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Lumbar Vertebral Marrow Metastasis: A Comparison of Three-Field and Four-Field Three-Dimensional Conformal Radiotherapy (3DCRT)

Wisam Nghaimesh Tuaib[1], Ruwaidah Abd Aalameer Mussttaf[2]

[1] Physiology and Medical Physics Department, College of Medicine, Al-Nahrain University, Baghdad, Iraq

[2] Oncology and radiotherapy center, Al-Nasiriyah Teaching Hospital, Dhi-Qar, Iraq

Abstract:

Background: Metastasis to the bone marrow in the vertebrae is a symptom of cancer that may be treated palliative. The purpose of this research was to evaluate the relative merits of the three-field and four-field approaches to 3D conformal radiation.

Materials and Methods: Forty patients with malignancies that had spread to their lumbar vertebral marrow received CT simulation as part of their radiation treatment plan. The obtained CT images were then used with the Monaco v5.3 Treatment Planning System (TPS) for delineation and treatment planning. The Elekta-made agility linear accelerator was used to administer the radiation. To facilitate this evaluation, two separate plan types were developed: the three-field approach and the four-field approach.

Results: The statistical analysis of lumber vertebral marrow metastasis tumors using the PTV 95%, PTV 105%, and PTV 2% parameters shows that the four-field technique is superior to the three-field technique. The four-field technique provides a greater mean dose to the tumor volume for PTV 95%, PTV 105%, and PTV 2%. These results suggest that the four-field technique may be a more effective treatment option for patients with vertebral marrow metastasis tumors. The research used the homogeneity index (HI), the conformity index, and the efficiency index to evaluate strategies for three and four fields. According to the findings, the Homogeneity Index (HI) and the Conformity Index (CI) were both considerably higher for the four-field method than for the three-field method (CI). The strategies of both methods were consistent with one another. The kidneys are more protected by the three-field approach, whereas the spinal cord is better shielded by the four-field method.

Conclusion: The four-field approach is more successful than the three-field strategy in reducing radiation dosage to the spinal cord. In contrast, the three-field strategy is more successful than the four-field technique for protecting the kidneys. The four-field planning approach achieves a more uniform dose distribution within the target volume for lumbar spinal bone metastases.

Key words: 3DCRT, Three-Field Techniques, Four-Field Technique, Bone Metastases

Address for correspondence:
Wisam Nghaimesh Tuaib
Physiology and Medical Physics Department, College of Medicine, Al-Nahrain University, Baghdad, Iraq
E-mail: wsamnghymysh@gmail.com

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INTRODUCTION

As cancer patients live longer, bone metastases become an increasingly pressing oncological concern [1]. When metastatic illness strikes, the spine is still a common target. At autopsy, 36% of 832 cancer patients were found to have the disease spread to their vertebrae. Painful bone metastases are often treated with external beam radiation treatment. In terms of pain relief, radiation treatment has a 50%-80% success rate [2]. The optimal dosage and fractionation required to produce long-term palliation have been the subject of several publications, including as randomized controlled trials, meta-analyses, and recommendations. Most patients choose for either a 30 Gy in 10 fractions or a 20 Gy in 5 fractions schedule. It seems that a single 8 Gy fraction is just as effective as extended treatment plans [3].

The standard method for treating metastases of the spine is tailored to each individual patient's lesions. Depending on the skin-target distance, lumbar fields may consist of a single posterior beam or AP-PA portals [4]. Reduced radiation toxicity to healthy tissue is a major benefit of three-dimensional conformal radiation treatment (3DCRT). It is difficult to develop a conformal plan that protects at-risk organs without compromising the Planning Target Volume (PTV) when the PTV is both big and irregular in shape [5-9].

There are many techniques are used to treat spinal cord tumors. The first technique contains three fields one is anterior and two other posterior fields are oblique. The second technique is the box technique which contains four fields each one opposite to the other [10, 11].

