

# A Super-selective Wada Test Successfully Detected an Artery That Supplied Broca's Area in a Case of Left Frontal Lobe Glioblastoma: Technical Case Report

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## Abstract

In cases of malignant gliomas located at language eloquent area, it is often difficult to preoperatively detect those area with functional MRI. Awake surgery is often used to spare the language eloquent area during surgery for such tumors; it is not available for a patient whose intracranial pressure is elevated due to the malignant tumor. The Wada test involves infusing anesthetic agents into the internal carotid artery to determine language dominance before surgery for epilepsy or brain tumor. The super-selective Wada test is a technique to detect more detailed functional localization by infusing anesthetics into far distal middle cerebral artery branches. We present a 37-year-old man suffering from a left frontal lobe glioblastoma, in whom detection of an artery supplying Broca's area was attempted by a super-selective Wada test. The super-selective Wada test successfully detected the branch of middle cerebral artery supplying Broca's area. Total resection of the contrast-enhancing area was achieved without damaging the artery supplying Broca's area without any neurological sequelae. This is the first report describing the usefulness of the super-selective Wada test in glioblastoma treatment. Our findings suggest that the super-selective Wada test is a powerful and useful means to distinguish the artery that supplies the language area from the tumor feeding artery in cases of tumors in the language eloquent area.

Keywords: functional localization, glioblastoma, language area, propofol test, Wada test

## Introduction

Glioblastoma is one of the primary brain tumors with the most malignant course. It is widely known that the extent of surgical resection or the volume

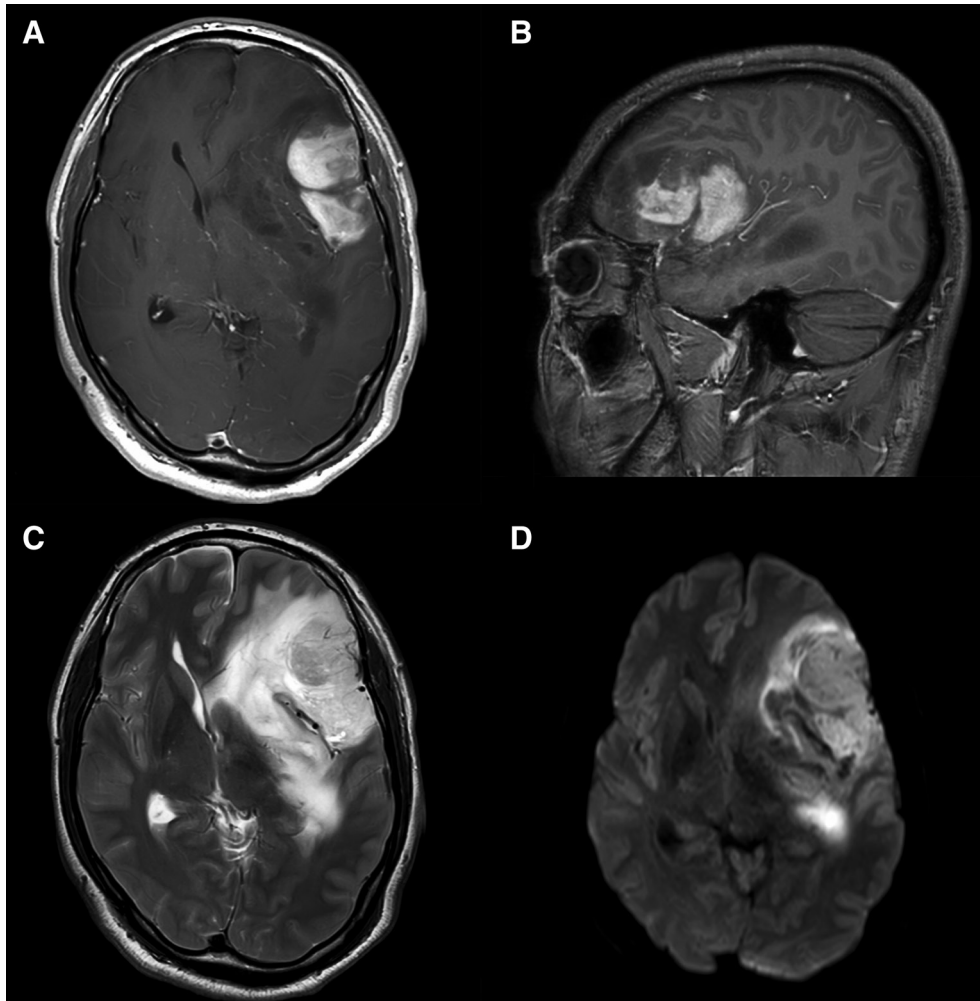
of residual tumor is a significant prognostic factor for overall survival in newly diagnosed glioblastoma.<sup>1–6</sup> In recent studies, both postoperative residual contrast-enhancing tumor volume and non-enhancing volume significantly influenced overall survival.<sup>7</sup> In contrast, when tumor involves or is next to an eloquent area, the risk of functional deterioration should be considered, and every effort should be made to preserve function.

