Neurol Med Chir (Tokyo) 52, 119～141, 2012

The Guidelines for Awake Craniotomy

Guidelines Committee of The Japan Awake Surgery Conference

Preface

Cortical mapping by awake craniotomy has become frequently used worldwide as part of the treatment strategy for brain lesions located near language areas. However, no systematic guidelines have been established for this surgery. The Japan Awake Surgery Conference has now created guidelines for awake craniotomy for brain lesions near language areas.

The Japan Awake Surgery Conference was established in 2002 for the purpose of continuing research into neurocognitive functions as well as establishing and promoting safe methods of awake craniotomy. The 4th annual meeting of this conference decided to establish guidelines for awake craniotomy and organized a guidelines committee. Members specializing in the fields of neurosurgery, neurology, and anesthesiology took part in discussions, a systematic review was carried out, and the guidelines committee attempted to create guidelines in compliance with evidence-based medicine methods as far as possible. However, the absence of randomized control trials of awake craniotomy forced the guidelines committee to use ''de facto standards'' to create the guidelines.

The guidelines consist of three parts: 1) Surgical maneuvers for awake craniotomy, 2) Anesthetic management for awake craniotomy, and 3) Language assessment during awake craniotomy. The guidelines are not intended to override the methods of experienced practitioners, and are not intended to exclude methods other than those included. We hope that these guidelines will improve the safety of awake surgeries and promote the development of the neuroscience of neurocognitive function.

President of The Japan Awake Surgery Conference
Takamasa KAYAMA, MD

I. SURGICAL MANEUVERS FOR AWAKE CRANIOTOMY

Indications

1. Age

[Recommendation]

While there is no specific upper age limit, an anesthesiologist, surgeon, and speech therapist should consider the condition of each patient carefully. Surgeons with little experience of awake craniotomy should try to perform awake surgery only in patients aged from 15 to 65 years.

[Commentary]

Awake surgery is usually performed in patients aged from 15 to 65 years. However, patients indicated for such surgery are not only specified by age. If the required tasks can be handled correctly, awake surgery can be performed in persons younger than 15 years and older than 65 years. Patients can undergo such surgery at any age if they are considered to be suitable candidates after other factors have been assessed. The cortex is difficult to excite by electrical stimulation in children aged 7 years or younger, so they do not fulfill the criteria for cortical electrical stimulation.[1] Patients older than 70 years, who may develop delirium or marked emergent increase in blood pressure, require especial attention.

Reference

1) Berger MS, Ojemann GA, Lettich E: Neurophysiological monitoring during astrocytoma surgery. *Neurosurg Clin N Am* 1: 65–80, 1990

These guidelines are approved by The Japan Neurosurgical Society. The part on anesthetic management is approved by the Japan Society of Anesthesiology and the part on language assessment during awake craniotomy is approved by the Neuropsychology Association of Japan.

Correspondence to: Takamasa Kayama, MD, Department of Neurosurgery, Yamagata University Faculty of Medicine, 2–2–2 Iida-nishi, Yamagata, Yamagata 990–9585, Japan.
Phone: +81–23–628–5349; FAX: +81–23–628–5351.

2. Diseases

[Recommendation]

In principle, the indication is for intramedullary diseases that can be treated surgically.

[Commentary]

Epilepsy without macroscopic demarcation between the normal brain tissue and the lesion, gliomatosis with indistinct borders, and cavernous hemangiomas that can only be reached through normal brain regions are typical indications.[1] Metastatic brain tumors are sometimes an indication. Extramedullary tumors such as meningioma are a less common indication, depending on the case.[2] For example, extramedullary tumor corresponding to brain disease with extended motor nerve involvement may be an indication.

References

1) Muragaki Y, Maruyama T, Iseki H, Takakura K, Hori T: [Functional brain mapping and electrophysiological monitoring during awake craniotomy for intraaxial brain lesions]. *No Shinkei Geka Journal* 17: 38–47, 2008 (Japanese)
2) Shinoura N, Yoshida M, Yamada R, Tabei Y, Saito K, Suzuki Y, Takayama Y, Yagi K: Awake surgery with continuous motor testing for resection of brain tumors in the primary motor area. *J Clin Neurosci* 16: 188–194, 2009

3. Sites

[Recommendation]

Areas indicated for awake surgery are locations where surgical procedures may lead to worsening of neurological symptoms, but can be assessed by the performance of intraoperative tasks.

[Commentary]

Lesions in and around the anatomical language areas, lesions in the lateral parietal lobe of the dominant hemisphere (mainly including the angular gyrus), lesions adjacent to the arcuate fibers (superior longitudinal fasciculus), lesions adjacent to the motor cortex, etc.

Awake surgery is indicated for lesions affecting the triangular and opercular regions of the posterior part of the inferior frontal gyrus (Brodmann's areas 44 and 45) or the inferior part of the precentral gyrus with respect to the language motor center, as well as lesions in the posterior half of the superior, middle, and inferior temporal gyri of the temporal lobe (areas 41, 42, 22, and 37) or the supramarginal and angular gyri of the parietal lobe (areas 40 and 39) with respect to the sensory language center. Awake surgery is also indicated for lesions adjacent to the arcuate fibers (superior longitudinal fasciculus) that appear to connect the motor and sensory language areas. The hippocampus is located deep inside the temporal lobe, and is associated with verbal memory, and includes the insular gyri.[1] If a lesion is located near any of the above sites in the dominant hemisphere or if the lesion cannot be confirmed to affect the nondominant hemisphere, identify the functional areas by stimulation.

Reference

1) Muragaki Y, Maruyama T, Iseki H, Takakura K, Hori T: [Functional brain mapping and electrophysiological monitoring during awake craniotomy for intraaxial brain lesions]. *No Shinkei Geka Journal* 17: 38–47, 2008 (Japanese)

4. Other indications such as neurological symptoms

[Recommendation and commentary]

The patient has to participate in awake surgery, so the patient, assessors, surgeons, and anesthesiologists must all fully understand the meaning of aggressive resection and possible complications, and be able to recognize whether or not the patient can tolerate awake anesthesia.

If patients have already developed moderate or severe symptoms, mapping and monitoring are difficult to perform. For example, patients with impairment of language functions, such as understanding, reading, repetition, and object naming, are not suitable for awake surgery. Among patients who cannot speak fluently but have no disorders of understanding, those with minor naming disorders and decreased word enumeration are candidates, although severe disorders may develop during surgery.[1]

Patients with serious intracranial hypertension and those with serious systemic complications are not suitable.

Reference

1) Berger MS, Ojemann GA, Lettich E: Neurophysiological monitoring during astrocytoma surgery. *Neurosurg Clin N Am* 1: 65–80, 1990

5. Determination of the dominant hemisphere

[Recommendation]

Performance of a provocation test (Wada test) by cerebral angiography is desirable. If determination of the dominant hemisphere is done by noninvasive tests such as functional magnetic resonance imaging (fMRI), the therapeutic strategy should be defined after considering the possibility of pseudolocalization.

[Commentary]

Various advanced procedures such as fMRI, magnetoencephalography (MEG), and near infrared spectroscopy (NIRS) have been developed as functional tests. These procedures are noninvasive and have made substantial contributions to neuroscience and neurology. However, for decision-making about surgical resection, the ''gold standard,'' which is the most reliable procedure available (the procedure used to define the ''correct answer'' as the standard for comparison with new procedures), should be used. The gold standards for identification of the dominant hemisphere, functional areas, and neuronal functions are the provocation test (Wada test), that involves infusion of anesthetic during cerebral angiography, identification of functional sites by electrical stimulation, and neurological testing, respectively. Although the anesthetic for the Wada test was amobarbital in the original proposal, propofol is primarily used these days because amobarbital is not currently marketed in Japan.[3] These ''gold standard'' procedures should be used despite being more invasive because, if less invasive but less reliable procedures are used and an incorrect result is obtained, the invasiveness of surgery may become greater than necessary. Determination of the dominant hemisphere in patients with tumors causing compression based on fMRI may have left-right errors (pseudolocalization) in 14%.[4] The surgical strategy largely depends on whether or not a lesion affects the dominant hemisphere and incorrect information naturally increases the risk, so performing the Wada test (the gold standard preoperative procedure) is considered to be necessary. Although textbooks state that 99% of right-handed persons are left hemisphere dominant, a meta-analysis of 734 patients undergoing the Wada test (including 121 of our patients)[2] revealed that the dominant hemisphere for right-handed persons was the left hemisphere in 88%, the right in 5%, and both in 7%.[1] The dominant hemisphere determined by electrical stimulation is the left hemisphere in 91% and the right in 9%. Thus, around 90% of right-handed persons are left hemisphere dominant and around 10% are right hemisphere dominant, which is not a low prevalence, suggesting that careful attention should be paid during surgery to lesions in functional areas of the dominant hemisphere. The results of the Wada test in left-handed people have shown that the left dominant:right dominant ratio ranges from 1:1 to 3:1, with a slightly higher rate of left dominance.

In recent years, the increasing accuracy of noninvasive procedures such as fMRI, MEG, and NIRS has provided us with more and more knowledge. In addition, when a gradual transition from invasive to noninvasive procedures occurs because of the risk of complications of cerebral angiography, including the Wada test, the risk of pseudolocalization should be accepted. Feedback with respect to comparison of the results of the Wada test and those of mapping by electrical stimulation is needed.

References

1) Ishikawa T, Muragaki Y, Maruyama T, Ono Y, Abe K, Tanaka M, Amano K, Inoue T, Kubo O, Iseki H, Hori T, Sakai K: [Efficacy of the determination of the dominant hemisphere by Wada test and functional MRI for tumors around language areas]. Presented at the 65th Annual Meeting of the Japan Neurosurgical Society; October 18–20, 2006; Kyoto (Japanese)
2) Medina LS, Bernal B, Ruiz J: Role of functional MR in determining language dominance in epilepsy and nonepilepsy populations: a Bayesian analysis. *Radiology* 242: 94–100, 2007
3) Takayama M, Miyamato S, Ikeda A, Mikuni N, Takahashi JB, Usui K, Satow T, Yamamoto J, Matsuhashi M, Matsumoto R, Nagamine T, Shibasaki H, Hashimoto N: Intracarotid propofol test for speech and memory dominance in man. *Neurology* 63: 510–515, 2004
4) Ulmer JL, Hacein-Bey L, Mathews VP, Mueller WM, DeYoe EA, Prost RW, Meyer GA, Krouwer HG, Schmainda KM: Lesion-induced pseudo-dominance at functional magnetic resonance imaging: implications for preoperative assessments. *Neurosurgery* 55: 569–581, 2004

Methods

1. Preoperative treatment

1–1. Status and details of simulation

[Recommendation]

The tasks that will be performed during surgery should be preoperatively rehearsed in the ward. Simulation of the surgical posture, equipment set-up, and role sharing, as well as rehearsal of the tasks for the patient, surgeons, anesthesiologists, and other surgical staff (such as nurses) should also be performed in the operating room.

[Commentary]

For successful intraoperative mapping with awake anesthesia, it is important to reduce the patient's anxiety as much as possible by maintaining a comfortable environment during surgery. Bring the patient to the operating room on the day before surgery, and take enough time to explain what will be done on the next day (including the posture that the patient will be placed in by the surgeon, anesthesiologists, and nurses). Then have the patient actually adopt that posture. If possible, show the patient a video of surgery on previous patients for better understanding. If functional language mapping is performed, conduct higher function examination before surgery, perform the tasks that will done during surgery in the ward in advance, and select intraoperative tasks, for example, by showing the patient pictures or photographs of common objects used in object naming and selecting some that the patient can answer correctly. If there has been a long interval between examination and surgery in a patient with progressive symptoms due to a tumor adjacent to the language areas, the tasks should be selected immediately before surgery.

