# Volumetric Modulated Arc Therapy as an Example of the Advanced Capability of Modern Radiotherapy

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**ABSTRACT:** **Background:** Family physicians and internal medicine specialists play an essential role in treating cancer patients. Modern technological advances in radiotherapy are not widely appreciated by primary care physicians. Bone metastases are a frequent complication of cancer. Palliative radiation therapy, as a component of modern advances in radiation treatments, should not subject normal bodily structures to excessive doses of irradiation. The sacrum is a common destination site for bone metastases, yet its concave shape along with its proximity to the rectum, intestines, and femoral heads creates treatment-planning challenges.

**Objectives:** To investigated whether the volumetric modulated arc therapy (VMAT) technique is preferable to more conventional radiation strategies.

**Methods:** The study comprised 22 patients with sacral metastases who were consecutively treated between 2013 and 2014. Two plans were generated for the comparison: three-dimensional (3D) and VMAT.

**Results:** The planning target volume (PTV) coverage of the sacrum was identical in VMAT and 3D planning. The median values for the rectal dose for 3D and VMAT were 11.34 ± 5.14 Gy and 7.7 ± 2.76 Gy, respectively. Distal sacral involvement (S4 and S5) was observed in only 2 of 22 cases, while the upper pole of the rectum ended at the level above S3 in just 3 cases.

**Conclusions:** Radiation therapy continues to be an integral component of the palliative armamentarium against painful metastases. Radiation oncologist, in conjunction with referral physicians, can tailor treatment plans to reflect the needs of a given patient.

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**KEY WORDS:** bone metastases, intensity modulated radiation therapy (IMRT), palliation, sacrum, volumetric modulated arc therapy (VMAT)

Family physicians and internal medicine specialists assume an essential role in treating cancer patients. Accordingly, they interact with all streams of oncological professionals including surgeons, medical oncologists, and radiation oncologists. Radiation oncologists, in particular, have witnessed many technological breakthroughs in cancer therapy during the past decade [1]. Yet, there is limited awareness of these technological improvements outside the discipline of radiation oncology.

Prior to these advances, treatment planning in radiotherapy was predicated on relatively primitive diagnostic tools and imaging studies, such as fluoroscopic visualization. Moreover, there was no ability to modify radiation portals as a function of tumor response in real time (adaptive treatment). Patients undergoing the ensuing treatment methods encountered uncertainty with unknown increases in side effects due to the potentially high radiation exposure of normal tissue [2].

Most of the optimized technologies that are currently available in modern radiotherapeutic facilities have been applied to cases treated with definitive intent. Yet, there is growing recognition that even patients treated with palliative intent are worthy of novel, sophisticated, safe treatments. In the current report, we discuss the use of a palliative treatment concept as a springboard to inform those with limited exposure to modern radiotherapy to these modern options.

Advances in the treatment of metastatic disease with the availability of new medications and supportive care prolong the life of patients with cancer and, in some respects, render the disease almost chronic in nature [3]. Modern radiotherapy has also made great strides not only in the definitive treatment of cancer but also in the palliation of symptoms and relief of pain and discomfort. Notwithstanding, bone metastases are a frequent and disturbing complication of cancer [4]. In an era of patient-centric medicine, symptoms associated with bone metastases must be addressed and discomfort and distress alleviated [5]. We believe that the relatively common phenomenon of bone metastases offers a window for viewing some of the progress made with sophisticated radiation treatment.

Metastatic deposition in the sacrum is relatively common. The incidence of pelvic bone involvement in the setting of metastatic breast cancer patients, for example, is 49% at any time during the course of follow-up [6]. The concave shape of the sacrum along with its close proximity to the rectum, intestines, and femoral heads led us to investigate whether the technique of volumetric modulated arc therapy (VMAT) is superior to three-dimensional (3D) treatment in the clinical setting.

We performed an extensive literature search of a direct comparison between VMAT and classical 3D planning for the treatment of pelvic bone metastases, but could not identify any

*The first and second authors contributed equally to this study such studies. However, it is understood that the general principle of the lowest possible dose exposure should be used for all techniques. Ostensibly, total palliative doses of 30 gray (Gy) in conventional fractionation would not be associated with rectal toxicity; however, based on recent reports [7] radiation oncologists must consider even low doses deposited in the rectum so that the patient who is referred for symptom alleviation does not develop iatrogenic toxicity.

