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The effect of increased intracranial EEG sampling rates in clinical practice

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Abstract

Objective—Recent research suggests that high frequency intracranial EEG (iEEG) may improve localization of epileptic networks. This study aims to determine whether recording macroelectrode iEEG with higher sampling rates improves seizure localization in clinical practice.

Methods—14 iEEG seizures from 10 patients recorded with >2000 Hz sampling rate were downsampled to four sampling rates: 100, 200, 500, 1000 Hz. In the 56 seizures, seizure onset time and location was marked by 5 independent, blinded EEG experts.

Results—When reading iEEG under clinical conditions, there was no consistent difference in time or localization of seizure onset or number of electrodes involved in the seizure onset zone with sampling rates varying from 100–1000 Hz. Stratification of patients by outcome did not improve with higher sampling rate.

Conclusion—When utilizing standard clinical protocols, there was no benefit to acquiring iEEGs with sampling rate >100 Hz. Significant variability was noted in EEG marking both within and between individual expert EEG readers.

Significance—Although commercial equipment is capable of sampling much faster than 100 Hz, tools allowing visualization of subtle high frequency activity such as HFOs will be required to

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Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

I confirm that I 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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improve patient care. Quantitative methods may decrease reader variability, and potentially improve patient outcomes.

Keywords

high frequency; macroelectrode; seizure onset

1. Introduction

For the ~1/3 of epilepsy patients who are not controlled by medications alone, epilepsy surgery or the possibility of implantable devices to treat their seizures may be the only therapeutic option. However, the success rates of epilepsy surgery vary broadly from 40–80% (Cohen-Gadol et al., 2006; Lee et al., 2005; Mohammed et al., 2012; de Tisi et al., 2011), and these numbers have not changed in many years. It is clear that the standard practice of evaluating epilepsy surgical candidates needs improvement. For this reason, the epilepsy community has great interest in identifying additional biomarkers to localize and characterize epileptic networks.

EEG has been the standard diagnostic tool for epilepsy for decades, and recent technological advances now enable much higher resolution. Originally, pen-and-paper EEGs had a mechanical limitation to sampling rate, which led to the traditional ‘Berger bands’ (0.1–30 Hz) that define the vast majority of EEG reading. With the advent of digital EEG, there is growing research interest in utilizing broadband recordings (i.e. sampling rates of 1000 Hz or greater) to better localize the ictal onset during intracranial EEG (iEEG) during presurgical evaluation. Current evidence supports two types of high frequency signals as biomarkers of epileptic networks. The first is low voltage fast activity seen at seizure onset. In several studies examining an array of clinical metadata, surgically removing regions producing this activity (also known as focal ictal beta, focal ictal gamma, beta/gamma buzz, etc) was highly associated with good outcomes (Park et al., 2002; Wetjen et al., 2009; Zakaria et al., 2012). This ictal biomarker is now highly regarded among clinicians and widely used in practice. The second are high frequency oscillations (HFOs), which are used primarily in research because they require significant processing. There is mounting evidence that interictal HFOs are highly localizing to the seizure onset zone (SOZ) (Jacobs et al., 2016, 2008; Park et al., 2014; Worrell et al., 2008, 2004), and surgical outcomes are improved if regions generating high rates of HFOs are resected (Haegelen et al., 2013; Usui et al., 2015). Much of the HFO research utilizes experimental microelectrodes, which sample from much smaller regions of brain and allow evaluation of unit activity (Weiss et al., 2016). However, HFOs are also detected in standard iEEG macroelectrodes, provided data are sampled fast enough (Worrell et al., 2012). The major limitation with HFO research is that these signals are too small to visualize on standard EEG viewers (10 seconds/page) and require bandpass filtering and thresholding that are not readily available (Worrell et al., 2012). These two biomarkers—low voltage fast activity and HFOs—have generated demand for EEG equipment capable of higher sampling rates. The hope is that increased temporal resolution will better localize seizure networks, and hopefully lead to better surgical outcomes.

