



Research Article

A PROSPECTIVE STUDY TO COMPARE THE EFFECT OF SINGLE (8Gy) vs MULTIFRACTION (20Gy/5#) RADIOTHERAPY IN PALLIATION OF PAINFUL BONE METASTASIS

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ABSTRACT

Aim: To assess pain control and symptomatic relief while using 8Gy single fraction versus 20Gy/5# in palliation of painful bone metastasis.

Materials and Methodology: This is a prospective study of 180 patients with painful bone metastasis who were treated at our centre. Ninety patients in one arm received 8Gy single fraction and ninety patients in other arm received 20Gy/5#. Primary goal is symptomatic pain relief, whereas secondary endpoints were decreased analgesic requirement, mean duration of response, improved performance status and reirradiation.

Results: Both single and multifraction RT produces more or less same symptomatic pain relief. However single fraction group required re irradiation more commonly when compared to multifraction group.

Conclusion: More than 80% patients got pain relief at 3-weeks post radiotherapy (82.2% in SF groups & 85.5% in MF group) which was maintained up to 3rd month. There was a reduction in the percentage of patients with overall pain relief 3rd month onward follow up. This study concludes that single fraction is as effective as multifraction for the palliation of painful bone metastasis.

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INTRODUCTION

Metastatic bone disease is a common problem encountered in oncology practice. Many patients with cancer, though heavily treated, ultimately metastasize and a large number of patients present as metastatic disease from the beginning. One of the important sites of metastasis is bone. Bone is a common site of metastases from solid tumors. In advanced cancer, bones are the third most common site of metastases following lung and liver. In most cases, bone metastasis is detected after diagnosis of primary. However, in 10 to 15 % cases bone metastases may be the presenting feature.

Of all cancer patients, about 50% develop metastases in their lifetime. Metastatic bone disease is most commonly seen with specific cancer types notably those with metastasis from the breast (70%), prostate (85%), lung (40%) and kidney (40%), thyroid carcinoma (20%) as well as multiple myeloma (MM) (95%). Bone metastases most frequently affect the axial skeleton and often cause skeletal complications known as skeletal related events (SREs): pathological fracture, radiotherapy (RT) to bone, surgery to bone, spinal cord compression (SCC) and hypercalcaemia, although the last may be of paraneoplastic origin and occur without bone metastases.

Typically, SREs are associated with loss of mobility and social functioning, reduced quality of life (QOL), increased health care expenditure and worse survival. Bone metastases are classified as osteolytic, osteoblastic or mixed variety.

Radiotherapy is the most effective treatment for bone metastases. External beam radiotherapy (EBRT) for bone metastasis is one of the most common uses of palliative radiation therapy. EBRT provides effective and time-efficient pain control with few side effects.

There are various fractionation regimens of radiotherapy used for the palliation of bone metastasis. Various studies conducted worldwide have shown single session radiotherapy to be equally effective as multifractionated radiotherapy in palliation of bone metastases. A prolonged fractionation schedule is restricted to those being considered for local control. Patients receiving surgery for spinal metastases can also be offered RT postoperatively, with evidence that EBRT or stereotactic body RT (SBRT) can improve local control and ambulation.

The present study has been designed to assess the pain control and symptomatic relief while using 8Gy single fractions versus 20Gy/5 fractions in the palliation of painful bone metastasis.

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MATERIALS AND METHODS

- **Study area:** Department of Radiation oncology, S.M.S, Medical college and hospital, Jaipur, Rajasthan.
- **Study period:-** Recruitment of patients was started after approval of institutional ethical committee from May 2019 to April 2020 and thereafter 2 months period further required for analysis of collected data.
- **Study universe:** Patients with secondaries bone from proven malignancy, attending Department of Radiation Oncology, S.M.S. Hospitals, Jaipur. All patients included in the study were previously untreated, histopathologically proven and registered at Department of Radiation Oncology.
- **Study type and design:** - A Hospital based quantitative prospective follow up study.
- **Sample size:** - Sample size was calculated 90 patients in each of two groups at alpha error 0.05 and power 80% assuring complete response rate in patients receiving 8 Gy single fraction versus 20Gy/5 fractions for painful bone metastasis. Assuming 10% attrition, sample size was enhanced up to 99 patients in each group.
- **Method of randomization:** Patients were randomized with chit box method with replacement.

Inclusion Criteria

- Patients of secondaries bone from proven malignancy.
 - Radiological evidence of bone metastases.
 - Age 18-70 years.
 - Patients willing to give written informed consent.
 - ECOG Performance score 0-3.
 - Patients having normal hematological parameters to receive radiotherapy:
1. Hemoglobin .9 gm%
 2. Absolute Neutrophil count > 1,500/uL.
 3. Platelet count >100,000/uL.
 4. Serum Creatinine level < 1.4mg/dl.
 5. Serum Bilirubin < 2 mg%.

Exclusion Criteria

- Patients who had previously received radiotherapy to the region concerned.
 - Any co-morbid conditions to which the patients symptoms could be attributed.
 - Pregnant and lactating mothers.
- Multiple myeloma.

