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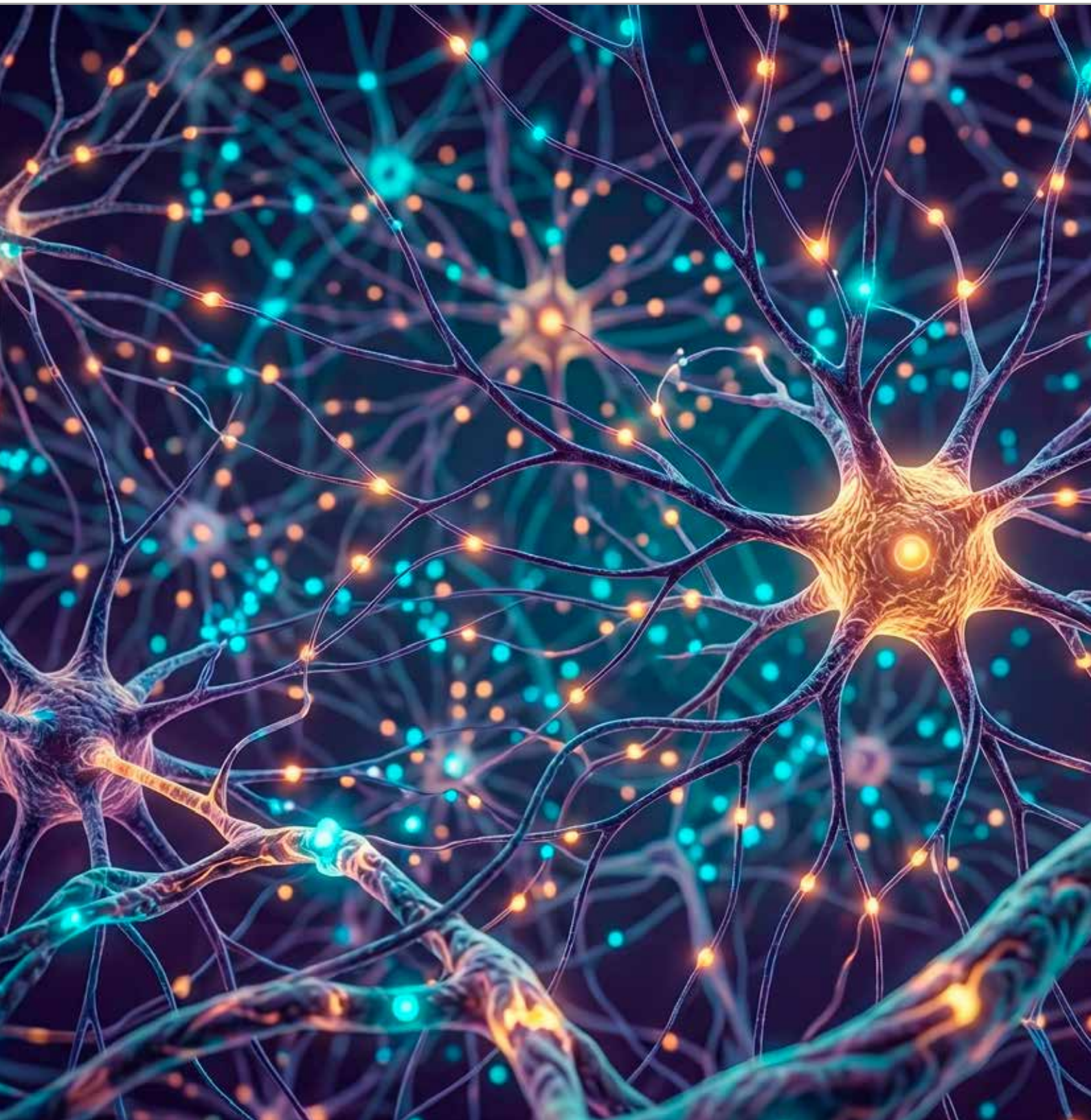

Contents

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Instruction To Authors

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EDITORIAL

Multiple-Target Deep Brain Stimulation: Current Evidence

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CONFLICT OF INTEREST
None

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Deep brain stimulation (DBS) represents a well-established neurosurgical intervention for treating severe neurological disorders resistant to pharmacological management. The procedure delivers precisely calibrated electrical impulses to targeted brain nuclei, modulating dysfunctional neural circuits [1]. While the precise mechanisms underlying DBS efficacy remain incompletely understood, substantial clinical evidence has established its therapeutic value, particularly in movement disorders [1–3].

The selection of brain nuclei to be targeted is driven by various factors, such as underlying disease, predominant symptoms, individual patient characteristics, and anatomical feasibility [4,5]. Common targets include the subthalamic nucleus (STN) and globus pallidus internus (GPi) DBS for motor symptom control in advanced Parkinson's Disease (PD), and ventral intermediate thalamic nucleus (Vim) for tremor-dominant Parkinsonism [3].

Due to its proven efficacy, its range of application is expanding and at the same time new approaches are being developed. A relatively new, evolving clinical approach combines simultaneous stimulation of anatomically distinct targets to address symptom combinations inadequately controlled by single-target interventions, aptly named multiple-target DBS. The rationale derives from neurocircuit topology: different basal ganglia structures contribute differentially to distinct symptom domains. For instance, STN-DBS effectively reduces bradykinesia and rigidity but may inadequately address tremor or gait disturbance; respectively, GPi-DBS controls dyskinesia more effectively than STN-DBS but produces less rigidity reduction [6].

Retrospective studies and small RCTs suggest that multiple-target DBS, such as GPi+VIM for dystonia, VIM+VOA (thalamic Ventralis Oralis Anterior) for essential tremor, as well as STN+GPi, STN+VIM and STN+SNr (Substantia Nigra) for PD can offer feasibility, safety, and situational superiority over single-target stimulation [7–10]. The research is still ongoing as it is hard to procure definite results in such small subsets of patients.

A critical concern regarding multiple-target DBS is the cumulative adverse effects from expanded hardware and surgical intervention. However, empirical evidence suggests that this concern may be overstated. The available evidence from small series indicates that despite requiring more complex surgical approaches and additional hardware, multiple-target DBS does not produce substantially elevated adverse effect frequencies [11–13]. Especially regarding stimulation-induced adverse effects, a small downwards trend could potentially be associated with a smaller need for increased current density required; symptoms can be adequately controlled with smaller current densities.

Despite accumulating evi-

dence, no formal clinical indications currently exist for multiple-target DBS outside structured research protocols. The evidence base remains limited to case reports, small retrospective case series (typically 3-8 patients), and preliminary open-label trials with up to 18 patients. Long-term follow-up data extending beyond 2-3 years remain scarce, limiting assessment of durability and cumulative adverse effects [8].

Several methodological limitations warrant acknowledgment. Study heterogeneity complicates a systematic approach : variable follow-up intervals, inconsistent outcome measurement protocols, and disease severity or comorbidity differences across studies hinder definitive comparisons. Additionally, small sample sizes create statistical instability; single patient outcomes can substantially impact reported efficacy percentages. Meanwhile, the very limited number of controlled clinical trials with pre-specified trial plans significantly increases the overall risk of bias. Lastly, smaller studies with statistically significant results may be overrepresented compared to studies which show no benefit.

Overall, current evidence could support multiple-target DBS as a viable option in carefully selected patients with documented poor response to optimized single-target DBS and symptoms spanning multiple functional domains (motor planning, tremor control, gait) not well-addressed by any single target. Interdisciplinary preoperative assessment remains essential, with the aim to systematically evaluate motor and non-motor symptom profiles to predict which additional target(s) may provide complementary benefit.

REFERENCES

1. Neumann W.-J., Steiner L. A., and Milosevic L., "Neurophysiological mechanisms of deep brain stimulation across spatiotemporal resolutions," Brain, vol. 146, no. 11, pp. 4456–4468, Nov. 2023, doi: 10.1093/brain/awad239.
2. Chiken S. and Nambu A., "Mechanism of Deep Brain Stimulation," The Neuroscientist, vol. 22, no. 3, pp. 313–322, June 2016, doi: 10.1177/1073858415581986.
3. Mao Z. et al., "Comparison of Efficacy of Deep Brain Stimulation of Different Targets in Parkinson's Disease: A Network Meta-Analysis," Front. Aging Neurosci., vol. 11, Feb. 2019, doi: 10.3389/fnagi.2019.00023.
4. Reese R. and Volkmann J., "Deep Brain Stimulation for the Dystonias: Evidence, Knowledge Gaps, and Practical Considerations," Mov. Disord. Clin. Pract., vol. 4, no. 4, pp. 486–494, Aug. 2017, doi: 10.1002/mdc3.12519.
5. Lizarraga K.J., Luca C.C., De Salles A., Gorgulho A., Lang A.E., and Fasano A., "Asymmetric neuromodulation of motor circuits in Parkinson's disease: The role of subthalamic deep brain stimulation," Surg. Neurol. Int., vol. 8, p. 261, Oct. 2017, doi: 10.4103/sni.sni_292_17.
6. Zhang C. et al., "Combined Unilateral Subthalamic Nucleus and Contralateral Globus Pallidus Interna Deep Brain Stimulation for Treatment of Parkinson Disease: A Pilot Study of Symptom-Tailored Stimulation," Neurosurgery, vol. 87, no. 6, pp. 1139–1147, May 2020, doi: 10.1093/neuros/nyaa201.
7. Schmidt S.L. et al., "At home adaptive dual target deep brain stimulation in Parkinson's disease with proportional control," Brain J. Neurol., vol. 147, no. 3, pp. 911–922, Mar. 2024, doi: 10.1093/brain/awad429.
8. Kalogirou E., Voulgaris S., and Alexiou G.A., "Efficacy and safety of multiple-target deep brain stimulation in non-parkinsonian movement disorders: a systematic review," Neurosurg. Rev., vol. 48, no. 1, p. 512, June 2025, doi: 10.1007/s10143-025-03661-4.
9. Fayed I. et al., "Combination targeting of subthalamic nucleus and ventral intermediate thalamic nucleus with a single trajectory in deep brain stimulation for tremor-dominant Parkinson's disease," J. Clin. Neurosci., vol. 85, pp. 92–100, Mar. 2021, doi: 10.1016/j.jocn.2020.12.022.
10. Weiss et D. al., "Nigral stimulation for resistant axial motor impairment in Parkinson's disease? A randomized controlled trial," Brain J. Neurol., vol. 136, no. Pt 7, pp. 2098–2108, July 2013, doi: 10.1093/brain/awt122.
11. Artusi C.A. et al., "Subthalamic and nigral stimulation for freezing of gait in Parkinson's disease: Randomized pilot trial," J. Park. Dis., vol. 14, no. 8, pp. 1602–1613, Nov. 2024, doi: 10.1177/1877718X241292315.
12. Isaacs D.A. et al., "Confined Thalamic Deep Brain Stimulation in Refractory Essential Tremor," Stereotact. Funct. Neurosurg., vol. 96, no. 5, pp. 296–304, 2018, doi: 10.1159/000493546.
13. Oliveria S.F. et al., "Safety and efficacy of dual-lead thalamic deep brain stimulation for patients with treatment-refractory multiple sclerosis tremor: a single-centre, randomised, single-blind, pilot trial," Lancet Neurol., vol. 16, no. 9, pp. 691–700, Sept. 2017, doi: 10.1016/S1474-4422(17)30166-7.

REVIEW

Posterior Subthalamic Deep brain stimulation for the treatment of Essential tremor: A Systematic Review

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CONFLICT OF INTEREST
None

FUNDING
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ABSTRACT

Background: Deep Brain Stimulation (DBS) to Ventral Inter Mediate nucleus (VIM) has been the first line surgical treatment for medically refractory essential tremor (ET). Several studies have suggested that Posterior Subthalamic Area (PSA) -DBS could be more effective in controlling tremor symptoms and at the same time is associated with fewer adverse events. Our aim was to provide an overview of the data on the efficiency of PSA-DBS in symptom control of ET.

Methods: A systematic review on PubMed, Embase, and the Cochrane Library until 2nd of July 2025 was performed using the following keywords: "Deep Brain Stimulation"; "essential tremor"; "posterior subthalamic area"; "caudal zone incerta"; "complications"; "adverse events". We included studies with patients with a confirmed diagnosis of ET that were treated with PSA-DBS and had a documented change in any objective tremor rating scale at baseline and at the last follow up. The risk of bias was assessed using the ROBINS-I tool.

Results: A total of 13 studies including 394 patients treated with PSA-DBS were included. The overall risk of bias, based on the ROBINS-I tool, was judged to be serious across all included studies. The average follows up ranged from 12-64.8 months. The pre and post DBS (on) tremor improvement rate ranged from 40.54 -89.47%. During the off stimulation setting the improvement rates when compared to baseline ranged from 1-23.68% with two studies reporting worse tremor rates than baseline. In the studies that reported adverse events post treatment, these rates ranged from 24.5-71.42%.

Conclusions: Our study demonstrated that PSA-DBS is an effective alternative to VIM-DBS in the treatment of patients with medically refractory ET. However, larger and better-structured studies are needed to confirm these findings.

Keywords: Deep Brain Stimulation; essential tremor; posterior subthalamic area; caudal zone incerta; complications; adverse events.

ΠΕΡΙΛΗΨΗ

Εισαγωγή: Η εν τω βάθει εγκεφαλική διέγερση (Deep Brain Stimulation, DBS) του πυρήνα Ventral Intermediate nucleus (VIM) αποτελεί την πρώτη γραμμή χειρουργικής θεραπείας για τον ανθεκτικό στη φαρμακευτική αγωγή ιδιοπαθή τρόμο (Essential Tremor, ET). Αρκετές μελέτες έχουν υποδείξει ότι DBS με στόχο την Posterior Subthalamic Area (PSA) ενδέχεται να είναι πιο αποτελεσματική στον έλεγχο των συμπτωμάτων του τρόμου και ταυτόχρονα να σχετίζεται με λιγότερα ανεπιθύμητα συμβάντα. Στόχος μας ήταν να παρέχουμε μια συνολική επισκόπηση των διαθέσιμων δεδομένων σχετικά με την αποτελεσματικότητα του PSA-DBS στον έλεγχο των συμπτωμάτων του ET.

Μέθοδοι: Πραγματοποιήθηκε συστηματική ανασκόπηση στη βάση δεδομένων PubMed, Embase και Cochrane έως τις 2 Ιουλίου 2025, χρησιμοποιώντας τις ακόλουθες λέξεις-κλειδιά: «Deep Brain Stimulation», «essential tremor», «posterior subthalamic area», «caudal zona incerta», «complications», «adverse events». Συμπεριλήφθηκαν μελέτες με ασθενείς με επιβεβαιωμένη διάγνωση ET που υποβλήθηκαν σε PSA-DBS και παρουσίαζαν τεκμηριωμένη μεταβολή σε οποιαδήποτε αντικειμενική κλίμακα αξιολόγησης τρόμου κατά την έναρξη και κατά την τελευταία παρακολούθηση. Ο κίνδυνος μεροληψίας αξιολογήθηκε με το εργαλείο ROBINS-I.

Αποτελέσματα: Συμπεριλήφθηκαν συνολικά 13 μελέτες με 394 ασθενείς που υποβλήθηκαν σε PSA-DBS. Ο συνολικός κίνδυνος μεροληψίας, βάσει του εργαλείου ROBINS-I, αξιολογήθηκε ως σοβαρός σε όλες τις συμπεριληφθείς μελέτες. Η μέση διάρκεια παρακολούθησης κυμάνθηκε από 12 έως 64,8 μήνες. Το ποσοστό βελτίωσης του τρόμου πριν και μετά το DBS (σε κατάσταση ενεργοποίησης) κυμάνθηκε από 40,54% έως 89,47%. Στην κατάσταση απενεργοποίησης της διέγερσης, τα ποσοστά βελτίωσης σε σύγκριση με την αρχική τιμή κυμάνθηκαν από 1% έως 23,68%, ενώ δύο μελέτες ανέφεραν επιδείνωση του τρόμου σε σχέση με την αρχική κατάσταση. Στις μελέτες που ανέφεραν ανεπιθύμητα συμβάντα μετά τη θεραπεία, τα ποσοστά αυτά κυμάνθηκαν από 24,5% έως 71,42%.

Συμπεράσματα: Η μελέτη μας έδειξε ότι το PSA-DBS αποτελεί αποτελεσματική εναλλακτική του VIM-DBS στη θεραπεία ασθενών με ανθεκτικό στη φαρμακευτική αγωγή ιδιοπαθή τρόμο. Ωστόσο, απαιτούνται μεγαλύτερες και καλύτερα σχεδιασμένες μελέτες για την επιβεβαίωση αυτών των ευρημάτων.

Λέξεις κλειδιά: Εν τω βάθει εγκεφαλική διέγερση, ιδιοπαθής τρόμος, οπίσθια υποθαλαμική περιοχή, caudal zone incerta, επιπλοκές, ανεπιθύμητα συμβάντα.

INTRODUCTION

Essential tremor (ET) is defined as a bilateral, symmetric postural or kinetic tremor involving hands, forearms, and possibly other body parts. [1] It is the most prevalent movement disorder as it is estimated that up to 4% of the adult population is affected. [2] The management of this hyperkinetic movement disorder is generally initially pharmacologic treatment. This is effective in 30–70% of patients with an average tremor reduction of 50-60%. [3] For medically refractory cases, deep brain stimulation (DBS) is now the preferred surgical treatment. Initially, the target of choice was the thalamic Ventral Inter Mediate nucleus (VIM). Vim stimulation was introduced in the early 1990s as a replacement of thalamotomies.[4]

In the only randomized trial comparing VIM DBS with traditional radiofrequency thalamotomy in patients with tremor, DBS and thalamotomy were equally effective for the suppression of drug-resistant tremor, but the former was associated with fewer adverse effects and a greater improvement in function. [5] The main limitation of DBS is stimulation induced adverse events such as ataxia, dysarthria and paraesthesia which often narrow the therapeutic window, especially when the disease severity progresses. [6] Also, it is difficult to assess disease progression in the "off" condition given the rebound effect of tremor in some patients, that lead to an immediate worsening of tremor after stimulation is stopped [7]

However, during the last years, increasing interest has focused on DBS in the posterior subthalamic area (PSA) and the caudal Zona incerta (Zi). A positive correlation between tremor inhibition and stimulation of dentato-rubro-thalamic tract (DRTT) was shown by many imaging studies. Therefore, the proximity of DRTT fibers in PSA makes it a good target for DBS. The superior anatomic location of PSA is thought to contribute to the better results of tremor suppression [8].

In recent years, the question of which structure is responsible for the tremor-suppressive effect of PSA-DBS on ET has attracted extensive research attention. ZI has been suggested as a target to control tremor of various pathologies including ET [9]. DRTT simulation has been correlated with tremor inhibition by many studies. According to a recent study, tremor suppression efficacy is directly associated with the distance of the target to the center of the DRTT. The authors also suggest that the reported superior results of PSA DBS versus VIM on ET symptom control can be explained by the close proximity of PSA to the DRTT. [9]

The primary goal of the current study is providing an overview of the long-term effect of this treatment for patients with drug resistant ET. This is the first study that focuses primarily on the long-term outcomes of PSA-DBS for ET and summarises the latest data.

MATERIAL AND METHODS

The present systematic review was conducted using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 guidelines

Search strategy

Articles describing the effect of PSA- DBS on ET were selected from three electronic databases (PubMed, Embase, and the Cochrane Library). We searched all articles related to DBS treatment for ET until 2nd of July 2025. A flow chart of the literature search is shown in Figure 1. The following keywords were used: Deep Brain Stimulation; essential tremor; posterior subthalamic area; caudal zone incerta; complications; adverse events. The titles, abstracts, full texts, and references were independently read and assessed by two investigators (TS and ER).

