

Advances in the Radiological Assessment of Melanoma Metastases in the Central Nervous System: Integrative Literature Review

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Avanços na Avaliação Radiológica das Metástases de Melanoma no Sistema Nervoso Central: Revisão Integrativa da Literatura
Avances en la Evaluación Radiológica de las Metástasis de Melanoma en el Sistema Nervoso Central: Revisión Integradora de la Literatura

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ABSTRACT

Introduction: Melanoma metastases in the central nervous system (CNS) represent a significant clinical challenge due to their high aggressiveness and prognostic impact. In this context, advances in imaging techniques have expanded the ability to detect, characterize, and differentiate these metastases. **Objective:** To analyze advances in the radiological assessment of melanoma metastases in the CNS. **Method:** An integrative literature review was conducted using the PubMed, SciELO, and Virtual Health Library databases, including articles published between 2015 and 2025, following the PICO strategy. **Results:** Eleven studies highlighted relevant advances in imaging techniques, particularly magnetic resonance imaging (MRI). Contrast-enhanced T1-weighted MRI was identified as the most sensitive technique for early detection of brain metastases, outperforming sequences such as T2-FLAIR and susceptibility-weighted imaging (SWI). Although SWI is useful in specific contexts, it has limitations in the diagnosis of melanotic metastases. Advanced techniques such as perfusion and diffusion provided complementary benefits in differentiating types of metastases but showed limitations in distinguishing their primary origins. The presence of leptomeningeal micrometastases and multiple lesions was associated with poorer prognosis, emphasizing the importance of a more detailed prognostic assessment. **Conclusion:** The combination of advanced imaging techniques is essential for a comprehensive assessment, providing valuable information for clinical and therapeutic management while emphasizing the need for multidimensional approaches to improve the diagnosis and treatment of these metastases.

Key words: Melanoma; Neoplastic Metastasis; Central Nervous System; Diagnostic Imaging.

RESUMO

Introdução: Metástases de melanoma no sistema nervoso central (SNC) representam desafio clínico significativo pela alta agressividade e impacto prognóstico. Nesse contexto, a evolução das técnicas de imagem tem ampliado a capacidade de detecção, caracterização e diferenciação dessas metástases. **Objetivo:** Analisar avanços na avaliação radiológica das metástases de melanoma no SNC. **Método:** Revisão integrativa da literatura, utilizando as bases PubMed, SciELO e Biblioteca Virtual em Saúde, abrangendo artigos entre 2015 e 2025, mediante a estratégia PICO. **Resultados:** Onze artigos destacaram avanços relevantes nas técnicas de imagem, especialmente na ressonância magnética (RM). A RM ponderada em T1 com contraste foi apontada como a técnica mais sensível para detecção precoce de metástases cerebrais, superando sequências como T2-FLAIR e RM ponderada por susceptibilidade magnética (SWI). A SWI, apesar de útil em certos contextos, tem limitações no diagnóstico das metástases melanóticas. Técnicas avançadas como perfusão e difusão mostraram benefícios complementares na diferenciação de tipos de metástases, mas com restrições em distinguir diferentes origens. A presença de micrometástases leptomeningeas e múltiplas lesões está associada a pior prognóstico, ressaltando a importância de uma abordagem prognóstica mais detalhada. **Conclusão:** A combinação de técnicas de imagem avançadas é essencial para uma avaliação abrangente, proporcionando informações valiosas para a gestão clínica e terapêutica, ao mesmo tempo que enfatiza a necessidade de abordagens multidimensionais para melhorar diagnóstico e tratamento dessas metástases.

Palavras-chave: Melanoma; Metástase Neoplásica; Sistema Nervoso Central; Diagnóstico por Imagem.

RESUMEN

Introducción: Las metástasis de melanoma en el sistema nervioso central (SNC) representan un desafío clínico debido a la alta agresividad e impacto pronóstico. La evolución de las técnicas de imagen ha ampliado la capacidad de detección, caracterización y diferenciación de estas metástasis. **Objetivo:** Analizar los avances en la evaluación radiológica de las metástasis de melanoma en el SNC. **Método:** Revisión integradora de la literatura utilizando las bases PubMed, SciELO y la Biblioteca Virtual en Salud, incluyendo artículos publicados entre 2015 y 2025, siguiendo la estrategia PICO. **Resultados:** Once estudios destacaron avances en las técnicas de imagen. La resonancia magnética (RM) ponderada en T1 con contraste fue identificada como la técnica más sensible para la detección temprana de metástasis cerebrales, superando secuencias como T2-FLAIR y RM ponderada por susceptibilidad magnética (SWI). Aunque la SWI es útil en contextos específicos, presenta limitaciones en el diagnóstico de metástasis melanóticas. Técnicas avanzadas, como la perfusión y la difusión, mostraron beneficios complementarios en la diferenciación de tipos de metástasis, pero con limitaciones para distinguir sus orígenes. La presencia de micrometástasis leptomeningeas y lesiones múltiples se asociaron con peor pronóstico, resaltando la importancia de una evaluación pronóstica detallada. **Conclusión:** La combinación de técnicas avanzadas de imagen es esencial para una evaluación integral, proporcionando informaciones valiosas para la gestión clínica y terapéutica, y enfatizando la necesidad de enfoques multidimensionales para mejorar el diagnóstico y tratamiento de estas metástasis.

Palabras clave: Melanoma; Metástasis Neoplásica; Sistema Nervioso Central; Diagnóstico por Imagen.

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INTRODUCTION

Skin cancer is the most common type of cancer, originating from different dermis and epidermis cells. The main types are basal cell carcinoma and squamous cell carcinoma, also known as non-melanoma skin cancer, the most frequent type, and melanoma, which is less common but more aggressive. A total of 9,360 new melanoma cases is estimated for Brazil annually, with a higher incidence in the South Region for both sexes, corresponding to a risk of 4.71 per 100 thousand inhabitants. It is more prevalent in light-skinned people over 40 years old, although the incidence in young people has increased due to high sun exposure. Ultraviolet (UV) radiation is the main risk factor for all skin cancer types, as it causes cumulative DNA damage. In the case of melanoma skin cancer, risks associated with artificial UV radiation also stand out, like that emitted by lamps and tanning booths, in addition to exposure to polychlorinated biphenyls¹.

Melanoma is an aggressive form of skin cancer, originating from epidermal melanocytes, which can evolve to metastasis from a small primary tumor, responsible for the highest number of deaths from skin cancer. Its high rate of metastases, especially for the brain and cerebrospinal fluid, is attributed to its capacity to escape hosts' defenses, genetic variability, and similarity with vasculature cells^{2,3}. During its development, melanoma accumulates mutations that facilitate its dissemination to the leptomeninges, including cellular adhesion molecules that allow metastatic cells to resist blood flow, extravasate from vessels, and adhere to other organs^{3,4}.

Melanoma is the third most common origin of brain metastases, behind only lung and breast cancer. It is also the solid tumor with the highest tendency to spread to the brain. Historically, the life expectancy of patients with melanoma that affects the central nervous system (CNS) is short, with average survival lower than six months. However, an improvement in the average overall survival from 14 months to 23 months has been identified for metastatic melanoma since the introduction of targeted therapies and immunologic checkpoint inhibitors. Early diagnosis and differentiation from other CNS tumors are important⁵⁻⁷. Despite therapeutic advances, patients with melanoma and CNS metastases continue to present poor survival results⁸.

In case of CNS tumors, glioblastoma and primary tumor metastases are the most common in adults. However, imaging exams are often unable to differentiate these tumors due to similarities in imaging characteristics and relief patterns between these entities, especially in solitary lesions in patients with no known history of malignancy. In lesions with a peripheral ring pattern,

differentiating between glioblastoma and metastasis based only on morphological imaging is often impossible. However, distinction between primary and metastatic brain lesions is essential to an appropriate initial treatment, due to differences in therapeutic approaches⁹.

The interest in researching this theme is justified, since melanoma metastases in the CNS represent a frequent and challenging complication, with a direct impact on the morbidity and mortality of patients. Radiological assessment, either through computed tomography (CT) or magnetic resonance imaging (MRI), albeit challenging at times, plays an important role in early diagnosis, therapeutic planning, and monitoring the response to treatment of these lesions.

Over the past years, advances in imaging techniques have contributed to a more detailed characterization of metastases, enabling specialists to differentiate malignant lesions from other neurological conditions, such as abscesses and gliomas. However, there are still gaps in the consolidation of knowledge on the efficacy and limitations of these radiological tools in the context of CNS melanoma metastases.

This study is relevant given the need to collect, analyze, and synthesize recent literature findings, contributing to improving radiological diagnosis and implementing more precise, effective approaches to clinically managing these patients. Moreover, integrating information on technological advances in imaging exams can offer important subsidies to clinical decisions and future studies.

The general objective of this research was to analyze advances in the radiological assessment of melanoma metastases in the CNS. The specific objectives of the study were to identify the main radiological patterns of melanoma metastases in the CNS, assess the role of advanced imaging techniques in the diagnosis and monitoring of these metastases, and compare the efficacy and limitations of these techniques in the diagnosis and follow-up of patients with metastatic melanoma in the CNS.

METHOD

Integrative literature review on the advances in radiological assessment of melanoma metastases in the CNS. The research was conducted in PubMed, SciELO, and *Biblioteca Virtual em Saúde* (BVS) databases, including articles published between 2015 and 2025. The following combination of English-language descriptors was used, along with the Boolean operator AND: *Melanoma metastasis* AND *central nervous system* AND *imaging diagnosis*.

The study selection criteria were defined based on the PICO strategy, which helps formulate research questions

and identify more relevant studies to answer the proposed issue. The PICO acronym refers to the following elements:

- P (Population): Patients diagnosed with melanoma metastases in the CNS.
- I (Intervention): Imaging techniques.
- C (Comparison): Melanoma metastases images compared to other CNS neoplasms, seeking to identify differences or similarities in radiological patterns.
- O (Outcome): Identification of radiological patterns of melanoma metastases and assessment of the utilized imaging techniques.

The PICO strategy involves the elaboration of a problem-question, defined as follows: “What are the advances in imaging diagnosis techniques in the assessment of melanoma metastases in the CNS, as demonstrated in the recent scientific literature?”

To answer this question, original articles (clinical trials, cohort, observational studies, or case reports) available in the aforementioned databases that approached the

use of imaging diagnosis in the assessment of melanoma metastases in the CNS, as defined by the predefined PICO strategy guidelines, were selected. Studies with non-specific populations for melanoma metastases in the CNS, review studies, articles unavailable for full reading, and duplicate publications were excluded.

The selected articles were analyzed qualitatively, with a focus on the advances in radiological techniques and imaging patterns described. The information of interest was organized in a chart, enabling comparison between the studies' results.

RESULTS

This research leveraged 75 articles from PubMed, 50 from BVS, and 1 from SciELO. There were 48 duplicates in the search results; therefore, this study presented a total of 78 articles for analysis. After applying the inclusion and exclusion criteria, 11 articles were included in this study (Figure 1¹⁰).

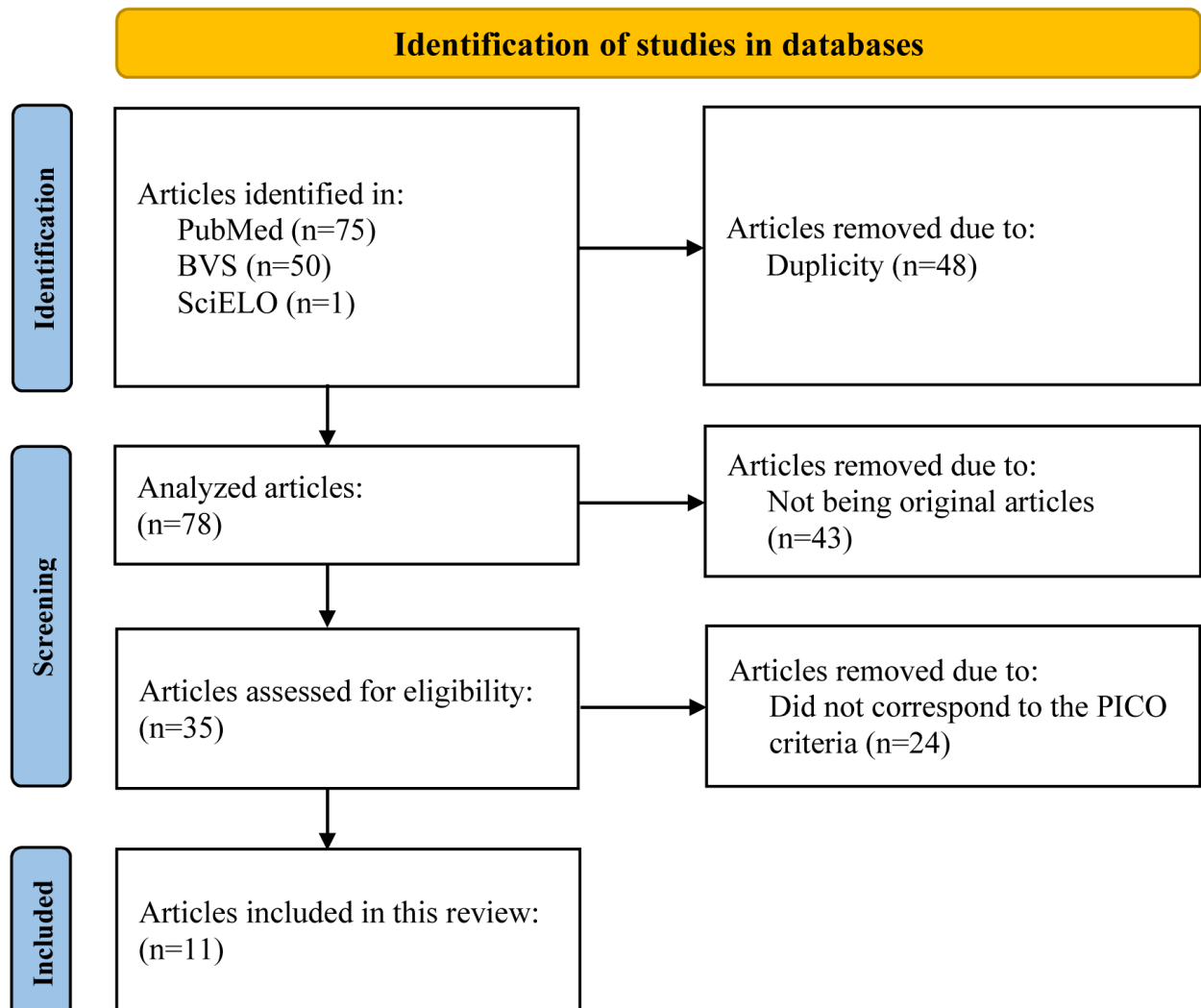


Figure 1. PRISMA flowchart of articles searched in databases

Source: Elaborated based on the PRISMA flowchart¹⁰.



The contents of the 11 articles selected in the present study can be analyzed in the following Chart 1^{2,6,9,11-18}, which includes data such as year of publication, authors, research method, objective of the study, and main results.

The analysis of results from these 11 selected articles reveals significant advances in radiological assessment of melanoma metastases in the CNS. Next, the main findings from the studies will be discussed, comparing results and highlighting each one's contribution to recent scientific literature.

DISCUSSION

The analyzed studies demonstrated that MRI is a fundamental tool in the detection of melanoma metastases in the CNS, with several sequences showing different sensitivities and specificities. According to Deike-Hofmann et al.¹⁵, contrast-enhanced T1-weighted MRI was the most sensitive for early detection of melanoma brain metastases, overcoming other sequences like T2-weighted fluid-attenuated inversion recovery MRI (T2w-FLAIR) and susceptibility-weighted MRI (SWI). This reinforces the findings by Reiter et al.¹¹, who reported a miliary dissemination of metastases in a patient with melanoma, evidenced by MRI in a short period, underscoring the importance of MRI in dynamically monitoring patients with metastatic melanoma.

In this context, it is worth mentioning the role of post-contrast FLAIR, especially when acquired late, in the assessment of leptomeningeal involvement. The study by Ibrahim, Rahman, and Elnekeidy¹⁹ demonstrated that the late post-contrast FLAIR sequence presented superior sensitivity compared to conventional contrast-enhanced T1-weighted imaging for detecting brain metastatic lesions, with greater conspicuity of lesions and better differentiation between pathological leptomeningeal enhancement and enhanced cortical vessels, frequently responsible for false positives in post-contrast T1. The authors reported a 98.98% sensitivity and 100% specificity for late post-contrast FLAIR, reinforcing its potential for identifying superficial and leptomeningeal involvement.

Although this study has not specifically assessed melanoma brain metastases — reason for which it was not included in the review results chart —, its findings were incorporated into the discussion as they add relevant evidence on the incremental value of post-contrast FLAIR in the detection of leptomeningeal dissemination, a particularly pertinent aspect in melanoma, given its known propensity to leptomeningeal involvement and unfavorable prognostic impact.

The study by Schwarz et al.¹⁶ showed that although SWI is useful for detecting blooming artifacts (signal expansion),

its additional diagnostic utility is limited, especially in melanotic metastases, in which the contents of melanin do not cause relevant blooming. This discovery reflects an important limitation of SWI, which, despite being useful to observe secondary phenomena such as micro-hemorrhages and post-radiotherapy parenchymal changes, is not determinant in identifying viable metastases.

Regarding perfusion and diffusion in MRI, the study by Jung et al.¹² highlighted the use of perfusion in dynamic contrast-enhanced T1-weighted MRI, which demonstrated efficacy in distinguishing melanoma metastases from glioblastomas and other brain tumors based on the analysis of contrast dynamics. This finding complements Askaner et al.⁹, who investigated MRI perfusion and the capacity to differentiate glioblastomas from brain metastases. Although relative cerebral blood volume (RCBV) has been useful to distinguish glioblastomas, it could not differentiate metastases of different origins, including melanoma. This suggests that perfusion can be a complementary, but not decisive, technique for differentiating types of brain metastases.

In addition to conventional sequences and functional MRI techniques, advanced metabolic methods have also demonstrated potential to increase the diagnostic specificity of brain metastases. In this context, Ostojic et al.¹⁸ reported the presence of a prominent peak at approximately 2.0 ppm in MRI spectroscopy (MRIS), mimicking amino acid N-acetylaspartate (NAA), in histologically confirmed solid metastatic brain lesions. Although NAA is classically considered a neuronal marker, found exclusively in CNS and at high concentrations in neurons, the authors demonstrated that this peak may be present in mucin-expressing metastases, including metastatic melanomas, mucinous breast carcinomas, mucinous non-small cell lung adenocarcinomas, and metastatic non-small cell lung cancer.

This finding suggests that identifying a peak similar to NAA in single ring-enhancing lesions may represent a relevant metabolic marker for differential diagnosis, especially in challenging cases in which conventional morphological characteristics are unspecific. Thus, MRIS can offer incremental value in differentiating between primary and secondary CNS lesions, amplifying diagnostic specificity when integrated with MRI structural sequences.

The studies by Sarbu, Pujol, and Oleaga¹³ and Nabavizadeh et al.¹⁴ explored perilesional T1-hyperintensity, a characteristic sign of melanoma metastases, but also observed in other conditions, such as cavernous malformations. The study by Nabavizadeh et al.¹⁴ demonstrated that perilesional hyperintensity on T1-weighted imaging has high specificity for metastases and cavernous malformations, being a useful indicator

Chart 1. Result of the content analysis of the 11 articles included in this integrative review

Year of publication, Authors, and Method	Objective	Results
2019 Berk et al. ² Retrospective observational study	Assess a possible negative association of white substance vascular lesions and vascular risk factors with brain metastases in patients with melanoma, through a three-dimensional brain MRI	The study compared hyper-intense lesions in T2-FLAIR in the white substance between patients with and without brain metastases, classified by Fazekas' score (grades I-III). Patients without metastases showed more pronounced lesions. Additionally, brain metastases were more probable in patients with no vascular risk factors. It was concluded that lesions in the white substance and vascular risk factors may reduce the risk of brain metastases and their presence can influence the choice of treatment
2024 Serra et al. ⁶ Cohort study	Identify patients with a higher risk of developing melanoma metastases in the CNS and assess associated prognostic factors	Among discoveries, it was confirmed that CNS involvement with multiple metastases and leptomeningeal involvement is correlated with worse survival
2019 Askaner et al. ⁹ Prospective observational study	Investigate if weighted MRI in perfusion can differentiate glioblastoma metastasis and if it is possible, in that last group, to predict the primary site of the neoplasm	Relative cerebral blood volume (RCBV) in the peritumoral edema is significantly higher in glioblastomas (average 3.2) than in metastases (average 0.9). However, there are no significant differences in RCBV among metastases of different origins or in solid tumoral areas adjacent to the edema. Thus, RCBV in the peritumoral edema can differentiate glioblastomas from metastases, but not metastases from different primary tumors (lung, breast, melanoma, or gastrointestinal)
2015 Reiter et al. ¹¹ Case Report	Report on the case of a patient with malignant melanoma with sharp, progressive worsening of neurological symptoms until loss of consciousness	MRI did not show evidence of a brain tumor. A second MRI, 5 days later, performed due to sharp, inexplicable worsening of neurological symptoms, revealed the emergence of numerous miliary lesions with contrast enhancement, especially in the gray matter, which were confirmed as malignant melanoma metastases in histopathology
2016 Jung et al. ¹² Retrospective observational study	Compare glioblastoma and brain metastases using dynamic contrast-enhanced T1-weighted MRI perfusion	Dynamic contrast-enhanced T1-weighted MRI perfusion demonstrated potential to differentiate glioblastomas, melanoma metastases, and hypovascular brain tumors. The logarithmic inclination of the washout phase (period after administering a contrast agent in which the contrast begins to be eliminated from the tissue) and the area under the curve (AUC) of the signal intensity curve over time were the best parameters for discriminating between hypervascular and hypovascular neoplasms
2016 Sarbu, Pujol, Oleaga ¹³ Case report	Report three cases showing T1-hyperintense perilesional edema of brain masses, an unusual radiological finding, one case representing cerebral hemorrhagic cavernous malformation (CCM, cavernoma) and the other two, melanoma metastases	The association between this signal (hyperintense perilesional edema) and cavernoma was recently acknowledged. On the other hand, in melanotic lesions, the relationship with the hyperintense perilesional edema in T1 has not yet been described. Although it is a rare sign, it can significantly help with differential diagnosis, conferring it a high clinical value. Moreover, due to the high prevalence of conditions that present this imaging characteristic, it can be observed occasionally

To be continued



Chart 1. Continuation

Year of publication, Authors, and Method	Objective	Results
2017 Nabavizadeh et al. ¹⁴ Retrospective observational study	Investigate the frequency of perilesional T1-hyperintensity in patients with intra-axial non-hemorrhagic and hemorrhagic cerebral masses	All the lesions with perilesional hyperintensity showed acute or subacute hemorrhage. Perilesional hyperintensity in T1-weighted images demonstrated high specificity in groups of metastases and cavernous malformation (94%). Although perilesional T1-hyperintensity is characteristic of cavernous malformations, it is also frequently observed in melanoma and other cerebral hemorrhagic metastases. However, it was not observed in high-grade gliomas, primary CNS lymphomas, or brain abscesses
2018 Deike-Hofmann et al. ¹⁵ Retrospective observational study	Investigate the sensitivity of 6 clinical MRI sequences in the early detection of melanoma cerebral metastases: Non-contrast T1-weighted (T1w) MRI, contrast-enhanced T1-weighted MRI (ceT1w), T2-weighted MRI (T2w), T2-weighted fluid-attenuated inversion recovery MRI (T2w-FLAIR), SWI MRI, and diffusion-weighted imaging (DWI)	Contrast-enhanced T1-weighted imaging is more sensitive than the other sequences for detecting melanoma cerebral metastases. Disruption of the blood-brain barrier is consistently the earliest sign in melanoma brain metastases, appearing before perifocal edema, signal loss on SWI, or restricted diffusion
2019 Schwarz et al. ¹⁶ Retrospective observational study	Systematically analyze the scope of intracerebral findings in malignant melanoma brain metastases in SWI and determine the diagnostic value of cerebral SWI-weighted imaging	Melanotic and amelanotic metastases showed no significant differences regarding blooming artifacts on SWI. SWI offers little additional diagnostic benefit in relation to T1-weighted imaging, as the isolated content of melanin does not cause relevant blooming. Signal transition can indicate secondary phenomena, like micro-hemorrhages or metal recovery. Isolated SWI artifacts do not represent vital tumoral tissue, but nonspecific micro-hemorrhages, post-radiotherapy parenchymal changes or remnants of treated metastatic lesions
2020 Lasocki et al. ¹⁷ Retrospective observational study	Systematically investigate the development of small intracranial melanoma metastases using fine cuts in modern MRI	Most intracranial melanoma metastases, with diameters between 2 and 9 mm, are corticomeningeal nodules, suggesting a possible leptomeningeal origin. These data suggest that deeper invasion of the parenchyma by intracranial melanoma metastases occur secondarily. If leptomeninges really offer a preferential location for the establishment of these metastases, a deeper investigation of the biology underlying this phenomenon can open new possibilities for therapeutic strategies targeted at these patients
2024 Ostojic et al. ¹⁸ Clinical trial	Present the occurrence of a prominent peak at approximately 2.0 ppm, mimicking the amino acid N-acetylaspartate, found exclusively in the CNS and in high concentrations in neurons, in histologically proven solid metastatic brain lesions	The identification of a prominent peak at 2.0 ppm can be a valuable diagnostic marker to distinguish single ring-enhancing lesions, potentially associated with metastases that express mucin, offering a new path for diagnostic specificity in challenging cases. Among them: brain metastases from mucinous breast carcinoma, non-small cell lung mucinous adenocarcinoma, metastatic melanoma and metastatic non-small cell lung cancer

Captions: MRI = magnetic resonance imaging; CNS = central nervous system; SWI = susceptibility-weighted imaging.

for differential diagnosis. This result was corroborated by Sarbu, Pujol, and Oleaga¹³, who observed this characteristic in melanoma metastases, despite its rarity.

The study by Lasocki et al.¹⁷ revealed that many small-sized (2-9 mm) intracranial melanoma metastases originate in the leptomeninges, suggesting a possible preferential route for the dissemination of melanoma in the CNS. These discoveries open new perspectives for targeted therapeutic strategies, since leptomeningeal involvement may have important prognostic and therapeutic implications.

In turn, the study by Serra et al.⁶ identified that the presence of multiple metastases and leptomeningeal involvement is associated with worse survival in patients with metastatic melanoma in the CNS. This result is important for prognostic assessment, as it can guide therapeutic decisions and help identify patients with a high risk of negative evolution. Additionally, Berk et al.² indicated that lesions in the white matter, often associated with vascular risk factors, can interfere with the risk of brain metastases, suggesting that these factors must be considered when planning treatment.

CONCLUSION

Advances in imaging techniques, especially MRI, have significantly contributed to the assessment of melanoma metastases in the CNS. Contrast-enhanced T1-weighted MRI is still the technique of choice for early detection of brain metastases, while SWI, despite being useful in certain contexts, has limitations in the diagnosis of melanotic metastases.

The use of advanced techniques, such as perfusion and diffusion, offers complementary benefits but also presents challenges in terms of distinguishing between different types of metastases. Furthermore, the identification of leptomeningeal micrometastases and consideration of prognostic factors are essential for clinical and therapeutic management of patients with metastatic melanoma in the CNS.

These results emphasize the importance of combining imaging techniques, including advanced sequences, such as late post-contrast FLAIR in specific contexts, to provide an encompassing assessment of melanoma metastases in the CNS, in addition to highlighting the need for multidimensional approaches for early detection, screening, and differentiation of types of metastases.

CONTRIBUTIONS

Both authors have substantially contributed to the study design, acquisition, analysis, and interpretation of the data, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the contents associated with the article are included in the manuscript.

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