

Retrospective analysis of the effectiveness of volumetric modulated arc therapy half-body irradiation in palliation of pain in patients with multiple bone metastases

ADAM KLUSKA^{1,2}, BARTŁOMIEJ TOMASIK³, ARKADIUSZ OSADNIK⁴,
NATALIA TRACZ², BERENIKA TRĄBSKA-KLUCH⁴, PAWEŁ MATYSIAK³,
JOLANTA ŁUNIEWSKA-BURY², JACEK FIJUTH^{1,4} and LESZEK GOTTFELD^{1,4}

¹Department of Radiotherapy, Medical University of Lodz; ²Department of Brachytherapy, Regional Cancer Center, Copernicus Memorial Hospital of Lodz, 93-509 Łódź; ³Department of Biostatistics and Translational Medicine, Medical University of Lodz, 92-215 Łódź; ⁴Department of Teleradiotherapy, Regional Cancer Center, Copernicus Memorial Hospital of Lodz, 93-509 Łódź, Poland

Received October 21, 2021; Accepted August 24, 2022

DOI: 10.3892/mco.2022.2586

Abstract. Bone metastases are the most common cause of cancer-related pain. It has been reported that radiotherapy is efficient in the palliation of pain caused by bone metastases. Half-body irradiation (HBI) is a method of palliative treatment in patients with multiple metastases to bones. The present study aimed to evaluate the efficiency of upper and lower HBI in reducing pain in patients with multiple bone metastases treated with volumetric modulated arc therapy (VMAT) HBI. A total of 22 patients received HBI based on the VMAT technique between July 2018 and July 2020. Treatment plans were subject to a dosimetric analysis. The absorbed doses ranged from 6 to 8 Gy in a single fraction. The patients rated pain on the 11-point (0-10) verbal numeric pain score (VNPS) before irradiation and after 1 month of follow-up. To assess the analgesic effect of HBI radiotherapy, data from 19 patients who attended the follow-up visit were analyzed. Before the treatment, the median VNPS of pain was 5 (IQR, 3-8); after the follow-up period, it was 3 (IQR, 1-4) ($P=0.003$). The median VNPS of the maximum pain within the last month before treatment was 8 (IQR, 7-10) and after irradiation it was 5 (IQR, 4-7) ($P<0.001$). The median VNPS of the average pain within the last month before the treatment was 5 (IQR, 4-7); after the treatment, it was 3 (IQR, 2-5) ($P=0.003$). In conclusion, conformal VMAT-intensity-modulated radiation therapy HBI is an effective method for reducing pain in patients with painful multiple bone metastases. Conformal techniques of

radiation allow for the reduction of doses to organs at risk thus potentially reducing the toxicity of treatment.

Introduction

Bone metastases occur in 60-84% of metastatic cancers and are the most common cause of cancer-related pain (1). Primary tumors that are responsible for the majority of cases are cancers of prostate, kidney, thyroid gland, lung and breast (2). Usually, bone metastases are associated with incurable diseases with significant morbidity and severe pain (3). In patients with bone metastases, radiotherapy has appeared to be efficient in palliation of pain (4). Local field radiotherapy is a safe option for relieving pain caused by localized bone metastases. All fractionation schemes: 30 Gy in 10 fractions, 20 Gy in 5 fraction and 8 Gy in single fraction are considered effective and widely accepted (5,6). In oligometastatic setting of the disease, defined as single or few (up to five) metastases (7), stereotactic body radiotherapy (SBRT) may be considered (5).

Multiple locations of painful bone metastases occur in many patients. Half-body irradiation (HBI) is an alternative to local field radiotherapy. It shortens treatment time and its pain palliation is effective (8-10). Historically, HBI was categorized into upper HBI (UHBI), lower HBI (LHBI) and mid-body irradiation (MBI) (11). For UHBI, the inferior margin of the radiation field corresponded to the bottom of the 4th lumbar vertebra. For LHBI, the superior margin corresponded to the inferior one for UHBI, while the inferior margin extended to mid-ankles and MBI that consisted of a field that reached from the top of the diaphragm to the bottom of the obturator foramina (11). Such treatment is advantageous as it allows to deal with multiple lesions simultaneously within a short period of time. On the other hand, wide field radiotherapy leads to frequent irradiation of healthy tissue and therefore may cause acute and long-term toxicity.

