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[¹⁸F]2-Fluoro-2-Deoxyglucose–Positron Emission Tomography Correlation of Gadolinium-Enhanced MR Imaging of Central Nervous System Neoplasia

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PURPOSE: To correlate the findings of gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA)enhanced MR imaging with positron emission tomography (PET) in the evaluation of central nervous system neoplasia. MATERIALS AND METHODS: Thirty-six lesions identified on noncontrast MR in 35 patients with biopsy-proved intracranial tumors were imaged with both T1-weighted Gd-DTPA MR at 1.5 T and [18F]2-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET). Eighteen women and 17 men with a mean age of 47.1 years (range 22-72) were studied. The degrees of Gd-DTPA enhancement and FDG uptake were rated separately, and then all scans were reviewed together. FDG uptake was graded 1-5. RESULTS: Of the 35 lesions rated, 30 had Gd-DTPA enhancement and 28 of these were hypermetabolic (FDG accumulation greater than white matter) on PET (93% concordance). Twenty-six of 32 neoplastic lesions had Gd-DTPA enhancement. Twenty-four of these enhancing tumors were hypermetabolic. Only one lesion was completely missed on PET but identified on routine spin echo MR. CONCLUSION: Gd-DTPA MR and FDG-PET are complementary and there is a high concordance of Gd-DTPA-enhancing tumors displaying FDG hypermetabolism. Although FDG hypermetabolism and Gd-DTPA enhancement are usually suggestive of high-grade malignancy, anaplastic astrocytomas may not enhance with Gd-DTPA and can be hypometabolic. In addition, benign intracranial tumors (two cases of meningioma) and radiation necrosis can be associated with both FDG uptake and Gd-DTPA enhancement.

Index terms: Positron emission tomography (PET); Magnetic resonance, comparative studies; Brain neoplasms

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The evolving role of gadopentetate dimeglumine (Gd-DTPA) in imaging cerebral neoplasms is being established (1, 2). The mechanism of enhancement is attributed to leakage of the paramagnetic contrast agent into the extravascular space in regions of blood-brain barrier disruption (3–6). Gd-DTPA enhancement of cerebral astrocytomas has been associated with histologic areas of malignant neovascularity and endothelial proliferation (7) and can be associated with a higher tumor malignant grade, as has been determined for computed tomography (CT) enhancement of gliomas (8).

Positron emission tomography (PET) provides functional information and is showing efficacy in characterizing the degree of brain tumor malignancy by the relative amount of [¹⁸F]2-fluoro-2deoxyglucose (FDG) metabolism (9–13). Correlation of PET imaging with C-11-I-methionine and Gd-DTPA enhancement in patients with central nervous system neoplasm has been reported in a small series of 14 patients (14). We report our correlation of Gd-DTPA magnetic resonance (MR) with FDG-PET imaging.

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Materials and Methods

Thirty-five patients, including 17 men and 18 women with cerebral neoplasms, comprised the patient study group. Both MR and PET studies were performed preoperatively on 20 patients; both studies were performed after surgical resection for 15 patients. No change in therapy occurred between the two studies. For 28 patients, the two scans were performed within 1 month of each other. The age range of the patients was 22 to 72 years (mean age = 47.1 years).

MR imaging was performed on a 1.5-T spectrometer (GE Signa). T1-weighted (500/20; repetition time/echo time), proton density, and T2-weighted images (2000/40, 80) were acquired axially with a 5-mm slice thickness and 2.5-mm interslice gap. Additional T1-weighted images were obtained after the intravenous administration of 0.1 mmol/kg Gd-DTPA. All PET studies were on an ECAT-911 scanner (CTI, Knoxville, TN). For each patient, 12 to 15 images were obtained parallel to the orbitomeatal line starting 30 minutes after the intravenous administration of 10 mCi of FDG.

