SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Radiation Oncology

Clinical Outcomes of Stereotactic Radiotherapy for Brain Metastases: A Retrospective Single-Center Cohort Study from Morocco

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DOI: https://doi.org/10.36347/sasjm.2026.v12i09.010 | **Received:** 11.06.2026 | **Accepted:** 21.08.2026 | **Published:** 12.09.2026

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Abstract **Original Research Article**

This study evaluates the clinical outcomes, treatment patterns, and safety of brain SRT for limited brain metastases (BM) in a Moroccan tertiary oncology center, addressing the scarcity of North African real-world data. We retrospectively analyzed patients with brain metastases treated with SRT (2022–2025), assessing survival outcomes using Kaplan–Meier analysis and toxicity according to CTCAE v5.0. A total of 70 patients were analyzed. The median age was 59 years (mean ± SD: 58 ± 10 years), and 54.3% (n = 38) were female. Lung (44.3%) and breast (38.6%) cancers were the most common primary malignancies. Most patients presented with oligometastatic intracranial disease (71.4% with a single lesion; mean: 1.6 lesions per patient). Prior neurosurgical resection was performed in 51.4% of cases. The median tumor size was 20 mm (range: 5–53 mm). The most frequently prescribed fractionation schedule was 27 Gy in 3 fractions (44.3%), followed by 30 Gy in 5 fractions (21.4%). The median interval between consultation and SRT initiation was 13 days (IQR: 10–20 days). The median follow-up duration was 18.6 months (IQR, 11.2–27.4 months). The median OS was 22 months, with 6-month and 12-month OS rates of 85.0% and 72.7%, respectively. The median iPFS was not reached, with 6-month and 12-month iPFS rates of 81.6% and 62.5%, respectively. Treatment was well tolerated, with no Grade ≥3 treatment-related toxicities or symptomatic radionecrosis reported. Brain SRT is a safe, effective, and feasible treatment for oligometastatic brain disease in Morocco, achieving outcomes comparable to international standards despite resource limitations.

Keywords: Brain metastases, Stereotactic radiotherapy, Oligometastatic disease, Morocco, Survival, Toxicity.

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INTRODUCTION

Brain metastases (BM) are the most common intracranial tumors in adults and represent a major cause of cancer-related morbidity and mortality. Approximately 20–40% of patients with solid malignancies develop brain metastases during the course of their disease, with lung cancer, breast cancer, and melanoma accounting for the majority of cases. The incidence of BM continues to increase because of improvements in neuroimaging, prolonged survival resulting from advances in systemic therapies, and more intensive surveillance of high-risk patients. As systemic disease control improves, the central nervous system (CNS) has become a frequent site of disease progression owing to the limited penetration of many anticancer agents across the blood–brain barrier, making intracranial disease management an essential component of modern oncology care [1–5].

The management of brain metastases has undergone profound changes over the past two decades. Historically, whole-brain radiotherapy (WBRT) represented the standard treatment for patients with multiple intracranial metastases because it addressed both visible lesions and occult microscopic disease. However, although WBRT reduces intracranial recurrence, randomized trials have consistently demonstrated its detrimental effects on neurocognitive function, memory, and health-related quality of life, particularly among long-term survivors [6,7]. Consequently, treatment strategies have progressively shifted toward focal therapies capable of achieving durable local tumor control while minimizing irradiation of healthy brain tissue and preserving neurological function.

Stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (SRT) have therefore become the cornerstone of local treatment for patients with limited brain metastases. These highly conformal techniques deliver ablative radiation doses with submillimetric precision, achieving steep dose gradients outside the planning target volume while sparing surrounding normal brain tissue. Compared with WBRT, stereotactic irradiation provides excellent local control with substantially lower risks of neurocognitive deterioration, allowing better preservation of functional independence and quality of life [2–5,7]. In addition to intact metastases, postoperative irradiation of the surgical cavity has become a widely accepted indication, significantly reducing local recurrence after resection while avoiding the long-term cognitive toxicity associated with WBRT [2–4].