1–2. Monitoring of anticonvulsants

[Recommendation]

In patients who are scheduled to undergo awake surgery, it is desirable to initiate the administration of anticonvulsants in advance and maintain effective blood concentrations if enough time is available. Phenytoin can be administered and the concentration increased to the upper limit of the effective range (target level 20 mg/dl) by the day before surgery.

[Commentary]

Even if an effective blood concentration of an anticonvulsant has been maintained since before surgery, there is some risk of convulsions during awake surgery (as described below). Therefore, sufficient preoperative antiepileptic drug saturation is desirable to prevent intraoperative convulsions and for easy drug loading after the onset of convulsions. Regarding the selection of drugs, phenytoin is recommended, since intravenous administration can be performed immediately before or during surgery when oral administration is not possible, rapid saturation is easy, a steady-state blood concentration can be obtained after a relatively short time (4–5 days), and regulation of the blood concentration is easy.

The bioavailability of phenytoin is high (98%) and there is little difference between systemic absorption after intravenous and oral administration. If there are 3 or more days before surgery, it is desirable to achieve the target blood concentration by oral administration to reduce patient discomfort. If rapid saturation immediately before surgery is selected, the target blood concentration can be obtained promptly by intravenous administration of phenytoin.

Especially for patients with tumors located near the motor cortex, after obtaining an adequate preoperative blood concentration of phenytoin, the blood level should be monitored every 2 hours during surgery. If the concentration is low, intravenous administration of 250 mg of phenytoin should be given to raise the concentration to the normal upper limit (this dose increases the blood level by approximately 6 mg/dl in a patient weighing 60 kg), or 100–200 mg of phenytoin should be given every 4 hours during surgery (this dose will increase the blood level by approximately 2.4–4.7 mg/dl in a patient weighing 60 kg).

Sixteen (16%) of the 100 patients who underwent awake surgery at Tokyo Women's Medical University from 2004 to the present developed seizures under awake conditions, whereas 48 (48%) of these 100 patients had a history of seizures before surgery. Twelve (24.5%) of the 49 patients with tumors near the motor cortex developed seizures during awake surgery and this rate was higher than at other sites. Occurrence of seizures during awake surgery is defined as clinically obvious convulsions and does not include patients who only have afterdischarges.

Among the 80% or more of our 100 patients who had received preoperative antiepileptic drug therapy, patients with lesions near the motor cortex and a preoperative blood level within or above the effective range accounted for 70% of patients both with and without intraoperative convulsions, although the blood level was not measured in all patients. Thus, even if the blood level of an antiepileptic drug is within the effective concentration range, there is no improvement of the preventative effect against intraoperative seizures, which is more likely to depend on the conditions of electrical stimulation.

Preoperative phenytoin loading is not performed at Tokyo Women's Medical University, so its efficacy has not been demonstrated there. Therefore, the frequency of intraoperative convulsions in patients with brain lesions at each site should be compared with that determined at institutions where rapid preoperative phenytoin saturation is performed to assess the usefulness of this procedure. It may also be necessary to assess the conditions employed for electrical stimulation, especially for the motor cortex, as well as the use of rapid anticonvulsant saturation.

[Saturation][1,2]

Initial loading dose [mg]: target blood concentration [mg/dl] × volume of distribution Vd [l/kg] × body weight [kg] = 20 × 0.7 × body weight [kg]..(a)

Additional loading dose [mg]: {target blood concentration − measured value [mg/dl]} × volume of distribution Vd [l/kg] × body weight [kg] = (20 − measured value) × 0.7 × body weight [kg] ....(b)

Where target blood concentration is 20 mg/dl, and Vd is specific value for each drug: phenytoin 0.6–0.8 (approximately 0.7) l/kg.

For example, in a patient weighing 60 kg, the initial loading dose calculated using (a) is 840 mg, which is administered as three divided doses every 2 to 4 hours. This will avoid cardiovascular adverse reactions such as hypotension, bradycardia, and arrhythmia, as well as gastrointestinal symptoms. After 12 to 24 hours of administration at the above dose, initiate therapy at the usual maintenance dose (200–400 mg/day). Measure the blood concentration 2 to 3 days after finishing the initial loading dose for oral administration, and at 24 hours after or immediately before surgery when rapid saturation has been achieved by intravenous administration, and calculate the additional loading dose using (b).

The saturation period for phenytoin should be within the range of 3 to 5 days to avoid the development of adverse reactions when the blood level is maintained at the upper limit of the effective concentration range for too long (1 week or more) before surgery. There have been many reports about phenytoin-induced skin disorders such as disseminated erythematous papules after approximately 2 weeks and serious drug-induced hypersensitivity syndrome after 2 to 6 weeks in most cases.[3]

Because the protein-binding rate of phenytoin is high (90–95%), even if the blood level of the drug is within the effective range in patients who have a low serum albumin concentration, the concentration of free drug (not bound to albumin) will be increased and measured values may not reflect the actual levels. If the serum albumin is 3 g/dl or lower, free phenytoin should be simultaneously measured or the effective phenytoin concentration estimated using the following formula for correction: Measured phenytoin level/$\{(0.2 \times \text{albumin level}) + 0.1\}$ ......(c)

Where target range for free phenytoin is 2 to 2.5 mg/dl.

References

1) Lacy CF, Armstrong LL, Goldman MP, Lance LL: *Lexi-Comp's Drug Information Handbook, 13th ed.* Ohio, Lexi-Comp Inc, 2005, pp 1195–1199
2) Ogata H, Masuhara K, Matsumoto Y: [*Clinical Pharmacokinetics*]. Osaka, Maruzen, 2001, 181 pp (Japanese)
3) Shiohara T, Miyachi Y, Takigawa M (*eds*): [*Dermatology Practice 19; Master Drug Eruption*]. Tokyo, Bunkodo, 2006, 301 pp (Japanese)

2. Various intraoperative methods

2–1. Sites and methods of local scalp anesthesia

[Recommendation]

For local anesthesia of the scalp, it is common to use long-acting local anesthetics in combination with invasive anesthesia and nerve blocks.

[Commentary]

Analgesia by local anesthesia is often performed by the combination of infiltration with local anesthetic and nerve blocks. At some institutions, anesthesia is performed only by local injection or only by nerve block. Long-acting local anesthetics such as ropivacaine and bupivacaine are often used and these are combined with lidocaine at some institutions.[3] Supraorbital nerve block is used if the skin incision is primarily located in the frontal region, whereas auriculotemporal nerve block is used for an incision in the temporal region. Greater or lesser occipital nerve blocks can be added to these blocks. If head fixation is used, an anesthetic is administered at the sites of the pins in addition to the skin incision sites. Sufficient anesthetic should be provided at the pin sites because many patients complain of pain at these sites during emergence.

Preoperative simulation of temporary pseudoemergence can be performed after fixing the head in a specific posture before the initiation of surgery, to confirm whether tasks can be performed or whether there are any problems with the removal and reinsertion of a laryngeal mask.[1,2]

References

1) Fukaya C, Katayama Y: [Intraoperative wake up procedure using propofol total intravenous anesthesia and laryngeal mask]. *No Shinkei Geka Journal* 8: 332–337, 1999 (Japanese)
2) Fukaya C, Katayama Y, Yoshino A, Kobayashi K, Kasai M, Yamamoto T: Intraoperative wake-up procedure with propofol and laryngeal mask for optimal excision of brain tumour in eloquent areas. *J Clin Neurosci* 8: 253–255, 2001
3) Sato K, Kawamata M, Nagata O, Kawaguchi M, Morimoto Y, Kato M, Sakabe T: [Present state of anesthetic management for awake craniotomy in Japan]. *Masui* 57: 492–496, 2008 (Japanese)

2–2. Head fixation and posture setting

[Recommendation]

Successful awake functional brain mapping/monitoring depends on whether the patient's cooperation can be maintained for a long time. Therefore, head fixation and posture setting are important to keep the patient in a comfortable position for a long period.

Although there is no definitive method of head fixation and posture setting, continuous feedback is essential about whether functional brain mapping/monitoring is successful or not, and whether or not the patient can comfortably cooperate with surgery and functional brain mapping/monitoring, and the surgeon should continue to assess whether the selected method is correct or not.

The basic procedure is as follows:

i) Preoperative explanation: It is important to create an image of surgery for the patient and family. If this is not done, the patient will not understand what to do and how to cooperate, and will be uneasy during the surgery. The preoperative explanation should include basic issues related to brain functional differentiation, association of the extent of tumor invasion with functional areas, neurosurgical procedures, and functional brain mapping/monitoring procedures, and be illustrated with pictures, slides, and videos. Also, bring the patient to the actual operating room before surgery, perform head fixation and posture setting, and allow enough time to perform surgical simulation that includes meeting with the surgeons and nurses.

ii) Head fixation: Whether complete restriction of movement of the head by pin fixation or to allow movement of the head by not performing fixation is better has not been decided. The purpose of surgery is to safely and reliably resect the tumor, and the method should be established at each institution that both maintains patient comfort and allows surgery to achieve its purpose.

iii) Posture setting: To perform functional mapping of motor and sensory areas including functional language mapping, craniotomy must extend to sites that include normal brain tissue as well as the tumor. A posture that allows the performance of wide frontal-temporal-parietal craniotomy is generally used. For posture setting, given that the body weight is supported by various parts of the body, individual differences with regard to a comfortable posture and how painful maintaining the same posture for a long time can be for patients must be fully understood. Setting a posture that is only tolerable for a short time and attempting to maintain it for a long time leads to pain at unexpected sites. How many times the posture can be changed during surgery and the patient's desired temperature (hot or cold) must also be confirmed.

[Commentary on approach without head fixation]
Posture setting

What surprised us most when we visited the institution of Berger et al., who are pioneers in the use of this method for maximum resection of gliomas, is that Dr. Berger himself took time to carefully set each patient's posture with pads that were tailor-made for size, shape, and thickness. Their stock of prepared pads and linen was much larger than ours. Awake surgery provides us with a good opportunity to realize how inadequate our previous posture setting is for general anesthesia. The following posture setting and head fixation procedures are basically according to the method of Berger et al.[1–3)]

Preparation on the day before surgery: Bring the patient to the actual operating room on the day before surgery, and take enough time to explain what will be done on the next day, including posture setting. It is important for the patient to meet the surgeons, assistants, anesthesiologists, and nurses. At that time, detailed explanation of the patient's pathological condition, and explanation using videos about tumor resection in combination with awake functional brain mapping/monitoring should be provided to the patient (permission for the use of videos should be obtained because they contain personal information). It is as important for the patient to have an understanding of the surgery as it is for the surgeons to develop an image of the procedure.

Fig. 1 Posture setting in the Department of Neurosurgery of Tohoku University.

To perform functional mapping of motor and sensory areas, including functional language mapping, craniotomy needs to expose normal brain tissue as well as the tumor. In general, to allow for wide frontal-temporal-parietal craniotomy, the head is tilted 75° to the opposite side. The next section covers whether head fixation should be performed or not. Place a large pad supporting the whole body from the shoulder to the waist to avoid torsion of the shoulders and head. To improve venous return, slightly raise the upper part of the body. Find the most comfortable positions for both the upper and lower extremities, and be careful not to overload any part of the body. It is desirable to fill little empty spaces with small pads. During posture setting, maintain an environment similar to that during the actual surgery as far as possible, continue conversation, and take time to check for the presence or absence of pain and to be careful not to have any body part unsupported (Fig. 1).

