CASE REPORT

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Repeated Stereotactic Radiosurgery for Recurrent Brain Metastases from Non-Small Cell Lung Cancer: A Changing Paradigm of Survival

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ABSTRACT: **Introduction**: The brain is a common site of metastasis in non-small cell lung cancer, historically associated with poor prognosis. Advances in systemic therapies and radiotherapy techniques have improved overall survival and preserved neurological function. **Case report:** A 51-year-old patient with lung adenocarcinoma, diagnosed in 2021, developed multifocal and recurrent brain metastases over a four-year period. He underwent chemoradiotherapy, immunotherapy, stereotactic radiosurgery, and palliative radiotherapy. The patient currently maintains a good functional status. **Discussion:** Repeated stereotactic radiosurgery, integrated with evolving systemic therapies, enabled successive intracranial recurrences to be treated focally, achieving prolonged disease control while delaying whole-brain radiotherapy and preserving functional independence. **Conclusion:** This case illustrates how repeated stereotactic radiosurgery, integrated within a multidisciplinary treatment strategy, can contribute to prolonged survival and preservation of neurological function in selected patients with metastatic non-small cell lung cancer, challenging the historical perception of brain metastases as an invariably terminal event.

KEYWORDS: Lung adenocarcinoma; brain metastases; radiosurgery; re-irradiation; survival.

INTRODUCTION

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related mortality worldwide. In patients with advanced disease, brain metastases (BM) are among the most frequent complications, affecting approximately 25–40% of patients during the course of the disease [1].

Historically, the presence of BM was associated with a median overall survival of less than six months. However, the clinical landscape has changed considerably with the introduction of targeted systemic therapies, immunotherapy, and high-precision radiotherapy techniques, particularly stereotactic radiosurgery (SRS) [2–4]. These advances have contributed to improved survival, enhanced local control, and preservation of neurological function. Consequently, the therapeutic goal in selected patients has shifted from short-term palliation towards sustained intracranial disease control, with increasing emphasis on minimizing the long-term neurocognitive burden of treatment. We report the case of a patient with PD-L1-negative lung adenocarcinoma (ADC) who devel-

oped recurrent brain metastases and achieved survival exceeding four years following a sequential multimodal treatment strategy, while maintaining functional and cognitive integrity.

CASE REPORT

A 51-year-old man, former light smoker (5 pack-years), with no relevant comorbidities or associated weight loss, was diagnosed in April 2021 with left lung adenocarcinoma (T2N3M0, PD-L1 0%). He underwent concurrent chemoradiotherapy to the primary tumour and involved nodal stations using volumetric modulated arc therapy (VMAT), with a total dose of 66Gy delivered in 33 fractions, followed by consolidation immunotherapy within the SKYSCRAPER-03 clinical trial (atezolizumab ± tiragolumab) until August 2022.

In August 2022, he developed progressive aphasia. Brain magnetic resonance imaging (BMRI) revealed a left middle frontal space-occupying lesion. Complete surgical resection was performed on September 15, 2022, confirming a brain metastasis from lung adenocarcinoma. Postoperative BMRI identified an additional right frontal lesion. In November 2022, SRS was delivered to the left frontal postoperative cavity and to the newly detected right frontal metastasis (20Gy and 24Gy, respectively). Systemic therapy with platinum-pemetrexed chemotherapy was subsequently initiated, with continued central nervous system (CNS) surveillance.

In July 2023, the patient presented with persistent left frontoparietal headache. BMRI demonstrated dural thickening consistent with extra-axial disease. Palliative three-dimensional conformal radiotherapy to the cranial vault was delivered in August 2023, with a dose of 20Gy in five fractions.

In September 2023, follow-up BMRI revealed a left parietal epicranial subcutaneous lesion. The patient underwent metastasectomy in November 2023, and histopathological examination confirmed metastatic lung adenocarcinoma. This was followed by palliative three-dimensional conformal radiotherapy to the left parietal scalp surgical bed (20Gy in five fractions). Following systemic progression and identification of a HER2 mutation, treatment with trastuzumab deruxtecan was initiated.

In January 2024, the patient experienced two episodes of right hemifacial twitching. Subsequent imaging performed in March 2024 revealed recurrence adjacent to the left parietal surgical cavity and a new right frontal lesion, both of which were treated with SRS. The left parietal cavity recurrence received 18Gy, while the right middle frontal gyrus lesion received 20Gy in a single fraction.

The patient remained under surveillance until January 2025, when enlargement of a right parietal meningeal lesion was observed. A new systemic treatment line with docetaxel was initiated, and a third course of SRS was delivered to the lesion, prescribing 21Gy.

He remained clinically stable and did not require corticosteroid treatment, however, speech therapy was initiated because of aphasia associated with radiation necrosis.

In August 2025, BMRI demonstrated four new right temporal metastases, which were treated with a fourth course of SRS (Figure 1), delivering 18Gy to the largest and most superior lesion and 21Gy to the remaining lesions.

At the most recent follow-up, the patient remains under clinical and radiological surveillance, and is receiving low-dose corticosteroid therapy, with good functional status (ECOG performance status 1) and complete independence in activities of daily living.

