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Laser-Induced Thermal Therapy in the Management of Low-Grade Gliomas: A Narrative Review

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Abstract—Background: **Low-grade gliomas (LGGs) are slow-growing, World Health Organization Grade I and II tumors that can transform into more aggressive malignancies over time. This transformation presents significant challenges in managing the burden of health care. Laser-induced thermal therapy (LITT) has emerged as a promising minimally invasive treatment option for LGGs, offering precise tumour ablation with minimal damage to surrounding tissues.**

Method: **This narrative review synthesizes data from relevant studies on the evolution, clinical manifestations, molecular characteristics, and emerging management strategies for LGGs, with a focus on the role of LITT.**

Results: **LITT, a minimally invasive technique, offers targeted tumour ablation with the added benefit of disrupting the blood-brain barrier to enhance drug delivery. Studies have shown that LITT can effectively reduce tumour size and improve survival rates in patients with both primary and recurrent gliomas. However, challenges such as procedure-related complications, including motor deficits and cerebral oedema, as well as the need for further research on long-term efficacy, remain.**

Conclusion: **LITT represents a significant advancement in the treatment of LGGs, combining precision and minimal invasiveness. Future studies should focus on optimizing protocols, integrating molecular and genetic insights, and assessing long-term outcomes to enhance therapeutic efficacy and patient quality of life.**

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***Index Terms*—Blood-Brain Barrier; Glioma; Laser Therapy.**

I. INTRODUCTION

Gliomas are a common type of tumour in the central nervous system (CNS), originating from glial cells [1]. These tumours diffusely infiltrate the surrounding brain tissue. Gliomas are classified into grades I to IV, based on molecular and histopathological markers, among other factors [2]. According to the WHO classification system, low-grade gliomas (LGGs) are benign tumours that fall within the first two grades. Although typically slow-growing, LGGs can transform into malignant grades over decades [3]. Survival rates for LGGs are relatively high compared with other gliomas [1]. The exact cause of gliomas is unknown, but risk factors include environmental and genetic factors, particularly therapeutic radiation [4].

Despite being generally non-threatening and slow-growing, LGGs have a strong tendency to infiltrate surrounding tissues, raising concerns [5]. The disease course varies greatly, leading to differing clinical approaches, with some clinicians favouring surveillance and others proactive surgical resection [6]. Understanding the nature of LGGs is crucial to optimize their management and improve outcomes [6].

The natural history of LGGs is influenced by various factors, including clinical presentation, radiological imaging, genetic characteristics, and treatment timing [5]. These factors contribute to the complexity of LGGs and necessitate individualized treatment plans [5]. The natural history of LGGs can be divided into three phases: an initial silent phase, a symptomatic phase, and a progressive phase [5]. The increased use of MRI has led to more incidental discoveries of LGGs [5]. While early discovery is promising, managing incidentally discovered LGGs remains challenging [5]. A clinical trial by Potts et al. compared the natural surgical history and management of inci-

dental and symptomatic gliomas, finding that patients with incidental LGGs had smaller tumours, a higher likelihood of complete surgical resection, and improved overall survival, though progression rates were similar in both groups [7]. Common symptoms of symptomatic LGGs include seizures, headaches, and vision problems [8].

Treatment for LGGs typically involves surgery, radiation therapy, and chemotherapy, each with its own challenges, such as impacts on brain function and side effects. The National Comprehensive Cancer Network's guidelines recommend surgery as the primary approach, aiming for gross total resection if feasible, otherwise subtotal resection [9]. Pathological assessment of the resected tumour helps determine the glioma type and presence of specific biomarkers, guiding further management [9]. Patients are classified based on their risk of tumour regrowth, with low-risk patients typically undergoing surveillance and high-risk patients receiving adjuvant radiotherapy and chemotherapy [9]. Follow-up is biannual to monitor for recurrence and manage treatment-emergent adverse events (TEAEs) [9].

Achieving maximally safe resection while maintaining neurological function is challenging due to anatomical variations between patients [10]. Radiotherapy toxicity can cause cognitive, visual, and auditory dysfunction, as well as complications such as radiation necrosis, secondary neoplasms, and hypopituitarism [8]. Chemotherapy, while beneficial for some, can cause side effects such as nausea, alopecia, myelosuppression, liver toxicity, and neurotoxicity, limiting patients' quality of life [8]. The invasive nature of the tumour and restricted therapeutic strategies result in high relapse rates and generally poor outcomes [11].

