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Guidelines for Awake Surgery

Guidelines Committee of the Japan Awake Surgery Conference

CONTENTS

Preface

The Japan Awake Surgery Conference presented the prototype of guidelines at a meeting of the World Federation of Neurosurgical Societies (President, Prof. Heros: Harvard Univ.) in Boston for the first time in 2009 and published it as the “Guidelines for awake surgery (Japanese, English)” in 2013. Subsequently, there were various advances, especially in brain science, linguistics, cognitive science, anesthesiology, brain oncology, and surgical methods. The steering committee members, Japan Awake Surgery Conference, started working on a revision, and the 2nd version of the Guidelines for Awake Surgery, “Guidelines for Awake Surgery,” was published last year＊. I thank all the members responsible for working on the guidelines.
The present guidelines were prepared by discussing/reviewing matters considered the best in clinical practice by the guideline-preparing committee because conducting a clinical trial for medical devices is diffi-

＊The Japanese version of these guidelines was published as Awake Surgery Guidelines in January 2022 by Tohoku University Press, Sendai, edited by Japan Awake Surgery Conference.

The members of the Guidelines Committee of the Japan Awake Surgery Conference are listed in the Appendix in the text.

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cult. Therefore, the guidelines were prepared following "de fact standard."

However, various findings were presented from the world during this period, including Japan, with the widespread application of awake surgery in many countries. However, reports only show factual, non-comparative studies. In this revision session, articles in all fields, namely "surgical procedure," "anesthetic management," and "language assessment," were narrowed, and the guidelines were revised based on a systematic review.

In the "surgical procedure," the indication of this surgery were added: age, application for cerebrovascular disorder, and sites. Reports on brain plasticity, one of the great advances in brain science, were also added. Concerning "anesthetic management," the following sentence was added: Using airway devices with laryngeal masks as supraglottic airway devices is recommendable. Furthermore, it was added that remifentanil and dexmedetomidine are recommended as anesthetics.

Concerning "language assessment," available language tasks agreeing with patients were introduced along with nerve bundles associated with language, conventional naming, and explanatory naming.

The respective parent societies, the Japan Neurosurgical Society, Japanese Society of Anesthesiologists, and Neuropsychology Association of Japan evaluated and approved the above contents of the revision.

I believe that the present guidelines will academically contribute to advances in neuroscience, anesthesiology, and neuropsychology. In addition, the present guidelines have a socially and medically important significance. To provide safe, reliable medical practice to citizens, our conference held training sessions following the present guidelines required for performing awake surgery and obtaining medical fees. This revision may open the academia to society.

It should be recognized that the highest-degree priority of the present guidelines is preserving the brain/nerve functions after surgery and contributing to patients' benefits through the most appropriate resection.

Lastly, I thank all the investigators from the revision working committee for cooperating and finishing the "For the publishing" section.

President of the Japan Awake Surgery Conference
6th- and 7th-term chairman, Japan Neurosurgical Society
Takamasa KAYAMA

Keywords: awake surgery, guidelines

I. Surgical Maneuvers for Awake Surgery

Indications

1. Age

[Recommendation] While there is no specific upper age limit, an anesthesiologist, surgeon, and speech therapist should consider each patient's condition carefully. Surgeons with little experience should try to perform awake surgery only in patients aged 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 specified by age. If the required tasks are handled correctly, awake surgery can be performed in persons below 15 and above 65 years old. Patients can undergo such surgery at any age if they are considered suitable candidates after assessing other factors. However, many children aged <10 years are non-cooperative, and exciting the cortex with electrical stimuli is difficult in those aged ≤7 years[1]; therefore, awake surgery should be indicated for persons aged ≥10 years, considering its purpose and patient stress/effects.[2] We have encountered patients above 70 years old showing delirium or a marked increase in blood pressure on awakening; caution is needed. However, a study indicated that no significant difference exists in the incidence of complications between groups aged equal or above 64 years (n = 90) and below 65 years (n = 334).[3] Currently, an experienced anesthesiologist/surgeon/speech therapist could perform awake surgery in elderly patients through sufficient conferences. Furthermore, awake surgery in pregnant women was reported, but whether or not awake surgery is indicated should be determined in cooperation with the Department of Anesthesiology and Department of Obstetrics and Gynecology.[4]

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 reachable only through normal brain regions are typical indications.[5] Metastatic brain tumors are sometimes an indication. Depending on the case, extramedullary tumors, such as meningioma, are a less common indication.[6] For example, an extramedullary tumor corresponding to brain disease with extended motor nerve involvement may be an indication. Recently, several studies reported awake surgery for cerebrovascular disorder,[7,8] but whether awake surgery is indicated should be determined in cooperation with the Department of Anesthesiology.

3. Sites

[Recommendation] Surgical procedures may worsen neurological symptoms in areas indicated for awake surgery, which can be assessed by performing intraoperative tasks.

[Commentary] Awake surgery is primarily indicated for lesions of the anatomical language area of the cortex or its periphery, lesions at the lateral parietal lobe of the dominant hemisphere involving the angular gyrus, arcuate fasciculus (superior longitudinal fasciculus)-adjacent lesions, and motor area-adjacent lesions. However, the indication range is increased to preserve various brain functions, as described below.

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, including 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. The hippocampus is deep in the temporal lobe, is associated with verbal memory, and includes the insular gyri.[9] Functional areas must be identified through stimulation, whether a lesion is located near any of the above sites in the dominant hemisphere or cannot be confirmed to affect the nondominant hemisphere.

Recently, the importance of nerve fiber preservation has been emphasized. Concerning its background, most intraoperative symptoms appear during subcortical operations (90%). A study reported that symptoms during subcortical operations correlate with postoperative defect symptoms.[10] Awake surgery is indicated for lesions adjacent to language-associated fibers, especially the arcuate fasciculus/superior longitudinal fasciculus.[11] In addition, several studies have focused on the functions of the inferior fronto-occipital fasciculus,[12] frontal aslant tract (FAT),[13-15] uncinate fasciculus,[16] and sagittal stratum.[17] Meanwhile, a study indicated that nerve fibers other than the arcuate fasciculus/superior longitudinal fasciculus had a circuit to detour their functions.[18] The relationship between injury and long-term functional prognosis must be investigated.

Furthermore, mapping of the optic radiation[19,20] or inferior longitudinal fascicle[21] for preserving the visual function/visual cognitive function has been increasingly reported.

In addition to language and motor/sensory/visual functions, an increasing number of studies have reported awake functional mapping and monitoring of other functions, such as nondominant hemisphere functions, including calculation and spatial perception:[22,23] calculation function in the parietal lobe of the nondominant hemisphere[24] and working memory in the frontal lobe of the nondominant hemisphere.[25,26] To clarify whether these are universal facts and whether functional mapping contributes to maintaining the patient's QOL, its necessity must be investigated from the viewpoint of long-term prognosis.

4. Other indications including neurological symptoms

[Recommendation] Since the patient has to participate in awake surgery, the patient, assessors, surgeons, and anesthesiologists must all fully understand the meaning of aggressive resection and possible complications and recognize whether or not the patient can tolerate awake anesthesia.

[Commentary] Mapping and monitoring will be difficult if patients have already developed moderate or severe symptoms. For example, patients with impaired language functions, such as understanding, reading, repetition, and object naming, are unsuitable for awake surgery. Among patients who cannot speak fluently but have normal understanding, those with minor naming disorders and decreased word enumeration are candidates, although severe disorders may develop during surgery.[1]

According to the University of California's (U.S.) 27-year single-center study involving 859 patients, stimulation-related convulsive attacks were observed in 3% of the patients regardless of the tumor size, site, pathology, risk of anesthesia, degree of obesity, smoking, mental state, or frequency of attacks, and there were only three patients in whom mapping could not be accomplished during surgery (0.5%); the incidence of complications was extremely low.[27] However, in general institutions, awake surgery should not be indicated for patients with seriously increased intracranial pressure or those with serious systemic complications.

Addendum. Determination of the dominant hemisphere

[Recommendation] A provocation test (Wada test) by cerebral angiography may be conducted. If the dominant hemisphere is determined through 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, have been developed as functional tests. These procedures are noninvasive and have substantially contributed to neuroscience and neurology. fMRI is an excellent method, but a study indicated that the left or right was incorrect in 14% concerning the dominant hemisphere identification for tumorous lesions with compression (pseudolocalization).[28] Furthermore, according to another study regarding fMRI involving 214 patients using the simple verbal fluency task and word fluency test, no significant signal could be identified in 40% (85 patients), and when comparing the site of identification with awake language mapping in the other 129 patients, the sensitivity and specificity of the anterior language area of the cortex (Broca area) were 91% and 64%, respectively. Those of the posterior language area of the cortex (Wernicke area) were 93% and 18%, respectively. It was indicated that fMRI was not useful for predicting postoperative complications, and verbal fMRI was an unnecessary current routine preoperative examination.[29] Currently, fMRI may be incomplete in predicting the language area.

Meanwhile, a provocation test by anesthetic infusion on cerebral angiography (Wada test) is the gold standard to determine the dominant hemisphere (the procedure used to define the "correct answer" as the standard for comparison with new procedures) in addition to electrical stimulation to identify functional sites. According to a study, evaluation was possible in 99% of the 74 patients; the left hemisphere was dominant in 92%, the right hemisphere was dominant in 5.4%, and the bilateral hemispheres were dominant in 1.4%.[30] This is the most reliable method for determining the indication of awake surgery, but the sales of amobarbital were discontinued, and propofol is used as an alternative.[31] However, permission for off-label use should be obtained in the institution. Concerning the comparison between the risk of cerebral angiography and that of predicting left dominance and extirpating a right-dominant right lesion, there is an opinion that the latter risk should be managed (awake surgery) without performing the Wada test. A more accurate, noninvasive test should be developed.

