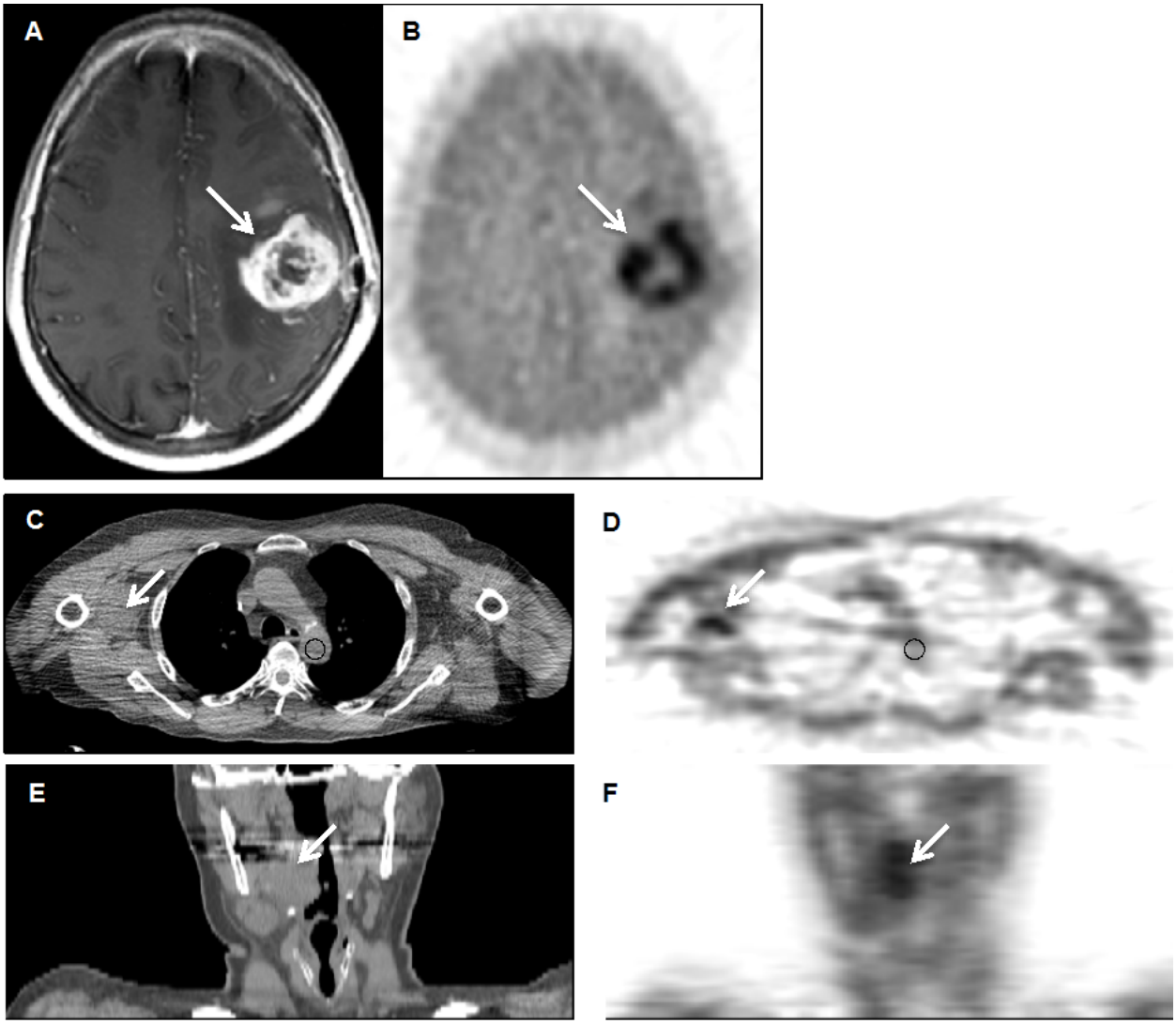
Supplemental Methods:

