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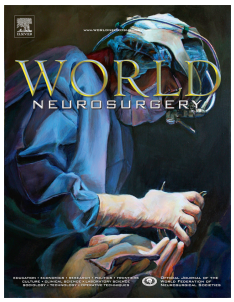

VALUE OF INTRAOPERATIVE COMPUTED TOMOGRAPHY IN INTRAAXIAL BRAIN TUMOUR SURGERY: A SYSTEMATIC REVIEW

Mohammad Ashraf, MBChB, Sophia Ahmed, Muhammad Asfandyar Nadir, Zuha Tariq, Mahrukh Iqbal, Maha Malik, Muhammad Haris Khan, Arfa Ahmed Assad, Abdul Rafeh Awan, Abdul Rehman Saeed, Javed Iqbal, Conor S. Gillespie

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VALUE OF INTRAOPERATIVE COMPUTED TOMOGRAPHY IN INTRAAXIAL BRAIN TUMOUR SURGERY: A SYSTEMATIC REVIEW

SHORT TITLE: INTRAOPERATIVE CT IN BRAIN TUMOR SURGERY

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ABSTRACT

Real-time intraoperative imaging with neuronavigation is a valuable adjunct in the surgical management of intra-axial brain tumours. While intraoperative magnetic resonance imaging (iMRI) is the gold standard, recent advances in technology have explored the utility of

intraoperative computed tomography (iCT) as an alternative. A systematic review was conducted by searching multiple databases, including MEDLINE, PubMed, Scopus, Cochrane Library, and Web of Science, for studies published from 1982 to 2024. Studies that evaluated the use of iCT in intra-axial brain tumour surgeries and reported on outcomes such as the extent of tumour resection (EOTR), residual tumour detection, and postoperative complications were included. Thirteen studies met the inclusion criteria. Overall, recent improvements in iCT's soft tissue imaging quality have increased its utility in intra-axial brain tumour surgeries. iCT was found to improve tumour resection accuracy in some instances, helping neurosurgeons detect residual tumours and refine surgical strategies. However, conclusions about its impact on long-term outcomes are limited by the lack of data on molecular tumour characteristics and adjuvant therapies. Further high-quality prospective work is needed to validate the role of iCT in improving key outcome parameters in neuro-oncology. Until then, iCT remains an adjunct whose use can be considered in select cases. Continued research on iCT is warranted to determine further indications in intra-axial brain tumour surgery.

KEYWORDS

Intraoperative Computed Tomography; Brain Tumours; Intra-axial; Systematic Review.

1) INTRODUCTION

Preoperative image-based navigation systems have been the primary tools for guiding surgeons during brain tumour surgeries. However, the brain shift phenomenon significantly reduces accuracy and precision, as these images usually do not coincide with the intraoperative neuroanatomy[1–3]. Several intraoperative imaging methods have been developed to address the limitations posed by the brain shift, including intraoperative magnetic resonance imaging (iMRI), intraoperative ultrasound, 5-aminolevulinic acid (5-ALA) fluorescence, and sodium fluorescein[3,4]. These imaging techniques allow surgeons to monitor brain shifts and other changes during tumour resection, guiding additional resection if possible. These imaging techniques also detect operative complications, such as hematomas, that can be addressed perioperatively[3,5].

While iMRI is often regarded as the preferred approach due to its excellent soft tissue resolution and ability to capture brain shifts, improving patient outcomes[1,6,7] and increasing progression-free survival in patients with contrast-enhancing brain tumours[8], it has significant drawbacks. It is resource-intensive, expensive , and can extend surgery time by up to 2 hours. As a result, iMRI is not practical for many setups[4,5,8]. Furthermore, newer low-field portable MRI technology has not shown clinical benefits, questioning its cost-effectiveness[9].

Intraoperative computed tomography (iCT), first introduced in the 1980s, was initially hindered by poor image quality and hardware limitations. However, it has dramatically improved in recent years, with modern iCT offering enhanced soft tissue resolution, lower costs, and significantly reduced radiation exposure. The image quality now matches that of advanced CT machines found in radiology departments.[4,5]. iCT has gained growing support as a valuable tool for neurosurgeons across various subspecialties. In neurovascular surgery, it can detect impending ischemia, enabling timely interventions like repositioning clips in aneurysm cases, especially

when paired with iCT-perfusion and angiography[10]. iCT also aids in deep brain stimulation (DBS) by ensuring precise and efficient electrode placement[11]. Its greatest value lies in its proven use in spinal surgery, improving screw placement and reducing the need for repeat spinal operations, mainly due to CT technology's exceptional ability to visualize bony anatomy[12].

The use of iCT in neuro-oncology as an adjunct to improve extent-of-tumour-resection (EOTR) and, hence, overall survival, is evidenced by studies demonstrating iCT improving not only surrogate markers such as EOTR but also overall survival rates in brain tumour patients[13].

Although the image resolution of iCT for intra-axial tumours is lower than that of iMRI, iCT addresses several challenges associated with iMRI. It is more affordable, portable, and accessible to incorporate into existing surgical workflows. Its small size and mobility enable its use in various surgical settings without requiring significant operating room modifications[4,5,14]. This systematic review seeks to evaluate the emerging evidence on the utility of iCT on surgical outcomes of intraaxial brain tumours.

2) MATERIALS AND METHODS

2.1) Study Protocol

This systematic review was conducted in accordance with the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Our review protocol consisted of a detailed research question, a search strategy, screening criteria for titles and abstracts, and screening criteria for full-text articles. The detailed research question was structured using the patient/population, intervention, comparison, outcomes and study design (PICOS) approach formulated as follows: What are the surgical outcomes of utilising iCT in brain tumour patients? Search databases were Google Scholar, MEDLINE (PubMed), Cochrane Library, Embase, Science Direct, and Scopus.

2.2) Eligibility Criteria and Search Strategy

The eligibility of the studies was evaluated under the primary criteria set by our PICOS research question. No restriction was applied based on the publication date or status, language, or length of follow-up. MEDLINE (PubMed) was used as the primary data source, and "Brain Neoplasm" and "Tomography, X-Ray Compute" were included as medical subject headings (MeSH) to specify the search results. Other databases were also searched to find additional literature concerning our research question. After deleting duplicate records, titles and abstracts were screened and included if they represented studies of patients with intra-axial brain tumours who underwent surgery using iCT. Studies focusing on non-humans, those not concerned with intra-axial brain tumours, or those not using iCT were excluded. Of the remaining records, full-text articles were assessed according to the same criteria, with one additional inclusion criterion: studies had to report quantitative surgical outcomes of using iCT.

The applied search strategies are given in ***Table 1***.

2.3) Study Selection and Data Collection

A total of 23,194 results were obtained across all databases. After exporting the results and removing the duplicates, the data was screened according to the mentioned inclusion and exclusion criteria. Four authors contributed to the screening process. An initial 37 articles were deemed eligible for our study. Upon conducting an assessment of the full-text, 24 articles were excluded. The remaining 13 articles were used for qualitative synthesis.

A summary of the study selection process is provided as a PRISMA flow diagram in ***Figure 1***.

2.4) Quality Assessment

We employed the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series to evaluate the quality of the included studies, focusing on essential elements of research design and reporting. This tool comprises ten questions addressing various areas of potential bias. Every question is evaluated as "Yes," "No," "Unclear," or "Not Applicable." The 10 questions evaluate factors including the clarity of inclusion criteria, standardisation and reliability of measurements, reporting of participant demographics and clinical data, and transparency of outcomes and interventions.

The Risk of Bias in Non-randomised Studies - of Interventions (ROBINS-I) tool was employed to evaluate the risk of bias in observational studies across seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results.

Quality assessment was conducted independently by all authors, with the final version reflecting the areas of least conflict and highest agreement, achieved through unanimous consensus.

The results of the quality assessment are provided in ***Figure 2.1, Figure 2.2, Table 2.1 and Table 2.2***.

