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

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ABSTRACT

Purpose: Epilepsy surgery is the most successful method of treating medically unresponsive epilepsy, but carries a risk of morbidity. PET/MR is an emerging technique that increases detection of focal lesions whose resection may result in symptom remission.

Methods: Retrospective review of 74 focal epilepsy patients over a period of 3 years who had a PET/MR was performed following IRB permission and informed consent. 27 patients underwent surgery or RNS (responsive neurostimulator) placement.

Results: Hybrid PET-MR identified new anatomic or functional lesions in 10 patients not identified with standalone 3 T MR. Of the 27 patients who underwent focal surgery (19) or RNS placement (8), 24 showed improvement (Engel's I-III), 2 did not (Engel's IV), and one had an RNS explanted due to infection. MR and PET were read by 2 separate neuroradiologists and nuclear medicine physicians, respectively. Modalities were evaluated in terms of ability to detect the correct lobe and side for a focal lesion whose resection improved symptoms. Prior standalone MR exhibited 71–77% sensitivity and 0% specificity (as there were only 2 non-responders), MR associated with PET/MR had 68–71% sensitivity and 0–50% specificity (depending on whether a lesion was seen on one of the nonresponders), and PET had 68–71% sensitivity and 25–33% specificity. Using either PET or MR to identify a focal lesion, PET/MR had sensitivity of 78–82% and specificity 0–50%.

Conclusions: PET-MR provides additional sensitivity when used as two combined modalities for detecting possible epileptic foci.

1. Introduction

Epilepsy surgery is a well-known method of treatment for patients with medically refractory epilepsy with a clearly defined focal onset. If a focal, radiographically identifiable lesion can be found, usually on MRI (magnetic resonance imaging), the prognosis for resection of the epileptic focus is significantly better, 60–90% free from disabling seizures, versus 20–65% if no lesion is found [1].

A variety of other techniques have been suggested to aid in localization, including radionuclide SPECT (single photon emission computed tomography) and PET (positron emission tomography) which can identify MRI negative lesions. Overall sensitivity for these methods varies with assessment. An early meta-analysis of SPECT for temporal lobe epilepsy has suggested a sensitivity of 97% for ictal SPECT against other diagnostic data such as EEG, but comparisons against actual surgical data was sparse (only 12 patients) [2] and capture of ictal data is challenging. A meta-analysis of ictal and interictal SPECT coregistered to MRI (SISCOM) gave a positive predictive value of 55–56% for a concordant localization [3]. A meta-analysis looking at temporal lobe epilepsy only found a positive predictive value of 72–89% (depending on the standard) for PET [4]. Another meta-analysis of patients with MRI-negative epilepsy found that PET did not predict seizure freedom [5].

PET-MR is a relatively new technique that allows for acquisition of both PET and MR in one session, simultaneously in some cases. Some preliminary studies have suggested that PET may be more sensitive than MR or SPECT [6], whereas others suggest PET is of little added utility. In particular, hybrid PET-MR has been less well studied for epilepsy, largely due to its novelty and lack of sites with the equipment. Early pilot studies have shown correlation between PET and MR abnormalities in patients with epilepsy [7]. Some sources have also combined PET/MR with EEG [8]. Metabolic abnormalities as detected

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Table 1
Standard epilepsy MR protocol used at our institution.

Sequence	FOV	Slice thickness	Distance factor
Sagittal T1	230	4 mm	20%
Axial T1 FS	220	4 mm	20%
Axial T2	220	4 mm	20%
Axial FLAIR	220	4 mm	20%
Coronal T2	200	3 mm	10%
Coronal FLAIR	180	2 mm	55%
Coronal IR	220	3 mm	20%
Coronal MPRAGE	220	1 mm 3D isotropic	n/a

by PET correlate well with perfusion abnormalities as detected by arterial spin labelling [9]. Despite prior concerns about attenuation correction with PET/MR instead of PET/CT, diagnostic accuracy for epilepsy evaluation appears to be similar [10].

Our prior work demonstrated that PET/MR identified additional lesions over and above MR alone, including lesions seen on MR only in retrospect after being detected on PET [11]. Three years after the initial study, we have collected 45 additional patients, many of whom have undergone surgery, allowing us to evaluate not only detection of lesions, but the effectiveness of surgery for those lesions with long-term follow-up in many cases. We have examined both the original set of patients and new patients collected over time, and are now presenting the aggregate both sets of patients with follow-up, so as to assess the clinical improvement rather than simply lesion detection.

2. Material and 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, epilepsy monitoring evaluation, and clinical semiology with video EEG evaluated by board certified epileptologists. Before PET/MRI became available, patients underwent PET/CT when MR was negative or clinical and EEG findings suggested multiple seizure foci. In some cases, a prior PET/CT was followed by a PET/MRI if there was need for further imaging studies for fine localization before invasive monitoring or resection. A total of 74 patients underwent pre-surgical evaluations with hybrid PET/MR from June 2013 through June 2017.