Several landmark studies have established stereotactic radiotherapy as the preferred treatment for patients with limited intracranial disease. The randomized trial by Brown *et al.,* demonstrated that stereotactic radiosurgery alone resulted in significantly less cognitive decline than stereotactic radiosurgery combined with WBRT, without compromising overall survival in patients with one to three brain metastases [7]. Subsequently, the prospective multi-institutional JLGK0901 study showed that carefully selected patients harboring five to ten brain metastases achieved overall survival comparable to those with two to four lesions when the cumulative intracranial tumor volume remained limited, shifting patient selection from the absolute number of metastases toward the overall intracranial disease burden [8]. These findings fundamentally transformed clinical decision-making and considerably expanded the indications for stereotactic treatment.

Technological advances have further broadened the role of SRT. While single-fraction radiosurgery remains appropriate for small lesions, hypofractionated stereotactic radiotherapy has gained increasing acceptance for larger tumors, postoperative cavities, and lesions located near critical organs at risk. Fractionated regimens such as 27 Gy in three fractions and 30 Gy in five fractions deliver high biologically effective doses while reducing the risk of radiation-induced brain injury, particularly symptomatic radionecrosis, by allowing repair of normal brain tissue between fractions [9–10]. Consequently, treatment is now individualized according to lesion size, anatomical location, cumulative tumor volume, and prior surgical management.

Current international guidelines consistently recommend stereotactic radiotherapy as the preferred local treatment for patients with limited brain metastases. The joint ASCO–SNO–ASTRO Guideline, the ASTRO Clinical Practice Guideline, the EANO–ESMO Clinical Practice Guideline, and the recent ESTRO–EANO Guideline all emphasize multidisciplinary decision-making based on performance status, cumulative intracranial tumor volume, extracranial disease control, expected survival, and technical feasibility rather than simply the number of metastatic lesions [2–5]. These recommendations reflect the growing recognition that treatment should maximize intracranial disease control while preserving long-term neurocognitive function and quality of life.

The therapeutic landscape has also evolved substantially with the introduction of molecularly targeted therapies and immune checkpoint inhibitors exhibiting meaningful intracranial activity. Modern systemic agents, including osimertinib for *EGFR*-mutated non-small-cell lung cancer, tucatinib-based regimens for *HER2*-positive breast cancer, and combined nivolumab–ipilimumab immunotherapy for melanoma have significantly improved intracranial response rates and overall survival in selected patient populations [11–14]. Rather than replacing local treatment, these therapies complement stereotactic radiotherapy within a multidisciplinary strategy integrating neurosurgery, precision radiotherapy, and systemic treatment according to tumor biology and disease burden [1–5].

Despite these major therapeutic advances, important disparities remain in access to stereotactic radiotherapy worldwide. Most available evidence originates from high-income countries with well-established stereotactic programs, whereas real-world data from low- and middle-income countries remain scarce. In North Africa, and particularly in Morocco, published studies evaluating the clinical characteristics, treatment patterns, survival outcomes, and toxicity of patients treated with brain SRT are extremely limited. Differences in healthcare infrastructure, access to advanced imaging, molecular diagnostics, targeted therapies, and radiotherapy resources may influence treatment delivery and clinical outcomes, highlighting the importance of generating regional evidence.

The National Institute of Oncology (INO) in Rabat is one of the leading referral centers for stereotactic radiotherapy in Morocco and has progressively implemented contemporary image-guided stereotactic techniques for the management of brain metastases. Evaluating the effectiveness and safety of these treatments in routine clinical practice is essential to determine whether outcomes achieved in a resource-constrained healthcare system are comparable with those reported by major international institutions. Therefore, the present retrospective single-center study aimed to describe the demographic and clinical characteristics of patients with brain metastases treated with stereotactic radiotherapy, evaluate treatment patterns, overall survival, intracranial progression-free survival, and treatment-related toxicity, and compare these real-world outcomes with contemporary international evidence. By providing one of the first comprehensive Moroccan experiences, this study seeks to contribute to the

optimization of multidisciplinary management of brain metastases and to support the broader implementation of high-precision radiotherapy in middle-income countries.