To perform mapping, you need to have a clear space in front of the patient's eyes and to have enough space to place a portable computer within the vision, which is used for object naming in functional language mapping. At our hospital, this space is created with L-shaped bars and infusion stands

Fig. 2 Conditions used for the first case in the Department of Neurosurgery of Tohoku University (1996).

(Fig. 2), and transparent drapes may be used to allow vision.[6] Surgery takes a long time and osmotic diuretics such as mannitol may be used because of the inability to employ hyperventilation to control brain swelling, so continuous urine flow is required.

If intraoperative motor functional mapping is done under general anesthesia, unlike awake anesthesia, freer setting of the posture and head position (including use of the prone position) is available. However, functional brain mapping takes time to perform without administration of muscle relaxants, so whether the patient will feel comfortable in an unforced posture should be considered when setting the posture.

Posture setting on the day of surgery: Even if the posture has already been confirmed on the day before surgery, take enough time to set the patient's posture again and ensure that he/she is comfortable. To confirm whether the patient feels comfortable or not, hold a conversation and do not induce anesthesia until the completion of posture setting.

Head fixation

There is no consensus at this time about whether head fixation should be done or not. If we give first priority to the patient's comfort, no fixation would seem to be more desirable. However, lack of fixation will lead to constant movement of the surgical field. To continually respond to unexpected movements for a long time when manipulating deep brain regions or blood vessels is very stressful for surgeons. For surgery combined with awake functional brain mapping/monitoring, which is based on cooperation and achieving a balance between the surgeons and the patient, determine whether head fixation should be used or not after careful consideration at each institution. Even without head fixation, continuous navigation is available[5] by fixing the reference points to the skull.[4]

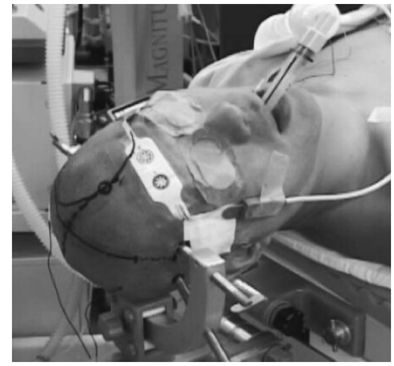

Fig. 3 Approach with head fixation.

[Commentary on approach with head fixation]

The advantages of head fixation include a fixed operating field and complete fixation of the conventional navigation system, retractor, electroencephalograph, or other instruments, so that the surgeon can operate as under general anesthesia. The disadvantages of this approach include more patient discomfort compared with the absence of head fixation, due to pain at the pin fixation sites, and difficulty of moving the body and changing the head position. Also, treatment of vomiting or convulsions and reintubation may be difficult, so sufficient simulation is necessary. A patient with a left frontal lobe glioma receives 4-point fixation after insertion of a laryngeal mask (Fig. 3). As with 3-point fixation, it is difficult to rotate and move the head after application of 4-point fixation, so simulation of emergency situations is very important.

References

1) Berger MS: Malignant astrocytomas: Surgical aspects. *Semin Oncol* 21: 172–185, 1994
2) Berger MS, Kincaid J, Ojemann GA, Lettich E: Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. *Neurosurgery* 25: 786–792,1989
3) Berger MS, Ojemann GA, Lettich E: Neurophysiological monitoring during astrocytoma surgery. *Neurosurg Clin N Am* 1: 65–80, 1990
4) Fukaya C, Katayama Y, Yoshino A, Kobayashi K, Kasai M, Yamamoto T: Intraoperative wake-up procedure with propofol and laryngeal mask for optimal excision of brain tumour in eloquent areas. *J Clin Neurosci* 8: 253–255, 2001
5) Leuthardt EC, Fox D, Ojemann GA, Dacey RG, Grubb RL, Rich KM, Ojemann JG: Frameless stereotaxy without rigid pin fixation during awake craniotomies. *Stereotact Funct Neurosurg* 79: 256–261, 2002
6) Walsh AR, Schmidt RH, Marsh HT: Cortical mapping and local anaesthetic resection as an aid to surgery of

low and intermediate grade gliomas. *Br J Neurosurg* 6: 119–124, 1992

2–3. Awake state and surgery: Status of anesthesia and status of electrical stimulation during resection

[Recommendation]

Resection is often performed under anesthesia or sedation, and the methods vary among institutions. With subcortical mapping, electrical stimulation needs to be continued even during resection. There is no established method at this time and the value of the procedure is uncertain.

[Commentary]

Although the use of sedation is common during resection of the lesion, it is done on a case-by-case basis or never performed at some institutions because it is still controversial. Propofol is often used, but dexmedetomidine, sevoflurane, nitrous oxide, etc., can also be employed.

For subcortical mapping, electrical stimulation needs to be continued even during resection. However, there is no established method of subcortical stimulation and the methods employed vary among institutions at present. For subcortical mapping of the corticospinal tract, the method of recording the electromyogram by using Ojemann-type bipolar electrodes as in cortical mapping seems to be employed relatively often. With bipolar recording, however, the stimulation range is limited to the immediate vicinity of the electrodes and injury has often already occurred when a response is detected. If the presence of the corticospinal tract cannot be predicted at a certain distance, subcortical mapping may well be useless. A method of recording corticospinal motor-evoked potentials (D-wave) that descend through the corticospinal tract from spinal epidural electrodes for subcortical mapping is being discussed. The amplitude of D-waves evoked by monopolar stimulation may reflect the distance between the stimulation points and the corticospinal tract to some degree, so the method of recording the D-wave amplitude under given stimulus conditions seems to be promising.

Also, in subcortical mapping of language functions, conventional bipolar stimulation limits the range as for mapping the corticospinal tract, so whether language area-derived speech arrest can be certainly detected is unclear and the reliability of subcortical electrical stimulation during resection is difficult to determine.

References

1) Duffau H: Contribution of cortical and subcortical electrostimulation in brain glioma surgery: methodological and functional considerations. *Neurophysiol Clin* 37: 373–382, 2007
2) Fukaya C, Katayama Y, Kobayashi K, Kasai M, Oshima H, Yamamoto T: Impairment of motor function after frontal lobe resection with preservation of the primary motor cortex. *Acta Neurochir Suppl* 87: 71–74, 2003
3) Katayama Y, Tsubokawa T, Maejima S, Hirayama T, Yamamoto T: Corticospinal direct response in humans: identification of the motor cortex during intracranial surgery under general anaesthesia. *J Neurol Neurosurg Psychiatry* 51: 50–59, 1988
4) Keles GE, Lundin DA, Lamborn KR, Chang EF, Ojemann G, Berger MS: Intraoperative subcortical stimulation mapping for hemispherical perirolandic gliomas located within or adjacent to the descending motor pathways: evaluation of morbidity and assessment of functional outcome in 294 patients. *J Neurosurg* 100: 369–375, 2004
5) Nagaoka T, Fukaya C, Katayama Y: [Neurosurgical procedures, and electroencephalogram and evoked potentials, 5. Subcortical mapping]. *Rinsho Noha* 48: 321–325, 2006 (Japanese)
6) Sato K, Kawamata M, Nagata O, Kawaguchi M, Morimoto Y, Kato M, Sakabe T: [Present state of anesthetic management for awake craniotomy in Japan]. *Masui* 57: 492–496, 2008 (Japanese)

2–4. Conditions and timing of stimulation

2–4–1. Cortical stimulation: type of electrode, intensity of stimulation, and duration

[Recommendation]

In the setting of brain electrical stimulation for functional mapping, because of its effect and to maintain the safety of the brain tissues, the following methods of using probe electrodes and subdural electrodes are recommended:

Probe electrodes: Interpolar distance of 5 mm and diameter of 1 mm for bipolar electrodes or diameter of 1 mm for monopolar electrodes; square wave pulses (0.2 or 0.3 or 1 msec) with alternating polarity and frequency of 50 or 60 Hz, and stimulus duration of up to 4 seconds; and current from 1.5 (or 2) mA with maximum intensity of 16 mA.

Subdural electrodes: Interpolar distance of 5 mm to 1 cm and diameter of 3 mm for bipolar electrodes; square wave pulses (0.2 or 0.3 msec) with alternating polarity and frequency of 50 or 60 Hz, and stimulus duration of up to 10 seconds; and current from 1 mA with maximum intensity of 16 mA.

[Commentary]

Stimulation conditions vary among the types of electrode and purposes of functional mapping. The recommendations cover typical methods for cortical language mapping. When stimulating the primary motor area under awake conditions, use of low frequency stimulation or one to five repetitive stimuli is desirable to prevent convulsions.

For identification of false-positive responses to peripherally spreading electrical stimulation, afterdischarges should be monitored.[1,2] Cortical excitability differs between children and adults and also varies between individuals, so false-negative results can occur.

References

1) Ebner A, Luders HO: Subdural electrodes, *in* Luders HO, Comair YG (*eds*): *Epilepsy Surgery*. Philadelphia, Lippincott Williams & Wilkins, 2000, pp 593–596
2) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med* 358: 18–27, 2008

2–4–2. Subcortical stimulation: type of electrode, intensity of stimulation, and duration

[Recommendation]

The conditions for stimulation are the same as those for ''cortical stimulation.''

Alternative method for stimulation (subcortical): 0.2 msec, 50 Hz, stimulus duration of up to 4 seconds, from 1 mA to maximum intensity of 20 mA.

Implanted subdural electrode (deep electrode): Used for hippocampal lesions. The interpolar distance is 1 cm or 5 mm.

[Commentary]

Experience shows that responses are often identified by the same tasks and current intensity as with cortical stimulation. If maximum resection is performed while checking the response to subcortical stimulation, 80% of patients develop transient neurological symptoms, but 94% of them recover within 3 months.[1] Subcortical stimulation also allows identification of the following language-related fibers, by which various findings have been obtained[2,3]: superior longitudinal fasciculus, arcuate fasciculus, subcallosal fasciculus, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, uncinate fasciculus, orofacial motor fibers, etc.

References

1) Duffau H, Capelle L, Denvil D, Sichez N, Gatignol P, Taillandier L, Lopes M, Mitchell MC, Roche S, Muller JC, Bitar A, Sichez JP, van Effenterre R: Usefulness of intraoperative electrical subcortical mapping during surgery for low-grade gliomas located within eloquent brain regions: functional results in a consecutive series of 103 patients. *J Neurosurg* 98: 764–778, 2003
2) Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, Sichez JP, Bitar A, Fohanno D: Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. *Brain* 125: 199–214, 2002
3) Muragaki Y, Maruyama T, Iseki H, Takakura K, Hori T: [Functional brain mapping and electrophysiological monitoring during awake craniotomy for intraaxial brain lesions]. *No Shinkei Geka Journal* 17: 38–47, 2008 (Japanese)

2–5. Treatment of convulsions

Risk: Convulsion can develop during intraoperative mapping and tumor resection.

Measures: Reduce the stimulus intensity. Do not persist with mapping. For tumors near the motor cortex, raise the concentrations of phenobal and phenytoin to the upper normal limits and check the levels every 2 hours during surgery. If the levels are lower than the limits, appropriately administer 250 mg of intravenous phenytoin and 100 mg of intramuscular phenobal to increase the concentrations to the upper limits. If convulsions occur, put cold water or cold artificial cerebrospinal fluid (e.g., Artcereb®; Otsuka Pharmaceutical Factory, Inc., Tokyo) on the brain surface and wait until the convulsions cease. If convulsions occur frequently, switch to general anesthesia and then switch back to awake surgery if possible after adequately raising the concentrations of anticonvulsants. (For tumors near the motor cortex, surgery can continue while checking the motor-evoked potentials [second best method].)

