Perspective review on applications of optics in cerebral endovascular neurosurgery

Christopher R. Pasarikovski
Jillian Cardinell
Victor X. D. Yang

Perspective review on applications of optics in cerebral endovascular neurosurgery

Christopher R. Pasarikovski,a,b Jillian Cardinell,c,d and Victor X. D. Yangab,c,d,*

*Address all correspondence to Victor X. D. Yang, E-mail: victor.yang@sunnybrook.ca

Abstract. Cerebral endovascular neurosurgery has transformed the way we manage cerebrovascular disease. Several landmark trials have demonstrated the effectiveness of endovascular techniques leading to continued technological development and applications for various diseases. The utilization of optical technologies and devices is already underway in the field of endovascular neurosurgery. We discuss the contemporary paradigms, challenges, and current optical applications for the most common cerebrovascular diseases: carotid atherosclerotic disease, cerebral aneurysms, intracranial atherosclerosis, and dural arteriovenous fistulas. We also describe needs-based opportunities for future optical applications, with the goal of providing researchers a sense of where we feel optical technologies could impact the way we manage cerebral disease.© The Authors. Published by SPIE under a Creative Commons Attribution 4.0 Unported License. Distribution or reproduction of this work in whole or in part requires full attribution of the original publication, including its DOI. [DOI: 10.1117/1.JBO.24.3.030601]

Keywords: cerebrovascular; endovascular; carotid; cerebral aneurysm; dural fistula; optics.

Paper 180684-PER received Dec. 28, 2018; accepted for publication Feb. 19, 2019; published online Mar. 26, 2019.

1 Introduction

Cerebral endovascular neurosurgery has transformed the way we manage cerebrovascular disease. The appeal of treating vascular diseases through minimally invasive intraluminal techniques without the need for open surgery has led to continued technological innovation and device development. In the era of evidence-based medicine, several landmark trials have demonstrated the effectiveness of endovascular techniques for various cerebral vascular diseases. The ISAT trial in 2005 showed that endovascular aneurysmal embolization resulted in increased independent survival at 1-year when compared to surgical clipping for ruptured brain aneurysms. The CREST trial in 2012 showed that carotid stenting was effective and safe when compared to surgical endarterectomy for carotid artery stenosis. Finally, for the management of stroke, the DAWN trial in 2018 revealed that endovascular thrombectomy was far superior to standard medical care even for patients 6 to 24 h after stroke onset. This has revolutionized stroke care for patients.

The mounting evidence behind the effectiveness of endovascular treatments and the general desire toward minimally invasive procedures will likely lead to an even greater role for endovascular management. The utilization of optical technologies and devices is already underway in the field of endovascular neurosurgery. In this paper, we highlight our perspective on current challenges faced by clinicians for various cerebrovascular diseases. Furthermore, we describe existing optical applications and opportunities for future applications.

2 Carotid Atherosclerotic Disease

2.1 Current Paradigm and Challenges

Stroke is one of the leading causes of morbidity and mortality in the developed world and 20% to 30% of strokes can be attributed to carotid atherosclerotic disease. The management algorithm for carotid atherosclerotic disease begins with patients differentiated based on the presence or absence of neurological symptoms attributed to the stenosis. Subsequently, patients are grouped based on the degree of radiographic stenosis as mild (<50%), moderate (50% to 69%), and severe (70% to 99%). The landmark NASCET trial in 1991 showed that surgical intervention is highly beneficial for symptomatic patients with moderate and high-grade stenosis. The results of the NASCET trial remain influential today, and the current American Heart Association/American Stroke Association recommends carotid revascularization for symptomatic patients with moderate and severe stenosis.

However, there is mounting evidence that the degree of radiographic stenosis fails to identify those patients with vulnerable carotid plaques. Several authors have reported carotid plaque morphological features, such as degree of lipid content, thickness of the fibrous cap, calcification, and intraplaque hemorrhage could all indicate plaque instability, and thus higher risk of stroke (Fig. 1). Identifying these high-risk morphological features would change the way we treat patients with carotid stenosis. Current noninvasive imaging techniques include MRI, CT, and ultrasound. However, no modality has proven reliable in identifying vulnerable plaques in relation to future stroke development.

Furthermore, once the decision is made to treat the carotid stenosis, physicians have two options: carotid endarterectomy and carotid artery stenting (CAS). The CREST trial showed that carotid stenting was associated with increased risk of
perioperative stroke compared to endarterectomy. Authors have hypothesized that plaque prolapse through the stent-struts as a major cause of perioperative stroke. Currently, imaging modalities are unable to detect this prolapse after stent placement.

### 2.2 Current Optical Applications

With respect to noninvasive carotid stenosis imaging, authors have described imaging the plaques with laser ultrasound. They report improved vessel wall spatial resolution compared to CT and the ability to detect calcification. However, the high acoustic contrast factor between calcium and surrounding tissue results in shadowing beyond the calcified plaques, leading to an inability to image beyond the lesion. With respect to invasive imaging, the United States Food and Drug Administration (FDA) approved the use of optical coherence tomography (OCT) for intravascular imaging in 2010. The commercially available OCT catheter is approved for coronary imaging and not carotid imaging. Given et al. were the first group to describe the use of OCT for carotid plaques using saline without proximal balloon occlusion. Since then, several authors have studied carotid plaque morphology and composition. Others have described the use of OCT for detecting plaque prolapse and stent-strut malapposition during CAS (Fig. 1).