PATIENTS AND METHODS

Study Design and Patient Selection

This retrospective, observational, single-center study evaluated consecutive patients with brain metastases who underwent high-precision brain SRT at the Department of Radiation Oncology of the National Institute of Oncology (INO) in Rabat, Morocco, between April 2022 and March 2025.

Eligible patients met the following inclusion criteria:

- Age ≥18 years.
- Histologically confirmed primary solid malignancy with radiologically documented brain metastases (via contrast-enhanced MRI or CT scan).
- Treated with upfront, adjuvant, or salvage brain SRT (single-fraction or hypofractionated).
- Complete medical, dosimetric, and follow-up records.

Exclusion criteria included patients with leptomeningeal carcinomatosis, primary CNS malignancies, or incomplete radiotherapy planning data. The study was conducted in accordance with the Declaration of Helsinki and approved by the local institutional review board.

Radiotherapy Planning and Delivery

All patients underwent CT simulation in the supine position with individualized thermoplastic immobilization. Contrast-enhanced 3D T1-weighted brain MRI was rigidly co-registered with planning CT for accurate target delineation. The GTV included contrast-enhancing lesions, while the CTV encompassed the surgical cavity and preoperative tumor extent in previously resected patients. A 1–2 mm isotropic margin was added to generate the PTV.

Treatment planning was performed using Monaco® v6.1.4.0, and SRT was delivered on an Elekta Versa HD™ linear accelerator equipped with an Agility™ multileaf collimator. VMAT was used to achieve highly conformal dose distributions and steep dose gradients while minimizing exposure to healthy brain tissue. Plan evaluation included PTV coverage, D2%, homogeneity index, gradient index, and dose-volume histogram analysis, with strict adherence to predefined OAR constraints.

Image-guided radiotherapy was performed using 2D kV imaging and 3D CBCT with the Elekta XVI platform for accurate target localization and setup verification. Patient-specific QA was conducted using the PTW Octavius® 4D system and VeriSoft® software. Dose distributions were evaluated using a 3%/2 mm gamma analysis, with a minimum passing rate of 95% required for treatment approval.

Data Collection and Variables:

The following data were extracted from the institutional electronic medical records and oncology database:

- **Demographics:** Age, sex, geographic origin, and health insurance status.
- **Clinical Characteristics:** Primary tumor histology, extracranial disease status, performance status (KPS or ECOG), number of BM, anatomical location, and maximum tumor diameter.
- **Treatment Details:** History of prior surgical resection, prescription dose, fractionation schedule, systemic therapy type (chemotherapy, immunotherapy, or targeted therapy), and concurrent supportive medications (corticosteroids and anti-epileptic drugs).
- **Timeliness of Care:** The interval (in days) from the initial radiation oncology consultation to the first day of SRT delivery.
- **Follow-up and Outcomes:** Intracranial local and distant control, overall survival (OS), intracranial progression-free survival (iPFS), and treatment-related acute or late toxicities.

Statistical Analysis:

Continuous variables were summarized as means ± standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate. Categorical variables were expressed as absolute frequencies and percentages.

Overall survival (OS) was defined as the interval from the initiation of stereotactic radiotherapy (SRT) to death from any cause or the date of the last follow-up, with surviving patients censored at the time of the last follow-up. Intracranial progression-free survival (iPFS) was defined as the interval from SRT initiation to the first documented intracranial progression (local or distant) or death, whichever occurred first.

Survival curves were estimated using the Kaplan–Meier method. Differences in survival between groups were compared using the log-rank test.

Treatment-related toxicities were classified and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

RESULTS

Patient and Disease Characteristics

A total of 70 patients met all study criteria and were included in the final analysis. The demographic and clinical characteristics of the cohort are detailed in Table 1. The median age was 59 years (range: 30–87 years), and the cohort exhibited a slight female predominance (55.7%). Approximately 60% of the patients resided within the Rabat-Salé-Kénitra region, while 40% traveled from other regions of Morocco.