3) RESULTS

3.1) Study Characteristics

Thirteen studies met our inclusion criteria. They consisted of eleven case series, one observational study, and one technical report. No randomised controlled trial (RCT) matched our defined criteria. Publication years for the included studies were between 1982 and 2024. Nearly all studies documented the baseline characteristics of patients, including the number of subjects, age, and sex. Most of the studies specified the type and location of tumours that were operated on. Overall, high-grade gliomas (HGGs), including glioblastomas, were the most common tumours navigated through iCT, and the most common location for tumours was the frontal lobe.

The contrast media predominantly used was Iomeprol, as reported by three studies. No specific positioning was required for the patient while undergoing iCT-navigated surgery. The position of the patient during surgery depended on the type of tumour. Nearly all studies reported the model of the CT scanner used, and some studies also stated the resolution of the CT scanner. Six studies have also reported on operating surgeons. The operators were either neurosurgeons or ear, nose and throat (ENT) surgeons.

Common outcomes observed across different studies were EOTR and detection of residual tumours, the time required to perform a surgery with a CT scanner, postoperative Karnofsky Performance Status (KPS) score, and Kaplan-Meier survival curve values.

A summary of the common outcomes is provided in ***Table 3***.

3.2) Results of Individual Studies

Barbagallo et al.[15], in their 2018 case series, evaluated the use of iCT during awake craniotomy in three patients with intra-axial brain lesions located in eloquent areas (two low-grade gliomas, one high-grade glioma). iCT was used to verify the completeness of tumour resection and correction for brain shift. In all cases, iCT confirmed the extent of resection, showing complete removal in two cases and a small residual tumour in one, where resection was halted due to the risk of language deficits. iCT added precision by providing updated neuronavigation, allowing surgeons to adjust real-time brain mapping. It did not significantly prolong surgery (iCT scan duration: 8–14 minutes) or cause additional patient stress. Postoperatively, all patients had stable outcomes, with mild, transient deficits in two cases.

Schichor[4], in their technical report, documented the application of iCT in intracranial surgeries for both high-grade and low-grade tumours. Twelve out of 23 cases presented were found to have residual tumours on iCT that were not grossly visible to the surgeon. The authors opined that the iCT data could be used to continue the resection in these cases.

Barbagallo et al.[16] conducted an observational study of 25 patients with high-grade gliomas (HGGs) undergoing surgery using iCT and 5-ALA. A control group of 25 cases utilising 5-ALA without iCT was included. iCT allowed the precise localisation of unrecognised tumours in 8 patients in the intervention group, 4 of which had multifocal neoplasms, and led to the further resection of these neoplastic foci detached from the primary lesion. The mean preoperative neoplastic volume of 30.90 cm^3 was reduced to a postoperative mean residual disease volume of 1.16 cm^3 in the iCT group, while it reduced from 36.90 cm^3 to 0.628 cm^3 for the control group. There was no statistically significant difference in the EOTR for the two groups. For the iCT group, the preoperative mean KPS score changed from 66.80 to a postoperative mean KPS score of 69.20. The change in KPS score from preoperative to postoperative value for both groups showed negligible difference. The difference between the postoperative KPS score for the two groups did not show any statistical significance. The values for overall survival (OS) and progression-free survival (PFS) were estimated by the Kaplan-Meier method. The log-rank test suggested no statistically significant difference in OS and PFS values between the control group and the iCT group.

Hosoda et al.[13] conducted a case series of 46 patients undergoing surgery for low-grade gliomas, of whom 23 patients were included in the iCT group. Among the 23 patients in the iCT group, additional resection could be performed in 11 patients (47.8%), and a more significant number of patients in the iCT group had gross total resection (9/23 vs. 0/23 in the non-iCT group) as well as

subtotal resection (8/23 vs. 3/23) when compared to the non-iCT group. The patients in the iCT group had a better postoperative KPS score (91.7 ± 10.3) than the non-iCT group (78.6 ± 24.4), although this difference was insignificant. Kaplan-Meier survival curves showed that the iCT group had significantly better overall survival than the non-iCT group. The five-year survival rates were also better for the iCT group (87.0%) than the non-iCT group (56.5%).

Uhl et al.[17], in a case series, evaluated the use of iCT in eight intra-axial brain tumour surgeries. All cases included patients with gliomas, and the grades of the tumours were not reported. They found that iCT took about 10–15 minutes and provided precise intraoperative imaging, including detecting residual flow in aneurysm cases. The study reported no iCT-related complications and highlighted the high-quality imaging from modern multi-slice CT scanners.

Gumprecht et al.[18], in a case series, evaluated iCT in 76 patients, including 43 patients with gliomas, during tumour resection surgeries. The grade of gliomas was not reported. They found tumour remnants in 27 of the 43 glioma cases (62.8%) using iCT. iCT allowed for the detection of residual tumour tissue that was missed during the initial resection. No significant postoperative complications were reported.

Nakao et al.[14] conducted a case series and utilised iCT in five patients undergoing intra-axial tumour resections, including cases with four high-grade gliomas and astrocytomas and one glioblastoma recurrence. iCT was able to detect the residual intra-axial lesions in all cases efficiently. The use of iCT led to maximum safe resection of these tumours and complete resection of glioblastoma in one case. There were no significant complications, and the authors reported that iCT was beneficial in detecting intraoperative bleeding impacting the course of surgery.

Haberland et al.[19] conducted a case series and evaluated iCT for neuronavigation in intracranial tumour surgeries in 57 patients. The accuracy of stereotactic biopsies was 91.4%, with no difference between iCT and conventional CT. However, iCT significantly reduced procedure time, with a mean duration of 2.6 ± 0.4 hours compared to 4.4 ± 0.5 hours for conventional CT, without increasing postoperative complications. In 49 patients with tumours in functionally critical brain areas, iCT was used for neuronavigation, benefiting 25 patients who also had preoperative brain mapping with magnetoencephalography (MEG) to guide surgical planning. Postoperatively, patients showed an improvement in their KPS from 80% to 86% at eight weeks, and there were no mortalities. In four cases, brain shifts during surgery were corrected, two using iCT and two with 3D ultrasonography.

Gwinn et al.[20], in a case series, assessed the use of a portable iCT scanner in four pediatric patients for the resection of two low-grade and two high-grade astrocytomas. iCT was employed to guide resection in areas where tumours were adjacent to vital structures, particularly in the hypothalamic and midbrain regions. The average imaging time was 20 minutes per scan, and iCT allowed surgeons to identify residual tumour tissue despite materials in the surgical field. iCT enabled the complete resection of tumours in one patient and helped in visualising the exact margins of the tumours and the placement of ventriculostomy catheters in the rest of the three patients, leading to maximum safe debulking of the tumours. While it did not guarantee complete resection, it aided in reducing postoperative morbidity. Postoperative pneumocephalus, hemiplegia or paresis observed in the patients improved with time, and patients were seen doing well throughout follow-ups.

Matsumoto et al.[21] conducted a case series and reported seven surgeries for deep-seated tumours utilising iCT. These tumours consisted of four high-grade astrocytomas and gliomas, two low-

grade astrocytomas, and an ependymoma. iCT was used to localise the tumour, followed by catheter placement for guidance. This approach ensured accurate tumour localisation during surgery, preventing displacement due to factors like gravity, position changes, or cerebrospinal fluid (CSF) aspiration. In all cases, lesions were quickly localised, enabling radical tumour removal without complications. Out of the seven cases, four patients presented with hemiparesis preoperatively, and one showed improvement post-surgery. At follow-up, two of the patients had passed away, while four showed normal clinical status.

Engle et al.[22], in their case series, analysed nine cases of iCT-assisted neurosurgery for brain tumours, including six high-grade gliomas and astrocytomas. The study focused on three primary objectives: tumour localisation, identification of residual tumours, and exclusion of postoperative complications. In three cases, iCT was utilised for precise localisation of lesions, while in seven cases, it was employed to identify residual tumours, which were detected in three cases (42.86%). In one of these cases, the tumour was inaccessible, while in another, the identification of contrast-enhancing tissue, which had not been visible grossly, led to additional tumour removal. Postoperatively, iCT was utilized in six cases to successfully confirm the absence of surgical complications.

Lunsford et al.[23] conducted a case series with three patients undergoing brain tumour surgery, including two with glioblastoma multiforme and one with astrocytoma. The grade of astrocytoma has not been reported in the study. The use of iCT provided precise intraoperative imaging to guide the resection. While specific operating times and resection extents were not provided, the study emphasised iCT's potential to improve surgical accuracy. No postoperative complications related to iCT were reported.