2–6. Necessity and usefulness of confirming afterdischarges: methods and evaluation

[Recommendation]

Confirmation of stimulation-induced convulsions by evaluating the occurrence of afterdischarges on the electrocorticogram should be a basic procedure.[2] At the very least, until the number of cases experienced by the institution increases, it is essential that the stimulation conditions are standardized, and the method of functional evaluation is established. The risk of mistakenly identifying motor, sensory, and language disorders induced by development of brain dysfunction at distant sites because of stimulation-induced afterdischarges should be avoided. To confirm whether electrical stimulation is actually being delivered (i.e., the current is flowing), electroencephalography is useful. Position the electrocorticographic electrodes and record the electrocorticogram without stimulation (Fig. 4). Place small pieces of paper with numbers, etc. on the brain surface so that surgeons, staff performing electrophysiological mapping, and staff performing higher function examination can mutually confirm the stimulation sites. Stimulate the brain surface for 2 to 3 seconds by applying biphasic rectangular pulses of 50 Hz and 0.3 msec pulse width with

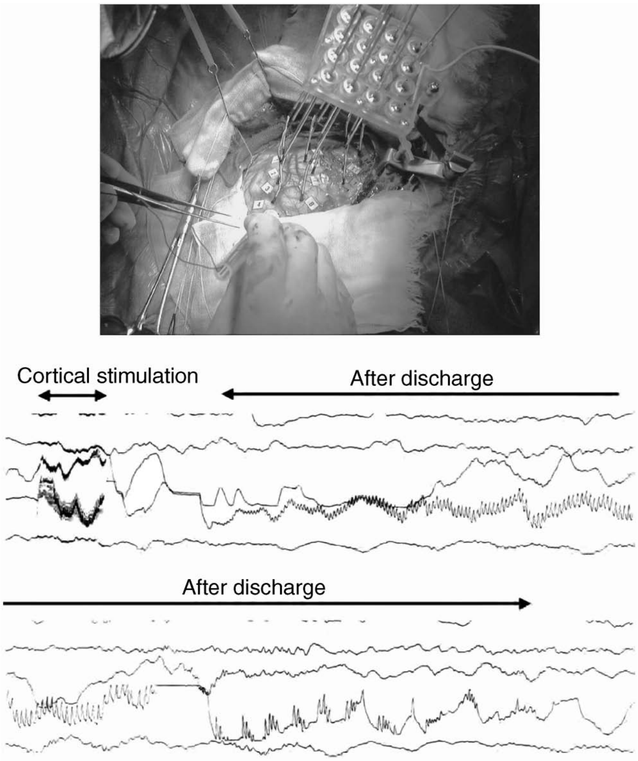

Fig. 4 Setting the electrocorticograph and electrocorticographic stimulation with bipolar electrodes.

bipolar electrodes using an inter-electrode distance of 5 mm. For stable stimulation, the brain surface should be kept moist by using a nebulizer. Increase the stimulus current from 4 mA in increments of 1 mA and determine the optimal current for achieving stable muscle contraction without afterdischarges in the cortical electroencephalogram. Under the above conditions (which we use), effective stimulation is often obtained at 8–11 mA. Under awake anesthesia, a lower stimulus current is optimal and 4–8 mA is often used. For the sensory areas, because instantaneous brain-surface stimulation with a low current leads to complaints of numbness and discomfort by the patient, it is desirable to initiate mapping of the sensory areas first. Stimulation is done at the sites predicted using the neuronavigation system or from anatomical landmarks such as sulci, gyri, and superficial veins, and from the somatosensory-evoked potentials obtained by median nerve stimulation or labial stimulation, and the aim is to achieve effective results from the first stimulus. The motor cortex does not cover all of the precentral gyrus, but lies between the anteroposterior regions on the side of the central sulcus. Therefore, stimulation should be applied along the central sulcus first. Bipolar electrodes are used to apply stimulation perpendicular to the central sulcus. If the craniotomy does not extend as far as the finger area during tumor resection in the frontal opercular region, you can place strip electrodes across the central sulcus underneath the dura for stimulation. Electromyography[3] is not performed for all muscles, so the extremities and face must be carefully observed at sites where stimulation is expected to induce movement.

After completion of mapping of the motor and sensory areas, initiate functional language mapping. First, ask the patient to count from 1 to 50 continuously. At this time, increase the stimulus current in increments of 1 mA, while confirming that there are no afterdischarges in the cortical electroencephalogram. A current of up to about 16 mA may be used. Record the sites associated with speech arrest and hesitation. When stimulating the lower portion of the precentral gyrus, a negative motor response[1] may inhibit speech. One of the methods for confirming this is to apply stimulation to the brain surface i) while instructing the patient to project the tongue and move it from side to side, ii) while continuing countermovement of the thumb and forefinger, and iii) while bending and extending the ankle joints. If arrest of movement of the tongue or countermovement of the fingers and movement of the ankle joints is observed, the inhibition is associated with a negative motor response and not with language dysfunction. By these procedures, the optimal stimulus current can be determined and the frontal language areas identified to some extent. Then, perform object naming while continuing stimulation.

No abnormalities of counting does not always correspond with no disorders of object naming. Show the patient slides for approximately 2–3 seconds each. Assess whether there is speech arrest, hesitation, or wrong answers after presenting the stimulus. If these occur, you always need to confirm whether they are induced by actual stimulation of language function areas, fatigue, inability to see the slides, or the development of seizures. Using the sentence pattern for naming ''This is ###'' allows us to determine whether abnormalities are associated with arrest of speech itself by stimulation of the tongue motor areas or negative motor areas, or are due to stimulation of language function areas. Because identification of language areas needs repeated confirmation of the results, patients have to expend a large amount of energy. Therefore, functional brain mapping/monitoring requires complete cooperation of the patient.

References

1) Nagamatsu K, Kumabe T, Suzuki K, Nakasato N, Sato K, Iizuka O, Kanamori M, Sonoda Y, Tominaga T:

[Clinical features and significance of negative motor response in intraoperative language mapping during awake craniotomy]. *No Shinkei Geka* 36: 693–700, 2008 (Japanese)
2) Ojemann G, Ojemann J, Lettich E, Berger M: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg* 108: 411–421, 2008
3) Yingling CD, Ojemann S, Dodson B, Harrington MJ, Berger MS: Identification of motor pathways during tumor surgery facilitated by multichannel electromyographic recording. *J Neurosurg* 91: 922–927, 1999

2–7. Complications other than convulsions and countermeasures

2–7–1. Pain

Risk: Pain can develop in the skin, muscles, dura mater, and sites on the underside of the body.

Measures: Ask the patient about painful sites and treat with local anesthesia as far as possible. Fix the head with 3 or 4 pins (if you use a head frame) and place something soft under the body to allow for movement. For surgery on the temporal lobe, turn the waist up as far as possible to prevent pain caused by compression of the underside of the waist, which often occurs in the lateral position.

2–7–2. Air embolism

Risk: Tumors of the inner motor cortex are associated with a risk of air embolism because the surgical field is placed in the highest position.

Measures: Bend the head forward without affecting respiration, raise the lower extremities, and bend the abdomen slightly forward to increase the jugular venous pressure. Cover the skull with fibrin, thrombin, and Calcicol immediately after opening the skull. Keep the head down until the dura mater is opened and then gradually raise the head while observing SaO_2. If there are symptoms such as cough and a decrease of SaO_2, immediately put the head down and hold the neck.

2–7–3. Delirium and emotional incontinence

Risk: There are some reports of delirium developing when anesthesia is stopped to obtain the awake state. Intraoperative anxiety and pain may also cause emotional incontinence.

Measures: Avoid decreasing the level of consciousness by use of local anesthetic as far as possible. Play the patient's favorite music or take measures to avoid anything that makes the patient uncomfortable so that the patient can undergo surgery easily. Depending on the patient's condition and the progress of surgery, decide whether it should be continued under awake conditions, should be continued without awake conditions, or should be discontinued. If continuation of awake conditions is needed, deal with the patient's complaints (primarily pain) as far as possible, but sometimes encourage the patient to tolerate the discomfort.

2–7–4. Increased intracranial pressure

Risk: Increased intracranial pressure may develop in patients with brain tumors, but seldom in those with epilepsy. During awake surgery, arterial carbon dioxide tension ($PaCO_2$) tends to be higher than under general anesthesia, leading to a higher risk of increased intracranial pressure.

Measures: If there is evidence of increased intracranial pressure on imaging studies, general anesthesia should be employed. If awake surgery is considered to be absolutely necessary, the decision can be made after dural incision following standard intubation. If there is no brain swelling induced by increased intracranial pressure, switch to awake surgery after extubation. If brain swelling occurs during awake surgery, consider switching to general anesthesia.

2–7–5. Others

There are reports about the development of air embolism and pneumonia, although whether these are characteristic problems of awake surgery is controversial. Air embolism can be caused by raising the head excessively (for example, locating the operating field at the highest position in the motor cortex 1). As with general anesthesia, bend the head forward without affecting the respiration, raise the lower extremities, and bend the abdomen slightly forward to increase the jugular venous pressure. Cover the skull with bone wax, fibrin, and thrombin immediately after opening the bone. Keep the head down until the dura mater is opened and then gradually raise the head while observing arterial oxygen percent saturation (SaO_2). If there are symptoms such as cough and decrease of SaO_2, immediately put the head down and hold the neck. Also, for prevention of pneumonia, it seems to be important to prevent lowering of consciousness and vomiting (refer to the section on anesthetic management for details about dealing with nausea and vomiting).

Reference

1) Shinoura N, Yamada R, Kodama T, Suzuki Y, Takahashi M, Yagi K: Association of motor deficits with head position during awake surgery for resection of medial motor area brain tumors. *Minim Invasive Neurosurg* 48: 315–321, 2005

2–8. Decision-making based on the results of stimulation

2–8–1. Epilepsy

[Recommendation]

In the case of epilepsy, consider whether the results of functional brain mapping by electrical stimulation are reliable. Epileptic foci often include functional brain sites and the extent of resection influences postoperative seizure control. It is desirable to fully assess the extent and overlap of epileptogenic foci and functional sites, and then carefully discuss the indications for resection of functional areas in individual cases depending on the pathological condition.

[Commentary]

Epilepsy is a functional disease, and the presence or absence of functional disorders associated with surgery influences the indications for surgery. For decision-making about additional surgical treatment and the extent of resection in individual cases, it is important to fully understand the pathology of epilepsy. Assessment of the results obtained by functional brain mapping with electrical stimulation requires attention to the following points. In patients with epilepsy, cortical excitability at functional sites is variable and both false-positive and false-negative results of electrical stimulation can occur.[1] Displacement of brain function sites from their anatomical positions can also occur. Therefore, functional brain mapping by electrical stimulation should be performed carefully, and it is desirable to undertake subdural electrode placement with reference to the results of various noninvasive physiological tests, such as fMRI, positron emission tomography, and MEG, for detailed mapping. The use of brain surface electrodes allows for complementary cortical function testing to assess the development of symptoms and to measure evoked potentials during voluntary activity after electrical stimulation. Epileptogenic foci often overlap with functional sites in the brain. In such a situation, resection of the focus is superior to multiple subpial transection and more complete resection results in better postoperative control of epileptic seizures.[2] It is reported that 0% to 63% of patients develop persistent functional disorders after resection of functional brain areas involved by epileptic foci. However, due to the small number of cases, it is unclear whether we should resect all the functional sites, whether we should consider the resection of sites with a possible compensatory function, and how to decide on the discontinuation of resection.

