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Original Article

Correlation between FDG-PET uptake and survival in patients with primary brain tumors

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Abstract: This study evaluates F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) semi-quantitative analysis as biomarker of tumor aggressiveness and predictor of survival in patients with primary brain tumors. Semi-quantitative analyses (SUVmax, SUVmean) were derived from FDG PET images in 78 patients with suspected recurrence of primary brain tumors based on MRI. SUVmax and the ratio of lesion SUVmax to the SUVmean of contralateral white matter (SUVmax/WM) were measured. A one-way Analysis of Variance (ANOVA), Kaplan-Meier analyses and the log rank test for evaluating statistical significance were utilized. There was statistical significance for time between FDG-PET and patient death. There was a significant difference with respect to FDG-PET time to death between patients with glioblastoma and patients with anaplastic oligodendroglioma, oligodendroglioma, and other histological subtypes. There is significant correlation with SUVmax/WM and patient survival following FDG-PET when a cut-point ratio of 1.90 is used. A 1.90 cut-point ratio of SUVmax/WM was associated with a difference in survival. GBM was associated with a significant difference in terms of reduced survival following FDG PET compared to most other histological sub-types. These results may inform current treatment and counseling strategies for patients with primary brain tumors.

Keywords: FDG, PET, brain, survival, primary brain tumor, postoperative imaging, postoperative FDG-PET, glioma

Introduction

There are approximately 24,000 new cases of central nervous system (CNS) tumors diagnosed in the United States each year [1]. The overall incidence of primary brain tumors has increased significantly in the last decade with about half of these lesions consisting of supratentorial high-grade gliomas [1, 2]. Anaplastic astrocytoma (World Health Organization (WHO) Grade III) and glioblastoma (GBM) (WHO grade IV) are the most common glial primary brain tumors [1, 3, 4]. Patients with newly diagnosed malignant gliomas are usually treated with surgical debulking or resection followed by radiation therapy and/or chemotherapy, depending on their functional status.

Glioblastoma is the most common and aggressive primary brain tumor. Despite multimodal treatment strategies including surgical resection, local radiation, and systemic chemotherapy; the median survival time following diagnosis is approximately 12 months [5, 6]. Moreover, overall survival for GBM remains poor even with the addition of temozolomide drug therapy. In a large randomized trial comparing the efficacy of temozolomide alone versus radiotherapy alone in elderly patients with anaplastic astrocytoma or glioblastoma, Wolfgang et al. [7] found temozolomide alone is not inferior to radiotherapy alone. The National Cancer Institute of Canada Clinical Trials Group reported improved median and 2-year survival for glioblastoma patients treated with concomitant and adjuvant temozolomide and radiotherapy [5]; although related work suggests that the survival benefit of combined therapy is mostly attributable to a subset of patients having inactivation of the MGMT promotor gene [6-8].

Positron emission tomography (PET) with [^{18}F]-2 fluoro-2-deoxy-d-glucose (F18-FDG-PET) is a well-validated and important imaging technique for diagnosis, staging, and monitoring response to therapy of patients with cancer [9, 10]. The majority of malignant tissues have increased FDG uptake associated with an increased rate of glycolysis as well as increased glucose transport. Warburg first described this fundamental aberration of malignant cells in the 1930's [11]. More recently, Weber described the specific cellular mechanisms associated with glucose uptake in malignant tissue [12, 13]. The increased FDG uptake noted in malignant tissue is related in a complex manner to the proliferative activity of malignant tissue and to viable tumor cell number. F18 FDG-PET has been used in evaluation of primary brain tumors to assess progression of disease [14, 15], differentiate recurrence from radiation necrosis/treatment effect [16-18], and also as a prognostic indicator [14, 19, 20]. There are few studies assessing the correlation between FDG-PET tumor uptake and survival time in patients with primary brain tumors, including glioblastoma. Moreover, these particular studies were almost exclusively based on visual grading [15, 19, 21, 22]. The purpose of the current study is to examine the use of semi-quantitative techniques (standardized uptake values) to assess FDG uptake as a biomarker of primary brain tumor aggressiveness and survival.

