Review

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Optical coherence tomography for precision brain imaging, neurosurgical guidance and minimally invasive theranostics

Yingwei Fan[1], Yan Xia[1], Xinran Zhang[1], Yu Sun[2], Jie Tang[2], Liwei Zhang[2], Hongen Liao[1,*]

[1] *Department of Biomedical Engineering, School of Medicine, Tsinghua University, Beijing, China;*
[2] *Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China.*

Summary **This review focuses on optical coherence tomography (OCT)-based neurosurgical application for imaging and treatment of brain tumors. OCT has emerged as one of the most innovative and successful translational biomedical-diagnostic techniques. It is a useful imaging tool for noninvasive, *in vivo*, *in situ* and real-time imaging in soft biological tissues, such as brain tumor imaging. OCT can detect the structure of biological tissue in a micrometer scale, and functional OCT has some clinical researches and applications, such as nerve fiber tracts and neurovascular imaging. OCT is able to identify tumor margins, and it gives intraoperative precision identification and resection guidance. OCT-based theranostics is introduced into preclinical neurosurgical resection, such as the integration of OCT and laser ablation. We discuss the challenges and opportunities of OCT-based system in the field of combination of intraoperative structural and functional imaging, neurosurgical guidance and minimally invasive theranostics. We point out that OCT and laser ablation-based theranostics can give more precision and intelligence for intraoperative diagnosis and therapeutics in clinical applications. The theranostics can precisely locate, or specifically target cancerous tissues, and then as much as possiblly eliminate them.**

Keywords: Optical coherence tomography, brain imaging, neurosurgical guidance, brain tumor, minimally invasive theranostics

1. Introduction

Minimally invasive theranostics is one of the most recent clinical hot topics. Theranostics will give huge simplification for clinical application in the future (*1*). Optical coherence tomography (OCT) is one of the most promising, innovative and rapidly emerging biomedical imaging modalities. It gradually serves for minimally invasive surgical guidance. It can acquire real-time tomographic images with micrometer resolution by using visible or infrared light (*2,3*). OCT imaging has been diffusely implemented across various disciplines due to its high-resolution, high-speed, low-cost, radiative-free, invasive-free, and convenience performance (*4*). Typical types of OCT scanning include galvanometer scanning, microscope, fiber-optic catheter, handheld probe, endoscope, *etc*. Therefore, OCT is widely used in intraoperative imaging, pre-operative diagnostic and postoperative evaluation (*2,5-9*), especially, in ophthalmic lesion detection and diagnosis (*10-12*). OCT is treated as a minimally invasive, real-time diagnostic approach for minimally invasive integration of diagnostics and therapeutics.

Intraoperative neurosurgical imaging with real-time identification are special and significant research for neurosurgical guidance and resection, which can save patients' lives and improve postoperative quality of lives. Furthermore, many advanced technologies are widely used in intraoperative brain tumor detection and neurosurgical guidance, including computer tomography (CT) (*13*), diffusion-weighted magnetic resonance imaging (MRI) (*14*), fluorescence (*15,16*) and fluorescence spectral analysis (*17*), Raman spectroscope (*18,19*), ultrasound (*20*), photoacoustic imaging (*21*), biomarkers (*22*), and evaporative ionization mass spectrometry (*23*) *etc*. OCT can visualize sub-surface

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**Address correspondence to:*
Dr. Hongen Liao, Department of Biomedical Engineering, School of Medicine, Tsinghua University, Beijing 100084, China.
E-mail: liao@tsinghua.edu.cn

tissue structure non-invasively, the micro-meter depth microstructure of tissue also has an intuitive demonstration for neurosurgeons, and the research of neurosurgical OCT are launching gradually in neurosurgical diagnostics and guidance.

In clinical applications, the precision of minimally invasive theranostics, which integrates multimodal diagnosis and therapeutic methods, plays an important role in the treatment of lesions (*1*). A 5-aminolevulinic acid (5-ALA) guided laser ablation system has been proposed, and it has been applied in clinical research by Liao *et al*. (*17,24,25*). A fluorescence-guided laser ablation system to resect residual cancer for soft tissue sarcoma has been investigated in a mouse model by Lazarides *et al*. (*26*). Integration of diagnostics and therapeutics has been used in the treatment of tumorous tissue, such as the integration of ultrasound and robotic technology (*27-29*). OCT has been widely used in imaging to improve diagnostic accuracy and precision, and it can guide therapies *via* providing intraoperative *in situ* abundant information of tumorous tissue (*30-32*).

In this paper, we review brain imaging, neurosurgical guidance and theranostics using OCT-based system. In brain imaging, "optical biopsy", brain cerebral vascular detection, and fiber nerve tracts are the preclinical and clinical targets. In neurosurgery, the neurosurgical guidance-based OCT system can realize the identification of tumorous tissue and non-tumorous tissue, as well as intraoperative guidance. As future research and clinical applications, we introduce the key technologies and clinical research of theranostics, which is the integration of OCT and other therapies in neurosurgery. Furthermore, we discuss the development and future application of integrated OCT and laser ablation for minimally invasive theranostics in a prospective intelligent medical system.