Table 1: General demographic characteristics of the study cohort

Variable	Patients (N = 70)	%
Sex		
Female	38	54.3
Male	32	45.7
Age		
Median	59 years	—
Mean ± SD	58 +/- 10 years	—
Range	30–87 years	—
Geographic Origin		
Rabat-Salé-Kénitra	42	60.0
Other Moroccan regions	28	40.0

Lung cancer was the most common primary tumor histology (44.3%), followed closely by breast cancer (38.6%). Together, these two malignancies accounted for 82.9% of all SRT indications (Table 2).

Table 2: Distribution of primary tumor sites

Primary Malignancy	Patients (n)	Percentage (%)
Lung	31	44.3
Breast	27	38.6
Melanoma	2	2.9
Thyroid	1	1.4
Ovarian	1	1.4
Bladder	1	1.4
Other	7	10.0

Intracranial Disease Burden and Location

The cohort represented a predominantly oligometastatic population, with 71.4% of patients presenting with a single brain lesion (Table 3). The mean number of brain lesions was 1.6 per patient.

Table 3: Distribution of the number of brain lesions treated per patient

Number of Brain Lesions	Patients (n)	Percentage (%)
1	50	71.4
2	5	7.1
3	10	14.3
4	2	2.9
5	3	4.3

The lesions were distributed across various intracranial compartments, with the parietal lobe (30.0%) and the cerebellum (28.0%) being the most frequent sites of metastasis, followed by the frontal lobe (18.0%) (Table 4).

Table 4: Anatomical distribution of brain metastases

Location of brain metastasis	Percentage (%)
Parietal lobe	30.0
Cerebellum	28.0
Frontal lobe	18.0
Temporal lobe	8.0
Occipital lobe	7.0
Corpus callosum	3.0
Sellar region	2.0
Other locations	4.0

The median maximum tumor diameter was 20 mm (22 ± 9 mm; range: 5–53 mm) (Table 5).

Table 5: Tumor size characteristics

Variable	Value
Median maximum tumor diameter, mm	20
Mean ± SD, mm	22 ± 9
Range, mm	5–53

Prior neurosurgical resection was performed in 36 patients (51.4%), whereas 34 patients (48.6%) underwent definitive upfront SRT (Table 6).

Table 6: Previous neurosurgical resection before stereotactic radiotherapy

Previous neurosurgical resection	Patients, n (%)
Yes	36 (51.4)
No	34 (48.6)

Prior to undergoing SRT, most patients received medical management to control peritumoral edema and symptoms (Table 7).

Table 7: Supportive medical treatment before stereotactic radiotherapy

Supportive treatment before SRT	Patients, n (%)
Corticosteroids alone	60 (86.0)
Corticosteroids plus antiepileptic drugs	10 (14.0)

Treatment Patterns and Fractionation

A wide variety of dose and fractionation schedules were employed, reflecting an individualized approach based on lesion size, postoperative status, and anatomical location. The single most common prescription was 27 Gy delivered in 3 fractions (44.3%), followed by 30 Gy in 5 fractions (21.4%) and 25 Gy in 5 fractions (14.3%), as detailed in Table 8.

Table 8: Details of stereotactic radiotherapy dose and fractionation schedules

Total Prescribed Dose	Number of Fractions	Patients (n)	Percentage (%)
15 Gy	1	1	1.4
18 Gy	1	5	7.1
20 Gy	1	4	5.7
21 Gy	3	1	1.4
24 Gy	3	3	4.3
25 Gy	5	10	14.3
27 Gy	**3**	**31**	**44.3**
30 Gy	5	15	21.4

Timeliness of Care

The median interval between the initial consultation in the radiation oncology department and the actual initiation of SRT was 13 days (IQR: 10–20 days; range: 3–97 days), representing rapid, high-quality clinical care in a tertiary public center (Table 9).