Spinal tumors are masses of abnormal cells that develop in or around the spinal column. Only 5%-10% of all primary Central Nervous System (CNS) malignancies are brain tumors, making them a very rare primary malignancy. These tumors are broadly classified based on their anatomical locations into two distinct groups [12]: initially, tumors outside the dural sac, where the boney structures meet the soft tissue. In the second section, we distinguish between extramedullary and intramedullary intradural cancers. The term "extramedullary" describes a location outside of the spinal cord, whereas

"intramedullary" describes a location inside the spinal cord. Intramedullary spinal cord tumors are the most prevalent kind.

With the use of contouring and planning algorithms for three distinct treatment modalities, Rhee planned to explore the possibility of completely automating cervical cancer radiation planning. The authors used an existing auto-contouring system to automate the planning process for 2D 4-field-box (4-field-box), 3D conformal radiotherapy (3D-CRT), and volumetric modulated arc treatment (VMAT). An internal field-in-field (FIF) automation tool was used to improve the quality of 4-field-box and 3D-CRT layouts. Almost 90% of 4-field-box plans, 98% of 3D-CRT plans, and 94% of VMAT plans were determined to fulfill clinical acceptability requirements without any further tweaking on the part of the researchers. However, radiation oncologists' preferences necessitated certain adjustments to the FIF design, and in some situations, plan renormalization was needed to meet their requirements. According to the authors' analysis, almost 90% of the clinically acceptable plans were created automatically across all three planning methods. For further assessment in low- and middle-income country radiotherapy centers with limited resources, a completely automated planning system has been included into the radiation planning assistant [13].

This study aimed to compare the following indices for the two techniques (three field and four field techniques) of 3D conformal radiotherapy such as Conformation Index (CI), Homogeneity Index (HI), and the dose reached to the spinal cord, and Kidneys organ dose.

MATERIALS AND METHODS

This is a prospective clinical study conducted at Al-Nasiriyah Teaching Hospital's Oncology and Radiotherapy Center in Dhi-Qar, Iraq. The research was done from December 2022 to May 2023. The Institute Review Board (IRB) of the College of Medicine at Al-Nahrain University approved approval for the study, since it was a required research component for earning a Master of Science in medical physics. The study focuses on forty instances utilizing CT simulations of lumbar vertebral bone marrow metastases patients. These individuals had been previously diagnosed by an oncologist and were advised to undergo radiation.

Three field technique

Initially, a unique treatment technique was designed utilizing the program Monaco v5.3. As a basis for this approach, CT simulation pictures were used. As indicated in Figure 2 and 3 the procedure required a thorough evaluation of the unique requirements and characteristics of each patient's situation. Subsequently, a dedicated interface inside the program displayed several treatment planning strategies. In this study's setting, the 3D approach was chosen the most appropriate. The selection of the 3D method was likely based on its capacity to capture the CT scans' detailed three-dimensional anatomical insights with precision. This accuracy enabled thorough treatment planning and accurate radiation dose delivery. Choosing the 3D approach was intended to improve treatment planning by utilizing CT imaging' substantial spatial data. This technology has the ability to more precisely tailor the treatment plan to the patient's anatomy, hence improving tumor targeting and minimizing radiation exposure to adjacent healthy tissues and organs.

In the first phase, the angle of the main radiation beam was set at zero degrees. This served as the standard for beam layouts that followed. Next, a replica of the first beam was created, with the angles adjusted. The second and third beams were given oblique angles of 140 and 210 degrees, respectively. The inclusion of oblique angles in the second and third beams was likely intended to maximize the treatment plan by allowing tumor targeting from a variety of orientations and angles. This method enhanced the dispersion of radiation doses, which may have enhanced the treatment's effectiveness. As the radiation beams interacted with the patient's anatomy from non-standard directions, the addition of oblique angles to the treatment plan increased its complexity and required additional considerations. This required thorough planning to guarantee appropriate dose distribution while reducing vital structural exposure to radiation. The beam with an angle of 140° was given collimator angles of 90°, while the beam with an angle of 210°was given collimator angles of 270°.

