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Review Article

Laser application in neurosurgery

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Abstract

Background: Technological innovations based on light amplification created by stimulated emission of radiation (LASER) have been used extensively in the field of neurosurgery.

Methods: We reviewed the medical literature to identify current laser-based technological applications for surgical, diagnostic, and therapeutic uses in neurosurgery.

Results: Surgical applications of laser technology reported in the literature include percutaneous laser ablation of brain tissue, the use of surgical lasers in open and endoscopic cranial surgeries, laser-assisted microanastomosis, and photodynamic therapy for brain tumors. Laser systems are also used for intervertebral disk degeneration treatment, therapeutic applications of laser energy for transcranial laser therapy and nerve regeneration, and novel diagnostic laser-based technologies (e.g., laser scanning endomicroscopy and Raman spectroscopy) that are used for interrogation of pathological tissue.

Conclusion: Despite controversy over the use of lasers for treatment, the surgical application of lasers for minimally invasive procedures shows promising results and merits further investigation. Laser-based microscopy imaging devices have been developed and miniaturized to be used intraoperatively for rapid pathological diagnosis. The multitude of ways that lasers are used in neurosurgery and in related neuroclinical situations is a testament to the technological advancements and practicality of laser science.

Key Words: Laser, laser-induced thermal therapy, neurosurgery, photodynamic therapy, transcranial laser therapy

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INTRODUCTION

Investigation of medical applications of lasers began shortly after their creation in 1960. Even the earliest studies suggested great therapeutic value in this newfound technology.[95-97] Since those early studies, low-power lasers have been used in diagnostic and therapeutic applications in a wide variety of medical areas. However, this modality of therapy continues to be highly controversial because of uncertainty regarding the mechanism of action by which therapy is achieved and a lack of consensus protocols for certain applications because of the large number of parameters (e.g., frequency, energy, treatment timing, positioning) that can be selected. Since the 1980s, researchers have studied the effects of laser-induced hyperthermia and changes in brain tissue, meninges, and various tumor tissues in experimental models.[31,138,139] The effect of laser on tissue depends on the intensity and wavelength of the light used, absorption characteristics of the tissue, and various biological responses to the energy of the laser.[9] An increase in the intensity of laser energy applied to tissues provides a range of changes from the closest point of contact to the tissue, where the most destructive effects occur, to the most distant areas, where low-energy laser light may cause a biostimulative effect [Table 1].[9] Different types of lasers have specific applications because of their unique wavelengths, which result in various penetration depths into the tissue before vaporization of the surface layers occurs.

In the present paper, we review the current technology and application of lasers in neurosurgery. The topics covered include magnetic resonance (MR)-guided percutaneous ablation, anastomosis, therapeutic applications, and diagnostic applications [Table 2].[3,7,11,12,15,17,25,27,33-35,38,44,53,61,65,67,74,83,85,92,108,112,113,116,119,120,127,130,131,133,136,137,140,146-148,151]

SURGICAL LASERS

Lasers in open surgery

Since the first use of a laser in human patients with malignant gliomas was reported in 1966,[117] the utility of lasers as a neurosurgical instrument has been researched extensively. In one of the earliest and largest case studies, Takizawa[140] concluded that using the CO_2 laser as a complement to traditional neurosurgical instruments allowed for less manipulation and invasion of normal brain tissue [Figure 1]. However, enthusiasm for the use of lasers in open neurosurgery has diminished since then because of the risks and limitations of the technology. CO_2 lasers require transmission through an optic fiber, and their long wavelength limits their capacity to deliver sufficient energy to the surgical site.[80] Endoscopes using neodymium-doped-yttrium aluminium garnet (Nd:YAG) or argon lasers have also been found to damage healthy brain tissue adjacent to the ablation area.[110,145,149] Despite these drawbacks, new technological advancements in the field and recent studies, especially with CO_2 lasers using novel energy transmission designs [Figure 2],[119] suggest that these devices may be used more often in the future for open neurosurgery. Pioneering applications with new CO_2 laser instrumentation by Ryan *et al*.[120] have led to the reintroduction of highly controllable and precise CO_2 laser use for neurosurgery.

Laser-assisted endoscopic neurosurgery

Using lasers to treat arachnoid cysts has provided good results. Choi *et al*.[21] performed the largest prospective study assessing the efficacy of laser-assisted endoscopic treatment.[51] They reported a 79% success rate with an Nd: YAG laser (30 W) for incision and coagulation of the cyst wall. A pediatric case report by Van Beijnum *et al*.[146] also demonstrated successful laser-assisted endoscopic fenestration of a suprasellar arachnoid cyst. Overall, the limited evidence suggests that using lasers endoscopically is safe and beneficial. However, comparisons of surgical results from laser-assisted endoscopic cyst fenestration with microsurgical cyst excision, stereotactic aspiration, or cystoperitoneal shunting are still lacking in the literature. Calisto[15] reported using a 15-W thulium: YAG surgical laser to make a surgical cut for resection of a hypothalamic hamartoma from the third ventricular wall through a contralateral endoscopic approach. He noted

Table 1: Approximate interaction of laser light with living tissue*

Energy density (J/cm²)	Biological effect
<4	Biostimulation
>4	Biosuppression
40	Nonthermal cytotoxic phototherapy with sensitizing agents
400	Photocoagulation and thermal effects
4,000	Vaporization and thermal effects

*Table used with permission from Brown SG: Phototherapy of tumors, World J Surg 1983;7:700-9

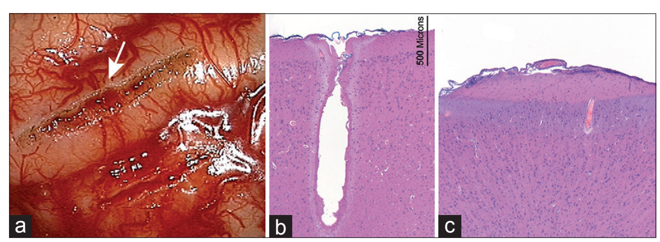

Figure 1: (a) Gross appearance of pial incisions made by a 7 W CO_2 laser (*top, arrow*) and with bipolar microscissors (*bottom*) (*in vivo* experiment, porcine brain). (b) Hematoxylin-and-eosin (H and E) stain shows a deep laser cut through the brain without extensive peripheral damage. Three zones of effect are visible: vaporized crater, desiccated zone, and edematous zone. The transition of the effect is rapid. (c) H and E stain of a drain shows the effect of bipolar coagulation. Two zones of effect are visible (desiccated and edematous) with no pial incision visible. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*

Table 2: Brief summary of laser technologies in neurosurgery and potential future applications