Materials and methods

Patient information

This retrospective study was performed with IRB approval. The study patients had a clinical diagnosis of a primary brain tumor referred for FDG-PET imaging to assess tumor recurrence versus radiation necrosis/treatment effect following MRI. The study included 78 evaluable adult patients (47 male, 31 female; mean age at time of FDG-PET of 47.1 years (standard deviation (sd) 12.01, range 18-75)) with histologically proven grade II or greater primary brain tumors. All patients had received radiotherapy with or without chemotherapy prior to enrollment. Radiation therapy had been completed a minimum of 4 months prior to evaluation. All subjects had a new or enlarging focus of enhancement on MRI within the radiation field demonstrated by a clinical gadolinium-enhanced (Gd) MRI. All subjects had a clinical FDG-PET scan of the brain within one month of the Gd-MRI for the purpose of differentiating radiation necrosis/treatment effect from tumor recurrence. Necessary data including demographic information, histology, time from completion of therapy to MRI abnormality concerning for tumor recurrence, and date of death were obtained from the electronic medical record.

Gadolinium-enhanced MRI

All Gd-MRI scans were performed according to clinical protocols on Siemens 1.5T or 3T systems (Erlangen, Germany) with the following parameters: sagittal T1 fast spin echo (FSE), axial T1 FSE, axial T2 FSE, axial fluid-attenuated inversion recovery (FLAIR), axial gradient-recalled-echo (GRE), axial diffusion tensor imaging (DTI) or diffusion-weighted imaging (DWI), as well as axial and coronal T1 weighted images following the administration of intravenous gadolinium (Gd-DTPA). The presence of a new or enlarging area of enhancement within the radiation port and follow-up assessment of progression, stability or regression of this specific lesion was documented in the clinical report by a neuroradiologist.

FDG-PET

All FDG-PET scans were performed according to clinical protocol. Patient preparation included 6 hours without caloric intake or insulin administration. 370 MBq (10 mCi) of FDG was given intravenously through a peripheral vein. Patients rested quietly in a dimly lit room in a reclining chair during the uptake period of approximately 45 minutes without physical activity and with minimal verbal contact. A FDG-PET scan was performed for 30 minutes over a single bed position. Three different PET scanners were used over the course of this study: a GE Advance PET scanner (GE Healthcare Milwaukee, WI) in 3-D mode, with measured attenuation (germanium rod source), a GE ST PET/CT scanner (GE Healthcare Milwaukee, WI) with CT attenuation correction and a GE Discovery 710 scanner with CT attenuation correction and time of flight (GE Healthcare Milwaukee, WI). The full width at half maximum spatial resolution of the GE Advance and GE ST scanners were almost identical at 4.8 mm and 5.0 mm,

respectively and the field of view for reconstruction was set to 25.6 cm on each scanner to generate a pixel size of 2.0 mm × 2.0 mm (image matrix size 128 × 128), resulting in identical spatial resolution for both scanners. The GE Discovery 710 also has a spatial resolution of ~5 mm FWHM with time of flight (ToF) and various reconstruction options including point spread function correction (Sharp IR) although for clinical brain imaging, standard iterative reconstruction without ToF or Sharp IR was utilized to more closely match the other scanners. Brain imaging and reconstruction protocols were created using a set of parameters to produce images that were virtually identical in quality, including image noise and contrast. The native slice thickness was 4.25 mm for the GE Advance, 3.27 mm for the GE ST system and 3.27 mm for the GE Discover 710. The CE Discovery 710 scanner has a bias towards higher SUVmax values, however, this is negligible [23].

