Acta Neurochirurgica (2020) 162:3055–3065
https://doi.org/10.1007/s00701-020-04561-w

ORIGINAL ARTICLE - BRAIN TUMORS

Experience with awake throughout craniotomy in tumour surgery: technique and outcomes of a prospective, consecutive case series with patient perception data

Jose E. Leon-Rojas[1] · Justyna O. Ekert[2] · Matthew A. Kirkman[3] · Darreul Sewell[4] · Sotirios Bisdas[5] · George Samandouras[1,3]

Received: 19 May 2020 / Accepted: 28 August 2020 / Published online: 2 October 2020

Abstract

Background Awake craniotomy is the standard of care in surgery of tumours located in eloquent parts of the brain. However, high variability is recorded in multiple parameters, including anaesthetic techniques, mapping paradigms and technology adjuncts. The current study is focused primarily on patients' level of consciousness, surgical technique, and experience based on a cohort of 50 consecutive cases undergoing awake throughout craniotomy (ATC).

Methods Data was collected prospectively for 46 patients undergoing 50 operations over 14-month period, by the senior author, including demographics, extent of resection (EOR), adverse intraoperative events, surgical morbidity, surgery duration, levels of O_2 saturation and brain oedema. A prospective, patient experience questionnaire was delivered to 38 patients.

Results The ATC technique was well tolerated in all patients. Once TCI stopped, all patients were immediately assessable for mapping. Despite > 75% of cases being considered inoperable/high risk, gross total resection (GTR) was achieved in 68% patients and subtotal resection in 20%. The average duration of surgery was 220 min with no episodes of hypoxia. Early and late severe deficits recorded in 12% and 2%, respectively. No stimulation-induced seizures or failed ATCs were recorded. Patient-recorded data showed absent/minimal pain during (1) clamp placement in 95.6% of patients; (2) drilling in 94.7% of patients; (3) surgery in 78.9% of patients. Post-operatively, 92.3% of patients reported willingness to repeat the ATC, if necessary.

Conclusions The current ATC paradigm allows immediate brain mapping, maximising patient comfort during self-positioning. Despite the cohort of challenging tumour location, satisfactory EOR was achieved with acceptable morbidity and no adverse intraoperative events.

Keywords Awake throughout craniotomy · Brain mapping · Gross total resection · Patient satisfaction · Glioma surgery

This article is part of the Topical Collection on *Brain Tumors*

Portions of this work were presented in poster form at the European Low-Grade Glioma Network meeting 15/06/2019, London and the Congress of Neurological Surgeons 19/10/2019.

✉ Jose E. Leon-Rojas
jose.rojas.18@ucl.ac.uk

George Samandouras
g.samandouras@ucl.ac.uk

[1] Institute of Neurology, University College London, Queen Square, London, UK

[2] Wellcome Centre for Human Neuroimaging, University College London, 12 Queen Square, London, UK

[3] Victor Horsley Department of Neurosurgery, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

[4] Department of Neuroanaesthesia, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

[5] Lysholm Department of Neuroradiology, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

Introduction

The value of brain mapping during awake craniotomies (AC) in safely maximising tumour resection is firmly established [13, 27]. A meta-analysis of 90 observational studies examining the role of intraoperative stimulation mapping (ISM) in surgery for supratentorial gliomas found that gross total resection (GTR) in patient cohorts with and without ISM was 75% and 58%, respectively; in addition, persistent neurological deficits were recorded in 3.4% and 8.2% of cases, respectively [13].

However, variability in anaesthetic techniques [3, 7, 37, 49]; mapping paradigms [16, 35, 44, 48]; selection and interpretation of intraoperative tasks [10, 34, 52]; acceptance of semantic errors and surgery termination points [40, 52]; and technology adjuncts cannot be overlooked [21, 50]. Each of these components and critical steps, uniformly grouped under the general term of AC, is executed in considerably different ways by surgical teams in institutions all over the world.

The present study examines one of the critical components of the AC, the patient's level of consciousness, which determines a number of parameters including the time interval between emergence from general anaesthesia (GA) and ability to participate in neuropsychological testing; positional discomfort or pain; intraoperative pain; and patient's ability to withstand extended and meticulous mapping which may determine final extent of resection (EOR) and preservation of function. Moreover, the lack of patient collaboration can result in failure of the AC as shown in a recent retrospective patient cohort, with a 21% rate of failed AC, 13.3% of which was attributed to lack of patient compliance [51].

While the vast majority of ACs are performed using the asleep-awake-asleep (SAS) technique [12, 14, 15, 17, 23, 26, 51, 53], numerous groups reported anaesthetic protocols ranging from intravenous conscious sedation or monitored anaesthetic care (MAC) to ACs without any sedation, called the "Awake-Awake-Awake Technique" (AAA) [24]. In the latter category, Hansen et al. (2013) reported a protocol employing cranial scalp nerve blocks, the presence of a contact person and psychological guidance [24]. Their approach was predicated in avoidance of propofol-based sedation with complications ranging up to 32% in some series [20]; hypertensive reactions and tachycardia episodes in > 30% and 7% of patients, respectively, and respiratory depression and desaturation rates of 7.1% and 4.8%, respectively [24].

SAS craniotomies performed by experienced teams remain effective and safe techniques [24, 49]. However, factors that prompted us to revise our previous SAS paradigm included the variable time of recovery from anaesthesia; the agitation during recovery observed in a number of patients, particularly in cohorts over 65 years of age and a small number of younger patients who were dislodged from the fixation device of the intraoperative MRI during emergence from GA; and the inability of the patient to reposition, once they recover from GA.

Patient comfort and compliance are crucial in outcomes and patient satisfaction in AC [12, 49]. In a series of 140 cases with intermittent GA and controlled ventilation (SAS), positional discomfort was reported in 17.8% of cases. Painful positioning was the second source of discomfort, after head fixation, in a prospective multicentre study of the European Low-Grade Glioma Network [3].

In addition, in SAS craniotomies, the interval from anaesthetic agent termination to fully conscious states is very variable. Montpellier's experience had mean time of emergence from anaesthesia 14 ± 6 min and an interval mean time for performing complex neuropsychological tests of 20 ± 9 min after discontinuation of the IV infusion [12, 15]. Another group reported an emergence time of 5–8 min after discontinuation of either propofol-remifentanil or dexmedetomidine (DEX) for conscious sedation [22]. Other studies have shown longer arousal times of propofol-based SAS up to 39 min [46].

Hansen et al. (2013) reported on 50 awake craniotomies over a period of almost 7 years, focusing mainly on anaesthetic aspects and proposed psychological strategies. Their report provided limited data on EOR and quoted a rather high rate of stimulation-induced seizures of 16% [24].

In the current report, we describe our experience with the awake throughout craniotomy (ATC) technique in a series of 50 cases, collected prospectively during a 14-month period.

