ON-LINE APPENDIX

Detailed Image Postprocessing

First, the ROIs were drawn by the consensus of 2 neuroradiologists blinded to the clinical information, using a semiautomatic signal-intensity-threshold method to include the entire enhanced portion of the tumors on 3D postcontrast T1-weighted images, while avoiding necrotic or cystic portions. Masks of enhancing tumors were generated from 3D postcontrast T1-weighted images. Second, the 3D postcontrast T1-weighted images were coregistered to the last phase of DCE-MR imaging source images, with an affine transformation and normalized mutual information. With the resulting matrix, the enhancing tumor masks were coregistered to the DCE MR imaging source images. Third, on DCE-MR imaging source images, the region outside the enhancing tumor was removed for ease of computation, using the coregistered masks. Finally, the wash-in phase was determined from each pixel of the enhancing tumors, and the corresponding IAUC values were calculated.

Genetic Profile Analysis

MGMT promoter methylation status was evaluated with the methylation-specific polymerase chain reaction, which was retrospectively recorded from pathologic reports. Along with *MGMT* promoter methylation status, 3 other genetic or molecular profiles of glioblastoma, including *IDH1* mutation, EGFR expression, and 1p/19q codeletion were identified. *IDH1* mutations were identified with *IDH1* mutation–specific immunohistochemical staining. The expression status of the EGFR protein was visually scored on a medium-power field (×200), with the scale from 0 to 3+. We defined 0, 1+, and 2+ as negative EGFR expression, and 3+ as positive EGFR expression for statistical analysis. The 1p/19q status was analyzed by polymerase chain reaction–based loss of heterozygosity analysis. Tumors were considered 1p/19q codeleted if there was an entire loss of 1p and an entire loss of 19q with centromeric breakpoints.

Differences in IAUC Parameters according to IDH1 *Mutations, EGFR Expression, and 1p/19q Codeletion*

The IAUC parameters showed a trend toward higher values in the tumors with *IDH1* mutations, compared with those with wild type *IDH* (14.6 ± 1.5 versus 12.6 ± 2.2, $P = .052$ for $IAUC30_{mean}$; 35.1 ± 4.0 versus 32.2 ± 4.6, $P = .179$ for $IAUC60_{mean}$). In linear regression with *MGMT* and *IDH1* mutation status to assess the significant determinant of IAUC values, *IDH1* mutation status was not significant ($P = .212$ and 0.460 for $IAUC30_{mean}$ and $IAUC60_{mean}$, respectively) and only *MGMT* status was a significant determinant ($P = .020$ and 0.047 for $IAUC30_{mean}$ and $IAUC60_{mean}$, respectively). No significant differences in IAUC parameters were found according to EGFR expression (12.8 ± 2.0 versus 12.7 ± 2.4, $P = .777$ for $IAUC30_{mean}$; 32.7 ± 4.2 versus 32.1 ± 4.9, $P = .542$ for $IAUC60_{mean}$) and 1p/19q codeletion (12.6 ± 2.3 versus 12.7 ± 2.2, $P = .858$ for $IAUC30_{mean}$; 32.1 ± 4.4 versus 32.4 ± 4.6, $P = .823$ for $IAUC60_{mean}$).

On-line Table 1: *MGMT* promoter methylation status and other clinical characteristics of the patients[a]