A hybrid PET-MR (Siemens Biograph mMR, Siemens Healthcare) capable of simultaneous PET and MR acquisition was used to obtain PET and 3 T MR images using a 12-channel head coil. The MR sequences were the same as the standard epilepsy protocol, although 5 early cases used a more limited MR protocol for the PET-MR (these patients had a full 3T MR earlier). The standard MRI epilepsy protocol used at our institution is described below in Table 1. MRI (both the prior studies and those with the accompanying PET) and PET studies were downloaded and blindly re-interpreted, separately by two separate neuroradiologists (for MR) and nuclear medicine physicians (for PET). The two MR studies were interpreted separately from each other by each of the neuroradiologists. PET attenuation correction was performed using vendor-provided two-point Dixon-VIBE method. For interpretation, PET was fused to the highest-resolution MR sequence available using MIMfusion by MIM Software (Cleveland, OH). In general, the PET was called as positive if there was an area substantially different from the contralateral side without underlying explanation visible on MR such as a resected lobe. This retrospective study was approved by the institutional review board.

3. Calculation

27 out of 74 patients underwent resective epilepsy surgeries or responsive neuro-stimulator (RNS) placement. Assessment of response to RNS and resection were as follows. A ‘true negative’ was a case where the study found no focal source, and surgery or RNS proceeded, but the patient did not improve. (One case where one site was indicated, a different site was operated on, and the patient did not improve was counted as ‘true negative’ as well.) In a ‘false negative’, the study was again negative for a focal source, but the patient improved (Engel I-III). In a ‘false positive’, the study indicated a focal lesion, that area was resected or RNS placed, and the patient did not improve. A case where the study found a focal lesion or lesions, and resection of lesions or RNS placement *in a different location* led to a *resolution* of seizures were also treated as ‘false positive’, as the putative lesion was not responsible for the patient’s epilepsy. Cases where placement in a different location only led to a decrease in seizures (Engel’s II or III) wouldn’t be considered ‘false positive’ as the untreated location indicated by SPECT might theoretically have been responsible for the remaining seizures. In a ‘true positive’, the study indicated a focal lesion, that area was resected or RNS placed, and the patient improved. For example, if a PET/MR demonstrated a left temporal abnormality and the patient underwent bilateral temporal RNS and improved, represents a true positive case, particularly when further improvement occurred with a subsequent left temporal lobectomy. Data is presented below in Tables 2 and 3.

4. Results

Median and mean age of the 74 patients at the time of study were 28 and 31 years respectively. 42 of 75 patients were found to have structural lesions on the MR portion of PET-MR, while 48 were found to have abnormal FDG uptake during the PET portion of the hybrid PET-MR. Hybrid PET-MR identified new anatomic or functional lesions in 10 patients over and above standalone 3 T MR on reinterpretation of both, without changes in seizure frequency between studies. 5 of these were on PET, 5 on MR. Interestingly, in all cases PET and MR identified different lesions not seen on the initial MR; in no case did they identify the same lesion not seen on the initial MR. An example of a lesion not considered significant on prior stand-alone MR that was identified as such on PET is shown in Fig. 1; a lesion shown on MR but not PET is shown in Fig. 2, and a lesion seen on both in Fig. 3. Kappa coefficient between standalone MR and MR from PET-MR was 0.582, whereas agreement between the MR and the PET in PET-MR was 0.456, or moderate agreement between MR and PET and substantial agreement between MR performed as part of PET-MR and standalone MR.

Of the 27 patients who had surgical treatment or RNS placement, 24 reported at least some improvement in seizure control (Engel’s score I-

Table 2
Sensitivity, specificity, positive and negative predictive value, and accuracy of all modalities. Readers are separated by a semicolon; for evaluation of PET and/or MR, all possible combinations of the 2 readers on each modality are given.

Modality	FN	FP	TN	TP	Sens	Spec	PPV	NPV	Accuracy
Outside MR	5; 6	2; 3	0; 0	17; 15	71-77	0	83-89	0	63-71
PET	7; 6	2; 3	1; 1	15;15	68-71	25-33	83-88	13-14	64
PET/MR MR	4; 4	1; 2	1; 0	14; 14	78	0-50	88-93	0-20	70-75
PET or MR	4; 4; 4; 4	2; 1; 3; 3	1; 1; 0; 0	19; 19; 18; 19	78-82	0-50	86-95	0-20	72-80
PET and MR	7; 6; 7; 6	1; 3; 1; 3	1; 1; 1; 1	11; 10; 11; 10	61-63	25-50	77-92	13-14	55-60

Table 3
Sensitivity, specificity, positive and negative predictive value, and accuracy of all modalities for surgical patients counting only Engel I as improvement. Readers are separated by a semicolon; for evaluation of PET and/or MR, all possible combinations of the 2 readers on each modality are given.