Methods

1. Preoperative preparations

1-1. Informed consent (explanation regarding surgery and the patient's consent)

[Recommendation] The purpose/methods of awake surgery, the extent of resection, and possible complications should be explained. Furthermore, strategies including a switch to general anesthesia should be reviewed, assuming a case in which it becomes impossible to continue awake surgery. The contents of the surgery should be explained, and informed consent should be obtained from the patient.

[Commentary] Functional preservation and an improvement in the resection rate, as the purpose of awake surgery, concrete methods, and specific complications, should be explained.

On preoperative explanation, surgical strategies (1. Tumorectomy is discontinued, biopsy alone is conducted, and surgery is again considered later, 2. Resection is continued within appropriate limits based on the knowledge/findings obtained previously, and 3. Other strategies are considered) in the following case should be discussed and decided with the patient in the informed consent process after explaining that awake surgery must be promptly switched to general anesthesia when it becomes impossible to continue awake surgery for some reasons (the appearance of neurological symptoms, poor awakening, generalized seizures, restlessness, brain swelling, etc.).

1-2. Status and details of the simulation

[Recommendation] It is recommended that the tasks to be performed during surgery should be preoperatively rehearsed in the ward. In the initial introduction phase, the surgical posture, equipment set-up, and role sharing, including rehearsing the tasks for the patient, surgeons, anesthesiologists, and surgical staff (such as nurses), should also be simulated in the ward or operating room before surgery.

[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 the day before surgery, and take enough time to explain what will be done the next day (including the posture that the patient will assume following the surgeon, anesthesiologists, and nurses). Then have the patient 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 be done during surgery in the ward in advance, and select intraoperative tasks 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.

1-3. Presence or absence of premedication

[Recommendation] To obtain accurate intraoperative awakening, premedication prolonging the sedative actions should be avoided.

If necessary, benzodiazepines, which can be antagonized, should be administered (other drugs with another action should be reviewed with anesthesiologists).

The preoperative administration of antiepileptic drugs should be consulted with an attending physician.

1-4. Intraoperative administration of antiepileptic drugs

[Recommendation] A history of preoperative seizure is a risk factor for intraoperative convulsion, but the efficacy of additional antiepileptic drug administration for preventing intraoperative convulsion has not been demonstrated.

[Commentary] The incidence of convulsion during awake surgery is 2%-20%. According to a study, patients in whom awake surgery was switched to general anesthesia due to protracted seizures/status epilepticus accounted for 1.2%.[32,33] Phenytoin, an antiepileptic drug administered before surgery to prevent convulsion during awake surgery, has been routinely used. However, no study has indicated its efficacy. An investigational study involving 2,098 patients in whom intraoperative mapping was performed showed no difference in the incidence of intraoperative seizures between institutions where an antiepileptic drug (levetiracetam or phenytoin) was additionally administered or the dose was increased immediately before surgery and institutions where no prophylactic antiepileptic drug was administered among 863 patients who underwent awake surgery (12% vs. 12%, respectively, $p = 0.2$).[32] A single-center retrospective study involving 424 patients who underwent awake surgery further examined 27 patients (6.4%) in whom awake surgery could not be performed and indicated that the reasons were language disorder in 18 (4.2%) and epileptic seizures in 9 (2.1%). General anesthesia was required in five patients with epileptic seizures. The presence of preoperative mixed aphasia, oral administration of phenytoin, and a Karnofsky Performance Status of <70 were associated with intraoperative language disorder ($p < 0.001$, $p = 0.0019$, $p = 0.07$). This study also showed that, concerning the adjunct antiepileptic drug before surgery, there was no influence of the type of drug, timing, or blood concentration on intraoperative convulsion development.[33]

Factors associated with intraoperative convulsion include a history of preoperative seizure, seizure control by polypharmacy, low-grade glioma, site of tumor localization (left hemisphere, frontal lobe, primary motor cortex, supplementary motor area, temporal lobe),[32-34] and tumors with IDH mutations.[3] However, even though a history of preoperative seizure is a risk factor for intraoperative convulsion, there is no evidence that the additional administration of an antiepileptic drug before/during surgery prevents intraoperative convulsion.

Since antiepileptic drugs induce adverse reactions, such as central nervous system depressant actions, including somnolence and a reduction in attention/concentration, and motor function-inhibiting actions, caution is needed for the additional administration of a new antiepileptic drug or dose-elevation of the drug that has been taken. Generally, these are frequently observed at the start of treatment in a dose-dependent manner. In particular, somnolence reportedly occurs in 5%-32.4% of patients from the initial phase of treatment. To acquire resistance, ≥2 weeks are required. In addition, phenytoin induces psychotic symptoms, such as coma, a reduction in the consciousness level, restlessness, confusion, syncope, increased intracranial pressure, coordination disorder, hyperreflexia, bradykinesia, anarthria, hypoesthesia, and nervousness, in 0.5%-5% of patients. Levetiracetam induces anxiety, hypoesthesia, dysthymia, psychotic disorder, or irritability in 1%-3%, and confusion, impatience, agitation, or aggression in <1%. Considering these adverse reactions, pre-/intraoperative prophylactic administration should be performed based on its risk-benefit assessment.

In high-risk patients for intraoperative seizures, sufficient seizure control or prophylaxis with an antiepileptic drug that can be used during surgery should be performed before surgery, and subsequently, the intraoperative blood concentration of the same component should be maintained. Concerning the degree of seizure control by phenytoin preparations and levetiracetam, although intraoperative seizure control was not compared, the results of several comparative studies involving phenytoin or levetiracetam administration for preventing convulsive seizures early (7 days) after intracranial tumor craniotomy were reported: A randomized phase II trial indicated that the incidence of seizures in the levetiracetam group was significantly lower (15.1% vs. 1.4%, respectively, $p = 0.005$),[35] and a retrospective analysis showed that there was no difference in the incidence of seizures (4.5% vs. 2.5%, respectively).[36] These results suggest that the inhibitory effects of the two drugs on seizures are similar or that the effects of levetiracetam are more potent than that of phenytoin.

However, when performing awake surgery in the Department of Epileptic Surgery, various methods are used for the intraoperative diagnosis of an epileptic focus (generally, the dose of a preoperative antiepileptic drug is slightly decreased, and electrical stimulation is not conducted during surgery), differing from awake surgery for glioma resection in this article.

Coverage of intravenous drugs that are intraoperatively available by health insurance

Antiepileptic drugs that can be intravenously injected as of 2018 are phenytoin, fosphenytoin, phenobarbital, and levetiracetam. Fosphenytoin is a water-soluble prodrug of phenytoin. This preparation was developed to reduce tissue damage related to the strongly alkaline and hyperosmolar properties of phenytoin at the administration site. In vivo, it is hydrolyzed to phenytoin, and its pharmacological actions are similar to those of phenytoin. Intravenous phenobarbital is indicated for status epilepticus only, and its sedative effects are potent; therefore, it is not appropriate for awake surgery. Intravenous levetiracetam is indicated as "alternative therapy from oral levetiracetam for partial epileptic seizures treatment (including secondary generalized seizures) in patients in whom oral administration is transiently impossible." As a rule, intravenous levetiracetam is available only for patients in whom seizure control with levetiracetam has been performed before surgery. This must be considered.

2. Various intraoperative methods

2-1. Sites and methods of local scalp anesthesia

[Recommendation] For local scalp anesthesia, using long-acting local anesthetics is common in combination with invasive anesthesia and nerve blocks.

[Commentary] Analgesia by local anesthesia is often performed by combining infiltration with local anesthetic and nerve blocks. Some institutions perform anesthesia only by local injection or nerve block. Long-acting local anesthetics, such as ropivacaine and bupivacaine, are often used and are combined with lidocaine at some institutions.[37]

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.

When adopting fixation with pins, 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 experience pain at these sites during emergence. Meanwhile, the total dose of a local anesthetic tends to be relatively high; therefore, caution is needed so that the maximum dose may not be exceeded.

Preoperative simulation of temporary pseudo-emergence can be performed after fixing the head in a specific posture before initiating surgery to confirm whether tasks can be painlessly performed or whether problems could arise with removing/reinserting a laryngeal mask.[38,39]

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, whether or not the patient can comfortably cooperate with surgery and functional brain mapping/monitoring, and whether the selected method is correct or not following the surgeon's assessment.

The basic procedure is as follows:

1) Preoperative explanation: Creating an image of surgery for the patient and family is important. If this is not done, the patient will not understand what to do and how to cooperate and will be uneasy during the surgery. In particular, females and patients aged ≤60 years become highly anxious, and head fixation with pins and a specific posture contribute to the patient's discomfort.[40] Furthermore, awake surgery is not always performed in a completely awake state; sleepiness is present.[41] 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, which should 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, including meeting with the surgeons and nurses.
2) Head fixation: Whether to completely restrict head movement by pin fixation or to allow head movement by not performing fixation is yet to be decided. Surgery aims to safely and reliably resect the tumor, and the method should be established at each institution that maintains patient comfort and allows surgery to achieve its purpose.
3) 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 and the tumor. A posture allowing the performance of wide frontal-temporal-parietal craniotomy is generally used. However, skilled surgeons can extirpate only the tumor and its periphery under minor craniotomy. For posture setting, since various parts of the body support the body weight, individual differences must be fully understood concerning a comfortable posture and how painful it can be for patients to prolong the same posture. Setting a posture tolerable only for a short time and attempting to maintain it for a long time leads to pain at unexpected sites. How often 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:

The following posture setting and head fixation procedures follow the method of Berger et al.[1,42,43]

Preparation on the day before surgery:

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

To perform functional mapping of motor and sensory areas, including functional language mapping, craniotomy must expose normal brain tissue and the tumor. Generally, to allow for wide fronto-temporo-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. This is also an important point on reinserting a supraglottic airway device in awake surgery by asleep-awake-asleep with a supraglottic airway device. To improve venous return, slightly raise the upper part of the body. Find the most comfortable positions for the upper and lower extremities, and be careful not to overload any part of the body. A small pad should supplement even a narrow space between the operating table/fixing device and the body. During the posture setting, maintain an environment similar to that during the actual surgery as much as possible, continue conversation, check for the presence or absence of pain, and 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 have enough space to place, within the vision, a portable computer used for object nam-

Fig. 1 Posture setting.

