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The Development and Application of the Device for Intraoperative Examination Monitor for Awake Surgery

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Intraoperative brain mapping is generally considered as an effective technique for identification of the cortical speech centers during surgery for cerebral gliomas. However, several pitfalls may interfere with correct interpretation of the obtained functional information. To facilitate application of this technique, Intraoperative Examination Monitor for Awake Surgery (IEMAS) was developed by us. View of the patient's face and examination task, level of sedation, view of the surgical field and display of the neuronavigation system can be observed simultaneously on IEMAS. We applied IEMAS in 96 awake craniotomies for gliomas adjacent to the cortical speech centers. In this series true positive intraoperative identification of Broca's area was done in 43 patients, Wernicke's area in 15, and both areas in 2. In 13 cases the functionally preserved speech area was identified within the tumor mass itself. In 26 cases false positive speech arrest due to stimulation either motor (13 cases), or negative motor (13 cases) cortex was noted. In 30 patients continuous monitoring of the speech function during tumor removal revealed appearance of its disturbances, and in 21 of them aggressive resection of the neoplasm was abandoned. Use of IEMAS was effective in determination of the cause of speech arrest, differentiation of true positive and false positive identification of the cortical speech centers, and precise localization of the functioning eloquent cortex with regard to tumor mass itself.

Key Words: intraoperative examination, language area, awake surgery, functional monitoring, functional mapping

Introduction

Contemporary surgical management of intracranial gliomas is directed on the maximal resection of the lesion with preservation of the adjacent functionally-important brain tissue [1)~3)]. However, such a goal is frequently significantly challenged due to non-clear tumor border caused by its infiltrative growth. Additionally, at least in cases of cortical neoplasms, identification of the eloquent brain areas, such as speech centers, may be complicated due to known anatomical variations of their location and possible shift during growth of the neoplasm[4)5)]. It necessitates individual assessment of the functional importance of the cerebral tissue adjacent to the lesion, which can be done either preoperatively, or using intraoperative brain mapping[1)2)6)].

Awake craniotomy showed a great usefulness in cases of gliomas adjacent to the cortical speech centers[7)~9)]. This technique provides the surgeon an opportunity to have a verbal contact with fully anesthetized patient, to control correctness of his or her responses to various tasks during direct cortical stimulation, to identify precisely localization of the Broca's and/or Wernicke's areas and their relationships to the tumor mass, and consequently, to perform maximal possible resection of the lesion without permanent damage of the speech function[5)10)~12)]. Nevertheless, interpretation of results of the intraoperative cortical mapping during awake craniotomy is neither simple nor straightforward, and their application to decision-making on the optimal tumor resection may be rather complicated[13)~16)]. To facilitate the use of this technique, we developed the Intraoperative Examination Monitor for Awake Surgery (IEMAS). The purpose of this paper is to report on the evaluation of our experience with this device in cases of gliomas adjacent to the cortical speech centers.

Materials and Methods

IEMAS was used for functional brain mapping in 96 patients who underwent awake craniotomy for gliomas of various WHO histopathological grades (from I to IV) adjacent to Broca's and/or Wernicke's area, or to the left supplementary motor cortex.

There were 68 men and 28 women. Their ages varied from 19 to 65 years old (median, 40 years old). All surgical procedures were performed in the intelligent operating theater of the Tokyo Women's Medical University[3)17)] equipped with 0.3 Tesla open intraoperative MRI (AIRIS II™, Hitachi Medical Co., Chiba, Japan) and dedicated neuronavigation system (PRSnavi, Toshiba Medical Systems Co., Tokyo, Japan), between January, 2005 and December, 2008. Before surgery, all patients were provided informed consent and fully informed on possible complications of the surgery itself, as well as of intraoperative functional examinations and neurophysiological monitoring.

Intraoperative cortical mapping

In all patients, laryngeal masks were used during anesthesia, and their extubation was performed after completion of craniotomy in advance of intraoperative brain mapping and speech examinations. Cortical stimulation was done with Ojemann Cortical Stimulator (OCS-1, Radionics, USA) with the currency ranged from 1 to 16 mA, output frequency of 50 Hz, and 0.5 ms biphasic rectangular waves. The examination tasks included words' repetition and number counting for the screening purpose, and object naming and verb generation for the diagnostic one.