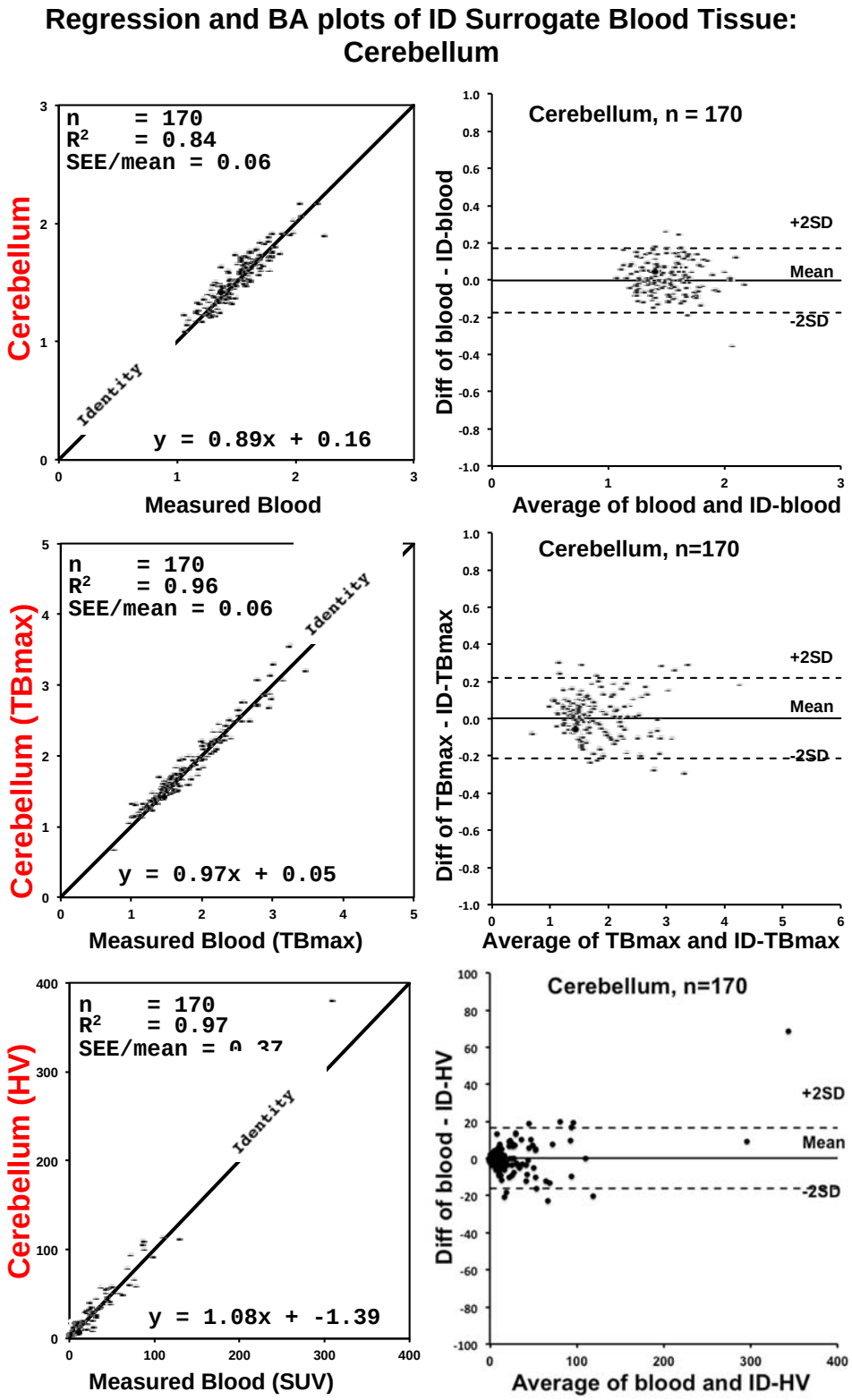
Patient Descriptions: Sixty-four patients (45 males, 19 females; mean age = 54, range 21-77) with pathologically confirmed brain tumor at various stages of treatment underwent 93 standard FMISO PET imaging studies described below. Of these, 9 scans were performed prior to treatment; 40 scans followed surgical resection, but before radiotherapy; 4 patients were imaged shortly after therapy began; and 40 had scans following radiation therapy with concurrent chemotherapy. In a prior report [20], a subset of 22 patients imaged with FMISO before conventional therapy showed that hypoxic parameters were independent predictors of overall survival and TTP.

