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Deep Brain Ablation (DBA) Techniques for Central Nervous System Pathologies: A Comprehensive Review

Andrés Fonnegra Caballero[1], Thiago Andrés Navarro Álvarez[2], Jaime Antonio Navarro Álvarez[3], María Sofía González Casagua[4], Ricardo Andrés Novoa Álvarez[5]

1. *https://orcid.org/0000-0003-0453-5646 Medical School, Navarra University Foundation, Neiva, Huila, Colombia*
2. *https://orcid.org/0000-0002-3272-471Medical School, Navarra University Foundation, Neiva, Huila, Colombia Corresponding Author's Email: thiago.navarro@uninavarra.edu.co*
3. *https://orcid.org/0009-0006-0464-7380 Medical School, Navarra University Foundation, Neiva, Huila, Colombia*
4. *María Sofía González Casagua - https://orcid.org/0000-0002-4023-3517 Medical School, Navarra University Foundation, Neiva, Huila, Colombia*
5. *https://orcid.org/0000-0001-9892-3468 Medical School, Navarra University Foundation, Neiva, Huila, Colombia*

Abstract
Goal: The objective of this review is to identify relevant studies on ablative techniques for central nervous system (CNS) pathologies.
Methods: A comprehensive literature search was conducted using electronic databases including PubMed, OVID, Scopus and Web of Science. The systematic selection of articles was performed through peer review using the intelligent research collaboration platform Rayyan.
Results: The selected studies evaluated the use of ablative techniques for the treatment of Central Nervous System Pathologies and 104 studies were included in the review.
Conclusions: Ablation techniques, including catheter ablation and laser therapy, offer promising options for the treatment of CNS pathologies for patients who are not ideal candidates for conventional surgery. Future research should focus on conducting well-designed randomized controlled trials for define standardized treatment protocols that increase survival rates and quality of life.

Keywords: Ablation Techniques, Laser Therapy, Catheter Ablation, Central Nervous System Neoplasms, Brain Neoplams.

Introduction
Laser ablation therapies have emerged as a promising approach for the treatment of intracranial pathologies, utilizing selective thermal intervention in neural tissue to modulate neurological dysfunctions associated with structural and/or functional abnormalities. These interventions are carried out through stereotactic or image-guided neurosurgical techniques, aiming to provide minimally invasive therapeutic alternatives with shorter recovery times and the potential to impact patients' quality of life positively (Ashraf et al., 2018; Hawasli et al., 2013; 2014).

These therapies have been favorably employed primarily and/or complementarily, particularly in neurodegenerative diseases such as Alzheimer's and Parkinson's, neoplasms, refractory pathologies, and hard-to-reach lesions. They have shown significant benefits in terms of precision, effectiveness, preservation of healthy tissue, and minimization of neurocognitive damage, leading to symptomatic improvements and slowing down the progression of the disease (Liu et al., 2014; Avecillas-Chasin et al., 2020).

Therefore, the focus of higher education should include interdisciplinary work with the aim of optimizing the implementation times of ablative therapies in the field of neuroscience, thus facilitating the development of new technologies and promoting quality of life from different perspectives. This approach should also complementarily utilize academic resources and didactic learning strategies (Navarro-Parra & Chiappe, 2024).

