

Figure S1. Histograms of tumour diameter, core tumour, and whole tumour volumes before and after logarithmic transformation

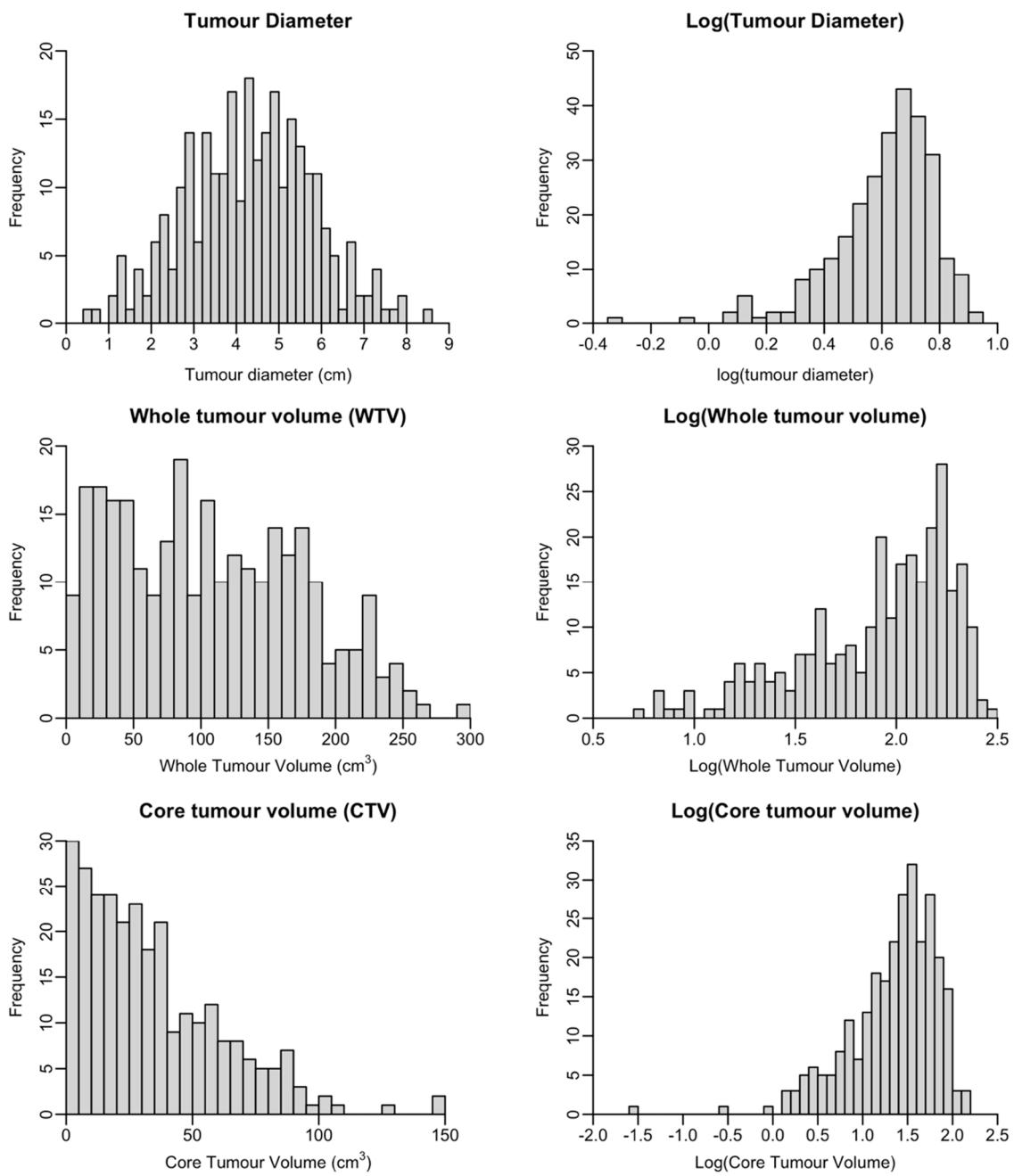


Figure S2a. Non-linear modelling of tumour diameter with log-transformation and penalised splines.

