Undiff.
[Jennings et al., 2006]	161 (149)	166 (51)	132 (48)	
[Usuda et al., 1994]	164 ± 178 (165)	223 ± 209 (86)	105 ± 106 (67)	79 ± 52 (12)
[Arai et al., 1994]	166 (237)	222 (133)	115 (69)	68 (9)
[Mizuno et al., 1984]	136 (50)	178 ± 157 (23)	103 ± 78 (22)	111 ± 57 (5)
[Geddes, 1979]	102 (228)	161 (60)	88 (111)	86 (44)
[Weiss, 1974]	183 ± 85 (28)	214 ± 73 (11)	78 ± 29 (8)	109 ± 72 (7)
[Spratt and Spratt, 1964]	88 (34)	118 (8)	70 (13)	93 (13)
[Spratt et al., 1963]	112 (22)	269 (7)	93 (6)	90 (9)
[Garland et al., 1963]	162 (41)	222 (7)	126 (22)	123 (9)
[Schwartz, 1961]	78 ± 48 (13)	72 ± 77 (2)	79 ± 46 (11)	
Average*	143	201	104	91

Reports of volume doubling times from routinely detected primary NSCLC tumors from the literature (extended from [Detterbeck and Gibson, 2008] and [Friberg and Mattson, 1997]). Note: squamous cell carcinoma = epidermoid carcinoma and undifferentiated carcinoma cell carcinoma = large cell carcinoma. All denotes all histology from lung cancer together (including both NSCLC and small cell carcinomas).

Undiff. = undifferentiated carcinoma.

Mean ± standard deviation.

In parenthesis are the number of patients.

*Average was computed as the weighted mean of each study with weights the number of patients.

Figure S1: Comparison of exponential and Gompertz predictions of pre-clinical phase of growth