Nowadays, more conformal techniques, such as volumetric modulated arc therapy (VMAT) or tomotherapy with 3D planning, are available, which allows to irradiate smaller fields and

Correspondence to: Mr. Adam Kluska, Department of Radiotherapy, Medical University of Łódź, ul. Paderewskiego 4, 93-509 Łódź, Poland
E-mail: adamkluska88@gmail.com

Key words: pain, bone metastases, half-body irradiation, palliative radiotherapy

avoid unaffected bones. Thus, it helps to reduce doses in organs at risk and may decrease the incidence of acute toxicity (8). The safest and most effective single HBI doses are 6 Gy for UHBI and 8 Gy for both LHBI and MBI (12). Lately, fractionated schemes: 15 Gy/5 fractions/5 days, 8 Gy/2 fractions/1 day and 12 Gy/4 fractions/2 days have been reported to relieve pain in 91% of cases (13). A response to treatment is usually prompt and manifests itself with relieved pain, observed as early as within 48 h following the initiation of the treatment (11,12). In UHBI, the main organs at risk are lungs affected by post-radiation pneumonitis, especially when the dose absorbed to a lung was above 6 Gy (14). Irradiation of great volume of the digestive system leads to nausea, vomiting and diarrhea, being the most common acute complications of HBI (4). Hospitalization may be required for hydration and administration of antiemetics. Myelosuppression is another common HBI-induced toxicity. Patients undergoing HBI demonstrate more hematologic toxicity in comparison to those who undergo a local field treatment alone, with approximately 10% of patients presenting leukopenia, anemia or thrombocytopenia (15).

Although HBI radiotherapy utilizes modern techniques which aim at reducing doses to organs at risk, there are only limited data regarding the effectiveness and side-effects of such treatment. The objective of our study was to evaluate efficiency of upper and lower half body irradiation (UHBI, LHBI) in reduction of pain in patients with painful multiple bone metastases, treated with VMAT HBI.

Materials and methods

Study population. Our retrospective analysis covered the period from July 2018 to July 2020. The study group included 22 patients treated with HBI in Regional Cancer Center, Copernicus Memorial Hospital of Lodz (Łódź, Poland). All patients were referred to radiotherapy department with multiple painful bone metastases in cases where pain could not be controlled with analgesics drugs and were qualified to palliative radiotherapy. Patients were qualified to HBI treatment when pain was present in more than 5 localizations and standard palliative treatment could not be performed quickly and there was no further systemic therapy planned. In most cases of patients that were qualified to HBI, number of bone metastases was not given in imaging results, and were described as multiple or uncountable. All the patients have been admitted to hospital one day prior to the treatment. Before hospitalization, all the patients have undergone computed tomography (CT) scanning for the elective treatment. Upon admission, the patients rated pain in 11 points (0-10) according to the verbal numeric pain score (VNPS). The patients were also asked to rate the maximum and average pain experienced in the last month period. All patients provided written informed consent to undergo the treatment.

Treatment. Hospitalization lasted 3 days, and the treatment procedure was performed on the second day. According to the protocol used in our center, inclusion criteria for HBI were the following: diagnosed cancer with multiple, symptomatic bone metastases, ECOG PS 0-4, WBC $\geq 3,000/\mu\text{l}$, PLT $\geq 100,000/\mu\text{l}$, Hgb level above 8.5 g/dl and submission of a written informed consent to undergo the treatment. The patients were prehydrated intravenously. On the day of irradiation, the patients were administrated

steroids (dexamethasone 8 mg i.v.), antiemetics (metoclopramide 10 mg i.m.), and additionally, anti-diarrheal drugs (loperamide 2 mg p.o. every 8 h) when LHBI was performed. The treatment procedure was conducted in the supine position, with hands above the head when UHBI was planned.

Clinical target volume (CTV) was delineated by a radiation oncologist, comprising the whole bone tissue extending from lumbar vertebrae to cervical vertebrae, depending on the metastases localized most superiorly and most inferiorly.

