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TECHNICAL NOTE

# The use of intraoperative near-infrared indocyanine green videoangiography in the microscopic resection of hemangioblastomas

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**Abstract**
*Background* The authors assessed the usefulness of intraoperative near-infrared indocyanine green videoangiography (ICG-VA) in the microscopic resection of hemangioblastomas.
*Methods* From January 2009 to February 2012, nine consecutive patients (seven men, two women) who underwent surgery for hemangioblastomas using intraoperative ICG-VA were included in this study. Surgery was performed on four cystic cerebellar lesions with mural nodules, two solid tumors (one in the cerebellar hemisphere and one in the medulla oblongata), one spinal tumor and multiple tumors in two patients with von Hippel-Lindau disease. Of the nine patients, three were treated for recurrent tumor. The ICG-induced fluorescence images of hemangioblastomas with variable presentation were evaluated.
*Results* All tumors could be completely removed en bloc. Blood flow in the tumor and tumor-related vessels at the brain surface were clearly detected by ICG-VA in all cases, except one recurrent tumor where postoperative adhesive scar tissue obstructed ICG-induced fluorescence resulting in poor delineation of the blood flow patterns and tumor margins. ICG-VA was also helpful for detecting the multiple small mural nodules within the cyst or the tumors buried under thin gliotic neural tissue despite reduced fluorescence.
*Conclusion* Intraoperative ICG-VA is a safe and easy modality for confirming the vascular flow patterns in hemangioblastomas. In addition, ICG-VA provided useful information for intracystic small lesions or lesions concealed under thin brain tissue in order to accomplish total resection of these tumors.

**Keywords** Hemangioblastoma · Indocyanine green videoangiography · Microsurgery

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## Introduction

Hemangioblastomas are benign, highly vascular neoplasms of the central nervous system that account for 2% of all intracranial tumors, 10% of primary posterior fossa tumors, and 2-3% of intramedullary spinal tumors [7, 11]. Surgical management of these lesions entails complete en bloc tumor removal [9, 11–13]. In order to achieve this goal, it is essential to have an ongoing intraoperative anatomical understanding of the feeding arteries and the main draining veins. Recently, intraoperative near-infrared indocyanine green videoangiography (ICG-VA) has been considered as the standard technique for confirming vascular patency in a variety of cerebrovascular diseases [1–3, 6, 8, 10]. In the present study, ICG-VA was applied in the microsurgery of hemangioblastomas. To evaluate the usefulness of ICG-VA in tumor resection, we assessed the flow dynamics patterns and the ability of intraoperative fluorescence images to delineate tumors.

## Patients and methods

### Patient population

From January 2009 to February 2012, nine consecutive patients with hemangioblastoma underwent microsurgical resection using ICG-VA (seven men and two women; median age 48.6 years; range 32-72 years; Table 1). Three patients

**Table 1** Clinical summary of characteristics in nine patients with hemangioblastoma

| Case no. | Age (years)/ sex | Initial symptoms | Tumor location | Surgical procedure | Postoperative course |
|---|---|---|---|---|---|
| 1 | 53/M | Motor weakness of bilateral legs | MO and left CH | Total removal | Rehabilitation for gait disturbance |
| 2 | 47/M | Cerebellar ataxia | Left CH | Removal of MN | Uneventful |
| 3 | 33/F | Cerebellar ataxia | Left CH | Removal of MN | Uneventful |
| 4 | 59/M | Paresthesia of left arm and face | Left C1 cervical cord | Total removal | Left facial pain 1 month postop. |
| 5 | 44/M | Motor weakness of right arm, VHL disease | Multiple lesions, MO and cerebellum | Total removal of 4 tumors | Rehabilitation for transient worsening motor weakness of right arm |
| 6 | 58/M | Cerebellar ataxia | Right CH | Total removal | Mild cerebellar ataxia |
| 7 | 72/F | Cerebellar ataxia | Left CH | Removal of MN | Uneventful |
| 8 | 32/M | Cerebellar ataxia | Left CH | Removal of MN | Uneventful |
| 9 | 39/M | Cerebellar ataxia, VHL disease | Multiple lesions, MO and cerebellum | Total removal of cerebellar tumor | Rehabilitation for gait disturbance |

*M* male, *F* female, *CH* cerebellar hemisphere, *MO* medulla oblongata, *MN* mural nodule, *VHL* von Hippel-Lindau

demonstrated clinical or radiographic evidence of tumor recurrence and of them two were diagnosed with von Hippel-Lindau (VHL) disease.

