



Effectiveness of two Palliative Radiotherapy Regimens (20 Gy in five fractions versus 8 Gy in one fraction) for Thoracic Spine Bone metastases. Experience of Saudi Arabia

Alsaeed E^{1,2}, Tunio M³ , Salah T^{2,4} , Marie A^{3,5}, Abdelmalik NA^{2,6}, Deyab M⁷

¹ Faculty of Medicine, King Saud University, Saudi Arabia.

² Radiation Oncology Unit, King Khalid University Hospital, King Saud University Riyadh, Saudi Arabia.

³ Radiation Oncology Department, King Fahad Medical City, Riyadh, Saudi Arabia.

⁴ Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Egypt.

⁵ Clinical Oncology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

⁶ Radiotherapy and Nuclear Medicine Department, South Egypt Cancer institute, Assiut University, Assiut, Egypt.

⁷ Radiation Therapy Treatment Unit, Radiation Oncology, King Fahad Medical City, Riyadh, Saudi Arabia.

Received: 6 October 2021

Accepted: 12 October 2021

Authors Information:

Eyad Alsaeed

Faculty of Medicine, King Saud University, Saudi Arabia.

Radiation Oncology Unit, King Khalid University hospital, King Saud University, Riyadh, Saudi Arabia.

email: EALSAEED@YAHOO.CA

Mutahir Tunio

Radiation Oncology Department, King Fahad Medical City, Riyadh, Saudi Arabia

email: drmutahirtonio@hotmail.com

Tareq Salah

Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Egypt.

Radiation Oncology Unit, King Khalid university hospital, King Saud university Riyadh, Saudi Arabia.

email: TAREQSALAH41@YAHOO.COM
DRTAREQSALAH@AUN.EDU.EG

Amal Marie

Radiation Oncology Department, King Fahad Medical City, Riyadh, Saudi Arabia.

Clinical Oncology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

email: yomna1552001@yahoo.com

Noha Ali Abdelmalik

Radiotherapy and Nuclear Medicine Department, South Egypt Cancer institute, Assiut University, Assiut, Egypt.

Radiation Oncology Unit, King Khalid University Hospital, King Saud University Riyadh, Saudi Arabia

email: nohaabdelmalik@aun.edu.eg

Mohamed Deyab

Radiation Therapy Treatment Unit, Radiation Oncology, King Fahad Medical City, Riyadh, Saudi Arabia

email: mdeyab@kfmc.med.sa

Corresponding Author:

Tareq Salah

Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Egypt.

Radiation Oncology Unit, King Khalid university hospital, King Saud University Riyadh, Saudi Arabia.

email: TAREQSALAH41@YAHOO.COM
DRTAREQSALAH@AUN.EDU.EG

Abstract:

Background: In spite of wider use of 8 Gy in one fraction palliative radiotherapy regimen for bone metastases in the Western world, data is scanty in the Middle East. We aimed to compare a single dose of 8 Gy vs. 20 Gy in 5 fractions for thoracic spine metastases.

Materials and methods: Forty patients with metastatic breast, prostate and lung cancers were randomized to receive a single dose of 8 Gy (n =20) vs. 20 Gy in 5 fractions (n =20) for thoracic spine metastases. Relief of pain and intensity was assessed prospectively via a pain questionnaire prior to treatment and every 4 weeks thereafter, using a 4-point scale (none, mild, moderate, severe), along with need for types of analgesic drugs and doses taken.

Results: Complete pain relief was achieved in 9 patients (45%) treated with one fraction of 8 Gy and in 11 patients (55%) who received 20 Gy in 5 fractions (P=0.61). Similarly, no difference between the two treatment regimens according to duration of pain relief (medians of 9 and 9.5 months, respectively) P = 0.42. No difference in nausea and vomiting (N&V) was seen (5 patients in 20 Gy in 5 fractions vs. 7 patients in 8 Gy in one fraction). However, N&V was significantly prolonged in patients who received 8 Gy in one fractions (15 days vs. 7 days in 20 Gy in 5 fractions) P=0.03.

Conclusions: No difference in pain relief and duration was noticed between two palliative radiotherapy regimens (8 Gy in one fraction vs. 20 Gy in 5 fractions) for painful thoracic spine metastases, however, nausea and emesis was prolonged with single fraction of 8 Gy, which warrants further larger trials of 8 Gy in single fractions in painful thoracic spine metastases.