## PATIENTS AND METHODS

Our study was comprised of 22 patients with sacral metastases, for whom comprehensive data were available, who were consecutively treated in 2013–2014. Permission for the analysis was obtained from the institutional review board (committee reference number: 0546-16 TLV). Patient characteristics are presented in Table 1. Two plans were generated for the comparison: 3D conformal and VMAT. Treatment planning proceeds with an understanding of several at-risk volume margins:

- Gross tumor volume (GTV): Gross palpable or visible/demonstrable extent and location of malignant growth
- Clinical target volume (CTV): includes the GTV and the subclinical microscopic extent of the disease (usually 5 to 10 mm around the GTV)
- Planning target volume (PTV): additional 5 to 10 mm extension around the CTV and arranged to compensate the uncertainness of the patient's positioning, internal organ movements, and set-up error

**Table 1.** Patient characteristics

| Number | Gender | Age, years | Diagnosis | Treatment plan | Bone involvement | End of rectum |
|---|---|---|---|---|---|---|
| 1 | Male | 54 | osteosarcoma | 3D | S1-3 | S2-3 |
| 2 | Female | 50 | NSCLC | 3D | S1-2 | S3-4 |
| 3 | Female | 58 | SQCC of cervix | 3D | S1-3 | S3-4 |
| 4 | Female | 56 | Ca of breast | 3D | S1-2 | S4 |
| 5 | Female | 37 | Ca of breast | 3D | S1-2+SIJ | S3 |
| 6 | Male | 70 | Myeloma | 3D | S1-3 + presacral mas | S4 |
| 7 | Female | 45 | STS | 3D | S1-2+ SIJ | S3 |
| 8 | Female | 70 | Ca of pancreas | 3D | S1-2 | S3-4 |
| 9 | Female | 67 | Ca of breast | 3D | S1 | S3-4 |
| 10 | Female | 83 | STS | 3D | S2-5+ presacral mass | S3 |
| 11 | Female | 69 | RCC | 3D | S2-3+ presacral mass | S3-4 |
| 12 | Female | 80 | NSCLC | 3D | S1-2 | S3 |
| 13 | Female | 60 | Ca of breast | 3D | S1-2+ SIJ | S3-4 |
| 14 | Male | 38 | Ca of breast | 3D | S1 | S3-4 |
| 15 | Female | 70 | STS | 3D | L5-S3 | S2 |
| 16 | Male | 62 | NSCLC | 3D | S1-2 | S2 |
| 17 | Male | 64 | NSCLC | 3D | S1-2+ SIJ | S3 |
| 18 | Female | 62 | NSCLC | 3D | S1-2 | S3 |
| 19 | Male | 49 | NPC | 3D | S1-2 | S3 |
| 20 | Female | 80 | Ca of breast | 3D | S5 | S4 |
| 21 | Male | 67 | RCC | 3D | S1-3 | S3-4 |
| 22 | Female | 46 | Ca of thyroid | 3D | S3 | S3-4 |

SQCC = squamous cell carcinoma, NSCLC = non-small cell lung cancer, Ca = carcinoma, S = sacrum, STS = soft tissue sarcoma, RCC = renal cell carcinoma, NPC = nasopharyngeal carcinoma, 3D = three-dimensional

Outcome data were retrospectively evaluated after permission for analysis was obtained from the institutional review board. All patients underwent standard simulation in the supine position on a CT Big Bore unit (Philips, Eindhoven, Netherlands). Lasers were used for localization. The sacrum was uniformly delineated from the L5-S1 intervertebral disk until the bottom of S5. The entire rectum as a whole organ, individual bowel loops within the irradiated fields, and heads and necks of the femurs were defined as organs at risk.

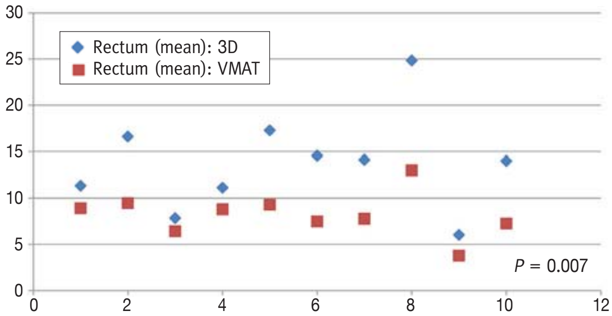
A dose of 30 Gy in 10 fractions was prescribed to the middle of the sacrum in the case of 3D planning and 5 mm around the GTV (visible bone edges of sacrum) when the VMAT technique was used. Typical 3D planning includes three field arrangements (e.g., two opposed lateral beams and one posterior field), which were best for conformity and minimizing exposure of the organs at risk. VMAT planning was devised to achieve 95% isodose coverage of the CTV, which typically shows minimal small bowel exposure. The results of the PTV coverage, mean rectal dose, mean dose, and the volume receiving 15 Gy (V15) to the intestines as well as the mean dose to the head/neck of the femurs were registered for the plans generated by 3D and VMAT techniques, respectively.