Clinical Characteristics	*MGMT* Status			*P* Value[b]
	Total (*n* = 88)	Unmethylated (*n* = 51)	Methylated (*n* = 37)	
Median OS (days)	521	442	790	.014
No. of deaths	50 (57%)	34 (67%)	16 (43%)	
Median PFS (days)	376	272	657	.003
No. of tumor progression	64 (72%)	42 (82%)	22 (59%)	
Age (yr)				
Median (range)	59.4 (1.2)	58.0 (1.7)	61.2 (1.7)	.199
Sex				
Male	44 (50%)	23 (45%)	21 (57%)	.280
Female	44 (50%)	28 (55%)	16 (43%)	
KPS				
Median (range)	73.4 (1.5)	72.5 (2.0)	74.6 (2.2)	.496
Extent of resection				
Total	46 (52%)	25 (49%)	21 (57%)	.338
Subtotal	32 (36%)	18 (35%)	14 (38%)	
Partial	6 (7%)	4 (8%)	2 (5%)	
Biopsy only	4 (5%)	4 (8%)	0 (0%)	
Postoperative treatment				
CCRT	74 (84%)	44 (86%)	30 (82%)	.261
RTx	7 (8%)	5 (10%)	2 (5%)	
CTx	2 (2%)	0 (0%)	2 (5%)	
None	5 (6%)	2 (4%)	3 (8%)	
Histopathology				
GBM	77 (87%)	46 (90%)	31 (84%)	.369
GBM with oligodendroglial component	11 (13%)	5 (10%)	6 (16%)	
Conventional MRI findings				
Volume of enhancing tumor (cm^3)	25.3 (2.4)	26.2 (3.2)	24.1 (3.6)	.673
Edema				
None	21 (24%)	10 (20%)	11 (30%)	
Mild to moderate	27 (31%)	16 (31%)	11 (30%)	
Severe	40 (45%)	25 (49%)	15 (40%)	
nCET				
Negative	44 (50%)	24 (47%)	20 (54%)	.517
Positive	44 (50%)	27 (53%)	17 (46%)	
Eloquent brain involvement				
Yes	27 (31%)	15 (29%)	12 (32%)	.762
No	61 (69%)	36 (71%)	25 (68%)	
Deep white matter invasion				
Yes	55 (63%)	33 (65%)	22 (60%)	
No	33 (37%)	18 (35%)	15 (40%)	

Note:—KPS indicates Karnofsky performance status; CCRT, concurrent chemoradiotherapy; RTx, radiotherapy; CTx, chemotherapy.

[a] Data are expressed as mean with SD in parentheses or number with percentage in parentheses.

[b] Calculated from the Student *t* test for continuous variables and the χ^2 test for categoric variables, if not otherwise mentioned.

[c] Calculated from the log-rank test.

On-line Table 2: Genetic characteristics in 88 patients[a]

Parameters	Value
MGMT promoter methylation status	
Methylated	51 (58%)
Unmethylated	37 (42%)
IDH1 status	
IDH1 mutation[b]	5 (6%)
IDH1 wild type	82 (93%)
NA	1 (1%)
EGFR	
High (3+)	44 (50%)
Low (0–2+)	44 (50%)
1p/19q codeletion	
Codeleted	10 (12%)
Not codeleted	76 (86%)
NA	2 (2%)

Note:—NA indicates not applicable.

[a] Data are No. of patients with percentages in parentheses.

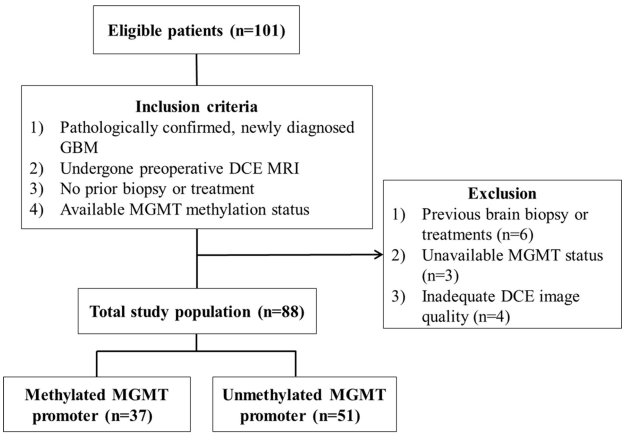
[b] All patients with *IDH1* mutation belonged to the methylated *MGMT* group.

