

# Recovery of visual field after awake stimulation mapping of the optic pathway in glioma patients

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#### **Research Article**

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# Abstract

Brain mapping during awake craniotomy for gliomas can help preserve neurological functions, including maintenance of central and peripheral vision. However, the consecutive changes in the visual field remain unknown. We retrospectively assessed 14 patients who underwent awake craniotomy for gliomas infiltrating into the optic radiation. Cortico-subcortical direct electrical stimulation (DES) was intraoperatively applied until transient visual symptoms were elicited and recorded. The visual fields were examined consecutively in the preoperative period and postoperative subacute and chronic periods. To evaluate the anatomo-functional validity of the recordings, all DES-elicited points were overlaid onto a three-dimensional template that included the optic radiation, using voxel-based morphometry (VBM) mapping. All patients experienced visual symptoms that were classified as phosphenes, blurred vision, or hallucinations during DES, and surgical resection was limited to within the functional boundaries. In VBM, almost all the subcortical positive mapping points overlapped with the surface of the optic radiation, and the distribution of sites that induced visual phenomena in the upper or lower visual fields could be differentiated in the anatomical space. We observed no postoperative visual deficit in four patients (29%), time-dependent improvements in five out of eight patients that presented transient quadrantanopia or partial visual defect (36% out of 57%), and permanent hemianopsia (14%) in two patients with occipital lesions. Intraoperative DES that identifies and preserves optic radiation in awake craniotomy for gliomas is a reliable and effective technique to avoid permanent deficit, but has a low success rate in patients with occipital involvement.

## Introduction

Recent developments in surgical and anesthetic techniques have enabled the treatment of intracerebral lesions while the patent is awake, under local anesthesia. This technique is particularly valuable in some cases such as supratentorial gliomas that are located adjacent to critical brain areas. Awake craniotomy has made it possible to identify neurofunctional networks involved in sensory, motor, and language functions, and it has contributed to accurate boundary identification for safe tumor resection (Duffau et al. 2005, 2008; Maldaun et al. 2014; Maldonado et al. 2011; Sanai et al. 2008). Furthermore, the technique can improve not only the oncological and functional outcomes but also the quality of life (QOL) of patients with gliomas (Duffau and Taillandier 2015; Kinoshita et al. 2016a; Nakajima et al. 2019).

Homonymous hemianopsia can severely affect QOL (Papageorgiou et al. 2007), while quadrantanopia is often symptomatic only in the inferior field and asymptomatic in the superior field (Krolak-Salmon et al. 2000). Hence, it is crucial to avoid permanent homonymous hemianopsia during surgeries for gliomas infiltrating near the optic radiation. For a safe resection of the tumor in the temporal and occipital lobes, various neuroimaging modalities including preoperative functional MRI, neuronavigation based on tractography, and intraoperative MRI are used to identify anatomical relationships between the visual pathway and adjacent lesions (Curatolo et al. 2000; Kamada et al. 2005; Winston et al. 2014). Intraoperative mapping and visual evoked potential monitoring of the visual pathway have also been attempted for the preservation of the visual pathway. In particular, it has been reported that direct

electrical stimulation (DES) of the optic radiation can prevent visual field deficits in patients with temporo-occipital gliomas (Gras-Combe et al. 2012; Mazerand et al. 2017; Nguyen et al. 2011). However, changes in the visual field after intraoperative preservation of the visual pathway by awake craniotomy for gliomas have not been studied.

In the current study, we retrospectively evaluated the time-dependent changes in visual field in patients who underwent surgical resection of temporo-occipital gliomas using intraoperative direct electrical mapping of the optic radiation. Furthermore, based on the results of the anatomo-functional analysis of the visual mapping, we describe the detailed relationship between the visual pathway and the distribution of subcortical mapped regions reproduced by DESs in awake condition.

# **Material And Methods**

This study was approved by the Medical Ethics Committee at Kanazawa University (identifier No. 2020-032 [3359]).

## Patients

Fourteen consecutive patients with supratentorial gliomas who were symptomatic due to stimulation of the visual pathway during awake surgery at the Department of Neurosurgery, Kanazawa University Hospital were retrospectively assessed in this study. Patient characteristics (i.e., age, gender, location, and diagnosis) are presented in Table 1. The tumor was located in the temporal lobe in 8 patients, occipital lobe in 3 patients, temporo-occipital lobe in 2 patients, and parieto-temporal lobe in 1 patient. We defined postoperative period within 1 month as subacute phase and more than 3 months after the surgery as chronic phase. All patients underwent static visual field tests (Humphrey 24-2 test) before and after the operation (within 1 month and 3 months or more after surgery); five patients presented with quadrantanopia prior to surgery.

