Utility of Indocyanine Green Videoangiography with FLOW 800 Analysis in Brain Tumor Resection - Venous Protection Technique

yue sun  
the First Affiliated Hospital of Soochow University

Zilan Wang  
the First Affiliated Hospital of Soochow University

Fan Jiang  
the First Affiliated Hospital of Soochow University

Xingyu Yang  
the First Affiliated Hospital of Soochow University

Xin Tan  
The Affiliated Hospital of Nanjing Medical University, Suzhou Municipal Hospital

Zhouqing Chen  
the First Affiliated Hospital of Soochow University

Yanfei Liu  
Suzhou Integrated Traditional Chinese and Western Medicine Hospital

Yun Zhu  
the First Affiliated Hospital of Soochow University

Zhong Wang ( wangzhong761@163.com )  
the First Affiliated Hospital of Soochow University

Research Article

Keywords: FLOW 800, ICG-VA, venous preservation, brain tumor, neurosurgery

Posted Date: January 4th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-862229/v2

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

**Background:** When it comes to central nervous system tumor resection, preserving vital venous structures to avoid devastating consequences such as brain edema and hemorrhage is important. Whereas, in clinical practice, it is difficult to obtain clear and vivid intraoperative venous visualization and blood flow analysis.

**Methods:** We retrospectively reviewed patients underwent brain tumor resection through the application of indocyanine green videoangiography (ICG-VA) integrated with FLOW 800 from February 2019 to December 2020 and presented our clinical cases to demonstrate the process of venous preservation. Galen vein, sylvian vein and superior cerebral veins were included in our cases.

**Results:** Clear documentations of the veins from different venous groups were obtained via ICG-VA integrated with FLOW 800, which semiquantitatively analyzed the flow dynamics. ICG-VA integrated with FLOW 800 enabled us to achieve brain tumor resection without venous injury and obstructing the venous flux.

**Conclusions:** ICG-VA integrated with FLOW 800 is an available method for venous preservation, though further comparison between ICG-VA integrated with FLOW 800 and other techniques of intraoperative blood flow monitoring is needed.

Introduction

A great number of post-operative complications after resection of central nervous system tumors are related to the lack of prevention or recognition of venous problems.[1] Vital venous structures include the major dural sinuses like the superior sagittal sinus, the deep veins like the vein of Galen and some dominant superficial veins like the vein of Labbe.[2] Iatrogenic venous injury may manifest as brain edema, intracranial hypertension and hemorrhagic infarcts. Therefore, having a good knowledge of venous anatomy and physiology is critical.

Besides magnetic resonance angiography (MRA), magnetic resonance venography (MRV), transcranial doppler (TCD) and digital subtraction angiography (DSA), microscope-integrated indocyanine green videoangiography (ICG-VA) has been recognized as a beneficial adjunct to figure out the flow dynamics of cerebral vessels nowadays.[3] The flow dynamics were semiquantitatively analyzed with FLOW 800 software integrated in the surgical microscope. Fluorescence intensities in regions of interest were calculated based on the average arbitrary intensity units. And then the algorithm reconstructed colorful maps based on maximal fluorescence intensities and delay times. ICG-VA integrated with FLOW 800 was widely used in neurosurgery, especially for the evaluation of aneurysmal clipping, cerebral arteriovenous malformation resection and the flow patency during bypass surgery. [4-9] And previous studies presented the guide effects of ICG-VA and FLOW 800 in the venous sacrifice decision process.[10, 11] However, the venous protection effects of ICG-VA and FLOW 800 was still lack of attention. Here, we report four typical cases of central nervous system (CNS) tumors in close proximity to important venous structures. ICG-VA
integrated with FLOW 800 were used before or after tumor resection in these cases to individuate landmarks for the surgical approach, confirm the venous patency and prevent potential complications caused by venous problems.