Patients with H&N, breast, sarcoma, lung cancer, lymphoma and melanoma had a combined total of 130 FMISO scans. Seventy-nine H&N squamous cell carcinoma patients were studied prior to therapy (68 male, 11 female; mean age 61, range 41 - 90) with primary tumor locations of the tongue base, tonsil, larynx, soft palate, hypolarynx, epiglottis and sinuses [18]. Seventy-three of these H&N patients have been used to show that quantitative FMISO imaging prior to therapy can predict outcome [18]Breast cancer patients (n = 14) underwent 15 studies, where and were all imaged prior to surgery; 10 had infiltrating ductal carcinomas and 4 had lobular; all were female with an average age of 46 (range 32 - 84). Patients with sarcoma (n = 17, 10 female, 7 male; mean age 50, range 40 - 61) underwent 23 FMISO imaging studies, of which 15 were prior to chemotherapy, 3 early into therapy and 5 post chemotherapy; tissue pathologies included fibrosarcoma, liposarcoma, rhabdomyosarcoma, and chondrosarcoma. Lung patients (n = 10) were all male with non-small cell lung cancer studied prior to neoadjuvant therapy, average age 56 (range 32-84). Of two lymphoma patients, one was imaged prior to therapy (male) and one following therapy (female). One melanoma patient was a male age 35 with metastatic melanoma to the chest wall with prior radiation to metastatic sites.

Patient Examples of FMISO Uptake in Tumors:

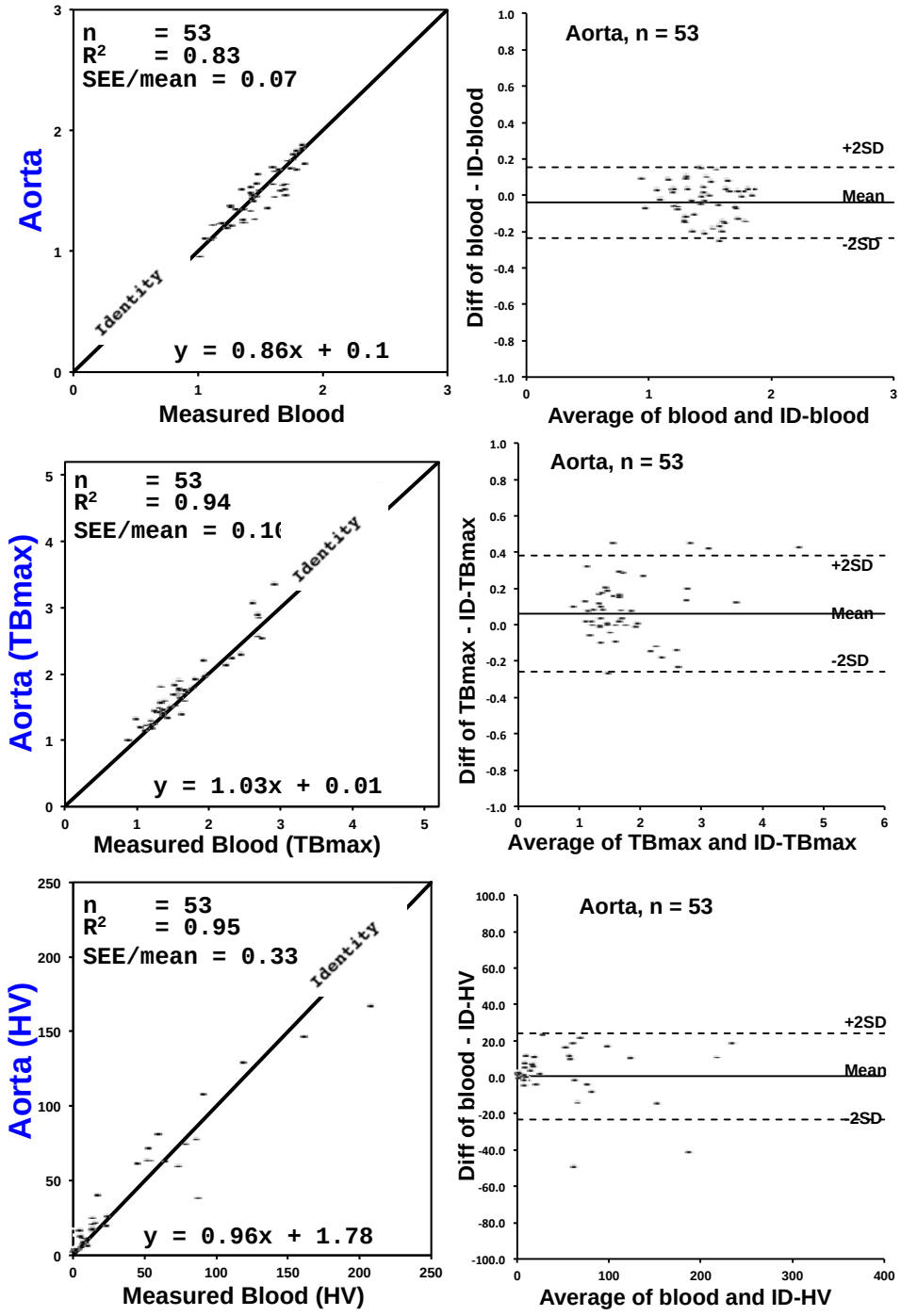


Supplemental Figure 1: *Cancer imaging with ^{18}F-FMISO.* (A) 61 year old female patient with biopsy confirmed glioblastoma multiforme imaged conventionally with gadolinium contrast enhanced MR, then with (B) FMISO, where the arrow indicates the tumor location. (C) A 74 year old male patient with right axillary synovial sarcoma cancer grade 2 with a low dose CT and (D) FMISO PET imaging, where the arrow indicates the tumor location, and the circle indicates the aorta blood surrogate tissue reference region. (E) Low-dose CT image of a 64 year old female patient with untreated T2, N2b squamous cell carcinoma at the base of the tongue and (F) an ^{18}F-FMISO image with an arrow indicating the tumor location.