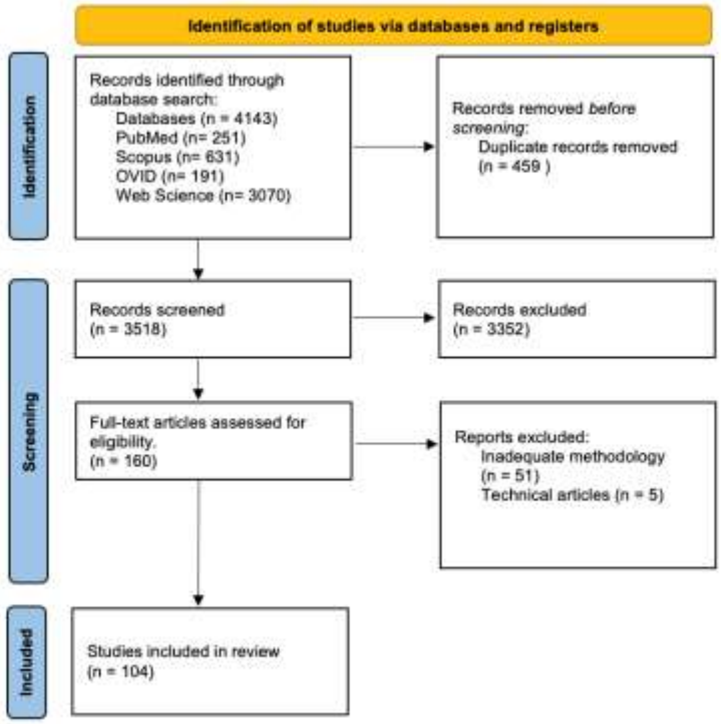
Methods

A comprehensive literature search was conducted using electronic databases, including PubMed, OVID, Scopus and Web of Science. The search strategy incorporated Medical Subject Headings (MeSH) terms and keywords such as "Ablation Techniques" or "Laser Therapy" or "Catheter Ablation" and "Central Nervous System Neoplasms" or "Brain Neoplams". The search was limited to studies published in the last 10 years, adult population and written in English or Spanish. Studies in animals, those not focused specifically on ablative techniques for CNS neoplasms or functional neurological therapies, and those with small sample sizes or insufficient results were excluded. The systematic selection of articles was performed through peer review using the intelligent research collaboration platform Rayyan.

Results

The search yielded a total of 4.143 articles from the selected databases. After screening for relevance and applying the inclusion criteria, 104 studies were included in the review. The selected studies evaluated the use of ablative techniques for the treatment of Central Nervous System Pathologies and reported history, indication and complications. These techniques offer precise tumor destruction through various wavelengths, delivery systems and imaging support to ensure accurate targeting for ablation of CNS lesions. A PRISMA flow diagram showing the number of studies identified can be found in Figure 1.

Figure 1
PRISMA flow diagram



History

Hypothermic therapy for tissue ablation constitutes a novel treatment alternative in the field of neuroscience (Grabowski et al., 2021; Lumenta, 2013). Its use was first described in the 1960s through the implementation of ruby and/or CO2 lasers capable of generating thermal energy through non-ionizing radiation for the recession of malignant tumors through localized cellular damage, protein denaturation, and cell death (Lee et al., 2014; Mahmoudi et al., 2018; Kamath et al., 2017). However, various limitations related to the size and volume of these systems, the precision of the therapy, the limited benefits in deep tissue lesions, and the scant guarantee of quality on clinical outcomes were documented (Ashraf et al., 2018; Bozinov et al., 2020.; Hurwitz M., 2014; Di et al., 2021).

Therefore, essential technological tools were developed in the late 20th century, such as thermographic magnetic resonance and the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, consisting of a flexible optical fiber cable, capable of generating hemostatic and coagulant action without vaporizing tissue above 60ºC, thus achieving broad acceptance in the scientific community, primarily in industrialized countries in Europe and Asia (Ashraf et al., 2018; Bozinov et al., 2020; Hurwitz M., 2014; Millesi & Wolfsberger, 2017). However, the use and commercialization of two laser systems in North America called Visualase and NeuroBlate have now been consolidated, which have reported comparatively better clinical results and fewer complications (Bozinov et al., 2020).

The NeuroBlate system, authorized by the Food and Drug Administration (FDA) since 2009, is equipped with a 1064 nm, 12 W Nd:YAG laser with a sapphire capsule, an internal gas cooling mechanism, 2.2 and 3.3 mm catheters with a directional firing mode, and a mechanism for delineating thermal damage thresholds, useful in tumor lesions with asymmetric distribution (Kim et al., 2020; Mohammadi & Schroeder, 2014; Lagman et al., 2017). Meanwhile, the Visualase system, approved since 2007, consists of a 980 nm, 15 W diode laser with a 1.65 mm polycarbonate catheter with saline irrigation, with advantages for rapid ablation due to greater tissue penetration through a higher degree of photon dispersion (Ashraf et al., 2018; Grabowski et al., 2021; Patel et al., 2020; Rennert et al., 2018).

Types of thermal therapies

Laser interstitial thermal therapy (LITT)

A minimally invasive procedure supported by stereotactic neuronavigation systems guided by magnetic resonance thermometry, with or without a frame, involving the insertion of a laser probe. This procedure has a spatial resolution of 1-2 mm and thermal precision of 1ºC (Patel et al., 2016; Buttrick & Komotar, 2016; Silva et al., 2017). It is performed through a small burr hole, no larger than 5 mm, facilitating the generation of thermal energy that induces cellular apoptosis. The effectiveness of LITT depends on various factors such as time, speed, temperature, laser type, and the intrinsic properties of the tissue being treated (Patel et al., 2020; Patel & Kim, 2020; Karampelas & Sloan, 2018).