All tumors were histologically proved by either open or stereotactic biopsy. The majority of tumors were gliomas (n = 22); other tumors included lymphomas (n = 2), metastases (n = 4), and meningiomas (n = 4). The histology of the four meningiomas were re-reviewed as to cellularity (normal or hypercellular), nucleoli size (+1 (micro) to +3 (macro)), and mitoses (absent or present). The gliomas were characterized histologically as glioblastoma multiforme, anaplastic astrocytoma (AA), astrocytoma (astro), anaplastic oligodendroglioma, or ependymoma. Two patients had biopsy-proved radiation necrosis, and no tumor was identified in three patients who had undergone total surgical resection of their primary brain tumors.

Two observers (W.K.D., O.B.B.) retrospectively reviewed the MR scans as a consensus opinion blinded to the PET scan results. Classification of Gd-DTPA enhancement was made qualitatively by comparing intensity of lesion enhancement with the normal enhancement of the choroid plexus. Lesions were divided qualitatively into three enhancement groups: 1) none, 2) less than choroid plexus, and 3) equal to choroid plexus.

Two different observers (J.M.H., M.W.H.) reviewed the PET scans as a consensus opinion without knowledge of the results of the Gd-DTPA MR study. The PET studies were graded as either normal or abnormal. Using only the noncontrast MR images for anatomic localization, FDG accumulation in a lesion was compared with corresponding contralateral hemisphere white and gray matter that had normal signal intensity on the MR scans. Lesion uptake of FDG was graded: 0 (equal to background), 1 (less than white matter), 2 (equal to white matter), 3 (between white and gray matter), 4 (equal to gray matter), or 5 (more than gray matter). Lesions of PET Grade 2 or less were considered hypometabolic, and lesions of PET Grade 3 or more were considered hypermetabolic. For purposes of statistical analysis, the average FDG uptake was determined for each tumor or lesion type. Statistical analysis included crosstabulation with determination of chi-square and P value. Heterogeneous lesions were graded according to the region with the highest grade on both histologic and imaging studies.

All four observers made a final group review of MR and PET scans. One tumor was scored as not being detected by PET (Case 24). Only one lesion fell in the group of enhancement less than that of choroid; this lesion was combined into the larger group of enhancement equal to choroid plexus.

Results

In the 35 patients studied, the MR and PET findings in 37 suspected lesions were reviewed (Table 1). All lesions were identified on spin echo MR imaging, but only one (case 24) could not be visualized by FDG-PET. One lesion thought to be present on PET showed normal signal intensity on MR and was considered a false-positive (case 35), giving a total of 35 lesions rated.

Thirty lesions demonstrated Gd-DTPA enhancement and the majority of these (28 lesions) were graded on FDG-PET as Grade 3 or greater (hypermetabolic). Only two hypermetabolic lesions (cases 13 and 14; grades 4 and 5) did not enhance with Gd-DTPA.

The six nonenhancing lesions showed FDG uptake grade ranging from 1 to 5 (Table 1). The Gd-DTPA-enhancing lesions correlated significantly (chi-square = 12.3, P = .02) with an increasing grade of FDG uptake (Table 2). Hypometabolic lesions (less than or equal to grade 2) showing enhancement included an AA (case 8) and a meningioma (case 28).

Based on histologic category, higher grade tumors demonstrated a trend of increased FDG uptake and Gd-DTPA enhancement (Table 2). The two meningiomas (cases 29 and 31) having Grade 5 FDG uptake had marked hypercellularity, with +3 nucleoli size and mitoses present. The other two meningiomas (cases 28 and 30) with Grade 2 or 3 PET were normocellular, with +1 or +2 nucleoli size and no mitoses.

When correlating Gd-DTPA enhancement with FDG-PET metabolic profile, four trends were seen, as described below.