References

1) Palmini A, Gambardella A, Andermann F, Dubeau F, da Costa JC, Olivier A, Tampieri D, Gloor P, Quesney F, Andermann E, Paglioli E, Paglioli-Neto E, Andermann LC, Leblanc R, Kim HI: Intrinsic epileptogenicity of human dysplastic cortex as suggested by corticography and surgical results. *Ann Neurol* 37: 476–487, 1995
2) Pondal-Sordo M, Diosy D, Téllez-Zenteno JF, Girvin JP, Wiebe S: Epilepsy surgery involving the sensory-motor cortex. *Brain* 129: 3307–3314, 2006

2–8–2. Brain tumors

[Recommendation]

Functional tissues revealed by mapping should be preserved unless consent giving priority to resection is obtained or the surgeon determines that resection is feasible. Accumulate experience with mapping and pay careful attention to false-positive results (nonfunctional brain tissues despite positive findings on stimulation).

[Commentary]

Intraoperative functional testing during awake surgery involves mapping by electrical stimulation and monitoring to observe neurological findings. Mapping is performed to identify functional brain tissues and to prevent neurological complications induced by resection and damage to functional tissues during brain tumor removal. Therefore, the sites where symptoms occur during mapping should be preserved in principle because they are likely to be functional tissues. If they are not preserved, we see no point in performing awake surgery. However, if tumors coexist with functional tissues[2] and preoperative consent has been obtained, functional tissues may not be preserved if the decision is confirmed to give priority to tumor resection after accepting the risk of complications and the fact that postoperative symptoms are likely to develop even with a response (e.g., negative motor areas in the supplementary motor cortex). Because responses are sometimes false-positive, you should acquire proficiency in mapping. False-positive findings are primarily obtained because awake conditions are poor and do not allow patients to perform their tasks, and sometimes because the basic conditions for the tasks are poor (e.g., the patient cannot see the screen because a drape covers his/her eyes). At our hospital, some patients could not perform the naming task due to inability to see the screen because of conjugate deviation induced by stimulation of oculomotor fibers, but they were regarded as having language arrest (the truth was recognized by reviewing videos). Recently, Berger et al.[1] have insisted on the validity of a ''negative mapping strategy,'' suggesting that language areas do not have to be identified as a positive control (and major craniotomy does not have to be performed for identification), and that resection can be performed if language areas do not exist within the resection zone under certain conditions (60 Hz, maximum 6 mA). Given that this is a report from the most experienced institution, resection after identifying the language areas seems to be safer at less experienced institutions. It is significant that their report indicates that awake language mapping allows us to perform even aggressive resection with a very low incidence of complications and that a report on language mapping was published in a top clinical journal, suggesting that evaluation of its usefulness as a surgical procedure for glioma has been established.

References

1) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med* 358: 18–27, 2008
2) Skirboll SS, Ojemann GA, Berger MS, Lettich E, Winn HR: Functional cortex and subcortical white matter located within gliomas. *Neurosurgery* 38: 678–685, 1996

II. Anestheic Management for Awake Craniotomy

1. Introduction

In the 1800s, resection of foci in epileptic patients was performed by craniotomy under local anesthesia.[6] With no electroencephalogram, direct stimulation of the cortex was employed to detect the epileptic focus and identify functionally important sites, which seems to be the prototype of current awake craniotomy. In the 1900s, with addition of sedation, surgery became more comfortable for patients.[8] Using codeine, thiopental, and meperidine, management was conducted under spontaneous respiration or partially by tracheal intubation. Epileptic surgery then came to emphasize intraoperative electroencephalography.[9] In the 1960s, neuroleptanalgesia was introduced into anesthesia, and the combination of droperidol and fentanyl was considered especially useful for surgery in patients with temporal lobe epilepsy because it had less influence on the intraoperative electroencephalogram.[5] In addition, the development of a long-acting local anesthetic, bupivacaine, facilitated awake craniotomy. As a result, many procedures for intractable epilepsy employed neuroleptanalgesia.[1,7] Thereafter, short-acting analgesics such as sufentanil and alfentanil were introduced.[4] Propofol was introduced for awake craniotomy because it is short-acting and has anticonvulsant and antiemetic effects.[10] It is now widely used as the main sedative. Recently, new anesthetics such as dexmedetomidine[2] and remifentanil[3] have been introduced, while use of a laryngeal mask has been initiated for airway management.[11] Because procedures that are not necessary during ordinary general anesthesia, such as airway management and treatment of intraoperative convulsions, are required, we would like you to refer to these guidelines for reliable and safe anesthetic management. There is limited evidence about anesthetic management during awake craniotomy, so the methods in actual use and those recommended by the review committee are presented. Also, because there is "awake surgery" in the cardiac surgery field and the "wake-up test" in orthopedic surgery, we are using the term "awake craniotomy" here to distinguish awake brain surgery from those procedures.

References

1) Archer DP, McKenna JMA, Morin L, Morin L, Ravussin P: Conscious-sedation analgesia during craniotomy for intractable epilepsy: a review of 354 consecutive cases. *Can J Anaesth* 35: 338–344, 1988
2) Bekker AY, Kaufman B, Samir H, Doyle W: Use of dexmedetomidine infusion for awake craniotomy. *Anesth Analg* 92: 1251–1253, 2001
3) Berkenstadt H, Perel A, Hadani M, Unofrievich I, Ram Z: Monitored anesthesia care using remifentanil and propofol for awake craniotomy. *J Neurosurg Anesthesiol* 13: 246–249, 2001
4) Gignac E, Manninen PH, Gelb AW: Comparison of fentanyl, sufentanil and alfentanil during awake craniotomy for epilepsy. *Can J Anaesth* 40: 421–424, 1993
5) Gilbert RGB, Brindle GF, Galindo A: Anesthesia for neurosurgery. *Int Anesthesiol Clin* 4: 842–847, 1966
6) Horsley V: Brain-surgery. *Br Med J* 2: 670–675, 1886
7) Manninen P, Contreras J: Anesthetic considerations for craniotomy in awake patients. *Int Anesthesiol Clin* 24: 157–174, 1986
8) Pasquet A: Combined regional and general anesthesia for craniotomy and cortical exploration. II. Anesthetic considerations. *Curr Res Anesth Analg* 33: 156–164, 1954
9) Penfield W: Combined regional and general anesthesia for craniotomy and cortical exploration. I. Neurosurgical considerations. *Curr Res Anesth Analg* 33: 145–155, 1954
10) Silbergeld DL, Mueller WM, Colley PS, Ojemann GA, Lettich E: Use of propofol for awake craniotomies. *Surg Neurol* 38: 271–272, 1992
11) Tongier WK, Joshi GP, Landers DF, Mickey B: Use of the laryngeal mask airway during awake craniotomy for tumor resection. *J Clin Anesth* 12: 592–594, 2000

2. Basic policy

i) Communicate with the surgeons and operating room staff based on a detailed surgical and anesthetic plan.

ii) To handle intraoperative respiratory problems and rapidly changing risks, management and supervision by anesthesiologists who have acquired extensive experience with awake craniotomy is required.

iii) To safely manage rapidly changing intraoperative conditions, ensure that backup anesthesiologists are available in addition to the attending anesthesiologists.

iv) To allow smooth switching to general anesthesia if the anesthesiologist considers it difficult to continue awake craniotomy, establish a system for cooperation with the surgeons and operating room staff.

v) Do not use inhalational anesthetics that are absorbed and excreted by the respiratory system because a definitive airway is not established. (Inhalational anesthetics that could possibly cause an increase of brain volume should not be used because of the uncertain management of $PaCO_2$ during awake craniotomy.) Use propofol as the basic sedative.

vi) Because management is performed under spontaneous respiration, carefully titrate the sedative and analgesic drugs. Maximize the use of local anesthesia for analgesia. (During the unconscious period, management with controlled respiration via the laryngeal mask airway [LMA], etc. is available.)

vii) Take measures to prevent nausea and vomiting that could lead to respiratory complications.

viii) Electrical stimulation during functional mapping may induce convulsions, occasionally resulting in inability to continue the procedure, which then requires rapid countermeasures to be taken.

[Commentary]

Awake craniotomy was used for surgical treatment of epilepsy in the early 20th century, and then was applied to surgery for brain tumors, cerebral arteriovenous malformations, and cerebral aneurysms associated with important areas such as the motor or sensory cortex and language cortex.[2,3] The purpose of awake craniotomy is to prevent brain dysfunction induced by surgery and to precisely resect the disease focus in order to improve the patient's prognosis and quality of life. The purpose of anesthetic management is, while putting the patient's safety first, to remove psychophysical pain and allow the necessary surgery to be done. Each of the sections in these guidelines and the corresponding commentary describe the details of anesthetic management for awake craniotomy. Because there have not been enough randomized controlled studies of anesthetic management for awake craniotomy, management that is not based on such evidence in these guidelines is based on the methods recommended by institutions familiar with awake craniotomy. Therefore, if anesthetic management based on randomized controlled study evidence is reported in the future, these guidelines will be appropriately reviewed.

For successful awake craniotomy, the first point is that the patient's cooperation is essential. Second, preoperative and intraoperative communication and agreement among neurosurgeons, anesthesiologists, and operating room staff familiar with awake craniotomy is required. For anesthetic management, it is necessary to establish the airway, stabilize hemodynamics, and prevent increase of intracranial pressure. Because management of $PaCO_2$ is more difficult during awake craniotomy, inhalational anesthetics that could possibly increase brain volume should be avoided. Hence, sedation and general anesthesia with propofol is currently the standard for awake craniotomy. While the patient is unconscious, respiratory management with an LMA can be used. Each of the sections in these guidelines describes the details of respiratory management.

During awake craniotomy, because scalp block and infiltrational anesthesia for sufficient pain control require a large volume of local anesthetics, caution should be paid with regard to local anesthetic toxicity.[1] During awake craniotomy, it is also necessary to prevent adverse reactions such as nausea, vomiting, and convulsions, and to deal with such reactions immediately if they occur. If establishment of an airway is difficult or if other adverse reactions interfere with the patient's safety, after discussion between the anesthesiologists and neurosurgeons, awake craniotomy should be speedily discontinued and switching to general anesthesia should be considered.[4]

References

1) Archer DP, McKenna JMA, Morin L, Ravussion P: Conscious sedation analgesia during craniotomy for intractable epilepsy: a review of 354 consecutive cases. *Can J Anaesth* 35: 338–344, 1988

2) Burchiel KJ, Clarke H, Ojemann GA, Dacey RG, Winn HR: Use of stimulation mapping and corticography in the excision of arteriovenous malformations in sensorimotor and language-related neocortex. *Neurosurgery* 24: 322–327, 1989

3) Duffau H, Capelle L, Sichez JP, Faillot T, Abdennour L, Law Koune JD, Dadoun S, Bitar A, Arthuis F, Van Effenterre R, Fohanno D: Intra-operative direct electrical stimulations of the central nervous system: the Salpêtrière experience with 60 patients. *Acta Neu-*

rochir (Wien) 141: 1157–1167, 1999
4) Piccioni F, Fanzio M: Management of anesthesia in awake craniotomy. *Minerva Anesthesiol* 74: 393–408, 2008

3. Premedication

i) To allow complete intraoperative emergence, do not administer premedication that could possibly cause residual sedation.
ii) If there is no choice but to administer premedication, use a benzodiazepine that could possibly produce antagonism.
iii) Make a decision about premedication with anticonvulsants after consulting the patient's physician.