The statistical analysis included the *t*-test, assuming unequal variance (one-tail). Calculation of the *P* value for the comparative results was performed. Our hypothesis was that VMAT was superior to the 3D technique.

## RESULTS

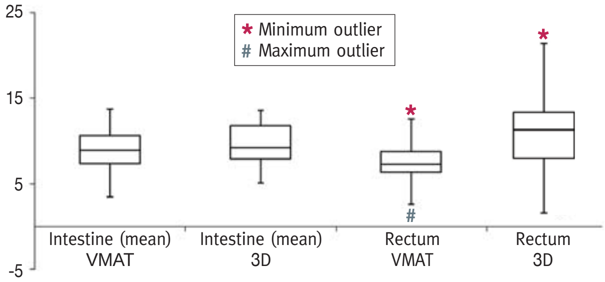
The PTV coverage was identical in VMAT and 3D planning. Mean values and V15 for the intestinal exposure showed no statistically significant difference between the 3D planning and VMAT: 9.28 ± 2.25 Gy and 47.0 ± 68.62 ml vs. 8.97 ± 2.18 Gy and 18.45 ± 69.56 ml, $P = 0.126$ and $P = 0.173$, respectively [Figure 1, Figure 2]. The mean values for the rectum 3D and VMAT were 11.34 ± 5.14 Gy and 7.7 ± 2.76 Gy, respectively, $P = 0.007$ [Figure 1]. The median 3D and VMAT exposure of the femoral head were 1.78 ± 2.94 Gy vs. 4.006 ± 2.1 Gy on the left, and 1.74 ± 0.9 Gy and 4.26 ± 1.8 Gy on the right side for the 3D

**Figure 1.** Comparative mean rectal dose for 3D and VMAT. The graph describes mean dose to the rectum in 3D and VMAT plans



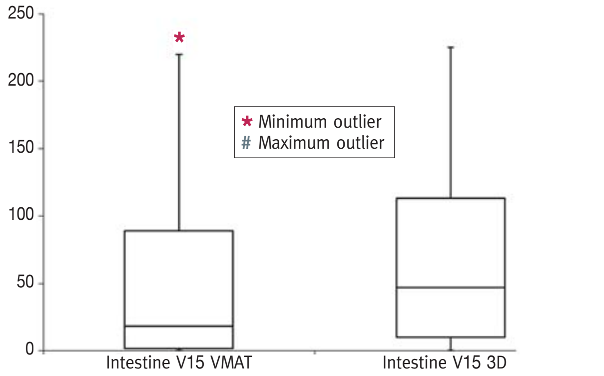

VMAT = volumetric modulated arc therapy, 3D = three-dimensional

**Figure 2. [A]** Box plot graph for the mean doses of the intestine and rectum (3D and VMAT). The graph describes the box plot for the small bowel and rectum for the 3D and VMAT plans. Boxes represent the median and interquartile range. Whiskers represent the spread of the data. Outliers are denoted by an asterisk



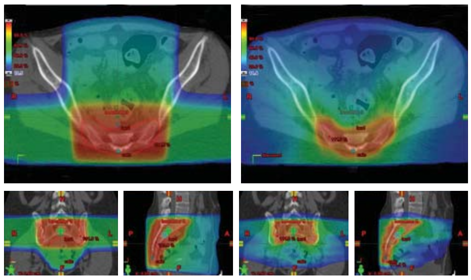

intestine mean ($P$ = 0.13), rectum mean ($P$ = 0.007)

**[B]** Box plot graph for the V15 of the intestine (3D and VMAT). The graph describes the box plot for the V15 of the small bowel for the 3D and VMAT plans. Boxes represent the median and interquartile range. Whiskers represent the spread of the data. Outliers are denoted by an asterisk




intestine ($P$ = 0.17)
VMAT = volumetric modulated arc therapy, 3D = three-dimensional

**Figure 3.** VMAT and 3D comparative plans of the scrum irradiation. The figure depicts comparative plans of the sacrum irradiation with the 3D and VMAT



VMAT = volumetric modulated arc therapy, 3D = three-dimensional

and VMAT, $P = 0.2$ and $P = 0.001$, respectively. Box plot analysis for the mean values and V15 of the small bowel and rectum are presented in Figures 2A and 2B. Figure 3 shows the preferred rectal sparing using the VMAT compared with the 3D plans.