Gd-DTPA Enhancement and Hypermetabolism

The majority of the lesions demonstrated both enhancement with Gd-DTPA and hypermetabolism with FDG (93% concordance) (case 27, Fig. 1). One patient had a hypermetabolic region on FDG-PET slightly separated from an area of Gd-

Histology ^a	Case No ^b	FDG-PET Uptake Grade and Total Lesion Number ^c						Gd-DTPA
		0	1	2	3	4	5	Enhancement ^d
GBMF	1-7	-	_	_	_	2	5	+
AA	8-12	-	-	1	1	_	3	+
	13, 14	-	-	-	-	1	1	-
Astro	15, 16	-	-	_	2	-	-	+
	17-19	_	3	-	-	_	-	-
A oligo	20, 21	-	-	-	-	1	1	+
Lymphoma	22, 23	-	-	-	-	-	2	+
Ependymoma	24	ND	-	_	-	-	-	—
Metastasis	25, 26	-	-	-	1	-	1	+
	27	-	_	-	-	-	2	+
Meningioma	28-31	-	-	1	1	-	2	+
Necrosis	12, 32	-	-	-	2	-	_	+
No tumor	33, 34	-	-	_	_	_	2	+
	35	-	-	-	1	_	-	_

TABLE 1: Tabulation of histology, PET metabolism, and Gd-DTPA enhancement

^e GBMF, glioblastoma multiforme; Astro, astrocytoma; A oligo, anaplastic oligodendroglioma.

^b 35 patients were studied; case 12 had two lesions graded (FDG uptake grade 5 for AA and FDG uptake grade 3 for necrosis), as did case 27 (metastasis).

^c Grading criteria summarized in Materials and Methods.

^d +, Present and equal to choroid plexus enhancement; -, not present.

ND, lesion not detected.

TABLE 2: FDG uptake grade versus Gd-DTPA enhancement

FDG-PET	Gd Enha		
Uptake Grade ^a	No	Yes	
0	0	0	
1	3	0	
2	0	2	
3	1	7	
4	1	3	
5	1	18	
ND	1	0	

^a Grading summarized in Materials and Methods. ND, not detected.

DTPA enhancement (case 33, Fig. 2). This patient had undergone total resection of a glioma, with the enhancement being postoperative change confirmed on follow-up MR studies (Figs. 2A and 2B). The small focal area of hypermetabolism on the PET studies was initially suspicious for residual or recurrent tumor (Fig. 2C). An electroencephalogram, however, revealed that the patient was having episodes of recurrent subclinical seizure activity at the time of FDG-PET imaging. The patient was placed on anticonvulsant medication. The metabolism of the left temporal lobe on the follow-up PET study was normal (Fig. 2D), suggesting that this small area of abnormal metabolism represented a seizure focus.

One patient (case 12) had two lesions biopsied. One biopsy revealed AA and the other biopsy revealed radiation necrosis. These two Gd-DTPA- enhancing lesions had different intensities of FDG uptake (Fig. 3), but were identical in their Gd-DTPA enhancement pattern.

No Gd-DTPA Enhancement and Hypometabolism

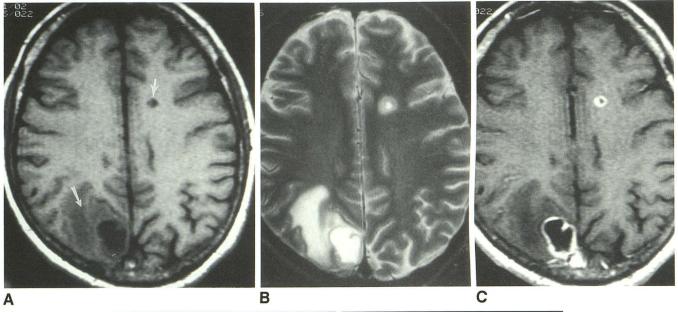
Three lesions in this study demonstrated no Gd-DTPA enhancement and were hypometabolic in the FDG-PET study (case 19, Fig. 4). These were all well-differentiated astrocytomas.

No Gd-DTPA Enhancement and Hypermetabolism

Three patients had hypermetabolic lesions by PET and no Gd-DTPA enhancement. Two lesions were AAs (cases 13 and 14, Fig. 5). One patient (case 35) had a focal FDG uptake between that of white and gray matter, but the contrast-enhanced MR study showed no enhancement and there were no abnormalities on T2-weighted images. In this particular instance, grade 3 FDG uptake would have been suggestive of tumor; however, in this case only normal signal intensity was present on MR.

