JCOMS eISSN:2783-3127 https://journalofcoms.com

Journal of

Current Oncology and Medical Sciences

Vol. 5, No. 2

Case report **Free Access**

Stereotactic fractionated radiotherapy for multiple brain metastasis treated with single isocenter multitargeted approach: a case report

Siddharth Arora [1] *, Kriti Grover [1]

[1] Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

Abstract

Introduction: Adult patients with solid cancers frequently develop brain metastases. Whole brain radiotherapy (WBRT) alone or Stereotactic radiosurgery/radiotherapy (SRS/SRT) alone or in combination can be considered in Brain metastasis. Stereotactic radiosurgery has been effective in brain metastasis. Linac-based stereotactic radiosurgery has made use of volumetric modulated arc therapy (VMAT), which enables the simultaneous treatment of many targets with a single plan and isocenter.

Case presentation: A 62-year-old Asian presented to us with complaints of headache and blurring of vision. Disease mapping with positron emission tomography (PET) revealed Lung primary. Magnetic resonance imaging (MRI) of brain revealed multiple brain metastasis. He was planned with fractionated stereotactic radiotherapy. Plan involved volumetric arc therapy - Stereotactic radiosurgery (VMAT-SRS) treatment with single isocenter multiple target stereotactic fractionated radiotherapy, which was delivered post stringent quality assurance.

Discussion: SRS immobilization System has become more patient specific. Multiple challenges are encountered with single isocenter multiple target stereotactic fractionated radiotherapy. Essential yet challenging aspect of SRS is dosimetry. It requires a comprehensive Quality assurance to treatment planning to its delivery.

Conclusion: LINAC based VMAT SRS plans are more conformal with prescribed isodose line up to 75%. Hence, optimization strategies should be applied for better plan outcome. Our patient completed treatment without any major side effects. Planned imaging with the CEMRI brain showed complete response with no new findings.

Keywords: Whole-brain radiotherapy, Fractionated stereotactic radiotherapy, Brain metastasis, Non-small cell lung cancer, Metastatic non-small cell lung cancer

*** Corresponding Authors:** Siddharth Arora

Email: drsiddhartharora25@gmail.com

Received: 2025.4.4, Accepted: 2025.6.8

Introduction

Lung cancer is the most common cause of cancer deaths in men, with non-small cell lung cancer (NSCLC) being most common. About 30-40% of NSCLC patients present with metastatic disease at the time of diagnosis (1). Bone is the most common metastatic site, followed by the lungs, brain, liver and adrenal glands. Brain metastasis is considered to be an unfavorable prognostic factor. Palliation of symptoms and preservation of neurologic function are the main goals of treatment for many patients with brain metastases. Survival has improved by inclusion of MRI brain in early detection. Whole brain radiotherapy alone or Stereotactic radiosurgery/radiotherapy alone or in combination can be considered in brain metastasis. Stereotactic radiosurgery is a non-surgical radiation therapy that aims to deliver precisely targeted radiation in fewer high-dose treatments than traditional therapy (2, 3). The size and location of lesions, the proximity of organs at risk (OARs), and the biologically effective dose (BED) of each treatment plan all influence the SRT dose and fractionation schemes. Multiple factors influence the decision on SRS vs FSRS or WBRT. Graded prognostic assessment (GPA) score, recursive partitioning analysis (RPA) class, synchronous or metachronous diagnosis of Brain metastasis, and specifically volume > 10 cc influences decisions. Similarly age, sex and tumor histology have been analyzed for survival (4).

Current National Cancer Care Network (NCCN) guidelines recommend the use of volume instead of the absolute number of metastases as the limit to determine eligibility for SRS, with potential cutoffs being ≤15 cc. Yamamoto et al.'s 2014 multi-institutional prospective observational analysis showed no difference in OS or treatment-related adverse events between treating 2-4 brain lesions and 5-10 lesions (total volume 6 cm are not treated with SRS (5). The Radiation Therapy Oncology Group Trial developed dose limits for SRS of 24 Gy for lesions less than 2 cm, 18 Gy for lesions 2 to 3 cm and 15 Gy for tumors 3 to 4 cm. We used 24Gy in 3 fractions as prescription dose.