Risk of bias and applicability assessment

Two independent (ER, TS) authors assessed the risk of bias in included studies using the Risk of Bias in Non-randomized Studies (ROBINS-I) tool for non-randomized studies. Any disagreements were settled by a third author (GA)

The articles selected were then classified according to an evidence-based classification proposed by Wright et al. [10]: I: High-quality randomized controlled trial, II: Lesser quality randomized controlled trial; prospective comparative study, III: Case–control study; retrospective comparative study IV: Case series. Expert opinion.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) Patients with a diagnosis of ET according to the consensus statement of the Movement Disorder Society treated with DBS [11] (2) essential tremor treated medically without satisfactory tremor control (3) Age>18 years (4) Studies reporting a change in any objective tremor rating scale at baseline and at the last follow up (5) Studies that the DBS target was the PSA/ZI.

The exclusion criteria were: (1) Conference presentations, editorials, reviews, non-English studies, and duplicate publications, (2) follow up of less than 6 months, presence of

another movement disorder apart from essential tremor for example Parkinson's disease. (3) Failed DBS and need for re-operation, not providing separate outcomes for Vim and PSA – ZI. (4) Dual DBS targeting of regions other than the PSA or ZI.

Data extraction

Our study looked at the following items: (1) baseline characteristics of the patients (age, sex, disease duration), (2) laterality of DBS (unilateral or bilateral) (3) clinical outcomes including symptom severity pre and post DBS. Because we wanted to compare the differences between the outcomes of PSA and VIM, adverse events related to DBS surgery were excluded, and only common stimulation-related complications (SRCs) (for example dysarthria, dysphagia, ataxia, and gait impairment) were included in the statistical analysis. The rate of SRCs (SRCR) was calculated as [(the number of patients who occurred gait ataxia + (the number of patients who occurred dysphagia) + ... + (the number of patients who occurred one type of SRCs)/the total number of patients × 100%]. Given the heterogeneity of the TRS scales, no pooled statistical analysis could be performed. The effect size was determined by calculating the percentage improvements in tremor rating scale scores ([(the presurgical score - the postsurgical score)/the presurgical score × 100%].

RESULTS

Literature Search

According to our keywords, our initial search yielded 1268 studies. Five additional studies were identified after manually searching the references of the included studies. After excluding duplicates and careful screening, 252 studies were retrieved for full-text analysis based on the title and abstract. Finally, thirteen studies which met our inclusion and exclusion criteria were finally selected for analysis. The screening process is illustrated in Figure 1.

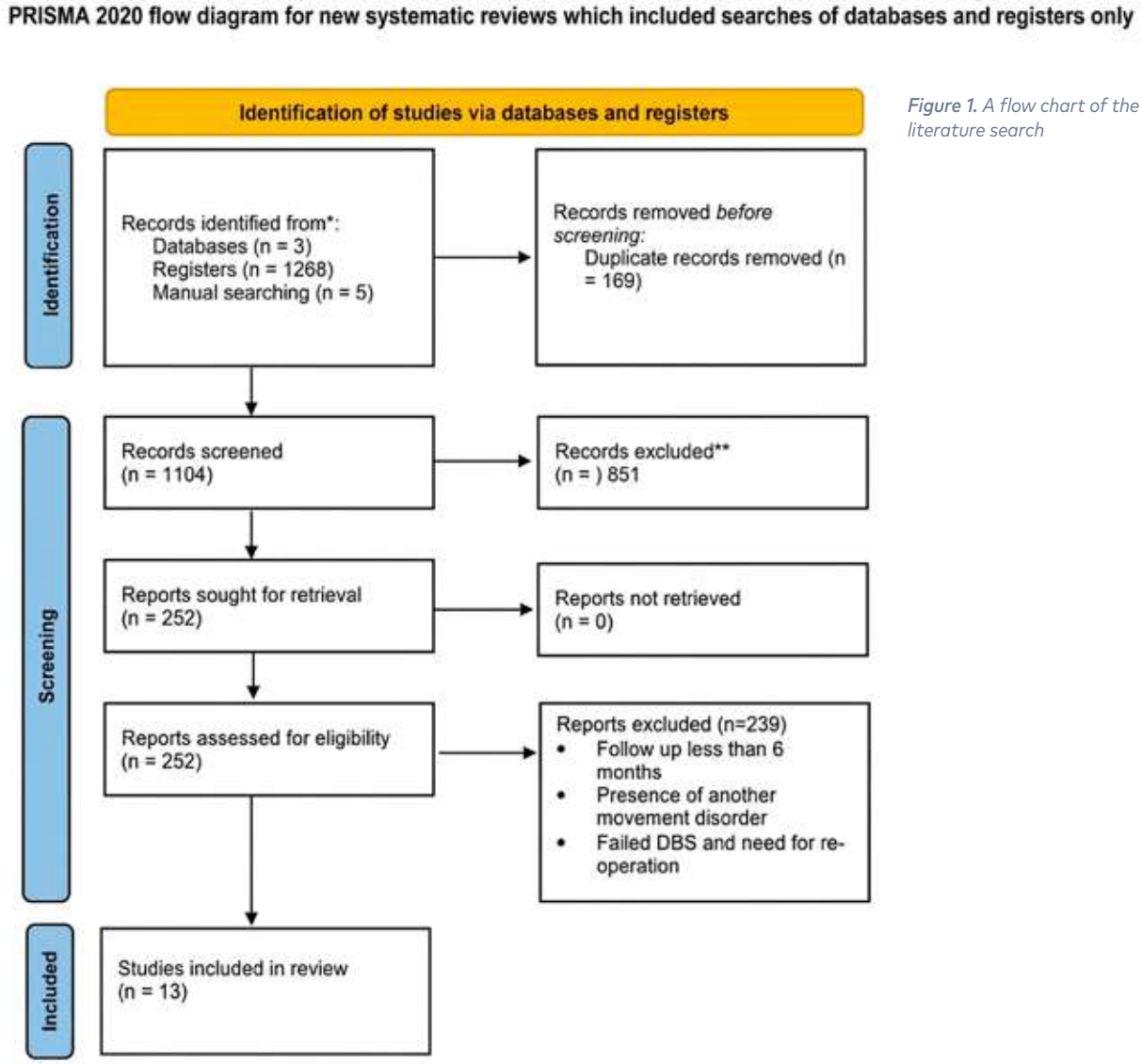


Figure 1. A flow chart of the literature search

Risk of bias and applicability assessment

Risk of bias was assessed using the ROBINS-I tool for all 13 included studies. Overall, every study was judged to be at serious risk of bias. The domain most frequently contributing to this judgment was confounding (D1), which was rated as serious in 10 studies [12,13,15,17-20,22-23], moderate in 2 [16,21], and low in 1[14]. Classification of interventions (D2) was generally well addressed, with most studies (n = 8) judged at low risk [12,14,15,17-20,22], three at moderate risk [21,23,24], and two at serious risk [13,16].

Selection into the study (D3) was rated low in 11 studies [12-14,17-24], while one was judged serious [16] and one provided insufficient information [15]. For deviations from intended interventions (D4), the majority (n = 9) were rated moderate [12,13,17-22,24], three serious [14,16,23], and one low [15]. Missing data (D5) was poorly reported: in seven studies the risk was not assessable [19-24], while four were judged serious [13-16], one moderate [17], and one low [18]. Measurement of outcomes (D6) was commonly rated serious (n = 10) [12-14,17-22,24], with only one low [18], one moderate [17], and one unreported [16]. Selection of reported results (D7) was predominantly moderate (n = 10) [12,13,17-24], with two serious [15,16] and one unreported [14].

Taken together, all 13 studies [12-24] were judged overall at serious risk of bias, primarily due to confounding, unblinded outcome measurement, and incomplete or selectively reported data.

These results are illustrated in Figure 2.

A detailed summary of the quality of the included studies with the Wright et al. evidence-based classification system can be found in Table 1 and Table 2.

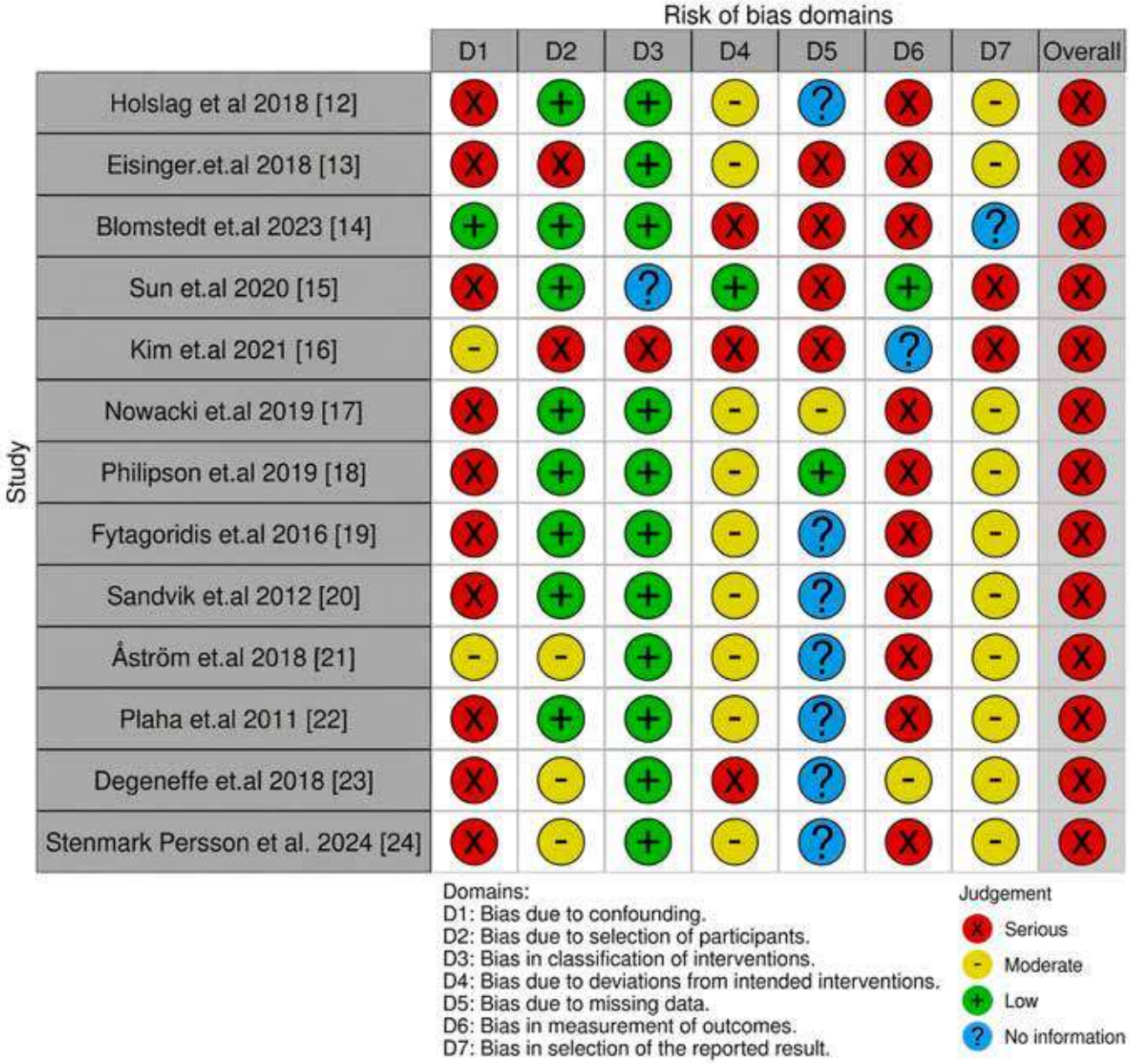
Table 1. Wright et al. Evidence-Based Classification (2003)

LEVEL	DESCRIPTION
I	High-quality randomized controlled trial (RCT)
II	Lesser-quality RCT or prospective comparative study
III	Case-control or retrospective comparative study
IV	Case series
V	Expert opinion, case report, or method paper without patient data

Table 2. Classification of the included studies and main characteristics

Study	Target(s)	Design	Wright Level	Rationale
Holslag et al., 2018	VIM vs. PSA	Retrospective comparative	**Level III**	Retrospective compares two DBS targets
Eisinger et al., 2017	VIM vs. ZI	Retrospective comparative	**Level III**	Multi-center, retrospective comparison
Blomstedt et al., *n.d.*	cZI/PSA	Long-term follow-up	**Level IV**	Case series with long-term results
Sun et al., 2020	PSA	Case series	**Level IV**	Case series, no control group
Kim et al., 2021	VIM & PSA	Retrospective	**Level III**	Compares side effects between targets retrospectively
Nowacki et al., 2018	PSA	Anatomical proposal	**Level V**	Anatomical landmark study, no outcomes
Philipson et al., 2019	cZI	Prospective	**Level II**	Prospective, clinical cognitive outcomes
Fytagoridis et al., 2016	cZI	Retrospective	**Level III**	Tremor control analysis vs. stimulation field
Sandvik et al., 2012	cZI	Prospective	**Level II**	Prospective QoL evaluation
Åström et al., 2018	cZI	Simulation/modeling	**Level V**	Predictive model, no direct patient data
Plaha et al., 2011	cZI	Prospective	**Level II**	Prospective outcomes and QoL
Degeneffe et a., 2018	VIM vs. PSA	Retrospective comparative	**Level III**	Comparison between targets, retrospective
Stenmark Persson et al. 2024	BcZI	Retrospective comparative	**Level III**	Comparison between awake ans asleep DBS retrospective

Figure 2. Plot of risk of Bias using ROBINS-1 risk score for non-randomised clinical trials



Characteristics of the Included studies

A total of 13 studies was included in the final analysis [12-24]. A total of 394 patients were identified. The detailed report of the patient's demographics is shown in Table 2. The mean age of the included patients ranged from 59-65.7 years of age. The number of the included patient was range from 7 to 86 with the male patient ration range from 23.53 to 85.71. The mean follow-up time after DBS ranged from 12 to 64.8 months. There were only 7 studies that used bilateral DBS [14] [15] [18-21][24]. The mean disease duration prior to surgery ranged from 21.4 to 29.2 years. Only one study has evaluated awake versus asleep DBS in the PSA, and it reported no significant differences between the two approaches with respect to stimulation effectiveness or side effects.

Qualitative synthesis

Effectiveness of DBS Based on Tremor rating Scales

There was significant heterogeneity in the tremor scales used to assess response to DBS. Essential Tremor Rating Scale (ETRS) [27] was the most frequently used [14,15,17-24]. Therefore, no pooled statistical analysis could be performed. The Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) rating scale [25] was only used in one study [12] and the Clinical Rating Scale for Tremor (CRST) [26] in another study [16]. The improvement in tremor rates scores was calculated by dividing pre with post DBS (stimulation on) severity scoresMost of the studies reported a mean follow-up period of 12 months [14,15,17–21]. Two studies did not report the mean follow-up period but instead provided the follow-up range, which was 6–48 months [13] and 11–24 months [24], respectively. The overall rate of improvement during the follow-up period ranged

from 40.54% to 89.47%There were 5 studies [14] [15] [18] [19] [21] that suggested that during the off stimulation setting the improvement rates compared to baseline ranged from 1-23.68% with three studies reporting worse tremor rates than baseline.

PSA DBS and effect on Quality of Life

In our study, there were only two studies assessing the effect of DBS on quality of life. [15] [20] More specifically, Sun et.al [15] showed that in patients with ET their quality of life increased by 81.25% after DBS at 1-month follow-up. Sandvik et.al assessed the QOF using Quality of Life in Essential Tremor Questionnaire (QUEST) score which showed statistically significant improvements in the psychosocial and activities of daily living subscores in patients with ET undergoing DBS. Given the different methods of assess effect of surgery on quality of life, a direct comparison with VIM DBS would be of limited value.

Adverse Events (AE)

From the 13 studies that have been analysed ,7 studies [13] [18-23] did not report any adverse events (AE) after DBS treatment. In the 6 studies that reported complications post DBS, the AEs rates ranged from 24.5-71.42%. Gait ataxia and dysarthria were some of the most commonly reported AEs. A summary of DBS related AEs is reported in Table 4.

Table 4. Outcomes of patients with ET treated with PSA-DBS

Study	Adverse event (number)	Adverse event rates (%)	Tremor scale	Symptom severity prior DBS	Symptom severity post DBS (off)	Symptom severity post DBS (on)	Improvement rates (%)
Holslag et al 2018 [12]	Gait ataxia (4), dysarthria (5) , HTN (1) intracranial hemorrhage (1), dysphasia (1)	41.37	WHIGET	3.7	NA	2.2	40.54
Eisinger et.al 2018 [13]	NA	NA	ETRS	48.8	NA	NA	35-96% improvement
Blomstedt et.al 2023 [14]	Stroke (1) Dysphasia (8) gait (6)	44.11	ETRS	51.2	46.1	17.2	66.4
Sun et.al 2020 [15]	Dysarthria (4) (1) Post op arm paralysis	71.42	ETRS	19	14.5	2	89.47
Kim et.al 2021 [16]	GAIT (13) Dysarthria (4) Paraesthesia (13)	54.54	CRST	17.63	NA	5.32	69.82
Nowacki et.al 2019 [17]	Dysarthria (4) Paraesthesia (1)	45.45	ETRS	47.2	NA	21.3	54.87
Philipson et.al 2019 [18]	NA	NA	ETRS	46.32	53.26	17	63.29
Fytagoridis et.al 2016 [19]	NA	NA	ETRS	47.6	47.9	19.3	59.45
Sandvik et.al 2012 [20]	NA	NA	ETRS	48.1	NA	18.8	60.91
Åström et.al 2018 [21]	NA	NA	ETRS	49.7	49.2	19.2	61.36
Plaha et.al 2011 [22]	NA	NA	ETRS	63.9	NA	16.7	73.86
Degeneffe et.al 2018 [23]	NA	NA	ETRS	21	NA	10	52.38
Stenmark Persson et al. 2024 [24]	upper limb ataxia (9), habiluation (7), dysarthria (5), gait disturbance (1), slight incoordination (1), paraesthesia (1)	24.5 % (awake group 25% and asleep group 24.2%)	ETRS	51.1	53.2	21.1	58.9

DISCUSSION

In this systematic review, we demonstrated that PSA DBS is an effective alternative to VIM DBS in the treatment of patients with medically refractory ET with a mean follow-up period ranging from 1 to 5 years and an improvement rate of up to 89.47%.

Different targets for DBS in ET management

There is still lack of evidence regarding which DBS target is superior for the treatment of ET. A direct comparison between the PSA and VIM is challenging. The is due to a number of factors including different scales used to assess tremor improvement, combination of bilateral and unilateral targets and also the close proximity of the two targets [28] In a recent meta-analysis by Fan et.al [29] PSA-DBS for ET was found to be more effective and associated with less adverse reactions for than VIM-DBS in 12–24 months, with both PSA-DBS and VIM-DBS being effective in suppressing tremor symptoms. To date, there is only two randomized controlled trial that has compared outcomes between targeting VIM and PSA in patients with ET, suggesting the latter to be potentially more efficient [30,31]. Sun et al. reported that PSA and VIM can be equal effective, and PSA-DBS can have a more effective anti-tremor effect in head tremor [31].

Another important consideration is the preoperative visualisation of the surgical target. VIM has been challenging to visualise with conventional MRIs and surgical planning is therefore based on atlas-defined co-ordinates. PSA on the other hand is much easier to locate with conventional imaging and therefore the therapeutic effect is less affected by incorrect target positioning [32].

In recent years, given their anatomical location, there are studies looking at the possibility to align these two targets with one trajectory. In a small sample of 6 patients, Hou et.al [32] investigated the efficacy of Vim–PSA double-target DBS for ET. Interestingly, when it comes to controlling tremor symptoms, the authors found that the efficacy of double-target stimulation is similar to that of single-target stimulation (Vim or PSA). A possible advantage of double target DBS could be that the chances of missing the optimal target would be diminished and therefore the potential need for re-operation would decrease. Shepherd et al [33] found that bilateral ViM-cZI DBS treatment had a favourable effect on overall tremor score sustained over the 5-years in ET group of patients.

In a recent randomised control trial, clinical benefit happened at a significantly lower stimulation intensity under PSA DBS versus VIM DBS, with the latter providing greater improvement in head tremor and disease-specific quality of life [34].

