

Brain metastases

- [Systematic review and epistemic meta-analysis to advance binomial AI-radiomics integration for predicting high-grade glioma progression and enhancing patient management](#)
 - [Carboplatin, etoposide, atezolizumab, and bevacizumab in the first-line treatment of patients with extensive stage small-cell lung cancer: the GOIRC-01-2019 CeLEBrATE study](#)
 - [Predicting the efficacy of bevacizumab on peritumoral edema based on imaging features and machine learning](#)
 - [A quantitative characterization of the heterogeneous response of glioblastoma U-87 MG cell line to temozolomide](#)
 - [RANO criteria for response assessment of brain metastases based on amino acid PET imaging](#)
 - [Fusion-Brain-Net: A Novel Deep Fusion Model for Brain Tumor Classification](#)
 - [Directional interactions from non-small cell lung cancer to brain glucose metabolism revealed by total-body PET imaging](#)
 - [\[⁶⁸Ga\]Ga-NOTA-T4 ImmunoPET imaging for evaluating TROP2 expression in patients with solid tumors](#)
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see also [Intracranial metastases](#).

Epidemiology

[Brain Metastases Epidemiology](#).

Classification

[Brain Metastases Classification](#).

Scales

[Karnofsky Performance Score](#).

[Response Assessment in Neuro-Oncology Brain Metastases \(RANO-BM\)](#).

Trials

Despite the frequency of brain metastases, prospective trials in this patient population are limited, and the criteria used to assess response and progression in the CNS are heterogeneous ¹⁾.

This heterogeneity largely stems from the recognition that existing criteria sets, such as RECIST ^{2) 3)}.

Genes involved

Whether brain metastases harbor distinct genetic alterations beyond those observed in primary tumors is unknown.

Brastianos et al. detected alterations associated with sensitivity to PI3K/AKT/mTOR, CDK, and HER2/EGFR inhibitors in the brain metastases. Genomic analysis of brain metastases provides an opportunity to identify potentially clinically informative alterations not detected in clinically sampled primary tumors, regional lymph nodes, or extracranial metastases ⁴⁾.

COX2

HBEGF

ST6GALNAC5

HK2

FOXC1

HER2

VEGFA

LEF1

[HOXB9](#)

CDH2, KIFC1, and FALZ3

STAT3

$\alpha v \beta 3$

[HDAC3](#), [JAG2](#), [NUMB](#), [APH1B](#), [HES4](#), and [PSEN1](#)

Molecular Biology

Brain metastasis is a complex process where cancer cells from a primary tumor spread to the brain and establish secondary tumors. The molecular biology of brain metastasis involves multiple steps, including:

Intravasation: cancer cells break away from the primary tumor and enter the bloodstream.

Circulation: cancer cells circulate through the bloodstream and eventually reach the brain.

Extravasation: cancer cells leave the bloodstream and enter the brain tissue.

Colonization: cancer cells establish themselves in the brain and begin to grow.

Evasion of immune response: cancer cells evade the immune system and avoid destruction by

immune cells.

The molecular biology of brain metastasis is influenced by many factors, including the characteristics of the primary tumor, the genetic makeup of the cancer cells, and the microenvironment of the brain. Understanding the molecular biology of brain metastasis is important for the development of new treatments that can effectively target and eliminate cancer cells in the brain.

Molecular biology, genetics, and epigenetics are rapidly expanding, enabling us to advance our knowledge of the underlying mechanisms involved. Research approaches using cell lines that preferentially metastasize in vivo to the brain and in vitro tissue-based studies unfold new molecular leads into the disease. It is important to identify and understand the molecular pathways of the metastatic cascade in order to target the investigation and development of more effective therapies and research directions ⁵⁾.

Tumor immune microenvironment

[Brain metastases immune microenvironment.](#)

Clinical Features

see [Brain metastases Clinical Features.](#)

Diagnosis

see [Brain metastases diagnosis.](#)

Differential diagnosis

see [Brain metastases differential diagnosis.](#)

Treatment

see [Brain metastases treatment.](#)

Outcome

[Brain metastases outcome.](#)

Recurrence

see [Brain metastases recurrence](#).

Systematic review and meta-analysis

Suppre et al. conducted a systematic review and meta-analysis to investigate the local [recurrence](#) rate following surgical [resection](#) of a brain metastasis without [adjuvant therapy](#). The analysis included four studies with a total of 235 cases. It was found that the rate of local recurrence by 12 months was 48.1% (95% CI 41.2-58.9). These findings underscore the high rate of patients who will experience local recurrence within 12 months of surgery, emphasizing the need for vigilant surveillance when omitting adjuvant radiotherapy in favor of systemic treatments with potential but unproven CNS penetrance. The analysis highlights unmet needs in this patient population ⁶⁾.

