

## Intraoperative Seizures During Awake Craniotomy for Brain Tumours

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### Abstract

Awake craniotomy (AC) is becoming increasingly popular for brain tumour surgery. The procedure allows better preservation of eloquent cortex and helps achieve greater tumour resection. However, a potential problem with the procedure is intraoperative seizures (IOS) that may affect the mapping and monitoring of awake patients and may even lead to abandoning of the awake procedure.

**Keywords:** Awake Craniotomy, Intraoperative Seizures, Brain Tumours.

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### Introduction

Awake craniotomy (AC) is the gold standard procedure for tissue resection close to eloquent areas of the brain.<sup>1,2</sup> AC was historically used for the surgical treatment of drug-resistant epilepsy but more recently, it has become even more popular in brain tumour resections.<sup>3</sup> Surgical removal of brain tumours adjacent to the eloquent cortex poses significant risks of postoperative neurological deficits. To minimize these neurological deficits, AC involves mapping of cortical areas controlling speech, motor, and sensory functions and optimizing the benefit-risk ratio of tumour resection.<sup>4</sup> As compared to conventional tumour resections, AC patients also recover faster with fewer neurological deficits.<sup>5</sup> Intraoperative seizures (IOS) are a known operative nuance of AC and can complicate the procedure by affecting the mapping and monitoring of the awake patient and might be a serious cause of surgical failure.<sup>5</sup>

### Review of Evidence

We reviewed relevant literature on Google Scholar and PubMed to find the incidence and any potential risk factors associated with IOS in AC. Nossek et al., prospectively reviewed one of the largest cohorts of 477 patients who had undergone AC for tumours within or near eloquent areas.<sup>6</sup> All included patients received preoperative anticonvulsant medications, irrespective of their seizure history. Patients who experienced clinical seizures during functional mapping were included in the seizure group and

any patients who may have had an epileptiform activity on the neurophysiological monitor but did not experience a clinical seizure were excluded. Overall, 60 (12.6%) patients experienced IOS which included 50 patients with focal seizures and either motor or language symptom, and 10 patients with secondary generalized seizures. Univariate analysis revealed that patients with IOS were younger ( $45 \pm 14$  years vs.  $52 \pm 16$  years,  $p=0.003$ ), with a tumour involving the frontal lobe (86% vs. 57%,  $p<0.0001$ ), and a prior history of seizures ( $p=0.008$ ). For IOS termination, brain was irrigated with iced Ringer's lactate and mapping was paused for 5 minutes until the patient regained speech/motor abilities. Patients whose seizures were not controlled in 5 minutes, or had evolved to status epilepticus were given antiepileptic drugs followed by induction of general anaesthesia and urgent intubation. In patients who had IOS, short-term post-operative motor deterioration was observed (20% vs. 10.1%,  $p=0.02$ ) and their hospital course was prolonged ( $4 \pm 3$  days vs.  $3 \pm 3$  days,  $p=0.045$ ). Overall AC had to be abandoned due to IOS in only 11 patients (2.3%).<sup>6</sup>

Boetto et al., conducted a prospective study on 374 patients who underwent AC for supratentorial brain lesion.<sup>4</sup> Most patients (83%) were diagnosed preoperatively with seizures (20% had intractable seizures) with a mean Karnofsky performance scale (KPS) score of 91. Preoperatively no anxiolytic or sedative medication was administered and only patients with a history of seizures received anticonvulsant medications. IOS occurred in only 13 (3.4%) patients, and these were partial seizures, which quickly resolved with cold Ringer's lactate irrigation. No anticonvulsants were administered. Patient age, sex, history of seizure, lesion side, and mean stimulation current intensity were taken into account and no statistically significant difference was seen between the IOS group and the non-IOS group. In the immediate postoperative period, the IOS group had transient worsening, however, no patients had new severe permanent neurologic deficit 3 months following surgery. No procedure failed because of IOS.<sup>3</sup>

Gonen et al.,<sup>7</sup> reviewed 137 consecutive cases of AC for the removal of supratentorial brain tumours. Patients were divided into two groups depending on the tumour location; 15 patients with tumours located in the supplementary motor area were compared to 70 patients

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with tumours in the non-supplementary motor area. The mean age, KPS, and handedness of patients were similar between both groups and a slight male predominance was seen in both groups. Eleven patients (73%) with tumours located in the supplementary motor area (SMA) experienced intraoperative seizures, compared with 17 (13.9%) with tumours in the non-SMA brain regions and this was statistically significant ( $p < 0.0001$ ). There was no statistically significant relationship between the occurrence of intraoperative seizures and the extent of resection, current intensities used during cortical mapping, and length of hospital stay. Many of the patients (63.6%) with a tumour in the SMA region had an IDH1 mutation compared with those who had tumours in non-SMA regions. In multivariate analysis, it was seen that tumour location was a significant predictor of IOS ( $p = 0.002$ ). Interestingly, a trend toward IDH1 mutation as a predictor of IOS was also found ( $p = 0.06$ ). It was also concluded that IOS were not associated with worse outcomes in AC.<sup>7</sup>

The most recent study was conducted by Ikechukwu et al., where 57 patients undergoing AC for a peritumoral region glioma were studied.<sup>8</sup> All patients, irrespective of their seizure history were treated with preoperative antiepileptic loading doses which included either levetiracetam (500–1,000 mg) or fosphenytoin (15–20 mg/kg). Cases were divided into two cohorts; patients who had positive mapping (PM) or intraoperative identification of motor regions in the cortex using direct cortical stimulation and patients with no positive motor mapping following direct cortical stimulation or negative mapping (NM). PM cohort included 33 patients whereas the NM cohort included 24 patients and the overall incidence of IOSs was 8.8%; none of which aborted the case. For IOS, cold saline irrigation was poured and stimulation was stopped. In cases where seizures persisted, additional intravenous levetiracetam and/or midazolam were administered. Postoperatively patients without a seizure history received levetiracetam, whereas a neurologist was asked to tailor the antiepileptics of patients with a preoperative history of seizures. The incidence of intraoperative and postoperative seizures was significantly higher in the PM cohort (15.5% and 30.3%, respectively) compared with the NM patients (0% and 8.3%, respectively;  $p = 0.046$  and  $0.044$ ). Univariate logistic regression showed that PM (odds ratio [OR]: 1.16; 95% confidence interval [CI], 1.01–1.34;  $p = 0.035$ ) and preoperative tumour volume (OR: 0.998; 95% CI, 0.996–0.999;  $p = 0.049$ ) were significant predictors for IOS in patients with peritumoral gliomas.<sup>8</sup>

Some recent advancements in the AC procedure have led to a significant reduction in IOS. One such advancement is the use of propofol for sedation which significantly reduces IOS risk.<sup>9</sup> Furthermore, longer stimulus durations, restimulating an epileptogenic area, and 50–60 Hz of stimulation are discouraged because they are associated with IOS.<sup>10</sup>

## Conclusion

The available evidence suggests IOS is infrequent, dependent on tumour location and positive mapping, and if aborted in time, will not lead to AC failure or permanent postoperative neurological deficits.

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