Shalit et al.[24], a case series, evaluated the use of iCT scanning in 10 patients with malignant brain tumours, including high-grade gliomas and astrocytomas. Postoperative CT scans indicated extensive tumour resection in all patients, with five showing no visible residue immediately postoperatively. However, tumour recurrence was observed in two cases during follow-up. Two patients had tumours in critical brain areas, with no neurological deterioration postoperatively. Overall, the use of iCT improved the extent of tumour resection and resulted in a smooth postoperative course for all patients. The authors noted that iCT might be valuable in managing invasive brain tumours.

4) DISCUSSION

This systematic review assesses the surgical outcomes associated with the use of iCT in intra-axial brain tumor surgeries. While iCT is a valuable tool for enhancing surgical navigation, current evidence does not convincingly demonstrate a significant improvement in key neuro-oncological outcomes compared to other imaging modalities, including iMRI and 5-ALA fluorescence.

Residual tumour detection was reported in nine of the thirteen included studies[4,13–16,18,22–24]. All of these studies reported that iCT successfully identified residual tumours in a majority of the patients, with seven studies noting its use for further debulking of these identified tumours[4,13–16,22,24]. The invasiveness of individual tumours is a factor to consider, which can vary even within the same histopathological tumour type[28]. This variability presents significant challenges during resection, as these tumours often infiltrate healthy tissue and mimic normal anatomical

structures, making them difficult to detect and completely remove. iCT not only enhances intraoperative visualization but also enables surgeons to identify and resect deep-seated residual tumours that might otherwise go unnoticed.

There was significant variability in the reported outcomes amongst different studies. Hosoda et al.[13] reported significantly higher five-year survival rates in the iCT group (87%) compared to the non-iCT group (57%) ($p < 0.00001$) for patients with low-grade gliomas. In contrast, Barbagallo et al.[16] found no significant differences in outcomes between the iCT and non-iCT groups. The interpretation of Barbagallo et al.'s findings is complicated by the use of 5-ALA in both study arms. The use of 5-ALA is known to enhance tumour visualization and improve the extent of resection in high-grade glioma surgeries, and it has been shown to be on par with iMRI[25]. This potentially diminishes any observable differences attributable to iCT alone.

However, it is important to note that outcomes are influenced by multiple factors such as patient condition and tumour biology[27], which are inadequately addressed in the current evidence base. As such, the independent contribution of assistive technologies like iCT to overall outcomes remains uncertain.

KPS scores were reported in three studies[13],[16],[19], with two showing a trend toward better postoperative scores, but the differences were not statistically significant[13],[16]. Notably, one of these studies[16] included the use of 5-ALA in both the iCT and non-iCT groups, which introduces a significant uncontrolled confounder, as the improved visualization from 5-ALA could independently contribute to better surgical outcomes, regardless of iCT usage[26]. The third study, a case series without a control group, reported a significant improvement in KPS scores from

80% preoperatively to 86% postoperatively. However, without a comparison group, these results cannot be considered significant[19].

Although EOTR showed favorable results, only two studies reported this as an outcome[15],[16], and the improvements in one of these studies were not statistically significant, where the use of 5-ALA in both iCT and non-iCT groups likely influenced the extent of resection[16]. The EOTR reported by these studies may be influenced by certain biases mainly due to the absence of a control group in both studies, as well as various factors including the surgeon's skill and the tumour's type, grade, location, and accessibility, which influence the complexity of resection, regardless of advanced intraoperative techniques like iCT. Since iCT generally led to an increase in the EOTR, a greater extent of resection would intuitively allow for a more optimized treatment course. While iCT itself does not change the treatment strategy per se, better intraoperative tumour visualization may enable more informed surgical decisions and potentially enhance treatment outcomes.

Most studies indicate that iCT adds time to surgeries due to preoperative setup and intraoperative scanning, with an average increase of 8 to 20 minutes. The added duration, particularly under general anaesthesia, may elevate patient risks and require closer monitoring. High-grade tumours may need multiple scans, further extending surgery time. However, studies like Haberland et al.[20] suggest that iCT can actually shorten total surgery time by enhancing surgical precision, enabling quicker neuronavigation, and correcting brain shifts mid-procedure.

Most studies reported few or no significant peri-operative adverse events associated with iCT, confirming the safety and tolerability of iCT and supporting its potential value in neurosurgical practice and operative workflow. Among the thirteen studies included, only four reported

postoperative complications[15],[16],[19],[21], which were generally minor and transient, including cases of hemiparesis and biopsy channel bleedings that resolved spontaneously before discharge. The lack of reported postoperative complications significantly limits the evidence quality. Without comprehensive outcome data, drawing firm conclusions on iCT's effectiveness in reducing complications remains untenable.

iCT systems have demonstrated more convincing utility in other areas, particularly where iMRI uses are limited. In spinal surgeries, for example, iCT's excellent bony visualization makes it the preferred intraoperative imaging modality[29]. iCT also excels in neurosurgical applications, such as DBS[30] and aneurysm surgeries, where iMRI may fall short. For aneurysm procedures, iCT's intraoperative and postoperative assessment capabilities offer critical advantages, as demonstrated in studies by Uhl et al.[20] and Barbagallo et al.[16], where iCT angiography was used to monitor residual aneurysmal flow. Recent advancements in ultra-high-resolution CT technology from Japan further enhance iCT's precision by minimizing imaging artefacts[31],[32].

This discussion would be amiss without delving into the utility of 5-ALA and iCT for glioma surgery and improving EOTR. 5-ALA is particularly effective in high-grade gliomas, where its fluorescence significantly enhances tumour visualization. In these cases, iCT can complement 5-ALA by improving residual tumour detection or serve as an alternative when 5-ALA is unavailable. However, the combined use of these modalities remains underexplored.

Barbagallo et al.[16] investigated the use of both iCT and 5-ALA but could not isolate iCT's contribution due to 5-ALA's presence in both study arms. In contrast, Hosoda et al. demonstrated the effectiveness of iCT alone in low-grade glioma resection, where 5-ALA's utility is limited due to insufficient fluorescence properties. This highlights iCT's versatility,

offering enhanced neuronavigation and tumour delineation, particularly for infiltrative tumours near eloquent brain areas.

Overall, iCT proves valuable across glioma grades—serving either as an adjunct to 5-ALA in high-grade gliomas or as a standalone tool in low-grade gliomas and cases where 5-ALA is not feasible. Its ability to improve tumour visualization and aid in achieving a more complete resection may help reduce residual tumour burden and improve long-term outcomes.

Overall, recent improvements in iCT's soft tissue imaging quality, though not yet equal to iMRI, have increased its utility in intra-axial brain tumour surgeries. This resurgence is driven by iCT's improved imaging capabilities, seamless integration into existing operating room setups, and versatile utility in various neurosurgical subspecialties. Pragmatically, if we consider iCT as an adjunct in the armamentarium of neurosurgeons and the operating room, then its use in intra-axial tumours can be justified in specific scenarios and nuanced cases, as highlighted in this review. However, the current literature cannot provide any significant evidence that iCT may improve patient-oriented outcomes, such as quality of life, or progression-free outcomes across the board. However, it may provide more benefits in individual cases, as highlighted by more recent publications utilizing newer iCT systems.

