

# Reliability of Seizure Semiology in Patients With 2 Seizure Foci

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**Objective:** To determine whether seizure semiology is reliable in localizing and distinguishing seizures at 2 independent brain foci in the same patient.

**Design:** Two masked reviewers localized seizures from 2 foci by their clinical semiology and intracranial electroencephalograms (EEGs).

**Setting:** Epilepsy monitoring unit of referral comprehensive epilepsy program.

**Patients:** Seventeen consecutive patients (51 seizures) with sufficient video and intracranial EEG data were identified by reviewing medical records of 366 patients older than 10 years.

**Main Outcome Measures:** The primary outcome measures were interobserver agreement between the 2 masked reviewers; the proportion of seizures localized by semiology; the proportion of localized seizures concordant

with intracranial EEG localization; and comparison between concordant and nonconcordant seizures in latency of intracranial EEG seizure spread.

**Results:** Interobserver agreement was 41% ( $\kappa$  score, 0.16). Only 30 of 51 seizures (59%) were localized by seizure semiology. The focus localized by semiology was concordant with the location of intracranial EEG seizure onset in 16 of 30 seizures (53%). No significant difference was observed between concordant and nonconcordant seizures in relation to the speed with which the EEG discharge spread from the location of seizure onset to another lobar region ( $P = .09$ , Wilcoxon rank sum test).

**Conclusion:** Clinical seizure semiology is not as useful as intracranial EEG in localizing seizure onset in patients with dual seizure foci.

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**V**IDEO ELECTROENCEPHALOGRAPHIC (video-EEG) monitoring is essential for localizing the seizure focus before epilepsy surgery.<sup>1</sup> Many semiologic features of seizures are valuable for localizing seizure onset.<sup>2</sup> Seizure semiology has been reported to be accurate in localizing seizures in 80% to 90% of patients with focal epilepsy.<sup>3,4</sup> Lateralizing semiology has also been reported to predict favorable outcomes of epilepsy surgery.<sup>5</sup> However, these observations have been made mainly on patients with only 1 seizure focus. We have observed among our patients that clinical seizure semiology often appears to be indeterminate when there is more than 1 seizure focus. A previous report of patients with unilateral hippocampal atrophy or sclerosis showed that clinical seizure lateralization is more often incorrect in patients who have interictal epileptiform discharges at both temporal lobes compared with patients with interictal discharges at only 1 temporal lobe.<sup>6</sup> How-

ever, patients in that report were not shown to have multiple seizure foci by either surface or intracranial EEG recording. Therefore, the localizing value of seizure semiology in epilepsy with multiple seizure foci is unknown. This study's objective was to determine whether seizure semiology is reliable in localizing and distinguishing seizures from 2 foci in the same patient.

## METHODS

Seventeen consecutive patients with sufficient video and intracranial EEG data of dual ictal foci were identified from review of medical records of 366 patients older than 10 years in our 1996 to 2000 listing of epilepsy patient monitoring. (None of the 366 patients had  $\geq 3$  ictal foci.) Dual ictal foci in each patient were determined when intracranially recorded seizures commenced independently at different lobar regions of 1 or both hemispheres. Seizures that began at different contacts of the same depth or subdural grid electrodes were not considered multifocal when all involved

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contacts were located within the same lobe. This method of distinguishing seizure onset location provided a clear way to identify independent seizure onset foci. Also, seizure semiology is generally more reliable in distinguishing seizure onset at different lobar regions of the brain than in localizing seizure onset to specific locations within each lobe.<sup>3</sup>

Two EEG/epilepsy specialists (B.S. and A.J.F.) who were masked to all prior clinical and EEG information reviewed the first 2 seizures with sufficient data from 1 focus, and the first seizure with sufficient data from another focus, in each patient. Video recording of each seizure was reviewed independently by each reviewer without knowledge of the corresponding EEG recording. The reviewer localized each seizure separately by semiologic features and by EEG. Each reviewer was blinded to the results of the assessment made by the other reviewer. The morphologic pattern of EEG seizure onset was determined by the reviewers.<sup>7</sup> The reviewers also specifically watched for the following semiologic features<sup>2,3</sup>: initial motionless stare, oral automatism, unilateral manual automatism, bimanual automatism, bipedal automatism, vocalization, dystonic extremity posturing, fencing posturing, tonic limb posturing, unilateral clonic activity, early nonforced head turn, forced head turn, restless trunk movement, postictal confusion, postictal dysphasia, postictal nose wiping, and postictal motor paresis (Todd paresis).

After reviewing each seizure, the reviewer indicated the side (lateralize) and the lobar region of seizure onset (localize). When this was not possible, the seizure was judged to be indeterminate in seizure onset. Seizures that could be lateralized but not localized are also considered indeterminate. Thus, the primary outcome measures were interobserver agreement between the 2 masked reviewers, the proportion of seizures that could be localized by semiology, the proportion of localized seizures that were concordant with intracranial EEG localization, and a comparison between concordant and nonconcordant seizures in latency of intracranial EEG seizure spread.

