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Initial experience in hybrid PET-MRI for evaluation of refractory focal onset epilepsy

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ABSTRACT

Purpose: We aim to evaluate the utility/improved accuracy of hybrid PET/MR compared to current practice separate 3 T MRI and PET-CT imaging for localization of seizure foci.
Method: In a pilot study, twenty-nine patients undergoing epilepsy surgery evaluation were imaged using PET/MR. This subject group had 29 previous clinical 3 T MRI as well as 12 PET-CT studies. Prior clinical PET and MR images were read sequentially while the hybrid PET/MR was concurrently read.
Results: The median interval between hybrid PET/MR and prior imaging studies was 5 months (range 1–77 months). In 24 patients, there was no change in the read between the clinical exams and hybrid PET/MR while new anatomical or functional lesions were identified by hybrid PET/MR in 5 patients without significant clinical change. Four new anatomical MR lesions were seen with concordant PET findings. The remaining patient revealed a new abnormal PET lesion without an MR abnormality. All new PET/MR lesions were clinically significant with concordant EEG and/or SPECT results as potential epileptic foci.
Conclusion: Our initial hybrid PET-MRI experience increased diagnostic yields for detection of potential epileptic lesions. This may be due to the unique advantage of improved co-registration and simultaneous review of both structural and functional data.

1. Introduction

Epilepsy surgery is an effective and safe alternative form of therapy for patients with focal onset medically refractory epilepsy. Radiographically identifiable epileptogenic lesions can provide good prognostic information for focal resective epilepsy surgery resulting in up to 60–90% freedom from disabling seizures [1,2]. When MRI fails to detect a potentially epileptogenic lesion, the chances of an excellent surgical outcome are significantly lower, ranging from 20 to 65% [2,3]. This may reflect the difficulty in localizing and resecting the epileptogenic zone [3]. In order to improve the radiographic detection of epileptogenic lesions, more advanced imaging techniques have been suggested such as 7T MRI, susceptibility weighted imaging, spectroscopy, volumetric analysis, diffusion tensor Imaging, arterial spin labeling, BOLD and PET [4–6]. The concept that combining different modaities is intuititvely beneficial. In particular, simultaneous acquisition also should improve detection since the patient is in the same physiologic state during both studies.

FDG-PET scan has been shown to provide additional information of functionally identifiable epileptogenic lesions and is widely used in epilepsy surgery evaluation [7]. More recently, hybrid PET-MRI has become available in clinical practice and may yield a potential benefit in various neurological disorders [5,8–10]. Garibotto and colleagues showed utility of hybrid PET-MRI in presurgical evaluation of epilepsy in 6 patients with four cases of PET concordant findings to MRI identified structural lesions [5]. Also, Ding and colleagues showed potential usefulness of this new technique to understand etiopathogenesis and localization of seizure foci by finding specific patterns of metabolic abnormalities and asymmetry in 11 epilepsy patients, compared to 6 controls [10]. However, there are no larger scale studies to show the clinical

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role of PET-MRI in epilepsy surgery evaluation. To our knowledge, preliminary evaluation of our pilot case series study is the first one to evaluate the potential improvement of radiographically identifiable epileptogenic lesions using a hybrid PET-MRI scanner in routine epilepsy surgery evaluation, compared to separate 3 T MRI and PET-CT.

2. Methods

This study is a retrospective data analysis in a single tertiary academic medical center. Potential epilepsy surgery candidates were identified during routine epilepsy clinic visits and epilepsy monitoring unit evaluation. Their clinical semiology and video EEG were evaluated by board certified epileptologists. These patients underwent a regular brain 3 T MRI unless there were contra-indications. Prior to the hybrid PET/MRI available in our institution, PET-CT was performed when there is no clear lesion found in brain MRI or suspected dual pathology from clinical and electric information such as neocortical seizure pattern with hippocampal sclerosis. Some patients repeated PET study with hybrid PET-MRI when there were need for more updated imaging studies, initially thought non-lesional cases, or further fine localization required prior to the invasive monitoring or resection. Patients with contraindication for 3 T MRI were excluded in hybrid PET-MRI studies. After hybrid PET-MRI available in our institution, PET-CT was no longer performed routinely unless the patient cannot have MR studies. Instead, hybrid PET-MRI has been performed. Twenty-nine patients underwent epilepsy pre-surgical evaluations with hybrid PET-MRI from June 2013 until October 2014.