Laser Technology	Applications	Competing standard practices	Comment on the potential role in neurosurgery
Surgical lasers			
CO_2 laser scalpel[119,120,140]	Coagulation and cutting tissues during open surgical approaches	Scalpel, bipolar, and monopolar electrical coagulators	May be used by few neurosurgeons, arguably because electrocoagulation is more readily available and clinical benefit is not firmly defined
Nd:YAG[146] and thulium: YAG[15] endoscopic laser scalpels	Coagulation and cutting tissues during endoscopic approaches	Endoscopic bipolar and monopolar electrical coagulators	Few reports in human endoscopic surgeries are available. Incisions may be more precise than with cautery, making this laser technology interesting for future neuroendoscopic use, although rivalry with ubiquitously available electrocautery limits its further spread
Excimer laser-assisted nonocclusive anastomosis (ELANA)[61,137,147]; a sutureless ELANA technique[133,148]	Microvascular anastomosis	Manual suturing with microinstruments and thin sutures	Human studies demonstrated safety of ELANA for bypass surgeries; however, the low volume of vascular bypasses and conservatism among neurosurgeons limit widespread use of this technology
Laser-induced thermal therapy			
NeuroBlate System; Visualase[92]	Magnetic resonance navigated and thermal-controlled transcutaneous laser-induced thermal destruction of targeted tissue Potential indications: Lesional epilepsy[27,38,53] Hypothalamic hamartoma[27] Brain metastases[17] Ependymomas[108]Gliomas[33,131] Radiation necrosis[113] Disruption of blood–brain barrier to enhance drug delivery	Open and endoscopic surgery, stereotactic radiotherapy (Gamma Knife, CyberKnife)	Viewed as a good, new, minimally invasive alternative for many open neurosurgical procedures. The novelty of this technique and lack of long-term results are current limitations. With more experience and studies being performed, laser-induced thermal therapy may solidify its position in the neurosurgical armamentarium
Laser photodynamic therapy (PDT)			
Laser photodynamic therapy with a photosensitizer[7,112,116,127,136]	Adjuvant treatment for malignant brain tumors, primarily gliomas	Surgical tumor removal, chemotherapy, radiotherapy	Although studies demonstrated slightly prolonged survival,[34,35] PDT is still limited to clinical trials and is not a commonly used treatment strategy. It will probably not become a cure for glioma patients but may become an adjuvant option at the end of surgery because of the lack of other better solutions
Lasers in spinal neurosurgery			
Percutaneous laser disk decompression[25]	Spinal nerve root decompression by evaporating nucleus pulposus of intervertebral disc, desensitizing nerve endings in disc	Conservative therapy, open and endoscopic discectomies, spinal fusion	Positive reports on the use of PLDD are regularly published. However, randomized controlled trials showed no benefit over the standard treatment options. Currently viewed as a controversial technique[12,130]
Epiduroscopic laser neural decompression (ELND)[67]	Epiduroscopic ablation of herniated disc material and adhesions	Conservative therapy, open and endoscopic discectomies, spinal fusion	ELND is a new technique with lack of clinical data. The overall value of ELND and epiduroscopic approaches is yet to be defined. ELND could potentially gain a small niche in minimally invasive spinal neurosurgery
Laser tissue soldering			
Laser tissue soldering for dural reconstruction[44,151]	Dural repair: reattaching dural edges with a soldering material	Conventional dural suturing, various fibrin glue polymers, artificial dural grafts, and autologous fascial grafts	Only a limited number of animal studies are available so far. Sutureless dural repair could potentially be beneficial in complex dural repair in skull base approaches, although the clinical benefit and cost-efficiency of laser dural soldering have yet to be defined

Contd...

Table 2: Contd...

Laser Technology	Applications	Competing standard practices	Comment on the potential role in neurosurgery
Therapeutic applications of lasers			
Laser phototherapy for peripheral nerve regeneration	Promoting regeneration of peripheral nerves	Surgical repair; no therapy with proven efficacy is currently available to promote peripheral nerve regeneration	Laser treatment appears to be a promising application for nerve regeneration therapy in animal studies, but clinical studies are required to better assess its therapeutic potential
Transcranial laser therapy	Transcranial neuro-therapy for ischemic stroke (failed to show clinical benefit),[83] traumatic brain injury, neurodegenerative disorders	Supportive therapy, few drugs with limited clinical benefit	TLT has no treatment role for patients with ischemic stroke.[83] The application of TLT for traumatic brain injury and neurodegenerative diseases is questionable and viewed with caution despite a few positive animal studies
Diagnostic applications of lasers in neurosurgery			
Laser scanning endomicroscopy	*In vivo* and *ex vivo* morphological tissue diagnostics	Conventional tissue slicing and staining, benchtop confocal laser scanning microscopes with various dyes	An evolving technology with proven diagnostic value in other specialties (e.g., dermatology and gastroenterology). It is an encouraging diagnostic platform, but the exact clinical value of LSM with currently available fluorophores for routine brain tumor surgery is yet to be defined. Development of tumor-specific fluorescent molecular probes may increase the intraoperative use of LSM in the future
Raman spectroscopy	*In vivo* and *ex vivo* morphological tissue diagnostics	Conventional tissue slicing and staining, benchtop confocal laser scanning microscope with various dyes	An evolving technology for unstained tissue diagnostics. It is a promising technology that may gain a place in surgical neuro-oncology to expedite and improve intraoperative histological diagnosis of brain and tumor tissue
Laser Doppler imaging, flowmetry, and laser speckle blood flow imaging[3,11,65,74,85]	Measuring blood perfusion and flow in the vessels and tissues	Ultrasound Doppler flow measurement	Currently, a widely-used technology for measuring tissue perfusion. Its intraoperative use is limited to investigational studies but may be adopted for routine use by specialized neurovascular surgeons in the future for accurate monitoring of local microcirculation and possible detection of early ischemic changes. However, such measurements are unlikely to significantly alter current treatment paradigms or outcomes. Its main use is envisioned as a tool to measure the effects of other techniques

that the laser aided in making a precise incision in the deep brain region.

Laser-assisted microanastomosis

Excimer laser-assisted nonocclusive anastomosis (ELANA; Elana, Inc., Columbia, Maryland, USA) is a technology used to create a high-flow bypass for cerebral revascularization.[147] Advantages of the ELANA system include no risk of stroke due to temporary occlusion of vessels which occurs with other treatments[137] and fewer distal-end graft complications due to the stability provided by metal-ring placement during the procedure sequence. In addition, the technique does not increase the operation time. ELANA includes the following steps: (1) A metal ring of at least 3 mm in diameter is sutured to the end of the graft vessel and then to the recipient vessel without flow occlusion. (2) The ELANA catheter, containing circumferentially placed optic fibers, is introduced into the saphenous vein graft, and a circular arteriotomy in the recipient vessel wall is created by applying two laser episodes (10 mJ, 40 Hz) of 5 seconds. The catheter has a suction vacuum integrated at the center of the tip to retract the cut vessel wall.[134] The XeCl excimer laser (CVX-300; Spectranetics Corp., Colorado Springs, Colorado, USA) serves as a source of coherent light. Interestingly, this intravascular circular laser technology is gaining popularity in cardiovascular surgery for removal of cardiac stimulator leads and for removal of atheromas in patients with in-stent restenosis.[29,51]