CTV varied from C2-C7 to L1-L4 and was evaluated by the attending physician. The skull was not delineated if there were no metastases. In LHBI, borders extended from the mid-length of the femur to the most inferiorly located metastasis if there were no more metastases in lower extremities. With regards to UHBI, the border extended as far as L1-L4 vertebrae, depending on how much superiorly the metastasis was localized. The patients who were qualified for both UHBI and LHBI, received simultaneous planning and treatment with at least a two-week interval. Planning target volume (PTV) was created by adding a four-five mm margin to CTV. Organs at risk that were delineated included: the heart, lungs, kidneys, spinal cord and liver in UHBI and kidneys, rectum, spinal cord and bladder in LHBI. The dose prescribed to PTV was 6 Gy in one fraction in UHBI and 8 Gy in one fraction in LHBI. When both UHBI and LHBI were planned, the dose of LHBI changed and ranged from 6 to 8 Gy, depending on the decision of the attending physician.

All patients' plans were prepared with the use of the VMAT technique. Aimed dosimetry constraints were at least 90% of the prescribed dose covering the whole PTV and organs at risk with mean doses smaller than 2.5 Gy for kidneys, 3 Gy for the rectum, bladder and heart, 4 Gy for the liver and 4 Gy for lungs. Image verification with kV images was performed before each arc. Plans for all 22 patients were subject to a dosimetric analysis.

Follow-up. During a follow-up visit one month after finishing the treatment, the patients were asked once again to rate the pain on the day of the visit as well as the maximum and average pain experienced within the last month. Of 22 patients, 3 were lost to the follow-up, so the influence of HBI radiotherapy on severity of pain was assessed on the base of data obtained from 19 patients. Characteristics of the study group are presented in Table I. De-escalation of pain on the day of interview, manifesting itself with the value of 0-1 in the VNPS Scale was considered a complete response, whereas relieved pain, characterized with at least 2 points less than before the treatment, was regarded as a partial response.

Statistical analysis. All statistical analyses were performed using Statistica 13.1 software (Statsoft). The Wilcoxon signed-rank test was used to compare VNPS before and after the treatment in the whole group of patients. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Dosimetric analysis. Thirteen UHBI plans were prepared: 6 of patients were planned for UHBI alone and 7 were planned for both UHBI and LHBI for which the total number of both plans was created to assess doses in PTVs and OARs, before

Table I. Characteristics of the study group.

Characteristic	Value
Median age at time of treatment, years	68 (IQR, 61-75)
Sex	
Female	7 (37%)
Male	12 (63%)
Localization of primary tumor	
Prostate	10 (53%)
Breast	7 (37%)
Bladder	1 (5%)
Unknown primary	1 (5%)
Treatment performed	
UHBI	8 (42%)
LHBI	5 (26%)
UHBI + LHBI	6 (32%)
ECOG performance status	
0-1	7 (37%)
2-3	12 (63%)

LHBI, lower half-body irradiation; UHBI, upper half-body irradiation; ECOG, Eastern Cooperative Oncology Group.

implementing the treatment. All patients received the dose of 6 Gy prescribed to UHBI PTV volume. Plans consisted of 6 arcs in six patients, 5 arcs in two patients, 4 arcs in four patients and 3 arcs for one patient. The mean minimum absorbed dose that covered 90% of the PTV volume (D90) was 5.89 ± 0.33 Gy and the mean minimum absorbed dose that covered 95% of the PTV volume (D95) was 5.68 ± 0.21 Gy. The mean dose in PTV was 6.08 ± 0.09 Gy with the mean volume that absorbed 90% of the prescribed dose (5.4 Gy)-V90 of $98.30 \pm 2.20\%$. Lungs were the main organs at risk taken into account during an audit of UHBI treatment plans. The mean doses administered to the left and right lungs were 4.09 ± 0.47 Gy and 4.02 ± 0.46 Gy, respectively. Other OARs that were delineated and in which the mean dose was checked included: the spinal cord with the mean dose of 5.79 ± 0.94 Gy, the liver with the mean dose of 3.69 ± 0.72 Gy and the heart with the mean dose of 2.50 ± 0.70 Gy.

LHBI plans were prepared for 16 patients: 9 were qualified for LHBI alone and 7 were qualified for sequential treatment with UHBI and LHBI for which the total number of both plans was created. Eleven patients were prescribed a dose of 8 Gy, 3 patients-a dose of 6 Gy and 2 patients-a dose of 7 Gy prescribed to LHBI PTV. A dosimetric analysis in the homogeneous group of 11 plans with a prescribed dose of 8 Gy was conducted. The plans consisted of 6 arcs in two patients, 5 arcs in two patients, 4 arcs in two patients and 3 arcs in five patients. The mean D90 was 7.77 ± 0.16 Gy and D95 was 7.64 ± 0.25 Gy. The mean dose prescribed to PTV was 8.04 ± 0.09 Gy with the mean volume that absorbed 90% of the prescribed dose (7.2 Gy)-V90 of $99.51 \pm 0.61\%$. The rectum, spinal cord and urinary bladder were organs at risk, taken into account during an audit of LHBI treatment plans. The mean doses applied to the rectum, spinal cord and urinary bladder were respectively: 3.41 ± 0.95 , 4.51 ± 1.93 , and 3.80 ± 0.96 Gy.