Randomized controlled trials

There is a lack of prospective randomized studies. Based on retrospective case series, international [guidelines](#) recommend the harvesting (if required, stereotactically guided) of tissue for histological and molecular [diagnosis](#) in cases of unknown or possibly competing for underlying systemic [malignant](#) diseases, in cases of suspected [tumor recurrence](#), and with regard to the evaluation of targeted therapies taking into account molecular [heterogeneity](#) of primary and secondary tumors. Surgical [resection](#) is particularly valuable for the treatment of up to three space-occupying cerebral metastases, especially to achieve clinical stabilization to allow further non-surgical treatment. For cystic metastasis, a combination of stereotactic puncture and radiotherapy may be useful. [Meningeal carcinomatosis](#) can be treated with [intrathecal](#) medication via an intraventricular catheter system. [Ventriculoperitoneal shunts](#) represent an effective treatment option for patients with tumor-associated hydrocephalus.

Neurosurgical procedures are of central importance in the multimodal treatment of cerebral metastases. The indications for neurosurgical interventions will be refined in the light of more effective radiation techniques and systemic treatments with new targeted therapeutic approaches and immunotherapies on the horizon ⁷⁾.

Prospective observational studies

A study provides insights into the prevalence and nature of adverse events (AEs) following intracranial surgery in patients aged 65 years and older. It highlights the complexities and implications of treating this demographic patient population and identifies risk factors associated with AEs. This prospective study includes patients aged 65 years and older with BM who underwent surgery between January 2022 and December 2023. A detailed assessment of AEs, defined as any complication occurring within the first 30 days post-surgery, was conducted. Potential risk factors for the occurrence of AEs were examined. The study encompassed 104 patients, averaging 70.1 ± 2.8 years, with 102 undergoing surgery. The mean age-adjusted Charlson Comorbidity Index (CCI) score was 8.9 ± 1.2 , indicating a significant comorbidity burden, predominantly cardiac conditions. The Karnofsky

Performance Scale (KPS) showed substantial improvement post-surgery, increasing from $71.3\% \pm 7.8$ to $75.1\% \pm 5.0$ ($p = 0.045$). The average hospital stay was 10.6 days. Four non-surgery-related mortalities occurred within the 30-day postoperative period. Surgery-related AEs included wound complications in two patients, with one necessitating surgical revision. Advanced age and comorbidities emerged as significant predictors of AEs. Our findings suggest that neurosurgical intervention for BM in the elderly is a feasible and safe option, demonstrating favorable morbidity and mortality rates. However, careful postoperative monitoring is crucial, especially considering the baseline health status of these patients, which increases their susceptibility to AEs. Standardizing protocols for AE reporting and analysis is essential for improving clinical outcomes and maintaining the quality of healthcare for this patient population ⁸⁾.

This [study](#) is a valuable addition to the literature on geriatric neuro-oncology, offering real-world data on a topic with limited prospective evidence. While the findings are encouraging, future studies with larger cohorts, comparative groups, and broader outcome measures are warranted to guide individualized treatment strategies in elderly patients with brain metastases.

Case series

see [Brain metastases case series](#).

Research

Zhu et al. reported a medium-throughput [drug screening](#) platform (METPlatform) based on [organotypic cultures](#) that allow evaluating inhibitors against [metastases](#) growing in situ. By applying this approach to the unmet clinical need of [brain metastases](#), they identified several vulnerabilities. Among them, a [blood-brain barrier](#) permeable [HSP90](#) inhibitor showed high potency against [mouse](#) and human [brain metastases](#) at clinically relevant stages of the [disease](#), including a novel model of local relapse after neurosurgery. Furthermore, in situ [proteomic](#) analysis applied to metastases treated with the chaperone inhibitor uncovered a novel molecular program in brain metastases, which includes [biomarkers](#) of poor prognosis and actionable mechanisms of resistance. The work validates METPlatform as a potent resource for metastases research integrating [drug screening](#) and unbiased [omics](#) approaches that are compatible with human samples. Thus, this clinically relevant strategy is aimed to personalize the management of metastatic disease in the brain and elsewhere ⁹⁾.