## Surgical Procedure

All surgical procedures were performed in the lateral position using the sleep-awake-sleep technique by the same operator (M.K.), and the cortical and subcortical functions were evaluated during DES. We used a bipolar probe to deliver biphasic current (pulse frequency, 60 Hz; amplitude, 2–6 mA; pulse duration, 0.2 ms), as in previous studies (Duffau et al. 2008; Kinoshita et al. 2016a). To identify the visual cortex and pathway, we introduced to each patient a four-screen naming task (E-card 2001, Escor, Chiba, Japan) for subcortical mapping. For this task, two pictures were displayed diagonally on the screen (*Figure in Online Resource 1*), as reported by Gras-Combe et al. (Gras-Combe et al. 2012). One image was presented in the quadrant to be documented and another image in the opposite quadrant as control. The image was switched depending on the quadrant to be noted. We used a multi-monitor to record real-time information of the patient, a task screen, an operative field, and a neuronavigation image. If an abnormal finding appeared in the visual field during DES in the cortical or subcortical area, the symptom and positive mapping sites were recorded using intraoperative videos and reconfirmed by a neuronavigation system

(Curve system and iPlan3.0 software, BrainLab, Feldkirchen, Germany), and the region was subsequently documented in three-dimensional (3D) space.

### Image Acquisition and Analysis

Structural magnetic resonance imaging (MRI) was performed during preoperative and postoperative (2–3 months after surgery) periods using a 3.0-T MR imager (Signa Excite HDx 3.0 T; General Electric Medical Systems, Waukesha, WI, USA). A series of diffusion-weighted (DW) axial images with (b-value = 1,000 s/mm<sup>2</sup>) and without (b-value = 0 s/mm<sup>2</sup>) a diffusion-sensitizing gradient along 30 directions was preoperatively obtained, as reported in our previous study (Kinoshita et al. 2016b). The DW-MR images were transferred to a workstation *via* the iPlan Cranial 3.0 software (BrainLab, Feldkirchen, Germany), which was used to reconstruct qualitative maps. Regions of interest targeting the optic radiations were selected manually by referring to a diffusion tensor imaging (DTI) tractography atlas and the result of previous study (Catani and Thiebaut de Schotten 2008). All 3D tracts were reconstructed with fiber propagation that terminated at a fractional anisotropy threshold of >0.18, as suggested in a previous report (Kinoshita et al. 2016b).

The anatomical relationship between the resection boundary and visual pathway was analyzed by voxelbased morphometry (VBM) mapping. The structural MRIs of all the 14 patients were transformed into the standardized Montreal Neurological Institute (MNI) 152 space (resolution of 1 × 1 × 1 mm) using Statistical Parametric Mapping 12 implemented in a MATLAB environment (R2018b, version 9.5; The MathWorks, Inc., Natick, MA, USA) with cost function masking (Brett et al. 2001) and MRIcron software (https://www.nitrc.org/projects/mricron/). Each 3D volume of interest (VOI) of the resection cavities was reconstructed and overlaid on an MNI152 template. All symptom-induced points were mapped and reconstructed as 4 mm-spherical VOIs, which were compared with non-normalized images and intraoperative records, as in a previous report (Nakajima et al. 2020). Initially, the surgical reports and intraoperative video records were used to plot the positive-mapping sites on the corresponding original 3DT1 images for each patient. These were made as accurate as possible by confirming spatial relationships with anatomical landmarks such as gyri, sulci, vessels, midline, and lateral ventricles (Tate et al. 2014). Next, each positive-mapping site on the original 3DT1 images was transferred to a normalized T1 image, and the spatial location of the mapping-positive sites was overlapped on a 3D MNI template using MRIcron software. Finally, the anatomical locations of the positive mapping sites on the 3D MNI template were reconfirmed. Each reconstruction was first constructed by R.N. and then systematically checked by a neurosurgeon (M.K.) (Liu et al. 2020). All VOIs were flipped to the left side and overlaid onto an MNI152 brain template that included the tracts of the optic radiation, the threshold of which was 0.5, based on the tractography-based white matter atlas, as reported by Rojkova et al (Rojkova et al. 2016). We then reconstructed all subcortical symptom-induced points as 1 mm-spherical VOIs, and measured the shortest distance between ipsilateral optic radiation and subcortical positive mapping sites using a software to calculate the distance in 3D space using the MATLAB environment. The tract probability of optic radiation was more than the threshold of 0.5, similar to a previous study (Nakajima et al. 2018). To assess the accuracy of electrical stimulations of the optic pathway, we

evaluated relationships between the distance and postoperative visual defect using Wilcoxon signed-rank test with JMP, version 14.3.0 (SAS Institute, Inc., Cary, NC, USA).