On-line Table 3: Univariate analysis of initial area under the curve histogram parameters, *MGMT* status, clinical factors, and conventional MRI findings as predictors of overall survival and progression-free survival in the entire cohort ($n = 88$)

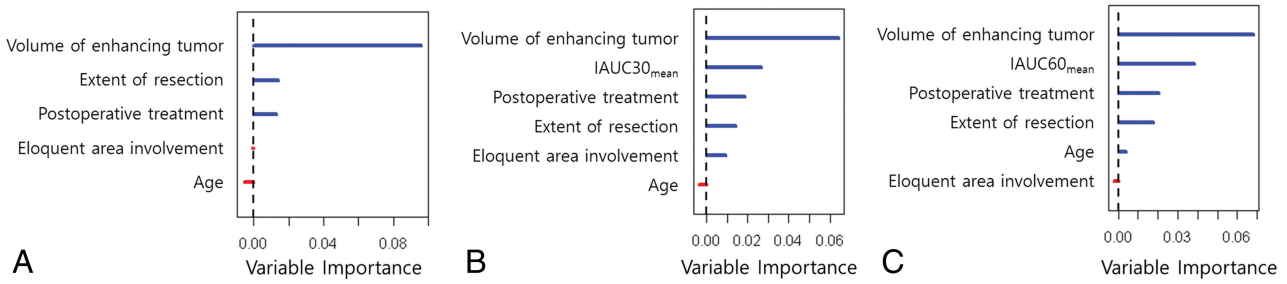
	OS			PFS		
Parameters	Cutoff Value	HR (95% CI)	*P* Value[a]	Cutoff Value	HR (95% CI)	*P* Value[a]
IAUC parameters						
$IAUC30_{mean}$	≥10.9	1.86 (0.90–3.84)	.090	≥15.2	0.60 (0.28–1.25)	.166
$IAUC60_{mean}$	≥28.4	2.16 (0.91–5.10)	.072	≥35.7	0.62 (0.31–1.26)	.186
MGMT	Unmethylated	2.14 (1.15–4.00)	.014	Unmethylated	2.23 (1.29–3.84)	.003
Other prognostic factors						
Age (yr)	≥66	1.81 (1.01–3.25)	.042	≥70	1.98 (1.07–3.66)	.027
Sex	Male	0.97 (0.55–1.69)	.906	Male	1.17 (0.71–1.92)	.541
KPS	≥0	0.70 (0.40–1.23)	.213	70	0.69 (0.39–1.22)	.199
Extent of resection	Subtotal, partial resection or biopsy only	1.94 (1.10–3.43)	.020	Subtotal, partial resection or biopsy only	1.65 (1.01–2.71)	.045
Postoperative treatment	RTx, CTx, or none	2.92 (1.52–5.63)	.001	RTx, CTx, or none	2.84 (1.53–5.29)	.001
Histopathology	GBM with oligodendroglial component	0.96 (0.41–2.25)	.918	GBM with oligodendroglial component	0.91 (0.41–2.00)	.813
Conventional MRI findings						
Volume of enhancing tumor (cm^3)	≥30.2	2.88 (1.62–5.12)	<.001	≥30.2	1.93 (1.13–3.30)	.015
Edema	≥Mild or severe edema	0.83 (0.47–1.46)	.517	Mild or severe edema	0.74 (0.45–1.22)	.236
nCET	Positive	1.33 (0.76–2.32)	.321	Positive	1.54 (0.93–2.54)	.093
Eloquent brain involvement	Yes	1.83(1.04–3.23)	.033	Yes	1.34(0.80–2.26)	.264
Deep white matter invasion	Yes	1.52 (0.83–2.79)	.170	Yes	1.14 (0.69–1.91)	.607

Note:—KPS indicates Karnofsky performance status; HR, hazard ratio.

