

**On-line Table 1: The clinical details of patients with cryptogenic epilepsy**

| Case No. | Age (yr) | Sex | Age of Onset (yr) | Duration of illness (yr) | Hypothesis | PET/CT/MRI         | Expert Consensus Epilepsy Surgery Case Conference                                               | Intracranial EEG          | Surgery | Outcome after Surgery | Seizure-Free Duration | Histopathologic Findings | Neuropsychological Assessment | Noninvasive Video-EEG Monitoring                             |
|----------|----------|-----|-------------------|--------------------------|------------|--------------------|-------------------------------------------------------------------------------------------------|---------------------------|---------|-----------------------|-----------------------|--------------------------|-------------------------------|--------------------------------------------------------------|
| 1        | 36       | F   | 10                | 25                       | R-F        | Hypometabolism R-F | Concordant hypothesis, intracranial EEG indicated                                               | R-F                       | Yes     | Seizure-free          | 12 mo (Engel I)       | Unremarkable CNS tissue  | L/R-F                         | Interictal: rare sharp waves L-F/T; ictal: R-F/C             |
| 2        | 50       | M   | 8                 | 42                       | R-T        | Unremarkable       | Concordant hypothesis, intracranial EEG indicated                                               | R-T                       | Yes     | Not seizure-free      | 1 mo (Engel II)       | Hippocampal sclerosis    | R-F/T                         | Interictal: R-F and L-T; ictal: R-F/T                        |
| 3        | 31       | F   | 10                | 21                       | R-F/T      | Unremarkable       | Concordant hypothesis, intracranial EEG indicated                                               | —                         | —       | —                     | —                     | —                        | R-F/T                         | Interictal: spikes and focal slowing R-F/T; ictal: R-F/T     |
| 4        | 38       | F   | 0                 | 38                       | R-F        | Unremarkable       | Concordant hypothesis, intracranial EEG indicated                                               | Multifocal, core area R-F | —       | —                     | —                     | —                        | R-F                           | Interictal: spikes R-F/C and R-F/T; ictal: R-F/C             |
| 5        | 55       | M   | 38                | 17                       | L/R-T      | —                  | Concordant hypothesis, intracranial EEG indicated                                               | —                         | —       | —                     | —                     | —                        | No localization possible      | Interictal: spikes and focal slowing L/R-F/T; ictal: L/R-F/T |
| 6        | 37       | F   | 9                 | 27                       | L-T/P/O    | Unremarkable       | Concordant hypothesis, intracranial EEG indicated                                               | L-T/P/O                   | Yes     | Not seizure-free      | 12 mo (Engel I)       | Unremarkable CNS tissue  | No localization possible      | Interictal: spikes L-O and L-T/P/O; ictal: L-T/P/O           |
| 7        | 18       | M   | 17                | 1                        | L-F        | —                  | Concordant hypothesis due to eventual medical seizure freedom, no further diagnostics indicated | —                         | —       | —                     | —                     | —                        | —                             | Interictal: spikes L-F/C; ictal: L-F/C                       |
| 8        | 24       | M   | 20                | 4                        | L-F/T      | —                  | Concordant hypothesis due to eventual medical seizure freedom, no further diagnostics indicated | —                         | —       | —                     | —                     | —                        | L-F/T                         | Interictal: unremarkable; ictal: L-F/T                       |
| 9        | 33       | M   | 15                | 18                       | L-T        | —                  | Concordant hypothesis due to eventual medical seizure freedom, no further diagnostics indicated | —                         | —       | —                     | —                     | —                        | No localization possible      | Interictal: spikes and slowing L-F/T; ictal: L-F/T           |
| 10       | 42       | F   | 8                 | 34                       | R-F/T      | —                  | Concordant hypothesis due to medical seizure reduction, no further diagnostics indicated        | —                         | —       | —                     | —                     | —                        | No localization possible      | Interictal: unremarkable; ictal: R-F/T                       |
| 11       | 27       | F   | 10                | 17                       | L/R-T      | Unremarkable       | Concordant hypothesis, intracranial EEG indicated                                               | L/R-T (bilateral)         | —       | —                     | —                     | —                        | L/R-F/T                       | Interictal: spikes and slowing L/R-F/T; ictal: L/R-F/T       |
| 12       | 33       | M   | 18                | 15                       | L-T        | —                  | Concordant hypothesis, intracranial EEG indicated, patient declined                             | Offered                   | —       | —                     | —                     | —                        | L-F/T                         | Interictal: spikes L/R-F/T; ictal: L-F/T                     |
| 13       | 43       | M   | 14                | 29                       | L/R-T      | —                  | Concordant hypothesis, intracranial EEG indicated, patient declined                             | Offered                   | —       | —                     | —                     | —                        | L-F/T                         | Interictal: spikes R-T; ictal: spikes L/R-T                  |

**Note:**—L/R indicates left/right; F/T/P/O/C, frontal/temporal/parietal/occipital/central; —, was not done/not available.