Pretreatment Evaluation

1. Complete detailed history & general physical examination.
2. Local examination of the area concerned.
3. Systemic examination.
4. Hematological investigations: CBC, LFT, KFT
5. Screening for HIV/HBsAg
6. Biopsy from the primary tumor.
7. X-ray Chest (PA view).
8. CECT/MRI of the area of interest.
9. Bone scan/PET CT (optional).

Patients’ selection: A total of 180 bone metastasis patients fulfilling the eligibility criteria were selected. Patients were randomly assigned to treatment groups Group A-Single fraction 8Gy & Group B-Multifraction 20Gy/5Fr.

Positioning and technique: The patients were treated on a BHABHATRON-2 Telecobalt machine. Treatment for spinal metastasis was done in prone position. Radiation to the spinal bones was prescribed to the mid vertebral body with inclusion of vertebral body above and below the painful vertebral body level or levels. Treatment for long bone and pelvic bone metastases was done in supine position with at least a 2cms margin proximal and distal to the radiographically evident abnormality. The field placement was done based on clinical and radiological investigations. Treatment fields were planned to include adequate margins from the known skeletal manifestation.

Follow up

Patients were followed up for a total period of 6 months, that is, weekly for 1 month, after completion of radiotherapy and then for 3rd and 6th month. At each follow up patients were assessed for pain palliation using the Visual analog scale/NRS, analgesic requirement and functional outcome using the ECOG performance scale.

Statistical analysis

Data obtained was compiled on a MS Office Excel Sheet (v 2019, Microsoft Redmond Campus, Redmond, Washington, United States). Data was subjected to statistical analysis using Statistical package for social sciences (SPSS v 26.0, IBM). Descriptive statistics like frequencies and percentage for categorical data, Mean & SD for numerical data has been depicted. Qualitative data was presented as ratios and proportions. Comparison of quantitative data was done by ANOVA test after confirming the normality of the data. Chi square test was applied between qualitative variables to see the association. Chi square test for proportions was applied to compare the proportions between the groups. Point of statistical significance was set as P<0.05.

RESULTS

Following are the baseline characteristics in table 1.

Table 1 Patients baseline characteristics

	Single Fraction Group Patients n= 90 (%)	Multiple Fraction Group Patients n= 90 (%)
Age		
<50 years	18 (16.2%)	27 (24.3%)
>50 years	72 (83.8%)	63(75.7%)
Gender		
Male	63 (70%)	54 (60%)
Female	27 (30%)	36 (40%)
Performance status		
ECOG<2	67 (74.4%)	69 (76.7%)
ECOG>2	23 (25.6%)	21 (23.3%)
PRIMARY SITE OF TUMOUR		
Lung	44 (48.9%)	47 (52.2%)
Breast	23 (25.5%)	20 (22.2%)
Prostate	8 (8.9%)	7 (7.8%)
Others	15 (16.6%)	16 (17.8%)
SITE OF BONE METASTASIS		
Spine	27 (30%)	29 (32.2%)
Pelvis	15 (16.7%)	12 (13.3%)
Ribs	2 (2.2%)	1 (1.1%)
Axial skeleton	10 (11.1%)	16 (17.8%)
Siteof palliative radiotherapy		
Spine	34 (37.8%)	37 (41.1%)
Pelvis	21 (23.3%)	19 (21.1%)
Limbs	12 (13.4%)	15 (16.7%)
Others	23 (25.5%)	19 (21.1%)

There was male predominance in both groups. Seventy five percent patients had ECOG upto 2. Lung was the most common primary site comprising more than 50% of cases followed by breast and prostate. Spine was the most common site of metastasis followed by pelvis.

Table 2 Post Treatment Evaluation

	1 st week	2 nd week	3 rd week	4 th week	3 rd month	6 th month	P-value
Overall Pain Relief							
Study arm N=90 (%)	49 (54.4%)	68 (75.5%)	74 (82.2%)	74 (82.2%)	74 (82.2%)	72 (80%)	0.874
Control arm N=90 (%)	53 (60%)	71 (78.9%)	77 (85.5%)	77 (85.5%)	77 (85.5%)	75 (83.3%)	
Complete Pain Relief							
Study arm N=90 (%)	0	0	9 (10%)	21 (23.3%)	21 (23.3%)	0	0.833
Control arm N=90 (%)	0	0	5 (5.5%)	21 (23.3%)	23 (25.5%)	2 (2.2%)	
Performance Status							
Single fraction group N=90 (%)	0	5 (5.5%)	20 (22.2%)	67 (74.5%)	62 (68.9%)	20 (22.2%)	0.977
Multiple fraction group N=90 (%)	0	4 (4.4%)	23 (25.5%)	65 (72.2%)	63 (70%)	18 (20%)	
Decreased Analgesic Requirement							
Single fraction group N=90 (%)	0	12 (13.3%)	56 (62.2%)	78 (86.7%)	73 (81.1%)	42 (46.7%)	0.991
Multiple fraction group N=90 (%)	0	10 (11.1%)	59 (65.5%)	82 (91.1%)	75 (83.35)	43 (47.85)	

More than 80% patients got pain relief in both groups which was maintained upto 3months.23.3% of patients achieved complete pain relief in both groups at 4 weeks.