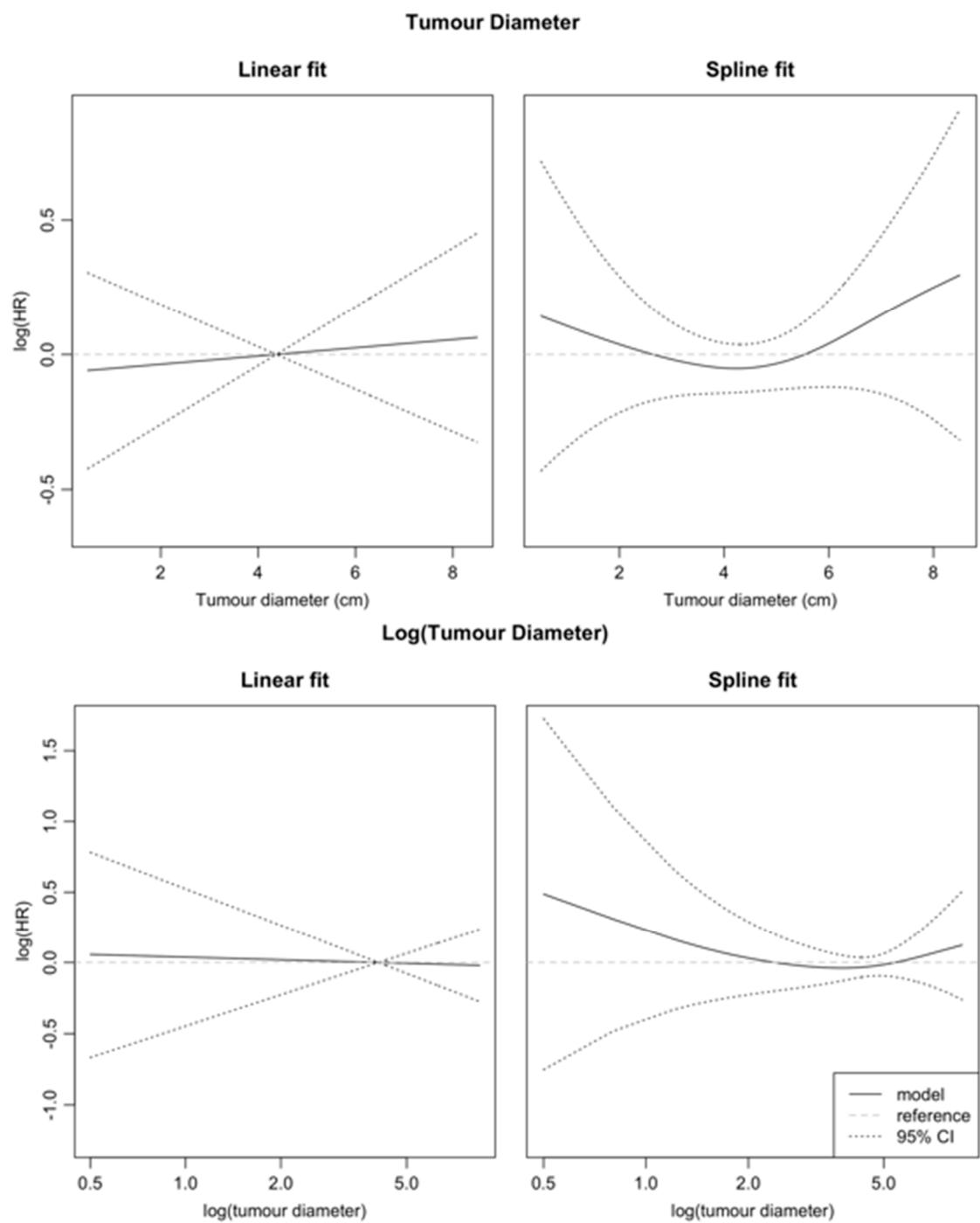


Figure S2b. Non-linear modelling of whole tumour volume with log-transformation and penalised splines.

