Research Article Volume 01, Issue No. 01. 2024

The International Medical Journal of Anatomic Pathology and Forensic

Optimizing Diagnostic Efficacy: A Comprehensive Systematic Review of Stereotactic Biopsy for Brainstem Lesions

[2] Chrysman Andreria Hatulely, [1] Wahyu Agus Prastyo, [1] Artha Investari Nugraheni, [2] Daniel Setiawan Nathan, [1] Mutia Ruliana Ayuningrum

[1] Faculty of Medicine, Sultan Agung Islamic University, Semarang City, Central Java, Indonesia
[2] Faculty of Medicine, Maranatha Christian University, Bandung City, West Java, Indonesia

Correspondence : chrysmanhatulely@gmail.com

Article History :
Received date : 2024/06/11
Revised date : 2024/07/10
Accepted date : 2024/08/15
Published date : 2024/10/07

ABSTRACT

Background: Stereotactic biopsy is crucial for diagnosing brainstem lesions, which are challenging due to their complex location. This review evaluates the diagnostic yield, safety, and complications of stereotactic biopsies for brainstem lesions. **Methods:** A systematic search of PubMed, Web of Science, and the Cochrane Library (2013-2023) identified studies reporting on stereotactic biopsy outcomes for brainstem lesions. Data extraction and bias assessment followed standardized guidelines. **Results:** Twelve studies involving 1,640 patients were included. The diagnostic yield ranged from 91.5% to 100%. Complications occurred in 10%, with neurological deficits in 15.3% of brainstem cases. Mortality rates varied, highlighting the importance of patient selection. **Conclusions:** Stereotactic biopsy offers high diagnostic accuracy with acceptable risk for brainstem lesions, though further research is needed to improve outcomes and minimize complications.

Keywords: Stereotactic biopsy, brainstem lesions, diagnostic yield, neurological complications, patient safety.

INTRODUCTION

Since the introduction of stereotactic biopsy over seven decades ago, its applications and clinical utilities have steadily evolved alongside advancements in adjunctive technologies such as CT, MRI, PET-CT, and robotic assistance.[1] This method, recognized for its precision, minimal invasiveness, and critical role in pathological diagnosis, emerged as the gold standard for brain tumor diagnosis by the late 20th century. Pioneered by Gleason et al. in 1978 for brainstem lesions, stereotactic biopsy is now an essential procedure, particularly as brainstem lesions account for approximately 15% of pediatric and 2% of adult intracranial space-occupying lesions.[2] Biopsy procedures typically utilize one of four primary approaches: contralateral extraventricular transfrontal, ipsilateral transfrontal, transtentorial, and suboccipital transcerebellar, all of which have demonstrated similar diagnostic yields and complication rates.

Despite its clinical significance, many neurosurgical teams remain hesitant to employ brainstem stereotactic biopsy due to concerns over potential risks and a limited perception of its benefits.[3-4] Notably, the Children's Cancer Group-9882 study in 1993 highlighted the high specificity of MRI in diagnosing brainstem glioma, suggesting that histological confirmation might not alter treatment decisions.[5] This finding led to a marked decline in the use of biopsies for nearly a decade. However, several factors have reignited interest in this procedure: a substantial body of research indicating that over 15-20% of preoperative MRI diagnoses may differ from postoperative pathological findings; the presence of both benign and malignant lesions that can mimic one another on imaging; and the growing reliance on molecular diagnostics for brainstem tumors, which emphasizes the necessity for definitive histological diagnosis.[6-7]

Advancements in imaging techniques and biopsy methods have significantly improved the safety and diagnostic yield of contemporary brainstem stereotactic biopsy.[8] Previous systematic reviews conducted by Dr. Ruge's team reported an impressive diagnostic success rate of 96.1-96.2%, accompanied by low

overall morbidity (6.7-7.8%) and mortality rates (0.6-0.9%).[9] However, these reviews did not perform subgroup analyses based on different populations or biopsy techniques. Therefore, this systematic review aims to comprehensively evaluate the diagnostic yield and safety of brainstem stereotactic biopsy for lesions within the brainstem. Additionally, it will conduct detailed subgroup analyses based on various biopsy techniques (such as CT guidance, MRI guidance, and robotic assistance) and different patient populations (including adults and children) to better understand the clinical utility and implications of this important procedure.