Methods

Data collection

Over a 14-month period, 50 consecutive ATCs were performed in 46 patients, by the senior author. All data were collected prospectively. In addition to standard demographics, supplemental data included mode and timing of clinical presentation; duration of surgery; recordings and variations of SaO_2; anaesthetic complications; surgical complications; and EOR. Cases were numbered from 1 to 50 according to the chronological order of surgical intervention at our institution. Interestingly, 75.6% of cases were considered inoperable by other groups or deemed of high surgical morbidity risk due to involvement of eloquent brain structures. Cases were discussed at and consensus for surgical intervention was obtained from the hospital's tumour board. The questionnaire data is anonymised and cannot be attributed to specific individuals.

Definitions of outcome measures

Major outcome measures used in our study were similar to the largest reported meta-analysis of ISM in glioma surgery,

totalling 8091 adult patients [13]. Consequently, new post-operative deficits were defined, according to severity, as severe and less severe; and according to duration, as early or late. Accordingly, severe deficits included motor power 1–3, on the Medical Research Council (MRC) scale [56], aphasia or severe dysphasia, hemianopia or vegetative state; less severe included MRC grade 4 monoparesis, and somatosensory or parietal syndrome. According to the criteria of the same study, deficits were categorised as early when present immediately or within 3 months of surgery, and late when present 3 months after surgery, with diminished possibility of recovery [13].

An AC was considered failed in inability to complete brain mapping and tumour resection, usually secondary to intraoperative seizures or patient's emotional intolerance [39]. Finally, despite the absence of firmly accepted hypoxia threshold, $SaO_2 < 95\%$ was considered abnormal [11].

Patient questionnaire

In the cohort of consecutive patients 13–50, a simple, patient experience questionnaire was administered before and immediately after (24–48 h) surgery to ensure recollection of surgery, with the following 5 stems: (a) level of pre-operative apprehension/anxiety; (b) level of intraoperative pain on a standard 11-point numeric rating scale (NRS) ranging from 0 (no pain at all) to 10 (excruciating, unbearable pain) for three parts of surgery: (b1) clamp placement, (b2) bone drilling and (b3) main operation and tumour removal; and finally (c) willingness to repeat the same procedure/have a similar experience in the future, if deemed medically necessary. The patient experience questionnaire was devised and implemented after the onset of study and was delivered prospectively in cases 13–50. Questionnaires were not sent to patients 1–12 to avoid violating the prospective nature of data collection.

Measurement of intraoperative pain

Levels of intraoperative pain at b1, b2 and b3 were measured using the standard 11-point NRS pain intensity scale anchored on extremes, used widely in assessing acute post-surgical pain and correlating well with the visual analogue scale (VAS) with a numerical value of 4 accepted as a threshold for tolerable level of pain [4, 6, 25].

Imaging studies

All patients had a standard post-operative MRI scan, requested to be completed within 24 h; in a small number of cases, scans were performed after 24 but within 48 h. Resection was stratified as gross total (GTR) ($\geq 95\%$); subtotal (STR) (80–94%); and partial (PR) ($< 80\%$). Complete resection was defined as (a) the absence of enhancement on immediate post-operative T1W MRI after administration of gadolinium in high-grade gliomas (HGGs) and metastases and (b) the absence of residual hyperintense signal change in Fluid Attenuated Inversion Recovery (FLAIR) MRI sequences in low-grade gliomas (LGGs). All cases were reviewed by experienced neuroradiologists (1) at the time of initial post-operative MRI sequences acquisition and (2) during data analysis of the current study.

Anaesthetic parameters

A circumferential scalp block with equal parts of lidocaine 1% with epinephrine (1:200,000) and bupivacaine 0.25% was used while the patient had a small amount of target-controlled infusion (TCI) of propofol and remifentanil aiming to target blood concentrations of 0.8–1.2 micrograms/ml and 1–2 nanograms/ml, respectively. Infusion rates were typically 15–50 mcg/kg/min for propofol and 0.03–0.1 mcg/kg/min for remifentanil, respectively, allowing rapid titration and rapid offset. No intubation or laryngeal mask was used. Once contact was made with the Mayfield pins, an additional small amount of lidocaine and bupivacaine was used to infiltrate the pin sites, before a standard pin pressure of 270 N (60 lbs) was applied, following which all TCI was stopped. The depth of anaesthesia during the operation was measured using the Richmond Agitation-Sedation scale, aiming for score between − 1 (drowsy) and − 2 (light sedation) [45].

Surgical and stimulation parameters

For delivery of DES, a 5 mm, handheld bipolar probe attached to Ojemann Cortical Stimulator, model OCS2 (Integra, Plainsboro, NJ) was used, with stimulation parameters including pulse duration 0.5 ms, pulse rate 50 Hz and current output 2.0–5.0 mA, maintaining contact with the neural tissue for 3 s at a time, with ice-cold saline irrigation between stimulation episodes. Emphasis was placed on largely subpial resections preserving even small arteries and veins to avoid cortical or subcortical infarcts (Fig. 1).

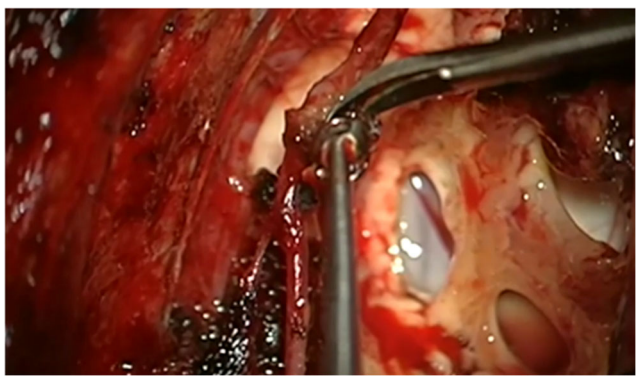

Fig. 1 Preservation of a small diameter, long, intra-parenchymal artery and resection of small tumour remnant attached to its surface (case 14)

The importance of EOR, procedural steps, mapping and their involvement in successful completion of surgery was explained to patients before and during surgery. All patients underwent routine pre-operative neuropsychology testing.

Results

Patient demographics

Over a 14-month period, 46 patients (26 males; 20 females) underwent 50 ATCs. The median age was 52 years, range 26–78. The tumour was located in the left hemisphere in 27 cases and right hemisphere in 23 cases. In the latter group, the tumours were largely located close to primary motor cortex and corticospinal tract.

The mean pre-operative tumour volume was 37.30 ml. Most tumours crossed, one or more, conventional lobar boundaries but based on the location of the most voluminous component, the lobar distributions of tumours, in order of decreasing frequency, were frontal (24); parietal (13); temporal (9); occipital (3); and thalamic (1). Thirty-seven cases were of glial histology (WHO grade I, 2; WHO grade II, 7; WHO grade III, 4; WHO grade IV, 24) and 13 cases were metastatic disease in deep-seated and eloquent locations.

Intraoperative events

In all 50 cases, the 46 patients tolerated the ATC technique well and were immediately assessable for detailed cortical and subcortical mapping. There were no stimulation-induced seizures (0/50; 0%).