Fig. 1 Components of the IEMAS
Laptop computer for examiners (a), task display monitor (b), signal circuits (c), and information display monitor (d).

IEMAS and its use during awake craniotomy

IEMAS consists of the (1) laptop computer with which examiner of the cortical functions can select the type of the examination task, (2) a display monitor that shows the task to the patient, (3) signal circuits, which collect and integrate in real-time the intraoperative information from the various sources, and (4) a display monitor that provided the visualization of the integrated data to the members of the surgical team (Fig. 1).

In the laptop computer the various examination tasks, such as naming, reading, and word creation, are stored as digital data. A selected task is projected on the display monitor just in front of the patient's face. This monitor is additionally equipped with a small video camera for monitoring the facial movements, and a microphone for detection of the verbal response during examination. The signal circuits integrate various intraoperative data during brain mapping. The images from the several

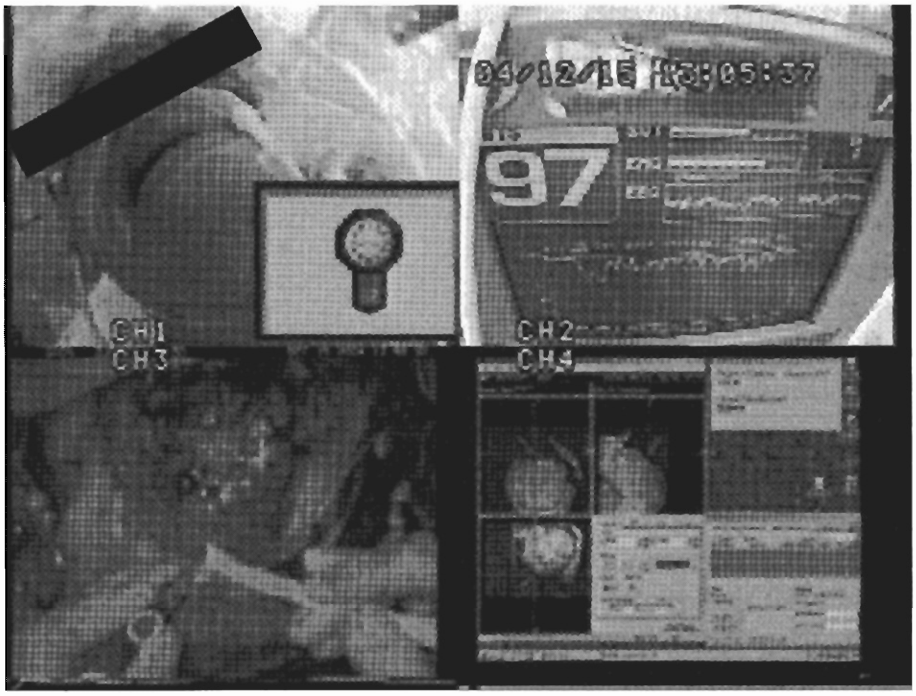

Fig. 2 Real-time integrated intraoperative information displayed on the monitor of IEMAS
View of the patient's face and examination task (Channel 1-upper left), anesthesia parameters displayed on BIS monitor (Channel 2-upper right), view of the surgical field via intraoperative microscope during electrical stimulation of the cortex (Channel 3-lower left), and display of the intraoperative neuronavigation device (Channel 4-lower right).

Fig. 3
Position of IEMAS in the intelligent operating theater during awake craniotomy with intraoperative cortical stimulation for resection of the cerebral glioma.

sources are integrated in real time on the same monitor of the IEMAS. Therefore, the view of the patient's face and the examination task, the level of sedation according to the anesthetic monitor (BIS A1000, Aspect Medical Systems, Inc., USA), the view of the surgical field through the operative microscope, and the display of the neuronavigation system can be observed simultaneously on one screen (Fig. 2). This integrated information can be seen not only on the monitor of the IEMAS itself, but projected on the several in-room liquid crystal displays (LCD), so that all members of the surgical team can share these information.

