The Utility of a 3-Dimensional, Large-Field-Of-View, Sodium Iodide Crystal–Based PET Scanner in the Presurgical Evaluation of Partial Epilepsy

Terence J. O'Brien, Rodney J. Hicks, Robert Ware, David S. Binns, Michael Murphy, and Mark J. Cook

Australian Center for Clinical Neuropharmacology and Victorian Epilepsy Centres, St. Vincent's, Royal Melbourne, and Alfred Hospitals, Fitzroy, Victoria; and Center for Positron Emission, Peter MacCallum Cancer Institute, University of Melbourne, Fitzroy, Victoria, Australia

^{18}F-FDG PET is an accurate and reliable technique for localizing medically refractory temporal lobe epilepsy, but widespread use has been hindered by limited reimbursement in many countries because of the high cost of traditional PET equipment and radioisotopes. Additionally, the place of FDG PET as a cost-effective tool for presurgical evaluation of epilepsy has been questioned because of limited data showing that FDG PET provides localization information incremental to that provided by more established techniques, particularly MRI and ictal electroencephalography (EEG). Three-dimensional (3D), large-field-of-view, sodium iodide crystal–based scanners have lower equipment and running costs and better multiplanar resolution than traditional 2-dimensional bismuth germanate (BGO) systems but have not yet been validated for evaluation of epilepsy. Our purpose was to investigate the localization rate, accuracy, and prognostic value of FDG PET images acquired on a 3D, large-field-of-view, sodium iodide crystal–based PET scanner in the presurgical evaluation of intractable partial epilepsy. We also wanted to establish the incremental value of FDG PET over established MRI and ictal EEG techniques. **Methods:** Fifty-five patients who were surgical candidates because of medically refractory partial epilepsy were examined. For most of these patients, the lesions had not been clearly localized on conventional assessment. The FDG PET scans were reviewed independently by 2 reviewers who were unaware of the patients' clinical details, ictal EEG findings, and volumetric MRI results, and the FDG PET results were correlated with those of MRI and EEG and with postsurgical outcome. **Results:** Forty-two patients (76%) had localizing FDG PET images (37 temporal, 5 extratemporal). The ictal EEG recordings were localizing in 66%, and the MRI findings were localizing in 27% (which increased to 35% after the MRI findings were reviewed again after PET). Concordance between the site of the PET localizations and the site of the MRI or EEG localizations was 100%. The PET images were localizing in 63% and 69% of patients with nonlocalizing ictal EEG and MRI findings, respectively. Twenty-one of 24 patients who subsequently underwent epilepsy surgery had localizing FDG PET images; of these 21 patients, 18 (86%) had a class I outcome. Multiple regression analysis showed the FDG PET results to be predictive of postsurgical outcome independently of the MRI findings. **Conclusion:** For intractable partial epilepsy, FDG PET using a 3D, large-field-of-view, sodium iodide crystal–based scanner provided clinically useful localizing information that was at least as accurate as the results reported for traditional BGO-based scanners. The PET images provided prognostically significant localization information incremental to that provided by volumetric MRI and ictal EEG, particularly if 1 of these studies was nonlocalizing.

Key Words: FDG PET; sodium iodide crystal; MRI; epilepsy surgery

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Interictal ^{18}F-FDG PET has been used for more than 2 decades to evaluate patients with medically refractory partial epilepsy. PET produces potentially quantifiable data with a superior resolution to SPECT data but lower than the resolution of MRI data. FDG PET images have been shown to be highly reliable in lateralizing temporal lobe epilepsy (TLE) in patients without a discrete neocortical mass lesion, with most studies finding sensitivities between 60% and 90% and few falsely lateralized cases (*1–4*). However, the localization rate in patients with extratemporal lobe epilepsy (ETLE) in the absence of a discrete lesion on MRI has generally been significantly lower (*4–9*).

Almost all published studies of interictal FDG PET in epilepsy have used bismuth germanate (BGO) crystal scanners operating in 2-dimensional (2D) mode. However, these scanners have several disadvantages. Probably the most important disadvantage is the relatively high establishment and operating cost, which has limited the general availability of PET imaging (*10–13*) and has raised questions about its cost-effectiveness as a routine part of epilepsy evaluation (*4,12,14–16*). In addition, 2D scanners have relatively poor resolution when their images are reformatted out of the

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For correspondence or reprints contact: Terence J. O'Brien, MD, Department of Clinical Neuroscience, St. Vincent's Hospital Melbourne, Fitzroy, 6035, Victoria, Australia.

original plane of acquisition, because the scanners require multiple, parallel lead septa for the acquisition of axial slices. This requirement results in interslice gaps that degrade the resolution of images on reformatting. The capacity for 3-dimensional (3D) acquisition and processing has now been developed for BGO systems using retractable septa. The development of lower cost 3D PET imaging systems during the past 10 y offers an opportunity to expand the availability and clinical utility of PET imaging.