Limitations

The limitations of this systematic review primarily arise from the study designs and quality of the included studies. Eleven of the thirteen studies were case series without control groups, which weakened the overall evidence. The absence of randomized controlled trials comparing iCT with other modalities strongly limits the ability to draw definitive conclusions on the clinical benefits of iCT, hinders the development of standardized guidelines, and raises concerns about

selection bias and confounding factors. Even in studies with control groups, small sample sizes limited the ability to detect statistically significant differences and reduced the generalizability of the findings. None of the included studies reported on the molecular status of the tumours. This may introduce potential bias in our review, as tumour-associated morbidity can be influenced by molecular profiling such as IDH (Isocitrate Dehydrogenase) or MGMT (O6-Methylguanine-DNA Methyltransferase) status. Many studies also focused more on the technical aspects of iCT rather than directly evaluating surgical outcomes, diminishing the relevance to our research objectives. Variability in reported outcomes further complicated the analysis, as not all studies assessed the same surgical outcomes, and methodological differences led to heterogeneity. One inherent limitation of our study is the wide time span of the included studies, ranging from 1982 to 2018, a period during which CT technology has undergone substantial advancements. Variations in imaging quality, resolution, and diagnostic capabilities across different time points may have influenced reported outcomes, making direct comparisons challenging. However, this limitation is not unique to our analysis but rather reflects a constraint within the existing literature. Despite these differences, the inclusion of studies across this extended timeframe remains valuable, as it offers a broad perspective on the evolution of intraoperative CT (iCT)-based assessments. By encompassing studies from different technological eras, our review highlights the gaps in the field and serves as a foundational proof of concept for understanding long-term trends in clinical outcomes. Most studies exhibited moderate bias, further reducing the evidence's strength. Furthermore, the literature presented a lack of detailed reporting on adjuvant treatment received by the patients. This can affect the clinical outcomes significantly, as adjuvant treatment protocols are associated with better prognosis and reduced morbidity. The potential influence of publication bias cannot be overlooked, as studies demonstrating positive outcomes

with iCT are more likely to be published, while negative or inconclusive findings may be underreported, potentially overestimating its benefits.

Future studies should ideally be of high quality and prospective in design, incorporate a control group, include sufficiently long follow-up periods to evaluate overall outcomes, and provide more detailed reporting of both preoperative and postoperative parameters. Most importantly, comparative studies must have a large enough sample of individual intra-axial tumours by molecular and histopathological subtypes to make any meaningful comparison.

5) CONCLUSION

ICT technology has significantly improved, and it is a valuable tool in the armamentarium of neurosurgeons and operating rooms. Its use specifically in intra-axial brain tumours may be of benefit in specific cases; however, the current evidence does not support that the use of iCT as an adjunct contributes to improved overall survival or better functional outcomes in general. The application of iCT might seem revolutionary on the outside but literature is only sparsely populated with trials and studies proving the absolute superiority of iCT over other neurosurgical radiological investigations in use currently. This is primarily due to a lack of appropriately designed high-quality studies. Smaller experiences of individual authors/centres provide some argument for iCT's utility in specific cases and warrant further work.

6) CREDIT AUTHOR CONTRIBUTION STATEMENT

Mohammad Ashraf: Conceptualization, Validation, Project administration, Visualization, Writing – review & editing. Sophia Ahmed: Project administration, Visualization, Data curation, Writing – original draft, Writing – review & editing. Muhammad Asfandyar Nadir: Writing – original draft, Writing – review & editing. Zuha Tariq: Writing – original draft, Writing – review & editing. Mahrukh Iqbal: Data curation, Writing – original draft, Writing – review & editing. Maha Malik: Data curation, Writing – original draft, Writing – review & editing. Muhammad Haris Khan: Writing – original draft, Writing – review & editing. Arfa Ahmed Assad: Writing – original draft, Writing – review & editing. Abdul Rehman Saeed: Data Curation. Abdul Rafeh Awan: Writing – original draft. Javed Iqbal: Writing – review & editing. Conor S Gillespie: Writing – review & editing.

7) DECLARATIONS

7.1) Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or

professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

7.2) Competing Interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

7.3) Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

7.4) Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

7.5) Availability of data and materials

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

7.6) Formal consent

For this type of study formal consent is not required.

7.7) Informed Consent

This article does not contain any studies with human participants performed by any of the authors.

9) ACKNOWLEDGEMENTS

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10) GLOSSARY

Astrocytomas: A type of glioma originating from astrocytes, star-shaped glial cells in the brain or spinal cord.

Deep brain stimulation (DBS): A neurosurgical procedure involving the implantation of electrodes to modulate neural activity, typically used for movement disorders like Parkinson's disease.

High-grade gliomas (HGGs): Aggressive brain tumors classified as Grade III or IV by the World Health Organization, often associated with poor prognosis.

Intraxial brain tumors: Tumors that originate within the brain parenchyma, such as gliomas or astrocytomas.

Intraoperative computed tomography (iCT): Imaging performed during surgery to guide procedures, confirm resection, and minimize complications.

Intraoperative magnetic resonance imaging (iMRI): MRI technology used during surgery to enhance tumor resection accuracy and reduce residual tumor volume.

Kaplan-Meier survival curves: Statistical graphs used to estimate survival probabilities over time, often applied in medical research.

KPS (Karnofsky Performance Status) score: A scale used to assess a patient's functional status and ability to carry out daily activities, often in cancer treatment.

Neuronavigation: A surgical navigation system that provides real-time imaging and guidance to enhance precision in neurosurgery.

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines: A standardized framework for conducting and reporting systematic reviews to ensure clarity, transparency, and reproducibility.

10) REFERENCES

1. Kim JT, Di L, Etame AB, Olson S, Vogelbaum MA, Tran ND. Use of virtual magnetic resonance imaging to compensate for brain shift during image-guided surgery: illustrative case. *Journal of Neurosurgery: Case Lessons*. 2022;3(24):CASE21683. doi:10.3171/CASE21683

2. Nabavi A, McL. Black P, Gering DT, et al. Serial Intraoperative Magnetic Resonance Imaging of Brain Shift. *Neurosurgery*. 2001;48(4). https://journals.lww.com/neurosurgery/fulltext/2001/04000/serial_intraoperative_magnetic_resonance_imaging.19.aspx

3. Renfrow JJ, Strowd RE, Laxton AW, Tatter SB, Geer CP, Lesser GJ. Surgical Considerations in the Optimal Management of Patients with Malignant Brain Tumors. *Curr Treat Options Oncol*. 2017;18(8):1-15. doi:10.1007/S11864-017-0487-8/METRICS

4. Schichor C, Terpolilli N, Thorsteinsdottir J, Tonn JC. Intraoperative Computed Tomography in Cranial Neurosurgery. *Neurosurg Clin N Am*. 2017;28(4):595-602. doi:10.1016/J.NEC.2017.05.010

5. Noh T, Mustroph M, Golby AJ. Intraoperative Imaging for High-Grade Glioma Surgery. *Neurosurg Clin N Am*. 2021;32(1):47-54. doi:10.1016/J.NEC.2020.09.003

6. Gandhe RU, Bhave CP. Intraoperative magnetic resonance imaging for neurosurgery - An anaesthesiologist's challenge. *Indian J Anaesth*. 2018;62(6):411-417. doi:10.4103/IJA.IJA_29_18

7. Kilcoyne RF, Richardson ML, Porter BA, Olson DO, Greenlee TK, Lanzer W. Magnetic resonance imaging of soft tissue masses. *Clin Orthop Relat Res*. 1988;(228):13-19.

8. Senft C, Bink A, Franz K, Vatter H, Gasser T, Seifert V. Intraoperative MRI guidance and extent of resection in glioma surgery: a randomised, controlled trial. *Lancet Oncol*. 2011;12(11):997-1003. doi:10.1016/S1470-2045(11)70196-6

9. Makary M, Chiocca EA, Erminy N, et al. Clinical and economic outcomes of low-field intraoperative MRI-guided tumor resection neurosurgery. *J Magn Reson Imaging*. 2011;34(5):1022-1030. doi:10.1002/JMRI.22739

10. Thorsteinsdottir J, Sandner T, Biczok A, et al. Detection of impending perfusion deficits by intraoperative computed tomography (iCT) in aneurysm surgery of the anterior circulation. *Acta Neurochir (Wien)*. 2021;163(12):3501-3514. doi:10.1007/S00701-021-05022-8

11. Carl B, Bopp M, Gjorgjevski M, Oehrn C, Timmermann L, Nimsky C. Implementation of Intraoperative Computed Tomography for Deep Brain Stimulation: Pitfalls and Optimization of

Workflow, Accuracy, and Radiation Exposure. *World Neurosurg*. 2018;124:e252-e265. doi:10.1016/J.WNEU.2018.12.079