One of the earliest clinical research studies to assess intraoperative flow through the ELANA system was performed by van der Zwan *et al.*,[147] who examined 26 patients with giant aneurysms and 8 patients with ischemia. The results showed that ELANA had a higher flow capacity than conventional techniques, leading the

Figure 2: A CO_2 surgical laser, the UniPulse COL-1040 (Nidek, Hiroshi, Japan), has an articulated arm through which the irradiation is delivered. Five regimens of irradiation effects range from cutting to coagulation. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*

authors to suggest that the ELANA system be denoted as a "high-flow" external-internal carotid bypass. Another study reported excellent results with high flow using an ELANA bypass technique in 7 patients with giant intracranial aneurysms.[61]

A sutureless ELANA technique (SELANA) was subsequently developed and is being tested. Its main improvement over ELANA is that it uses a special metal ring that is first mounted on the end of the graft vessel and then attached to the recipient vessel tightly with two pins. The anastomosis is then sealed by a circumferential layer of BioGlue surgical adhesive (CryoLife, Inc., Kennesaw, Georgia, USA) before an arteriotomy is created by the laser as in the ELANA technique.[133,148] Another laser-assisted anastomosis technique uses a Trinity Clip anastomotic connector to create an oval 0.8 × 2.0-mm end-to-side sutureless anastomosis that could feasibly be used for cerebrovascular bypass in the future.[132]

The ELANA system appears to be a safe and effective tool in intracranial bypass surgery. However, despite potential benefits of nonocclusive anastomoses, cerebrovascular high-flow bypasses are still relatively uncommon procedures used in select patients and most surgeries are still performed with manual suturing of the anastomosis.[71] High-flow bypasses are usually indicated for difficult cases that would otherwise have poor prognoses, hence neurological complications are not simply a result of the difficulty of microsuturing and vessel occlusion time. This partially explains the fact that ELANA is not commonly used in intracranial bypass.

LASER-INDUCED THERMAL THERAPY

The goal of laser-induced thermal therapy (LITT) (also referred to as laser interstitial thermal therapy, percutaneous laser ablation, laser heat ablation, MRI-guided laser surgery, and MRI-guided percutaneous laser ablation) is to achieve selective thermal injury of pathological tissue while maintaining a sharp thermal border between the tumor and normal brain tissues.[131] LITT involves the creation of a small cranial bur hole, through which a thin laser fiber is introduced into the brain until the tip reaches the targeted location. The procedure is performed under stereotactic guidance with a precision of 1 mm or less. Practical use of LITT was restrained by the absence of methods to monitor the extent of thermal destruction; however, recent advancements in MR thermometry have rejuvenated this approach. Laser-induced brain temperature change is monitored by MR thermometry and correlated with predicted cell death by computer models, all in real time. Such prediction has a high level of specificity and sensitivity (98.1% and 78.5%, respectively), as reported by Breen *et al*.[10]

Current systems use cooling with a constant stream of cooled water or CO_2 to prevent carbonization and adhesions to the probe, thus providing smooth energy distribution around the probe. LITT is initiated by the neurosurgeon and stopped manually or automatically if any monitored temperature limits are exceeded.[131]

The need to preserve a sharp border between surrounding normal brain tissue and the area of ablation necessitates the use of wavelengths for rapid energy deposition and high absorption by the lesion.[18] Light from the laser distributes in all directions, warming the tissues at the same distance evenly around the beam. Propagation of the thermal ablation zone to areas perpendicular and even backward to the probe is observed, creating one of the current technical challenges for controlled dose delivery.[131]

Currently available systems

The three main components of the LITT system include a flexible laser probe for transmission of laser light, a laser emitter, and an MRI-compatible head-fixation frame. A software platform with a monitor displays the estimate of predicted cell death and real MRI thermal-dose contours. After the probe is inserted in the operating room, the thermal ablation procedure is performed in the MRI suite. Thereafter, the patient is moved back into the operating room for probe removal. Alternatively, the whole procedure could be performed under intraoperative MRI monitoring. Correlation among the preoperative tumor volume, postoperative ablated volume, intraoperative critical temperature volume, and intraoperative critical dose volume is essential to assess the accuracy of LITT.

NeuroBlate system

The NeuroBlate system (Monteris Medical Corp., Plymouth, Minnesota, USA) incorporates an Nd: YAG laser that produces light transmitted through a laser-delivery probe. The directional gas-cooled probe decreases the coagulation effect near the tip of the probe, allowing more even energy penetration into the brain tissue. The tip of the probe also contains a thermocouple to monitor temperature. The laser-delivery probe is positioned by using stereotactic navigation frames and connects to the robotic probe driver.

The workstation is located in the MRI control room. The surgeon creates a procedure plan using NeuroBlate system software to control a robotic mechanism for laser depth and rotation. This remote manipulation allows repetitive ablations in different positions until the planned thermal dose reaches the desired boundaries. A 3D display provides the opportunity for multiplane assessment and better visualization of thermal therapy zones and surrounding structures.

This system received U.S. Food and Drug Administration (FDA) 510(k) clearance for planning, monitoring under MRI visualization, and use of 1,064-nm lasers to ablate, necrotize, or coagulate soft tissue through interstitial irradiation or thermal therapy in neurosurgery. So far, more than 300 procedures have been performed with this system in the United States and the results have yet to be published (ClinicalTrials.gov NCT02389855). Twelve-month results from 1,000 patients are expected by 2020 (ClinicalTrials.gov NCT02392078).

Visualase system

The Visualase system (Medtronic, plc., Dublin, Ireland) is an integrated, MRI-guided, minimally invasive laser-ablation system. The ablation system comprises a 15-W, 980-nm diode laser, flexible fiber-optic probe, and 17-gauge (1.65-mm diameter) internally cooled catheter.[1] The cooling catheter is connected to a peristaltic roller pump that circulates sterile saline to cool the probe tip and surrounding tissue. The light-diffusing tip of the silica fiber-optic applicator has a 10-mm length and a 0.76-mm outer diameter leading to an elliptical heating volume [Figure 3].

