ScienceDirect

Neurochirurgie

Volume 71, Issue 2, March 2025, 101629

Review Article

Synergistic effects of laser interstitial thermal therapy (LITT) and immunotherapy for brain tumor recurrence: A systematic review and meta-analysis

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https://doi.org/10.1016/j.neuchi.2025.101629

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Highlights

- LITT and immunotherapy show promise as a synergistic approach for recurrent brain tumors.
- Combined therapy resulted in a median survival of 12.8 months for treated patients.
- Only 6% of patients experienced adverse events, demonstrating a favorable safety profile.
- LITT may enhance immunotherapy efficacy by boosting the immune response against tumors.

Abstract

Purpose

The confluence of laser interstitial thermal therapy (LITT) with immunotherapeutic approaches represents a promising option for managing recurrent brain lesions. However, the potential synergy between these modalities is still unclear. This meta-analysis examines the literature to elucidate the adverse effects and overall survival associated with this combination in treating recurrent brain metastases and glioblastoma.

Methods

Systematic searches were performed on PubMed, Embase, and Web of Science databases. Inclusion criteria comprised studies investigating the combined utilization of LITT with immunotherapy, among adult patients diagnosed with recurrent brain metastases and recurrent glioblastoma. Our analysis, using a random-effects model, pooled Overall Survival (OS) and Adverse events (AEs) from all the included studies.

Results

We analyzed 162 patients from one RCT and three non-randomized studies. The pooled analysis of all patients revealed a median OS of 12.8 months (95% CI = 8.31–17.31; $p < 0.01$) with the combined treatment of LITT and immunotherapy. Similarly, approximately 6% of patients experienced AEs (95% CI = −0.01–0.11; $p = 0.03$). Subgroup analysis further demonstrated that among patients with recurrent glioma, the combined treatment showed pooled OS of 11 months (95% CI = 7.13–16.62; $p < 0.01$), while AEs were observed in 4% of patients (95% CI = −0.02–0.10; $p = 0.21$).

Conclusion

This meta-analysis showed a potentially comparable safety profile and overall survival to conventional treatment modalities. Further research is warranted to test differences in the incidence of AEs and OS from LITT with immunotherapy versus a control.

Introduction

Recurrent brain cancer, particularly glioblastoma (GBM), remains a devastating diagnosis with a poor prognosis. Despite advancements in standard therapies like surgery, radiation, and chemotherapy, the median survival for recurrent GBM patients is often less than two years [1]. This highlights the urgent need for novel therapeutic strategies to improve treatment outcomes.

Laser interstitial thermal therapy (LITT) has emerged as a promising minimally invasive technique for recurrent brain tumors. LITT utilizes a laser probe inserted directly into the tumor to deliver localized thermal ablation, destroying cancer cells [2]. Immunotherapy, which harnesses the body's immune system to fight cancer, has also shown promise in treating various malignancies [3]. Recent clinical and preclinical studies suggest a potential synergistic effect when combining LITT with immunotherapy for brain tumors [4].

The rationale behind this synergy is multifaceted. LITT can trigger the release of tumor antigens,

which can prime the immune response against cancer cells [5]. Additionally, LITT may enhance the effectiveness of immunotherapies by improving their infiltration into the tumor microenvironment [6]. However, the clinical evidence for the combined use of LITT and immunotherapy in recurrent brain cancer remains limited. Existing studies are often small and lack control groups. Therefore, a comprehensive evaluation of the current evidence is crucial.

This systematic review and meta-analysis investigates the effectiveness and safety of combining LITT with immunotherapy for the treatment of cytoreduction of brain cancer. By evaluating outcomes such as overall survival and treatment-related adverse events, the analysis aims to provide valuable insights into the potential of this novel therapeutic approach and inform future research directions.

Section snippets

Methods

To ensure transparency and completeness, this systematic review was conducted following the 2020 Preferred Reporting Items for Systematic Literature Reviews and Meta-Analyses (PRISMA) guidelines. The review protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO) under the registration ID “CRD42024528064”. …

Study selection and characteristics

As detailed in Fig. 1, the initial search yielded 200 results. After the removal of duplicate records and ineligible studies, 105 remained and were fully reviewed based on inclusion criteria. Of these, a total of 4 studies were included, comprising 162 patients from 1 randomized controlled trial (RCT) [9], and 3 non-randomized cohorts [10], [11]. No gray literature was included. A total of 81 (50%) patients received LITT and Immunotherapy combined, and 81 (50%) received immunotherapy alone. …

Discussion

To the best of our knowledge, this was the first systematic review and meta-analysis to investigate the potential synergy between laser interstitial thermal therapy (LITT) and immunotherapy for intracranial lesions. Our analysis included four studies (one RCT, one prospective cohort study, one prospective open-label nonrandomized study, and one prospective multicenter study) encompassing a total of 162 patients. Our main findings were: (1) combined treatment of LITT and immunotherapy had 12.81 …

Limitations

Our meta-analysis has limitations. Firstly, the incorporation of observational studies may

inherently introduce bias into the analysis. Quality assessments of individual studies revealed variance in study quality. Secondly, a notable number of the incorporated studies failed to account for the potential influence of underlying comorbidities and factors such as tumor location, expressed molecular markers, and specific immunotherapeutic agents used, number of intracranial metastasis, presence of …

Conclusion

In this meta-analysis evaluating the combined approach of LITT and immunotherapy for recurrent brain metastases and brain gliomas, suggests promising overall survival rates and a low occurrence of adverse events. A sub-analysis of patients with recurrent glioblastoma also found comparable survival benefits with minimal adverse events. Further studies are necessary to confirm our findings and future trials should compare the potential synergistic effects of LITT and immunotherapy with both …

CRediT authorship contribution statement

ES conceived and designed the study. MR, AA, and AC collected data. ES, OKS, and PL analyzed and interpreted the data. ES, OKS, ARA, NR, and YPS drafted the manuscript. WF provided a final review. All authors contributed to earlier versions of the manuscript, reviewed, and approved the final manuscript. …

Informed consent

The authors affirm that human research participants provided informed consent for the publication of the images in Figures. …

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript. The authors have no relevant financial or non-financial interests to disclose. …

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request. …

Declaration of competing interest

All authors report no relationships that could be construed as a conflict of interest. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. …

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1 Equal contribution.

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