2. Basic policy

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

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

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

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

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

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

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

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

[Commentary]

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

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

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

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3. Premedication

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

[Commentary]

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

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

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

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4. Basic monitoring and preparation

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

[Commentary]

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

There have been reports of air embolism during awake surgery. Especially when surgery is performed under spontaneous respiration without an LMA, caution is required. In this case, end-tidal carbon dioxide is not so useful as described above, and it is difficult to determine whether changes of saturation of peripheral oxygen result from worsening of respiratory status or air embolism.[2,5] Upper airway obstruction causes lower negative intrathoracic pressure and may result in increased risk of air embolism. Although a bispectral index (BIS) monitor is generally considered to be useful, its value is limited

and is not strongly recommended in the field of neurosurgical anesthesia. There have been reports that a BIS monitor is useful even if placed at sites other than the forehead. However, because shaving of the head recently tends to be minimized, the site where the monitor can be placed is actually limited to the forehead. Even if a pediatric BIS sensor is used, disinfectant or blood often enters the connections of the sensors and interferes with analysis. In addition, a BIS monitor is mainly useful on emergence, and its value before that is limited by contamination from electromyogram signals and noise from electric scalpels used during craniotomy.

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

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

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5. Admission, induction, and local anesthesia

i) Initiate oxygen delivery after validation of the vital signs with a patient monitor.
ii) Induce anesthesia with only propofol, or in combination with fentanyl/remifentanil. A target-controlled infusion (TCI) system should be used for propofol administration to precisely manage the level of sedation. The administration of fentanyl before emergence should be minimal.
iii) Maintain general anesthesia under spontaneous respiration with a facemask, or under assisted/controlled ventilation after insertion of an LMA.
iv) Insert a urethral catheter.
v) Provide effective analgesia with local anesthetics by infiltration at the site of skin incision, and/or by selective nerve blocks of, for example, the supraorbital nerve and the greater occipital nerve. Ropivacaine is commonly used as a long-acting local anesthetic.

[Commentary]

Management of general anesthesia with inhalation anesthetics is ineffective when the airway is poorly established. The main impediments are uncertain delivery of the anesthetics and hazardous contamination of the operating room with the anesthetics. Propofol should be used as a hypnotic agent. Propofol is an intravenous anesthetic drug that permits faster and clearer emergence than inhalation anesthetics, which affect the electroencephalogram and sometimes induce excitement at

emergence from anesthesia. A TCI system can reasonably be used for propofol in order to maintain an optimal hypnotic level by adjusting the effect-site concentration of the agent, as the sedative effect depends on the effect-site concentration. In the case of anesthetic management without the TCI system, the propofol administration should preferably be managed by continuous infusion combined with repetitive injection based on the effect-site concentration calculated with pharmacokinetic simulation. Opioids are sometimes used for sedation, but give some residual effects to the consciousness level after emergence. Remifentanil is therefore suitable in the management of strong surgical stimulation before emergence, as its effect rapidly disappears. It is also reasonable to administer small dose of fentanyl repeatedly, expecting only a slight residual analgesic effect.

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

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

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6. Before emergence

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

[Commentary]

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

During the period of strong surgical stimulation, including scalp incision, muscle detachment, and removal of the bone flap and dural incision, provide adequate sedation and analgesia, and discontinue propofol on completion of dural manipulation.[2] Body movement sometimes occurs during emergence as with other surgical anesthesia practice. Because sudden body movement can be more harmful when the skull is fixed with head pins and opened, sufficient vigilance is required and anesthesiologists should be prepared to control body movement. Anesthesiologists should promptly control major changes in circulatory and respiratory systems,

which often occur during this period.[3] When a gastric tube or LMA is used, check spontaneous respiration and remove on emergence. Due to restlessness, the patient may not remain still and cooperate with functional tests.[1] If restlessness is considered to be caused by excitation, pain, poor posture, low temperature, residual anesthetic, or a painful urethral catheter, deal with the cause. If the cause is unknown or cannot be controlled, after discussion with the attending surgeon, intraoperative emergence may be abandoned and surgery may be discontinued or performed under general anesthesia.

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7. Awake period

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

[Commentary]

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

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

The incidence of convulsions during awake craniotomy depends on the underlying disease and is reported to be approximately 0–24%.[2,8] Convulsions are more likely to develop during electrical

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

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8. Reinduction and completion of craniotomy

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

[Commentary]

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

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9. Emergence and discharge

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

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

[Commentary]

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

III. LANGUAGE ASSESSMENT DURING AWAKE CRANIOTOMY

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

[Recommendation]

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

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

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

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

[Commentary]

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

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

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

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

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

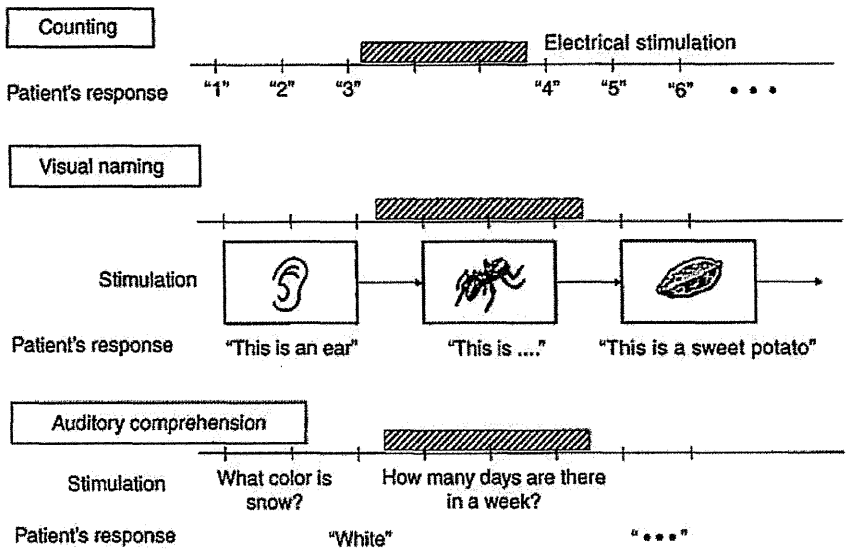

Fig. 5 Flow chart of language tasks. Initiate electrical stimulation before presenting the language tasks.

