# Value of semiology in predicting epileptogenic zone and surgical outcome following frontal lobe epilepsy surgery

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Abstract

**Objective:** To evaluate the ability of semiology alone in localising the epileptogenic zone (EZ) in people with frontal lobe epilepsy (FLE) who underwent resective surgery.

**Methods:** We reviewed data on all individuals who had FLE surgery at our centre between January 01, 2011 and December 31, 2020. Descriptions of ictal semiology were obtained from video-EEG telemetry reports and presurgical multidisciplinary meeting summaries. The putative EZ was represented by the final site of resection. We assessed how well initial and combined set-of-semiologies correlated anatomically with the EZ, using a semiology visualisation tool to generate probabilistic cortical heatmaps of involvement in seizures.

**Results:** Sixty-one individuals had FLE surgery over the study period. Twelve months following surgery, 28/61 (46%) were completely seizure-free, with a further eight experiencing only auras. Comparing the semiology database with the putative EZ, combined set-of-semiology correctly lateralised in 77% (95% CI: 69%-85%), localised to the frontal lobe in 57% (95% CI: 48%-67%), frontal lobe subregions in 52% (95% CI: 43%-62%), and frontal gyri in 25% (95% CI: 16%-33%). No difference in degree of correlation was seen comparing those with ongoing seizures 12 months after surgery to those seizure free.

**Significance:** Semiology alone was able to correctly lateralize the putative EZ in 77%, and localise to a sublobar level in approximately half of individuals who had FLE surgery.

Semiology is not adequate alone and must be combined with imaging and EEG data to identify the epileptogenic zone.

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## INTRODUCTION

Seizure semiology helps identify areas of the brain involved in the onset and propagation of epileptic seizures. (1) This aids in determining the epileptogenic zone (EZ), which is a critical step in evaluating the feasibility of epilepsy surgery. (2) The lateralising and localising value of semiology varies according to which features occur. Many of these observations, however, relate to temporal lobe seizures, where semiological patterns are often clearer than in frontal lobe epilepsy. (3)

Frontal lobe epilepsy (FLE) can be associated with a wide variety of clinical manifestations, reflecting the rich and diverse connectivity of frontal lobe networks. (4) Furthermore, frontal seizures are frequently brief and may manifest complex behaviours that can be difficult to accurately describe. (5) In these cases, semiology often arises from interaction of many brain regions, which may not be intimately related to the epileptogenic zone (6). Although characteristic seizure patterns have been described, there is only modest correlation with anatomical origin, particularly at the sublobar level. (7, 8) This may relate to rapid propagation of epileptic discharges within widely connected frontal networks, which leads to activation of areas distinct from the seizure onset zone. (9, 10) In most cases of FLE, seizure propagation over a distance of at least 2cm occurs before the onset of subjective symptoms or objective clinical signs. (10)

Recent advances in correlating semiology with sublobar regions have come primarily from stereo-EEG studies. (11-15) In FLE, several different electroclinical subgroups have been described. (5, 15) For example, seizures involving precentral or premotor regions are characterised by elementary motor signs, whereas those involving lateral prefrontal cortex or the frontal pole are associated with gestural motor behaviour with distal stereotypies. (5) By their nature, however, observations during stereo-EEG are limited to the areas they sample.

Prediction of the EZ should take into account multiple sources of data, including clinical, neuroimaging and electroencephalography (EEG) data. The lateralising and localising value of semiology has been estimated to be approximately 60-90%, equivalent to scalp EEG and MRI. (16-18) These studies again, however, tend to focus on seizures which originate in the temporal lobe.

We sought to evaluate how well semiology alone performed in lateralising and localising the EZ in people with FLE who underwent resective surgery. In these individuals, the site of resection following multimodal investigation and multidisciplinary team discussion was used as a surrogate for the presumed epileptogenic zone, with subgroup analysis based on 12-month postsurgical seizure freedom.

**METHODS**

**Participants and Setting**

We reviewed electronic records of all individuals who had FLE surgery at the National Hospital for Neurology & Neurosurgery, London, UK, over a 10-year period between January 01, 2011 and December 31, 2020. All individuals had been discussed in presurgical multidisciplinary meetings having undergone scalp video-EEG telemetry, neuropsychology and neuropsychiatry assessments, MRI imaging, and in selected cases FDG-PET, ictal SPECT or

intracranial EEG monitoring before proceeding to resective surgery. We excluded those in whom surgery was primarily performed for reasons other than epilepsy.

Seizure outcomes 12 months after surgery were obtained from a prospective epilepsy surgery database at our centre. Outcomes were classified according to the International League Against Epilepsy (ILAE) surgery outcome scale. (19)

**Data: Semiology**

Detailed descriptions of ictal semiology and their evolution were obtained from video-EEG telemetry reports and summaries of multidisciplinary team (MDT) meetings. Semiologies were documented from review of video-EEG and MDT data using a consistent, predetermined format, and independently categorised by two investigators, with any discrepancies resolved by discussion. Semiology included signs obtained from video-EEG as well as symptoms noted by the patients, documented in a standardised MDT proforma (20). Semiological features were categorised using the descriptions listed in Supplementary Table 1, based on previously described semiological seizure classification (21), and subsequently categorised according to the latest ILAE classification of seizure types. (22)

Initial semiology was defined as the first seizure manifestation described by the patient or witnessed on video telemetry. Combined set-of-semiology included all ictal manifestations, as witnessed on video-EEG telemetry. The most frequently encountered chronological sequence for included semiologies is noted in Supplementary Table 2.