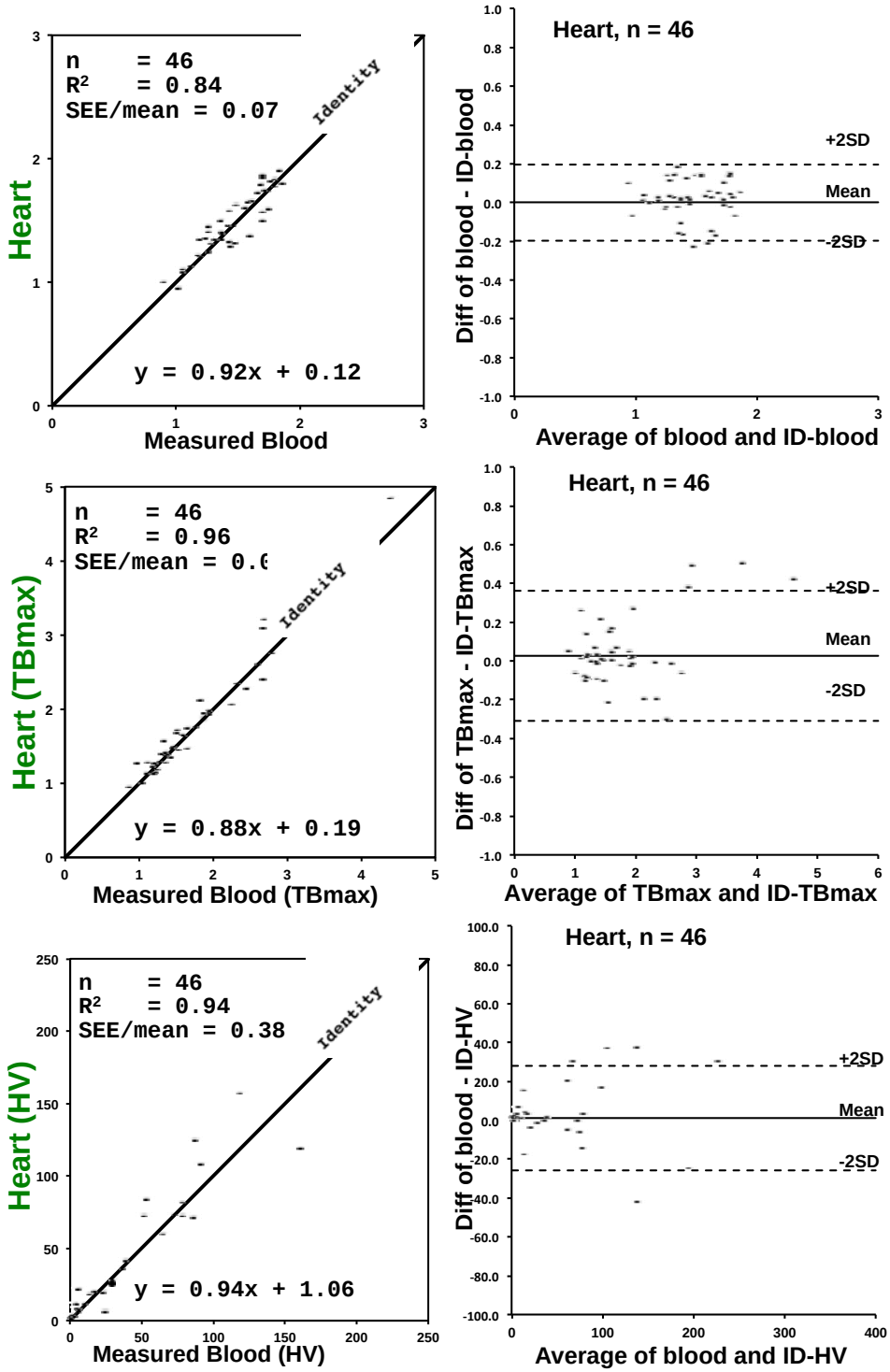
Supplemental Figure 2: Blood, TBmax and HV plots for values from sampled blood and the ID surrogate, cerebellum.