Image analysis

FDG-PET images were fused with the most recent prior Gd-MRI T1 post contrast images for target lesion confirmation. This allowed for unequivocal localization of the area of enhancement on the FDG-PET images. The maximum standardized uptake value (SUVmax) corrected for body weight was measured on the non-fused attenuation corrected emission images at the same area of enhancement on Gd-MRI. Individual image slices of all areas of concern based on the MRI enhancement were examined to determine the SUVmax for the tumor volume. A circular region of interest was placed on each image slice avoiding adjacent cerebral cortex to determine SUVmax. The tumor SUVmax value was determined by using the highest SUVmax value obtained on the individual image slices. This SUVmax assessment of FDG tumor uptake was used rather than SUVmean or SUVpeak because many of the lesions were small and irregular in shape, located within or adjacent to metabolically active cortex, and were sensitive to user variability in region-of-interest placement. In addition, a 1 cm circle was used in the contralateral white matter to obtain a weight-corrected SUVmean. In certain patients multiple distinct enhancing areas were noted (GBM = 5, anaplastic astrocytoma = 3, anaplastic oligodendroglioma = 1, oligodendroglioma = 1, and other = 1). In these cases, regions of interest were obtained as described above for each distinct enhancing area to obtain an average SUVmax. The tumor SUVmax and average SUVmax were also normalized to the contralateral white matter by dividing by the SUVmean of the contralateral white matter region of interest (SUVmax/WM). This SUVmax/WM ratio was also used in all analyses.

Data and statistical analysis

The data was retrospectively reviewed and included FDG-PET studies from May 2008 to December 2017. Standard statistical analyses were performed with a one-way Analysis of Variance (ANOVA) to assess for differences between the histologic tumor type and age, SUVmax, average SUVmax, SUVmax/WM, average SUVmax/WM, and time from FDG-PET to death. A Tukey HSD post-hoc test (also known as “Honestly Significant Difference”) was done to assess for significant differences between the histologic tumor types with respect to age, SUVmax, SUVmax/WM, average SUVmax/WM, and time from FDG-PET to death. Four predictors of overall survival were evaluated: SUVmax, average SUVmax, SUVmax/WM, and average SUVmax/WM. Kaplan-Meier methods analyses were used for determining survival and the log rank test was used for evaluating statistical significance.

Two methods were used in the data analysis from subjects with multiple lesions: the highest SUVmax value among all of the lesions determined the SUVmax for each subject and the SUVmax from all lesions was averaged to determine an average SUVmax for each subject. Out of our data set, 9 patients had 2 lesions, one patient had 3 lesions, and one patient had 4 lesions. Since most subjects had one lesion, the difference between these methods was small. In addition, cut-points were chosen in two ways, one pre-defined and one data-driven. The pre-defined cut-point was the median. The data-driven cut-point was based on the minimum *p*-value over all cut-points. For this data-driven cut-point, a simple complete search procedure was used to select cut points that minimized the *p*-value. The analysis was repeated with every observed value as a candidate cut point, and the cut-point with the smallest

Table 1. Demographic information based on patient central nervous system tumor histological sub-type

Tumor Histology	WHO grade	Number of patients	Number of discrete lesions	Average age at PET	Age range at PET	Male	Female
GBM	IV	50	56	53.8 ± 10.7	19-75	35	15
AA	III	8	12	47.9 ± 12.5	33-66	3	5
Ana Olig	III	10	10	47.6 ± 11.8	31-65	6	4
Oligo	II	4	5	46.8 ± 8.1	35-52	1	3
Other*	N/A	6	7	42.7 ± 15.2	18-59	2	4
Totals		78	90	47.8	18-75	47	31

*Other comprised 2 patients with astroblastomas, 1 patient with brainstem anaplastic astrocytoma, 1 patient with anaplastic ependymoma, 1 patient with gliosarcoma and 1 patient with CNS lymphoma. Abbreviations: WHO = World Health Organization; SD = standard deviation; GBM = glioblastoma multiforme; AA = anaplastic astrocytoma; Ana Olig = anaplastic oligodendroglioma; Oligo = oligodendroglioma.