More than 70% patients had improved performance status in both groups at 4 weeks.

Decreased analgesic requirement maximum at 4 weeks in both groups.

Table 3 Re-irradiation

Groups	SF Group (N= 90) (%)	MF Group (N= 90) (%)	P value
Patients underwent re-irradiation	24(26.7%)	7(7.8%)	0.002

More patients underwent re irradiation in single fraction group compared to other group which was statistically significant.

DISCUSSION

Metastatic bone disease is a common problem encountered in oncology practice. Bone is a common site of metastases from solid tumours. In advanced cancer, bones are the third most common site of metastases following lung and liver. Of all cancer patients, about 50% develop metastases in their lifetime. The common primary sites causing bone metastases are lung, breast and prostate. However, in 10 to 15 % cases, bone metastases may be the presenting feature. Of all cancer patients, about 50% develop metastases in their lifetime.

The present study was carried out on 180 histopathologically proven patients of malignancy with bone metastases from any primary site attending the Department of Radiotherapy, S.M.S. Medical College & Hospitals, Jaipur for their treatment by radiation therapy. These patients were randomly divided into single fraction and multifraction group. All patients in SF group received palliative external radiation therapy 8Gy single fraction to the involved site. Patients in MF group received palliative external radiation therapy 20 Gy in 5 fractions for 1 week to the involved site.

In our study patient’s age ranged from 35 to 70 years (mean 58.6 & 60.5 years in SF and MF group respectively). A similar study conducted by Jillaet al. in India had similar age distribution of patients with a peak age of 40 to 70 years as seen in study.

In our study seventy percent of patients were males and the remaining 30% were females. There was male predominance in both group (70% & 65% in SF group and MF group respectively). Majumder et al. observed similar male predominance (82.7% of all patients in the study were males) as seen in our study. The Bone Trial Working Party Study Group (BTWPG) in a similar study also reported 52% patients to be males while the rest 48% were females. Arnalot et al. in a similar study found 57% patients to be males. There was thus, always a slight male predominance in patients with bone metastases.

In our study overall, ca lung was the most common primary site comprising more than 50% of all cases followed by breast and prostate (23.9% and 8.3% respectively). However, metastasis of unknown origin or others primary sites comprising 17.2% patients. According to literature, the common primary sites causing bone metastases are lung, breast and prostate. In a study conducted by Arnalot et al. the common sites of primary were lung, breast and prostate as seen in our study. Bayard et al. also reported prostate to be the most common site of primary followed by breast and lung.

In our study, most patients presented with multiple sites of bony metastases (40% and 35.5% in SF and MF group respectively). Spine was the most common site of metastases (30% and 32.2% respectively) followed by pelvis (16.6% and 13.3% respectively). In both group spines was the most common site of radiotherapy (37.8%, and 41.1 % in SF and MF group respectively) followed by pelvis (23.3% and 21.1% respectively). Arnalot et al. & Anter et al. had similar findings with spine being the most common site of radiotherapy followed by pelvis

In our study, more than 80% patients got pain relief at 3-weeks post radiotherapy (82.2% in SF groups & 85.5% in MF group respectively which was maintained up to 3rd month. There was a reduction in the percentage of patients with overall pain relief 3rd month onward follow up. There was no significant statistical difference in number of patients with overall pain relief in these groups at each follow up. Our results are consistent with that of a similar study conducted by Jilla et al. where overall pain relief for single fraction arm was 78% and for the multifraction arms were 80 each.

The complete pain relief was achieved by 23.3% patients in both groups at 4-weeks. However at 6th month follow up, pain recurred in all patients of SF group while in MF group, only 2 patients out of 90 were pain free. There was no significant statistical difference in number of patients with complete pain relief in both groups at any time during follow up. Our findings are consistent with a study conducted by Hartsell et al. where complete pain relief in the single fraction arm was 17% and that in the multifraction arm was 15%.

In SF group, 24 patients were irradiated again compared to 7 patients in MF group. However, this was not statistically significant. The Bone Trial Working Party Study Group (BTWPG) reported retreatment in 23% patients of the single fraction arm and 10% in the multifraction arms. Hartsell et al.

reported retreatment in 18% patients in the single fraction group compared to 9% in the multifraction group.

CONCLUSION

We have observed that there was no significant statistical difference in outcomes as overall or complete pain relief, decreased analgesic requirement, and improved performance status in single (8Gy/1Fr) versus multifraction (20Gy/5Fr) group. However, we noted a higher incidence of retreatment in the single fraction arm compared to the multifraction arms.

Radiotherapy requires daily hospital attendance at a Radiotherapy center. This may be at some distance from the patient's home. Thus, a protracted course of radiotherapy may cause considerable problems for patients and their attendance, especially those with poor performance status and limited life expectancy. It also increases the workload of the treatment center. Hence, our study concludes that 8 Gy single fraction is as effective as multifraction radiotherapy for the palliation of painful bone metastases.

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