Additionally, SRT calls for extra caution when it comes to prescribing, documenting, and reporting. The potential advantages of SRS, include, its quick treatment duration and high likelihood of treated-lesion control. Here we report a case of metastatic lung carcinoma with multiple brain metastasis treated with single isocenter multiple target stereotactic fractionated radiotherapy at our institute.

Case presentation

A 62-year-old male previously treated for stage IIIC Adenocarcinoma elsewhere with chemotherapy presented to us with severe and persistent headache, worsening over time since 6 months. The headache was more in the morning and was associated with nausea and vomiting. Associated other symptoms include blurring of vision. Neurological examination was within normal limits except for vision impairment. He underwent Contrast enhanced magnetic resonance imaging (CEMRI) of brain in view of suspected brain metastasis as radiological imaging to evaluate the symptoms. Disease mapping with PET CT was suggestive of enhancing irregular margined left infrahilar and suprahilar mass measuring 5.8 x 6.6 cm (SUV max 18.18). Biopsy from Hilar growth was suggestive of non-small cell Lung Carcinoma. Immunohistochemistry results were positive for CK7 and negative for P63, P40, CK20, Synatophysin, chromogranin, CD56 and TTF-1. Overall favoring as poorly Differentiated Adenocarcinoma. He was prescribed dexamethasone at 16 mg /day in divided doses along with tab emset 4 mg thrice daily, tab pantop 40mg once daily and pain medications to relieve the symptoms.

Radiological Imaging:

Contrast enhanced MRI (CEMRI) of the brain revealed multiple intracranial brain lesions suggestive of metastasis. An irregular thick walled conglomerated peripherally enhancing lesion involving the right occipital lobe measuring 18 x 16 mm, another lesion in the left parietal lobe measuring 17 x 19 mm at the gray white junction with surrounding parietal edema and a tiny ring enhancing intra- axial lesion measuring 5 x 0.7 x 5 mm in the left high parietal lobe with minimal surrounding edema (Figure 1). These radiological and pathological findings were consistent with multiple brain metastases in a previously treated case of pulmonary adenocarcinoma.

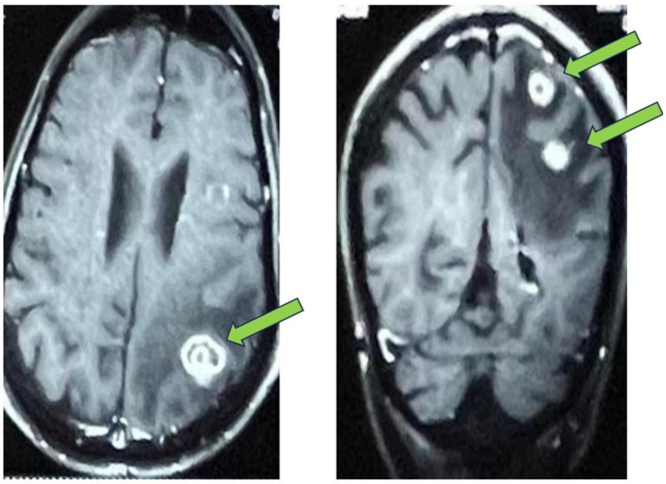

Figure 1. CEMRI Brain showing multiple brain metastasis.

He was discussed in multidisciplinary committee composed of neurosurgeon, radiation oncologist, and medical oncologist, and was planned with fractionated stereotactic radiosurgery (FSRS). He was planned with single isocenter multiple target FSRS using 3 Planning target volumes (PTV), each against the gross tumor volume (GTV) (enhancing lesions in right occipital lobe, left parietal lobe and high parietal lobe). In the present case, there were multiple, 3 brain metastasis of diameter 2.2 cm, 1.8 cm and 1.6 cm, the radiation tumor board decided for multi fraction SRS with 24 Gy marginal dose as per RTOG 9005. Multiple plans were generated, and best plan was delivered post stringent and recommended dosimetry and quality check by medical dosimetrist.