Table 9: Key intervals (in days) from radiation oncology consultation to SRT initiation

Parameter	Value (Days)
Median	13
Mean	16
First Quartile (Q1)	10
Third Quartile (Q3)	20
Minimum	3
Maximum	97

Survival Outcomes:

Overall survival (OS) and intracranial progression-free survival (iPFS) were analyzed using the Kaplan–Meier method.

The median follow-up duration was 18.6 months (IQR, 11.2–27.4 months). The median overall survival was 669 days (22 months), with estimated 6- and 12-month OS rates of 85.0% and 72.7%, respectively, indicating prolonged survival in a substantial proportion

of patients following stereotactic radiotherapy (Table 10, Figure 1).

Intracranial disease control was similarly favorable. The median iPFS was not reached, with 6-month and 12-month iPFS rates of 81.6% and 62.5%, respectively. The iPFS curve reached an apparent plateau of approximately 56.8% beyond 13 months, suggesting durable intracranial disease control among long-term survivors (Table 10, Figure 2).

Table 10: Kaplan–Meier estimates of overall survival and intracranial progression-free survival

Outcome	Parameter	Estimate
Overall Survival (OS)	Median OS	669 days (22.2 months)
	6-month OS rate	≈85.0%
	12-month OS rate	≈72.7%
Intracranial Progression-Free Survival (iPFS)	Median iPFS	Not reached (NR)
	6-month iPFS rate	≈81.6%
	12-month iPFS rate	≈62.5%

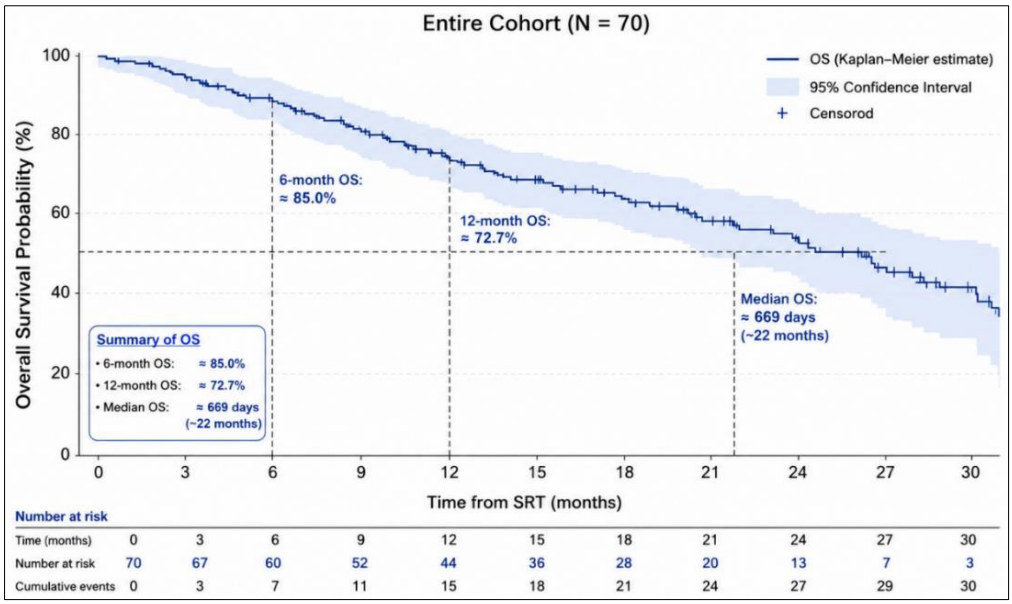

Figure 1: Kaplan–Meier estimate of Overall survival (OS) in the entire cohort (N = 70). The solid line represents the Kaplan–Meier estimate, the shaded area corresponds to the 95% confidence interval, and vertical tick marks indicate censored observations

