



Contents lists available at ScienceDirect

Technical Innovations & Patient Support in Radiation Oncology

journal homepage: www.sciencedirect.com/journal/technical-innovations-and-patient-support-in-radiation-oncology



Reduction of oesophageal toxicity with VMAT dose-sparing radiotherapy in thoracic metastatic spinal cord compression: A feasibility study

Vanja Remberg Gram^{a,b}, Daniel Gram^{a,c}, Gitte Fredberg Persson^{b,d}, Morten Hiul Suppli^a, Sarah Barrett^{e,*}

^a Department of Oncology, Section of Radiotherapy, Rigshospitalet, University Hospital of Copenhagen, Denmark

^b Department of Oncology, University Hospital Herlev-Gentofte Hospital, Copenhagen, Denmark

^c Department of Clinical Oncology and Palliative Care, Radiotherapy, Næstved, Zealand University Hospital, Denmark

^d Department of Clinical Medicine, Faculty of Health Science, University of Copenhagen, Denmark

^e Applied Radiation Therapy Trinity, Discipline of Radiation Therapy, Trinity St James's Cancer Institute, Trinity College Dublin, Ireland

ARTICLE INFO

Keywords:

Metastatic spinal cord compression
Palliative radiotherapy
Oesophageal toxicity
Dysphagia
Volumetric modulated arc therapy

ABSTRACT

Background: Palliative radiotherapy for metastatic spinal cord compression (MSCC) is given to halt disease progression and sustain quality of life for patients with advanced cancer. Radiotherapy can however induce toxicity, contradicting treatment intention. Advanced radiotherapy offers possibility of sparing organs at risk (OARs). The purpose of this dosimetric study is to establish the feasibility and potential benefits of dose sparing of the oesophagus.

Materials and methods: 30 patients receiving radiotherapy of 30 Gy/10# for MSCC were retrospectively included and the oesophagus delineated. Two new dose plans were created for each patient (eso-crop and PTV-crop) with the intention of optimising the oesophageal dose. In the eso-crop plan maintaining full target volume coverage was prioritised, for the PTV-crop plan oesophageal dose was further reduced through cropping the planning target volume (PTV) overlapping oesophageal/PTV-area. Time added for delineation was measured. Plans were compared using Wilcoxon signed rank test with $p < 0.05$ considered statistically significant. Bivariate associations between dose metrics and patient characteristics were quantified using linear regression models.

Results: Oesophageal delineation took a mean of 8.6 min. There was significant dose reduction for both V7.7 Gy, D2% and mean oesophageal dose, without significant change in CTV coverage. The mean achievable oesophageal dose reduction was 29.1% and 50.4% for the eso-crop and PTV crop plans, respectively. Minor changes in dose distribution to the lungs was observed, with increased mean and V20Gy for the eso-crop plan and decreased V5Gy to the PTV-crop plan.

Conclusion: This study demonstrated the possibility of significant dose sparing of the oesophageal dose using single arc VMAT without impacting on CTV coverage.

Introduction

The bone structure, including the vertebral column, is the most commonly affected site for metastatic cancer [1]. Vertebral body metastases occur in approximately 5–10% of all cancer patients as a result of advanced cancer [2]. These lesions can cause metastatic spinal cord compression (MSCC). This is a disabling complication, which, untreated, can lead to pain, paralysis and loss of motor function distally of the compression, and incontinence [3]. Symptoms are severe, unremitting pain, progressive discomfort, neurological symptoms and motor

function deficit, numbness or weakness and bladder or bowel dysfunction [4,5].

In palliative radiotherapy (RT), life expectancy may be short, with a median survival rate of less than 6 months [6] however, patients may present with favourable prognostic factors with increased life expectancy [7]. Interventions in palliative care focus on preservation of quality of life (QoL) by reducing pain and preserving functional and mobile ability as a part of the end-of-life care [8]. Options of treatment and symptom relief include corticosteroids, surgical decompression of the involved vertebrae and palliative RT, or a combination of these, with

* Corresponding author.

E-mail address: barrets7@tcd.ie (S. Barrett).

