

ORIGINAL ARTICLE

Single vs multiple fraction palliative radiotherapy for uncomplicated painful bone metastases treated at University of Malaya Medical Centre: A single institutional Malaysian experience

Ina Shaliny Duraisamy  | Marniza Saad | Adlinda Alip

Clinical Oncology Unit, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

Correspondence

Ina Shaliny Duraisamy, Clinical Oncology Unit, University of Malaya Medical Centre, Kuala Lumpur, Malaysia.
Email: i_shaliny@yahoo.com

Abstract

Introduction: This study was conducted to compare pain response between single and multiple fraction palliative radiotherapy and to describe prognostic factors affecting treatment response in University of Malaya Medical Centre (UMMC).

Methods: The case records of 162 patients with uncomplicated painful bone metastases treated with palliative radiotherapy from 2006 to 2014 were analyzed. Treatment outcomes were pain score response, analgesic score response, response according to International Consensus Endpoints (complete response and overall response) at 4, 12, and 24 weeks, retreatment rate, symptomatic skeletal events (SSEs), and prognostic factors.

Results: At 24 weeks, pain score response for single and multiple fraction group was 82.3% and 88.5%, analgesic score response was 54.8% and 61.5%, and overall response according to International Consensus Endpoint was 61.3% and 67.7%, respectively. There was no statistically significant difference in treatment response between the 2 treatment groups for all endpoints. ECOG (<2 vs ≥2: aOR 3.405, 95% CI 1.708-6.790, $P = .001$) and primary breast and prostate (breast vs others: aOR 5.231, 95% CI 1.973-13.869, $P = .001$; prostate vs others: aOR 5.522, 95% CI 1.493-20.420, $P = .01$) were significant variables on multivariate analysis.

Conclusion: Single fraction radiotherapy is as effective as multiple fraction radiotherapy for the palliation of uncomplicated bone metastases.

KEYWORDS

bone metastases, pain, palliative radiotherapy

1 | INTRODUCTION

Many advanced cancer patients are surviving longer with improvements in anticancer therapy. Pain from bone metastases accounts for 75% of the presenting complaint in these patients¹ and can be a debilitating problem. It is important to manage

pain adequately so that these patients can have a good quality of life.

The role of radiotherapy for palliation of painful bone metastases has been well established. It has been shown to provide pain relief in 50%-80% of treated patients with a complete response rate of 20%-50%.^{2,3} Nevertheless, the optimal dose fractionation remains

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uncertain. Some studies suggested that single fraction radiotherapy is equally effective to multiple fraction in providing pain relief,^{4–11} while others showed that higher dose fractionation provides more effective pain relief than single fractionation schedule.^{12,13} Evidence from several studies demonstrated that single fraction radiotherapy may be associated with higher rates of retreatment and pathological fracture postirradiation.^{9,10}

We conducted this study to compare outcomes between single and multiple fraction palliative radiotherapy in terms of pain response, retreatment rate, and symptomatic skeletal events, and to describe potential factors affecting treatment outcomes in our patients.

2 | METHODS

2.1 | Data collection

This is a retrospective analysis of patients with bone metastases treated with external beam radiotherapy in University of Malaya Medical Centre (UMMC) between January 2006 and December 2014. The study was approved by the Medical Ethics Committee of UMMC (201510-1789). The radiotherapy database was retrieved and screened for patients with bone metastases. Patient case records, medication chart, and radiotherapy treatment sheet were reviewed to identify eligible patients.

Patients were considered eligible for this study if they had histologically proven primary malignancy with radiologically confirmed bone metastasis and received palliative radiotherapy for pain relief. Patients were excluded if the painful site had been irradiated before the study period (ie, before 2006), the presence of spinal cord compression, pathological fracture or history of surgical intervention at treatment site, and nonsolid primary tumor. Each patient was evaluated only once, that is the first radiation treatment for one particular site.

Relevant data collected include patient demographics, primary tumor details, bone metastasis details, pain severity, analgesic consumption, radiotherapy treatment details, adverse events after radiotherapy, use of bone-targeting agents, systemic therapy, and retreatment details.

Response evaluations were documented at 4, 12, and 24 weeks after radiotherapy. Patients who died within 24 weeks of evaluation period were excluded from this study. Retreatments occurring within the evaluation period were reported as progression at evaluation endpoint and were excluded from further analysis. Retreatment outcomes were not assessed. Results were reported and compared in 2 treatment groups, that is single and multiple fractions.