Molecular and genetic data, such as IDH mutation and 1p/19q co-deletion, are important biomarkers that affect tumour behaviour and treatment outcomes. Molecular characteristics can aid in the diagnosis and prognosis of LGGs [8]. IDH mutations are common in gliomas and can sub-classify LGGs [8]. Tumors with IDH mutations and 1p/19q co-deletions are more likely to be oligodendrogliomas, while those with IDH and TP53 mutations but without 1p/19q co-deletion are more likely astrocytomas [8]. IDH-mutated tumours generally have favourable prognoses and are more chemosensitive [8]. Tumours with 1p/19q deletions have improved median survival times [8]. Molecular neuropathology in LGGs continues to be a focus of research, with ongoing exploration of targeted therapies [8,10].

However, despite these advances, there are significant unmet needs in the management of LGGs. Existing therapies often fall short of achieving long-term control and can have substantial side effects [7-9]. This highlights the need for innovative treatments that can provide better outcomes with fewer complications. Laser-induced thermal therapy (LITT) is one such emerging modality. LITT is a minimally invasive technique that uses laser energy to ablate tumour tissue precisely, with the added benefit of disrupting the blood-brain barrier to enhance drug delivery [5,8].

The therapeutic implications of molecular biomarkers, such as IDH mutations and 1p/19q deletions, are crucial in the context of LITT. These biomarkers not only aid in diagnosis and prognosis but also influence the response to therapies, including LITT [10,9]. Understanding these molecular characteristics can help tailor LITT protocols to improve efficacy and patient outcomes.

II. METHODOLOGY

This narrative review aims to provide an in-depth analysis of laser-induced thermal therapy (LITT) in the management of low-grade gliomas (LGGs). The review process involved an extensive search of major academic databases, including PubMed, ScienceDirect, and Scopus, to identify relevant studies published between January 2000 and December 2024. Inclusion criteria encompassed clinical trials, observational studies, and systematic reviews focusing on LITT, its effectiveness, and its role in glioma treatment. Only studies published in peer-reviewed journals and written in English were included. Key search terms included "laser-induced thermal therapy," "low-grade gliomas," "treatment," "laser ablation," and "blood-brain barrier." After the initial

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search, studies were selected based on their relevance to the research question, with a focus on those that discussed LITT's clinical application, technological advancements, and potential to enhance treatment outcomes for LGGs.

The selected articles were analysed for their findings on the efficacy of LITT in comparison with traditional treatment modalities, its safety profile, and any complications or limitations associated with the procedure. Data from these studies were synthesized to highlight the advantages and challenges of using LITT in LGG management.

Laser-induced thermal therapy (LITT) is a minimally invasive surgical technique that uses laser-induced heat to ablate pathological tissue. It was first introduced in the early 2000s and has since gained traction as a treatment option for low-grade gliomas (LGGs), particularly in cases where conventional therapies such as surgery, radiation, or chemotherapy are not viable or have proven ineffective. LITT is performed under MRI guidance, allowing for precise targeting of the tumour while minimizing damage to surrounding brain tissue.

Several studies have highlighted the effectiveness of LITT in treating both primary and recurrent gliomas, with promising results in improving survival rates and reducing tumour size. For instance, a systematic review and meta-analysis by Ivan et al. (2016) reported an overall survival (OS) of 14.2 months for patients with glioblastoma and WHO grade III astrocytoma treated with LITT, with a complication rate of 3.4% [12]. However, for low-grade gliomas specifically, studies have shown more favourable outcomes. A study by Strauss et al. (2024) reported a progressive reduction in tumour volume and a median survival time of 36 months for patients with LGGs treated with LITT [4]. Additionally, LITT has been shown to offer advantages over traditional open craniotomy, particularly in patients with inoperable or deeply seated tumours. LITT's ability to disrupt the blood-brain barrier (BBB) temporarily increases the permeability of therapeutic agents, such as chemotherapy drugs, allowing for more effective drug delivery to the tumour site [13]. This effect has been particularly beneficial in treating gliomas resistant to conventional treatments.