The PENN PET scanner (UGM Medical Systems, Inc., Philadelphia, PA) is a dedicated 3D device that has several potential cost and imaging advantages over traditional 2D PET scanners (*17*). First, it uses sodium iodide crystals, which are more readily available and cheaper to produce than BGO crystals. As a result, the purchase cost is less than that of traditional BGO PET scanners (approximately US $1.1 million vs. US $1.4 million for current-generation 3D BGO scanners). Furthermore, the administered activity used for clinical studies with this scanner is typically 25% of that for traditional scanners operating in 2D mode and approximately half that for BGO systems operating in 3D mode. A lower administered activity potentially reduces the operating costs if FDG is purchased by activity rather than unit dose. Also reduced are patient radiation exposure and the occupational exposure of the PET facility staff (*18*). The large axial field of view allows the whole brain to be imaged with 1 bed position, resulting in shorter imaging times, less chance for patient movement, and a higher throughput, which further contributes to lower running costs. New-generation 3D BGO PET scanners also generally have a sufficient axial field of view to encompass the whole brain, with improved sensitivity and reduced acquisition time. The ultimate cost of clinical PET is complex and depends on the number of patients scanned, the availability and cost of radiopharmaceutical supplies, and the case mix of PET studies.

Three-dimensional scanners (both PENN PET and BGO PET) produce images of dramatically improved resolution when reformatted out of the plane of acquisition, because unlike the traditional 2D scanners, images are acquired as an isotopic 3D volume with no interslice gap (*17*). There is little published information validating the localization rate and accuracy of dedicated 3D sodium iodide devices such as the PENN PET scanner in the evaluation of medically refractory partial epilepsy. The primary aim of this study was to investigate the localization rate, accuracy, and prognostic value of FDG PET images acquired on a 3D PENN PET scanner in presurgical evaluation of medically refractory partial epilepsy. The study also aimed to establish the incremental value of FDG PET over established MRI and ictal electroencephalography (EEG) techniques in the presurgical evaluation of epilepsy, with particular focus on patients with seizures that are difficult to localize.

MATERIALS AND METHODS

Patients

Fifty-five patients (31 males, 24 females; age range, 16–63 y; mean age, 34 y) were referred for an FDG PET scan between November 1996 and April 1999 as part of their presurgical evaluation for medically refractory partial epilepsy at the Victorian Epilepsy Centres (St. Vincent's and Alfred Hospitals, Melbourne, Australia). They had been classified as having medically refractory epilepsy because treatment trials with 3 or more different antiepileptic drugs had failed. The patients had been selected for PET primarily because other standard noninvasive tests (particularly MRI and ictal EEG) had not provided a confident enough localization to enable the patients to proceed to surgery. However, these guidelines were not strictly enforced, and the clinicians were free to order a PET examination if they believed it might yield useful additional information. The final localization, based on all available information, for these patients found the epilepsy syndrome to be TLE in 41 and ETLE in 14 (frontal in 2, frontoparietal in 4, temporoparietal in 1, parietal in 1, and unlocalized in 6).

PET Methods

All patients were imaged as outpatients in the interictal state on a PENN PET 300H Tomograph scanner with sodium iodide crystals, using a 25-cm field of view and 3D whole-head acquisition. For the 2-mm slice thickness used for whole-body imaging, the measured resolution was 4.2 mm at full width at half maximum transaxially and 5.4 mm at full width at half maximum out of plane (based on National Electrical Manufacturers Association–specified testing at the time of installation). The use of a 1-mm slice thickness for brain acquisitions has been estimated to improve spatial resolution by approximately 0.5 mm (G. Muehllehner, oral communication, 2001). Patients prepared by fasting for 4 h before the scan and resting in a quiet, darkened room for 30 min before FDG administration and for at least 30 min afterward. Scanning commenced 45–60 min after radiotracer administration. Routine EEG monitoring was not performed because we and others (*4,19*) have found that it adds little useful information for most patients and increases the cost and resource intensiveness of the imaging. Patients were, however, asked to report any seizures experienced on the day of the scan, whether before or after the FDG injection; a second examination was considered for patients with such seizures if the images were inconclusive.