2. Brain tissue imaging with OCT system

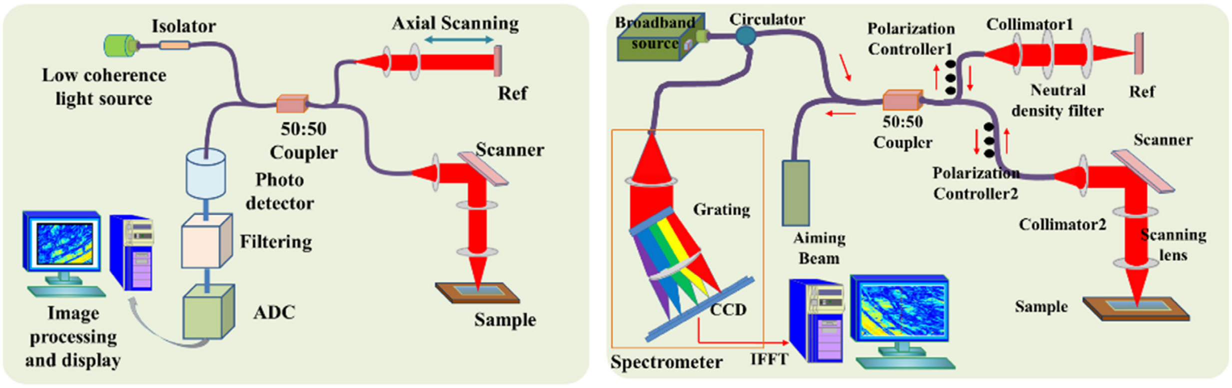
Optical imaging and detection are a non-invasive or minimally invasive method to diagnose lesions, so that the optical imaging system can widely be devoted to biomedical imaging. Due to the feature of high resolution, OCT can present a more precise microstructure of brain tissue. Moreover, functional imaging based on the polarization property and Doppler effect has been applied in detecting brain function for nerve fiber tracking and cerebral metabolism. The functional imaging also includes angiography imaging to detect blood flow information.

Time domain (TD) and Fourier domain (FD) OCT system are usually devoted in biomedical imaging. A coupler divides a beam of low-coherence light into two paths. The two light beams, which reflect or scatter from the sample and reference arm, form an interference field in a coupler. The ability to discriminate two scattering objects in-depth is up to coherence length of the low coherence light source (*2,33*). The fundamental principal schematic of time domain OCT is as shown in Figure 1A. By contrast, in FD-OCT, the reference mirror keeps motionless. The basic principal of FD-OCT is that optical coherence frequency of the coherence pattern within the envelope of the light source spectrum increases with the distance of the scattering event from a reference mirror increase (*33*). Applying a Fourier transform provides the reflectivity profile as a function of depth along the A-scan within the sample or biological tissue (Figure 1B). The depth information of sample is an afforded signal transform without A-scan.

In brain imaging, OCT is a useful tool for detecting brain tissue and lesions. It can provide micrometer level information and the function of optical biopsy. Functional information such as cerebral vascular and fiber bundle, gives an important indicator for avoiding this position to save brain function.

2.1. *Brain imaging and 'biopsy'with OCT system*

OCT is high-resolution imaging for brain imaging and optical biopsy (*34*). OCT demonstrates that micrometer-



(a) (b)

Figure 1. Basic schematic representation. (a) Time domain optical coherence tomography. (b) Spectral domain optical coherence tomography.

scaled, cross-sectional imaging could provide micromorphological information to diagnose and analyze. Therefore, OCT has the potential to serve as a type of optical biopsy where morphology is assessed with *in situ*, real-time imaging, unlike histological section, which needs removal of specimens and long-time processing for microscopic examination (*35*). It is possible that OCT will replace histological section in some degree.

Ultrahigh resolution (UHR) OCT, of which the resolution can reach one micrometer or sub-micrometer level, is investigated to image high scattering tissue. Ultrahigh resolution has remarkable characteristics for detecting microstructure in OCT imaging. OCT has been widely used in brain imaging (*36-38*). Bizheva *et al*. reported that UHR OCT was investigated for imaging of brain tissue morphology using a number of animal models *ex vivo* and *in vitro* (*39*). The scale of UHR OCT imaging is from neuron cells to an intact animal brain. Moreover, UHR OCT is a successfully translational diagnosis tool, since it is capable of discriminating healthy brain tissue and various neuro-pathologies. For imaging deep brain tissue *in vivo*, a forward scanning single mode fiber (φ125 μm) is used as detecting probe (*40,41*). Some advanced technologies have been integrated into the OCT system for improving light penetration to enhance imaging depth in highly scattering brain tissue. Imaging depth of OCM is improved through intrinsic scattering contrast (*41*). This method does not require the addition of dyes or contrast agents. Vertical cavity surface emitting laser (VCSEL) sweep source OCT offers an extended imaging depth range of more than 2 mm in highly scattering turbid biological tissue (*42*). With technical improvement, imaging depth of OCT will increase in research and clinical application. Whole brain imaging in an animal model is a big challenge in the current optical field, especially in a freely moving animal. It is meaningful for future research in brain imaging. Whole brain imaging has been developed through techniques for reconstruction and segmentation of sliced brains (*43*), and quantitative analysis make brain imaging a more practical clinical value (*44*). However, whole brain imaging is unnecessary with OCT-based system in intraoperative brain imaging, while a large-field view can provide a great amount of information for a specialist to guide and identify brain tissue feature.