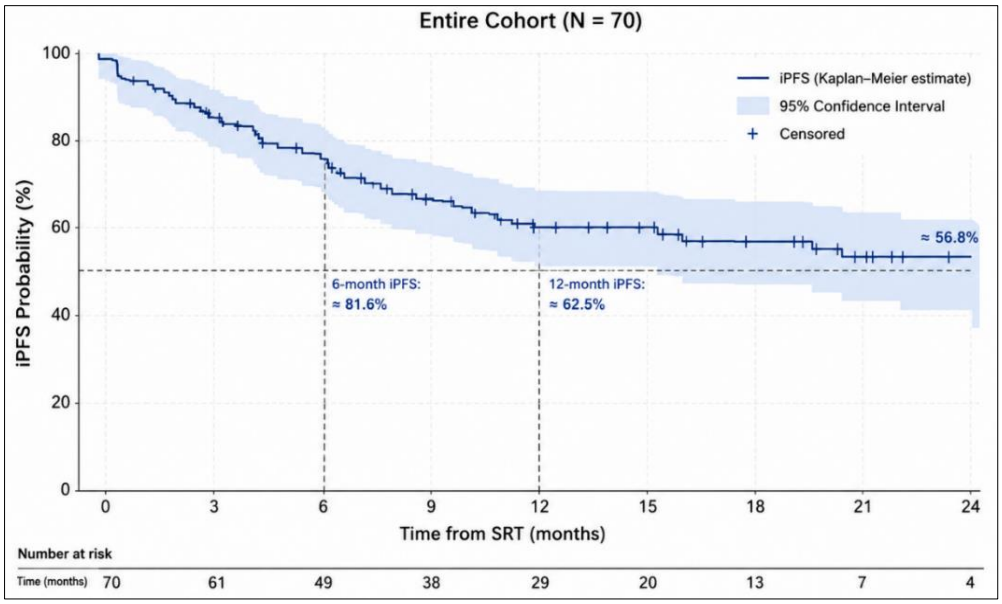

Figure 2: Kaplan–Meier estimate of intracranial progression-free survival (iPFS) in the entire cohort (N = 70). The solid line represents the Kaplan–Meier estimate, the shaded area corresponds to the 95% confidence interval, and vertical tick marks indicate censored observations

Overall Survival Stratified by Primary Tumor Histology

A subgroup analysis was performed to evaluate overall survival (OS) according to the primary tumor histology. Patients were categorized into three groups: breast cancer (n = 39), lung cancer (n = 24), and other primary malignancies (n = 7).

Significant differences in OS were observed among the three groups (log-rank $\chi^2 = 8.78$, p = 0.012) (Figure 3). Patients with breast cancer demonstrated the most favorable survival outcomes, with estimated 6-month and 12-month OS rates of 90.2% and 79.5%, respectively. In comparison, patients with lung cancer had corresponding survival rates of 77.1% and 60.6%, whereas patients with other primary malignancies experienced substantially poorer outcomes, with 6-month and 12-month OS rates of 57.1% and 28.6%, respectively.

The median OS was not reached for patients with breast cancer, whereas it was 17.2 months for patients with lung cancer and 7.6 months for those with other primary malignancies. The median OS for the entire cohort was 22.2 months.

Pairwise comparisons demonstrated significantly longer OS in patients with breast cancer than in those with lung cancer (p = 0.028) and other primary malignancies (p = 0.006). The difference between the lung cancer and other malignancy groups did not reach statistical significance (p = 0.094). These findings indicate that primary tumor histology is an important determinant of survival following stereotactic radiotherapy for brain metastases.