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

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

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

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

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

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

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2. Task details

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

Table 2 Examples of questions used to test auditory comprehension

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

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

Appendix: Guidelines Committee of the Japan Awake Surgery Conference

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CASE REPORT

Neurol Med Chir (Tokyo) 52, 439–442, 2012

Ruptured Aneurysm With Delayed Distal Coil Migration Requiring Surgical Treatment

—Case Report—

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Abstract

A 64-year-old woman with subarachnoid hemorrhage manifesting as sudden onset of severe headache visited our hospital on post-onset day 8. Diagnostic cerebral digital subtraction angiography revealed an aneurysm located at the left internal carotid-anterior choroidal artery with diffuse cerebral arterial spasm. Coil embolization was selected because of diffuse spasm in spite of parent artery elongation at the extra-cranial portion. A small portion of the coil migrated to the parent artery, but coil embolization was successfully completed. The patient developed delayed spasm, which required arterial fasudil hydrochloride injection. After the acute phase of subarachnoid hemorrhage, the patient's symptoms disappeared. However, on day 24 after subarachnoid hemorrhage, the patient showed right hemiparesis and total aphasia, and skull radiography revealed that the migrated coil had moved into the M1 portion of the left middle cerebral artery. Craniotomy was performed to retrieve the coil and clip the aneurysm neck. However, the migrated coil could not be retrieved because of adhesion to the arterial wall. Delayed coil migration is very rare in the chronic phase.

Key words: subarachnoid hemorrhage, coil embolization, delayed coil migration, clipping, complication

Introduction

The International Subarachnoid Aneurysm Trial (ISAT) is the only multi-center prospective randomized clinical trial, considered the gold-standard in study design, comparing surgical clipping and endovascular coiling of ruptured aneurysm. The ISAT found that patients equally suited for both treatment options achieved substantially better outcomes after endovascular coiling treatment than after surgery in terms of survival-free disability at one year. However, the coiling technique is technically developing and continues to carry risks of unexpected complications. Coil migration is one of the rare complications, but might be related to poor functional outcome. Therefore, evaluation techniques such as volume embolization ratio (VER) and new embolization devices have been developed to improve aneurysm stability after endovascular treatment with platinum coils.

We describe a case of bizarre coil migration in a patient with a ruptured internal carotid-anterior choroidal artery aneurysm treated by surgical excision of the migrated part for rescue treatment.

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Case Report

A 64-year-old woman visited the emergency service of Nayoro City Hospital because of severe headache persisting for a week. She had suffered sudden onset of headache and nausea for 8 days. Head computed tomography (CT) demonstrated residual clot in the subarachnoid space (Fig. 1A, B; Fisher group 3), and the diagnosis was subarachnoid hemorrhage (SAH) on the 8th day after occurrence (Hunt and Kosnik grade 2). Emergent angiography revealed an aneurysm at the left internal carotid-anterior choroidal artery (4.5 × 5.4 × 3.2 mm, neck: 3.9 mm) with severe intracranial arterial vasospasm (Fig. 1C). In addition, the internal carotid artery (ICA) in the cervical portion was tortuous and had a loop, which suggested difficulty in accessing the aneurysm by the endovascular approach (Fig. 1D). However, considering the vessel structure anomaly and vasospasm, we selected aneurysm embolization by endovascular coils.

Under general anesthesia, a Slimguide catheter (6 Fr; Medikit, Tokyo) with a 6-Fr sheath was inserted via the right femoral artery and positioned at the proximal portion of the cervical ICA. An Excelsior SL-10® 45 preshaped microcatheter (Stryker Neurovascular, Fremont, California, USA) was carefully navigated to the aneurysm using a Synchro² Soft 0.014 micro guidewire (Stryker Neu-

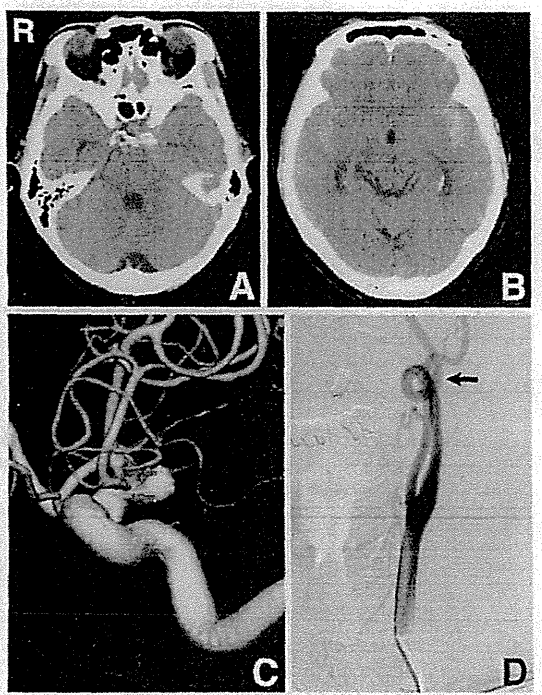

Fig. 1 A, B: Computed tomography scans on admission showing subarachnoid hemorrhage. C: Three-dimensional digital subtraction angiogram revealing an anterior choroidal artery aneurysm. D: Left common carotid angiogram showing coiling of the extracranial internal carotid artery (arrow).