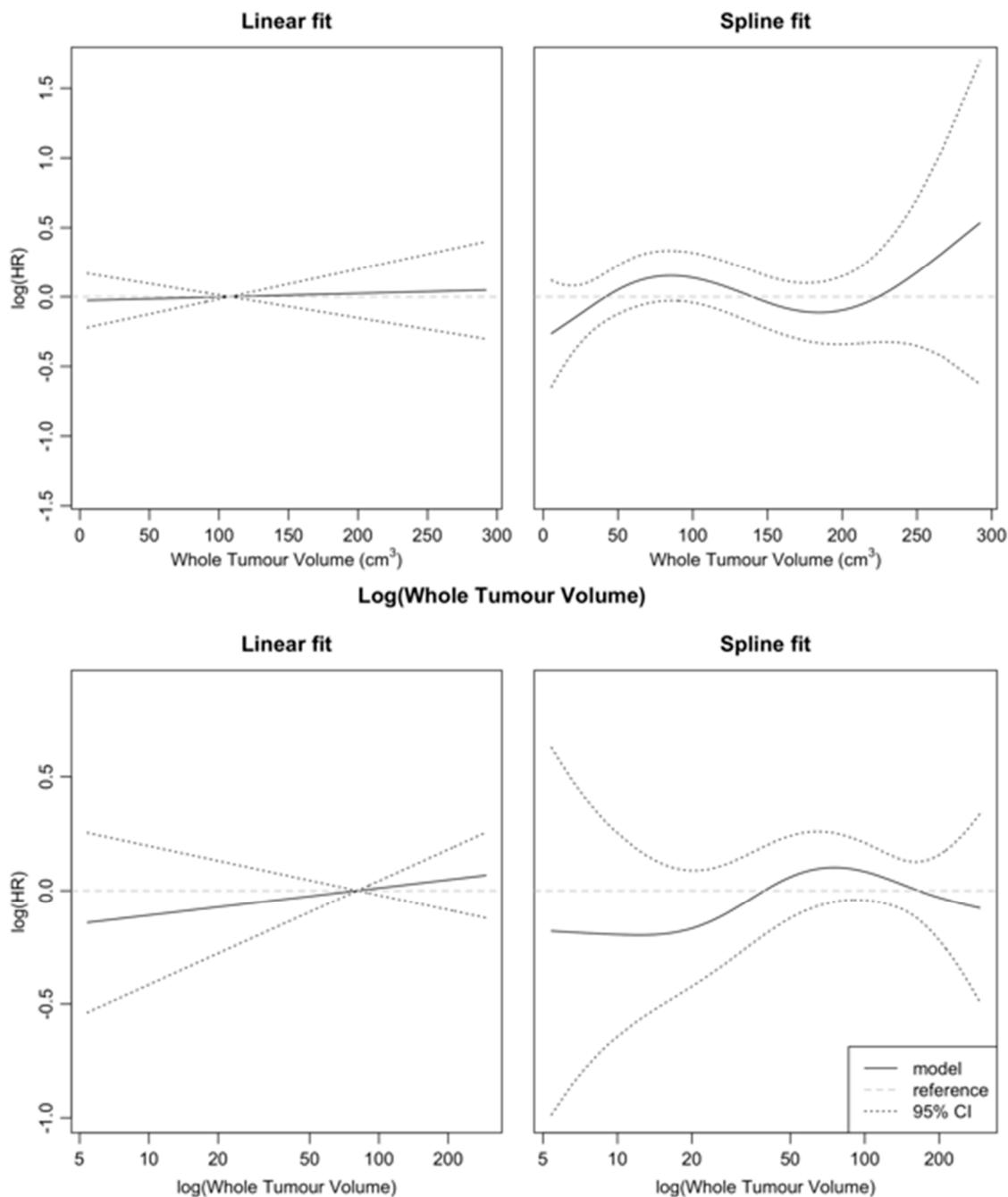