Failed awake craniotomies

In our series there were no failed awakes with no cases had to be converted to an asleep procedure, due to anaesthetic or physiological reasons (0%). One patient (case 11) developed unexpected mutism only after successful language mapping had been completed. A laryngeal mask airway (LMA) was easily inserted and the procedure was converted to GA for patient comfort but despite this, complete tumour removal was achieved with post-operative imaging showing 100% tumour resection; the deficit recovered completely in the sixth post-operative day, thereby not fulfilling the criteria for failure of AC (FAC).

Neurological events

There was no surgery-related mortality in our cohort of patients (30-day mortality, 0%). Early, severe deficits were observed in six patients (12%) and early, less severe deficits were observed in eight patients (16%). Late, severe deficits were observed in one patient (2%) and late, less severe deficits, were observed in five patients (10%).

EOR

Independent analysis of post-operative imaging in the cohort of 50 patients showed GTR in 34 patients (68%), STR in 10 patients (20%) and PR in six patients (12%) (Fig. 2). Pre- and post-operative scans from representative cases from the current series are shown in Figs. 3 and 4.

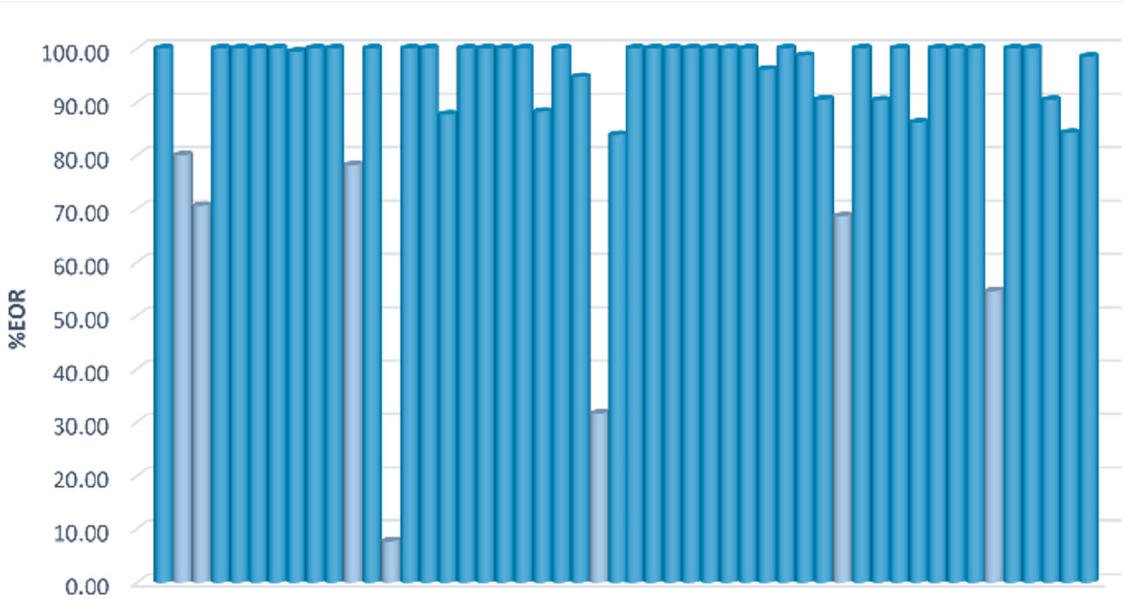

Fig. 2 EOR in 50 consecutive cases operated on with the ATC technique. GTR (≥ 95%) and STR (80–94%), both dark blue, as 78% EOR is considered to be a threshold required to achieve a survival benefit; PR (< 80%), light blue

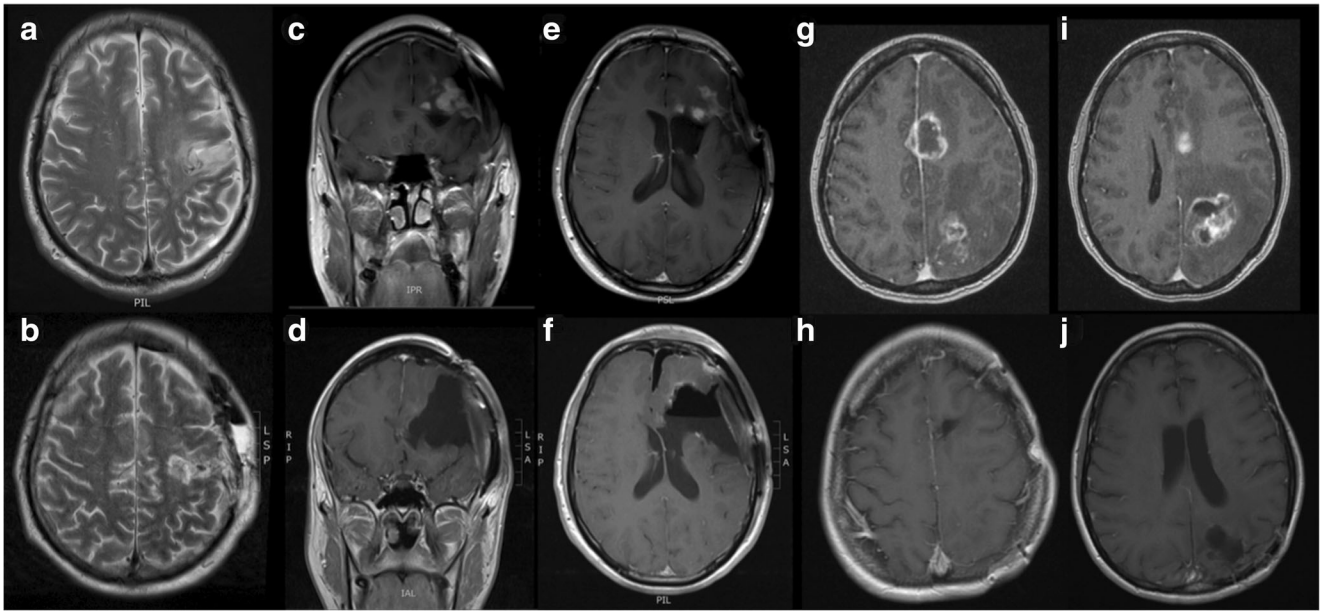

Fig. 3 T2W MRI showing infiltration of the arm, hand and face motor area of the left M1, previously debulked at another institution (**a**), immediate post-operative T2W MRI scan showing resection of the lesion histologically proven to be a LGG (case 37) (**b**), T1W MRI sequences after administration of gadolinium on a patient with left frontal HGG involving the left Broca's area, previously operated on at another institution (**c**, **e**), immediate post-operative MRI scan shows resection of all enhancing neoplastic tissue and resection of the traditional territory of Broca's area (case 1) (**d**, **f**), T1W MRI scan after administration of gadolinium showing a multicentric HGG initially deemed inoperable (cases 10 and 11) (**g**, **i**), post-operative T1W MRI scan after administration of gadolinium showing complete excision of both lesions (cases 10 and 11) (**h**, **j**)