A hybrid PET-MRI (mMR, Siemens Healthcare) capable of acquiring both MRI and PET images simultaneously was used for acquiring PET and MRI images. This is 3 T MRI, using 12 channel head coil same as stand-alone 3 T MRI commonly used in our practice. Both studies were acquired same MRI sequences when epilepsy protocol was ordered. The PET portion of the PET-CT and hybrid PET-MRI studies were all interpreted and compared as routine clinical examinations by experienced Board Certified Nuclear Medicine physicians who had full access to other imaging modalities and clinical history while MRI portion of PET-MRI studies were all interpreted by board certified neuro-radiologists. Prior clinical PET-CT and MRI images were read sequentially while the hybrid PET-MRI was concurrently read. PET attenuation correction was performed using the vendor-provided two-point Dixon-VIBE AC method. The clinical PET images were visually interpreted, and additional tools such as normal databases (Scenium) were variably used at the discretion of the interpreting physician. Only images that were clinically reported as discordant between the PET-CT and PET-MRI images formally compared retrospectively by the study Nuclear Medicine physician and neuroradiologist to see whether prior lesions might have been present in retrospect, and were called only if a lesion was newly appreciated. To examine the magnitude of agreement between results from hybrid PET-MRI and separate acquisition of PET and MRI, we analyzed the data with Kappa statistics [11,12]. This study was approved by the institutional review board.

3. Results

Median and mean age of the 29 patients at the time of hybrid PET-MRI studies were 28 and 30.9 (years), respectively. Table 1 illustrates findings of 3 T MRI, hybrid PET-MRI, PET-CT and clinical semiology and/or EEG findings. Median and mean time interval among 3 T stand-alone MRI, hybrid PET-MRI and PET-CT were 5 and 10.2 months respectively. Nineteen of 29 patients were found to have structural lesions on the MRI portion of hybrid PET-MRI, while 23 were found to have abnormal FDG uptake during the PET portion of the hybrid PET-MRI. Hybrid PET-MRI identified new anatomical or functional lesions in 5 patients without significant clinical changes between studies with the average interval of 12.4 months between two studies. New anatomical MRI lesions were seen in four patients (patients # 15, 18, 26, and 28). Fig. 1 shows hybrid PET-MRI images, compared to PET-CT in patient #15. All of these new MRI lesions were consistent with PET findings. In patient #20 with negative MRI findings, new abnormal FDG uptake (PET lesion) in right frontal lobe was noted in hybrid PET-MRI compared to PET-CT. The cases with the new PET lesion and three out of the four new MRI lesions except patient # 18 appeared to be clinically significant with concordant EEG and/or SPECT results and potentially epileptic foci.

In one patient (patient # 14), a previously seen MRI abnormality was not appreciated in hybrid PET-MRI and was thought to be due to the post-ictal signal changes on the previous MRI. Also, a previously seen FDG hypo-metabolic area on PET-CT was not seen on a more recent PET-MRI in patient # 11. However, this patient underwent left anterior temporal lobectomy between PET-CT and PET-MRI over a time interval separated by 6 years.

Kappa co-efficiency between MRIs is 0.6437, indicating substantial agreement between the results of stand-alone 3 T MRI and the MRI portion of the hybrid PET-MRI. The 95% confidence interval of 0.3667 and 0.9208 suggests at least fair agreement. Kappa co-efficiency between PETs are 0.6250, indicating substantial agreement between the results of the PET-CT and the PET portion of the hybrid PET-MRI. However, from the 95% confidence interval of −0.0273 and 1, it is hard to determine whether an agreement better than chance truly exists but this may be due to small sample size of 12 cases. Also, concordant PET and MRI findings in PET-MRI are seen in 20 out of 29 (69.0%) which are similar to a previous study [9].

Ten out of 29 patients underwent focal resective epilepsy surgeries. Eight of the 10 patients underwent invasive EEG monitoring with concordant findings of seizure foci to PET-MRI. Two patients underwent direct resective surgeries. Six additional patients underwent Phase II evaluation without resection: three of which declined resection due to the potential neurological deficits and three patients were not surgical candidates due to the inability to localize seizure foci. All patients with identified seizure focus had concurrent PET-MRI abnormalities in the same location except Patient #10 who declined surgery showed a different seizure focus (left anterior temporal lobe), compared to a PET abnormality in the posterior temporal lobe. Nine out of 10 surgical patients showed a good surgical outcome, Engel's I-III outcome for 5 months up to 20 months.

4. Discussion

The increased yield to capture anatomical and functional abnormalities on hybrid PET-MRI in our initial experience is thought to be due to the concurrent review of both MRI and PET images by the neuro-radiologist and nuclear medicine specialist, or possibly due to better correlation of anatomic and function imaging.