Gd-DTPA Enhancement and Hypometabolism

Two patients exhibited Gd-DTPA enhancement with hypometabolism on PET. These le-



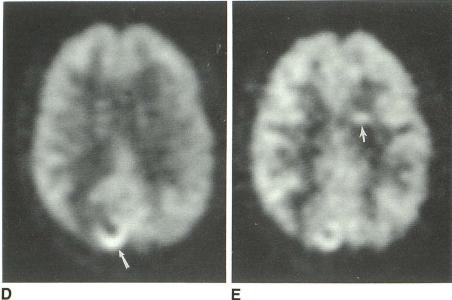


Fig. 1. A 64-year-old man (case 27) with metastatic undifferentiated adenocarcinoma.

A, T1-weighted MR (500/20) shows a lesion with low signal intensity in the right occipital pole and the left frontal subcortical white matter (*arrows*).

B, T2-weighted image (2800/80) shows high signal intensity in the same regions.

C, Gd-DTPA T1-weighted image (500/20) demonstrates the right occipital lobe lesion to be ring enhancing. An area of near-homogeneous enhancement is present in the left frontal deep white matter.

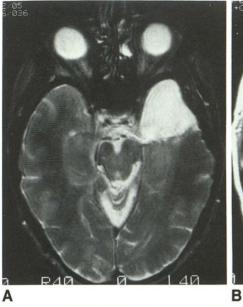
D and E, Both lesions had increased FDG uptake (grade 5), and the uptake of the right occipital lobe lesion was in a ring-like pattern (arrow). This case illustrates concordance of Gd-DTPA enhancement with hypermetabolism as determined by FDG-PET.

sions included a meningioma and an AA.

The one lesion not detected by FDG-PET was an ependymoma (case 8).

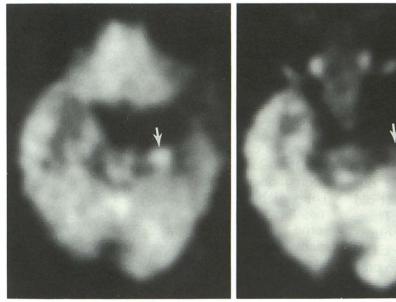
Discussion

Gd-labeled DTPA cerebral enhancement is associated with blood-brain barrier disruption (1– 3). Histologic studies have demonstrated tumor neovascularity and endothelial proliferation in areas of enhancement (7). Gd-DTPA has a molecular weight of 938, which is similar to the molecular weight of iodinated contrast agents used in CT (6). With CT contrast agents, as with Gd-DTPA (7), higher grade gliomas are associated with enhancement (8, 15). The presence of enhancement can be used as an imaging criterion associated with tumors of higher histologic grade





D



C

(14). Enhancement, though, can be a nonspecific finding and can occur with radiation necrosis (7, 16) and postsurgical change (17).

Similarly, PET is being used to characterize tumor grade, with higher grade tumors tending to be hypermetabolic (9-11, 13). As with contrast agents, PET hypermetabolism can be nonspecific and can occur with inflammatory processes such as abscess (18) and, as shown in this study, with seizure foci.

Our report correlates the Gd-DTPA enhancement findings and the FDG-PET metabolic findings in a group of brain tumor patients. In our study group of 35 patients, 32 patients had biopsy confirmation of tumor. Of these 32 tumors, 26 showed Gd-DTPA enhancement, and 24 of

Fig. 2. A 66-year-old woman (case 33) with recently resected oligodendroglioma localized to the left temporal lobe.

A, T2-weighted MR image (2000/80) shows a lesion with high signal intensity localized to the left anterior temporal region.

B, The T1-weighted Gd-DTPA image (500/20) shows minimal enhancement along the posterior margin of the resection site (arrow).

C, FDG-PET scan showed focal hypermetabolic abnormality localized to the left mesial-temporal region (grade 5) (arrow).