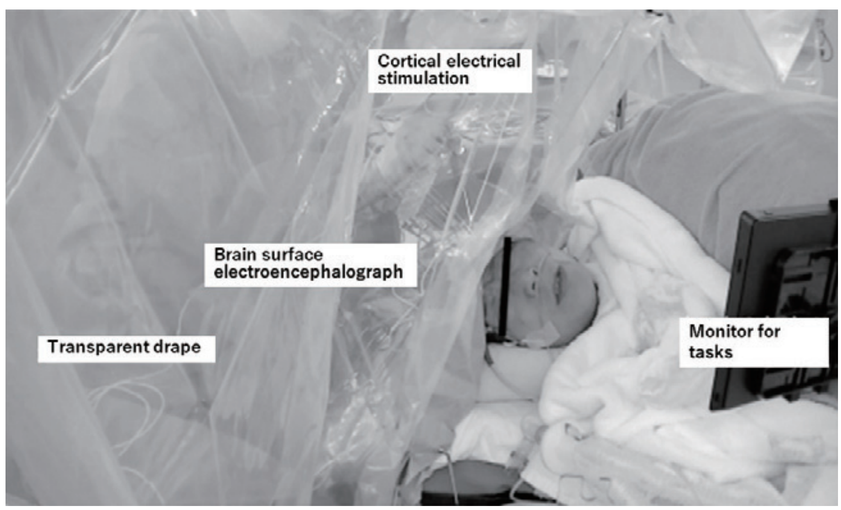

Fig. 2 Intraoperative setting.

ing in functional language mapping. Transparent drapes may be used to allow vision (Fig. 2).

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, a freer setting of the posture and head position (including using the prone position) is available. However, functional brain mapping takes time to perform without administering muscle relaxants, so whether the patient will feel comfortable in an unforced posture should be considered when setting the posture.

To avoid air embolism, the patient's head should be set as low as possible and legs should be elevated.

Posture setting on the day of surgery:

Even if the posture has already been confirmed on the day before surgery, consider setting the patient's posture again to ensure comfort. To confirm whether the patient feels comfortable or not, hold a conversation and do not induce anesthesia until completing the posture setting.

There is no consensus at this time about whether head fixation should be done or not. Berger et al. (2007) initially proposed in the Journal of Neurosurgery a head-fixation-free method but described that the head should be fixed with pins so that a neuronavigation system may be used.[44] However, the neuronavigation system does not always require head fixation with pins, as they had understood the best and as described below. If we prioritize the patient's comfort, no fixation would seem desirable. Pin fixation, including the patient's discomfort during surgery, cannot be ignored.[40] However, lack of fixation will constantly move 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 cooperating and achieving a balance between the surgeons and the patient, determine whether head fixation

Fig. 3 An optical neuronavigation system with fixation of reference points to the skull (left) and an electromagnetic neuronavigation system (right): Head fixation was not conducted. For introduction, a laryngeal mask[39] was used.

should be used or not after careful consideration at each institution.

Even without head fixation, continuous optical navigation is available by fixing the reference points to the skull[45,46] (Fig. 3, left). If an electromagnetic navigation system is used, the reference points for skull fixation may be unnecessary (Fig. 3, right).

Recently, navigation has been combined with intraoperative MRI in many institutions. Respective fixing devices-/imaging methods-matched management should be manualized.

[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 the surgeon can operate under general anesthesia. However, this approach induces more patient discomfort than without head fixation due to pain at the pin fixation sites and difficulty in moving the body and changing the head position. Also, treating vomiting or convulsions and reintubation may be difficult, so sufficient simulation is necessary. A patient with a glioma of the left frontal lobe in whom head fixation with four pins (Sugita frame) was performed by inserting a supraglottic airway device is presented (Fig. 4). Head fixation with four pins (Sugita frame) facilitates head rotation but makes moving the body difficult, as demonstrated for 3-pin fixation. Simulation for emergencies is important.

Fig. 4 Awake surgery with a craniostat.
(edited by the Japan Awake Surgery Conference: Guidelines for Awake Craniotomy, IGAKU-SHOIN, reprinted from 2013; p14).

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

[Recommendation] It depends on lesions or institutions whether a lesion is extirpated under sedation or awakening. When extirpating lesions, such as glioma in the white matter, resection control should be performed while conducting functional assessment (monitoring) and subcortical mapping by electrical stimulation under awakening during resection.

[Commentary] Examinations during awake surgery aim to identify functional areas by electrical stimulation (mapping) and confirm functional preservation by neurological examinations (monitoring). As general procedures for white-matter-infiltrating glioma resection, the extent of cortical resection is determined by cortical mapping and confirmed through monitoring at appropriate times under awakening on resection, and subcortical mapping is performed at a site where important nerve fibers are suspected.[47-52] However, when the results of cortical mapping are almost sufficient for determining the extent of resection, as indicated for epileptic focus resection, sedation is sometimes provided on resection after completing cortical mapping.

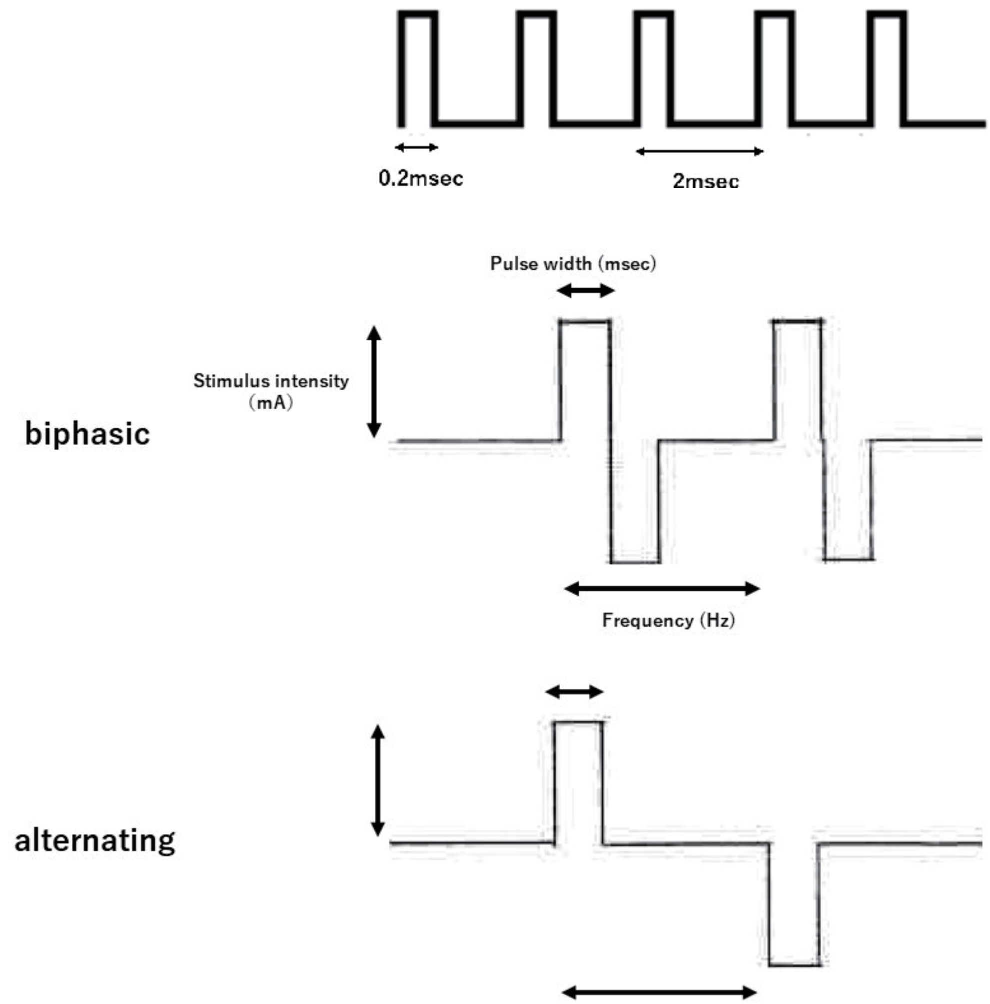

Fig. 5 Electrical stimulation: for motor-evoked potential (upper), for cortical language mapping (lower).