2.2 | Evaluation and definition of response

2.2.1 | Pain score

Pain was measured by a 4-point scale with numbers 1–4 with pain documented as none—score 1, mild—score 2, moderate—score 3, and

severe—score 4.^{5,14} Partial response was defined as relief of pain by at least ≥ 1 category (eg, severe to moderate) or score of at least 1 (eg, 4–3). Complete response was defined as the absence of pain (pain score of 1) at treated site. Progression was considered as an increase in pain score by ≥ 1 category or the need for retreatment.

2.2.2 | Analgesic scoring system

Patient analgesic consumption was recorded and scored as follows: analgesic score 0—analgesic not required, score 1—nonopioid analgesic irregularly required, score 2—nonopioid analgesics regularly required, score 3—oral or parenteral opioids occasionally required, and score 4—oral or parenteral opioids regularly required.¹⁵ The response was defined as a reduction in analgesic score by at least 1 step or an unchanged analgesic score but reduction in daily dose by $\geq 25\%$. Progression was defined as an increase in the analgesic score by $\geq 25\%$ or the need for retreatment. The stable response was defined as a state between response and progression.

2.2.3 | International consensus endpoints

The outcomes were further analyzed using International Consensus Endpoints, which incorporates pain score response and analgesic consumption.¹⁶ Complete response was defined as a pain score of 0 at the treated site with no increase in analgesic intake (ie, stable or reducing analgesic intake). Partial response was defined as a reduction in pain score by at least 1 (scale 1–4) at the treated site without analgesic intake or analgesic reduction by at least 25% from baseline without an increase in pain. Pain progression was defined as an increase in pain score by at least 1 above baseline at the treated site with stable analgesic usage or an increase in analgesic requirement by at least 25% from baseline with stable pain score.

2.3 | Statistical methods

The sample size was calculated using Stata software, based on the information gathered from a study by Arcangeli et al.¹² The sample size was calculated on the basis of a 0.05 alpha, with a power 80% and hazard ratio 0.44 (total dose variable). Based on this calculation and accounting for 20% dropout, each treatment arm required 63 patients. Therefore, the minimum sample size required for this study was 126 patients.

Descriptive analysis of all the demographic and outcome variables was performed. Results of the continuous variables were described with mean and standard deviation or median and interquartile range, where appropriate. Results of categorical variables were described with frequency and percentage. Mann-Whitney *U* test, chi-square test, and Fisher's exact test were used to compare the demographic and predictor variables with the outcome variables. All statistical analysis was performed using Statistical Package for the Social Sciences (SPSS), ver 22.0. Statistical significance was defined as $P < .05$. Using univariate analysis, all variables were analyzed and variables were considered significant if $P < .25$ by applying

the preliminary main-effect model. Significant variables were then included in multivariate analysis using the forward and backward logistic regression. Hosmer and Lemeshow test was carried out to test for interaction and multicollinearity between significant variables and is significant for $P > .05$.

3 | RESULTS

3.1 | Overview of patient characteristics

Between January 2006 and December 2014, 584 patients with bone metastases received palliative radiotherapy in University of Malaya Medical Centre (UMMC). Of the 584 case records reviewed, 162 patients were eligible for this study. A total of 422 patients were excluded from analysis due to prior irradiation ($n = 4$), nonsolid tumor ($n = 5$), prior surgical intervention with or without pathological fracture ($n = 44$), spinal cord compression ($n = 113$), death within 24 weeks of study period ($n = 12$), lost to follow-up ($n = 124$), and missing records ($n = 120$). Baseline characteristics of the patients are summarized in Table 1. The parallel-opposed technique was used to treat pelvis and extremity, while the direct posterior technique was used to treat spine. Treatment was delivered with a linear accelerator using megavoltage beams.

3.2 | Pain response according to fractionation group

The mean baseline pain and analgesic score at the treated site were 3.4 (SD \pm 0.5) and 3.2 (SD \pm 0.7), respectively. Response evaluation according to treatment groups is shown in Table 2. There was an increasing trend of pain score response and analgesic score response noted in both the treatment groups from 4 to 24 weeks. Using chi-square test, the difference in response rates between the 2 treatment groups was not statistically significant. However, there was a statistically significant difference in analgesic score progression between the 2 fractionation groups seen at 24 weeks, $P = .019$. When the results were reported in terms of International Consensus Endpoint, the difference in overall response rates and pain progression between the 2 treatment groups was not statistically significant.

