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Case Report

Good seizure outcome after focal resection surgery for super-refractory status epilepticus: Report of two cases

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ABSTRACT

Background: There is scarce evidence regarding focal resection surgery for super-refractory status epilepticus (SRSE), which is resistant to general anesthetic treatment over 24 h. We report two patients with SRSE, in whom good seizure outcomes were obtained following focal resection surgery.

Case Description: Patient 1: A 58-year-old man who underwent left anterior temporal lobectomy with hippocampectomy at the age of 38 years after being diagnosed left medial temporal lobe epilepsy. After 19 years of surgery with no epileptic attacks, the patient developed SRSE. Electroencephalogram (EEG) demonstrated persistence of lateralized periodic discharges in the left frontotemporal region. On the 20th day after SRSE onset, resection of the frontal lobe and temporal lobe posterior to the resection cavity was performed. Patient 2: A 62-year-old man underwent craniotomy for anaplastic astrocytoma in the left frontal lobe at the age of 34 years. Since the age of 60 years, he developed SRSE 3 times over 1 and 1/12 years. On EEG, repeated ictal discharges were observed at the medial part of the left frontal region during the three SRSEs. Corresponding to the ictal EEG findings, high signals on diffusion-weighted magnetic resonance images and focal hypermetabolism on fluorodeoxyglucose-positron emission tomography were observed around the supplementary motor area, medial to the resection cavity. Resection surgery of the area was performed during the interictal period.

Conclusion: Good seizure outcome was obtained in the two cases which provide additional support for the recent concept of focal resection surgery as an indication for SRSE.

Keywords: Astrogliosis, Diffusion-weighted image, Electrocorticography, Electroencephalography, Positron emission tomography

INTRODUCTION

Status epilepticus (SE) is a condition in which one seizure lasts for 5 min or more, or two or more seizures occur consecutively without the patient regaining normal level of consciousness.[16] There is an established methodology for the treatment of SE. The first line of treatment involves administration of benzodiazepines or Lorazepem.[16] If SE is resistant to the first treatment, it is considered an established SE, and treatment with intravenous administration of antiepileptic

drugs (AEDs) is attempted.[16] However, if SE is refractory to treatment with intravenous administration of AEDs, it is called refractory SE (RSE), and treatment with general anesthesia is considered.[1-3,8] Further, when SE continues despite general anesthetic treatment for RSE over 24 h, it is called "SRSE."[2,3,6,9,10,12,15] It has been reported that 24–48% of SE progresses to RSE and 15%–22% of RSE progresses to SRSE.[2,15]

SRSE is recognized as a neurological emergency disease that is difficult to treat and has a poor prognosis, with death occurring in 35% of cases and 13% suffering from serious neurological sequelae.[3,5,6,8-10,12] To date, there is no clear protocol or evidence regarding the treatment of SRSE.[3,9,10,12] Among the various treatments, focal surgical resection is recommended for SRSE patients with a well-localized epileptogenic zone in the non-eloquent cortex.[9] However, the actuality and usefulness of focal resection surgery have not been fully clarified, as limited reports are available.[4,7,9,17] We treated two SRSE patients who underwent resection surgery and obtained good seizure outcomes. Herein, we retrospectively analyze the clinical findings of these patients and discuss the usefulness of resection surgery for SRSE.

CASE DESCRIPTION

Patient 1

A 58-year-old man underwent anterior temporal lobectomy with hippocampectomy at the age of 38 years, with a diagnosis of left medial temporal lobe epilepsy (MTLE). In the Wada test performed as a preoperative examination at that time, it was determined that the right hemisphere was dominant in both language and memory. All clinical findings were typical of MTLE, and the findings of magnetic resonance (MR) images were characterized by a small left calvarium and left entire hemisphere, not just the left temporal lobe [Figures 1a and b]. The patient was seizure-free for more than 10 years after the operation, and the AED was gradually reduced and discontinued.