Long term effects of PSA-DBS

The main drawback of VIM is that despite good patient selection and significant initial tremor suppression achieved, around 40-70% of patients will show worsening tremor over time [35]. Differentiating between disease progression of ET from habituation remains a challenge. Eisinger et.al reported a potential long-term advantage for applying stimulation to the VIM region due to a gradual worsening in tremor scores over time in patients stimulated chronically in the cZI region [14].

Little is known however regarding the long-term effects of PSA-DBS in patients with ET as most of the studies limit their follow up period to a maximum of 4 years. Blomstedt et.al [14] studies the long-term effect of DBS for ET when targeting PSA and showed no progress of disease at 10 years of follow up. Notably, a significant improvement was maintained on ETRS scores at 10 years follow up (66.4% improvement at 1 year vs 50.8% at 10 years) [14].

Imaging for PSA-DBS treatment

Another important factor when planning PSA-DBS treatment for ET is the ability to reliable visualise the ZI, given that the success of the intervention is indispensably dependent on the reliable visualisation of the ZI. Pre-stereotactic 1.5 Tesla (T) magnetic resonance imaging (MRI) alone has limitations [36]. Kerl et.al found that the ZI was optimally visualised on T2*-FLASH2D and SWI imaging in coronal orientation, with only the rostral part being reliably visualised [37].

Unilateral vs Bilateral Surgery

With regards in bilateral DBS, in our results it was only assessed in 6 studies that included a total of 30/308 patients [14-15] [18-21]. Bilateral VIM-DBS had been reported to be more effective in tremor control than unilateral VIM-DBS but also has been associated with higher rates of adverse events including dysarthria and gait ataxia [38] [39]. Sun et.al [15] assessed the clinical outcomes of a series of patients with medically refractory ET who underwent bilateral PSA-DBS. The results showed that bilateral PSA-DBS was associated with a significant improvement in patients' motor symptoms, particularly upper limb tremor and quality of life. There is also data that suggests that stimulation effect weaned over time in both groups, with the difference being more pronounced in bilateral patients [15].

Simulation-induced side effects of PSA DBS

Like any surgical treatment, DBS can cause post operative complications. Serious adverse event rates for DBS are relatively rare and can include intracranial haemorrhage and soft tissue infections [40]. The vast majority are stimulation-related and thus can usually be improved or resolved with adjustments in stimulation parameters but this could potentially result in less tremor control benefit [41]. Dysarthria and gait ataxia have been reported as two of the most common AEs in DBS, something which is confirmed in our study. According to literature, the pooled percentages of complication rates after PSA-DBS were significantly lower than that after VIM-DBS [30]. In our study, the AEs rates were reported only in 5 studies and ranged from 41.37-71.42%. Gait changes can be either acute or a delayed side effect of the treatment. Worsening of pre-existing or new-onset gait impairments after thalamic DBS affects has been reported between 5–50% of patients with ET [42].

Awake versus Asleep

In our review, we included only one study that compared awake and asleep DBS cZi, involving both unilateral and bilateral electrode implantations[24]. This study reported no significant differences between the groups in terms of efficacy or side effects. However, the awake group required low-

er stimulation parameters and had a shorter operation time compared to the asleep group. On the other hand, during the off-stimulation period, the awake group had worse ETRS scores than the asleep group, but after stimulation, the scores were similar. Regarding unilateral versus bilateral stimulation, no significant differences in improvement were observed between the two groups. This study suggests that both asleep and awake DBS in cZi can be safe and effective for patients with essential tremor [24].

Limitations

Our study has several limitations. First of all, we included DBS outcomes on medium- to long-term follow-up as there were very few studies that had reported data beyond several years, with only one study extending up to 10 years. Sample sizes were generally small, with only one study including 86 patients, while most ranged from 7 to 55. With regard to adverse events (AEs), some may occur shortly after treatment but improve later during the postoperative period and therefore not be evident at the time of the last follow-up. Others may have been alleviated or disappeared after adjustment of stimulation parameters and consequently not reported. It is also important to note that there was heterogeneity in the outcome scales used to assess tremor: although the majority of studies employed the ETRS, some used WHIGET or CRST, which may limit comparability. In terms of methodological quality, all included studies were judged to be at serious risk of bias according to the ROBINS-I tool, mainly due to confounding, unblinded outcome assessment, missing data, and selective reporting. Furthermore, one of the included studies was a small case series [15] , for which ROBINS-I may not be the most appropriate instrument for risk-of-bias assessment, thereby adding further uncertainty.

CONCLUSION

Our study demonstrated that PSA DBS is an effective alternative treatment option for the management of patients with medically refractory ET. This is the first study that summarises the data regarding the tremor control post DBS in the offsetting. More studies are needed that assess the QOL post DBS treatment. Future randomised control trials are needed to provide more evidence on the outcomes of PSA DBS in the treatment of ET.

REFERENCES

1. Louis, E.D., 2011. Treatment of Essential Tremor: Are there Issues We are Overlooking? Front Neurol 2, 91. https://doi.org/10.3389/fneur.2011.00091
2. Deuschl, G., Raethjen, J., Hellriegel, H., Elble, R., 2011. Treatment of patients with essential tremor. Lancet Neurol 10, 148–161. https://doi.org/10.1016/S1474-4422(10)70322-7
3. Deuschl, G., Bain, P., Brin, M., 1998. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. Mov Disord 13 Suppl 3, 2–23. https://doi.org/10.1002/mds.870131303
4. Benabid, A.L. et al. (1991) 'Long-term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus', Lancet (London, England), 337(8738), pp. 403–406. Available at: https://doi.org/10.1016/0140-6736(91)91175-t
5. Schuurman, P.R., Bosch, D.A., Bossuyt, P.M., Bonsel, G.J., van Someren, E.J., de Bie, R.M., Merkus, M.P., Speelman, J.D., 2000. A comparison of continuous thalamic stimulation and thalamotomy for suppression of severe tremor. N Engl J Med 342, 461–468. https://doi.org/10.1056/NEJM200002173420703
6. Iorio-Morin, C., Fomenko, A. and Kalia, S.K. (2020) 'Deep-Brain Stimulation for Essential Tremor and Other Tremor Syndromes: A Narrative Review of Current Targets and Clinical Outcomes', Brain Sciences, 10(12), p. 925. Available at: https://doi.org/10.3390/brainsci10120925.
7. Kumar, K., Kelly, M., Toth, C., 1999. Deep brain stimulation of the ventral intermediate nucleus of the thalamus for control of tremors in Parkinson's disease and essential tremor. Stereotact Funct Neurosurg 72, 47–61. https://doi.org/10.1159/000029671
8. Middlebrooks, E.H., Okromelidze, L., Carter, R.E., Jain, A., Lin, C., Westerhold, E., Peña, A.B., Quiñones-Hinojosa, A., Uitti, R.J., Grewal, S.S., 2022. Directed stimulation of the dentato-rubro-thalamic tract for deep brain stimulation in essential tremor: a blinded clinical trial. Neuroradiol J 35, 203–212. https://doi.org/10.1177/19714009211036689
9. Akram, H., Dayal, V., Mahlknecht, P., Georgiev, D., Hyam, J., Foltynie, T., Limousin, P., De Vita, E., Jahanshahi, M., Ashburner, J., Behrens, T., Hariz, M., Zrinzo, L., 2018. Connectivity derived thalamic segmentation in deep brain stimulation for tremor. Neuroimage Clin 18, 130–142. https://doi.org/10.1016/j.nicl.2018.01.008
10. Wright JG, Swiontkowski MF, Heckman JD (2003) Introducing levels of evidence to the journal. J Bone Joint Surg Am 85:1–3
11. Deuschl, G., Bain, P., Brin, M., 1998. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. Mov Disord 13 Suppl 3, 2–23. https://doi.org/10.1002/mds.870131303
12. Holslag, J.A.H., Neef, N., Beudel, M., Drost, G., Oterdoom, D.L.M., Kremer, N.I., van Laar, T., van Dijk, J.M.C., 2018. Deep Brain Stimulation for Essential Tremor: A Comparison of Targets. World Neurosurg 110, e580–e584. https://doi.org/10.1016/j.wneu.2017.11.064
13. Eisinger, R.S., Wong, J., Almeida, L., Ramirez-Zamora, A., Cagle, J.N., Giugni, J.C., Ahmed, B., Bona, A.R., Monari, E., Wagle Shukla, A., Hess, C.W., Hilliard, J.D., Foote, K.D., Gunduz, A., Okun, M.S., Martinez-Ramirez, D., 2017. Ventral Intermediate Nucleus Versus Zona Incerta Region Deep Brain Stimulation in Essential Tremor. Mov Disord Clin Pract 5, 75–82. https://doi.org/10.1002/mdc3.12565
14. Blomstedt, Y., Stenmark Persson, R., Awad, A., Hariz, G.-M., Philipson, J., Hariz, M., Fytagoridis, A., Blomstedt, P., n.d. 10 Years Follow-Up of Deep Brain Stimulation in the Caudal Zona Incerta/Posterior Subthalamic Area for Essential Tremor. Movement Disorders Clinical Practice n/a. https://doi.org/10.1002/mdc3.13729
15. Sun, X., Huang, L., Pan, Y., Zhang, C., Wang, T., Li, H., Sun, B., Ding, J., Wu, Y., Li, D., 2020. Bilateral Posterior Subthalamic Area Deep Brain Stimulation for Essential Tremor: A Case Series. Frontiers in Human Neuroscience 14.
16. Kim, M.J., Chang, K.W., Park, S.H., Chang, W.S., Jung, H.H., Chang, J.W., 2021. Stimulation-Induced Side Effects of Deep Brain Stimulation in the Ventralis Intermedius and Posterior Subthalamic Area for Essential Tremor. Front Neurol 12, 678592. https://doi.org/10.3389/fneur.2021.678592

17. Nowacki, A., Debove, I., Rossi, F., Schlaeppi, J.A., Petermann, K., Wiest, R., Schüpbach, M., Pollo, C., 2018. Targeting the posterior subthalamic area for essential tremor: proposal for MRI-based anatomical landmarks. Journal of Neurosurgery 131, 820–827. https://doi.org/10.3171/2018.4.JNS18373

18. Philipson, J., Blomstedt, P., Hariz, M., Jahanshahi, M., 2019. Deep brain stimulation in the caudal zona incerta in patients with essential tremor: effects on cognition 1 year after surgery. Journal of Neurosurgery 134, 208–215. https://doi.org/10.3171/2019.9.JNS191646

19. Fytagoridis, A., Åström, M., Samuelsson, J., Blomstedt, P., 2016. Deep Brain Stimulation of the Caudal Zona Incerta: Tremor Control in Relation to the Location of Stimulation Fields. Stereotact Funct Neurosurg 94, 363–370. https://doi.org/10.1159/000448926

20. Sandvik, U., Hariz, G.-M., Blomstedt, P., 2012. Quality of life following DBS in the caudal zona incerta in patients with essential tremor. Acta Neurochir (Wien) 154, 495–499. https://doi.org/10.1007/s00701-011-1230-z

21. Åström, M., Samuelsson, J., Roothans, J., Fytagoridis, A., Ryzhkov, M., Nijlunsing, R., Blomstedt, P., 2018. Prediction of Electrode Contacts for Clinically Effective Deep Brain Stimulation in Essential Tremor. Stereotact Funct Neurosurg 96, 281–288. https://doi.org/10.1159/000492230

22. Plaha, P., Javed, S., Agombar, D., O' Farrell, G., Khan, S., Whone, A., Gill, S., 2011. Bilateral caudal zona incerta nucleus stimulation for essential tremor: outcome and quality of life. J Neurol Neurosurg Psychiatry 82, 899–904 https://doi.org/10.1136/jnnp.2010.222992

23. Degeneffe, A., Kuijf, M.L., Ackermans, L., Temel, Y., Kubben, P.L., 2018. Comparing deep brain stimulation in the ventral intermediate nucleus versus the posterior subthalamic area in essential tremor patients. Surg Neurol Int 9, 244. https://doi.org/10.4103/sni.sni_234_18

24. Stenmark Persson R, Blomstedt Y, Fytagoridis A, Hariz M, Blomstedt P. Awake versus asleep deep brain stimulation targeting the caudal zona incerta for essential tremor. NPJ Parkinsons Dis. 2024 Nov 22;10(1):226. doi: 10.1038/s41531-024-00833-9.

25. Fahn, S., Tolosa, E., and Marín, C. (1988). "Clinical rating scale for tremor," in Parkinson's Disease and Movement Disorders, eds J. Jankovic, and E. Tolosa, (Munich: Urban & Schwarzenberg), 225–234

26. Louis, E.D., Wendt, K.J., Albert, S.M., Pullman, S.L., Yu, Q., Andrews, H., 1999. Validity of a performance-based test of function in essential tremor. Arch Neurol 56, 841–846. https://doi.org/10.1001/archneur.56.7.841

27. Elble, R., Bain, P., Forjaz, M.J., Haubenberger, D., Testa, C., Goetz, C.G., Leentjens, A.F.G., Martinez-Martin, P., Pavy-Le Traon, A., Post, B., Sampaio, C., Stebbins, G.T., Weintraub, D., Schrag, A., 2013. Task force report: scales for screening and evaluating tremor: critique and recommendations. Mov Disord 28, 1793–1800. https://doi.org/10.1002/mds.25648

28. Bruno, S., Nikolov, P., Hartmann, C.J., Trenado, C., Slotty, P.J., Vesper, J., Schnitzler, A., Groiss, S.J., 2021. Directional Deep Brain Stimulation of the Thalamic Ventral Intermediate Area for Essential Tremor Increases Therapeutic Window. Neuromodulation 24, 343–352. https://doi.org/10.1111/ner.13234

29. Fan, H., Bai, Y., Yin, Z., An, Q., Xu, Y., Gao, Y., Meng, F., Zhang, J., 2022. Which one is the superior target? A comparison and pooled analysis between posterior subthalamic area and ventral intermediate nucleus deep brain stimulation for essential tremor. CNS Neurosci Ther 28, 1380–1392. https://doi.org/10.1111/cns.13878

30. Barbe, M.T., Reker, P., Hamacher, S., Franklin, J., Kraus, D., Dembek, T.A., Becker, J., Steffen, J.K., Allert, N., Wirths, J., Dafsari, H.S., Voges, J., Fink, G.R., Visser-Vandewalle, V., Timmermann, L., 2018. DBS of the PSA and the VIM in essential tremor: A randomized, double-blind, crossover trial. Neurology 91, e543–e550. https://doi.org/10.1212/WNL.0000000000005956

31. Sun X, Shen R, Lin Z, Wang T, Wang L, Huang P, Feng T, Liu J, Ding J, Zhang C, Li D, Wu Y. Optimizing Deep Brain Stimulation in Essential Tremor: A Randomized Controlled Trial for Target Consideration. Neurosurgery. 2024 Jan 25;95(1):63–75. doi: 10.1227/neu.0000000000002839.

32. Hou, X., Mo, Y., Zhu, Z., Zhang, H., Liu, X., Zou, Z., He, X., Xue, S., Li, J., Li, M., Zhang, S., 2023. Technical Issues of Vim–PSA Double-Target DBS for Essential Tremor. Brain Sci 13, 566. https://doi.org/10.3390/brainsci13040566

33. Shepherd, H., Heartshorne, R., Osman-Farah, J., Macerollo, A., 2024. Dual target deep brain stimulation for complex essential and dystonic tremor - A 5-year follow up. J Neurol Sci 457, 122887. https://doi.org/10.1016/j.jns.2024.122887

34. Sun, X., Shen, R., Lin, Z., Wang, T., Wang, L., Huang, P., Feng, T., Liu, J., Ding, J., Zhang, C., Li, D., Wu, Y., 2024. Optimizing Deep Brain Stimulation in Essential Tremor: A Randomized Controlled Trial for Target Consideration. Neurosurgery 95, 63–75. https://doi.org/10.1227/neu.0000000000002839

35. Pilitsis, J.G., Metman, L.V., Toleikis, J.R., Hughes, L.E., Sani, S.B., Bakay, R.A.E., 2008. Factors involved in long-term efficacy of deep brain stimulation of the thalamus for essential tremor. J Neurosurg 109, 640–646. https://doi.org/10.3171/JNS/2008/109/10/0640

36. Cho, Z.-H., Min, H.-K., Oh, S.-H., Han, J.-Y., Park, C.-W., Chi, J.-G., Kim, Y.-B., Paek, S.H., Lozano, A.M., Lee, K.H., 2010. Direct visualization of deep brain stimulation targets in Parkinson disease with the use of 7-tesla magnetic resonance imaging. J Neurosurg 113, 639–647. https://doi.org/10.3171/2010.3.JNS091385

37. Kerl, H.U., Gerigk, L., Huck, S., Al-Zghloul, M., Groden, C., Nölte, I.S., 2012. Visualisation of the zona incerta for deep brain stimulation at 3.0 Tesla. Clin Neuroradiol 22, 55–68. https://doi.org/10.1007/s00062-012-0136-3

38. Obwegeser, AA, Uitti, RJ, Turk, MF, Strongosky, AJ & Wharen, RE 2000, 'Thalamic stimulation for the treatment of midline tremors in essential tremor patients', Neurology, vol. 54, no. 12, pp. 2342-2344. https://doi.org/10.1212/WNL.54.12.2342

39. Mitchell, K.T., Larson, P., Starr, P.A., Okun, M.S., Wharen, R.E., Uitti, R.J., Guthrie, B.L., Peichel, D., Pahwa, R., Walker, H.C., Foote, K., Marshall, F.J., Jankovic, J., Simpson, R., Phibbs, F., Neimat, J.S., Stewart, R.M., Dashtipour, K., Ostrem, J.L., 2019. Benefits and risks of unilateral and bilateral ventral intermediate nucleus deep brain stimulation for axial essential tremor symptoms. Parkinsonism Relat Disord 60, 126–132. https://doi.org/10.1016/j.parkreldis.2018.09.004

40. Lu, G., Luo, L., Liu, M., Zheng, Z., Zhang, B., Chen, X., Hua, X., Fan, H., Mo, G., Duan, J., Li, M., Hong, T., Zhou, D., 2020. Outcomes and Adverse Effects of Deep Brain Stimulation on the Ventral Intermediate Nucleus in Patients with Essential Tremor. Neural Plast 2020, 2486065. https://doi.org/10.1155/2020/2486065

41. Shetty, N., 2022. Essential Tremor—Do We Have Better Therapeutics? A Review of Recent Advances and Future Directions. Curr Neurol Neurosci Rep 22, 197–208. https://doi.org/10.1007/s11910-022-01185-8

42. Martinez-Nunez, A.E., Sarmento, F.P., Chandra, V., Hess, C.W., Hilliard, J.D., Okun, M.S., Wong, J.K., 2024. Management of essential tremor deep brain stimulation-induced side effects. Front. Hum. Neurosci. 18. https://doi.org/10.3389/fnhum.2024.1353150

TITLE

Review and Meta-Analysis of Literature Comparing Robotic Versus Frame Based Stereotactic Biopsies

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ABSTRACT

Purpose: Frame-based stereotaxy remains the gold standard for diagnostic brain biopsies. Over the past three decades, robotic stereotaxy has emerged alongside frameless techniques as an approach positioned between conventional neuronavigation and frame-based procedures. This systematic review and meta-analysis aimed to directly compare frame-based and robotic stereotactic brain biopsies (SBB).

Methods: A comprehensive search of the Medline and Scopus databases was conducted up to March 12, 2025. Studies directly comparing robotic and frame-based SBB within the same patient cohorts were included. Risk of bias was assessed using the QUADAS-2 tool. Pooled analyses were performed using random-effects models to estimate odds ratios (OR), risk ratios (RR), and mean differences (MD) with 95% confidence intervals (CI).

Results: Four retrospective studies, including 656 patients met the inclusion criteria. Risk of bias varied, with high risk related to patient selection in two studies and unclear risk regarding the reference standard in one study. Diagnostic yield was high and comparable between robotic and frame-based groups (pooled OR 1.86, p = 0.28; pooled RR 1.03, p = 0.33). Procedure times showed substantial heterogeneity. Complication rates were low and similar between groups (OR 0.86). Differences in targeting metrics were reported in one study, and they are not associated with significant differences in diagnostic yield or safety outcomes.