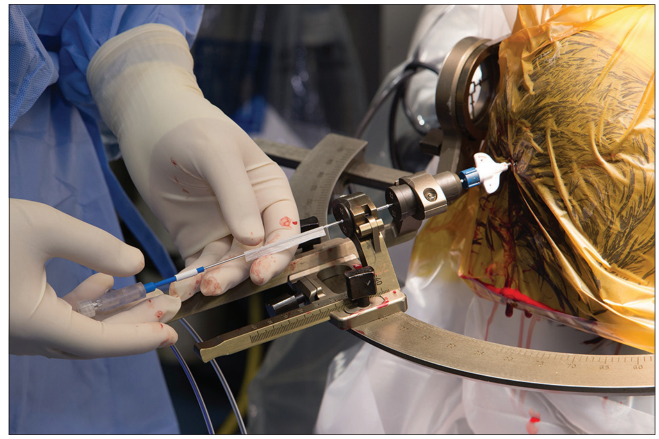

Figure 3: A Visualase laser catheter (Medtronic, plc, Dublin, Ireland) is stereotactically placed through a small bur hole to the required position for an interstitial laser ablation procedure. ***Used with permission from Barrow Neurological Institute, Phoenix, Arizona***

The system is connected to a computer workstation in the MRI unit, which allows the display of real-time thermographic data at the treatment site.[92] Extracted MR thermal imaging data produce color-coded "thermal" and "damage" images, providing feedback to control the extent of thermal therapy [Figure 4].

The neurosurgeon controls the probe position manually inside the MRI and regulates ablation time and intensity on the workstation. The ablation may be intentionally stopped by the surgeon or automatically stopped by the system when the planned ablation has been achieved or when measured temperatures at specifically predetermined voxels exceed the operator-defined threshold. After ablation, the tissue is given time to cool to prevent carbonization and vaporization, and ablation may then be repeated in the same or a different location, producing a sausage-shaped area of damage.

Surgical applications

Lesional epilepsy

MRI-guided laser thermal ablation for epilepsy is emerging as a technique to treat a variety of epileptogenic foci, such as hypothalamic hamartomas, cortical dysplasias, cortical malformations, or the amygdalohippocampal complex. Visualase laser probe positioning by the robotic stereotactic assistant, ROSA (Medtech SA, France), with MR-guided thermal ablation for medically refractory epilepsy, has been successful.[53] Multiple entry-point trajectories and repetitive ablations after pullback of the probe could be performed to shape the ablation area in larger epileptogenic foci.[38] The procedure may be done when the patient is awake, but is usually performed with the patient under general anesthesia. Only one study with a limited number of patients has been reported, which showed good outcomes and a low complication rate.[27] The ablation of the amygdalohippocampal complex was shown to produce curative effects similar to those with open surgical procedures but in a less invasive manner; however, the shortcoming of this study is its small number of patients.[27]

Hypothalamic hamartomas

Hypothalamic hamartomas are a rare type of non-neoplastic lesion located on the floor of the third ventricle. They are more common in children, and patients may present with gelastic seizures, precocious puberty, hormone imbalances, cognitive impairment, behavioral problems, and emotional difficulties. The indications for more invasive treatment options arise because of intolerance to, or ineffectiveness of, conservative therapy, most frequently caused by side effects of antiseizure therapy. Surgical resection

Figure 4: Visualase laser workstation setup in the magnetic resonance imaging (MRI) control room during a procedure. Monitor shows actual MRI thermal map image and predicted zone of damage, automatically calculated based on the temperature and duration of treatment. The laser source is located on the lower rack of the workstation. The blue cord is a laser fiber that transports the laser light to the patient inside the MRI machine. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*

and Gamma Knife (Elekta AB, Stockholm, Sweden) radiotherapy are possible options but carry a high risk of damage to adjacent eloquent brain structures. Therefore, laser ablation is an attractive alternative for such patients. During a single procedure, laser ablation can be stereotactically delivered with high accuracy to the place where the hamartoma attaches to the brain tissue, thus disconnecting the abnormal firing neurons from the normal tissue [Figure 5]. A biopsy can be obtained via the same probe prior to ablation. The main risk of this procedure is hypopituitarism and severe memory deficit caused by damage to the column of the fornix, mammillary body, or mammillothalamic tract. Therefore, when performing ablations, surgeons may leave some abnormal hamartoma connections to spare structures related to memory function. Subsequent ablation with a slightly different trajectory can be performed if the first procedure is not effective. Short-term memory disturbance is usually transient in half of the cases. The effect of treatment may develop within 3 months, usually within the first 2 weeks after the procedure. Additional ablation is usually attempted only after follow-up examination when deemed necessary. Hypothalamic hamartomas are composed of relatively avascular tissue that heats faster than the surrounding normal brain tissue; thus, it may reach the point of permanent damage before surrounding structures. In addition, when ablation is repeated, the energy deposited in the hamartoma is greater. Curry *et al.*[27] reported seizure freedom after LITT in 12 of 14 (86%) hypothalamic hamartoma patients, with a mean follow-up of 9 months, without surgical complications, neurologic deficits, or neuroendocrine disturbances.

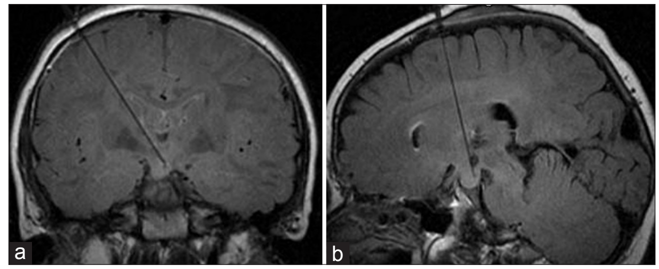

Figure 5: (a) Coronal and (b) oblique sagittal views of intraoperative magnetic resonance images show the laser probe trajectory during interstitial laser treatment of a hypothalamic hamartoma in a pediatric patient. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*

In general, MR-guided laser thermal ablation holds significant promise as a minimally invasive alternative for surgical treatment of brain epileptogenic foci. However, its long-term efficacy is unknown. Evidence is forthcoming as more centers conduct clinical trials of this new technology (e.g., ClinicalTrials.gov NCT01703143) and begin to adopt it.[38]

Brain metastases

Laser treatment has been successfully applied to cerebral metastases. This approach could be applied for lesions less than 3 cm in diameter, even those with elongated shapes, and especially for radioresistant lesions. However, one study was terminated due to slow accrual (ClinicalTrials.gov NCT00720837). Initially, tumor volume increases after the procedure, but over time, tumor volume decreases and may progress to complete absence in most cases.[17] Carpentier *et al.*[17] demonstrated no recurrences within thermal ablation zones 30 months after laser thermal treatment in 7 patients with 15 metastatic brain tumors. Although small case series have demonstrated good control, 2 cases of recurrences after LITT have been reported: metastatic lung adenocarcinoma 11 months after LITT and metastatic breast adenocarcinoma 6 months after LITT.[41] Larger studies with different histological tumor types are required to determine the types of tumors and the subpopulation of patients who could benefit from laser thermal ablation. Simultaneous photodynamic therapy with interstitial MRI-guided thermal ablation is a potentially beneficial concept but little clinical data have been reported.[70]

Ependymomas

Ependymomas are a relatively radiosensitive but chemoresistant type of brain tumor, which usually progresses if complete resection of the tumor cannot be accomplished. The standard management approach for ependymomas is surgery followed by radiotherapy, depending on tumor grade.[103] Patel *et al.*[108] presented their initial experience of MRI-guided LITT for recurrent intracranial ependymomas in 9 ablations for 5 tumors. They reported the possibility of long-term control for these tumors; however, radical ablation is paramount because an incompletely ablated ependymoma will inevitably recur.