12. Hagan MJ, Syed S, Leary OP, et al. Pedicle Screw Placement Using Intraoperative Computed Tomography and Computer-Aided Spinal Navigation Improves Screw Accuracy and Avoids Postoperative Revisions: Single-Center Analysis of 1400 Pedicle Screws. *World Neurosurg*. 2022;160:e169-e179. doi:10.1016/J.WNEU.2021.12.112

13. Hosoda T, Takeuchi H, Hashimoto N, et al. Usefulness of intraoperative computed tomography in surgery for low-grade gliomas: a comparative study between two series without and with intraoperative computed tomography. *Neurol Med Chir (Tokyo)*. 2011;51(7):490-495. doi:10.2176/NMC.51.490

14. Nakao N, Nakai K, Itakura T. Updating of neuronavigation based on images intraoperatively acquired with a mobile computerized tomographic scanner: technical note. *Minim Invasive Neurosurg*. 2003;46(2):117-120. doi:10.1055/S-2003-39344

15. Barbagallo GMV, Morrone A, Certo F. Intraoperative Computed Tomography and Awake Craniotomy: A Useful and Safe Combination in Brain Surgery. *World Neurosurg*. 2018;119:e159-e166. doi:10.1016/J.WNEU.2018.07.078

16. Barbagallo GMV, Palmucci S, Visocchi M, et al. Portable Intraoperative Computed Tomography Scan in Image-Guided Surgery for Brain High-grade Gliomas. *Operative Neurosurgery*. 2016;12(1):19-30. doi:10.1227/NEU.0000000000001112

17. Uhl E, Zausinger S, Morhard D, et al. Intraoperative computed tomography with integrated navigation system in a multidisciplinary operating suite. *Neurosurgery*. 2009;64(5 Suppl 2). doi:10.1227/01.NEU.0000340785.51492.B5

18. Gumprecht H, Lumenta CB. Intraoperative imaging using a mobile computed tomography scanner. *Minim Invasive Neurosurg*. 2003;46(6):317-322. doi:10.1055/S-2003-812496

19. Haberland N, Ebmeier K, Hliscs R, et al. Neuronavigation in surgery of intracranial and spinal tumors. *J Cancer Res Clin Oncol*. 2000;126(9):529-541. doi:10.1007/S004320000122

20. Gwinn R, Cleary K, Medlock M. Use of a portable CT scanner during resection of subcortical supratentorial astrocytomas of childhood. *Pediatr Neurosurg*. 2000;32(1):37-43. doi:10.1159/000028895

21. Matsumoto K, Higashi H, Tomita S, Furuta T, Ohmoto T. Resection of deep-seated gliomas using neuroimaging for stereotactic placement of guidance catheters. *Neurol Med Chir (Tokyo)*. 1995;35(3):148-155. doi:10.2176/NMC.35.148

22. Engle DJ, Lunsford LD. Brain tumor resection guided by intraoperative computed tomography. *J Neurooncol*. 1987;4(4):361-370. doi:10.1007/BF00195607

23. Lunsford LD, Parrish R, Albright L. Intraoperative imaging with a therapeutic computed tomographic scanner. *Neurosurgery*. 1984;15(4):559-561. doi:10.1227/00006123-198410000-00017

24. Shalit MN, Israeli Y, Matz S, Cohen ML. Experience with intraoperative CT scanning in brain tumors. *Surg Neurol*. 1982;17(5):376-382. doi:10.1016/0090-3019(82)90319-6

25. Golub D, Hyde J, Dogra S, et al. Intraoperative MRI versus 5-ALA in high-grade glioma resection: a network meta-analysis. *J Neurosurg*. 2020;134(2):484-498. doi:10.3171/2019.12.JNS191203

26. Zeppa P, De Marco R, Monticelli M, et al. Fluorescence-Guided Surgery in Glioblastoma: 5-ALA, SF or Both? Differences between Fluorescent Dyes in 99 Consecutive Cases. *Brain Sci*. 2022;12(5). doi:10.3390/BRAINSCI12050555

27. Verma S, Malviya R, Uniyal P. Survival of Patients with Primary Brain Tumor: A Data Analysis of 10 Years. *Curr Pharm Des*. 2024;30(15):1129-1132. doi:10.2174/0113816128306113240328050608

28. Vollmann-Zwerenz A, Leidgens V, Feliciello G, Klein CA, Hau P. Tumor Cell Invasion in Glioblastoma. *Int J Mol Sci*. 2020;21(6). doi:10.3390/IJMS21061932

29. Florkow MC, Willemsen K, Mascarenhas V V., Oei EHG, van Stralen M, Seevinck PR. Magnetic Resonance Imaging Versus Computed Tomography for Three-Dimensional Bone Imaging of Musculoskeletal Pathologies: A Review. *Journal of Magnetic Resonance Imaging*. 2022;56(1):11. doi:10.1002/JMRI.28067

30. Shahlaie K, Larson PS, Starr PA. Intraoperative computed tomography for deep brain stimulation surgery: technique and accuracy assessment. *Neurosurgery*. 2011;68(1 Suppl Operative). doi:10.1227/NEU.0B013E31820781BC

31. Iwata N, Sakamoto M, Sakou T, Uno T, Kurosaki M. Utility of follow-up ultra-high-resolution CT angiography with model-based iterative reconstruction after flow diverter treatment for cerebral aneurysms. *Radiol Med*. 2023;128(10):1262-1270. doi:10.1007/S11547-023-01692-9

32. Kayano S, Ito A, Endo T, et al. Efficacy of ultra-high-resolution computed tomographic angiography for postoperative evaluation of intracranial aneurysm after clipping surgery: A case report. *Surg Neurol Int*. 2022;13(85):85. doi:10.25259/SNI_1190_2021

9) TABLES

Table 1: Applied search strategies for different databases.

Database	Search Strategy
Embase	"Brain cancer*" or "brain tumor*" or "brain neoplas*" or "brain carcino*" or "brain metastas*" or "brain malignanc*" or "intracranial tumor*" or "intracranial neoplas*" AND "Intraoperative computed tomography" or "iCT*" or "Intraoperative CT" or "X-ray computed tomography" or "computerized axial tomography scan" or "CAT scan" or "computer aided tomography" or "computed tomography scan"
PubMed	("Brain Neoplasm*"[Mesh] OR "Brain neoplasm*"[All Fields] OR "Brain cancer*"[All Fields] OR "Brain tumor*"[All Fields] OR "Brain carcinoma*"[All Fields] OR "Brain Malignanc*"[All Fields] OR "Intracranial lesions"[All Fields]) AND ("Tomography, X-Ray Compute*"[Mesh] OR "iCT"[All Fields] OR "intraoperative CT"[All Fields] OR "intraoperative computed tomography"[All Fields] OR "intraoperative computed tomography scan"[All Fields] OR "intraoperative CT scan"[All Fields])
Cochrane Library	((“Brain Neoplasm” OR “Brain Cancer” OR “Brain carcinoma” OR “Brain malignancy” OR “Intracranial lesions”) AND (“iCT” OR “X-ray computed tomography” OR “computerized axial tomography scan” OR “CAT scan” OR “computer aided tomography” OR “computed tomography scan”))
Google Scholar	"Intraoperative Computed Tomography" in “Brain Tumor Surgery”
Science Direct	(Intraoperative Computed Tomography OR Intraoperative Computerized Tomography Scan OR Intraoperative CT) AND (Brain Tumor OR Brain Neoplasm OR Brain Carcinoma)
Scopus	(TITLE-ABS-KEY ("Brain cancer*" or "brain tumor*" or "brain neoplas*" or "brain carcino*" or "brain metastas*" or "brain malignanc*" or "intracranial tumor*" or "intracranial neoplas*")) AND (TITLE-ABS-KEY ("Intraoperative computed tomography" or "iCT*" or "Intraoperative CT" or "X-ray computed tomography" or "computerized axial tomography scan" or "CAT scan" or "computer aided tomography" or "computed tomography scan")) AND (LIMIT-TO (DOCTYPE , "ar", Medicine and Neuroscience))

Table 2.1: Quality Assessment JBI*.