During surgery, IEMAS was positioned near the operating table and was operated by the examiner of the cortical functions (Fig. 3). The validity of the patient's responses during brain mapping was checked using strict algorithm with assessment of data visualized on the information display monitor of the IEMAS (Fig. 4). The special emphasis was put on the appropriate visualization of the examination task by the patient, sufficiency of his or her awaken-

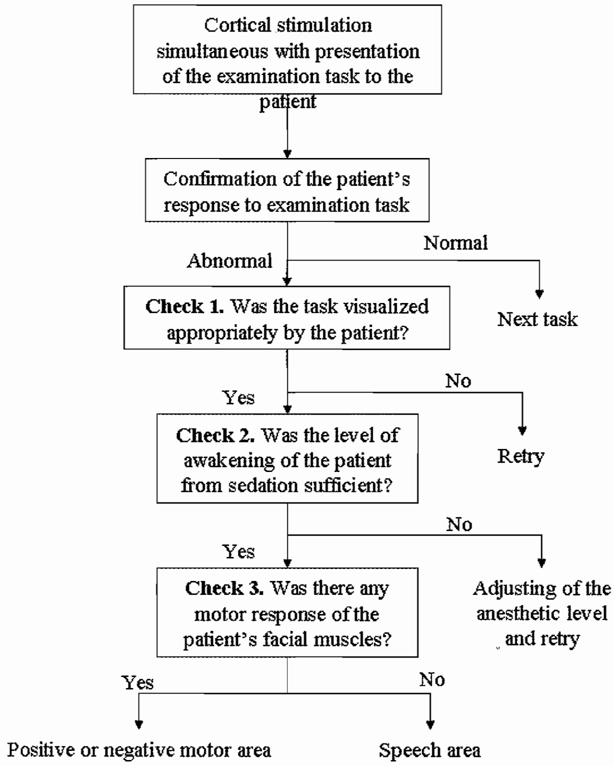

Fig. 4

Algorithm for evaluation of validity of the patient's response during intraoperative cortical mapping with the use of IEMAS.

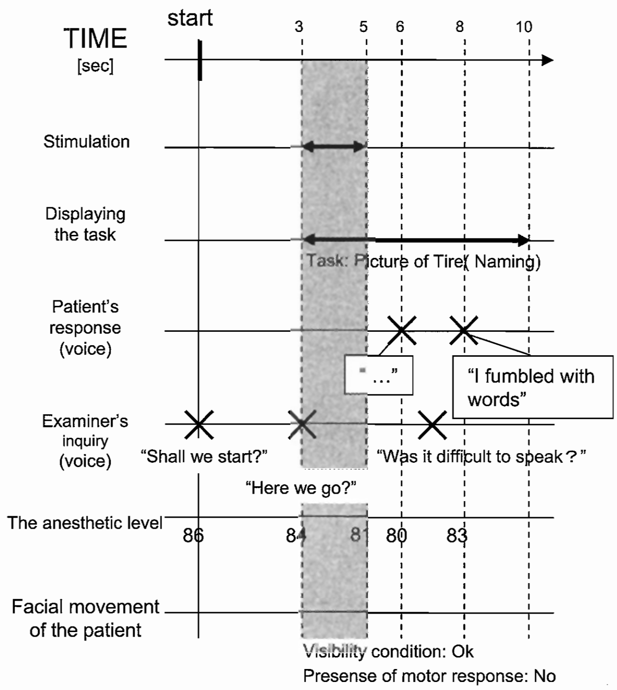

Fig. 5

Example of the time chart of the cortical mapping during awake craniotomy (Illustrative Case 1). All required items can be identified simultaneously either on the monitor of IEMAS or with its sound recorder, which significantly facilitate real-time integrative assessment of the intraoperative information.

ing from sedation, and evaluation of the motor response of the facial muscles.

Results

Intraoperative cortical mapping with the use of IEMAS during awake surgery for cerebral gliomas adjacent to the speech areas was successfully completed in 91 out of 96 patients (95%). In other 5 cases the procedure was interrupted due to either insufficient awakening of the patient from sedation, or development of the epileptic seizure.