Modality	FN	FP	TN	TP	Sens	Spec	PPV	NPV	Accuracy
Outside MR	2; 2	6; 6	2; 2	9; 9	82	25	60	50	58
PET	0; 3	6; 6	3; 2	10; 8	73-100	25-33	57-63	40-100	58-68
PET/MR MR	2; 2	5; 6	1; 0	7; 7	78	0-17	54-58	0-33	47-53
PET or MR	0; 1; 0; 2	8; 7; 7; 8	1; 1; 2; 0	10; 10; 10; 9	82-100	0-22	53-59	0-100	47-63
PET and MR	2; 3; 1; 3	4; 5; 4; 5	2; 2; 2; 2	7; 5; 8; 5	63-89	29-33	40-67	40-67	47-67

III), 2 reported no improvement or worsening (Engel's score IV), and one had an RNS that became infected and had to be explanted, and hence could not be assessed. 1 of the 24 patients who improved had a vagal nerve stimulator (VNS) which did decrease seizures, but this is hard to classify as regards to focality. Descriptive statistics are given below in Table 2, and actual data with locations of lesions detected by PET and MR in Appendix A, and treatment, demographic information, clinical semiology, scalp EEG, and invasive monitoring (Phase II) in Appendix B. Case 14 was treated as a 'true negative' or 'false positive' (depending on reader response) as resection of a right frontal glioma did not lead to improvement. (The additionally detected MTS cannot be evaluated as it was not resected.) Note that we considered case 17 'false negative' with negative MR, and 'false positive' with positive PET. This is because PET indicated a lesion in the left temporal lobe but resection of the right temporal lobe resulted in improvement—thus, the MR failed to detect a resectable lesion (false negative) and the PET incorrectly localized the resectable lesion to the left temporal lobe (false positive). Cases 25 and 27 were excluded from analysis of sensitivity and specificity as the RNS 25 had to be explanted (so it is not clear if the RNS would have helped) and 27 had a VNS, which is nonfocal.

Standalone MR found lesions in 23 of 26 patients who had a prior MR according to at least one reader. (Notably, some prior standalone MRs were obtained a few years before the PET-MR, with an average of 261 days.) In addition, with PET-MR, one lesion noted on the prior MR was not described on the PET-MR, and overall the MR found lesions in 18 of 22 patients (excluding the early patients with a limited MR protocol) according to at least one reader, whereas the PET found lesions in 21 of 27 patients according to at least one reader. Treating the diagnostic study as a test for a lesion whose resection will improve seizures, and excluding the explanted and VNS patients, 'plain' MR had a sensitivity of 68–74% and specificity of 0% (due to the small number of negative studies), PET-MR MR had a sensitivity of 74% and specificity of 0–50% (as can be seen, this may not be relevant due to the small number of cases which did not show at least some improvement), and PET had a sensitivity of 70–74% and specificity of 25–33%. Overall agreement between readers was moderate for prior MR (0.50) and PET (0.44), with good agreement for MR concurrent with PET (0.68), perhaps due to greater protocol uniformity.

One might argue that only an Engel's I outcome, however, justifies the morbidity and possible functional loss of surgery. Redoing the analysis with Engel's I treated as 'positive' and Engel's II-IV treated as 'negative', and looking only at surgical cases (of which there were 19), PET now proves to be the most sensitive, specific, and accurate modality (though specificity for other modalities has declined).

5. Discussion

Interestingly, standalone MR did better in some cases than the MR performed with the PET-MR, possibly due to differences in protocol and/or coils. This, however, could also be related to timing between MRI and PET and recent unknown seizure. While PET does appear to find additional cases, many of which are negative on MRI, at least from our results, the PET and MR studies seem to be primarily useful as independent indicators of possible surgical targets rather than confirmatory of a strongly indicated lesion. In particular, we are more concerned with false negatives than false positives in this particular case. It is much less likely a false positive will result in wrongly removing a part of the brain, as PET and MR are not used in isolation, but together with EEG, semiology, and possibly other studies as well. As a result, the increased sensitivity from using PET and MR together to find lesions is of greater utility.