The dose distribution was then estimated using the optimization function to assess the extent to which the prescribed dosage reached both the Planned Target Volume (PTV), which comprised the tumor, and the nearby organs at risk. The purpose of this stage was to evaluate the geographical distribution of radiation doses within the treatment region and their possible influence on vital structures. The optimization tool inside the treatment planning system enables the radiation oncologist to refine and change the dose distribution depending on particular limitations and goals. This function allowed the treatment plan to be fine-tuned to obtain the appropriate dose coverage of the PTV while reducing radiation exposure to important organs.

Four field technique

Initially, the four-field approach used in this research was comparable to the aforementioned three-field technique.

However, there were differences in the amount of fields and angles used. Four beams were positioned at angles of 0, 180°, 90°, and 270°, respectively, for the four-field approach. Notably, each beam's collimator angle was adjusted at zero degrees. This arrangement guaranteed that radiation beams were supplied perpendicular to the treatment region, allowing for constant and uniform dosage distribution.

This diagram displayed the geographical distribution of radiation doses inside the treatment region. By assessing this distribution, physicians might determine the degree of dosage coverage to the target volume as well as the possible impacts on nearby essential structures. Compared to the three-field approach, the four-field technique delivered higher dosage compliance, improved target coverage, and more preservation of healthy tissues. It permitted more thorough and precise radiation administration, which might result in improved patient outcomes.

Evaluation parameters

Dosage homogeneity refers to the consistency of dose distribution across the target volume. In the context of the Planning Target Volume (PTV), a uniformly distributed dose would manifest as a distinct increase in the differential Dose-Volume Histogram (DVH) or a sharp decrease in the cumulative DVH curve at that specific absorbed dose level. For a well-constructed treatment plan, the differential DVH of the PTV should exhibit a Gaussian-like shape, demonstrating a concentrated distribution around the mean absorbed dose. Various radiation techniques have led to diverse interpretations of a homogeneity index.

The International Commission on Radiation Units and Measurements (ICRU) established an improved homogeneity index definition in 2010 to address the limits of prior indices, which were largely focused on minimum, maximum, and reference point doses. The proposed definition of the homogeneity index is as follows:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (1)$$

Where:

- $D_{2\%}$ represents the absorbed dose at the 2 percent isodose line.
- $D_{98\%}$ represents the absorbed dose at the 98 percent isodose line.
- $D_{50\%}$ represents the absorbed dose at the 50 percent isodose line.

The value "HI" signifies the Homogeneity Index. An HI value of 0 indicates nearly uniform distribution of absorbed dose.

Dose conformance describes the adequacy of the high-dose area conforming to the target volume, often the PTV. Conformity Index (CI) measures the degree to which the isodose volume of the treatment plan successfully covers the PTV:

$$CI = \frac{V_{PTV} \times V_{TV}}{TV^2_{PV}} \quad (2)$$

Where:

- CI represents the Conformity Index.
- V_{TV} represents the volume of the actual prescribed dose.
- V_{PTV} represents the volume of the PTV.
- TV_{PV} represents the volume of the PTV covered by the prescribed dose volume.

Optimal treatment conformity is achieved when CI equals 1.

In terms of statistical analysis, the collected data were examined using the widely used Statistical Packages for the Social Sciences - version 28. (SPSS-28). To thoroughly represent data distribution and variability, descriptive metrics such as percentages, means, standard deviations, and ranges were applied. The Student's T-test for the difference between three means was used to assess significant differences among means in quantitative data. This test helps determine the statistical significance of reported group differences. In addition, the Spearman's rank correlation test was used to investigate relationships between variables in the dataset. This non-parametric test evaluates the strength and direction of monotonic relationships between variables, revealing possible linkages. When the p-value for a particular test was equal to or less than 0.05, statistical significance was attributed. This threshold shows that observed results are unlikely to be the product of random chance, hence enhancing the validity and reliability of the statistical findings.

RESULTS

The statistical analysis of lumber vertebral marrow metastasis tumours in three and four field techniques was presented in Table 1. The 95% coverage of the tumour volume (PTV 95%) was calculated the mean dose in cGy, while the dose at 105% of the tumour volume (PTV 105%) represents the hot area. The PTV 2% represents the dose reached 2% of tumour volume, named the cold zone. The analysis shows that the four-field technique is significantly better than the three-field technique, where

the four-field technique distributes more maximum and mean dose to the tumour volume for PTV 95, PTV 105%, and PTV 2%, as shown in figures 1, 2, 3 respectively.

