Low Rate of Intraoperative Seizures During Awake Craniotomy in a Prospective Cohort with 374 Supratentorial Brain Lesions: Electrocorticography Is Not Mandatory

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■ OBJECTIVE: **Awake craniotomy (AC) in brain lesions has allowed an improvement of both oncologic and functional results. However, intraoperative seizures (IOSs) were reported as a cause of failure of AC. Here, we analyze the incidence, risk factors, and consequences of IOSs in a prospective cohort of 374 ACs without electrocorticography (ECoG).**

■ METHODS: **We performed a prospective study including all patients who underwent AC for an intra-axial supratentorial cerebral lesion from 2009–2014 in our department. Occurrence of IOS was analyzed with respect to medical and epilepsy history, tumor characteristics, operative technique, and postoperative outcomes.**

■ RESULTS: **The study comprised 374 patients with a major incidence of low-grade glioma (86%). Most of the patients (83%) had epilepsy history before surgery (20% had intractable seizures). Preoperative mean Karnofsky performance scale (KPS) score was 91. IOSs occurred in 13 patients (3.4%). All IOSs were partial seizures, which quickly resolved by irrigation with cold Ringer lactate. No procedure failed because of IOS, and the rate of aborted AC whatever the cause was nil. Mean stimulation current intensity for cortical and subcortical mapping was 2.25 ± 0.6 mA. Presurgical refractory epilepsy was not associated with a higher incidence of IOS. Three months after surgery, no patients had severe or disabling permanent worsening, even within the IOS group (mean KPS score of 93.7).**

■ CONCLUSIONS: **AC for intra-axial brain lesion can be safely and reproducibly achieved without ECoG, with a low rate of IOS and excellent functional results, even in patients with preoperative intractable epilepsy.**

INTRODUCTION

Awake craniotomy (AC) associated with intraoperative electrical cortical and subcortical mapping represents a reliable method to optimize the benefit-risk ratio of surgery for intra-axial supratentorial brain lesions, including gliomas, metastasis, and cavernomas.[1–3] Indeed, many recent series have shown that this technique enabled surgical removal of tumors in highly functional regions previously considered as inoperable,[4,5] with nonetheless a preservation (or even an improvement) of quality of life thanks to mechanisms of neuroplasticity (especially in slow-growing lesions as low-grade gliomas[6]) and with an increase of the extent of resection.[7–12]

In spite of these favorable results, some authors have nonetheless reported that intraoperative seizures (IOSs) could represent a regular complication of AC technique and might be a serious cause of surgical failure.[13–16]

We investigated the incidence and risk factors of IOS on the basis of a prospective series with 374 ACs for cerebral lesions. Clearly, our aim was not to study the impact of ACs on the oncologic outcomes but to specifically analyze the possible consequences of IOS on the surgical procedure itself and on the postoperative functional results. In addition, to simplify the surgical procedure, we did not use intraoperative electrocorticography (ECoG). Our goal was also to investigate whether the rate of IOS was modified by the lack of ECoG in comparison with the classical literature on AC.

Key words
- Awake craniotomy
- Brain tumor surgery
- Low-grade glioma
- Seizures

Abbreviations and Acronyms
AC: Awake craniotomy
ECoG: Electrocorticography
IOS: Intraoperative seizures
KPS: Karnofsky performance scale
WHO: World Health Organization

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PATIENTS AND METHODS

Patient Population

Between January 2009 and November 2014, baseline and perioperative data were recorded prospectively on all patients undergoing awake craniotomy for resection of an intra-axial supratentorial brain lesion. All patients were operated on by the senior author (HD) at the same institution. Information concerning the following parameters was obtained for all patients: sex; age; Karnofsky performance scale (KPS) score; eventual epilepsy history (preoperative seizures, administration of antiepileptic drugs, intractable seizures under multiple antiepileptic drugs); tumor characteristics (side, pathology); possible previous surgery or biopsy; intraoperative findings (intensity of stimulation, eventual IOS or AC failure); postsurgical course with eventual onset of seizures within the 3 months following resection; and neurologic outcomes, as well as KPS at 3 months.

Of note, any partial or generalized IOSs occurring during AC were diagnosed by the anaesthesiologist, speech therapist, neuropsychologist, or surgeon and collected in our database.

