

## Original Article

# The potential role of modern radiotherapy techniques in the treatment of malignant spinal cord compression: a dose planning study

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## Abstract

**Aim:** To investigate the doses given to the kidneys and the small intestines for three radiation therapy techniques [anterior–posterior (APPA) fields, three fields and volumetric-modulated arc therapy (VMAT)] for spinal cord compression (SCC) patients with metastatic disease in the lower thoracic or lumbar spine and to monitor the time spent by clinicians and dose planners.

**Introduction:** Radiation therapy is one of the main treatment modalities for SCC. Typical palliative radiation therapy techniques have used APPA fields or a three-field technique.

However, as delivery techniques have evolved dramatically over the past decades, VMAT has gained wide acceptance. VMAT allows for a dose reduction in the organs at risk. Such a dose reduction may result in less toxicity.

The use of the VMAT technique may require more time for contouring and planning compared with the APPA and three-field techniques. Any potential dosimetric benefit of VMAT must not be outweighed by large amounts of extra time spent by clinicians and dose planners.

**Materials and methods:** For 20 patients treated with radiation therapy for SCC at our hospital, we created a VMAT plan, and the more traditionally used APPA and three-field plans. The mean kidney doses and the volume of bowel, which received 20 Gy, were extracted for each plan. The correlations between parameters for three techniques were determined.

Furthermore, the time required for contouring targets for five patients; and the time required to plan five patients, was recorded.

**Results:** VMAT lead to the most conformal distributions: the high-dose areas were restricted to the target volume, whereas the healthy tissue, especially the bowel, received a lower dose. In contrast, the APPA plan lead to a larger volume of bowel being irradiated, whereas the three-field technique spared the bowel at the expense of a higher dose to the kidneys.

The average contouring time was 16 minutes, the average planning time was 38 minutes.

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**Conclusion:** Patients treated for SCC in the lower thoracic or lumbar region may benefit from VMAT treatment, as it reduces the dose to the bowel and kidneys compared with APPA or three-field treatments.

**Keywords:** conformal; IMRT; palliative; radiotherapy; spinal cord compression

## INTRODUCTION

Spinal compression lesions occur in about 5% of patients with metastatic cancer,<sup>1</sup> usually with breast, prostate, lung or kidney cancer as a primary diagnosis. Treatment in the form of surgery, radiation therapy or chemotherapy, aims at restoring (or maintaining) functional capacity as well as providing pain relief and improving quality of life. Radiation therapy is a main component of treatment for many of these patients. Fractionation schedules vary (from 8 Gy in a single fraction to up to 30 Gy in 10 fractions).<sup>1–3</sup> Preservation of motor function does not depend on fractionation; however, in-field recurrences occur more frequently in patients treated with a single fraction.<sup>1</sup>

Delivery techniques have evolved dramatically over the past decades, with intensity-modulated radiation therapy and image-guided radiation therapy gaining wide acceptance. Most of the reports indicate the benefit in curatively intended treatments; however, in palliative-intended treatments improved techniques also seem to be increasingly warranted. The potential of better local control and reduced toxicity have consistently justified the allocation of additional resources.<sup>4</sup>

Typical radiation therapy techniques in cancer patients with spinal cord compression (SCC) have used weighted anterior–posterior (APPA) fields (where the APPA field may have zero weight). An alternative technique consists of three fields: one posterior and two lateral fields, reducing the dose to anterior structures like the intestines.

At our institution, we introduced volumetric-modulated arc therapy (VMAT) in 2008<sup>5</sup> and today we offer this treatment modality to >50% of our cancer patients coupled with daily image guidance. VMAT allows for a far more

conformal dose delivery than what can be achieved with APPA or three-field techniques. With VMAT, the dose to organs at risk (e.g., intestines and kidneys) can be reduced. Since 2012, VMAT has been the standard delivery technique of radiation therapy for SCC at our institution.

SCC patients may develop acute toxicity in the kidneys and the small bowel following radiation therapy.<sup>6,7</sup> Dose limits for the small bowel are specified by QUANTEC.<sup>8</sup> The dose limit for the average kidney dose at our institution is 10 Gy.