Reviewers also compared the semiologic features of each seizure with those of the other 2 seizures in each patient and determined whether the pair of seizures compared was similar or dissimilar in semiology. The secondary outcome measures were the proportion of seizure pairs that had dissimilar semiology, despite the same location of EEG seizure onset, and the intracranial EEG seizure onset pattern in seizure pairs that had similar vs dissimilar seizure semiology.

In all comparisons, if the 2 reviewers disagreed, a third masked reviewer (E.L.S.) was used. The study was approved by the Mayo Clinic Institutional Review Board.

## RESULTS

Fifty-one seizures in 17 patients were analyzed. **Table 1** shows the intracranial EEG and semiologic localizations of each seizure, with the latency of spread from the lobar region of onset to another lobe. Fourteen patients had independent bitemporal EEG seizures, 2 had independent left and right frontal seizures, and 1 had independent left frontal and left temporal seizures. Interobserver agreement between the 2 primary reviewers on localization by seizure semiology was only 41% ( $\kappa$  score, 0.16). Only 30 of the 51 seizures (59%) could be localized by seizure semiology. Moreover, the focus localized by semiology was concordant with the location of intracranial EEG seizure onset in only 16 of the 30 seizures (53%). There was no significant difference between concordant and nonconcordant seizures in rela-

tion to the speed with which the EEG discharge spread from the location of seizure onset to another lobar region ( $P=.09$ , Wilcoxon rank sum test).

Semiology was frequently dissimilar between pairs of seizures that arose from the same focus in the same patient (8 of 17 seizure pairs [47%]). The pattern of intracranial EEG discharge at seizure onset was compared in the 17 pairs of seizures that arose from the same focus. Seven of these 8 seizure pairs (88%) with dissimilar semiologies had different patterns of EEG discharge at seizure onset (**Table 2**), whereas none of the 9 seizure pairs with similar semiologies had dissimilar EEG onset patterns ( $P<.001$ , Fisher exact test). Only 5 patients proceeded to have epilepsy surgery (patients 1, 2, 7, 12, and 16; Table 1).

## COMMENT

Our study disclosed that seizure semiology is often poorly localized in patients with dual seizure foci. Their seizures lack consistently localizing clinical features, so much so that agreement between masked reviewers was low for localizing seizures. Semiology in 41% of the seizures was not helpful in localizing seizure onset. When seizure semiology is localizing, the localization disagrees with the location of intracranial EEG seizure onset in nearly half the patients.

Seizures arising from the same focus are expected to have identical or similar semiologies. However, such was not the case in our patients with dual seizure foci. Therefore, seizure semiology does not reliably distinguish between seizure types or foci in these patients. The basis for the lack of distinguishing features of seizures in these patients is not clear. We found in this study that seizures with dissimilar semiologies are more likely to have different EEG discharge patterns than seizures with similar semiologies, despite arising from the same focus. This finding supports a previous report that several seizure generators may be present within a single ictal EEG onset zone.<sup>7</sup> Alternatively, differences in spreading patterns of seizures may explain the variable seizure semiology in our patients.<sup>8</sup> Intracranial EEG recording in occipital epilepsy suggests that variability in clinical seizure characteristics is related to different pathways of seizure propagation.<sup>9</sup>

Our study could have been strengthened by the inclusion of subjects with unifocal epilepsy for comparison with subjects with bifocal epilepsy. The design of our study was influenced by prior clinical observation that seizure semiology appeared to be nonlocalizing in patients with bifocal epilepsy, regardless of whether the seizures being compared came from the same focus. In contrast, a previous study had shown that agreement between masked reviewers of unifocal seizures was very good ( $\kappa$  score, 0.68).<sup>10</sup> Moreover, semiology was localizing in 80% of these patients compared with the localization rate of 53% in our study.

Ideally, the seizure episodes in our study should have been randomly selected, but the limited number of seizures that met our study criteria prevented randomization. We had to use only seizure episodes that had sufficient views of the patients on the video image. Not