Quality of life and functional outcomes post-LITT have also been positive. A pilot study by Peña Pino et al. (2024) found that patients reported less pain and narcotic use post-LITT compared with craniotomy, with 89% of patients preferring LITT over craniotomy [1]. Another study by Srinivasan et al. (2022) showed that LITT patients had shorter ICU and hospital stays and similar functional outcomes at 180 days post-treatment than those who underwent resection [2].

Despite its advantages, LITT is not without risks. Complications such as motor deficits, aphasia, intracerebral haemorrhage, and cerebral oedema have been reported in a small subset of patients. These complications are often related to the proximity of the tumour to critical brain structures, such as the corticospinal tracts and language centres, highlighting the importance of careful pre-operative planning and real-time imaging during the procedure [14-20]. In a review of the literature, five articles reported complication rates ranging from 3% to 10%, while two articles highlighted the effectiveness of LITT, with survival outcomes ranging from 24 to 36 months for LGGs.

III. DISCUSSION

Laser-induced thermal therapy (LITT) has emerged as a promising technique for managing low-grade gliomas (LGGs), particularly for tumours that are inoperable, recurrent, or located in regions that are difficult to access through traditional surgery. Several studies highlight the advantages of LITT over traditional surgical approaches, primarily due to its minimally invasive nature and precision in targeting tumour tissue while sparing surrounding healthy brain structures. LITT has demonstrated promising results in treating both primary and recurrent gliomas.

Studies have shown that LITT is effective in reducing tumour volume, leading to improved survival outcomes. A systematic review and meta-analysis by Ivan et al. (2016) reported an overall survival (OS)

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of 14.2 months for patients treated with LITT, including those with glioblastomas and WHO Grade III astrocytomas, with a complication rate of only 3.4% [12]. Similar survival outcomes were noted by Muir et al. (2022) for patients with newly diagnosed gliomas treated with LITT [21].

Additionally, LITT has been particularly useful in patients with recurrent gliomas, which have typically exhausted other treatment options such as surgery, chemotherapy, or radiation therapy. LITT has been shown to be an effective alternative in these cases, offering the possibility of repeated treatments without the limitations imposed by traditional surgical interventions. Mohammadi et al. (2019) reported comparable survival rates for patients treated with LITT as upfront therapy for newly diagnosed glioblastomas (nGBM) compared to a matched cohort of biopsy-only patients [22]. Furthermore, the use of LITT allows for a less invasive procedure with shorter recovery times, enabling patients to return sooner to their normal activities.

One of the significant advantages of LITT is its ability to disrupt the blood-brain barrier (BBB), which often limits the effectiveness of conventional chemotherapy in treating gliomas. Recent studies have shown that LITT can temporarily disrupt the BBB, allowing for enhanced drug delivery. For example, Leuthardt et al. (2016) demonstrated that LITT caused a temporary disruption of the peritumoral blood-brain barrier in glioblastoma patients, improving the permeability of chemotherapy agents [23]. This effect is particularly important for gliomas, as the BBB poses a significant challenge to the effective delivery of many therapeutic agents. In a study by Salehi et al. (2020), LITT was shown to increase the permeability of the BBB for up to 30 days following the procedure, which could facilitate better drug delivery for treating gliomas [24]. LITT's ability to enhance drug delivery is an important factor in improving patient outcomes, particularly for tumours resistant to conventional therapies. While LITT is generally considered a safe and effective procedure, it is not without its risks. The most common complications associated with LITT include neurological deficits, intracerebral haemorrhage, and cerebral oedema. Neurological deficits, particularly motor deficits and aphasia, have been reported in studies involving LITT. The incidence of motor deficits ranges from 11.6% to 29.0%, while aphasia occurs in approximately 6.0% to 17.6% of patients [14-20]. These deficits are often transient, but in some cases they can be permanent. The risk of motor deficits is particularly high when tumours are located near the corticospinal tracts (CSTs). Sharma et al. (2016) used diffusion tensor imaging (DTI) to map and delineate the CSTs in 80 patients, finding that the risk of motor deficits was significantly higher when there was overlap between the thermal injury zone and the CST [25].