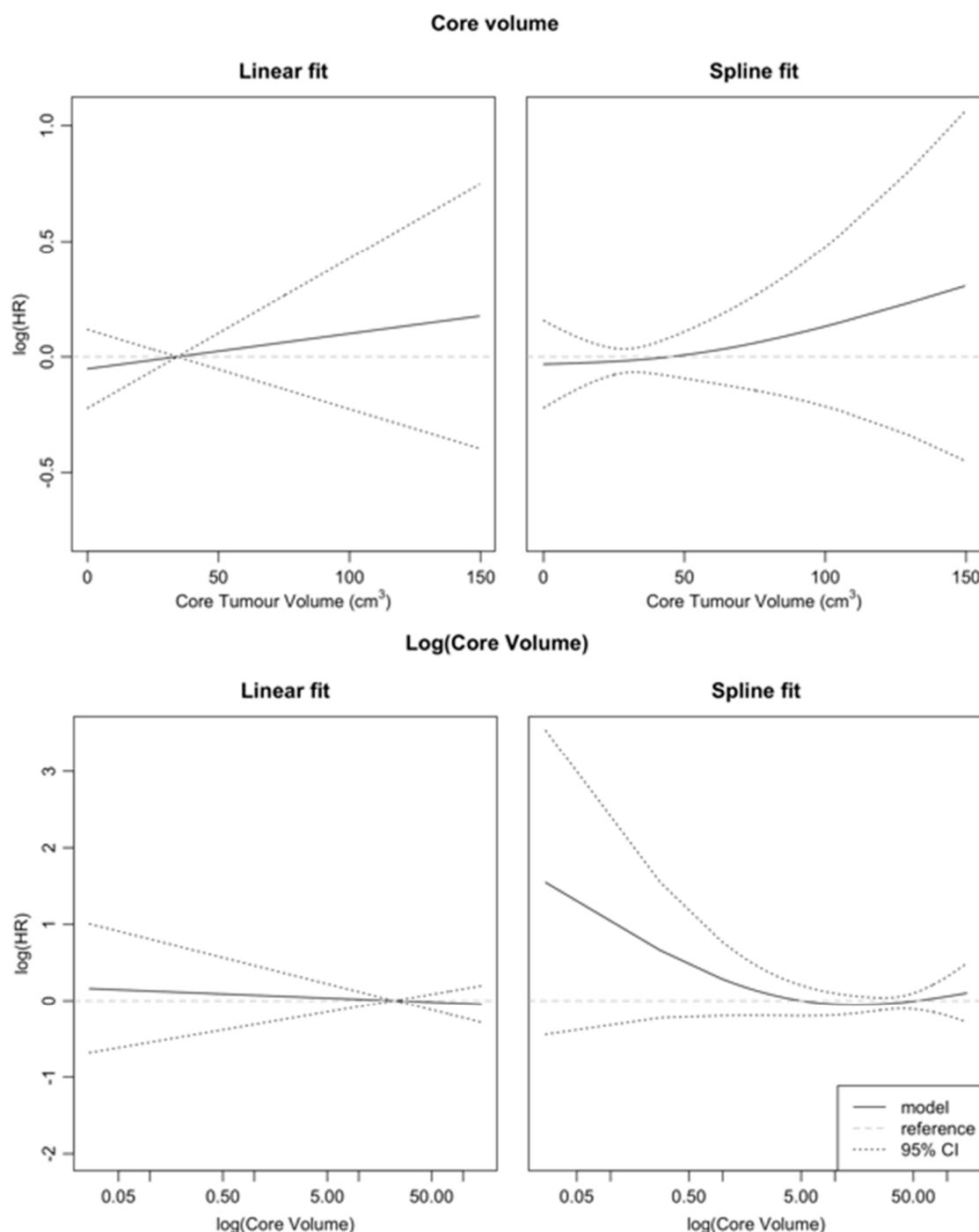