The dose of FDG PET administered was 37–111 MBq (1–3 mCi). One bed position was used. The acquisition time was 30–40 min, achieving total counts of >40 million. An empiric attenuation correction (ellipse) was applied. The data were processed using a Wiener prefilter (scaling value = 0.5) and ordered-subsets expectation maximization iterative reconstruction. Wiener filtering attempts to reduce blurring of an object by restoring the amplitude of the object's power spectrum in certain ranges. In particular, the filter identifies frequencies that define the resolving power of the spectrum (*20*). The images were reconstructed into a 256 × 250 mm cylindric volume with a 2-mm slice thickness. The reconstruction process created a standard series of contiguous images oriented in the transaxial, coronal, sagittal, and transtemporal planes.

The FDG PET images were reviewed independently by 2 reviewers using a high-resolution computer monitor and a standard rainbow-color lookup table (Fig. 1). The visual presentation of the images was previously optimized by studying 10 patients with well-localized TLE using the range of color scales available on the system as supplied commercially. We found that localization of

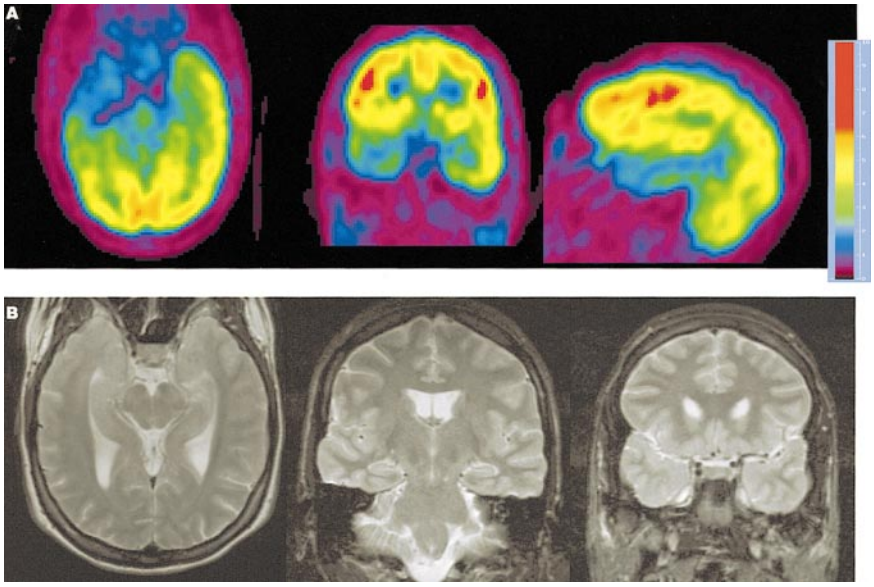

FIGURE 1. (A) From left to right, axial (plane of acquisition) and reformatted coronal and sagittal FDG PET images from 39-y-old man with medically refractory right TLE show prominent focal hypometabolism anteromesially in right temporal lobe. (B) MR images show no significant abnormalities.

focal hypometabolism was best seen using the rainbow color scale set at a power factor of 0.65. No background subtraction was used. This image display methodology was applied prospectively to the analysis of patients evaluated in this study.

The reviewers were unaware of the patients' clinical details, EEG findings, and MRI results. After reviewing all PET images in multiple planes for each patient, the reviewers determined whether the images showed localization to a single brain region or were nonlocalizing. To be considered localizing, an image had to clearly show a single focus of decreased image intensity in 2 or more contiguous slices (each of 2-mm thickness) in 2 or more planes. For the images that were considered localizing, the reviewers were asked to classify their confidence in the localization as high or low. If the findings of the 2 reviewers showed any discrepancy, either in whether the images were localizing or in the site of the localization, a consensus was obtained through joint review. Quantitative measurements were not used for this study.

Comparison with MRI and Video-EEG Findings

All patients were scanned on high-resolution 1.5-Tesla scanners (Vision; CTI, Knoxville, TN/Siemens Medical Systems, Inc., Hoffman Estates, IL, or Signa; General Electric Medical Systems, Milwaukee, WI) according to a standardized epilepsy protocol for MRI, and studies included formal measurement of hippocampal volume (*21*). The protocol included a whole-brain volumetric T1-weighted sequence acquired in the coronal plane, with a slice thickness of 1.5 mm and no interslice gap. Axial and coronal T2-weighted images and axial proton density–weighted images were acquired. In most cases, coronal fluid attenuated inversion recovery sequences were obtained. Comparisons were made both with the MRI results, as initially reported by the radiologists, and with the MRI results as reported in the final opinion of the epilepsy treatment team. This final opinion was based on careful reevaluation of the MR images after the FDG PET results and other localizing information had been made available. For patients with an initial report of normal MRI findings, we determined the proportion in whom a subtle MRI abnormality was uncovered after focal hypometabolism was found on the FDG PET scan.