3.3 | Factors affecting pain response

Several factors that could potentially affect overall pain response at 4 weeks were analyzed using simple logistic regression. The univariate analysis is shown in Table 3, and using the preliminary main-effect model ($P < .25$), this suggests that gender, ECOG, primary tumor, and bone-targeting agent could possibly be significant prognostic factors affecting pain response, with significantly different rates of overall pain response, when other confounders are not adjusted.

For these variables, forward and backward logistic regression was carried out. Following this, only 2 of the variables, that is primary tumor and ECOG, were found to be significant in the main-effect model, as shown in Table 4. There is no interaction and

TABLE 1 Baseline characteristics of patients

	Single fraction (N = 65)		Multiple fraction (N = 97)		All patients (N = 162)	
	N	%	n	%	N	%
Age						
< 65	41	63	72	74.2	113	69.8
≥ 65	24	37	25	25.8	49	30.2
Mean	58.9		54.9		56.6	
Median	60.0		55.0		57	
Sex						
Male	20	30.8	34	35	54	33.3
Female	45	69.2	63	65	108	66.7
ECOG						
1	37	57	57	58.8	94	58
2	22	33.8	36	37.1	58	35.8
3	6	9.2	4	4.1	10	6.2
Comorbidities						
Yes	17	26.2	20	20.6	37	22.8
No	48	73.8	77	79.4	125	77.2
Primary tumor						
Breast	33	50.8	51	52.6	84	51.9
Lung	16	24.6	15	15.5	31	19.1
Prostate	7	10.8	12	12.4	19	11.7
Others	9	13.8	19	19.5	28	17.3
Extent of bone metastases						
Single	6	9.2	3	3.1	9	5.6
Multiple	59	90.8	94	96.9	153	94.4
Visceral metastases						
Yes	31	47.7	42	43.3	73	45.1
No	34	52.3	55	56.7	89	54.9
Baseline pain score^a						
2	1	1.5	2	2.1	3	1.9
3	36	55.4	52	53.6	88	54.3
4	28	43.1	43	44.3	71	43.8
Baseline analgesic score^b						
2	13	20	16	16.5	29	17.9
3	29	44.6	47	48.5	76	46.9
4	23	35.4	34	35	57	35.2
Treatment site						
Spine	29	44.6	62	63.9	91	56.2
Pelvis	25	38.5	30	30.9	55	34.0
Extremities	5	7.7	2	2.1	7	4.3
Others	4	6.2	5	5.2	9	5.5
Systemic therapy						
Yes	52	80	79	81.4	131	80.9
No	13	20	18	18.6	31	19.1

(Continues)

TABLE 1 (Continued)

	Single fraction (N = 65)		Multiple fraction (N = 97)		All patients (N = 162)	
	N	%	n	%	N	%
Fractionation schedule						
10 Gy in 1#	-	-	-	-	5	3.1
8 Gy in 1#	-	-	-	-	60	37
30 Gy in 10#	-	-	-	-	5	3.1
20 Gy in 5#	-	-	-	-	92	56.8

^aThere were no patients with pain score 1.

^bThere were no patients with analgesic score 0-1.