In this paper, we seek to demonstrate whether increased sampling rate provides additional information to clinicians under standard clinical procedures—reading an iEEG in traditional viewing software. The goal is not to test whether either of these specific biomarkers can be seen, but rather to assess whether the current trend of steadily increasing technical capability has led to any improvement in accuracy of reading clinicians and clinical care. This increased technical capability comes at a cost, both to purchase newer equipment and to store the vast datasets. We specifically measure whether time and location of seizure onset, as determined by expert reviewers, is affected by higher iEEG sampling rates. Prior literature supports our hypothesis that increased EEG sampling rates would allow for earlier and perhaps better localized detection of low voltage fast activity and HFOs in the SOZ. We also estimate whether patient outcome would have been affected. We believe these results will help demonstrate the utility of incorporating broadband EEG into standard clinical practice, and the need for better clinical tools to leverage these data.

2. Methods

2.1 Patient Data

Ten patients from the Mayo Clinic in Rochester, MN with medically refractory epilepsy believed to be of neocortical origin underwent implantation of standard subdural electrodes (Ad Tech Medical Instruments, Racine, WI) to localize the SOZ after noninvasive monitoring was indeterminate. All data were acquired with approval of the local Institutional Review Board, then de-identified. These patients were monitored with a Neuralynx Digital Lynx amplifier (Bozeman, MT) at 32556 samples/s and 9 kHz low pass anti-aliasing filters. The data were downsampled to 2713 Hz in Matlab (Mathworks, Natick, MA) and stored on the cloud-based International Epilepsy Electrophysiology Portal (IEEG Portal) (Wagenaar et al., 2013). Each patient had at least 1 seizure captured. The location, number, and type of intracranial electrodes (grid and/or strip and/or depth electrodes) were determined by a multidisciplinary team, including neurosurgeons, neurologists, neuroradiologists, and neuropsychologists, as part of routine clinical care. Nine patients underwent surgical resection and the regions of resection are known. One patient did not undergo surgical resection due to co-localization of the SOZ with eloquent speech cortex as established on cortical mapping. Patient outcome as determined by the International League Against Epilepsy (ILAE) Classification was available in the 9 patients who underwent resection (Wieser et al., 1997). Table 1 provides detailed clinical information for all subjects.

2.2 EEG processing and marking

Seizures were identified in each patient from their clinical metadata, and then seizure “clips” with a randomized lead time of at least 10 minutes prior to EEG onset were extracted from the IEEG Portal. Fourteen seizures were identified and clipped. Each of these clips was then downsampled in Matlab (‘decimate.m’) four times (to 100, 200, 500 and 1000 Hz) independently. This function automatically low-pass filters the data prior to downsampling in order to avoid aliasing. Each of these new clips was saved with a randomized filename in BNI file format, leading to 56 EEG files.

Human marking of seizure onsets was performed by five full-time clinical epileptologists. The clinicians opened each file in the same, standard EEG viewing software that allows control of high- and low-pass filters, horizontal and vertical scaling. The clinicians were instructed to determine the timing and location of the seizure onset in each file, according to their own personal interpretation. They then marked the seizures for the Earliest EEG Change (EEC) (Litt et al., 2001). The EEC is identified by first determining the unequivocal electrographic onset and then looking backwards in time to find the first departure from normal background on the EEG leading to a seizure. Reviewers were instructed to mark as many channels as they felt were involved in the EEC for each seizure. All clinicians were aware that this study was assessing whether high frequency data could improve detection, and were also instructed to set the display to 2 seconds per page on a 2560-by-1600 pixel resolution 30 inch monitor when making determination of the EEC. Clinicians were free to use any tools or interpretations at their disposal, duplicating their standard clinical practice.

3. Results

Two measures are considered in order to evaluate the quality of the response of the neurologist to the EEG data prior to seizure: the onset time of the seizure (earlier onset superior) and the number of channels in the SOZ. Fourteen seizures were observed across nine patients; one patient had three seizures, three patients had two seizures and the remaining five each had one seizure. Five expert EEG readers evaluated each of the fourteen seizures at four different frequencies: 100, 200, 500, 1000 Hz. We assessed whether reader performance improves as frequency cutoff increases.