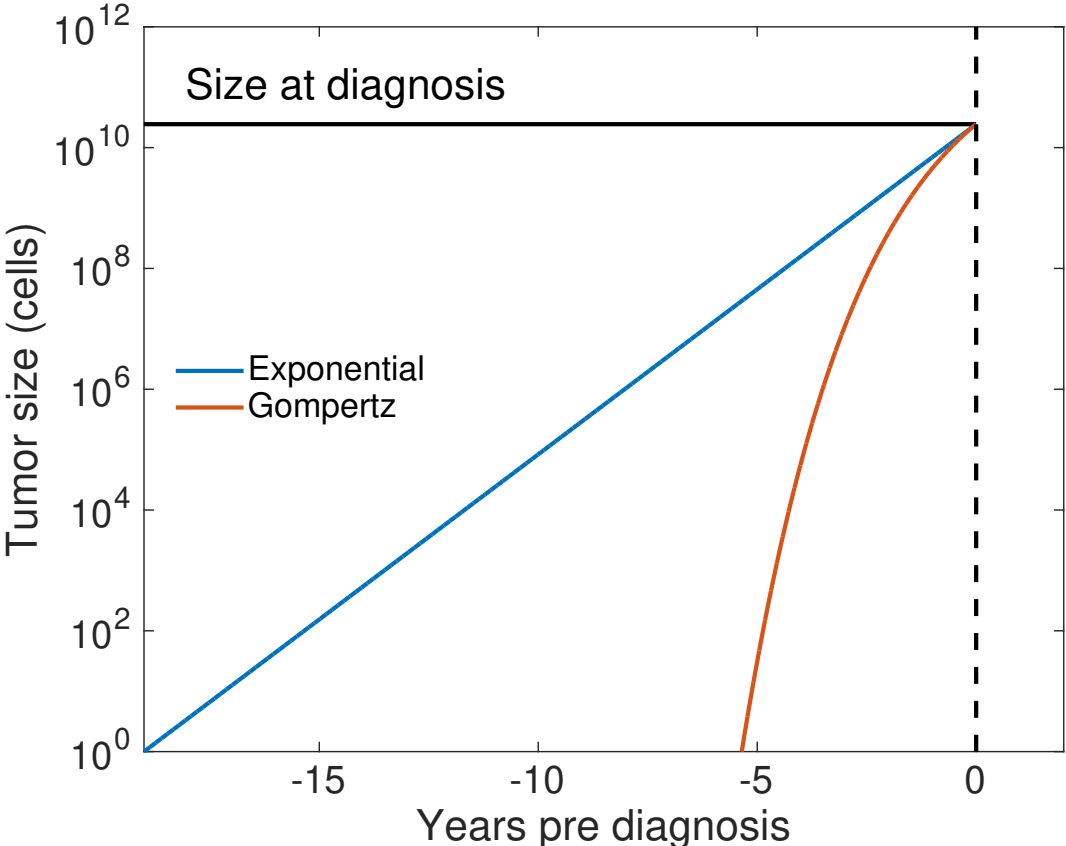
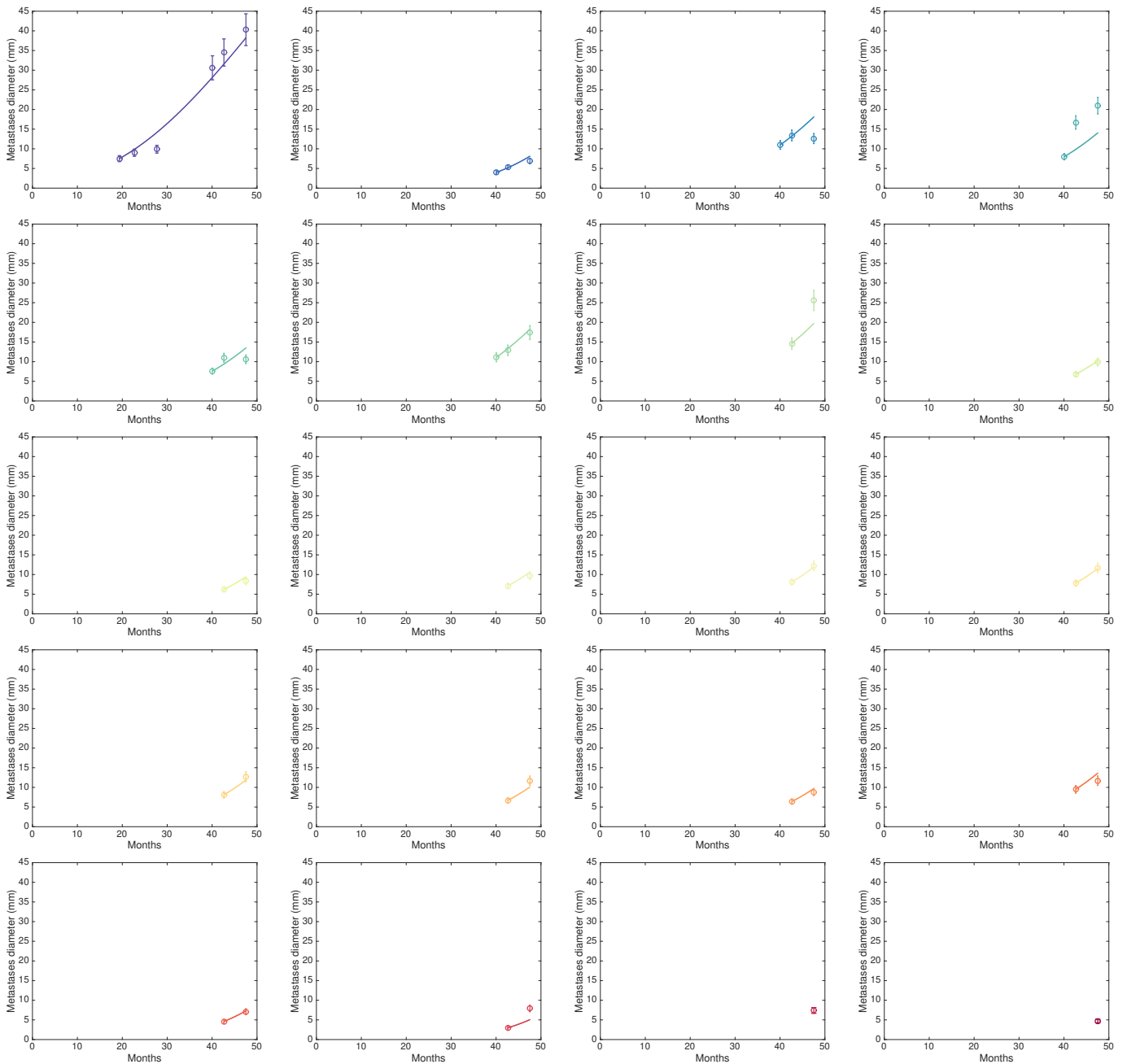