Discussion

The concept of SRS was introduced by Larks Leksell in 1951 as an alternative treatment option to conventional WBRT (2). It can be delivered with the help of Gamma knife which uses 192 small beams of gamma rays or with LINAC which uses X-rays (photons) to target and treat cancerous (Gliomas, brain metastasis, meningiomas, vestibular schwannomas) and noncancerous brain abnormalities (vascular pathologies, and functional disorders) (6). Charged particle radiosurgery or Proton therapy is relatively new and is available at very few centers. SRS Delivery is done accurately within 1-2 mm. When given in two or more fractions, it is termed as fractionated radiotherapy (3).

Immobilization: The radiotherapy procedure involves frameless immobilization, imaging, dose planning and radiation delivery after quality assurance. We used Encompass SRS immobilization System. It provides noninvasive stereotactic immobilization by using a patient-specific thermoplastic mask. It is designed for precisely targeting brain treatments. Furthermore, it conforms to patient features to provide accurate, reproducible positioning, repositioning and immobilization. Likewise, it also allows for diagnostic imaging in the same position. The mask features the Integra Bite, which reduces motion, allowing for maximum dose to the tumor and minimizing radiation delivered to the surrounding healthy tissue. The mask utilizes a posterior thermoplastic and anterior open view for use with an optical tracking system to allow for real-time monitoring. Encompass insert attaches to KVue Couch top and K Vue CT using One TOUCH Latch. The integrated Shim System on anterior thermoplastic masks allows for a minimal invasive approach to height adjustments. Shim adjustments are in increments of 0.5 mm. Recommended height is 2 mm. The posterior thermoplastic mask adds support under the patient's neck. The IntegraBite System is designed to immobilize the intracranial during treatment, allowing replication of position. Three fiducial markers are placed on the device around the head of the patient.

CT simulation: Planning CT was acquired at 1.0 mm slice spacing. After simulation, the DICOM CT, images were sent to server which was then imported for delineation of target and organ at risk (OAR). Planning CT was fused with brain MRI. Brain MRI was done in neutral neck position with no gap, no tilt with sequences at 1 mm interval. Sequences used included T1, T2 and FLAIR. MRI -CT fusion helped in delineating OARS and Gross treatment volume (GTV).

Target and OARs delineation: GTV was contoured as gross volume on post-Contrast T1 weighted MRI sequences. PTV was generated by geometric expansion of GTV + 2 mm margin. OARs delineated include brainstem, optic nerve, optic chiasm, and lens. Hippocampal sparing SRS planning was done (7). Fused MRI helped in delineating the above OARs and contouring.

Radiotherapy technique: Planning was done on Varian Truebeam equipped with 120 HDMLC using Eclipse treatment planning system (17.0 - External beam planning). The calculation algorithm utilized was the Anisotropic Analytical Algorithm (version 17.0.1). Prescribed doses were 24Gy in 3 fractions. The plan was made using one co-planar full arc and three non-coplanar partial arcs. An avoidance sector of 50 degrees was used for the third partial arc (Couch 270). This was done to avoid exit beam through body via vertex. A non-coplanar beam was used to reduce skin dose so that beam entry could be done from different angles. Figures 2 describe the collimator angles.

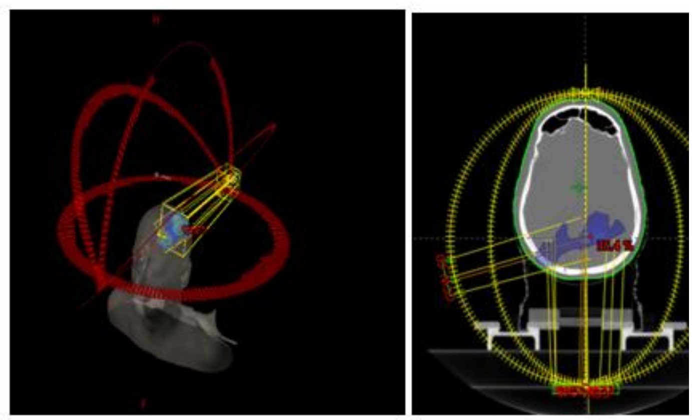

Figure 2a: Selection of collimator angle; Figure 2b: Spillage for Arc1 at Gantry 255 with collimator 95 degree (16% dose spill); Figure 2c: Changed collimator angle to 5-degree, to reduce spillage

Plan optimization was obtained with the help of Optimizer. Photon Optimizer (version 17.0.1) was utilized, which helps to generate shells to reduce dose fall off. For planning purposes, we have made 2 shells for each PTV. In total, 6 shells were drawn. First shell for controlling dose falls off at the border of PTV and the second shell for sharp dose fall outside PTV. Multiple plans (5 plans) were created.