In this study, we investigate how well the plans generated with APPA, three-field and VMAT techniques comply with these dose limits. Compliance could contribute to improved treatment outcomes for cancer patients with SCC in terms of less organ toxicity.

The use of the VMAT technique may require more time for contouring and planning compared with the APPA and three-field techniques. Any potential dosimetric benefit of VMAT must not be outweighed by large amounts of extra time spent by oncologists and dosimetrists.

Thus, the aim of the study was to investigate the doses given to the kidneys and the small intestines for three radiation therapy techniques (APPA fields, three fields and VMAT) for SCC in patients with metastatic disease in the lower thoracic or lumbar spine and to monitor the time spent by clinicians and dosimetrists.

## MATERIALS AND METHODS

### Patients

In total, 20 patients with a single to multiple spinal metastases in the lower thoracic or lumbar

region were selected from the cohort of patients treated at our clinic. Their primary diagnoses were lung (seven patients), breast (six patients), prostate (two patients), kidney (one patient), cholangiocarcinoma (one patient), oesophagus (one patient) cancer and unknown primary tumour (two patients). The patients were scanned on a Siemens Sensation Open CT scanner (Siemens Healthcare, Erlangen, Germany), with 2.5 mm slices in a supine position, using a knee cushion and foot support.

For each patient, the vertebrae requiring treatment were evaluated by an oncologist and radiologist. The gross tumour volume (GTV) was then delineated by the oncologist. A 5 mm planning target volume (PTV) margin was added to all GTVs to account for daily variations in patient positioning. Image guidance in the form of cone-beam computed tomography was performed daily in order to position the patients as accurately as possible on the treatment couch. All patients were treated with VMAT to a total dose of 30 Gy delivered in 10 fractions (5 fractions/week).

### Planning study

APPA as well as three-field plans were generated retrospectively for this analysis. The bowel and kidneys were also contoured retrospectively. All contouring and planning was performed in Eclipse (Varian Medical Systems, Palo Alto, CA, USA).

#### *APPA plans*

APPA plans were retrospectively generated following our former clinical guidelines. According to these, the GTV contours were not used in the APPA planning, but the field edges were positioned such that the treatment field included the processus spinosi laterally; and one additional vertebrae cranially and caudally (see Figure 1).

The beam energy (6 or 18 MV) was chosen in order to provide the best coverage of the vertebrae. The fields were weighted to ensure that the maximum dose was <114% of the total prescribed dose and the vertebrae requiring treatment were covered by the 95% isodose contour. In the planning, the anterior fields were given as low a weight as possible in order to

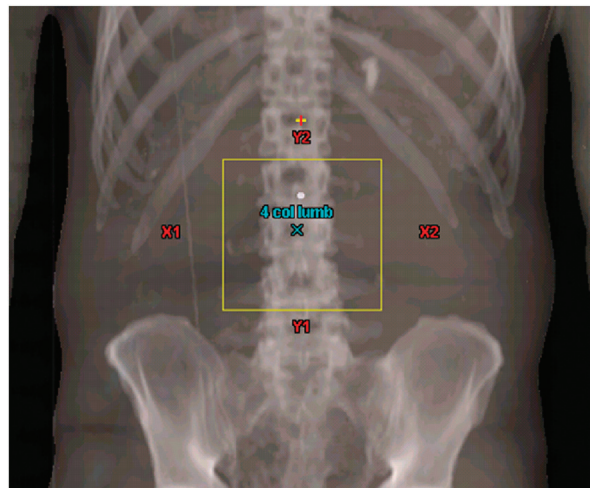


Figure 1. A beam's eye view of a posterior field in a typical anterior–posterior treatment.

comply with the hot spot dose limit to avoid unnecessary exposure of the bowels.

#### *Three-field plans*

For the three-field plan, two lateral fields and one posterior field were used. Multileaf collimators (MLCs) were positioned with a 7 mm distance to the GTV at the isocentre. The beam energy was chosen to provide the best coverage of the PTV. MLCs defined the field with a 7 mm margin to the PTV edge. The treatment fields were weighted such that the maximum dose was <114% and the PTV was covered at the 95% isodose line.