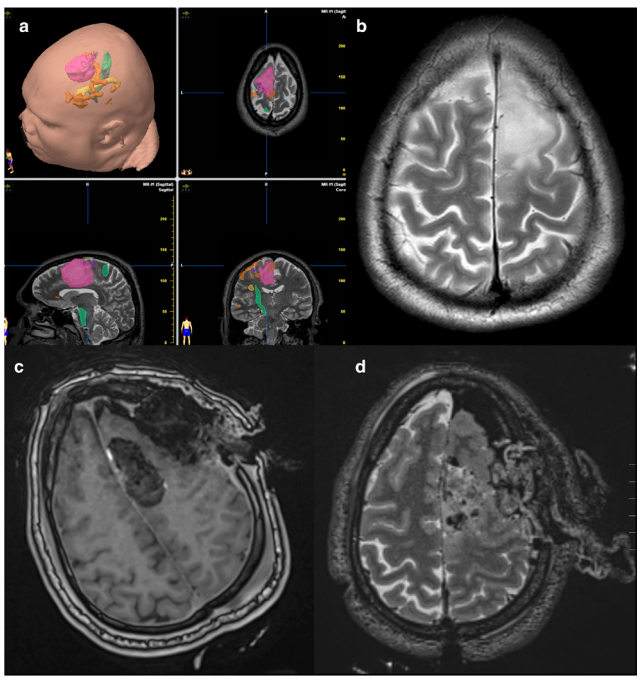

Fig. 4 Functional imaging with delineation of the tumour volume (magenta), and corticospinal tract (green) (**a**), T2W MRI showing infiltration of the pre-SMA, SMA and medial M1 (**b**), intraoperative T2W and FLAIR T1 MRI scan showing resection of the lesion histologically proven to be a LGG (case 26) (**c**, **d**)

Duration of surgery

The duration of surgery was recorded for each case with the start and the end of procedure defined in accordance with the National Quality Forum (NQF) consensus report [38]. The total time of surgery ranged from 80 to 513 min, with a mean of 220 min (median = 200 min; interquartile range 148.5–269.25 min).

Oxygen saturation recordings

In the current series, the average oxygen saturation (SaO_2) was 97.8% (SD = 1.39) and was found not be significantly different from the universally accepted normal threshold of 95% SaO_2 ($p < 0.001$).

Patient questionnaire

From the 38 patients who participated in the questionnaire, clamp pain was absent/minimal (0–3/10) in 37 patients (95.6%); drilling pain was absent/minimal (0–3/10) in 36 patients (94.7%); and intraoperative pain was absent/minimal (0–3/10) in 30 patients (78.9%) (Fig. 5). Additionally, no positional-related discomfort was recorded. Pre-operative anxiety was reported in 68.4% of the patients; however, post-operatively, 92.3% of patients reported that they would be willing

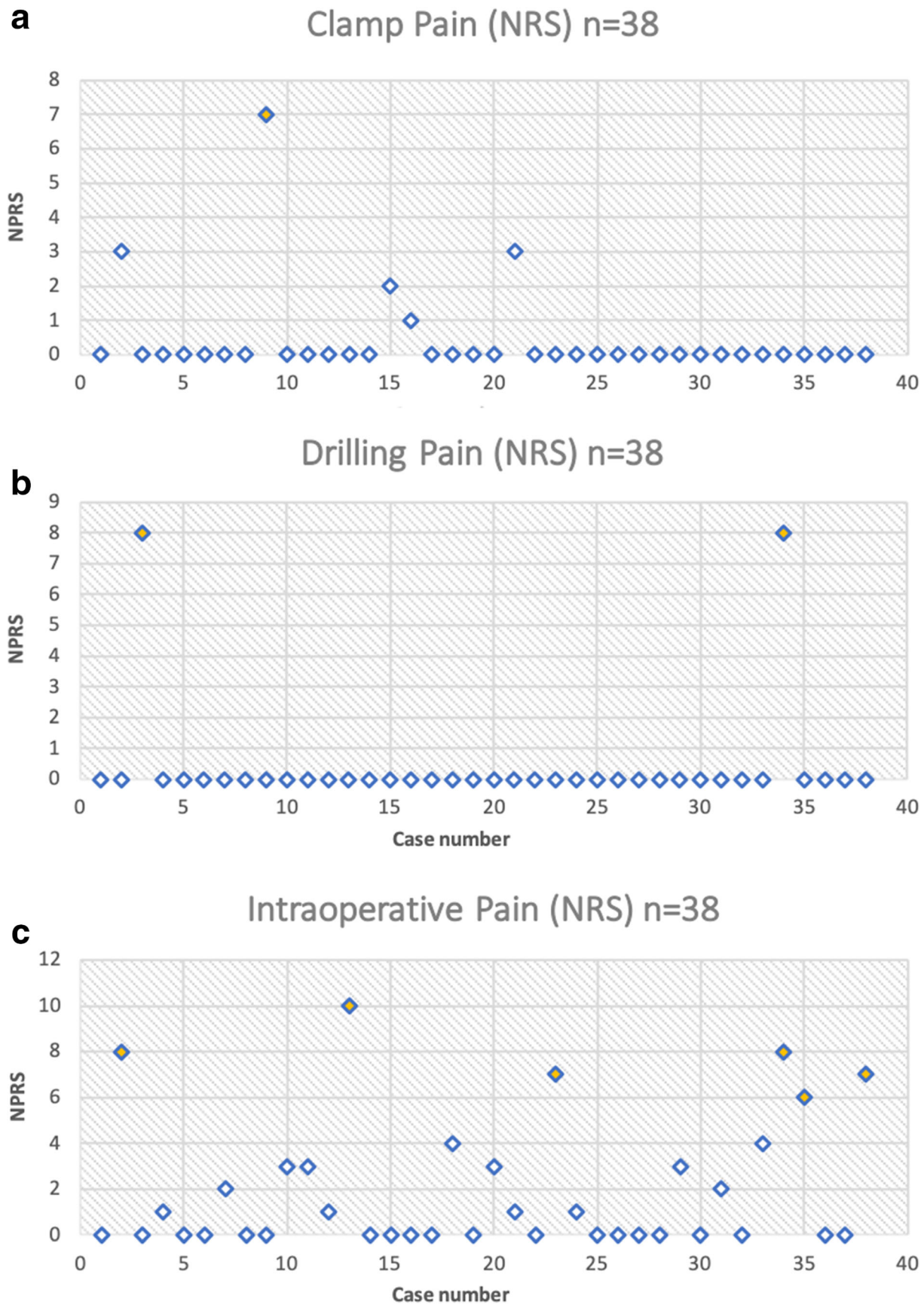

Fig. 5 Clamp (a), drilling (b) and intraoperative (c) pain expressed as numeric value on the numeric rating scale (NRS) scale. 0–4: no/mild/tolerable pain. Yellow diamonds indicate pain levels above NRS level 4

to repeat the ATC procedure, if deemed medically necessary (Fig. 6).

Discussion

Maximum safe resection of gliomas is strongly supported by the current literature [9, 28–30, 42, 47, 57] with a minimum EOR of > 90% required to produce survival benefit. More recently, even small residual tumour volumes stratified between 0 cm^3, 0.1–5.0 cm^3 and > 5.0 cm^3 were associated with progressively decreased survival benefit [57]. Furthermore, in a "near-randomised" trial, Roelz et al. (2016) reported that no survival benefit was recorded in patients with residual tumour volume of < 15 cm^3 and fared similarly to the biopsy only group. In addition, the value of GTR in HGGs was also shown by a systematic review and meta-analysis of 37 articles totalling 41,117 patients diagnosed with HGGs, with likelihood of 1- and 2-year survival of 61% and 19% at 1 and 2 years, respectively [8].

De Witt et al. (2012) showed that awake DES is associated with more extensive resections and fewer, late neurological deficits. However, patients' anxiety and pain levels have been shown to influence their ability to collaborate during awake DES [3, 31, 54, 58]. A patients' experience and satisfaction questionnaire study reported overall good patient tolerance to the MAC technique; however, 24% of patients experienced discomfort during surgery, often related to positioning [55]. In comparison, none of our patients reported positional discomfort.

Intraoperative pain and patient experience

Patients' intraoperative pain was measured using the standard 11-point NRS with a threshold of tolerable pain set to 4 [19]. Different sources of discomfort during AC have been reported with the application of the Mayfield Clamp as a consistent source, by 50% of respondents in one study [31]. In our series, 95.6% reported an NRS of three or less during Mayfield clamp application and 94.7% reported NRS of three or less during drilling pain (Fig. 5) while during the same stages, 33 and 36 patients, respectively, out of 38, reported complete lack of pain (NRS = 0). In a prospective randomised trial comparing dexmedetomidine and combination of propofol and remifentanil, participants reported excessive pain in 22% and 20% of cases, respectively [22], which is higher than our current findings.

In this context, compared with SAS craniotomies, ATCs allow a successive, linear protocol, accommodating active patient participation and feedback, lack of airway instrumentation and nearly instant intraoperative testing. By way of comparison, in the SAS paradigm, if patients feel muscle strain or pain, upon regaining consciousness, a common complaint, they cannot reposition as this will inevitably result in breaching surgical field sterility and neuronavigational registration loss [12, 49]. In addition, in the SAS practice, there may be considerable interval until consciousness is regained, and particularly until a stage allowing detailed neuropsychological testing is reached [12, 15, 46]. Coughing during airway instrumentation, particularly during emergence from GA, may raise the ICP. However, the SAS paradigm allows better CO_2 control and airway management and protection [2].

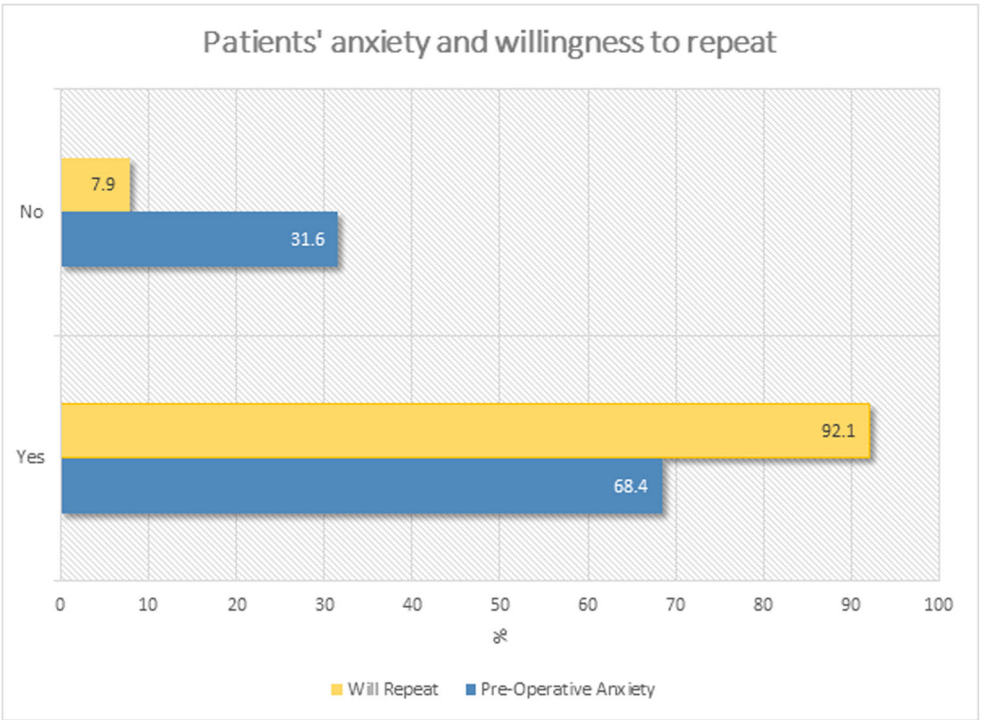

Fig. 6 Comparison of the levels of pre-operative anxiety experienced by the patient and the post-surgery willingness to repeat the procedure if necessary. Despite > 68% of patients having pre-operative anxiety, following ATC, > 92% would be prepared to repeat the procedure, if indicated

During the ATC, there might be a risk of apnoea, particularly at the beginning, linked to levels of sedation, requiring close monitoring. In addition, difficulties to control CO_2 may be encountered increasing the ICP. Finally, there might be a higher risk of stimulation-induced seizures. However, in our series, and the technique described, we had no incidences of stimulation-induced seizures or raised ICP. Pre-operative anxiety is likely; hence, the ATC requires extensive patient coaching before and during the operation, on the required steps and importance of their participation. In addition, collaborative experience between team members requires regular, rather than sporadic, engagement in ATC.

EOR and neurological events

The largest meta-analysis of 90 studies, totalling 8091 adult patients, found that with the use of DES, GTRs were achieved in 74.9% of patients (95% CI, 67.1 to 81.9%) while without DES, EOR was recorded as 58.1% (95% CI, 47.4 to 68.6%) [13]. However, the rate of early, and late, severe deficits with DES was 36% (95% CI, 2.3 to 4.8%) and 3.4% (95% CI, 24.9 to 49.1%), respectively. In the current series, early, and late, severe deficits amounted to 12% and 2%, respectively, which are comparable with other reported series [13].

Duration of surgery

A literature search on the duration of SAS procedures identified eight studies reporting average duration of surgeries from 159 to 404 min. In our series, the total surgery time ranged from 80 to 513 min (mean, 220 min; median, 200 min; interquartile range 269.25–148.5 min), placing the current study in the lower range of reported series to date (Fig. 7).