Conclusion: Robotic-assisted stereotactic brain biopsy can be an alternative to frame-based biopsy. However, current evidence does not demonstrate superiority over frame-based stereotaxy, which remains the reference standard. Further prospective, multicenter studies are required to validate these findings.

Keywords: Stereotactic Brain Biopsies, Robotic, Frame-based, Diagnostic accuracy, Complications, Neurosurgery

ΠΕΡΙΛΗΨΗ

Σκοπός: Η στερεοταξία με πλαίσιο παραμένει το πιο ακριβές για λήψη βιοψίας. Κατά τις τελευταίες τρεις δεκαετίες, οι στερεοτακτικές τεχνικές χωρίς πλαίσιο εξελίχθηκαν σημαντικά, ενώ η ρομποτικά υποβοηθούμενη στερεοταξία αναπτύχθηκε επίσης. Σκοπός της παρούσας συστηματικής ανασκόπησης και μετα-ανάλυσης είναι η σύγκριση της στερεοτακτικής βιοψίας με πλαίσιο και της ρομποτικά υποβοηθούμενης στερεοτακτικής βιοψίας.

Μέθοδοι: Πραγματοποιήθηκε αναζήτηση στις βάσεις δεδομένων Medline και Scopus έως τις 12 Μαρτίου 2025. Συμπεριλήφθηκαν μελέτες που συνέκριναν ρομποτική και στερεοταξία με πλαίσιο. Ο κίνδυνος μεροληψίας αξιολογήθηκε με το εργαλείο QUADAS-2. Οι αναλύσεις πραγματοποιήθηκαν με μοντέλα τυχαίων επιδράσεων για τον υπολογισμό λόγων πιθανοτήτων (OR) και λόγων κινδύνου (RR) με 95% διαστήματα εμπιστοσύνης (CI).

Αποτελέσματα: Τέσσερις αναδρομικές μελέτες, συνολικού αριθμού 656 ασθενών, πληρούσαν τα κριτήρια ένταξης. Ο κίνδυνος μεροληψίας διέφερε μεταξύ των μελετών. Η διαγνωστική απόδοση ήταν υψηλή και συγκρίσιμη μεταξύ των δύο τεχνικών, χωρίς στατιστικώς σημαντική διαφορά (συνδυαστικό OR 1,86, p = 0,28· RR 1,03, p = 0,33). Οι χρόνοι επέμβασης παρουσίασαν σημαντική ετερογένεια. Τα ποσοστά επιπλοκών ήταν χαμηλά και παρόμοια μεταξύ των ομάδων (OR 0,86). Διαφορές σε δείκτες στόχευσης αναφέρθηκε σε μια μελέτη, χωρίς επίδραση στη διαγνωστική απόδοση ή την ασφάλεια.

Συμπεράσματα: Η ρομποτικά υποβοηθούμενη στερεοτακτική βιοψία αποτελεί μια εναλλακτική τεχνική της στερεοταξίας με πλαίσιο. Ωστόσο, τα διαθέσιμα δεδομένα δεν τεκμηριώνουν σαφή κλινική υπεροχή. Απαιτούνται περαιτέρω προοπτικές, πολυκεντρικές μελέτες για την επιβεβαίωση των ευρημάτων.

INTRODUCTION

Stereotactic brain biopsy (SBB) remains a cornerstone in the diagnosis of intracranial lesions, particularly for deep-seated, inoperable, or radiologically indeterminate tumors [1]. Among the available techniques, frame-based stereotactic biopsy remains the gold standard, underpinned by more than six decades of methodological refinement demonstrating high precision, particularly in phantom-based targeting accuracy studies, consistent reproducibility, and widespread clinical applicability. Frame-based stereotaxy entails specific procedural requirements, including rigid cranial fixation by stereotactic frame placement [2].

In recent years, robotic-assisted systems have been introduced as an alternative approach to frame-based stereotaxy, incorporating mechanically guided trajectory execution based on preoperative imaging data. However, targeting accuracy remains primarily determined by imaging quality and registration methodology rather than by the guidance platform itself. Robotic systems may influence procedural workflow depending on institutional practice, but they do not inherently reduce operator dependency or expand anatomical access beyond that achievable with frame-based stereotaxy. Despite increasing availability of robotic platforms, the comparative efficacy and safety of robotic-assisted versus frame-based stereotactic brain biopsy remain subjects of ongoing debate [3].

To date, no large-scale consensus exists regarding whether robotic assistance confers a clinically meaningful advantage over frame-based stereotactic biopsy. Previous systematic reviews and meta-analyses have primarily evaluated robotic-assisted stereotactic brain biopsy as a standalone modality or compared frame-based with frameless techniques, rather than providing direct head-to-head comparisons with frame-based stereotaxy [4-6]. These studies consistently report high diagnostic yield and low complication rates for robotic-assisted biopsy but are limited by non-randomized designs, heterogeneous accuracy metrics, and the absence of comparative outcome data demonstrating superiority over frame-based techniques [4-5]. Consequently, existing literature does not establish clear clinical superiority of robotic-assisted stereotactic brain biopsy over frame-based methods, underscoring the need for direct comparative analyses [4-6]. To address this gap, we conducted a systematic review and meta-analysis restricted to studies that directly compared robotic-assisted and frame-based SBB within the same clinical cohorts. Our objective was to evaluate and synthesize current evidence regarding diagnostic yield, procedure time, complication rates, and targeting accuracy, thereby offering a clearer understanding of the relative strengths and limitations of each technique.

MATERIALS AND METHODS

The present systematic review was conducted using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 guidelines [7].

Search Strategy

We conducted a systematic search to identify relevant studies comparing robotic and frame-based SBB techniques. The databases MEDLINE and Scopus were searched using the following query, which was designed and approved by all authors: [(frame-based OR frame OR manual arm-based) AND (robot OR robotic OR robotic device) AND (biopsy OR biopsies) AND (stereotactic OR stereotaxic) AND (brain OR cerebral OR cerebellar OR brainstem)]. The final search across all databases was conducted on March 12, 2025.

Selection Process

Two independent investigators (ER and PB) screened all retrieved studies by title and abstract. Any disagreements during this stage were resolved by a third reviewer (JK). In our study, we exclusively included studies that directly compared robotic-assisted SBB with frame-based SBB. We did not include available studies involving robotic or frame-based SBB individually. This selective inclusion criterion was applied to ensure that our analysis focused on head-to-head comparisons between the two techniques, thereby providing a more accurate assessment of their relative efficacy and safety.

Inclusion and exclusion criteria

Studies were included if they 1) involved patients undergoing SBB, 2) provided a direct comparison between robotic and frame-based approaches within the same manuscript, 3) evaluated clinical, procedural, accuracy, or diagnostic outcomes, and 4) were original research articles such as randomized clinical trials, case series, or cohort studies. Full texts of potentially eligible studies were reviewed using the same inclusion strategy prior to final inclusion in the analysis.

Studies were excluded if they 1) included fewer than ten patients undergoing SBB, 2) were published in a language other than English, 3) lacked the ability to assess diagnostic accuracy (including case reports, reviews, editorials, conference abstracts, and animal or cadaveric studies), or 4) did not report outcomes for both robotic and frame-based techniques within the same cohort.

Risk of Bias and Applicability Assessment

Two authors independently evaluated the risk of bias and applicability of each included study using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. A standardized quality assessment template was used throughout the process. Any disagreements were resolved through consensus among the reviewers [8,9].

Data Extraction

A standardized data extraction table, pre-approved by all authors, was developed to ensure consistent and comprehensive data collection. Two authors (ER and PB) independently completed the table for each included study. The table included the following fields: eligibility (yes/no), first author, year of publication, study design (prospective or retrospective), title, type of study, study population, number of patients, number of patients in the robot-assisted group, number of patients in the frame-based group, mean age, sex distribution, targeting accuracy, sensitivity, specificity, area under the curve (AUC), total number of SBB, number of diagnostic SBBs, diagnostic yield (in percentage), reported complications, additional comments, authors, journal name, and study DOI.

Statistical Analysis

Meta-analysis was performed using Review Manager (RevMan) and SPSS. For binary outcomes (e.g., diagnostic yield, complications), pooled odds ratios (OR) or risk ratios (RR) were calculated with 95% confidence intervals (CI). For continuous outcomes (e.g., operative time), mean differences (MD) were used.

A random-effects model was employed for all analyses to account for between-study variability. Heterogeneity was assessed using the I^2 statistic, with thresholds of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. The Chi^2 test was also used to evaluate statistical significance of heterogeneity, with $p < 0.05$ indicating significance. The Z-test was used to assess overall effect estimates, and statistical significance was defined as $p < 0.05$. All statistical analyses were performed using Review Manager (RevMan) version 5.4.

Subgroup and Sensitivity Analyses

Subgroup analysis was performed for each outcome separately: diagnostic yield, operative time, and complications. Sensitivity analysis was considered by excluding studies with high risk of bias or outliers where applicable..

RESULTS

Following the systematic search, 43 records were identified through the MEDLINE/PubMed database and 12 through the SCOPUS database, yielding a total of 55 records. No duplicates were found. All 55 records were screened by title and abstract, resulting in the exclusion of 19 studies that did not meet the inclusion criteria. The remaining 36 studies were retrieved in full text and assessed for eligibility.

Of these, two studies were excluded due to the absence of a direct comparison between robotic and frame-based techniques. Nineteen studies were excluded because they evaluated only robotic SBB, while four focused solely on frame-based SBB. Two additional studies were excluded as they contained only technical notes without outcome data. Finally, two studies were excluded for being reviews or meta-analyses rather than original research.

As a result, four studies [10-13] met all inclusion criteria and were included in the systematic review, comprising a total of 656 patients. The search results and study selection process are illustrated in the PRISMA 2020 flow diagram for systematic reviews involving database, register, and other source searches [7], as shown in Figure 1.

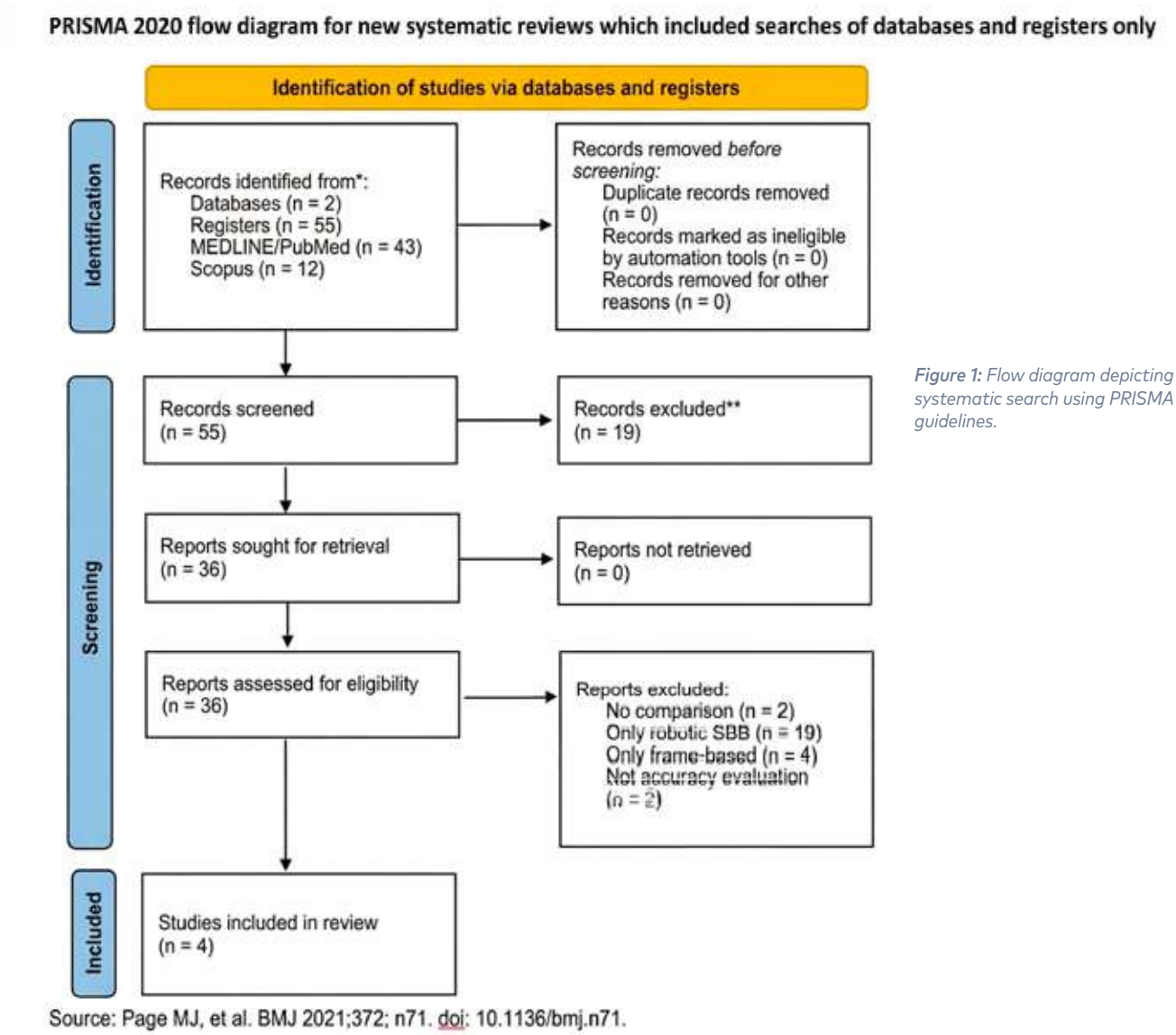


Figure 1: Flow diagram depicting systematic search using PRISMA guidelines.

Source: Page MJ, et al. BMJ 2021;372: n71. doi: 10.1136/bmj.n71.

Risk of Bias and Applicability Assessment

The four included studies were assessed for risk of bias across four domains using the QUADAS-2 tool, across four domains: patient selection, index test, reference standard, and flow and timing. Within the patient selection domain, two studies [12,13] were judged to have a high risk of bias, while the other two [10,11] showed a low risk. None of the studies exhibited a high risk of bias in the index test domain [10–13]. In the reference standard domain, three studies were found to have a low risk of bias [10, 11, 13], whereas one study demonstrated an unclear risk [12]. Regarding the flow and timing domain, one study [12] was rated as having a high risk of bias, while the remaining three studies showed a low risk [10, 11, 13].

Applicability concerns were also evaluated using the QUADAS-2 tool across three domains. In the patient domain, two studies had low concerns [10, 11], while two had high concerns [12, 13]. All four studies were judged to have low applicability concerns in both the patient selection and index test domains. In the reference standard domain, one study [12] showed unclear applicability concerns, whereas the other three studies [10, 11, 13] presented low concerns.

A visual summary of the risk of bias and applicability assessments for each study is presented in Figure 2.

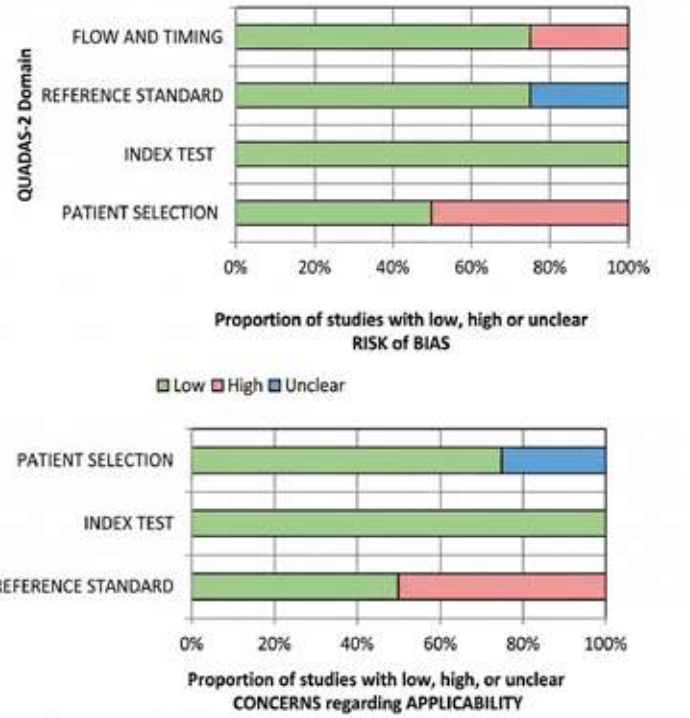
Figure 2. Summary of the risk of bias and applicability assessments for each study

A

STUDY	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Li et al.	Low	Low	Low	Low
Hu et al.	Low	Low	Low	Low
Spyrantis et al.	High	Low	Unclear	High
Wu et al.	High	Low	Low	Low

STUDY	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Li et al.	Low	Low	Low
Hu et al.	Low	Low	Low
Spyrantis et al.	High	Low	Unclear
Wu et al.	High	Low	Low

B



Characteristics of the Included Studies

This systematic review and meta-analysis included four retrospective studies published between 2021 and 2023, comprising a total of 656 patients undergoing SBB. Two studies enrolled mixed pediatric and adult populations [10,11], with children constituting up to 54.5% of the sample in one study [10]. The total sample size ranged from 33 to 406 patients per study. The robotic-assisted biopsy groups included 22 to 148 patients, while the frame-based groups had 11 to 258 patients. Mean patient age varied substantially among studies, reflecting differences in population focus: robotic groups ranged from 17.3 ± 18.7 years to 62 years, while frame-based groups ranged from 32.8 ± 17.1 to 60 years. The sex distribution was generally balanced, with male-to-female ratios roughly similar between groups. The robotic systems assessed were Remebot [10,13], Sino [11], and ROSA [12]. Frame-based stereotactic biopsies, considered the standard approach, served as comparators in all studies.

The characteristics of the studies are summarized in Table 1.

Table 1. Characteristics and results of the included studies.

Author (Year)	Study Design	Population	Sample Size	Robotic Group	Frame-Based Group	Age (Mean ± SD)	Sex (M/W)
Li et al. (2023)	Retrospective	Children and adults (54.5% <16 yrs)	33	22 (Remebot)	11	ROB: 17.3 ± 18.7 FRAME: 32.8 ± 17.1	ROB: M7/W15 FRAME: M7/W4
Hu et al. (2022)	Retrospective	Children and adults	151	104 (Sino)	47	SINO: 45.3 ± 19.2 FRAME: 49.2 ± 15.8	SINO: M62/W42 FRAME: M28/W19
Spyrantis et al. (2021)	Retrospective	Adults	406 (416 biopsies)	148 (ROSA, 150 biopsies)	258 (266 biopsies)	ROSA: 62 yrs (24–88) FRAME: 60 yrs (18–88)	ROSA: M87/W61 FRAME: M157/W101
Wu et al. (2021)	Retrospective	Adults	66	31 (Remebot)	35	ROB: 46 ± 13 FRAME: 45 ± 16	ROB: M18/W13 FRAME: M21/W14

Qualitative Synthesis

Across the four included studies, robotic-assisted SBB demonstrated comparable diagnostic yield and safety profiles to conventional frame-based techniques. Diagnostic yield was consistently reported in all studies, with the robotic biopsy groups achieving yields ranging from 91.5% to 98%, while the frame-based groups demonstrated yields between 91% and 95.9%. In three of the four studies, the differences in diagnostic yield between the two modalities were not statistically significant [10,11,13]. However, Spyrantis et al. reported a significantly higher diagnostic yield in the robotic group compared to the frame-based group (98% vs. 91%, p = 0.0036) [12]. This isolated finding was not reproduced in other studies and therefore does not provide sufficient evidence to support a consistent clinical advantage of robotic assistance.

Only one included study reported quantitative metrics of procedural accuracy [11]. However, no corresponding differences were observed in diagnostic yield or complication rates between techniques. Similarly, Wu et al. reported that patients undergoing robotic biopsies experienced lower levels of procedural discomfort, as measured by visual analog scale (VAS) scores, indicating lower reported patient discomfort tolerance [13].