We first focus on the onset time of the seizure, the EEC, as marked by each reader. The results were similar with comparison of any of the six possible pairs of frequencies (e.g. 100 versus 200, 100 versus 500, etc.). Thus, we only report the comparison of 100 to 1000 Hz. We defined an improvement in EEC marking if the time at 1000 was at least one second (s) earlier than the time marked at 100. Figure 1 demonstrates the transition into a seizure for the first patient (P001) in the study in a selection of channels. The figure is a screenshot of the same seizure shown with 100, 200, and 1000 Hz sampling rate. This particular patient had low voltage fast activity at seizure onset, which is seen equally well in the 200 and 1000 Hz data but not at 100 Hz. All five reviewers agreed on the seizure onset time, which did not differ with different sampling rate. Another example with more ambiguous onset was the second seizure in P013 (Fig. 2). In this case, an early discharge with low voltage fast activity was followed by mild attenuation, then the seizure becomes readily apparent. Reviewers were inconsistent in picking the two potential starting points. Note that although the early fast activity is better visualized at 1000 Hz at the scale in the figure, it can be seen at lower sampling rates (albeit low pass filtered to its constituent gamma frequencies) when expanded to 2 s/page.

For all of the EEG readers there was no significant difference in the EEC across all frequency cutoffs in the majority of seizures. Below, we present the specific results for each reader. Table 2 summarizes the results.

EEG reader 1—There were 12 cases in which the times were in essence the same. In the other two cases, there was one instance where the time was 1.7s earlier at 1000 Hz and in the other case the time was 1.1s later at 1000 Hz.

EEG reader 2—There were 9 cases where the times were in essence the same. In three cases the times were earlier at 1000 Hz (1.1, 1.5 and 1.9s). There were two anomalous cases which point out disparities between readers. In one case (second seizure in P013), the EEC marked at 100 Hz was 232s and at 1000 Hz it was 226s, or 6 seconds earlier. In this same seizure, two of the other four readers marked the EEC at the 226s range twice (at 100 and 1000 Hz) and at the 232s range twice (at 200 and 500 Hz), i.e. without any consistent relationship with sampling rate. The other two readers' EEC was in the 232s range for all frequency cutoffs. The difficulty of the analysis is even more evident for the second anomalous case (P036). Reader 2 marked the EEC at 78s at 1000 Hz and 159s for all other sampling rates. Two of the other readers marked the EEC at 159s at all frequency cutoffs, while the other two marked 78s at 100 Hz and 159s at 1000 Hz. These cases highlight the high degree of intra- and inter-rater variability in EEG marking that we observed in our results.

EEG reader 3—There were 8 cases where the times were in essence the same. In two cases, the EEC marked times were earlier at 1000 Hz by amounts of 2.7s and 4.8s and in four cases the times were later at 1000 Hz by amounts of 5.3, 5.8, 1.8 and 4.2s.

EEG reader 4—There were 9 cases where the times were in essence the same. In two cases the EEC markings were earlier by amounts of 3.3 and 1.7s at 1000 Hz and in two cases it was earlier at 100 Hz by the amounts of 5.5s and 5.4s. In P036, this Reader marked the EEC as 78s for 100 Hz and 500 Hz and 159s at 200 and 1000 Hz.

EEG reader 5—This reader was least like the other four. For example, in one instance the other four readers all marked EEC within 0.1s at all frequencies, while Reader 5 marked the EEC 4s earlier. In only six cases were the EEC markings in essence the same when comparing 1000 Hz to 100 Hz. In three cases the EEC times were earlier at 1000 Hz by the amounts 1.9, 9 and 7.3s. In three cases it was later at 1000 Hz by the amounts 5, 7.5, and 3.1s. There were two anomalous cases. In P036 the Reader marked the EEC at 78s for 100, 200, and 500 Hz and 159s at 1000 Hz. In P034 this reader was an outlier, marking 60s at 100 Hz and 72s at 1000 Hz, while the other 4 Readers all marked around 84s.