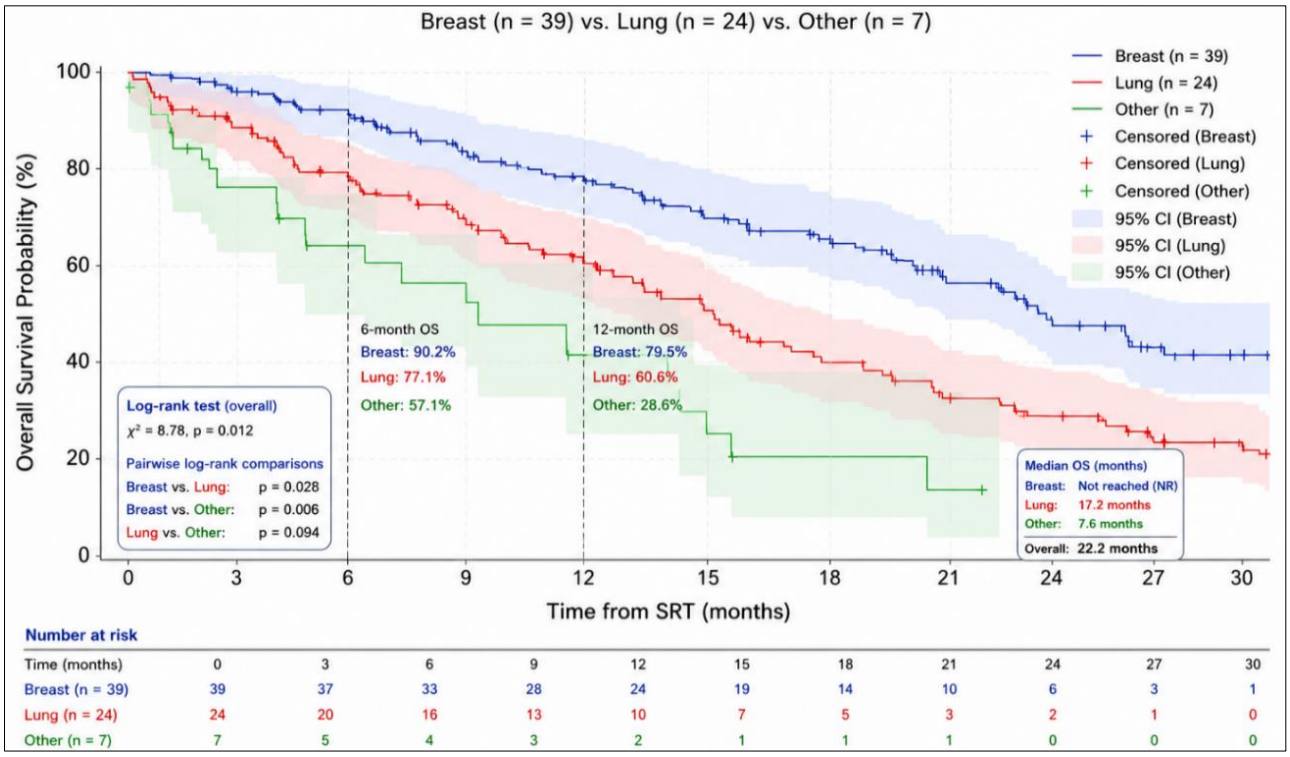

Figure 3: Kaplan–Meier estimates of overall survival (OS) according to primary tumor histology. Patients with breast cancer (n = 39), lung cancer (n = 24), and other primary malignancies (n = 7) are represented by the blue, red, and green curves, respectively. Shaded areas indicate the corresponding 95% confidence intervals, and the numbers at risk are displayed beneath the curves. Overall survival differed significantly among the three groups (log-rank p = 0.012)

Safety and Toxicity Profile:

Treatment was well tolerated. No Grade ≥3 treatment-related toxicities or symptomatic radionecrosis were documented during the follow-up period. Owing to the retrospective design of the study, low-grade (Grade 1–2) adverse events may have been underreported in the medical records and were therefore not analyzed.

DISCUSSION

This retrospective single-center study represents one of the first real-world evaluations of stereotactic radiotherapy (SRT) for brain metastases in Morocco and one of the few published experiences from North Africa. Our findings demonstrate that modern image-guided SRT can be safely implemented in a resource-constrained healthcare setting, providing favorable overall survival, durable intracranial disease control, and minimal treatment-related toxicity. The predominance of patients with oligometastatic disease, the frequent use of postoperative cavity irradiation, and the excellent safety profile observed in our cohort are consistent with current international recommendations supporting SRT as the preferred local treatment for

patients with limited brain metastases. These findings confirm that high-quality stereotactic treatment can be successfully delivered outside high-income countries when standardized planning, image guidance, and quality assurance procedures are applied [1–5].