#### *VMAT plans*

The VMAT plans we evaluated were those used for treatment of patients at our clinic and 6 MV was used for all plans. For most plans, only one arc was required; however, when the PTV could not be adequately covered by the 95% isodose in these plans, two arcs were used. In the plan optimisation, constraints were used to ensure adequate coverage of the PTV and to reduce the dose to a ring structure defined around the PTV.

#### *Comparison of plans*

All plans were calculated using an anisotropic analytical algorithm (Eclipse v. 11.0.31) with a calculation grid of 2.5 mm.

For each plan, the following parameters were extracted: the mean dose to the left and right kidney were extracted. Our institutional dose limit to the kidneys is that the mean kidney dose should be <10 Gy whenever possible.

The QUANTEC<sup>8</sup> recommendation is that for a 3–5 fraction treatment, a maximum 15 Gy should be delivered to 120 cc. Using an  $\alpha/\beta$  ratio of 8,<sup>9</sup> and comparing with a 4-fraction treatment, this corresponds to a dose limit of 20 Gy when delivered in 10 fractions.

For each plan, we determined whether the mean kidney dose was <10 Gy, and whether a volume of the small intestine >120 cc received more than 20 Gy.

The two-tailed *p* value for correlations between parameters for three techniques was determined (ref <http://vassarstats.net/>) for correlated datasets.

**Time required for contouring and planning**

In a separate investigation, the time spent by the oncologist consultant contouring the GTV in five SCC patients, and the time spent by a dose planner creating VMAT plans for five patients, were recorded (Figure 2).

**RESULTS**

The mean doses to the kidneys, and the volume of bowel which received at least 20 Gy, are shown in