<sup>a</sup> Clinical details of the patients comprising patient No., age, sex, age of onset, duration of illness, PET/CT/MRI availability, expert consensus, availability of intracranial EEG data, surgery, outcome after surgery, seizure-free duration, histopathologic findings, neuropsychological assessment, and noninvasive video-EEG monitoring are shown.

**On-line Table 2: AUC values for all VBM models at different smoothing levels<sup>a</sup>**

| VBM         | 4 mm | 6 mm | 8 mm | 10 mm | 12 mm | 14 mm | 16 mm |
|-------------|------|------|------|-------|-------|-------|-------|
| GMC         |      |      |      |       |       |       |       |
| T1          | 0.09 | 0.11 | 0.17 | 0.26  | 0.35  | 0.34  | 0.30  |
| T1+T2       | 0.07 | 0.10 | 0.16 | 0.24  | 0.29  | 0.23  | 0.15  |
| T1+FLAIR    | 0.05 | 0.10 | 0.21 | 0.33  | 0.42  | 0.41  | 0.35  |
| T1+T2+FLAIR | 0.09 | 0.11 | 0.22 | 0.30  | 0.36  | 0.35  | 0.29  |
| GMV         |      |      |      |       |       |       |       |
| T1          | 0.08 | 0.08 | 0.08 | 0.12  | 0.12  | 0.08  | 0.04  |
| T1+T2       | 0.10 | 0.11 | 0.11 | 0.06  | 0.05  | 0.02  | 0.0   |
| T1+FLAIR    | 0.12 | 0.05 | 0.09 | 0.8   | 0.12  | 0.11  | 0.09  |
| T1+T2+FLAIR | 0.15 | 0.08 | 0.12 | 0.11  | 0.11  | 0.09  | 0.06  |

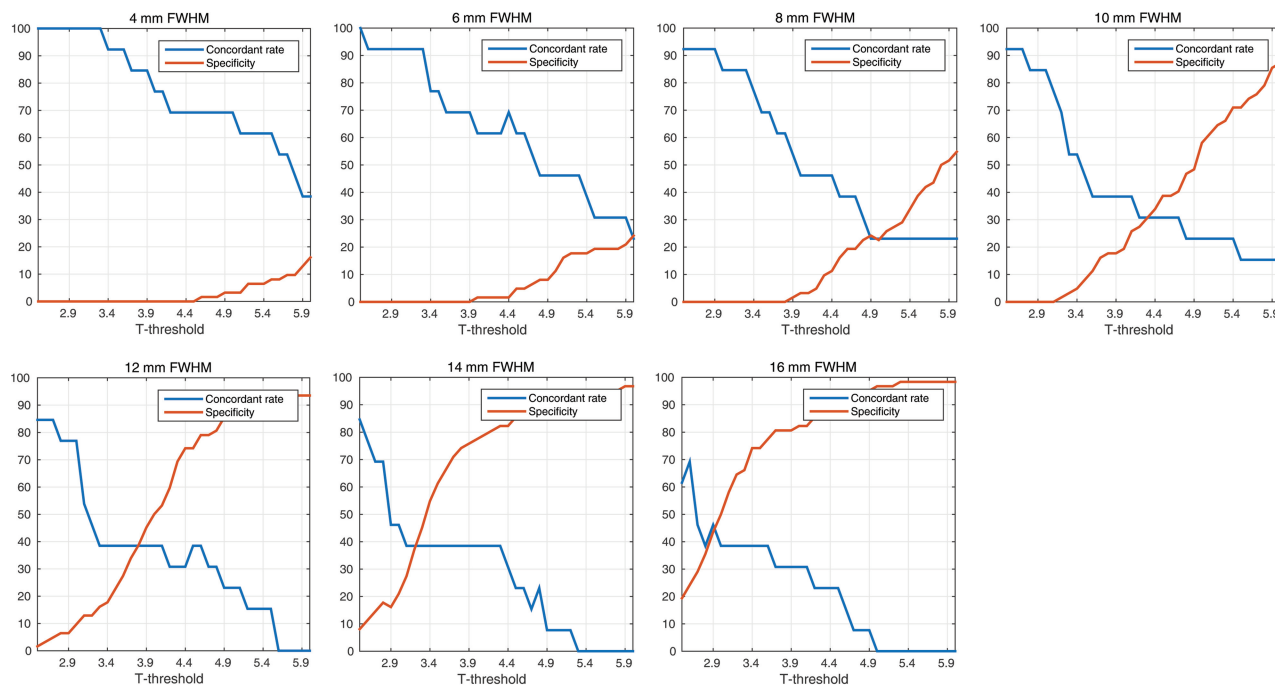
<sup>a</sup> All the AUC values across statistical cutoffs (2.5–6 in a step size of 0.1) are shown for each smoothing level from 4 to 16 mm for all VBM models.