Key words: Thoracic Spine metastases. 8 Gy in one fraction, 20 Gy in 5 fractions, pain relief

Introduction:

Bone metastasis (BM) are serious sequelae of many types of malignancy, especially in breast, prostate and lung cancer who accounts for up to 70%. [1] Frequent involved site BM include spine and pelvic bones. [2] Moreover, spine metastases result into gradual decline in the quality of life (QoL), and eventually death due to skeletal and metastatic complications. Many radiation therapy regimens are in practice for palliating symptoms of spine metastasis; 30 Gy in 10 fractions over two weeks and 20 Gy in five over one week being the more commonly used regimens [3]. However, the optimal radiation dose, fractionation regimen and treatment time remains controversial. Currently, there is increasing interest in resource sparing single fraction of 8 Gy in one fraction for palliating painful spine metastasis [4, 5]. Many randomized trials have reported that single fraction of 8 Gy is equivalent to higher radiation doses (20 Gy in 5 fractions or 30 Gy in 10 fractions) [6, 7]. However, 8 Gy in one fraction for palliative radiotherapy for spine metastases has not yet been experienced prospectively in our population yet.

We aimed to determine the effectiveness of 8 Gy in one fraction radiotherapy for thoracic spine metastasis, its duration of response and toxicity profile as compared to higher dose fractionated radiotherapy (20 Gy in 5 fractions) in Saudi patient with metastatic breast, lung and prostate cancers.

Patients and Methods:

After taking formal approval from Institutional ethical committee, total of forty patients were accrued in this pilot study, and were randomized to receive either 20 Gy in 5 fractions or 8 Gy in one fraction. Inclusion criteria was; (a) histopathological confirmed diagnosis of breast, prostate and non- small cell lung cancers (NSCLC); (b) painful thoracic spine metastases evident on magnetic resonance imaging (MRI and computed tomography (CT)); (c) Life expectancy > 3 months and (d) ECOG <4. Patients with vertebral compression fracture or spinal cord compression or previous irradiation to the metastatic sites were excluded.

Radiation therapy was given with either single postero-anterior (PA) or two parallel-opposed field techniques. For single PA field, the dose was specified on the lesion depth, whereas for parallel opposed fields the dose was specified in the mid-plane, using 6 MV photon energy.

Assessment for pain relief was performed using a pain questionnaire, in which patients were asked to score their pain intensity using a 4-point scale (none, mild, moderate, severe), as well as analgesics use, types and the doses. This questionnaire was filled up at baseline, then every 4 weeks of follow ups. Complete response was defined as complete absence of pain and withdrawal of all types of analgesic drugs taken by the patient. Acute toxicity was graded according National Cancer Institute-Common Toxicity Criteria 1.1 (NCI-CTCv1.1) [8].

For all categorical and numerical data frequencies and percentages were calculated. Fischer' Exact test was used to compare the categorical data and T-Test for continuous data.

Results:

Forty patients with metastatic bone disease with spine metastases were treated. The most common sites for spine metastases was the T7-T10 (22 patients) and T2-T5 (18 patients). The most frequent primary tumor was breast cancer (47.5%), followed by lung (27.5%) and prostate cancers (25%). Both groups were well balanced in regard to age, gender, ECOG, primary tumor location, metastatic spine site location and treatment technique used, as shown in Table 1.

Table 1: Patients' characteristics

Variable	20 Gy in 5 fractions (n =20)	8 Gy in one fraction (n = 20)
Median age (years)	62 (55-70)	62 (54-68)
Sex		
Male	6 (30%)	6 (30%)
Female	14 (70%)	14 (70%)
ECOG		
2	14 (70%)	13 (65%)
3	6 (30%)	7 (35%)
Primary tumor		
Breast	10 (50%)	9 (45%)
Lung	5 (25%)	6 (30%)
Prostate	5 (25%)	5 (25%)
RT technique		
PA	2 (10%)	1 (5%)
AP/PA	18 (90%)	19 (95%)

ECOG = Eastern Cooperative Oncology Group, RT = radiation therapy, PA = Postero-anterior, AP = Antero-posterior

Regarding the response rates, complete remission of pain was achieved in 11 patients (55%) who received 20 Gy in 5 fractions, and in 9 patients (45%) who were treated with single fraction of 8 Gy (P = 0.61). Similarly, the median duration of pain relief was 9.5 months and 9 months in patients received 20 Gy in fractions and 8 Gy in one fraction respectively (P = 0.42). Two patients who received 20 Gy in 5 fractions and 3 patients who received 8 Gy in one fraction did not achieve any type of pain relief (P = 0.55). No difference in nausea and vomiting (N&V) was seen (5 patients in 20 Gy in 5 fractions vs. 7 patients in 8 Gy in one fraction) P = 0.61. Interestingly, median duration of nausea and emesis was 15 days in 8 Gy in one fraction as compared to 7 days in 20 Gy in 5 fractions (P = 0.03). Table 2

Table 2: Treatment Response rates and outcomes

Outcome	20 Gy in 5 fractions (n = 20)	8 Gy in one fraction (n = 20)	P value
Complete response	11 (55%)	9 (45%)	0.61
Marked response	7 (35%)	8 (40%)	0.52
No response	2 (10%)	3 (15%)	0.55
Median duration of pain relief	9.5 months	9 months	0.42
Median duration of post treatment nausea and emesis	7 days (5-10)	15 days (12-30)	0.03

Discussion:

Present study for metastatic thoracic spine metastasis did not determine any difference between treatment outcomes achieved by palliative radiotherapy with 8 Gy in one fraction and 20 Gy in 5 fractions. Similarly, the duration of pain relief was not significantly different in both radiotherapy regimens. These results were in agreement with other randomized studies comparing single fraction of 8 Gy with various fractionation schedules [9-11]. However, percentages of nausea and emesis were higher, which persisted significantly longer in 8 Gy in one fraction as compared to 20 Gy in five fractions, which in discordance with study by Bone Pain Trial Working Party [12].

