

## STUDY OF EFFICACY OF HYPOFRACTIONATED RADIOTHERAPY 8 GRAY IN SINGLE FRACTION IN PALLIATION OF PAIN SECONDARY TO BONE METASTASIS

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### ABSTRACT

**Objectives:** To determine the efficacy of hypo-fractionated radiotherapy 8 Gray in 1 fraction for palliation of pain secondary to bone metastasis.

**Study Design:** Quasi-experimental study.

**Place and Duration of Study:** Oncology department, Combined Military Hospital, Rawalpindi, Sep 2012 to Nov 2013.

**Patients and Methods:** Forty three patients were included after permission from concerned authorities and Hospital Ethical Committee. OPD registration numbers, name, age, gender, Eastern Cooperative Oncology Group (ECOG) performance status (PS), diagnosis of primary malignancy along with histopathology and sites of skeletal metastasis were recorded. Radiotherapy 8 Gy in 1 fraction was administered using 6MV (mega voltage) Primus Linear Accelerator with 2-2.5 cm margin around the gross disease at the Oncology department, CMH Rawalpindi. Pain score was recorded using visual analogue scale on the day of administering radiotherapy (day 0) and thirty days (day 30) after radiotherapy to assess response to treatment.

**Results:** There was a statistically significant (<0.001) improvement in the scores of pain with treatment at day 30. Thirty four out of forty three patients (86%) showed an improvement in pain score.

**Conclusion:** Based on our results hypofractionated radiotherapy 8 Gy in 1fraction is an effective modality in the palliation of pain secondary to bone metastasis.

**Keywords:** Bone metastasis, Palliative, Radiotherapy.

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### INTRODUCTION

Bone is one of the most common sites of metastasis in solid tumors, especially when primary malignancy is found in breast, lung and prostate. More than 70% of patients with solid tumors develop painful bone metastases during the course of their disease in the spine, pelvis, and extremities<sup>1</sup>. Most common symptom in advanced cancer is pain which is experienced by up to 86% of the patients<sup>2</sup>. Around 30-40% of patients experiencing such pain is due to bone metastases<sup>3</sup>. A major cause of mortality and morbidity in men with prostate cancer is bone metastasis. The aim of treatment of patients with bone metastases is pain relief and prevention of skeletal related events. Localized external beam radiation is an effective modality of treatment when bone pain is limited to a single or a limited

number of sites. It provides pain relief in up to 80 to 90% of cases, with complete response obtained in 50 to 60% of patients<sup>4</sup>. Numerous external beam RT fractionation schedules have been reported in the literature including 30 Gy in 10 fractions, 20 Gy in five fractions and 8 Gy in a single fraction being practiced in United States, Canada and some European countries respectively. Multiple randomized clinical trials have compared various fractionated schedules with a single fraction RT. American Society of Radiation Oncology (ASTRO), recommend the use of 8 Gy in a single fraction as it has similar efficacy but is more convenient for the patient and is cost effective compared to other regimens. Eight Gy is a single fraction treatment which is less recourses intense for the radiotherapy departments<sup>5</sup>. In Pakistan very few studies have been conducted on shorter fractionation schedules. The resources are very limited with few centers equipped with modern Radiotherapy machines. Longer

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Received: 06 Dec 2017; revised received: 29 Jan 2018; accepted: 31 Jan 2018

fractionation protocols lead to increased work load on our linear accelerator machine and increases the number of patient visits leading to poor quality of life. The purpose of this study is to explore the efficacy of single fraction (in one visit) radiotherapy in decreasing pain secondary to bone metastasis so that better management protocols can be recommended locally.