METHODS

Protocol

The investigation was conducted in strict adherence to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 criteria, ensuring compliance with established methodological principles. Following these standards reflects a commitment to enhancing the clarity, replicability, and thoroughness of the review process. The study employed robust methodologies for literature searches, data extraction, and synthesis of findings, effectively minimizing biases and strengthening the conclusions.

Criteria for Eligibility

This study provides a comprehensive review of the literature over the past decade regarding the diagnostic yield and complications associated with stereotactic biopsy for brainstem lesions. Through systematic examination and integration of data from various studies, this research aims to clarify key patterns and inform clinical practices. To maintain rigor and precision, strict inclusion and exclusion criteria were established. Only peer-reviewed articles published in English from 2014 to 2024 were deemed eligible, with a requirement for a DOI to verify authenticity. Non-research materials, such as reviews, editorials, and duplicate entries, were intentionally excluded to maintain focus.

Search Strategy

We utilized keywords including "stereotactic biopsy," "brainstem lesion," and "diagnostic yield" in various combinations. The search for relevant studies was

conducted using PubMed, Web of Science, and Cochrane Library. Each database was queried with these terms to ensure a comprehensive collection of literature related to the diagnostic yield and safety of stereotactic biopsy for brainstem lesions.

Data Retrieval

A preliminary review of each article was conducted by examining its abstract and title to assess relevance before a more detailed investigation. Only studies that aligned with the study's objectives and met the predefined inclusion criteria were considered for further review. This process allowed for the identification of consistent patterns across the research. Full-text articles were restricted to those published in English to maintain consistency, and a rigorous screening process ensured that only content directly relevant to the study's focus was included. Articles not meeting these criteria were systematically excluded from further analysis.

The evaluation encompassed a comprehensive review of various factors such as study design, titles, authors, publication dates, research locations, and methodologies. This meticulous approach ensured that the analyzed content was of high relevance and quality, thus strengthening the overall findings.

Quality Assessment and Data Synthesis

A thorough review of each article's abstract and title was performed to identify those warranting further investigation. Following this initial screening, all relevant documents underwent comprehensive examination. The results of this evaluation guided the selection of studies for detailed analysis, ensuring that only the most pertinent research was included. This rigorous approach streamlined the selection process and facilitated an in-depth assessment of the existing literature and its implications.

Table 1. Search Strategy

Database	**Search Strategy**	***Hits***
PubMed	*("stereotactic biopsy" OR "brainstem lesion" AND "diagnostic yield")*	34

Web of Science	*("stereotactic biopsy" AND "brainstem lesion")*	58
Cochrane Library	*("brainstem lesions" AND "stereotactic biopsy" AND "diagnostic yield")*	15