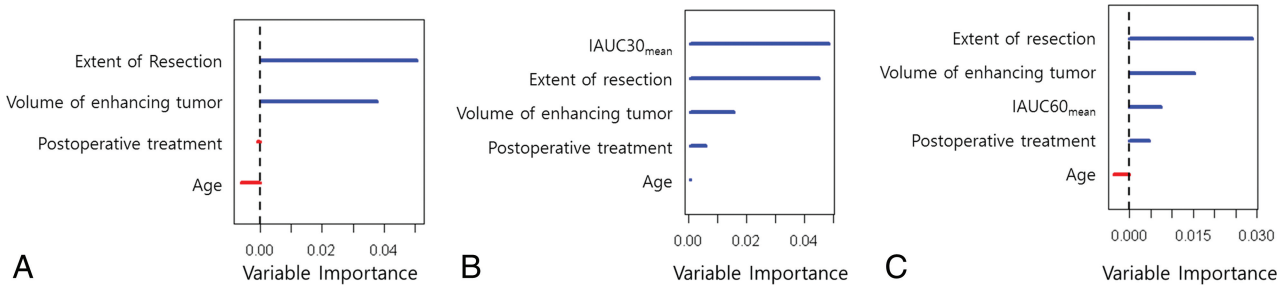
[a] Calculated from the log-rank test.



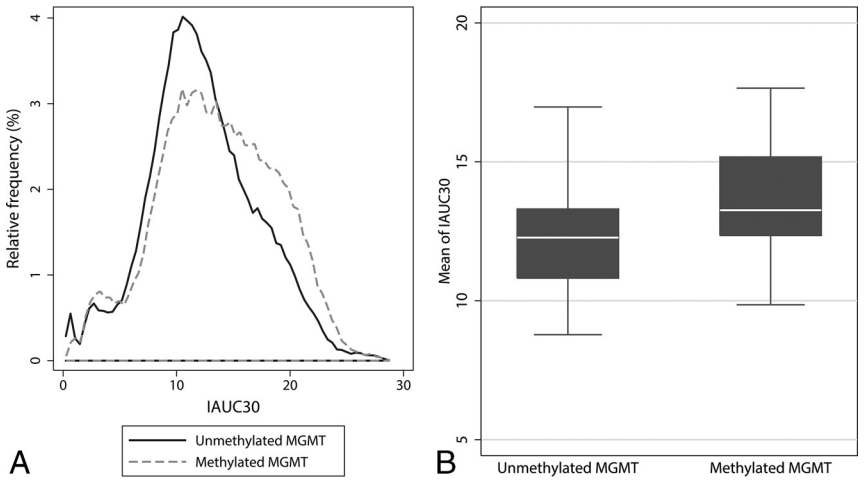
ON-LINE FIG 1. Flowchart showing the enrollment process of the study population.



ON-LINE FIG 2. Graphs depicting variable importance scores from random survival forests for OS. *A*, In OS model 0 without IAUC parameters, the volume of enhancing tumor was the top predictor. In OS model 1 with $IAUC30_{mean}$ (*B*) and OS model 2 with $IAUC60_{mean}$ (*C*), the IAUC parameters were the second most important variable, following the volume of enhancing tumor as the top variable, and followed by postoperative treatment as the third most important variable. Variable importance is denoted positively (*blue bars to the right*) or negatively (*red bars to the left*), depending on whether inclusion of that variable in the classification increases or reduces the accuracy of survival prediction.



ON-LINE FIG 3. Graphs depicting the variable importance scores from random survival forests for PFS. *A*, In PFS model 0 without IAUC parameters, the extent of resection was the top predictor. *B*, In PFS model 1, $IAUC30_{mean}$ was the most important variable, followed by extent of resection and volume of enhancing tumor as the second and third most important variables, respectively. *C*, On the contrary, in PFS model 2, $IAUC60_{mean}$ was the third most important variable, following the extent of resection and volume of enhancing tumor as the first and second most important variables, respectively. Variable importance is denoted positively (*blue bars to the right*) or negatively (*red bars to the left*), depending on whether inclusion of that variable in the classification increases or reduces the accuracy of the survival prediction.



ON-LINE FIG 4. Relative frequency histogram of IAUC30 (*A*) and boxplot of $IAUC30_{mean}$ (*B*) according to the *MGMT* status. Tumors with methylated *MGMT* promoter status showed a greater percentage of pixels of high IAUC30 values than those with unmethylated *MGMT* promoter status. $IAUC30_{mean}$ was significantly higher in the methylated *MGMT* group (13.5 ± 2.2) than in the unmethylated *MGMT* group (12.2 ± 2.1, $P = .007$).