Figure S2c. Non-linear modelling of core tumour volume with log-transformation and penalised splines



Supplementary Figure 2a-c. For each 2×2 plot, the top row shows models before log-transformation and the bottom row shows them after log-transformation. The graph on the left illustrates a linear fit to the data points and the graph on the right shows a fit of a penalised spline function to fit the data points more closely. HR—hazard ratio.

Table S1. Summary of MRI acquisition parameter per imaging sequence

| Sequence | Parameter summary |
|----------|--|
| T1 | Slice thickness 5mm (0 – 5 mm), spacing between slices 5.5 mm (0.6 – 7mm), echo time 7.8 ms (3.0 – 58 ms), repetition time 550 ms (7.0 – 3200 ms), field strength 1.5 T (1.5 – 3.0 T), flip angle 90 deg (8 – 150 deg) |
| T2 | Slice thickness 5 mm (1.2 – 7 mm), spacing between slices 5.5 mm (0.6 – 7.7 mm), echo time 98 ms (25 – 171 ms), repetition time 5268.6 ms (660 – 6600 ms), field strength 1.5 T (1.5 – 3.0 T), flip angle 150 deg (20 – 180 deg) |
| FLAIR | Slice thickness 5mm (0.7 – 5 mm), spacing between slices 5.5mm (0.6 – 7 mm), echo time 109 ms (82 – 474 ms), inversion time 2500 ms (1660 – 2880 ms), repetition time 9000 ms (4610 – 14788 ms), field strength 1.5 T (1.5 – 3.0 T), flip angle 150 deg (90 – 180 deg) |
| T1Gd | Slice thickness 1.1 mm (0 – 7 mm), spacing between slices 5.9 mm (0.5 – 7.7 mm), echo time 3.9 ms (2.3 – 46 ms), repetition time 700 ms (7.5 – 3200 ms), field strength 1.5 T (1.5 – 3.0 T), flip angle 15 deg (8 – 150 deg) |

Values for acquisition parameters are presented as median (range). FLAIR—Fluid attenuated inversion recovery.

T1Gd—Post-gadolinium T1-weighted imaging.

Table S2a. Univariable association between clinical variables and overall survival.

| Characteristic | N | Event N | HR | 95% CI | p-value |
|----------------------------|------------------|---------|------|------------|---------|
| Age | 279 | 236 | 1.01 | 1.00, 1.03 | 0.060 |
| Sex | 279 | 236 | | | |
| Female | | | — | — | |
| Male | | | 1.26 | 0.96, 1.64 | 0.091 |
| Operation | 279 | 236 | | | |
| Biopsy | | | — | — | |
| 100% resected ^a | | | 0.34 | 0.23, 0.50 | <0.001 |
| ≥90% resected ^a | | | 0.38 | 0.27, 0.54 | <0.001 |
| <90% resected ^a | | | 0.50 | 0.35, 0.71 | <0.001 |
| Stupp | 279 | 236 | | | |
| No Stupp | | | — | — | |
| Full Stupp ^b | | | 0.29 | 0.20, 0.41 | <0.001 |
| Partial Stupp ^c | | | 0.49 | 0.36, 0.67 | <0.001 |
| MGMT | 258 ^d | 219 | | | |
| Unmethylated | | | — | — | |
| Methylated | | | 0.56 | 0.42, 0.74 | <0.001 |

HR—Hazard ratio; CI—Confidence interval.

^aPercentage of contrast enhancing and necrotic tumour core removed.^bCompleted 60Gy in 30 fractions radiotherapy with concomitant temozolomide and 6 cycles adjuvant temozolomide.^cCompleted 60Gy in 30 fractions radiotherapy but stopped temozolomide either during radiotherapy or adjuvant course.^dNumber of cases with known result.