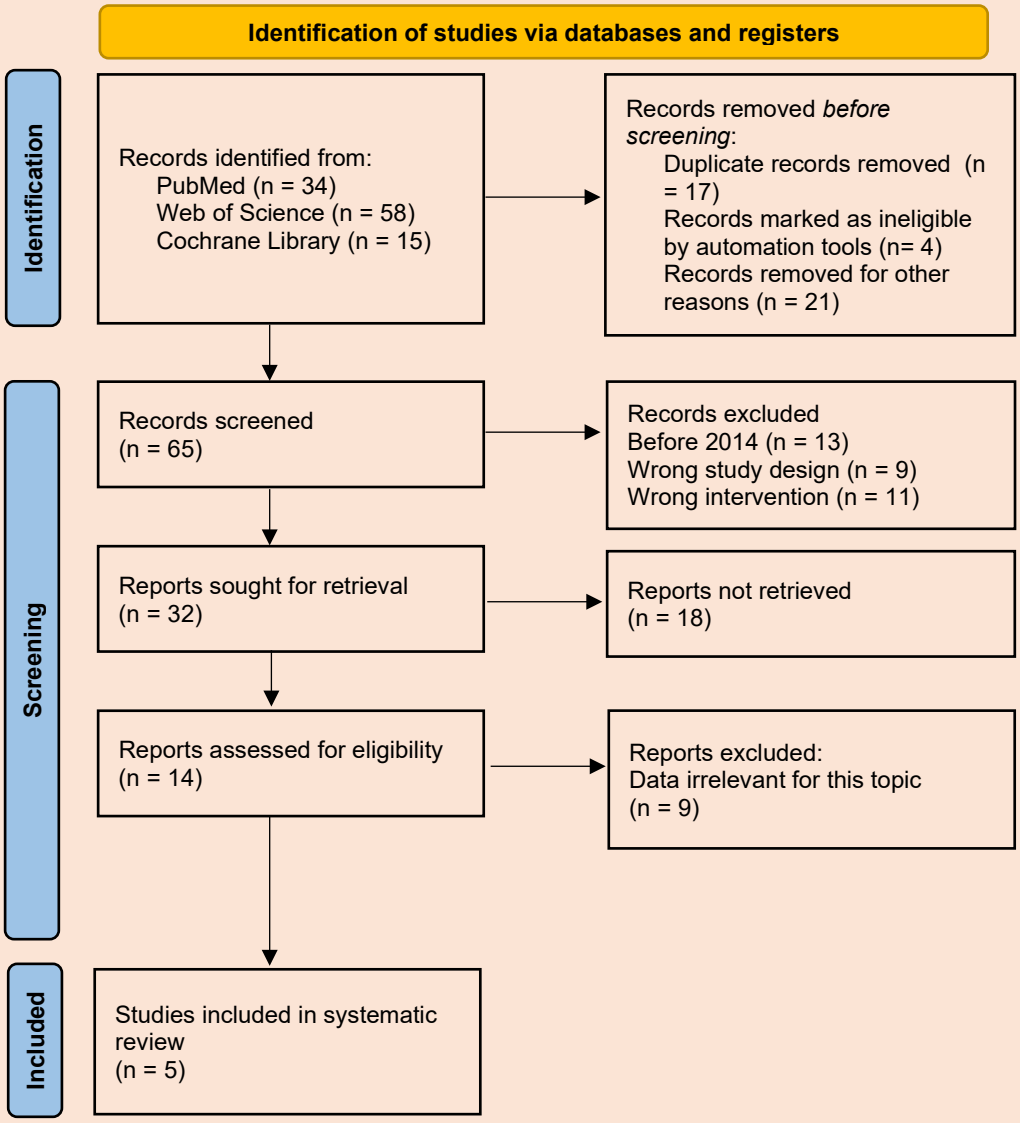

Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	(Birski et al., 2021)	(Cheng et al., 2020)	(Akay et al., 2019)	(Gupta et al., 2018)	(Manoj et al., 2014)
1. Bias related to temporal precedence					
Is it clear in the study what is the "cause" and	Yes	Yes	Yes	Yes	Yes

what is the "effect" (ie, there is no confusion about which variable comes first)?					
2. Bias related to selection and allocation Was there a control group?	No	No	No	Yes	No
3. Bias related to confounding factors Were participants included in any comparisons similar?	Unclear	Unclear	Yes	Yes	Unclear
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Yes	Yes	Yes	Yes	Yes.
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Unclear	Unclear	Yes	Yes	Unclear
Were the outcomes of participants included in any comparisons measured in the same way?	Unclear	Unclear	Yes	Yes	Unclear
Were outcomes measured in a reliable way?	Unclear	Unclear	Yes	Yes	Unclear
6. Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Unclear	Unclear	Yes	Yes	Unclear
7. Statistical conclusion validity Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes

RESULT

We initiated the investigation by systematically gathering a significant assortment of papers from reputable sources such as PubMed, Web of Science, and Cochrane Library. After a thorough three-stage screening process, we selected five papers that were considered very pertinent to our ongoing systematic inquiry. Subsequently, we selected certain topics for further examination and meticulously evaluated each report. In order to expedite our study, we have included a concise summary of the evaluated information in Table 3.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result

Birski et al.[10] (2021)	Poland	Retrospective analysis	85 participants	19 patients with ventricular lesions, aged 18 to 84, underwent 123 biopsies (85 stereotactic and 38 endoscopic). The diagnostic yield was 98% for stereotactic and 92% for endoscopic biopsies, though the total nondiagnostic rate was 6% for stereotactic and 11% for endoscopic procedures, with no significant differences between groups. Complications occurred in 11% of patients, including three fatal cases due to bleeding and brain edema. The overall mortality rate for ventricular biopsies was 2.4%, significantly higher than the 0.3% mortality rate for intracranial biopsies elsewhere ($p = 0.016$).
Cheng et al.[11] (2020)	China	Retrospective analysis	111 participants	145 patients (mean age 32.9 years) with brain lesions underwent stereotactic biopsies (STB). Lesions were located primarily in the brainstem (76.6%), pineal region (12.4%), and sellar region (11.0%). A 100% diagnostic rate was achieved for patients with sellar and pineal region lesions, while a 96.4% rate was obtained for brainstem lesions. Among brainstem biopsy patients, 15.3% experienced neurological complications, including facioplegia, facial pain, and changes in vital signs, with a 2.7% mortality rate. No complications were reported for patients with pineal or sellar region biopsies.