**Data: Localisation and Lateralisation**

Surgical records and post-operative MRI imaging were reviewed to identify the site and extent of resective surgery. Resections were visually categorised into those that involved orbitofrontal,

frontomedial, dorsolateral, and/or frontocentral regions, as has been previously described. (23,

24) An example of each region is demonstrated in Figure 1.
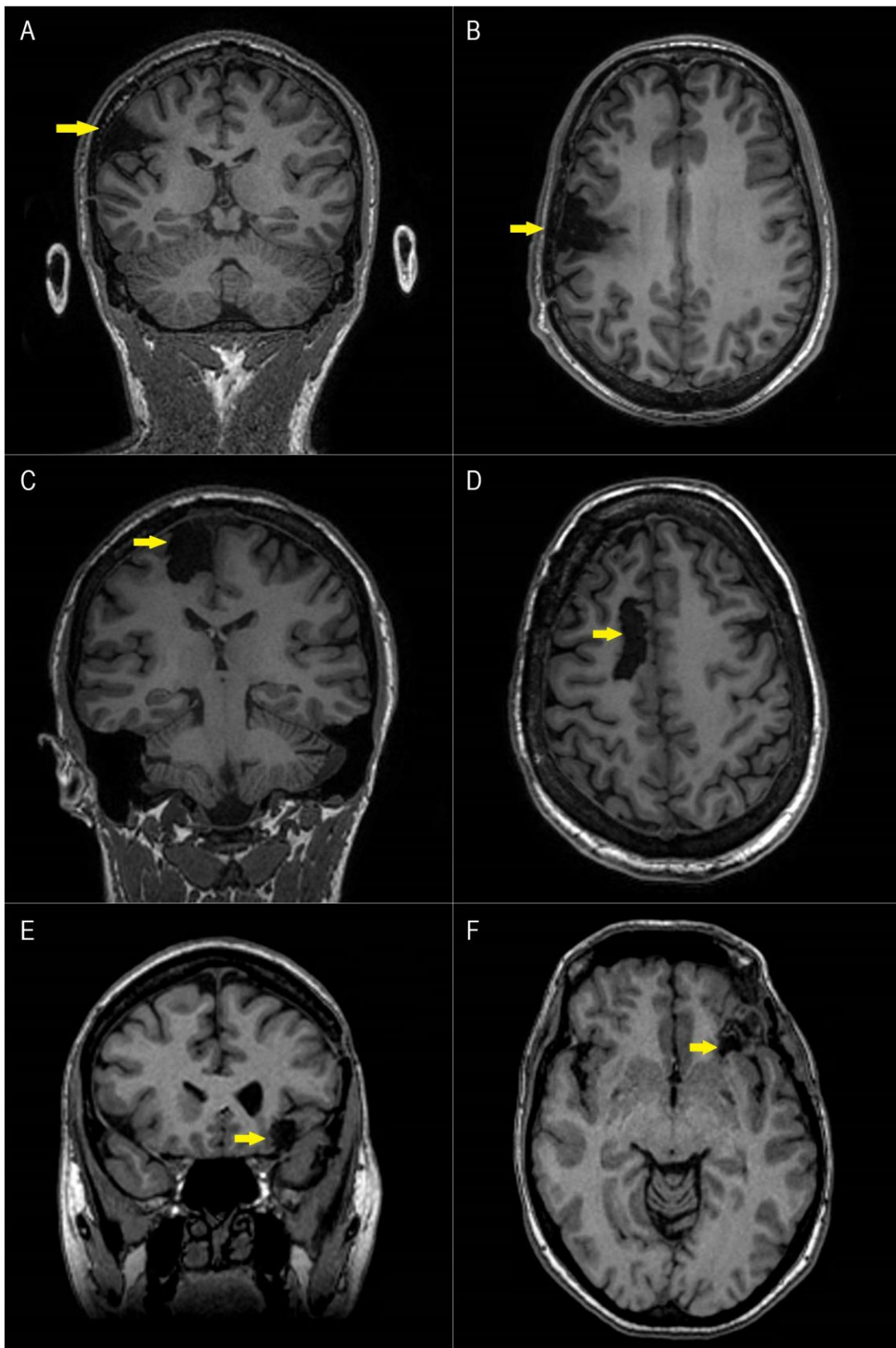
**Figure 1: Imaging categorisation example. Right dorsolateral resection in coronal (A) and axial (B) views. Right frontomedial resection in coronal (C) and axial (D) views. Left orbitofrontal resection in coronal (E) and axial (F) views. All images are T1-weighted 3T MRI sequences; yellow arrows indicate site of resection.**

Surgical operations were deemed extensive if they involved two or more of these regions. Localisation was then further categorised at the gyral level, with resections involving the precentral gyrus, superior, middle or inferior frontal gyri as well as those that extended into the anterior cingulate and insula. Although these are distinct brain areas, frontal lobe resection for non-lesional frontal lobe epilepsy may involve part of the anterior cingulate gyrus. (25, 26) For the one individual who had more than one procedure, only data for the first surgical resection were included.

**Predictions: Semiology-to-Brain Visualisation Tool**

We assessed how well initial and combined set-of-semiologies anatomically correlated with surgical resections, using a Semiology Visualisation Tool (SVT) to generate probabilistic cortical heatmaps of involvement in seizures. (27-29) This software uses the Semio2Brain database which links descriptions of semiologies to brain regions using data from 4,643 patients across 309 peer-reviewed articles, and generates probabilities of brain regions being involved in the generation of the semiology. (27-29) We used default SVT settings: proportions, global lateralisation, using all ground-truths irrespective of patients' ages, including the normalisation and high-resolution options, and on non-topological data to mitigate publication bias that favours temporal lobe epilepsies.