Prolonged video-EEG was performed using 32-channel systems with the electrodes arranged on the scalp according to a modified 10–20 system, which included subtemporal electrodes. Five patients had further prolonged video-EEG monitoring after implantation of intracranial electrodes (3 bitemporal depth electrodes and 2 subdural grid electrodes). The localization shown by the ictal EEG tracings was determined by retrospective review of the reports and was then compared with the localization shown by PET.

Assessment of Clinical Impact

For all patients, the clinical impact of PET findings on the presurgical evaluation was retrospectively assessed. The impact was considered high if the seizures had been unlocalized before PET and the PET findings allowed further evaluation for epilepsy surgery. The impact was considered moderate if localizing information was available from other modalities but the PET findings improved the confidence of localization and enabled an offer of epilepsy surgery. The impact was considered low if the seizure had been localized by other noninvasive tests and the PET findings were confirmatory but did not significantly change the management decisions. PET findings were considered contradictory if they conflicted with other localizing information.

Relationship with Outcome After Epilepsy Surgery

In patients who subsequently underwent epilepsy surgery and were then followed up for at least 6 mo (none were lost to follow-up), the postsurgical outcome for seizures was classified at the last follow-up point according to a modification of the scale of Engel et al. (*22*). Class I was assigned to patients who were free of seizures, had auras only, or experienced a single seizure associated with discontinuation of medication; class II, to patients who had a >95% reduction in seizure frequency; class III, to patients who had an 80%–94% reduction in seizure frequency; and class IV, to patients who had a <80% reduction in seizure frequency.

Statistical Methods

The Fisher exact test (2-tailed) was used to test for differences between dichotomous variables. Agreement between the 2 PET reviewers was determined using Cohen's κ scores calculated for 5 possible choices (right TLE, left TLE, right ETLE, left ETLE, and nonlocalizing). Agreement was considered poor for $\kappa < 0.4$, good for $0.4 \leq \kappa < 0.75$, and excellent for $\kappa \geq 0.75$ (*23*). Multiple

TABLE 1
FDG PET Localization Rates

Epilepsy location	Reviewer 1	Reviewer 2	Final localization
Temporal (n = 41)	37 (90%)	33 (80%)	37 (90%)*
Extratemporal (n = 14)	6 (43%)	5 (36%)	5 (36%)*
Frontal	1	—	—
Frontoparietal	2	2	2
Temporoparietal	—	—	—
Parietal	1	1	1
Unlocalized	2	2	2
Total patients (n = 55)	43 (79%)	38 (69%)	42 (76%)

*Localization rate was significantly higher in temporal vs. extratemporal cases (P = 0.0001, Fisher exact test).

regression analysis was conducted using the modified Engel scale (classes I–IV) as the dependent variable and the results of preoperative MRI (i.e., definite focal lesion vs. no focal lesion) and FDG PET (i.e., localizing vs. nonlocalizing) as the independent variables. The significance level was set at $P < 0.05$ for all tests.

RESULTS

FDG PET Localization

The results of the FDG PET review are summarized in Table 1. The images were agreed to be localizing in 42 (76%) of 55 patients, with the localization rate being significantly higher for TLE than for ETLE (90% vs. 36%, P = 0.0001, Fisher exact test). Agreement between the 2 reviewers was 91% (κ = 0.87). For 38 patients, the reviewers agreed on the cerebral region of localization shown by the images; for 12 patients, the reviewers agreed that the images were nonlocalizing. For 5 patients (9%), 1 reviewer believed the images were localizing whereas the other classified them as nonlocalizing. For no patients did the 2 reviewers disagree on the region of localization shown by the images.

Of the 43 images classified by the first reviewer as localizing, his confidence in this localization was high in 25 (58%) (e.g., Figs. 1 and 2). The second reviewer rated his localization confidence as high in 23 (61%) of the 38 images he classified as localizing. In all but 1 of the 5 disputed cases, both reviewers rated their localization confidence as low (e.g., Fig. 3).

Comparison with Ictal EEG, MRI, and Final Seizure Localization

Table 2 compares the localization rate for MRI and ictal EEG with that for FDG PET. The MR images were reported as showing a single, focal, potentially epileptogenic lesion in 15 patients (27%) (mesial temporal sclerosis in 10, focal cortical dysplasia in 3, and tumors in 2). The FDG PET localization was concordant with the site of the MRI lesion in all patients (100%). After the FDG PET results had been obtained, the MRI findings were carefully reviewed again, revealing a subtle, focal structural abnormality in another 4 patients (2 with mesial temporal sclerosis and 2 with focal cortical dysplasia) (Fig. 2). In an additional 13 patients, a focal signal change (an increase on T2-weighted images and a decrease on T1-weighted images) was noted in the anterior pole of the ipsilateral temporal lobe, with accompanying blurring of the gray matter–white matter junction and often with unilateral atrophy of the pole. This last finding is of uncertain significance.