**Methods**

This is a single-center, retrospective study of patients with CNS tumor close to important veins who underwent microsurgical operations using ICG-VA and FLOW 800 from February 2019 to December 2020. The exclusion criteria include (a) patients allergic to ICG, (b) patients younger than 18 years old, (c) patients with life-threatening conditions. Written informed consent was obtained from all patients.

All the patients underwent magnetic resonance imaging (MRI) as a routine examination before surgery to confirm tumor size and location. 3D imagings were reconstructed preoperatively based on the contrast enhanced MRI to clarify the relationship between tumor and blood vessels, especially the veins. The solution of ICG was prepared in advance and administrated intravenously before and after tumor resection upon required by the neurosurgeon.

We gave patients 25mg of ICG intravenously. Then, the integrated light source induced the fluorescence, and INFRARED 800 (IR800) video filmed it. FLOW 800 software integrated in the surgical microscope (Release 2.21, Carl Zeiss Co., Germany) generated a color-coded map timely for blood flow assessment via IR800 video, using red for early appearance, yellow or green for medium appearance, blue for late appearance. Fluorescence intensity curves of regions of interest (ROIs) were also provided by FLOW 800 software for hemodynamic analysis.

We collected series of information from every patient, including age, gender, clinical manifestations, radiological manifestations which demonstrated the relationship of tumor and vasculars, intraoperative findings, Flow 800 results and prognosis.

**Results**

Based on the exclusion criteria, our study included 23 patients with various clinical presentations and tumor types. The age of our patients ranged from 19 to 70 (mean age of 53) and the ratio of male to female is 4:5. What the patients had in common was the their tumors were in close proximity to veins, even encased them. Galen vein, sylvian vein and superior cerebral veins were involved in our study. ICG-VA integrated with FLOW 800 semiquantitatively analyzed the flow dynamics of the different venous groups. The following four cases showing the protection of veins mentioned above were presented to show the value of ICG-VA with Flow 800 in the surgery of tumor resection.

**Case presentation**
Case 1

A 30-year-old woman revealed a mass located at posterior horn of the right lateral ventricle with no apparent clinical symptoms (Figure 1A, B). As shown in the 3D reconstruction imaging, the mass was close to the Galen vein (Figure 1C). Intraoperative neurosurgery navigation was used. During the surgical process (Figure 1D), with the aid of ICG-VA integrated with FLOW 800, the visualization and identification of the deep veins were achieved (Figure 1E, F). Galen vein was protected intact and the patient had a good prognosis.

Case 2

A 58-year-old woman who complained about intermittent headache showed a large cystic mass in the frontotemporal lobe. The mass was sized 7.7*5.4*5.3 cm, with midline shift and compression on the lateral ventricle (Figure 2A, B). The 3D reconstruction imaging revealed that the right middle cerebral artery was displaced and encased by the mass (Figure 2C), and the sylvian vein was also compressed by the mass (Figure 2D). The mass was removed via pterional approach (Figure 2E, I). With the help of ICG-VA and FLOW 800, we removed the tumor with minimizing injury of the sylvian vein (Figure 2E-G, I-K). The pre- and post- FLOW 800 analysis on the same two veins also indicated that the venous flow was almost unaffected. The patient was also discharged soon after operation without any complications.

Case 3

A 36-year-old woman presented with persistent headache. Magnetic resonance imaging (MRI) with contrast showed a left parietal lobe lesion which was approximately 4.5*5 cm in size. (Figure 3A, B). The lesion had a close relationship with these superior cerebral veins according to 3D reconstruction. (Figure 3C, D) The patient underwent tumor resection. The patient's pre- and post-central gyrus and surrounding vein such as central sulcus vein and postcentral sulcus vein were all anatomically preserved under the microscope. After administering the intravenous bolus of ICG, the veins were marked clearly and the mapping reconstructed by the software demonstrated the blood flow condition. However, ICG-VA with FLOW 800 indicated the occlusion of the postcentral sulcus vein (Figure 3F). We then noticed the hyaline thrombus in the postcentral sulcus vein, which might be caused by the traction and compression during tumor resection (Figure 3E). Special attention was paid for postoperative management to prevent brain edema, epilepsy and bleeding after venous infarction. The patient did well and was discharged soon after operation.