In summary, if we eliminate the anomalous cases in each reader and utilize a marking time at least 1s earlier at 1000 Hz to define improvement, we observe an EEC marked earlier by >1s in: 1/14, 3/12, 2/14, 2/13 and 3/12 cases across the 5 EEG readers. In aggregate, there were 11 out of 65 cases in which the EEC was earlier. This produces an estimate of 16.9% of cases have earlier EEC with higher sampling rate (95% standard confidence interval: 7.8% to 26%). However, there were 10 cases in which the EEC was later at higher sampling rate. Thus, even excluding the anomalous cases, there is no appreciable earlier identification of the EEC when sampling the iEEG at higher rates.

We next assessed the impact of sampling frequency on localization of the seizure onset zone (SOZ) in terms of the number of electrodes marked as involved at seizure onset at the time of earliest EEG change (EEC) at different sampling rates. These results also varied significantly across the five EEG readers. Again, the results were similar when comparing any of the six possible pairs of frequencies. Thus, we only report the comparison of 100 to 1000 Hz. We hypothesized that EEG readers would be able to localize seizure onset to a smaller number of electrodes within the EEC at higher sampling rates. Specific results for the two examples in Fig. 1–2 are shown in Table 3. The EEC channels marked per seizure varied widely both within individual EEG readers and across all readers. Across all seizures and readers, the average total number of channels marked within the EEC per seizure was 4.7 at 100 Hz, 6.0 at 200 Hz, 5.0 at 500 Hz, and 4.5 at 1000 Hz, though the absolute number of channels varied widely. Therefore, for this comparison it was necessary to compare a given reader's specific results only with themselves, as the assignment of number of involved electrodes is very subjective and varied widely between readers.

The most relevant comparisons, particularly given that the number of total electrode channels varied across patients, is an assessment of the number of times that more EEC channels were found at 100 Hz relative to 1000 Hz. Table 3 shows that slightly more EEC channels are marked at the higher sampling frequency, but that result varied by reader and most frequently the number of EEC channels marked were not different.

If we aggregate across the 5 readers, there are 12 seizures at 100 Hz versus 19 seizures at 1000 Hz with a larger number of electrodes marked within the EEC indicating a trend toward higher frequency cutoffs leading to a larger number of electrodes marked within the EEC. Using a binomial model to assess if this difference is significant, the p value is 0.141. What is more telling is that the difference is often very small. The most extreme case was 46 more onset channels at 100 Hz for one patient (P011) for one EEG reader, but in most cases the difference was at most 2 electrode channels. Therefore, our conclusion is that sampling rate produced no consistent difference in the number of channels for any of the readers.

We further stratified the data to see if the results were affected by patient outcome. For instance, it is possible that patients with diffuse seizure onset, wherein there is less chance of good outcome from surgery, could have different results with higher sampling rates. Two of the 9 patients who underwent surgical intervention met our criteria for poor surgical outcome (ILAE score = 3). When restricting our analysis to the remaining 7 patients with good outcomes (ILAE score = 1), or to the two patients with poor outcome, we again found that sampling rate made no difference in the time of EEC nor in the number of channels within the SOZ.

It is important to note that the data were not processed to identify HFOs. Identification of HFOs requires specialized filtering and usually utilizes software specifically designed to identify them (Navarrete, et al. 2016, Worrell, et al. 2012). Nevertheless, each of the reviewers was aware that HFOs could be present and the expansion to 2 seconds per page was designed to allow them to potentially visualize HFOs. However, the reviewers could not discern any HFO data from the preictal period nor at the time of seizure onset. There were rare instances in which HFOs were visible within the standard EEG. The best example was

P002, who had HFOs visible on spikes during the seizure (Fig. 3). As expected, HFOs were not visible in the 100 Hz data, though even at 200 Hz there were oscillations visible. However, although HFOs were prominent at higher frequency during seizures, HFOs were not visible interictally and were not a factor in determining the location and time of seizure onsets. Thus, none of the reviewers were able to utilize HFO data to help in their determination of the EEC or electrode localization.

4. Discussion

In the clinical setting, iEEG was traditionally recorded over a narrow frequency bandwidth (~0.1–100 Hz) from large surface area (~1–10 mm²), widely spaced (5–10 mm) macroelectrodes. As technology has advanced, there have been only subtle changes to this paradigm. The electrode size and spacing has changed little, although stereo-EEG now has reduced the scale by about half. On the other hand, sampling rate has increased considerably, largely fueled by demand for acquiring broadband signals such as HFOs and low voltage fast activity. But the question remains: is there any benefit from higher sampling rates in standard clinical practice--how high is high enough?