2.2. *Cerebral vascular and angiography imaging with OCT-based system*

Brain is a complicated and comprehensive component in the central nervous system. A brain tumor will affect nervous function and quality of patients' lives. OCT is gradually applied into cerebral functional imaging during brain activity or disease progression. Recently, to investigate blood flow and cerebral hemodynamics in neuroscience, many researchers have been investigating the angiography and Doppler effect-based OCT imaging system. Furthermore, a novel technique combining optogenetic stimulation and OCT technology can monitor blood flow and cerebral hemodynamics.

During seizures' progression, optical characteristics will change with cerebral function. Yaseen *et al*. reported that OCT detects the changes of optical properties of cortical tissue in mice during the induction of global and focal seizures *in vivo* (*45*). Yashin *et al*. investigated a contrast-enhanced optical Doppler tomography system (ODT) with intralipid to provide monitoring of cerebral blood flow velocity (*46*). Furthermore, imaging of the hippocampal area and white matter are presented by OCT system *in vivo* in an animal model (*47*). Optogenetic stimulation combined with OCT system is proposed for monitoring cerebral hemodynamics (*48*). Srinivasan *et al*. proposed an optical microscopic method with a multiparametric OCT platform for measuring blood flow and recovery of ischemic stroke in brain (*49*). Recent development of OCT-based angiography has started to shed some new light on cerebral hemodynamics in neuroscience. Baran *et al*. demonstrated the effectiveness of proposed automatic image segmentation and enhancement methods for OCT-based microangiography (OMAG) and tissue injury mapping (TIM) in a mouse cerebral cortex (*50,51*).

Multimodal optical imaging system can acquire the information of multiple intrinsic visualization view and facets of cerebral blood flow, and metabolism in healthy tissue and tumorous tissue (*52,53*). Moreover, a summary of OCT angiography studies is provided for stroke, traumatic brain injury, and subarachnoid hemorrhage cases on rodents (*54*). This review gave an overview of the recent developments of angiography-based OCT imaging techniques for neuroscience applications in an animal model. Figure 2 shows that dual-wavelength laser speckle contrast imaging (DWLS) (Figure 2A) enabled rapid prediction of the intact infarct area and hemoglobin oxygenation throughout the intact brain in a mouse model. The OMAG system (Figure 2B) provides detailed information of blood perfusion dynamics down to the microvascular or capillary level in a region of interest (ROI) in regard to ischemia.

2.3. *Brain nerve fiber bundle imaging based on functional OCT/OCM*

Fiber bundle imaging and orientation tracts are outstanding doubts and troubles. The method of nerve fiber tracts imaging is usually based on MRI-diffusion tensor imaging (MRI-DTI) tractography (*55*) with a high intensity MRI imaging system. However, this diagnosis method is not enough accurate due to the low resolution of MRI imaging compared to other modal imaging systems. Thus, the nerve fiber tracts will give more intuitive and more precise viewing with micrometer-level resolution imaging. Recently, Wang *et al*. reported

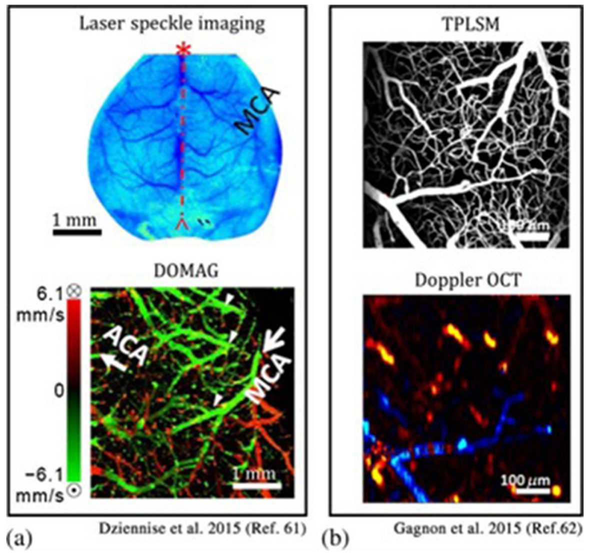


Figure 2. (a) A system combined DWLS with OCT used to monitor microvasculature and microstructure in mouse cortex through whole skull. (b) Combination of TPLSM angiography with Doppler OCT imaging for blood flow in the mouse cortex. From Ref. (*54*) (Reprinted with permission).

that a multi-contrast OCT (MC-OCT) shows nerve fiber tracts and comprehensive brain anatomy *ex vivo* in animal brain. The MC-OCT has a novel high resolution and improvement of scanning structure with a serial optical coherence scanner (SOCS). Neighboring fiber tracts with different orientations can be distinguished in tomographic optical slices, two-dimensional *en face* images and three-dimensional volumetric images (*56,57*). Furthermore, a combination of diffusion tensor imaging (DTI) and SOCS imaging can describe the orientation of nerve fiber tracts on postmortem human medulla (*58,59*). Figure 3 shows the *en face* optic axis orientation maps in fiber orientations of the coronal plane. Different colors represent the different fiber directions as shown on the color wheel; the brightness of colors is determined by the *en face* retardant values (*58*).