Case 4

A 56-year-old woman presented with a one-month history of headache and intermittent vomit. Symptoms worsen with urinary and fecal incontinence for 20 days. MRI with contrast showed a necrotic mass with
irregular shape on the bilateral frontal lobe and corpus callosum (Figure 4A, B). We also used ICG-VA and FLOW 800 to guide the preservation of the two superior cerebral vein when performed transcortical surgical approach to remove the tumor (Figure 4C, D). The patient was discharged without worsen of symptoms.

**Discussion**

In recent decades, increasing number of neurosurgeons have realized the importance of venous preservation because the injury or occlusion of important intracranial venous structures might lead to severe complications, such as hematoma, epilepsy, cerebral edema, hemiplegia, and aphasia.[12] Instead of depending heavily on their own surgical experience, neurosurgeons took advantage of neuroimaging tools such as DSA, MRA, MRV and TCD preoperatively to analyze the vascular structures surrounding the lesion. In addition, the development of intraoperative microvascular Doppler (MVD) and ICG-VA has made the visualization of intraoperative blood flow possible. These technics that help neurosurgeons to understand the dynamic flow of the venous system and how to preserve them are welcoming.

Groups of veins were treated differently after neurosurgeons made surgical judgement, considering whether to preserve them.[13] As for the superficial cerebral veins, they are strongly interconnected, making it acceptable to sacrifice one of them. Additionally, once the terminal ends of the Sylvian left the fissure and entered the sphenobasal, sphenoparietal, or cavernous sinus, they can be sacrificed safely. [14] However, known as central group of veins, bridging veins should not be stretched, injured or sacrificed in avoidance of devastating consequences including contralateral hemiplegia. When it came to the vein of Labbe, surgeons usually preserved it to avoid venous infarction of the temporal lobe at all costs. As injury to the deep venous system led to diencephalic edema, hyperpyrexia and death, preservation of deep veins like the vein of Galen aroused great concern.[15-18] However, there were no clear guidelines for venous preservation. And it was important to make surgical judgment on a case-by-case basis with the help of imaging tools.

In patients undergoing craniotomy for tumor resection, thrombosis of the cerebral veins and sinuses happened from time to time. The symptoms were highly variable including headaches, seizures and delirium, which resulted in the difficulty of timely diagnosis.[19] When the infarcts were associated with increased intracranial pressure, patients might die because of cerebral herniation. In order to clarify the formation of vein thrombosis and take treatment as soon as possible, it was important to use ICG-VA integrated with FLOW 800 during the surgical process.

As the first to report the use of microscope-integrated quantitative analysis of ICG-VA for blood flow assessment, Kamp et al. showed the great value of the maps and promoted clinical applications of FLOW 800 analysis.[6] However, few articles reported the use of ICG-VA along with FLOW 800, especially in the field of surgery for brain tumors, cerebral and spinal hemangioblastomas.[20-22] In present case reports, we described our experience with using ICG-VA integrated with FLOW 800 in brain tumor resection to
observe venous flux and detect obstruction of venous reflux timely. All of our patients had good prognosis after surgery.

There were several limitations of our study. First, we included a small number of participants. Second, the use of ICG-VA with Flow 800 was subjective based on the experience of the surgeon. We have not reached an optimal protocol to use it routinely throughout the procedure. In addition, quantitative data of Flow 800 was not collected and analyzed systematically. Furthermore, long-term follow up investigation was needed.

Comparison between ICG-VA integrated with FLOW 800 and other techniques of blood flow monitoring was needed in order to demonstrate the sensitivity and specificity. We believe the application of ICG-VA integrated with FLOW 800 will be expanded in the future.