[Commentary]

During awake craniotomy, it is important for patients to be sufficiently awakened during surgery to perform language and motor tasks that yield reliable results, based on which the extent of resection is determined. Therefore, as a matter of principle, drugs that could affect emergence should not be administered. For successful awake craniotomy, it is crucial to build a relationship of trust among the patient, the surgeons, the anesthesiologists, and the operating room staff.[1)] The establishment of such a patient-centered relationship reduces the need for sedatives. However, if sedatives have to be administered, benzodiazepines are recommended as antagonists are available. If surgery is being done for a tumor, hypercapnia induced by sedation can possibly result in an increase of intracranial pressure, and this requires special caution.

Convulsions are one of the most significant complications of awake craniotomy. Difficulty in ventilating the patient when convulsions persist and respiratory arrest occurs can lead to a fatal outcome. Because the patient's condition needs to be considered, preoperative administration of anticonvulsants should only be done after discussion with the attending physician. Note that propofol also has an anticonvulsant effect. With regard to other drugs such as H2 blockers that are administered during general surgery, the policy of the institution should be adopted.

Among antiemetics, metoclopramide hydrochloride (Primperan®; Sanofi-Aventis K.K., Tokyo) is not recommended because of potential adverse effects caused by enhanced peristalsis. Some reports of dexamethasone being administered to control the intracranial pressure and prevent vomiting have been described in other countries. However, this procedure is not covered by health insurance in Japan. Also, propofol has a useful antiemetic effect.

Reference

1) Whittle IR, Midgley S, Georges H, Pringle AM, Taylor R: Patient perceptions of ''awake'' brain tumor surgery. *Acta Neurochir (Wien)* 147: 275–277, 2005

4. Basic monitoring and preparation

i) Monitor the electrocardiogram, invasive arterial blood pressure, percutaneous oxygen saturation, expiratory partial pressure of carbon dioxide, urine volume, and body temperature.
ii) Create peripheral venous access for continuous administration of anesthetics and blood transfusion.
iii) Procedures are performed without a secure airway, so careful respiratory management is needed. Management can be done with spontaneous breathing or assisted ventilation via the LMA, etc.

[Commentary]

Basically, comply with the guideline of the Japanese Society of Anesthesiologists for installation of monitors. If sedation is used during awake craniotomy, regardless of the method of establishing the airway, different precautions from those during tracheal intubation should be taken. If a device such as the LMA is not used to establish the airway, precise management of $PaCO_2$ is difficult and careful observation is necessary to assess the frequency of breathing and the presence or absence of forced respiration. Therefore, for good anesthetic management, an environment that allows easy observation of the respiratory status is required, including use of transparent drapes to allow sufficient observation of the patient's mouth, neck, and chest. A stethoscope taped to the chest wall is one method. Some nasal cannulae have ports for measurement of expiratory carbon dioxide, but sometimes accurate data are not obtained, indicating limited usefulness. For management with an LMA, even if spontaneous ventilation is maintained, measure expiratory carbon dioxide tension and support respiration if necessary. Ventilation does not often allow for sufficient respiratory management, so an arterial cannula should be placed for easy arterial gas analysis when needed.

There have been reports of air embolism during awake surgery. Especially when surgery is performed under spontaneous respiration without an LMA, caution is required. In this case, end-tidal carbon dioxide is not so useful as described above, and it is difficult to determine whether changes of saturation of peripheral oxygen result from worsening of respiratory status or air embolism.[2,5)] Upper airway obstruction causes lower negative intrathoracic pressure and may result in increased risk of air embolism. Although a bispectral index (BIS) monitor is generally considered to be useful, its value is limited and is not strongly recommended in the field of neurosurgical anesthesia. There have been reports that a BIS monitor is useful even if placed at sites other than the forehead. However, because shaving of the head recently tends to be minimized, the site where the monitor can be placed is actually limited to the forehead. Even if a pediatric BIS sensor is used, disinfectant or blood often enters the connections of the sensors and interferes with analysis. In addition, a BIS monitor is mainly useful on emergence, and its value before that is limited by contamination from electromyogram signals and noise from electric scalpels used during craniotomy.

Maintenance of the airway during awake craniotomy is done by one of two methods; one method is to depend on spontaneous respiration with no devices and the other method is to use a device such as the LMA. If a device is used, we can rely on spontaneous respiration and, if necessary, provide respiratory support, or we can actively perform ventilation. In Japan, the LMA has tended to be used recently. Tracheal intubation is not recommended since it is likely to interfere with an awake study because of complications caused by emergence-induced coughing and depressed laryngeal function including hoarseness. Although a tracheal tube can be placed in the pharynx via the nose for respiratory support, if necessary, or emergency intubation can be done with a bronchoscope, nasal bleeding can become a problem. If management is performed by spontaneous respiration without devices, hypercapnia will become a problem, but can often be dealt with by target controlled infusion, avoiding narcotics, or large craniotomy.[1,3,4] Partly to decrease the dose of narcotics, it is important to administer sufficient local anesthesia as described in the next section.

If 3-point fixation is performed, it is assumed that reinserting the LMA or tracheal intubation will be difficult in some cases. It is important to test removal and reinsertion of the LMA, to sufficiently discuss measures to tracheal intubation when the aggravation of the breathing state occurs during surgery. Also, when 3-point fixation is employed, check with the surgeons that the neck has not been twisted or anteflexed. As it is known that more problems related to the respiratory tract and respiration develop in patients with a body mass index >30, be careful about deciding to perform awake craniotomy in such patients.[6]

References

1) Herrick IA, Craen RA, Gelb AW, Miller LA, Kubu CS, Girvin JP, Parrent AG, Eliasziw M, Kirkby J: Propofol sedation during awake craniotomy for seizures: patient-controlled administration versus neurolept analgesia. *Anesth Analg* 84: 1285–1291, 1997

2) Morimoto Y, Sakabe T: [Practical side of awake craniotomy—primarily anesthetic management for stereotactic surgery], *in* Furuya H (*ed*): [*Practice of Awake Craniotomy—Main Points of Anesthetic Management*]. Tokyo, Shinko Trading Co., Ltd. Publication Department of Medical Books, 2003, pp 38–60 (Japanese)

3) Nagaoka Y, Miura Y, Takaoka S, Iwabuchi M, Amagasa S, Kotani N: [Considerations for awake craniotomy in our hospital—especially respiratory complications and brain edema]. *Rinsho Masui* 29: 836–840, 2005 (Japanese)

4) Sarang A, Dinsmore J: Anaesthesia for awake craniotomy—evolution of a technique that facilitates awake neurological testing. *Br J Anaesth* 90: 161–165, 2003

5) Scuplak SM, Smith M, Harkness WF: Air embolism during awake craniotomy. *Anaesthesia* 50: 338–340, 1995

6) Skucas AP, Artru AA: Anesthetic complications of awake craniotomies for epilepsy surgery. *Anesth Analg* 102: 882–887, 2006

5. Admission, induction, and local anesthesia

i) Initiate oxygen delivery after validation of the vital signs with a patient monitor.

ii) Induce anesthesia with only propofol, or in combination with fentanyl/remifentanil. A target-controlled infusion (TCI) system should be used for propofol administration to precisely manage the level of sedation. The administration of fentanyl before emergence should be minimal.

iii) Maintain general anesthesia under spontaneous respiration with a facemask, or under assisted/controlled ventilation after insertion of an LMA.

iv) Insert a urethral catheter.

v) Provide effective analgesia with local anesthetics by infiltration at the site of skin incision, and/or by selective nerve blocks of, for example, the supraorbital nerve and the greater occipital nerve. Ropivacaine is commonly used as a long-acting local anesthetic.

[Commentary]

Management of general anesthesia with inhalation anesthetics is ineffective when the airway is poorly established. The main impediments are uncertain delivery of the anesthetics and hazardous contamination of the operating room with the anesthetics. Propofol should be used as a hypnotic agent. Propofol is an intravenous anesthetic drug that permits faster and clearer emergence than inhalation anesthetics, which affect the electroencephalogram and sometimes induce excitement at emergence from anesthesia. A TCI system can reasonably be used for propofol in order to maintain an optimal hypnotic level by adjusting the effect-site concentration of the agent, as the sedative effect depends on the effect-site concentration. In the case of anesthetic management without the TCI system, the propofol administration should preferably be managed by continuous infusion combined with repetitive injection based on the effect-site concentration calculated with pharmacokinetic simulation. Opioids are sometimes used for sedation, but give some residual effects to the consciousness level after emergence. Remifentanil is therefore suitable in the management of strong surgical stimulation before emergence, as its effect rapidly disappears. It is also reasonable to administer small dose of fentanyl repeatedly, expecting only a slight residual analgesic effect.

The airway before emergence is usually managed with a facemask or an LMA. Airway management under assisted/controlled ventilation and spontaneous respiration can be performed safely with LMA, though it is generally difficult to extubate safely and smoothly at awakening. The incidence of muscle weakness in the conscious state is rare with LMA, as muscle relaxants are not necessary for LMA insertion. A nasogastric tube should not be inserted, as it leads to discomfort in the pharynx, nausea, and vomiting during the conscious state. Remove the nasogastric tube before emergence if it has to be inserted during general anesthesia. Insert a urethral catheter after induction of anesthesia, as the operation will take a long time.

The key to anesthetic management for awake craniotomy is to achieve a ''pain-free'' state with multimodal pain management. Since intravenous anesthetics affect the state of consciousness and respiration, local anesthetics are essential for assured analgesia. This is achieved with the use of long-acting local anesthetics such as ropivacaine or bupivacaine, or lidocaine combined with epinephrine. Problems such as local anesthetic toxicity did not occur even at a mean ropivacaine dose of 3.6 mg/kg in a study of the blood concentration of local anesthetics for awake craniotomy. Local anesthetics are administered by infiltration around pin fixation and the site of the skin incision, along with selective nerve blocks (supraorbital nerve, greater occipital nerve, etc.) Gauze soaked with local anesthetics can be pressed against the wound. Because direct contact of local anesthetics with the brain parenchyma causes central nervous system symptoms such as convulsions, the administration of local anesthetics after dural incision should be performed carefully.

References

1) Costello TG, Cormack JR, Hoy C, Wyss A, Braniff V, Martin K, Murphy M: Plasma ropivacaine levels following scalp block for awake craniotomy. *J Neurosurg Anesthesiol* 6: 147–150, 2004
2) Sato K, Kawamata M, Nagata O, Kawaguchi M, Morimoto Y, Kato M, Sakabe T: [Present state of anesthetic management for awake craniotomy in Japan]. *Masui* 57: 492–496, 2008 (Japanese)

6. Before emergence

i) In principle, sedative and analgesic drugs should not be used during the awake time. Check the surgeons' preference for the level of consciousness (level of sedation).
ii) Discontinue propofol after the dural incision has been made. If sedation is to be continued, provide the required dose of propofol, etc.
iii) Closely monitor the patient because body movements may occur suddenly during the course of emergence.
iv) If an LMA and a gastric tube are used, confirm spontaneous respiration before removal.
v) If the patient exhibits restlessness and cannot keep still, intraoperative emergence may be abandoned after discussion with the surgeon and the procedure may instead be performed under standard general anesthesia.