TABLE 2 Response according to treatment group

	Total, N = 162	Single fraction, N = 65	Multiple fraction, N = 97	P-value
Pain score response				
4 wk	129/162 (79.6%)	50/65 ^a (76.9%)	79/97 (81.4%)	.394
12 wk	138/159 (86.8%)	54/63 (85.7%)	84/96 (87.5%)	.938
24 wk	136/158 (86.1%)	51/62 (82.3%)	85/96 (88.5%)	.228
Pain score progression				
4 wk	6/162 (3.7%)	4/65 (6.2%)	2/97 (2.1%)	.176
12 wk	5/159 (3.1%)	2/63 (3.2%)	3/96 (3.1%)	.986
24 wk	11/158 (6.9%)	4/62 (6.5%)	7/96 (7.3%)	.839
Analgesic score response				
4 wk	81/162 (50%)	30/65 (46.2%)	51/97 (52.6%)	.155
12 wk	92/159 (57.9%)	34/63 (54%)	58/96 (60.4%)	.319
24 wk	93/158 (58.9%)	34/62 (54.8%)	59/96 (61.5%)	.056
Analgesic score progression				
4 wk	16/162 (9.9%)	10/65 (15.4%)	6/97 (6.2%)	.054
12 wk	20/159 (12.6%)	11/63 (17.5%)	9/96 (9.4%)	.133
24 wk	27/158 (17.1%)	16/62 (9.9%)	11/96 (11.5%)	.019*
International consensus endpoint				
4 wk				
CR	52/162 (32.1%)	18/65 (27.7%)	34/97 (35.1%)	
PR	39/162 (24.1%)	15/65 (23.1%)	24/97 (24.7%)	
ORR	92/162 (56.2%)	33/65 (50.8%)	58/97 (59.8%)	.364
Progression	54/162 (33.3%)	22/65 (33.8%)	32/97 (33.0%)	.910
12 wk				
CR	55/159 (34.6%)	21/63 (33.3%)	34/96 (35.4%)	
PR	44/159 (27.7%)	18/63 (28.6%)	26/96 (27.1%)	
ORR	99/159 (62.3%)	39/63 (61.9%)	60/96 (62.5%)	.466
Progression	38/159 (23.9%)	13/63 (20.6%)	25/96 (26.0%)	.384
24 wk				
CR	89/158 (56.3%)	33/62 (53.2%)	56/96 (58.3%)	
PR	14/158 (8.9%)	5/62 (8.1%)	9/96 (9.4%)	
ORR	103/158 (65.2%)	38/62 (61.3%)	65/96 (67.7%)	.259
Progression	28/158 (17.7%)	10/62 (16.1%)	18/96 (18.8%)	.599

CR, complete response; PR, partial response; ORR, overall response (CR + PR).

^aNumber of patients within treatment group.

* $P < .05$.

multicollinearity seen among the variables. The Hosmer and Lemeshow test is significant at 0.492 (>0.05). The logistic regression has a Nagelkerke R^2 of 0.202.

3.4 | Retreatment

The overall retreatment rate was 20.4% ($n = 33$). Retreatment was observed in 16 patients (24.6%) in the single fraction group and 17 patients (17.5%) in the multiple fraction group. Although the retreatment rate was higher in the single fraction group, this was not statistically significant ($P = .552$). Mean duration to retreatment was 35.1 (SD \pm 22.4) weeks in the single fraction group and 57.6

TABLE 3 Univariate analysis of prognostic factors and overall pain response

Variable	Odds ratio	95% confidence interval	Wald statistic	P-value
Age				
< 65	1.000	-	-	-
≥65	1.193	0.605-2.353	0.258	.611
Gender				
Male	1.000	-	-	-
Female	1.823	0.942-3.527	3.178	.075*
ECOG				
< 2	3.240	1.689-6.213	12.526	<.001*
≥2	1.000	-	-	-
Primary tumor				
Breast	5.000	1.959-12.762	11.333	.001*
Lung	2.344	0.795-6.908	2.385	.122*
Prostate	4.286	1.238-14.831	5.279	.022*
Others	1.000	-	-	-
Extent of bone metastases				
Single	1.000	-	-	-
Multiple	1.027	0.265-3.973	0.001	.969
Treatment site				
Spine	1.067	0.269-4.235	0.008	.927
Pelvis	1.033	0.250-4.269	0.002	.964
Extremities	0.600	0.082-4.400	0.253	.615
Others	1.000	-	-	-
Fractionation				
Single	1.000	-	-	-
Multiple	1.299	0.690-2.446	0.658	.417
Bone-targeting agent				
Yes	1.693	0.898-3.192	2.650	.104*
No	1.000	-	-	-
Systemic treatment				
Yes	1.256	0.573-2.752	0.323	.570
No	1.000	-	-	-

*The variables selected ($P < .25$) for the preliminary main-effect model are gender, ECOG, primary tumor, and bone-targeting agent.

(SD ± 54) weeks in the multiple fraction group. Using Mann-Whitney U test, there was no statistically significant difference in mean duration to retreatment in the 2 groups ($P = .656$). At evaluation period of 24 weeks, 11 (33.3%) patients had retreatment. The main reason for retreatment was worsening pain seen in 16 (48.5%) patients, cord compression with pain in 14 (42.4%) patients, and pathological fracture with pain in 3 (9.1%) patients.