DISCUSSION

This case reflects the evolving therapeutic paradigm of metastatic NSCLC. The historically poor prognosis associated with brain metastases has been substantially transformed through the integration of multimodal treatment approaches and individualized clinical decision-making [1,5]. Advances in systemic therapies and high-precision radiotherapy techniques have changed the natural history of the disease, allowing selected patients to achieve prolonged survival while maintaining neurological function and quality of life.

Improved survival has led to a new clinical scenario in which brain metastases no longer necessarily represent a terminal event but may instead constitute a potentially controllable manifestation of disease over time. In this setting, successive intracranial recurrences require a dynamic therapeutic strategy integrating local and systemic treatments while maintaining close surveillance for late treatment-related toxicities, particularly radiation necrosis. This shift is especially relevant for radiation oncologists, who are increasingly involved in the long-term management of patients with recurrent intracranial disease.

SRS has demonstrated local control rates comparable or superior to those achieved with whole-brain radiotherapy (WBRT), while reducing neurotoxicity and preserving neurocognitive function [3,6]. Current international guidelines favour SRS for selected patients with brain metas-

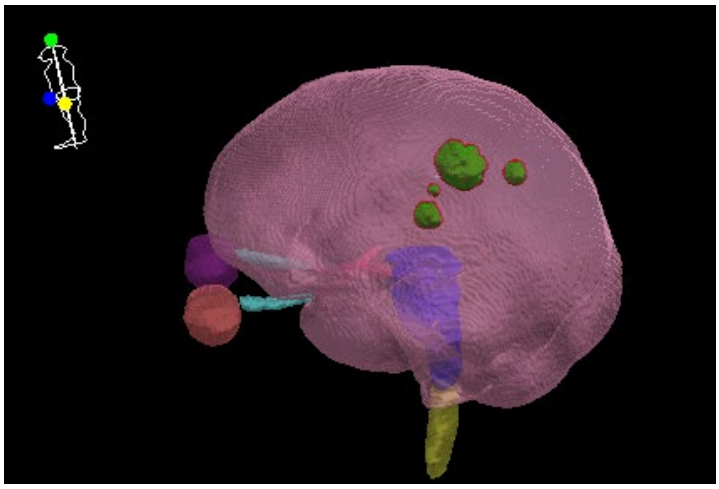

FIGURE 1. Target volume delineation for the fourth course of SRS (representative three-dimensional reconstruction)

tases, reserving WBRT for specific situations because of its association with greater neurocognitive decline [7]. Repeated SRS for oligorecurrent disease has proven safe and effective, particularly in patients with good performance status and controlled systemic disease. In the present case, four courses of SRS allowed successive intracranial recurrences to be treated focally, avoiding WBRT and its associated neurocognitive burden while maintaining functional independence over several years.

The decision to perform repeat cranial irradiation must be individualized, taking into account cumulative dose, lesion location, and the interval between treatments. Recent studies have shown that repeated SRS, even after multiple sessions, may be associated with overall survival exceeding 24 months in carefully selected patients [8]. The present case further illustrates how repeated focal treatments can contribute to long-term intracranial control in patients who continue to benefit from advances in systemic therapy. However, radiation necrosis (RN) remains an increasingly relevant late toxicity, particularly in the setting of prolonged survival.

RN results from radiation-induced endothelial injury and chronic inflammation, leading to tissue hypoxia and fibrinoid necrosis [9]. Its incidence increases with cumulative dose and repeated irradiation, ranging from approximately 5% to 25% following SRS and potentially higher after re-irradiation [10]. Clinically, RN may present with focal neurological deficits, seizures, or cognitive decline, often mimicking tumour recurrence. Distinguishing RN from tumour progression therefore remains a significant challenge.

In this patient, aphasia secondary to RN following multiple SRS courses improved with corticosteroids and speech therapy, highlighting the importance of multidisciplinary management and supportive care. From a systemic perspective, initial chemoradiotherapy followed by consolidation immunotherapy provided prolonged locoregional control [11], while subsequent treatment with trastuzumab deruxtecan and docetaxel illustrates the growing personalization of NSCLC management [12].

Overall survival exceeding four years, together with preservation of functional independence, underscores the value of integrating neurosurgery, radiation oncology, and thoracic oncology within a strategy focused on durable disease control, rigorous imaging surveillance, and quality-of-life preservation. More importantly, this case exemplifies the changing natural history of metastatic NSCLC, in which recurrent brain metastases may no longer represent an immediate determinant of mortality but rather a chronic and potentially controllable manifestation of disease. This case highlights the potential of repeated focal therapies to achieve long-term intracranial control while emphasizing the importance of recognizing and managing late complications such as RN.

CONCLUSION

In selected patients with metastatic NSCLC and recurrent brain metastases, repeated SRS can form the backbone of a longitudinal intracranial treatment strategy, integrated with evolving systemic therapies. This

approach may provide prolonged disease control while preserving neurocognitive function, functional independence, and quality of life.

This case illustrates the changing paradigm of survival in metastatic NSCLC, where brain metastases may no longer represent an immediate determinant of mortality but can instead be managed as a recurrent and treatable manifestation of disease. As survival improves, careful recognition and management of late toxicities, particularly radiation necrosis, become increasingly important components of long-term care.

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