Published in final edited form as:

Clin Imaging. 2013 ; 37(3): 451–457. doi:10.1016/j.clinimag.2012.08.008.

Comparison of the effectiveness of MRI Perfusion and Fluorine-18 FDG PET-CT for differentiating radiation injury from viable brain tumor

Vaios Hatzoglou, MD^{1,2}, Gary A. Ulaner, MD¹, Zhigang Zhang, PhD³, Kathryn Beal, MD⁴, Andrei I. Holodny, MD^{1,2}, and Robert J. Young, MD^{1,2}

¹Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York

²Brain Tumor Center, Memorial Sloan-Kettering Cancer Center, New York, New York

³Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York

⁴Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, New York

Abstract

Objectives—Differentiating radiation injury from viable tumor is important for optimizing patient care. Our aim was to directly compare the effectiveness of fluorine-18 fluorodeoxyglucose (FDG) PET-CT and dynamic susceptibility-weighted contrast-enhanced (DSC) MR perfusion in differentiating radiation effects from tumor growth in patients with increased enhancement following radiotherapy for primary or secondary brain tumors.

Materials and Methods—We retrospectively identified 12 consecutive patients with primary and secondary brain tumors over a 1-year period that demonstrated indeterminate enhancing lesions after radiotherapy and that had undergone DSC MR perfusion, FDG PET-CT, and subsequent histopathologic diagnosis. The maximum SUV of the lesion ($SUV_{\text{lesion max}}$), SUV_{ratio} ($SUV_{\text{lesion max}}/SUV_{\text{normal brain}}$), maximum relative cerebral blood volume ($rCBV_{\text{max}}$), percentage of signal intensity recovery (PSR) and relative peak height (rPH) were calculated from the PET and MR perfusion studies. A prediction of tumor or radiation injury was made based on these variables while being blinded to the results of the surgical pathology.

Results— SUV_{ratio} had the highest predictive value (area under the curve = 0.943) for tumor progression, although this was not statistically better than any MR perfusion metric (area under the curve = 0.757–0.829).

Conclusions—This preliminary study suggests that FDG PET-CT and DSC MR perfusion may demonstrate similar effectiveness for distinguishing tumor growth from radiation injury. Assessment of the SUV_{ratio} may increase the sensitivity and specificity of FDG PET-CT for differentiating tumor and radiation injury. Further analysis is needed to help define which modality has greater predictive capabilities.

Keywords

Differentiating radiation injury and tumor; MRI perfusion versus FDG PET/CT; $rCBV_{\text{max}}$; PSR; rPH; SUV_{ratio}

Introduction

Radiation therapy can help prolong survival for many patients with primary or metastatic brain tumors (1, 2). To assess treatment response, the current standard of care involves following patients clinically and with serial MRI examinations in order to assess treatment response. The detection of new or increased enhancement at the site of previously irradiated tumor may represent radiation injury or tumor growth. Resolving the etiology of increasing enhancement is frequently very difficult because radiation injury and tumor growth often demonstrate a similar appearance with conventional imaging (3, 4).

MR perfusion and FDG PET-CT are advanced imaging techniques that are commonly utilized as problem-solving tools to help make the correct diagnosis in this setting. Both studies provide insightful data about the biology and physiology of abnormal tissue enhancement that cannot be perceived with conventional imaging alone. Even though radiation injury and tumor can both enhance on MR imaging, they are fundamentally different on a pathologic and mechanistic basis. Tumor growth promotes angiogenesis and microvascular proliferation (5, 6). In contrast, radiotherapy decreases microvascular density and capillary perfusion because it typically induces endothelial cell damage and small-vessel injury (7–9). Additionally, histology-based research has demonstrated that the degree of capillary permeability is significantly different between the two entities (10, 11).

The ability of MR perfusion to quantify certain hemodynamic properties of enhancing brain lesions has shown promise for distinguishing malignant gliomas and metastases from radiation injury (12–14). Several retrospective studies have also suggested the efficacy and usefulness of FDG PET/CT for differentiating tumor growth from radiation injury based on the quantification of their metabolic activities (15–17). Although both MR perfusion and PET/CT are commonly performed, their comparative predictive value, sensitivity, specificity and indications remain uncertain.