3.5 | Symptomatic skeletal events

The occurrence of pathological fracture in the treated site was seen in 4 (2.5%) patients, 2 (3%) patients in the single fraction group and

TABLE 4 Multivariate analysis for overall response

Variable	Adjusted odds ratio (aOR)	95% confidence interval	Wald statistic	P-value
ECOG				
< 2	3.405	1.708-6.790	12.112	.001
≥2	1.000	-	-	-
Primary tumor				
Breast	5.231	1.973-13.869	11.064	.001
Lung	2.817	0.907-8.747	3.210	.073
Prostate	5.522	20.420-6.557	6.557	.010
Others	1.000	-	-	-

2 (2.1%) patients in the multiple fraction group. Spinal cord compression was seen in 14 (8.6%) patients, 5 (7.7%) patients in the single fraction group, and 9 (9.3%) patients in the multiple fraction group. There was no significant difference in the occurrence of SSEs between the 2 treatment groups, $P = 1.00$.

3.6 | Bone metastases

Mean time from diagnosis of bone metastases to first irradiation for pain was 20.2 weeks (SD ± 40.3 weeks). Mean duration of diagnosis of bone metastases to first irradiation was 14.3 weeks (SD ± 18) in the single fraction group and 24.11 (SD ± 49.7) weeks in the multiple fraction group. Using Mann-Whitney U test, there was no significant difference in duration of diagnosis of bone metastases to time of first irradiation between single and multiple fractionation group ($P = .492$).

3.7 | Bone-targeting agents and systemic therapy

The administration of bone-targeting agent and systemic therapy in both the fractionation groups is shown in Table 5. Mean time from diagnosis of bone metastases to initiation of bone-targeting agent was 44.9 (SD ± 58) weeks. There was a significant association for usage of bone-targeting agents and occurrence of pathological fracture and cord compression ($P = .004$).

4 | DISCUSSION

The results of our study showed that there is no significant difference in pain relief between single and multiple fraction radiotherapy for palliation of painful bone metastases. This is consistent with several published studies⁵⁻⁷ and meta-analyses.^{10,11} Although we employed the verbal rating scale which is less sensitive than the numerical rating scale,¹⁷ it is a reliable method for pain assessment.¹⁸ Pain response rates from trials which used a categorical scale as a measure of pain showed response rates of 76%,¹⁴ 72%,⁷ 83.7%⁵ in the single fraction group and 84%,¹⁴ 90%,⁷ 89.2%⁵ in the multiple fraction group. This is compatible with our pain response rates of 76.9%-85.7% in the single fraction

TABLE 5 Concomitant therapy according to fractionation group

	Single fraction (N = 65) (%)	Multiple fraction (N = 97) (%)	Total (N = 162) (%)	Retreatment (N = 33)	P-value [†]	Pathological fracture/Cord compression (N = 18) (%)	P-value [‡]
Bone-targeting agents (N = 71)	29 (44.6) ^a	42 (43.3) ^a	71 (43.8) ^b	12 (36.4) ^c	.43	2 (11.1) ^d	.004*
Pamidronate	2 (3.1)	4 (4.1)	6 (3.7)				
Zoledronic A.	24 (36.9)	33 (34.0)	57 (35.2)				
Denosumab	3 (4.6)	5 (5.2)	8 (4.9)				
Systemic therapy (N = 131)	52 (80)	79 (81.4)	131 (80.9)	28 (84.8)	.625	15 (83.3)	1.000
Chemotherapy	32 (49.2)	40 (41.2)	72 (44.4)				
Hormonal therapy	15 (23.1)	32 (33)	47 (29)				
Tyrosine kinase inhibitor	5 (7.7)	5 (5.2)	10 (6.2)				
Radioiodine therapy	0 (0)	2 (2.1)	2 (1.2)				

^aPercent within treatment group.

^bPercent within total number of patients.

^cPercent within retreatment.

^dPercent within pathological fracture/cord compression.

* $P < .05$.

[†]P-value for retreatment.

[‡]P-value for pathological fracture/cord compression.

group and 81.4%–88.5% in the multiple fraction group. A recent systematic review¹⁹ comparing various single fraction doses for the palliation of painful bone metastases showed a higher overall response rate for higher doses, that is an overall response rate of 84% for 10 Gy and 72% for 8 Gy in evaluable patients, which was representative of the single fraction doses that were used in our study, as 92.3% of our patients were prescribed 8 Gy and the remaining 10 Gy.

When results were reported using International Consensus Endpoints, we obtained an overall response rate of 56.2% and 62.3% at 4 and 12 weeks, respectively, in the entire cohort of patients. Our results were comparable with published data of overall response rates in evaluable patients according to International Consensus Endpoint at 1 month of 58% and 3 months of 67%.²⁰ The reported estimated spinal adverse event (SAE) rate (which include uncontrolled pain) of >40% at 6 months²¹ could explain the significant requirement for more analgesia at 24 weeks that was seen in our study.