The ictal scalp EEG tracings were localizing in 36 (72%) of 50 patients for whom seizures were recorded. In all patients for whom both EEG and PET were localizing, there was concordance between the sites of localization. In 5 patients, seizures were localized with prolonged intracranial

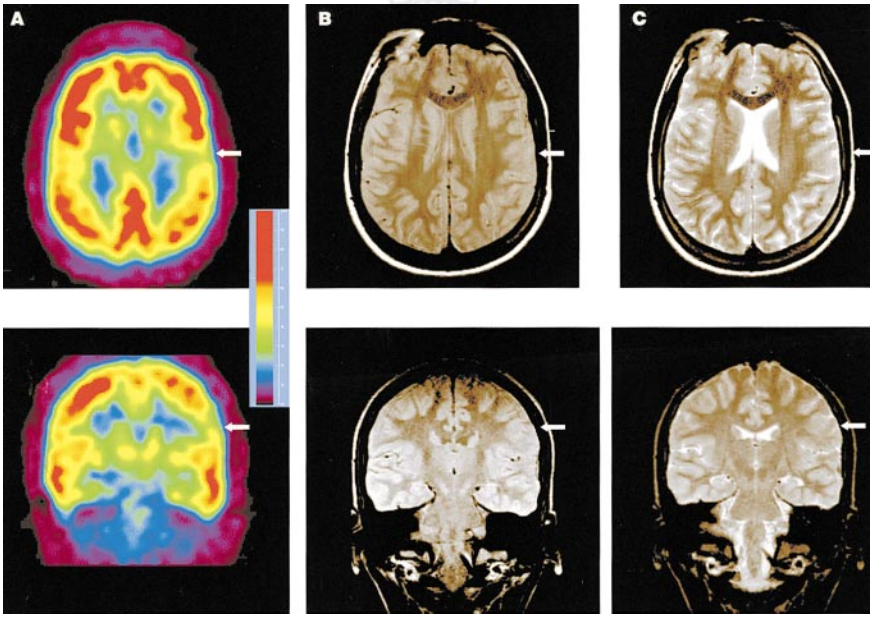

FIGURE 2. Axial and coronal FDG PET (A), proton density–weighted MRI (B), and T2-weighted MRI (C) images from 13-y-old girl with medically refractory extratemporal seizures. MRI findings were initially reported as normal, whereas FDG PET showed region of focal hypometabolism around left inferior rolandic area (arrows). Review of MR images showed small region of cortical signal change with blurring of gray matter–white matter junction corresponding to region of PET hypometabolism, consistent with focal cortical dysplasia.

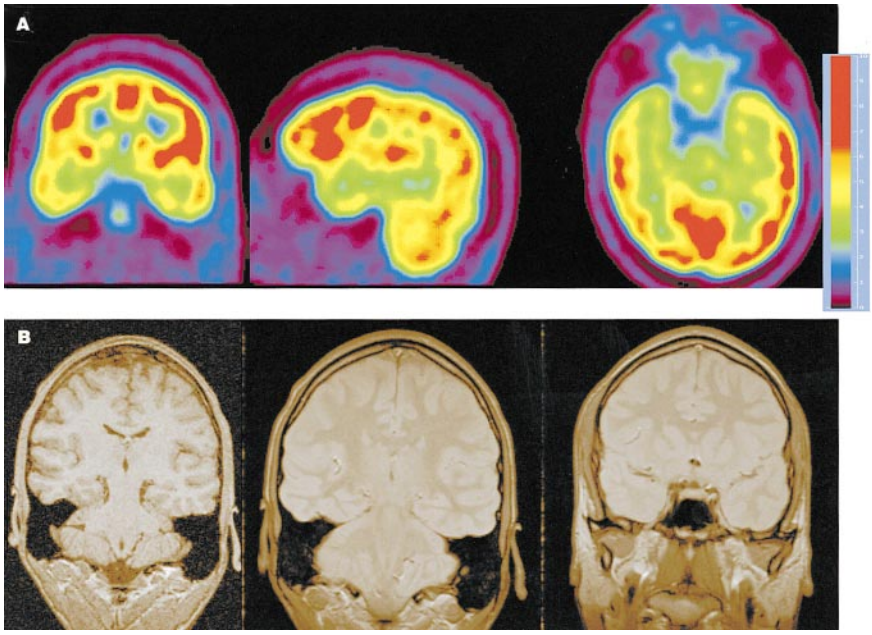

FIGURE 3. From left to right, coronal, sagittal, and axial FDG PET images (A) from patient with right temporal lobe seizures (on ictal EEG) but normal MRI findings (B). Interpretation of FDG PET images was discordant between the 2 independent reviewers, with 1 initially diagnosing right temporal hypometabolism with low confidence. On joint review, reviewers decided that PET images were nonlocalizing.