The nerve fiber tracts are equally important for neuroimaging and neurosurgical guidance. Deep-OCM allows, after minor surgery, *in situ* imaging of single myelinated fibers over a large fraction of the sciatic nerve (*60*). To detect nerve fiber bundles based on measurement of birefringence, polarization sensitive OCT (PS-OCT) demonstrated good quality for detection (*61-63*). However, these studies are still based on animal experiments, and usually implement the detection of brain function the brain *in vivo* living mouse. These studies are meaningful and significant to recognize brain function of nerve fiber tracts.

3. Neurosurgical monitoring and neurosurgical guidance based on OCT technology

OCT-based clinical application in neurosurgical procedures is a main direction in biological tissue. It is more important for intraoperative imaging with high spatial resolution and identification of tumor margins for neurosurgical guidance.

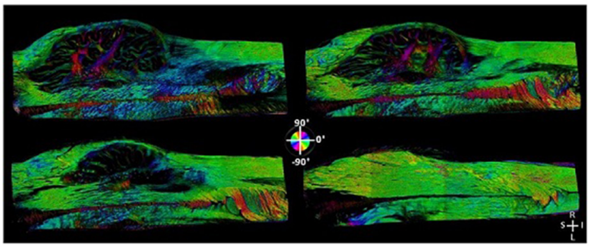


Figure 3. *En-face* optic axis orientation maps produced by SOCS quantitatively depict in-plane fiber orientations in the medulla. Each map is composed of eight (2 × 4) serial scans. The color wheel shows the orientation values ranging between −90° and 90°. The brightness of colors in the images is determined by the *en-face* retardance values. From Ref. (*58*) (Reprinted with permission).

In neurosurgery, OCT-related system will give real-time information for guiding neurosurgical resection. The information can include morphology of tumorous tissue and non-tumorous tissue. In order to acquire more information and a larger imaging field of view, integration of OCT and other imaging modalities can provide appropriate neurosurgical guidance and treatment. Furthermore, integration of OCT and laser ablation system can give precision treatment for brain tumors.

3.1. *Identification of tumorous and non-tumorous tissue with OCT system*

High-resolution cerebral tumor imaging is very useful for reseting of brain tumors, where the tumor or abnormal lesion can be discriminated from normal brain tissue by OCT system. Many scientists and surgeons are turning *in vivo* OCT tumor imaging research and clinical translational practice into reality. OCT imaging plays a significant role in the resection of brain tumors. Deep brain tumor imaging also has profound significance for identification of tumorous tissue.

During neurosurgical tumor resection, real-time identification of tumors gives ample evidence for operation. Boppart *et al.* reported that an intraoperative OCT system could identify tumor regions and localize tumor margins based on the optical attenuation in backscatter intensity. OCT images of the cortex were acquired in two and three dimensions in the cadaveric human cortex with metastatic melanoma (*64*). Bizheva *et al.* reported the first studies on *ex vivo* human tissues (*65*). Böhringer e*t al*. reported imaging of human brain tumor specimens using TD-OCT and SD-OCT system to identify tumor and normal tissue using optical characteristics (*66-68*). Due to the intrinsic optical property of brain tissue, near-infrared OCT has a deeper viewing field/range than visible light used in the OCT system (*42,67-69*). For the discrimination of tumor, the longitudinal tomographic OCT image is the basis through measuring the optical attenuation of signal in three-dimensional topology. Furthermore, brain tumor has a more complex microstructure and micromorphology. However, it is difficult to identify tumor margins from the longitudinal/axial map, because the algorithm based on the optical attenuation coefficient of A-scan will get the map of an alignment in the B- or C-scan. Such an algorithm adds the longitudinal analysis to identify the boundary of tumorous tissue.

Multimodal optical imaging can image the microstructure, cerebral oxygen delivery and energy metabolism of brain tumors. Yaseen *et al.* investigated the combination of two-photon microscopy (TPM) and confocal lifetime microscopy, laser speckle imaging, OCT imaging, and optical intrinsic signal imaging to monitor cerebral oxygen delivery and energy metabolism (*51*). It will be used into intraoperative imaging and neurosurgical guidance for detecting metabolism and identification of tumorous tissue. Two-imaging modalities, including cross-polarization OCT and microangiographic OCT, are integrated into multimodal (MM) OCT system for differential diagnostics of normal and diseased brain tissue with glioblastoma (*52*). Microangiographic OCT allowed the visualization of blood vessels in brain tissues, revealing changes in the form and sizes typical of the tumor vessels.