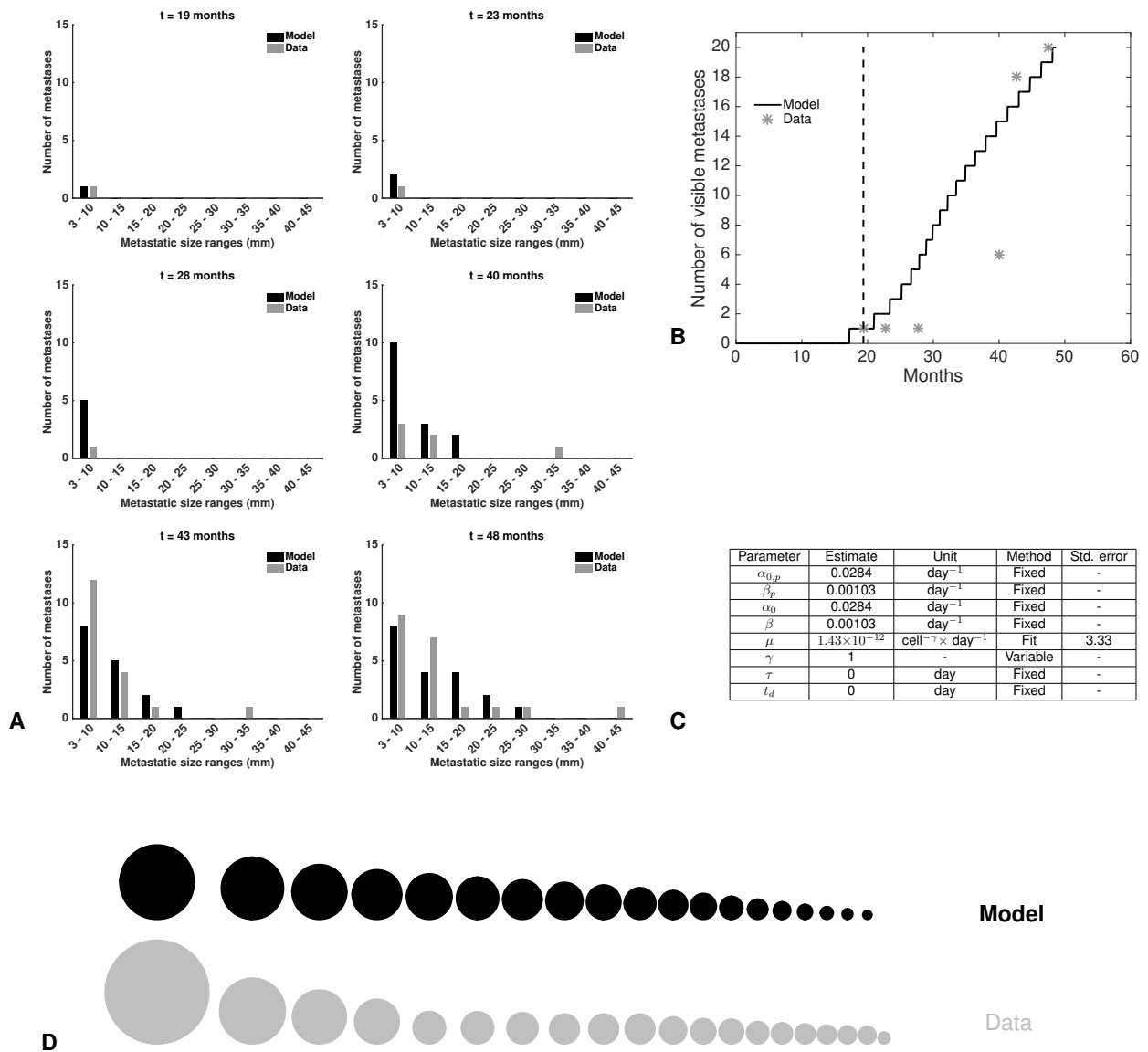