<https://doi.org/10.1016/j.tipsro.2022.07.001>

Received 9 May 2022; Received in revised form 8 July 2022; Accepted 13 July 2022

Available online 16 July 2022

2405-6324/© 2022 Published by Elsevier B.V. on behalf of European Society for Radiotherapy & Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

primary RT being a favoured treatment option for those with poorer prognostic factors [3,7,9].

For curatively intended treatments, there is a focus on reducing the long-term adverse effects of RT by reducing the dose and thereby also the toxicity to organs at risk (OARs) to increase life span and QoL [10]. However, for palliative patients, the acute toxicity from radiation therapy may create adverse effects, reducing their QoL. Studies have shown that palliative patients may be affected by acute toxicity, including gastro-intestinal toxicity, mucositis, bone-marrow suppression and myelopathy, depending on the OARs close to the target volume [2,11].

The cervical and thoracic part of the spinal column is situated posteriorly to the oesophageal tract, which is considered an OAR in thoracic radiotherapy [12]. Although there is a paucity of research on patient reported acute toxicity <grade 3 from palliative RT, one study by Gram et al included all grades of patient self-reported outcomes [13]. This study reported that for patients irradiated at the level of the oesophagus, the incidence of patient experienced toxicity was 79%, which patients also reported impacted on their well-being [13]. The study also demonstrated a correlation between the mean and maximum oesophageal dose metrics and the risk of developing toxicity; [13]. The average mean and maximum oesophageal dose for patients reporting toxicity was 7.7 Gy and 30.4 Gy respectively, in comparison this was 0.2 Gy and 0.5 Gy for patients without self-reported toxicity [13]. Modulated techniques have been suggested in the palliative setting to reduce patient reported side effects.

For patients with a short life expectancy, it is particularly important to reduce acute toxicity as the aim of treatment is to maintain or improve QoL. Dose fractionation schemes for MSCC vary, with life expectancy being a key factor influencing the choice of prescription [2]. Common prescriptions are 8 or 10 Gy in 1 fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions, 37.5 Gy in 15 fractions and 40 Gy in 20 fractions [2].

Delineation of the oesophageal tract as an OAR is not standard practice for MSCC. As a large part of the oesophageal tract can be directly adjacent to the vertebral body, this also means that parts of the planning target volumes (PTV) may overlap with the oesophagus. Optimising the dose to the oesophagus may therefore not be feasible without some compromise of the PTV coverage. Considering that the clinical objective for MSCC is symptom relief above local tumour control, it is reasonable to evaluate the impact of partial PTV compromise to achieve sparing of the oesophagus. Clinically this compromise of PTV would be located at the anterior PTV, distal to the spinal canal and location of cord compression. Reducing the acute toxicity within palliative RT may contribute to an increase in the benefits of this treatment and provide further incentive to using RT to treat MSCC and improve patient outcome.

Volumetric modulated arc therapy (VMAT) has demonstrated desirable dose optimisation and sparing of OARs for curative treatments, such as head and neck cancer [14,15], oesophageal cancer [16], as well as for patients with cancer in the pelvic area [17] and is a technique that is continuously recommended for treatments requiring OAR sparing. This technique also offers a reduced treatment time when using single arc therapy, compared to intensity modulated radiation therapy (IMRT).

The purpose of this study was to assess the feasibility and potential benefits of oesophageal dose sparing VMAT for MSCC, compared to the standard, single arc treatment without dose optimisation of the oesophagus.

Materials and methods

Study population and simulation

This retrospective dose comparative planning study included 30 consecutive target volumes of adult patients (n = 29, one patient was treated to 2 thoracic vertebral sites) treated for MSCC using VMAT, between January and May 2016. Ethical approval was obtained from the

local ethics board, the Danish Patient safety Authority and the Danish Data Protection Agency. Inclusion criteria were patients with an estimated remaining life expectancy of ≥ 6 months, receiving 30 Gy in 10 fractions for MRI-confirmed MSCC in the thorax. Patients irradiated above or below the thoracic level (including the level of C7) of the oesophagus, post-stabilisation-surgical patients, and patients with large soft-tissue components included in the target volume were excluded.