## Results

All 3D-VOIs of the resection cavities were overlapped on an MNI152 template (*Fig. 1*). The clinical, radiological, and surgical characteristics of the 14 patients are summarized in Table 2.

## Summary of Intraoperative Mappings

A total of 33 symptom-induced points related to visual phenomena were obtained from the 14 patients who underwent awake functional mapping (Table 2). Of these, there were 26 subcortical mapping points; the remaining seven were cortical mapping points around the calcarine sulcus, including one point that was counted as two points because of the appearance of both upper and lower symptoms. The average stimulation intensity was 4.6 mA (3-6 mA). Three differentiated symptoms were identified during DES: phosphenes were the most observed symptom (85%), followed by blurred vision (12%), and hallucinations (3%). An intraoperative video of each illustrative intraoperative symptom is presented in Video in Online Resource 2.

## **Imaging Analysis**

All 33 positive mapping sites were overlaid onto a normal brain atlas (MNI152) that included optic radiations using VBM analysis (*Fig. 2 and Figure in Online Resource 3*). Almost all the subcortical induced sites were on the surface of optic radiations, and the distribution corresponded to the passage of optic radiation in subcortical regions (*Fig. 2A*). The distribution from the anterior to the posterior direction could be divided into two groups based on the location of the mapped visual field phenomena, while the distributions of the upper and lower visual phenomena were polarized and spread upside down in the horizontal direction (*Fig. 2B*). According to the anatomo-functional map, the center of the distributions of visual symptoms statistically deviated in two locations associated with the differentiated visual field (*Fig. 2C*).

Figure 2D shows the spatial distributions of the three kinds of symptoms elicited by DES: blurred vision, hallucinations, and phosphenes. Phosphenes were classified into two different types of flashes: an uncolored (white) type that characterized most phosphenes and a colored type (*Table in Online Resource 4*). A colored flash was observed around the calcarine sulcus. Hallucinations were observed at the leading edge of the optic radiation in the anterior temporal lobe at a DES of 6 mA, while phosphenes appeared at the same point at a lower intensity (3 mA). Blurred vision could also be induced at the anterior temporal lobe.

Finally, we measured the shortest distance between symptom-induced points and optic radiation on a normal brain atlas during intraoperative subcortical mapping. In all patients, the distance between the symptom-induced points and the optic radiation was within 10 mm (*Figure in Online Resource 5*). Next,

we examined the relationship between the distance and the appearance of new postoperative visual field abnormalities, but there were no apparent differences (*Figure in Online Resource 6*).

## Postoperative Course of Visual Field

There was no postoperative visual field deficit in four patients, while visual field deficits appeared after surgery in 10 patients, five of whom surprisingly exhibited improvement during the chronic period. Additionally, the visual field was successfully preserved in eight patients; however, the other six patients who exhibited visual field defect immediately after surgery continued having visual impairments in the postoperative chronic phase. There was no significant difference between intraoperative visual phenomena and stimulation thresholds (*Table in Online Resource 7*).

The relationship between the locations of induced visual symptoms and time-dependent changes are shown in Figure 3. Among the patients with positive mappings in the temporal lobe, 4 out of 11 patients exhibited no postoperative visual impairments, and 7 patients presented with visual field disorders that appeared immediately after the surgery. However, four of them (57%) presented with an improvement in visual field deficits during the postoperative chronic period. Homonymous hemianopsias was prevented in 12 patients (86%), including in all patients with temporal lesions. Only two patients eventually presented with a permanent hemianopsia, both of whom presented with occipital lesions prior to the surgery.

In the group of patients with postoperative new visual field disorders, when we compared the group whose symptoms improved over time with the group whose symptoms stabilized, no statistically significant differences were found (p = 0.24) in distance between stimulation sites and optic radiation (data not shown).

## **Case Presentation**

Two illustrative cases (Case No. 3 and No. 5) are shown in Figure 4 and Figure 5, respectively.