Table 2. Summary between histologic sub-types (max ± standard deviation) in regards to SUVmax, average SUVmax, SUVmax/SUVmean of contralateral white matter (SUVmax/WM), age at time of PET imaging, and survival following PET imaging

Tumor Histology	SUVmax all lesions*	Average SUVmax, multiple lesions averaged**	SUVmax/ WM*	Average SUVmax/WM**	Time FDG-PET to death (days)	Age at time of PET (years)
GBM	7.92 ± 2.54	7.82 ± 2.20	2.76 ± 0.99	2.74 ± 0.94	426 ± 391	53.8 ± 10.7
AA	8.42 ± 4.74	9.15 ± 5.19	2.39 ± 0.77	2.52 ± 0.67	374 ± 232	47.9 ± 12.5
Ana Olig	9.10 ± 9.12	9.36 ± 6.61	3.11 ± 2.50	3.13 ± 2.60	897 ± 858	47.6 ± 11.8
Oligo	6.56 ± 2.67	7.11 ± 2.64	2.50 ± 1.04	2.73 ± 1.01	1660 ± 971	46.8 ± 8.1
Other***	8.99 ± 2.75	8.66 ± 1.88	3.16 ± 1.26	3.17 ± 1.25	1164 ± 1001	42.7 ± 15.2

*At the lesion level; **At the patient level; ***Other comprised 2 patients with astroblastomas, 1 patient with brainstem anaplastic astrocytoma, 1 patient with anaplastic ependymoma, 1 patient with gliosarcoma and 1 patient with CNS lymphoma. Abbreviations: GBM = glioblastoma multiforme; AA = anaplastic astrocytoma; Ana Olig = anaplastic oligodendroglioma; Oligo = oligodendroglioma.

p-value was chosen as this will have the best separation in prediction of survival probability for those above and below the cut-point *p*-value. Using the same data to both select and evaluate cut-points is known to lead to bias. For this reason, a resampling method was used to adjust the *p*-value. The sample outcome (alive or dead) was permuted 1,000 times so that death indicator was unrelated to the predictors. The minimum *p*-value was calculated over all possible splits to get an empirical null distribution. The Cox proportional hazard model and associated Wald tests was used for survival analysis. Survival analysis was performed using R version 3.2.1 [24]. Analysis of variance was used to determine if there were significant differences in continuous variables between histological groups. The "optimal *p*-value" method split the data into groups with "high" and "low" values of a predictor at the value with the smallest nominal *p*-value. The nominal *p*-values from this search procedure will be biased since the same data set was used to select the split point and for analysis. Permutation methods were used to adjust the *p*-values. Results are summarized in **Table 4**.

Results

Demographic and other information including tumor histology, WHO grade, number of patients, average age at FDG-PET, and sex is provided in **Table 1** based on histological sub-type. There was no statistically significant difference in age at time of FDG-PET between the histologic sub-types (**Tables 1** and **2**). Standard statistical analyses were performed with a one-way Analysis of Variance (ANOVA) to assess for differences between the histologic tumor types with respect to age, SUVmax, SUVmax/WM, average SUVmax/WM, and time from FDG-PET to death. No statistically significant differences

Table 3. Univariate Survival Analysis demonstrating method and optimal cut-off values for prediction of survival probability as a function of central nervous system tumor FDG uptake

Predictor	Method of Combining Lesions	Value	Method to Find Cut Point	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	*P*-value	Adj *p* value
Average SUVmax/WM	average	2.56	Median	1.26	0.77	2.02	0.36	---
SUVmax/WM	maximum	2.64	Median	1.33	0.82	2.12	0.25	---
Average SUVmax	average	7.83	Median	1.25	0.77	2.02	0.36	---
SUVmax	maximum	7.90	Median	1.23	0.76	1.99	0.40	---
Average SUVmax/WM	average	1.90	Optimal *P* value	2.05	1.07	3.93	0.030	0.45
SUVmax/WM	maximum	1.90	Optimal *P* value	2.18	1.11	4.31	0.021	0.39
Average SUVmax	average	10.80	Optimal *P* value	0.47	0.20	1.09	0.077	0.35
SUVmax	maximum	12.4	Optimal *P* value	0.36	0.11	1.14	0.082	0.66
Force the hazard ratio to be > 1:								
Average SUVmax	average		Optimal *P* value	1.25	0.77	2.02	0.37	0.33
SUVmax	maximum	7.83	Optimal *P* value	1.35	0.83	2.19	0.22	0.32

Abbreviation: WM = white matter.