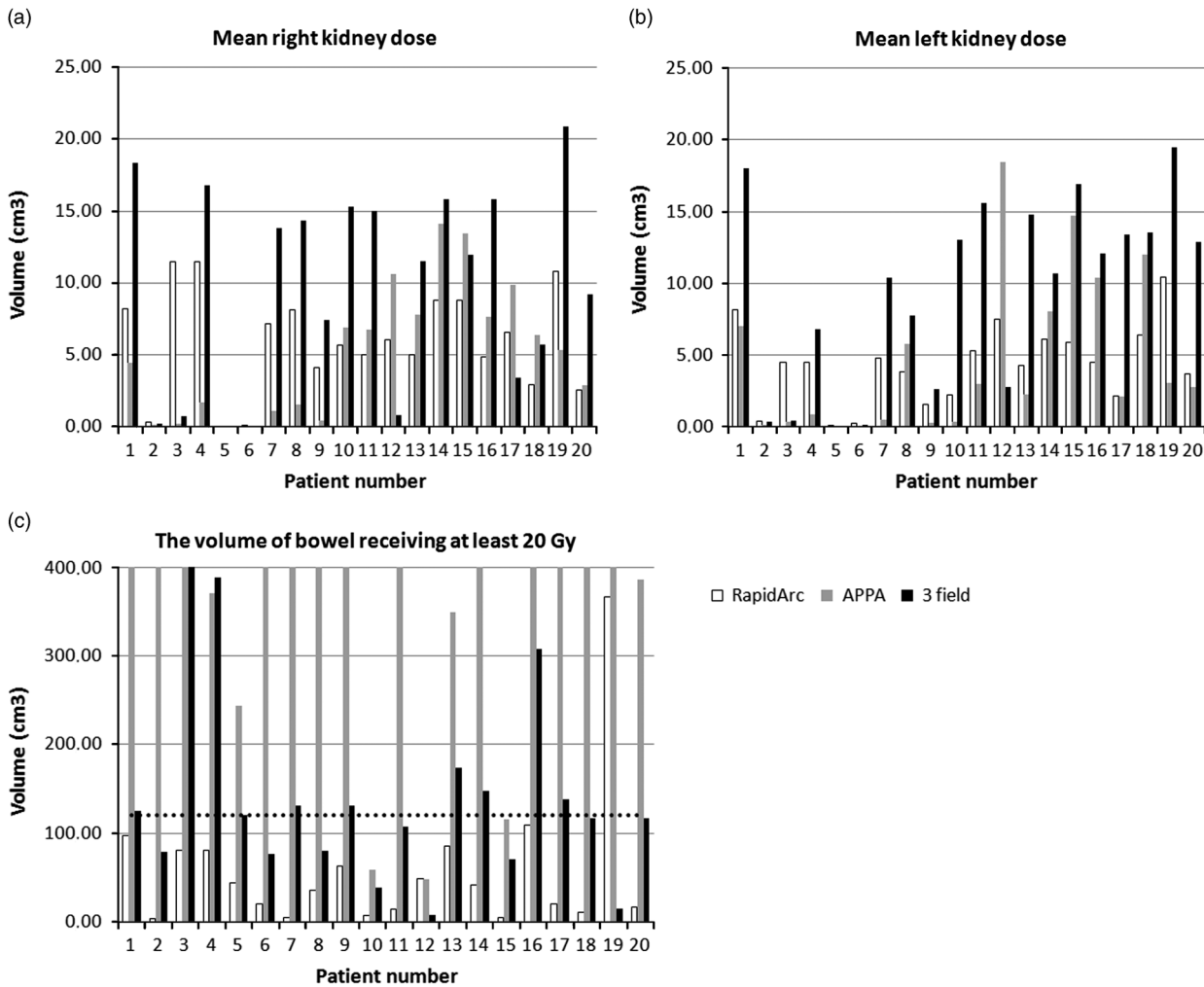


Figure 2. Mean left (a) and right (b) kidney dose, and the volume of bowler receiving  $\geq 20$  Gy (c), for the anterior–posterior (APPA), the three-field and the volumetric-modulated arc therapy techniques.

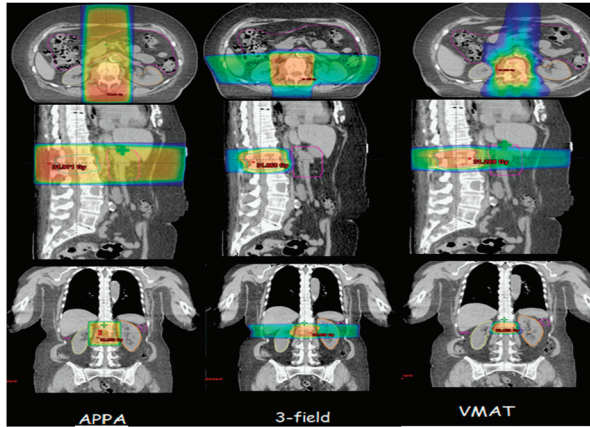


Figure 3. Dose ‘colour wash’ overlay for volumetric-modulated arc therapy (VMAT), anterior–posterior (APPA) and three-field plans for one of the 20 patients. Notes: The minimum dose shown is 33%, the maximum 110% of the prescribed dose. The planning target volume is contoured in light blue, the bowel in purple and the kidneys in yellow and orange.

Figure 2. An example of the resulting plans are presented in Figure 3. VMAT lead to the most conformal distributions: the high-dose areas (represented as the red overlay) were restricted to the target volume, whereas the healthy tissue, especially the bowel, received a lower dose (green–blue overlay). In contrast, the APPA plan lead to a larger volume of bowel being irradiation, whereas the three-field technique spared the bowel at the expense of a higher dose to the kidneys.

At least one of the kidneys received >10 Gy on average for four patients (APPA technique), 15 patients (three-field technique) and one patient (VMAT technique).

In the small bowel, >120 cm<sup>3</sup> received 20 Gy for 18 patients (APPA technique), nine patients (three-field technique) and one patient (VMAT technique).

The mean kidney doses were significantly higher with the three-field techniques than the other techniques ( $p = 0.0002–0.008$ ); however, there is no significant difference between the APPA and VMAT techniques ( $p = 0.138–0.775$ ).