Case No. 3: A 47-year-old woman who had previously undergone a surgery for a right parietal oligodendroglioma (WHO Grade II) 5 years ago was hospitalized for tumor recurrence. The lesion exhibited fluid-attenuated inversion recovery (FLAIR) hyperintensity in the right temporo-occipital region (*Fig. 4A*), and no gadolinium-enhanced mass was observed. During awake craniotomy, a visual disorder, phosphene at the left upper quadrant of the visual field, was induced in a deep region of the temporal lobe through which the optic radiations are known to pass, using a four-screen naming task (*Fig. 4B*). The optic radiation was identified on the medial surface of the tumor in the preoperative DTI (Fig. 4C). The recurrent tumor was removed while preserving the positive mapping areas (*Fig. 4D*). The diagnosis was anaplastic oligodendroglioma, WHO Grade III. Although the patient had no visual disorder before the surgery (*Fig. 4E*), she postoperatively presented with left hemianopsia during the subacute period (*Fig. 4F*). Subsequently, the left hemianopsia dynamically improved with only a partial defect persisting 6

months after surgery (*Fig. 4G*). The patient was aware of visual field recovery for the first time in the chronic phase.

Case No. 5: A 40-year-old man presented with seizures in our hospital. The first MRI revealed a gadolinium-enhanced mass accompanied by brain edema in the near-field region of the left temporal lobe including the insular cortex (*Fig. 5A*). During awake craniotomy, visual symptoms were reproduced by DES in the subcortical area where optic radiations are known to be located. The patient presented flashes of light, or phosphenes, at the right upper and lower quadrant visual fields in different subcortical regions when a four-screen naming task was used (*Fig. 5B*). In the preoperative DTI tractography, the arcuate fasciculus, inferior fronto-occipital fasciculus, and optic radiations could be identified near the tumor (*Fig. 5C*). The surgery was completed without complications, preserving the positive mapping area (*Fig. 5D*). The diagnosis was anaplastic astrocytoma, WHO Grade III. The patient presented with a visual defect at the lower right quadrant 1 month after surgery, which had not been present before surgery; however, this visual defect vastly improved 6 months after surgery (*Fig. 5E, F, and G*).

## Discussion

To the best of our knowledge, this is the first study to evaluate the time-dependent improvements in visual field deficits after awake craniotomy for supratentorial gliomas. Moreover, we showed by anatomofunctional analysis that intraoperative DES to identify and preserve the optic radiation appears to be a reliable and effective technique to avoid permanent hemianopsia with visual plasticity in awake craniotomy for gliomas.

## Visual Phenomena Elicited by Direct Electrical Stimulation

In the current study, three visual symptoms were intraoperatively observed: phosphene, blurred vision, and hallucinations, as reported previously (Gras-Combe et al. 2012). Contrary to the observations of the present study, blurred vision has been reported to be the most frequently observed intraoperative symptom (Gras-Combe et al. 2012). There are two possible reasons for this discrepancy. First, differences in stimulation intensity (a weak stimulation, 2-4 mA) might account for differences in the symptoms observed by DES. Interestingly, two different symptoms (hallucination and phosphenes) were observed at the same point by changing the stimulus intensity in the same patient (Case No. 8), which strongly supports the notion that stimulus intensity levels can differentially influence intraoperative provoked symptoms. The second possible reason could be the differences in stimulated locations. In our patients, hallucinations were observed at the anterior temporal lobe during subcortical mapping, consistent with the cortical mapping study by Penfield (Penfield and Rasmussen 1950). The hallucinations were described as dream-like "flickering fancies," and occurred when the DESs activated the temporal lobe cortex and evoked an experience memory. Additionally, they also addressed phosphenes elicited at the posterior temporal and occipital lobes, the symptoms of which included the perception of colors upon stimulation of the calcarine sulcus. These findings are similar to those observed in the subcortical mapping in our study. Thus, evoked symptoms may differ and may indicate differences (including the

presence or absence of color perception) in visual cognitive functions, depending on the stimulation site, regardless of whether the site is in a cortical or subcortical region.

VBM analysis of the anatomic relationship between the stimulation site and optic radiation revealed that most of the positive intraoperative subcortical mapping were obtained near or on the optic radiation. Thus, the three aforementioned visual symptoms are the stimulation symptoms to the optic radiation itself. The results also suggest that other white matter networks, which were reported to be associated with visual-related processing (Herbet et al. 2018), such as the inferior longitudinal bundle, inferior fronto-occipital bundle, and vertical occipital bundle, were not the subcortical pathways responsible for the three visual symptoms.