The palliative effect of bone radiotherapy for pain relief is postulated from killing the radiosensitive pro-inflammatory cells (macrophages secreting various cytokines and osteoclasts responsible for bone destruction). Few pre-clinical studies have shown reduction of levels of osteoclast activity markers and more re-calcification after palliative radiotherapy as compared to non-irradiated ones [6, 13]. Similar, various studies have shown no treatment outcome benefit with utilization of use below 8 Gy in one fraction for pain relief [6, 14].

Limitations of present study were; (a) short sample size, and (b) short follow up period.

In conclusion, present pilot study demonstrates that 8 Gy in one fraction palliative radiotherapy is as effective as 20 Gy in 5 fractions in the treatment of painful thoracic spine metastases. However, increased percentages of nausea and emesis along with role of osteoclast markers in palliative radiotherapy warrants further investigation in larger trials.

References:

1. Chow E, Danjoux C, Wong R, et al. Palliation of bone metastases: a survey of patterns of practice among Canadian radiation oncologists. *Radiother Oncol.* 2000 Sep;56(3):305-14.

2. Roos DE. Continuing reluctance to use single fractions of radiotherapy for metastatic bone pain: an Australian and New Zealand practice survey and literature review. *Radiother Oncol.* 2000 Sep;56(3):315-22.
3. Wu JS, Wong RK, Lloyd NS, et al. Radiotherapy fractionation for the palliation of uncomplicated painful bone metastases—an evidence-based practice guideline. *BMC Cancer.* 2004 Oct 4;4:71.
4. Kirkbride P, Warde P, Panzarella A, et al. A randomised trial comparing the efficacy of single fraction radiation therapy plus ondansetron with fractionated radiation therapy in the palliation of skeletal metastases (Abstract). *Int J Radiat Oncol Biol Phys* 2000; 48 (suppl 3): 185.
5. Shuja M, Elghazaly AA, Iqbal A, et al. Efficacy of 8 Gy Single Fraction Palliative Radiation Therapy in Painful Bone Metastases: A Single Institution Experience. *Cureus.* 2018 Jan 8;10(1):e2036.
6. Koswig S, Budach V. Remineralization and pain relief in bone metastases after different radiotherapy fractions (10 times 3 Gy vs. 1 time 8 Gy). A prospective study. *Strahlenther Onkol.* 1999 Oct;175(10):500-8.
7. Steenland E, Leer JW, van Houwelingen H, et al. The effect of a single fraction compared to multiple fractions on painful bone metastases: a global analysis of the Dutch Bone Metastasis Study. *Radiother Oncol.* 1999 Aug;52(2):101-9.
8. National Cancer Institute. Common toxicity criteria. 1999. 26: p. 1084-1144.
9. Lievens Y, Kesteloot K, Rijnders A, et al. Differences in palliative radiotherapy for bone metastases within Western European countries. *Radiother Oncol.* 2000 Sep;56(3):297-303.
10. Nielsen OS, Bentzen SM, Sandberg E, et al. Randomized trial of single dose versus fractionated palliative radiotherapy of bone metastases. *Radiother Oncol.* 1998 Jun;47(3):233-40.
11. Wu JS, Wong R, Johnston M, et al. Meta-analysis of dose-fractionation radiotherapy trials for the palliation of painful bone metastases. *Int J Radiat Oncol Biol Phys.* 2003 Mar 1;55(3):594-605.
12. Yarnold JR. 8 Gy single fraction radiotherapy for the treatment of metastatic skeletal pain: randomised comparison with a multifraction schedule over 12 months of patient follow-up. On behalf of the Bone Pain Trial Working Party. *Radiother Oncol.* 1999 Aug;52(2):111-21.
13. Hoskin PJ, Stratford MR, Folkes LK, et al. Effect of local radiotherapy for bone pain on urinary markers of osteoclast activity. *Lancet.* 2000 Apr 22;355(9213):1428-9.
14. Jeremic B, Shibamoto Y, Acimovic L, et al. A randomized trial of three single-dose radiation therapy regimens in the treatment of metastatic bone pain. *Int J Radiat Oncol Biol Phys.* 1998 Aug 1;42(1):161-7.