Table S2b. Prognostic effect of each clinical variable within a multivariable model adjusted for all other clinical variables.

| Characteristic | HR | 95% CI | p-value |
|----------------------------|------|------------|---------|
| Age | 1.00 | 0.98, 1.02 | 0.98 |
| Sex | | | |
| Female | — | — | |
| Male | 1.31 | 0.99, 1.75 | 0.061 |
| Operation | | | |
| Biopsy | — | — | |
| 100% resected ^a | 0.38 | 0.25, 0.56 | <0.001 |
| ≥90% resected ^a | 0.36 | 0.25, 0.52 | <0.001 |
| <90% resected ^a | 0.43 | 0.29, 0.63 | <0.001 |
| Stupp | | | |
| No Stupp | — | — | |
| Full Stupp ^b | 0.34 | 0.23, 0.50 | <0.001 |
| Partial Stupp ^c | 0.56 | 0.39, 0.79 | <0.001 |
| MGMT | | | |
| Unmethylated | — | — | |
| Methylated | 0.67 | 0.50, 0.90 | 0.007 |

HR—Hazard ratio, CI—Confidence interval. Multivariable model included age, sex, operation type, Stupp status, and MGMT methylation.

n = 258 (219 events) = cases with complete results for all clinical variables.

^aPercentage of contrast enhancing and necrotic tumour core removed.

^bCompleted 60Gy in 30 fractions radiotherapy with concomitant temozolomide and 6 cycles adjuvant temozolomide.

^cCompleted 60Gy in 30 fractions radiotherapy with concomitant temozolomide and began adjuvant temozolomide.

Table S3a. Percentage of univariable tumour size models with model p-values <0.05 during the resampling study.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 5.43 | 5.95 | 5.14 | 5.20 | 5.07 | 7.07 |
| 100 | 5.60 | 5.94 | 5.12 | 5.94 | 5.73 | 7.57 |
| 150 | 5.84 | 6.00 | 5.21 | 6.93 | 6.53 | 8.00 |
| 200 | 6.05 | 6.04 | 5.35 | 8.00 | 7.32 | 8.36 |
| 250 | 6.25 | 6.07 | 5.53 | 9.04 | 8.15 | 8.68 |
| 279 | 6.39 | 6.13 | 5.60 | 9.70 | 8.60 | 8.94 |

CV— Core volume; WV— Whole volume.

Table S3b. Percentage of univariable tumour size models with model p-values <0.01 during the resampling study.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 1.12 | 1.31 | 1.05 | 1.06 | 0.91 | 1.66 |
| 100 | 1.16 | 1.26 | 1.03 | 1.26 | 1.13 | 1.91 |
| 150 | 1.26 | 1.31 | 1.05 | 1.57 | 1.39 | 2.12 |
| 200 | 1.34 | 1.33 | 1.09 | 1.90 | 1.66 | 2.26 |
| 250 | 1.40 | 1.34 | 1.15 | 2.29 | 1.93 | 2.39 |
| 279 | 1.44 | 1.33 | 1.16 | 2.51 | 2.08 | 2.49 |

CV— Core volume; WV— Whole volume.

Table S3c. Percentage of univariable tumour size models with model p-values <0.001 during the resampling study.

| Sample size | Tumour Diameter | | Whole volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 0.11 | 0.15 | 0.11 | 0.11 | 0.08 | 0.21 |
| 100 | 0.12 | 0.14 | 0.10 | 0.14 | 0.10 | 0.27 |
| 150 | 0.14 | 0.14 | 0.10 | 0.18 | 0.14 | 0.30 |
| 200 | 0.15 | 0.15 | 0.11 | 0.22 | 0.18 | 0.34 |
| 250 | 0.16 | 0.15 | 0.11 | 0.30 | 0.22 | 0.36 |
| 279 | 0.17 | 0.15 | 0.12 | 0.33 | 0.24 | 0.39 |

CV—Core volume; WV—Whole volume.