In addition to preserving the cortical language area by monitoring or subcortical mapping, the importance of preserving eloquent connecting fibers associated with language has been recognized. Hence, selecting an adequate issue per site and intraoperatively evaluating it based on findings regarding white matter fibers and their function is important.[49,51] However, the history of subcortical mapping is short, and the significance of intraoperative findings remains to be clarified: Whether positive-finding-site resection leads to permanent dysfunction, especially language and other high brain functions. Currently, physicians should not consider that awake surgery assesses all brain functions. Concerning motor function, simultaneous MEP monitoring during awake surgery is also effective.[48,52]

2-4. Conditions and timing of stimulation

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

[Recommendation] When performing cerebral cortex electrical stimulation for functional mapping, monopolar or bipolar stimulation is conducted using probe[1] or subdural[2] electrodes (Fig. 5). From the viewpoint of efficacy and tissue safety, their use is recommended as follows:

Probe electrodes[1]	Interelectrode distance: 5 mm or 1 cm, Electrode diameter: 1 or 2 mm
Subdural electrodes[2]	Interelectrode distance: 5 mm or 1 cm, Electrode diameter: 2.3 or 3 mm

Cortical electrical stimulation for motor-evoked potential (MEP) recording

- Polarity: monophasic
- Pulse width: 0.2 msec
- Type of stimulation: Train of five pulses
- Interstimulus interval: 2 msec
- Intensity: stimulation threshold + 2 mA (maximum: 20 mA)

Cortical electrical stimulation for language mapping

- Polarity: biphasic or alternating
- Pulus width: 0.2-1 msec
- Frequency: 50-60 Hz
- Intensity: 1-20 mA
- Stimulus duration: 6 sec at maximum

[Commentary] Subdural electrodes are manufactured by NIHON KOHDEN CORPORATION (by ADTECH Corporation) and UNIQUE MEDICAL Co., Ltd. In 2016, health insurance covered disposable subdural electrodes for electrical stimulation. Electrical brain stimulation during awake surgery may induce convulsion, and understanding the characteristics of stimulation conditions is important. The conditions differ among institutions, and a value calculated by multiplying the surface charge density (calculated by dividing the quantity of electric charge per pulse: stimulus intensity x pulse duration by the contact surface area) by the stimulus frequency or duration corresponds to the intensity of electrical stimulation. The quantity of electric charge on biphasic stimulation is 2-fold that on alternating stimulation. In addition to the quantity of electric charge, the type of electrode, interelectrode distance, and tissue state are involved in the extent of electric stimulation. A post-stimulation discharge monitor is required to confirm false-positive responses related to electrical stimulus spread to the periphery.[53,54] Furthermore, cortical excitability depends on the condition or age, and there are individual differences; therefore, false-negative responses may occur. When measuring motor-evoked electromyograms by 5-shot electrical stimulation, awake recording may provide more stable results than under general anesthesia recording.[55]

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

[Recommendation] The conditions for subcortical 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 those recover within 3 months.[56]

Subcortical stimulation also allows identifying the following language-related fibers, by which various findings have been obtained[5,57]: superior longitudinal fasciculus, arcuate fasciculus, subcallosal fasciculus, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, uncinate fasciculus, orofacial motor fibers, etc. Furthermore, a study indicated the importance of paying attention (cross-road) to the lateral side (sagittal stratum) of the lateral ventricle involving the superior longitudinal fascicle, arcuate fasciculus (AF), inferior fronto-occipital fascicle, and frontal aslant tract (FAT).[58]

In addition, another study reported language-fiber-associated cortico-cortical evoked potentials for confirming the connection and preservation of subcortical fibers,[59] suggesting the association between a reduction in the potential and postoperative complications.[60]

2-5. Treatment of convulsions

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

Measures: Reduce the stimulus intensity. Mapping at the same point should not be repeatedly performed. Attacks may increase intracranial pressure, making surgical-field development difficult. If the tumor is adjacent to the motor cortex, the concentrations of phenobarbital and phenytoin should be increased to the upper limits of effective blood concentrations and checked every two hours during surgery. If the concentrations are low, the intravenous injection of phenytoin at 250 mg and intramuscular injection of phenobarbital at 100 mg should be performed appropriately to correct the concentrations to the upper limits of effective blood concentrations. If convulsions occur, put cold water or cold artificial cerebrospinal fluid (e.g., Artcereb®: Otsuka Pharmaceutical Factory, Inc., Tokyo, Japan) 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. (Surgery can continue for tumors near the motor cortex while checking the MEP [second best method].) If the anesthetic state does not return to sufficient awakening, additional surgery may be selected. This possibility should be explained before surgery.

2-6. Necessity and usefulness of confirming afterdischarge: methods and evaluation

[Recommendation] Confirmation of stimulation-induced convulsions by evaluating afterdischarge occurrence on the electrocorticogram should be a basic procedure.[61] 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.[62] The risk of mistakenly identifying motor, sensory, and language disorders induced by brain dysfunction development at distant sites because of stimulation-induced afterdischarge should be avoided. An electrocorticography is useful to confirm whether electrical stimulation is being delivered (i.e., the current is flowing). However, there is an article describing that afterdischarge confirmation with electrocorticography is unnecessary at institutions where stable conditions are secured with much experience regarding awake surgery.[63]

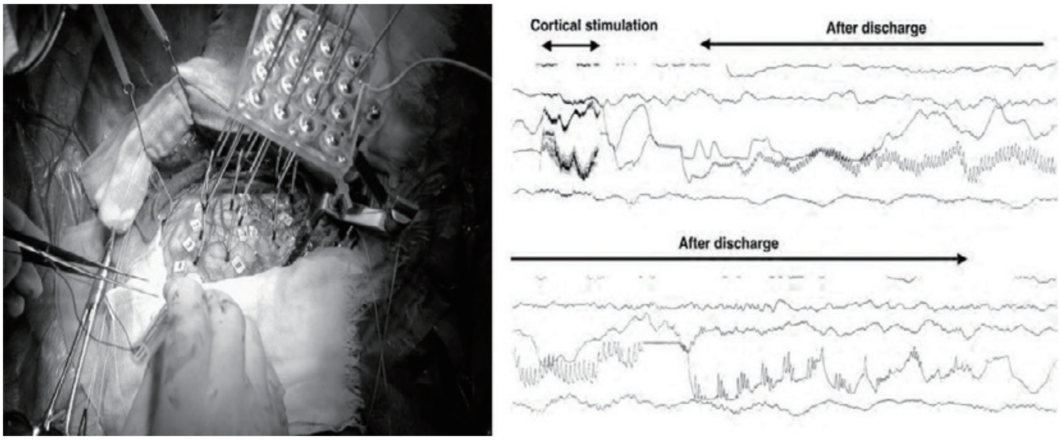

Fig. 6 Setting the electrocorticography and cortical stimulation with a bipolar stimulation probe (left). A case in which afterdischarge induced by electrical stimulation is presented (right) (edited by the Japan Awake Surgery Conference: Guidelines for Awake Craniotomy, IGAKU-SHOIN, reprinted from 2013; p19).

[Commentary] Position the electrocorticographic electrodes and record the electrocorticogram without stimulation (Fig. 6). Locate small pieces of paper with numbers, etc., on the cortical surface so the surgeons, staff performing electrophysiological mapping, and staff performing higher function examination can mutually confirm the stimulation sites.

Stimulate the cortical surface for 2-3 sec by applying biphasic rectangular pulses of 50 Hz and 0.3 msec pulse width using bipolar electrodes spacing 5 mm. For stable stimulation, the brain surface should be kept moist 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 while avoiding afterdischarge on the cortical electroencephalogram. Under the above conditions, effective stimulation is often obtained at 8-11 mA. Under awake condition, a lower stimulus intensity is optimal, and 4-8 mA is often used. For the sensory areas, since instantaneous cortical-surface stimulation with a low current lead to patient's numbness and discomfort, initiating mapping of the sensory areas first is desirable. 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 elicited by median nerve stimulation or labial stimulation; it aims to achieve effective results from the first stimulus. The primary motor area does not exist in all of the precentral gyrus but lies on the anteroposterior direction toward the central sulcus. Therefore, stimulation should be applied along the central sulcus first. Applying stimulation perpendicular to the central sulcus uses a bipolar probe. 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. Electromyogram[64] is not obtained from all muscles, so the extremities and face must be carefully observed at sites where stimulation is expected to induce movement.

After completing the motor and sensory area mapping, 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 no afterdischarge on the electrocorticogram. A current 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[65] may elicit speech arrest. One of the methods for confirming this is applying stimulation to the brain surface i) while instructing the patient to protrude the tongue and move it from side to side, ii) while continuing countermovement of the thumb and forefinger, and iii) during flexion and extension of the ankle joint. If movement arrest 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, not with language dysfunction. These procedures determine the optimal stimulus current and identify the frontal language areas to some extent. Then, perform object naming while continuing stimulation.

Normal counting does not always correspond to normal object naming. Show the patient the slides for approximately 2-5 sec each. Assess whether there is speech arrest, hesitation, or wrong answers (such as semantic/phonemic paraphasia) after presenting the stimulus. If these occur, you must always confirm whether they are induced by actual stimulation of the language areas, fatigue, inability to see the slides, or seizures development. Using the sentence pattern for naming "This is ...," allows us to determine whether abnormalities are associated with speech arrest by stimulating the tongue motor areas or negative motor areas or are due to stimulation of language areas. Since identifying language areas needs repeated confirmation of the results, patients must expend a large amount of energy. Therefore, functional brain mapping/monitoring requires the patient's complete cooperation.

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 much as possible. During continuous tasks, management with remifentanil should be performed in a dose range in which there may be no decreased consciousness. The head should be fixed with pins, but soft material should be placed below the body so there may be enough space to move the body. 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: The risk of air embolism is higher in awake surgery than in general anesthesia because of negative pressure respiration during the procedure. Air embolism can be caused by raising the head excessively (for example, locating the operating field at the highest position in the motor cortex).[66]

Measures: As with general anesthesia, 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 cutting edge with bone wax, fibrin, and thrombin immediately after craniotomy. Keep the head down until the dura mater is opened, and then gradually raise the head while observing the 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.

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 using local anesthetic as much as possible. Play the patient's favorite music or take measures to avoid anything that makes the patient uncomfortable so 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 much 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 tumor but seldom in those with epilepsy. Arterial carbon dioxide tension ($PaCO_2$) tends to be higher during awake surgery than during under general anesthesia, leading to a higher risk of increased intracranial pressure.

Measures: If there is evidence of increased intracranial pressure in imaging studies, general anesthesia should be employed. If awake surgery is necessary, the decision can be made after dural incision following standard intubation. If no brain swelling is 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 pneumonia development, although whether these are characteristic problems of awake surgery is controversial. To prevent pneumonia, it seems important to prevent lowering of consciousness and vomiting (refer to the section on anesthetic management for details about dealing with nausea and vomiting).