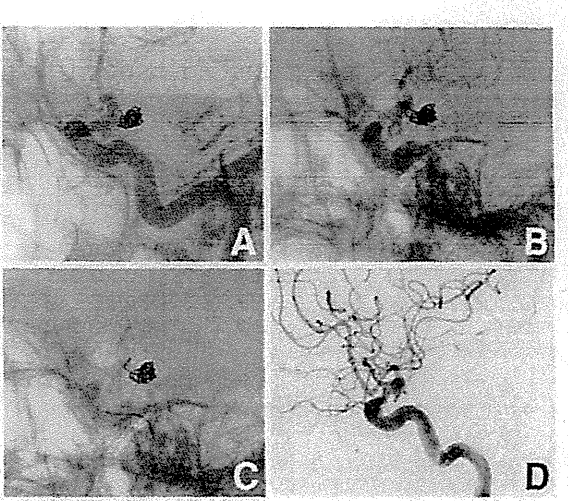

Fig. 2 A–C: Left internal carotid angiograms, lateral view, showing placing the 3rd coil into the aneurysm (A), but a loop protruded into the left internal carotid artery (B). The loop was unraveled and moved into the left internal carotid artery (C). Then, we abandoned detaching the fourth coil. D: Post-coil embolization subtraction image showing only a small neck remnant, so we decided that this operation should be abandoned.

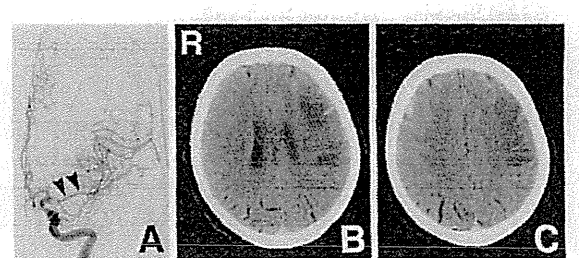

Fig. 3 A: Left carotid angiogram, anteroposterior view, before arterial injection of 30 mg of fasudil hydrochloride on day 10 revealing delayed arterial spasm (arrowheads). B, C: Computed tomography scans on day 10 showing low density areas in the left frontal lobe.

rovascular). For the first coiling, a cage formation was created inside the aneurysm using DCS complex fill 5 × 5 (Cordis Corporation, Bridgewater, New Jersey, USA) (Fig. 2). After successful cage formation, flexible platinum coils were introduced such as DCS mini-complex fill 3 × 4 coils to fill the inner cavity of the aneurysm, and moderate aneurysm packing was confirmed. After intravenous administration of 3,000 units of heparin, GDC UltraSoft 3 × 4 coils (Stryker Neurovascular) were inserted for complete embolization. The last coil was too soft and redundant, resulting in a loop which protruded into the parent artery and pushed the microcatheter away from the aneurysm. Although we tried to achieve complete packing using a shorter coil (GDC UltraSoft 2 × 2), the aneurysm neck was too wide to hold the looped coil, and coil manipulation was severely disturbed by the cervical ICA anomaly. We abandoned further procedures because blocking of the blood flow into the aneurysm had been completed, and we planned to observe the remaining coil loop. The total coil length was 9 cm, and the VER was 17.4%.

After the endovascular treatment, the patient had no neurological deficit. Cerebrospinal fluid was continuously drained with intrathecal administration of urokinase (6,000 units/day) and aspirin (100 mg/day) was orally administered to prevent deterioration of vasospasm. Two days later (10th day after onset), she suffered right hemiparesis and aphasia, and emergent cerebral angiography disclosed narrowing of the bilateral anterior cerebral arteries and middle cerebral arteries (MCAs) (Fig. 3A). Severe vasospasm was considered to be the cause of the symptoms and 30 mg of fasudil hydrochloride was administered via the 4-Fr angiographic catheter. No displacement or migration of the coils in the aneurysm and improvement of vasospasm were confirmed. The symptoms persisted until the 12th day and head CT revealed a low density area in the left frontal region (Fig. 3B, C). Cerebral angiography was repeated and 30 mg of fasudil hydrochloride injected into the left ICA for symptomatic vasospasm. The coil shape including the protrusion maintained stable. After the 3rd angiography, she gradually

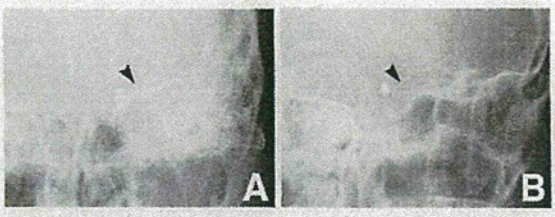

Fig. 4 Skull radiographs, Town's (A) and lateral views (B), on day 24 showing the migrated coil portion (*arrowhead*).

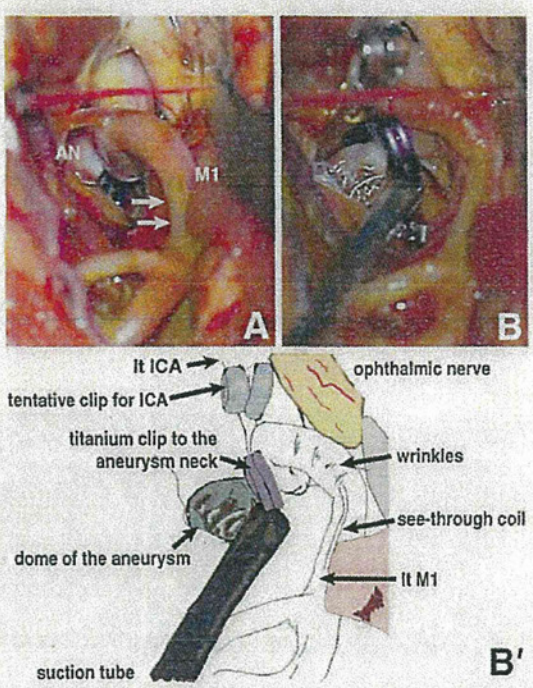

Fig. 5 Intraoperative photographs. A: After opening the left sylvian fissure, the migrated coil was seen through the middle cerebral arterial wall (*arrows*). AN: aneurysm dome, M1: M1 portion of left middle cerebral artery. B: A clip was applied to the neck of the aneurysm, and the cut anterior aneurysm wall and coils were seen. The clip head was opened slightly, to try to retrieve the migrated coil. However, the coil was adhered to the arterial wall. When the coil was pulled, a wrinkle was caused on the wall of the M1 artery. The coil could not be removed. B': Illustration of B. ICA: internal carotid artery.