Another potential limitation of LITT in intraventricular or paraventricular lesions is the presence of cerebrospinal fluid neighboring the ablation site, which likely acts as a heat sink preventing the spread of thermal energy.[108] One study concluded that new thermal-damage estimate software based on MR-thermal imaging may increase the efficacy of LITT for recurrent ependymomas.[108]

Gliomas

MRI-guided LITT may be implemented in patients with glioblastoma multiforme (GBM) who would otherwise undergo biopsy only.[33] Indications include deep-seated or difficult-to-access lesions, elderly age, and comorbidities that preclude open surgical procedures because of potentially high risks of morbidity and mortality.[59] Such a minimally invasive procedure provides cytoreduction, disrupting the blood–brain barrier in the peritumoral areas and thus fostering drug delivery to the possible remaining tumor cells, which may increase the efficacy of adjunct treatment options.[59,104] LITT may be delivered after treatment with other minimally invasive options, such as Gamma Knife or CyberKnife (Accuray, Inc., Sunnyvale, California), or it can preserve such options for use as future treatments. Moreover, thermal cytoreduction allows minimal subsequent radiation doses to be used. Thus, LITT is used to increase treatment options for patients with GBM in whom maximal treatment modalities are applicable. Limited evidence regarding the survival benefit after LITT for GBM patients warrants future clinical studies.

In a Phase I trial, adult patients with recurrent or progressive GBM in whom standard therapy (radiotherapy with or without chemotherapy) failed were candidates for NeuroBlate MRI-guided LITT and were followed for a minimum of 6 months or until death.[131] Although this study was not designed to investigate efficacy but rather to show safety, it gives hope for better outcomes as patients received actual treatment instead of only a biopsy. The study confirmed the safety of LITT for patients with recurrent GBMs in whom safe, conventional surgery is impractical or impossible.[131] Posttreatment edema was observed in all patients on 48-hour postprocedure MRI and was successfully managed with corticosteroids.

Carpentier *et al*.[16] performed LITT as a salvage procedure for 4 patients with recurrent glioblastoma and found no significant differences in survival compared with previously reported cases in the literature. They concluded that GBM recurrence may not be the optimal indication for LITT.[65] Nevertheless, LITT may be useful in two other situations involving gliomas: newly diagnosed, deep-seated, high-grade gliomas <30 mm in diameter, and deep-seated, low-grade gliomas <30 mm in diameter with well-defined boundaries. A prospective study with 10-year follow-up was launched in 2015 to assess morbidity and efficacy of LITT for pediatric brain tumors (ClinicalTrials.gov NCT02451215).

Another possible use of MRI-guided LITT is disruption of the peritumoral blood–brain barrier to enhance drug delivery and efficacy for treatment of pediatric brain tumors. This use is under investigation in a phase 0 trial (ClinicalTrials.gov NCT02372409). Phase 1 and 2 trials to investigate a synergetic effect with MK-3475, a molecule that was designed to restore the natural ability of the immune system to recognize and target cancer cells, are also underway (ClinicalTrials.gov NCT02311582). Results of a pilot study of LITT and doxorubicin hydrochloride in treating patients with recurrent glioblastoma are also awaited (ClinicalTrials.gov NCT01851733).

Radiation necrosis

Radiation necrosis develops months to years after intracranial radiotherapy and is difficult to distinguish from tumor recurrence on standard MRI.[20] Patients with radiation necrosis can present with an increased rim of enhancement and brain edema on MR imaging, headache, nausea, and somnolence. Biopsy and resection can be considered for symptomatic steroid-refractory radiation necrosis or when the diagnosis is unclear. Several case reports have shown that LITT may be an effective treatment option for radiation necrosis.[40,113,114] The trial "Laser Ablation After Stereotactic Radiosurgery" was completed in 2016 but study reports are not yet available (ClinicalTrials.gov NCT01651078). Only case reports [40,113] and limited case series[114,142] of cerebral edema resolution in postradiosurgery metastasis after LITT are currently available in support of LITT for radiation necrosis.

Safety and limitations of LITT

Specific risks of LITT include damage to the cerebral vasculature by the laser probe, which could result in hemorrhage or pseudoaneurysm that may require subsequent open or endovascular surgery. Although MR thermometry allows precise control of the ablated tissue, the risk of damage to the critical cortex areas and white matter tracts by the probe or thermal energy remains.[131] Delayed transitory neurologic deficits due to increasing brain edema usually resolve after steroid therapy. Other potential limitations of LITT include the necessity of training in stereotactic surgery, which requires the availability of special equipment and established logistics with an MR scanner. Despite its minimally invasive nature, this technology takes a relatively long time in clinical practice and requires costly equipment.

Nonspecific adverse effects include balance disorder, dizziness, and headache. Brain abscess, seizures, and wound infection have also been reported after LITT.[131] Risks and contraindications for MRI are also applicable to

LITT. The exact rates of various complications have not yet been defined for LITT. Overall, nonspecific risks, such as surgical site infections, bleeding, and anesthesia-related risks in LITT, are thought to be lower than those in open craniotomy, which allows neurosurgeons to balance the potential benefits of surgical treatment with the risks of surgery in patients with comorbidities.

LASER PHOTODYNAMIC THERAPY FOR BRAIN TUMORS

Laser photodynamic therapy (PDT) uses a photosensitizer that accumulates in the tumor. After illumination with a light source at the photosensitizer's absorption wavelength, the photosensitizer excites to a singlet state of higher energy. The relaxation from an excited state to a ground state after emission of a fluorescent photon generates singlet oxygen, which leads to mitochondrial and nuclear DNA damage and cell death.[141] Effects are also caused by vascular damage and an immune reaction, which might be important factors for long-term tumor control.[19]

Various compounds such as porphyrin, m-tetrahydroxyphenylchlorin (temoporfin), 5-aminolevulinic acid (5-ALA), boronated porphyrin, and talaporfin sodium have been used as photosensitizers administered orally, intravenously, or locally in clinical and *in-vitro* trials for gliomas.[141] Each sensitizer has a unique absorption wavelength and emission wavelength that influence the rate of energy deposition and penetration depth.