However, at the age of 57, he had two generalized seizures, and AED administration, such as levetiracetam (LEV) and lacosamide (LCM), were resumed. Further, at the age of 58 years, he developed a third generalized seizure and was admitted because of SE (day 1). Intravenous injections of diazepam (DZP) and fosphenytoin (fPHT) resulted in cessation of the seizures, but impaired consciousness was subsequently prolonged. On the electroencephalogram (EEG), lateralized periodic discharges (LPD) with the maximum amplitude at F7 of the International EEG 10–20 system were recorded in the left frontotemporal region [Figures 1c and d]. MR images showed gliosis in the temporal lobe posterior to the resection cavity [Figure 1e]; however, no definite abnormality was noted in the left frontal lobe [Figure 1f]. In addition, MR angiography (MRA) showed increased signals of the peripheries of the left middle and anterior cerebral arteries due to "ictal hyperperfusion"[14] [Figure 1g]. The patient was diagnosed with subtle non-convulsive status epilepticus (NCSE). In addition to the administration of AEDs, including LEV, LCM, perampanel (PER), and clobazam (CLB), general anesthesia with thiamylal, propofol, and midazolam (MDZ), was induced after endotracheal intubation.

General anesthesia was maintained with the appearance of a suppression-burst on the EEG monitoring, and the ictal hyperperfusion demonstrated by MRA improved on day 9 [Figure 1h]. However, when the amount of anesthetic was reduced, LPD appeared again in the left frontotemporal region, and it was judged to be difficult to control SRSE with medical treatment alone. On day 12, tracheal intubation was replaced with tracheostomy, and a preoperative examination was performed. On day 17, MRA was performed which did not show ictal hyperperfusion [Figure 1i], and positron emission tomography with fluorodeoxyglucose (FDG-PET) on day 19 showed rather low metabolism in the entire left hemisphere [Figures 1j and k].

Based on the EEG findings, we considered that there was an epileptogenic region at the left fronto-temporal lobe, and on day 20, the fronto-temporo-parietal craniotomy was performed under general total intravenous anesthesia (TIVA) with propofol. Intraoperative electrocorticography (ECoG) showed high-amplitude periodic discharges in the frontal lobe. Asynchronous small-amplitude paroxysms were also recorded in the temporal lobe posterior to the resection cavity [Figures 1l and m]. These areas were resected [Figures 1n and o]. No paroxysmal discharges were recorded in the medial temporal lobe. After resection, no paroxysmal discharge was observed from the cortex of the excision margin.

After the operation, general anesthesia was discontinued under EEG monitoring for 2 days, and controlled ventilation was withdrawn. The patient was completely awake on the 10th postoperative day. Postoperative EEG occasionally showed low-amplitude paroxysmal discharges in the left frontotemporal region, but no seizures occurred. On the 15th postoperative day, the patient was transferred to a rehabilitation hospital with the prescription of LEV, LCM, PER, CLB, and phenytoin, and the tracheostomy was closed on the 43rd postoperative day. Pathological examination of the resected frontal and temporal lobes revealed marked astrogliosis centered on the corticomedullary junction. Nine months after the operation, he only had one seizure due to a decrease in the dose of PER (Engel class ID).

Patient 2

A 62-year-old man underwent resection of an anaplastic astrocytoma in the left frontal lobe through a left fronto-