## The Visual Field and Quality of Life

Visual field deficit is a commonly observed postoperative complication after glioma surgery, particularly in cases where lesions are located in the temporal and occipital lobes. Inferior quadrantanopia is often symptomatic and results in a reduced QOL, although less than that due to hemianopsia. Hemianopsia significantly affects QOL, particularly, the ability to drive a vehicle. In European directives for driving licenses, which state the minimum visual standards for driving safely in Europe, the visual acuity standard is at least binocular vision of 20/40 and a visual field extending to 120° in the horizontal meridian (Bron et al. 2010). These criteria differ between countries; for example, Japanese driving licenses require both, a monocular vision greater than 20/28 feet and a visual field extending to 150° in the horizontal meridian. Driving a vehicle is an important life skill that allows individuals to maintain their independence and mobility; therefore, an attempt to prevent the exacerbation of vision disorders, at least to limit to a quadrantanopia, could lead to improvements in QOL. Furthermore, in a previous study that examined the relationship between intracranial disease and visual field abnormalities, it was revealed that all patients who were aware of their visual field abnormality had a visual defects in the central 5° field area by the Goldmann perimeter test (Horibe et al. 2005). Thus, prevention of visual defects in the central visual field could also help maintain a high QOL.

Postoperative visual outcomes are given much attention when surgical procedures are performed for brain tumors near the visual pathway. To date, several intraoperative techniques and modalities to prevent postoperative loss of the visual field have been attempted, and an awake craniotomy is one of the most efficient techniques to maintain the visual field. As early as the 1950s, Penfield first evaluated cortical visual function using DES (Penfield and Rasmussen 1950). After more than half a century, Duffau et al. reported the usefulness of direct electrophysiological detection of the optic radiation. This was the first report describing awake craniotomy for low-grade glioma to identify and preserve optic radiation in subcortical areas of the temporal lobe and temporo-occipital junction (Duffau et al. 2004). During the surgery, neurosurgeons terminated tumor resection when the patient experienced a visual field disturbance as an impression of "shadows" in the contralateral hemifield. Postoperatively, the patient presented with a mild visual disorder in the form of left and upper quadrantanopia. The same group subsequently proposed an intraoperative four-screen picture-naming test consisting of two objects

situated diagonally on a screen divided into four guadrants (Gras-Combe et al. 2012). They performed awake resection in 14 cases of glioma (1 WHO Grade I, 11 WHO Grade II, 2 WHO Grade III) and was able to avoid postoperative homonymous hemianopsia in 13 of the 14 patients (93%), while 1 patient had no postoperative visual disorder (7%). In our study, using the same intraoperative task, we successfully prevented homonymous hemianopsia in all patients except for patients with occipital lesions (86%), and four patients exhibited no new visual field deficits after surgery (29%). The main factors contributing to more patients with postoperative hemiparesis in the present report than in previous reports (Gras-Combe et al. 2012) could have been the inclusion of lesions in the occipital lobe and the inclusion of more highgrade tumor cases. In the patients with temporal lesions, the postoperative visual field was asymptomatic or improved in 72% of the patients, and there were no patients with permanent hemianopsia. Meanwhile, two out of three patients with occipital lobe lesions suffered from hemianopsia without improvement of the visual field defect even in the postoperative chronic period. These findings indicate that intraoperative electrophysiological monitoring of the optic radiation is feasible but with limitations in preserving the functional integrity of the posterior optic radiation near the visual cortex in the occipital lobe. Moreover, our results suggest that intraoperative mapping of the visual field with the four-screen picture-naming test is an effective method for preventing postoperative visual defects, especially in patients with temporal lesions.

### **Recovery of Postoperative Visual Field**

Although the mechanisms underlying the recovery of the visual field is not well understood, neuronal reorganization is considered to be one of the factors. From their extensive research on vision and plasticity, Hubel and Wiesel (1963) reported that neurons in the primary visual cortex of the kitten became unresponsive after elimination of visual input to the eye because of poor synapse formation from the lateral geniculate body to the visual cortex (Hubel and Wiesel 1963). Since then, increased attention has been given to visual cortex reorganization, particularly in peripheral vision disorders (Berardi et al. 2003; Maya-Vetencourt and Pizzorusso 2013; Papanikolaou et al. 2014). Regarding stroke, there are a few reports about visual functional reorganization in infants but with an unexpected absence of visual field deficits (Bova et al. 2008; Guzzetta et al. 2013). However, postoperative functional recovery in language, motor, and attentional networks after surgical resection of brain tumors has been reported (Charras et al. 2015; Shinoura et al. 2006). Duffau et al. reported that functional plasticity led to reorganization within 3 months after surgical resection of low-grade gliomas (Duffau et al. 2003). In the current study, reorganization is considered to be a mechanism for the postoperative improvements in visual field deficits because of the following three reasons. First, postoperative MRI assessments indicated that postoperative visual disorders were not caused by postoperative cerebral ischemia (data not shown). There are several reports of recovery of visual field deficits associated with cerebral infarction; the involvement of a resumption of blood flow via collateral circulation is considered to be one possible mechanism underlying this recovery (And and Kolmel 1991; Çelebisoy et al. 2011). Second, visual field defects were too prolonged to be caused by transient postoperative events, although immediate postoperative visual field deficits are typically associated with transient parenchymal edema or temporary damage of the area adjacent to the resection region. Our study indicated that the time