Procedure duration varied across the studies. Wu et al. observed significantly shorter procedure times with robotic-assisted biopsies, whereas both Hu et al. and Spyrantis et al. found that robotic procedures took longer than frame-based biopsies. In contrast, Li et al. reported no significant difference in operative time between the two approaches [10]. These discrepancies likely reflect differences in the type of robotic platform used, operator familiarity with robotic systems, and institutional protocols.

Patient comfort appeared to be improved with robotic techniques in the study by Wu et al., where subjects reported less discomfort during the procedure [13]. However, findings regarding procedural efficiency remained inconsistent. The substantial variability in reported durations and patient experiences may be attributed to heterogeneous factors, including robotic system design, technical workflow, and surgical team experience.

Notably, the study by Spyrantis et al. was the only investigation to demonstrate a statistically significant improvement in diagnostic yield favoring robotic SBB [12]. This isolated finding raises the hypothesis that robotic systems could influence targeting precision; however, this was not supported by consistent improvements in diagnostic yield or safety and therefore remains speculative. Furthermore, this finding was not consistently reproduced across the included studies and requires confirmation in well-designed prospective investigations.

The outcomes of the studies are summarized in Table 2.

Table 2. Comparative Outcomes of Robotic and Frame-Based Stereotactic Brain Biopsy Technique

Author (Year)	Diagnostic Yield	Procedure time (Mean ± SD minutes)	Visual Analog Scale (VAS)	Complications	Accuracy /Technical Findings	Key Conclusions
Li et al. (2023)	ROB: 21/22 (95.9%) FRAME: 10/11 (95.9%) *p > 0.9*	ROB: 44.14 ± 1.4 FRAME: 45.35 ±2.67	Not reported	No significant difference	Not reported	No significant differences in yield or complications
Hu et al. (2022)	SINO: 45/47 (98.1%) FRAME: 102/104 (95.7%) *p > 0.05*	SINO:59.1 ± 9 FRAME:49.4 ± 12.1	Not reported (comfort/ discomfort is discussed but not measured)	No significant difference	Entry error: FRAME: 1.33 ± 0.40 mm, ROBOT: 0.92 ± 0.27 mm Target error: FRAME: 1.63 ± 0.41 mm, ROBOT: 1.10 ± 0.30 mm (p < 0.001)	Robotic biopsy is more accurate; no increase in complications
Spyrantis et al. (2021)	ROSA: 147/150 (98%) FRAME: 242/266 (91%) *p = 0.0036*	ROSA: 140 ± 32.6 FRAME: 113 ±30.7	Not reported	No significant difference	Operating time similar (100–113 min) ROSA is slightly faster with local anesthesia	Robotic method offers higher yield and shorter overall time
Wu et al. (2021)	ROB: 29/31 (93.5%) FRAME: 32/35 (91.5%) *p = 0.75*	ROB: 29.25 ± 1.4 FRAME: 45.45 ± 2.67	ROM: 1.5 FRAME: 2.7 *(p < 0.001)*	No significant difference	Patients reported lower discomfort with robotics	Robotic approach is better tolerated by patients

Technical Registration and Accuracy Metrics

Registration and technical accuracy-related metrics were inconsistently reported across studies (Table 3).

Only one study [11] provided quantitative measures of stereotactic accuracy, reporting both EPE and TPE. In that study, significantly lower target entry point error (TPE) and entry point error (EPE) were observed in the robotic group compared with the frame-based group [TPE : 1.10 ± 0.30 (0.69–2.03) mm vs 1.63 ± 0.41 mm (0.74–2.65), P < 0.001 and EPE: 0.92 ± 0.27 mm (0.35–1.65) vs 1.33 ± 0.40 mm (0.47–2.30) vs. P < 0.001][11].

The remaining studies did not report quantitative targeting accuracy metrics. Instead, they provided technical parameters related to registration and instrumentation, including registration modality (e.g., surface matching, skin markers, bone fiducials, or frame-based CT registration), CT slice thickness, burr hole diameter, and needle dimensions. Registration methods varied between robotic and frame-based approaches, with robotic systems relying on CT and surface matching, skin markers, or bone fiducials, whereas frame-based systems used CT or MRI with frame-based coordinates.

Trajectory length was reported in one study [10], with shorter mean trajectories in the robotic group compared with the frame-based group (71.3 mm vs. 91.1 mm). However, no study systematically evaluated the impact of these technical differences on clinical outcomes.

For frame-based SBB, all included studies utilized the Leksell Frame G stereotactic frame (Elekta Inc., Stockholm, Sweden) [10–12]. In robotic-based SBB, head fixation was achieved using a Mayfield clamp (Integra Neurosciences Inc., Plainsboro, NJ, USA) [10–13]. Hu et al. employed five bone fiducials placed on the patient's head in combination with a Mayfield head holder connected to the robotic system [11].

In three studies, the same surgeon performed both procedures [10,11,13].

Table 3. Technical registration and accuracy-related metrics in included studies

Study (Year)	Technique	Head Fixation	Registration Method	Accuracy Metrics (Mean in mm)	Other Technical Metrics
Spyrantis et al. (2021)	ROSA robot-guided biopsy	Mayfield skull clamp	Facial laser scan (surface matching)	Not reported	Burr hole 2.1 mm; CT slice 1.25 mm
	Frame-based biopsy	Leksell frame fixed to OR table	CT with frame (1.25 mm)	Not reported	Burr hole ~10 mm
Wu et al. (2021)	Remebot robot-assisted biopsy	Mayfield clamp	CT with skin markers	Not reported	Burr hole 10 mm; needle 2.5 mm
	Frame-based biopsy	Leksell Frame G	MRI planning + frame coordinates	Not reported	Burr hole 10 mm; needle 2.5 mm
Hu et al. (2022)	SINO robot-assisted biopsy	Mayfield head holder	Bone fiducials + CT	EPE 0.92 mm TPE 1.10 mm	Drill 3.0 mm; nails 4×5 mm; CT 1 mm
	Frame-based biopsy	Leksell frame	CT with frame (1 mm)	EPE 1.33 mm TPE 1.63 mm	Drill 3.0 mm
Li et al. (2023)	Remebot frameless brainstem biopsy	Mayfield clamp	Laser-based surface registration	Trajectory length 71.3 mm	CT slice 0.625 mm; needle 2.5 mm
	Frame-based brainstem biopsy	Leksell Frame G	MRI + frame coordinates	Trajectory length 91.1 mm	Burr hole 10 mm; needle 2.5 mm

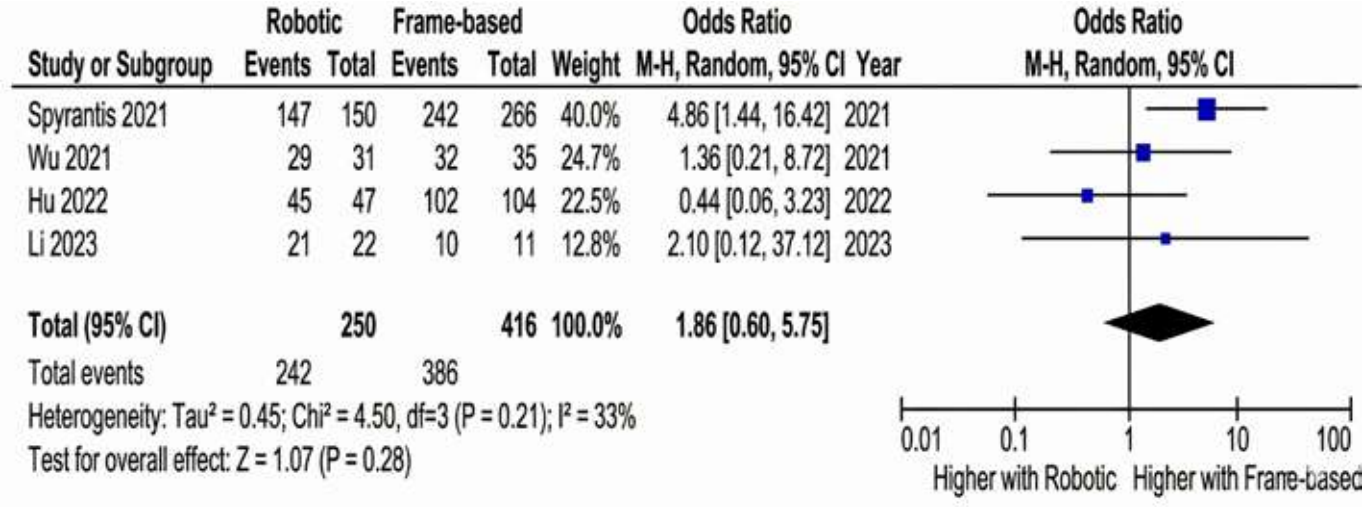
EPE: Entry Point Error, TPE: Target Point Error, Or: Operation Room, CT: Computer Tomography, MRI: Magnetic Resonance Imaging

Meta-analysis

Diagnostic Yield

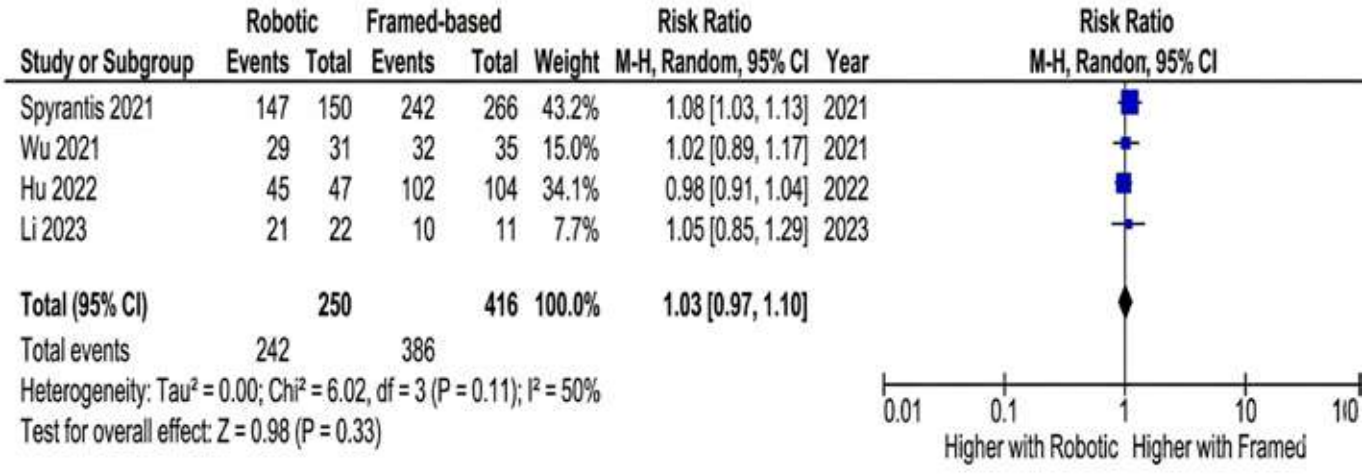
The meta-analysis for diagnostic yield incorporated data from all four included studies, encompassing a total of 656 patients. Across the four comparative studies, diagnostic tissue was obtained in 242 of 250 robotic-assisted biopsies and 386 of 416 frame-based biopsies. The pooled OR for obtaining a diagnostic result using robotic-assisted SBB, compared to frame-based biopsy, was 1.86 with a 95% CI of 0.60 to 5.75. Although the point estimate numerically favored robotic-assisted biopsy, this difference was not statistically significant. (p = 0.28). Moderate heterogeneity was observed among the studies (I^2 = 33%, Chi^2 = 4.50, p = 0.21), indicating acceptable variability and allowing for meaningful synthesis of results (Figure 3).

Figure 3. Forest plot of the diagnostic Yield with Odds Ratio



A pooled RR was also computed to further assess the relative performance of the two techniques. The RR was 1.03 (95% CI: 0.97 to 1.10), suggesting that robotic biopsies were marginally more likely—by approximately 3%—to yield a diagnostic result compared to frame-based approaches. However, this difference was also not statistically significant (Z = 0.98, p = 0.33), and the CI crossed the null value of 1.0. Moderate heterogeneity was again noted (I^2 = 50%, Chi^2 = 6.02, p = 0.11), reflecting some degree of methodological and clinical diversity across the included studies (Figure 4).

Figure 4. Forest plot of the diagnostic yield with Risk Ratio



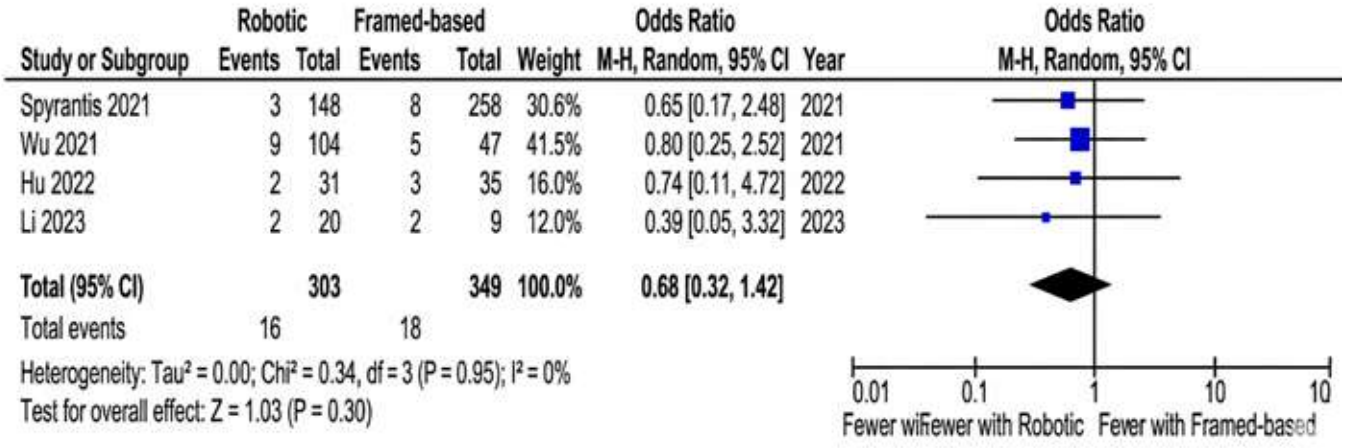
Procedure Time

All four studies provided data on procedure duration, but results were highly inconsistent. Due to high heterogeneity between the four studies no meta-analysis of duration time has been conducted.

Complications

Complications occurred in 16 of 303 robotic-assisted biopsies (5.3%) and 18 of 349 frame-based biopsies (5.2%). Pooled analysis using a random-effects Mantel–Haenszel model demonstrated no statistically significant difference between groups (OR 0.68, 95% CI 0.32–1.42; p = 0.30). Statistical heterogeneity was negligible (I^2 = 0%, Chi^2 = 0.34, p = 0.95 (Figure 5). While heterogeneity was low, this likely reflects uniformly low event rates and limited statistical power. Therefore, the absence of a statistically significant difference should not be interpreted as evidence of equivalence between techniques.

Figure 5. Forest plot of complications



DISCUSSION

This systematic review and meta-analysis synthesize available evidence comparing robotic-assisted and frame-based stereotactic brain biopsy based on four retrospective studies involving a total of 656 patients. The results demonstrate low complication rates and similar diagnostic yields in both groups; however, the limited number of studies, retrospective design, and low event rates substantially restrict the strength of comparative conclusions.

No statistically significant differences were identified in complication rates or diagnostic yield between robotic-assisted and frame-based techniques. Claims regarding improved targeting accuracy, patient comfort, or procedural efficiency with robotic-assisted biopsy could not be substantiated, as these outcomes were not consistently measured or reported across the included studies. Moreover, differences in fixation methodology, rigid stereotactic frames versus Mayfield head clamp–based immobilization, were not evaluated in terms of mechanical stability or targeting precision.

Procedure duration did not demonstrate consistent or statistically significant differences between techniques. Given the long-standing clinical use and validated accuracy of frame-based stereotactic biopsy, which remains a reference standard in many centers, the available data do not support claims of superiority or equivalence of robotic-assisted approaches.

Notably, only one included study employed bone fiducials for registration in robotic-based SBB [11]. This heterogeneity in registration methodology limits comparability of targeting accuracy and technical performance metrics across studies.

Diagnostic Yield

All included studies reported high diagnostic yields for both techniques, with successful tissue diagnosis achieved in 96.8% (242/250) of robotic-assisted biopsies and 92.8% (386/416) of frame-based biopsies. Pooled results suggesting a non-significant trend favoring robotic-assisted biopsies (OR 1.86, p = 0.28; RR 1.03, p = 0.33). Only one study demonstrated a statistically significant benefit for robotic systems (98% vs. 91%, p = 0.0036) [12]. These findings indicate that according to authors reports, robotic platforms may achieve high diagnostic success in selected settings; however, the overall evidence is insufficient to establish superiority over frame-based techniques.

The moderate heterogeneity observed (I^2 = 33–50%) reflects some variability in study populations, lesion characteristics, and robotic platforms used. A meta-analysis by Porto Junior et al. reported a pooled diagnostic yield of 98% (95% CI: 97–98%) and another one by Marcus et al. reported a rate from 75 to 100% [4,5]. In contrast, our analysis of head-to-head comparative studies found yields ranging from 91.5% to 98% in the robotic group, with pooled risk and odds ratios that did not reach statistical significance (RR 1.03; OR 1.86). These findings may suggest comparable diagnostic performance when directly compared with frame-based biopsy, without definitive evidence of superiority.

Procedure Time

Findings related to procedural duration were inconsistent across studies. While Wu et al. reported significantly shorter operative times with robotic assistance, Hu et al. and Spyrantis et al. found the opposite, and Li et al. observed no meaningful difference. These discrepancies are likely attributable to institutional workflow differences, operator experience, and platform-specific setup times. Thus, procedure time should be interpreted as context-dependent rather than inherently superior in either modality. In recent meta-analysis the mean time for robotic SBB was 52.45 min (95% CI: 37.83-67.07) [4].

Complications and Safety

Across all included studies, complication rates were low for both robotic-assisted and frame-based biopsies. Porto Junior et al. reported postoperative hemorrhage rates of approximately 6%, transient neurological deficits of 4%, and no procedure-related mortality, findings that are consistent with the low complication rates observed in the studies included in the present review [4]. The pooled complication analysis demonstrated no statistically significant difference between techniques (OR 0.68, 95% CI: 0.32–1.42; p = 0.30).

Although heterogeneity was negligible (I^2 = 0%), this likely reflects uniformly low event rates and limited statistical power rather than robustness of the pooled estimate. Therefore, these findings indicate that both techniques are associated with low reported complication rates, but they do not establish equivalence of safety profiles or procedural mechanics.

Targeting Accuracy and Patient Comfort

In the literature, targeting errors reflecting the precision achievable with robotic guidance vary from 0.9 to 4.5 mm [4], and a recent meta-analysis reported a mean error of 1.08 mm (95% CI: 0.49–1.66) [5]. Only one study [11] provided quantitative targeting accuracy data, limiting the strength of any comparative conclusions. However, this finding was based on a single study using a specific registration method and did not translate into improvements in diagnostic yield or complication rates. Moreover, these measurements likely reflect clinical workflow accuracy rather than intrinsic system precision and were influenced by differing registration strategies between techniques. Reported accuracy for Remebot systems in the literature was approximately 3 mm, which is inferior to that typically achieved with frame-based systems [10,13].

Importantly, the observed differences in localization error did not translate into statistically significant improvements in diagnostic yield or reductions in complication rates. When considered alongside evidence from phantom-based assessments, frame-based stereotaxy remains the gold standard for stereotactic accuracy, and both techniques appear comparably effective and safe in clinical practice. Wu et al. also reported lower patient discomfort scores for robotic-assisted procedures, likely due to the elimination of the stereotactic head frame [13]. While this may affect patient experience in selected settings, these findings are based on limited data and do not alter diagnostic or safety outcomes.