recovered from the symptoms. In the early morning of the 24th day after onset, severe right hemiparesis and total aphasia suddenly appeared. Emergent magnetic resonance (MR) imaging demonstrated no new lesion on diffusion-weighted images except for old ischemic changes due to the vasospasm. MR angiography showed uncertain signal loss between the peripheral portion of the left ICA and the proximal site of the MCA. Radiography depicted part of the embolization coils was stretched and

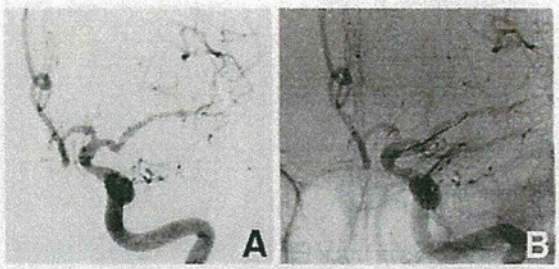

Fig. 6 Left internal carotid angiograms, anteroposterior view, showing no aneurysm in the digital subtraction image (A), and the remaining coil and clips (B).

had migrated from the aneurysm neck to the MCA (Fig. 4). Although the symptoms diminished within 6 hours without special treatment, we decided to retrieve the migrated part of the coils by open surgery, to avoid embolic events or arterial wall injury and aneurysm re-rupture.

The left ICA and the aneurysm were exposed by left fronto-temporal craniotomy and part of the migrated coil was observed between the ICA top and proximal MCA (Fig. 5). After temporary clips were placed at the proximal and distal sites of the aneurysm on the ICA, the translucent aneurysm sac was opened for complete removal of the coils. However, the entire coil was impossible to withdraw because of severe adhesion between the migrated part and the MCA arterial wall. As the coil was pulled, a wrinkle was caused on the wall of the M1 artery. Therefore, we removed only the coils in the aneurysm, preventing further coil migration, since aggressive manipulation might worsen arterial wall injury. Aneurysm clipping was achieved with 2 titanium clips (Yasargil 720T; Aesculap AG, Tuttlingen, Germany) and the coil remnant was cut at the aneurysm neck inlet, leaving the migrated part in the M1. Postoperative angiography demonstrated 8 mm of the remnant coil remained between the ICA top and proximal MCA with complete aneurysm clipping (Fig. 6). Six months after the open surgery, she had suffered no new neurological deficit, and the remnant coil had not migrated or caused any new ischemic event.

Discussion

The present case of SAH caused by a ruptured aneurysm and associated with severe vasospasm initially treated with endovascular embolization. Although serial angiography showed no deformity or dislocation of the coils during the acute period, coil migration was found more than 3 weeks after the embolization. The superiority of coil embolization over clipping for ruptured aneurysms within 2 years after onset has been proposed. In particular, the endovascular procedure causes fewer ischemic complications during the vasospasm phase in patients with SAH.[1,7] In this case, coil embolization was appropriate to avoid re-bleeding in the acute period.

In general, migration of the coil outside the aneurysm is caused by stopping packing while the coil partially pro-

trudes. Other causes are wide aneurysm neck or loose packing of coils. We could not help ending in such a situation in the acute stage. If a little more coil can be packed into the aneurysm tightly regardless of the coil type, this complication would not occur. Assisting techniques with balloon or stent are effective and used worldwide to reduce migration of the coil. On the other hand, delayed coil migration after embolization has been recently reported. There are two main reasons for the migration. One reason is the stent technique used with the embolization.[2,4] Although stent devices are expected to stably support embolizing coils, fine coils might escape from the stent struts with loose mesh design. The other reason is the combination of the ultrasoft coil, which was recently developed for better embolization, and the balloon remodeling technique.[3,5,8] This technique may simply compress the ultrasoft coils in the coil complex by the balloon. In our case, no stent, balloon, or ultrasoft coil was used. Therefore, our endovascular strategy had less risk of coil migration than previous methods. Coil migration usually occurs during or within a day after the embolization procedure (acute phase). Since vessel endothelium cells might proliferate within a week after treatment, the coils might become stable in the subacute phase. Delayed coil migration, as experienced in the present case, is relatively rare. Surgical removal failed to retrieve the migrated coils because of severe adhesion related to endothelial proliferation and inflammation on the arterial wall. On the basis of our experience, we have to carefully check for coil migration, even some weeks after completing treatment with no negative occurrences.

Our patient had two associated pathological conditions, vasospasm and tortuous cervical ICA. In particular, the tortuous cervical ICA hindered balloon remodeling and fine control of the microcatheter. As a result, the coil packing ratio did not reach adequate values. Such multiple factors might still make endovascular treatment complex. Catheterization to treat peripheral severe tortuous arteries is difficult. Treatment must be planned on the assumption of difficulty in using a balloon in the acute phase, and the possibility of clipping. To employ catheterization to complete treatment without a balloon, we should use a triple coaxial system, such as the Cerulean catheter (Medikit), or the head position should be rotated beforehand to release coiling of the cervical ICA.

The coil placed in the aneurysm was displaced and embolization became incomplete, so we performed craniotomy and clipping to prevent re-rupture. Coil embolectomy, vessel repair, and clipping of the aneurysm are necessary for surgical treatment after such distal coil migration. Coil embolectomy and neck clipping is the optimum treatment strategy. However, removal of intravascular coils is not always possible due to adhesion to the arterial wall. Symptomatic arterial stenosis has been caused by a coil which migrated into the peripheral artery during an operation.[8] Therefore, surgical management that considers even revascularization procedures such as superficial temporal artery-MCA bypass is necessary. Coil manipulation should be carefully performed because the dynamics of coils inserted into the human body are difficult to predict.[9,10]

The present patient with SAH was treated with coil embolization in the spasm phase, but part of a protruding coil migrated distally in the chronic phase. Although endovascular treatment is useful for SAH in the spasm phase, application may be difficult in some cases and should be carefully performed. If a protruding coil is detected at the finish of endovascular treatment, we should consider additional endovascular treatment in the chronic stage. Surgical treatment of a migrating coil may be difficult due to adhesion to the vascular wall.