For identifying different kinds of brain tumors, full-field OCT (FF-OCT) system, which can detect the microstructure of tumor, has been proposed. Assayag *et al.* applied a FF-OCT imaging system to structural imaging of brain tumor specimens (70). However, the diagnostics of brain tumors are only implemented in brain specimens *ex vivo*. FF-OCT in *LLTech Corporation* (*71*) uses infrared light to take optical biopsies beneath the surface of tissue under analysis instead of histological section. Intraoperative precision diagnostics has some space for improvement. Figure 4 demonstrates that FF-OCT detects cerebral tissue architecture modification. Infiltrating tumorous glial cells are not detectable in this system, but low-grade gliomas are mistaken for normal brain tissue on FF-OCT images. However, in high-grade gliomas (Figure 4 G-K), the infiltration zone of brain tumors has occurred to such an extent that normal parenchyma structure is lost (*70*).

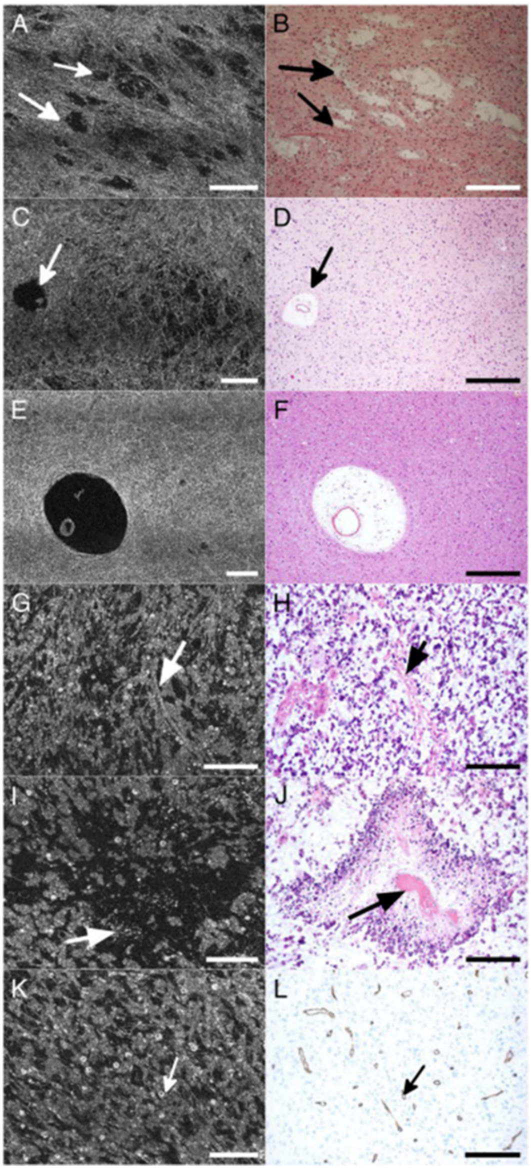


Figure 4. Glioma. Assayag et al. reported three different cases shown in (A-B; C-F; G-L). (A-B) Microcysts (arrows) in an oligo-astrocytoma grade 2; **(C-D)** microcystic areas and Virchow-Robin space (arrows) in an astrocytoma grade 2; **(E-F)** enlarged Virchow-Robin spaces in an astrocytoma grade 2; **(G-H)** microvessels (arrow) and tumorous glial cells in an oligoastrocytoma grade 3; and **(I-J)** pseudo-palisading necrosis in an oligo-astrocytoma grade 3. **(K-L)** Vasculature (arrows) in an oligo-astrocytoma grade 3. **(B, D, F, H** and **J)** Hemalun and phloxin stainings and CD34 immunostaining **(L)**.Scale bars show 250 μm **(A, B)**, 100 μm **(C-F)**, 20 μm **(G, H)**, and 10 μm **(I-L)**. From Ref. (*70*) (Reprinted with permission).

3.2. *Neurosurgical guidance with intraoperative OCT imaging and integrated multi-modality imaging*

Intraoperative neurosurgical imaging and guidance are crucial for non-invasive identification of brain tumor and non-tumor tissue on a facial map together with longitudinal tumor margin in real time. However, the image quality and the imaging depth limits the identification of longitudinal tumor margin. During neurosurgery, intraoperative diagnosis plays an important role in surgical guidance. The speed of OCT imaging will strongly influence intraoperative diagnosis and visualization. The improvement of imaging speed promotes the efficient of identification and diagnosis.

For giving an intuitive view of brain tissue, some researchers have designed and manufactured a neurosurgical probe of OCT, including endoscopic, needle-type, hand-held probe, and other kinds of neurosurgical OCT robotic arms (*68,72-79*). Böhringer *et al.* used a modified rigid endoscopic probe to mount OCT device for detecting tumor during resection of intrinsic brain tumors (*68*). In microsurgery, Kang *et al*. proposed a common-path OCT system with an applicable fiber-optic endoscopic probe (*74,76*). Furthermore, a hand-held forward-viewing probe is useful for neurosurgical imaging and residual tumor detection due to the irregular and limited resection cavity. Liang *et al*. and Sun *et al*. developed a needle-type forward-imaging OCT probe, which was fit for minimally invasive tools (*77-79*).