Predictions of the EZ from SVT were visually assessed using the probabilistic colour bar, in which any brain region highlighted in bright yellow on the viridis colourmap spectrum signified high probability of being involved in that semiological feature. SVT predictions were categorised using seven top level brain regions (frontal lobe, cingulate cortex, insula, hypothalamus, temporal, occipital, and parietal lobes). Inevitably, if SVT predicts a large area of involvement there is more likely to be a stronger correlation with the resection volume.

**Comparison of Predicted and Resected Localisation and Lateralisation**

Predictions from SVT were scored in comparison with resections at three levels: 1) frontal lobe (all frontal lobe regions, including extension into cingulate cortex and insula); 2) frontal lobe regions (orbitofrontal, frontomedial, dorsolateral, or frontocentral); 3) at the level of the gyri (precentral gyrus, superior, middle or inferior frontal gyri, anterior cingulate, and insula).

For all three levels, if the top predicted region(s) ("bright yellow") on SVT overlapped with the resection, it was regarded as a congruent prediction. Conversely, if the top predicted brain region(s) in SVT did not overlap with the resection, an incongruent prediction was recorded.

Lateralisation was scored correctly if SVT's top predicted region was on the same side as the resection. If lateralisation was bilateral or toward the opposite side of the resection it was scored as incorrect.

The proportion lateralising and localising correctly at all three levels were compared between initial and set-of-semiologies using two-sided Fisher's exact tests with a p-value of <0.05 considered significant.

An example of SVT is shown in Figure 2.
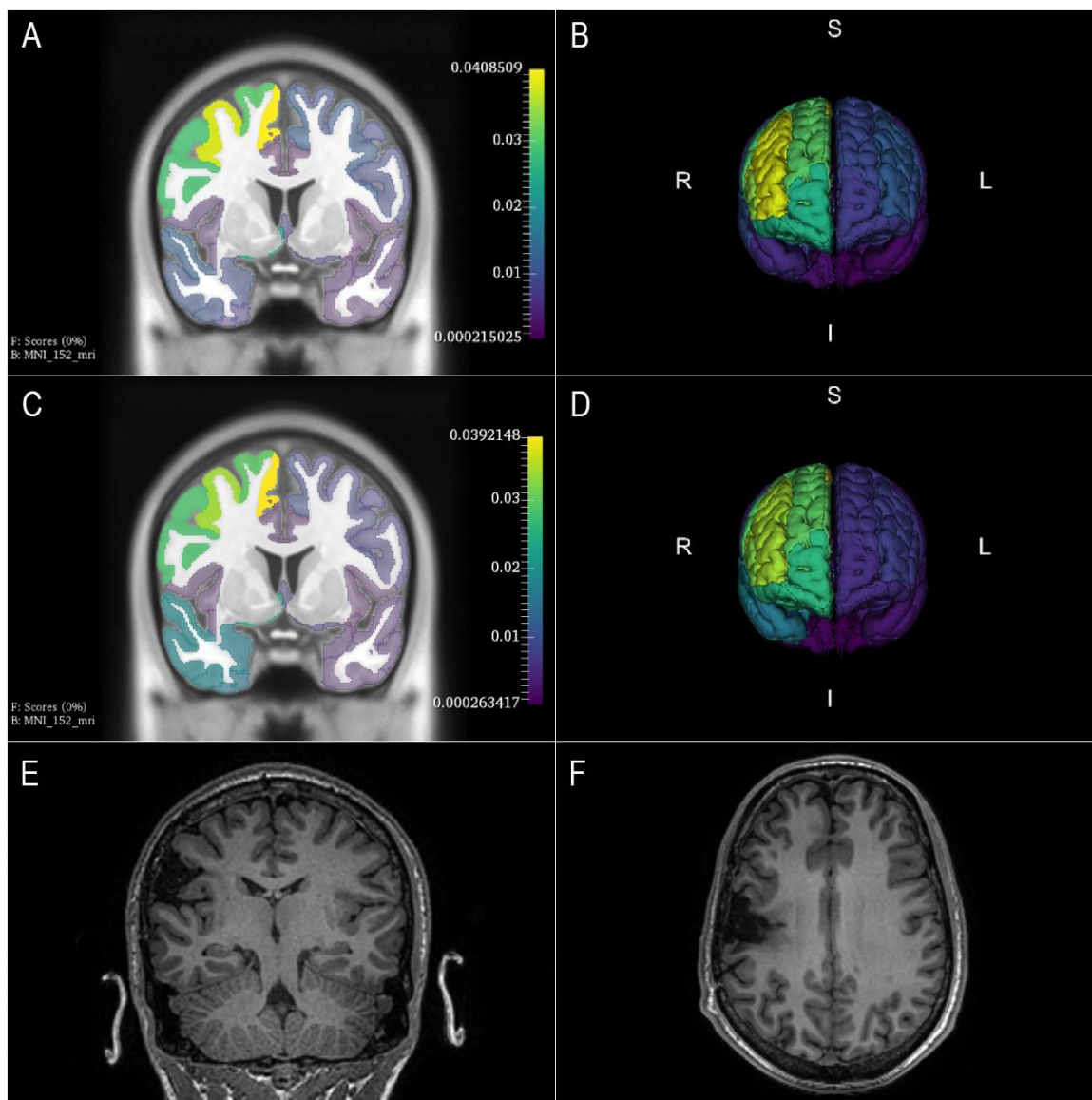
**Figure 2: Example of Semiology Visualisation Tool. The top row demonstrates the epileptogenic zone prediction using initial semiology in coronal (A) and 3D (B) views. The middle row demonstrates the epileptogenic zone prediction using combined set-of-semiology in coronal (C) and 3D (D) views. The bottom row demonstrates the postoperative MRI in T1 coronal (E) and axial (F) views.**