Our results demonstrate that there is no appreciable difference in the time of EEC marking or the number of electrodes identified within the SOZ with higher sampling rates in this set of 10 patients. While it is impossible to generalize these results to all patients, there are several reasons that they are pertinent to standard practice: intra/interrater variability, the fact that low voltage fast activity is visible at lower sampling rates, and the fact that HFOs are very difficult to find under clinical conditions.

Even with standardized training of the participants in this study, the markings between readers were highly variable, and intrarater reliability was also highly variable. These findings are not surprising given EEG readers are known to be inconsistent even with their own markings (Abend et al., 2011; Benbadis et al., 2009; Spring et al., 2017). We expect that similar variability would occur if the data were processed to find HFOs: previous work showed that human reviewers agree in only 21% of HFOs events (Blanco et al., 2010; Gardner et al., 2007), and, in another recent study HFO identification agreement was poor between human reviewers (mean Cohen's Kappa=0.403) (Spring et al., 2017). In total, these results show that, using standard EEG viewing software, higher sampling rates appear not to affect clinical decisions.

These results may seem disappointing, especially given the current technological improvements and the mounting evidence that high frequency data should help with seizure localization. There is also data suggesting that more sophisticated computational modeling may better localize epileptic networks, and perhaps these methods too will benefit from high frequency data, but this has not been tested (Khambhati et al., 2016, 2015; Sinha et al., 2016). Clinical data clearly show that low voltage fast activity is a strong indicator of the epileptogenic zone (Park et al., 2002; Wetjen et al., 2009; Zakaria et al., 2012). However, our data suggest that this activity can be seen adequately even with 100 Hz sampling rate. HFOs are also very promising biomarkers, but clinicians cannot consistently see them in the iEEG without custom processing. Both of these results are a direct result of current clinical

practice, in which EEG is viewed with standard display software at about 10 seconds per page.

In clinical practice, epileptologists put the most emphasis on seizure onset and propagation patterns to determine regions to resect during iEEG evaluations. Currently, interictal data, although examined, does not play as important of a role in determining resection region. In fact, it is unknown what an interictal “spike” represents, with respect to the epileptic network, particularly with regard to seizure generation versus propagation and how reliable the presence of these epileptiform discharges is as a biomarker of underlying epileptogenic tissue(Rathore and Radhakrishnan, 2010). In contrast, much of the high frequency EEG literature has focused on interictal quantification of ripples and fast ripples. The majority of these studies are very labor intensive, taking a human many hours to mark 10 minutes of data on a 10 channel recording(Zijlmans et al., 2011). For obvious reasons, this highly laborious methodology is not practical in clinical practice. But there is clear motivation to incorporate this information in clinical decision making, for example literature indicating that high frequency activity increases 20 minutes prior seizures(Worrell et al., 2004), and even more so in several seconds before onset(Khosravani et al., 2009).

A common electrophysiology board question is to determine the maximum frequency that can be resolved with a monitor showing 10 seconds: at 2560 pixels, peak frequency is 128 Hz. These practical aspects of viewing hardware are such that sampling faster than 500 Hz makes little difference for common EEG reading using this equipment. Expanding the EEG to 2 seconds/page allows the reader to visually resolve activity up to 640 Hz, which makes sampling up to double this frequency (Nyquist criteria) practically feasible; however, our study suggests that clinicians do not base their decisions on such high frequency information, even when specifically looking for it. Physicians are typically trained to read EEGs and to recognize seizure onset patterns on a time scale of 10–15s per page (more with wider monitors). The vast majority of EEGs are read at that scale, meaning the higher frequency data are mostly ignored. Thus, while it is now possible to see higher frequencies on the iEEG, it appears that clinicians do not yet utilize them in their standard practice, with the exception being low voltage fast activity, which can be seen easily at sampling rates 200 Hz and higher.