Another issue is the intraoperative detection of residual tumor in neurosurgery. Giese *et al*. reported that tumorous tissues of human brain and areas of the resection cavity were analyzed during the resection of gliomas within OCT guidance (*80*). Recently, excellent research reported by Kut *et al*. investigated a self-regulating OCT system on *ex vivo* human tissue specimens of 32 patients (*81*), and the method to discriminate between normal and tumorous tissues is based on the optical attenuation coefficient measured by developing nanoparticle-based OCT imaging contrast agents during operation (*82,83*). The substantial contribution of this research is the performance of diagnostic analysis to derive an attenuation threshold to distinguish tissues with high sensitivity and specificity. For the identification of tumor margins, some algorithms assist the diagnosis of tumorous tissue, such as pixel classification-based method (*84*), and attenuation coefficient-based method (*85*). Machine learning method has been used in the classification of skin tumors with OCT images (*86*), it has potential application on brain tumor imaging. Furthermore, on the aspect of imaging speed, the technology of graphic processing unit (GPU)-based acceleration provides a huge potential application. Zhang *et al*. use the dual GPU to accelerate the speed of FD-OCT system so that the system can be used in the intraoperative microscopic guidance. This research provides an access to fast image processing for microscopic surgery. It has potential to translate into a typical clinical application in the future (*87*). The intraoperative real-time identification of cancerous tissue and non-cancerous tissue provides a similar function for real-time histological section to guide neurosurgery. OCT system is a promising intraoperative imaging tool for neurosurgical guidance (*88*). However, there is still lack of brain functional information in the cerebral cortex and deep brain tissue. Figure 5 shows that OCT attenuation maps aided the neurosurgeon in identifying regions of tumorous tissue versus non-tumorous tissue (white matter) before and after surgery.

Multimodal imaging system is more convenient for neurosurgical guidance for tumor resection. Sun *et al*. reported that a hand-held probe has been proposed in the cadaveric *in situ* testing for providing updated image information; however, the probe has a forwarding viewing for neurosurgical OCT attached with tracking markers (*89*). Liang *et al*. investigated a combination of OCT with an MRI-compatible needle-type probe for tumor resection in neurosurgical guidance. The probe has capability of providing microscale architecture in conjunction with macroscale MRI tissue morphology for human patients in real-time for *in situ* imaging and neurosurgical guidance (*90*). An integrated system of photoacoustic OCT and surgical microscope has been proposed, and it can guide surgeons through providing the intraoperative real-time tumor margins, tissue structure and a magnified view of region of interest (*91*). Multimodal imaging system will acquire multi-

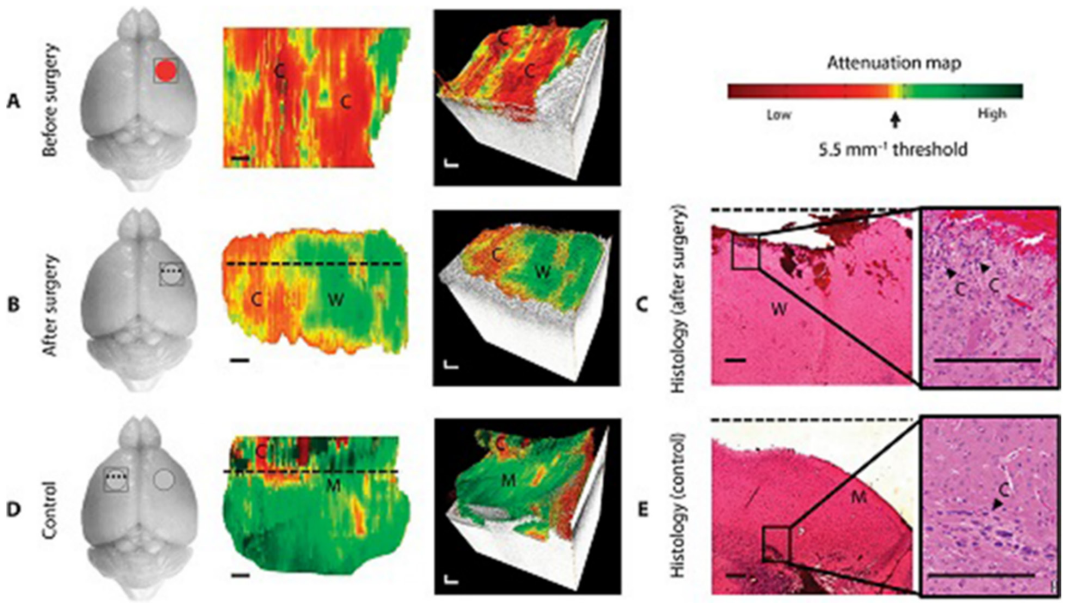


Figure 5. *In vivo* OCT imaging brain cancer in a mouse with patient-derived high-grade brain cancer (GBM272). From *Ref.* (*81*). (Reprinted with permission).

dimension information of intraoperative biological tissue for helping real-time surgical diagnosis and analysis. It can decrease the difficulty of intraoperative identification of tumor margins for neurosurgical guidance.

The main challenges of large-scale/wide-field scanning of the resection zone are the creating a map of the cavity, scanning of the perpendicular surface and merging an intraoperative visualization of the three-dimensional data. Some novel techniques may assist surgeons to achieve micrometer precision incisions, reducing the risks of damage to the surrounding tissue, and minimizing intraoperative complications (*92*). Overlaying microscopy images with depth information from OCT could lead to improved detection of residual tumor cells (*58,93*). Combining OCT imaging with an operating microscope (*94,95*) can offer intuitionistic viewing of the surgical area. Robotized operating microscope integrated OCT imaging could scan larger scale tissue surface area through automated movement of the microscope. Hence, the microscope assisted OCT-based neurosurgical guidance can provide more high-resolution and wild-field intuitive viewing to perform precision surgical resection.