**In this example, initial semiology and combined set-of-semiology correctly lateralised the seizure focus to the right hemisphere and localised to the frontal lobe, however neither correctly localised to the inferior frontal gyrus.**

**Subgroup Analysis: Predicting Seizure Freedom**

Subgroup analysis was performed to determine if the correlation between predicted and actual resections were different between those who were completely seizure free (ILAE outcome score 1) and those who were not (ILAE outcome score 2-6). This would help identify individuals in whom discordance between semiology and site of resection was a consequence of an inadequately localised EZ, as implied by ongoing seizures following surgery. Additionally, we evaluated the univariate association between the presence of any semiology in predicting seizure freedom. Subgroup analysis for both individual semiologies and set-of-semiology were compared between seizure free and not seizure free groups using two-sided Fisher's exact test with a p-value $<0.05$ considered significant.

**Ethical Approval**

This study used de-identified data collected as a service evaluation into postsurgical outcomes following frontal lobe epilepsy surgery at University College London Hospitals NHS Trust (registration number 135-202021-SE). As a service evaluation posing no risk, individual informed consent was not required.

**Results**

A total of 61 individuals had FLE surgery at our centre during the 10-year study period. The median age at surgery was 33.9 (IQR 28.1-43.1) years, with a median duration of epilepsy of 21.9 (IQE 21.3-25.1) years. An abnormal MRI was present in 43 (70%) individuals, with a focal abnormality in 35 (57%). All individuals with a normal MRI (n=18) had icEEG prior to resection. All those who proceeded to resection without icEEG (n=20) had a focal abnormality on MRI.

Operations comprised 52 (85%) cortical resections and 9 (15%) lesionectomies. In 23/61 (38%) people, frontal lobe resections also included regions of anterior cingulate cortex, and one individual had a resection that extended into the insula. A higher percentage of those who had icEEG had 'extensive' resections (reflecting the larger number of non-lesional cases) compared to those who did not have icEEG, however this was not statistically significant (29% vs 10%, p = 0.12).

Baseline characteristics of all individuals and site of resections are summarised in Table 1.

| Table 1: Characteristics of 61 individuals who had frontal lobe epilepsy surgery ||
|---|---|
| **Characteristic** | |
| Age of epilepsy onset, yr, median (IQR) | 12.0 (6.8-18.0) |
| Age at time of surgery, yr, median (IQR) | 33.9 (28.1-43.1) |
| Duration of epilepsy, yr, median (IQR) | 21.9 (21.3-25.1) |
| Abnormal MRI, n (%) | |
|   Focal abnormality | 35 (57) |
|   Diffuse abnormality | 8 (13) |
| Intracranial EEG performed, n (%) | 41 (67) |
| Side of resection, n (%) | |
|   Left | 32 (53) |
|   Right | 29 (47) |
| Location of resection, n (%) | |
|   Orbitofrontal | 4 (7) |
|   Frontomedial | 22 (36) |
|   Dorsolateral | 20 (33) |
|   Frontocentral | 1 (2) |
|   Extensive | |
|    OF+FM+DL | 9 (15) |
|    OF+FM | 2 (3) |
|    FM+DL | 3 (5) |
| Pathology in surgical specimen, n (%) | |
|   Focal cortical dysplasia | 26 (43) |
|   Cavernoma | 6 (10) |
|   Dysembryoplastic neuronal tumour | 6 (10) |
|   Low grade glioma | 3 (5) |
|   Gliosis | 7 (12) |
|   No abnormality / non-specific changes | 13 (22) |
| Abbreviations – MRI: Magnetic Resonance Imaging, EEG: electroencephalography, OF: orbitofrontal, FM: frontomedial, DL: dorsolateral, IQR: interquartile range ||

A variety of seizure manifestations were noted on ictal video telemetry. The frequency of initial and subsequent semiologic features are noted in Table 2. The most common initial semiology was loss of awareness, seen in 12 (20%) individuals, focal aware seizures (non-specific auras) in 9 (15%), cognitive seizures (such as déjà vu, hallucinations or perceptual distortions (30)) in 6 (10%) and focal sensory (somatosensory) seizures in 6 (10%). The most frequently observed chronological semiologic features in these 61 individuals are displayed in Supplementary Table 2.

| Table 2: Semiologies identified on ictal video telemetry | | |
|---|---|---|
| | **Initial semiology** | **Combined (set of) semiology** |
| **Semiology** | **Frequency, N = 61 (%)** | **Frequency, N = 61 (%)** |
| Focal cognitive (aphasia) | 1 (2) | 3 (5) |
| Focal motor (unilateral tonic) | 0 (0) | 11 (18) |
| Focal motor (atonic) | 0 (0) | 2 (3) |
| Focal sensory (auditory) | 1 (2) | 1 (2) |
| Focal motor (automatisms) | 2 (3) | 13 (21) |
| Autonomic | 2 (3) | 9 (15) |
| Focal motor (clonic) | 2 (3) | 7 (11) |
| Complex behaviour | 3 (5) | 12 (20) |
| Impaired awareness | 12 (20) | 25 (41) |
| Focal motor (dystonic) | 0 (0) | 2 (3) |
| Eye movements | 1 (2) | 2 (3) |
| Eye version | 0 (0) | 4 (7) |
| Focal non-motor (emotional) | 2 (3) | 3 (5) |
| Focal sensory (gustatory) | 2 (3) | 2 (3) |
| Head/Body turn | 3 (5) | 6 (10) |
| Head version | 1 (2) | 12 (20) |
| Hyperkinetic | 0 (0) | 6 (10) |
| Ictal speech | 0 (0) | 2 (3) |
| Focal motor (myoclonic) | 0 (0) | 5 (8) |
| Focal aware (non-specific aura) | 9 (15) | 10 (16) |
| Focal cognitive (deja vu/jamais vu) | 6 (10) | 6 (10) |
| Focal sensory (somatosensory) | 6 (10) | 9 (15) |
| Focal motor (tonic – bilateral) | 3 (5) | 23 (38) |
| Focal sensory (vestibular) | 1 (2) | 1 (2) |
| Vocalisation | 4 (7) | 7 (11) |