We hypothesized that DSC MR perfusion is more effective than FDG PET-CT in distinguishing radiation injury from viable tumor. The high metabolic activity of background normal brain on FDG PET-CT often limits optimal assessment of brain lesions. Additionally, there are several studies that suggest FDG PET-CT is not sensitive or specific enough to be used routinely for this task (18–20). Therefore, the main objective of this preliminary study was to directly compare the effectiveness of MR perfusion and FDG PET-CT for discriminating between radiation injury and viable tumor with pathologic tissue diagnosis as the reference standard in all cases.

Materials and Methods

Patient Population

This study was performed after local Institutional Review Board approval and in compliance with Health Insurance Portability and Accountability Act regulations. We retrospectively identified 12 consecutive patients using a departmental database from January 2009 to January 2010 who met the following criteria: diagnosis of primary or metastatic intra-axial brain tumor, treatment with radiotherapy, subsequent new or increased enhancing brain lesions on MRI within the radiation field that were indeterminate by conventional imaging for radiation induced injury versus tumor growth, DSC MR perfusion and FDG PET-CT evaluation of the enhancing lesions, and subsequent histopathologic diagnosis. To limit major potential changes in the characteristics of the lesions, patients that had their MR perfusion and FDG-PET examinations greater than 1 month apart were excluded. Patients with gliomas who demonstrated increased enhancement within 6 months of treatment with

radiation and temozolomide were also excluded, as changes to their images were potentially attributable to pseudoprogression rather than the effects of radiotherapy (21).

DSC T2* MR Perfusion Protocol and Analysis

DSC gradient-echo echo-planar (TR/TE, 1050/20 ms; flip angle, 20–40°) images were obtained with a 5-mm section thickness and no intersection gap. Up to 16 slices were acquired to cover the entire lesion volume as identified by FLAIR and fast-spin echo images. A series of 60 multi-slice acquisitions were performed at 1-second intervals. The first 10 acquisitions were performed prior to the contrast agent injection to establish a pre-contrast baseline. At the 10th acquisition, a standard dose of gadopentate diglumine (Gd-DTPA; 0.1 mmol/kg of body weight) was injected with a power injector at a flow rate of 4–5 mL/sec through an intravenous catheter (18–21 gauge), followed immediately by a 20-mL continuous saline flush. The raw DSC images were transferred to a commercially available perfusion image processing workstation (Advantage Workstation, GE Healthcare). A board-certified neuroradiologist processed the images using commercially available software (Functool 4.3, GE Healthcare) while blinded to the FDG PET/CT results and histopathologic outcome. T2* susceptibility signal-intensity time curves were derived on a voxel-by-voxel basis from the DSC data. Standard algorithms without leakage correction have been described as achieving approximately 81% accuracy (22) and have provided acceptable results in our experience. A 50-mm² region-of-interest (ROI) was drawn around the enhancing region with the highest CBV and another 50-mm² ROI was drawn around the contralateral normal-appearing white matter in the same plane. Small, fixed diameter ROIs have been described as providing accurate and reproducible perfusion results (23–25). Areas of hemorrhage, nonenhancing cystic or necrotic change, blood vessels and susceptibility artifact were explicitly excluded. The T2* signal-intensity time curves generated for the ROI were used to quantify rCBV_{max}, rPH and PSR as described by Barajas et al in previous studies (12, 13).

Fluorine-18 fluorodeoxyglucose (FDG) PET-CT Protocol and Analysis

All patients fasted for at least 6 hours prior to the study and blood glucose was checked by finger stick. If the blood glucose was >60 and <200mg/dL the study continued as planned. If the blood sugar was between 200 and 300mg/dL, a standard insulin administration protocol was used to bring the blood glucose below 200. If blood glucose was > 300mg/dL or <60, the study was rescheduled.

10 mCi of Fluorine-18 fluorodeoxyglucose (FDG) was injected intravenously and the patient remained seated quietly in the injection room for 60 minutes. The patient was then positioned on a GE Discovery ST or STE PET/CT. A scout view of the head was acquired at 30 mA, 120 kVp. Once the scanning field was determined from the scout, a spiral CT was acquired using a full helical acquisition at 1 sec/rotation, 30 mA, 140 kV, 5.0 mm slice thickness, and 4.5 mm interval. Immediately upon completion of the CT, acquisition of a 10-minute 3D brain PET scan was performed. CT and PET data were re-reconstructed using a 30 cm field of view. CT, PET, and hybrid images were evaluated in transaxial, coronal, and sagittal planes. The SUV_{lesion max}, SUV of normal white matter (SUV_{normal brain}) and SUV_{ratio} were calculated using standard ROI tools by a board-certified nuclear medicine physician blinded to both MR perfusion results and histopathologic outcome.