To identify the language area before or during surgical resection, various means have been used

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**Fig. 1** Preoperative magnetic resonance images—contrast-enhanced T1-weighted images (A and B), non-contrast-enhanced T2-weighted image (C), and diffusion-weighted image (D), a contrast-enhancing lesion in the left frontal lobe is shown with a large perifocal high-intensity area on the T2-weighted imaging in the left frontal lobe, the tumor showed high intensity on the diffusion-weighted image, indicating high cellularity.

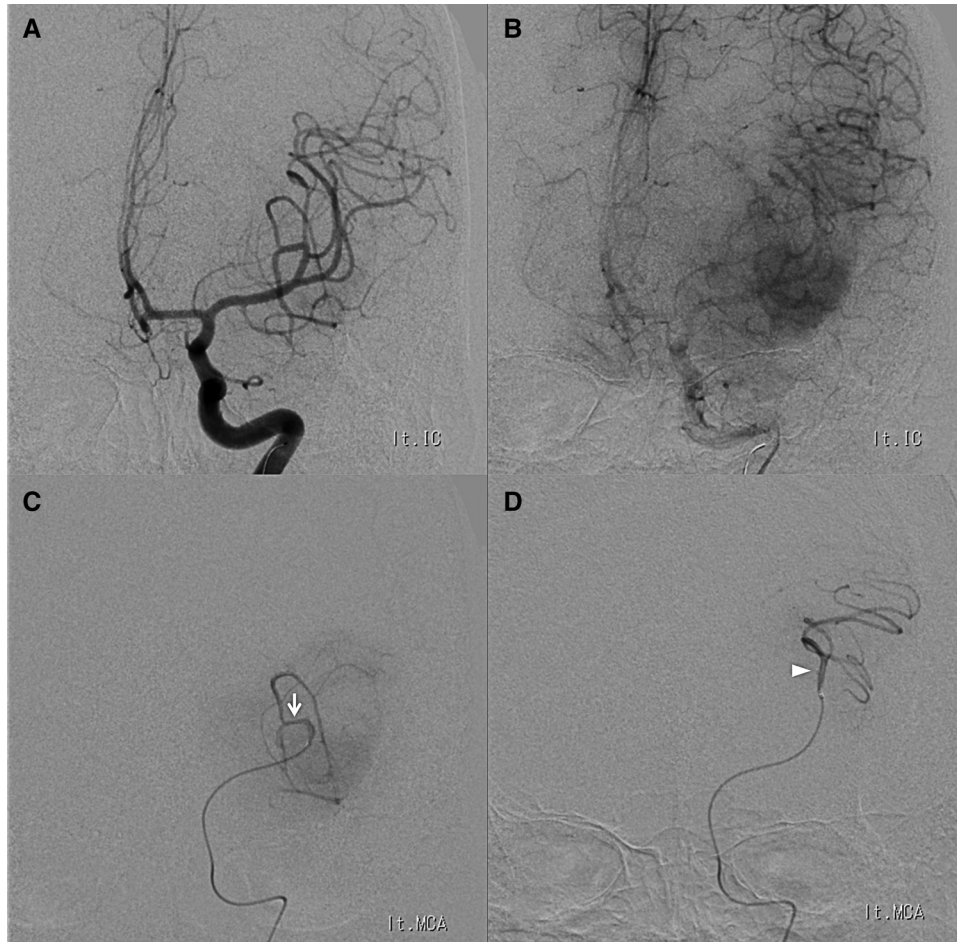
including functional magnetic resonance (fMR) imaging,<sup>8,9)</sup> magnetoencephalography,<sup>10,11)</sup> the Wada test,<sup>12)</sup> and awake surgery.<sup>13,14)</sup> Though fMR imaging and magnetoencephalography are less invasive than the Wada test, it is sometimes difficult to identify the language area, especially in patients with gliomas.<sup>15,16)</sup> In this study, we report our experience of a 37-year-old male suffering from a left frontal lobe glioblastoma in whom preoperative determination of the artery supplying Broca's area (the language eloquent area) with a super-selective Wada test was useful.