Following surgery, 28 (46%) people were completely seizure free at 12 months, with a further eight (13%) experiencing only focal aware seizures. Eight (13%) had experienced only one to three seizure days in the preceding year (ILAE outcome class 3), thirteen (21%) experienced a >50% reduction in seizure frequency (ILAE outcome class 4), and three (5%) people noted no change in seizure frequency following surgery (ILAE outcome class 5).

Seizure outcomes for all individuals are listed in Table 3.

| Table 3: Seizure frequency 12 months following frontal lobe epilepsy surgery | | |
|---|---|---|
| Postsurgical ILAE outcome score | Description | Number of individuals, n = 61 (%) |
| 1 | Completely seizure-free; no auras | 28 (46) |
| 2 | Only auras; no other seizures | 8 (13) |
| 3 | One to three seizure days per year; +/- auras | 8 (13) |
| 4 | Four seizure days per year to 50% reduction of baseline seizure days; +/- auras | 13 (21) |
| 5 | Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; +/- auras | 3 (5) |
| 6 | More than 100% increase of baseline seizure days; +/- auras | 0 (0) |
| Other | Lost to follow-up | 1 (2) |

No significant differences in 12-month seizure freedom rates were seen between those who had icEEG (44% seizure free) and those who did not (50% seizure free), p=0.65.

We compared how well the first reported semiology and set of combined semiologies performed in localisation and lateralisation of the presumed EZ. Analysis was divided into those individuals who were completely seizure free following surgery (ILAE outcome group 1) and those who had ongoing seizures (ILAE outcome group 2-6).

Initial semiology alone was able to correctly lateralise the EZ in 26%, localise to the frontal lobe in 18%, localise to subregions of the frontal lobe in 15% and localise to frontal lobe gyri in 8%. Combined set-of-semiology lateralised correctly using SVT in 47/61 (77%), lateralised to the opposite hemisphere in 8/61 (13%) and was non-lateralising in 6/61 (10%). Of the 8 people with mis-lateralised predictions, 3/8 (38%) were seizure free at one year, compared to 1/6 (17%) of those with non-lateralising predictions, and 24/47 (51%) who had congruent predictions.

Combined set-of-semiology was able to correctly localise to the frontal lobe in 57%, localise to frontal lobe subregions in 52% and localise to frontal gyri in 25% (Table 4). Of the 26 (43%) individuals in whom SVT did not correctly localise to the frontal lobe, most incorrect localisations were to the ipsilateral mesial temporal lobe (n = 19), and less commonly to contralateral mesial temporal lobe (n = 4) or other extrafrontal areas (n = 3). Combined set-of-semiologies were superior to initial semiology alone for lateralization and localization at all levels (p<0.05).

| Table 4. Retrospective lateralization and localization of seizure onset focus by semiology in patients who had frontal lobe epilepsy surgery | | |
|---|---|---|
| | **Initial semiology alone** | **Combined set-of-semiology** |
| Lateralization | 26% (95% CI: 18%-35%) | 77% (95% CI: 69%-85%) |
| Localize to frontal lobe | 18% (95% CI: 10%-26%) | 57% (95% CI: 48%-67%) |
| Localize to frontal sub-region | 15% (95% CI: 8%-22%) | 52% (95% CI: 43%-62%) |
| Localize to frontal gyri | 8% (95% CI: 3-14%) | 25% (95% CI: 16%-33%) |

No significant differences were found in SVT semiology prediction scores comparing those who were seizure free to those who were not seizure free for either initial or set-of-semiologies (Supplementary table 3). No significant differences in prediction scores were seen among those

with focal MRI abnormalities compared with diffuse MRI abnormalities or normal imaging. Similarly, no differences in rates of correct lateralisation or localisation to any of the levels were seen among those with lobar resections compared with those with lesionectomies.

**Discussion**

Several semiologic features, such as adopting a 'fencing posture' and duration of postictal confusion, have been demonstrated to distinguish between frontal and temporal lobe epilepsy (6, 31, 32). Sub-lobar identification of ictal foci within the frontal lobe on the basis of semiology alone is, however, more challenging. Certain clinical features such as focal clonic activity can be characteristic of frontal lobe involvement and may have lateralising value however do not always localise to specific frontal lobe regions (8, 15, 32).

Intracranial studies have suggested that certain semiologic features can be correlated with specific frontal lobe areas, organised along a rostrocaudal axis (5). Seizures originating from rostral prefrontal regions have been associated with integrated behaviours that resemble natural activities, whereas those from more posterior regions produce elementary motor manifestations. In practice, however, accurate localisation can be challenging due to rapid propagation through shared networks (5, 15, 32). Semiologic features of mesial frontal lobe seizures have not been consistently elicited during electrocortical stimulation (9). A key point in the correlation of semiology and anatomy is that the inferred localisation of a semiology is based on seizure freedom following resection, intracranial ictal onset and congruent structural imaging lesions. The network sustaining semiology may of course be distant from the site of seizure onset. SVT uses a Bayesian framework and inverse variance weightings where the more focal a semiology localises in the database, the higher the anatomical weighting. Our study was not designed to interrogate the reliability of individual FLE semiologies. However, SVT correctly predicted frontal lobe involvement in those with elementary motor manifestations (such as tonic and clonic activity) or hyperkinetic movements (Supplementary Table 4).