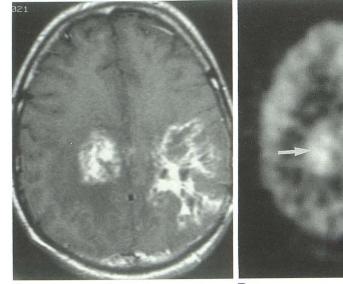
D, FDG-PET scan performed approximately 3 months later, after the patient had been placed on anticonvulsant medications, does not show a hypermetabolic abnormality. This patient was having subclinical seizure activity that had been documented by electroencephalogram the evening before the PET scan. This is an example of a falsepositive hypermetabolic lesion caused by seizure activity rather than tumor. MR enhancement was false-positive for tumor and was secondary to surgery.

these 26 tumors were hypermetabolic on the PET study. Thus, there was 93% concordance (28 of 30 enhancing lesions) of FDG hypermetabolism and Gd-DTPA contrast enhancement (Fig. 1), or 92% concordance (24 of 26 tumors) when considering only neoplastic lesions. Of 19 grade 5 FDG-PET lesions, 18 enhanced with Gd-DTPA. Thus, the presence of Gd-DTPA enhancement in a lesion tends to be associated with FDG-PET hypermetabolism. A previous study of 14 patients showed concordance between Gd-DTPA enhancement in gliomas and positive 11-C-I-methionine accumulation on PET (14). Two cases of hypermetabolic pediatric posterior fossa astrocytomas that enhanced have also been reported (19).

Fig. 3. A 40-year-old man (case 12). This individual had two distinct lesions, both of which were biopsied.

A, Gd-DTPA-enhanced T1weighted (500/20) image shows two enhancing abnormalities (localized to the posterior white matter bilaterally).

B, The FDG-PET study reveals one hypermetabolic abnormality (grade 5) localized to the deep white matter of the right hemisphere that revealed AA on biopsy (large arrow). In the deep left white matter, however, FDG uptake was graded between that of gray and white matter (grade 3) (small arrow). Biopsy revealed the majority of the lesion to be necrosis with focal astrocytoma. This is a complex situation in which two lesions are present. On the MR study with Gd-DTPA enhancement, the lesions appear identical and the etiology of the lesions cannot be differentiated. This is an excellent example of the complementary information gained from both studies. The FDG-PET study was helpful in assessing which lesion most likely represented metabolically active tumor.



A

B

But discordant findings also are evident from our study. This discordancy included two AA tumors that were hypermetabolic and did not enhance (cases 13 and 14) and one AA that did enhance but was hypometabolic (case 8). Thus, higher grades of gliomas are not always contrast enhancing on MR and hypermetabolic on PET.

FDG-PET has been previously reported to provide added diagnostic information in cases of radiation necrosis (16, 20-22). Our findings in two cases also show a discordance with the concept that radiation necrosis is hypometabolic (16, 19-21), since in two of our cases we had findings of grade 3 PET (hypermetabolic). The concomitant histologic presence of tumor and radiation necrosis has been reported (22, 23), and our FDG-PET findings may reflect that even in histologic areas of radiation necrosis, tumor cells may be present that are not actively undergoing mitosis, but may have a background FDG metabolic profile (case 12) as well as viable surrounding brain parenchyma (case 32). Valk et al (22) demonstrated that the FDG-PET study correlated with clinical outcome in 18 patients who showed viable tumor as well as necrosis on histologic examination.

A third discordant finding in our study is the fact that 2 of 16 grade 5 FDG-PET tumors were nonmalignant neoplasms (both meningiomas). The variable FDG metabolic profile of meningiomas has been previously reported (24). There is some suggestion that hypermetabolic FDG-PET meningiomas may be associated with increased aggressiveness or propensity for recurrence (24). It is interesting that the two grade 5 PET meningiomas had mitoses and macro nuclei in our study and bordered on histologic atypia, but were not considered to be atypical meningiomas. Further studies are warranted to formulate this correlation better as far as recurrence.