## Clinical Presentation

### History and presentation

A 37-year-old right-handed man presented with headache. He had neither significant medical history

nor family history. Neurological examination revealed trivial anomia while Western Aphasia Battery aphasia quotient score and cortical quotient score were well preserved, which were 100 and 98.7, respectively. Brain MRI revealed a contrast-enhancing lesion in the left frontal lobe (Fig. 1A and 1B), with a large perifocal high intensity area on the T2-weighted imaging (Fig. 1C). The tumor showed high intensity in the diffusion-weighted images, indicating a highly cellular malignancy (Fig. 1D). The lesion appeared to involve the frontal operculum that might involve the language area.<sup>17)</sup> Based on the anatomical localization of the contrast-enhancing lesion, safety total removal of the tumor was possible if the anterior language area could be identified and preserved. However, fMR imaging failed to identify the anterior language area (Broca's area), partly because of the mass effect of the tumor.



**Fig. 2** Digital subtraction angiograms—anteroposterior view of the digital subtraction angiography of the left internal carotid artery (A: arterial phase, B: capillary phase) demonstrates tumor stain fed by the superior trunk of the left MCA; super-selective angiography during a selective/super-selective Wada test from the superior trunk of M2 segment of the MCA reveals small feeding arteries of the tumor originating from the medial branch of the M2 superior trunk (C: arrow) and the “missing branch” (lateral branch) of the superior trunk (D: arrowhead indicates the other branch supplying Broca’s area). MCA: middle cerebral artery.

High intracranial pressure and the risk of herniation made awake surgery difficult. Therefore, he underwent a Wada test to determine the language dominance, and identification of the Broca’s area and discrimination of arteries that supply the language area if possible.

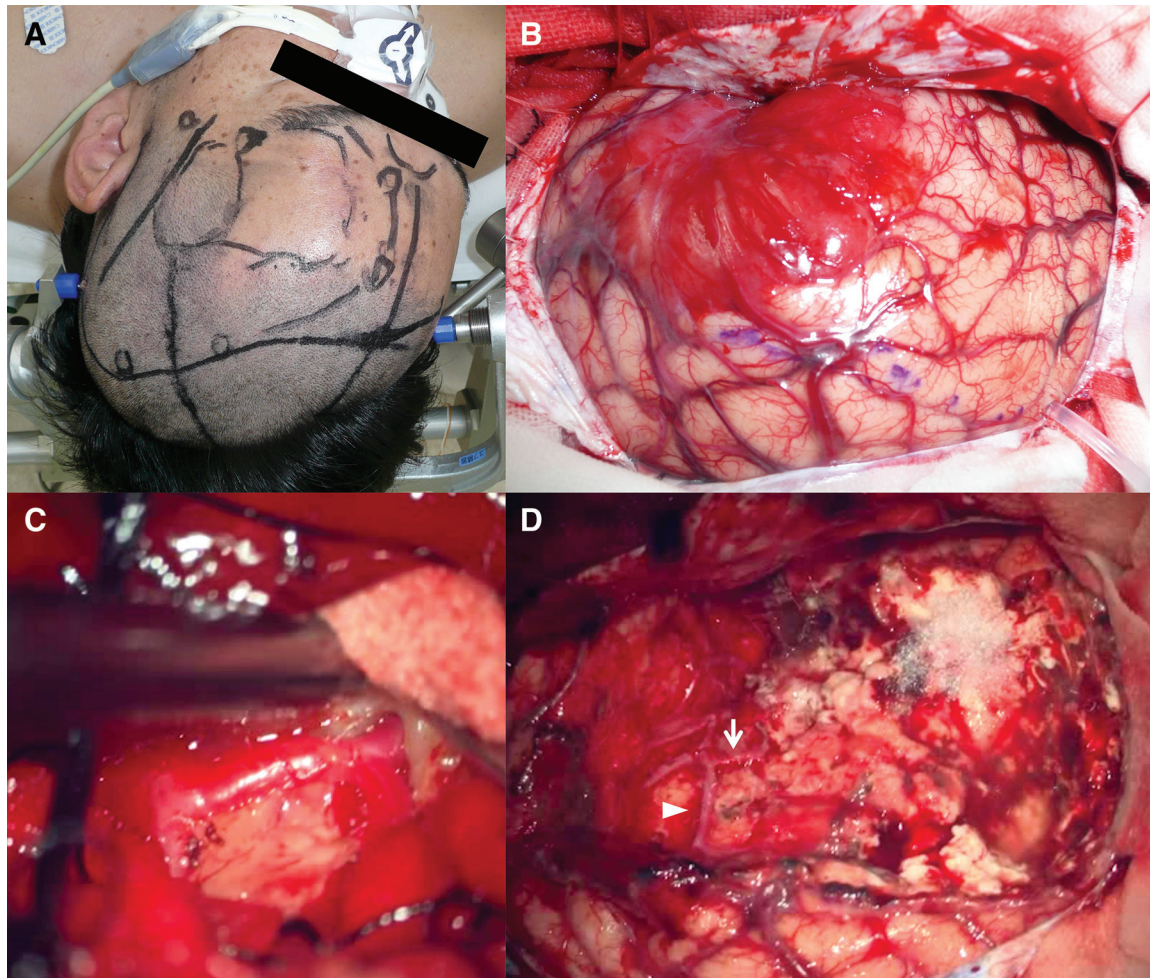
#### **Selective/Super-selective Wada test**