[Commentary]

Because the tasks and tests used for brain functional mapping and electrocorticography to determine the extent of epileptic focus resection are generally susceptible to sedative and analgesic drugs, in principle, such drugs should not be administered during the awake time. Since even analgesics administered before emergence influence the extent of emergence, check the neurosurgeon's preference about the tests and sufficiently control the depth of anesthesia while considering the patient's preoperative condition. Poor emergence may make functional assessment difficult.[4)]

During the period of strong surgical stimulation, including scalp incision, muscle detachment, and removal of the bone flap and dural incision, provide adequate sedation and analgesia, and discontinue propofol on completion of dural manipulation.[2)] Body movement sometimes occurs during emergence as with other surgical anesthesia practice. Because sudden body movement can be more harmful when the skull is fixed with head pins and opened, sufficient vigilance is required and anesthesiologists should be prepared to control body movement. Anesthesiologists should promptly control major changes in circulatory and respiratory systems, which often occur during this period.[3] When a gastric tube or LMA is used, check spontaneous respiration and remove on emergence. Due to restlessness, the patient may not remain still and cooperate with functional tests.[1] If restlessness is considered to be caused by excitation, pain, poor posture, low temperature, residual anesthetic, or a painful urethral catheter, deal with the cause. If the cause is unknown or cannot be controlled, after discussion with the attending surgeon, intraoperative emergence may be abandoned and surgery may be discontinued or performed under general anesthesia.

References

1) Berkenstadt H, Perel A, Hadani M, Unofrievich I, Ram Z: Monitored anesthesia care using remifentanil and propofol for awake craniotomy. *J Neurosurg Anesthesiol* 13: 246–249, 2001
2) Huncke K, Van de Wiele B, Fried I, Rubinstein EH: The asleep-awake-asleep anesthetic technique for intraoperative language mapping. *Neurosurgery* 42: 1312–1316, 1998
3) Keifer JC, Dentchev D, Little K, Warner DS, Friedman AH, Borel CO: A retrospective analysis of a remifentanil/propofol general anesthetic for craniotomy before awake functional brain mapping. *Anesth Analg* 101: 502–508, 2005
4) Sato K, Kawamata M, Nagata O, Kawaguchi M, Morimoto Y, Kato M, Sakabe T: [Present state of anesthetic management for awake craniotomy in Japan]. *Masui* 57: 492–496, 2008 (Japanese)

7. Awake period

i) In principle, systemic administration of sedatives and analgesics should not be done.
ii) For light sedation, administer propofol, etc. at the minimum required dose. (There are reports on the use of dexmedetomidine as a sedative. Use of remifentanil in patients with spontaneous respiration is not recommended because of respiratory depression.)
iii) If the patient complains of pain, provide additional local anesthesia first.
iv) If nausea and/or vomiting occur: Discontinue the surgical procedure, administer metoclopramide or a serotonin receptor antagonist, and wait for the subsidence of symptoms. Remove vomitus to prevent aspiration. If symptoms are severe and do not subside, consider sedation with propofol and discuss with the surgeons regarding the discontinuation of awake craniotomy.
v) If convulsions develop: Discontinue the surgical procedure, especially electrical stimulation. (If the electroencephalogram is being monitored, the operation should be discontinued when the first spike is seen.) Cool the brain surface with cold water. Administer propofol at a sleeping dose. Give an intravenous infusion of 250 mg of phenytoin. If convulsions do not cease even after additional administration of propofol, midazolam, or thiopental, discontinue awake craniotomy.

[Commentary]

During the awake period, as a general rule, systemic application of sedatives or analgesics should not be done in order to minimize the influence on functional mapping or the identification of epileptic foci. To deal with pain, add local anesthetics. If a small dose of a sedative or narcotic is considered to prevent worsening of the patient's mental state and excitation, the potential influence on functional assessment should be assessed. Recently, there have been several reports about anesthesia during awake surgery in which dexmedetomidine or remifentanil was used during the awake period.[1,3–6,9] However, there have also been reports that poor emergence of patients given dexmedetomidine required a decrease of the dose or discontinuation, and dexmedetomidine is not covered by health insurance in Japan. The use of remifentanil at low doses with spontaneous respiration on emergence has also been reported, but is not considered to be safe due to the potential for respiratory depression or brain swelling induced by hypercapnia, so this method would require careful attention.

Although the incidence of nausea and vomiting during awake surgery varies among reports, it has been reported to be approximately 0–10% when anesthetic management is primarily done with propofol.[8] Nausea and vomiting, in addition to causing discomfort for the patient, increases the risk of respiratory complications due to aspiration, and body movement and increased brain swelling associated with nausea/vomiting may make the surgical procedure more difficult. Nausea and vomiting may be induced by the surgical procedure or by use of narcotics. At the onset, immediately discontinue the surgical procedure and administer metoclopramide or a serotonin receptor antagonist. However, serotonin receptor antagonists are only available off label in Japan, requiring the decision to be made at each institution. If symptoms are severe and do not improve, consider sedation with propofol and even consider the discontinuation of awake craniotomy in certain cases. Although there are some reports about medications to prevent nausea and vomiting, the efficacy during awake surgery is unknown.

The incidence of convulsions during awake craniotomy depends on the underlying disease and is reported to be approximately 0–24%.[2,8] Convulsions are more likely to develop during electrical stimulation for brain functional mapping. If convulsions develop, discontinue electrical stimulation during the surgical procedure and cool the brain with cold Ringer's solution or saline. If the electroencephalogram is being monitored, discontinue the procedure at the onset of a spike. Most convulsions cease with discontinuation of the surgical procedure and cooling of the brain. If these measures are ineffective, administer propofol or phenytoin at a sleeping dose. The preventative effect of phenytoin has not been confirmed, so it is considered desirable to achieve an effective blood concentration before surgery. If convulsions do not cease with additional propofol, midazolam, or thiopental, discontinue awake craniotomy. There has been a report that intractable convulsions required general anesthesia with tracheal intubation.[7] During awake craniotomy, it is necessary to be prepared for emergency transition to airway management or general anesthesia at any time.

References

1) Ard JL Jr, Bekker AY, Doyle WK: Dexmedetomidine in awake craniotomy: a technical note. *Surg Neurol* 63: 114–116, 2005
2) Conte V, Baratta P, Tomaselli P, Songa V, Magni L, Stocchetti N: Awake neurosurgery: an update. *Minerva Anesthesiol* 74: 289–292, 2008
3) Herrick IA, Craen RA, Blume WT, Novick T, Gelb AW: Sedative doses of remifentanil have minimal effect on ECoG spike activity during awake epilepsy surgery. *J Neurosurg Anesthesiol* 14: 55–58, 2002
4) Lobo F, Beiras A: Propofol and remifentanil effect-site concentrations estimated by pharmacokinetic simulation and bispectral index monitoring during craniotomy with intraoperative awakening for brain tumor resection. *J Neurosurg Anesthesiol* 19: 183–189, 2007
5) Mack PF, Perrine K, Kobylarz E, Schwartz TH, Lien CA: Dexmedetomidine and neurocognitive testing in awake craniotomy. *J Neurosurg Anesthesiol* 16: 20–25, 2004
6) Sarang A, Dinsmore J: Anaesthesia for awake craniotomy—evolution of a technique that facilitates awake neurological testing. *Br J Anaesth* 90: 161–165, 2003
7) Serletis D, Bernstein M: Prospective study of awake craniotomy used routinely and nonselectively for supratentorial tumors. *J Neurosurg* 107: 1–6, 2007
8) Skucas AP, Artru AA: Anesthetic complications of awake craniotomies for epilepsy surgery. *Anesth Analg* 102: 882–887, 2006
9) Souter MJ, Rozet I, Ojemann JG, Souter KJ, Holmes MD, Lee L, Lam AM: Dexmedetomidine sedation during awake craniotomy for seizure resection: effects on electrocorticography. *J Neurosurg Anesthesiol* 19: 38–44, 2007

8. Reinduction and completion of craniotomy

i) When the cooperation of the patient is not required any further, induce sedation with propofol.
ii) In principle, manage the patient with spontaneous respiration. However, if the airway needs to be secured because of oversedation, use the LMA. (Anesthesiologists who are experienced in handling the LMA may perform anesthetic management by deliberately using it at closure.)
iii) If needed, add more local anesthesia. However, if there is evidence of local anesthetic toxicity, discontinue additional anesthesia and provide necessary treatment such as establishment of an airway and countermeasures for convulsions.
iv) If the airway is established with an LMA, the required dose of fentanyl or remifentanil can be given for analgesia.

[Commentary]

Propofol is generally used as the anesthetic at the end of craniotomy, as it is during craniotomy.[1] Determine whether tumor resection will be performed in the awake state or under sedation with propofol, considering the conditions at each institution and each patient. Some surgeons want patients to be re-awakened after tumor resection to check for neurological symptoms.[1] Insertion of an LMA should be done via a lateral caudal approach and requires some degree of proficiency when the head is fixed with pins. There is a risk of difficulty with airway establishment or vomiting and is recommended for at least two anesthesiologists to be involved in inserting the LMA. After establishment of the airway with an LMA, management can be achieved by controlled respiration with remifentanil or fentanyl. If establishment of the airway takes a long time, tracheal intubation[2] can be considered. If establishment of the airway is not done, add further local anesthetic to continue surgery. Preparations should be made to allow for establishment of the airway with an LMA immediately after a sudden change of the patient's state, such as the onset of convulsions. If analgesia is insufficient, add a small dose of fentanyl. Caution is required with regard to the use of remifentanil with spontaneous respiration during craniotomy, as on emergence.

References

1) Sato K, Kawamata M, Nagata O, Kawaguchi M, Morimoto Y, Kato M, Sakabe T: [Present state of anesthetic management for awake craniotomy in Japan]. *Masui* 57: 492–496, 2008 (Japanese)
2) Suzuki A, Terao M, Aizawa K, Yamagishi A, Kurosawa A, Iwasaki H: [Experience of the use of airway scope and airtrack in a face-to-face sitting position]. *Rinsho Masui* 32: 1327–1334, 2008 (Japanese)

9. Emergence and discharge

i) After the completion of surgery, discontinue sedatives and analgesics.

ii) Confirm emergence and the return of spontaneous respiration, remove the LMA if used, and transfer the patient to the intensive care unit.

[Commentary]

Follow the regular procedures for neurosurgical anesthetic management of emergence and discharge.

III. Language Assessment During Awake Craniotomy

1. Methods of language mapping by cortical electrical stimulation during awake craniotomy

[Recommendation]

Indications: Patients with lesions around the perisylvian language areas of the dominant hemisphere. Patients without apparent aphasia who are able to fully understand the language tasks and cooperate with them.

Preoperative preparation: Set language tasks that can easily be performed by patients and fully familiarize them with the tasks.

Electrical stimulation: A stronger stimulus intensity (6–12 mA) and longer duration (2–4 sec) are required than for motor and sensory mapping. Initiate electrical stimulation immediately before presenting the language stimulus (line drawing or question) and continue it during presentation.

Language tasks: Perform counting, visual naming, and listening comprehension tasks for cortical mapping. If electrical stimulation reveals any dysfunction, assess reproducibility. Monitor language functions primarily on the basis of spontaneous speech during resection. If an abnormality is suspected, perform language mapping with visual naming and/or listening comprehension.

[Commentary]

Purpose: The purpose of language mapping is to identify the language areas and to avoid postoperative aphasia by preserving these areas. Because the extent of the language areas varies among individuals and it is difficult to accurately identify them anatomically, the areas should be determined for each individual.[5] If language areas are identified outside the resection zone and language functions are confirmed to be localized away from the lesion to be resected, the neurosurgeon can resect the lesion with confidence.

Indications: Because patients must have full understanding and good cooperation to perform language mapping, we should consider the preoperative cognitive level and mental maturity of the patient. Because some patients cannot adapt to the special circumstances of the operating room environment, after providing sufficient explanation and practice of the tasks, determine whether they are suitable candidates for awake surgery or not. Be especially careful with young and elderly persons. Children and patients with obvious aphasia before surgery are not suitable for language mapping. Patients showing slight anomia or word finding difficulty (poor word production by category or initial phonemes) during preoperative examination may attempt language mapping, but their language function can become worse than preoperatively because of drowsiness, which can make language mapping difficult.

