Laser-Induced Thermal Therapy in Neuro-Oncology: A Review

Omar Ashraf, Nitesh V. Patel, Simon Hanft, Shabbar F. Danish

Key words
- Ablation
- Lasers
- Laser therapy for brain tumors
- Magnetic resonance-guided laser-induced thermal therapy

Abbreviations and Acronyms
BBB: Blood—brain barrier
GBM: Glioblastoma multiforme
LITT: Laser-induced thermal therapy
MRI: Magnetic resonance imaging
SRS: Stereotactic radiosurgery
WBRT: Whole brain radiation therapy

Division of Neurosurgery, Rutgers University, Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA

To whom correspondence should be addressed:
Shabbar F. Danish, M.D.
[E-mail: shabbar.danish@rutgers.edu]

Citation: World Neurosurg. (2018) 112:166-177.
https://doi.org/10.1016/j.wneu.2018.01.123

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

■ OBJECTIVES: **Laser therapy has become an appealing treatment modality in neurosurgery. In this review, we report on the history, physics, surgical steps, indications and uses, and complications that have been reported to date.**

■ METHODS: **An extensive literature search was performed for laser interstitial thermal therapy (LITT) and laser therapy in the context of glial tumors, metastatic lesions, pediatric brain tumors, and radiation necrosis. Reported complications in each series also were reviewed.**

■ RESULTS: **In the past decade, multiple studies have demonstrated the use, outcomes, and complications associated with LITT in neurosurgery. These same studies have consistently reported an overall benefit of LITT in cases in which traditional surgical approaches may be limited by the patient's clinical status, tumor location, or overall prognosis. However, there have been complications reported from local effects of thermal damage, technical error, and edema development. Increased experience has reduced complications and brought more promising results.**

■ CONCLUSIONS: **With the advent of real-time monitoring and damage estimation, LITT has gained ground in the management of intracranial tumors. Larger scale trials must be performed to develop standard protocols to define specific indications for use. Further large clinical studies for LITT in non-oncologic cases are also of interest.**

INTRODUCTION

Laser-induced thermal therapy (LITT) is a novel and minimally invasive procedure that has revolutionized the use of lasers in the treatment of various intracranial pathologies. Previously, limitations on the control of thermal damage to the tissue prevented the widespread application of this therapy. Recent advances in technology have allowed the integration of LITT and magnetic resonance imaging (MRI), giving surgeons the ability to operate on lesions located in deep parts of the brain with accurate estimates of thermal damage.[1,2]

The use of LITT in treating brain tumors dates back to the 1990s.[3,4] Although it is not currently a first-line option for treating intracranial tumors, LITT has been shown to treat many tumor-specific pathologies such as gliomas, recurrent metastases, radiation necrosis, and pediatric brain tumors.[5-12] LITT has proved useful for cases in which tumors are in difficult to access locations, patients are greater risk surgical candidates, or in cases involving multiple recurrences and repeat resections. In this review, the authors aim to present an overview of the technology as well as indications, uses, known complications, and future directions of LITT, specifically in the treatment of brain tumors.

HISTORICAL PERSPECTIVES

Laser use in neurosurgery has a deep history that spans more than 50 years. In 1966, ruby lasers were used to treat malignant gliomas,[13,14] and in 1969, CO_2 lasers were used by surgeons to treat recurrent glioblastoma multiforme (GBM).[15] However, these initial lasers were limited in their use; the large size and bulk of the laser delivery systems made them impractical for the treatment of tumors located deep in the tissue.[13]

The use of LITT can be traced back to the original Nd:YAG laser in 1980.[16] Along with its ability to penetrate deeply into neuronal tissue with a flexible fiberoptic cable, the Nd:YAG laser gave surgeons the power to promote hemostasis and coagulation, an inherent advantage over other surgical lasers used at the time.[13,17] In conjunction with new techniques integrating LITT and imaging methods such as magnetic resonance thermography, surgeons gained the ability to plan laser trajectories for optimal laser placement as well as assess thermal damage in real-time.[1,18] This ushered in a new age for laser use in neurosurgical procedures.

LITT TECHNOLOGY

Lasers are a form of nonionizing radiation that produce a coherent and collimated beam of light energy.[19,20] The effectiveness of a laser on tissue can be determined by 2 principles: absorption and scatter (**Figure 1**). Absorption occurs when the laser energy is converted to heat after its photons hit molecules in the target tissue called chromophores. The energy transfer to chromophores results in the release of heat, allowing photothermal heating to take place, which directly damages adjacent cells and structures.[20] Scatter takes place when the trajectory of the photon is deviated by its interaction with particles in the tissue, resulting in an increased spatial distribution of light.[20] To promote selective photothermolysis of tissue, a wavelength must be chosen in which photon scatter and absorption optimize tissue heating and penetration of light.[19-21] Several properties of tissue, such as perfusion, conductivity, specific heat, and density, are also critical components of how laser light may affect tissue ablation.[19,22]