One interesting finding was that in the case where only surgical patients are looked at, PET is much more sensitive specifically for Engel's I outcomes. While this may be simply the result of a small sample size (27 cases decline to 19), it is possible that PET positivity may have additional value in terms of identifying lesions that will result

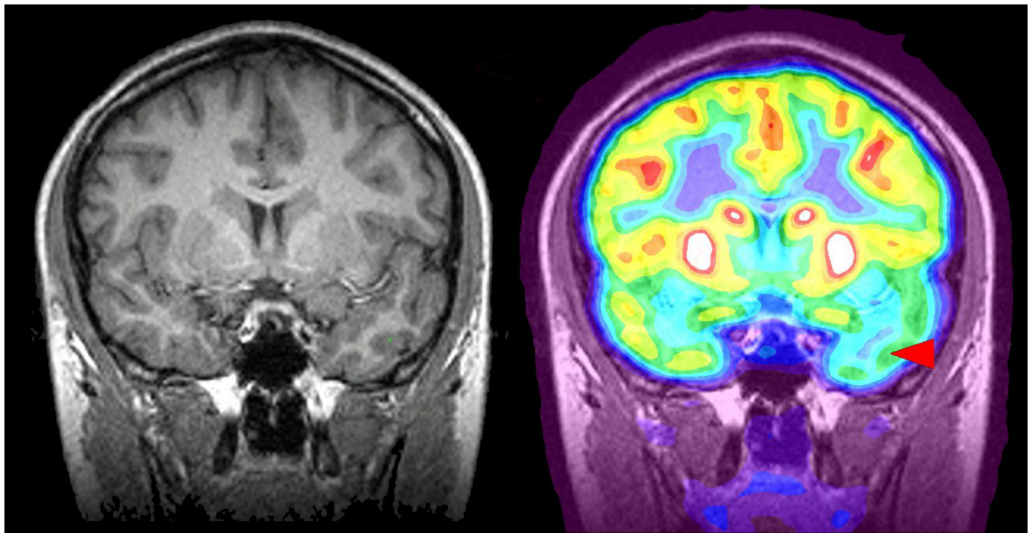

Fig. 1. PET demonstrates decreased uptake in the left temporal lobe (red arrowhead), not visible on either standalone MR or MR concurrent with PET. Hippocampus and remainder of MRI study were normal. The patient had RNS to left frontal and temporal lobes and showed a decrease in seizures (Case #10). (For interpretation of the references to colour in the text, the reader is referred to the web version of this article.)

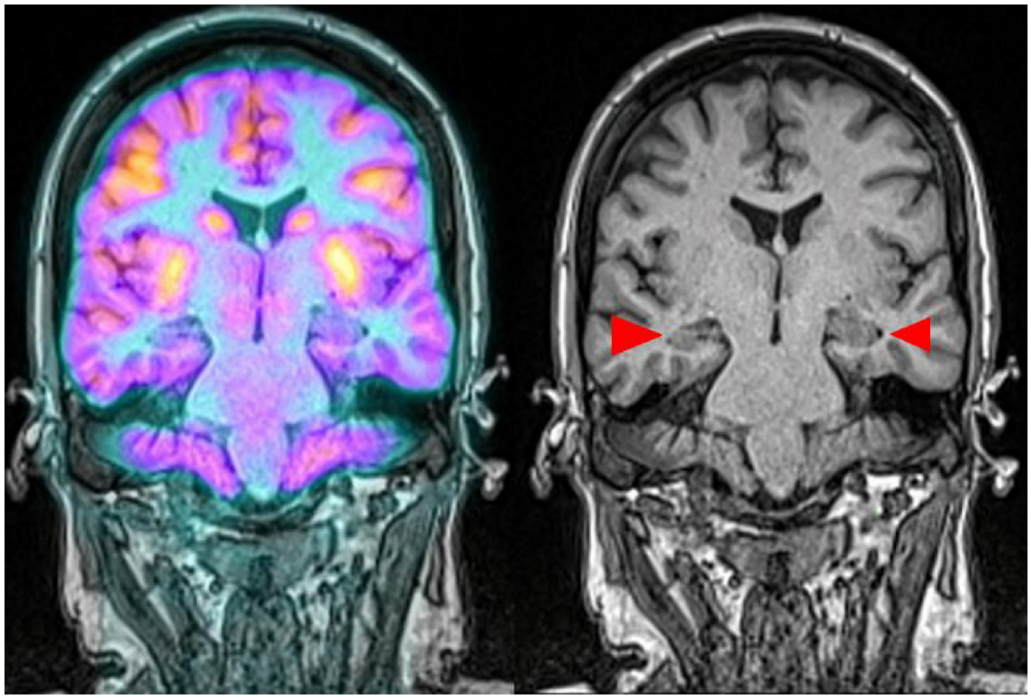

Fig. 2. The difference in hippocampal size (left greater than right-red arrowheads) was visible on both prior standalone MR and PET-MR MR, but did not correspond to a significant difference in uptake on PET. Focal cortical dysplasia on the left was resected, and the patient experienced a decrease in seizures (Case #26). Gliosis in the right temporal lobe was also described on MR as an incidental finding. (For interpretation of the references to colour in the text, the reader is referred to the web version of this article.)

in a complete remission of seizures on surgical resection. This may make it particularly useful in the case where the patient will only undergo surgery if complete remission is likely.