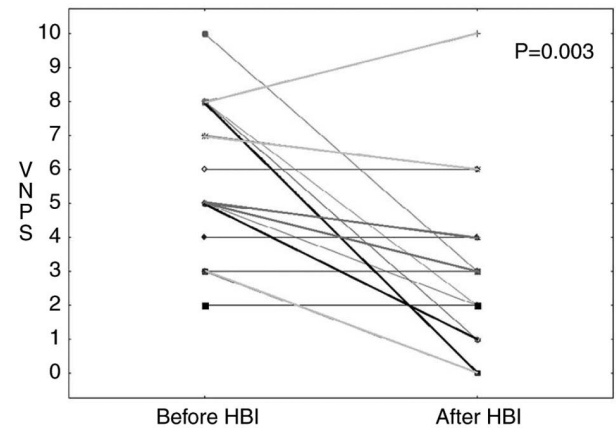


Figure 1. Change in VNPS at the day of the questionnaire for each patient. Before the treatment, the median VNPS score of pain was 5 (IQR 3-8); after the follow-up period, it was 3 (IQR 1-4) ($P=0.003$). VNPS, verbal numeric pain score; HBI, half-body irradiation.

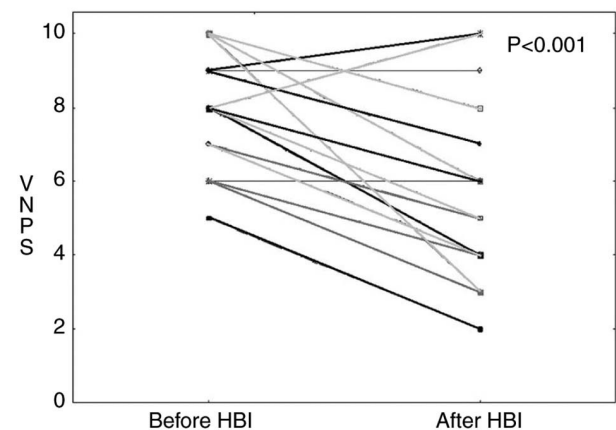


Figure 2. Change in VNPS of maximum pain during the last month for each patient. The median VNPS score of the maximum pain in the last month before the treatment was 8 (IQR 7-10) and after irradiation it was 5 (IQR 4-7) ($P<0.001$). VNPS, verbal numeric pain score; HBI, half-body irradiation.

Pain palliation. The median age of 19 patients included in the analysis was 68 (IQR 61-75) years. Primary tumors included prostate cancer diagnosed in 10 cases, breast cancer diagnosed in 7 cases, and bladder cancer detected in 1 case. A primary tumor of the unknown origin was diagnosed in 1 case. Eight patients were treated with LHBI, 5 patients-with UHBI and 6 patients-with both UHBI and LHBI (Table I).

The median pain, measured in the VNPS on the day prior to the treatment was 5 (IQR 3-8) and 3 (IQR 1-4) on the day of the follow-up visit ($P=0.003$) (Fig. 1). The median VNPS of the maximum pain in the last month before the treatment was 8 (IQR 7-10) and 5 (IQR 4-7) on the follow-up visit ($P<0.001$) (Fig. 2). The median VNPS of the average pain calculated in the last month before the treatment was 5 (IQR 4-7) and 3 (IQR 2-5) on the day of the follow-up visit ($P=0.003$) (Fig. 3). A short-term complete response was noted in 31.6% of patients (6 out of 19) and a partial response was observed in 52.4% of patients (10 out of 19).

The VNPS of pain on the day before the treatment in the UHBI group ($n=5$) was 5 (IQR 3-5) and 3 (IQR 2-3) on

Table II. Summary of the palliation effect in all subgroups.