In some cases, antineoplastic effects have been described for tumor cells at temperatures of 42ºC, and damage to normal parenchyma occurs above 43ºC (Rohatgi et al., 2014; Murayi et al., 2020; Diaz et al., 2016). Therefore, accurate classification of the neoplasm is crucial for defining the therapeutic window and the specific thermal dose for tissue necrosis and coagulation, which depend on the heat capacity (Chaunzwa et al., 2018; Norred & Johnson, 2014). After the procedure, all patients should undergo at least 24 hours of in-hospital monitoring (Patel et al., 2020; Patel & Kim, 2020; Sano F. Washio T., 2019; Karampelas & Sloan, 2018).

Focused ultrasound thermal ablation

A non-invasive thermoablation technique using radiofrequency at a frequency of 434 MHz for the treatment of head and neck tumor lesions operates through acoustic energy that releases thermal energy capable of inducing local tissue changes (Oberacker E., Kuehne A., 2020; Franzini et al., 2019; Toccaceli et al., 2018; Yan et al., 2018). Currently, these therapies have been approved in the United States in the field of neurosurgery for the treatment of essential tremor, chronic neuropathic pain, obsessive-compulsive disorders, and depression, showing good clinical outcomes (Toccaceli et al., 2018; Alkins & Mainprize, 2018; Banerjee et al., 2015).

Radiofrequency thermal ablation

It creates tissue changes through thermal energy generated by an intracranially active electrode stimulated by an external generator that induces ionic oscillation via radiofrequency waves at frequencies of 500,000 cycles per second, producing current densities that heat the tissue and create current-dependent localized lesions (Franzini et al., 2019; Stea & Witte, 2022; Shah et al., 2019; MacDonell et al., 2018).

Radiosurgery

It is an external ablative treatment alternative generated by image-guided stereotaxy, which delivers a large single dose of ionizing radiation to induce cellular apoptosis and halt mitosis (Hernandez et al., 2019; MacDonell et al., 2018; Palmer et al., 2020; Buckley et al., 2016). One of the most prominent devices is the Gamma Knife radiosurgery, which uses gamma rays from excited nuclei of 60Co (Franzini et al., 2019; Torcuator et al., 2016; Stea & Witte, 2022).

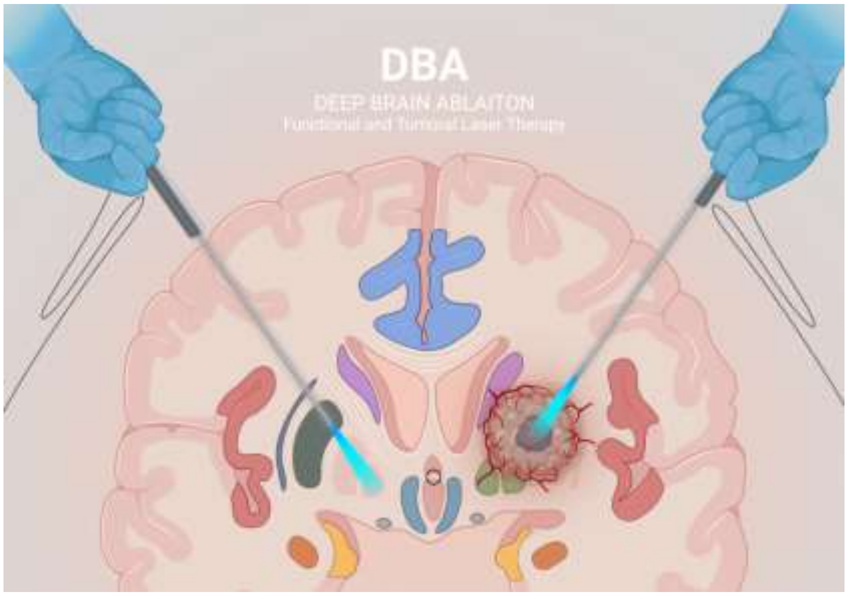
In a group of 63 patients with high-grade glioblastomas, a treatment regimen with LITT was performed, resulting in neurological deficits in 12% of cases, followed by vascular lesions (3%) and surgical site infections (1%). It is considered that selection criteria for initiating ablative therapies, especially in cases of recurrence, compared to conservative therapies, are still lacking (Lee et al., 2016; Montemurro et al., 2020; Rivera et al., 2021).