Table 4. All pairwise comparisons for Time of FDG-PET to death between different central nervous system tumor histologic subtypes*

Reference Histology	Tested Histology	HR	Low	High	*p*-value	Adj p (Holm)
GBM	AA	1.03	0.46	2.30	0.940	1
GBM	Anaplastic Oligo	0.37	0.16	0.83	0.016	0.15
GBM	Oligodendroglioma	0.16	0.04	0.67	0.013	0.13
GBM	Other**	0.25	0.08	0.83	0.023	0.19
AA	Anaplastic Oligo	0.46	0.14	1.49	0.195	1
AA	Oligodendroglioma	0.12	0.01	1.04	0.054	0.38
AA	Other**	0.40	0.10	1.57	0.189	1
Anaplastic Oligo	Oligodendroglioma	0.60	0.15	2.37	0.462	1
Anaplastic Oligo	Other**	0.62	0.16	2.42	0.493	1
Oligodendroglioma	Other**	1.06	0.21	5.37	0.945	1

*The omnibus F test from ANOVA with Tukey's HSD to control familywise error was used for all variables except for Time FDG-PET to death. The Cox proportional hazards model was used for Time FDG-PET to death. Significant findings for Time FDG-PET to death have P < 0.05 (unadjusted). There are no significant differences after familywise multiple comparison adjustment using the method of Holm. **Other comprised 2 patients with astroblastomas, 1 patient with brainstem anaplastic astrocytoma, 1 patient with anaplastic ependymoma, 1 patient with gliosarcoma and 1 patient with CNS lymphoma.

were noted between the histologic types and the variables of interest. A summary of those results are provided in **Table 2**.

Survival analysis was performed based on the time from the FDG-PET scan and death with adjustment for *p*-value as outlined in the data analysis section. For average SUVmax the cut-point of 10.8 was optimal, with higher average SUVmax uptake predicting a lower survival probability. However, it was not statistically significant (*p*-value of 0.077). Similarly, for SUVmax the cut-point of 7.9 was optimal, with higher SUVmax uptake predicting lower survival probability, but this was also not statistically significant (*p*-value of 0.4). When average SUVmax and SUVmax were normalized to the contralateral white matter (average SUVmax/WM and SUVmax/WM), these were both statistically significant with a cut-point of 1.90 (*p*-value of 0.03 and 0.021, respectively). However, when adjusted with familywise multiple comparison with the method of Holm, statistical significance was not present. Nevertheless, these results do show correlation between SUVmax alone and SUVmax/WM with survival.

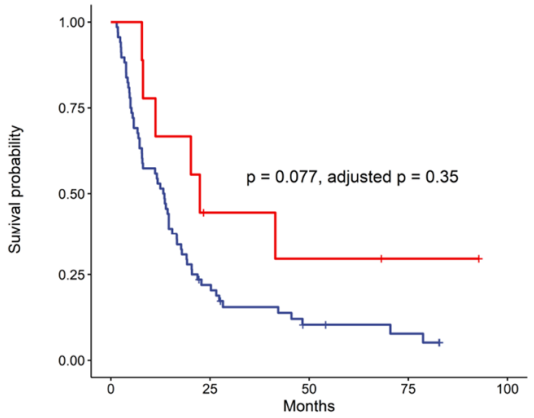

Figure 1. Average SUVmax optimal cut based on minimum *p*-value over all cut-points as a function of patient survival with regard to direction of effect. For average SUVmax the optimal cut point for prediction of patient survival was 10.8. Survival probability over time for patients with average SUVmax greater or less than 10.8 is shown.