There are limitations to this study. EEG readers did not have access to the video recordings of patient seizures, which may have had impact on SOZ determination, particularly in the 2 anomolous seizures. The patient population included only neocortical seizure onsets and 10 patients. In addition, there were very few patients who met criteria for poor surgical outcome. A useful future study would be to utilize quantitative analysis in a larger population of patients to determine if automated detection algorithms applied to broad bandwidth iEEG can improve seizure network localization and epilepsy surgical outcomes. Successful application of automated detection would allow this technology to be utilized in clinical practice.

To be clear, some might argue that there is little to lose by sampling at high frequency rates, given how easy this is to do with present equipment. But such a practice is not without cost, particularly for institutions that own older equipment that is not capable of sampling at

higher bandwidths, and secure storage at many institutions remains one of the higher associated costs of epilepsy monitoring. For these reasons, this study points out that at least the current standard of care for intracranial EEG monitoring does not require high sample rates for routine reading.

Given that our collaborative group has spent a great deal of time analyzing high bandwidth iEEG data, it is important to state that we aggressively support collecting and utilizing these data for research purposes. We also believe that more standard tools to leverage these data may increase the clinical utility of high frequency EEG, provided they can be rigorously proved to be of value. In particular, there could be great value in having HFOs or other high frequency activity identified and marked within the EEG to aid clinicians in their interpretation. Our point in presenting this study is to make a clear distinction between what is theoretically possible, what may be important to research and what is actually important to current clinical practice. In an era when epilepsy surgery remains underutilized, particularly in many developing parts of the world, an appreciation of minimum requirements for functionality remains an important area for discussion, as opposed to pushing for the most expensive equipment available prior to rigorously demonstrating its value.

In summary, there is ample evidence that high resolution iEEG can be helpful in patient care, but our results show that simply sampling at a higher rate, while utilizing the same, traditional strategies for reading EEG, does not have a clear effect on reading accuracy or patient outcome. To our knowledge, most modern systems sample at > 200 Hz at least, which is sufficient to see low voltage fast activity. But other high frequency activity such as HFOs and similar phenomena are not readily visible on standard EEG viewers. Additional strategies such as automated detectors and efficient, enhanced clinical interfaces will be needed before routine mapping of HFOs and other high frequency activity is likely to influence clinical practice. Without such tools, higher sampling rates do not appear to enhance EEG interpretation.

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Highlights

- 1.** Increased sampling rates did not improve seizure onset human marking under clinical conditions.
- 2.** Interrater and intrarater reliability of visually evaluated intracranial EEG is poor.
- 3.** Automated detection algorithms are needed to utilize higher EEG sampling rates in clinical practice.

Fig. 1.

Comparison of EEG in patient 1 for 100 (top), 200 (middle), and 1000 (bottom) Hz sampling rate. The low voltage fast activity (red *) is clearly seen even at 200 Hz, and is visible as beta/gamma oscillations at 100 Hz. All five reviewers marked the onset at 2:32.2 seconds at all sampling rates. There was variability in the number of channels felt to be within the seizure onset zone, but no consistent correlation with sampling rate.

Figure 2.

Comparison of EEG for patient 13 for 100 (top), 200 (middle) and 1000 (bottom) Hz sampling rate. There is a single broad area discharge (blue *), which at higher sampling rate is accompanied by low voltage fast activity, followed by a clear synchronous oscillations (red *) 6 seconds later. Reviewers picked between the two onset times, but were inconsistent.

Figure 3. Visualization of HFOs

One second of 4 channels of data is shown from patient P002 during a seizure for 100 (top), 200 (middle) and 1000 Hz (bottom). Likely HFOs are shown with red bars. As expected, HFOs are poorly visualized by lower sampling rates. Although HFOs were visible during this seizure, no readers were able to identify interictal HFOs. Scale bar: 100 ms x 5 mV.

Table 1

Detailed clinical information regarding each of the 10 patients with drug resistant epilepsy included in this study. For each patient, 1–3 seizures were analyzed at 4 different frequency cutoffs. A total of 56 seizures were marked by 5 independent expert EEG readers (sz=>seizures).

