# Laser/Light Applications in Neurology and Neurosurgery

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**Abstract**

Applications of light in neurology and neurosurgery can be diagnostic or therapeutic. Neurophotonics is the science of photon interaction with neural tissue. Photodynamic therapy (PDT) has been attempted to destroy infiltrative tumor cells in tissue. Spatially modulated imaging (MI) is a newly described non-contact optical technique in the spatial domain. With this technique, both quantitative mapping of tissue optical properties within a single measurement and cross sectional optical tomography can be achieved rapidly. The ability to control the activity of a defined class of neurons has the potential to advance clinical neuromodulation.

**Keywords**

LITT · Laser interstitial thermal therapy
Optical Coherence Tomography
Fluorescence assisted surgery
Raman spectroscopy · $CO_2$ laser

- Applications of light in neurology and neurosurgery can be diagnostic or therapeutic.
- Optical Coherence Tomography (OCT) is a non-invasive imaging technique that uses the back scattering of light at different depths from tissue to generate micron scale resolution images from a single imaging plane.

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- Laser interstitial thermal therapy (LITT) is a method for tissue ablation that has shown promising results as a new minimally invasive method for treating brain tumors, radiation necrosis, and epileptogenic tissue.
- Photodynamic therapy (PDT) has been attempted to destroy infiltrative tumor cells in tissue.
- Raman spectroscopy involves rare photon-electron interactions in a molecule and has clinical promise in identifying CNS tumors.

## Introduction

The application of lasers to the medical fields of neurology and neurosurgery is described in this chapter. We begin with an overview of laser physics in relation to the nervous system and progress to describing specific applications in neurology and neurosurgery. In general, the use of lasers in neurology and neurosurgery can be classified into the following categories: diagnostic imaging, thermal tissue ablation, photodynamic therapy, and neuromodulation. While laser technology is becoming increasingly useful in neurosurgical treatment of brain tumors, radiation necrosis, and epilepsy, its use in the treatment of non-surgical neurological disorders is still theoretical and experimental.

## Laser Interaction with Brain Tissue

Laser light can interact with neural tissue in five principal modalities: absorption, phosphorescence, fluorescence, elastic scattering, and inelastic scattering. Absorption involves the effect of photon electromagnetic energy on chromophores in the tissue and conversion of that energy into heat. Phosphorescence describes the release of a photon with similar or lower energy with a delay period after the incident photon interacts with the tissue. Fluorescence involves the excitation of electrons to higher energy orbitals with electron transitions resulting in release of a photon of lower energy. Elastic scattering involves the deviation of the photon path with no change in energy. Inelastic scattering involves an increase in the wavelength (reduction in energy) of a photon after interaction with molecular components of the tissue, the magnitude of the change being determined by individual molecular components of the tissue.

Light traveling in tissue shows decay in intensity due to absorption of photons by the tissue. The intensity decays exponentially with the depth of penetration ($z$) at a rate determined by the absorption coefficient of the tissue ($\alpha$), according to the Beer-Lambert law, $I(z) = I_{(0)}e^{-\alpha z}$. Chromophores are the light absorbing molecules in the tissue. Ultraviolet light has very short penetration due to avid absorption by organic molecules such as DNA and proteins. The principle brain chromophore for light in the visible range is hemoglobin. Near-infrared (NIR) wavelength light is used in lasers designed to generate thermal energy in brain tissue in order to permit greater penetration into tissue since water is the main chromophore for NIR light and NIR light shows less scattering than visible light in tissue. In the NIR region, the absorption spectra of water and other primary chromophores, such as lipids, and oxy and de-oxy hemoglobin are different (Fig. 10.1). The greater brain penetration of NIR light (940 nm) versus blue light (453 nm) has been confirmed experimentally in mouse brain [1]. Lipids absorb avidly in the NIR range, which suggests theoretically faster heating of white matter than grey matter may be achieved with NIR laser light given the lipid density of white matter. The absorption coefficients of astrocytoma is higher than that of normal brain, allowing for preferential deposition of light energy in these tumors [2].