Patients were scanned in a supine position on a head and neck board with one of the standard pillows fitted to each patient. For patients treated at the level of the fifth thoracic vertebra or above, a 5-attachment point mask was made to ensure reproducibility of the neck position. The entire vertebral column was scanned with a slice thickness of 2,5mm.

Patients were treated with daily image guided radiation therapy using cone beam computed tomography (CT).

Patient characteristics are noted in Table 1.

Delineation

The clinical target volume (CTV), included the entire affected vertebrae, with corpus, associated posterior arch, processus spinosus and processus transversus, if affected, as well as extracorporeal tumour (Fig. 1), if relevant, without extending target volumes to the neighbouring vertebrae. The CTV to planning target volume (PTV) expansion was 5 mm margin. The bone structure and body contours were delineated according to local protocols, as well as oesophagus and lungs in coherence with RTOG 1106 atlas for thoracic OARs [11]. The entire oesophagus was delineated from the cricoid to the gastro-oesophageal junction by one observer (VG). The time required to delineate the oesophagus was recorded in full minutes.

Treatment planning

Plans were created using Eclipse™ treatment planning system (TPS) version 13.7, Varian Medical Systems, Palo Alto, CA, USA) Clinical treatment plans met the institutional guidelines for palliative RT

Table 1
Patient characteristics for all included patients.

	Mean	Range	SD
Age (y)	68.9	47–83	8.2
Treated vertebra (n)	2.4	1–8	1.7
Field length (cm)	5.2	1.9–16.3	3.5
	n	%	
Sex			
Male	21	70	
Female	9	30	
Primary disease			
Prostate cancer	9	30	
Breast cancer	4	13.3	
Pulmonary cancer	4	13.3	
Rectal cancer	3	10	
Head and neck cancer	2	6.7	
Multiple myeloma	2	6.7	
Oesophagus cancer	2	6.7	
Neuroendocrine cancer	2	6.7	
Unknown primary cancer	2	6.7	
Vertebral level			
C7 – Th4 (Upper thoracic oesophagus)	12	40.0	
Overlapping both regions	6	20.0	
Th5 – Th8 (Mid thoracic oesophagus)	11	36.7	
Overlapping both regions	1	3.3	
Th9 – Th12 (Lower thoracic oesophagus)	0	0	

Abbreviations. C = Cervical vertebra, Th = Thoracic vertebra.

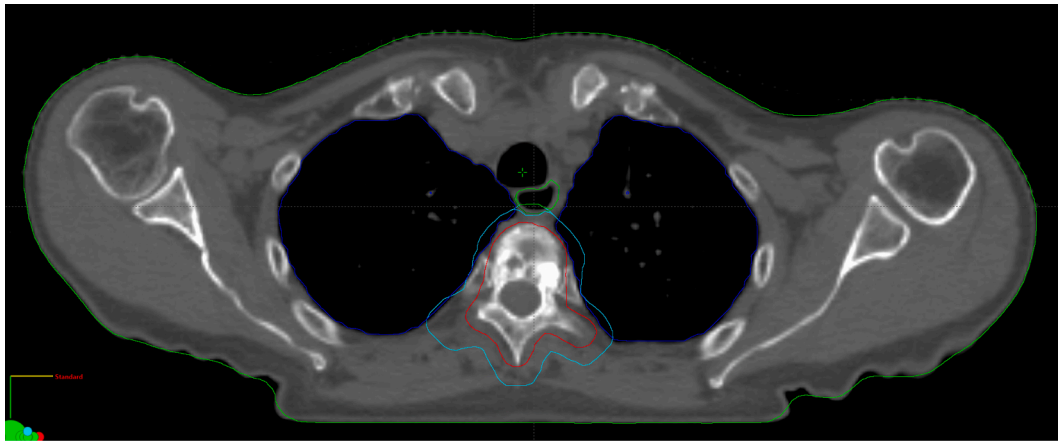


Fig. 1. Shows the delineation of GTV, PTV, cropped PTV, lungs and oesophagus as well as body contour.

planning with PTV $V_{90\%} = 98\%$ and CTV $V_{98\%} = 90\%$ of the CTV dose coverage required. Maximum dose up to 110% was deemed acceptable. No optimisation specific to the oesophagus was performed.