The Wada test was performed according to our team protocol. We infused 0.1% propofol at the rate of 1 ml/s from a Marksman microcatheter (Covidien, Chicopee, MA, USA) navigated into the target artery. The volume of propofol injected was 10 ml for the M1 segment of the middle cerebral artery (MCA) and 7.5 ml for the M2 segment of the MCA, which could gain enough time to examine tasks to evaluate neurological symptoms but less likely to induce adverse effects such as disturbance of consciousness.

During the test, both electroencephalography (EEG) and neurological examinations (motor, sensory, vision, cognition, and language) were repeatedly evaluated. The emergence of the effect of propofol was judged by the appearance of slow-wave activity on the EEG and any neurological symptoms, and the disappearance of the effect of propofol was judged by the normalization of the EEG and all neurological symptoms. Between the sessions, more than three times the time length between the emergence of and the disappearance of the effect of propofol was waited.

In this case, digital subtraction angiography showed the tumor stain in the left frontal lobe supplied from the MCA (Fig. 2A and 2B). Infusion of 10 ml 0.1% propofol from the microcatheter navigated into the distal M1 segment of the MCA induced a significant sensory aphasia, but motor aphasia was not obvious.





**Fig. 3** Intraoperative views—skin incision planning (A), very red tumor protruded from the brain surface (B), the tumor feeder identified with a super-selective Wada test was detected (C), the tumor was totally removed (D), the tumor feeders were cut (arrow), and the other branch supplying Broca's area was preserved (arrowhead).

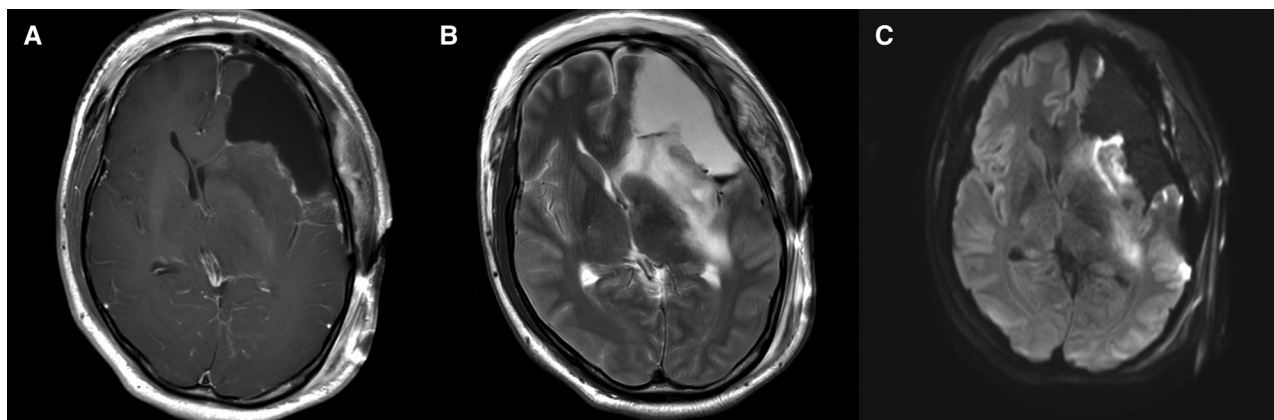
Subsequently, navigating the microcatheter further into the superior trunk of the M2 segment of the MCA, 7.5 ml 0.1% propofol was infused revealing no verbal symptoms (Fig. 2C). However, with detailed examination of the images acquired at this infusion, we noticed that several branches of the M2 superior trunk were missing compared with the initial scan. We considered that this was a result of a “steal phenomenon” by the hypervascular tumor and that these non-imaged branches might be the feeder of Broca's area. The microcatheter was therefore navigated into these missing branches. Significant verbal paraphasia, dysgraphia, and difficulty of word recall were observed upon infusion of 7.5 ml 0.1% propofol into one of the frontal branches that supplied the area adjacent to the tumor (Fig. 2D). The effect of propofol was observed from 6 to 9.5 minutes in each session.