PET-MR allows for acquisition of PET and MR in rapid succession (or simultaneously for systems such as ours). The opportunity to acquire studies in one session decreases the number of studies a patient must undergo, which is helpful given the huge number of studies involved in preparing for epilepsy surgery. Having a registered PET and MR obtained through a single acquisition is also useful in interpretation, although this advantage can be somewhat replaced by a high-quality fusion algorithm. As we had both, this is difficult to assess.

The other principal advantage of PET-MR is the lack of radiation exposure from CT. The big question is, can the joint use of PET and MR be helpful in confirming data? As with many other medical diagnostic tests, there appears to be a trade-off between sensitivity and specificity; however, in our particular case, the data seem to suggest that PET and MR are better at widening the range of possible targets rather than confirming a single one that should definitely be resected. The identification of more foci with PET MRI may have an impact upon the extent of subdural electrodes places for EEG monitoring to evaluate for resection. This may in turn result in greater accuracy of resection.

We found lesions in about 70–80% of patients depending on the precise method of evaluation. This is somewhat lower than the 80% usually cited for temporal lobe epilepsy (TLE), although the inclusion of

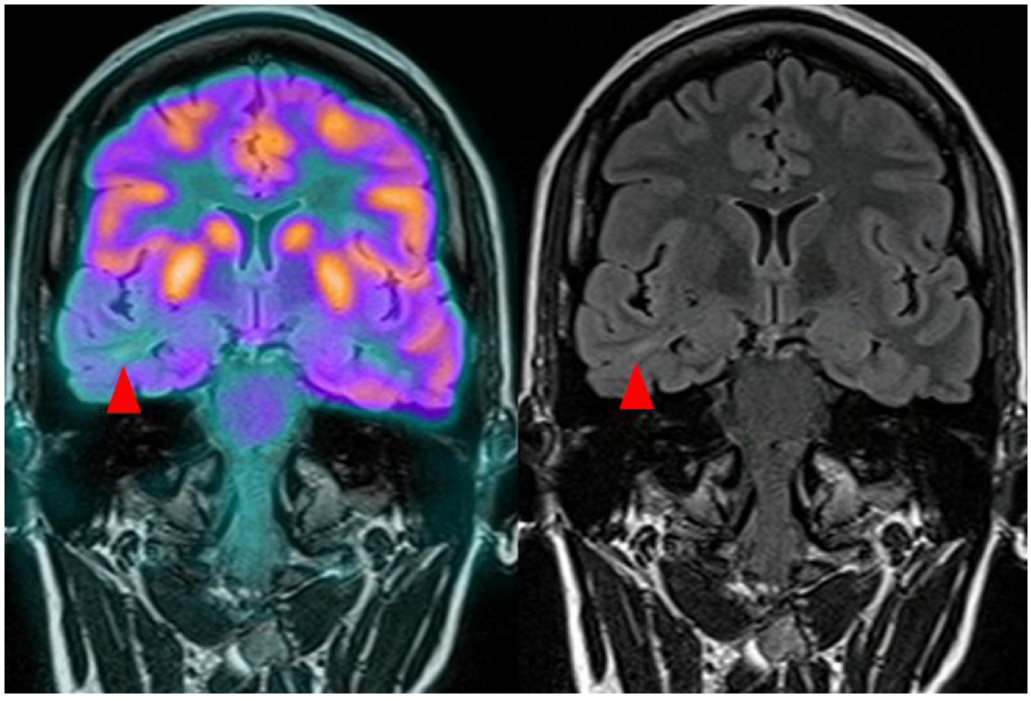

Fig. 3. Diffuse cortical dysplasia was visible on both MRI and PET. The patient's seizures resolved after resection of the abnormal right temporal lobe (red arrowheads). Mesial temporal sclerosis was found as well at pathology, not identified on MR (Case #21). (For interpretation of the references to colour in the text, the reader is referred to the web version of this article.)

non-TLE etiologies will be expected to lower lesion detection [12]. Our Engel's outcome (I-III) improvement in 24/27 (89%) of patients who had surgery or VNS is slightly better than the literature. One meta-analysis shows that at least some decrease in seizures (an Engel's I-III outcome) occurs in about 86% of patients with a seizure focus shown by PET, 80% if MR is normal and 73% if EEG is nonfocal [4].