3.3. *Integrated OCT and laser ablation system for real-time treatment of diseased tissue*

Minimally invasive theranostics for treatment of the diseased soft biological tissue is a developmental and potential clinical application. Integration of *in vivo/in situ* imaging and therapy will provide some more possibilities for intraoperative diagnosis and therapeutic (*17,24-29,96*). With respect to tumor resection in soft biological tissue, OCT-guided laser ablation is a novel theranostics method, especially in brain tumor resection. Some research demonstrated that the integration of OCT and laser ablation provide a novel treatment approach for the tissue's lesion. For malignant tumor treatment, the challenge is visualization of the treatment response dynamics in microscale spatiotemporal resolution during the surgical operation. Minimally invasive integration of diagnosis and therapy will decrease the radiative dose and increase the efficiency of tumor treatment.

In surgical procedures, OCT can monitor and capture the dynamic changes during the laser ablation or laser surgery for the diseased tissue. OCT-guided laser surgery has been developed for use in ophthalmic surgery (*97,98*). Boppart *et al*. reported that it is a new approach, where the integration of real-time high-resolution OCT and laser ablation can realize the treatment of brain tumors *in vivo* and *in situ*; the system could image the dynamic changes before, during, and after intraoperative laser ablation scenarios (*30*). Meng-Tsan Tsai *et al*. proposed an OCT guided laser-assisted drug delivery system, which can monitor drug diffusion through an induced microthermal ablation zones array (*99*). The integration of OCT and laser ablation will provide an intuitive view for real-time treatment of diseased tissue.

With respect to soft tissue *in situ* treatment, the *in situ* monitoring of laser ablation results provides intuitive observation for evaluating the laser ablation during the operation. Ohmi and Haruna *et al*. demonstrated an effective method for *in situ* observation of laser ablation of soft-biological tissue based on OCT imaging (*100,101*). For the improvement of imaging speed, the swept source OCT has been investigated in the system with 25 Frames/s imaging speed for *in situ* observation (*102-104*). In Ohmi's research, OCT system is only used in monitoring the process of laser ablation and post-operation imaging. It is still a dilemma how to use integration of OCT and laser ablation treatment. OCT guided laser resection in surgery has also been developed by Nitesh Katta *et al*. The smart laser knife system is used for surgical guidance (*105,106*). These research methods take the utility of OCT imaging and monitoring the laser ablation into consideration. Enhanced tissue ablation efficiency with a mid-infrared nonlinear frequency conversion laser system has been proposed, and the results can be monitored using OCT imaging (*107*). However, a large-scale OCT scanning and laser ablation model during OCT-guided laser ablation treatment are still problematic, as well as real-time monitoring laser ablation. The integration of OCT and laser ablation has met same dilemmas. Therefore, we proposed a novel SD-OCT guided laser ablation system for resection of brain tumors (*109*). We have proposed and designed the prototype of integration of diagnosis and therapeutic systems, which is an optical theranostics system, and includes OCT imaging, analytical outcome of laser ablation, and automatic scanning platform. It has a promising application for neurosurgical treatment. Figure 6 shows the *ex vivo* porcine brainstem validation experiment for evaluating OCT imaging of pre- and post-ablated craters. In the future, integration of OCT and laser ablation will provide more precise diagnosis and therapy through precisely controlled radiation power and duration times.

In the imaging and treatment of brain tumors, OCT-related system can give an optional approach for precision identification and therapy. OCT-based diagnosis has the function of intraoperative histological sections for real-time identification of tumorous tissue, non-tumorous tissue, and infiltrated zone. In the future, a combination of morphological and functional information for imaging brain tumors will further prompt the clinical application of OCT in neurosurgery. Some novel optical attenuation coefficient- and artifact intelligence-based approaches of OCT image processing will play a greater advantage in diagnostics for real-time identification, classification and segmentation of tumorous tissue. Minimally invasive theranostics is the developmental trend for future clinical practice. Integration of OCT and laser ablation system