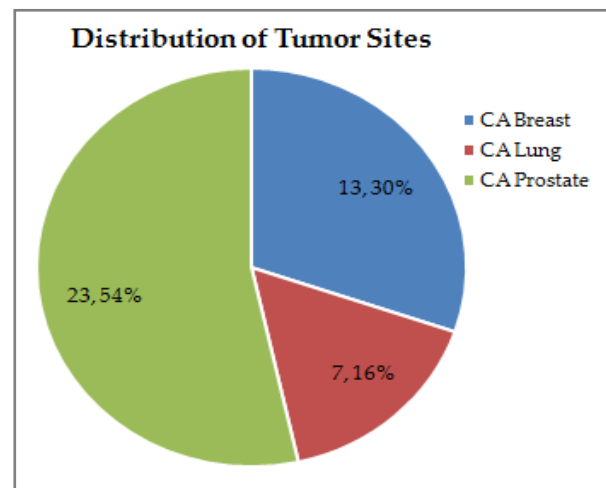
### PATIENTS AND METHODS

This quasi-experimental study was conducted in Oncology department, CMH Rawalpindi from September 2012 to November 2013. Sample size was calculated using WHO sample size calculator. Forty three patients using simple random sampling were selected from Oncology department, outpatient department (OPD) at CMH Rawalpindi with histologically confirmed carcinoma of lung, breast and prostate having age more than or equal to 18 years, including both genders, with Eastern Cooperative Oncology Group Performance Status (ECOG PS) 1 to 2 and radiological evidence of skeletal metastasis (bone scan and/or radiographs and/or CT Scan and/or MRI scans) causing pain which could be measured objectively by visual analogue scale were included in this study after informed written consent. Patients who had received previous radiotherapy to the same site, pain secondary to causes other than skeletal metastasis, impending pathological fractures and cases of spinal cord compression or impending collapse/fracture were excluded from the study. OPD registration numbers, name, age and gender, ECOG PS, diagnosis of primary malignancy along with histopathology and sites of skeletal metastasis were recorded. Radiotherapy 8 Gy in single fraction was administered using 6MV (mega voltage) Primus Linear Accelerator, with 2-2.5 cm margin around the gross disease at the Oncology department, CMH Rawalpindi. Pain score was recorded using visual analogue scale to assess response to pain. Pain score was recorded at day 0 and day 30 respectively to establish the efficacy of radiation protocol. Treatment was accepted to be effective if an improvement of at least 2 steps in pain score was observed on visual analogue scale.

Data analysis was done using SPSS version 19. For numerical variables mean and standard deviation were calculated while for categorical data frequency and percentages were calculated. Paired t-test was applied to compare the scores of pain before and after treatment.

### RESULTS

A total number of 43 patients of secondary bone metastasis were enrolled in the study from Oncology outpatient department. There were 28 (65%) males and 15 (35%) females in the study. The mean age of the patients included in our study was  $59.12 \pm 12.66$  years with minimum age



**Figure-1: Distribution of tumor sites.**

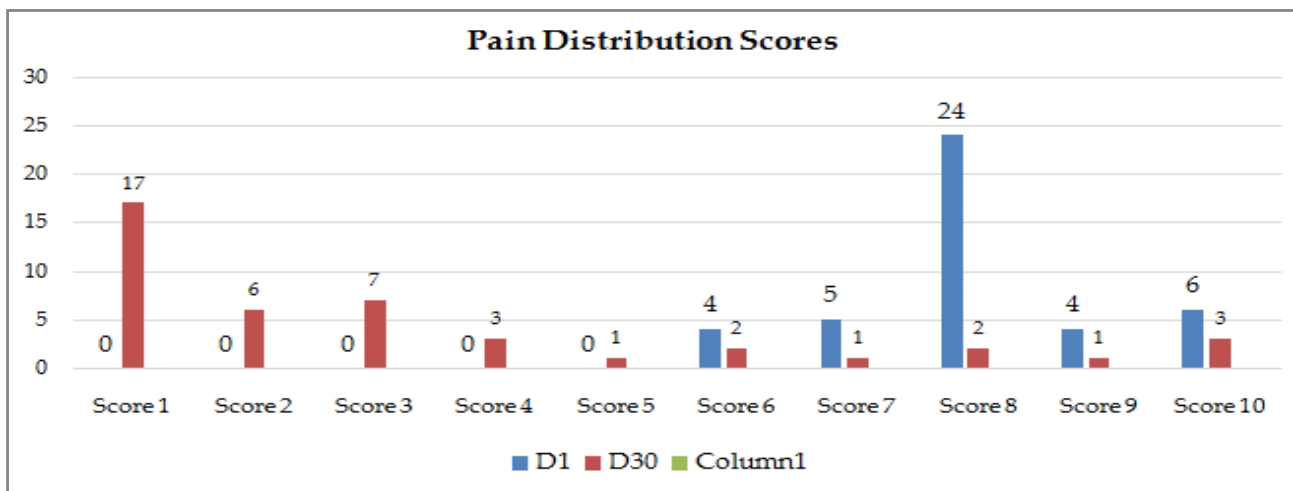
of 29 years and maximum age of 78 years. The mean weight was  $74.30 \pm 11.649$  kg with minimum of 54 kg and maximum of 98 kg. Distribution of tumor site is shown in fig-1. Mean pain score at D0 was  $8.07 \pm 1.07$  which improved to  $2.49 \pm 3.23$  at D30 with a *p*-value of  $<0.001$ . The distribution of grades of pain is shown in fig-2 which shows that maximum frequency 24 (55.8%) was of score 8, followed by score 10 which had a frequency of 6 (13.9%) at day 0 (before RT). At day 30 (after RT) maximum frequency 17 (39.5%) was of score 1, while the second most common score was 3 with a frequency of 7 (16.2%). Eighty six percent of patients showed an improvement in pain with the radiotherapy at day 30. The comparative analysis by using paired t-test, showed a statistically significant improvement