Figure S2: Gompertz growth predictions of individual brain metastases



Comparison between the Gompertz growth model predictions and the lesion size data of individual BMs. The Gompertz growth parameters were determined only from the primary tumor size at diagnosis and histology (adenocarcinoma, see Methods). Apart from the first measurements used as initial conditions, no other future measurements were used to make the predictions. Error bars represent 10% error on the size measurement.

Figure S3: Fit of the basic model



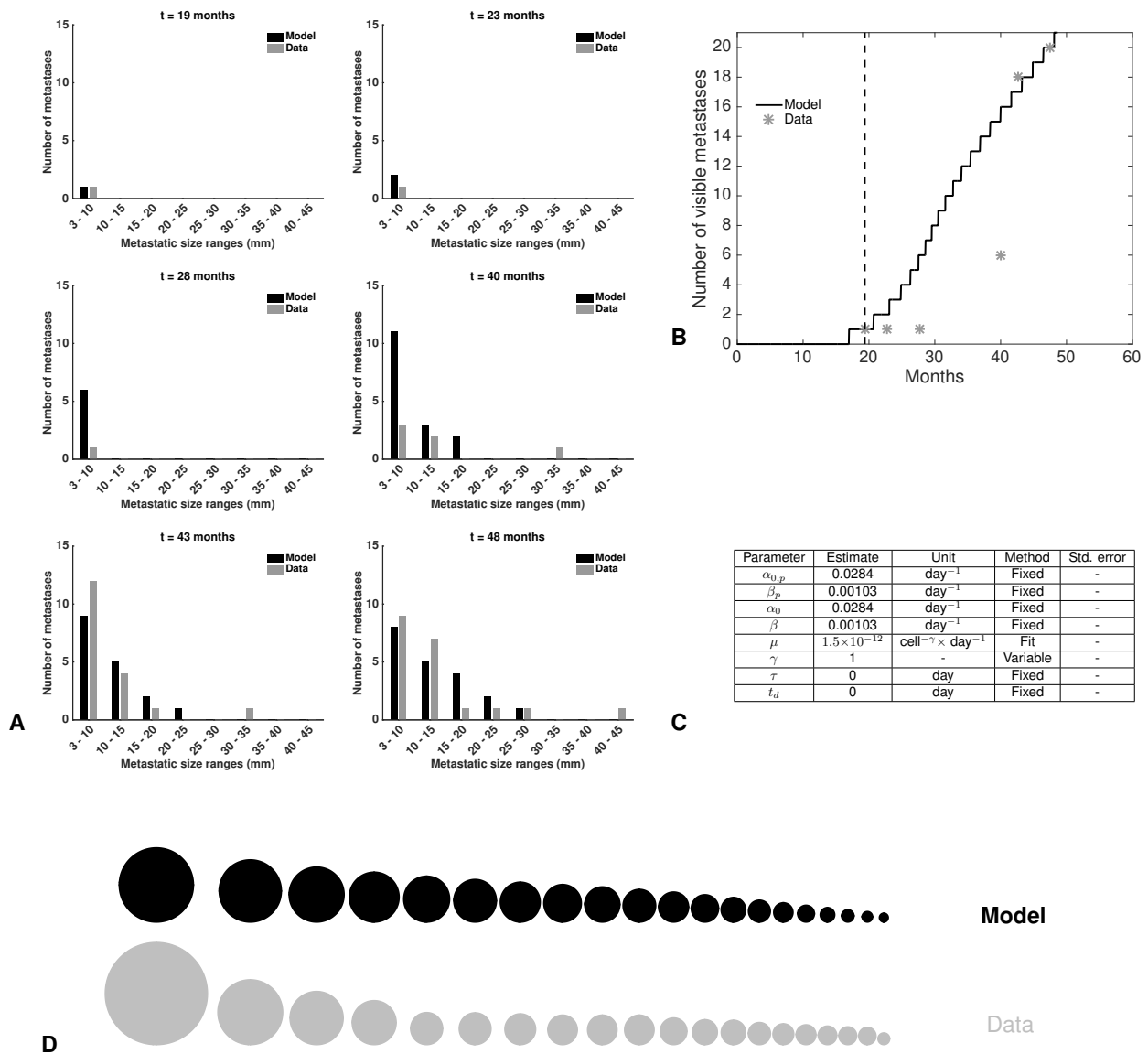
A. Time course of the visible brain metastases (BMs) size distributions during follow-up. Comparison between model calibration and data.