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Shalit 1982	Unclear	Yes	Yes	No	Unclear	Yes	Yes	Yes	No	N/A

Lunsford 1985	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Engle 1987	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Matsumoto 1995	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Gwinn 2000	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Barbagallo 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Barbagallo 2018	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	N/A

***** *Below are the 10 questions included in the JBI critical appraisal tool for case series:*

1. Were there clear criteria for inclusion in the case series?

2. Was the condition measured in a standard, reliable way for all participants included in the case series?

3. Were valid methods used for identification of the condition for all participants included in the case series?

4. Did the case series have consecutive inclusion of participants?

5. Did the case series have complete inclusion of participants?

6. Was there clear reporting of the demographics of the participants in the study?

7. Was there clear reporting of clinical information of the participants?

8. Were the outcomes or follow-up results of cases clearly reported?

9. Was there clear reporting of any interventions or treatments received by participants?

10. Were the presenting sites (clinics) or participant populations included in the case series similar to those of the target population?

Answers are:

Yes

No

Unclear

Not applicable (N/A)

Table 2.2: Quality Assessment ROBBINS.

Study	D1	D2	D3	D4	D5	D6	D7	Overall
Haberland 2000	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Uhl 2000	Serious	Serious	Moderate	Moderate	Serious	Serious	Serious	Serious
Gumprecht 2003	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Nakao 2003	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Hosoda 2011	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Schichor 2017	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate

Table 3: Summary of common outcomes.

StudyID	Population	Age (years)	Males	Type and Location of tumor	Neuronavigation modalities	iCT Scanner characteristics	Contrast Media Used	Outcomes	Adverse Events
Gumprecht 2003	76	-	-	Glioma: 43 Meningioma: 11 Metastasis: 11 Catheter placement: 4 Cavernoma: 2 Others: 5	i-CT	Philips Tomoscan Mobile CT scanner	Gadolinium	**Residual Tumor Detection:** 32 patients (42%) **Image Quality:** High **Comparison with iMRI:** in 6 of 44 cases iMRI demonstrated residual tumor compared to iCT (14%). In 2 cases, iCT identified residual tumor not detected by iMRI	-
Lunsford 1984	3	28	-	Glioblastoma Multiforme: 2 Astrocytoma: 1 Frontal: 2/Thalamic: 1	Contrast Enhanced i-CT	GE 8800 CT/T scanner (General Electric Medical Systems, Milwaukee, Wisconsin)	Yes	**Residual Tumor Detection:** 2 patients (67%)	-
Nakao 2003	8	46	2	Glioblastoma: 3 Anaplastic Astrocytoma: 1 Astrocytoma: 1 Metastasis: 2 Cavernoma: 1 Frontal: 3/Temporal: 2/ Basal Ganglia: 2/Suprasellar: 1	i-CT and i-MR	Mobile CT Scanner. 2mm slice thickness.	Yes	**Residual Tumor Detection:** 7 patients (88%) on iCT **Comparison with iMRI:** 7/8 residual lesions detected by iCT while only 4/8 (50%) were detected by iMRI	-
Uhl 2009	136	51±17	72	Meningioma: 34 Pituitary lesion: 45 Glioma: 8 Metastasis: 7 Other: 20 Aneurysm: 7 Cerebellar pathology: 3 Ventricular lesion: 9	i-CT (111/136 had an iCT scan)	40-multislice CT scanner (Somatom Sensation Open Sliding Gantry; Siemens Medical Solutions, Forchheim, Germany). Slice thickness in cranial surgery 0.6, 1.0, 1.5, 2.0, 5.0 mm CTA: 1.0mm Spinal surgery: 3mm	Imeron 300; Bracco-Altana-Pharma, Konstanz, Germany.	**Residual Tumor Detection:** 9 patients of 64 iCT patients for complete resection (14.1%) **Image Quality:** Excellent	No adverse events or postoperative complications
Barbagallo 2016	50	Group A: 58 Group B: 61	Group A: 15 Group B: 13	High Grade Gliomas:25 Glioblastoma Multiforme: 21 Anaplastic Astrocytoma: 2 Anaplastic oligodendroglioma: 2 Frontal: 9/Rolandic: 3/Parietal: 3/Insular: 2/Cerebellum: 1/Temporal: 1/Multicentric: 4/Frontoinsular: 2	i-CT+5-ALA fluorescence (**Group A, n: 25**) vs. 5-ALA fluorescence surgery alone (**Group B, n: 25**)	8-slice small-bore portable CT scanner (CereTom; NeuroLogica, Danvers, Massachusetts) 1.25 mm slice thickness with 5-ALA contrast enhancement	1. Iodinatedcontrast (Iomeron [Bracco, Milan, Italy] 300 mg/mL, containing 61.24 g Iomeprol in 100 mL) 2. 5-ALA	**Residual Tumor Detection:** 8 patients (32%) **Post-op KPS Score:** 69.2 **EOTR:** Group A: 97.3%, Group B: 98%	**Post-op complications:** One patient in Group B experienced a transient worsening of preoperative neurological condition
Engle 1987	9	Range: 2-87	4	Glioblastoma Multiforme: 4 Anaplastic Astrocytoma: 1 Astrocytoma: 1 Intracranial Hematoma: 1 Metastatic Carcinoma: 1 Frontal: 3/Occipital: 1/Parietal: 3/Thalamic: 2	i-CT	GE 8800 CT/T scanner (General Electric Medical Systems, Milwaukee, Wisconsin)	Yes	**Residual Tumor Detection:** 7 patients (78%)	6 patients had intraoperative CT scan to ensure no operative complications had occurred
Haberland 2000	57	43	33	-	i-CT, i-US and i-MR	Lerch Microstereotaxy system 2001. 2mm slice thickness	-	**Karofsky Index**: Improved from 80% preoperatively to 86% postoperatively. **Time:** Accelerated workflow, time reduced from a mean time of 4.4 hours to 2.6 hours	**Post-op complications:** Small bleedings along the biopsy channel were seen in 2.4% of patients
Hosoda 2011	46	Non-ICT Group: 39.5 ICT Group: 42.0	Non-ICT group: 16 ICT group: 7	Astrocytoma: 27 Oligodendroglioma: 19	i-CT	X vision /SP; Toshiba Corp, Tokyo. 2mm slice thickness	-	**Post-Op KPS score:** Non ICT group 78.6±24.4 ICT group 91.7±10.3. **Residual Tumor Detection:** 11 patients in the iCT group (48%) **Image Quality:** Less than intraoperative MRI **5 year survival rate:** 87% in iCT group vs 57% in non-iCT group	-
Matsumoto 1995	15	42.3	7	Astrocytoma Grade II: 7 Astrocytoma Grade III: 3 Ependymoma: 1 Glioblastoma: 4 Frontal: 8/Parietal: 2/Thalamus: 5	i-CT (6/15 underwent CT guided stereotactic surgery) and i-MR	A Brown Roberts-Wells (BRW) CT stereotactic system. 5 mm axial CT	Yes	**Post-op neurological status improvement:** 2 patients (1 of CT surgery)	**Post-op complications:** 1 patient (MR stereotactic surgery) suffered transient hemiparesis after the resection of the lesion in the pyramidal tract
Schichor 2017	23	-	-	Skull base tumors	i-CT and i-CTA	Siemens SOMATOM. 40-slice sliding-gantry	Iomeron 300	**Residual Tumor Detection:** 12 patients (52%) **Image Quality:** Excellent	No intraoperative or postoperative complications.

Table 3: Summary of common outcomes (continued).

StudyID	Population	Age (years)	Males	Type and Location of tumor	Neuronavigation modalities	iCT Scanner characteristics	Contrast Media Used	Outcomes	Adverse Events
Shalit 1982	10	37.4	3	Malignant Melanoma: 1 Glioma: 9	i-CT	-	-	**Residual Tumor Detection:** 6 patients (60%)	-
Gwinn 2000	4	9.75	3	Astrocytomas: 4 Thalamus: 2/Midbrain: 1/Caudate Nucleus: 1	i-CT	-	-	**Post-operative residual tumor detection:** 3 (75%) but these were due to surgeon choice to avoid further morbidity	**Post-op complications:** 2 patients with hemiparesis, 1 patient with no improvement of pre-op symptoms.
Barbagallo 2018	4	48.5	2	Low-Grade Glioma (LGG): 2, high-grade glioma (HGG): 1, cavernous hemangioma: 1	i-CT and i-US	Small-bore portable scanner (CereTom; NeuroLogica, Danvers, Massachusetts, USA) in 3 of 4 cases, and a portable scanner with a large bore	-	**EOTR:** 98.2%	**Postoperative neurological complications:** 100%

10) FIGURE LEGENDS

Figure 1: PRISMA Flow Diagram.