Previous studies of patients with multiple sclerosis receiving corticosteroid therapy have shown an effect on plaque enhancement for both CT and MR (25–27) by a presumed mechanism of improved integrity of the blood-brain barrier. Our study did not address the issue of steroid effect, but this can be proposed as a limitation of any study using Gd-DTPA enhancement as a criterion. Certainly, a limitation to Gd-DTPA enhancement's providing information about cerebral neoplasms is the presence of enhancement due to postoperative change (20). FDG-PET may be helpful in these cases (28) in which hypometab-

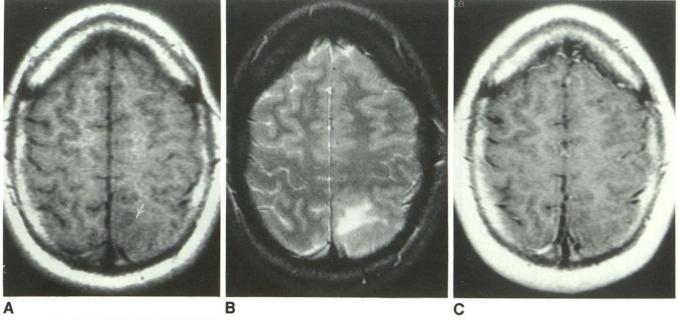




Fig. 4. A 35-year-old man with a low-grade astrocytoma (case 19).

A, The unenhanced T1-weighted image (500/20) reveals a low signal abnormality localized to the deep white matter of the left occipital region (*arrow*).

B, Corresponding T2-weighted image (2800/80) shows an abnormality with high signal intensity localized to the left deep occipital white matter.

C, Gd-DTPA T1-weighted image (500/20) shows no enhancement.

D, The FDG-PET study shows FDG uptake to be less than white matter in this corresponding region (grade 1) (*arrow*). This is an example of nonenhancing lesion on MR with FDG hypometabolism. Histology revealed a well-differentiated astrocytoma, which is consistent with both the MR and FDG imaging findings.

D

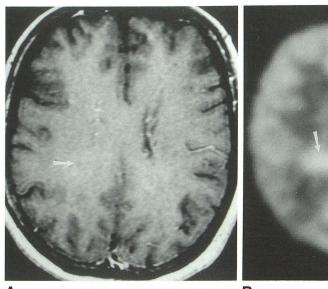
olism would suggest no viable tumor, as long as the patient was seizure-free and a well-differentiated astrocytoma was not suspected. A potential pitfall of FDG-PET is the fact that a temporal lobe seizure focus (Fig. 2) can be misinterpreted as a hypermetabolic tumor. However, the pitfall can be avoided by clinical assessment or electroencephalogram monitoring if seizures are suspected.

Our report further suggests the potential clinical role of PET scanning in the preoperative evaluation of brain tumors, as previously reported from our institution, where hypermetabolism on FDG-PET in correlation with Gd-DTPA enhancement was used in selecting which brain lesion to biopsy stereotactically (29). In our limited subgroup of brain tumors that showed no enhancement but were hypermetabolic on PET (Fig. 5), future clinical experience may indicate that in such cases, PET may assist in preoperative planning and in selecting which patients may receive an open biopsy and resection rather than a limited or stereotactic type of biopsy.

In conclusion, our study indicates a high concordance (92%) of Gd-DTPA-enhancing lesions and increased FDG uptake of neoplasm, indicating that blood-brain disruption can be associated with lesions having a hypermetabolic state. Gd-DTPA MR and FDG-PET can provide complementary information. Fig. 5. A 60-year-old woman with AA (case 14).

A, T1-weighted Gd-DTPA-enhanced MR (500/20) does not show enhancement in the area of known tumor in the right posterior deep white matter (*arrow*).

B, The FDG-PET study shows the tumor to be hypermetabolic (*arrow*). This is an example of a discordant result with no Gd-DTPA enhancement, but a hypermetabolic tumor (grade 5) on FDG-PET.



A

В

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Please see Commentary by Di Chiro on page 524.