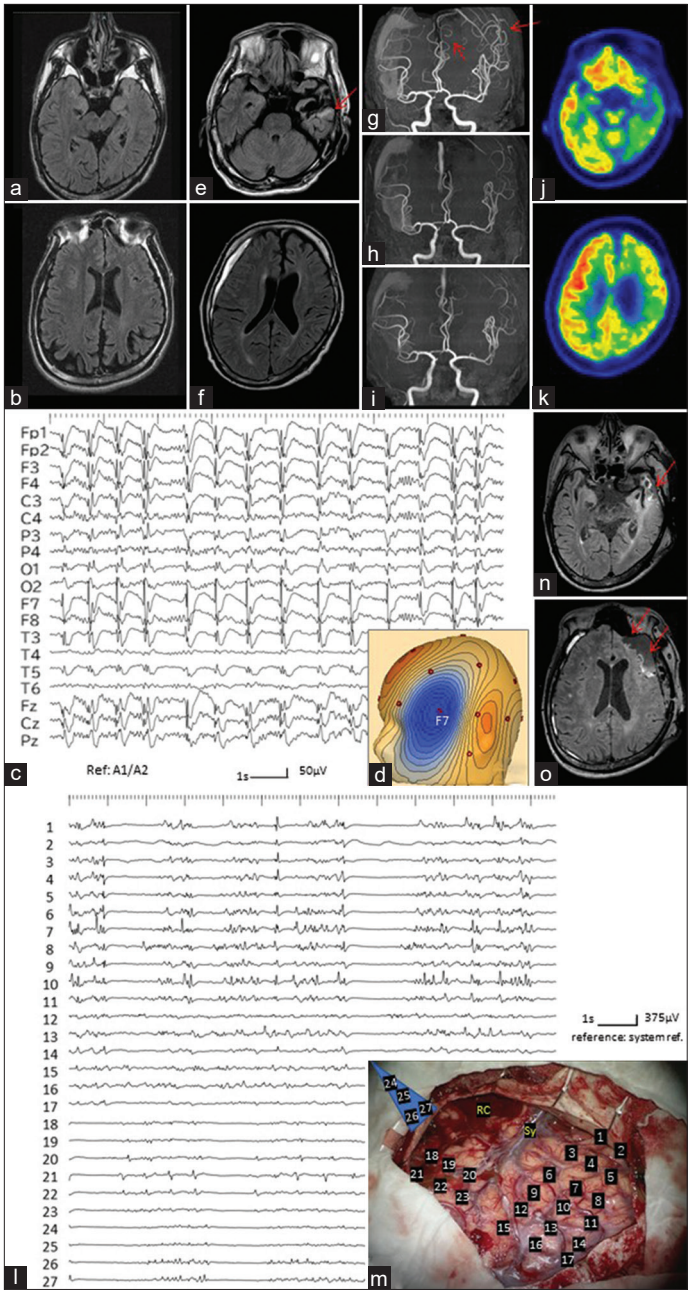

Figure 1: (Patient 1) (a and b) Oblique views, along with the long axis of the hippocampus, of the magnetic resonance (MR) images with fluid attenuated inversion recovery (FLAIR) sequences, before the left anterior temporal lobectomy at the age of 38, demonstrate a small size of the left calvarium and left entire hemisphere, not just the left temporal lobe. (c) Electroencephalogram (EEG) on day 1 shows lateralized periodic discharges (LPD) at the left fronto-temporal region. (d) Voltage topography of LPD indicates that the maximum amplitude of LPD is located at F7 of International EEG 10–20 system. Blue indicates negativity. (e and f) Axial views of FLAIR images on day 2 depict gliosis in the temporal lobe posterior to the resection cavity (red arrow in e). No definite abnormality is noted at the left frontal lobe (f). Thin chronic subdural hematoma, caused by a fall due to generalized seizure, is also noted on the right side. (g) MR angiography shows increased signals of the peripheries of the left middle and anterior cerebral arteries due to "ictal hyperperfusion" (red arrows). (h and i) On MR angiography of day 9 (h) and day 17 (i), the ictal hyperperfusion is improved. (j and k) Positron emission tomography with fluorodeoxyglucose on day 19 shows rather low metabolism not just in the left temporal lobe, posterior to the resection cavity, but the left entire hemisphere. (l) Intraoperative electrocorticography depicts high-amplitude periodic discharges on the frontal lobe (electrode No 1-10). Asynchronous small-amplitude paroxysms are also recorded on the temporal lobe posterior to the resection cavity (electrode No. 18-22). No paroxysmal discharges are recorded from the medial part of the temporal lobe (electrode No. 24-27). (m) The location and number of the electrodes are indicated on the operative view. Blue trapezoid electrode (No. 24-27) is placed adjoining the medial and basal aspects of the temporal lobe, as described before.[11] Sy: Sylvian veins, RC: Resection cavity at the previous craniotomy. (n and o) Oblique views of FLAIR images, immediately after the operation, showing the resection area (red arrows).

parietal craniotomy at 34 years of age. He underwent radiation therapy (whole brain 40 Gy, local 20 Gy) and chemotherapy, including interferon-β and nimustine hydrochloride. No subsequent tumor recurrence was observed. He never experienced seizures and did not take any AED.