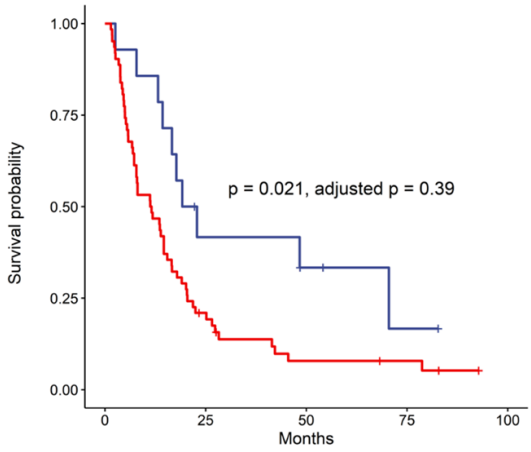

Figure 2. SUVmax/white matter (SUVmax/WM) optimal cut based on minimum *p*-value over all cut-points as a function of patient survival with regard to direction of effect. For SUVmax/WM the optimal cut point for prediction of patient survival was 1.9. Survival probability over time for patients with SUVmax/WM greater or less than 1.9 is shown.

These results are summarized in **Table 3**. The Kaplan-Meier survival curves for the metrics that show the cut-points that are most predictive of survival are shown in **Figures 1** and **2**.

There was statistical significance for only the length of time between the FDG-PET scan and death based on the histologic subtypes. In terms of discrete histologic sub-types, there was a significant difference with respect to survival between glioblastoma and oligodendroglioma, anaplastic oligodendroglioma, and other histologic subtypes. There was a correlation between survival with anaplastic astrocytoma and oligodendroglioma; however this was not significant (*p*-value of 0.054). These results are summarized in **Table 4**.

Representative Gd-MRI and FDG-PET images of patient CNS tumors along with SUVmax and SUVmax/WM values with patient-specific survival are shown in the images and legends for **Figures 3**-**5**.

Discussion

Important clinical information on primary brain tumors can be obtained using FDG-PET. This technique has been used to evaluate progression of malignancy, differentiate recurrence from necrosis, and also as a prognostic indicator [22, 25-28]. However, the reliability of FDG-PET as a prognostic predictor has been questioned by other studies [15, 18, 19, 21, 22, 28-31]. Glial tumors have significant histologic heterogeneity that may affect biopsy results, and ultimately the treatment course [32, 33]. Therefore, predicting postoperative and post treatment prognosis of such patients is complicated and challenging.

Research that indirectly supports the degree of uptake on FDG-PET as predictive of survival has been mounting. Cerebral metabolism and circulation have been found to be of ancillary significance in predicting prognosis in patients with primary brain tumors [34]. In a small prospective study population of 20 patients with primary brain tumors, Schifter et al. [35] demonstrated a significant association between tumor SUV average over serial examinations and survival. High-grade gliomas (anaplastic astrocytoma, anaplastic oligodendroglioma, and glioblastoma) are generally hypermetabolic on FDG-PET. In FDG-PET performed in 30 patients with high-grade gliomas, De Witte et al. [15] found that metabolic grade was predictive of survival in patients with glioblastoma, but was not superior to pathological grading in lesser grade malignant gliomas. Other prognostic indicators have been identified in patients with primary brain tumors including patient age, tumor location, and neurological status; however, FDG-PET tumor metrics have yet to be established as a practical indicator of survival time [36]. Numerous studies have