Preoperative Preparation

The preoperative preparation for our institutional protocol was multidisciplinary and required at least 3 appointments per patient: with the neurosurgeon, anaesthesiologist, and speech therapist and/or neuropsychologist in charge of the preoperative, intraoperative, and postoperative cognitive testing (see[17] for a detailed description of this protocol). During these appointments, the patient and relatives were fully informed about the procedure modalities, their inherent risks and benefits, and the safety measures that might be undertaken. In particular, the sequence of events that would occur during the awake procedure and the moment at which patient cooperation would be required were accurately detailed. All patients gave informed consent to participating in the study.

The evening before the procedure, an oral sedative (zolpidem tartrate, 10 mg) was administered. The day of the procedure, no anxiolytic or sedative medication was given to avoid compromising the patient's cooperation during the awake phase. Anticonvulsants were administered as usual (i.e., with no systematic antiepileptic drugs in patients with no preoperative seizures), as well as a 400-mg dose of cimetidine.

OPERATIVE PROCEDURE

Anaesthetic Management

Our institutional asleep-awake-asleep anaesthetic protocol has previously been described[18] and shown its reliability and safety. Briefly, two intravenous lines were placed in the patient, who was monitored by a pulse oximeter, a noninvasive blood pressure monitor, electrocardiography, an end-tidal carbon dioxide partial pressure analyzer, and a respiratory rate monitor. Urinary catheters and temperature probes were used routinely. The position used was the lateral decubitus on a thick foam mattress. The head was placed in a Mayfield head holder, in neutral position with respect to the head-neck-trunk axis. The environmental temperature in the operating room was also controlled to avoid shivering, and a forced-air warming device was systematically used.

Total intravenous general anaesthesia with a laryngeal mask airway was used in the first asleep phase for all patients, using a target-controlled infusion of propofol and remifentanil to regulate the depth of anaesthesia and to facilitate ventilation, respectively. Noninvasive blood pressure monitor, pulse oximeter, electrocardiography, and respiratory rate monitor were used to monitor the patient. All patients received ondansetron 4 mg, acetaminophen 1 g, and cefamandole 1.5 g intravenously for antibiotic prophylaxis. The scalp was infiltrated with local anaesthetic (20 mL lidocaine 2% with epinephrine) before placement of the Mayfield head holder and all along the skin incision, as well as at the level of specific regional anaesthesia points (e.g., temporal, supraorbital, or occipital nerve blocks). Once the craniotomy was performed, the temporal muscle and the dura mater were also infiltrated with lidocaine.

Once the craniotomy was completed, the general anaesthesia was stopped at the surgeon's request and the laryngeal mask was removed when the patient opened his or her eyes. The examiner (speech therapist and/or neuropsychologist) was able to start working a few minutes after the patient was conscious and fully cooperative. The neurologic tests were then performed during whole cortical and subcortical mapping, as well as throughout the tumor resection. The anesthesiologist treated any discomfort, but no sedative medications and no antiepileptic drugs were administered during this phase. Again, the awake period ended at the surgeon's request. General anaesthesia with intravenous propofol and remifentanyl was also used after the awake phase, for possible additional resection in noneloquent areas and closure.

Cortical Mapping

Technical details of our functional mapping-guided surgical procedure have been described in previous reports.[19,20] In all cases, bone flap and dura mater opening were wide enough to expose primary motor area and ventral premotor cortex, in order to obtain a positive mapping. Indeed, before lesion resection, stimulation of the entire exposed cortical surface was achieved using a bipolar electrode with 5-mm spaced tips (Nimbus, Innopsys, France), delivering a biphasic current (pulse frequency 60 Hz, single pulse phase duration of 1 msec, amplitude from 1–4 mA), with a maximum duration of stimulation of 4 seconds.

Firstly, ultrasonography was used before any resection to identify the tumor limits and the main sulci and gyri. Next, speech and sensory-motor cortical mapping was performed in all cases, over the ventral premotor cortex and primary sensory-motor area until a positive response was evoked (i.e., articulatory disorders eliciting a complete speech arrest while the patient was asked to count and/or induction of involuntary movements or paraesthesia in the contralateral hemibody), indicating the optimal threshold of stimulation.[21] The current of intensity was determined for each patient by progressively increasing the amplitude of stimulation in steps of 0.5 mA starting from a 1-mA baseline until a response was elicited. Once the threshold was defined, that current amplitude was used for the remainder of the cortical and subcortical mapping. Of note, in order to simplify the surgical procedure, no EcoG was used.