In 26 cases, false positive speech arrest due to stimulation either motor (13 cases), or negative motor (13 cases) cortex was noted. Its identification was based on the observed facial muscle contractions around the mouth or deviation of the eyes, which were clearly seen on the monitor of IEMAS. True positive intraoperative identification of Broca's area was done in 43 patients, Wernicke's area—in 15, and both areas—in 2. In 13 cases, the functionally preserved speech area was identified within the tumor mass itself, which precluded aggressive resection of the neoplasm for avoidance of permanent damage of the speech function. In 30 patients continuous monitoring of the speech function during tumor removal revealed appearance of its disturbances (mainly, aphasia). In 21 of these patients, aggressive resection of the neoplasm was abandoned. No permanent postoperative neurological morbidity was observed in 91 patients.

Illustrative cases

Case 1

A 42-year-old man was operated on for glioblastoma located in the inferior frontal gyrus. Intraoperative brain mapping resulted in straightforward identification of the Broca's area, with reproducible speech arrest in response to cortical stimulation during object naming. The verbal response was blocked completely beside production of the unrecognizable sounds during approximately 3 seconds after application of the stimulation and was followed by the patient's claim that he had not been able to speak (Fig. 5). Subsequently correct response to ex-

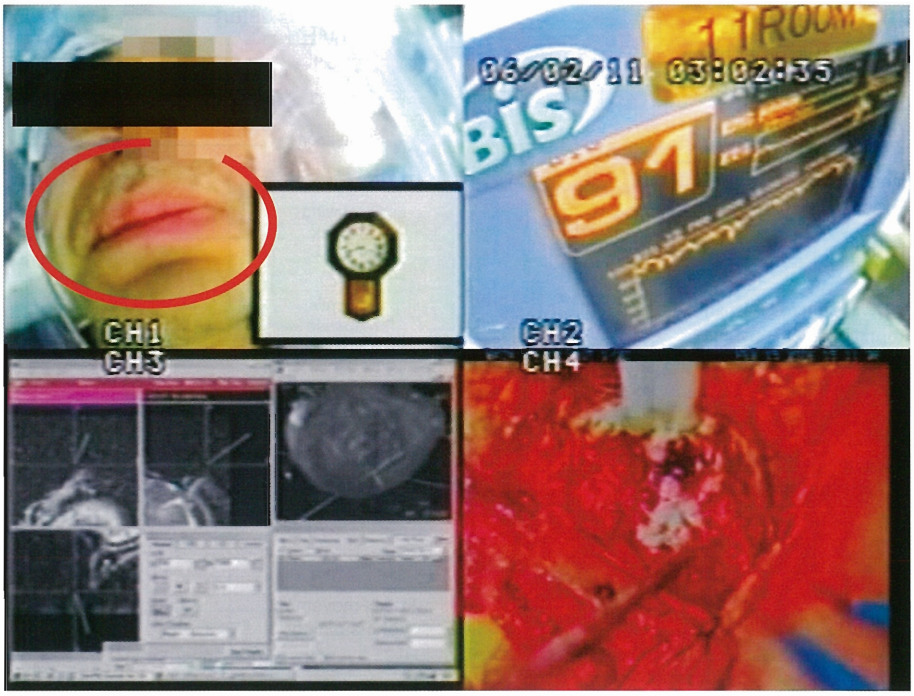

Fig. 6

Real-time integrated intraoperative information displayed on the monitor of IEMAS at the time of speech arrest simultaneous to electrical stimulation of the cortex during object naming test. Note strain of the facial muscles around the mouth (dashed line on the upper left display) considered as a sign of false positive identification of the cortical speech area and result of stimulation of the motor cortex.

amination task was fully restored. The level of awakening was sufficient and no movements of the facial muscles were observed. Therefore, speech arrest was considered as true positive identification of the Broca's area. According to IEMAS-based integration of the functional cortical mapping and real-time neuronavigation with the use of intraoperative MRI, the identified speech area was located within the tumor mass itself. Therefore, aggressive resection of the neoplasm was abandoned for preservation of the speech function.