Limitations

This analysis has several limitations. First and foremost, our study exclusively included research that directly compared robotic-assisted SBB with frame-based SBB within the same patient cohorts. While this head-to-head design enhances the internal validity of our comparative analysis, it also resulted in the exclusion of a broader body of literature involving single-arm studies, which may contain valuable insights into each technique's individual performance, safety, and operational nuances. By focusing solely on comparative studies, we may have inadvertently omitted high-quality data on robotic-assisted or frame-based SBB that could have enriched our understanding of each modality's strengths and limitations in isolation. This exclusion limits the generalizability of our findings to settings where only one modality is in use.

Moreover, all included studies were retrospective in nature, which introduces inherent selection bias and limits the ability to establish causality. Furthermore, variations in robotic platforms, surgical techniques, and patient populations introduce heterogeneity, especially regarding procedure time and accuracy outcomes. Only one study provided data on quantitative targeting error [11], and none included long-term follow-up on neurological outcomes. The small number of directly comparative studies limits the statistical power and generalizability of our findings.

Implications and Future Directions

Robotic-assisted SBB constitutes may be an alternative to frame-based SBB for some neurosurgeons. However, current evidence does not support definitive clinical superiority over frame-based stereotaxy, which remains the reference standard. Further well-designed, prospective, multicenter studies employing standardized protocols are required to confirm these findings and to evaluate cost-effectiveness, training requirements, and long-term outcomes.

CONCLUSIONS

This systematic review and meta-analysis evaluated the comparative performance of robotic-assisted and frame-based stereotactic brain biopsy across four retrospective studies involving 656 patients. The findings demonstrate that both techniques are associated with high diagnostic yields and low complication rates, with no statistically significant differences in diagnostic success, safety, or procedure duration.

However, the strength of these conclusions is limited by the small number of studies, retrospective design, low event rates, and heterogeneity in study populations, robotic platforms, and outcome definitions. Importantly, the absence of statistically significant differences should not be interpreted as evidence of equivalence or superiority of robotic-assisted approaches. Outcomes related to fixation stability, targeting precision, patient positioning, and surgical access were not systematically assessed and therefore cannot be inferred from the current data.

Frame-based stereotactic biopsy remains the reference standard due to its rigid cranial fixation, unrestricted patient positioning, and broad surgical access. Frame-based systems permit flexible trajectory planning and positioning strategies. In contrast, current robotic-assisted systems typically require straight head positioning and predominantly limit trajectories to frontal or central approaches.

Based on the available evidence, robotic-assisted SBB should be regarded as a complementary, indication-specific technique rather than a replacement for established frame-based stereotactic methods, which remain the reference standard. Further prospective, multicenter studies using standardized protocols and objective accuracy metrics are required to better define the role of robotic systems in stereotactic brain biopsy, including their potential benefits, limitations, and cost-effectiveness.

ABBREVIATIONS LIST

AUC	Area Under the Curve
Chi²	Chi-square test
CI	Confidence Interval
CT	Computed Tomography
EPE	Entry Point Error
I²	Higgins' inconsistency index
MD	Mean Difference
MRI	Magnetic Resonance Imaging
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies 2
RevMan	Review Manager
RR	Risk Ratio
SBB	Stereotactic Brain Biopsy
SPSS	Statistical Package for the Social Sciences
TPE	Target Point Error
VAS	Visual Analog Scale

REFERENCES

1. Gkampenis A, Romeo E, Koukoulithras I, Lampros M, Voulgaris S, Tzakos AG, Alexiou GA. A systematic review evaluating the effectiveness of nuclear medicine techniques in enhancing the diagnostic accuracy of stereotactic brain biopsies. Neurosurg Rev. 2025 Jul 1;48(1):538. doi: 10.1007/s10143-025-03698-5

2. Smith JS, Quiñones-Hinojosa A, Barbaro NM, McDermott MW. Frame-based stereotactic biopsy remains an important diagnostic tool with distinct advantages over frameless stereotactic biopsy. J Neurooncol. 2005 Jun;73(2):173-9. doi: 10.1007/s11060-004-4208-3.

3. Bex A, Mathon B. Advances, technological innovations, and future prospects in stereotactic brain biopsies. Neurosurg Rev. 2022 Dec 6;46(1):5. doi: 10.1007/s10143-022-01918-w..

4. Porto Junior S, Meira DA, da Cunha BLB, Fontes JHM, Pustilnik HN, Medrado Nunes GS, Cerqueira GA, Vassoler MEM, Monteiro PQ, da Silva da Paz MG, Alcântara T, Carlos Dourado J, de Avellar LM. Robot-assisted stereotactic brain biopsy: A systematic review and meta-analysis. Neurosurg Rev. 2024 Dec 4;47(1):886. doi: 10.1007/s10143-024-03122-4. PMID: 39627622

5. Marcus HJ, Vakharia VN, Ourselin S, Duncan J, Tisdall M, Aquilina K. Robot-assisted stereotactic brain biopsy: systematic review and bibliometric analysis. Childs Nerv Syst. 2018 Jul;34(7):1299-1309. doi: 10.1007/s00381-018-3821-y. Epub 2018 May 10. PMID: 29744625; PMCID: PMC5996011.

6. Dhawan S, He Y, Bartek J Jr, Alattar AA, Chen CC. Comparison of Frame-Based Versus Frameless Intracranial Stereotactic Biopsy: Systematic Review and Meta-Analysis. World Neurosurg. 2019 Jul;127:607-616.e4. doi: 10.1016/j.wneu.2019.04.016

7. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration:

updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.

8. Reitsma JB, Rutjes AW, Whiting P, Yang B, Leeflang MM, Bossuyt PM, et al. Assessing risk of bias and applicability. In: Deeks JJ, Bossuyt PM, Leeflang MM, Takwoingi Y, editors. Cochrane Handb Syst Rev Diagn Test Accuracy [Internet]. 1st ed. Wiley; 2023 [cited 2024 Mar 19]. p. 169–201. Available from: https://onlinelibrary.wiley.com/doi/10.1002/9781119756194.ch8

9. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011; 155:529–36.

10. Li C, Wu S, Huang K, Li R, Jiang W, Wang J, Shu K, Lei T. A Comparison of the Safety, Efficacy, and Accuracy of Frame-Based versus Remebot Robot-Assisted Stereotactic Systems for Biopsy of Brainstem Tumors. Brain Sci. 2023 Feb 20;13(2):362. doi: 10.3390/brainsci13020362.

11. Hu Y, Cai P, Zhang H, Adilijiang A, Peng J, Li Y, Che S, Lan F, Liu C. A Comparation Between Frame-Based and Robot-Assisted in Stereotactic Biopsy. Front Neurol. 2022 Jul 18;13:928070. doi: 10.3389/fneur.2022.928070

12. Spyrantis A, Woebbecke T, Constantinescu A, Cattani A, Quick-Weller J, Willems LM, Marquardt G, Seifert V, Freiman TM. Comparison of frame-less robotic versus frame-based stereotactic biopsy of intracranial lesions. Clin Neurol Neurosurg. 2021 Aug;207:106762. doi: 10.1016/j.clineuro.2021.106762.

13. Wu S, Wang J, Gao P, Liu W, Hu F, Jiang W, Lei T, Shu K. A comparison of the efficacy, safety, and duration of frame-based and Remebot robot-assisted frameless stereotactic biopsy. Br J Neurosurg. 2021 Jun;35(3):319-323. doi: 10.1080/02688697.2020.1812519

CASE REPORT

Upper cervical schwannoma in a 46- year- old male patient: an interesting case report in our clinic

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ABSTRACT
Schwannomas are a rare type of benign tumors, which typically develop without presenting any neurological symptoms, due to their slow- growth. While they can occur anywhere along the peripheral nerves, upper cervical spinal schwannomas are extremely rare and often pose diagnostic and surgical challenges. We present a case of a 46-year-old male patient, who complained about progressive weakness and numbness of his right arm and headache for one year. Neurological examination showed hypoesthesia in the C3-C4 dermatomes with mild motor weakness. MRI demonstrated a well-circumscribed, enhancing mass at the C2-C3 level, suggestive of a schwannoma. The patient underwent a posterior cervical laminectomy and gross total excision of the tumor. Histopathological examination confirmed the diagnosis of schwannoma. Early post- operative recovery was uneventful, but due to severe surgical site infection, the patient was hospitalized for intravenous antibiotic therapy. He was discharged after approximately one month, without any neurological symptoms..

Keywords: Upper cervical, schwannoma, spine surgery, posterior laminectomy

ΠΕΡΙΛΗΨΗ
Τα σβαννώματα είναι ένας σπάνιος τύπος καλοηθών όγκων, οι οποίοι συνήθως αναπτύσσονται αργά, χωρίς να παρουσιάζουν νευρολογικά συμπτώματα. Ενώ μπορούν να εμφανιστούν οπουδήποτε κατά μήκος της σπονδυλικής στήλης, τα σβαννώματα της άνω αυχενικής μοίρας της σπονδυλικής στήλης είναι εξαιρετικά σπάνια και συχνά αποτελούν διαγνωστική και χειρουργική πρόκληση. Παρουσιάζουμε την περίπτωση ενός 46χρονου άνδρα, ο οποίος ανέφερε προοδευτική αδυναμία και αιμωδίες του δεξιού άνω άκρου και κεφαλαλγία από έτους. Η νευρολογική εξέταση έδειξε υπαισθησία στα δερμοτόμια A3-A4 με ήπια μυϊκή αδυναμία. Η μαγνητική τομογραφία απεικόνισε μια καλά περιγεγραμμένη, ενισχυόμενη μάζα στο επίπεδο A2-A3, με χαρακτηριστικά σβαννώματος. Ο ασθενής υποβλήθηκε σε αυχενική πεταλεκτομία και υφολική εκτομή του όγκου. Η ιστοπαθολογική εξέταση επιβεβαίωσε τη διάγνωση του σβαννώματος. Η πρώιμη μετεγχειρητική ανάρρωση ήταν ομαλή, αλλά λόγω σοβαρής λοίμωξης της χειρουργικής περιοχής, ο ασθενής νοσηλεύτηκε για ενδοφλέβια αντιβιοτική θεραπεία. Πήρε εξιτήριο μετά από περίπου ένα μήνα, χωρίς νευρολογική συμπτωματολογία..

Λέξεις κλειδιά: Άνω αυχενική μοίρα, σβάννωμα, χειρουργική επέμβαση σπονδυλικής στήλης, πεταλεκτομία.

INTRODUCTION

Schwannomas are benign peripheral nerve sheath tumors, accounting for approximately 25-30% of all spinal tumors [1]. Although, atypically presented in the thoracic or lumbar spine area, cervical spine schwannomas are extremely rare cases and can present with variable, non-specific clinical symptoms [2].

Especially in terms of upper cervical region, this anatomical area contains critical neurovascular structures, the medulla oblongata, spinal cord, vertebral arteries, and the spinal nerve roots of C1–C3, making neoplasms in this area diagnostically and surgically challenging. Patients may present with neck pain, sensory disturbances, radiculopathy, or even signs of myelopathy depending on the size and location of the lesion [3].

Magnetic resonance imaging (MRI) is "gold standard" imaging method for diagnosis and pre- operative planning, typically revealing a well-demarcated, iso- to hypointense lesion on T1-weighted images and hyperintense on T2-weighted sequences, with homogeneous or heterogeneous enhancement after contrast administration [4]. Computed tomography (CT) may be helpful to assess bony involvement or foraminal widening [5].

Surgical resection remains the treatment of choice for symptomatic schwannomas. The goal is gross total resection while preserving neurological function. Histological examination should be always undertaken, in order to confirm the diagnosis. The prognosis is generally favorable, with low recurrence rates following complete resection.

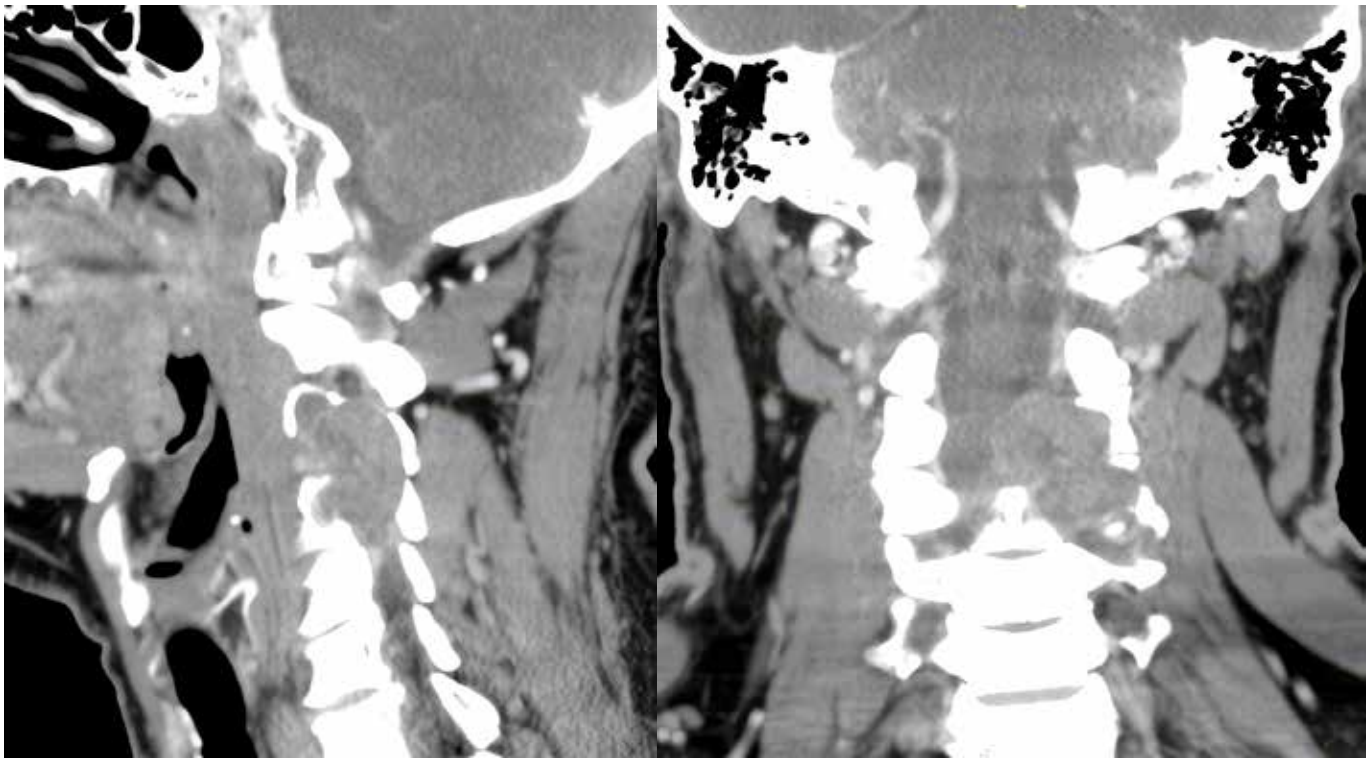
In this case report, we present a rare case of an upper cervical schwannoma in a male patient, highlighting the clinical presentation, radiological features, surgical approach, and outcome.

CASE REPORT

A 46- year- old male patient came to our outpatient clinic, complaining about progressive weakness and numbness of his right arm and headache for one year. He did not mention any severe traumatic brain or cervical injury, but he experienced intense physical fatigue through work. Neurological examination showed hypoesthesia in the C3-C4 dermatomes with mild motor weakness of the shoulder in the right upper limb. Further clinical examination was without pathological findings. Upon taking his medical history, only the intake of anti- hypertensive therapy during the last two years was noted.

Brain and cervical MRI were performed. The former did not show any pathological issues, the latter were performed with intravenous contrast and showed a well-demarcated, hypointense lesion on T1-weighted images and hyperintense

Figure 1: CT scan



on T2-weighted sequences, located intradural extramedullary mainly in the third cervical vertebrae, extended also in the second and fourth cervical vertebrae, with heterogeneous enhancement after contrast administration. In order to identify the bony involvement, we also prescribed a cervical CT, which showed vertical scalloping of the third cervical vertebrae, without osteolytic characteristics. [Figure 1]. Due to the neurological symptoms that reduce the patient's quality of life and the diagnosis of schwannoma, we suggested surgical excision.

We performed C2, C3 and C4 posterior laminectomy and gross total resection of the tumor. [Figure 2] There were no peri- operative complications and the patient was transferred to our clinic. During the first 3 days post- operatively, he complained about mild motor weakness of the right upper and lower limb, with symptoms disappearing gradually. He was discharged 6 days post- operatively, without any complications.

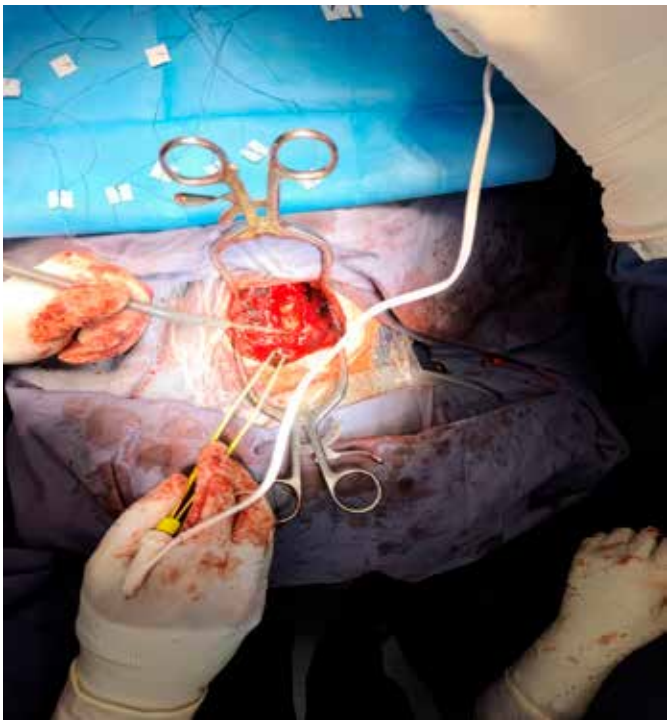


Figure 2: Intraoperative picture

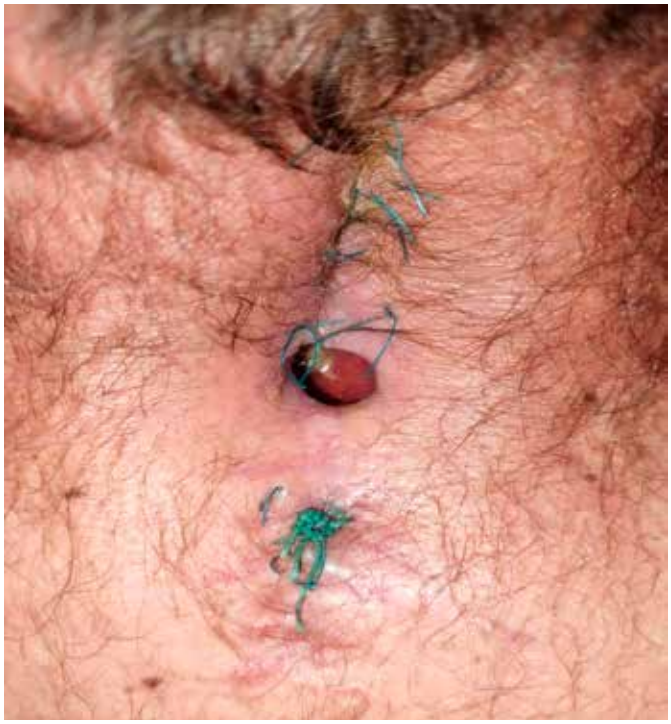


Figure 3. *20th day postoperatively*

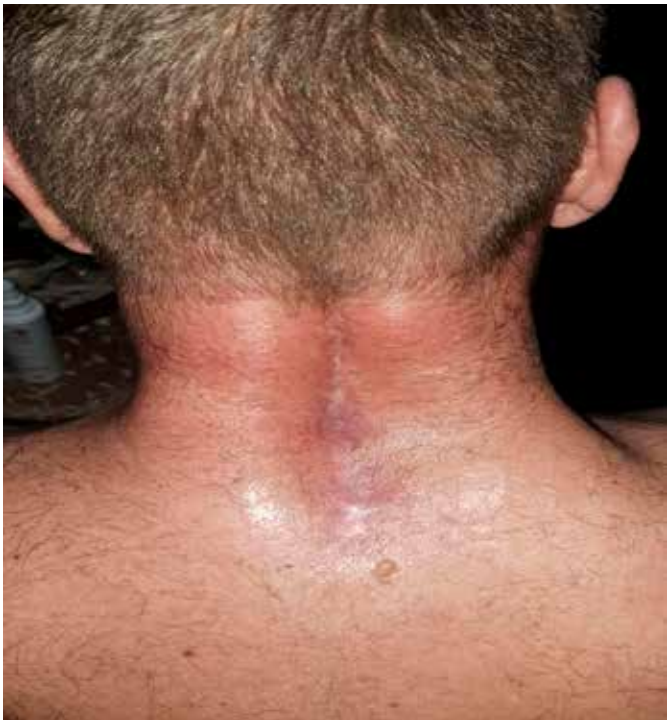


Figure 4. *First day after discharge*

In the twelfth post- operative day, he complained about severe headache, fever and malodorous trauma leakage. [Figure 3] We took cultures from different sides of the traumatic area, and the patient was hospitalized and received intravenous empirical antibiotics (meropenem, polymyxin E), after taking into consideration the infectious data of our hospital. The cultures were positive for Pseudomonas Aeruginosa and Enterococcus faecalis. The patient was discharged after appropriate antibiotic therapy for approximately one month, without any neurological symptoms. [Figure 4] The histopathological examination confirmed the diagnosis of slow-growing (Ki- 67< 3%) schwannoma.