Preoperative preparation: Examination: Perform neurological and neuropsychological testing. Explanation: Fully explain the language tasks that will be used for mapping. Establishment of tasks: After performing the standard tasks once, exclude stimuli that evoke unstable responses, leaving only the stimuli for which the patient can definitely provide correct answers. Determine the rate of presenting line drawings at which the patient can answer comfortably (2–5 sec intervals). Practice: The selected tasks should be practiced several times until the patient can answer with confidence. If examination reveals suspected decrease of language function, perform the standard aphasia tests to measure the severity of aphasia. Identification of language-related sites by fMRI might be useful to limit the area that has to be explored by intraoperative mapping.[6]

Electrical stimulation: Follow the usual standards, but remember that stronger and longer stimulation is required for language mapping. Employ a stimulus intensity of 6–12 mA if no afterdischarge is evoked. Because electrical stimulation is initiated immediately before presenting a line drawing or question and is continued during presentation, stimulation needs to be applied for between 3 and 4 seconds (Fig. 5). It is desirable to present the language tasks at regular intervals so that the neurosurgeons get used to the timing of electrical stimulation. Also, adjust the location of the screen so the surgeons are able to monitor stimulation during the language tasks.

Language tasks: Language tasks to be performed: For all areas to be tested, counting and visual nam-

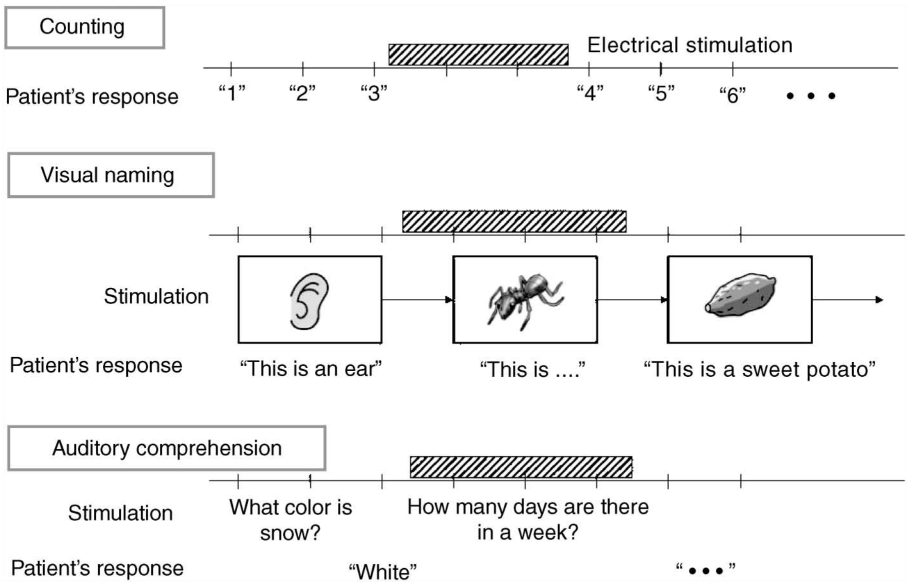

Fig. 5 Flow chart of language tasks. Initiate electrical stimulation before presenting the language tasks.

ing should be performed. With counting, check speech arrest and delay. Confirm that the site of speech arrest does not correspond to the negative motor area. During the visual naming task (picture naming), record slips of the tongue (errors), delayed responses, or no response. Words for the naming task are selected from among high-frequency words, such as cat, knife, desk etc. For the temporal lobe, also perform auditory comprehension. Frequency: Stimulate each site twice or more with the maximum current to check whether a language abnormality is detected. If any language abnormality is detected, stimulate the site twice or more again to check reproducibility. Interpretation of results: If three stimuli induce at least two incorrect responses, the site should be designated as a language-related site (Fig. 5).

Cortical mapping: Counting (from 1 to 30): Perform electrical stimulation while asking the patient to count from 1 to 30 at approximately one number per second. After the patient reaches 30, he/she starts from 1 again. Identify the sites where stimulation leads to abnormalities of speech (arrest, delay, dysarthria). Regarding the sites associated with these abnormalities, ask about the patient's subjective symptoms (e.g., inability to move the tongue). Then, assess whether or not the sites are primary motor areas or negative motor areas related to articulation. Visual naming[7]: Present line drawings (on paper or a monitor) at the interval predetermined for each patient and instruct the patient to name them using a carrier phrase like ''This is...''. Anomia or paraphasia: After saying ''This is'' fluently, patients cannot recall the name or substitute one word for another. Speech arrest: The patient cannot say ''This is''. Auditory comprehension: The patient answers an easy question with a single word. Because this involves both word recall and listening comprehension, electrical stimulation at sites different from those related to visual naming induces abnormalities.[3] Language mapping is based on the above three tasks. If time permits, other language tasks can be added as required.

Subcortical mapping: This is required if nerve fibers immediately below or adjacent to the language areas are to be resected. Continue conversation between the patient and examiner during resection and perform mapping with electrical stimulation at the sites with possible abnormalities. Use visual naming and, for the posterior language areas, listening comprehension as well. The intensity of electrical stimulation should be equal to or slightly greater than that for cortical stimulation. Identification of nerve fascicles by preoperative tractography might be useful to determine the sites for subcortical mapping.[1,2,4]

References

1) Berman JI, Berger MS, Chung SW, Nagarajan SS, Henry RG: Accuracy of diffusion tensor magnetic resonance imaging tractography assessed using intraoperative subcortical stimulation mapping and magnetic source imaging. *J Neurosurg* 107: 488–494, 2007

2) Duffau H: The anatomo-functional connectivity of language revisited. New insights provided by electrostimulation and tractography. *Neuropsychologia*

Table 1 Examples of line drawings used in the visual naming task

Grape	Ear	Ant	Potato	Train	Strawberry	Eye	Cat	Truck	Rabbit
Bus	Scissors	Patrol car	Carrot	Plane	Chicken	Pencil	Motorcycle	Apple	Cup

Words are selected from among high-frequency words in the vocabulary test for aphasia and color drawings without copyright are used.

46: 927–934, 2008

3) Hamberger MJ, Seidel WT: Auditory and visual naming tests: normative and patient data for accuracy, response time, and tip-of-the-tongue. *J Int Neuropsychol Soc* 9: 479–489, 2003
4) Henry RG, Berman JI, Nagarajan SS, Mukherjee P, Berger MS: Subcortical pathways serving cortical language sites: initial experience with diffusion tensor imaging fiber tracking combined with intraoperative language mapping. *Neuroimage* 21: 616–622, 2004
5) Ojemann G, Ojemann J, Lettich E, Berger M: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg* 108: 411–421, 2008
6) Rutten GJ, Ramsey NF, van Rijen PC, Noordmans HJ, van Veelen CW: Development of a functional magnetic resonance imaging protocol for intraoperative localization of critical temporoparietal language areas. *Ann Neurol* 51: 350–360, 2002
7) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med* 358: 18–27, 2008

2. Task details

Examples of line drawings used in the visual naming task and questions used to treat auditory comprehension are shown in Tables 1 and 2, respectively.

Table 2 Examples of questions used to test auditory comprehension

1. What is your name?
2. What color is snow?
3. What color is a sunflower?
4. What color is a crow?
5. What color is a banana?
6. What color is a fire truck?
7. How many days are there in a week?
8. How many minutes are there in an hour?
9. How many legs has a dog?
10. What day is after Tuesday?
11. What season is after spring?
12. What month is New Year's Day in?
13. What month is the Bon Festival in?
14. Which direction the sun sets in?
15. What is the offspring of a frog called?
16. What is the offspring of a chicken called?
17. A mother is a woman. What is a father?
18. A brother is a man. What is a sister?
19. The sun shines during the daytime. When do the stars come out?
20. Cherry blossom is seen in spring. How about red leaves?
21. Where do you buy postage stamps?
22. What do you use to cut vegetables?
23. What do you use to cut paper?
24. What do you use to tell the time?
25. Hot water is hot. How about ice?
26. Iron is heavy. How about feathers?
27. The sea is deep. How about mountains?
28. You wear clothes. How about shoes?
29. Birds fly. How about fish?
30. You listen to music. How about paintings?

Questions that can be answered within approximately 2 seconds are prepared based on the Wechsler Intelligence Scale for Children-Revised, Illinois Test of Psycholinguistic Abilities, Western Aphasia Battery test, etc.

Appendix: Guidelines Committee of the Japan Awake Surgery Conference

Chairman of the Committee

Takamasa KAYAMA	(National Cancer Center & Dept. of Neurosurgery, Yamagata University Faculty of Medicine)

Co-Chairman of the Committee

Hiroshi ISEKI	(Tokyo Women's Medical University, Faculty of Advanced Techno-Surgery)
Yoshitsugu YAMADA	(Dept. of Anesthesiology, Faculty of Vital Care Medicine, The Graduate School of Medicine, The University of Tokyo)

Committee Members

Tatsuya ABE	(Dept. of Neurosurgery, Oita University Faculty of Medicine)
Chikashi FUKAYA	(Dept. of Neurosurgery and Applied System Neuroscience, Nihon University School of Medicine)
Hidekatsu FURUTANI	(Dept. of Anesthesia, Kyoto University Hospital)
Kazuhiro HONGO	(Dept. of Neurosurgery, Shinshu University School of Medicine)
Tohru ITAKURA	(Wakayama Medical University)
Koji KAJIWARA	(Dept. of Neurosurgery, Yamaguchi University Graduate School of Medicine)
Kyosuke KAMADA	(Dept. of Neurosurgery, Asahikawa Medical University)
Masahiko KAWAGUCHI	(Dept. of Anesthesiology, Nara Medical University)
Mikito KAWAMATA	(Dept. of Anesthesiology and Resuscitology, Shinshu University School of Medicine)
Toshihiro KUMABE	(Dept. of Neurosurgery, Tohoku University Graduate School of Medicine)
Junichi KURATSU	(Dept. of Neurosurgery, Kumamoto University School of Medicine)
Masanori KURIMOTO	(Dept. of Neurosurgery, University of Toyama, Faculty of Medicine)
Nobuhiro MIKUNI	(Dept. of Neurosurgery, Sapporo Medical University, School of Medicine)
Yasuhiro MORIMOTO	(Dept. of Anesthesiology, Yamaguchi University Graduate School of Medicine)
Yoshihiro MURAGAKI	(Tokyo Women's Medical University, Faculty of Advanced Techno-Surgery)
Osamu NAGATA	(Dept. of Anesthesiology, Tokyo Women's Medical University)
Kaori SAKURADA	(Dept. of Neurosurgery, Yamagata University Faculty of Medicine)
Kiyotaka SATO	(Dept. of Anesthesiology, Kohnan Hospital)
Shinya SATO	(Dept. of Neurosurgery, Yamagata University Faculty of Medicine)
Nobusada SHINOURA	(Dept. of Neurosurgery, Komagome Metropolitan Hospital)
Morihiro SUGISHITA	(Institute of Brain Vessels)
Masahiko SUMITANI	(Dept. of Anesthesiology and Pain Relief Center, The University of Tokyo)
Kyoko SUZUKI	(Dept. of Clinical Neuroscience, Yamagata University Faculty of Medicine)
Seiji TAKAOKA	(Dept. of Anesthesiology, Yamagata City Hospital Saiseikan)