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Invited review

Publication criteria for evoked magnetic fields of the human brain: A proposal

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Magnetic fields
Publication criteria
A region of interest
A root mean-squared (RMS) waveform
A contour map
A normal database

HIGHLIGHTS

- In this article, we propose publication criteria for studies of an evoked or event-related magnetoencephalogram (MEG).
- The criteria include original waveforms and a root mean-squared waveform in a region of interest with a contour map at an appropriate time.
- This three set of presentations will allow comparison of evoked or event-related MEG signals recorded with different MEG sensors.

ABSTRACT

Magnetoencephalography (MEG) is a record of the magnetic fields produced by the electrical activities of the brain using MEG systems. There are three types of sensors for MEG systems: magnetometer and two types of gradiometer. Among them, two types of gradiometer, axial and planar, have been used worldwide. Unfortunately, the waveforms recorded by the two types of gradiometer are often different from each other. This poses a serious problem in comparing and evaluating the data from the two gradiometers. We consider that the MEG study should be published in a way that allows other workers using different types of gradiometer to evaluate and replicate the results of MEG studies. There have been, however, no publication criteria for reports of studies on stimulus-evoked or event-related magnetic fields in human subjects. In this article, we propose publication criteria for evoked or event-related magnetic fields of the human brain: original waveforms of selected channels covering a region of interest, a root mean-squared (RMS) waveform and a contour map at an appropriate time.

Contents

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1. Introduction

Magnetoencephalography (MEG) is a totally non-invasive technique for providing spatially and temporally accurate information about the distribution of current sources in the cerebral cortex. Spatial resolution of MEG is considered superior to that of scalp electroencephalography (EEG), because magnetic fields recorded outside the scalp are unaffected by the electrical and geometrical properties of brain, skull and scalp. MEG can visualise travelling impulses from the thalamus to the primary somatosensory cortex (Kimura et al., 2008), but it has been believed insensitive to radially oriented currents; activated area confined to the cortex of a certain geometry that produces radially oriented currents, such as gyral cortices of the lateral surface of the brain, can be overlooked in MEG records. As to clinical application of MEG for epilepsy, MEG is reportedly limited to detect spikes originating from mesial temporal lobes based on a combination study of electrocorticogram (cortical EEG) and MEG (Agirre-Arrizubieta et al., 2009). In this sense, one should be modest about accuracy regarding the spatial resolution of MEG. Further, as compared to EEG, MEG has a great disadvantage of much higher cost for maintenance such as keeping an appropriate level of liquid helium; a recycling system for helium at each MEG facility is awaited from an economical and ecological point of view.

Nevertheless, the total non-invasiveness of MEG has the benefit of repeat examinations in patients suffering from epilepsy or progressive neurodegenerative diseases and children with such diseases. However, MEG has not been either widely used or reached a high status for a functional brain mapping method as yet, though the number of MEG facilities was gradually increased worldwide (more than 140 in the year 2011). It is more than 30 years since MEG was introduced to basic and applied neuroscience, but standardisation of the MEG technique, which includes a recording or stimulating procedure of MEG and publication criteria of results, has not been established. This may have caused MEG to meet with severe criticism from inside and outside the MEG community; among the published papers on MEG, though novel, some articles are not rigorous enough because no original waveforms of MEG but a root mean-squared (RMS) waveform alone or the traces obtained from a couple of sensors (out of 100–200 sensors!) are presented as figures or because, without any MEG waveforms, the location of equivalent current source superimposed onto the subject's brain magnetic resonance imaging (MRI) alone is shown. It seems as if authors of such kind of papers wanted to avoid the results from standing up to a searching scrutiny. Inappropriate presentation of the results in experimental papers does not give the details of how the experiments were carried out and what results were obtained and analysed; therefore, other researchers cannot fully evaluate and replicate the data. As a result, since the year 2005 the number of annual original articles on MEG has begun to plateau.

There are other embarrassing situations in analysis of MEG; one is an inverse problem. At the time when MEG was introduced to neuroscience, a single dipole modelling method was developed to compute localisation of the equivalent current source. It works well for analysing the initial cortical response of stimulus-evoked MEG and localising the equivalent current source. When activated areas are overlapping in a time course or when two or more areas are simultaneously activated, recorded MEG waveforms become more complicated and difficult to analyse by using a single dipole method. Then, many algorithms to calculate the localisation of the multiple equivalent current sources have been published (e.g., for minimum norm estimates, see Hämäläinen and Ilmoniemi, 1994; for spatial filtering, see Taniguchi et al., 2000; and for hierarchical Bayesian estimation, see Sato et al., 2004), but unfortunately, one cannot judge which kind of method among the previously published algorithms is the best to use as their accuracy or correctness has not been proven yet by a proper method between the researchers. In fact, a recent bibliographic survey on the clinical application of MEG for epilepsy has disclosed that a single dipole method is commonly used to verify accuracy of MEG in localisation of epileptogenesis as compared to other methods such as cortical EEG (Hirata et al., 2012). Another problematic issue in MEG is that several different sensors for MEG systems have been developed to pick up magnetic flux from the outside of the brain: a magnetometer and two types of gradiometer. Among them, two types of gradiometer, axial and planar, have been used worldwide. However, the waveforms of individual MEG sensors inherently differ between the two types of gradiometer; for the planar gradiometer (Elekta Neuromag VV (Elekta Oy, Helsinki, Finland)), the response with the maximal amplitude is recorded from the sensor located just above the equivalent current source; for the axial gradiometer, the maximal positive and negative responses are obtained from a pair of sensors apart from each other that sandwiches the equivalent current source. Whereas a unit of amplitude of EEG waveforms is the 'micro Volt' regardless of which EEG equipment is used for recording, a unit of amplitude of MEG waveforms differs between the two types of gradiometer: 'femto Tesla' in the axial gradiometer and 'femto Tesla/cm' in the planar gradiometer. Therefore, when looking at responses from individual sensors, original MEG waveforms alone are inadequate for evaluating and replicating evoked-MEG responses. As a result, users of an axial gradiometer sometimes cannot appropriately evaluate the results of MEG recorded from the planar gradiometer, and vice versa. Furthermore, as previously described, some researchers of the MEG demonstrate an RMS waveform alone in an article (see Haueisen et al., 2000); and others do not show any waveforms (see Mogilner et al., 1993; Elbert et al., 1995; Braun et al., 2000; Breier et al., 2004; Periáñez et al., 2004). Therefore, neuroscientists or physiologists both familiar and unfamiliar with MEG cannot fully evaluate some of the results on MEG that have been published. Perhaps, the situations described above have made it difficult to conduct a multicentre study on MEG or to expand clinical application of MEG testing. To make the MEG become a more favourable and reliable tool for mapping human brain function, we consider it obligatory to find a way to present MEG data common to the two different MEG systems, to build a consensus on the minimum requirement for publication criteria of MEG data and thereby, to allow workers to compare and replicate the results of published MEG data easily.