Two new dose plans were created for each included target volume, totalling 60 new dose plans.

The Eso-Crop Plan aimed to improve oesophageal sparing without compromise of PTV target coverage. As a result, only the region of the oesophagus outside the PTV overlap was included in the plan optimisation.

The PTV-Crop Plan prioritised oesophageal dose sparing over PTV coverage, but without any compromise to CTV, see Fig. 2 for an example of the plans generated.

For treatment planning, the upper objective for oesophageal dose was set as low as possible for each individual plan. CTV coverage was not compromised on either of the new dose plans. All plans were created using a single arc VMAT technique using 6 megavolts.

Evaluation metrics

Oesophageal metrics of Dmean, $V_{\geq 7.7\text{Gy}}$ and D_{2%} were recorded. Lung $V_{5\text{Gy}}$, $V_{20\text{Gy}}$ and Mean Lung Dose (MLD) were also recorded to assess if re-optimisation impacted nearby OARs. Target volume coverage was measured as CTV and PTV for the Eso-crop plans and CTV for the PTV-crop plans.

The resulting dose metrics from both the Eso-Crop and the PTV-Crop plans were compared to the baseline plan metrics.

Statistical analysis

Shapiro-Wilk tests and visual inspection of scatter plots and histograms were used to test the variables for normal distribution and linearity. Metrics were

compared for all plans using Wilcoxon signed rank tests and $p < 0.05$ was considered statistically significant.

Bivariate associations between field length and mean oesophageal dose, as well as field length and mean lung dose were quantified by using Spearman's rank correlation coefficient. The linear regression models provide the following relationship ($y_i = b_0 + b_1x_i + \varepsilon_i$) which describes the line y where x is the sample data used, b_0 is the sample estimate for vertical intercept, b_1 is the sample estimate of the slope of the regression line and ε_i is the residual error.

Results

Delineation time

Mean time required to delineate entire oesophagus was 8.6 min (range 4–18 min).

One included patient had two eligible targets, however, as the oesophagus is only delineated once, the delineation time is only registered once, therefore all 29 included patient's delineation time are represented in Fig. 3. For all included patients the oesophagus was situated in close proximity of the target volumes. In 27/30 cases the oesophagus overlapped with the PTV to various extents.

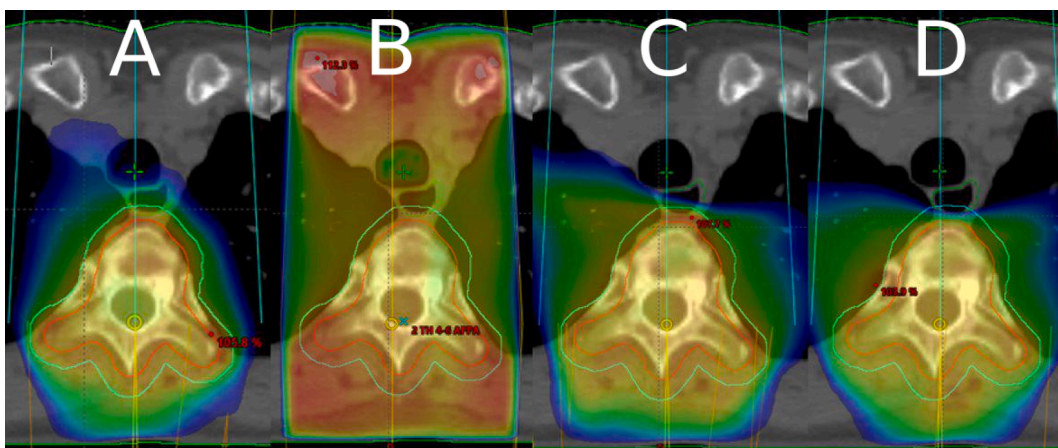


Fig. 2. Showing dose distribution of the 60–110% dose. All images are same slice of the same patient. A is the original plan, B is AP-PA plan for illustrational purposes only, C the eso-crop plan and D the PTV-crop plan.