Several limitations of carotid atherosclerotic OCT imaging exist. Clinicians have described satisfactory imaging without proximal balloon occlusion, though it is our institutional experience that the highest quality images are obtained with proximal occlusion. The occlusion temporarily blocks blood flow to the brain and consequently has potential for ischemic injury. We have not encountered complications in our experience given the short (6 s) acquisition time. Furthermore, the FDA-approved device is designed for imaging vessels 2 to 3 mm in diameter and the carotid artery is 5 to 8 mm in diameter, leading to an inability to image the entire vessel in certain patients. Lesions such as calcium or red thrombus also cause shadowing.

Intraluminal angioscopic imaging for carotid atherosclerotic disease has also been described with excellent visualization of the plaques. The major disadvantage for this technology is the requirement of long-duration proximal balloon occlusion during acquisition. Newer laser-based angioscopes have showed promise discerning the different phases of atherosclerotic plaque evolution in animal models.

### 2.3 Future Directions

The calculation of radiographic degree of stenosis to determine which patients should be treated for carotid disease is likely rudimentary. Ideally, a noninvasive technology would exist to image a carotid plaque for features that would predict future risk of stroke. Shindo et al. in 2015 showed that carotid plaque fibrous cap thickness <130 μm was associated with increased risk of rupture, and thus any new technology would need superb spatial resolution. The device would also need to be able to differentiate a lipid core, calcium deposits, intraplaque rupture, and thrombus on the surface of the plaque. A clinical trial to assess the predictive value of a noninvasive optical device able to detect vulnerable plaque features would be very appealing to clinicians given the massive burden of stroke.

A device to detect plaque prolapse through the struts of a stent during CAS would also be an extremely valuable tool for clinicians. As described above, we know from the CREST trial that periprocedural stroke was higher in the CAS group and some authors have hypothesized that plaque prolapse through the stent could be the cause. The device must have the spatial resolution adequate to identify plaque on the micrometer scale and be able to image a vessel with ~5 to 8 mm diameter. The detection of plaque prolapse would be done after stent placement by imaging over the stent mesh. If thrombus/prolapse were detected, periprocedural anticoagulation could be used to decrease the risk of thromboembolism.

What we envision is a not a new standalone optical technology to detect plaque prolapse, rather a combination of several different technologies into an all-purpose stenting device with imaging capability (Fig. 2). The device would ideally be comprised of a distal embolization protection system, a dual-lumen transparent angioplasty balloon filled with saline that optical imaging can be acquired through the balloon, a stent, and a proximal balloon for occlusion during stent deployment. This would save a significant amount of time during the procedure, as several catheters would not need to be exchanged during optical imaging.

### 3 Cerebral Aneurysm

#### 3.1 Current Paradigm and Challenges

The prevalence of intracranial aneurysms in the population is ~3.2%. Cerebral catheter angiography remains the gold-
standard in diagnosing cerebral aneurysms. The anatomic location, shape (saccular or fusiform), and size can all be determined (Fig. 4). Mathews et al.39 were the first to use a custom-built OCT device to image the cavernous internal carotid artery in three patients who previously underwent aneurysmal coiling. They showed that the internal elastic lamina and external elastic lamina of the vessel wall could be imaged intracranially with excellent resolution. Guerrero et al.40 examined neoendothelialization over a flow-diverting stent placed 8-weeks prior using a commercially available OCT catheter in the posterior circulation and found that there was concentric neoendothelialization over the stent, except in areas where the stent was not in contact with the vessel wall.

### 3.3 Future Applications

Our current knowledge of rupture risk for intracranial aneurysms is limited due to a poor understanding of the natural history. This is likely due in part to our inability to image the aneurysm wall and understand the histologic composition. Knowledge of aneurysm wall composition could have immense diagnostic potential in evaluating rupture risk for patients, and thus guide the clinical decision making process. The benefit solely from invasive aneurysmal wall imaging with an optical technology would unlikely outweigh the risks. However, the device could be utilized during diagnostic cerebral angiography and as an adjunct before/after aneurysmal treatment to provide information regarding wall histologic features.
A device that can be navigated intracranially and confirm acceptable stent-strut apposition against the vessel wall during aneurysm embolization would be extremely valuable as an adjunct during aneurysm embolization. The lack of neendothelialization over a stent is thought to be a risk factor for aneurysm recurrence. Intraprocedural knowledge of stent malapposition could guide the clinician to reposition the stent. Furthermore, evidence of complete neendothelialization of stents could also help direct management with respect to duration of antiplatelet medications. Blood-thinners are needed after stent deployment because stents are thrombogenic. A stent that is completely excluded from the vessel lumen due to neendothelialization would of course be at a decreased risk for thromboembolic events, and patients may not require blood-thinning medication.