(*p*-value <0.001) in the score of pain with treatment.

**DISCUSSION**

Bone metastasis is a common presentation from a number of solid cancers, particularly of the breast, lung and prostate. The patients of bone metastasis are already in advanced stage of disease and most of them are inoperable. In patients who do not warrant surgery, the primary objective is to relieve pain, preserve function and maintain skeletal integrity to improve living standards. A wide variety of fractionated schedules are in practice around the world for palliation in bone metastasis ranging from 30 Gy

pain relief was 72% in the single fraction arm as compared to 69% in the multifractionation arm<sup>6</sup>. In the RTOG-9714 (Radiation Therapy Oncology Group) trial 949 patients with painful bone metastases from prostate or breast cancer were randomly assigned to 8 Gy in a single fraction or 30 Gy in 10 fractions<sup>7</sup>. No significant difference was found in the complete and partial response rate for relief of pain. It was noted that patients on hypofractionation were twice as likely to get retreatment. i.e. 18% versus 9%. Both the studies mentioned above were multicentric randomised trials which compared hypofractionation versus multifractionated treatments with long term



**Figure-2: Pain Distribution scores at Day 0 and Day 30.**

in 10 fractions, 20 Gy in 5 fractions to 8 Gy in a single fraction, but there is no consensus on a single fractionation regime. The efficacy of 8Gy single fraction has not been studied in out center previously. Therefore, keeping in view the high load on radiation services in our hospital, it was decided to carry out this study to determine the efficacy of single fraction radiotherapy for palliation in skeletal metastasis. Our study showed statistically significant benefit of hypofractionated palliative RT for relief of pain secondary to bone metastasis. Similar results were achieved in Dutch multicenter trial for pain palliation in which 1171 patients with pain due to bone metastases were randomly assigned to 8 Gy in a one fraction versus 24 Gray in 6 fractions. The overall

patient follow-ups. A British trial studied 765 patients with painful bone metastasis. At a median follow-up of 12 months, 8 Gy in single fraction, 20 Gy in 5 fractions, or 30 Gy in ten fractions. All the three groups has similar overall response rates i.e. 78 percent. No difference whatsoever was found in the rate of response which was one month on the average<sup>8</sup>. The above mentioned trials clearly depict that the efficacy of single fraction radiation treatment schedules. We have used simple planning system as compared to the three dimensional system widely used in protracted radiotherapy schedules. The results clearly indicate that this easy to administer and convenient regimen has resulted in effective pain palliation secondary to bone metastasis. The short

duration of treatment is convenient for patients with advanced disease and decreases the burden on the radiotherapy machines in terms of palliative cases, thus allowing more time for curative cases which require higher dose protracted radiation therapy. By this study it is expected that other oncologists will also consider shifting to hypofractionated regimes for palliation of pain secondary to bone metastasis rather than following the traditional lengthy radiotherapy schedule.

### CONCLUSION

Based on our results hypofractionated radiotherapy 8 Gy in 1fraction is an effective modality in the palliation of pain secondary to bone metastasis.

### CONFLICT OF INTEREST

This study has no conflict of interest to declare by any authors.

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