However, he had a generalized seizure for the 1st time at the age of 60 years. Intravenous administration of DZP and LEV stopped his seizures, but impaired consciousness was subsequently prolonged. EEG revealed ictal discharges with evolution continued on the medial part of the left frontal region [Figure 2a], which occasionally propagated to the surroundings. Subsequent MR images failed to reveal tumor recurrence [Figures 2b and c]; however, gliosis was noted medial and posterior to the resection cavity [Figure 2d]. Diffusion-weighted images (DWI) showed a strong hyperintensity at the medial part of the resection cavity in the left frontal lobe and laminar hyperintensity along with the cortex, named "cortical hyperintensity,"[13] in the left parietal lobe [Figure 2e]. In addition, FDG-PET showed a strong accumulation in the medial part of the resection cavity [Figures 2f and g]. The patient had subtle NCSE and the treatment included two rounds of general anesthesia with MDZ for 3 days, in addition to the administration of LEV, PER, sodium valproate (VPA), and CBZ.

Nine months after the initial SRSE, the patient had an aphasia attack with impaired consciousness. EEG demonstrated repeated ictal discharges at the medial part of the left frontal region, as observed at the 1st SRSE. Treatment for this NCSE required 7 days of general anesthesia with MDZ, in addition to intravenous fPHT.

He developed the same NCSE in the 4th month after the 2nd SRSE. In addition, EEG showed repeated ictal discharges at the medial side of the left frontal region. Eleven days of general anesthesia with MDZ were required to control the 3rd SRSE.

Based on the EEG findings corresponding to the 3 SRSEs and the concordant DWI and FDG-PET findings at the 1st SRSE, we considered that there was an epileptogenic region at the medial part of the left frontal lobe. Three months after recovery from the 3rd SRSE, during the interictal period, reopening of the fronto-parietal craniotomy was performed under TIVA with propofol. Intraoperative ECoG showed frequent paroxysmal discharges on the interhemispheric surface, medial to the surgical defect in the left frontal lobe [Figures 2h and i], and the area was resected [Figures 2j and k].

Postoperative mild right hemiparesis and aphasia were transiently observed, but no seizures occurred. On the 20th postoperative day, he was transferred to a rehabilitation hospital with prescriptions of LEV, LCM, VPA, and CLB. Pathological examination of the resected frontal lobe showed marked astrogliosis, but no tumor recurrence was observed. Postoperative EEG failed to reveal a paroxysmal discharge. No seizures occurred during the 3-year postoperative follow-up (Engel class IA).

DISCUSSION

In both patients with SRSE, good seizure outcomes were obtained by performing focal resection surgery. In Patient 1, resection surgery was performed during the super-refractory seizure episode to recover from SRSE. In Patient 2, the purpose of the surgery was to prevent recurrence of SRSE, which occurred 3 times in 1 year and 1 month, and the surgery was performed during the interictal period at 3 months after recovery from the 3rd SRSE.

In both patients, the EEG findings during SRSE, that is, the "ictal" EEG findings, were the most useful for the preoperative identification of the epileptogenic region, confirming the previous reports.[7,17] In Patient 1, LPD was observed in the left frontotemporal region, and in Patient 2, repeated ictal discharges were consistently observed in the medial part of the left frontal region during the three SRSEs. Furthermore, in Patient 2, a high signal on DWI and focal hypermetabolism on FDG-PET were observed at the site corresponding to the ictal EEG findings. However, in Patient 1, FDG-PET failed to reveal focal hypermetabolism in the left frontal and temporal lobes. In addition, ictal hyperperfusion on MRA, which was observed immediately after the onset of NCSE, was not noted before surgery. One possible reason is that FDG-PET and MRA are performed under general anesthesia with thiamylal and propofol, which may have affected the cerebral circulation and metabolism. Moreover, since these examinations were conducted on the 17–19th days after the onset of SRSE, it is possible that the mechanism of secondary increase in the blood flow in response to SRSE[13] could not be sustained, and the metabolism was also decreased. Caution should be taken in the evaluation of these examinations, which are performed under prolonged general anesthesia for SRSE.