### Surgical procedure and method of ICG-VA

All patients underwent routine surgical procedures for treatment of intracranial and spinal hemangioblastomas. After careful dural opening with avoidance of injury to the draining veins, ICG was administrated as an intravenous bolus. Information regarding blood flow within the tumor and in the surrounding tumor-related vessel was obtained by an initial ICG-VA. Each artery was carefully identified with ICG-VA as either a feeding or passing artery, and only the feeding arteries were interrupted. If necessary, ICG-VA was repeated during temporary occlusion of the vessels. Subsequently, dissection was performed until the tumor no longer demonstrated ICG-induced fluorescence, at which point the main draining veins were then sacrificed. When only a few draining veins appeared during surgical resection, the small draining veins were sacrificed, followed by direct confirmation of delayed blood flow by ICG-VA. Next, if the tumor enhanced with ICG in the final phase, any feeding arteries concealed behind the main draining veins were sacrificed simultaneously. Lastly, the resection bed was carefully inspected for hemostasis and any evidence of residual tumor was confirmed by additional ICG-VA as necessary. None of the patients were treated with preoperative embolization. Postoperative enhanced magnetic resonance (MR) imaging was performed in all cases within 24 h of surgery.

ICG-VA was performed using two microscope systems integrated with ICG technology (OPMI Pentero, Carl Zeiss, Oberkochen, Germany and MM80 with F-light 300, Mitaka Kohki, Mitaka, Japan). The technique of ICG-VA has already been described elsewhere in detail [1, 6, 8]. ICG dosing was 0.125–0.15 mg/kg allowing for intravenous injection. ICG-VA was repeated at intervals of more than 10 min.

## Results

All tumors were removed en bloc via ICG-VA with no evidence of residual hemangioblastoma as measured by intraoperative ICG-VA or postoperative MR imaging. In two patients with VHL disease (cases 5 and 9), the asymptomatic tumors outside the operative field were treated conservatively. There were no complications in any patient due to the intravenous administration of ICG.

### ICG-VA findings

The flow dynamics of the feeding arteries, the tumor itself and the draining veins appeared within 10 s after intravenous administration of ICG. In the early arterial phase, the tumors emitted ICG-induced fluorescence, while the draining veins were detected in the late arterial phase of ICG-VA (Fig. 1, case 2). During occlusion of the feeding arteries, ICG-induced fluorescence of the tumor and the draining veins was delayed or disappeared partially. When the arterial supply was completely interrupted, there was no apparent evidence of ICG-induced fluorescence within the tumor.

Only the superficial vessels of the brain or the exposed portion of the tumor could be clearly visualized by ICG-VA because of the limited penetration depth of the ICG dye. Tumor margins buried beneath postoperative adhesive scar tissue could not be clearly defined with ICG-VA (case 6),

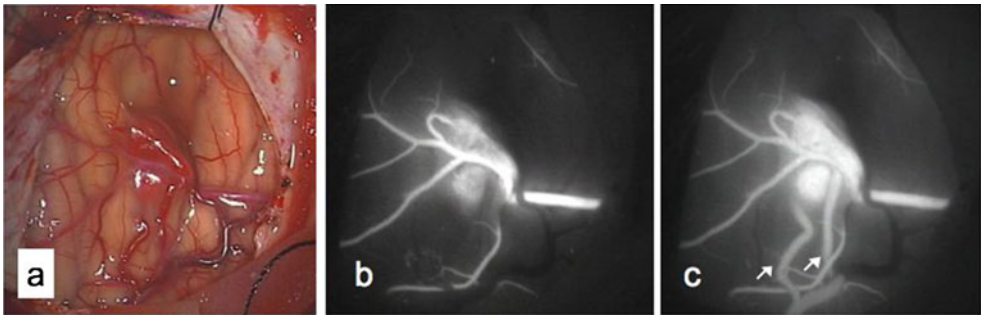


**Fig. 1** Intraoperative photogram (**a**) showing the mural nodule and tumor-related vessels in the cerebellar cortex. The early (**b**) and late (**c**) arterial phase of initial ICG-VA revealing the blood flow through the feeding artery, the mural nodule, and draining veins. The draining veins (*arrows*) were detected in the late arterial phase (case 2)