The brain has intrinsic fluorescence when excited by high-energy light in the UV to green range due to high proportion of aromatic amino acids (tryptophan, tyrosine, phenylalanine), high NADH content due to energy demands, and presence of lipids and vitamins (A, K, D). Fluorescence involves the transfer of energy from a photon to a lower molecular orbital electron transition to a higher molecular orbital, and decay of the electron down to a lower energy molecular orbital releasing a photon of lower energy.

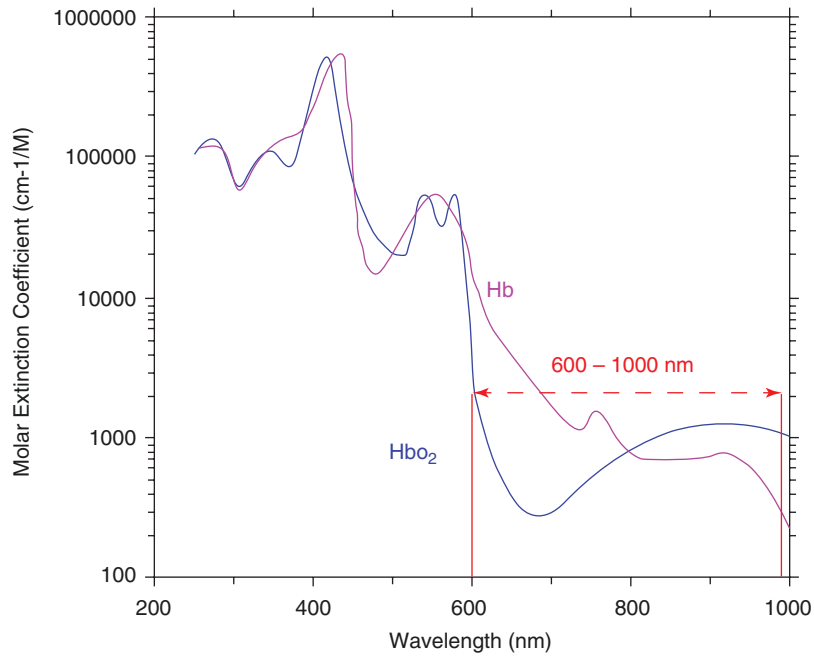


**Fig. 10.1** Graph showing the molar extinction coefficients of oxy (*HbO2*) and deoxy (*Hb*) hemoglobin. Between wavelengths of 600–1000 nm the extinction coefficients of the two states of hemoglobin show low absorption with distinct spectral features. This provides a spectral window of good tissue penetrance of photons as well as allows better resolution of their individual chromophore concentrations from the Beer-Lambert Law

The process is affected by the environment of the molecule, such as pH, as well as the presence of other fluorophores with absorption maxima in the range of the emitted photons resulting in quenching. Because the microenvironment is an important determinant of brain fluorescence the emission spectra of tumor infiltrated brain and normal brain have been compared. Tumor infiltrated brain shows a shift of 10–20 nm in peak autofluorescence and the overall autoflourescence intensity can vary 15–30% [3].

Laser light scattering by brain tissue has become a useful tool in the laboratory to assess the physiological properties of brain tissue. The scattering properties of different brain regions differ, so that photostimulation with light requires specific understanding of the optical properties of the target region in order to use adequate light intensity to achieve effects at a distance from the light source [1]. Measurement of light scattering can give important information about the functional status of brain tissue. Changes in neuronal membrane potential result in alterations in the light scattering, which can be used to monitor neuronal function in real-time [4]. This enables experimentation to determine the effects of integrated neuronal circuits, alterations in membrane ion channel composition, or testing new drugs to alter neuronal excitability in a contact free manner compared to standard patch clamping. Changes in membrane potential can also be recorded using specialized laser microscopy technique involving second harmonic generation from the membrane surface. This type of imaging has been used to characterize membrane potential dynamics in cultured hippocampal neurons [5]. The changes in scattering of light associated with spreading depolarization in brain can be used to assess brain function in pathological states such as trauma, subarachnoid hemorrhage, and ischemia. Increase in scattering at 500 and 584 nm and decrease at 800 nm was found to occur in synchrony with cortical spreading depression in rats [6].

Recently inelastic scattering of laser light has been used to evaluate surgical specimens obtained during brain tumor surgery or to determine the transition from brain densely infiltrated with tumor from that less densely infiltrated. Inelastic scattering involves the absorption and emission of light by a molecule resulting in bond vibrations that generate a unique spectral emission pattern based on the identity of that molecule and therefore the molecular composition of a tissue

[7]. These electronic transitions may be stimulated or alternatively enhanced by electromagnetic interactions of molecules with the surface of roughened metals or metallic nanoparticles.

## Neurodiagnostic Application of LASER Light

### Optical Coherence Tomography

Optical Coherence Tomography (OCT) is a non-invasive imaging technique that uses the back scattering of light at different depths from tissue to generate micron scale resolution images from a single imaging plane. By using scattering signal from a defined depth to generate the image, optical sections through the tissue can be imaged. This allows visualization of tissue microstructure without the need for fixation or use of a contrast agent or dyes. However, due to the limits of light penetration, the depth of imaging is small (200–300 μm), compared to other imaging tools such as ultrasound. It is structurally based on the Michelson's interferometer [8] (see Fig. 10.2). Brain structures that show high intrinsic optical contrast are myelinated fiber tracts and blood vessels [9]. OCT has been proposed as a potential guidance tool for deep brain stimulation, permitting the identification of blood vessels to avoid injury [9]. Because of the lack of contrast in OCT, tumor infiltrated brain cannot be distinguished from normal brain. Thus, OCT for pathologic analysis of low-grade gliomas is not effective [10]. When the tissue architecture changes due to tumor growth and associated changes such as the case of necrosis, microvascular proliferation, and high cell density in glioblastoma, OCT may detect these changes as a function of their effects on tissue optical contrast. The advantages of using OCT for tissue evaluation at the time of surgery it that the tissue sample does not require preparation and image acquisition is rapid [10]. OCT does not replace histological assessment, but can serve as a rapid technique to identify changes at the resection margin or identify tissue that should be sent for histologic assessment. Similarly to its use in assessment of tissue architecture in tumors, OCT can be used for imaging of the luminal wall in the assessment of cerebral aneurysms [11]. This technology provides a more detailed assessment of aneurysm healing after coil embolization than can be provided with standard angiography; however the application in current clinical practice is still under investigation.

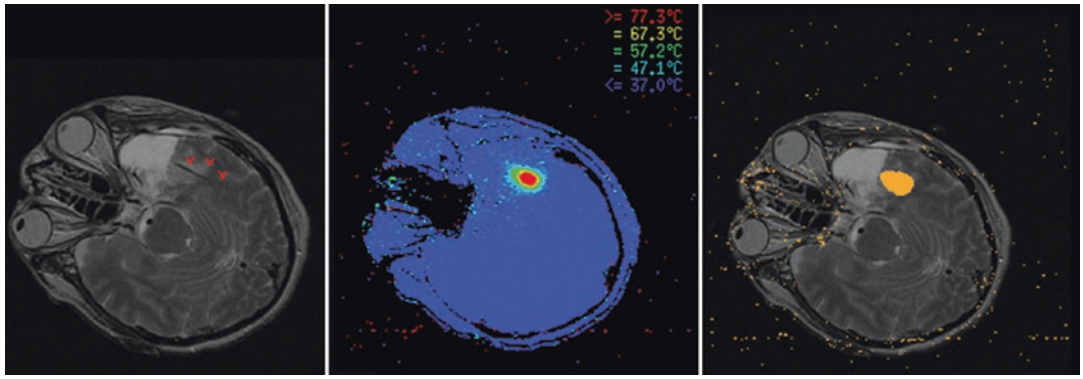


**Fig. 10.2** Schematic diagram of a high speed, high resolution spectral domain OCT system which reconstructs vessel structure image. The system is constructed along the lines of a Michelson interferometer. Eighty percent of the incident power is coupled into sample arm while 20% is fed into a reference arm by a 1 × 2 fiber coupler. The reference power is attenuated by an adjustable neutral density attenuator for maximum sensitivity. Two circulators are used in both reference and sample arms to redirect the backreflected light to the second 2 × 2 fiber coupler (50/50 split ratio) for balanced detection. The signal collected by a photodetector is digitized with an analog-digital acquisition card and transferred to a computer for processing

## Neurotherapeutic Applications of LASER and Light

Laser light can be used a tool to ablate or anneal tissue based on the transfer of photon energy to heat within tissue and the ability to select a specific wavelength and tune the laser power, beam width, and pulse characteristics.

## Pediatric Applications

Spinal lipomas involving the conus and cauda equina are challenging surgical lesions. The intimate association with the spinal cord and nerve roots requires accurate and minimal manipulation to avoid neurological injury during debulking and untethering. The $CO_2$ laser, invented by Kumar Patel at Bell labs in 1964, has become an important surgical laser due to its efficiency and capacity to function as a continuous wave laser. The light generated by the $CO_2$ laser is in the infra-red range and readily absorbed by water and lipid molecules in tissue. McLone and Naidich decribed the advantages of the $CO_2$ laser in the treatment of spinal lipomas as shortening operation time, reducing blood loss, and reducing the degree of manipulation of the spinal cord and nerve roots [12]. A flexible $CO_2$ laser system was recently used to achieve subtotal to near-total resection of eight conus lipomas without causing new neurological deficit [13]. The $CO_2$ laser can be used for the cutting and cauterization of intramedullary tumors with minimal energy dispersion to adjacent tissue as described for an intramedullary dermoid tumor in a 11 month old child [14].

## Cerebrovascular Applications

### Laser Assisted Vascular Anastomosis

Laser assisted vascular anastomosis was first performed by Yahr and colleagues in the mid 1960s [15]. While early studies described an increased risk of aneurysm formation with laser anastomosis compared to suture anastomosis [16, 17], more recent use of an excimer (ultraviolet light) laser system has resulted in high patency rates with no increased complication rate in cerebral vascular bypass. Excimer laser assisted nonocclusive anastomosis (ELANA) has been used for bypass in the treatment of large or giant aneurysms of the internal carotid artery or middle cerebral artery [18, 19]. The use of ELANA for bypass of large caliber cerebral vessels has also been reported in the treatment of ischemia and tumors [20]. This technology works by creating a window in the recipient vessel wall and welding the donor blood vessel to the recipient vessel wall without occlusion of flow in the recipient vessel.

## Neuro-Oncologic Applications

### Extra-Axial Intracranial Tumors

Similar to the use of the $CO_2$ laser in spinal lipomas, to reduce neural tissue manipulation while permitting precision tumor destruction, the $CO_2$ laser can be used for the resection of meningiomas [21, 22]. The Nd:YAG laser has been combined with the $CO_2$ laser in order to take advantage of the hemostatic action of Nd:YAG in meningiomas [23]. In a large series of meningiomas operated with laser versus conventional techniques, patients with eloquent region tumors operated with the laser showed better outcomes [24]. Use of laser-assisted resection of meningioma may enhance the ability to resect difficult to reach meningiomas and increase the extent of resection [25, 26]. Vaporization and shrinkage of meningiomas with a safety margin beyond 2 mm of the laser-tissue interface can be achieved with the 2-μm thulium laser [27, 28]. This laser allows removal of tumor while maintaining hemostasis and visualization due to its coagulation ability.

## Vestibular Schwannomas

Vestibular schwannomas commonly arise in the superior vestibular nerve just proximal to Scarpa's ganglia and are intimately related to the cochlear nerve and the facial nerve. Due to the close rela-

tionship of these cranial nerves to the tumor and the small working space for tumor resection through a retrosigmoid or middle cranial fossa approach, use of laser for tumor precision vaporization while maintaining hemostasis in these tumors is appealing to the surgeon. The flexible $CO_2$ laser has been used in the middle cranial fossa approach to vestibular schwannoma with similar cranial nerve function results to conventional resection [29]. Eiras et al. compared $CO_2$ laser excision of giant vestibular schwannomas versus conventional surgery finding that facial nerve function was better in laser treated patients, although the duration of surgery was longer [30].

## Fluorescence Assisted Surgery

A growing body of evidence has associated extent of resection with increased survival and greater effect of adjuvant therapy in malignant gliomas [31–35]. Due to the intrinsic nature of this tumor and its invasive potential along white matter tracts and the perivascular niche, surgical resection is abound with challenges. Pre-operative MR imaging has allowed the assessment of enhancing tumor boundaries and demonstrates the invasiveness in extension of FLAIR signal along white matter tracts. Intra-operative neuronavigation using pre-operative images has enabled accurate operative planning of the surgical approach and surface mapping of tumor boundaries. However, as surgical resection is carried out the accuracy of neuronavigation for defining the enhancing tumor boundary is altered by brain shift secondary to CSF egress, tumor debulking, and gravity. In addition, distinguishing enhancing tumor margin from surrounding non-enhancing brain tissue becomes dependent on surgeon experience and assessment of tissue texture and other qualities such as color and softness, which are subjective measures. To address the challenge of intra-operative tumor delineation three different strategies have been previously employed: intra-operative MRI, ultrasound, and tumor cell labeling with 5-aminolevulenic acid (5-ALA).

Fluorescence guided glioblastoma resection using the tumor cell specific agent 5-ALA has been shown to have a benefit on extent of resection and 6 month progression free survival [36]. Adoption of 5-ALA fluorescence guided surgery in the US has been hindered by lack of FDA approval of 5-ALA for clinical use. From a technical standpoint, surgical resection using 5-ALA is affected by the requirement for low ambient light levels, blue hue to the adjacent non-tumor tissue, and black colored blood [37]. Use of 5-ALA requires the administration of 20 mg/kg orally 3 h prior to the surgical procedure and protection of the patient from light sources for 24 h after administration [38]. In the circulation 5-ALA is converted to protoporphyrin IX. It is the accumulation of violet-blue light fluorescing protoporphyrin IX that allows demarcation of glioma cells. A filter attachment is provided on the operative microscope that permits the excitation of PPIX in malignant tumor tissue with blue light ($\lambda = 400–410$ nm), which emits a red-violet light of 635 nm. Preclinical studies of 5-ALA demonstrated preferential uptake of into C6 rat glioma cells [39, 40].

Passive labeling by sodium fluorescein of regions of blood-brain barrier disruption associated with the infiltrative tumor margin is hypothesized to provide another means to delineate and resect brain tumors up to the enhancing tumor margin. This provides for real-time surgical delineation and resection of a glioblastoma, which is limited with intra-operative MRI and 3D-ultrasound. Unlike 5-ALA, which is currently not approved for clinical use in the US, fluorescein sodium has been used extensively in clinical practice for retinal angiography with a proven safety record. Fluorescein is a water-soluble dye that has been used in clinical medicine for retinal angiography and dermatofluorometry [41]. Use of intravenous fluorescein for the demarcation of parenchymal brain tumors was first reported in 1947 [42, 43]. However, use of fluorescence to guide tumor resection was not practical at that time given the lack of surgical fluorescence microscopy. In 1998, Kuriowa et al. [44] described the first microscope mounted fluorescein fluorescence excitation and emission filter system with white-light switching capability. Subsequently, Zeiss has developed a module for the xenon-light operating microscope that enables visualization of fluorescein fluorescence through the eyepieces using excitation via light yellow ($\lambda$ = 560 nm),

thereby facilitating microscopic tumor dissection [37, 45]. Recently, investigation of the mechanism of tumor demarcation using two animal models of glioblastoma have demonstrated that fluorescein labels regions of blood-brain barrier disruption and does not concentrate inside glioblastoma cells [46]. Thus, while fluorescein will identify enhancing tumor with high sensitivity it is not specific for glioblastoma cells. Fluorescein fluorescence allows surgical resection under a more normal hue with blood having a red color. Furthermore, it is envisioned that fluorescein would be more rapidly adopted as a tool in the surgical resection of malignant enhancing gliomas within the US given FDA approval for clinical use, allowing the off-label use of fluorescein. There have been three case series reported in the literature demonstrating significantly higher rates of gross-total resection when using fluorescein fluorescence to guide resection (80–84%) compared to white light (30–55%) [47–49]. Currently, there are no reported randomized controlled trials evaluating the use of fluorescein to enhance the extent of resection or survival in patients with malignant gliomas.

## Laser Interstitial Thermal Therapy (LITT)

Given the optical properties of brain and capacity for conversion of light energy to heat in a controlled manner adjacent to a laser source, laser catheter ablation of intraparenchymal lesions and seizure foci has been developed and is currently undergoing clinical evaluation. Heat production by laser light can be monitored using MRI thermometry. Irreversible cell damage occurs between 46 and 60 °C [50]. The clinical platforms currently in use deliver light in the NIR-range (980 nm and 1064 nm). Ablation of metastatic or primary brain tumors can be achieved with placement of a catheter in the center of the mass and delivery of light energy in a time-dependent manner under MRI monitoring (Fig. 10.3). Specific neuroimaging changes occur after the ablation treatment, which have been described by Medvid et al. [51] The laser catheter tract is surrounded by a zone of coagulation

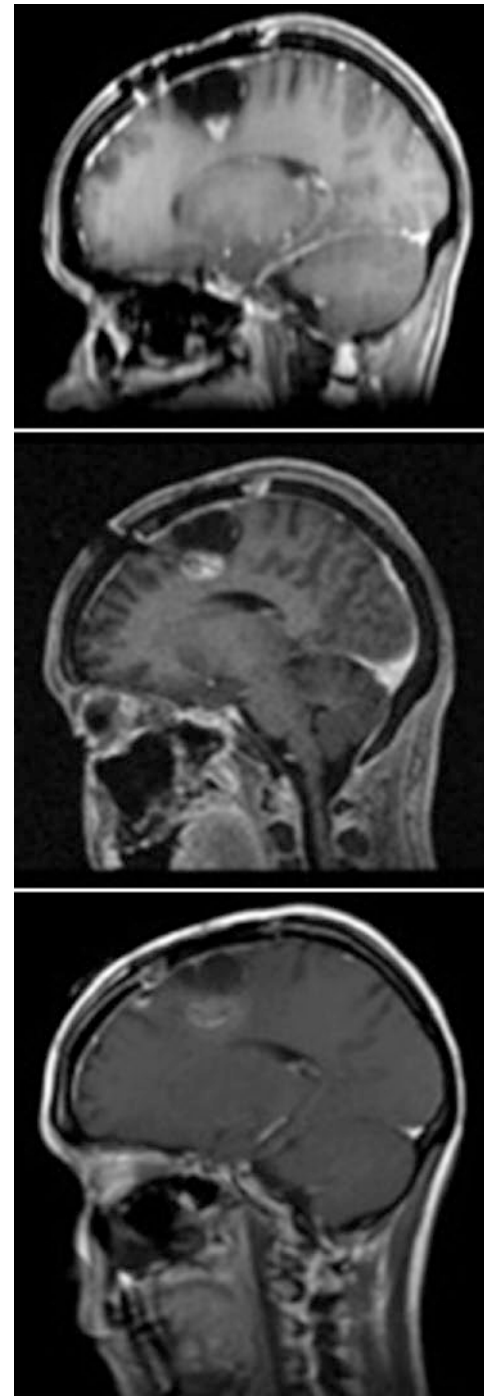

**Fig. 10.3** T2 MRI demonstrating a glioblastoma recurrence abutting the prior resection cavity with a LITT catheter inserted. Red cross-haired identify areas of temperature control high temperature limits set prior to ablation (Left). MRI thermometry of the lesion, with color correlating to the lesional temperature around the catherter tip. (Center). Damage estimate after ablation of the temporal lesion (Right)