Statistical Analysis

We determined the predictive value of FDG PET-CT and DSC MRI perfusion using various statistical tools, including two-sample t-test (previous analysis had shown PET and MRI perfusion measurements to be reasonably symmetric and have a small range). We also performed logistic regression and receiver operating characteristic (ROC) analysis. To

approximately assess the power of the analysis, we focused on the two-sample t-test with the type I error rate of 5%. For the ROC analysis, the area under the curve (AUC) was computed for both FDG PET-CT and DSC MR perfusion. Bootstrap confidence intervals were constructed to compare the predictive values of these advanced imaging methods and the difference was calculated and examined as to whether it was significantly different from 0. Cutoff values for the different imaging variables were estimated by maximizing the sum of sensitivity and specificity.

Results

Patient Population

There were 5 men and 7 women with a mean age of 56.7 years at the time increased intracranial enhancement was first identified by conventional MR imaging. Three patients had glioblastoma multiforme and 9 had brain metastases (4 non-small cell lung cancer, 2 breast cancer, 2 renal cell carcinoma, and 1 spindle cell sarcoma). Seven patients received stereotactic radiosurgery (SRS, 18–21 Gy), 2 patients whole brain radiation (35–52.5 Gy) and 3 patients partial brain radiation therapy (59.4–60 Gy). Each patient had a single indeterminate lesion for a total of 12 abnormalities that were evaluated by both FDG PET-CT and MR perfusion. Nine patients had both of their scans on the same date, 1 patient had 1 day between scans, 1 patient had 14 days between scans, and for one patient 28 days elapsed between scans. Seven of the 12 lesions were histopathologically diagnosed as radiation necrosis (6 by gross total resection and 1 via biopsy). Five lesions were diagnosed as recurrent tumor after gross total resection. These findings are summarized in Table 1.

Accuracy of DSC MR Perfusion Variables

Compared with lesions caused by radiation injury, lesions caused by tumor growth exhibited decreased PSR. ROC analysis demonstrated an area under the curve (AUC) of 0.829 for PSR as a predictive variable. An optimal cutoff value of 74% optimized differentiation of the histopathologic groups (Fig. 1a, b, c) with a sensitivity of 60% and a specificity of 100%. The lesions that were diagnosed as tumor growth demonstrated higher values for $rCBV_{max}$ than the lesions diagnosed as radiation injury (Fig. 1a, b, c and Fig. 2a, b). The AUC for this variable was 0.771 with an optimal cutoff value for tumor detection of 1.8. This threshold was 100% sensitive and 71% specific. Tumor demonstrated higher rPH values than did lesions caused by radiation injury. The AUC of relative peak height was 0.757 with an optimal cutoff value of 2.2. The sensitivity for tumor detection utilizing this threshold was 60% and the specificity was 100%.

Accuracy of FDG PET-CT

With a cutoff value of 1.4 (area under the curve = 0.943), SUV_{ratio} was 80% sensitive and 100% specific for detection of tumor recurrence (Fig. 1d, e and Fig. 2c, d). In addition, using the more traditional approach of visual analysis and consideration of only $SUV_{lesion\ max}$ (rather than looking at the ratio which also factors in the SUV of normal brain), ROC analysis demonstrated an area under the curve of 0.571 in predicting viable tumor rather than radiation injury. This was significantly worse than the performance of SUV_{ratio} .

Which variable is more accurate for predicting viable tumor or radiation injury?

In our study, SUV_{ratio} has the highest predictive value, but this superiority is not significant when compared to rPH, PSR, and $rCBV_{max}$ based on both permutation and bootstrap tests (the small sample size cannot generate p-values small enough when comparing these predictors). The proposed threshold values for these 4 variables based on our preliminary data are summarized in Table 2.

Discussion

Distinguishing between radiation changes and tumor progression in patients with brain tumors treated with radiation therapy and who later present with new enhancement is one of the frequent challenges in neuro-oncologic imaging. Radiation injury reflects a known complication of treatment that often requires chronic corticosteroid therapy or surgery. Tumor growth indicates a treatment failure and necessitates the exploration of a new therapeutic approach. Making an accurate distinction is paramount and the inability to differentiate between these two diagnoses weighs on both patients and physicians alike.