Although clinical teaching emphasises identification of initial semiology as helping to identify the epileptogenic zone (33, 34), this feature alone performed poorly in localising the presumed

epileptogenic zone. This is likely to be the result of many of these first manifestations involving consciousness or sensorial spheres, and in our cohort loss of awareness and a variety of auras were the most common initial semiologic features. This is consistent with a previous report in which over two-thirds of those with frontal lobe epilepsy reported some type of subjective sensation before their seizures. (8) These auras, which are classified in the latest ILAE seizure classification as focal aware, or focal sensory seizures, can be seen in seizures arising from both temporal or extratemporal regions. There are also some data suggesting that semiology in FLE is age-dependent (35), however we did not investigate this due to our centre being an adult neurology service.

Combined semiology performed better than initial semiology, and could successfully lateralise seizure foci in 77% of cases. These results are consistent with previous studies looking at the lateralising value of seizure semiology. (16, 36) There was no significant difference in semiology prediction rates between those with focal MRI abnormalities and those with diffuse MRI changes or normal imaging. This emphasises the important distinction between imaging abnormalities and the symptomatogenic zone, both of which may not always correspond to the epileptogenic zone. Notably, 13% of the whole cohort had combined semiology which SVT lateralised to the opposite hemisphere, highlighting the need for caution when lateralising seizure foci on the basis of semiology alone.

Localisation to sublobar frontomedial, dorsolateral, orbitofrontal and frontocentral regions by semiology alone remained relatively poor, and was correct in only half of all cases. This is lower than estimates in temporal lobe epilepsy, in which lobar localisation by semiology can be up to 90%. (16) It is likely that even in dorsolateral or ventrolateral prefrontal seizures, projection to medial structures plays an important role in observed motor semiology. (5, 15) This also highlights that semiology alone is not reliable for localization in FLE and needs to be

combined with other data such as neuroimaging, scalp video-EEG telemetry and, in selected cases, intracranial recording to adequately identify the seizure onset zone. (37) Over two-thirds of individuals who had frontal lobe epilepsy surgery during the 10-year study period had undergone intracranial EEG recordings prior to resection. In our cohort of individuals with FLE, semiological features in lesional and non-lesional cases were considered together. Notably, all those with non-lesional FLE required icEEG prior to resection, whereas all those who had a resection without icEEG had a focal abnormality on MRI. This highlights the differences in presurgical evaluation between those with lesional and non-lesional drug refractory focal epilepsy, and the importance of semiology in both of these settings. Semiology in non-lesional FLE is often utilised to help guide the extent of icEEG and formulate a surgical hypothesis. In those with a distinct lesion on MRI, the emphasis is primarily on looking for electroclinical concordance between semiology and other presurgical investigations, before deciding upon either icEEG or resection. (38)

No significant association was found between seizure outcome and accuracy of SVT predictions and no relationship was identified between outcome and specific site of resection. These results are consistent with previous reports in epilepsy surgery cohorts that suggest that focal semiology is an uncertain prognostic feature. (36, 39-41) Postsurgical outcome is influenced by a variety of other factors such as presence and location of focal MRI and EEG abnormalities, and the nature of the underlying pathology. (42)

Over 90% of those who had epilepsy surgery in our cohort experienced an improvement in seizure frequency at 12 months, and approximately half were seizure free. This shows the value of surgery in drug-resistant frontal lobe epilepsy, with seizure freedom rates considerably higher than those who complete presurgical evaluation but do not have a resection. (43)  Our present study nonetheless highlights the complex relationship between symptomatogenic and

epileptogenic zones in the workup for epilepsy surgery suitability, and suggests that relatively few frontal lobe seizures can be reliably localized to sublobar regions on clinical grounds alone. (44, 45)

There were limitations to our study, which was retrospective, so details of semiological features could not be probed, and limited to a single tertiary hospital in the UK. Although initial and subsequent semiology were analysed separately, seizure chronology – which can help distinguish between epileptogenic and symptomatogenic zones – was otherwise not examined. This was because the literature review that underpins SVT included studies of semiology devoid of chronological sequence. We used site of resection as a surrogate for the seizure onset zone. SVT predictions that extended across many gyri may have led to bias that favoured those with larger resections. Our cohort was also derived from consecutive individuals who had completed presurgical evaluation and subsequently proceeded to surgery, which may result in selection bias, as this group is likely to have more lateralising and localising semiology than those who are not deemed to be surgical candidates. Resections often involved combinations of the orbitofrontal, frontomedial, dorsolateral and precentral regions, reducing the granularity of our analysis. Finally, seizure outcomes in all cases were self-reported, which is susceptible to reporting bias, but reflects real world conditions.

**Conclusion**

Semiology alone was able to correctly localise the seizure focus to a sublobar level in approximately half of individuals who had frontal lobe epilepsy surgery, and correctly lateralised the focus in 77%. Semiology must be combined with other aspects of the multimodal presurgical evaluation to accurately predict the epileptogenic zone.

**Figure and Table Legend**

**Figure 1:** Imaging categorisation example. Right dorsolateral resection in coronal (A) and axial (B) views. Right frontomedial resection in coronal (C) and axial (D) views. Left orbitofrontal resection in coronal (E) and axial (F) views. All images are T1-weighted 3T MRI sequences; yellow arrows indicate site of resection.