Figure 2.1: Risk of Bias Domains.

Figure 2.2: Overall Risk of Bias.

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Embase	"Brain cancer*" or "brain tumor*" or "brain neoplas*" or "brain carcino*" or "brain metastas*" or "brain malignanc*" or "intracranial tumor*" or "intracranial neoplas*" AND "Intraoperative computed tomography" or "iCT*" or "Intraoperative CT" or "X-ray computed tomography" or "computerized axial tomography scan" or "CAT scan" or "computer aided tomography" or "computed tomography scan"
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Engle 1987	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Matsumoto 1995	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Gwinn 2000	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	N/A
Barbagallo 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Barbagallo 2018	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	N/A

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9. Was there clear reporting of any interventions or treatments received by participants?
10. Were the presenting sites (clinics) or participant populations included in the case series similar to those of the target population?
Answers are:
Yes
No
Unclear
Not applicable (N/A)

Table 2.2: Quality Assessment ROBBINS.

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Gumprecht 2003	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Nakao 2003	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Hosoda 2011	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Schichor 2017	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate

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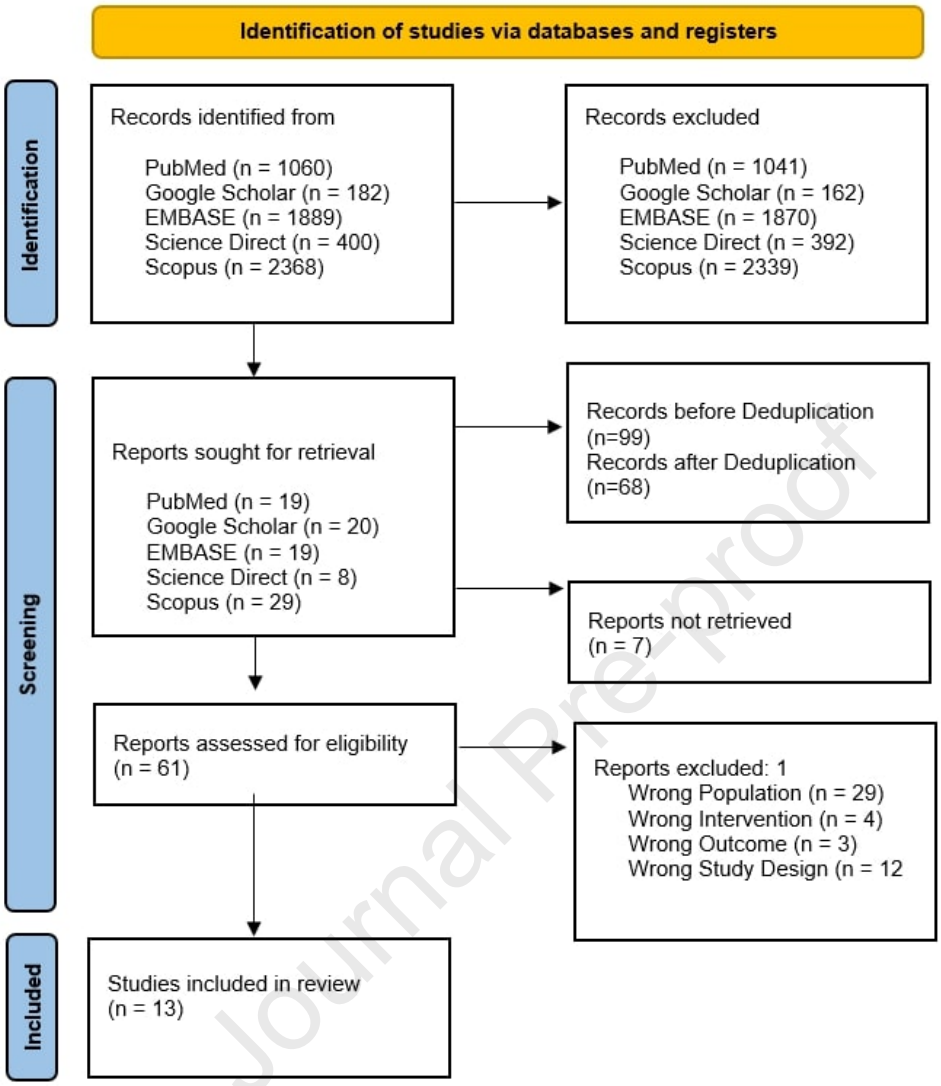
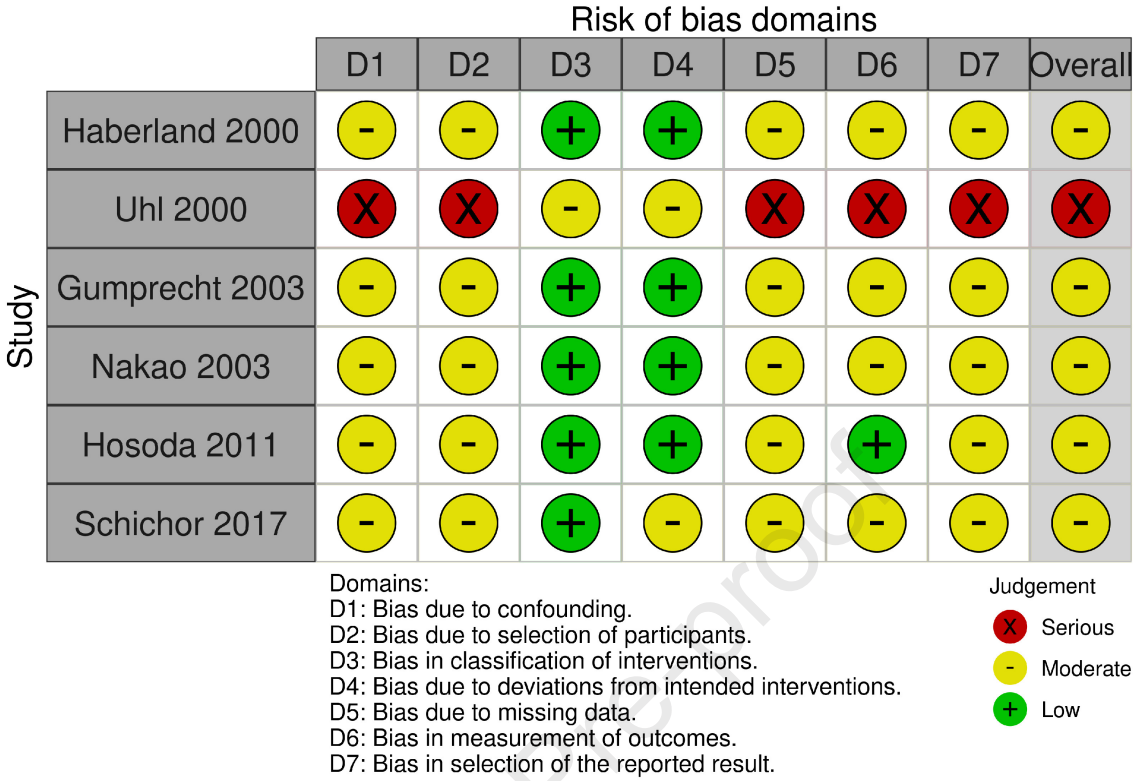
Lunsford 1984	3	28	-	Glioblastoma Multiforme: 2 Astrocytoma: 1 Frontal: 2/Thalamic: 1	Contrast Enhanced i-CT	GE 8800 CT/T scanner (General Electric Medical Systems, Milwaukee, Wisconsin)	Yes	**Residual Tumor Detection:** 2 patients (67%)	-
Nakao 2003	8	46	2	Glioblastoma: 3 Anaplastic Astrocytoma: 1 Astrocytoma: 1 Metastasis: 2 Cavernoma: 1 Frontal: 3/Temporal: 2/ Basal Ganglia: 2/Suprasellar: 1	i-CT and i-MR	Mobile CT Scanner. 2mm slice thickness.	Yes	**Residual Tumor Detection:** 7 patients (88%) on iCT **Comparison with iMRI:** 7/8 residual lesions detected by iCT while only 4/8 (50%) were detected by iMRI	-
Uhl 2009	136	51±17	72	Meningioma: 34 Pituitary lesion: 45 Glioma: 8 Metastasis: 7 Other: 20 Aneurysm: 7 Cerebellar pathology: 3 Ventricular lesion: 9	i-CT (111/136 had an iCT scan)	40-multislice CT scanner (Somatom Sensation Open Sliding Gantry; Siemens Medical Solutions, Forchheim, Germany). Slice thickness in cranial surgery 0.6, 1.0, 1.5, 2.0, 5.0 mm CTA: 1.0mm Spinal surgery: 3mm	Imeron 300; Bracco-Altana-Pharma, Konstanz, Germany.	**Residual Tumor Detection:** 9 patients of 64 iCT patients for complete resection (14.1%) **Image Quality:** Excellent	No adverse events or postoperative complications
Barbagallo 2016	50	Group A: 58 Group B: 61	Group A: 15 Group B: 13	High Grade Gliomas:25 Glioblastoma Multiforme: 21 Anaplastic Astrocytoma: 2 Anaplastic oligodendroglioma: 2 Frontal: 9/Rolandic: 3/Parietal: 3/Insular: 2/Cerebellum: 1/Temporal: 1/Multicentric: 4/Frontoinsular: 2	i-CT+5-ALA fluorescence (**Group A, n: 25**) vs. 5-ALA fluorescence surgery alone (**Group B, n: 25**)	8-slice small-bore portable CT scanner (CereTom; NeuroLogica, Danvers, Massachusetts) 1.25 mm slice thickness with 5-ALA contrast enhancement	1. Iodinatedcontrast (Iomeron [Bracco, Milan, Italy] 300 mg/mL, containing 61.24 g Iomeprol in 100 mL) 2. 5-ALA	**Residual Tumor Detection:** 8 patients (32%) **Post-op KPS Score:** 69.2 **EOTR:** Group A: 97.3%, Group B: 98%	**Post-op complications:** One patient in Group B experienced a transient worsening of preoperative neurological condition
Engle 1987	9	Range: 2-87	4	Glioblastoma Multiforme: 4 Anaplastic Astrocytoma: 1 Astrocytoma: 1 Intracranial Hematoma: 1 Metastatic Carcinoma: 1 Frontal: 3/Occipital: 1/Parietal: 3/Thalamic: 2	i-CT	GE 8800 CT/T scanner (General Electric Medical Systems, Milwaukee, Wisconsin)	Yes	**Residual Tumor Detection:** 7 patients (78%)	6 patients had intraoperative CT scan to ensure no operative complications had occurred
Haberland 2000	57	43	33	-	i-CT, i-US and i-MR	Lerch Microstereotaxy system 2001. 2mm slice thickness	-	**Karofsky Index**: Improved from 80% preoperatively to 86% postoperatively. **Time:** Accelerated workflow, time reduced from a mean time of 4.4 hours to 2.6 hours	**Post-op complications:** Small bleedings along the biopsy channel were seen in 2.4% of patients
Hosoda 2011	46	Non-ICT Group: 39.5 ICT Group: 42.0	Non-ICT group: 16 ICT group: 7	Astrocytoma: 27 Oligodendroglioma: 19	i-CT	X vision /SP; Toshiba Corp, Tokyo. 2mm slice thickness	-	**Post-Op KPS score:** Non ICT group 78.6±24.4 ICT group 91.7±10.3. **Residual Tumor Detection:** 11 patients in the iCT group (48%) **Image Quality:** Less than intraoperative MRI **5 year survival rate:** 87% in iCT group vs 57% in non-iCT group	-