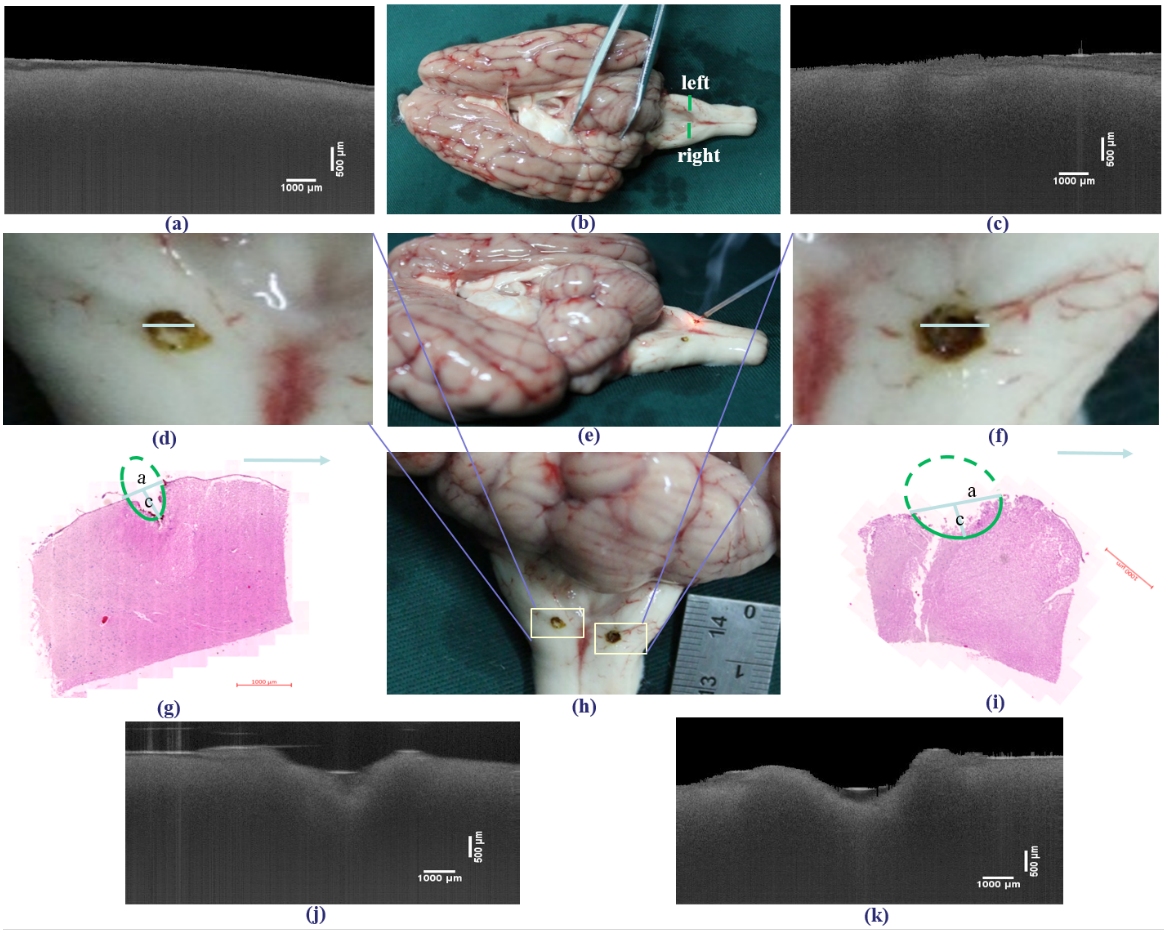


Figure 6. The validaion experiment of imaging the pre- and post-ablated craters on the *ex vivo* porcine brainstem (a) and (c). The OCT images of the pre-ablated craters corresponding to the left and right locations in ex vivo porcine brainstem. **(b)** The *ex vivo* porcine brainstem, with the green line showing the scanning location. **(d, f)** The ablated craters corresponding to a radiation power of 5 W and radiation durations of 5 and 10 s, respectively. **(e)** The performance of laser ablation on the porcine brainstem. **(g, i)** Histological sections corresponding to **(d)** and **(f)**, respectively (scale bar = 1,000 µm). **(h)** Laser-ablation results. **(j, k)** OCT images of post-ablated craters at a radiation power of 5 W for radiation durations of 5 and 10 s, respectively. From *Ref.* (*108*). (Reprinted with permission).

can carry out treatment of brain tumors. Endoscopic or robotic-assisted integration of OCT and laser ablation system will make minimally invasive theranostics a reality. This will be one of the clinical trends due to the characteristics of precision and real time in integration of diagnosis and therapeutics.

4. Conclusion

In summary, OCT has performed some advantages and has great potential in ultra-high resolution brain imaging, neurosurgical guidance, and minimally invasive theranostics integrated with laser ablation. Local intraoperative brain imaging can provide extensible sufficient structural and functional information including nerve fiber tracts and neurovascular structure. Improvement of OCT imaging depth is the trend for precision imaging and identification of brain tumorous and non-tumorous tissue. Functional imaging will provide more precise information for neurosurgical guidance. Optical Doppler tomography or Doppler OCT has also been used to acquire tomographic images of animals' brain hemodynamics in the cerebral cortex. Brain functional imaging, which includes nerve fiber tracts and cerebral vascular hemodynamics, can be incorporated into intraoperative neurosurgical imaging and guidance procedures to avoid damage of cranial nerve's function during resection treatment.

In OCT-guided neurosurgical theranostics, the system needs higher technical advancements for faster automatic diagnosis and therapy as well as fusion of multimodal information. The intelligence of theranostics system can be improved by adding visual feedback to make treatment safer, less invasive and more effective. Hence, minimally invasive theranostics, which combines OCT and laser ablation to reach high precision, automation and intelligence on intraoperative neurosurgical operation and treatment, is a novel method for diagnosis and therapy of brain tumor. It could be a promising technology in translational medicine.

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