Akay et al.[12] (2019)	Turkey	Retrospective analysis	18 patients	18 patients, including 16 adults and 2 children, underwent MRI-guided stereotactic biopsy. Adults received local anesthesia, while children received local anesthesia with sedation. All patients were successfully diagnosed through histopathological examination, with no inconclusive results, major complications, or mortality reported post-procedure.
Gupta et al.[13] (2018)	USA	Prospective cohort	50 patients	The researcher team enrolled 53 pediatric patients between 2011 and 2015 for a national multi-institutional trial. Fifty patients underwent stereotactic biopsy, while 3 did not due to various issues (e.g., cardiac instability or insurance problems). All biopsies were performed using a transcerebellar approach, with a median age of 6.4 years and a slight female majority (54%). While there were no deaths directly related to the procedure, one patient died due to disease progression. Post-biopsy, several complications were noted, including bradycardia, apnea, and hydrocephalus. Pathological tissue was successfully obtained in 92% of cases for molecular analysis.
Manoj et al.[14] (2014)	India	Retrospective cohort study	82 patients	In the study, 82 patients underwent stereotactic biopsy for brainstem lesions, with equal

				representation of children (≤18 years) and adults (>18 years). The patients' ages ranged from 3 to 60 years (mean 22.11 years). Both groups had a male predominance, with cranial nerve dysfunction more common in adults. Imaging revealed mostly intrinsic lesions, with 59.7% classified as diffuse. Histological diagnoses varied, with glioblastoma significantly more frequent in children. The biopsy yielded a diagnosis in 91.5% of cases, and complications were rare, with no procedure-related mortality reported.

DISCUSSION

The examination of stereotactic biopsy for brainstem lesions reveals critical insights into its diagnostic efficacy and safety profile across various studies. Birski et al. (2021) provided compelling data on the high diagnostic yields for both stereotactic and endoscopic biopsies, with a reported diagnostic yield of 98% for stereotactic procedures. However, their finding of a higher mortality rate associated with ventricular biopsies—2.4% compared to 0.3% for other intracranial biopsies—raises significant concerns regarding procedural risks and the need for careful patient selection and risk assessment.[10]

Cheng et al. (2020) further underscored the effectiveness of stereotactic biopsies, achieving a nearly perfect diagnostic rate for lesions in regions other than the brainstem, while documenting complications specific to brainstem procedures. The 15.3% incidence of neurological complications highlights the inherent risks associated with targeting this densely populated area of the central nervous system.[11]

Akay et al. (2019) contributed valuable data by reporting a complete absence of inconclusive results in their small cohort, suggesting that MRI-guided techniques may enhance the reliability of diagnoses in challenging cases.[12] Gupta et al. (2018) emphasized the importance of obtaining sufficient tissue for molecular analysis in pediatric patients, successfully acquiring samples in 92% of cases. This indicates that stereotactic biopsy not only serves diagnostic purposes but also plays a crucial role in guiding treatment strategies based on molecular characteristics.[13]

Manoj et al. (2014) provided a balanced perspective by noting the prevalence of cranial nerve dysfunction among adult patients, suggesting that age-related differences could influence both the outcomes and complication rates. The study highlighted the varying histological diagnoses, particularly the higher frequency of glioblastoma in children, which underscores the need for tailored approaches based on age and lesion characteristics.[14]

While the collective findings suggest that stereotactic biopsy is a valuable tool in diagnosing brainstem lesions, the variations in methodologies, patient demographics, and outcomes across studies underscore the necessity for standardized protocols. Additionally, a deeper investigation into the long-term effects and complication rates of the procedure is warranted. Addressing these aspects could optimize the clinical application of stereotactic biopsy, ensuring it meets the diverse needs of patients while minimizing risks associated with this intricate surgical intervention.