Indication

In the field of neuro-oncology, the use of hyperthermic therapies has gradually been incorporated for patients with deep-seated tumor lesions, unfavorable anatomical characteristics, recurrent metastases, and a history of surgical complications. It is established as a complementary therapeutic strategy for refractory or very challenging cases, and exceptionally as primary treatment (Figure 2) (Ashraf O. Arzumanov G., 2020; Johnson et al., 2022; Aizenberg, 2016; Skandalakis et al., 2020). Various authors predominantly describe the use of laser therapies in patients diagnosed with glial-origin neoplasms, with measurable clinical results in terms of increased progression-free survival rates and a reduction in average hospital stays (Torres-Reveron et al., 2013; Parikh & Neil, 2020; Thomas et al., 2016). Additionally, the use of ablative therapies for giant meningiomas, among others, has been reported (Yi et al., 2015; Yu & Mohammadi, 2020; Schupper et al., 2022).

Among the conditions to be evaluated for the proper and efficient implementation of therapy are the morphological characteristics of the neoplasms, such as size, location, and local perfusion. Thus, in smaller spherical tumors located away from strategic flow areas, there is a higher likelihood of generating complete ablative resections with fewer side effects due to more symmetrical thermal dispersion (Traylor et al., 2021; Del Bene et al., 2022). In contrast, ellipsoidal distribution lesions require directional firing devices with a higher number of interventions and the use of different types of catheters, which are commonly associated with a higher risk of significant post-ablation tissue edema (Ashraf et al., 2018; Torres-Reveron et al., 2013).

Figure 2
DBA indications



Source: Authors own elaboration

However, it is important to note that the conditions and indications for ablative therapies are currently an active area of study. Most authors describe treatment experiences with small patient populations, making it difficult to draw comparisons regarding clinical benefits, as described in relation to tumor size (Shao et al., 2020). Some studies suggest better clinical outcomes in patients with neoplastic lesions with diameters less than 3 cm^3, especially concerning mass effects, while other studies have documented positive experiences in neoplasms ranging from 6 to 9 cm^3 (Patel & Kim, 2020).

Furthermore, another aspect of hyperthermic therapies is the reversible disruption of the blood-brain barrier (BBB) to facilitate drug distribution through increased tissue perfusion and pharmacological permeability, leading to enhanced local bioavailability for up to 1 to 2 weeks after the start of therapy (Leuthardt et al., 2016; Lerner et al., 2022; Wise, 2016). Benefits are also described in relation to increased sensitivity to chemoradiotherapy, the activation of gene therapies, and the release of thermosensitive liposomal formulations (Alkins & Mainprize, 2018; Patel & Kim, 2020; Nagaraja & Lee, 2021).

Central Nervous System Neoplasms

Interstitial Thermal Laser Therapy (LITT) is an innovative minimally invasive procedure used for the treatment of intracranial lesions by inserting a laser probe through a trepanation hole to deliver optical radiation and localized tissue damage through one or several ablation paths, depending on the size and shape of the tumor, as well as therapeutic objectives (Ashraf O. Arzumanov G., 2020; Hawasli et al., 2013). Locally, hyperthermia stimulates the immune system through changes in T lymphocytes and macrophages, as well as changes in the neoplastic microvasculature (Karampelas & Sloan, 2018; Rodriguez & Tatter, 2015; 2016).

Ashraf et al. (2020) reported the clinical outcomes of a group of 58 patients treated with LITT for tumor lesions in the posterior fossa. They documented an average ablation volume of 2.24 cm^3 with an overall local control rate of 84% after an average follow-up of 9.5 months (Malone & Bruce, 2014). Additionally, there were 2 procedure-related complications and 12 cases of new-onset neurological deficits, requiring rehabilitation in 20.7% of cases (Ashraf O. Arzumanov G., 2020). Meanwhile, Di et al. (2021) performed ablative therapy on 20 patients with newly diagnosed glioblastoma with a total laser power ranging from 5.1 to 14.6 watts (W) and a total ablation time ranging from 54.7 to 1,780 seconds; achieving an overall survival of 36.2 months and a progression-free survival of 3.5 months. Better clinical outcomes were observed in those patients with ablation areas greater than 70% with chemotherapy regimens 16 days after the procedure (Di et al., 2021; Lara-Velazquez et al., 2017; Kamath et al., 2019; Rozumenko et al., 2018).