Plan evaluation: Treatment was evaluated using plan efficiency indicators derived from DVHs for target coverage and sparing of OARS. Conformity index (CI), Homogeneity index (HI RTOG), Quality of coverage were the plan quality metrics used. (8, 9) The dose falls off outside the target was assessed with Gradient index (GI).Gradient index was less than 2.5 (Table1).

Table 1. Plan efficacy indicators in our case.

PTV	Paddick conformity index ($CI_{Paddick}$)	Homogeneity index HI RTOG	Gradient Index
	Volume of prescription isodose in the area of interest ie PTV) / PTV volume × Volume of prescription isodose	Maximum dose / Prescription dose	Equivalent radius of 50% isodose – Equivalent radius of prescription isodose.
PTV1	0.801	1.3	2.5
PTV2	0.853	1.25	
PTV3	0.813	1.23	

Quality Assurance (QA): Patient-specific QA was done with a Pin point 3D chamber using Ruby Phantom. The point dose verification was done keeping the tolerance as 1 mm.

Challenges, advantages and drawbacks with single isocenter multiple target stereotactic fractionated radiotherapy

There are multiple challenges encountered with single isocenter multiple target stereotactic fractionated radiotherapy. The single isocenter multiple target stereotactic fractionated radiotherapy involves treating off targets. The dosimetry and modeling of small MLC opening, which are frequently employed in multitarget radiosurgery, makes it particularly difficult. Each plan isocenter is centered on a target when targets are addressed independently, allowing imaging-based alignment to concentrate mostly on that region of interest. Rotational errors up to a few degrees usually have a negligible dosimetric effect under these circumstances. On the other hand, since at least one target must be offset from the point of rotation, multi-target, single-isocenter SRS treatments are less robust to rotational errors. The impact of rotational errors on target coverage was examined by Justin Roper and colleagues in a variety of SRS scenarios (10, 11). The plan isocenter was placed at the geometric isocenter of three PTV's in our patient. Some clinics might rely on manual patient repositioning to account for rotational problems in the initial setup, even though our facility has a robotic another factor that will affect the dosimetric impact of rotational errors on the GTV is the margin. After characterizing rotational uncertainty, target coverage can be predicted using multivariate regression models with patient specific input characteristics. One benefit of treating several targets at once is that the treatment period is shortened .Thus, enhanced effectiveness enables the treatment of more patients.

The biggest drawback of this technique is its limited availability. Other frequently discussed drawback is risk of compromised coverage: This issue can be addressed by placing plan isocenter nearer the smaller PTV to reduce the chance of compromised coverage. Lastly, not all patients are considered good candidates for single isocenter multiple target stereotactic fractionated radiotherapy, if the gap in between the contours is significant, this approach may not be ideal. Our patient was an ideal candidate due to overlap contours. New optimization techniques were described by David et al. for VMAT SRS plan of brain tumor (12). With VMAT SRS more conformal plans can be made in the high and intermediate dosage regions (about 50% of the Prescription dose), where the Paddick conformity index (PCI) was enhanced and the dose in the target's core was noticeably raised while V12 and mean modified gradient index (mGI) were dramatically reduced. These techniques can be applied to treatment planning for various brain tumors when it is essential to preserve the surrounding tissue. In protocols 90-05 (13) and 93-05, the Radiation Therapy Oncology Group (RTOG) proposed the SRS quality assurance and plan evaluation guidelines based on three parameters: the homogeneity index (HI), the conformity index (CI) (8) and target coverage.

SRS's toxicities have been associated with the Paddick conformity index, mGI and V12. Larger the PCI and smaller V12/mGI, the lesser brain toxicity in form of radionecrosis. Side effects profile of SRS include headache, seizures, localized alopecia, worsening of neurological deficits, fatigue, radiation dermatitis or radiation-induced brain necrosis as late side effect (14, 15). Radiation-induced brain necrosis is due to vascular endothelial damage and demyelination of the white matter (16). Our patient completed treatment without any major side effects. Planned imaging with the CEMRI brain shows complete response with no new findings.