Regression and BA plots of ID Surrogate Blood Tissue: Aorta

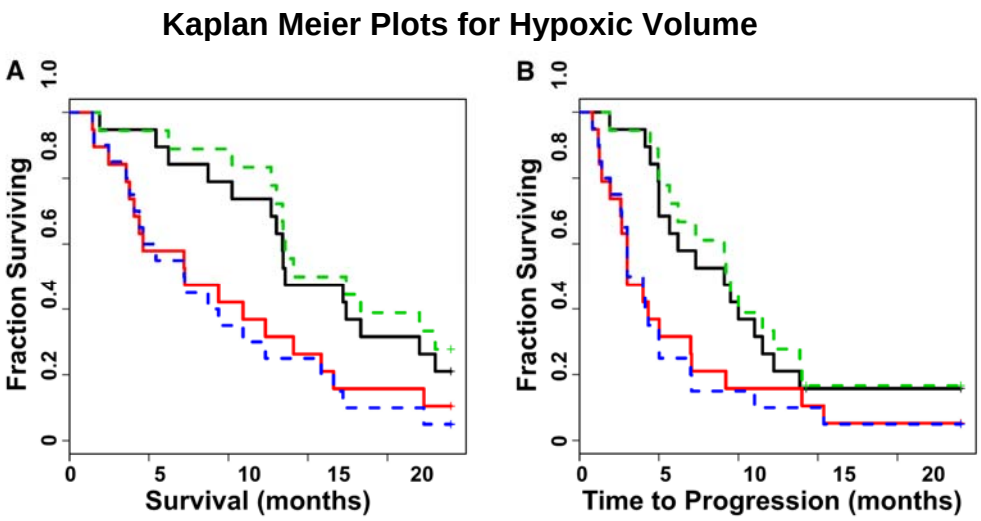


Supplemental Figure 3: Blood, TBmax and HV plots for values from sampled blood and the ID surrogate, aorta.

Regression and BA plots of ID Surrogate Blood Tissue: Heart

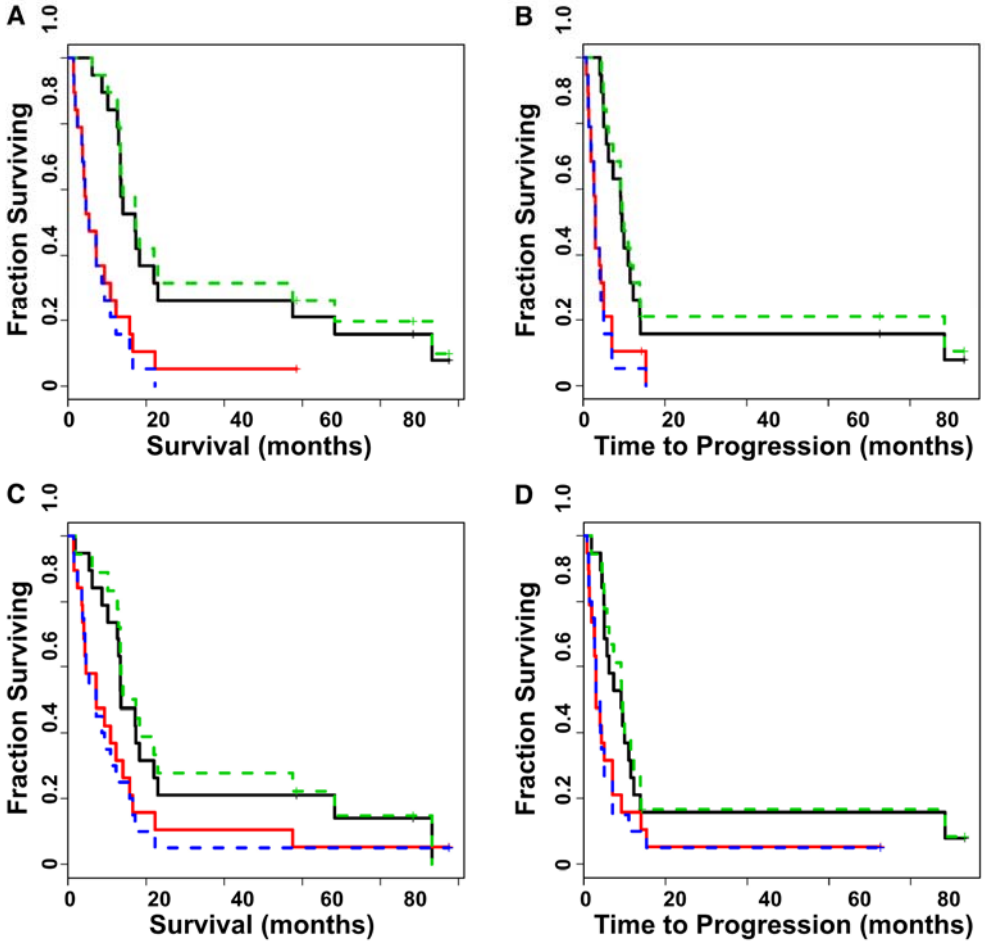


Supplemental Figure 4: Blood, TBmax and HV plots for values from sampled blood and the ID surrogate, heart.