Tab. 1. The lumber vertebral marrow metastasis tumour coverage for the three and four fields' techniques

Parameters	Three Field Technique	Four Field Technique	p-value
PTV 95%			
Mean dose (cGy)	1998.6 ± 356.7	2033.3 ± 309.7	0.0043*
V105%			
Mean dose (cGy)	2249.05 ± 543.4	2305.5 ± 443.3	0.0148*
PTV 2%			
Mean dose (cGy)	40.9 ± 15.5	53.2 ± 13.8	0.0295*

*Significant difference at p-value ≤ 0.05.

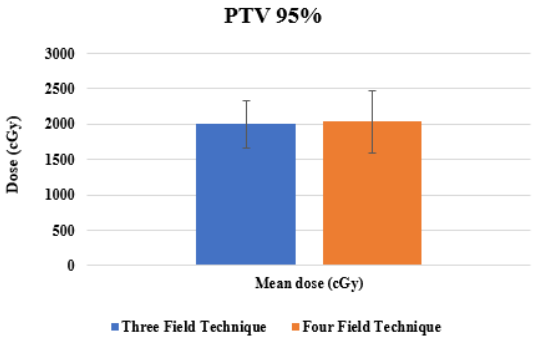

Fig. 1. Comparison of the dose coverage PTV 95% of the lumber vertebral marrow metastasis tumour between the three and four field's techniques

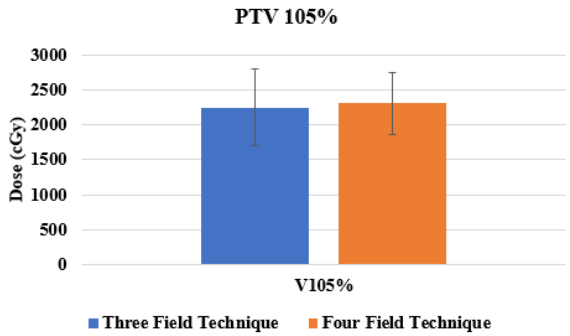

Fig. 2. Comparison of the hot are dose coverage PTV 105% of the lumber vertebral marrow metastasis tumour between the three and four field's techniques

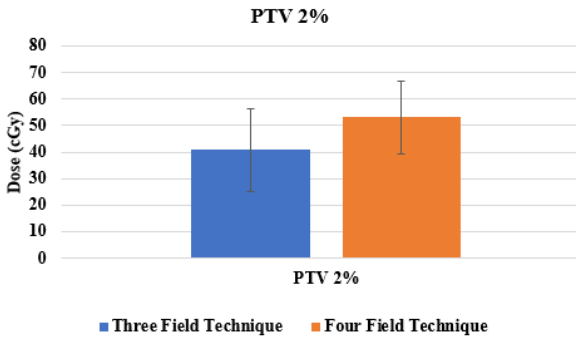

Fig. 3. Comparison of the cold area dose coverage PTV 2% of the lumber vertebral marrow metastasis tumour between the three and four fields' techniques

An index was measured for all the methods in three and four field's techniques to evaluate the efficiency of plans. These indexes are the Homogeneity Index (HI), and Conformity Index (CI). The resulting statistics of evaluation indexes are presented in Table 2. The analysis shows that the four field techniques had a significant difference better than the three field techniques for the Homogeneity Index (HI), as shown in Figure 4. No significant difference was found in the Conformity Index (CI). The plans were conformal for both techniques, as shown in Figure 5.

Tab. 2. The lumber vertebral bone marrow metastasis tumour evaluation indexes for the three and four fields' techniques

Parameters	Three Field Technique	Four Field Technique	*p*-value
HI	0.59 ± 0.02	0.46 ± 0.07	0.0065*
CI	1.14 ± 0.05	1.05 ± 0.06	0.0589

*Significant difference at p-value ≤ 0.05.