B. Time course of the number of visible BMs.

C. Parameter estimates. Std error = Standard errors expressed in percent.

D. Comparison of the BM size distribution between the model fit and the data at the last time point.

Figure S4: Fit of the model with secondary dissemination



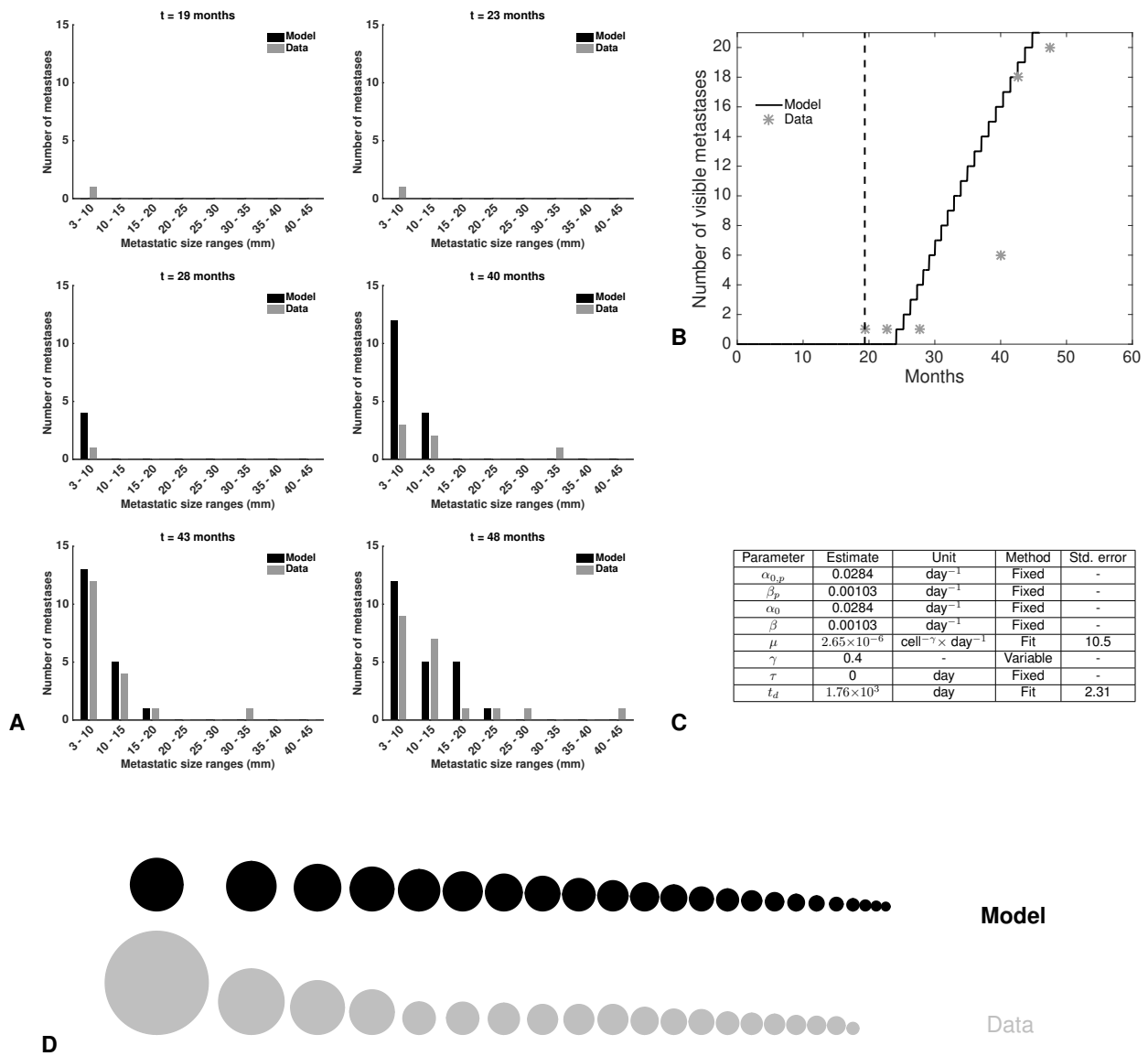
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Figure S5: Fit of the delay model



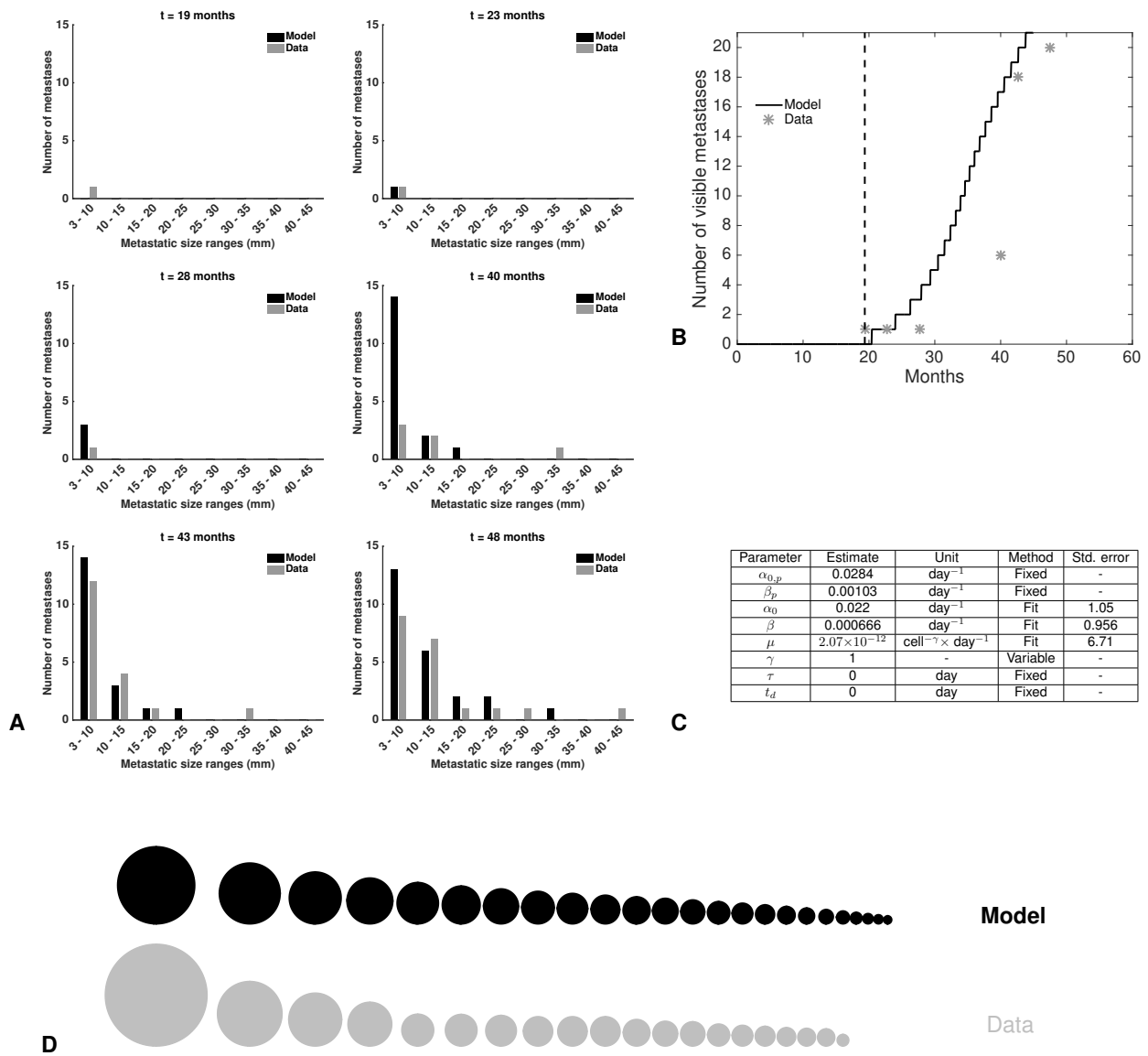
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B. Time course of the number of visible BMs.