while tumors concealed under thin brain tissue or deep-seated tumors within the cyst were only faintly detected despite reduced fluorescence (case 5)

## Case illustrations

### Brainstem hemangioblastoma (case 1)

This 53-year-old man presented with progressive tetraplegia and cerebellar ataxia. MR images revealed an enhancing mass lesion in the dorsal medulla oblongata (Fig.2a). A midline suboccipital approach with C-1 laminectomy was used for tumor resection. After completing careful dural opening, a reddish tumor was exposed in the cisterna magna (Fig.2b). Initial ICG-VA clearly defined the blood flow within the tumor and the surrounding vessels immediately after dye injection (Fig.2c). Main feeders from the vertebral artery were occluded using temporary clips. However, a second confirmatory ICG-VA showed delayed ICG-induced fluorescence in the entire tumor. After occluding a left PICA feeder, a defect of ICG-induced fluorescence was revealed in the left-rostral portion of the tumor (Fig.2d). In this fashion, ICG-VA was repeated throughout the dissection with interruption of further feeding arteries until a tumor devoid of ICG-induced fluorescence was demonstrated (Fig.2e). Subsequently, the main draining vein was sacrificed and the tumor was completely removed en bloc from the medulla oblongata. Postoperative MR images revealed total resection of the tumor (Fig.2f).

### Multiple hemangioblastomas in VHL disease (case 5)

This 44-year-old man who was originally diagnosed with VHL disease presented with right hemiplegia. MR images revealed multiple enhancing lesions with cysts in the brain stem and bilateral cerebellar hemisphere (Fig.3a). A midline suboccipital craniotomy was performed in the prone position. The dural opening revealed the mural nodules and surrounding vessels on the cyst wall (Fig.3b). Initial ICG-VA clearly detected the mural nodules on the surface of the cyst with tumor-related vessels. ICG-induced fluorescence was also visible through the cyst wall, enabling detection of