VNPS	UHBI (n=5)	LHBI (n=8)	UHBI + LHBI (n=6)
VNPS of pain at the day of the questionnaire			
Before treatment	5 (IQR, 3-5)	5.5 (IQR, 5-7.5)	6 (IQR, 3-8)
At follow-up	3 (IQR, 2-3)	3.5 (IQR, 1-5)	2 (IQR, 1-4)
P-value	0.068	0.028	0.144
VNPS of maximum pain during the last month			
Before treatment	7 (IQR, 6-8)	9 (IQR, 7.5-10)	8 (IQR, 7-9)
At follow-up	6 (IQR, 4-6)	5.5 (IQR, 4.5-8.5)	4 (IQR, 3-7)
P-value	0.068	0.028	0.059
VNPS of average pain during the last month			
Before treatment	4 (IQR, 4-5)	5.5 (IQR, 5-7)	6 (IQR, 5-8)
At follow-up	4 (IQR, 4-5)	3.5 (IQR, 2.5-6)	2 (IQR, 2)
P-value	0.29	0.128	0.028

VNPS, verbal numeric pain score; LHBI, lower half-body irradiation; UHBI, upper half-body irradiation.

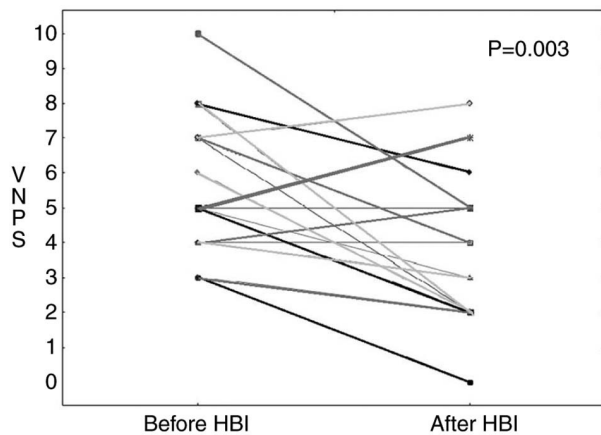


Figure 3. Change in VNPS of average pain during the last month for each patient. The median VNPS score of the average pain in the last month before the treatment was 5 (IQR 4-7); after the treatment, it was 3 (IQR 2-5) ($P=0.003$). VNPS, verbal numeric pain score; HBI, half-body irradiation.

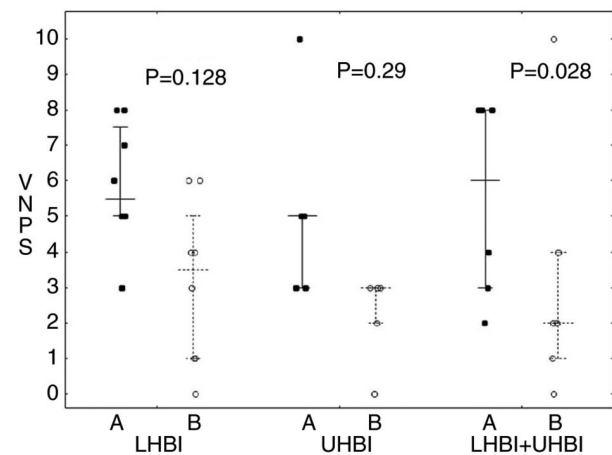


Figure 4. Summary of HBI impact on median average pain during the last month in LHBI, UHBI and LHBI + UHBI subgroups. A, before treatment; B, after treatment; HBI, half-body irradiation; LHBI, lower HBI; UHBI, upper HBI.

the day of the follow-up ($P=0.068$). The median VNPS of the maximum pain in the last month before the treatment in the UHBI group was 7 (IQR 6-8) and 6 (IQR 4-6) on the follow-up visit ($P=0.068$). The median VNPS of the average pain in the last month reported in the UHBI group before the treatment was 4 (IQR 4-5) and 4 (IQR 4-5) on the follow-up day ($P=0.29$). In the LHBI group ($n=8$), the VNPS of pain on the day before the treatment was 5.5 (IQR 5-7.5) and 3.5 (IQR 1-5) on the follow-up day ($P=0.028$). The maximum pain reported in this group in the last month before the treatment was 9 (IQR 7.5-10) and 5.5 (IQR 4.5-8.5) on the follow-up day ($P=0.028$). The average pain in the last month before the treatment was 5.5 (IQR 5-7) and 3.5 (IQR 2.5-6) on the follow-up procedure ($P=0.128$). In the group of patients with both UHBI and LHBI ($n=6$), the VNPS on the day before the treatment was 6 (IQR 3-8) and 2 (IQR 1-4) during the follow-up visit ($P=0.144$). According to the VNPS, the maximum pain in the last month prior to the treatment was 8 (IQR 7-9) and 4 (IQR 3-7) after

the treatment ($P=0.059$). The VNPS of the average pain during the last month before HBI in this group was 6 (IQR 5-8) and 2 (IQR 2) during the follow-up visit ($P=0.028$). Table II and Fig. 4 demonstrate the total value in all subgroups.