Case 2

A 35-year-old man was operated on for low-grade astrocytoma located in the precentral gyrus. Continuous monitoring of the speech function during tumor resection was done. While speech arrest had happened during electrical stimulation within the bulk of the neoplasm careful evaluation of the view of the patient's face on the monitor of IEMAS revealed strain of the facial muscles around the mouth, which was considered as a sign of false positive identification of the cortical speech area caused by stimulation of the motor cortex (Fig. 6). Aggressive tumor resection was accomplished.

Case 3

A 33-year-old man was operated on for low-grade astrocytoma located in the middle frontal gyrus. Cortical stimulation in the vicinity to the tumor was done and resulted in speech arrest. However, it was accompanied by rigid deviation of the patient's eyes to the right, which was clearly seen on the monitor of IEMAS (Fig. 7). Such response was clearly reproducible. Consequently, we judged that speech arrest was actually caused by stimulation of the supplementary motor cortex, but not Broca's area itself. Therefore aggressive tumor resection was performed.

Discussion

Use of updated intraoperative neuronavigation proved its high usefulness during resection of intracranial gliomas[3,18]. It provides for the surgeon a perfect opportunity to remove the bulk of the lesion from the peritumoral brain tissue. Moreover, introduction of the intraoperative MRI into clinical prac-

Fig. 7

View of the patient's face on the monitor of IEMAS at the time of speech arrest simultaneous to electrical stimulation of the cortex during object naming test. Note accompanied rigid deviation of the eyes to the right (left), which was considered as a sign of false positive identification of the cortical speech area caused by stimulation of the supplementary motor cortex. Subsequently the patient was able to respond correctly to the examination task and deviation of the eyes was resolved completely (right).

Table Possible problems of the intraoperative cortical mapping during awake craniotomy and technical solutions

Problem	Solution
Identification of neurological signs Speech arrest may be caused by stimulation of the different cortical areas, namely motor cortex, negative motor cortex, and speech area, which require to be precisely discriminated. In addition, insufficient awakening of the patient from sedation may result in pseudo speech arrest.	Monitoring of the patient's face, its mimics, involuntary movements of the facial muscles and the patient's sedation level at the time of speech arrest during cortical stimulation
Sharing information among the members of surgical team It may be difficult for the surgeon, the examiner and the anesthetist to share the information necessary to interpret the obtained functional information, such as the nuances of the cortical stimulation, the patient's sedation level, the examination tasks.	Real time integration of the information on the cortical stimulation observed by the surgeon through the operating microscope, the type of examination task, and his or her response and the share of these information among the members.
Integration functional information with anatomical information it may be difficult for the surgeon to integrate precisely the positioning of functional area with the anatomical details of the tumor location.	Integration of the information on the electrical cortical stimulation during intraoperative brain mapping with the data of intraoperative neuronavigation with 3-dimensional visualization of the tumor location.

tice resulted in significant reduction of the mislocalization errors resulted from the effect of "brain shift"[17)]. Nevertheless, despite high preciseness of such updated intraoperative neuronavigation, it is important to emphasize that it provides only morphological, but not functional information. Therefore, its use is not sufficient enough for solution of the extremely difficult surgical dilemma: whether the eloquent functionally-preserved cerebral structures are located within the mass of the infiltrating tumor or outside of it. It necessitates application of the various preoperative and intraoperative techniques for clinical brain mapping in individual patient.

Awake craniotomy is a widely used technique, which provides for the surgeon unique opportunities for intraoperative examination of the higher brain functions, detailed cortical and subcortical brain mapping, and precise identification of the functionally-important structures. However, presence of several medical, surgical, and technical pitfalls may interfere with interpretation of the obtained data, particularly during localization of the cortical speech centers (Table). The intraoperative neurosurgical device IEMAS was developed to eliminate the existing problems and facilitate the intraoperative cortical mapping.

Electrical stimulation of the several cortical areas may similarly result in speech arrest[19]. Particularly, in 13 cases of the present series false positive identification of the Broca's area was caused by stimulation of the primary or supplementary negative motor area, which represents a cortical center for synergistic movements. Differentiation of the speech arrest caused by stimulation of the negative motor area from the speech center itself can be done with testing of limb movements during the period of speech arrest. Meanwhile, in the present series, it was effectively done with assessment of the facial motor reaction, particularly strain of the muscles around the mouth or deviation of eyes, which were clearly seen on the monitor of IEMAS.