It has been hypothesized that functional techniques such as arterial spin labelling and blood oxygen-level dependent imaging (BOLD) would work synergistically with PET, which assesses interictal metabolism. To some extent, this has been performed with PET used together with BOLD [13,14] MR imaging during epilepsy imaging evaluation to select patients for resection to lower risk of loss of valuable memory or language function. However, the most common non-conventional imaging MR sequence, diffusion-weighted imaging is rarely utilized [15]. BOLD could be used on future PET/MR cases and correlating it with PET would be a useful direction for further study. Integration with MR spectroscopy, which has also been used for finding resectable lesions [16], could be another possible future area of study.

As with our previous study, there are several limitations. One major confounding factor with our results is our high rate of improvement post-surgery. Since we had very few patients who did not show at least some improvement, our assessment of negative predictive value and specificity are extremely limited. This is somewhat compensated for in clinical practice when considering that PET-MR is used together with other sources of data such as clinical seizure semiology and EEG to determine a resective site, so negative predictive value (and specificity) are less important; even if a PET or MR does not find a lesion, one of the many other data sources might.

MR-based attenuation correction of the brain does appear to be adequate. The positive with PET/MR is the avoidance of repeated radiation dose (from the CT in the PET/CT) in this largely young patient population. Patients often receive repeat scans, and the dose to the eyes and brain may become a concern, as does the long-term increased risk for meningiomas and gliomas. Other shortcomings of this study include the retrospective nature, small sample size (74 patients, 27 with surgery or RNS/VNS), although larger than our previously reported paper. Follow-up is longer in this study than in the prior one, but still quite limited with the more recently performed cases.

6. Conclusion

In this case series, 74 patients undergoing epilepsy pre-surgical evaluation were imaged using PET-MRI with 27 undergoing surgery or RNS/VNS placement. Our initial hybrid experience demonstrates improved diagnostic yields for detection of possible lesions, with MR being the most sensitive technique for detection of lesions and subsequent improved seizure control on resection. Furthermore, the use of PET or MR together appears to be the most sensitive test for detecting lesions that will aid epilepsy control if resected.

Conflict of interest

None of the authors has a conflict of interest.
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Appendix A. Results of MRI and PET

Index	Outside MR (R1)	Outside MR (R2)	PET (R1)	PET (R2)	PET-MR MRI (R1)	PET-MR MRI (R2)
1	R MTS CD (TP)	R ant/MTS (TP)	R T down (TP)	R T down (TP)	Not done	Not done
2	L F low grade tumor (TP)	L F mass? ODG (TP)	L F down (TP)	L F down (TP)	Not done	Not done
3	L hippo increased signal (TP)	L T lobectomy (FN)	no new focus (Neg); s/p L lobectomy (FN)	L T down over and above lobe resection (TP)	Not done	Not done
4	R MTS (TP)	R MTS (TP)	Neg (FN)	Neg (FN)	R MTS (TP)	R MTS (TP)
5	L MTS (TP)	Neg (FN)	Neg (FN)	Neg (FN)	Not done	Not done
6	L MTS (TP)	Neg (FN)	L T down (TP)	Neg (FN)	Not done	Not done
7	Neg (FN)	R uncus (TP)	R T down (TP)	R T down (TP)	Neg (FN)	R uncus (TP)
8	R FP CD (TP)	R FP CD (TP)	R FP CD (TP)	R T down (FP)	Right FP CD (TP)	R FP CD (TP)
9	L MTS (TP)	L hippo sclerosis (TP)	L T down (TP)	L T down (TP)	L MTS (TP)	L hippo sclerosis (TP)
10	Neg (FN)	Neg (FN)	Neg (FN)	L T down (TP)	Neg (FN)	Neg (FN)
11	R MTS (TP)	R MTS (TP)	R T down (TP)	R T down (TP)	R MTS (TP)	R MTS (TP)
12	R MTS (TP)	R MTS, R hemi atrophy (TP)	R T down (TP)	R T down (TP)	R MTS (TP)	R MTS, R hemi atrophy, R par CD (TP)
13	R amygdala, med T lobe enlarged (TP)	R T polar encephaloceles (TP)	R T down (TP)	R T down (TP)	R MTS (TP)	R T polar encephaloceles (TP)
14	L MTS (FP)	R F mass (FP)	Neg (TN)	Neg (TN)	Neg (TN)	R F mass (FP)
15	Neg (FN)	Neg (FN)	Neg (FN)	Neg (FN)	Neg (FN)	Neg (FN)
16	R T (TP)	R T mass (TP)	R T down (TP)	R T down (lobe resection) (TP)	R T (TP)	R T lobectomy, R hippo atrophy (TP)
17	Neg (FN)	Neg (FN)	L T down (FP)	Neg (FN)	Neg (FN)	Neg (FN)
18	L MTS (TP)	L MTS (TP)	L T down (TP)	L T down (TP)	L MTS (TP)	L MTS (TP)
19	L MTS (TP)	L MTS (TP)	L T down (TP)	L T down (TP)	L MTS (TP)	L MTS (TP)
20	L MTS (TP)	L MTS (TP)	L T down (TP)	L T down (TP)	L MTS (TP)	L MTS (TP)
21	R T CD (TP)	R T CD (TP)	R T down (TP)	R T down (TP)	R T CD (TP)	Neg (FN)