A retrospective analysis revealed grade 3 toxicity in one patient with breast cancer and metastases to bones, treated with UHBI. She needed to be admitted to hospital as well as administered transfusion of packed red blood cells. No other patient in this group demonstrated toxicity of grade 3 or higher.

Discussion

Our retrospective study shows that VMAT-based HBI is effective in palliation of pain, with relief in all measured scales of pain. Our findings are similar to results by another authors (8-10,12,13,16) are consistent with two prospective trials, where pain relief was reported in 76 and 73% of patients undergoing HBI (9,12). However, in both trials, radiotherapy

was applied in less conformal techniques. One retrospective analysis of 3D conformal radiotherapy with HBI, conducted in a large group (fractionation: 4 fractions of 3 Gy bind up to the total dose of 12 Gy) was presented, where pain reduction was observed in 76.3% of patients (16). To our knowledge, this is the first report of HBI delivered with highly conformal VMAT technique. In general, VMAT allows to deliver a prescribed dose to PTV, simultaneously protecting normal tissues outside PTV, as the high gradient of a dose at borders of PTV allows to reduce doses in OARs.

There is a number of studies on dose reduction in OARs due to the use of VMAT (17,18). Our dosimetric analysis showed that the VMAT technique, allows to reduce doses applied to lungs to 4 Gy, for 6 Gy prescribed to PTV. Therefore, potential escalation of dose to PTV can be safely achieved. The risk of radiation-induced pneumonitis, which tends to increase when a dose absorbed to a lung is higher than 6 Gy, is now lower (14). What is more, with the application of conformal techniques, doses to all OARs are reduced in comparison to those prescribed to PTV (8).

In our group, we did not report grade 1-2 toxicity due to lack of full retrospective data, which is a limitation of this study. It is the grade 1-2 toxicity that is considered a common adverse event of HBI (4,15). However, despite another limitation of our study that doses in ileum were not analyzed, a reduced radiation dose applied to the gastrointestinal system may potentially reduce the number of adverse events during the treatment. Results of our study confirmed that the VMAT technique has another benefit. It also ensures homogeneity of the dose delivered to PTV. This allows to treat all metastatic locations with the same effective dose. On the other hand, VMAT, being a highly conformal technique, needs image verification before each fraction, which may be problematic in highly symptomatic patients, treated with numerous arcs. Designing a treatment for our patients was not difficult; however, it was one-fraction treatment. Maintaining the same therapeutic position can be difficult for a greater number of fractions.