**Conclusion**

Venous preservation during brain tumors resection can be another valuable application of ICG-VA integrated with FLOW 800. This technology can demonstrate the blood flow information of the target vein.

**Abbreviations**

ICG-VA: indocyanine green videoangiography; MRA: magnetic resonance angiography; MRV: magnetic resonance venography; TCD: transcranial doppler; DSA: digital subtraction angiography; MRI: magnetic resonance imaging; CNS: central nervous system; MVD: microvascular Doppler.

**Declarations**

**Ethics approval and consent to participate:**

All procedures complied with ethical standards of institutional and/or National Research Council. The study was approved by the Institutional Review Board of the First Affiliated Hospital of Soochow University. Informed consent was obtained from patients.

**Consent for publication**

Consent to publish has been received from all participants

**Data availability statement**

All data included in this study are available upon request by contact with the corresponding author.
Competing interests

There was no competing interests among authors.

Funding

This work was supported by

1. the Suzhou Health Talents Training Project (GSWS2019002)
2. the Natural Science Foundation of Jiangsu Province (Grants No BK20200203)

Authors' contributions

YS and ZLW designed the study and wrote the article. FJ, XYY and XT revised the manuscript and polish the language. ZW and ZQC were the primary researchers.

References

1. Sindou, M., J. Auque, and E. Jouanneau, Neurosurgery and the intracranial venous system. Acta Neurochir Suppl, 2005. 94: p. 167-75.
2. Sindou, M. and J. Auque, The intracranial venous system as a neurosurgeon's perspective. Adv Tech Stand Neurosurg, 2000. 26: p. 131-216.
3. Raabe, A., et al., Near-infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow. Neurosurgery, 2003. 52(1): p. 132-9; discussion 139.
4. Oda, J., et al., Intraoperative near-infrared indocyanine green-videoangiography (ICG-VA) and graphic analysis of fluorescence intensity in cerebral aneurysm surgery. J Clin Neurosci, 2011. 18(8): p. 1097-100.
5. Faber, F., et al., Enhanced analysis of intracerebral arteriovenous malformations by the intraoperative use of analytical indocyanine green videoangiography: technical note. Acta Neurochir (Wien), 2011. 153(11): p. 2181-7.
6. Kamp, M.A., et al., Microscope-integrated quantitative analysis of intraoperative indocyanine green fluorescence angiography for blood flow assessment: first experience in 30 patients. Neurosurgery, 2012. 70(1 Suppl Operative): p. 65-73; discussion 73-4.
7. Xue, T., et al., Intraoperative indocyanine green video angiography (ICG-VA) with FLOW 800 software in complex intracranial aneurysm surgery. Chin Neurosurg J, 2021. 7(1): p. 28.
8. Rennert, R.C., et al., *Intraoperative Assessment of Cortical Perfusion After Intracranial-To-Intracranial and Extracranial-To-Intracranial Bypass for Complex Cerebral Aneurysms Using Flow 800*. Oper Neurosurg (Hagerstown), 2019. 16(5): p. 583-592.

9. Shah, K.J. and A.A. Cohen-Gadol, *The Application of FLOW 800 ICG Videoangiography Color Maps for Neurovascular Surgery and Intraoperative Decision Making*. World Neurosurg, 2019. 122: p. e186-e197.

10. Acerbi, F., et al., *Use of ICG videoangiography and FLOW 800 analysis to identify the patient-specific venous circulation and predict the effect of venous sacrifice: a retrospective study of 172 patients*. Neurosurg Focus, 2018. 45(1): p. E7.

11. Ferroli, P., et al., *Venous sacrifice in neurosurgery: new insights from venous indocyanine green videoangiography*. J Neurosurg, 2011. 115(1): p. 18-23.

12. Morcos, J.J. and S.A. Munich, *Editorial. The use of ICG videoangiography and FLOW 800 analysis*. Neurosurg Focus, 2018. 45(1): p. E8.