A principal requirement for efficacious PDT of brain tumors is to achieve adequate light illumination throughout the targeted tissue volume.[112] Recently, light-emitting diodes (LEDs)[126,127] have gained favor over argon and xenon arc light sources for PDT due to their higher power and narrower spectral characteristics.[112] Another important parameter is clearness and lack of bleeding on the ablated brain surface, which could significantly affect penetration and energy absorption rate.[135]

Several strategies have been proposed for even dispersion of the light. Standard approved PDT uses cylindrical diffusing fiber tips stereotactically placed for interstitial irradiation,[112] light-emitting sources positioned in the resection cavities,[111] or emitters placed in a balloon with a photodistributor solution positioned in the resection cavity.[101]

In glioma surgery, several PDT approaches have been used:[112] photofrin plus intracavitary PDT;[116,127,136] 5-ALA fluorescence guided resection plus PDT;[7] temoporfin fluorescence-guided resection and intracavitary PDT;[78] 5-ALA-guided resection plus PDT;[141] talaporfin plus optically guided cavitary spot light application;[2,102] and 5-ALA fluorescence-guided resection plus repeated postoperative photofrin PDT.[34,35] The last two approaches showed the most promise, with results better than those for control groups, but it still did not provide longer survival compared to that of historical controls. Dose-dependent death of meningioma cells under 5-ALA PDT was also recently demonstrated.[32]

Safety

Side effects of PDT are usually related to the sensitization of the skin to light and brain edema. Other adverse events are solely related to the surgical procedure. Laser-related potential risks include brain edema, hyperthermia injury, hemorrhages, and thrombus formation.[2,121]

LASERS IN SPINAL NEUROSURGERY

Percutaneous laser disk decompression

Degeneration of intervertebral disks and disk herniation are common causes of low-back pain and sciatica, affecting more than 80% of the population.[64] The application of lasers for treatment of intervertebral disk pathologies was first introduced in the 1980s by Choy *et al*.[25] Percutaneous laser disk decompression (PLDD) is a minimally invasive procedure usually performed in an outpatient setting with the patient under local anesthesia. Briefly, with the patient in a prone or lateral decubitus position, under the guidance of C-arm fluoroscopy, an 18-gauge 7-inch needle is inserted through the Kambin triangular safe entry zone (anterior to superior articular process and superior to transverse process) to the intervertebral disk. An optic fiber, from which laser energy is transmitted, is then run through the needle. Laser energy evaporates water in the nucleus pulposus, resulting in a decrease in intradiscal pressure. In addition, the heat generated by the laser causes denaturation of pain-promoting cytokines and desensitization of intradiscal nociceptors, relaxation of local macromolecular tensions, and potential creation of microchannels for nutrient transport.[13,14] Lasers have been reported with wavelengths varying from 514-nm potassium titanyl phosphate (KTP) to 10,200-nm (CO_2), of different power and pulse duration and pulse intervals, with total delivered energy ranging from 572 to 4000 J [Figure 6].[124] KTP, Nd: YAG, holmium (Ho):YAG, and diode lasers have been used to treat degenerative disks.[22,47,75] Studies investigating the efficacy of PLDD have reported a success rate of 70–89% in cases of radicular pain[23,46] and a low rate of overall complications.[60] Overall, this technique is currently viewed as controversial because of the lack of randomized clinical trials and the limited level of current evidence regarding its efficacy compared to that of more conventional therapies.[12,130]

Indications

Laser diskectomy has been shown to be beneficial in patients suffering from a single-level disk herniation with associated radicular pain refractory to conservative treatment. Optimal candidates are patients with limited bulging of the disk herniation.

Figure 6: The diode surgical laser Alod-01 (wavelength 810-1064 nm, power 1-30 W) used for percutaneous laser intervertebral disc surgery. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*

Contraindications include previous surgery at the same disk level, spinal stenosis, disk fragmentation, and migration with significant neurological deficits due to herniation. However, Choy *et al*.[24] reported that PLDD provides positive results in select cases of recurrent disk herniation.[91]

Currently used lasers

Nd:YAG laser

In the mid-1980s, Choy *et al*.[24,25] used an Nd: YAG laser to perform PLDD. After the fluoroscopically guided probe was positioned, 1,000–1,850 J of energy was delivered into the disk in continuous 1-second 20-W pulses and 1-second pauses, causing ablation of tissue within the nucleus of the disk. The vaporized products (water and carbon particles) escaped via the spinal needle. Currently, a 1.06 Nd: YAG laser has been approved by the FDA for PLDD.

KTP laser

Early findings by Davis *et al*.[28] suggested that KTP lasers for diskectomy were just as effective as Nd:YAG lasers. At present, KTP lasers are designed to deliver 1,250 J of energy. KTP has been found to be safe and beneficial, and it was also approved by the FDA for PLDD. Manufacturers have since improved this technique by developing side-firing probes that allow laser energy to be localized to specific areas, reducing the risk of injury to surrounding structures.

Ho:YAG laser

A Ho:YAG laser has mid-infrared wavelengths and is used in a pulsed mode to ablate the nucleus of the disk. The laser produces 1.6 J of energy per pulse with a pulse width of 250 microseconds at 10 Hz. Treating the disk with a pulsed laser, in comparison to continuous exposure, is assumed to provide no temperature rise in adjacent tissue, thus minimizing any harmful effects to normal tissue. The Ho:YAG laser is considered to be safe and effective, and it is FDA approved.

Safety

PLDD is considered a low-risk treatment option. The major potential complications associated with PLDD are nerve root injury from needle insertion or laser heat, or infectious spondylodiskitis attributed to nonsterile technique. Choy *et al*.[23] described a 0.4% complication rate, with the only complication being diskitis post PLDD. The long-term (5-year) success of PLDD in select patients was reported to be approximately 70% in a retrospective study.[93] Although PLDD is a relatively low-risk procedure, it should not be performed by specialists who are not trained in spinal surgery.[36]

Epiduroscopic laser neural decompression

Epiduroscopic laser neural decompression (ELND) is a new method for diagnosing and treating herniated disks, spinal stenosis, failed back surgery syndrome, and chronic refractory low-back pain. The technology utilizes an epiduroscope inserted in the sacral hiatus and passed into the epidural space with the patient under local anesthesia. The procedure is performed under fluoroscopic guidance through a Tuohy needle and the epiduroscope itself is approximately 3 mm in diameter (4007 Epiduroscopy Introducer Set, Myelotec, Roswell, Georgia, USA) and has dual working channels.[69] A laser fiber can be inserted through the working channel to directly cut fibrous bands or ablate protruded disk.[68] In a recent study, 85% of patients receiving ELND for chronic low-back or radicular pain were satisfied with the treatment.[67] On the basis of the limited amount of literature currently available, ELND may become a new treatment alternative for patients with an anatomically suitable spinal canal who have chronic radicular or back pain attributed to disk herniation or spinal stenosis, and for whom conventional therapies have failed. So far, epiduroscopy even without laser is a rare procedure; therefore, indications for ELND, risks of complications, and its place in spinal surgery are yet to be established.[68]