There was a significantly higher overall response rate observed in patients with ECOG < 2 and primary tumors of breast and prostate when compared to other primary tumors, which was compatible with evidence which demonstrated that patients with breast and prostate cancer had the best response rate.⁹

In addition to this, a study has reported that the single fraction group was associated with fourfold greater retreatment rate and higher pathological fracture rate.⁹ Our study did not demonstrate this. We found higher retreatment rates in the single fraction group, but this was not statistically significant. We obtained a retreatment rate of 24.6% in the single fraction group and 17.5% in the multiple fraction group, which was higher as compared to published data of 21%,¹⁹ 18.2%²¹ in single fraction group and 6%²¹ in the multiple fraction group. The highest percentage of retreatment was seen in

patients with lung primary, which could be due to the effect of tumor histology.^{9,12} At 4 weeks of evaluation endpoint, there were 3 (9%) retreatments involving the spine, 2 of them were in the single fraction group. The use of single fraction radiotherapy in patients with high spinal instability neoplastic score (SINS \geq 11) was associated with higher incidence of SAEs, with a reported cumulative incidence first with SAE rate at 30 days of 6.8% in the single fraction group and 3.5% in the multiple fraction group.²¹

Our results showed a lower pathological fracture rate of 3% in the single fraction group compared to 4%^{9,19} and 13.6%²¹ that have been reported. However, the pathological fracture rate obtained in the multiple fraction group of 2.1% was similar to published data of 2%⁹ and 3%.²¹ As for cord compression rate, we obtained rates of 7.7% in the single fraction group and 9.3% in the multiple fraction group compared to that reported in trials, that is, 3% to 7%,¹⁹ 10.5%²¹ in single fraction group and 1.7%²¹ in the multiple fraction group. The low spinal cord compression rate in the multiple fraction group²¹ may not be accurate as the recruitment of patients was not reflective of the true numbers of spinal cord compression cases. Furthermore, this trial only assessed patients that had spinal radiotherapy, which only account for 56.2% of our study patients.

The significant association between the development of pathological fracture and cord compression with the usage of bone-targeting agents is consistent with published trials on the efficacy of bone-targeting agents in reducing the risk of skeletal-related events.^{22,23}

There were several limitations to our study. Given the retrospective nature of this study, we were limited by the availability of data. Firstly, as our primary objective was to assess pain response, patients who did not have data or follow-up notes following irradiation were excluded. This included patients who had died within evaluation period of 24 weeks. We acknowledge that the number of

deaths reported in this study may not be accurate as there could be more deaths in the lost to follow-up and missing notes group that we were not able to trace. Hence, our study population may not be representative of the actual situation.

Secondly, we realized that patient-reported outcomes were as important as physician-assessed outcomes, as it provides evaluation of response on the patient's perspective. Results based on patient-reported outcomes showed an improvement of 70% in pain with no difference between single and multiple fraction groups.²⁴

The choice of single fraction radiotherapy is affected by cultural differences, physicians' experience, location of training, and practice location.²⁵ The reported single fraction utilization rate in Canada was 49.2%,²⁵ as compared to the United States of 4.7%.²⁶ There are no trials reporting on the single fraction utilization rate in Asian countries to date. As for cultural differences, 76% of Canadian patients favored single fraction²⁷ while 85% of Asian patients preferred the multiple fraction schedule.²⁸ Patients' preference toward treatment needs to be considered as well as 84% of Asian patients expressed positive opinions about being involved in the decision-making process.²⁸

Therefore, our study could be improved by including outcome assessment by physician and patient, SINS for patients with spinal metastases, patient involvement in treatment decision making, and exploration on physician judgment in choosing radiotherapy prescription. A prospective randomized trial should be performed in the future to verify our results. Importantly, despite our limitations, we were able to obtain comparable pain response rates to those found in the literature.

In conclusion, our study showed that there is no significant difference in terms of pain response, retreatment rate, and SSEs between single fraction and multiple fraction radiotherapy in patients treated for uncomplicated bone metastases. Single fraction radiotherapy should be the standard treatment and prescribed more frequently as it is more convenient and cost-effective.

CONFLICT OF INTEREST

None.

ORCID

Ina Shaliny Duraisamy  <http://orcid.org/0000-0002-7314-8220>

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