D<sub>20</sub> Gy<sub>bowel</sub> was significantly lower with VMAT than with each of the other two techniques ( $p < 0.0001$  and  $0.017$ ), and

significantly lower with the three-field technique than APPA ( $p < 0.001$ ), respectively.

The time spent contouring and planning is shown in Table 1. The average contouring time was 16 minutes, the average planning time was 38 minutes.

## DISCUSSION

Patients with malignant SCC have limited life expectancies and are in the palliative care phase of their diseases. Metastatic lung cancer has a mean survival time of 6 months. The mean survival after metastasis of breast, renal or prostate carcinoma is longer, averaging approximately 1.5–2 years. Less than 10% of patients with metastatic renal cancer survive >2 years.<sup>10</sup> However, owing to recent advances in antineoplastic treatments, especially in breast and prostate cancer, longer survival periods are continuously being achieved. Thus, a reduction of early toxicity in SCC patients is justified and likely to bring benefit to at least some patients in the palliative phase of the disease.

Early toxicity in SCC patients receiving radiation therapy includes nausea and vomiting,<sup>6,11</sup> diarrhoea,<sup>6,7</sup> esophagitis, pharyngitis<sup>6</sup> and dysphagia.<sup>6</sup> In many reports, late toxicity has not been well documented.<sup>6,7,11</sup> Interestingly, Maranzano et al.<sup>7</sup> reported that dysphagia for solid foods in one-third of patients irradiated on the thoracic spine may be owing to radiation-induced toxicity. This suggests that reducing the dose to healthy tissue in patients with SCC could result in an increased quality of life.

Table 1. The times required for GTV contouring, and planning, for 5 patients.

| Patient number | Time required by an consultant oncologist to contour the GTV (minutes) | Time required by an dose planner to create the plan (minutes) |
|----------------|--|---|
| 1              | 19   | 38  |
| 2              | 15   | 40  |
| 3              | 10   | 60  |
| 4              | 18   | 28  |
| 5              | 16   | 24  |
| Average        | 16   | 38  |

Abbreviations: GTV, gross tumour volume.

For SCC patients with disease in the lower thoracic or lumbar spine, the small intestine and the kidneys should therefore be treated as organs at risk and the irradiation dose delivered to them should be carefully considered.

We have shown that the doses to the kidneys and the small intestine can be reduced to what is probably a clinically meaningful level using VMAT instead of an APPA or three-field technique in patients with advanced cancer. Similarly, encouraging results indicating sparing of organs at risk with VMAT rather than APPA and three-field techniques have been reported for curative treatments in the literature.<sup>12–14</sup>

When VMAT plans are made, additional steps are necessary in the planning process. However, these are relatively few: we generate a PTV margin automatically and generate a ring around the PTV as a soft tissue surrogate. We do not consider these procedures prohibitively time consuming and demanding in the workflow of our clinic.

The time required to contour the target—16 minutes on average—seems short enough that the contouring required for VMAT plans is clinically feasible.

The time required to plan is not inconsiderable, but should be comparable with other reported treatment times.<sup>15,16</sup>

This study has several limitations: the patient cohort is limited to 20 patients, and for the sake of homogeneity, we focussed on a specific tumour location (lower thoracic and lumbar region). Hence, we cannot report dose reductions to other potentially relevant organs at risk, such as the lungs or the oesophagus. It should also be noted that our institution has many years of experience with VMAT; hence, the time evaluations reported here might not apply to institutions where VMAT has recently been implemented. The main limitation is the retrospective nature of this study and the fact that no direct patient outcome was reported. The evaluation of the clinical impact of VMAT would require a randomised setting and is well beyond the scope of this work.

In spite of these limitations, the data from this study will hopefully encourage institutions to consider offering advanced radiotherapy treatments to cancer patients in the palliative phase of their cancer diseases if these therapies are already available standard practice for curatively intended treatments. However, clinical studies of acute and long-term efficacy as well as toxicity studies in patients with advanced cancer are highly warranted.