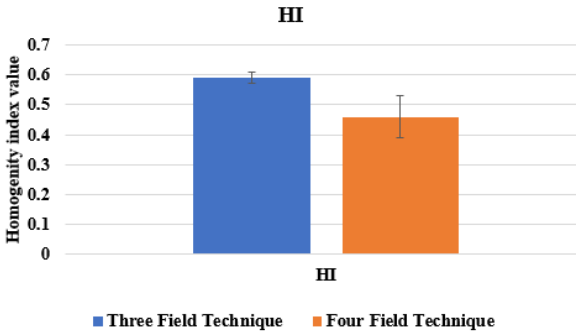

Fig. 4. Comparison of the Homogeneity Index (HI) for the lumber vertebral marrow metastasis tumour between the three and four fields' techniques

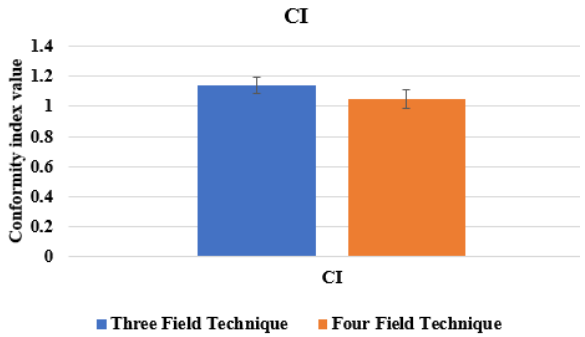

Fig. 5. Comparison of the conformity index (CI) for the lumber vertebral marrow metastasis tumour between the three and four fields' techniques

The results of Organs-At-Risks (OARs) in this study, such as the spinal cord and left and right kidneys were presented in Table 3. The results show that the right kidney volume is 133.554 cm^3 ± 16.44 cm^3, while the left is 157.38 cm^3 ± 14.07 cm^3. No significant difference was found between the volumes of kidneys. The four-field technique protects the spinal cord significantly better than the three fields. The results show that the four-field method has a significantly lower dose than the three-field technique for the mean dose of the right and left kidneys. No significant difference was established for the minimum and maximum doses for the left and right kidneys.

Tab. 3. The organs at risk (OARs) for patients with lumber vertebral marrow metastasis

OARs	Three Field Technique	Four Field Technique	p-value
Spinal cord			
Maximum dose (cGy)	34.97 ± 6.35	30.54 ± 9.43	0.0474 1*
Right Kidney			
Mean dose (cGy)	552.1 ± 29.57	1085.07 ± 448.6	<0.000 01*
Left Kidney			
Mean dose (cGy)	322.3 ± 43.9	1001.9 ± 53.3	<0.000 01*

* Significant difference at p-value ≤ 0.05.

DISCUSSION

Radiation therapy is considered as the primary therapeutic modality for spinal bone metastases, and the attainment of a uniform distribution of radiation dosage within the target volume is considered a critical aspect for ensuring favourable clinical outcomes [14].

The study examined the coverage of tumor volume at 95% (PTV 95%), the hot area at 105% of the tumor volume (PTV 105%), and the cold zone at 2% of the tumor volume (PTV 2%) of vertebral marrow metastasis tumors in the context of three and four field techniques. The results indicate that the four-field technique offers significantly better outcomes compared to the three-field technique. Specifically, the four-field technique distributes a greater mean dose to the tumor volume for PTV 95%, PTV 105%, and PTV 2%.

Pain from lumbar metastases is often treated with radiotherapy, and previous studies have focused on determining the optimal dose-fractionation correlations for this modality. However, there is a dearth of data on improved field designs for irradiating the lumbar spine, despite the fact that treatment planning technology has evolved. Although both designs may cover the PTV well, our results imply that the 3-D plan, which was designed for this very reason, results in a more uniform dosage distribution [15].

The use of external beam radiation therapy has been a longstanding approach for managing bone metastases, particularly those affecting the spine. For many years, radiation oncologists have been engaged in debates over the optimal dose-fractionation schedules for such lesions. These debates have been fuelled by not only retrospective studies, but also by a multitude of randomized controlled clinical trials. Interestingly, these trials have revealed that comparable levels of pain relief can be attained with both short and long courses of radiotherapy [16]. However, it is important to note that radiation treatment prescriptions must include more than just the delineation of dosage, beam energy, and total and fractional dose notation. Further research is necessary to determine the most effective and appropriate course of radiation therapy for bone metastases.