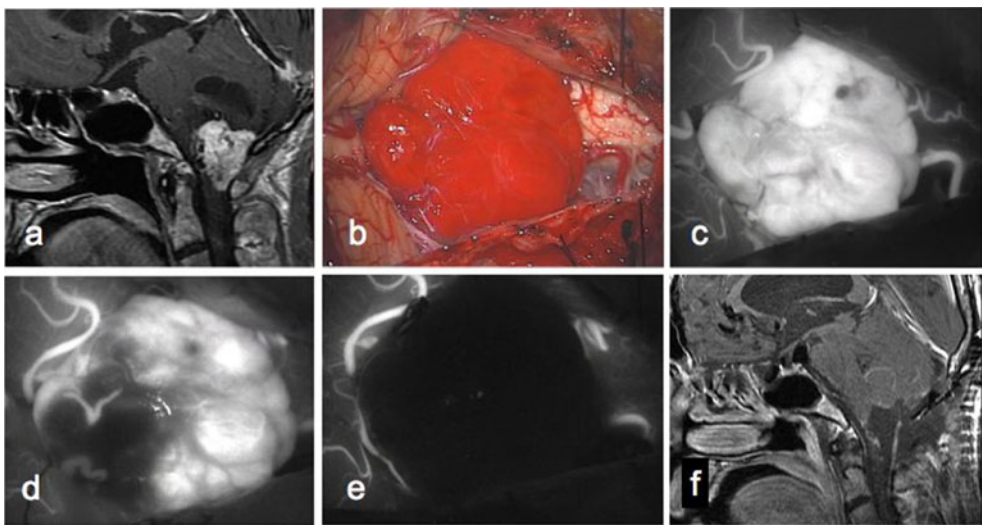


**Fig. 2** Sagittal enhanced MR image (**a**) demonstrating a solid tumor with a cyst in the dorsal medulla oblongata. Intraoperative photogram (**b**) showing a red tumor exposing the cisterna magna. Initial ICG-VA (**c**) showing blood flow in the tumor and surrounding vessels. After occlusion of feeders from the bilateral vertebral and the left PICA, ICG-induced fluorescence disappeared in the left-rostral component of the tumor (**d**). Final ICG-VA (**e**) showing the tumor with disappearance of ICG-induced fluorescence. Postoperative MR image (**f**) demonstrating complete en bloc resection of the tumor (case 1)

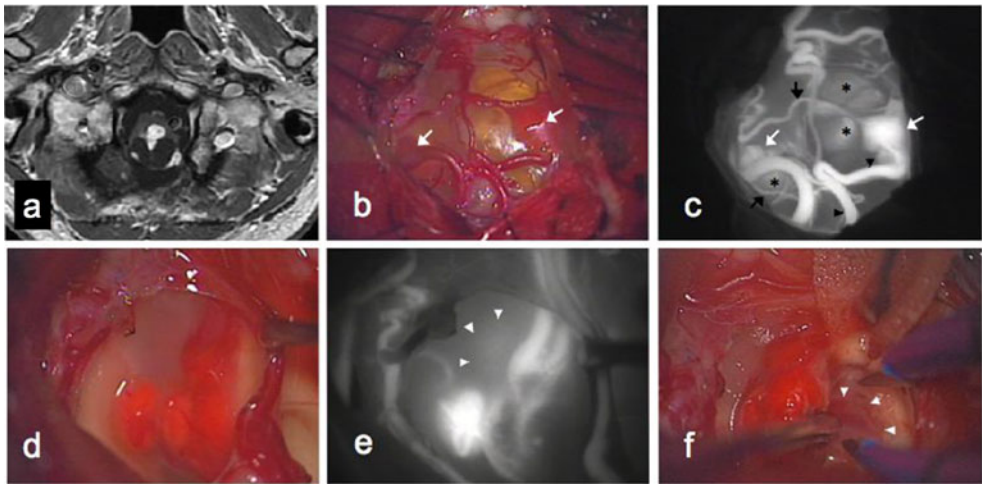


**Fig. 3** Axial enhanced MR image (**a**) demonstrating multiple small mural nodules with cysts in the medulla oblongata. Intraoperative photogram (**b**) showing two mural nodules (*white arrows*) and tumor-related vessels on the cyst wall. Initial ICG-VA (**c**) clearly revealing mural nodules on the cyst wall (*white arrows*), the feeding arteries (*black arrows*), the draining veins (*black arrowheads*) and faint appearance of the deep-seated mural nodule within the cyst (*black asterisks*). After opening the cyst, intraoperative photogram (**d**) show the deep-seated mural nodule. Second ICG-VA (**e**) faintly revealing the intramedullary component of the deep-seated mural nodule (*white arrowheads*). Intraoperative photogram (**f**) showing the intramedullary component (*white arrowheads*) located behind the mural nodule within the cyst (case 5)

the deep-seated mural nodule within the cyst (Fig.3c). The two dorsal mural nodules on the surface of the cyst wall were removed, followed by opening of the cyst wall (Fig.3d). ICG-VA was performed again and the deep-seated mural nodule, including tumor-related vessels, was more clearly visualized. The intramedullary component concealed under thin layers of gliotic neural tissue, however, was only faintly visualized (Fig.3e). After removal of the mural nodule on the internal wall of the cyst, the intramedullary component was gently removed (Fig.3f).