**Figure 2:** Example of Semiology Visualisation Tool. The top row demonstrates the epileptogenic zone prediction using initial semiology in coronal (A) and 3D (B) views. The middle row demonstrates the epileptogenic zone prediction using combined set-of-semiology in coronal (C) and 3D (D) views. The bottom row demonstrates the postoperative MRI in T1 coronal (E) and axial (F) views.

**Table 1:** Characteristics of 61 individuals who had frontal lobe epilepsy surgery

**Table 2:** Semiologies identified on ictal video telemetry

**Table 3:** Seizure frequency 12 months following frontal lobe epilepsy surgery

**Table 4.** Retrospective lateralization and localization of seizure onset focus in frontal lobe epilepsy by semiology in patients who remained seizure-free postoperatively

**Supplementary Table 1:** Standardised semiology categories

**Supplementary Table 2:** Sequential semiologic features identified in 61 individuals who had frontal lobe epilepsy surgery

**Supplementary Table 3:** Comparison of rates of correct lateralisation/localisation using SVT according to 12-month postoperative seizure freedom

**Supplementary Table 4:** Frequency of correct localisation of the symptomatogenic zone to the frontal lobe using SVT

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| Supplementary Table 1: Standardised semiology categories* | | |
|---|---|---|
| **Semiology** | **ILAE Seizure Classification** | **Subset Examples** |
| **Aphasia** | Focal cognitive (aphasia) | Mute, speech arrest, aphemia or anarthria |
| **Asymmetric Tonic** | Focal motor tonic (asymmetric) | Fencing, 'figure of 4' |
| **Atonic** | Focal motor (atonic) | Flaccid, jelly, head drop |
| **Auditory** | Sensory (auditory) | Hearing sounds, auditory hallucination |
| **Automatism - Manual & Oral** | Automatisms | Fiddling, peddling, lip smacking, chewing, orofacial movements, ictal drinking |
| **Automatisms - Other** | Automatisms | Blink, ictal cough, spitting, ictal nose wiping, ictal face rub |
| **Autonomic** | Autonomic | Cardiovascular e.g. ictal bradycardia, respiratory e.g. hypopnoea gastrointestinal: e.g. nausea |
| **Clonic** | Focal motor (clonic) | Repetitive or rhythmical jerks |
| **Complex Behavioural** | Emotional or Behavioural arrest | Behavioural change, fearful behaviour, wandering, awakening or arousal, compulsive checking |
| **Dialeptic** | Loss of awareness | Blank, unaware, loss of contact stare, distant gaze, dreamy state, psychomotor arrest |
| **Dysphasia** | Focal cognitive (aphasia) | Difficulty speaking or incoherent speech, expressive dysphasia, incomprehensible speech |
| **Dystonic** | Dystonic | Twisted posture |
| **Epigastric Aura** | Focal sensory | Abdominal aura, butterfly sensation, rising sensation |
| **Eye Movements** | | Nystagmus (fast phase direction), ocular flutter, complex ocular movements, gaze deviation and versive eye movements |
| **Fear-Anxiety** | Emotional | Sense of impending doom, fear, anxiety, negative emotion |
| **Gustatory** | Sensory | Taste aura |
| **Head or Body Turn** | | Head turn, gyroscopic or body turn |
| **Head Version** | | Forced head deviation over shoulder, extreme head turn |
| **Hypermotor** | Hyperkinetic | Large proximal limb or axial movements, hyperkinetic, head banging, kicking, pelvic thrust |

| | | |
|---|---|---|
| **Ictal Pout** | | Chapeau de gendarme |
| **Ictal Speech - Formed Words** | Vocalisation | Ictal speech, palilalia, coprolalia |
| **Mimetic Automatisms** | Automatisms | Grimace, raising of eyebrows, mimetic, facial expression, fearful expression |
| **Myoclonic** | Focal motor (myoclonic) | Jerk |
| **Non-Specific Aura** | Focal sensory | Vague, unspecified aura lightheaded, dizzy, indefinable feeling, cephalic sensation |
| **Olfactory** | Focal sensory (olfactory) | Smell |
| **Psychic** | Focal Cognitive | Déjà vu, jamais vu, derealisation, depersonalisation |
| **Somatosensory** | Focal sensory (somatosensory) | Tingling, touch sensation |
| **Spasms** | Spasms | Infantile spasm and epileptic spasms |
| **Tonic** | Focal motor (tonic) | Stiff, tonic posturing |
| **Vestibular** | Focal sensory (vestibular) | Vertigo, spinning sensation |
| **Visual** | Focal cognitive (hallucinations) | Formed visual hallucinations e.g. people or objects, movement of objects (not vestibular), phosphene, macropsia, micropsia, metamorphopsia |
| **Vocalisation - Unintelligible Noises** | Vocalisation | Grunt, mumble, hum |
| *Adapted from ILAE and semiological seizure classifications (2, 22) | | |