Of interest, we observed a skewing of the anatomic involvement of the sacrum by metastatic disease. Specifically, distal involvement of the sacrum (i.e., S4 and S5) was present in only 2 of the 22 cases reviewed. Simultaneously, it was noted that the upper pole of the rectum only reached the level of S3 in three cases [Table 1].

## DISCUSSION

Primary care physicians are actively involved in treating cancer patients. The latest advances in radiotherapy are not well known outside the field of radiation oncology. Radiation therapy is a well-established and effective treatment for bone metastases [8]. Numerous publications reveal the indications and effectiveness of different doses and fractionation regimens of radiotherapy [9-11]. There is consensus among radiation oncologists that different schemes of radiation therapy are equivalent in term of palliative effect; however, single fractionation is associated with a higher level of recurrent pain and a greater need for re-treatment [9]. The cornerstone of modern radiation therapy is the delivery of the required dose to the target with a minimal normal tissue exposure. In this manner, the therapeutic ratio can be optimized. In treating the sacrum, the tolerance of the rectum to radiation injury is rate-limiting. It has been established that a rectal dose as low as 20 Gy, which was common in the older technique of the palliative sacral irradiation, is harmful in terms of the acute toxicity (diarrhea, cramps, and abdominal pain) [12].

The net effect of palliation was compromised by side effects of the excessive dose to normal structures. In the preceding decades, 3D conformal radiotherapy achieved this goal using computed tomography scans or magnetic resonance imaging (MRI)-based target delineation and physics calculations of creatively oriented fields with an array of energies.

Intensity Modulated Radiation Therapy (IMRT) implies variation of dose intensity to enable sculpting of the coverage of the target with simultaneous sparing of normal tissues. VMAT is the newest developmental step of the IMRT progression, which harnesses the dose delivery while the gantry moves around the patient in an arc-like fashion. The concave shape of the sacrum and the close proximity of the rectum make the IMRT and VMAT, at least theoretically, a preferred option of treatment.

Although much attention has been given to the optimization of stereotactic treatments for bone metastases, limited efforts have been devoted to improving the technical approach of conventional radiotherapy for this common problem [13,14]. Most modern radiotherapy departments retain high technology capabilities, such as IMRT and VMAT. These approaches are routinely used in treatment of primary and metastatic disease [15,16]. However, direct comparison of the VMAT vs. 3D planning of the treatment in different boney anatomical sites is scarce. Moreover, stereotactic body radiotherapy (SBRT) is frequently used and reported in the setting of bone metastases, despite the lack of theoretical rationale [17]. In American Society for Radiation Oncology (ASTRO) evidence-based guidelines for the treatment of bone metastases [18], the recommended treatment to vertebral bodies is conformal radiation that should be prescribed to the middle of the vertebral body. However, beyond that recommendation, there is no further technical specification offered. Specific attention was given to the spinal stereotactic radiosurgery (SRS) of the vertebral metastases with its ability to provide the highest dose with minimal exposure of the spinal cord and surrounding tissues. Simultaneously, the ASTRO guidelines caution against routine use of SBRT because that highly conformal treatment may exclude the subclinical disease [18] and increase the risk of tumor re-growth.

The results of our study show that the difference in intestinal exposure is not statistically significant using VMAT as compared to 3D planning. However, if the volume of the small bowel related to the volume of sacrum is greater than one, a benefit appears. The dose-volume histogram (DVH) for the median dose to the rectum was statistically preferred for the VMAT ($P = 0.001$). Even though the prescribed doses for the palliative effect were within a range of safety [19], the concept of the lowest possible dose to the surrounding normal tissue must be applied in decision making.

The femoral heads received lower doses of radiation in the 3D planning when compared to VMAT. The results were anticipated because the VMAT planning prioritized protection of the small intestine over the femoral heads. Prioritization of relative morbidities (e.g., injury to femoral head vs. injury to bowel) reflects the nuanced demands on the modern radiation oncologist in the clinical setting. For example, when dealing with a patients with underlying Crohn's disease, protection of the intestines may be emphasized. In contrast, when treating a patient with known osteoporosis, greater attention might be accorded to minimizing doses in the femurs.

Based on our findings, further prospective studies are crucial.

## CONCLUSION

Radiation therapy continues to be an integral component of the palliative armamentarium against painful metastases. Today's radiation oncologist, in conjunction with referral physicians, can tailor treatment plans to reflect the needs of a given patient.

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