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Figure S6: Fit of the model with different primary and secondary growth parameters



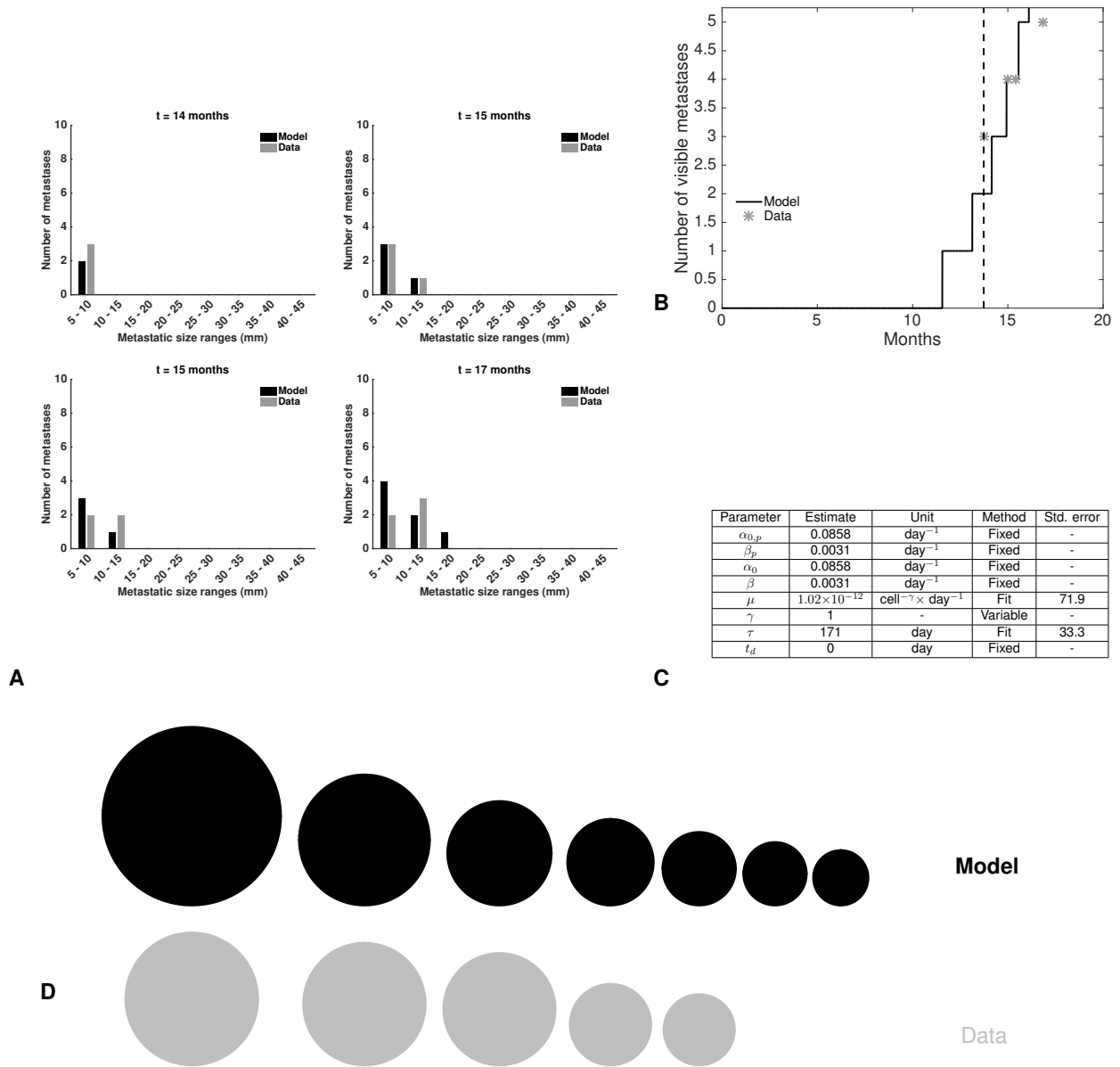
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B. Time course of the number of visible BMs.