### Surgical resection

To remove the contrast-enhanced tumor, a left frontotemporal craniotomy was performed (Fig. 3A). On opening the dura matter, a hypervascular tumor protruding from the brain surface was seen (Fig. 3B). Tracking the MCA from distal to proximal, the arterial branch detected with the super-selective Wada test was identified (Fig. 3C). The frontal branch that functioned as a main feeder of the tumor was coagulated and cut, and the contrast-enhanced tumor was totally removed while preserving the other branch that supplied the Broca's area (Fig. 3D). Pathological examination of the tumor revealed glioblastoma (IDH-1 mutant).

### Postoperative course

Postoperative MRI demonstrated total removal of the contrast-enhancing lesion, as well as the absence



**Fig. 4** Postoperative magnetic resonance images—contrast-enhanced T1-weighted image (A), non-contrast-enhanced T2-weighted image (B), and diffusion-weighted image (C).

of any new peritumoral ischemic lesion on the diffusion-weighted image (Fig. 4). The patient suffered from transient motor aphasia after surgery, but this resolved within a few weeks. Western Aphasia Battery was examined a month after the operation, and aphasia quotient score and cortical quotient score were 100 and 99.8, respectively. He was discharged home with no remaining neurological deficits.

### Discussion

The Wada test was first reported in 1960 to the English-speaking world. Originally, sodium amobarbital was injected into the internal carotid artery, but nowadays propofol is frequently used because amobarbital is not available in many countries.<sup>18,19)</sup> In Japan, although injection of propofol into the artery is off-label usage, the propofol Wada test is common and its safety is confirmed. This propofol usage has been approved by the institutional review board of our hospital. However, injection of propofol into the internal carotid artery was reported to induce consciousness disturbances, which affects the results of the Wada test.<sup>20)</sup> Fujii et al. reported the MCA Wada test that selectively infuses propofol into the M1 segment of the MCA.<sup>20)</sup> This method prevents the flow of propofol into the anterior choroidal artery, and avoids the induction of consciousness decline, and thus makes the results reliable. Our method, the super-selective Wada test, is a further refinement of the MCA Wada test. This procedure can separate not only anterior and posterior language areas but also proper tumor feeders and arteries supplying eloquent areas. By cutting this proper feeder in a precise manner, bleeding can be controlled during the surgery, especially in hypervascular glioma just as the present case.

In this case, injection of propofol into the M1 or the M2 superior trunk did not induce motor aphasia, while injection into the branch of the M2 superior trunk did. A possible explanation is that there was a “steal phenomenon” of the blood flow toward the Broca’s area by the hypervascular tumor. By selection of the artery that was not showing up, motor aphasia was evoked, suggesting that the artery supplying the Broca’s area had been found. Therefore, care should be taken when applying this technique for hypervascular lesions.

The super-selective Wada test may also help to map the localization of brain functions in detail before surgery, for example motor, sensory, vision, cognition, and language areas. Fusion of angiogram via this method and MR images<sup>21)</sup> may contribute to detailed functional mapping, and thus helps us determine the extent of resection, and preserve function.

### Conclusion

This is the first report describing the application of the super-selective Wada test to glioblastoma treatment. Our findings suggest that the super-selective Wada test enables more precise brain functional localization and thus preserves the vessels supplying language area in cases of tumors in the language-eloquent area.

### Conflicts of Interest Disclosure

All authors have no conflict of interest and have registered online Self-reported COI Disclosure Statement Forms through website for The Japan Neurosurgical Society members.