13. Elhammady, M.S. and R.C. Heros, *Cerebral veins: to sacrifice or not to sacrifice, that is the question*. World Neurosurg, 2015. 83(3): p. 320-4.

14. Heros, R.C. and S.H. Lee, *The combined pterional/anterior temporal approach for aneurysms of the upper basilar complex: technical report*. Neurosurgery, 1993. 33(2): p. 244-50; discussion 250-1.

15. Kunicki, A., *Operative experiences in 8 cases of pineal tumor*. J Neurosurg, 1960. 17: p. 815-23.

16. Rhoton, A.L., Jr., *The posterior fossa veins*. Neurosurgery, 2000. 47(3 Suppl): p. S69-92.

17. Stern, W.E., U. Batzdorf, and J.R. Rich, *Challenges of surgical excision of tumors in the pineal region*. Bull Los Angeles Neurol Soc, 1971. 36(4): p. 105-18.

18. Suzuki, J. and T. Iwabuchi, *Surgical removal of pineal tumors (pinealomas and teratomas). Experience in a series of 19 cases*. J Neurosurg, 1965. 23(6): p. 565-71.

19. Stam, J., *Thrombosis of the cerebral veins and sinuses*. N Engl J Med, 2005. 352(17): p. 1791-8.

20. Hojo, M., et al., *Usefulness of tumor blood flow imaging by intraoperative indocyanine green videoangiography in hemangioblastoma surgery*. World Neurosurg, 2014. 82(3-4): p. e495-501.

21. Takeshima, Y., et al., *Visualization of vascular structure of spinal hemangioblastoma using intraoperative indocyanine green videoangiography and temporary feeder occlusion*. Eur Spine J, 2015. 24 Suppl 4: p. S585-9.

22. Acerbi, F., et al., *The role of indocyanine green videoangiography with FLOW 800 analysis for the surgical management of central nervous system tumors: an update*. Neurosurg Focus, 2018. 44(6): p. E6.

**Figures**
Figure 1

A patient with a mass located at the posterior horn of the right lateral ventricle underwent operation. (A) T1-weighted axial and (B) T1-weighted sagittal MRI with contrast demonstrated a mass located at posterior horn of the right lateral ventricle. (C) The 3D imaging revealed the involvement of the Galen vein by the tumor. (D) During the surgical process, the Galen vein was preserved. (E, F) ICG-VA integrated with FLOW 800 clearly demonstrated the blood flow of the deep vein.
Figure 2

A patient with a large cystic mass in the right frontotemporal lobe underwent operation. (A) T1-weighted axial and (B) T1-weighted sagittal MRI with contrast demonstrated a cystic mass located at the right frontotemporal lobe. (C) The 3D reconstruction imaging showed the right middle cerebral artery was displaced and encased by the mass. (D) It also revealed the encased sylvian vein. (E) The mass was removed via pterional approach. (F, G) The sylvian vein was preserved and ICG-VA integrated with FLOW 800 semiquantitatively analyzed the blood flow of the protected vein.

Figure 3

A patient with left parietal lobe lesion underwent operation. (A) T1-weighted axial and (B) T1-weighted sagittal MRI with contrast demonstrated a large meningioma with significant mass effect. (C, D) The postcentral sulcus vein was encased and displaced by the tumor as demonstrated on the 3D
reconstruction imaging. (E) The postcentral sulcus vein was anatomically preserved under microscope, (F) but hyaline thrombus was found according to ICG-VA with FLOW 800.

Figure 4

A patient with mass on the bilateral frontal lobe and corpus callosum. (A, B) MRI with contrast showed a heterogeneous mass with cystic areas involving the body of the corpus callosum and extending into the frontal lobes bilaterally. FLOW 800 mapped the blood flow condition of the two superior cerebral vein (C) before and (D) after tumor resection.