necessary for visual neuronal circuits to reorganize for improvement in visual deficits is at least 6 months; this time period is similar to that reported in previous studies describing other neuronal symptoms (Jiao et al. 2020). Third, recent research suggested that neuronal synaptic plasticity could be activated by direct brain stimulation using repetitive transcranial magnetic stimulation for not only motor and language functions (Hartwigsen and Volz 2021) but also the visual system with large-scale brain network dynamics (Sabel et al. 2020). In neuronal synaptic microenvironments, electrical stimulation (Toni et al. 1999) and glutamate release (Kwon and Sabatini 2011) induce rapid structural changes (within minutes) and stabilization of stimulated dendritic spines, resulting in with long-term synaptic plasticity (Yuste and Bonhoeffer 2001). In our surgical procedure, frequent invasive DESs were applied adjacent to vision-related cortico-subcortical regions to identify the reproducible functions. However, the last hypothesis requires solid evidence from future basic and clinical studies.

Our study suggested that there was a poor prognostic factor, occipital lesion. In the present study, two out of three patients (66%) with occipital lesions continued exhibiting permanent hemianopsia. In a previous report, it was suggested that subcortical stimulation could identify the passage of the optic radiation when distances between the tip of the stimulating probe and the optic radiation were less than 10 mm, and that a proximate distance may lead to an increased risk of postoperative visual field deficits (Shahar et al. 2018). Therefore, postoperative visual disorder is more likely to occur in occipital lobe lesions with a short distance from the brain surface to the visual pathway. In this study, as in previous reports, the distance from the sites of symptom induction to the optic radiation was within 10 mm, but there was no significant difference in the relationship between the distance and presence of postoperative visual field symptoms. Furthermore, contrary to previous reports (Shahar et al. 2018), there was no correlation between postoperative visual impairment and stimulus intensity in our study, which could be because we used lower stimulus amplitudes of 2–6 mA compared to the 2–15 mA stimulus amplitudes used in previous studies.

# Conclusions

DES of the optic radiation is a reliable and effective neurophysiological technique to avoid permanent visual field deficits during surgery for glioma involving or infiltrating the visual pathway. We also demonstrated that postoperative visual field deficits had the potential to improve within and up to 6 months. Anatomically, if the risk of damage to vision due to surgery is assumed, visual tasks during awake procedures could be an efficient method for preserving the visual field after glioma surgery.

# Abbreviations

DES direct electrical stimulation

DTI diffusion tensor imaging

DWI diffusion weighted imaging

FLAIR fluid-attenuated inversion recovery

MRI magnetic resonance imaging

QOL quality of life

VEP visual evoked potential

3D three-dimensional

## Declarations

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#### **Competing interests**

The authors report no competing interests.

#### **Ethics approval**

The approval for this study was granted by the Medical Ethics Committee of Kanazawa University (2020-032 [3359]).

#### Consent to participate

Written informed consent for the use of the patient's images was obtained from all patients in this study.

#### Consent to publication

Written informed consent for the use of the patient's images was obtained from all patients in this study.

#### Data availability statements

Data will be made available on reasonable request.