C. Parameter estimates. Std error = Standard errors expressed in percent.

D. Comparison of the BM size distribution between the model fit and the data at the last time point.

Figure S7: Fit of the dormancy model for patient 2



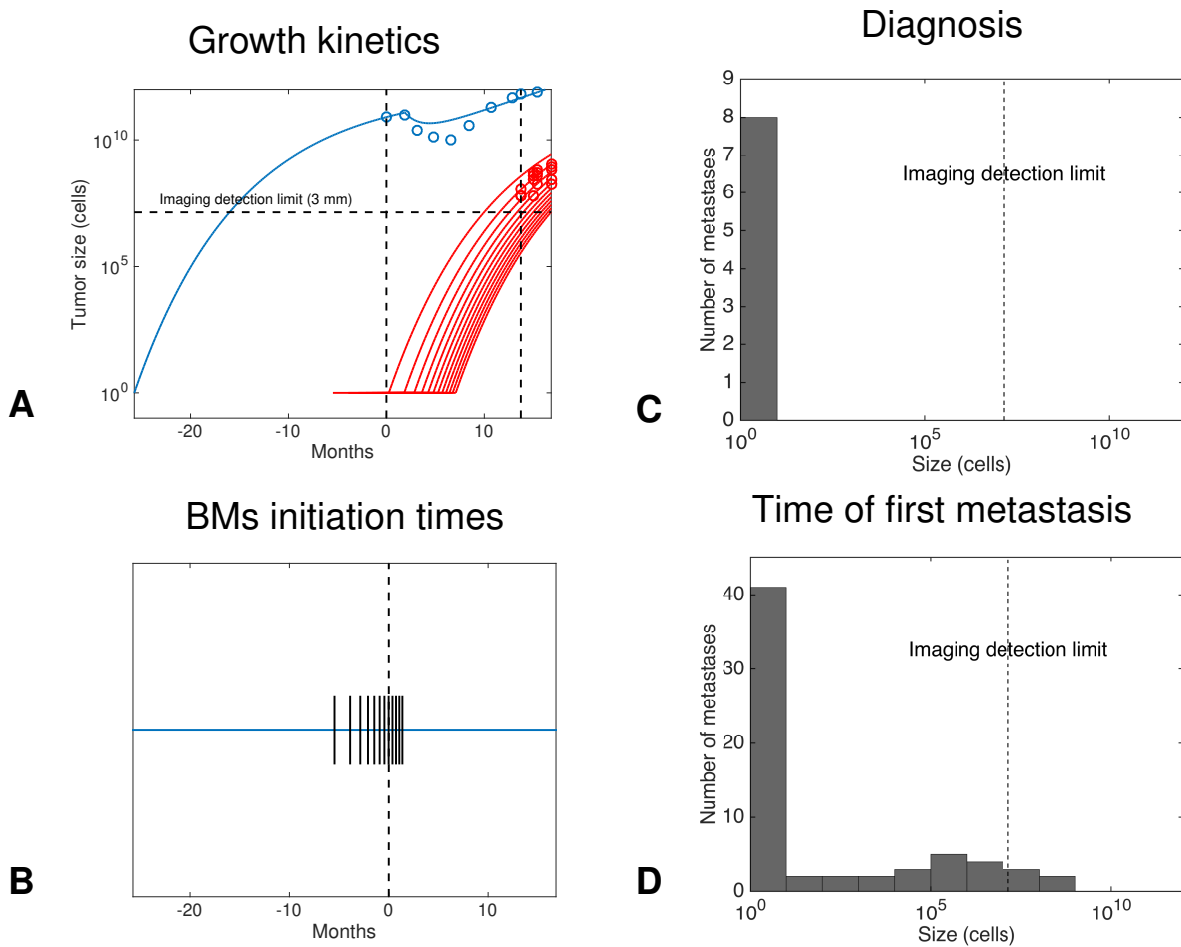
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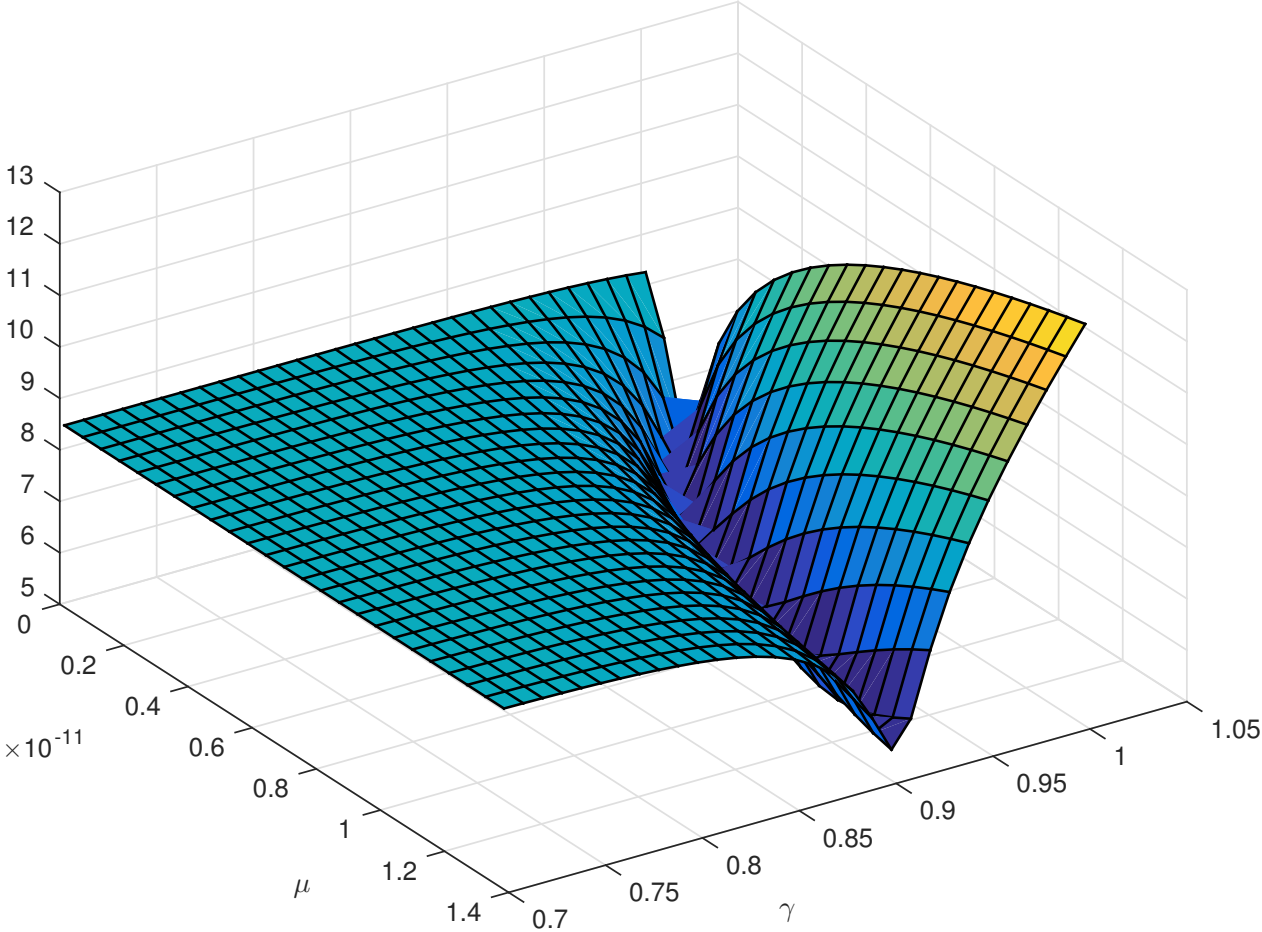
D. Comparison of the BM size distribution between the model fit and the data at the last time point.

Figure S8: Predictions for patient 2



- A. Inferred growth kinetics of the primary tumor (in blue) and the brain metastases (in red). Only brain metastases that will become visible are shown.
- B. Model predictions of the initiation times of the brain metastases.
- C. Predicted size distribution of the brain metastases at diagnosis.
- D. Predicted size distribution of the brain metastases at the time of clinical occurrence of the first one.

Figure S9: Shape of the objective as a function of μ and γ



References

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