In resection surgery during SRSE, such as in Patient 1, it was seen that it is highly possible to identify the epileptogenic region by intraoperative ECoG, instead of gold standard chronic intracranial EEG recording, and most of the reported cases achieved good seizure outcomes with the guidance of intraoperative ECoG recording.[7] In the previous reports regarding simultaneous intra- and extracranial EEG recordings, it has been demonstrated that synchronized periodic discharges with amplitudes of more than 600–800 μV were recorded at more than 10 cm^2 on the lateral cortex and were recorded as LPD on the scalp.[11] Consistent with these results, in Patient 1, periodic discharges with amplitudes of more than 400 μV synchronized at more than 10 cm^2 of the lateral frontal lobe were recorded.

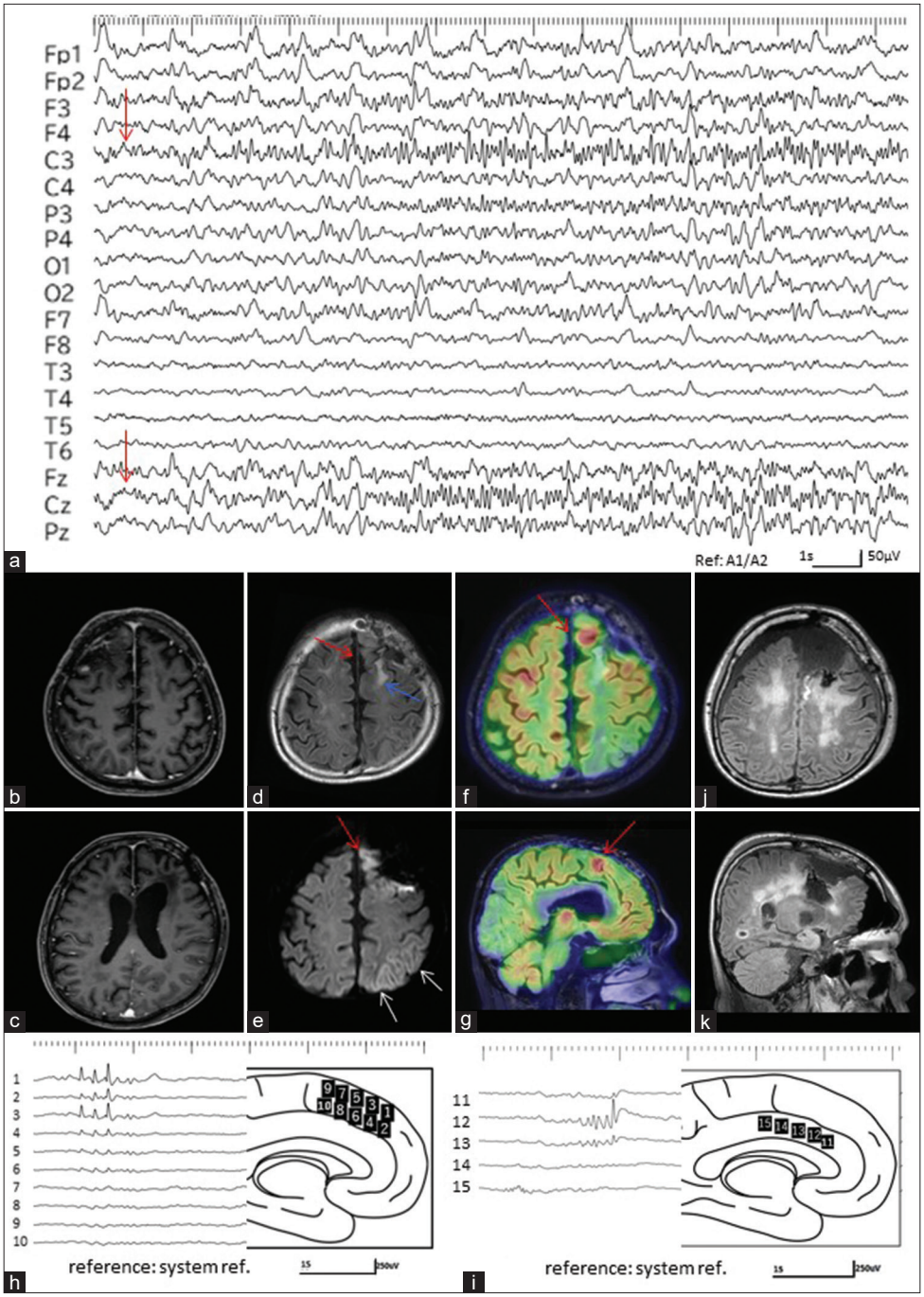

Figure 2: (Patient 2) (a) Electroencephalogram (EEG) at the 1st super-refractory status epilepticus depicts ictal discharges with evolution continued on the medial part of the left frontal region at the C3 and Cz (red arrows). (b and c) T1-weighted images with gadolinium enhancement fail to reveal the tumor recurrence in the left frontal lobe. (d) Fluid attenuated inversion recovery (FLAIR) image shows gliosis at the interhemispheric cortex medial to the resection cavity (red arrow), in addition to the frontal white matter posterior to the resection cavity (blue arrow). (e) Diffusion-weighted images depict a strong hyperintensity at the medial part of the resection cavity in the left frontal lobe (red arrow) and laminar hyperintensity along with the cortex in the left parietal lobe (white arrows). (f and g) Axial (f) and sagittal views (g) of the fusion images of positron emission tomography with fluorodeoxy glucose (FDG-PET) and FLAIR images demonstrate a strong accumulation at the interhemispheric cortex, medial to the resection cavity in the left frontal lobe (red arrows). (h and i) Intraoperative electrocorticography shows frequent paroxysmal discharges on the interhemispherical surface, medial to the surgical defect in the left frontal lobe. The location and number of the electrodes are indicated on the schematic drawing of the interhemispheric surface. (j and k) Axial (j) and sagittal views (k) of FLAIR images, immediately after the operation, show the resection area, which is identical to the high accumulation area on FDG-PET.

In Patient 2, since the surgery was performed during the interictal state, chronic intracranial EEG recording can be indicated as a presurgical evaluation. However, we selected intraoperative ECoG recording for guidance because it was anticipated that the 4th SRSE would be induced with the reduction of AED and electrical stimulation during functional mapping. In addition, the fact that the ictal EEG findings, which were consistent during all three SRSEs, were concordant with DWI and FDG-PET findings at the first SRSE was also one of the reasons for the selection of intraoperative ECoG guidance.