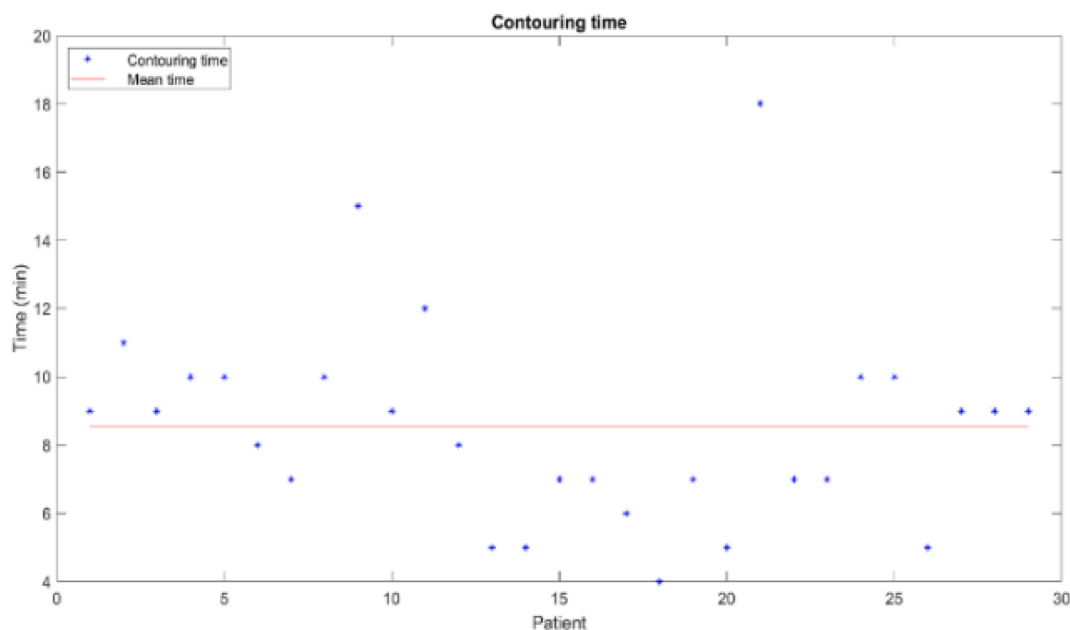


Fig. 3. Delineation and mean time (minutes) for delineating the entire oesophagus for all 29 patients.

Oesophageal dose

Both the eso-crop plans and the PTV-crop plans were compared to the original plans with data represented in Table 2.

A statistically significant reduction of the mean oesophageal dose, was found for the eso-crop and PTV-crop plans, compared to the original plan ($p < 0.001$). Scatter plots with identity lines visualise the difference in OAR sparing for all comparisons (Fig. 4).

The average oesophageal D_{mean} was reduced from 25.8% (7.7 Gy) in the original plans to 18.3% (5.5 Gy) for the eso-crop plans and 12.8% (3.8 Gy) for the PTV-crop plans. Additionally, the number of patients with $D_{mean} < 7.7$ Gy also increased from $n = 18$ in the original plans to $n = 24$ and $n = 28$ in the Eso-crop and PTV-crop plans respectively. This resulted in an average dose reduction of 29.1% and 50.4% for the Eso-crop and PTV-crop plans, when compared to the original plan ($p < 0.001$). For the original plans, oesophageal D_{mean} ranged from 10.5% (3.2 Gy) to 67.5% (20.3 Gy) of the prescribed dose. For the optimised plans, oesophageal D_{mean} ranged from 4.4% (1.3 Gy) to 43.6% (13.1 Gy) for the Eso-crop plans and 3.1% (0.9 Gy) to 31.7% (9.5 Gy) for the PTV-crop plans.

The eso-crop and PTV-crop plans had a statistically significant reduction in oesophageal volume receiving ≥ 7.7 Gy from 33.6% in the original plan, to 23.7% ($p < 0.001$) and 18.2% ($p < 0.001$) in the eso-crop and PTV-crop plans, respectively. The PTV-crop plan had a statistically significant lower oesophageal dose, compared to the eso-crop plan ($p = 0.001$).