Case reports from the HGUA

Q11824

A 77-year-old female with a history of [cholangiocarcinoma](#) and subsequent metastasis to the right [frontal lobe](#) cerebral region. The patient initially presented with generalized [tremors](#), [disorientation](#), and [drowsiness](#), prompting further investigation that revealed a [space-occupying lesion](#) in the right frontal lobe. Following surgical [resection](#) of the lesion, the patient exhibited a favorable [postoperative recovery](#) with no new neurological deficits. Imaging studies demonstrated an increase in the size of

the metastatic lesion and surrounding edema. Close follow-up is recommended to monitor disease progression.

Introduction: Metastatic brain tumors are a common complication of various malignancies, including cholangiocarcinoma. These tumors can present with a variety of neurological symptoms and pose significant challenges in management. We present a case of metastatic brain tumor resection in a patient with a history of cholangiocarcinoma, highlighting the diagnostic and therapeutic approach in such cases.

Case Presentation: A 77-year-old female with a medical history significant for cholangiocarcinoma, treated with chemotherapy and radiotherapy, presented with generalized tremors, disorientation, and drowsiness. Neurological examination revealed findings consistent with a right frontal cerebral lesion. Imaging studies confirmed the presence of a space-occupying lesion with characteristics suggestive of metastasis.

Management and Outcome: The patient underwent surgical resection of the right frontal cerebral lesion without complications. Postoperatively, she experienced a favorable recovery with no new neurological deficits observed. Follow-up imaging revealed an increase in the size of the metastatic lesion and surrounding edema, emphasizing the need for continued monitoring.

Discussion: Metastatic brain tumors represent a significant clinical challenge due to their potential for neurological compromise and limited treatment options. In cases of cholangiocarcinoma, the brain is an uncommon site of metastasis, making early detection and intervention crucial for optimizing outcomes. Surgical resection remains a cornerstone of treatment, often complemented by adjuvant therapies such as chemotherapy and radiotherapy.

Conclusion: This case highlights the importance of considering metastatic brain tumors in patients with a history of cholangiocarcinoma presenting with neurological symptoms. Timely diagnosis and multidisciplinary management, including surgical resection, can lead to favorable outcomes and improved quality of life for these patients. Close follow-up is essential for monitoring disease progression and guiding further therapeutic interventions.

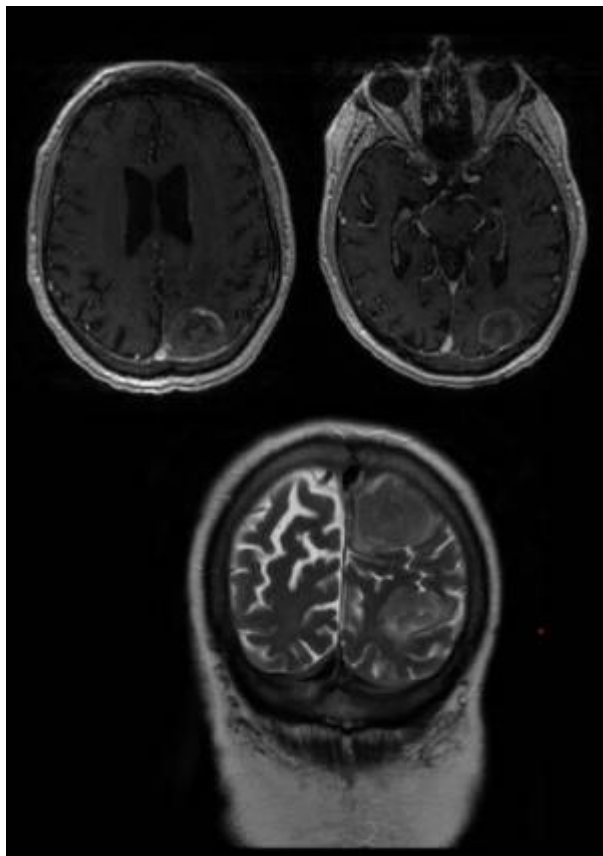
71-year-old male

Past medical History:

Arterial hypertension. Type 2 diabetes with polyneuropathy. dyslipidemia - digital agenesis MSD of birth - intermittent claudication.

Operated on cervical disc herniation, Peripheral arterial disease

Confusional picture, gait instability and hoarseness of 2 weeks evolution.



Two lesions left posterior parietal and occipital region, suggestive of brain metastases and a 6-mm pulmonary nodule in LSD and a 13-mm thyroid nodule in LTD, both with non-specific characteristics

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