LASER TISSUE SOLDERING FOR DURAL RECONSTRUCTION

Dural repair is a basic requirement for most neurosurgical procedures. Conventionally, dural reconstruction is achieved with sutures and fibrin glue. The laser tissue-soldering technique is a new alternative for dural reconstruction. The technique involves applying a soldering material (e.g. albumin) to the edges of the dura and binding the tissue using laser energy. The heat generated from the laser creates a bond between the soldering material and the dura. Results from studies comparing the efficacy of laser soldering with traditional dural closure are inconsistent. One of the earlier studies using a diode laser to repair dural lacerations in rat models reported desiccation of brain tissue.[45] Another study using a diode laser for tissue soldering to repair the dura in canine brainstems found postoperative leakage of cerebrospinal fluid.[57] However, recent studies using CO_2 lasers were more successful. In a porcine model, dural reconstructions using CO_2 lasers were significantly stronger than those performed with the suture technique.[44] Dural reconstruction by CO_2 laser soldering showed higher fibroblast cell density upon postoperative histological review than with conventional suture repair.[151] Although clinical trials for this technique have not been performed, recent preclinical studies are promising. Laser tissue-soldering could potentially benefit skull base approaches, accidental dural tears in spinal surgery, or other situations that require a watertight dural closure, which is difficult to achieve with traditional suturing. The cost of the laser tissue-soldering procedure should be low enough to compete with the cost of existing dural sealants.

THERAPEUTIC APPLICATIONS OF LASERS IN NEUROSURGERY

Nerve regeneration

Mester *et al*. were among the first to document the medical application of lasers by reporting in 1968 the ability of a helium-neon laser to increase hair growth[96] and by reporting in 1971 its ability to stimulate wound healing.[95] Since those early applications, several studies have shown low-level laser therapy to be efficacious for promoting peripheral nerve regeneration.

Rochkind *et al*.[115] demonstrated in rat models that peripheral nerves treated by 200-mW 780-nm laser therapy displayed an increase in myelinated axons.[99] Several other randomized controlled studies have also shown positive effects on peripheral nerve regeneration.[50,99] However, the optimal wavelength by which peripheral nerves should be treated for full recovery remains inconclusive. Barbosa *et al*.[5] found that rats treated with a gallium-aluminum-arsenide (GaAlAs) laser at 660 nm (30 mW, 10 J/cm^2) for regeneration of the sciatic nerve after a crush injury showed the most recovery. Other studies on sciatic nerve crush injuries in rats suggested continuous 808 nm (416 mW with energy density of 29 J/cm^2[49] or 170 mW with energy density of either 3 J/cm^2 or 8 J/cm^2[150]) and pulsatile 905 nm (28 W, 200 ns, 10 kHz, 40 J/cm^2[92]) irradiation generated by a GaAlAs laser was most effective.[49,150] Histological studies have also shown an increase in levels of the growth-associated protein 43 in injured peripheral nerves after laser therapy.[150] Phototherapy has been shown to promote Schwann cell proliferation *in vitro*,[54,88] but the exact mechanism by which nerve cell regeneration is stimulated by lasers is still not well understood. Laser treatment appears to be a promising application for nerve regeneration therapy, but clinical studies are required to better assess its therapeutic potential.

Transcranial laser therapy

Transcranial laser therapy (TLT) involves passing near-infrared light through the scalp and skull, with a small percentage reaching the cortex. Studies showed that TLT modulates brain function in a neurotherapeutic manner.[58] The primary biochemical mechanism underlying the potential beneficial effects of TLT is thought to involve increased mitochondrial activity mediated through photoenergy absorption by cytochrome oxidase.[153] Mitochondria upregulate cellular respiration in response to transcranial laser therapy.[55] In addition, TLT causes photodissociation of nitric oxide from intracellular stores,[86] increases production of proteins,[6] and modulates enzymatic activity.[87] These biochemical consequences of TLT are thought to collectively promote neuronal survival by promoting cerebral perfusion and fueling adenosine triphosphate–dependent transporters, which provide neuronal stability.[84,144] Initial studies on rat models that assessed TLT for treatment of acute stroke showed improved recovery and an increased number of newly formed neuronal cells at 3 weeks when treatment occurred 24 hours post stroke.[82,105,157] In 2007, a small randomized controlled trial, entitled the NeuroThera Effectiveness and Safety Trial (NEST-1), evaluated the efficacy and safety of TLT in humans treated within 24 hours of stroke onset. The study used the NeuroThera Laser System (ProThera, Inc. [now defunct]), which transmitted energy at a wavelength of 808 nm and penetrated the brain approximately 2 cm in depth. The results showed a strong 90-day functional benefit in patients treated with TLT, which prompted two more clinical trials (NEST-2 and -3).[83] However, both failed to show statistical significance in terms of efficacy, and the NEST-3 trial was halted for futility, as researchers concluded that TLT did not have a measurable neuroprotective effect in acute ischemic stroke within 24 hours after onset.[56]

TLT treatment of traumatic brain injuries has also been suggested. Oron *et al*.[106] conducted studies on animal models that suggested that TLT has long-term neurological benefits on traumatic brain injuries. Further studies conducted by other groups also found similar beneficial outcomes within animal models.[100,154] Although initial animal data are intriguing, TLT for traumatic brain injury is viewed with caution because of the previous failures in the NEST trials.

TLT for neurodegenerative diseases is a relatively new area of research. TLT has been shown to upregulate brain-derived neurotrophic factor expression and decrease cell loss in a transgenic mouse model for Alzheimer's disease.[94] Initial studies also suggest beneficial effects in other neurodegenerative diseases such as amyotrophic lateral sclerosis[98] and Parkinson's disease.[77,143] On the basis of the supporting literature, the minimally invasive and beneficial properties of TLT merit further investigation before consideration of its possible integration into clinical practice.

The discovery of LEDs as another source for light therapy comparable to laser therapy has further challenged the value of lasers in medical therapy. LEDs are remarkably cheaper than lasers and create a light with broader output peaks (less monochromatic); thus, a comparison of irradiation sources for therapy continues.

DIAGNOSTIC APPLICATIONS OF LASERS IN NEUROSURGERY

Neurosurgical laser-based endomicroscopy

Laser-scanning confocal microscopy (LSCM) has gained popularity in basic science research and has been applied intraoperatively for neurosurgery.[37,42,89] In LSCM, the specimen is irradiated in a point-by-point manner both in depth and at the surface in contrast to the conventional microscope. In this manner, at any moment only a small portion of the specimen is illuminated, whereas other lights from other locations on the specimen are rejected with the aid of a pinhole, which results in images with higher resolution. LSCM provides high-resolution images with depth selectivity that allows for 3D cellular and subcellular visualization *in vivo*. One cost of this imaging technique is that the point must be illuminated for a longer duration or with a high-intensity light. This technique has been used primarily with zirconium arc lamps or lasers.[129]