Level of the patient's consciousness may significantly influence the response to examination tasks, and in our experience, insufficient awakening from sedation was one of the main reasons of unsuccessful brain mapping. The level of consciousness should be preferably confirmed before initiation of the brain mapping for avoidance of unnecessary repetitions of the cortical stimulation. For this purpose, we performed not only checking of parameters of the BIS monitor, but applied preliminary screening with words' repetition and number counting tests. Use of IEMAS permitted easy assessment of the patient's consciousness level at the time of cortical stimulation and response to examination task, since all these data are co-registered in real time and presented on the same monitor. Additionally, such integrated information can be easily projected on several LCD within the operating theater, which results in its quick and easy visualization by all members of the surgical team, which may prevent missing of the important data or their incorrect interpretation.

Of special note, IEMAS provides a unique opportunity for integration of the functional data obtained during brain mapping with anatomical information based on the intraoperative MRI, which permits the surgeon direct 3-dimensional assessment of the localization of the stimulated cortex with regard to tumor location. In 13 patients of the present series, such co-registration of the functional and anatomical data revealed localization of the functionally preserved speech area within the tumor mass itself, which resulted in less aggressive lesion resection and prevention of the bothersome postoperative neurological morbidity. On the other hand, in several occasions IEMAS-based integrated assessment of the intraoperative data permitted to reveal false positive identification of the speech center within the tumor, which resulted in total removal of the neoplasm.

Between June, 2000 and December, 2004, before IEMAS was developed, we had performed 20 cases of awake craniotomy for gliomas various WHO histopathological grade (from II to IV) adjacent to Broca's and/or Wernicke's area, or to the left supplementary motor cortex in the intelligent operating theater of the Tokyo Women's Medical University, where 0.3 Tesla open intraoperative MRI and neuronavigation system had been already equipped. There were 12 men and 8 women. Their age varied from 26 to 57 years old (median, 34 years old), and postoperative neurological morbidity was observed in 2 patients (for 2 months and 3 weeks after surgery, each). In this study, no permanent postoperative neurological morbidity was observed.

Therefore, we think individually-based approach for surgical management of gliomas with IEMAS permits for the surgeon to attain maximal possible tumor resection with minimal risk of permanent postoperative neurological morbidity.

Conclusion

In our experience, use of IEMAS significantly facilitates registration, integration, and interpretation of the various intraoperative information obtained with functional brain mapping during awake craniotomy for gliomas adjacent to Broca's and/or Wernicke's areas. The device was helpful for determination of the cause of speech arrest and differentiation of true positive and false positive identification of the cortical speech centers. Additionally, possible co-registration of the functional and anatomical information was useful for precise localization of the functioning eloquent cortex with regard to tumor mass itself. Therefore, the IEMAS is considered to be an useful device for neurosurgical practice.