Regarding the identification of the non-eloquent cortex, in Patient 1, the preoperative evaluation of the initial surgery for MTLE revealed that the dominancy of both language and memory was located on the contralateral side. In Patient 2, although the localization of the dominant hemisphere was not apparent, the site indicated by FDG-PET was the site corresponding to the left supplementary motor area (SMA) or pre-SMA, and it was judged that this site was not eloquent. In fact, in Patient 1, no obvious exacerbation of higher brain function was observed after surgery. Postoperative right hemiparesis and aphasia in Patient 2 were transient, which are characteristic symptoms after resection of the SMA.

Regarding the timing of surgery for SRSE, in the literature, surgical interventions have been performed at least 2 weeks after persistent SE in all but one patient who was operated within 8 days of the onset.[4,7] Compared to these reports, surgery on the 20th day after the onset of SRSE in Patient 1 seems to be slightly delayed. The most likely reason is that the surgical indication was decided after evaluation with MRI and FDG-PET. In Patient 2, though each of the three previous SRSEs were successfully treated with medication, the stable results obtained with resection surgery indicated that surgical intervention should be considered in the earlier stages.

Both patients suddenly developed SRSE after a long period of time from the initial craniotomy. Patient 1 with MTLE had SRSE after a seizure-free period of 19 years, whereas in Patient 2, with no prior history of seizure, SRSE began to occur 26 years after the first craniotomy. In both cases, strong astrogliosis was histopathologically found in the resected epileptogenic area. After the initial surgery, prolonged astrogliosis progression was observed around the excision area, and the area was considered to have acquired strong epileptogenicity. In Patient 1, hypoplasia of the entire left hemisphere was already observed in the preoperative image of MTLE, and there was originally a pathological condition that caused epilepsy not only in the medial temporal lobe but also in the lateral temporal lobe and frontal lobe.

CONCLUSION

Although the number of cases presented here is minimal (two patients), the present findings provide additional support for the recent idea that focal resection can be indicated for SRSE, in which a well-localized epileptogenic area is identified in the non-eloquent cortex with EEG and intraoperative ECoG.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflict of interest.

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