The attachment of LSCM to endoscopes created laser-scanning confocal endomicroscopy (LSCE), which has a wide range of imaging applications in the medical sciences.[52,72] LSCE provides enhanced visualization of neoplasm margins within the brain.[43,91,123,125] Sankar *et al*.[123] and Martirosyan *et al*.[91] used a variety of fluorophores, including fluorescein sodium, 5-ALA, and indocyanine green with handheld LSCE and showed that histological information about normal and cancerous cells can possibly be obtained from the brain *in vivo* [Figure 7]. Intraoperative clinical use of LSCM with fluorescein sodium as a contrast medium for a variety of brain tumors showed initially good diagnostic results comparable to those of frozen section biopsies.[90] The application of exogenous fluorescent dyes available for neurosurgical use with LSCE provides enhanced morphological details.[156] By using confocal microscopy and sulforhodamine 101 (SR101), Georges *et al*.[48] showed that SR101-labeled astrocytoma cells have different morphological features than astrocytes and suggested that this method can be used to enhance visualization of tumor margins. Another wide-field laser fluorescence imaging technology, a scanning fiber endoscope, is being actively studied.[62,128] Although it lacks histology-like image resolution, patients undergoing surgery might benefit from interrogation of the large tissue areas visible with this tool. The continued development of laser imaging technology in neurosurgery may provide surgeons with better *in-vivo* imaging and thus may improve identification and resection of pathological tissue.[8]

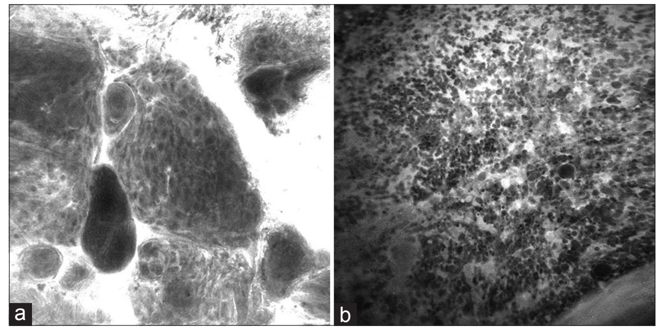

Figure 7: Images acquired by an OptiScan (OptiScan Pty. Ltd., Victoria, Australia) intraoperative confocal laser microscope with a 488-nm wavelength from brain tumor specimens treated with a fluorescein sodium dye show the clear differentiation of the cell pattern of (a) meningioma (psammoma bodies and whorling pattern) and (b) glioblastoma (multiple irregular cells with areas of necrosis). ***Used with permission from Barrow Neurological Institute, Phoenix, Arizona***

Current systems

OptiScan

The OptiScan system (OptiScan Pty. Ltd., Victoria, Australia, and Carl Zeiss Surgical GmbH, Oberkochen, Germany) is an endoscope-integrated system in which a miniaturized confocal microscope has been placed at the distal end of a conventional endoscope. The miniaturized confocal microscope is connected to optical and personal computer units, and it uses a distal scanner with a single optical fiber. The laser emits a wavelength of 488 nm for excitation with a maximum power of 1 mW.[37,122] The emitted fluorescence after excitation is collected using the same fiber to generate the image. An experimental but not yet commercialized system developed by OptiScan that is based on a near-infrared spectrum laser confocal endomicroscopy system has successfully used indocyanine green to identify glioma cells *in vivo*.[94]

Cellvizio

The Cellvizio LSCE (Mauna Kea Technologies, SA, Paris, France) is a compact maneuverable endomicroscopy system that permits multiple miniprobes to be inserted into the endoscope.[63] Miniprobes can differ by field of view, resolution capacity, and other technical parameters, for specific clinical circumstances. Similar to the OptiScan, it performs laser transduction (488–600 nm) and collection of emitted fluorescence using the same optic fiber. A 4-Hz oscillating mirror and a galvanometric mirror are used for horizontal and frame scanning, respectively, resulting in real-time imaging with a frame rate of 12 Hz.[81]

Raman spectroscopy

Raman spectroscopy is a method of spectroscopic analysis that involves laser light interaction with molecular vibrations, phonons, or other excitations. Krafft *et al*.[79] were able to distinguish between tumor and normal human brain tissue by using near-infrared Raman spectroscopy. Koljenovic *et al*.[76] applied Raman spectroscopy *in vivo* to develop a guidance method for meningioma resections. They compared the Raman spectra of meningioma and dural sections with histopathology results and produced 100% accuracy for the classifier model. A subsequent study for exploring the biochemical differences between necrosis and viable tissue had 100% accuracy on 9 test patients. In a recent study, a handheld contact Raman spectroscopy probe that was developed for *in-vivo* local detection of cancer cells in the human brain had 93% sensitivity and 91% specificity.[66] These results suggest that Raman spectroscopy has great potential for making enhancements in diagnosis and during tumor resection.

Intraoperative cerebral blood flow measurement

The capacity to assess cortical cerebral blood flow (CBF) has clinical value in neurosurgery. Three main blood flow assessment techniques, laser Doppler flowmetry (LDF), laser Doppler imaging (LDI), and laser speckle imaging (LSI) all use lasers as a source of coherent light.

LDF involves illuminating a tissue sample with a single-frequency light and measuring the frequency of backscattered light to estimate blood perfusion. This technique relies on the principle that light particles undergo a frequency or wavelength change (Doppler effect) after encountering moving red blood cells that can be detected by a sensor. A 5-mW laser diode is used in LDF with an emission wavelength of 780 nm.[65] This technique has been used for monitoring capillary blood flow in brain tissue drug treatment[74] and in clinical procedures as a potential intracerebral guide to differentiate between white and gray matter.[152] It was also used to measure blood flow in the skin after sympathectomy.[26]

LDI uses the same theoretical framework as LDF but it provides spatially resolved CBF images by measuring the change in frequency of backscattered light at multiple points.[3,85] LDI has been shown to be an effective imaging technique for a wide variety of disorders,[39] of blood flow reduction in smokers,[109] of altered vasodilation in diabetics,[73] and of altered brain perfusion in Alzheimer's patients.[4,107] Limitations of these two methods are that LDI does not provide real-time CBF information whereas LDF measures blood flow only at a single point.[11]

LSI generates CBF information from interference patterns produced by coherent light scattering due to moving red blood cells. Real-time CBF mapping is generated from a time-varying speckle pattern that is dependent on flow speed.[11,30] Recent studies have shown LSI to have superior temporal resolution with real-time visualization than that of the more conventional LDI and LDF.[30] A moorFLPI laser speckle contrast imager (Moor Instruments, GmbH, Cologne, Germany) was used that has a laser wavelength of 785 nm and power of 50 mW. Clinical applications of this technique have been studied for blood flow in skin, retina, and other tissues.[11,118,155]

CONCLUSION

Despite early skepticism by the medical community, the application of lasers in the neurosciences, in particular, shows promising results and merits further investigation. The multitude of ways that lasers are being used in neurosurgery and in related neuroclinical situations is a testament to the technological advancements and practicality of laser science.

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Conflicts of interest

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