In LITT, laser light is transmitted from the generator to the patient's tissue through the use of optical fibers. The optical fibers may exceed 10 m as they must reach from the laser source located outside of the MRI suite to the patient in the scanner.[19,23] Laser light is introduced into the patient through a diffusing tip that is approximately 1 cm in length.[23] Diffusing tips vary by manufacturer, and the 2 most commonly used LITT systems include the NeuroBlate system (Monteris Medical, Minneapolis, Minnesota, USA) and the Visualase Thermal Therapy System (Medtronic Inc., Minneapolis, Minnesota, USA). Diffusing tips radiate light in a cylindrical to ellipsoid distribution along the axis of the tip.[24,25] The NeuroBlate system has a directional-firing option that allows surgeons to conform to the complex shape of certain tumors with asymmetrical light distribution.[11,26] In addition, the Visualase system features a 15W, 980-nm diode laser, whereas the NeuroBlate system uses a 12W, 1064-nm Nd:YAG laser.[27-29] The optical properties of each laser lends itself to a different effect in the water-dominated environment of the brain. Because the absorptive properties of water are greater at 980 nm than at 1064 nm, the Visualase system has the advantage of producing rapid ablation of tissue with sharp boundaries.[30] The lower water absorption at 1064 nm implies a greater degree of photon scatter and ultimately increased tissue penetration.[31]

The optical fibers are housed inside a catheter sheath to ensure proper cooling of the fiber and clean energy dispersal.[23,32] Cooling mechanisms vary between LITT systems: the Visualase system incorporates a polycarbonate catheter, 1.65 mm in diameter, with saline irrigation, whereas the NeuroBlate system uses a sapphire capsule with an internal cooling mechanism using CO_2 gas.[11,31] The NeuroBlate catheters come in both 2.2 mm and 3.3 mm diameters.[31]

The thermal effects on tissue include DNA and protein denaturation, ultimately leading to cell death.[33] Up to 40°C, the cell can maintain homeostasis.[34] Temperatures ranging from 46°C to 60°C induce irreversible damage to cellular structures. In this range, the relationship between temperature and time to cytotoxicity is inversely proportional[35]; an increase in a couple of degrees noticeably decreases the time necessary to induce coagulation in the targeted region.[36] At temperatures greater than 60°C, cells undergo instantaneous protein coagulation, resulting in coagulation necrosis. Therefore, optimal temperature for tissue ablation ranges from 50 to 100°C.[34]

The LITT software allows for automatic deactivation of the laser at certain temperatures set by the surgeon.[25] Patel et al.[37] reported a temperature limit of 50°C at the border of the target area to prevent irreversible damage to adjacent structures, as well as a temperature limit of 90°C at the tip of the laser probe to avoid the production of steam and subsequent unintended tissue damage.

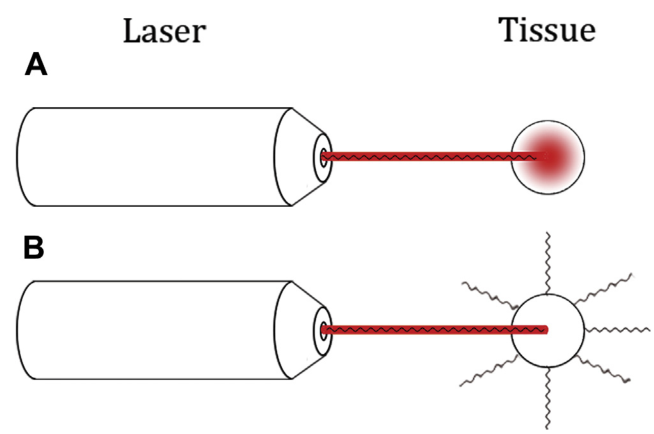

Figure 1. Photon absorption and scatter. The figure depicts the 2 dominating interactions between tissue and laser light: absorption and scatter. (**A**) Photothermal heating takes place at the target region after absorption of the laser light by the tissue. (**B**) Scatter occurs when photons radiate away from the target region after being deviated by particles in the tissue. Source: Franck P, Henderson PW, Rothaus KO. Basics of lasers: history, physics, and clinical applications. *Clin Plast Surg* 2016;43:505-513.[20]

SURGICAL PROCEDURE

To maximize thermal ablation of a target region, care must be taken to ensure precise laser placement. There are small variations in the procedure followed by surgeons because of the different LITT systems, software, and hardware available for use.[19] However, the general steps remain the same: stereotactic registration, catheter placement, thermal ablation, and postprocedural care (**Figure 2**).[19] The following steps detailing the surgical technique for the Visualase system are taken from Patel et al.[19]

Stereotactic registration is an important primary step for determining the appropriate entry point, target, and laser trajectory. The approaches to stereotactic registration include frameless, trajectory guide/platform, and stereotactic frames. Frameless techniques involve the use of anatomic landmarks, gadolinium fiducials, skull-implanted fiducials, and pattern tracing (**Figure 2A**). Frameless approaches give the surgeon the benefit of increased flexibility but the added risk of shifting the fiducials relative to the head, compromising the stereotactic registration. Trajectory guides and platforms are mounted to the skull and allow for instrument guidance as well as a reference for trajectory planning. Stereotactic planning with the use of a frame is one of the more traditionally