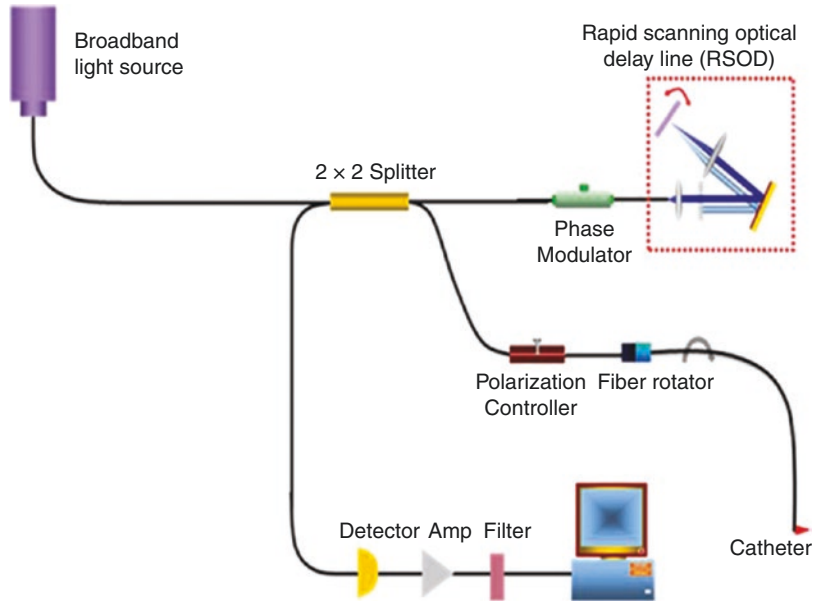


**Fig. 10.4** Contrast enhanced T1-weighted MRI showing a glioblastoma recurrence in the resection cavity margin before insertion of LITT catheter (top row), immediately after LITT ablation (middle row) and 18 h after LITT ablation (lower row)

necrosis, which appears hyperintense on T1-weighted and hypointense on T2-weighted imaging at 24 h (Fig. 10.4). Concentrically adjacent to the coagulative zone is the peripheral zone, which is an area of hypointense on T1 and hyperintense on T2 due to edema. Due to disruption of the blood-brain barrier at the margin of the peripheral zone, a thin enhancing rim appears on T1-weighted contrast-enhanced images. Post-ablation edema peaks around 3–4 days and is easily managed with a 2-week steroid taper, not necessitating inpatient management. Case series reported on the treatment of recurrent gliomas demonstrate a median survival of 9.9 months after laser ablation with the majority of these patients harboring glioblastoma [52–57]. In the treatment of metastatic lesions, post-ablation median survival ranges from 4.6–19.8 months [58–60]. While the current literature includes a heterogeneous population of treated patients, it provides evidence of a safe and potentially effective use of laser ablation to disrupt lesions that are difficult to reach by standard cranial surgical routes or for which open surgery would place the patient at risk of significant neurological deficit. For gliomas it appears that the extent of tumor ablation is an important determinant of the efficacy of LITT. As such LITT for glioma treatment is primarily used today in lesions that are difficult to reach with standard procedures and for which LITT treatment is predicted to result in total or near-total thermal ablation of the tumor. The technology is in ongoing development. With the introduction of pre-operative planning software greater degrees of ablation margin planning are envisioned. Furthermore, enhanced safety will be obtained with the used of safety temperature markers and margins based on functional MRI, and diffusion tensor tractography. The use of multimodality imaging and 3-D planning of thermal tissue injury will ultimately result in more efficient and safe application of this technology.

Several advantages of LITT over traditional open craniotomy exist. First, the procedure may reduce operative time and post-operative stay for patients who are already in a fragile health state. Secondly, the procedure permits treatment of tumors that would not have been considered operable in the past and offers the opportunity for repeated treatments in multiple orientations. In addition, there is no risk of ionizing radiation damage. Because the procedure involves a single 4 mm incision and 3.2 mm drill hole, patients can be quickly transitioned to receive adjuvant radiation or chemotherapy without the need to wait for tissue healing required after a craniotomy. The

indications and overall efficacy and safety of LITT for brain tumors is currently undergoing active investigation. Early studies show a similar complication rate to that of open surgery in patients with recurrent glioma (16.7% vs 11% major complication respectively) [61, 62].