Table S4a. Percentage of resamples in which the multivariable tumour size model adjusted for patient age (i.e., age + tumour size in the model) has a tumour size regression coefficient Wald test p-value <0.05.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 5.61 | 6.61 | 5.60 | 5.00 | 5.71 | 7.70 |
| 100 | 5.53 | 6.75 | 5.30 | 5.00 | 6.30 | 8.30 |
| 150 | 5.47 | 6.96 | 5.22 | 5.42 | 7.01 | 8.87 |
| 200 | 5.44 | 7.23 | 5.21 | 5.90 | 7.68 | 9.37 |
| 250 | 5.43 | 7.49 | 5.19 | 6.39 | 8.43 | 9.98 |
| 279 | 5.45 | 7.64 | 5.25 | 6.65 | 8.82 | 10.28 |

CV—Core volume; WV—Whole volume.

Table S4b. Percentage of resamples in which the multivariable tumour size model adjusted for patient gender (i.e., gender + tumour size in the model) has a tumour size regression coefficient Wald test p-value <0.05.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 5.40 | 6.63 | 5.58 | 4.74 | 5.33 | 8.30 |
| 100 | 5.30 | 6.65 | 5.28 | 4.78 | 5.54 | 9.08 |
| 150 | 5.27 | 6.78 | 5.19 | 5.10 | 5.77 | 9.82 |
| 200 | 5.24 | 6.95 | 5.12 | 5.57 | 6.07 | 10.62 |
| 250 | 5.27 | 7.15 | 5.07 | 6.03 | 6.32 | 11.39 |
| 279 | 5.20 | 7.28 | 5.10 | 6.33 | 6.48 | 11.90 |

CV—Core volume; WV—Whole volume.

Table S4c. Percentage of resamples in which the multivariable tumour size model adjusted for adjuvant oncology treatment received (i.e., oncology treatment + tumour size in the model) has a tumour size regression coefficient Wald test p-value <0.05.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|-------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 9.50 | 9.74 | 7.59 | 6.94 | 7.41 | 10.43 |
| 100 | 9.30 | 10.10 | 6.97 | 6.65 | 7.68 | 11.08 |
| 150 | 9.18 | 10.48 | 6.72 | 6.65 | 7.92 | 11.73 |
| 200 | 9.08 | 10.96 | 6.51 | 6.67 | 8.23 | 12.30 |
| 250 | 9.08 | 11.42 | 6.50 | 6.83 | 8.53 | 12.94 |
| 279 | 9.03 | 11.77 | 6.42 | 6.94 | 8.77 | 13.22 |

CV—Core volume; WV—Whole volume.

Table S4d. Percentage of resamples in which the multivariable tumour size model adjusted for MGMT promoter methylation (ie. MGMT methylation + tumour size in model) has a tumour size regression coefficient Wald test p-value <0.05.

| Sample size | Tumour Diameter | | Whole Volume (WV) | | Core Volume (CV) | |
|------------------|-----------------|---------------|-------------------|---------|------------------|---------|
| | Diameter | log(diameter) | WV | log(WV) | CV | log(CV) |
| 50 | 6.52 | 8.29 | 6.31 | 5.85 | 5.89 | 10.80 |
| 100 | 6.78 | 8.51 | 6.03 | 5.86 | 6.07 | 11.44 |
| 150 | 7.05 | 8.55 | 5.89 | 6.26 | 6.27 | 11.87 |
| 200 | 7.29 | 8.57 | 5.79 | 6.75 | 6.53 | 12.23 |
| 250 | 7.63 | 8.54 | 5.75 | 7.34 | 6.86 | 12.58 |
| 258 ^a | 7.80 | 8.52 | 5.74 | 7.63 | 6.97 | 12.74 |

CV—Core volume; WV—Whole volume.

^aMaximum sample size limited to 258 due to the number of cases with a known MGMT result.