EEG recordings; 4 of these EEG localizations were concordant with the PET localization, and PET was nonlocalizing in the other patient.

FDG PET images were localizing in 29 (72%) of 40 patients for whom MRI was initially reported to be nonlocalizing, 25 (69%) of 36 patients for whom the final MRI report showed MRI to be nonlocalizing, and 10 (62%) of 16 patients for whom scalp ictal EEG was nonlocalizing.

Assessment of Clinical Impact

The clinical impact of the FDG PET localization was considered to be high in 25 patients (45%), moderate in 7 (13%), and low in 23 (42%). Of the patients with high- or moderate-impact FDG PET images, 12 and 4, respectively, have subsequently undergone epilepsy surgery with at least 6 mo of follow-up. Of the 16 remaining patients with high- or moderate-impact images, 9 have declined to proceed to surgery at this stage, 6 are awaiting surgery or have had <6 mo of follow-up, and 1 is not currently a surgical candidate because of psychiatric concerns.

TABLE 2
Comparison of Localization Rates of MRI, Ictal EEG, and FDG PET

Epilepsy location	Initial MRI	Final MRI	Scalp Ictal EEG	FDG PET
Temporal (n = 41)	12 (29%)	15 (37%)*	30 (73%)	37 (90%)
Extratemporal (n = 14)	3 (20%)	4 (29%)	4 (29%)	5 (36%)
Frontal	—	—	—	—
Frontoparietal	1	2	2	2
Temporoparietal	1	1	1	—
Parietal	1	1	—	1
Unlocalized	—	—	1	2
Total patients (n = 55)	15 (27%)	19 (35%)*	34 (69%)†	42 (76%)

*A further 13 patients had focal signal change ± atrophy in ipsilateral temporal pole. Finding was of uncertain significance.
†Five patients did not have seizure recorded on video-EEG.

Relationship with Outcome After Epilepsy Surgery

Twenty-four of the patients have undergone epilepsy resection surgery (22 temporal and 2 extratemporal) and have had at least 6 mo of postoperative follow-up (median, 17 mo; range, 6–42 mo). Of the 31 remaining patients, 9 have declined to proceed to surgery at this stage, 7 are awaiting surgery or have had <6 mo of postoperative follow-up, and 15 cannot be offered surgery on the basis of the available information. Twenty-one of the patients who underwent surgery (20 temporal and 1 extratemporal) had a localizing FDG PET scan, and all of these scans were concordant with the site of the surgical resection. The impact of the PET images was rated as high in 13 patients (61.9%) and as moderate in 4 (19.0%). In 14 of the 24 surgical patients, MRI was initially reported as showing no focal, potentially epileptogenic lesion, and FDG PET was localizing in 13 of these 14. Careful review of the MRI images in light of the PET findings revealed a definite focal lesion in a further 2 patients.

At the last point of follow-up, 18 (86%) of the patients with localizing PET had a class I outcome, 2 (10%) had a class II outcome, and 1 (5%) had a class III outcome. Of the 3 surgical patients with nonlocalizing PET, 1 had a class I outcome, 1 had a class II outcome, and 1 had a class IV outcome (P = 0.099 for the difference in the rates of a class I outcome between the groups, Fisher exact test). Among the patients with localizing PET, 10 (90.9%) of 11 with a definite, focal lesion detected on MRI had a class I postsurgical outcome; in comparison, 7 (70%) of 10 with nonlo-

TABLE 3
Multiple Regression Analysis Models for Prediction of Postsurgical Outcome

Independent variable	Postsurgical outcome class (R^2 = 0.40; P = 0.004)		
	β	SE	P
MRI*	0.32	0.17	0.07
PET†	0.51	0.17	0.007

*MRI group 1: definite focal potentially epileptogenic lesion detected preoperatively; MRI group 2: no focal lesion detected.

†FDG PET group 1: focal localizing region of hypometabolism detected; FDG PET group 2: nonlocalizing findings.

R^2 is for the model. β is standardized regression coefficient for each independent variable. SE is for each independent variable. Data are for the 24 patients who underwent epilepsy surgery.

calizing MRI (P = 0.31, Fisher exact test) had a class I outcome.