22	R MTS (FP)	R MTS (FP)	R T down (FP)	R T down (FP)	R MTS (FP)	R MTS (FP)
23	L MTS and amygdala (TP)	L hippo (TP)	L T down (TP)	Neg (FN)	L MTS (TP)	L MTS, L hippo T2 bright (TP)
24	No MRI	No MRI	Neg (FN)	L T down (TP)	L MTS (TP)	L MTS (TP)
25	Neg (N/A)	Neg (N/A)	Neg (N/A)	Neg (N/A)	L FP centrum semiovale cort thick (N/A)	L F CD (N/A)
26	s/p R T mass resection (FN)	L F CD, L hippo change (FP)	Neg (FN)	R T down (FP)	L T lobe mass (TP)	R T mass; L F CD; L hippo sclerosis (TP)
27	Neg (N/A)	Neg (N/A)	Neg (N/A)	Neg (N/A)	Neg (N/A)	Neg (N/A)

Appendix B. Treatment and outcome data

Index	Engel score	Treatment	Age/ Sex	Clinical Semiology	scalp EEG	Phase II
1	II	R T resection same yr + RNS to R post T and occipital	25F	déjà vu, visual aura, staring and GTC	Electroclinical seizures from R posterior quadrant	Independent seizures from R hippocampus and R occipital lobe
2	I	L F lobe resection	35M	staring, head version to R and GTC	L anterior quadrant	L subF lobe > > L inferior P and posterior T lobe independently
3	II	Left posterior T lobe resection with previous left anterior T lobectomy over 10 years ago	19F	goose bump, staring, GTC	L mid T region	L sub/inferior/ middle T gyrus posteriorly > > superior T and P lobe
4	II	B. hippocampal RNS	24F	staring and GTC	B/l FT	B. hippocampi
5	I	RNS to left superior temp gyrus and hippocampus	42F	staring and GTC	L anterior T and L central region (C3)	L superior T gyrus
6	I	Left T resection	44F	staring/confusion and GTC	L T region	L anterior temp
7	I	R T resection	25M	dejavu/staring and dystonic posture with falling	R T	R anterior T
8	I	R P lobe resection	25F	screams, head version to R, GTC. Sometimes with B. shaking with intact consciousness	R centroparietal region	R P lobe
9	I	Left T resection	26F	staring, palpitation of heart, GTC	L T	N/A
10	III	RNS to left F and T lobe	20F	dystonic posturing on R, drop attacks, GTC	L anterior quadrant	L F lobe
11	II	R T resection	19F	staring, L facial twitching, olfactory aura, L thumb twitching with spread to arm/ face and whole body	R T	N/A
12	I	R T resection	9M	gastric aura, staring, drooling, R arm jerking and head version to L, gagging	R frontocentral and L T region	R mesial T lobe
13	II	R T resection	42F	Staring	R anterior to mid T	N/A
14	IV	R partial F lobe resection	21F	L leg shaking and GTC	vertex/central region but R > L	R F lobe
15	III	RNS to R P lobe and posterior T lobe	25F	auditory aura/R arm tingling/dystonic posture, GTC	L P and posterior T	L superior parietal lobe
16	I	R T resection	20M	nausea/vomiting/ staring	R hemispheric, T maximal	R subT lobe
17	I	R T resection	47F	GTC	BiT	R hippocampus
18	II	L T resection	16F	R arm/leg shaking/twitching, staring, sensation of nosebleed,	L hemispheric but cannot further localize	L hippocampus, anterior and mesial T lobe
19	III	L T resection	27F	staring and GTC	BiT but L > R	L anterior and mesial T lobe
20	I	L T resection	54M	chill, funny feeling, staring, right hand posturing, L hand automatism, lip smacking	L T	L anterior and mesial T lobe
21	I	R T resection	22F	staring and GTC	R FT region	broad from R mesial/ anterior T to posterior superior T gyrus

22	IV	RNS to R T lobe due to the stronger memory support from R	35F	gastric aura, staring, GTC	R hemispheric but not localizing	R anterior-mesial T lobe
23	I	L T resection	13M	staring, eye deviation upward, GTC	L T	L anterior-mesial T lobe
24	II	RNS to B. Hippocampi in 1 yr - > L temp resection with preserving RNS to R	25F	finger tingling, staring and GTC	independent L > R T	L anterior mesial temp
25	n/a	RNS to L F and explantation due to infection	21M	R facial drooping, right leg/face twitching and B. shaking	L > R F region	L F lobe with motor cortex involvment
26	III	L T resection	42F	Staring	L > R T	L > R anterior/mesial T
27	III	VNS, no resection	43F	Staring	L T	multifocal from L posterior subT, L anterior-mesial and L subF lobes

References

[1] Tellez-Zenteno JF, Hernandez Ronquillo L, Moien-Afshari F, Wiebe S. Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. Epilepsy Res 2010;89:310–8.