2. Recommended representation of evoked MEG data

For the analyses of stimulus-evoked MEG, we use the following information: original waveforms obtained from sensors, the iso-

contour field distributions of the magnetic field representing flux-out and flux-in at a certain time, orientation and location of an equivalent current source that produces a recorded magnetic field and results of spatial filtering such as Beamformer (Sekihara et al., 2001) and LORETA (Pascual-Marqui et al., 1994). Among various methods of MEG-data presentation, we consider it preferable to represent original waveforms of selected channels covering a region of interest, an RMS waveform in the region of interest and an isocontour field map at a certain time for evoked MEG as this three set of presentations will be shared between the axial and the planar gradiometer systems.

2.1. The need for presenting raw records: original waveforms of selected channels covering a region of interest and an RMS waveform in the region of interest

As emphasised in the publication criteria for studies of evoked potential (EP) (Donchin et al., 1977), an absolute acceptance criterion for all papers on stimulus-evoked MEG should be that they include actual records of averaged MEG waveforms. It is not required to publish all data of experiments; it is the authors' responsibility to select data to be presented, but figures should honestly reflect the quality of the data collected. It is also important to represent replications of the records under the same conditions to confirm reproducibility of the results and indicate the quality of the recording process. For EEG recording, as electrode placements are determined according to the International 10–20 system and are unchanged during experiments, it has been recommended to show duplication of representative waveforms at a certain electrode placement for two or more trials: for example, superimposed waveforms recorded from the Cz electrode for auditory evoked or event-related potentials (ERPs) or those obtained from the C3/4 electrode for somatosensory-evoked potentials after median nerve stimulation. In the case of recording MEG, sensor placements are fixed on the dewar but not on the subject's head so that sensor positions relative to the subject's head are changeable from one trial to another when the subject moves his or her head even a little within a dewar during an experiment. It is, therefore, quite difficult to choose a particular sensor channel for demonstrating a representative MEG waveform and to show superimposed records obtained from the particular sensor channel. In addition, as described previously, the response waveforms of individual sensors inherently differ between the planar and the axial gradiometer. For the planar gradiometer, the response with the maximal amplitude is recorded from the sensor located just above the equivalent current source; polarity change of the waveform directly indicates the opposite direction of the equivalent current dipole. For the axial gradiometer, the maximal positive and negative responses are obtained from a pair of sensors apart from each other that sandwiches the equivalent current source; a polarity change from positive to negative in the waveform at a certain sensor indicates the change from magnetic flux-out to flux-in across the scalp. Hence, to demonstrate raw MEG records that can be shared between users of a planar gradiometer and those of an axial gradiometer, we suggest that one should represent original waveforms of selected channels covering a region of interest in the case of stimulus-evoked or event-related MEG. When they are presented as superimposed records, the figure will reflect the quality of the data collected. In addition to original waveforms of selected channels covering a region of interest, we suggest that an RMS waveform should be presented because it easily shows culmination of a stimulus-evoked MEG response. To show replication of the results under the same conditions, two sets of the superimposed raw records obtained from selected channels covering a region of interest will be presented; or the calculated RMS waveforms for two trials can be superimposed.

2.2. The need for presenting spatial distribution of the magnetic field at an appropriate time: an isocontour field map representing flux-out and flux-in at a peak latency of an RMS waveform

The raw traces recorded from individual sensor channels show sequential changes of magnetic fields at their sensor placements; the RMS waveform obtained from selected channels covering a region of interest represents a global time-course of the stimulus-evoked or event-related brain responses. However, analysing spatial distribution of the electromagnetic field at an appropriate time is essential to know which area or areas in the brain are activated. Isocontour field distributions of the magnetic field representing flux-out and flux-in are very informative; when a response consists of a single equivalent current dipole, the isocontour field distributions of the magnetic field represent a pair of flux-out and flux-in; when a response consists of more than two equivalent current dipoles, they may show a complex pattern such as two or more pairs of flux-out and flux-in. Therefore, we suggest that isocontour field maps should be presented at a certain time such as a peak latency of an RMS waveform or at several successive times including an RMS peak.

2.3. Demonstration of examples of somatosensory- or auditory-evoked MEG signals

Fig. 1 illustrates somatosensory-evoked magnetic fields (SEFs) following left median nerve stimulation obtained from a representative subject, using an axial gradiometer system (A) or a planar gradiometer system (B). Looking at a topographic display of recorded MEG waveforms, spatial distributions of maximum and/or minimum responses and shapes of the MEG waveforms in a certain region differ between an axial gradiometer system and a planar gradiometer system. However, superimposed waveforms or RMS waveforms of the right hemisphere obtained by an axial gradiometer system and by a planar gradiometer system are quite similar. So are isocontour field distributions of the magnetic field at the peak latency of N20 m. Another example is demonstrated in Fig. 2 in which auditory-evoked magnetic fields (AEFs) following left ear 1000 Hz tone-burst stimulation are obtained from the subject as in Fig. 1, using an axial gradiometer (A) or a planar gradiometer (B). Isocontour field distributions of the magnetic field at the peak latency of N1 m, superimposed waveforms and RMS waveforms that are obtained by an axial gradiometer system are compatible with those obtained by a planar gradiometer system, though the sensor layout display of recorded MEG waveforms differs between the two systems.