On the other hand, a group of patients with recurrent glioblastomas treated with LITT reported an average survival of 11.6 months with a 16% morbidity rate after 30 days of treatment. In comparison, patients treated with adjuvant therapies reached 9.1 months with an incidence of adverse effects ranging from 40-60% (Ashraf O. Arzumanov G., 2020). For cases of posterior fossa tumors, a reduction of 2.90 cm^3 has been achieved after 9 months of follow-up, with a median progression-free survival of 7 months and an average overall survival of 40 months, without intraoperative complications (Traylor et al., 2019); Rennert et al., 2016). Likewise, LITT offers an alternative for cytoreduction of malignant tumors located in areas that are difficult to access due to depth or proximity to white matter structures (Vega et al., 2020; Luther et al., 2020). However, in elderly patients, comorbidities and conditions of frailty should be considered, as age is not regarded as an exclusion criterion for performing LITT (Ginalis & Danish, 2020).

LITT produced predictable treatment effects such as (1) hemorrhagic necrosis within the lesion, (2) a new diffusion restriction ring within the treatment area and at the edge of the treatment area, (3) a new enhancement ring at the edge of the treatment area, and (4) peritumoral edema. Although somewhat variable, delayed images often showed a loss of diffusion restriction, a stable or reduced enhancement ring, and a final decrease in edema. Clinical outcomes in patients with tumors varied (Beaumont et al., 2018; Bastos, Fuentes, et al., 2020). However, LITT is recommended as a first-line alternative for patients with recurrent neoplastic lesions, achieving minimal reductions in functionality scales and shorter hospital stays (Sharma, Habboub, et al., 2016). It is also recommended for cases of brain metastases post-radiosurgery, although the benefits may be temporary (Lara-Velázquez et al., 2017; Schwalb et al., 2022; Fabiano & Qiu, 2014; Silva et al., 2016; Ivan et al., 2017; Eichberg et al., 2020; Alattar et al., 2019).

Functional Disorders

Radiation necrosis: Brain tissue injury secondary to radiotherapy (5-10%) and stereotactic radiosurgery (10-20%) is common in neuro-oncology (Sharma, Balasubramanian, et al., 2016; Bastos et al., 2020). These conditions are generally managed conservatively in

asymptomatic patients, occasionally with dexamethasone, and in some cases with bevacizumab (Sujijantarat et al., 2020; Hong et al., 2020). However, the latter is used sparingly due to high costs and the risk of thrombotic events such as pulmonary embolism and deep vein thrombosis (Johnson et al., 2022; Medvid et al., 2015).
The spectrum of symptoms and imaging findings mimics the original tumor lesion, leading to confusion and diagnostic errors, as they are indistinguishable from brain metastases, even after further studies (Chaunzwa et al., 2018; Rao et al., 2014; Murovic & Chang, 2015). In refractory cases, surgical measures such as open craniotomy should be considered; however, the associated risks significantly increase morbidity and complications (Hong et al., 2019). Therefore, LITT has been included as a therapeutic alternative, with lesion control close to 100% (Grabowski et al., 2021; Patel et al., 2020; Shah et al., 2020; Swartz et al., 2019).

Ablative Laser Therapy for Movement Disorders: In certain movement disorders, such as essential tremor or Parkinson's disease, ablative laser therapy has been investigated to selectively destroy or lesion the brain areas responsible for the disorder. Therefore, in the early twentieth century, the first ablative procedures for movement disorders were performed targeting the precentral gyrus, brainstem peduncles, and other parts of the pyramidal tract, resulting in various neurological side effects (Franzini et al., 2019).

Laser Therapy for Epilepsy: Interstitial laser thermal therapy guided by magnetic resonance imaging is a novel treatment alternative approved by the US Food and Drug Administration since 2007 for cases of refractory epilepsy (Diaz et al., 2016; Zemmar et al., 2020). In this technique, the laser is directed at localized or deep-seated epileptogenic foci, such as in mesial temporal lobe epilepsy, hypothalamic hamartoma, and callosotomy, achieving outcomes comparable to open surgery by reducing abnormal activity and decreasing the frequency of epileptic episodes (Lee et al., 2019; Medvid et al., 2015; Willie et al., 2014).