[2] Devous Sr. MD, Thisted RA, Morgan GF, Leroy RF, Rowe CC. SPECT brain imaging in epilepsy: a meta-analysis. J Nucl Med 1998;39:285–93.

[3] Chen T, Guo L. The role of SISCOM in preoperative evaluation for patients with epilepsy surgery: a meta-analysis. Seizure 2016;41:43–50.

[4] Willmann O, Wennberg R, May T, Woermann FG, Pohlmann-Eden B. The contribution of 18F-FDG PET in preoperative epilepsy surgery evaluation for patients with temporal lobe epilepsy A meta-analysis. Seizure 2007;16:509–20.

[5] Wang X, Zhang C, Wang Y, Hu W, Shao X, Zhang JG, et al. Prognostic factors for seizure outcome in patients with MRI-negative temporal lobe epilepsy: a meta-analysis and systematic review. Seizure 2016;38:54–62.

[6] Won HJ, Chang KH, Cheon JE, Kim HD, Lee DS, Han MH, Kim IO, Lee SK, Chung CK. Comparison of MR imaging with PET and ictal SPECT in 118 patients with intractable epilepsy. AJNR Am J Neuroradiol 1999;20:593–9.

[7] Ding YS, Chen BB, Glielmi C, Friedman K, Devinsky O. A pilot study in epilepsy patients using simultaneous PET/MR. Am J Nucl Med Mol Imaging 2014;4:459–70.

[8] Grouiller F, Delattre BM, Pittau F, Heinzer S, Lazeyras F, Spinelli L, Iannotti GR, Seeck M, Ratib O, Vargas MI, Garibotto V, Vulliemoz S. All-in-one interictal presurgical imaging in patients with epilepsy: single-session EEG/PET/(f)MRI. Eur J Nucl Med Mol Imaging 2015;42:1133–43.

[9] Boscolo Galazzo I, Mattoli MV, Pizzini FB, De Vita E, Barnes A, Duncan JS, Jager HR, Golay X, Bomanji JB, Koepp M, Groves AM, Fraioli F. Cerebral metabolism and perfusion in MR-negative individuals with refractory focal epilepsy assessed by simultaneous acquisition of (18)F-FDG PET and arterial spin labeling. Neuroimage Clin 2016;11:648–57.

[10] Paldino MJ, Yang E, Jones JY, Mahmood N, Sher A, Zhang W, Hayatghaibi S, Krishnamurthy R, Seghers V. Comparison of the diagnostic accuracy of PET/MRI to PET/CT-acquired FDG brain exams for seizure focus detection: a prospective study. Pediatr Radiol 2017;47(Oct. (11)):1500–7.

[11] Shin HW, Jewells V, Sheikh A, Zhang J, Zhu H, An H, Gao W, Shen D, Hadar E, Lin W. Initial experience in hybrid PET-MRI for evaluation of refractory focal onset epilepsy. Seizure 2015;31:1–4.

[12] Theodore WH. Presurgical focus localization in epilepsy: PET and SPECT. Semin Nucl Med 2017;47:44–53.

[13] Reyes A, Thesen T, Wang X, Hahn D, Yoo D, Kuzniecky R, Devinsky O, Blackmon K. Resting-state functional MRI distinguishes temporal lobe epilepsy subtypes. Epilepsia 2016;57:1475–84.

[14] Abreu R, Leal A, Lopes da Silva F, Figueiredo P. EEG synchronization measures predict epilepsy-related BOLD-fMRI fluctuations better than commonly used univariate metrics. Clin Neurophysiol 2018;129:618–35.

[15] Bao Y, He R, Zeng Q, Zhu P, Zheng R, Xu H. Investigation of microstructural abnormalities in white and gray matter around hippocampus with diffusion tensor imaging (DTI) in temporal lobe epilepsy (TLE). Epilepsy Behav 2018;83:44–9.

[16] Caruso PA, Johnson J, Thibert R, Rapalino O, Rincon S, Ratai EM. The use of magnetic resonance spectroscopy in the evaluation of epilepsy. Neuroimaging Clin N Am 2013;23:407–24.