DISCUSSION

Spinal schwannomas are benign tumors arising from Schwann cells. While these tumors can occur anywhere along the spinal cord, upper cervical schwannomas are relatively rare. Due to their location at the C1–C3 level, they pose unique diagnostic and surgical challenges.

In our case, the patient presented unspecified symptoms, which were typically related to nerve root compression or direct spinal cord involvement. As in many cases, the insidious onset of symptoms often leads to a delay in diagnosis, resulting in surgical difficulties.

Complete surgical excision by minimizing neurological deficits is the treatment of choice for symptomatic schwannomas. In the upper cervical region, the posterior approach is most preferred, as it provides direct access to the lesion while preserving spinal stability. Advances in neurosurgical techniques and intraoperative neuro-monitoring have significantly improved surgical outcomes, allowing for safer resection even in this anatomical challenging area. Although intraoperative neuromonitoring (IONM) remains controversial in moderate cervical cases, in pathologies that may be difficult to resect (such as schwannomas) is highly recommended. [6] Approximately 20% of patients undergoing challenging cervical spine surgeries develop impermanent neurological symptoms that should be noticed. [6] As a result, IONM contributes to reducing postoperative deficits and supports more confident, precise removal of cervical schwannoma tumors.

Cervical laminectomy is a common surgical approach for resecting spinal schwannomas, providing wide exposure of the tumor while allowing careful neural decompression. The decision to perform spinal fusion in addition to laminectomy depends largely on the extent of bone removal and the patient's baseline spinal stability. In our case, we performed limited laminectomy unilaterally, which does not significantly compromise structural integrity, therefore fusion may be unnecessary. However, when multiple levels are removed, facetectomy is required, or there is preexisting deformity or instability, instrumented fusion is recommended to prevent postoperative kyphosis or instability. The choice is therefore individualized based on anatomical and surgical considerations.

Surgical site infection (SSI) risk after cervical schwannoma surgery is influenced by a combination of patient, tumor, and procedure-related factors. Patient-related risks include diabetes, smoking, obesity, advanced age, poor nutritional status, and immunosuppression. Surgery-related contributors, such as prolonged operative time, extensive soft-tissue dissection, multilevel laminectomy, cerebrospinal fluid leaks, and the use of instrumentation, may further elevate infection risk. Prior surgery or radiation can also impair tissue healing and increase susceptibility. Identifying these predictors allows for better perioperative optimization and targeted preventive measures.

Histopathological examination confirmed the diagnosis of schwannoma, typically characterized by Antoni A and B patterns and immunoreactivity to S-100 protein [7]. These tumors rarely undergo malignant transformation and have a favorable prognosis when completely resected. Recurrence is uncommon but can occur in cases of subtotal resection or in the context of neurofibromatosis type 2 [8].

REFERENCES

1. Tubbs RS, Malefant J, Loukas M, Jerry Oakes W, Oskouian RJ, Fries FN. Enigmatic human tails: A review of their history, embryology, classification, and clinical manifestations. Clin Anat. 2016;29(4):430-8.
2. Lu FL, Wang PJ, Teng RJ, Yau KI. The human tail. Pediatr Neurol. 1998;19(3):230-3.
3. Ackerman LL, Menezes AH. Spinal congenital dermal sinuses: a 30-year experience. Pediatrics. 2003;112(3 Pt 1):641-7.
4. Dao AH, Netsky MG. Human tails and pseudotails. Hum Pathol. 1984;15(5):449-53.
5. Chakrabortty S, Oi S, Yoshida Y, et al. Myelomeningocele and thick filum terminale with tethered cord appearing as a human tail. Case report. J Neurosurg. 1993;78(6):966-9.
6. McLone DG, Naidich TP. Terminal myelocystocele. Neurosurgery. 1985;16(1):36-43.
7. Hoffman HJ, Taecholarn C, Hendrick EB, Humphreys RP. Management of lipomyelomeningoceles. Experience at the Hospital for Sick Children, Toronto. J Neurosurg. 1985;62(1):1-8.
8. Belzberg AJ, Myles ST, Trevenen CL. The human tail and spinal dysraphism. J Pediatr Surg. 1991;26(10):1243-5.
9. Tavafoghi V, Ghandchi A, Hambrick GW, Jr., Udverhelyi GB. Cutaneous signs of spinal dysraphism. Report of a patient with a tail-like lipoma and review of 200 cases in the literature. Arch Dermatol. 1978;114(4):573-7.
10. Park K. Urological Evaluation of Tethered Cord Syndrome. J Korean Neurosurg Soc. 2020;63(3):358-65.
11. Cai C, Shi O, Shen C. Surgical treatment of a patient with human tail and multiple abnormalities of the spinal cord and column. Adv Orthop. 2011;2011:153797.
12. Matsumoto S, Yamamoto T, Okura K. Human tail associated with lipomeningocele--case report. Neurol Med Chir (Tokyo). 1994;34(1):44-7.

CASE REPORT

Coiling of a ruptured posterior inferior cerebellar artery aneurysm using the catheter assisted technique

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CONFLICT OF INTEREST

None

SOURCES OF SUPPORT

None

ABSTRACT

Aneurysms of the posterior inferior cerebellar artery (PICA) are rare lesions usually involving the antero-medullary segment of the vessel. We present the case of a 54 year old woman suffering a subarachnoid haemorrhage due to rupture of a 6mm right PICA aneurysm. and undergoing end-vascular treatment of the lesion. Due to the relatively wide neck of the lesion and partial incorporation of PICA's origin, we used a catheter assisted technique to coil the aneurysm achieving near total exclusion from the circulation. Technical details of the case as well as other considerations regarding PICA aneurysms are discussed. In an era of increasing use of adjunct endovascular devices, neurosurgeons and interventionists need to keep in mind that simpler alternatives - such as the catheter assisted technique described here - do exist and should not be ignored.

KEYWORDS

Aneurysm, PICA, embolism.

ΠΕΡΙΛΗΨΗ

Τα ανευρύσματα της οπίσθιας κάτω παρεγκεφαλιδικής αρτηρίας (PICA) είναι σπάνιες αλλοιώσεις που συνήθως αφορούν το εγγύς (πρόσθιο προμηκικό) τμήμα του αγγείου. Παρουσιάζουμε την περίπτωση ασθενούς 54 ετών η οποία υπέστη υποαραχνοειδή αιμορραγία μετά από ρήξη ανευρύσματος της δεξιάς PICA και υποβλήθηκε σε ενδαγγειακή αποκατάσταση αυτού. Λόγω του ευρύ αυχένα της βλάβης και της μερικής ενσωμάτωσης της έκφυσης της PICA σε αυτήν, χρησιμοποιήσαμε catheter assisted τεχνική για τον εμβολισμό του ανευρύσματος με σπειράματα, επιτυγχάνοντας τελικά τον σχεδόν πλήρη αποκλεισμό του. Παρά την αυξανόμενη χρήση ενδαγγειακών συσκευών στην σύγχρονη νευροεπεμβατική, καθιερωμένες τεχνικές όπως αυτή (catheter assisted coiling) θα πρέπει να παραμείνουν στο οπλοστάσιό μας και να μην παραγνωρίζονται, ειδικά σε ό,τι αφορά ραγέντα ανευρύσματα.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ

Ανεύρυσμα, PICA, εμβολισμός.

INTRODUCTION

Aneurysms of the posterior inferior cerebellar artery (PICA) are rare lesions usually involving the antero-medullary segment of the vessel. Endovascular treatment, although established nowadays as our first option, often proves challenging and special consideration is always needed. Unfavorably configurated lesions in the region require the application of advanced techniques in order for a good outcome to be achieved.

CASE DESCRIPTION

Our case is that of a 54-year-old woman presenting with subarachnoid haemorrhage (SAH) due to rupture of a 6mm right PICA aneurysm. Initial presentation was with a sudden collapse while the patient walking on the street. According to the records, she was reported by the paramedics to be unresponsive on the scene but later on she partly recovered, reaching a GCS of 10/15. A CT scan performed in the Emergency Department of her local hospital revealed a Grade IV on the Fisher scale subarachnoid haemorrhage. The blood was predominantly concentrated in the right cerebellopontine angle and extending, through the ipsilateral foramen of Luschka and Magendie, in the ventricular system. Incipient hydrocephalus was also noted.

On the basis of these findings the patient was intubated and transferred to the John Radcliff Hospital for further treatment. There, ICP monitoring was instituted (recorded values in the high twenties range) and a second CT scan followed by a CTA were performed (Fig. 1 & 2).

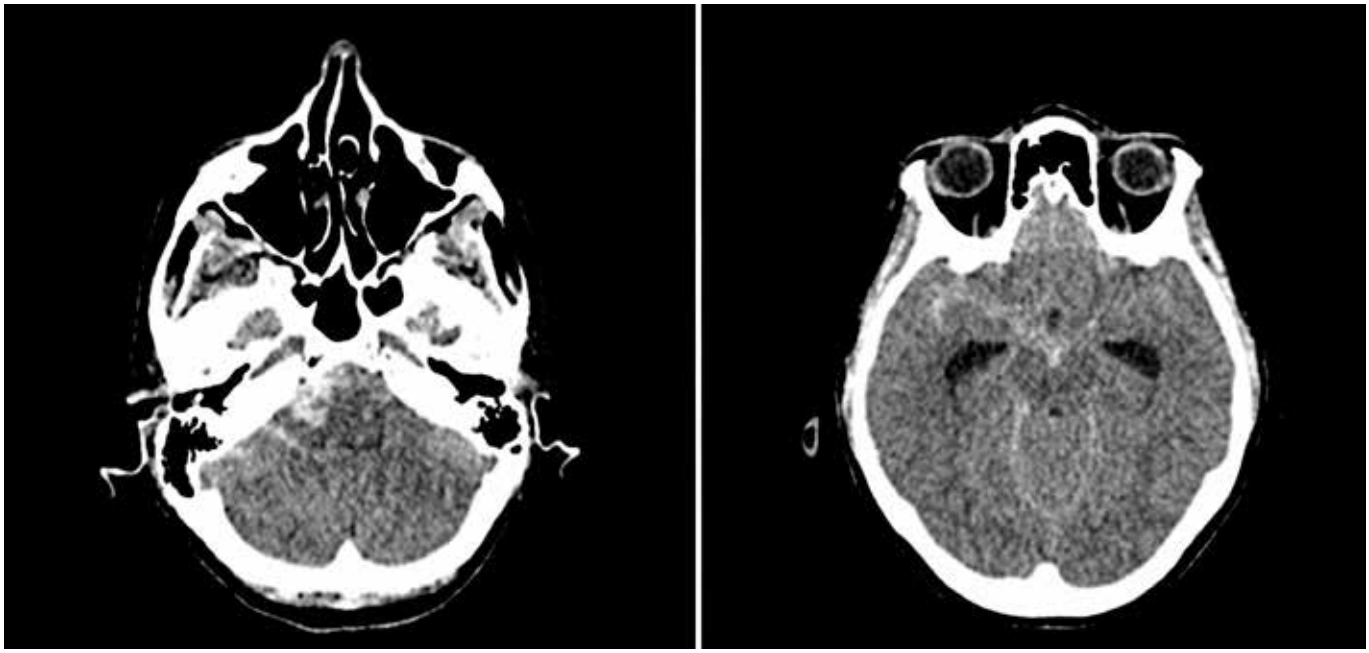


Figure 1. Unenhanced axial CT scans. Subarachnoid haemorrhage with blood is predominantly concentrated in the left cerebellopontine angle (Right). Signs of hydrocephalus (dilatation of temporal horns) (Left).

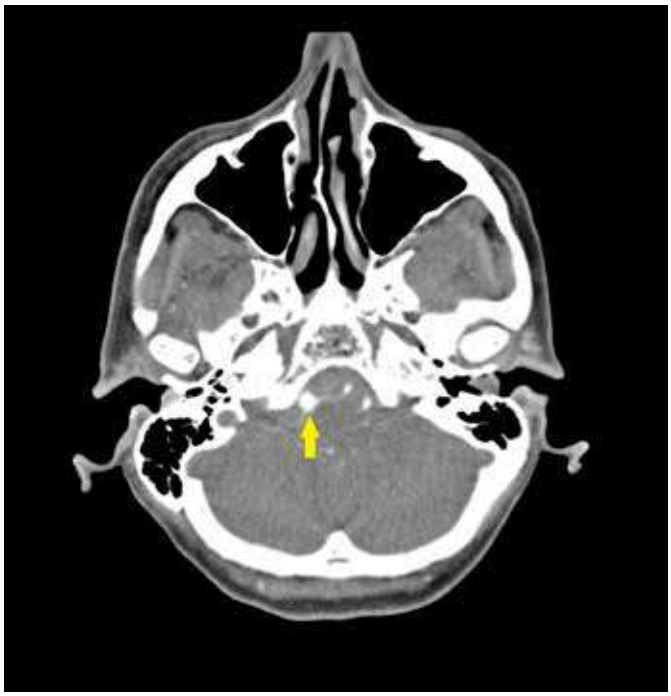


Figure 2. CTA, axial scan. A right PICA aneurysm is noted (yellow arrow).

The size of the ventricular system was reported slightly increased compared to previous imaging while the cause of the haemorrhage was found to be a 6mm proximal PICA aneurysm on the right. After discussion with the neurosurgical team, endovascular treatment of the lesion in question was offered and accepted by the patient's relatives (the patient herself was kept intubated throughout this period).

The procedure was performed within 24 hours of the initial haemorrhage, with the patient sedated and under continuous monitoring of both her activated clotting time (ACT) and intracranial pressure. 6F sheaths were placed in the common femoral arteries bilaterally, the right one under US guidance. Diagnostic injections in the left subclavian and the right vertebral arteries with a 5F Vertebral Catheter confirmed the presence of the previously identified PICA aneurysm (Fig. 3).

The lesion was relatively wide necked and it partly incorporated PICA's origin. A daughter sac, probably representing the rupture point, could also be seen. 6F Envoy guiders were used to selectively catheterize both vertebral arteries and a bolus dose of 5000 IU of heparin was administered intra-arterially. With the aid of a Synchro-14 guidewire, an SL-10 microcatheter was advanced through the left vertebral artery and over to the proximal right PICA where it was left in place throughout the procedure. A second SL-10 microcatheter, this time loaded over a Synchro-2 guidewire, was advanced through the right vertebral catheter, in the aneurysm dome (Fig. 4).

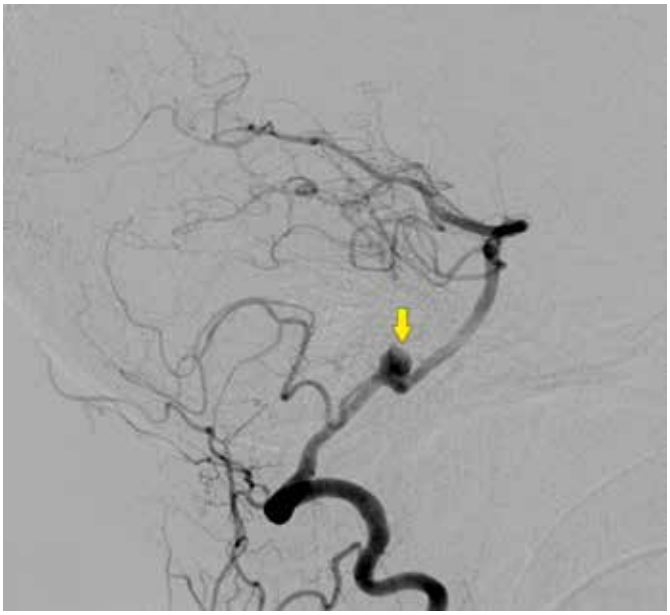


Figure 3. DSA (right vertebral artery injection, lateral projection). A 6mm aneurysm partly incorporating PICA's origin is noted (yellow arrow). A daughter sac, probably representing the rupture point, can also be seen projecting superiorly.

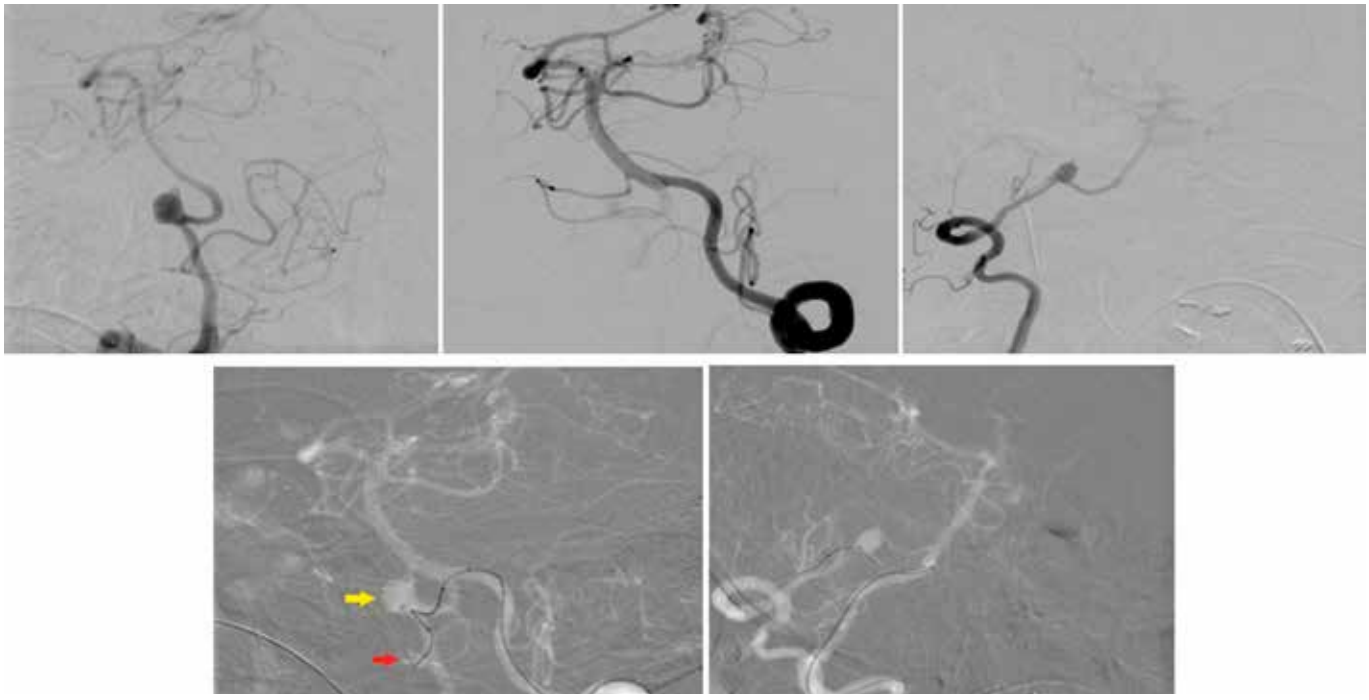


Figure 4. Intraprocedural images. (Top) Working projections, bilateral vertebral injections. On the left vertebral injection some degree of reflux into the right vertebral artery as well as the aneurysm dome can be seen. (Bottom) Roadmap images. The tip of an SL-10 microcatheter has been positioned in the aneurysmal sac (yellow arrow) while a second similar microcatheter with the guidewire still in place has been inserted in the proximal PICA (red arrow).