A small-sized group of patients and only one-month follow-up period are limitations of this analysis as well as only grade 3 toxicity reported. Due to these limitations, further relief of pain and grade 1-2 toxicity of this treatment remains unknown. Another limitation of this report is that exact analgesics doses and previous pharmacotherapy was analyzed and correlated with pain level and HBI effectiveness. Yet, VMAT HBI appeared to be clearly effective. Prospective trials followed by an analysis of toxicity are needed to clarify advantages of conformal techniques in HBI.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AK was involved in conception and design, acquisition and analysis of data, and was a major contributor in writing the manuscript. AK and LG confirm the authenticity of all the raw data BT analyzed and interpreted the data, and was involved in drafting the manuscript. AO, NT, BTK, JLB and PM performed treatment, acquired the data and critically revised the manuscript critically. JF and LG revised the manuscript critically, were involved in writing the manuscript, conception and design of the study, and gave final approval of the version to be published. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Consent was not required for this retrospective study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Mercadante S: Malignant bone pain: Pathophysiology and treatment. *Pain* 69: 1-18, 1997.
2. Tubiana-Hulin M: Incidence, prevalence and distribution of bone metastases. *Bone* 12 (Suppl 1): S9-S10, 1991.
3. Foley KM: The treatment of cancer pain. *N Engl J Med* 313: 84-95, 1985.
4. Lin A and Ray ME: Targeted and systemic radiotherapy in the treatment of bone metastasis. *Cancer Metastasis Rev* 25: 669-675, 2006.
5. De Felice F, Piccioli A, Musio D and Tombolini V: The role of radiation therapy in bone metastases management. *Oncotarget* 8: 25691-25699, 2017.
6. Wu JS, Wong RK, Lloyd NS, Johnston M, Bezjak A and Whelan T: Supportive Care Guidelines Group of Cancer Care Ontario: Radiotherapy fractionation for the palliation of uncomplicated painful bone metastases-an evidence-based practice guideline. *BMC Cancer* 4: 71, 2004.
7. Niibe Y and Hayakawa K: Oligometastases and oligo-recurrence: The new era of cancer therapy. *Jpn J Clin Oncol* 40: 107-111, 2010.
8. Furlan C, Trovo M, Drigo A, Capra E and Trovo MG: Half-body irradiation with tomotherapy for pain palliation in metastatic breast cancer. *J Pain Symptom Manage* 47: 174-180, 2014.
9. Berg RS, Yilmaz MK, Høyer M, Keldsen N, Nielsen OS and Ewertz M: Half body irradiation of patients with multiple bone metastases: A phase II trial. *Acta Oncol* 48: 556-561, 2009.
10. Pal S, Dutta S, Adhikary SS, Bhattacharya B, Ghosh B and Patra NB: Hemi body irradiation: An economical way of palliation of pain in bone metastasis in advanced cancer. *South Asian J Cancer* 3: 28-32, 2014.
11. Salazar OM, Rubin P, Hendrickson FR, Poulter C, Zagars G, Feldman MI, Asbell S and Doss L: Single-dose half-body irradiation for the palliation of multiple bone metastases from solid tumors: A preliminary report. *Int J Radiat Oncol Biol Phys* 7: 773-781, 1981.
12. Salazar OM, Rubin P, Hendrickson FR, Komaki R, Poulter C, Newall J, Asbell SO, Mohiuddin M and Van Ess J: Single-dose half-body irradiation for palliation of multiple bone metastases from solid tumors. *Final Radiation Therapy Oncology Group report. Cancer* 58: 29-36, 1986.

13. Salazar OM, Sandhu T, da Motta NW, Escutia MA, Lanzós-Gonzales E, Mouelle-Sone A, Moscol A, Zaharia M and Zaman S: Fractionated half-body irradiation (HBI) for the rapid palliation of widespread, symptomatic, metastatic bone disease: A randomized Phase III trial of the International Atomic Energy Agency (IAEA). *Int J Radiat Oncol Biol Phys* 50: 765-775, 2001.
14. Fowler JF and Travis EL: The radiation pneumonitis syndrome in half-body radiation therapy. *Int J Radiat Oncol Biol Phys* 4: 1111-1113, 1978.
15. Poulter CA, Cosmatos D, Rubin P, Urtasun R, Cooper JS, Kuske RR, Hornback N, Coughlin C, Weigensberg I and Rotman M: A report of RTOG 8206: A phase III study of whether the addition of single dose hemibody irradiation to standard fractionated local field irradiation is more effective than local field irradiation alone in the treatment of symptomatic osseous metastases. *Int J Radiat Oncol Biol Phys* 23: 207-214, 1992.
16. Macchia G, Ferro M, Cilla S, Buwenge M, Ianiro A, Boccardi M, Picardi V, Ferro M, Arena E, Zamagni A, *et al*: Efficacy and safety of 3D-conformal half body irradiation in patients with multiple bone metastases. *Clin Exp Metastasis* 35: 747-752, 2018.
17. Tamaki T, Hirai R, Igari M, Kumazaki Y, Noda SE, Suzuki Y and Kato S: Dosimetric comparison of three-dimensional conformal radiotherapy versus volumetric-arc radiotherapy in cervical cancer treatment: Applying the central-shielding principle to modern technology. *J Radiat Res* 59: 639-648, 2018.
18. Sudha SP, Seenisamy R and Bharadhwaj K: Comparison of dosimetric parameters of volumetric modulated arc therapy and three-dimensional conformal radiotherapy in postmastectomy patients with carcinoma breast. *J Cancer Res Ther* 14: 1005-1009, 2018.