Table 3 summarizes the results of the multiple regression analysis. The FDG PET localizations were independently predictive of postsurgical outcome with respect to seizures. There was also a strong trend for the MRI findings to be predictive, but this did not quite attain statistical significance.

DISCUSSION

The localization rate for the FDG PET images acquired on the PENN PET scanner in this study was 90% for the TLE patients (Table 1). This rate compares well with previously reported localization rates—generally 60%–90%—for TLE patients imaged on traditional BGO PET scanners (*1*–*5*). The localization rate for the patients with presumed ETLE, at just over one third, was significantly lower than that for the TLE patients. However, this rate is again consistent with rates found in many previous studies of visual analysis of BGO PET images in patients with nonlesional extratemporal seizures (*4*–*9*).

We acknowledge that the visual image analysis used in this study is, by definition, subjective and that some reduction and asymmetry in intensity is seen in the temporal lobes of healthy volunteers. However, our reviewers used quite conservative criteria for a localizing study, requiring detection of a single focus of prominent hypometabolism in at least 2 contiguous slices in at least 2 image planes. The size and shape of the foci of hypometabolism varied greatly but tended to be larger and more diffuse in the TLE than in the ETLE patients (e.g., Figs. 1 and 2), in keeping with previous findings (*4*). The objectivity of our image interpretation methods is attested by the excellent agreement, 91% (κ = 0.87), between the 2 reviewers. Importantly, there were no instances in which the reviewers localized the images to different brain regions. Of particular note, in the 5 ETLE patients for whom the PET images were determined to be localizing, both reviewers agreed precisely on the cerebral site.

The accuracy of the FDG PET localizations is attested by the 100% concordance found with the site of the potentially epileptogenic lesion found by MRI and with the localizations of the scalp ictal EEG and the intracranial ictal EEG (when both PET and MRI/EEG were localizing). No test is considered a gold standard for defining the true seizure location—all existing tests, including MRI and video-EEG, produce some false localizations. For this reason, we compared the concordance of the PET localization with the localizations from these well-accepted tests as a surrogate measure of their accuracy. Quantitative analysis methods (e.g., the asymmetry index) might have further improved the localization rate and accuracy of the PET images in this study (*4*); however, these methods are not routinely used in clinical practice and do not easily lend themselves to situations in which a putative seizure focus is unknown (i.e., TLE vs. ETLE), as in this study population.

Before being considered a cost-effective part of the presurgical evaluation, ancillary localizing tests such as PET must be shown to provide significant additional, rather than just confirmatory, information to that of the more routine tests, particularly EEG and MRI. The incremental value of the FDG PET images in this series is well illustrated by the comparison with the MRI and ictal EEG localizations given in Table 2. Although the PET analysis was localizing in 76% of patients, the initial report by the radiologist showed MRI to be localizing in only 27% of patients. After careful review of the images in light of other localizing information, particularly the FDG PET findings (e.g., Fig. 2), the proportion of patients with a definite focal and potentially epileptogenic MRI lesion increased to only 35%. The relatively low localization rate of MRI in our series reflects a pretest referral bias. During the study period, not all potential candidates for epilepsy surgery in our program were referred for a PET scan; the referred patients were mainly those whose epileptogenic zone had not been clearly localized by more routine methods (especially MRI). We believe that this selection process is clinically appropriate but would also be expected to decrease the apparent localization rate of PET. Nevertheless, the good localizing ability in patients without abnormal findings on MRI further attests to the impressive localization rate found in this series.

In 13 of the "MRI normal" TLE patients, MRI signal changes were noted diffusely in the anterior pole of the temporal lobe, with accompanying blurring of the gray matter–white matter junction and often subtle atrophy of the pole, ipsilateral to the side of the EEG seizure onset and coinciding with the region of focal hypometabolism on the FDG PET scans. This MRI finding is of uncertain clinical and pathologic significance. Mitchell et al. (*24*) recently reported similar MRI changes in the ipsilateral temporal pole in 58% of 50 patients with medically refractory TLE. Those authors did not report PET findings for that group. Histopathologic examination of the 42 surgically treated

patients in that study revealed a variety of underlying epileptogenic abnormalities but no specific abnormalities in the anterior temporal pole. Likewise, in our series, histopathologic examination of the anterior temporal pole in the 8 patients who subsequently went on to surgery showed changes of focal cortical dysplasia in 1 but only nonspecific changes in the other 7.