Adverse intraoperative events

Seizures

Stimulation-induced seizures (SIDs) are well documented and can inadvertently affect surgery, compromising airway and brain mapping [14, 17, 23, 32, 49, 51, 53]. SIDs during the SAS technique have a reported incidence of 0–8.5% [14, 17, 23, 26, 32, 49, 51], whereas their incidence with the MAC technique ranges from 4 to 19%. A retrospective study of 180 patients who underwent AC under either conscious sedation or SAS techniques showed an incidence of SIDs of 17.3% and 8.5%, respectively [51]. In one of the recent meta-analyses including 47 studies and totalling 4942 ACs, SIDs were reported in 351 cases (7.1%), with 23 incidents (0.5%) requiring conversion to GA [49]. In our series, no SIDs were recorded. In our practice, the

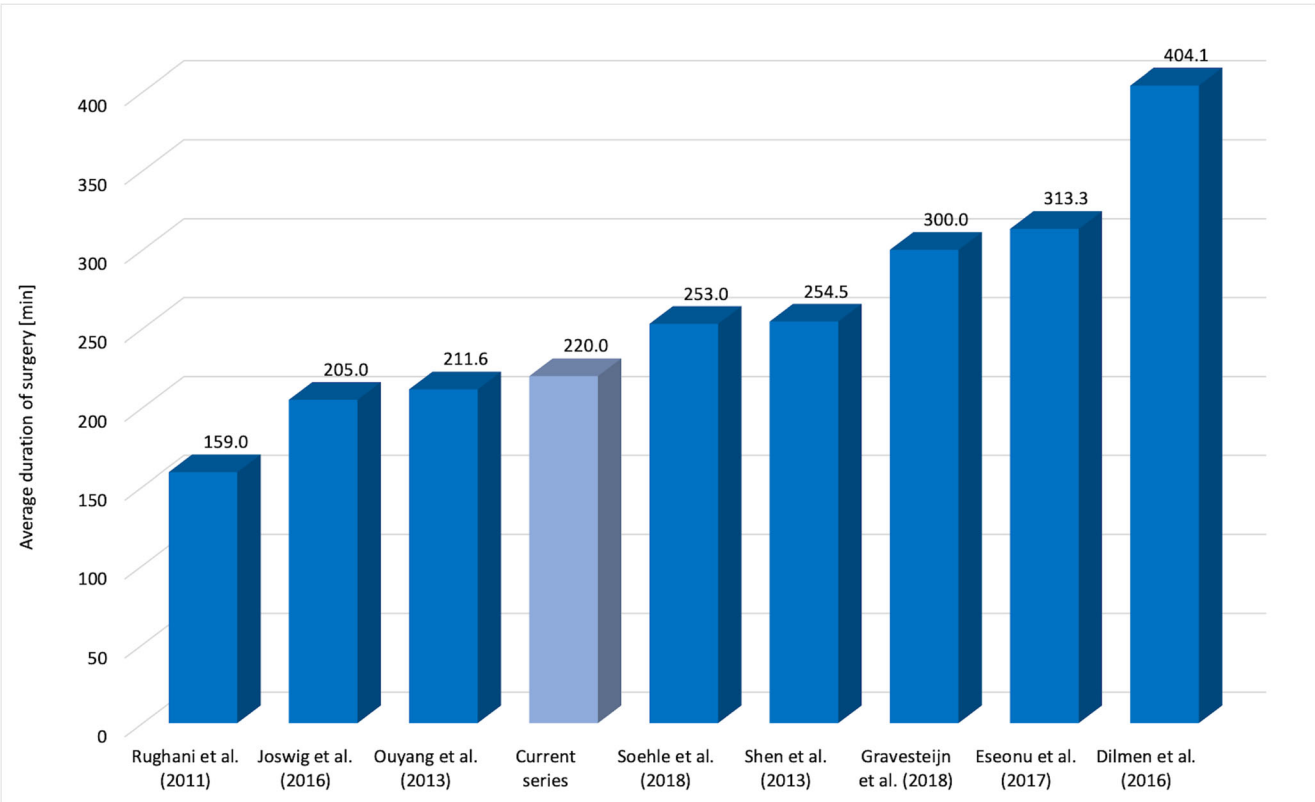

Fig. 7 The average duration of awake craniotomy reported in other studies

threshold of 5 mA during DES is rarely exceeded and the neural tissue is irrigated with cold saline between DES episodes, which may account for the absence of SIDs. The use of cold solutions such as Ringer's lactate has shown to decrease SIDs [43].

Failure of AC

Failed AC is defined as the inability to perform DES or the necessity to convert to GA during the awake phase [14, 17, 23, 26, 32, 49, 51, 53]. FAC rates for the SAS technique range from 0.5 to 21% [14, 17, 23, 26, 32, 49, 51, 53]. Studies using the MAC technique reported FAC rates ranging between 0 and 7.8% [14, 17, 22, 31, 36, 40, 51]. In our series, there were no instances of FAC (0%) for anaesthetic or physiological reasons.

Brain oedema

Brain oedema may lead to reduced level of consciousness and often requires invasive airway management during the awake phase in the SAS technique causing FAC [14, 17, 23, 32]. In addition, airway manipulation during the awake phase can lead to activation of the patient's cough reflex further increasing intracranial pressure and exacerbating oedema [14, 17, 41]. Existing series report rates of 0–14.3% [14, 17, 23, 32].

Despite the lack of use of prophylactic mannitol, in our series, no cases of brain oedema were recorded, which could be attributed to complete lack of airway manipulation or drug-induced respiratory depression. Indeed, in our series, the average oxygen saturation (SaO_2) was 97.8% (SD = 1.39) comparable with normal 95% SaO_2 threshold ($p < 0.001$).

Anaesthetic techniques

Numerous anaesthetic techniques attempt to achieve patient tolerance and compliance during the awake phase of the procedure [18, 22, 36, 46, 49, 51]. The use of DEX, a highly selective α_2-receptor agonist, has been described [49, 51]. However, DEX has been associated with bradycardia and hypotension [1, 5], rarely with respiratory depression and obstruction [46], subclinical seizures and interference with ECoG monitoring. Comparison of SAS and monitored anaesthesia care (MAC) has been reported in the literature [2].

In a recently published survey of the European Low-Grade Glioma Network sent to 28 centres, the responding 20 centres indicated that 56% and 44% of teams employed SAS and monitored sedation paradigms, respectively. In addition, hypnosis-aided awake surgery (HAS) has been considered helpful although surveys of the European Low-Grade Glioma Network (ELGGN) have shown that, in the centres surveyed, HAS remains an infrequently used technique [33]. Our ATC did not involve HAS, but was based on extensive pre- and intraoperative patients' coaching; our surgical and anaesthetic technique was associated with minimal pain scores, high patient satisfaction rates and no systemic, cardiovascular or respiratory adverse effects.

Limitations

The current study reports the experience of a single surgeon and supporting teams with a minimal incidence of postoperative complications and high patient satisfaction. Patient experience questionnaire was administered before and immediately after (24–48 h) surgery to ensure accurate recollection of patients' experience, although the patients were not asked during surgery to grade every incident of intraoperative discomfort or pain, and we did not record the exact timing of pain occurrence, as this would have been an excessive task for the patients and a distracting activity for the health care team.

The outcomes are likely related to meticulous surgical and anaesthetic technique as well as patient coaching; patients' active involvement and experience of teams are paramount. This paradigm has been developed and refined based on years of experience; hence, it is difficult to assess the learning curve and feasibility of its implementation at another institution. Replication of our results in a larger sample of patients would provide further evidence in support of this technique.