In an attempt to address this important issue, different imaging techniques such as MR perfusion (12–14), MR spectroscopy (26–28), diffusion tensor imaging (DTI) (29), and FDG PET-CT (15–20) have been utilized with varying degrees of success. As there is currently no clear consensus on which modality is the most reliable, our experience is that many treating physicians order multiple scans as a way of gathering complementary information and increasing diagnostic accuracy. This reasonable practice may not be sustainable as health care spending in the United States continues to outpace the growth of the economy. There is currently a powerful movement in the United States driving policy reform that seeks to not only to improve effectiveness but also cost-effectiveness, safety and the sustainability of health care (30). The costs of MR perfusion are less than FDG PET-CT in terms of price (no dedicated charge versus ~\$900 at our institution), time (60 second sequence versus 1 hour FDG uptake period and 20 minute scan), radiation (none versus ~5millisieverts), and convenience (no separate appointment needed for MR perfusion, as nearly all brain tumor patients already undergo MR imaging for routine surveillance). In this era of contracting health care dollars, it is expensive and inefficient to perform more than one advanced imaging study to answer the same question. There is an urgent need to determine which imaging technique is best suited for accurately predicting tumor growth and radiation injury in these patients.

Our objective was to approach an answer to this question by directly comparing the effectiveness of the two most commonly used techniques at our institution: DSC MR perfusion and FDG PET-CT. We found that DSC MR perfusion variables ($AUC=0.757-0.829$) outperformed PET imaging when subjective visual interpretation and standard SUV measurements were used to predict changes associated with either tumor growth or radiation effects ($AUC=0.571$). This was not the case when SUV_{ratio} was factored into the analysis. We found that the predictive value of SUV_{ratio} ($AUC=0.943$) was better than any of the MR perfusion metrics, although this was not statistically significant.

We decided to explore the utility of SUV_{ratio} because several prior reports have demonstrated that maximum uptake ratio (tumor to normal background) can predict characteristics and prognosis of brain tumors in addition to malignancies in other organ systems (31–33). SUV_{ratio} has been applied to help differentiate tumor from radiation effects in another recent short series (34). The ROC curve analysis for that study demonstrated an area under the curve of 0.875 for SUV_{ratio} with a cutoff value of 1.45 that was 100% sensitive and 75% specific. These results are similar to our preliminary findings that an optimal threshold of 1.4 is 100% sensitive and 81% specific (area under the curve =0.943) for accurately detecting tumor recurrence. Further evaluation of SUV_{ratio} is warranted in larger scale prospective studies to see if these results can be validated.

DSC MR perfusion allows the quantification of 3 hemodynamic variables (rCBV, rPH and PSR) that have been demonstrated to reflect vascular hyperplasia, total capillary volume and alterations in capillary permeability (35–37). Our findings that enhancing tumor demonstrates decreased PSR, increased rPH, and increased rCBV in comparison to radiation

injury are consistent with the existing literature. The optimal cutoff values for the hemodynamic variables that we report are also similar to findings of prior studies and confirm that DSC MR perfusion can be very useful as a problem-solving tool when conventional imaging cannot distinguish between tumor and radiation effects.

To our knowledge, there has only been one other study that directly compares the effectiveness of MR perfusion and FDG PET-CT in the same set of patients for predicting radiation injury or tumor growth (34). That short retrospective study, mentioned previously, investigated 10 patients, but only 3 indeterminate lesions had tissue analysis. Among the strengths of our study are that all 12 patients were confirmed to have tumor growth or radiation injury by histopathologic diagnosis (11 via gross total resection) which is the gold standard. We excluded any patients without tissue sampling in order to increase confidence in our data and proposed cutoff values for the 4 different variables we assessed.

Our study has several limitations in addition to its retrospective design. First, our strict inclusion criteria restricted our study population to 12 patients. The bootstrap and permutation tests we performed demonstrated that SUV_{ratio} had the highest predictive value, but this was not statistically superior to PSR, rPH and $rCBV_{max}$. Second, we included patients with both primary and metastatic brain tumors. Previous studies have looked at these populations separately when comparing their hemodynamic properties to radiation effects. By segregating the patients with brain metastases from those with high-grade gliomas, it may be possible to achieve more precise cutoff values than those achieved here, although recent data has demonstrated significant overlap in rCBV and relative peak height between the 2 entities (38, 39). In contrast, there is a more significant difference with assessment of PSR which is lower in metastatic lesions than high-grade gliomas. This finding is probably attributable to a complete absence of the blood-brain barrier in the setting of metastases, which results in increased capillary permeability (39). Notably, our optimal threshold value of 74% for PSR is very similar to the 76.3% recently determined by Barajas et al when comparing metastases (13) to radiation injury but is lower than the 87.3% from a study comparing GBM to radiation injury (12); this makes sense in that 9 of our 12 patients had metastases while only 3 had high-grade gliomas.