A statistically significant reduction of oesophageal $D_{2\%}$ was also observed in both eso-crop and PTV-crop plans ($p < 0.01$) compared to the original plans. The average oesophageal $D_{2\%}$ for the original plan was 92% (27.6 Gy), $D_{2\%} > 27.6$ Gy $n = 22$ reduced to 80.9% (24.3 Gy), $D_{2\%} > 27.6$ Gy $n = 17$ and 58.2% (17.5 Gy), $D_{2\%} > 27.6$ Gy $n = 4$ for the eso-crop and the PTV-crop plans respectively. The achieved dose reduction of the oesophagus varied between patients, depending on the anatomical positioning of the oesophagus and its proximity to the PTV.

The mean dose to the oesophagus was co-dependant on the length of the treatment field, as illustrated in Fig. 5.

Lung dose

The original plan had a statistically significant lower average mean

Table 2

Summary of dose metrics measured for all three VMAT treatment plans; original, eso-crop and PTV-crop plans, presented in mean percentage for each value. Bold values represent a statistically significant difference from the original plan.

	Dose Metric	Original plan	Eso-crop plan	PTV-crop plan
CTV dose (%)	Mean	100.19	99.9	100
	Min	92.9	92.5	91.5
	$D_{2\%}$	106.1	106.3	108.4
PTV dose (%)	Mean	100	100	96.7
	Min	84.9	83.9	39.8
	$D_{2\%}$	107.5	108.2	107.9
Mean oesophagus dose (%)	Mean	25.8	18.3	12.8
	Range	10.5–67.5	4.4–43.6	3.1–31.7
	SD	13.1	9.2	7.3
Oesophagus $V_{7.7}$ (%)	Mean	33.6	23.7	18.2
	Range	14.8–88.0	0.1–65.9	0.0–68.9
	SD	18.6	14.6	16.8
Oesophageal $D_{2\%}$ (%)	Mean	92.0	80.9	58.2
	Range	60.7–101.8	20.5–102.4	15.2–98.6
	SD	10.7	26.3	26.3
Mean lung dose (%)	Mean	11.7	12.6	11.4
	Range	2.3–32.0	2.4–34.4	1.7–31.6
	SD	7.8	8.2	7.9
Lung V_{5Gy} (%)	Mean	28.9	27.3	25.3
	Range	3.4–85.4	3.4–78.6	2.1–83.7
	SD	22	19.4	19.7
Lung V_{20Gy} (%)	Mean	1.7	2.6	2.0
	Range	0.0–6.8	0.0–9.3	0.1–6.7
	SD	1.6	2.5	2.0