Conclusion

Our present ATC paradigm appears to allow constant patient awareness of an uninterrupted, linear process, avoiding two intubation/extubation cycles; patient involvement in positioning; no systemic complications; and finally, immediate brain mapping with full patient co-operation. Emphasis is placed on the patient's engagement and on pre- and intraoperative patient coaching. This team effort allows instant mapping, minimal pain scores, high patient satisfaction rates and no stimulation-induced seizures or FAC. Although many successful models of AC are available, the described model should also be considered.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Arcangeli A, D'Alò C, Gaspari R (2009) Dexmedetomidine use in general anaesthesia. Curr Drug Targets 10(8):687–695

2. Arzoine J, Levé C, Pérez-Hick A, Goodden J, Almairac F, Aubrun S, Gayat E, Freyschlag CF, Vallée F, Mandonnet E (2020) Anesthesia management for low-grade glioma awake surgery: a European Low-Grade Glioma Network survey. Acta Neurochir: 1–7
3. Beez T, Boge K, Wager M et al (2013) Tolerance of awake surgery for glioma: a prospective European Low Grade Glioma Network multicenter study. Acta Neurochir 155(7):1301–1308
4. Berry PH, Covington EC, Dahl JL, Katz JA, Miaskowski C Pain: current understanding of assessment, management, and treatments Editorial Advisory Board
5. Bhana N, Goa KL, McClellan KJ (2000) Dexmedetomidine. Drugs 59(2):263–268 discussion 269-70
6. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EKB, Kvarstein G, Stubhaug A (2008) Assessment of pain assessment of pain intensity and pain relief in acute pain. Br J Anaesth 101:17–24
7. Brown T, Shah AH, Bregy A, Shah NH, Thambuswamy M, Barbarite E, Fuhrman T, Komotar RJ (2013) Awake craniotomy for brain tumor resection: the rule rather than the exception? J Neurosurg Anesthesiol 25(3):240–247
8. Brown TJ, Brennan MC, Li M et al (2016) Association of the extent of resection with survival in glioblastoma a systematic review and meta-analysis. JAMA Oncol 2(11):1460–1469
9. Capelle L, Fontaine D, Mandonnet E et al (2013) Spontaneous and therapeutic prognostic factors in adult hemispheric World Health Organization Grade II gliomas: a series of 1097 cases. J Neurosurg 118(6):1157–1168
10. Chang EF, Breshears JD, Raygor KP, Lau D, Molinaro AM, Berger MS (2016) Stereotactic probability and variability of speech arrest and anomia sites during stimulation mapping of the language dominant hemisphere. J Neurosurg:1–8
11. Collins JA, Rudenski A, Gibson J, Howard L, O'Driscoll R (2015) Relating oxygen partial pressure, saturation and content: the haemoglobin–oxygen dissociation curve. Breathe 11(3):194–201
12. Deras P, Moulinié G, Maldonado IL, Moritz-Gasser S, Duffau H, Bertram L (2012) Intermittent general anesthesia with controlled ventilation for asleep-awake-asleep brain surgery: a prospective series of 140 gliomas in eloquent areas. Neurosurgery 71(4):764–771
13. DeWitt Hamer PC, Robles SG, Zwinderman AH, Duffau H, Berger MS (2012) Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. J Clin Oncol 30(20): 2559–2565
14. Dilmen OK, Akcil EF, Oguz A, Vehid H, Tunali Y (2017) Comparison of conscious sedation and asleep-awake-asleep techniques for awake craniotomy. J Clin Neurosci 35:30–34
15. Duffau H (2014) The usefulness of the asleep-awake-asleep glioma surgery. Acta Neurochir 156(8):1493–1494
16. Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, Sichez J-P, Bitar A, Fohanno D (2002) Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomofunctional study. Brain 125(Pt 1):199–214
17. Eseonu CI, ReFaey K, Garcia O, John A, Quiñones-Hinojosa A, Tripathi P (2017) Awake craniotomy anesthesia: a comparison of the monitored anesthesia care and asleep-awake-asleep techniques. World Neurosurg 104:679–686
18. Garavaglia MM, Das S, Cusimano MD, Crescini C, Mazer CD, Hare GMT, Rigamonti A (2014) Anesthetic approach to high-risk patients and prolonged awake craniotomy using dexmedetomidine and scalp block. J Neurosurg Anesthesiol 26(3):226–233
19. Gerbershagen HJ, Rothaug J, Kalkman CJ, Meissner W (2011) Determination of moderate-to-severe postoperative pain on the numeric rating scale: a cut-off point analysis applying four different methods. Br J Anaesth 107(4):619–626
20. Geze S, Yilmaz AA, Tuzuner F, Abbas A, Tuzuner F (2009) The effect of scalp block and local infiltration on the haemodynamic and stress response to skull-pin placement for craniotomy. Eur J Anaesthesiol 26(4):298–303
21. Ghinda D, Zhang N, Lu J, Yao C-J, Yuan S, Wu J-S (2016) Contribution of combined intraoperative electrophysiological investigation with 3-T intraoperative MRI for awake cerebral glioma surgery: comprehensive review of the clinical implications and radiological outcomes. Neurosurg Focus 40(3):E14
22. Goettel N, Bharadwaj S, Venkatraghavan L, Mehta J, Bernstein M, Manninen PH (2016) Dexmedetomidine vs propofol-remifentanil conscious sedation for awake craniotomy: a prospective randomized controlled trial. Br J Anaesth 116(6):811–821
23. Gupta DK, Chandra PS, Ojha BK, Sharma BS, Mahapatra AK, Mehta VS (2007) Awake craniotomy versus surgery under general anesthesia for resection of intrinsic lesions of eloquent cortex-a prospective randomised study. Clin Neurol Neurosurg 109(4): 335–343
24. Hansen E, Seemann M, Zech N, Doenitz C, Luerding R, Brawanski A (2013) Awake craniotomies without any sedation: the awake-awake-awake technique. Acta Neurochir 155(8):1417–1424
25. Hawker G, Mian S, Kendzerska T, French M (2011) Measures of adult pain. Arthritis Care Res 63(11):240–252
26. Hervey-Jumper SL, Berger MS (2016) Maximizing safe resection of low- and high-grade glioma. J Neuro-Oncol 130(2):269–282
27. Hervey-Jumper SL, Li J, Lau D, Molinaro AM, Perry DW, Meng L, Berger MS (2015) Awake craniotomy to maximize glioma resection: methods and technical nuances over a 27-year period. J Neurosurg 123(2):325–339
28. Ius T, Isola M, Budai R, Pauletto G, Tomasino B, Fadiga L, Skrap M (2012) Low-grade glioma surgery in eloquent areas: volumetric analysis of extent of resection and its impact on overall survival. A single-institution experience in 190 patients. J Neurosurg 117(6): 1039–1052
29. Jakola AS, Myrmel KS, Kloster R, Torp SH, Lindal S, Unsgård G, Solheim O, Unsgård G, Solheim O (2012) Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. JAMA J Am Med Assoc 308(18): 1881–1888
30. Jakola AS, Skjulsvik AJ, Myrmel KS et al (2017) Surgical resection versus watchful waiting in low-grade gliomas. Ann Oncol 28(8): 1942–1948
31. Klimek M, van der Horst PH, Hoeks SE, Stolker RJ (2018) Quality and quantity of memories in patients who undergo awake brain tumor resection. World Neurosurg 109:e258–e264
32. Lu VM, Phan K, Rovin RA (2018) Comparison of operative outcomes of eloquent glioma resection performed under awake versus general anesthesia: a systematic review and meta-analysis. Clin Neurol Neurosurg 169(April):121–127
33. Madadaki C, Aubrun S, Bello L, Duffau H, Mandonnet E (2020) Reply to: letter to the editor regarding anesthesia management for low-grade glioma awake surgery: a European Low-Grade Glioma Network survey. Acta Neurochir (Wien) 1–2
34. Mandonnet E, Nouet A, Gatignol P, Capelle L, Duffau H (2007) Does the left inferior longitudinal fasciculus play a role in language? A brain stimulation study. Brain 130(3):623–629
35. Mandonnet E, Sarubbo S, Duffau H (2017) Proposal of an optimized strategy for intraoperative testing of speech and language during awake mapping. Neurosurg Rev 40(1):29–35
36. McAuliffe N, Nicholson S, Rigamonti A, Hare GMT, Cusimano M, Garavaglia M, Pshonyak I, Das S (2018) Awake craniotomy using dexmedetomidine and scalp blocks: a retrospective cohort study. Can J Anesth 65(10):1129–1137
37. Meng L, Berger MS, Gelb AW (2015) The potential benefits of awake craniotomy for brain tumor resection. J Neurosurg Anesthesiol 27(4):310–317