Brain tissue ablation for the treatment of mesial temporal lobe epilepsy is a novel non-invasive therapeutic application of LITT. Instead of performing a craniotomy and resecting the mesial temporal structures either through a selective amygdalohippocampectomy or a complete anterior temporal lobectomy, the laser delivery catheter is placed co-axial with the long-axis of the parahippocampal gyrus in a plane below the temporal horn of the lateral ventricle. Thermal ablation of the amygdala and hippocampus in this manner offers a safe and potentially effective treatment for mesial temporal sclerosis [63, 64]. Stereotactic laser amygdalahippocampectomy could be useful where temporal lobe neocortical function needs to be preserved. For example, object recognition and naming outcomes in dominant temporal lobe procedures and famous face recognition in non-dominant temporal lobe procedures is preserved in patients with stereotactic laser amygdalahippocampectomy compared to decline seen in most patients with standard surgical procedures to treat temporal lobe epilepsy [65]. Further long-term outcome studies and neuro-cognitive assessments done in a randomized fashion in anterior temporal lobectomy versus stereotactic laser amygdalahippocampectomy are needed.

## Emerging Optical Technologies

### Photodynamic Therapy

Photodynamic therapy involves the activation of a light-responsive chemical process that results in cellular toxicity or the release of a cell-damaging agent. Glioblastoma accumulation of 5-ALA derived protoporphyrin IX has been tested as a photodynamic therapy agent. In a xenograft mouse model of human glioblastoma, interstitial delivery of 635 nm light after injection of 5-ALA showed induction of necrosis when delivered in a fractionated fashion at high power [66]. Human application of this technology is in early stages; however, Stummer et al. have reported a response of recurrent glioblastoma to photodynamic therapy with 633 nm laser light in a patient after administration of 5-ALA [67]. Talaporfin sodium is another photosensitizer that has been demonstrated to induce programmed necrosis in glioblastoma cells [68]. Safety data from clinical trials with Talaporfin sodium show it is well tolerated in humans [69]. Multifunctional nanoparticle platforms which can be activated by light and carry brain tumor targeting moieties such as peptides or antibodies are being designed which could be used with NIR-light or interstitial laser light sources [70, 71].

### Stimulated and Surface-Enhanced Raman Spectroscopy

Raman spectroscopy involves rare photon-electron interactions in a molecule. It can be performed without the need for molecular immobilization in a discrete plane using stimulated electron transitions. A dual laser source is used to pump electrons in the molecules making up the tissue into higher energy states that show more rapid Raman inelastic scattering, allowing fast imaging. Pre-clinical studies of stimulated Raman scattering have demonstrated its use in identifying brain tissue consisting of a high tumor cell density [72]. Furthermore, application of this technology to the operative theatre using a pen-like device to probe tumor resection margins has been described [73].

Spherical and rod-shaped gold nanoparticles can be designed to have absorbance maxima in the near-infrared light wavelengths such that the particles can be heated with near-infrared (NIR) light in pulse patterns creating expansion and contraction that allows the detection of particles by their acoustic emissions (photoacoustic detection) [74, 75]. Alternatively, NIR light can be used to create a localized surface plasmon effect which allows the detection of unique Raman spectra from reporter molecules on the gold

nanoparticle surface—a process known as surface enhanced Raman spectroscopy (SERS) [76, 77]. NIR-SERS capable gold nanoparticles are of particular interest in that they have recently been shown useful in imaging U87 GBM and primary brain tumour xenografts in a mouse model [78]. Structures in this size range demonstrate unique chemical properties and phenomena that are dependent on size, shape and chemical composition [79].

## Summary

Laser technologies have undergone remarkable progress towards clinical application in the setting of neurological disease. In the basic science research sphere, lasers are routinely used for studying neuronal structure and function, assessment of brain microenvironment, and visualizing changes in cerebral vasculature. Clinical application of laser technology for the purposes of creating tissue damage is beginning to play a significant role in brain tumor and epilepsy surgery. Future development of laser imaging techniques for nanoparticle diagnostic and non-ablative therapeutic applications in the CNS can be envisioned. The combination of nanoparticles with light activated chemical agents may serve a role in phototherapy of brain tumors previously deemed inoperable or that have developed resistance to standard chemotherapy and radiation. Translating the basic science advances in laser technology to the clinical realm will require close collaboration between physicists, engineers, and clinicians.

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