Knowledge on whether an aneurysm has been excluded from the cerebral vasculature due to complete aneurysm neck endothelialization after stenting/coiling could also eliminate the need for routine follow-up imaging looking for recurrence (Fig. 3). The above concepts all fall under the umbrella of the need for routine follow-up imaging looking for recurrence. Endothelialization after stenting/coiling could also eliminate the cerebral vasculature due to complete aneurysm neck endothelialization after coiling. Satisfactory apposition of the stent-struts against the vessel wall can also be visualized.

4 Intracranial Atherosclerosis

4.1 Current Paradigm and Challenges

Intracranial atherosclerosis (ICAS) is also an important etiology of stroke, especially in Asian populations. The landmark WASID trial in 2005 studied medical management for patients with symptomatic large vessel ICAS of 50% to 99%. They compared Warfarin with Aspirin and found the primary endpoint of stroke, brain hemorrhage, or death from nonvascular causes occurred in 22% of patients in both groups. These poor outcomes lead the SAMMPRIS trial investigators in 2011 to compare medical management with intracranial stenting for patients with symptomatic large vessel ICAS of 70% to 99%. The trial was halted after interim analysis showed patients undergoing stenting had a 30-day perioperative stroke rate of 15%. The majority of strokes in the SAMMPRIS trial occurred due to adjacent arterial perforator occlusion. One proposed mechanism of perforator infarct during intracranial stenting is the displacement of unstable or complex plaques into adjacent perforating vessels.

4.2 Current Optical Applications

There have been no optical technologies directly utilized in the diagnosis or treatment of ICAS. Alles et al. were the first to image ex vivo aortic tissue with an optically transmitted acoustic beam. They demonstrated side-branch blood vessels with great accuracy (Fig. 5).

4.3 Future Applications

As described above, the majority of strokes in the SAMMPRIS trial occurred due to adjacent arterial perforator occlusion. The ability to directly visualize perforators before stent placement would greatly improve the safety of intracranial stenting. The perforators coming off the basilar artery or middle cerebral artery range between 80 and 1400 μm in size and thus the device to image these vessels would need excellent spatial resolution. Furthermore, the detection of vulnerable plaque features could be a warning sign for the interventionist and help decrease the perioperative stroke risk. If the risk of perforator occlusion were deemed high, the decision could be made not to place a stent. In other circumstances, different stent types (open/closed cell) could be used depending on plaque morphology. Future trials must select the appropriate patients for intervention, and a device that can identify both vulnerable plaque features and adjacent perforating vessels would certainly help identify these patients.

5 Concept

Arteriovenous fistulas are abnormal connections between arteries and veins. In the brain, dural arteriovenous fistulas (dAVF) acquired vascular malformations with arterial feeders from extracranial arteries. The venous system is a low-pressure system, and arterial pressure can cause symptoms varying from tinnitus (ringing in the ears) to fatal ruptures. With the evolution of endovascular neurosurgery, the first-line treatment option for
most dAVF is now endovascular embolization. Trans-arterial embolization techniques using glue are often very expensive, in the range of $20,000 per procedure, and may require multiple procedures.

We envision an optical device that can both image the arterial feeders to the fistula and ablate these arteries using a laser (Fig. 6). First, the device would be navigated transvenously to the site of the dural AVF. Next, through a transparent dual-lumen balloon, optical imaging is undertaken to identify the exact location of arterial feeders into the dural sinus. With the knowledge of the exact spatial position of the feeding arteries, laser ablation of the feeders is completed under image guidance through the saline-filled balloon. This could eliminate the need for expensive glue embolization material and multiple treatment sessions with the use of a single device.

6 Conclusion

Endovascular neurosurgical management of cerebrovascular disease will continue to expand. Optical devices have begun to play a role in diagnosis and treatment. We believe there remains significant opportunity for improvement of current optical systems and techniques, along with the development of devices to treat these complex diseases.

Disclosures

The other authors declare that they have no competing interests to disclose.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Research ethics board approval was not required for this systematic review of the literature.

References

Pasarikovski, Cardinell, and Yang: Perspective review on applications of optics in cerebral...
at the University of Toronto. Following his third year, Chris entered the surgeon-scientist training program and is currently enrolled as a PhD candidate in the Institute of Medical Science. His research focus is the application of optical coherence tomography imaging in cerebrovascular disease.

**Jillian Cardinell** is an undergraduate student at Ryerson University studying biomedical engineering. Her research focus is on the analysis of retinal and dermal optical coherence tomography images for diagnostics and characterization at Sunnybrook Health Sciences Center under the supervision of Dr. Yang. She has also participated in augmented reality studies for surgical navigation. She combines her artistic abilities with her cerebrovascular technical knowledge to generate descriptive diagrams for publications.

**Victor X. D. Yang** received his honors BASc degree in engineering science from the University of Toronto in 1997. He completed a master’s in electrical and computer engineering in 1998, then entered the University of Toronto MD-PhD program in the Department of Medical Biophysics, completed in 2004. Currently, he is an associate professor in the Division of Neurosurgery, University of Toronto, and Department of Electrical and Computer Engineering, Ryerson University, holding the Canada Research Chair (CRC) in Bioengineering and Biophotonics.