## References

- 1) Brown TJ, Brennan MC, Li M, et al.: Association of the extent of resection with survival in glioblastoma: a systematic review and meta-analysis. *JAMA Oncol* 2: 1460–1469, 2016
- 2) Chaichana KL, Jusue-Torres I, Navarro-Ramirez R, et al.: Establishing percent resection and residual volume thresholds affecting survival and recurrence for patients with newly diagnosed intracranial glioblastoma. *Neuro Oncol* 16: 113–122, 2014
- 3) Ellingson BM, Abrey LE, Nelson SJ, et al.: Validation of postoperative residual contrast-enhancing tumor volume as an independent prognostic factor for overall survival in newly diagnosed glioblastoma. *Neuro Oncol* 20: 1240–1250, 2018
- 4) Grabowski MM, Recinos PF, Nowacki AS, et al.: Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma. *J Neurosurg* 121: 1115–1123, 2014
- 5) Marko NF, Weil RJ, Schroeder JL, Lang FF, Suki D, Sawaya RE: Extent of resection of glioblastoma revisited: personalized survival modeling facilitates more accurate survival prediction and supports a maximum-safe-resection approach to surgery. *J Clin Oncol* 32: 774–782, 2014
- 6) Pan IW, Ferguson SD, Lam S: Patient and treatment factors associated with survival among adult glioblastoma patients: a USA population-based study from 2000–2010. *J Clin Neurosci* 22: 1575–1581, 2015
- 7) Kotrotsou A, Elakkad A, Sun J, et al.: Multi-center study finds postoperative residual non-enhancing component of glioblastoma as a new determinant of patient outcome. *J Neurooncol* 139: 125–133, 2018
- 8) Binder JR, Swanson SJ, Hammeke TA, et al.: Determination of language dominance using functional MRI: a comparison with the Wada test. *Neurology* 46: 978–984, 1996
- 9) Desmond JE, Sum JM, Wagner AD, et al.: Functional MRI measurement of language lateralization in Wada-tested patients. *Brain* 118 (Pt 6): 1411–1419, 1995
- 10) Doss RC, Zhang W, Risse GL, Dickens DL: Lateralizing language with magnetic source imaging: validation based on the Wada test. *Epilepsia* 50: 2242–2248, 2009
- 11) Papanicolaou AC, Simos PG, Castillo EM, et al.: Magnetoencephalography: a noninvasive alternative to the Wada procedure. *J Neurosurg* 100: 867–876, 2004
- 12) Wada J, Rasmussen T: Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. *J Neurosurg* 17: 266–282, 1960
- 13) Ojemann G, Ojemann J, Lettich E, Berger M: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg* 71: 316–326, 1989
- 14) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med* 358: 18–27, 2008
- 15) Ishikawa T, Muragaki Y, Maruyama T, Abe K, Kawamata T: Roles of the Wada test and functional magnetic resonance imaging in identifying the language-dominant hemisphere among patients with gliomas located near speech areas. *Neurol Med Chir (Tokyo)* 57: 28–34, 2017
- 16) Pallud J, Roux A, Mellerio C: Glioma resection unmasks eloquent brain areas. *World Neurosurg* 132: 251–252, 2019
- 17) Quiñones-Hinojosa A, Ojemann SG, Sanai N, Dillon WP, Berger MS: Preoperative correlation of intraoperative cortical mapping with magnetic resonance imaging landmarks to predict localization of the Broca area. *J Neurosurg* 99: 311–318, 2003
- 18) McCleary K, Barrash J, Granner M, Manzel K, Greider A, Jones R: The safety and efficacy of propofol as a replacement for amobarbital in intracarotid Wada testing of presurgical patients with epilepsy. *Epilepsy Behav* 78: 25–29, 2018
- 19) Takayama M, Miyamoto S, Ikeda A, et al.: Intracarotid propofol test for speech and memory dominance in man. *Neurology* 63: 510–515, 2004
- 20) Fujii M, Miyachi S, Matsubara N, et al.: Selective propofol injection into the M1 segment of the middle cerebral artery (MCA Wada test) reduces adverse effects and enhances the reliability of the Wada test for determining speech dominance. *World Neurosurg* 75: 503–508, 2011
- 21) Dasenbrock HH, See AP, Smalley RJ, et al.: Frameless stereotactic navigation during insular glioma resection using fusion of three-dimensional rotational angiography and magnetic resonance imaging. *World Neurosurg* 126: 322–330, 2019

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