3. Discussion

Stimulus-evoked or event-related changes in the electromagnetic fields of the brain can be extracted from the ongoing spontaneous MEG or EEG by means of filtering and signal averaging. As to ERPs or EPs, the guidelines for recording standards and publication criteria were proposed (Donchin et al., 1977; Picton et al., 2000) and have been recommended by the International Federation of Clinical Neurophysiology (IFCN) (for visual EPs, see Celesia et al., 1993; for auditory ERPs, see Goodin et al., 1994; for somatosensory-evoked potentials, see Nuwer et al., 1994) or by the American Clinical Neurophysiology Society (2006a–d). Further, the recommendations by IFCN for the clinical use of various EPs or ERPs have been updated (Cruccu et al., 2008; Duncan et al., 2009; Holder et al., 2010). As for MEG, the clinical practice guideline for MEG is proposed by the Japanese Society of Clinical Neurophysiology (Hashimoto et al., 2005) and by the American Clinical Magnetoencephalography Society (Bagić et al., 2011a,b; Burgess et al., 2011).

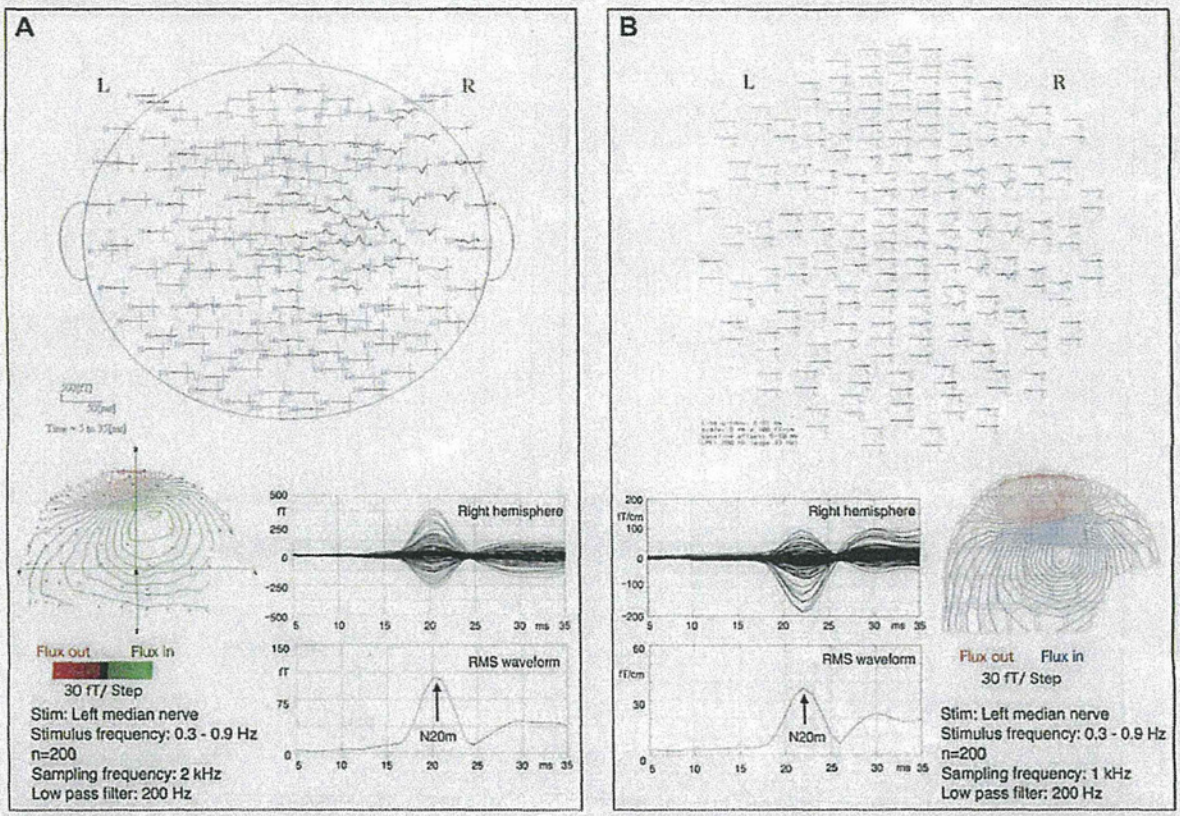

Fig. 1. Somatosensory evoked magnetic fields (SEF) following left median nerve stimulation obtained from a representative subject using an axial gradiometer system (A) (Yokogawa, MEGVision) or a planar gradiometer system (B) (Neuromag, Vector View). Upper column: sensor layout display of SEF waveforms (post-stimulus period of 5–35 ms). Lower column: right lateral view of isocontour field distributions of the magnetic field at the peak latency of N20 m, superimposed SEF waveforms and root mean squared (RMS) waveforms. Note that, although SEF waveforms at individual measurement sites and their spatial distribution differ between the axial and planar gradiometer systems, superimposed SEF waveforms, root mean squared (RMS) waveforms and contour maps are similar to each other.

These guidelines include technical issues in relation to recording and stimulating methods, the majority of which follow the practical standards for EEG, such as EPs and ERPs. Although the publication criteria for EPs emphasise the necessity for raw records of averaged EPs (Donchin et al., 1977; Picton et al., 2000), there have been no publication criteria for MEG: presentation of MEG waveforms as well as analysed MEG data. Here, for the first time we have proposed the publication criteria for stimulus-evoked or event-related MEG as the three set of presentations: original waveforms of selected channels covering a region of interest, an RMS waveform in the region of interest and an isocontour field map at a certain time for evoked MEG. As shown in examples of SEFs and AEFs (Figs. 1 and 2), the three set of presentations will allow investigators of MEG to share the results of evoked MEG. Similar to EPs or ERPs in EEG, the publication criteria for stimulus-evoked MEG or event-related MEG we propose will help not only neurophysiologists to examine patients by means of MEG testing and make a diagnosis of a neurological disease, but also scientists to evaluate and replicate previously published MEG data.