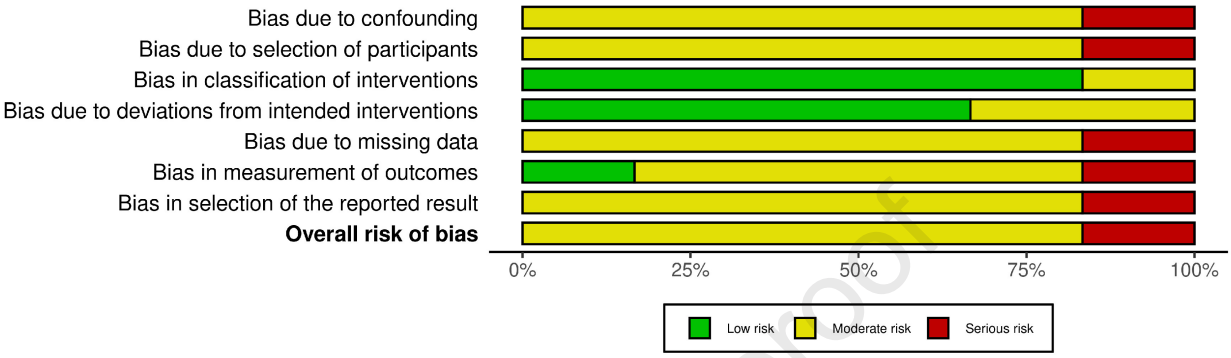
Table 3: Summary of common outcomes (continued).

Matsumoto 1995	15	42.3	7	Astrocytoma Grade II: 7 Astrocytoma Grade III: 3 Ependymoma: 1 Glioblastoma: 4 Frontal: 8/Parietal: 2/Thalamus: 5	i-CT (6/15 underwent CT guided stereotactic surgery) and i-MR	A Brown Roberts-Wells (BRW) CT stereotactic system. 5 mm axial CT	Yes	**Post-op neurological status improvement:** 2 patients (1 of CT surgery)	**Post-op complications:** 1 patient (MR stereotactic surgery) suffered transient hemiparesis after the resection of the lesion in the pyramidal tract
Schichor 2017	23	-	-	Skull base tumors	i-CT and i-CTA	Siemens SOMATOM. 40-slice sliding-gantry	Iomeron 300	**Residual Tumor Detection:** 12 patients (52%) **Image Quality:** Excellent	No intraoperative or postoperative complications.

StudyID	Population	Age (years)	Males	Type and Location of tumor	Neuronavigation modalities	iCT Scanner characteristics	Contrast Media Used	Outcomes	Adverse Events
Shalit 1982	10	37.4	3	Malignant Melanoma: 1 Glioma: 9	i-CT	-	-	**Residual Tumor Detection:** 6 patients (60%)	-
Gwinn 2000	4	9.75	3	Astrocytomas: 4 Thalamus: 2/Midbrain: 1/Caudate Nucleus: 1	i-CT	-	-	**Post-operative residual tumor detection:** 3 (75%) but these were due to surgeon choice to avoid further morbidity	**Post-op complications:** 2 patients with hemiparesis, 1 patient with no improvement of pre-op symptoms.
Barbagallo 2018	4	48.5	2	Low-Grade Glioma (LGG): 2, high-grade glioma (HGG): 1, cavernous hemangioma: 1	i-CT and i-US	Small-bore portable scanner (CereTom; NeuroLogica, Danvers, Massachusetts, USA) in 3 of 4 cases, and a portable scanner with a large bore	-	**EOTR:** 98.2%	**Postoperative neurological complications:** 100%







ABBREVIATIONS

5-ALA: 5-aminolevulinic acid

DBS: Deep brain stimulation

ENT: Ear, nose, and throat

EOTR: Extent of tumor resection

HGGs: High-grade gliomas

iMRI: Intraoperative magnetic resonance imaging

JBI: Joanna Briggs Institute

KPS: Karnofsky Performance Status

MeSH: Medical Subject Headings

MEG: Magnetoencephalography

OS: Overall survival

PFS: Progression-free survival

PICOS: Population, Intervention, Comparison, Outcome, Study design

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT: Randomized controlled trial

ROBINS-I: Risk of Bias In Non-randomized Studies - of Interventions

DECLARATIONS AND DISCLOSURE-CONFLICT OF INTEREST STATEMENTS

Conflict of interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: