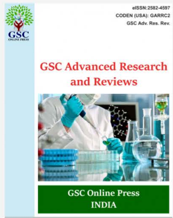
GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/



(Review Article)

MRI sequencing of brain metastasis from lung malignancy: Literature review

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GSC Advanced Research and Reviews, 2023, 15(03), 105–109

Publication history: Received on 10 April 2023; revised on 24 May 2023; accepted on 26 May 2023

Article DOI: https://doi.org/10.30574/gscarr.2023.15.3.0152

Abstract

Background: Lung cancer is ranked as the second most prevalent disease, with 2,2 million new cases anticipated by 2020. 85% of lung cancers are non-small-cell lung cancers (NSCLC), with 25-40% of NSCLC patients developing brain metastases during the course of the disease, typically within 2 years of the primary tumor's detection. Contrast-enhanced MRI is the preferred modality for judging cranial and intracranial metastases.

Methods: The most recent articles published between 2017 and 2023 were searched for in the databases of PubMed, Google Scholar, and Cochrane Library. Two reviewers (D and W, with more than 10 years of neurology and radiology experience, respectively) independently searched all papers.

Results: Cancer in the lung is most prevalent primary malignancy associated with CNS metastases, with 23% to 36% of lung cancer patients ultimately developing CNS metastases.[6] Patients with lung cancer and EGFR mutations in the brain metastases had a higher response rate to whole-brain radiation therapy and specific chemotherapy drugs.

For the detection of tiny metastases, MR is more sensitive than CT or even CT/PET. However, sensitivity on MR is variable, as various parameters of the MR capture can affect performance.[5] Therapeutically specialized brain metastases MRI procedures frequently include pre-contrast and post-contrast sequences.

Conclusion: MRI is the gold standard for evaluating patients with brain masses, such as primary and secondary due to metastatic malignancies. Brain metastases must be diagnosed early and distinguished from suspicion of other neuropathologies. Initial diagnosis influences prognosis and outcome.

Keywords: MRI; Metastasis; Brain; Lung cancer

1. Introduction

Globally, lung cancer is ranked as the second most prevalent disease, with 2,2 million new cases anticipated by 2020 (GLOBOCAN).[1] In East Asia, lung cancer is considered one of the primary causes of cancer-related mortality and the most widely known origin of cerebral metastases.[2] 85% of lung cancers are non-small-cell lung cancers (NSCLC), with 25-40% of NSCLC patients developing brain metastases during the course of the disease, typically within 2 years of the primary tumor's detection. According to the Surveillance, Epidemiology, and End Results (SEER) program, around 20% of patients with non-small cell lung cancer (NSCLC), 26.8% of patients with lung adenocarcinoma, and 15.9% of patients with squamous cell carcinoma manifest together with brain metastasis.[1,3] Metastatic central nervous system (CNS) neoplasms are more prevalent than primary brain malignancies.[4,13,16]

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Contrast-enhanced MRI is the preferred modality for judging cranial and intracranial metastases due to the increased detail and contrast of examined tissue, as well as the number of MRI sequences that can presently be used to define lesions in the intracranial. Brain metastases are localized anatomically and with a high degree of resolution by MRI. On T1-weighted images, parenchymal metastases are typically isointense to hypointense relative to the brain, while their intensity is variable on T2-weighted images. They have a shape that is approximately spherical. Frequently, metastatic lesions are encircled by vasogenic edema, which has a strong signal on T2-weighted imaging and a low signal on T1-weighted imaging. Compared to the extent of the main tumor, edema is frequently vast. Typically, edema is restricted to the white matter, making room for the cortical layer beneath. Cortical involvement should provoke the investigation of additional conditions, such as a primary brain tumor.[5,11,12]

2. Methods

The most recent articles published between 2017 and 2023 were searched for in the databases of PubMed, Google Scholar, and Cochrane Library. Two reviewers (D and W, with more than 10 years of neurology and radiology experience, respectively) independently searched all papers.

3. Results and Discussion

Cancer in the lung is most prevalent primary malignancy associated with CNS metastases, with 23% to 36% of lung cancer patients ultimately developing CNS metastases.[6] Patients with lung cancer and EGFR mutations in the brain metastases (BM) had a higher response rate to whole-brain radiation therapy and specific chemotherapy drugs, such as EGFR-associated tyrosine kinase inhibitors (TKIs), and a longer survival rate than patients with BM and wild-type epidermal growth factor receptor (EGFR). Individuals with EGFR mutations were more likely than patients with wild-type EGFR to develop brain or leptomeningeal metastases.[7] Patients who suffer non-small cell lung cancer may develop different patterns of brain metastases because these lesions depend on tumor nodules and are more or less linked to cystic and necrotic lesions.[8,9,15] For the detection of tiny metastases, MR is more sensitive than CT or even CT/PET. However, sensitivity on MR is variable, as various parameters of the MR capture can affect performance.[5] Therapeutically specialized brain metastases MRI procedures frequently include pre-contrast (i.e., T1-weighted, T2-weighted, diffusion-weighted) and post-contrast (i.e., FLAIR, T1-weighted) sequences. The essential sequence is a postcontrast 3D T1-weighted image acquired with either the Fast Spin-Echo (FSE) or 3D volumetric Fast Spoiled Gradient-Echo (FSPGR) technique. Magnetic resonance imaging (MRI) with contrast enhancement is the ideal imaging test for diagnosing brain metastases. The T2-weighted FLAIR and contrast-enhanced T1-weighted (CET1W) MRI sequences are most often used for assessing brain metastases and provide information on gross characteristics, morphology, and size. New MRI sequences have been developed to enhance the visibility of metastases. Recent developments in MRI have made it possible to characterize cellularity, microstructures, perfusion, physiology, and metabolism in addition to anatomy.[10] Brain metastases are frequently diagnosed with imaging examination such as computed tomography (CT) or magnetic resonance imaging (MRI). Brain abscess and brain metastases can be distinguished in suspected cases using apparent diffusion coefficient (ADC) and diffusion-weighted imaging (DWI). Brain abscesses and brain metastases both displayed high T1WI and low T2WI on the MRI. However, whereas brain abscesses have a high DWI and a low ADC, brain metastases often have a low DWI and a high ADC. Magnetic resonance spectroscopy (MRS), when used in conjunction with DWI, may also help in making a precise diagnosis.[9]

MRI is essential in the planning of treatment for brain metastases because it helps to spot the location, number, and size of lesions, directing more effective radiation-based and surgical therapies. FET PET may supplement conventional MRI for treatment planning optimization because it can detect areas of potential malignancy that widen beyond the contrast-enhancing zone on MRI. Comparing MET PET (11C methionine PET) to MRI for treatment planning in patients with iterative illness after gamma knife SRS (stereotactic radiosurgery) has also been the subject of research. The authors of one such study found that while MET PET imaging resulted in fewer irradiation volumes than MRI alone, survival durations were longer, giving the impression that MET PET targeted lesions more effectively than MRI. Since FET and MET uptake are analogous in pretreatment brain metastases, FET PET may elicit comparable results. Recurrence risk may also be reduced by treatment planning using diffusion imaging. The addition of ADC data to postcontrast T1 imaging did not affect the gross tumor volumes, but transformed the shape of the targets. It was discovered that the diffusion-based therapy region encompasses a larger proportion of subsequent tumor recurrences and, pending the results of survival studies, may therefore provide patient benefit. As invasion may be an underappreciated metastatic phenomenon, the ability to noninvasively recognize areas of infiltrative tumor spread may be useful for optimizing treatment strategies. Using ADC data analysis, this is feasible. Another study discovered that integrating ADC maps from intraoperative scans with anatomic imaging helped to characterize tumor boundary zone regions where parenchymal invasion was taking place and better define tumor borders.[5,11]

Table 1 Imaging techniques, features, and prospective applications are summarized.[5,10]

Technique	**Features**	**Potential applications**
Overlapping post-contrast 3D T1-weighted CUBE (oCUBE-MIP)	Enhancing lesions have a high contrast-to-noise ratio.	Rapid and sensitive detection of parenchymal and leptomeningeal brain metastases Clinically available and simple to use
Magnetic resonance spectroscopy	Identifies tumor metabolites	Lipids are present in glioblastomas and metastases NAA/Cr is greater in metastases compared to the original gliomas Cho/Cr and Cho/NAA are greater with tumor advancement compared to radiation necrosis; Clinically available, but more challenging and complex to execute; which complement each other in structural imaging Standardization across numerous MRI vendors is required
Quantitative magnetization transfer	Magnetization transfer ratio (MTR), macromolecular concentration (F), and exchange rate between bound and free water protons (kf) are all measured	Meningioma has the smallest peritumoral MTR in comparison to glioblastoma and metastases. The proportion of macromolecules in the non-contrast-enhancing zone of the tumor is greatest in metastases. At the moment, the focus is primarily on research. There is no standardized post-processing software.
Trans-membrane water exchange	Transmembrane intra-extracellular water exchange rate constant (kIE), which is sensitive to apoptosis, is measured.	kIE is higher in radiosurgery responders than in non-responders. At the moment, the focus is primarily on research
Chemical exchange saturation transfer	Measuring neoplasm milieu metabolites	With tumor progression, MTR_{Amide} and NOE levels are higher compared to radiation necrosis An exciting and immediately evolving molecular imaging technique More human research and standardized techniques to increase specificity are required.
Perfusion imaging	Relative cerebral blood volume and cerebral blood flow	Peritumoral rCBV and rCBF are higher in glioblastomas compared to metastases Intratumoral rCBV could assist in identifying tumor infection Intratumoral and peritumoral ASL-rCBF are greater in glioblastomas compared to metastases. Recurrent tumor has a lower PSR, a higher rCBV, a higher rPH, and a higher Ktrans; radiation necrosis has a higher PSR, a lower rCBV, a lower rPH, and a lower Ktrans. Available clinically with a variety of acquisition and post-processing techniques, restricting its ubiquitous use; complementary to structural imaging
Radiomics and textural analysis	Tumor quantitative patterns and inter-pixel connections are computed.	Certain textural criteria can differentiate glioblastomas from metastases. Some textural criteria can be used to categorize the major origins of brain metastases. Currently under investigation; validation requires massive multicenter datasets

Abbreviation: NAA: N-acetylaspartate; Cho:choline; Lp: lipid; Cr: creatine; MTR_{Amide}: magnetization transfer ratio for amide; NOE: nuclear Overhauser effect; rCBV: relative cerebral blood volume; rCBF: relative cerebral blood flow; ASL-rCBF: arterial spin labeling- relative cerebral blood flow; rPH: relative peak height; PSR: signal-intensity recovery

4. Conclusion

The magnetic resonance imaging (MRI) technique is the gold standard for evaluating patients with brain masses, such as primary and secondary due to metastatic malignancies. Brain metastases must be diagnosed early and distinguished from suspicion of other neuropathologies. Initial diagnosis influences prognosis and outcome. It is essential to differentiate between metastases and other etiologies. Despite the fact that a biopsy is frequently necessary for a fixed diagnosis, imaging can provide valuable evidence.

Compliance with ethical standards

Acknowledgments

The authors received no grants from any funding agency in the public, commercial, or non-for-profit sectors.

Disclosure of conflict of interest

There is no conflict of interest among the authors.

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