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 resectioning 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, fully understanding the pathology of epilepsy is important. 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 varies, and false-positive and false-negative electrical stimulation results can occur.[67] 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 following the results of various noninvasive physiological tests, such as fMRI, positron emission tomography, and MEG, for detailed mapping. Using brain surface electrodes allows for complementary cortical function testing to assess symptoms' development and 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 complete resection results in better postoperative control of epileptic seizures.[68] It is reported that 0%-63% of patients develop persistent functional disorders after resection of functional brain areas involved by epileptic foci. However, since only a few cases exist, it is unclear whether we should resect all the functional sites or consider only the resection of sites with a possible compensatory function, including how to decide on the discontinuation of resection.

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 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 could be functional tissues. We see no point in performing awake surgery if they are not preserved. Duffau et al. reported many patients in whom a negative response was detected at the same site on mapping during recurrence after functional preservation without resection of a positive site on the initial session, suggesting "plasticity." A study indicated that it occurred in approximately 33% of patients.[69)]

However, if tumors coexist with functional tissue[70)] and preoperative consent has been obtained, functional tissues may not be preserved if the decision is confirmed to prioritize tumor resection after accepting the risk of complications and the fact that postoperative symptoms are less likely to develop even with a response (e.g., negative motor areas in the supplementary motor cortex).

Since responses are sometimes false-positive, you should acquire proficiency in mapping. False-positive findings are primarily obtained either because awake conditions are poor and do not allow patients to perform their tasks or the basic conditions for the tasks are poor (e.g., the patient cannot see the screen because a drape covers their eyes). Some patients could not perform the naming task due to an inability to see the screen because of conjugate deviation induced by stimulation of the oculomotor fibers, but they were regarded as having language arrest (the truth was recognized by reviewing videos).

The "positive mapping" strategy, in which lesions are extirpated after identifying the language area accurately to avoid injury, is appropriate for risk reduction. However, the language area could not be identified in 17% (14/82) of patients, and much caution is needed when a tumor is present in the triangular part of the inferior frontal gyrus.[71)] Berger et al.[53)] proposed the "negative mapping" strategy in which there is no necessity to identify the language area as a positive control (under major craniotomy for identification), and resection may be performed under specific conditions (60 Hz, maximum: 6 mA) if the language area is absent in the extent of resection. When the result of "negative mapping" is finally obtained at an eloquent area before surgery, the tumor resection rate is high, confirming the efficacy of awake surgery.[72)] However, extirpation is performed after confirming positive findings involving the language area; its safety is secured.

According to stereotactic recording in 102 patients on dominant hemisphere language mapping with this negative mapping strategy, speech arrest was noted in 51% of patients, and the most frequent site was the posterior inferior frontal gyrus, followed by the dorsal premotor cortex and posterior superior temporal gyrus. Anomia occurred in 33% of patients, extensively involving the posterior superior temporal gyrus, posterior middle temporal gyrus, angular gyrus, and supramarginal gyrus. The probability that the language area may be identified at a nontypical site was significantly high in patients in whom classical Broca's or Wernicke's areas were affected or those with multilobular lesions.[73)]

Significantly, their report indicates that awake language mapping allows us to perform even aggressive resection with a very low incidence of complications, and a report on language mapping was published in a top clinical journal, suggesting that its usefulness as a surgical procedure for glioma has been established.

II. Anesthetic Management for Awake Surgery

Introduction

In the 1800s, foci resection in patients with epilepsy was performed by craniotomy under local anesthesia.[74)] With no electroencephalogram, direct cortex stimulation was employed to detect the epileptic focus and identify functionally important sites, which seems to be the prototype of current awake surgery. In the 1900s, owing to sedation, surgery became more comfortable for patients.[75)] Using codeine, thiopental, and meperidine, management was conducted under spontaneous respiration or partial tracheal intubation. Epileptic surgery then came to emphasize intraoperative electroencephalography.[76)] 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.[77)] Developing a long-acting local anesthetic, bupivacaine, also facilitated awake surgery. As a result, many procedures for intractable epilepsy employed neuroleptanalgesia.[78,79)] Thereafter, short-acting analgesics, such as sufentanil and alfentanil, were developed and adopted.[80)] Propofol was introduced for awake surgery because it is short-acting with anticonvulsant and antiemetic effects.[81)] It is now widely used as the main sedative. Recently, new anesthetics, such as dexmedetomidine[82)] and remifentanil[83)] have been introduced, while a laryngeal mask has been initiated for airway management.[84)] Since unnecessary procedures 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 surgery, so the methods in actual use and those recommended by the review committee are presented.

To introduce the above methods, the guidelines for anesthetic management during awake surgery were prepared in 2012. Subsequently, the number of institutions where awake surgery is performed and that of surgical sessions increased, and awake surgery became covered by health insurance through institutional authorization in 2015. Awake surgery should be addressed by a team comprising a neurosurgeon, anesthesiologist, speech therapist, nurse, and clinical engineer to preserve the patient's high functions, including language. Therefore, the guidelines for anesthetic management during awake surgery were not simply prepared for anesthesiologists, but to show other-field staff comprising the team standards for anesthetic management in the Department of Anesthesiology, namely basic attitudes. The basic policy ensures safety and improves the patient's peri-/postoperative quality of life. However, 8 years have passed since the first version was issued, and new anesthetic management methods were introduced. We prepared the second version of the guidelines for anesthetic management during awake surgery by incorporating these new methods into the present guidelines.

Anesthetic management

1. Basic policy

[Recommendation]

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

1.2 To handle intraoperative respiratory problems and rapidly changing risks, management and supervision by anesthesiologists with extensive experience in awake surgery are required.

1.3 To safely manage rapidly changing intraoperative conditions, ensure that backup anesthesiologists and attending anesthesiologists are available.

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

1.5 Do not use inhalational anesthetics absorbable and excretable through the respiratory system because a definitive airway is not established. (Inhalational anesthetics possibly causing brain volume increase should not be used because of the uncertain $PaCO_2$ management during awake surgery.) Use propofol as the basic sedative.

1.6 Since management is performed under spontaneous respiration, carefully titrate the sedative and analgesic drugs. Maximize using local analgesic anesthesia. (During the unconscious period, management with controlled respiration via a supraglottic airway device, etc., is available.)

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

1.8 Electrical stimulation during functional mapping may induce convulsions, occasionally resulting in the inability to continue the procedure, requiring rapid countermeasures.

[Commentary] Awake surgery was used for surgical treatment of epilepsy in the early 20th century and was then 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.[85,86] Awake surgery aims to prevent brain dysfunction induced by surgery and to precisely resect the disease focus to improve the patient's prognosis and quality of life. Anesthetic management aims to remove psychophysical pain, allowing the necessary surgery to proceed, while putting the patient's safety first. Each section in these guidelines and the corresponding commentary describe the details of anesthetic management for awake surgery.

Since there have not been enough randomized controlled studies of anesthetic management for awake surgery, management that is not based on such evidence in these guidelines is based on the methods recommended by institutions familiar with awake surgery. Therefore, if anesthetic management based on randomized controlled study evidence is reported in the future, these guidelines will be appropriately reviewed.

For successful awake surgery, the patient's cooperation is essential. Also, preoperative and intraoperative communication and agreement is required among neurosurgeons, anesthesiologists, and operating room staff familiar with awake surgery. For anesthetic management, establishing the airway, stabilizing hemodynamics, and preventing intracranial pressure increase are necessary. Since $PaCO_2$ management is difficult during awake surgery, inhalational anesthetics that could increase the brain volume should be avoided. Hence, propofol for sedation and general anesthesia is currently the standard for awake surgery. While the patient is unconscious, respiratory management with a supraglottic airway device can be used. Each section in these guidelines describes the details of respiratory management.

During awake surgery, since scalp block and infiltration anesthesia for sufficient pain control require a large volume of local anesthetics, caution to local anesthetic toxicity should be monitored.[87] During awake surgery, 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 establishing an airway is difficult or other adverse reactions interfere with the patient's safety, awake surgery should be discontinued and switching to general anesthesia should be considered after discussion between the anesthesiologists and neurosurgeons.[88]

2. Premedication

[Recommendation]

2.1 To allow complete intraoperative emergence, do not administer premedication that could cause residual sedation.

2.2 If there is no choice but to administer premedication, use a benzodiazepine that could produce antagonism.

2.3 The intraoperative administration of dexmedetomidine for sedation during emergence may reduce the risk of respiratory complications during awakening operations.

2.4 Decide which antiepileptic drug should be used for premedication after consulting the patient's physician.

[Commentary] During awake surgery, patients must be sufficiently awakened to perform language and motor tasks that yield reliable results. Based on that, the extent of resection is determined. Therefore, as a matter of principle, drugs that could affect emergence should not be administered.

For successful awake surgery, it is crucial to build a relationship of trust among the patient, the surgeons, the anesthesiologists, and the operating room staff.[89] Establishing a patient-centered relationship reduces the need for sedatives. However, if sedatives have to be administered, benzodiazepines are recommended since its antidotes are available. If surgery is being done for a tumor, sedation-induced hypercapnia can possibly increase intracranial pressure, and this requires special caution.

Convulsions are one of the most significant complications of awake surgery. 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 an antiepileptic drug should only be done after discussion with the attending physician. Note that propofol also has an anticonvulsant effect. Discontinuation during awakening operations increases the risk of postoperative complications, prolonging the admission period.[33] However, sedation with dexmedetomidine during awakening operations reduces the risk of respiratory complications; therefore, it may be useful.[90] Meanwhile, it may reduce the quality of tasks; it should be carefully indicated.

The institution's policy should be adopted concerning other drugs, such as H2 blockers, administered during general surgery.

Among antiemetics, metoclopramide hydrochloride (Primperan®; Sanofi-Aventis K.K., Tokyo, Japan) is not recommended because of potential adverse effects secondary to enhanced peristalsis. Some reports of dexamethasone being administered to control 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.

3. Basic monitoring and preparation

[Recommendation]

3.1 Before surgery, the patient's mental and physical states involving the airway should be evaluated.

3.2 Preoperative surgical simulation is effective in reducing the patient's anxiety.

3.3 A pressure-reduction, highly stable mattress should be used on the operating table.

3.4 The posture (supine position, side position), sedation (Asleep-Awake-Asleep, Monitored anesthesia care, Awake-Awake-Awake), respiratory care (spontaneous respiration, controlled respiration), and devices for airway management (supraglottic airway device, endotracheal intubation) should be confirmed before surgery.