**On-line Table 3: VBM findings rated as potentially epileptogenic stratified in concordant and discordant lobes for all models<sup>a</sup>**

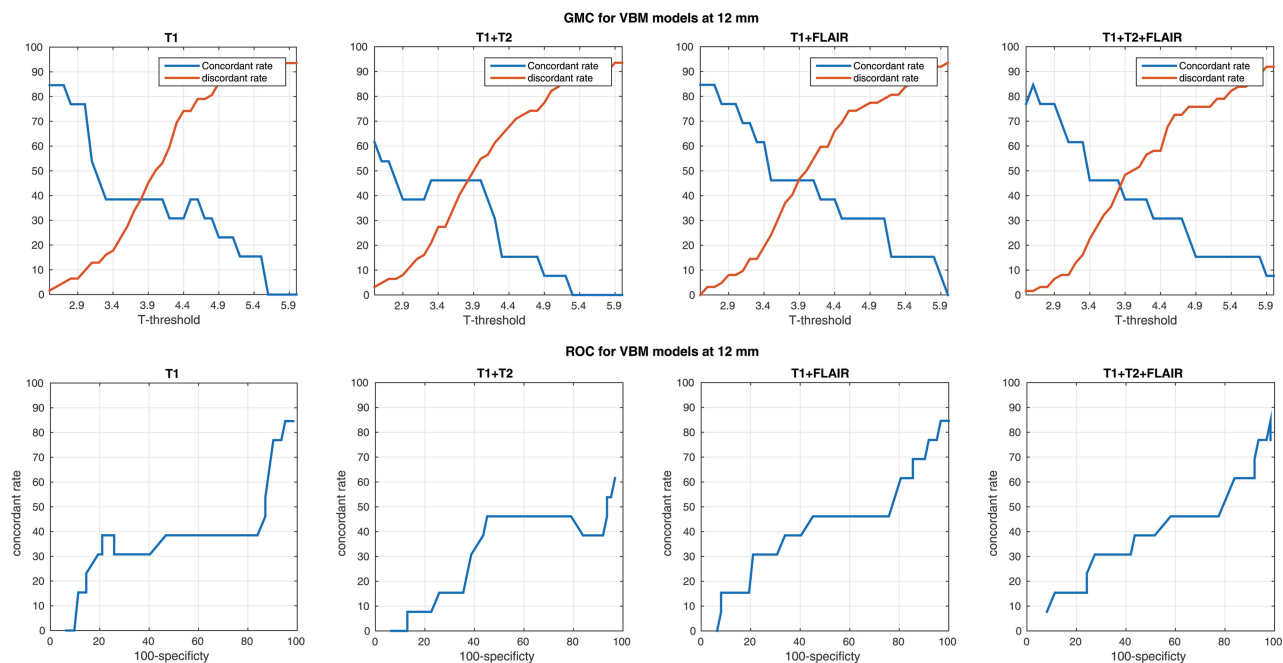
| Case No. | Concordant Lobe |       |          |             | Discordant Lobe |       |          |             |
|----------|-----------------|-------|----------|-------------|-----------------|-------|----------|-------------|
|          | T1              | T1+T2 | T1+FLAIR | T1+T2+FLAIR | T1              | T1+T2 | T1+FLAIR | T1+T2+FLAIR |
| 3        | —               | —     | Yes      | Yes         | Yes             | Yes   | Yes      | Yes         |
| 4        | Yes             | Yes   | Yes      | Yes         | Yes             | —     | Yes      | —           |
| 5        | Yes             | Yes   | Yes      | Yes         | Yes             | —     | —        | —           |
| 6        | Yes             | —     | Yes      | Yes         | —               | —     | —        | —           |
| 7        | Yes             | —     | Yes      | —           | —               | —     | —        | —           |
| 9        | —               | —     | —        | —           | —               | Yes   | Yes      | Yes         |
| 10       | —               | —     | —        | —           | Yes             | —     | —        | —           |
| 12       | —               | —     | —        | —           | Yes             | Yes   | Yes      | Yes         |
| 13       | —               | —     | Yes      | —           | Yes             | Yes   | Yes      | Yes         |

**Note:** — indicates that finding was not present.

<sup>a</sup> VBM findings in patients confirmed as potentially epileptogenic across all models for concordant and discordant lobes are presented.



**ON-LINE FIG 1.** Concordant rate and specificity for T1 VBM at variable statistical cutoffs and smoothing levels. Concordant rate and specificity for increasing smoothing levels from 4 to 16 mm are plotted for GMC analysis. As the smoothing level increases, the intersection point moves toward the left (lower T-threshold). FWHM indicates full width at half maximum.



**ON-LINE FIG 2.** Diagnostic performance for different VBM models. The plots show the concordant rate and specificity for different T-thresholds at 12-mm smoothing for all VBM models (*upper panel*). The *lower panel* shows receiver operating characteristic curves for all VBM models at 12-mm smoothing.