Coiling of the aneurysm was achieved with 2 framing and 6 filling coils. The former were Micrusphere Microcoils 6mm x 11.9cm and 5mm x 9.7cm respectively while the latter were Ultipaq Microcoils (4mm x 8cm, 3 mm x 8cm, 2.5mm x 6 cm, 2.5mm x 6cm, 2mm x 8cm, 2mm x 8cm) (Fig. 5). Having achieved a near total exclusion of the aneurysm from the circulation (OG I), the microcatheters were retrieved and a final angiogram confirmed patency of the PICA (Fig. 6).

Figure 5. Intraprocedural images under roadmap. Coils have been deployed in the aneurysmal sac. Stable presence of the assisting microcatheter within the proximal PICA.

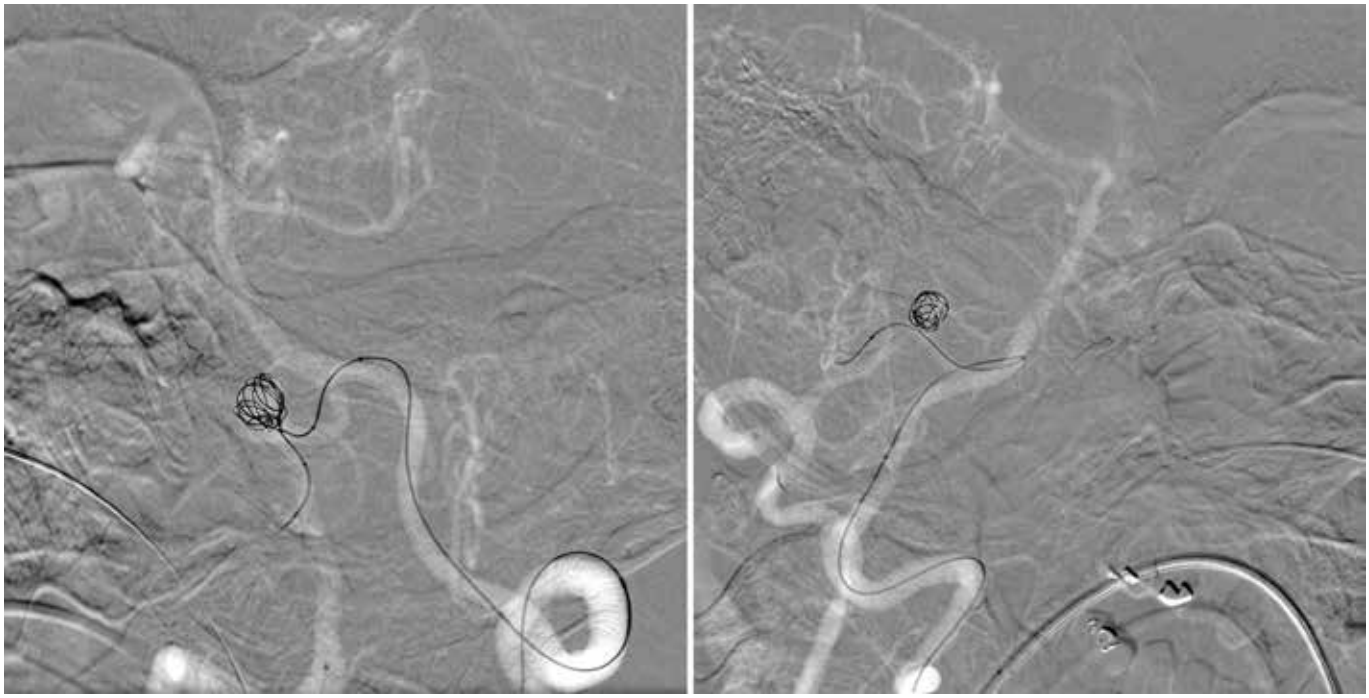
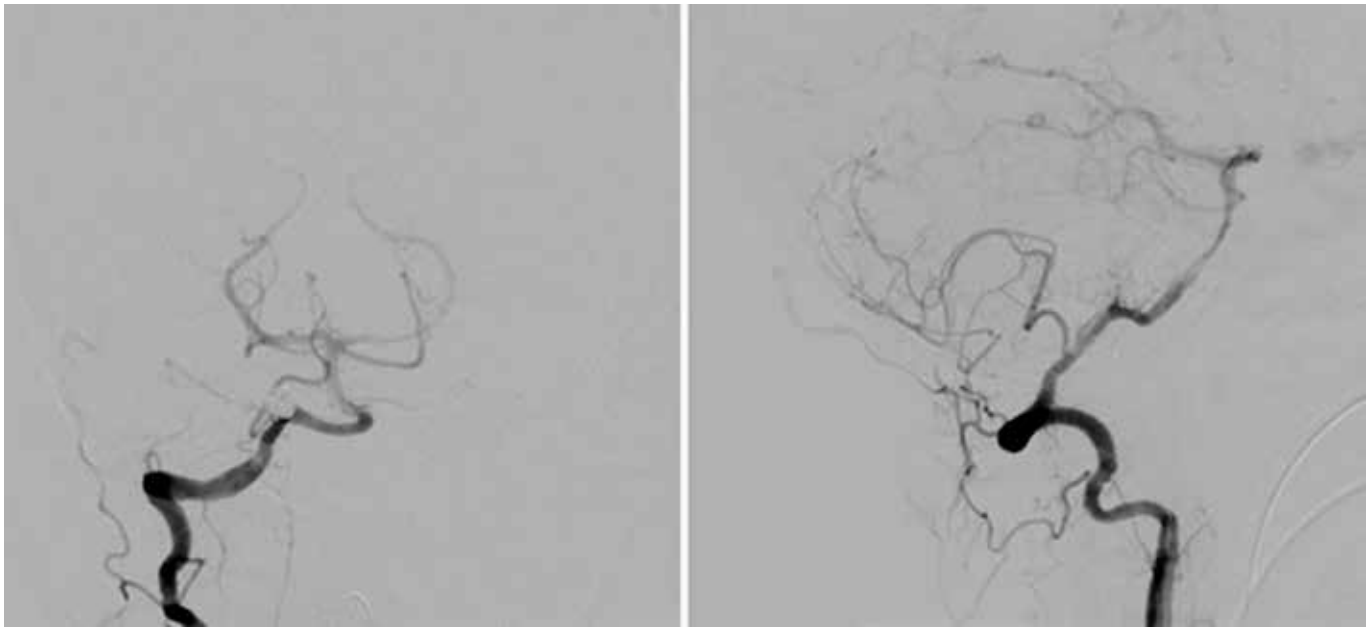


Figure 6. Post-procedural DSA. Right vertebral artery injection, AP (Left) and lateral (Right) views. Near total occlusion of the aneurysm dome (OG I..



The procedure was reported uneventful and the patient returned to neuro-ICU with her vital signs (including ICP) stable. The sheaths were left in place to be removed at a later stage. Post-procedural recovery was deemed satisfactory and the patient was discharged nearly 20 days after her initial admission

DISCUSSION

PICA aneurysms are rare lesions, accounting for 0.5-3% of all intracranial aneurysms [1]. Pointing usually upwards, they are categorized as either proximal or distal lesions. The former are found on the antero-medullary segment of the PICA or on its junction with the vertebral artery while the latter, far less common and usually of an irregular shape, arise more distally on the vessel (Ishihara, 2013) [2].

Despite our incomplete understanding of their natural history, it seems that PICA aneurysms have a higher risk of rupture compared to their anterior circulation counterparts [3]. As a result, most authors favor a more aggressive approach when it comes to unruptured lesions suggesting that aneurysms as small as 3mm should be treated [4].

Microsurgical treatment of PICA aneurysms is challenging due to their close proximity to the brainstem and the lower cranial nerves. Postoperative dysphagia and inability to protect the airway are not infrequent and, even though temporary, they are associated with prolonged hospitalization and risk of aspiration pneumonia. Other complications include infection, CSF leaks and hydrocephalus [5].

Endovascular therapy presents today as the primary treatment modality for PICA aneurysms. Despite satisfactory results, significant difficulties may occur. PICA's origin incorporation within the lesion often requires the application of advanced techniques in order to protect the branch while, in a substantial proportion of patients, parent artery occlusion will still be required. In our case, preservation of PICA's flow was achieved with the aid of a catheter assisted technique [6]. This involves insertion of one microcatheter into the endangered branch while the tip of another microcatheter is positioned into the aneurysm lumen for coil deployment. The catheter assisted technique is an alternative when a balloon or a stent cannot be used due to the branch's small size, tortuosity or acute angulation to the parent artery.

Prior to closing our discussion, it should be noted that PICA aneurysms are prone to intraprocedural rupture. This has been traditionally attributed to the geometry of these aneurysms: virtually all PICA aneurysms project upward and slack in the microcatheter caused by the V3 loop of the vertebral artery can easily be transferred in an upward jump during pushing, resulting in rupture of the aneurysm dome [7].

CONCLUSION

PICA aneurysms often prove to be a challenge for interventionists. Today's endovascular armatorium includes a wide range of adjunct devices (i.e., balloons and stents) that promise to facilitate such procedures. However, simpler alternatives are not to be ignored. Limiting the overall cost of endovascular therapy, such techniques still remain of great value in our everyday practice.

PATIENT CONSENT

Written informed consent was obtained from the patient.

REFERENCES

1. Hudgins R.J., Day A.L., Quisling R.G., Rhoton A.L., Sypert G.W., and Garcia-Bengochea F., "Aneurysms of the posterior inferior cerebellar artery. A clinical and anatomical analysis," J Neurosurg, vol. 58, no. 3, pp. 381–387, 1983, doi: 10.3171/JNS.1983.58.3.0381.
2. Ishihara H., Tateshima S., Jahan R., Gonzalez N., Duckwiler G., and Vinuela F., "Endovascular treatment of ruptured dissecting aneurysms of the posterior inferior cerebellar artery," J Neurointerv Surg, vol. 5, no. 6, pp. 557–561, Nov. 2013, doi: 10.1136/NEURINTSURG-2012-010500.
3. Tokimura H. et al., "Clinical presentation and treatment of distal posterior inferior cerebellar artery aneurysms," Neurosurg Rev, vol. 34, no. 1, pp. 57–66, Jan. 2011, doi: 10.1007/S10143-010-0296-Z.
4. Jeon S.G., Kwon D.H., Ahn J.S., Kwun B.D., Choi C.G., and Jin S.C., "Detachable coil embolization for saccular posterior inferior cerebellar artery aneurysms," J Korean Neurosurg Soc, vol. 46, no. 3, pp. 221–225, 2009, doi: 10.3340/JKNS.2009.46.3.221.
5. Liew D., Ng P.Y., and Ng I., "Surgical management of ruptured and unruptured symptomatic posterior inferior cerebellar artery aneurysms," Br J Neurosurg, vol. 18, no. 6, pp. 608–612, Dec. 2004, doi: 10.1080/02688690400022870.
6. Ryu C.W., Koh J.S., Lee C.Y., and Kim E.J., "Endovascular Management of the Wide-neck Aneurysms: the Applications of the Coils and Catheter.," Neurointervention, vol. 5, no. 2, pp. 71–78, 2010, doi: 10.5469/NEUROINT.2010.5.2.71.
7. Peluso J.P., Van Rooij W.J., Sluzewski M., Beute G.N., and Majoie C.B., "Posterior inferior cerebellar artery aneurysms: incidence, clinical presentation, and outcome of endovascular treatment," AJNR Am J Neuroradiol, vol. 29, no. 1, pp. 86–90, Jan. 2008, doi: 10.3174/AJNR.A0758.

CASE REPORT

Unexplained Intraoperative Elevation of Lactate During Anterior Cervical Discectomy and Fusion. A Case Report

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CONFLICT OF INTEREST
None

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None

ABSTRACT
Lactic acidosis is a rare but potentially serious complication during surgery, typically associated with tissue hypoxia, sepsis, or metabolic disorders. We present the case of a previously healthy patient who developed a significant intraoperative elevation in lactate levels (lactate = 10.5 mmol/L) during an anterior cervical discectomy and fusion (ACDF) for cervical disc herniation, with no identifiable cause. This case underscores the importance of vigilant intraoperative monitoring and the need for further investigation into atypical metabolic responses during routine spinal procedures.

KEYWORDS
Lactate acid, cervical hernia, ACDF, intraoperative complications, spinal surgery, metabolic abnormalities

ΠΕΡΙΛΗΨΗ
Η γαλακτική οξέωση αποτελεί μια σπάνια αλλά δυνητικά σοβαρή επιπλοκή κατά τη διάρκεια του χειρουργείου. Συνήθως σχετίζεται με ιστική υποξία, σήψη ή μεταβολικές διαταραχές. Παρουσιάζουμε την περίπτωση ενός προηγουμένως υγιούς ασθενούς που εμφάνισε σημαντική διεγχειρητική αύξηση των επιπέδων γαλακτικού οξέος (γαλακτικό = 10,5 mmol/L) κατά τη διάρκεια πρόσθιας αυχενικής δισκεκτομής και σπονδυλοδεσίας (ACDF) λόγω κήλης μεσοσπονδύλιου δίσκου, χωρίς να εντοπιστεί σαφής αιτία. Η περίπτωση αυτή αναδεικνύει τη σημασία της εντατικής παρακολούθησης κατά τη διάρκεια της επέμβασης και την ανάγκη περαιτέρω διερεύνησης άτυπων μεταβολικών αντιδράσεων κατά τη διάρκεια συνήθων επεμβάσεων στη σπονδυλική στήλη.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ
Γαλακτική οξέωση, κήλη αυχενικού μεσοσπονδύλιου δίσκου, ACDF, διεγχειρητικές επιπλοκές, χειρουργική σπονδυλικής στήλης, μεταβολικές διαταραχές.

INTRODUCTION

The normal value of lactate in arterial gas is < 2 mmol/L. Elevation of lactate can be present in cases of tissue hypoperfusion, mitochondrial dysfunction, or toxin exposure [1]. Intraoperative elevation of lactate acid in patients without significant previous medical history is uncommon in elective spinal surgery [2,3]. This case report describes an unusual presentation of severe lactate acid elevation up to 10 mmol/L with metabolic acidosis during anterior cervical discectomy and fusion (ACDF) in a patient without predisposing conditions.

CASE DESCRIPTION

A 50-year-old male patient presented with chronic neck pain, numbness in the right upper limb, and associated gait instability over the past four months. His medical history was notable for active smoking and arterial hypertension, for which he was under treatment with an angiotensin II receptor blocker. On neurological examination, he had a positive Hoffmann's sign, reduced muscle strength in the right upper limb (graded 4/5), and clonus in the right lower limb. Magnetic resonance imaging (MRI) of the cervical spine revealed disc herniations at the C4–C5 and C6–C7 levels, with evidence of cervical myelopathy and spinal cord compression. Following preoperative evaluation from cardiologists, anesthesiologists and examination of the respiratory system, the patient was cleared for surgery and scheduled for an elective ACDF at the two affected levels.

During the procedure, the first arterial blood gas (ABG) showed a lactate level of 5.8 mmol/L, pH = 7.34, bicarbonate levels = 21.2 mmol/L and potassium level of 2.5 mmol/L, with normal sodium level. Intravenous fluids were administered to correct the electrolyte imbalances, which were promptly normalized. Despite the absence of excessive bleeding or hemodynamic instability, the lactate levels continued to rise, with the last intraoperative ABG showing lactate at 10.2 mmol/L and a concomitant pH drop to 7.298. Consequently, following consultation with cardiologist and intensive care unit, the surgical team decided to terminate the procedure prematurely. Vital signs remained stable throughout the surgery (BP 110–125/70–85 mmHg, HR 75–90 bpm, SpO_2 97–100%).

Laboratory investigations, including cardiac troponin, were obtained and were negative. A computed tomography pulmonary angiography (CTPA) was subsequently performed and was negative for pulmonary embolism. The patient was admitted in the neurosurgery clinic postoperatively for close monitoring for potential infection, hypoxia, or renal or hepatic dysfunction. During the 5-day hospitalization, no underlying cause was identified for the lactic acidosis.

The lactate levels gradually normalized (<2 mmol/L) by the third day without additional intervention. Three weeks later, the patient underwent a rescheduled surgery, during which a two-level ACDF was successfully performed without any complications. Lactic acid levels remained within normal limits throughout the second procedure and postoperative period.

DISCUSSION

Lactic acidosis is a critical metabolic condition that is associated with several clinical entities and a range of metabolic disorders, particularly in critically ill patients. It is defined as a serum lactate concentration above 4 mmol/L, and is usually accompanied by a blood pH below 7.35 and low plasma bicarbonate levels [4]. Lactic acidosis during elective spinal surgery is rare and is typically associated with underlying systemic illness or major intraoperative events. In our case, the cause of intraoperative lactic acid elevation remains unclear. Common etiologies such as hypoxia, hypoperfusion, sepsis, or drug-induced mitochondrial dysfunction could not be identified. Lactic acidosis is generally divided into two types, depending on the underlying cause. Type A, is the most common form, is typically caused by tissue hypoperfusion and hypoxia (e.g., shock, sepsis, severe anemia, or cardiopulmonary arrest). These conditions force cells to rely on anaerobic glycolysis, resulting in excessive lactate production. Type A lactic acidosis is usually severe and requires immediate correction, as it is associated with high mortality rates. Type B is less common and occurs without evidence of tissue hypoxia or hypoperfusion. It is attributed to mitochondrial dysfunction and the inability to metabolize excess pyruvate. This type may result from various causes, including malignancies, liver disease, medications (such as metformin or propofol), HIV infection, trauma, alcohol abuse, and other metabolic disorders [5].

In our case, a possible explanation may involve a stress-related or idiopathic mechanism, most likely Type B lactic acidosis triggered by perioperative stress. Notably, three weeks later, the patient underwent surgery using the same anesthetic agents, including propofol, as used in all other cases of ACDF, without recurrence of lactic acidosis, further supporting the transient and idiopathic nature of the initial event. For this reason, close monitoring of metabolic parameters—even during routine surgeries—is crucial in neurosurgical patients, as it may allow for the early detection and management of unexpected metabolic disturbances.

CONCLUSION

This case illustrates an unusual occurrence of severe, unexplained lactic acid elevation during elective cervical spine surgery. Although the outcome was ultimately favorable, it underscores the importance of intraoperative vigilance and awareness of rare metabolic complications.

PATIENT CONSENT

Written informed consent was obtained from the patient.

REFERENCES

1. Kamel KS, Oh MS, Halperin ML. L-lactic acidosis: pathophysiology, classification, and causes; emphasis on biochemical and metabolic basis. Kidney Int. 2020; 97(1): 75-78.
2. Kondratowicz J, Najeeb H, Ali M, Torlinski T. An unusual cause of lactic acidosis following spinal surgery. BMJ Case Rep. 2022; 15(9): e252352.
3. Bangaari A, Chakravarthy S, Chockalingam S, Murugesan K. Perioperative intractable severe lactic acidosis in a spine patient: Is it always Type A? Clinical Case Reports: Open Access. 2024; 7(1): 285.
4. Baddam S, Tubben RE. Lactic Acidosis. 2025 Apr 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29262026.
5. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW. Etiology and therapeutic approach to elevated lactate levels. Mayo Clin Proc. 2013; 88(10): 1127-1140.

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