3.5 Monitor the electrocardiogram, percutaneous oxygen saturation, expiratory partial pressure of carbon dioxide, urine volume, and body temperature.

3.6 Create peripheral venous access for continuous administration of anesthetics and blood transfusion.

3.7 Create arterial access to directly measure arterial pressure and monitor the partial pressure of arterial carbon dioxide.

3.8 As the patient becomes awake during surgery, the patient's privacy protection and adequate room-temperature control must be considered.

[Commentary] Awake surgery is more mentally and physically stressful than surgery under general anesthesia for patients. As a requirement for awake surgery, the patient's positive, strong will is necessary.[91] Anesthesiologists can smoothly perform interventions for mental/physical stress on intraoperative emergence by seeing the patient and establishing a good relationship before the day of surgery.[92] Until intraoperative emergence, inaccurate airway management with a supraglottic airway device or airway-device-free sedation is sometimes conducted; therefore, preoperative airway assessment is also important.[27] Be careful in deciding to perform awake surgery in patients with a body mass index >30 because respiratory tract and respiration problems easily develop in them.[93]

Surgical simulation with the patient before the day of surgery effectively reduces anxiety. The patient is instructed to enter the operating room and take a position on the operating table so that the environment on the day of surgery may be accurately experienced. A mattress that equalizes the distribution of the patient's body pressure and facilitates the maintenance of a non-circulation-affected state should be prepared on the operating table so the patient may endure the same position even during surgery for many hours.

Concerning an intraoperative posture (supine position, side position), sedation (Asleep-Awake-Asleep, Monitored anesthesia care, Awake-Awake-Awake), respiratory care (spontaneous respiration, controlled respiration), and devices for airway management (supraglottic airway device, endotracheal intubation), various methods have been proposed, but the most appropriate method should be selected in the institution, considering techniques or patient factors, and necessary drugs or goods should be prepared.[94]

Basically, the guideline for installing an intraoperative monitor follows the Japanese Society of Anesthesiologists. For awake surgery, sedation is sometimes performed without endotracheal intubation; therefore, strict respiratory care is required. When maintaining spontaneous respiration without devices for airway management, it is necessary to carefully examine the respiratory rate and the presence or absence of respiratory efforts. For good anesthetic management, an environment allowing easy observation of the respiratory status is required, including using transparent drapes to allow sufficient observation of the patient's mouth, neck, and chest. Airway maintenance during awake surgery is done by one of two methods: one method depends on spontaneous respiration without devices, and the other method uses a device for airway management, such as a supraglottic airway device. If a device is used, we can rely on spontaneous respiration and, if necessary, provide respiratory support, or we can actively perform ventilation. Tracheal intubation is not recommended since it will likely 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.

When maintaining spontaneous respiration on sedation, respiratory depression or glossoptosis decreases the amount of ventilation, causing hypercapnia.[95] Hypercapnia induces increased intracranial pressure related to brain swelling, leading to nausea or vomiting on intraoperative emergence. Respiratory care by controlled respiration using a device for airway management, such as a supraglottic airway device, is advantageous for $PaCO_2$ control. For accurate $PaCO_2$ assessment, arterial gas analysis through arterial cannulation should be performed.

There have been reports of air embolism during awake surgery. Caution is required, especially when surgery is performed under spontaneous respiration without a supraglottic airway device. In this case, end-tidal partial pressure of CO_2 is not useful as described above, and it is difficult to determine whether changes in saturation of peripheral oxygen result from worsening respiratory status or air embolism.[96,97] Upper airway obstruction causes lower negative intrathoracic pressure and may increase the risk of air embolism. Concerning anesthetics, fast-metabolism drugs facilitating a prompt switch to a favorable awake state where brain function tasks can be performed should be selected. When administering fentanyl, it makes emergence poor, and its dose should be minimized. Asleep-Awake-Asleep anesthetic management with propofol and remifentanil target-controlled infusion is often performed. In the Asleep-Awake-Asleep method, it is effective to regulate the depth of anesthesia using an electroencephalographic monitor, such as the Bispectral index (BIS), until the start of brain function tasks.[98] Recently, dexmedetomidine became available for intraoperative sedation without intubation under local anesthesia, and anesthetic management by monitored anesthesia care can be selected.[99] Selective scalp nerve block with local anesthetics facilitates effective analgesia without influencing consciousness, providing a favorable awake state during brain function tasks.[100,101] It is necessary for anesthetic management during awake surgery. Also, when 3-point fixation is employed, check with the surgeons that the neck has not been twisted or anteflexed. Lastly, protecting the patient's privacy and patient-priority-based room-temperature control must be considered due to intraoperative emergence state.

4. Admission, induction, and local anesthesia

[Recommendation]

4.1 Initiate oxygen delivery after validating the vital signs with a patient monitor.

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

4.3 Maintain general anesthesia under spontaneous respiration with a facemask, or under assisted/controlled ventilation after inserting a supraglottic airway device.

4.4 Insert a urethral catheter.

4.5 Analgesia with local anesthetics should be sufficiently performed. A combination of infiltration anesthesia at the skin incision site and site-matched nerve block is more effective. Long-acting local anesthetics, such as ropivacaine and levobupivacaine, should be primarily used.

[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, an intravenous anesthetic drug, should be used as a hypnotic agent. Emergence is faster and clearer in propofol than in inhalation anesthetics, affecting the electroencephalogram and sometimes inducing excitement at emergence from anesthesia.[37]

A TCI system can reasonably be used for propofol 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, when used for sedation, have residual effects on the consciousness level after emergence. Therefore, Remifentanil is suitable for managing strong surgical stimulation before emergence, as its effect rapidly disappears. It is also reasonable to administer a small dose of fentanyl repeatedly, expecting only a slight residual analgesic effect.

A facemask or supraglottic airway device usually manages the airway before emergence. Airway management under assisted/controlled ventilation and spontaneous respiration can be performed safely with a supraglottic airway device, though it is generally difficult to extubate safely and smoothly at awakening. Even when a supraglottic airway device is used, muscle relaxants should not be administered as a rule.

A nasogastric tube should not be inserted, as it leads to discomfort in the pharynx and nausea during the conscious state. Remove the nasogastric tube before emergence if it has to be inserted during general anesthesia.

Insert a urethral catheter after anesthesia induction, as the operation will take a long time.

The key to anesthetic management for awake surgery 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 using long-acting local anesthetics, such as ropivacaine, levobupivacaine, or lidocaine combined with epinephrine. According to a study regarding the blood concentrations of local anesthetics during awake craniotomy, there was no problem, such as local anesthetic toxicity, even at a mean ropivacaine dose of 3.6 mg/kg.[102] However, local anesthetic toxicity must be considered. Local anesthetics are administered by infiltration around pin fixation and the skin incision site, along with selective nerve blocks (supraorbital nerve, greater occipital nerve, etc.). Gauze soaked with local anesthetics can be pressed against the wound. Since direct contact of local anesthetics with the brain parenchyma causes central nervous system symptoms, such as convulsions, administering local anesthetics after dural incision should be performed carefully.

5. Before emergence

[Recommendation]

5.1 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).

5.2 Discontinue propofol after the dural incision has been made. Suppose sedation is continued, provide the required dose of propofol, etc.

5.3 Closely monitor the patient because body movements may occur suddenly during emergence.

5.4 If a supraglottic airway device is used, confirm spontaneous respiration before removal.

5.5 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] Since the tasks and tests used for brain functional mapping and electrocorticography (ECoG) 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 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.[37]

During strong surgical stimulations, 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.[103] Body movement sometimes occurs during emergence, as with other surgical anesthesia practice. Since 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 the circulatory and respiratory systems, which often occur during this period.[104]

When using a gastric tube or supraglottic airway device, check for spontaneous respiration and remove it on emergence.

Due to restlessness, the patient may not remain still and cooperate with functional tests.[83] If restlessness is 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.

6. Awake period

[Recommendation]

6.1 In principle, systemic administration of sedatives and analgesics should not be done.

6.2 For light sedation, administer propofol, etc., at the minimum required dose. (There are reports on using dexmedetomidine as a sedative. Use of remifentanil in patients with spontaneous respiration is not recommended because of respiratory depression.)

6.3 If the patient experiences pain, provide additional local anesthesia first.

6.4 If nausea and/or vomiting occur:

- 6.4.1 Discontinue the surgical procedure, administer metoclopramide or a serotonin receptor antagonist, and wait for the subsidence of symptoms.
- 6.4.2 Remove vomitus to prevent aspiration. If the symptoms are severe and do not subside, consider sedation with propofol and discuss with the surgeons regarding discontinuing awake surgery.

6.5 If convulsions develop:

- 6.5.1 Discontinue the surgical procedure, especially electrical stimulation. (In electroencephalogram monitoring, the operation should be discontinued when the first spike is seen.)
- 6.5.2 Cool the brain surface with cold water.
- 6.5.3 Administer propofol at a sleeping dose.
- 6.5.4 Give an intravenous infusion of 250 mg of phenyt-

oin.

6.5.5 If the convulsions do not cease even after additional propofol, midazolam, or thiopental administration, discontinue awake surgery.

