# Intraoperative Coregistration of Magnetic Resonance Imaging, Positron Emission Tomography, and Electrocorticographic Data for Neocortical Lesional Epilepsies May Improve the Localization of the Epileptogenic Focus: A Pilot Study

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**Key words**
- Coregistration
- Electrocorticography
- Intraoperative
- Lesional epilepsy
- Multimodal imaging
- Neocortical epilepsy

**Abbreviations and Acronyms**
**EcoG**: Electrocorticography
**EEG**: Electroencephalography
**MRI**: Magnetic resonance imaging
**PET**: Positron emission tomography
**SPECT**: Single-photon emission tomography

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OBJECTIVE: **To objectively mark out abnormal areas of magnetic resonance imaging (MRI), positron emission tomography (PET), and electrocorticography (ECoG) using neuronavigation so as to 1) enhance the accuracy of margins of the epileptogenic zone and 2) understand the relationships of all the three modalities with each other.**

METHODS: **A prospective study was conducted of 37 patients with intractable epilepsy due to lesional, neocortical pathologies from noneloquent areas. Prior to surgery, fusion and transfer of MRI and PET images onto a neuronavigation system was performed. At surgery, this was correlated to intraoperative ECoG using the electrode as referential points. An objective score was created for every electrode point that was correlated with MRI and PET abnormality at the point. The extent of surgical resection was mapped out using these data.**

RESULTS: **From a total of the data recorded from 1280 electrode points, 23.5% were located over the lesion. In addition, over the lesions, 93% of PET and 66% of ECoG points were abnormal. Over the perilesional areas, 43% of PET and 45% of ECoG points were abnormal. Using these data for surgery, both lesional and perileisonal areas were resected; 33/37 patients had good outcome (25 Engel I, 8 Engel II) (mean follow-up: 23.6 ± 3.2 months; range 18–31 months).**

CONCLUSION: **Multimodal imaging and ECoG using this method seems to provide a better objective localization of the epileptogenic foci.**

## BACKGROUND

Localization of the epileptogenic zone in surgery for intractable epilepsy is yet to be optimally defined with the current technology. More than a decade ago, Holmes et al. (16) demonstrated that the lesion seen on magnetic resonance imaging (MRI) often does not correspond to electrical activity observed on invasive electroencephalography (EEG). The same is true for electrocorticography (ECoG) or even functional imaging techniques like positron emission tomography (PET) or single-photon emission tomography (SPECT). Although MRI, PET, and SPECT studies are used for preoperative localization, only ECoG is usually utilized to define the limits of resection intraoperatively. MRI-PET coregistration to accurately map the resective area preoperatively has been earlier utilized by the author in tuberous sclerosis along with abnormal diffuse tensor imaging (5).

Although multimodal imaging (MRI, PET, tryptophan-PET, video EEG) (7, 8, 19, 22, 48) has gained much acceptance in epilepsy surgery, its application was used to roughly define epileptogenic focus rather than to accurately mark the boundaries for surgical resection.

Neuronavigation provides an excellent opportunity to achieve this purpose. Despite the routine use of multimodality imaging, the overall concordance among all the techniques (MRI, video EEG, PET, and ictal SPECT) is approximately two thirds or less in lateralizing the epileptogenic foci (22-48). In addition, most times at surgery, intraoperative ECoG or data from invasive video EEG that is utilized for resection in lesional epilepsies is not correlated objectively with the PET/MRI data. Although data from MRI and PET scans (by visual "eyeballing") are used to plan the surgical craniotomy, they are not represented on the patient's brain to mark out the epileptogenic zone for resection.

To overcome this shortcoming, intraoperative multimodal imaging may be useful, by coregistering simultaneously with anatomical (MRI), functional (SPECT/PET), and electrical data (ECoG/invasive video EEG) on the patient's brain. This would allow the surgeon to have information to accurately and objectively obtain information from all the modalities required for surgery (31, 34).

With this background knowledge, the authors describe a simple procedure of utilizing the data intraoperatively from MRI, PET, and ECoG in patients undergoing surgery for lesional neocortical epilepsy. This would allow the surgeon to have

complete representation of all the three imaging modalities on the patient's brain in order to

1. improve the accuracy in marking out the epileptogenic zone
2. study the relationship among MRI, PET, and intraoperative ECoG.
3. develop a prototype technique that might allow further integration of other imaging modalities such as magnetoencephalography, ictal SPECT, and so forth.

Lesional neocortical epilepsies have been included in the present study, as the presence of a substrate on MRI would allow the surgeon to objectively define its relationship to PET and ECoG. In addition, only focal lesions with well-defined concordance have been included to minimize the preoperative variable factors.

### Hypotheses

The study is based on the following assumptions of our current knowledge on the neurobiology of lesional epilepsy (10, 19-24, 32).