The overall localization rate for ictal EEG, at 69%, was higher than that for MRI but was still lower than that for PET. Furthermore, almost one third of the 16 patients with a nonlocalizing scalp ictal EEG recording had localizing findings from PET, again showing its incremental value in the epilepsy surgery evaluation.

The ultimate proof, however, of the value of a test for presurgical evaluation is the test's allowing more patients to proceed to epilepsy surgery, improving the surgical outcome, or ideally both. The utility and prognostic importance of MRI in the epilepsy surgery evaluation is now well established (*25–27*); however, such importance has yet to be unequivocally established for FDG PET. Although potentially influenced by patient selection for PET evaluation, the impact of localizing information provided by the FDG PET images for presurgical evaluation in this series was substantial, having been rated as high or moderate in 58% of patients. These included 16 of the 24 patients who subsequently underwent epilepsy surgery, of whom 14 (88%) had a class I postoperative outcome. In all 16 of these patients, the localizing PET images were critically important in enabling the surgery to be performed. In 14 patients, the MRI scan was initially reported as showing no focal, potentially epileptogenic lesion, whereas the FDG PET images showed a focal region of hypometabolism in all but 1 patient. After careful review of the MRI images in light of the PET findings, a definite focal MRI lesion was detected in a further 2 patients. However, in 10 of the remaining 11 patients, PET was the primary imaging modality used to guide intracranial electrode implantation or surgical resection. In the 25 patients for whom the PET images were classified as being of low impact, 13 studies were nonlocalizing; the other 12 studies were still of clinical value because they provided additional confirmation of the epileptogenic site.

Multiple regression analysis showed the FDG PET results to be significantly predictive of the postsurgical outcome, independently of the MRI findings (Table 3). More than 90% of the patients for whom both MRI and PET were localizing had a class I outcome, in contrast to neither of the 2 patients for whom both tests were nonlocalizing. Particularly encouraging was the outcome in patients whose MR images did not show a definite focal lesion but whose PET images were localizing; 70% of such patients were rendered seizure free postoperatively. This result is considerably better than would be expected in patients with "nonlesional" MRI findings, with most series reporting class I outcomes in only 30%–50% of such patients (*22,28–33*). A major reason for the less satisfactory surgical outcome generally reported for this group of patients has been the difficulty in identifying the epileptogenic focus when a well-defined structural lesion is not detected by MRI (*29,34*). Our current results suggest that in these nonlesional ETLE patients, detection of a focus of hypometabolism on a 3D PET scan may serve a role similar to that of detection of a lesion on an MR image in identifying the epileptogenic zone and guiding surgical resection.

To our knowledge, this study is the first to show that visual analysis of FDG PET images provides prognostically significant localization that is statistically independent of that achieved through MRI performed using a modern, high-resolution, volumetric protocol (including hippocampal volume measurements). The findings provide a strong rationale for including FDG PET in the presurgical evaluation. Because MRI is less expensive and more widely available than PET, routine use of FDG PET for presurgical evaluation would be difficult to justify if the FDG PET findings reflect simply the presence of associated MRI abnormalities. Several studies of FDG PET have found an association between detection of unilateral focal temporal hypometabolism, by either visual or quantitative analysis, and a higher rate of good outcomes after surgery for TLE (*35–38*). Theodore et al. (*35*) found that among patients undergoing temporal lobectomy, a quantitative asymmetry index of >15% for the lateral temporal lobe was predictive of outcome even after controlling for the MRI results and the side of surgery. However, this finding was not shown for the visual analysis, the study did not include patients with ETLE, and the MR images were not acquired using a modern volumetric protocol (therefore, the sensitivity of the MRI findings was likely lower). The other studies did not compare PET results with MRI results or determine whether PET provided prognostic information independent of the information provided by MRI (*36–38*).

We acknowledge that the study participants did not represent a consecutive series of all patients with medically refractory partial epilepsy, but only those chosen to undergo FDG PET. Because of selection bias favoring patients with seizures that were not well localized by more standard methods, particularly MRI, the results of this study do not prove that PET provides independent prognostic information in an unselected group of patients. However, our results do indicate that PET added significant information to the MRI findings in this important group of patients with seizures that were difficult to localize.

CONCLUSION

The results of this study show that FDG PET using a 3D PENN PET scanner provides sensitive and specific localizing information in the presurgical evaluation of medically refractory partial epilepsy. This information is at least equivalent to the information that traditional BGO PET scanners have been reported to provide, thus validating use of the PENN PET scanner for evaluating epilepsy. Further-

more, in this selected group of patients, many of whom had difficult-to-localize seizures, FDG PET added information to that provided by MRI and ictal EEG and yielded prognostic information independent of that provided by MRI for outcome after epilepsy surgery.

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