[Commentary] During the awake period, generally, systemic application of sedatives or analgesics should be avoided 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 prevents the patient's mental state and excitation from worsening, the potential influence on functional assessment should be assessed. Recently, there have been several reports about anesthesia during awake surgery where dexmedetomidine or remifentanil was used during the awake period.[90,94,95,105-111]Dexmedetomidine, which facilitates sedation with only slight respiratory depression, is useful and can be effectively and safely administered even on mapping, according to a study. However, there have also been reports that poor emergence of patients receiving dexmedetomidine required a decrease of the dose or discontinuation. Furthermore, low-dose remifentanil is available under spontaneous respiration on emergence. For its use, acute tolerance must be inspected, considering the possibility of respiratory depression or hypercapnia-related brain swelling.[112]

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.[94] Nausea and vomiting, along with causing discomfort for the patient, increases the risk of respiratory complications due to aspiration, and body movement and swollen brain associated with nausea/vomiting may make the surgical procedure even more difficult. Nausea and vomiting may be induced either by the surgical procedure or narcotics use. 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 each institution to make the decision. If symptoms are severe and do not improve, consider sedation with propofol and even consider the discontinuing awake surgery 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 surgery depends on the underlying disease and is reported to be approximately 0%-24%.[93,113] 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 discontinuing 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 surgery. A report shows that intractable convulsions required general anesthesia with tracheal intubation.[114] During awake surgery, preparing for emergency transition to airway management or general anesthesia at any time is necessary.[115]

7. Reinduction and completion of craniotomy

[Recommendation]

7.1 When the patient's cooperation is not required any further, induce sedation with propofol or dexmedetomidine.

7.2 In principle, manage the patient with spontaneous respiration. However, use a supraglottic airway device if the airway must be secured because of oversedation. (Anesthesiologists with expertise in handling the supraglottic airway device may perform anesthetic management by deliberately using it at closure.)

7.3 If needed, add more local anesthesia. However, if there is evidence of local anesthetic toxicity, discontinue additional anesthesia and provide necessary treatment, such as establishing an airway and countermeasures for convulsions.

7.4 If the airway is established with a supraglottic airway device, the required dose of fentanyl or remifentanil can be given for analgesia

[Commentary] Anesthetic methods for awake surgery include the Asleep-Awake-Asleep technique (SAS), Monitored anesthesia care (MAC), and Awake-Awake-Awake technique (AAA).[94] Anesthesia on reintroduction/cranial closure depends on the selected method.

When adopting SAS or MAC, propofol is routinely used as an anesthetic on cranial closure, as selected for craniotomy.[37] 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.[37] In addition, several studies reported the use of dexmedetomidine for MAC. It was indicated that there were no marked differences in the quality of sedation or degree of emergence on mapping between propofol and dexmedetomidine.[90] For AAA, local anesthetics and analgesics should be administered without using sedatives.[94]

During SAS, a supraglottic airway device is routinely used for airway management. Insertion of a supraglottic airway device should be done via a lateral caudal approach and requires some degree of proficiency when the head is fixed with pins. During insertion, difficult airway management, body movement, cough, vomiting, or increased intracranial pressure may occur.[111] Management by at least two anesthesiologists is recommended. After establishing the airway with a supraglottic airway device, management can be achieved by controlled respiration with remifentanil or fentanyl. If airway management takes a long time, endotracheal intubation with a supraglottic airway device, airway scope, or air track[116] may be selected. Preparations should be made to establish the airway with a supraglottic airway device immediately after a sudden change in the patient's state, such as the onset of convulsions. If analgesia is insufficient, add a small dose of fentanyl. Caution is required for using remifentanil with spontaneous respiration during craniotomy, as on emergence.

III. Language Assessment during Awake Surgery

Language assessment during awake surgery

1. Language mapping

[Recommendation]

1.1. Indications

Patients with lesions around the perisylvian language areas of the dominant hemisphere.

Aphasia is absent, or even if it is present, it is mild. Patients can sufficiently understand examination and cooperate.

1.2. Preoperative preparation

Set language tasks that patients can easily perform and fully familiarize.

1.3. Cortical electrical stimulation

A stronger stimulus intensity (5-15 mA) and longer duration (3-5 sec) are required for motor and sensory mapping, respectively. The electrical stimulation should be initiated immediately before starting language tasks and continued during the tasks.

1.4. Language tasks

As cortical mapping, visual naming, and counting are adopted as basic tasks, tasks, such as auditory comprehension, repetition, and reading, are conducted following the site. If electrical stimulation reveals any dysfunction, assess reproducibility. On subcortical mapping, the language function should be continuously monitored with spontaneous speech or naming during resection. When an abnormality is suspected, mapping by electrical stimulation is conducted, if necessary.

[Commentary]

l. Purpose

Language mapping aims to identify the language areas in each patient and prevent postoperative language disorder by avoiding the areas during resection. Since the extent of the language areas varies among individuals and accurately identifying them anatomically is difficult, the areas should be determined for each individual.[117] "Negative mapping" indicates that the language areas are not included in the operative field. If the language areas are identified in areas other than the resection site (positive mapping), the possibility of postoperative language disorder is low.

Table 1 Brain regions for language mapping

Main regions associated with language	
Frontal lobe	Inferior frontal gyrus
	Posterior middle frontal gyrus
	Posterior superior frontal gyrus
	Precentral gyrus (middle and inferior parts)
Temporal lobe	Superior temporal gyrus
	Middle temporal gyrus
	Inferior temporal gyrus
Parietal lobe	Supramarginal gyrus
	Angular gyrus
White matter pathways related to language	
	Arcuate fasciculus
	Superior longitudinal fasciculus
	Inferior longitudinal fasciculus
	Inferior fronto-occipital fasciculus
	Uncinate fasciculus
	Frontal aslant tract

2. Indications

Language mapping is indicated for patients with foci in language-associated areas in/around the perisylvian cortex of the language-dominant hemisphere (Table 1). The language-dominant hemisphere should be comprehensively identified in advance based on the neuropsychological examination and functional MRI findings (Chapter 1, Addendum). Especially in patients with left-handedness or ambidexterity, the language-dominant hemisphere may be present on the right/bilateral sides in approximately 30%; confirmation is necessary. The Wada test should also be considered when the language-dominant hemisphere is unclear on functional MRI.

Diseases for which language mapping is indicated include low-grade glioma and cavernous hemangioma as primary indications. Although language mapping is sometimes performed in other cases, its indication should be comprehensively determined based on the patient's status, lesion site, functional outcome, prognosis, and patient's/family's wishes.

Since patients must fully understand and cooperate to perform language mapping, we should consider the patient's preoperative cognitive level and mental maturity. Since 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 patients. Language mapping is not indicated for children aged <10 years or patients with moderate or severe aphasia before surgery.

Language mapping is indicated for patients with mild aphasia on preoperative examination, but caution is needed because language symptoms become more marked than its preoperative state during surgery in many cases.

3. Preoperative preparation

3-1. Examination

Whether it is possible to perform the language tasks during surgery should be evaluated through neurological/neuropsychological examination. Initially, whether consciousness is clear and attention deficit is absent should be confirmed. If attention deficit is present before surgery, it may become more marked during awake surgery, increasing the number of mistakes in language responses; therefore, it is difficult to evaluate the language areas. Furthermore, the visual acuity and glasses requirement should be confirmed and prepared for using glasses during surgery, if necessary. Next, the presence or absence and degree of dysarthria or aphasia should be examined. Patients with moderate to severe aphasia cannot respond to the language tasks stably and correctly, and awake surgery is not indicated for these patients; therefore, the severity must be evaluated. If necessary, the neurologist/neurosurgeon should request a speech therapist to perform the standard aphasia battery. Concerning the language tasks to be used during awake surgery, a state in which the patient can completely provide correct answers on preoperative examination is necessary.

3-2. Explanation

Since the purpose and methods of awake surgery are explained by the attending neurosurgeon, those of language mapping should be concretely explained using actual stimuli. Electrical stimulation may induce language impairment depending on the stimulation site, but it will return to normal after completing stimulation. Informing the patient in advance about the necessary procedures to identify the language areas will prevent distraction during language mapping.

3-3. Establishment of tasks

Visual naming should be performed in all patients. The other tasks should be selected with reference to Table 2 following the lesion site. After performing the tasks once, exclude stimuli evoking unstable responses, leaving only the stimuli for which the patient can provide correct answers. Furthermore, the most appropriate stimulus-presenting interval should be determined while observing the patient's responses (2-5s).

3-4. Practice

The selected tasks should be practiced several times until the patient can confidently answer. Stimuli on which the correct answers are sometimes provided, but not at other points, including those on which the responses are delayed, should be excluded.

3-5. Others

Identification of language-related sites by fMRI might be useful to limit the area that has to be explored by intraoperative mapping.[118] Furthermore, assessing the courses of nerve fibers adjacent to the lesion using tractography is useful when subcortical mapping is necessary.[119-121]

Table 2 Tasks to be used for language mapping by electrical stimulation

Basic tasks	
	Naming
	Counting
Additional tasks in accordance with brain regions	
Frontal lobe	Oral diadochokinesis (repetition of "pa/ta/ka")
	Repetition
	(Verb generation)
Temporal lobe	Repetition
	Naming from verbal descriptions
	Sentence completion
Parietal lobe	Reading
	Repetition
	Naming from verbal descriptions
	Sentence completion

4. Intraoperative mapping

4-1. Electrical stimulation

Cortical stimulation should be performed using bipolar (interpolar distance: 5 mm) or unipolar probes for electrical stimulation. For stimulation, a 0.2-to 1-ms biphasic square wave and a frequency of 50-60Hz should be used. In using electroencephalography, the presence of afterdischarge should be monitored. The stimulus intensity should be initially set at 1 mA, and gradually increased to 15 mA unless afterdischarge, language impairment, or other neurological symptoms are induced. The stimulus duration should be 3-5 sec: Before the task presentation until the completion of presentation (Fig. 7). It is desirable to present the language tasks at regular intervals so that the neurosurgeons get used to the timing of electrical stimulation. Furthermore, preparations should be made so that the neurosurgeons can confirm the timing of line drawing presentation for visual naming tasks by screens or signal sounds. Mapping with electrical stimulation is performed at all sites around the lesion, and the area adjacent to a resection line must be intensively investigated. To prevent the afterdischarge, the interval between electrical stimulation should not be too short or the same area should not be stimulated repeatedly.