There is a lot written on the best ways to treat spinal metastases in terms of dose-fractionation, but much less about how these methods stack up against one another. Despite widespread use, cutting-edge technology such as stereotactic body irradiation may remain out of reach for the majority of the world's population. Therefore, it is important to conduct a formal assessment of more accessible technologies [1].

The findings of the analysis indicate that the four field techniques yielded significantly better results than the three field techniques for the Homogeneity Index (HI). This suggests that the four-field technique produces a more uniform dose distribution within the tumor volume and a steeper dose gradient outside the tumor volume compared to the three field technique. However, no significant difference was found in the Conformity Index (CI), indicating that both techniques were conformal, i.e., the treatment plans effectively conformed to the tumor volume.

Radiation oncologists are constantly concerned with the therapeutic index, which includes the treatment's

effectiveness and toxicity. Our findings indicate that the three-dimensional conformal approach is an effective palliative treatment for spinal metastases. However, different organs are at risk of radiation-related damage during lumbar spine treatment. Acute poisoning of the small intestine is of special concern since it may cause diarrhea and other gastrointestinal problems [17]. For instance, Baglan [18] showed that the incidence of grade 3 acute small bowel toxicity was close to 30% after irradiation of more than 15 Gy to at least 150 cm3 (as measured by the Common Toxicity Criteria).[19]. Similarly, Gunnlaugsson et al. found that the mean radiation dose at which diarrhea grade 2-3 occurred was 27 Gy [20].

The results of the study regarding the Organs-At-Risk (OARs) such as the spinal cord, left kidney, and right kidney. The findings show that the volume of the right kidney is 133.554 $cm^3 \pm 16.44$ cm^3, while the volume of the left kidney is 157.38 $cm^3 \pm 14.07$ cm^3, with no significant difference between the volumes of the two kidneys.

Furthermore, the results indicate that the four-field technique provided significantly better protection to the spinal cord compared to the three-field technique. The four-field technique resulted in a lower dose to the left and right kidneys compared to the three-field technique, as indicated by the mean dose results. However, no significant difference was observed between the two techniques in terms of the minimum and maximum doses for the left and right kidneys.

These findings suggest that the four-field technique may be a more appropriate treatment option in cases where the protection of the spinal cord and kidneys is crucial, particularly when compared to the three-field technique. Further studies are required to confirm these results and explore other factors that may influence the efficacy of treatment plans for OARs. Overall, the results of this study emphasize the importance of selecting the appropriate treatment technique to minimize the risk of OAR damage and maximize treatment efficacy.

Radiotherapy is the primary treatment for spinal bone metastasis, and achieving a homogenous dose distribution in the target volume is crucial for successful treatment outcomes.

According to the International Commission on Radiation Units and Measurements (ICRU) report, a homogenous dose within 95% to 107% of the prescribed dose is recommended for the target volume, with a variation of ± 10% from the prescribed dose widely used in clinical practice [21].

The results of Nehru similar to those seen in previous research [22]. Fundagul Andic of Turkey found that an AP/PA field reached the desired dosage ranges with a uniform dose distribution and with tolerable doses to the medulla spinalis, esophagus, and intestines. Particularly for those with lengthy expected life spans, insights gained by studying the correlation between radiation method and treatment result might be invaluable.

CONCLUSION

In conclusion, the four-field technique was superior in providing a greater mean dose to the tumor volume for PTV 95%, PTV 105%, and PTV 2%. In this study, which compared the effectiveness of the three-field and four-field techniques for treating vertebral marrow metastasis tumors. The homogeneity index were significantly better for the four-field technique, while there was no significant difference in the conformity index. The four-field technique was also found to be more effective in reducing radiation dose to the spinal cord, while the three-field technique was more effective in protecting the kidneys. This study suggests that the choice of technique should be tailored to the individual patient's needs and further studies are necessary to evaluate the long-term effects on organ function.

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