Intracerebral haemorrhage (ICH) is another potential complication, with an incidence ranging from 2.9% to 14.2% [26, 27-29]. These haemorrhages typically occur during the insertion of the laser fibre or stereotactic biopsy. Pruitt et al. (2017) identified that ICH could occur due to inadequate dural puncture or vascular injury during the procedure [30]. To minimize the risk of ICH, it is essential to use precise pre-operative imaging techniques, such as MRI and CT angiography, to guide the laser probe and avoid blood vessels. Cerebral oedema is a well-recognized complication following LITT, particularly when large tumours are treated. To mitigate this risk, corticosteroids like dexamethasone are often administered before and after the procedure [31]. In cases where oedema becomes severe and refractory, further interventions, such as hemicraniectomy, may be required. Jethwa et al. (2019) emphasized the importance of managing oedema carefully, especially in cases involving large tumours that require substantial ablation volumes [28].

While LITT offers numerous advantages, certain limitations need to be addressed. One major limitation is its effectiveness in treating larger, more irregularly shaped tumours. Larger tumours require the use of multiple catheters, and the risk of complications such as oedema and ICH increases. Spherical

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tumours, by contrast, are easier to treat due to the more predictable distribution of laser energy [32]. Tumours adjacent to cerebrospinal fluid (CSF) spaces or blood vessels pose additional challenges due to thermal energy distortion [33]. Moreover, LITT's role in the management of newly diagnosed glioblastomas is still under investigation. While LITT has shown promise for recurrent gliomas, the existing evidence does not yet support its widespread use as a first-line treatment for newly diagnosed gliomas. A study by Shah et al. (2019) reported that LITT-treated patients had lower progression-free survival (PFS) and OS compared with those undergoing surgical resection, particularly for deeply seated lesions [34]. This suggests that while LITT is a valuable tool, it is not a replacement for traditional surgical resection in many cases.

Future studies should focus on optimizing LITT protocols, refining imaging techniques, and developing more sophisticated laser probes to improve targeting accuracy. Additionally, combining LITT with other therapies, such as immunotherapy, chemotherapy, or gene therapy, could offer new avenues for improving treatment outcomes. For example, LITT's ability to disrupt the BBB may enhance the efficacy of immunotherapies by facilitating the delivery of immune cells or agents to the tumour site [34]. Long-term studies will be essential to assess the durability of LITT's effects, especially in terms of recurrence-free survival and overall survival.

Cost-effectiveness and accessibility are also important considerations for the broader adoption of LITT. A cost-effectiveness analysis by Voigt and Barnett (2016) found that LITT improves survival at a cost that is considered good value compared with traditional surgical options [35]. The minimally invasive nature of the procedure often results in shorter hospital stays and quicker recovery times, which can reduce overall healthcare costs [36]. However, the availability of LITT is currently limited to specialized centres with the necessary equipment and expertise, which may restrict access for some patients. Ongoing clinical trials and technological advancements continue to shape the future of LITT. For instance, real-time thermal mapping and advanced imaging techniques are being developed to enhance the precision and safety of the procedure [37]. Additionally, research into the use of nanotechnologies to improve heat conduction and expand treatment coverage is under way [37]. These innovations hold promise for making LITT a more effective and widely accessible treatment option for patients with LGGs and other brain tumours.

VI. CONCLUSION

Laser-induced thermal therapy (LITT) has proven to be a promising and effective treatment option for low-grade gliomas (LGGs), particularly for tumours that are difficult to access through conventional surgical methods or those that have recurred after previous therapies. The minimally invasive nature of LITT, combined with its ability to precisely target tissue while sparing healthy brain structures, offers significant advantages over traditional surgical approaches.

As LITT technology continues to evolve, further research is needed to optimize its protocols and refine its applications. Combining LITT with other treatment modalities, such as chemotherapy or immunotherapy, could open new avenues for improving outcomes in glioma treatment. Additionally, long-term clinical trials will be crucial in determining the long-term efficacy and safety of LITT in the treatment of LGGs.

In conclusion, while LITT is not a replacement for traditional resection in all cases, it offers a valuable adjunct in the treatment of low-grade gliomas, particularly for patients with tumours inoperable by conventional means or those with recurrent disease. With ongoing advancements in technology and technique, LITT has the potential to significantly improve the prognosis and quality of life for patients with low-grade gliomas.

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