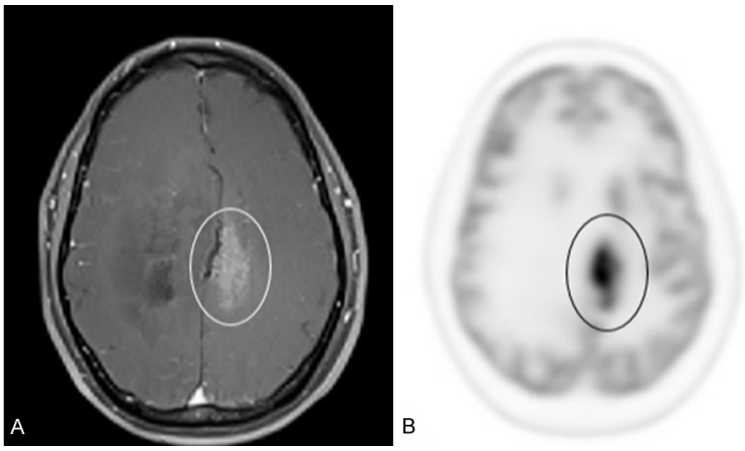

Figure 3. 39-year-old male at the time of imaging with initial pathology of low-grade glioma localized to the right parietal lobe treated with resection. Approximately 10 years later, follow-up Gd-MRI (A) showed a new focus of enhancement in the cingulate region contralateral to the treated lesion, which was suspicious for a recurrent high-grade anaplastic oligodendroglioma (white oval). FDG-PET scan (B) demonstrated an extremely hypermetabolic focus (SUVmax = 27.7, SUVmax/WM = 10.26) corresponding to the enhancing lesion on MRI (black oval). These values are consistent with recurrent high-grade tumor recurrence. Subsequent biopsy revealed malignant degeneration of the initial lesion to anaplastic oligodendroglioma. Despite the high FDG uptake the patient was still alive at the completion of our study, 87 months following the FDG-PET.

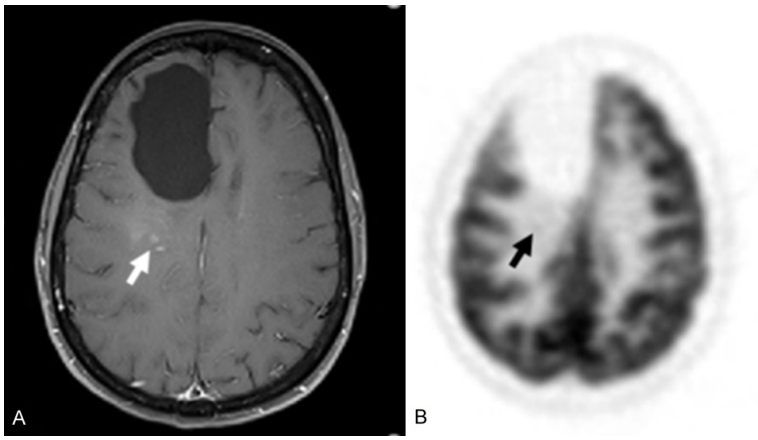

Figure 4. 37-year-old female with recurrent right frontal anaplastic astrocytoma treated with resection followed by radiation therapy with concurrent temozolomide and Carmustine. Follow-up Gd-MRI (A) showed small areas of nodular enhancement posterior to the resection cavity concerning for tumor recurrence (white arrow). FDG-PET scan (B) showed only subtle uptake posterior to the resection cavity corresponding to the foci of nodular enhancement on MRI (black arrow). (SUVmax = 3.1, ratio of SUVmax/WM = 0.95). The survival in this individual was 14 months from the time of FDG-PET.

shown that survival is longest in patients who have extensive tumor resection [37-46]. In a retrospective study examining pre-operative and post-operative tumor volumes in 92 patients with glioblastoma, Keles et al. [36] demonstrated a significant association between residual tumor volume and median survival time. However, there is not a widely accepted biomarker to predict survival during the course of therapy. FDG-PET has been used to differentiate recurrent tumor from radiation necrosis for nearly 30 years [18]. This underscores the potential utility in using FDG-PET semi-quantitative assessments such as SUVmax in predicting survival as an adjunct to multimodal treatment in patients with primary brain tumors. Although several imaging features have been established as prognostic correlates, conventional anatomic imaging with CT and MRI have not been well validated as reliable prognostic parameters in patients with primary brain tumors [47]. This current study is a prospective extension of a previous study performed at our institution [16]. In that study we noted that a ratio of tumor SUVmax to SUVmean of contralateral white matter with an optimized cut-off value of 1.90 was most predictive of detecting recurrent tumor vs. treatment effect. In the current study, the goal was to assess the ability of the semi-quantitative determinations of tumor SUVmax and the ratio of tumor SUVmax/WM to predict survival. This is a clinically relevant issue as many primary brain tumors become more aggressive over time and lower-grade tumors often dedifferentiate into higher-grade tumors. The challenges with such an approach are the variables of tumor location, size, age of patient, prior treatments, and other factors that all have potential effects on survival. An imaging assessment that would give a biologic or physiologic based snapshot at a critical time in the patient's treat-