Subject	Pre-operative imaging	Electrodes Implanted (total #)	Surgery	Pathology	# of sz	ILAE Outcome
P001	Nonlesional brain MRI and fdg-PET	4x6 grid (left temporal) 5 strips (left) 2 depths (left) (64)	Left temporal lobectomy	Periventricular white matter and mesial temporal cortex with marked gliosis	1	3 (>10 years follow-up)
P002	Brain MRI with left > right hippocampal volume loss, fdg-PET with left>right temporal hypometabolism	Bilateral hippocampal depths (16)	Left temporal lobectomy	Consistent with left mesial temporal sclerosis	1	1 (>10 years follow-up)
P005	Nonlesional brain MRI	3 strips (left) 2 depths (left temporal) (36)	Left temporal lobectomy	Cerebral cortex and white matter with nonspecific mild to moderate gliosis, amygdala and hippocampus with nonspecific mild gliosis	1	1 (>10 years follow-up)
P010	Known lesion concerning for neoplasm (imaging reports unavailable)	6x6 grid (left temporal) 3 strips (left) 2 depths (left) (56)	Left anterior temporal resection (excluding amygdala and hippocampus)	Ganglioglioma	3	5 (>10 years follow-up)
P011	MRI with two regions of signal abnormality in left parietal and anterolateral left frontal lobes	4x6 grid (left frontal) 6x6 grid (left frontoparietal) (60)	Resection of two focal areas of flair abnormality	Left frontal: malformation of cortical development. Left parietal: Taylor type IIB cortical dysplasia.	1	1 (>10 year follow-up)
P013	MRI brain with small focus of increased T2 signal adjacent to right frontal horn, otherwise unremarkable	8x8 grid (left posterior temporal-parietal) 4x4 grid (left posterior), 1 strip (84)	Left parietal cortical resection	Consistent with microdysgenesis	2	1(>10 years follow-up)
P015	Normal brain MRI, fdg-PET with left temporal hypometabolism	6x6 grid (left temporal) 4 strips (left) 2 depths (left) (68)	Left temporal lobectomy	Consistent with left mesial temporal sclerosis	1	1 (4 years follow-up)
P034	Previously resected oligodendroglioma, MRI suspicious for residual neoplasm right middle frontal gyrus	6x6 grid (right frontal) 1 strip (right motor cortex) (44)	Right frontal lobe prior resection extended	Oligodendroglioma	1	1 (1 year follow-up)
P036	MRI brain with chronic right middle cerebral artery vascular territory infarct	8x8 grid (right frontal) 6x4 grid (right temporal) 2 depths (right) (96)	Right temporal lobectomy (to temporal-occipital junction)	Gray and white matter gliosis, hippocampal structures without pathology	1	1 (7 years follow-up)
P040	focal cortical dysplasia inferior left parietal gyrus	8x8 grid (left parietal), left parietal depth (68)	Left parietal resection	no resection (eloquent speech cortex involved)	2	N/A

Table 2

Comparison of seizure onset zone (SOZ) time between 100 and 1000 Hz: For each EEG reader the number of seizures with marked seizure onset zone (SOZ) times within 1 second at 100 versus 1000 Hz (column 2), marked SOZ >1 second earlier at 100 Hz (column 3), and SOZ >1 second earlier at 1000 Hz (column 4). Anomalous cases are described in the text.

EEG reader	SOZ time same 100 and 1000 Hz	SOZ time >1s earlier 100 Hz	SOZ time >1s earlier 1000 Hz	Anomalous cases
1	12	1	1	0
2	9	0	3	2
3	8	4	2	0
4	9	2	2	1
5	6	3	3	2

Table 3

Number of channels determined to be in the Seizure Onset Zone in P001 and P013

Reviewer	P001 (100 200 500 1000 Hz)	P013 (100 200 500 1000 Hz)
1	4 4 4 4	2 2 2 20
2	7 23 22 22	8 8 8 12
3	5 7 5 7	13 4 7 13
4	1 1 1 1	2 5 2 2
5	6 5 6 7	12 26 23 21

For each reviewer, the number of channels they selected as comprising the Seizure Onset Zone (SOZ) is shown for P001 (left of column) and the second seizure of P013 (right of column) (seizures shown in Figs 1,2).