Supplemental Figure 5: Kaplan Meier plots of HV used to stratify 38 pretreatment glioma patients with respect to 2-year survival (A) and TTP (B) shows the separation of higher risk group (red line, HV > 7.36) from the lower risk group (black line). ID-HV risk groups are separated by the median HV = 6.91 (dotted lines) and show similar predictive power as HV (results in Table S3).

Kaplan Meier Plots of Hypoxia Parameters for Overall Survival



Supplemental Figure 6: Kaplan Meier plots of hypoxia parameters used to stratify 38 pretreatment glioma patients with respect to overall survival (A, C) and TTP (B, D). TBmax (A, B) shows risk group separation (high risk = red line, low risk = black line) at the median (TBmax = 1.83), while ID-TBmax separates the risk groups (high risk = blue dotted line, low risk = green dotted line) at ID-TBmax = 1.77. HV (C, D) shows the separation of risk groups at the median HV = 7.36 cc, while ID-HV risk groups are separated at ID-HV = 6.91 cc. ID parameters show similar predictive power as parameters using blood samples.

Supplemental Table 1
Additional descriptive statistics for hypoxia parameters:

Parameter	Min	1st Qt	Med	Mean	3rd Qt	Max
HV	0.09	3.00	7.36	20.52	21.71	129.30
ID-HV	0.02	2.95	6.91	20.02	16.29	109.10
TBmax	1.20	1.56	1.83	2.03	2.19	4.19
ID-TBmax	1.20	1.46	1.77	2.01	2.18	4.35

Descriptive statistics showing the similarities of distribution of hypoxia parameters derived from sampled blood and from surrogate blood regions from 18F-FMISO imaging.

Supplemental Table 2
Average Percent Difference Between Blood and ID values

Blood Surrogate	Blood SUV	TBmax	HV
Cerebellum (170)	0.1%	0.5%	6.1%
Aorta (53)	0.2%	1.1%	4.4%
Heart (46)	-2.8%	4.0%	8.4%
All Regions (269)	-0.4%	1.3%	6.9%

As a measure of bias, the average percent difference between blood and ID values were computed as (ID value - blood value)/blood value * 100.

Supplemental Table 3
Hypoxic Volume Multivariate Analysis Results

	Multivariate			
	Survival (0.506) †		TTP (0.515)	
	Hazard	P	Hazard	P
Age	1.39	0.245	1.53	0.094
Gender	2.22	0.126	2.47	0.069
KPS	0.88	0.661	0.96	0.881
HV	2.77	<0.001	2.65	<0.001
Resection*	0.71	0.425	0.70	0.366

	Survival (0.505)		TTP (0.533)	
	Hazard	P	Hazard	P
Age	1.36	0.267	1.48	0.118
Gender	1.75	0.246	2.02	0.127
KPS	0.89	0.686	0.95	0.836
ID-HV	2.76	<0.001	2.79	<0.001
Resection	0.76	0.523	0.73	0.426

* Resection is dichotomized as biopsy or other (gross/sub-total resection).
† The coefficient of determination (R^2) is given for each table.

Multivariate analysis of HV and clinical variables shows the hazard ratio with P values associated with survival and TTP at 2 years in 38 pretreatment glioma patients. After adjusting for clinical variables using a multivariate Cox proportional hazards model, greater tumor HV was still associated with shorter survival and TTP.