## CONCLUSION

Patients treated for SCC in the lower thoracic or lumbar region may benefit from VMAT treatment, as it considerably reduces the dose to the bowel and kidneys in a clinically meaningful way compared with APPA or three-field treatments. In clinics where VMAT is already implemented and widely available for curatively intended treatments, the extension of this treatment modality to cancer patients with SCC is feasible with only a modest increase in the consumption of resources and time and—most important—with a likely benefit to patients in palliative care owing to reduced organ toxicity. Future clinical studies should assess organ toxicities related to the various radiation therapy regimens in patients with malignant SCC.

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## Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guides on the care and use of laboratory animals and has been approved by the radiation therapy management group.

## References

1. Rades D, Stalpers L J, Hulshof M C et al. Comparison of  $1 \times 8$  Gy and  $10 \times 3$  Gy for functional outcome in patients with metastatic spinal cord compression. *Int J Radiat Oncol Biol Phys* 2005; 62 (2): 514–518.
2. Rades D, Stalpers L J, Veninga T et al. Evaluation of functional outcome and local control after radiotherapy for metastatic spinal cord compression in patients with prostate cancer. *J Urol* 2006; 175 (2): 552–556.
3. Maranzano E, Latini P, Checcaglini F et al. Radiation therapy in metastatic spinal cord compression. A prospective analysis of 105 consecutive patients. *Cancer* 1991; 67 (5): 1311–1317.
4. Nutting C, Dearnaley D P, Webb S. Intensity modulated radiation therapy: a clinical review. *Br J Radiol* 2000; 73 (869): 459–469.
5. Kjaer-Kristoffersen F, Ohlhues L, Medin J et al. Rapidarc volumetric modulated therapy planning for prostate cancer patients. *Acta Oncol* 2009; 48 (2): 227–232.
6. Maranzano E, Bellavita R, Rossi R et al. Short-course versus split-course radiotherapy in metastatic spinal cord compression: results of a phase III, randomized, multicenter trial. *J Clin Oncol* 2005; 23 (15): 3358–3365.
7. Maranzano E, Latini P, Perrucci E et al. Short-course radiotherapy ( $8 \text{ Gy} \times 2$ ) in metastatic spinal cord compression: an effective and feasible treatment. *Int J Radiat Oncol Biol Phys* 1997; 38 (5): 1037–1044.
8. Kavanagh B D, Pan C C, Dawson L A et al. Radiation dose–volume effects in the stomach and small bowel. *Int J Radiat Oncol Biol Phys* 2010; 76 (3): S101–S107.
9. Joiner M, van der Kogel A. *Basic clinical radiobiology*, 4th edition. Hodder Arnold, London, 2009.
10. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer* 2013; 49 (6): 1374–1403.
11. Maranzano E, Latini P, Beneventi S et al. Radiotherapy without steroids in selected metastatic spinal cord compression patients. A phase II trial. *Am J Clin Oncol* 1996; 19 (2): 179–183.
12. Shaffer R, Nichol A M, Vollans E et al. A comparison of volumetric modulated arc therapy and conventional intensity-modulated radiotherapy for frontal and temporal high-grade gliomas. *Int J Radiat Oncol Biol Phys* 2010; 76 (4): 1177–1184.
13. Zhang G G, Ku L, Dilling T J et al. Volumetric modulated arc planning for lung stereotactic body radiotherapy using conventional and unflattened photon beams: a dosimetric comparison with 3D technique. *Radiat Oncol* 2011; 6: 152.
14. Wolff D, Stieler F, Welzel G et al. Volumetric modulated arc therapy (VMAT) vs. serial tomotherapy, step-and-shoot IMRT and 3D-conformal RT for treatment of prostate cancer. *Radiother Oncol* 2009; 93 (2): 226–233.
15. Oliver M, Ansbacher W, Beckham W A. Comparing planning time, delivery time and plan quality for IMRT, rapidarc and tomotherapy. *J Appl Clin Med Phys* 2009; 10 (4): 117–131.
16. Craft D L, Hong T S, Shih H A et al. Improved planning time and plan quality through multicriteria optimization for intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2012; 82 (1): e83–e90.