Conclusions

It is important to establish useful quantitative parameters to accurately diagnose tumor growth and radiation injury in patients who have undergone radiotherapy and subsequently manifested increased enhancement. We compared the accuracy of four variables derived from lesions assessed with both DSC MR perfusion and FDG PET-CT and subsequently had pathologic diagnosis in all cases. Our preliminary data suggests similar predictive capabilities for both studies. SUV_{ratio} may increase the sensitivity of FDG PET-CT and further evaluation of this variable is warranted. Additionally, a large prospective trial directly comparing DSC MR perfusion and FDG PET-CT is needed to establish which modality physicians should be ordering for brain tumor patients and to validate associated biomarkers and optimal thresholds.

References

1. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *New Engl J Med*. 2005; 352:987–996. [PubMed: 15758009]
2. Mintz A, Perry J, Spithoff K, et al. Management of single brain metastasis: a practice guideline. *Curr Oncol*. 2007; 14:131–143. [PubMed: 17710205]
3. Valk PE, Dillon WP. Radiation injury of the brain. *AJNR Am J Neuroradiol*. 1991; 12:45–62. [PubMed: 7502957]

4. de Wit MC, de Bruin HG, Eijkenboom W, et al. Immediate post-radiotherapy changes in malignant glioma can mimic tumor progression. *Neurology*. 2004; 63:535–537. [PubMed: 15304589]
5. Brem S. The role of vascular proliferation in the growth of brain tumors. *Clin Neurosurg*. 1976; 23:440–453. [PubMed: 975695]
6. Gigtenbeek JM, Wesseling P, Maass C, et al. Three-dimensional reconstruction of tumor microvasculature: simultaneous visualization of multiple components in paraffin embedded tissue. *Angiogenesis*. 2005; 8:297–305. Epub 2005 Nov 19. [PubMed: 16328157]
7. Remler MP, Marcussen WH, Tiller-Borsich J. The late effects of radiation on the blood brain barrier. *Int J Radiat Oncol Biol Phys*. 1986; 12:1965–1969. [PubMed: 3771316]
8. Doms JC, Hecht S, Brant-Zawadzki M, et al. Brain radiation lesions: MR imaging. *Radiology*. 1986; 158:149–155. [PubMed: 3940373]
9. Nishimura R, Takahashi T, Morishita S, et al. MR Gd-DTPA enhancement of radiation injury. *Radiat Med*. 1992; 10:101–108. [PubMed: 1509101]
10. Long DM. Capillary ultrastructure in human metastatic brain tumors. *J Neurosurg*. 1979; 51:53–58. [PubMed: 448419]
11. Kamiryo T, Lopes MB, Kassell NF, et al. Radiosurgery-induced microvascular alterations precede necrosis of the brain neuropil. *Neurosurgery*. 2001; 49:409–415. [PubMed: 11504117]
12. Barajas RF, Chang JS, Segal MR, et al. Differentiation of recurrent glioblastoma multiforme from radiation necrosis after external beam radiation therapy with dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. *Radiology*. 2009; 253:486–496. [PubMed: 19789240]
13. Barajas RF, Chang JS, Sneed PK, et al. Distinguishing recurrent intra-axial metastatic tumor from radiation necrosis following gamma knife radiosurgery using dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. *AJNR Am J Neuroradiol*. 2009; 30:367–372. [PubMed: 19022867]
14. Hu LS, Baxter LC, Smith KA, et al. Relative cerebral blood volume values to differentiate high-grade glioma recurrence from posttreatment radiation effect: Direct correlation between image-guided tissue histopathology and localized dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging measurements. *AJNR Am J Neuroradiol*. 2009; 30:552–558. [PubMed: 19056837]
15. Petronas NJ, DiChiro G, Brooks RA, et al. Work in progress: [18F] fluorodeoxyglucose and positron emission tomography in the evaluation of radiation necrosis of the brain. *Radiology*. 1982; 144:885–889. [PubMed: 6981123]
16. Ericson K, Kihlstrom L, Mogard J, et al. Positron emission tomography using 18F-fluorodeoxyglucose in patients with stereotactically irradiated brain metastases. *Stereotact Funct Neurosurg*. 1996; 66(suppl 1):214–224. [PubMed: 9032864]
17. Chao S, Suh J, Raja S, et al. The sensitivity and specificity of FDG PET in distinguishing recurrent brain tumor from radionecrosis in patients treated with stereotactic radiosurgery. *Int J Cancer*. 2001; 96:191–197. [PubMed: 11410888]
18. Griffeth LK, Rich KM, Dehdashti F, et al. Brain metastases from non-central nervous system tumors: evaluation with PET. *Radiology*. 1993; 186:37–44. [PubMed: 8416584]
19. Kahn D, Follet KA, Bushnell DL, et al. Diagnosis of recurrent brain tumor: value of 201Tl SPECT vs 18F-fluorodeoxyglucose PET. *AJR Am J Roentgenol*. 1994; 163:1459. [PubMed: 7992747]
20. Ricci PE, Karis JP, Heiserman, et al. Differentiating recurrent tumor from radiation necrosis: time for re-evaluation of positron emission tomography? *AJNR Am J Neuroradiol*. 1998; 19:407–413. [PubMed: 9541290]
21. Brandsma D, Stalpers T, Taal W, et al. Clinical features, mechanisms, and management of pseudoprogression in malignant glioma. *Lancet Oncol*. 2008; 9:453–461. [PubMed: 18452856]
22. Hu LS, Baxter LC, Pinnaduwage DS, et al. Optimized preload leakage-correction methods to improve the diagnostic accuracy of dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging in posttreatment gliomas. *AJNR Am J Neuroradiol*. 2010; 31:40–48. [PubMed: 19749223]
23. Wetzel SG, Cha S, Johnson G, et al. Relative cerebral blood volume measurements in intracranial mass lesions: interobserver and intraobserver reproducibility study. *Radiology*. 2002; 224:797–803. [PubMed: 12202717]