Because of simultaneous acquisition of PET and MRI, it is possible to directly compare structural and functional information to better understand pathophysiologic changes in an epileptogenic lesion. In addition, this new technique will enable us to compare various functional images in real time such as FDG uptake and blood flow with arterial spin labeling and bold images to further enhance our understanding of relationships between different functional modalities. Furthermore, hybrid PET-MRI studies may be attractive to patients due to convenience and time efficiency of one study session rather than two separate studies. However, this needs to be formally confirmed in future studies.

Table 1
Summary of findings of hybrid PET-MR, separate 3 T MRI, PET-CT and clinical/EEG information.

Patient	3 T MRI finding	MR findings in hybrid MR-PET	PET findings in hybrid MR-PET	PET-CT	Time interval between 3 T MRI and hybrid PET/MR vs hybrid PET/MR and PET-CT (months)	Clinical semiology and/or EEG findings
1	Negative	Negative	Decreased FDG in R temporal	Decreased FDG in R temporal	5 vs 5	R temporal epilepsy
2	Negative	Negative	Decreased FDG in L temporal	Decreased FDG in L temporal	1 vs 5	L temporal epilepsy
3	Negative	Negative	Decreased FDG in L temporal	Decreased FDG in L temporal	3 vs 3	L temporal epilepsy
4	R fronto-temporal parietal Focal Cortical Dysplasia	R fronto-temporal parietal Focal Cortical Dysplasia	Increased FDG in R fronto-temporal parietal	Increased FDG in R fronto-temporal parietal	6 vs 8	R parietal epilepsy
5	L frontal tumor	L frontal tumor	Decreased FDG in L frontal	N/A	1 vs n/a	L orbitofrontal epilepsy
6	R temporal Focal Cortical Dysplasia	R temporal Focal Cortical Dysplasia	Decreased FDG in R temporal	N/A	1 vs n/a	R temporal and parieto-occipital epilepsy
7	L mesial temporal sclerosis	L mesial temporal sclerosis	Decreased FDG in L temporal	N/A	3 vs n/a	L temporal epilepsy
8	R parietal tumor	R parietal tumor	Decreased FDG in R parietal	N/A	2 vs n/a	R parieto-occipital epilepsy
9	R frontal tumor	R frontal tumor	Increased FDG in R frontal	Increased FDG in R frontal	3 vs 75	R frontal epilepsy
10	Negative	Negative	Decreased FDG in L posterior temporal	N/A	5 vs n/a	L temporal epilepsy
11	Previous L anterior temporal lobe resection	Previous L anterior temporal lobe resection	Negative	Decreased FDG in the anterior left temporal	4 vs 77	L temporal epilepsy
12	Small B. hippocampi	Small B. hippocampi	Decreased FDG in L temporal	N/A	8 vs n/a	Presumed L temporal epilepsy
13	R mesial temporal sclerosis	R mesial temporal sclerosis	Decreased FDG in R hippocampus	Decreased FDG in R hippocampus	2 vs 40	R temporal epilepsy
14	Flair signal abnormality in L mesial temporal and frontal lobes	Neg	Negative	N/A	8 vs n/a	Presumed L temporal epilepsy
15	Negative	Subtle L central temporal white matter abnormality	Decreased FDG in L central temporal	Decreased FDG in L central temporal	5 vs 5	L temporal epilepsy
16	R subtemporal focal cortical dysplasia	R subtemporal focal cortical dysplasia	Decreased FDG in R temporal	N/A	7 vs n/a	R temporal epilepsy
17	Negative	Negative	Negative	N/A	8 vs n/a	Bitemporal epilepsy
18	Negative	L mesial temporal signal abnormality	Decreased FDG in L temporal	N/A	14 vs n/a	L frontal epilepsy
19	L hemispheric atrophy	L fronto-temporal, R cerebellum atrophy	Decreased FDG in L fronto-temporal, R cerebellum	N/A	1 vs n/a	L frontal epilepsy
20	Negative	Negative	Decreased FDG in R temporal and frontal	Decreased FDG in R temporal	1 vs 1	R frontal epilepsy
21	R temporal focal cortical dysplasia	R temporal focal cortical dysplasia	Decreased FDG in R temporal	N/A	8 vs n/a	R temporal epilepsy
22	Negative	Negative	Negative	N/A	1 vs n/a	L temporal epilepsy
23	Negative	Negative	Decreased FDG in R temporal	N/A	1 vs n/a	R temporal epilepsy
24	R temporal tumor	R temporal tumor	Decreased FDG in R temporal	N/A	1 vs n/a	R temporal epilepsy
25	Periventricular heterotopia	Periventricular heterotopia	Decreased FDG in L temporal	N/A	3 vs n/a	L temporal epilepsy
26	Negative	L fronto-parietal focal cortical dysplasia	Increased FDG in L temporal and fronto-parietal	Increased FDG in L temporal and fronto-parietal	11 vs 11	L frontal epilepsy
27	Negative	Negative	Negative	N/A	11 vs n/a	R or Bilateral temporal epilepsy
28	Negative	L parieto-occipital deep sulcus subtle gray-white matter blurring	Decreased FDG in L post parieto-occipital lobe	Decreased FDG in L post parieto-occipital lobe	10 vs 11	L posterior temporal and parietal epilepsy
29	L mesial temporal signal abnormality	L mesial temporal signal abnormality	Negative	Negative	22 vs 22	L temporal epilepsy