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References

1) **Black PM**: Brain tumors. N Engl J Med **324**: 1471–1476, 1991
2) **Berger MS**: Minimalism through intraoperative functional mapping. Clin Neurosurg **43**: 324–337, 1996
3) **Muragaki Y, Iseki H, Maruyama T et al**: Information-guided surgical management of gliomas using low-field-strength intraoperative MRI. Acta Neurochir Suppl **109**: 67–72, 2011
4) **Ojemann G, Ojemann J, Lettich E et al**: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg **71**: 316–326, 1989
5) **Sanai N, Mirzadeh Z, Berger MS**: Functional outcome after language mapping for glioma resection. N Engl J Med **358**: 18–27, 2008
6) **Duffau H, Capelle L, Sichez N et al**: Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. Brain **125**: 199–214, 2002
7) **Ojemann GA**: Neurosurgical management of epilepsy: a personal perspective in 1983. Appl Neurophysiol **46**: 11–18, 1983
8) **Berger MS, Kincaid J, Ojemann GA et al**: Brain mapping techniques to meximize resection, safety, and seizure control in children with brain tumors. Neurosurgery **25**: 786–792, 1989
9) **Larkin M**: Neurosurgeons wake up to awake-brain surgery. Lancet **353**: 1772
10) **Taylor MD, Bernstein M**: Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. J Neurosurg **90**: 35–41, 1999
11) **Fukaya C, Katayama Y, Yoshino A et al**: Intraoperative wake-up procedure with propofol and laryngeal mask for optimal excision of brain tumor in eloquent areas. J Clin Neurosci **8**: 253–255, 2001
12) **Duffau H, Capelle L, Denvil D et al**: Usefulness of intraoperative electrical subcortical mapping during surgery for low-grade gliomas located within eloquent brain regions: functional results in a consecutive series of 103 patients. J Neurosurg **98**: 764–778, 2003
13) **Lüders H, Lesser RP, Dinner DS et al**: Localization of cortical function: new information from extraoperative monitoring of patients with epilepsy. Epilepsia **29**: 56–65, 1988
14) **Lim SH, Dinner DS, Pillay PK et al**: Functional anatomy of the human supplementary sensorimotor area: results of extraoperative electrical stimulation. Electroencephalogr Clin Neurophysiol **91**: 179–193, 1994
15) **Luders HO, Dinner DS, Morris HH et al**: Cortical electrical stimulation in humans. The negative motor areas. Adv Neurol **67**: 115–129, 1995
16) **Mikuni N, Ohara S, Ikeda A et al**: Evidence for a wide distribution of negative motor areas in the perirolandic cortex. Clin Neurophysiol **117**: 33–40, 2006
17) **Iseki H, Nakamura R, Muragaki Y et al**: Advanced computer-aided intraoperative technologies for information-guided surgical management of gliomas: Tokyo Women's Medical University experience. Minim Invasive Neurosurg **51**: 285–291, 2008
18) **Muragaki Y, Iseki H, Maruyama T et al**: Usefulness of intraoperative magnetic resonance imaging for glioma surgery. Acta Neurochir Suppl **98**: 67–75, 2006
19) **Schäffler L, Lüders HO, Dinner DS et al**: Comprehension deficits elicited by electrical stimulation of Broca's area. Brain **116**: 695–715, 1993

術中言語機能検査システム IEMAS の開発と臨床への適用

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グリオーマ摘出術において，最大限の病変摘出と機能温存の両立を図るために，術中言語機能検査が有効な手段の一つと考えられている．

覚醒下の患者に検査タスクを見せると同時に，脳を電極刺激し，患者の応答から言語野をはじめとする機能野を術中に同定し，適切な切除範囲を決定できる．しかし，術中言語機能検査では，患者の検査タスクへの応答から，言語野への刺激による失語症と，陽性運動反応，陰性運動反応を区別するのが難しい．

そこで我々は，この問題を解決するため，術中言語機能検査システム Intraoperative Examination Monitor for Awake Surgery（IEMAS）を開発した．IEMAS は，検査タスクを選択する PC，患者に検査タスクを提示するディスプレイと，患者の顔の映像，麻酔モニター，術野映像，手術ナビゲーション装置の画像情報を一つの画面に表示するディスプレイを備える装置である．IEMAS により，手術チームは，提示された検査タスク，応答する患者の顔，麻酔深度，術野映像と手術ナビゲーション装置上での刺激場所を簡便に確認できる．我々は，言語野近傍のグリオーマ摘出術 96 例に IEMAS を適用した．結果，43 例でブローカ野，15 例でウェルニッケ野が同定され，そのうち，13 例では，言語野が腫瘍領域内に存在することが分かった．また，陽性，陰性運動野が，それぞれ 13 例で同定された．また，腫瘍摘出途中に失語症を中心とした言語症状が出現した症例が 30 例あり，うち，21 例では摘出を終了した．

IEMAS による，術中検査に関連する情報の統合は，患者の失語症状，陽性運動反応，陰性運動反応を区別するのに有効であった．また，術者が，同定された機能野と腫瘍の位置関係を簡便に把握し，手技に反映させるのに有用であった．