1. The lesion seen on the MRI (anatomical substrate) does not correspond exactly to the epileptogenic zone.
2. Accurate multimodal imaging integration along with ECoG may prove to have a greater benefit for the surgeon to accurately mark out the epileptogenic zone.
3. No single investigation accurately marks out the epileptogenic zone; hence, under these circumstances, multimodal integration may provide the best possible localization.

## MATERIALS AND METHODS

### Patient Profile

The present study has been conducted at a center with a significant experience in performing epilepsy surgeries (more than 600 epilepsy cases have been surgically operated over 14 years) and under direct guidance of a neurologist with significant experience in intraoperative electrocorticography (1, 44, 45). The work was conducted per the guidelines of the Indian Council of Medical Research after clearance from the institute ethics committee.

The eligible population was a prospective cohort ($n = 37$, males $= 19$) between the ages of 15 and 45 years (mean age $= 24.8$ years), with well-characterized refractory neocortical epilepsy. Patients with an identifiable neocortical lesion on MRI with intractable epilepsy and showing concordance on presurgical investigations (interictal EEG, video EEG, ictal SPECT) were included. Patients with diffuse lesions or inaccurate concordance with respect to other investigations were not included. All cases were first discussed at a comprehensive epilepsy surgery meeting.

The duration of epilepsy for the population varied from 3 to 17 years (mean $7.6 \pm 3.4$ years), with a seizure frequency range between 2 and 32 seizures/week (mean $5.8 \pm 3.9$/week). Majority of the patients ($n = 34$) were maintained on a regimen of three antiepileptic drugs. Twenty-seven patients had changed at least one drug during their course of treatment (mean times of change: $1.4 \pm 1.2$). The commonest seizure pattern observed was complex partial type with generalization (19), with the rest being simple partial and myoclonic types ($n = 14$ and $n = 4$, respectively). Myoclonic seizures were seen in a younger spectrum of patients, where the generalized phenotype of myoclonias were seen in addition to focal semiologies. Six patients among the total study population were observed to have had multiple seizure patterns.

Patients were excluded if they had the presence of deep-seated lesions (e.g., hippocampal sclerosis), MRI-negative epilepsies, eloquent cortex lesions, or if they required chronic implanted electrodes.

### Investigations

All the patients underwent a detailed clinical examination and standard epileptic presurgical investigations (interictal EEG, video EEG, and MR imaging with special sequences) (4, 6, 44, 45).

A day prior to surgery, the patients underwent fiducial marker placement. This was followed by MRI (with gadolinium, magnetization-prepared rapid gradient echo, oblique coronal T2, fluid attenuation inversion recovery, T1 axial, T2 axial, T2 sagittal) on a 1.5-T MR Siemens machine (Siemens AG, Munich, Germany). Subsequently, fluorodeoxyglucose PET scan was performed on Siemens Biograph PET machine (Siemens AG) using neuronavigation protocol (contiguous, nonoverlapping slices of 1.0- to 3.0-millimeter thickness using matrix size $256 \times 256$ or $512 \times 512$ with no gantry tilt and circular or square field of vision). Scans were performed from hard palate to the top of the head with at least two or three slices in the air in the orbitomeatal plane. PET acquisition was performed 30 minutes following intravenous injection of 10 millicurie of $^{18}$F-fluorodeoxyglucose on a full-ring dedicated dual-slice lutetium oxyorthosilicate (LSO) PET three-dimensional scanner. PET was performed in the interictal period (at least 48 hours after a seizure) to avoid false positive results of postictal hypometabolism.

The images were then transferred to the neuronavigation system (Medtronic, stealth station [Medtronic, Minneapolis, Minnesota, USA]). Using the software (Stealth Merge), the PET and MR images were then fused. One could vary the intensity of MRI and/or PET images on the window scale. At one end, pure MRI images could be visualized, whereas at the other end, pure PET images were seen. Fusion images were visible in between. Colored images, rainbow, or heat option images were available depending on the choice of the operating surgeon for differentiation (Figure 1). The color coding was such that red represented hypermetabolic areas and blue represented hypometabolic areas. Other colors like yellow and green were termed as relatively hypometabolic.

***Neuropsychological Workup.*** All patients underwent a neuropsychological workup using the standard battery used at our institution (35). A repeat examination was performed 6–9 months after surgery.

### Mapping of the Epileptogenic Zone and Surgical Technique

All patients underwent surgery under general anesthesia. The surgical craniotomy was planned depending on concordance obtained from all the investigations. The ECoG recordings were performed using a 64-channel machine (Viasys [Carefusion, Alberqurque, New Mexico, USA]) with at least 32 grid electrodes to allow generous coverage of the lesional and perilesional areas. All the grid electrodes had a standard 10-mm interelectrode distance. The reference electrode was placed over the forehead. The recordings were performed both by the