Conclusion

Stereotactic radiosurgery is the new standard surgery for multiple brain metastasis. It doesn't require surgical incisions and is popular and suitable for patients with primary tumors and brain metastases. Stereotactic radiosurgery has been effective in brain metastasis. Brain metastasis trials yield has shown less deterioration of cognition with SRS use, although they do demonstrate benefits for local control with Combined WBRT therapy. Essential yet challenging aspect of SRS is dosimetry. It requires a comprehensive Quality assurance to treatment planning to its delivery. Proton SRS is an uncommon choice because of its high cost and space requirements. LINAC based VMAT SRS plans are more conformal with prescribed isodose line upto 75%. Hence optimization strategies should be applied for better plan outcome.

Author contribution

SA and **KG** write the main script, revised the script, conceptualized, and prepared figures.

Conflict of interest

The author declares no conflict of interest.

Funding

There is no funding.

References

1. Matsuda A, Matsuda T, Shibata A, Katanoda K, Sobue T, Nishimoto H. (Japan Cancer Surveillance Research Group). Cancer incidence and incidence rates in Japan in 2008: a study of 25 population-based cancer registries for the Monitoring of Cancer Incidence in Japan (MCIJ) project. Jpn J Clin Oncol. 2014;44:388–396.

2. Ganz JC. The journey from proton to gamma knife. Prog Brain Res. 2014;215:67-75. 7

3. Suh JH. Stereotactic radiosurgery for the management of brain metastases. N Engl J Med. 2010 Mar 25;362(12):1119-27.

4. Routman DM, Bian SX, Diao K, et al. The growing importance of lesion volume as a prognostic factor in patients with multiple brain metastases treated with stereotactic radiosurgery. Cancer Med. 2018;7:757-764.

5.Yamamoto, Masaaki et al. Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study The Lancet Oncology, Volume 15, Issue 4, 387 - 395

6.Chen JC, Girvigian MR. Stereotactic radiosurgery: instrumentation and theoretical aspects-part 1. Perm J. 2005 Fall;9(4):23-6.

7. Gondi V, Hermann BP, Mehta MP: Hippocampal dosimetry predicts neurocognitive function impairment after fractionated stereotactic radiotherapy for benign or low-grade adult brain tumors. Int J Radiat Oncol Biol Phys. 2012, 15:487-93.

8. Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R, et al. Radiation Therapy Oncology Group:Radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys. 1993;27:1231–9

9. Feuvret L, Noël G, Mazeron JJ, Bey P: Conformity index: a review. Int J Radiat Oncol Biol Phys. 2006, 1:333-42.

10. Roper J, Chanyavanich V, Betzel G. Single-Isocenter Multiple-Target Stereotactic Radiosurgery: Risk of Compromised Coverage. Int J Radiat Oncol Biol Phys. 2015 Nov 1;93(3):540-6.

11. Prentou G, Pappas EP, Logothetis A, Dosimetric impact of rotational errors on the quality of VMAT-SRS for multiple brain metastases: Comparison between single- and two-isocenter treatment planning techniques. J Appl Clin Med Phys. 2020 Mar;21(3):32-44.

12. Wang D, DeNittis A, Hu Y. Strategies to optimize stereotactic radiosurgery plans for brain tumors with volumetric-modulated arc therapy. J Appl Clin Med Phys. 2020 Mar;21(3):45-51.

13. Shaw E, Scott C, Souhami L, Dinapoli R, Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05. Int J Radiat Oncol Biol Phys. 2000 May 1;47(2):291-8.

14. Solberg TD, Balter JM, Benedict SH, Fraass BA, Kavanagh B, Miyamoto C, Pawlicki T, Potters L, Yamada Y. Quality and safety considerations in stereotactic radiosurgery and stereotactic body radiation therapy: Executive summary. Pract Radiat Oncol. 2012 Jan-Mar;2(1):2-9.

15. Redmond KJ, Gui C, Benedict S, et al. Tumor control probability of radiosurgery and fractionated stereotactic radiosurgery

16. Tofilon PJ, Fike JR. The radioresponse of the central nervous system: a dynamic pocess. Radiat Res. 2000 Apr;153(4):357-70.