The clinical characteristics of our cohort closely resemble those reported in contemporary international series. Lung and breast cancers accounted for more than 80% of primary tumors, reflecting the current epidemiology of brain metastases worldwide [1,15–17]. Similarly, most patients presented with a single intracranial lesion and underwent multidisciplinary evaluation before treatment, illustrating the current paradigm shift from whole-brain radiotherapy (WBRT) toward individualized focal therapy based on disease burden rather than simply the number of brain metastases [2–5,8].

The survival outcomes observed in our study compare favorably with those reported in recent stereotactic radiotherapy series. The median overall survival reached 22 months, whereas the median intracranial progression-free survival was not reached, indicating durable intracranial disease control. Breast cancer patients achieved significantly better overall survival than patients with lung cancer or other primary malignancies, consistent with previous studies demonstrating the prognostic influence of tumor biology and the availability of effective systemic therapies [12,13,18,19]. Current evidence indicates that survival following SRT is increasingly determined by performance status, extracranial disease control, molecular profile, and access to targeted therapies rather than by local treatment alone [1,15–19].

Treatment delivery in our institution closely followed contemporary international recommendations. Most patients received hypofractionated SRT, particularly 27 Gy in three fractions and 30 Gy in five fractions, schedules that are widely recommended for larger lesions and postoperative cavities because they provide excellent local control while reducing the risk of radionecrosis [2–5,9,10]. These treatment strategies reflect current evidence favoring individualized fractionation according to lesion size, location, surgical status, and proximity to critical organs at risk [4,9,10].

The safety profile observed in our cohort was excellent. No Grade ≥3 treatment-related toxicities or symptomatic radionecrosis were documented during follow-up. These findings are consistent with previous studies demonstrating that modern image-guided stereotactic radiotherapy, combined with meticulous treatment planning and rigorous quality assurance, minimizes radiation exposure to normal brain tissue while maintaining excellent tumor control [6,7,9,10]. Nevertheless, because radionecrosis may occur several months after treatment and low-grade adverse events may be underreported in retrospective studies, longer follow-up and prospective toxicity assessment remain warranted.

The present study has several strengths. It provides one of the first comprehensive reports describing stereotactic radiotherapy for brain metastases in Morocco, reflecting routine clinical practice in a national tertiary oncology center. Furthermore, all patients were treated using standardized MRI-based target delineation, VMAT planning, daily cone-beam CT image guidance, and quality assurance procedures, thereby ensuring treatment reproducibility and consistency.

However, several limitations should be acknowledged. The retrospective single-center design may have introduced selection bias, and the relatively limited sample size reduced the statistical power of subgroup analyses. In addition, comprehensive molecular profiling and standardized neurocognitive or quality-of-life assessments were unavailable for all patients. Future prospective multicenter studies incorporating molecular biomarkers, patient-reported outcomes, and longer follow-up are warranted to validate these findings and further optimize patient selection for stereotactic radiotherapy [1–5,15–19].

Overall, our results demonstrate that stereotactic radiotherapy is an effective, safe, and reproducible treatment for patients with limited brain metastases. The favorable survival outcomes and excellent safety profile observed in this Moroccan cohort support the broader implementation of contemporary stereotactic radiotherapy programs in Morocco and other low- and middle-income countries while reinforcing the central role of SRT in the multidisciplinary management of brain metastases [1–5].

CONCLUSION

This study demonstrates that stereotactic radiotherapy is an effective, safe, and reproducible treatment for patients with limited brain metastases in routine clinical practice. Favorable survival outcomes, durable intracranial disease control, and minimal treatment-related toxicity were achieved despite the resource-constrained setting. These findings support the broader implementation of modern stereotactic radiotherapy programs in Morocco and other middle-income countries. Future prospective multicenter studies integrating molecular biomarkers, neurocognitive outcomes, and patient-reported quality-of-life measures are warranted to optimize patient selection and treatment strategies.

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