The same area should be electrically stimulated at least twice in a single language task, and the area eliciting reproducible language impairment is identified as the language area. Thus, the appearance of ≥ 2 episodes of language impairment per 3 stimulation sessions is established as a criterion.

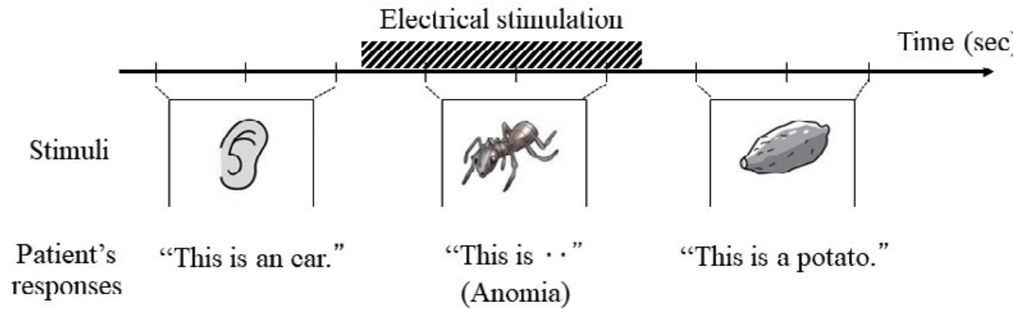

Fig. 7 Timeline of language tasks (visual naming) and electrical stimulation.
For visual naming, start electrical stimulation before line drawings appear and continue it for 3-5 seconds until the line drawings disappear with the patient's response. When the interval of the line drawing appears, the most appropriate time should be established in each patient. This figure shows that the patient's response was impaired only during electrical stimulation (shaded area) (edited by the Japan Awake Surgery Conference: Guidelines for Awake Craniotomy, IGAKU-SHOIN, 2013; p45 was modified).

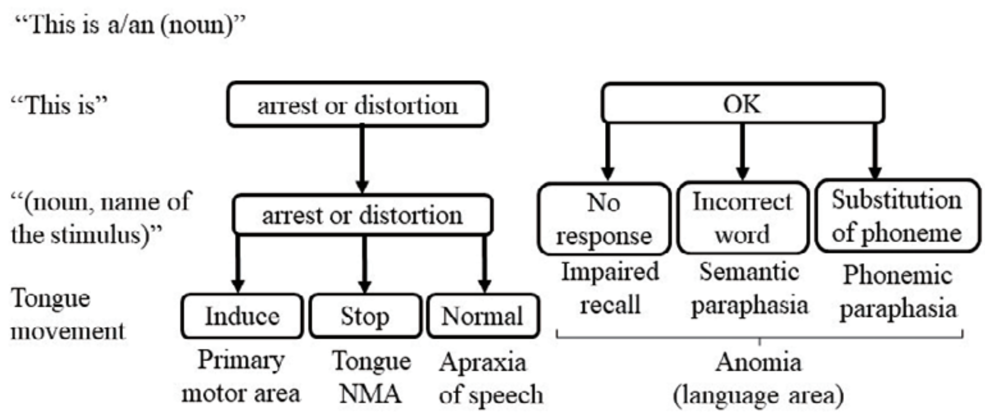

Fig. 8 Differentiation of symptoms in the naming task.
Instruct the patient to answer the name of the presented stimulus with the carrier phrase "This is ...." Examine whether the patient cannot say only names or whether they also cannot say "This is....', If the patient cannot say "This is," tongue movement should be examined.
NMA = Negative motor area

4-2. Cortical language mapping

Among the language tasks during awake surgery, the visual naming task is the most commonly used for the following reasons: naming disorder appears regardless of the type of aphasia; naming is associated with a broad neural network involved in language; and visual naming can be conducted in a limited time during surgery.

The language areas are determined by naming alone in some institutions,[122,123] but many studies adopted a combination of naming and counting.[124,125] A study proposed combining several language tasks according to mapping sites.[126] However, there has been little experience regarding tasks other than naming and counting during awake surgery, and their associations with functional prognosis have not been sufficiently investigated.[127] The basic and primary language tasks to be used following the sites are presented in Table 2.

1 Visual naming

Present line drawings or photos (on paper or a monitor) at the interval determined preoperatively for each patient and instruct the patient to name them using a carrier phrase like "This is···."[53]

Patients who can say the phrase "This is ..." fluently but not the name or answer incorrectly (paraphasia) are regarded as having anomia. Meanwhile, if the patient cannot even say "This is ...," the condition is considered speech arrest and should be differentiated from dysarthria or negative motor areas (Fig. 8).

Concerning the sites where speech arrest/delay appeared, ask the patient what symptoms they experienced (for example, cannot move the tongue, the tongue becomes numb). Then, assess whether or not the sites are primary motor areas or negative motor areas related to articulation. Stimulation of the primary motor areas induces muscular contraction, leading to lip or tongue movement regardless of the patient's intention. If the negative motor areas are stimulated while making the patient continue left-right tongue move-

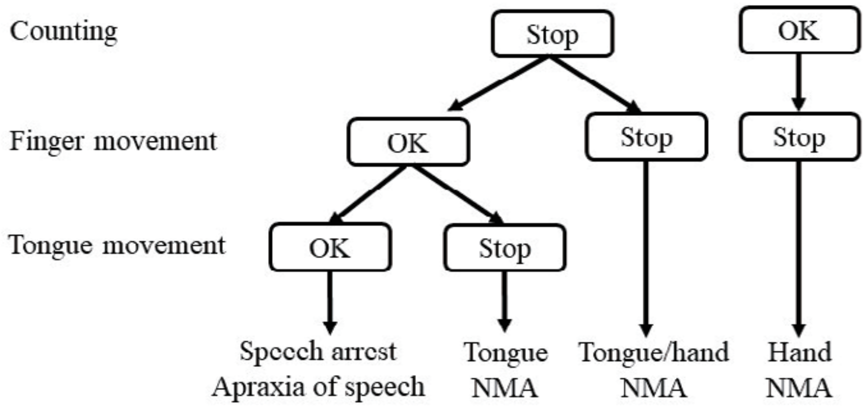

Fig. 9 Simultaneous tasks of counting and hand movement (prepared following Reference 13).
When counting stops without hand motor arrest, administer electrical stimulation of the same site during tongue movement. NMA = negative motor area

ment, motor arrest may occur. When the negative motor areas are stimulated, movement of the fingers other than the tongue also stops. When the language areas are stimulated, movement induction and influence on simple tongue motions are absent.

2 Counting

Perform electrical stimulation while asking the patient to count from 1 to 30 at approximately one number per second. After the patient reaches 30, they must begin from 1 again. Identify the sites where stimulation leads to speech abnormalities of (arrest, delay, dysarthria). The primary motor areas can be differentiated from the negative motor areas when speech arrest is present using the above methods. This procedure is especially useful in patients with frontal lobe foci. A study proposed a method to optimize the distinction between motor arrest, speech arrest, and anomia by combining upper limb movement, counting, and naming tasks (Fig. 9).[128]

3 Other tasks

The following tasks are sometimes used following the site of mapping. Considering the patient's condition and the time available for mapping, tasks should be carefully selected. Even when any task is selected, it should be confirmed that the patient can answer correctly before surgery.

(a) Repetition

Before surgery, confirm how many syllables the patient can repeat and instruct them to repeat a word/sentence of the length. If repetition impairment is absent, the patient can repeat approximately 17 syllables.

(b) Verbal diadochokinesis

Repetitive utterance of the same sound "pa pa pa…" or different sounds "pa/ta/ka/pa/ta/ka/pa/ta/ka…" should be performed. If same-sound repetition is possible despite poor repetitive utterance of different sounds, it is considered speech apraxia (anarthria).

(c) Verb generation

Show the patient a picture involving an action and instruct him/her to answer "He is ◯◯ ing"[129,130] or say a relevant verb by presenting a noun. Verb generation is associated with the frontal lobe.

(d) Naming from verbal description/sentence completion (auditory comprehension and word-finding abilities)

Instruct the patient to answer a noun after hearing verbal explanations or add a word to complete a sentence. For example, short sentences are used: "What is an animal that says bow wow? (dog) " and "The sun sets in the … (west)." As two aspects of language functions are involved, auditory comprehension and word-finding, abnormalities are induced by electrical stimulation at sites different from visual naming.[131] To examine auditory comprehension, verbal commands may be used to ask the patient to perform simple facial and hand movements that can be moved even during surgery.

(e) Reading

Words and sentences are presented visually to test oral reading and reading comprehension skills.

4-3. Subcortical language mapping

Subcortical language mapping is necessary when resecting an area immediately below the cortex, the language area with nerve fibers associated with language.[132] While proceeding with resection, free conversations or naming tasks is continued. If an abnormality in speech or word finding is suspected, mapping by electrical stimulation could be performed using a task in which an abnormality was induced on adjacent cortical stimulation. The intensity of electrical stimulation should be equal to or slightly greater than that of cortical stimulation. As described for cortical stimulation, abnormalities by subcortical electrical stimulation should be evaluated.

4-4. Mapping of cognitive functions other than language

Concerning the mapping of cognitive functions other than language, functional mapping of the right hemisphere has been reported.[133,134] However, the association between the results of intraoperative functional mapping of cognitive functions other than language and functional prognosis after surgery must be clarified. It should be systematically examined in the future. Currently, the clinical validity of mapping cognitive functions other than language in awake craniotomy has not been established. In some institutions, mapping of cognitive functions other than language is performed as neuroscientific research. It is not clinically recommended to map various cognitive functions other than language in institutions new to awake craniotomy.

Informed Consent

The patients/participants provided their written informed consent to participate in this study and for the use of their facial photographs in this article for publication.

Conflicts of Interest Disclosure

None

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Appendix: Guidelines Committee of the Japan Awake Surgery Conference

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