#### Code availability

Not applicable

#### Acknowledgments

Not applicable

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## Tables

## Table 1

#### Clinical characteristics of patients

Defect134MLeftParieto- temporalAnaplastic astrocytomaIIINo249MRightTemporalGlioblastoma, IDH- wildtypeIVNo347FRightTemporalOligodendrogliomaIIINo434MLeftTemporalOligodendrogliomaIIIYes540MLeftTemporalAnaplastic astrocytomaIIINo641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporalAnaplastic astrocytomaIIIYes844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- mutantIVNo1144FRightOccipitalEpendymomaIINo1224FLeftCecipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalAnaplastic astrocytomaIIIYes	No.	Age	Gender	Side	Location	Diagnosis	WHO Grade	Preoperative Visual Field —
134MLeftParieto- temporalAnaplastic astrocytomaIIINo249MRightTemporalGlioblastoma, IDH- wildtypeIVNo347FRightTemporo- OccipitalAnaplastic oligodendrogliomaIIINo434MLeftTemporalOligodendrogliomaIIYes540MLeftTemporalAnaplastic astrocytomaIIINo641MLeftTemporalGlioblastoma, IDH- 								Defect
249MRightTemporalGlioblastoma, IDH- wildtypeIVNo347FRightTemporo- OccipitalAnaplastic oligodendrogliomaIIINo434MLeftTemporalOligodendrogliomaIIYes540MLeftTemporalOligodendrogliomaIIINo641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporalGlioblastoma, IDH- mutantIVNo844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- mutantIVNo1144FRightOccipitalGlioblastoma, IDH- mutantIVNo1144FRightOccipitalGlioblastoma, IDH- mutantIVYes1144FRightOccipitalEpendymomaIINo1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	1	34	Μ	Left	Parieto- temporal	Anaplastic astrocytoma	III	No
347FRightTemporo- OccipitalAnaplastic oligodendrogliomaIIINo434MLeftTemporalOligodendrogliomaIIYes540MLeftTemporalAnaplastic astrocytomaIIINo641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporalGlioblastoma, IDH- mutantIVNo844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- 	2	49	Μ	Right	Temporal	Glioblastoma, IDH- wildtype	IV	No
434MLeftTemporalOligodendrogliomaIIYes540MLeftTemporalAnaplastic astrocytomaIIINo641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporo- OccipitalAnaplastic 	3	47	F	Right	Temporo- Occipital	Anaplastic oligodendroglioma	III	No
540MLeftTemporalAnaplastic astrocytomaIIINo641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporo- OccipitalAnaplastic astrocytomaIIIYes844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- 	4	34	Μ	Left	Temporal	Oligodendroglioma	II	Yes
641MLeftTemporalGlioblastoma, IDH- mutantIVNo733FLeftTemporo- OccipitalAnaplastic astrocytomaIIIYes844MLeftTemporal TemporalAnaplastic astrocytomaIIINo942MLeftTemporal TemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- wildtypeIVYes1144FRightOccipitalEpendymomaIINo1224FLeftTemporal OccipitalAnaplastic astrocytomaIINo1339MLeftTemporal Diffuse astrocytomaIIYes	5	40	Μ	Left	Temporal	Anaplastic astrocytoma	III	No
733FLeftTemporo- OccipitalAnaplastic astrocytomaIIIYes844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- 	6	41	Μ	Left	Temporal	Glioblastoma, IDH- mutant	IV	No
844MLeftTemporalAnaplastic astrocytomaIIINo942MLeftTemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- wildtypeIVYes1144FRightOccipitalEpendymomaIINo1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic 	7	33	F	Left	Temporo- Occipital	Anaplastic astrocytoma	III	Yes
942MLeftTemporalGlioblastoma, IDH- mutantIVNo1073MRightOccipitalGlioblastoma, IDH- wildtypeIVYes1144FRightOccipitalEpendymomaIINo1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	8	44	Μ	Left	Temporal	Anaplastic astrocytoma	III	No
1073MRightOccipitalGlioblastoma, IDH- wildtypeIVYes1144FRightOccipitalEpendymomaIINo1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	9	42	Μ	Left	Temporal	Glioblastoma, IDH- mutant	IV	No
1144FRightOccipitalEpendymomaIINo1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	10	73	Μ	Right	Occipital	Glioblastoma, IDH- wildtype	IV	Yes
1224FLeftOccipitalEpendymomaIINo1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	11	44	F	Right	Occipital	Ependymoma	II	No
1339MLeftTemporalAnaplastic astrocytomaIIIYes1446MLeftTemporalDiffuse astrocytomaIIYes	12	24	F	Left	Occipital	Ependymoma	II	No
14 46 M Left Temporal Diffuse astrocytoma II Yes	13	39	Μ	Left	Temporal	Anaplastic astrocytoma	III	Yes
	14	46	М	Left	Temporal	Diffuse astrocytoma	II	Yes

M = Male, F = Female

## Table 2

## Characteristics of intraoperative symptoms and postoperative visual field

No. Intraoperative Findings

Postoperative Defect of Visual Field

	Symptom	Induced Site	Stimulation (mA)	Location	Central Area	Time- Dependent Improvement
1	Blurred vision	Rt. 1/4, lower	5	No	No	Stable
2	Phosphene	Lt. 1/4, Iower	3.5	Lt. 1/4 upper	No	Yes
3	Phosphene	Lt. 1/4, upper	4	Lt. partial middle	Yes	Yes
4	Phosphene	Rt. 1/2	3	No	No	Stable
		Rt. 1/4, lower				
5	Phosphene	Rt. 1/4, upper Rt. 1/4, lower	3.5	Rt. lower 1/4	No	Yes
6	Phosphene	Rt. 1/4, upper	6	No	No	Stable
7	Phosphene	Rt. 1/4, Iower	4	No	No	Stable
8	Hallucination	Rt. 1/2	6	Rt. upper 1/4	No	No
	Phosphene	Rt. 1/4, upper	3			
9	Phosphene	Rt. 1/4, lower	6	Rt. upper 1/4	Yes	No
10	Phosphene	Lt. 1/4, upper	2 or 6	Lt. 1/2	Yes	No
11	Phosphene	Lt. 1/4, upper	5	Lt. 1/2	Yes	No
12	Phosphene	Rt. 1/4, upper Rt. 1/4, lower	б	Rt. middle partial	No	Yes
13	Blurred vision	Rt. 1/4, lower	4	Rt. 1/2 partial	Yes	Yes
14	Blurred vision	Rt. 1/4, upper	3.5	Rt. upper 1/4	Yes	No