**Table 1. Intracranial EEG Localization vs Semiologic Localization of 51 Seizures in 17 Patients**

Patient No.	Seizure No.	Intracranial EEG Localization	Semiologic Localization	Latency of Spread, s <sup>a</sup>	MRI Findings
1	1	LT	LT	NS	(-)
	2	RT	LT	19	
	3	RT	I	9	
2	1	RF	LF	NS	Right hippocampal malrotation
	2	RT	I	NS	
	3	RT	I	NS	
3	1	LT	I	26	Bifrontal white matter increased T2
	2	LT	LT	NS	
	3	RT	I	NS	
4	1	RT	LT	NS	(-)
	2	LT	RT	NS	
	3	RT	LT	NS	
5	1	LT	LT	9	(-)
	2	LT	RT	7	
	3	RT	RT	NS	
6	1	LT	I	NS	(-)
	2	RT	I	32	
	3	RT	I	46	
7	1	LT	LT	10	(-)
	2	LT	I	10	
	3	RT	RT	NS	
8	1	LT	LT	18	Left parieto-occipital NMD
	2	RT	RT	312	
	3	LT	LT	20	
9	1	LT	RT	6	(-)
	2	LT	RT	8	
	3	RT	I	13	
10	1	RT	I	25	(-)
	2	RT	RT	17	
	3	LT	LT	NS	
11	1	RF	I	NS	(-)
	2	LF	I	NS	
	3	LF	RF	NS	
12	1	RF	I	NS	Right frontal increased T2
	2	LF	I	NS	
	3	LF	I	NS	
13	1	RT	LT	NS	(-)
	2	RT	LT	NS	
	3	LT	LT	NS	
14	1	RT	RT	15	(-)
	2	LT	I	NS	
	3	LT	RT	NS	
15	1	LT	I	NS	(-)
	2	LT	I	NS	
	3	RT	I	NS	
16	1	RT	RT	27	Bilateral hippocampal atrophy
	2	RT	RT	39	
	3	LT	I	48	
17	1	LT	RT	90	(-)
	2	RT	LT	100	
	3	LT	LT	NS	

Abbreviations: EEG, electroencephalographic; I, indeterminate; LF, left frontal; LT, left temporal; MRI, magnetic resonance imaging; NMD, neuronal migrational disorder; NS, no spread; RF, right frontal; RT, right temporal; (-), nonlesional.

<sup>a</sup>Time for the seizure to spread from the lobar region of onset to another lobe.

infrequently, semiologic features of seizures recorded in the epilepsy monitoring unit are not observable because of an obstructed view or the patient's being out of view. We minimized selection bias by uniformly including only the first seizures that met study criteria, without prior knowledge of their semiologic or EEG localization. These seizure episodes were identified for the study by one of us (K.M.R.) who was not a reviewer of the seizures. We

avoided using seizures that had occurred later during the monitoring period to minimize inclusion of seizures with secondary generalization. Secondarily generalized seizures tend to evolve rapidly with consequent bilateral involvement, making semiologic lateralization difficult. Moreover, by using initial seizures from each focus, we also avoided the cluster effect of seizures on their lateralization and localization. Choi and colleagues<sup>11</sup> have dem-

**Table 2. Seven Pairs of Seizures With the Same Intracranial EEG Localization but With Different EEG Onset Patterns**

Pattern of EEG Seizure Onset	No. of Pairs
1st seizure: rhythmic beta discharge	4
2nd seizure: 3- to 5-Hz spike waves	
1st seizure: rhythmic beta discharge	1
2nd seizure: rhythmic theta discharge	
1st seizure: rhythmic beta discharge and electrodecree ment	1
2nd seizure: electrodecree ment only	
1st seizure: electrodecree ment	1
2nd seizure: 4-Hz spike wave	

Abbreviation: EEG, electroencephalographic.

onstrated that there is a significant difference in the interseizure interval between concordant and nonconcordant seizure pairs in patients with bilateral seizure foci.

Intracranial EEG recording is considered the criterion standard and clinical state of the art for localizing seizure onset in the evaluation of patients for epilepsy surgery.<sup>12</sup> We used intracranial EEG instead of surface EEG in determining the seizure onset foci in each patient. Nevertheless, sampling error is known to occur with intracranial EEG recordings if the intracranial electrodes still do not record the earliest EEG seizure activity because of the limited area of coverage by the electrodes.<sup>13</sup> The possibility of sampling error is minimized in our study by the fact that all seizures of surgical and nonsurgical patients had EEG onset preceding or simultaneous with clinical semiology onset. (The converse situation of clinical seizure onset preceding EEG onset would have raised the probability that the intracranial electrodes did not capture the earliest EEG seizure activity.) Therefore, the timing of EEG onset vs semiology onset did not distinguish between surgical and nonsurgical patients in our study. Magnetic resonance imaging findings also did not clearly distinguish between the 2 groups. Three of the 5 surgical patients vs 2 of the 12 nonsurgical patients had magnetic resonance imaging lesions ( $P=.12$ , Fisher exact test; Table 1). Moreover, the retrospective nature of our study does not permit us to determine the way in which magnetic resonance imaging results had independently influenced the surgical decision in each patient.

Our study did confirm our prior clinical observation that clinical seizure semiology is not reliable for localizing seizure onset in patients with dual seizure foci. We expect the same to hold true for patients with more than 2 seizure foci, but none of our study patients had more than 2 foci.

The *epileptogenic zone* has been defined as the area of the brain that is necessary to generate seizures, resection of which results in seizure control.<sup>14</sup> It would be useful to relate the findings of our study to the epileptogenic zone, but only 5 of 17 patients proceeded to epilepsy surgery. Given the presence of 2 seizure foci in each of our patients, it is not surprising that the proportion of our patients who proceeded to surgery is small.

In conclusion, caution should be exercised when clinical semiology of seizures is being assessed for epilepsy surgery in patients with 2 or more seizure foci. The un-

reliability of seizure semiology in these patients is currently not fully understood. Our study findings suggest that the symptomatogenic zone of seizures does not correspond well to the EEG seizure onset zone in these patients.

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