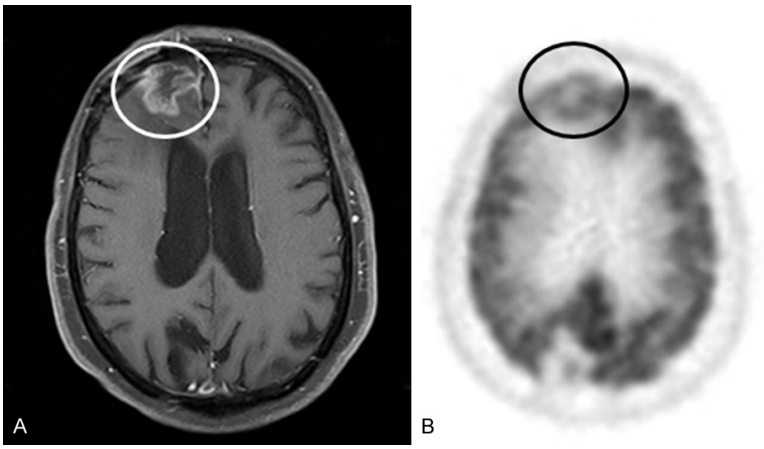

Figure 5. 75-year-old male with right frontal glioblastoma treated with resection followed by radiation therapy with neoadjuvant temozolomide. Follow-up Gd-MRI (A) showed nodular enhancement at the resection margins concerning for tumor recurrence (white circle). FDG-PET scan (B) showed a ring-like area of FDG uptake corresponding to the nodular enhancement on MRI concerning for recurrent tumor (black circle). (SUVmax = 9.03, Ratio of SUVmax/WM = 2.88). The survival in this individual was 8 months from the time of FDG-PET.

ment such as determining tumor recurrence versus treatment effect/radiation necrosis could provide important clinical information. The current study shows an association between a metabolic assessment with FDG-PET (SUVmax) and survival when a cut-point ratio of SUVmax/WM of 1.90 is used. There is also correlation of SUVmax alone with survival using a cut-point of 12.4, however, this value was not statistically significant. Finally, before corrections for multiple comparison adjustment there was a significant metabolic difference with respect to time of death between patients with GBM and oligodendroglioma, anaplastic astrocytoma and anaplastic oligodendroglioma with reduced survival from time of PET for patients with GBM.

There are some limitations to our study. We did not select a prospective absolute cut-point for either SUVmax or the ratio of SUVmax/WM. From our previous study [16], we postulated that the ratio cut-point should be close to 1.90. In fact, the current study also determines an optimized value of 1.90, which provides further evidence that the ratio method should be prospectively validated, in a potentially larger study. A potential confound of the study results is the use of 3 different PET/CT scanners. The GE Advance and GE ST scanner are equivalent in performance and reconstructed image quality. The majority of the patients (n = 70) were performed on one of those scanners. The GE Discovery 710 is a time of flight scanner. As noted previously, this scanner has an intrinsic bias to higher SUVmax values. However, this is negligible [23] and only a few patients were scanned using this system (n = 6). Furthermore, additional studies would also be necessary to determine whether reported SUV values from this study would apply to state-of-the-art PET scanners with digital PET detectors.

To date, no specific quantitative parameters have been widely accepted in predicting length of survival following post-treatment FDG-PET imaging. This study provides compelling evidence that a ratio of SUVmax to SUVmean of contralateral white matter when using a cut-point ratio of 1.90 may be appropriate for use in the clinical care of patients with primary brain tumors. Prospective studies with more participants would be necessary to confirm these findings.

In conclusion, semi-quantitative assessment of FDG uptake on PET is a potential metric for predicting survival in patients with primary brain tumors during the course of their treatment. This study demonstrates that FDG-PET demonstrates an association with survival in patients who have had treatment of a primary brain tumor when a cut-point ratio of SUVmax/WM of 1.90 is used. Additionally, before corrections for multiple comparison adjustment there was a significant metabolic difference with respect to time of death between patients with glioblastoma and oligodendroglioma and anaplastic oligodendroglioma. Our results may contribute to the refining of current treatment and counseling strategies for patients with primary brain tumors.

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Disclosure of conflict of interest

None.

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