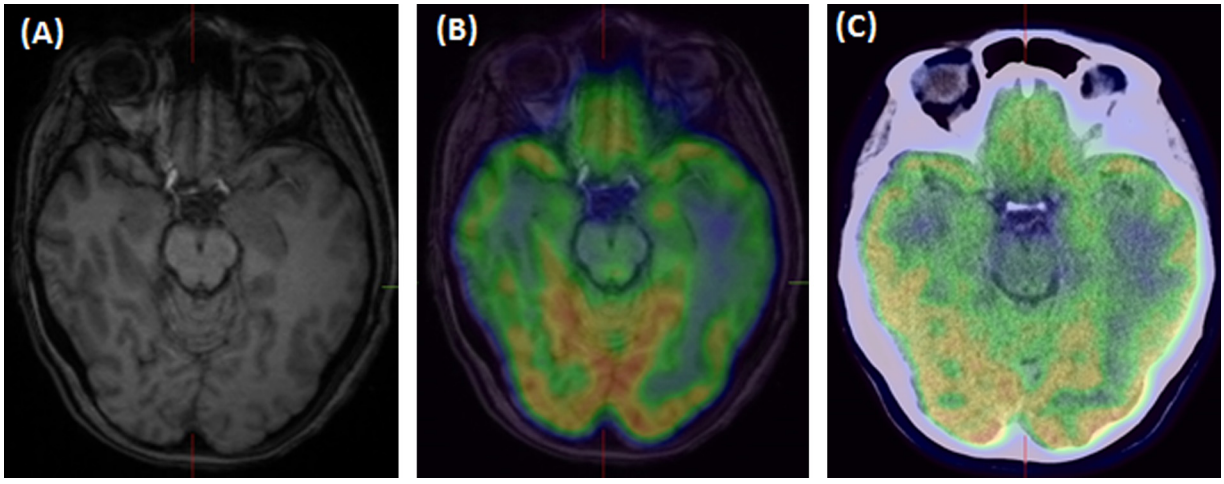

Fig. 1. Comparison between hybrid PET/MRI and PET-CT images in Patient # 15. (A) MR portion of hybrid PET/MRI showing increased abnormal white matter in the left temporal lobe. (B) The fused PET/MR acquired using hybrid PET/MRI showing decreased FDG uptake in the left central temporal lobe, correlating with increased white matter. (C) PET-CT showing similar but more subtle findings to the PET/MRI.

Despite apparent improved lesion detection with hybrid PET-MRI and potential benefits, there are multiple limitations in our pilot study including challenge of MRI based PET attenuation correction, small sample size, retrospective data analysis and various time intervals among different studies from 1 month up to over 6 years. Since the Dixon MRI based attenuation correction does not include bone, we expect underestimation of PET signal using PET-MRI. Various time intervals among different studies may raise the concern that new abnormalities seen in hybrid PET-MRI are due to progression of disease rather than its true sensitivity or specificity. However, none of these patients exhibited significant clinical changes. Future prospective studies with a larger sample size with short intervals among different studies and longer follow up may provide more useful information about the cost-effective benefit of hybrid PET-MRI and potential for epileptic lesion detection compared to the current standard of practice of 3 T MRI and interictal PET-CT.

5. Conclusion

In our pilot case series study, twenty-nine patients undergoing epilepsy surgery evaluation were imaged using PET-MRI. Our initial hybrid PET-MRI experience seems to have improved diagnostic yields for detection of potential epileptic lesions, but further analysis and future studies with more patients will be needed to assess clinical benefit.

Conflict of interest statement

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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