In general, developing a standardised method for data analysis accelerates propagation of a new research technology. In 1990, Ogawa et al. developed a new technique, using functional magnetic resonance imaging (fMRI) to provide focal haemodynamic changes in the brain of humans and animals (Ogawa et al., 1990), but it was not until the statistical parametric mapping (SPM) software was developed as a standardised method for analysis of brain MRI (Friston, 1995) that fMRI was used explosively for mapping the working brain. We think, therefore, that a standardised method for data analysis of MEG, such as the SPM for fMRI, is needed for propagation of MEG. As different types of sensors detecting MEG signals are commonly used, the most practical approach is to transform recorded magnetic signals from the brain into a virtual standard sensor configuration, as has been previously attempted for magnetocardiography (Burghoff et al., 2000). If all recorded magnetic signals from the brain are converted into signals of a virtual standard MEG system, direct comparison of signals obtained from different MEG recording devices will be available. However, apart from the impulse conduction system of the heart, there exists large intersubject variability in the sulci of the brain, confounding the transformation approach for MEG signals. The alternative transformation approach for each subject in which magnetic signals obtained from MEG sensors are converted into signals on the subject brain MRI will avoid intersubject variability in the sulci of the brain. However, this approach inevitably needs the brain MRI of the subject who undergoes MEG testing. In addition, there has been no consensus on building a virtual standard MEG system so that transforming recorded signals to source space via a localisation algorithm, or to signals of the virtual standard MEG system, awaits a general agreement. Currently, we have no choice other than to present signals from the sensors that are fixed within a dewar of an MEG system; the locations and types of the sensors differ among MEG recording devices. Therefore, we consider that our

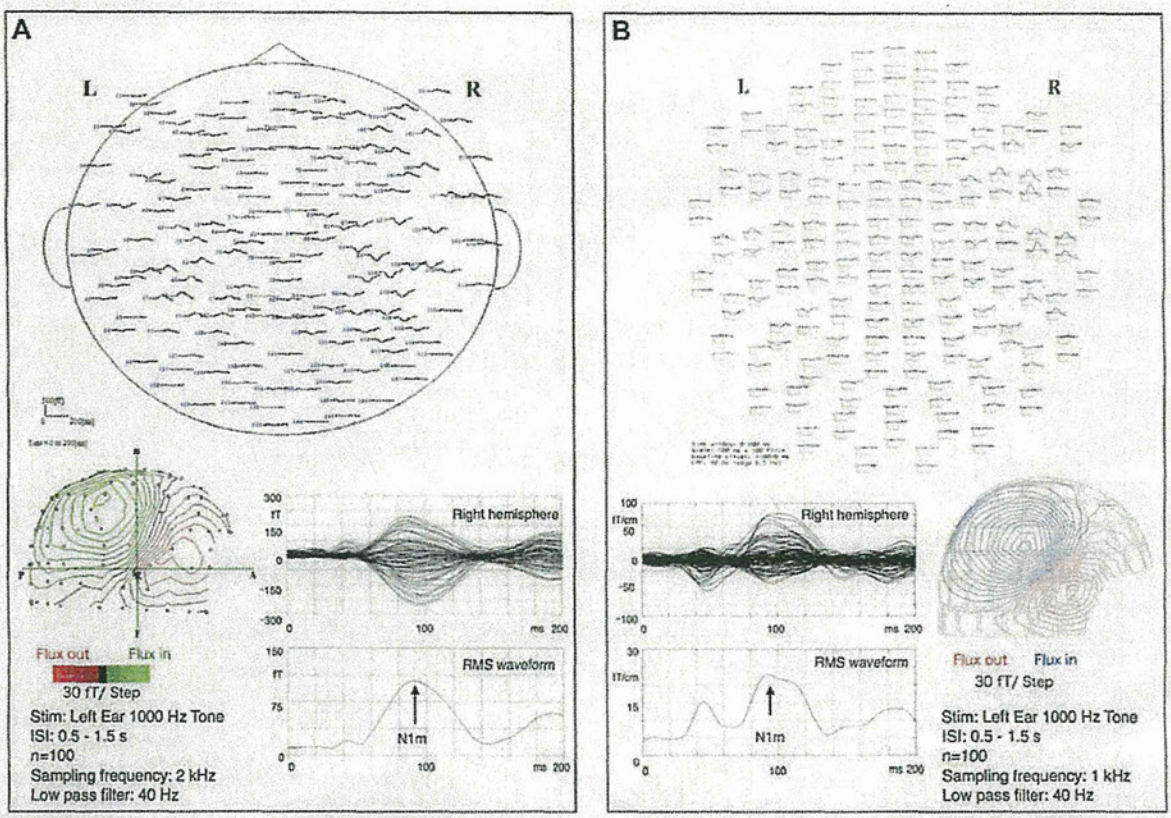

Fig. 2. Auditory evoked magnetic fields (AEFs) following left ear 1000 Hz tone burst stimulation obtained from a representative subject using an axial gradiometer system (A) (Yokogawa, MEGVision) or a planar gradiometer system (B) (Neuromag, Vector View). Upper column: sensor layout display of AEF waveforms (post-stimulus period of 200 ms). Lower column: right lateral view of isocontour field distributions of the magnetic field at the peak latency of N1 m, superimposed AEF waveforms and root mean squared (RMS) waveforms. Note that, although AEF waveforms at individual measurement sites and their spatial distribution differ between the axial and planar gradiometer systems, superimposed AEF waveforms, root mean squared (RMS) waveforms and contour maps are similar to each other.

proposal on publication criteria, comprising original waveforms of selected channels covering a region of interest, an RMS waveform in the region of interest and an isocontour field map at an appropriate time(e.g., an RMS peak), will allow comparison of event-related or stimulus-evoked MEG signals recorded with different MEG recording devices. This will specify minimal acceptance criteria for reports of studies in patients or normal humans. We hope that our proposal should facilitate conducting a multicentre study and building a normal database of stimulus-evoked and event-related MEGs in the near future, and that a standardised diagnostic protocol of MEG based on the normal database will be established, thereby enhancing clinical utility of MEG.

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