Recurrent cerebellar hemangioblastoma (case 6)

This 58-year-old man presented with progressive cerebellar ataxia. MR images revealed an enhancing mass lesion with accompanying cyst in the right cerebellar hemisphere (Fig.4a). The previous suboccipital craniotomy was employed and the dura mater was opened with difficulty because of dense adhesions on the surface of the tumor and on the cerebellar cortex (Fig.4b). Initial ICG-VA of the tumor margins and blood flow in the surrounding vessels was not clearly detectable (Fig.4c) due to postoperative adhesive scar tissue, which obstructed penetration of the ICG-induced fluorescence. The tumor was carefully dissected from the cerebellar hemisphere and removed en bloc. Finally, ICG-VA confirmed the presence of normal surrounding vasculature without evidence of residual tumor in the resection bed. Postoperative MR images demonstrated gross total resection of the tumor (Fig.4d).

## Discussion

Since the commercialization of an integrated microscopic ICG system technology, there has been a surge in use of ICG-VA in microsurgical procedures. ICG-VA has been recognized as a relatively noninvasive modality which can provide rapid acquisition of real-time intraoperative information on the vascular flow dynamics in the operative field. This modality has shown to be especially useful during cerebral aneurysm surgery for confirmation of complete aneurysm occlusion and preservation of patency in parent and perforating arteries [1, 2, 8]. Recently, ICG-VA has been applied in arteriovenous malformation (AVM) or arteriovenous fistula surgery for detection of vascular flow patterns prior to lesion expatriation as well as for confirmation of postoperative residual AVM vasculature [3, 6, 10].

Based on these multiple applications, we considered the possibility of ICG-VA for use in hypervascular brain tumor surgery. In particular, hemangioblastomas are vascular-rich tumors with variable presentations and in some instances can be approached using surgical strategies similar to that of AVMs [12]. Therefore, we assessed whether ICG-VA was useful in the surgical management of hemangioblastomas.

The most important point for safe surgical management of hemangioblastomas is preservation of the main draining veins until the arterial blood supply can be adequately controlled and interrupted [11–13]. If preservation of the main draining veins is neglected, catastrophic hemorrhage from the tumor can occur and subsequent hemostasis becomes extremely difficult. Therefore, a thorough understanding of the feeding and draining vasculature surrounding

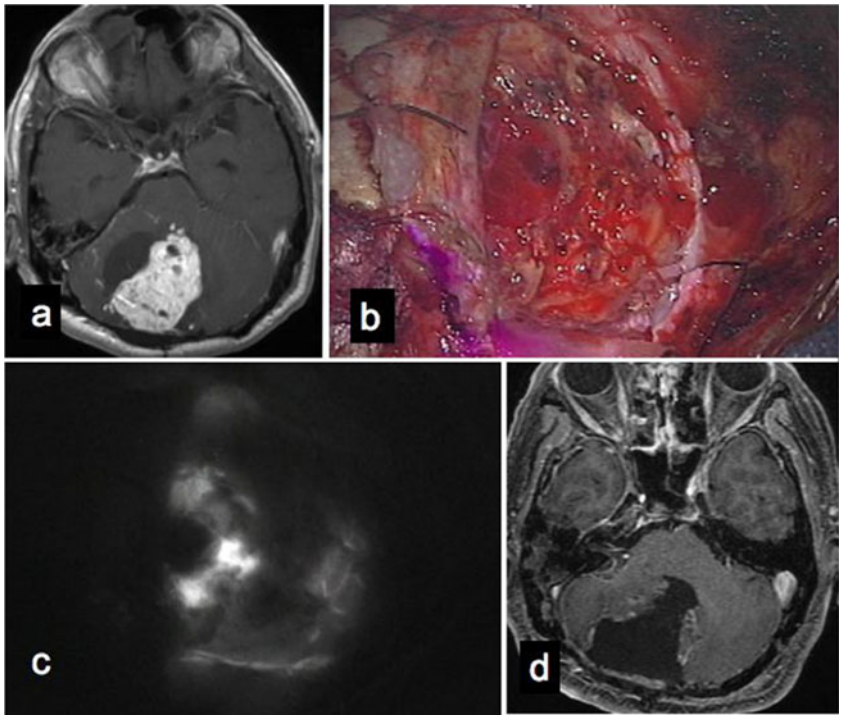


**Fig. 4** Axial enhanced MR image (**a**) demonstrating a solid tumor with cyst in the right cerebellar hemisphere. Intraoperative photogram (**b**) showing the tumor and the cerebellar cortex covered by postoperative adhesive scar. Initial ICG-VA (**c**) revealing poor visualization of the tumor and surrounding vessels due to obscuring of ICG-induced fluorescence by connective tissue. Postoperative MR image (**d**) demonstrating total resection of the tumor (case 6)