24. Young R, Babb J, Law M, et al. Comparison of region-of-interest analysis with three different histogram analysis methods in the determination of perfusion metrics in patients with brain gliomas. *J Magn Reson Imaging*. 2007; 26:1053–1063. [PubMed: 17896374]
25. Cha S, Knopp EA, Johnson G, et al. Intracranial mass lesions: dynamic contrast-enhanced susceptibility-weighted echo-planar perfusion MR imaging. *Radiology*. 2002; 223:11–29. [PubMed: 11930044]
26. Graves E, Nelson S, Vigneron D, et al. Serial proton MR spectroscopic imaging of recurrent malignant gliomas after gamma knife radiosurgery. *AJNR Am J Neuroradiol*. 2001; 22:613–624. [PubMed: 11290467]
27. Schlemmer H, Bachert P, Herfarth K, et al. Proton MR spectroscopic evaluation of suspicious brain lesions after stereotactic radiosurgery. *AJNR Am J Neuroradiol*. 2001; 22:1316–1324. [PubMed: 11498420]
28. Sundgren PC. MR Spectroscopy in radiation injury. *AJNR Am J Neuroradiol*. 2009; 30:1469–1476. [PubMed: 19369613]
29. Sundgren PC, Fan X, Weybright P, et al. Differentiation of recurrent brain tumor versus radiation injury using diffusion tensor imaging in patients with new contrast enhancing lesions. *Magn Reson Imaging*. 2006; 24:1131–1142. [PubMed: 17071335]
30. Institute of Medicine. Initial national priorities for comparative effectiveness research. Washington, DC: National Academies Press; 2009.
31. Kato T, Shinoda J, Nakayama N, et al. Metabolic assessment of gliomas using ^{11}C -methionine, ^{18}F fluorodeoxyglucose, and ^{11}C -choline positron-emission tomography. *AJNR Am J Neuroradiol*. 2008; 29:1176–1182. [PubMed: 18388218]
32. Borbely K, Nyary I, Toth M, et al. Optimization of semi-quantification in metabolic PET studies with ^{18}F -fluorodeoxyglucose and ^{11}C -methionine in the determination of malignancy of gliomas. *J Neurol Sci*. 2006; 246:85–94. [PubMed: 16603193]
33. Shiomi S, Nishiguchi S, Ishizu H, et al. Usefulness of positron emission tomography with fluorine-18-fluorodeoxyglucose for predicting outcome in patients with hepatocellular carcinoma. *Am J Gastroenterol*. 2001; 96:1877–1880. [PubMed: 11419843]
34. Kim YH, Oh SW, Lim YJ, et al. Differentiating radiation necrosis from tumor recurrence in high-grade gliomas: Assessing the efficacy of ^{18}F -FDG PET, ^{11}C -methionine PET and perfusion MRI. *Clin Neurol Neurosurg*. 2010; 112:758–765. [PubMed: 20619531]
35. Aronen HJ, Gazit IE, Louis DN, et al. Cerebral blood volume maps of gliomas: comparison with tumor grade and histologic findings. *Radiology*. 1994; 191:41–51. [PubMed: 8134596]
36. Lupo JM, Cha S, Chang SM, et al. Dynamic susceptibility-weighted perfusion imaging of high-grade gliomas: characterization of spatial heterogeneity. *AJNR Am J Neuroradiol*. 2005; 26:1446–1454. [PubMed: 15956514]
37. Cha S, Lu S, Johnson G, et al. Dynamic susceptibility contrast MR imaging: correlation of signal intensity changes with cerebral blood volume measurements. *J Magn Reson Imaging*. 2000; 11:114–119. [PubMed: 10713942]
38. Cha S, Lupo JM, Chen MH, et al. Differentiation of glioblastoma multiforme and single brain metastasis by peak height and percentage of signal intensity recovery derived from dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. *AJNR Am J Neuroradiol*. 2007; 28:1078–1084. [PubMed: 17569962]
39. Mangla R, Kholar B, Zhu T, et al. Percentage signal intensity recovery derived from MR dynamic susceptibility contrast imaging is useful to differentiate common enhancing malignant lesions of the brain. *AJNR Am J Neuroradiol*. 2011; 32:1004–1010. [PubMed: 21511863]