38. National Quality Forum (2010) Serious reportable events in health care-2010 update
39. Nossek E, Matot I, Shahar T et al (2013) Intraoperative seizures during awake craniotomy: incidence and consequences: analysis of 477 patients. Neurosurgery 73(1):135–140
40. Nossek E, Matot I, Shahar T, Barzilai O, Rapoport Y, Gonen T, Sela G, Korn A, Hayat D, Ram Z (2013) Failed awake craniotomy: a retrospective analysis in 424 patients undergoing craniotomy for brain tumor. J Neurosurg 118(2):243–249
41. Olsen KS (2008) The asleep-awake technique using propofol-remifentanil anaesthesia for awake craniotomy for cerebral tumours. Eur J Anaesthesiol 25(8):662–669
42. Roelz R, Strohmaier D, Jabbarli R, Kraeutle R, Egger K, Coenen VA, Weyerbrock A, Reinacher PC (2016) Residual tumor volume as best outcome predictor in low grade glioma-a nine-years near-randomized survey of surgery vs. Biopsy Sci Rep 6(August):1–9
43. Sartorius CJ, Berger MS (1998) Rapid termination of intraoperative stimulation-evoked seizures with application of cold Ringer's lactate to the cortex. J Neurosurg 88(2):349–351
44. Sefcikova V, Sporrer JK, Ekert JO, Kirkman MA, Samandouras G (2020) High inter-rater variability in intraoperative language testing and interpretation in awake craniotomies among neurosurgeons and neuropsychologists; an emerging need for standardization. World Neurosurg
45. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK (2002) The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 166(10):1338–1344
46. Shen SL, Zheng J, Zhang J, Wang W, Jin T, Zhu J, Zhang Q (2013) Comparison of dexmedetomidine and propofol for conscious sedation in awake craniotomy: a prospective, double-blind, randomized, and controlled clinical trial. Ann Pharmacother doi: https://doi.org/10.1177/1060028013504082
47. Smith JS, Chang EF, Lamborn KR, Chang SM, Prados MD, Cha S, Tihan T, Vandenberg S, McDermott MW, Berger MS (2008) Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. J Clin Oncol 26(8):1338–1345
48. Southwell DG, Hervey-Jumper SL, Perry DW, Berger MS (2016) Intraoperative mapping during repeat awake craniotomy reveals the functional plasticity of adult cortex. J Neurosurg 124(5):1460–1469
49. Stevanovic A, Rossaint R, Veldeman M, Bilotta F, Coburn M (2016) Anaesthesia management for awake craniotomy: systematic review and meta-analysis. PLoS One 11(5):12–23
50. Stummer W, Pichlmeier U, Meinel T (2006) Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol. https://doi.org/10.1016/S1470-2045(06)70665-9
51. Suero Molina E, Schipmann S, Mueller I, Wölfer J, Ewelt C, Maas M, Brokinkel B, Stummer W (2018) Conscious sedation with dexmedetomidine compared with asleep-awake-asleep craniotomies in glioma surgery: an analysis of 180 patients. J Neurosurg 1–8
52. Talacchi A, Santini B, Casartelli M, Monti A, Capasso R, Miceli G (2013) Awake surgery between art and science. Part II: language and cognitive mapping. Funct Neurol 28(3):223–239
53. Taylor MD, Bernstein M (1999) Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. J Neurosurg 90(1):35–41
54. van Ark TJ, Klimek M, de Smalen P, Vincent AJPE, Stolker RJ (2018) Anxiety, memories and coping in patients undergoing intracranial tumor surgery. Clin Neurol Neurosurg 170(April):132–139
55. Wahab SS, Grundy PL, Weidmann C (2011) Patient experience and satisfaction with awake craniotomy for brain tumours. Br J Neurosurg 25(5):606–613
56. Walton J, Gilliatt RW, Hutchinson M, O'Brien MD, Thomas PK, Willison RG (1986) Aids to the examination of the peripheral nervous system. 45(45):61
57. Wijnenga MMJ, French PJ, Dubbink HJ et al (2018) The impact of surgery in molecularly defined low-grade glioma: an integrated clinical, radiological, and molecular analysis. Neuro-Oncology 20(1):103–112
58. Wrede KH, Stieglitz LH, Fiferna A, Karst M, Gerganov VM, Samii M, Von Gösseln HH, Lüdemann WO (2011) Patient acceptance of awake craniotomy. Clin Neurol Neurosurg 113(10):880–884

Comments Tumor craniotomy with mapping in awake patients increases the chance of satisfactory macroradical resection and reduces the risk of complications. Most centres offering awake craniotomy to patients with brain tumours do so by combining it with some level of general anaesthesia before and after the mapping in itself. However, some authors have voiced concerns that short-lasting anaesthetics may affect the level of consciousness and cognitive function even after being stopped.

Here Leon-Rojas and colleagues report their experience with 50 procedures of brain-tumour craniotomy performed in 46 patients who remained awake throughout surgery. The patients presented neurosurgically challenging cases, as three out of four patients were considered inoperable by other groups; they were probably also highly selected and were all operated by the same neurosurgeon. Placement of skull pins was done using scalp block, local anaesthetic infiltration of pin holes, and light sedation, following which all sedatives were stopped. Results were favourable, with a low complication rate; no more than minor pain was reported by 95% of patients during clamp placement and drilling, and by 79% during the surgery itself. Ninety-two per cent were willing to undergo awake throughout craniotomy again. The results indicate that with careful selection, certain patients may be able to undergo tumour craniotomy with mapping using minimal levels of sedatives and analgesics.

Kirsten Møller
Copenhagen, Denmark.