this lesion is essential. ICG-VA is especially useful in evaluating individual feeding arteries, which may be quickly and easily confirmed. By temporary occlusion of the feeding arteries, ICG-induced fluorescence can be seen to disappear or to show delayed illumination in the tumor itself. In contrast, identification of the draining veins is not usually difficult because of the change in vessel tone due to the so-called "red veins" and vessel diameter expansion. ICG-VA provides exceptionally clear confirmation of the presence of these draining veins as evidenced by the appearance of dilated vessels in the late arterial phase.

Safe hemangioblastomas resection requires a careful dissection of the tumor-neural tissue interface with interruption of the feeding arteries which course through the dissection plane [5]. ICG-VA is not necessary for identifying the surgical dissection plane of intramedullary component because the typical reddish color of the tumor is clearly accentuated at the borders of the tissue plane. However, the real-time information of flow dynamics in the tumor itself could be obtained by repeated ICG-VA during interruption of each feeding artery. Diminished ICG-induced tumor fluorescence indicates that the tumor may be safely removed en bloc.

ICG-VA is also helpful for detecting small lesion or lesions concealed under thin brain tissue. This modality is especially useful in managing VHL disease with multiple tumors, where locations of the each tumor could be confirmed by ICG-induced fluorescence image. Likewise case 5, the multiple small mural nodules within the cyst were detectable and the tumors buried under thin gliotic neural tissue were faintly visible despite reduced fluorescence.

Hwang et al. [4] described how ICG-VA aided in defining the distinction of recurrent tumor extension from adhesive connective tissue. However, in our series, we found that it was difficult to clearly define the recurrent tumor and its surrounding vessel architecture compared with the initial surgical case. The reason for this was that adhesive postoperative scar and thick brain tissue obstructed the visualization of ICG-induced fluorescence. In such conditions, there may be a limit to detection of the tumors by ICG-VA due to such barriers interrupting penetration of the fluorescent dye.

## Conclusions

Hemangioblastomas are highly vascular lesions which require an intricate understanding of the feeding and draining vascular architecture in order to achieve safe and satisfactory treatment outcomes. The relatively novel integrated intraoperative ICG-VA microscopic imaging system is an ideal adjunctive modality for use in the surgical management of hemangioblastomas. In particular, repeated ICG-VA allows for easy, almost instantaneous, precise confirmation of the flow dynamics in the tumor and tumor-related vessels. Moreover, ICG-VA may be helpful for detecting the variable presentation of hemangioblastomas, such as small mural nodules within the cyst and intramedullary tumors covered by thin layers of brain tissue. Despite the small patient number in this study, ICG-VA is a safe and efficient real-time intraoperative vascular imaging technique,

which has potential for adjunctive use in hemangioblastoma surgery.

**Conflicts of interest** None.

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## Comments

In this article, the authors assessed the use of intraoperative near-infrared indocyanine green videoangiography (ICG-VA) in the microsurgical resection of nine cases of hemangioblastoma. Although this information is not completely new, the study provides some insights in the use of ICG-VA in the treatment of hemangioblastomas presenting different surgical challenges. According to the authors' experience, ICG-VA provided a valid contribution in most situations. This and other studies suggest that this technique has the potential to become the routine intraoperative vascular imaging during both cerebrovascular and tumour surgery. Nonetheless, it is worth mentioning the fact that the angiographic perspective provided by the ICG video technique is restricted to the field of view through the microscope. Furthermore, blood clots or, according to the authors' experience, scar tissue may hide relevant vascular structures. So, as the ICG fluorescence may be affected by calcifications and thick-walled atherosclerotic vessels, therefore its use in combination with other methods—including visual inspection, intraoperative angiography and Doppler ultrasonography—should be evaluated in difficult cases.

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