| Individual | First seizure manifestation | Subsequent set of semiology in order of occurrence | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **Subsequent set of semiology in order of occurrence** | | | | | | |
| 1 | Clonic (L) | Asymmetric tonic (L) | | | | | | |
| 2 | Vocalisation | Hyperkinetic | | | | | | |
| 3 | Somatosensory (L) | Autonomic | | | | | | |
| 4 | Non-specific aura | Asymmetric tonic (L) | Tonic (Bil) | Dialeptic | | | | |
| 5 | Vocalisation | Automatisms - oral & manual | | | | | | |
| 6 | Eye movements (R) | Aphasia | | | | | | |
| 7 | Autonomic | Head turn (L) | | | | | | |
| 8 | Tonic (L) | Clonic | | | | | | |
| 9 | Tonic (Axial) | Tonic (L) | Hyperkinetic | Behavioural | | | | |
| 10 | Automotor (R) | Tonic (R) | Clonic (R) | | | | | |
| 11 | Dialeptic | Custom (utilisation) | | | | | | |
| 12 | Psychic aura | Dialeptic | Head turn (R) | Tonic (R) | | | | |
| 13 | Asymmetric tonic (R) | Dialeptic | Clonic (R) | | | | | |
| 14 | Head turn (L) | Tonic (bil) | | | | | | |
| 15 | Psychic aura | Dialeptic | Eye movement (L) | Head version (L) | Asymmetric tonic (R) | | | |
| 16 | Non-specific aura | Somatosensory (R) | Myoclonic (R) | | | | | |
| 17 | Psychic aura | Aphasia | Head version (R) | Asymmetric tonic (R) | | | | |
| 18 | Fear-Anxiety | Hyperkinetic | | | | | | |
| 19 | Clonic (R) | Somatosensory (R) | | | | | | |
| 20 | Tonic (Bil) | Dialeptic | | | | | | |

**Supplementary Table 2: Sequential\* semiologic features identified in 61 individuals who had frontal lobe epilepsy surgery**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 21 | Dialeptic | Automatisms - manual (L) | | | | | | |
| 22 | Vestibular | Dialeptic | Head version (L) | Tonic (L) | | | | |
| 23 | Fear-Anxiety | Head version (L) | Eye version (L) | Dialeptic | | | | |
| 24 | Head turn (R) | Tonic (R) | Automotor (R) | | | | | |
| 25 | Dialeptic | Myoclonic (L) | Astatic | | | | | |
| 26 | Non-specific aura | Fear-Anxiety | Autonomic | | | | | |
| 27 | Gustatory aura | Dialeptic | Somatosensory aura | | | | | |
| 28 | Psychic aura | Head version (R) | Tonic (R) | Eye version (R) | | | | |
| 29 | Automotor | Dystonic (L) | | | | | | |
| 30 | Body turn (L) | Complex behavioural | Autonomic | | | | | |
| 31 | Non-specific aura | Head version (L) | Tonic (L) | Hyperkinetic | | | | |
| 32 | Gustatory aura | Dialeptic | | | | | | |
| 33 | Somatosensory aura | Body turn (R) | Complex behavioural | Hyperkinetic | | | | |
| 34 | Complex behavioural | Body turn | | | | | | |
| 35 | Dialeptic | Automotor | | | | | | |
| 36 | Automotor (mimetic) | Automotor (L) | Dialeptic | Autonomic | | | | |
| 37 | Autonomic | Clonic (L) | Asymmetric tonic (L) | | | | | |
| 38 | Somatosensory (R) | Aphasia | Atonic (R) | | | | | |
| 39 | Somatosensory (R) | Tonic (R) | | | | | | |
| 40 | Vocalisation | Tonic (Bil) | | | | | | |
| 41 | Non-specific aura | Tonic (Bil) | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 42 | Psychic aura | | | | | | | | |
| 43 | Non-specific aura | Automotor | | | | | | | |
| 44 | Dialeptic | Head version (R) | | | | | | | |
| 45 | Dialeptic | Head turn (R) | Clonic (R) | | | | | | |
| 46 | Dialeptic | Asymmetric tonic (R) | | | | | | | |
| 47 | Vocalisation | Hyperkinetic | | | | | | | |
| 48 | Vocalisation | Complex behavioural | | | | | | | |
| 49 | Complex behavioural | | | | | | | | |
| 50 | Dialeptic | Complex behavioural | Hyperkinetic | | | | | | |
| 51 | Somatosensory | Tonic (L) | Head version (L) | | | | | | |
| 52 | Aphasic | Complex behavioural | Head turn (L) | | | | | | |
| 53 | Vocalisation | | | | | | | | |
| 54 | Non-specific aura | Myoclonic | Automotor | | | | | | |
| 55 | Dialeptic | Ictal speech | | | | | | | |
| 56 | Automotor | Complex behavioural | | | | | | | |
| 57 | Somatosensory (R) | Tonic (R) | Myoclonic (R) | | | | | | |
| 58 | Dialeptic | | | | | | | | |
| 59 | Non-specific aura | Asymmetric tonic (L) | | | | | | | |
| 60 | Head version (R) | Tonic (L) | | | | | | | |
| 61 | Fear-Anxiety | Autonomic | Clonic (L) | Tonic (Bil) | | | | | |

Abbreviations – R: right, L: left, Bil: bilateral

*For individuals with several seizure types only the most frequently observed seizure chronology is listed

| Supplementary Table 3: Comparison of rates of correct lateralisation/localisation using SVT according to 12-month postoperative seizure freedom | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Lateralisation | | Lobar localisation | | Sublobar localisation | | Gyral localisation | |
| | Initial semiology | Combined semiology | Initial semiology | Combined semiology | Initial semiology | Combined semiology | Initial semiology | Combined semiology |
| Seizure Free | 28% | 78% | 22% | 50% | 17% | 47% | 6% | 17% |
| Not seizure free | 20% | 72% | 8% | 60% | 8% | 56% | 8% | 36% |

| Supplementary Table 4: Frequency of correct localisation of the symptomatogenic zone to the frontal lobe using SVT ||
|---|---|
| **Semiology** | **Percentage (%)** |
| Tonic (unilateral) | 100 |
| Clonic (unilateral) | 100 |
| Tonic (bilateral) | 100 |
| Hyperkinetic | 86 |
| Vocalisation | 67 |
| Complex behaviour | 63 |
| Head version | 56 |
| Focal sensory (aura) | 50 |
| Dialeptic | 45 |
| Automotor | 25 |
| Eye version | 25 |