Currently, it has been used for small lesions ≤2–3 cm and large, deep-seated lesions located in the insular lobe. It is important to note that the use of ablative laser therapies for functional central nervous system issues is an emerging practice, and its benefits, risks, and long-term outcomes are still under investigation (McCracken et al., 2016; Hedaya et al., 2022). Therefore, surgical interventions require well-defined plans to avoid complications from thermal damage to surrounding critical structures. Ablative therapy has been suggested particularly as a first-line surgical option in pediatric patients with hypothalamic hamartoma due to a lower risk of neurological deficits compared to open surgery, and better resolution of seizure episodes (Lee et al., 2019; Nagae et al., 2017).

Neuropsychiatric disorders: There have been isolated reports of the use of ablative treatments for the management of addictions and mood disorders through leucotomy, hypothalamotomy, anterior cingulotomy, and lesions in the nucleus accumbens with controversial results, achieving benefits in about 60% of the patients treated. However, there is a lack of clarity regarding the efficiency and safety of the procedure. In cases of patients with eating disorders, such as anorexia nervosa, ablations of the white matter of the frontal lobe, resection of the dorsomedial thalamus, and the anterior limb of the internal capsule have been performed, with variable improvement in neuropsychiatric symptoms and weight stabilization (Franzini et al., 2019).

Additionally, there are records of ablative treatments for disruptive behaviors and aggression through stereotactic amygdalotomies and hypothalamotomies, as well as anterior cingulotomy and anterior capsulotomy. These procedures have resulted in behavioral improvements in up to 70% of cases, although the patient cohorts recorded do not exceed 40 individuals. Therefore, studies are needed to standardize the evaluation processes and objective clinical assessment of patients (Franzini et al., 2019).

Chronic pain: In patients with chronic pain due to radicular disorders or secondary to neoplastic pain, thermocoagulation therapies using MRI-guided radiofrequency of the cingulum have been utilized to intervene in the pain pathways. However, solid studies are lacking to determine their efficacy and benefits (Salem et al., 2019).

Complications

Neurointerventions involving the use of thermal therapy are associated with transient and/or permanent complications, among which post-ablation edema, infections, and hemorrhages are noteworthy (Patel et al., 2020; Medvid et al., 2015; Chen et al., 2021).

Neurological Deficits

Neurological conditions with involvement of the brain and cerebellum have been documented, characterized by clinical presentations mainly including hemianopsia, hemiparesis, hemiplegia, dysphasia, amnesia, and seizures. These conditions are reported in 13% to 20% of intervened patients, with permanent neurological deficits occurring in 3% of cases. This is due to the thermal absorption properties of the tissue, which can lead to peripheral lesions beyond the ablation point, as well as tissue edema, potentially affecting white matter. Therefore, recommendations include the use of ablative catheters with a diffuser tip of less than 3 mm and pharmacological measures involving preoperative or postoperative use of antiepileptic and steroid medications (Jamshidi et al., 2020)

Hemorrhage

In the case of ablative therapies, hemorrhages occur in up to 2.5% of cases. This complication can be caused by catheter passage, tissue fragility, and the rate of thermal energy delivery (Ashraf et al., 2018). Therefore, it is recommended to limit the number of laser interventions and use needles with smaller diameters to minimize the risk of hemorrhage (Medvid et al., 2015).

Infections

The risk of infections associated with neurosurgical procedures remains a possibility (Ashraf et al., 2018). Some studies report surgical site infections due to contamination during the procedure, and only in exceptional cases are neurological complications such as ventriculitis and meningitis reported (Grabowski et al., 2021).

Cerebral Edema

There are records of patients with brain tumors treated with LITT and radiotherapy regimens who showed imaging evidence of cerebral edema on MRI. These patients required prolonged steroid management (>65 days) with successful clinical outcomes. However, a minority of patients with steroid-refractory edema required the use of bevacizumab (Maraka et al., 2018; Pisipati et al., 2016).

Conclusion

Ablation techniques, including catheter ablation and laser therapy, offer promising options for the treatment of CNS pathologies for patients who are not ideal candidates for conventional surgery. As technology and experience in these procedures continue to evolve, their clinical application is expected to expand and improve outcomes and quality of life for patients.

Future research should focus on conducting well-designed randomized controlled trials with standardized outcome measures to establish the role of ablative techniques in the treatment of CNS pathologies, define standardized treatment protocols and optimize patient outcomes, resulting in an innovative and effective neurosurgical management tool.

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