Fig 1.

This 52-year-old female patient with history of breast cancer metastasis demonstrates a right frontal enhancing lesion (A) that increased in size 23.2 months after treatment with stereotactic radiosurgery. The CBV map (B) with region of interest analysis and corresponding T2* signal intensity time curve (C) demonstrate 89% PSR and $rCBV_{max}$ of 1.2. The FDG PET-CT study (D, E) demonstrates that $SUV_{lesion\ max}$ (red box) is 4.9 and $SUV_{normal\ brain}$ is 3.9 (green box) with SUVratio (4.9/3.9) of 1.26. The lesion was resected and pathologically proven to be radiation necrosis.

Fig 2.

This male patient with a history of right frontal lobe glioblastoma multiforme presents with increased enhancement on axial T1-weighted imaging (A) 12.3 months after completion of radiation therapy. The region of interest analyses for the MRI perfusion (B) and FDG PET-CT (C, D) examinations demonstrate an $rCBV_{max}$ of 3.6 and SUV_{ratio} of 2.0. The $SUV_{lesion\ max}$ is 8.2 (red box) and the $SUV_{normal\ brain}$ is 4.1 (green box). The lesion was resected and pathologically proven to be recurrent tumor.

Table 1

Patient characteristics at the time increased enhancement was first identified

Mean Age	56.7 years
Diagnosis	
Glioblastoma multiforme	3
Metastasis to the brain [*]	9
Type of radiation received	
Stereotactic radiosurgery (18–21 Gy)	7
Whole brain radiation (35–52.5 Gy)	2
Partial brain radiation (59.4 – 60 Gy)	3
Days between the two scans, per patient	
Same day	9
1 day	1
14 days	1
28 days	1
Histopathologic findings upon resection	
Radiation necrosis	7 [†]
Recurrent tumor	5

^{*} 4 non-small cell lung cancers, 2 breast cancers, 2 renal cell carcinomas, 1 spindle cell sarcoma;

[†] Of these 7 one was diagnosed not by gross total resection but rather by biopsy

Table 2

Sensitivity and Specificity of Proposed Threshold Values for 4 Variables

	Threshold	AUC	Sensitivity	Specificity
SUV _{ratio}	1.4	0.943	80%	100%
rCBV _{max}	1.8	0.771	100%	71%
PSR	74%	0.829	60%	100%
rPH	2.2	0.757	60%	100%