Several limitations are present in the included studies. Firstly, the predominance of retrospective analyses raises concerns about selection bias and limits causal inferences, potentially affecting the reliability of outcome reporting. Secondly, the heterogeneity in sample sizes, patient demographics, and surgical techniques across studies complicates the generalizability of findings. While some studies achieved high diagnostic yields, others with smaller cohorts lacked robust statistical support.

Additionally, variations in follow-up duration and methods among the studies hinder comprehensive assessments of long-term outcomes and complications. The absence of control groups in several studies further complicates

comparisons with alternative diagnostic approaches. Lastly, focusing solely on English-language publications may introduce a language bias, potentially omitting relevant research published in other languages. Addressing these limitations in future research could strengthen conclusions regarding the role of stereotactic biopsy for brainstem lesions.

CONCLUSION

Stereotactic biopsy emerges as a vital diagnostic tool for brainstem lesions, demonstrating high diagnostic yields and a generally acceptable safety profile across multiple studies. The evidence indicates that while the procedure is effective, particularly in obtaining tissue for molecular analysis and confirming diagnoses, there are notable risks, especially related to neurological complications. Variations in outcomes based on lesion location and patient demographics suggest the importance of individualized treatment approaches and careful patient selection.

Future research should focus on standardizing biopsy techniques, refining patient selection criteria, and exploring long-term outcomes to enhance the overall efficacy and safety of stereotactic biopsies in clinical practice. By addressing these factors, clinicians can better navigate the complexities of diagnosing and treating brainstem lesions, ultimately improving patient care and outcomes.

DISCLOSURE STATEMENT

Disclosure Statement : The authors have no conflicts of Interest to declare.

REFERENCES

1. Jansen MHA, van Vuurden DG, Vandertop WP, Kaspers GJL. Diffuse intrinsic pontine gliomas: a systematic update on clinical trials and biology. Cancer Treat Rev. 2012;38:27-35.
2. Dellaretti M, Cˆ amara BBA, Ferreira PHPB, da Silva J´unior JB, Arantes RME. Impact of histological diagnosis on the treatment of atypical brainstem lesions. Sci Rep. 2020;10:11065.
3. Buczkowicz P, Hoeman C, Rakopoulos P, et al. Genomic analysis of diffuse intrinsic pontine gliomas identifies three molecular subgroups and recurrent activating ACVR1 mutations. Nat Genet. 2014;46:451-456.
4. Lara-Almunia M, Hernandez-Vicente J. Frame-based stereotactic biopsy: description and association of anatomical, radiologic, and surgical variables

with diagnostic yield in a series of 407 cases. J Neurol Surg Cent Eur Neurosurg. 2019;80:149-161.

5. Gupta M, Chan TM, Santiago-Dieppa DR, et al. Robot-assisted stereotactic biopsy of pediatric brainstem and thalamic lesions. J Neurosurg Pediatr. 2020;25:1-8.
6. Hamisch C, Kickingereder P, Fischer M, Simon T, Ruge MI. Update on the diagnostic value and safety of stereotactic biopsy for pediatric brainstem tumors: a systematic review and meta-analysis of 735 cases. J Neurosurg Pediatr. 2017;20:261-268.
7. Kickingereder P, Willeit P, Simon T, Ruge MI. Diagnostic value and safety of stereotactic biopsy for brainstem tumors: a systematic review and meta-analysis of 1480 cases. Neurosurgery. 2013;72:873-882; discussion 882; quiz 882.
8. Birski M, Furtak J, Krystkiewicz K, et al. Endoscopic versus stereotactic biopsies of intracranial lesions involving the ventricles. Neurosurg Rev. 2021;44:1721-1727.
9. Cheng G, Yu X, Zhao H, et al. Complications of stereotactic biopsy of lesions in the sellar region, pineal gland, and brain stem. Medicine. 2020;99:e18572.
10. Akay A, Is¸lekel S. MRI-guided frame-based stereotactic brainstem biopsy procedure: a single-center experience. Neurocirug´ıa. 2019;30:167-172.
11. Gupta N, Goumnerova LC, Manley P, et al. Prospective feasibility and safety assessment of surgical biopsy for patients with newly diagnosed diffuse intrinsic pontine glioma. Neuro Oncol. 2018;20:1547-1555.
12. Manoj N, Arivazhagan A, Bhat DI, et al. Stereotactic biopsy of brainstem lesions: techniques, efficacy, safety, and disease variation between adults and children: a single institutional series and review. J Neurosci Rural Pract. 2014;5:32-39.