Rt = Right, Lt = Left

# Figures

## Figure 1

Overlapping maps of resection cavities

A: An overlapping map of all resection cavities in axial images of Montreal Neurological Institute (MNI) coordinates.

B: An overlapping map of all resection cavities that are fused to the right side on an MNI template. A three-dimensional lateral image is shown on the right.

#### Figure 2

Voxel-based morphometry mapping of visual symptoms.

A total of 33 positive mapping sites (red) of visual phenomena were overlaid onto a normal brain template that included the optic radiation (green) (A). Visual symptoms were classified according to the elicited visual areas: Contralateral upper quadrant (yellow), lower area (blue), and optic radiations (green) (B). Each center of distribution was statistically deviated into the upper (-33, -58, -4; yellow) and lower (-34, -52, 0; blue) directions on the MNI coordinate space (C). All positive mapping sites were classified into phosphene with color (blue) or without color (yellow), blurred vision (red), and hallucination (green). Lateral view (left) and upward (right) view (D). Lateral (left) and upward (right) views in A, B, and D images.

#### Figure 3

Flowchart of time-dependent changes in visual field.

Fourteen patients were classified based on the positive mapping location (temporal lobe or occipital lobe) and the results of the first (1 month after surgery) and second (6 months after surgery) visual field tests, and thereafter categorized into good visual field (field-preserving group) and hemianopsia (field-loss group) groups.

An illustrative case (No. 3): perioperative MRIs, the intraoperative picture, intraoperative images of tractography, and time-dependent change in the visual field.

A: Fluid-attenuated inversion recovery (FLAIR) axial (left) and sagittal (right) images before awake craniotomy.

B: Intraoperative picture after mapping and resection of the tumor. Number tags 4-6 indicate positive sites with visual symptoms (phosphenes at the upper left quadrant of the visual field).

C: 3D-visualized neuronavigation images of the tumor (brown) and white matter tracts reconstructed by diffusion tensor imaging. Inferior fronto-occipital fascicle, blue; superior longitudinal fasciculus (SLF) II, magenta; SLF III, yellow; optic radiations, green. A white square is enlarged as the right image showing the relationship between positive mapping sites and tractography of the optic radiation (green). The sites of elicited symptoms were determined according to expected regions of the visual pathway. A doll in the lower left corner indicates the direction of the head. A, anterior; I, inferior; P, posterior; S, superior.

D: FLAIR axial (left) and sagittal (right) images after awake surgery.

E-G: The results of visual field examinations before surgery (E), 1 month after surgery (F), and 6 months after surgery (G). The visual field deficits showed a time-dependent improvement although a partial visual defect, including in the central visual field, persisted for 6 months after surgery.

A, anterior; I, inferior; P, posterior; S, superior.

## Figure 5

An illustrative case (No. 5): perioperative MRIs, intraoperative picture, intraoperative images of tractography, and the time-dependent changes in the visual field.

A: T1-weighted axial image with contrast enhancement before awake craniotomy

B: Intraoperative picture after mapping and resection of the tumor. Number tags 4, 6, and 7 indicate positive sites with visual symptoms. Phosphenes were reproduced at the upper right (tag no. 7) and lower right quadrant visual fields (tag no. 4, 6) by direct electrical stimulation.

C: 3D-visualized neuronavigation images of the tumor (brown) and white matter tracts reconstructed by diffusion tensor imaging. Superior longitudinal fasciculus III, yellow; arcuate fascicle, red; optic radiations, green. A white square is enlarged as the right 3D-reconstructed image indicating the relationship between positive mapping sites and tractography of the optic radiation (green) around the tumor (orange).

D: T1-weighted axial image with contrast enhancement after awake surgery. A doll in the lower left corner indicates the direction of the head.

E-G: The results of visual field examinations before surgery (E), 1 month after surgery (F), and 6 months after surgery (G). The visual field disturbance was greatly improved during the postoperative chronic period.

A, anterior; I, inferior; P, posterior; S, superior.

# **Supplementary Files**

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