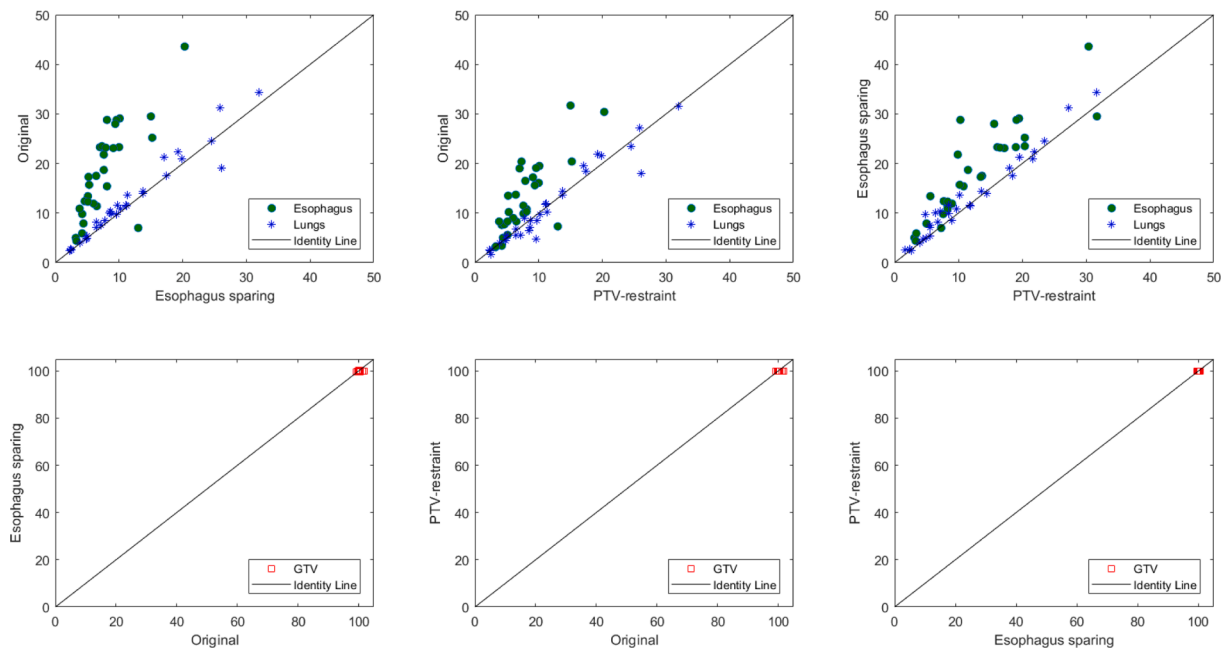


Fig. 4. Scatter plots with identity lines. The three top plots illustrate mean oesophageal and lung dose, demonstrating a statistically significant reduction of the mean oesophageal dose for the eso-crop and PTV-crop plans, compared to the original plan ($p < 0.001$). The three bottom plots illustrating the GTV coverage.

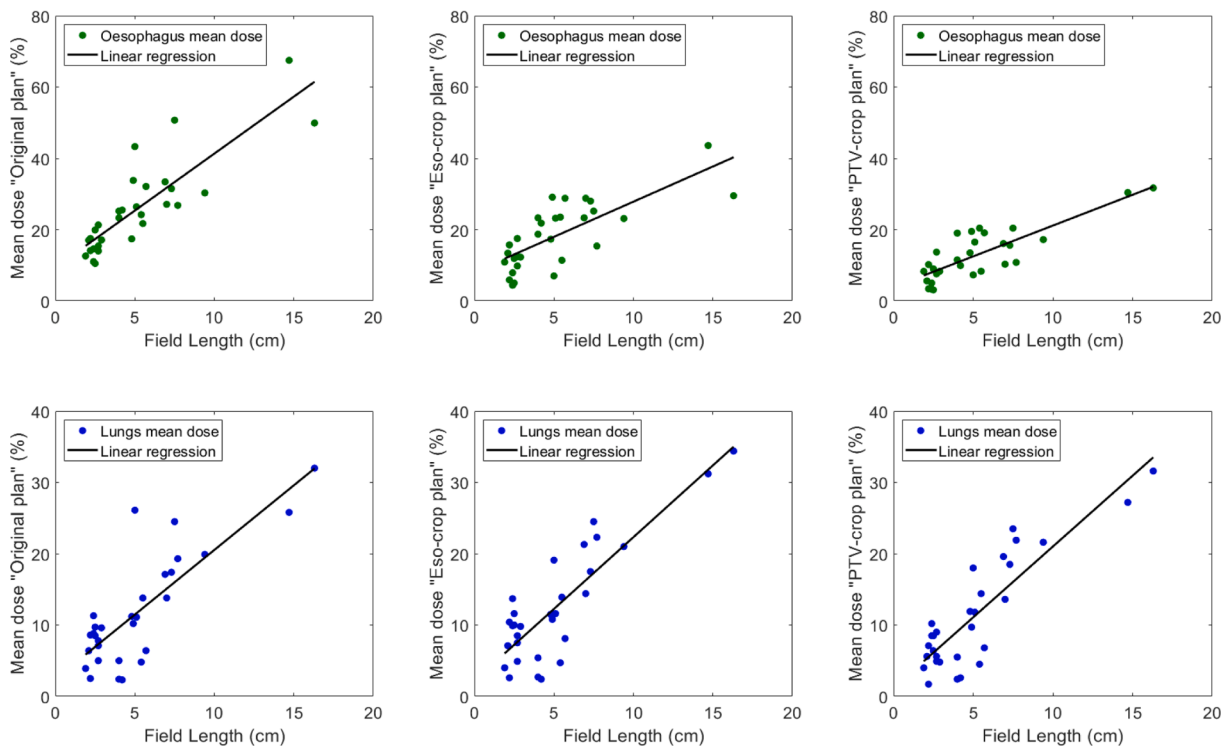


Fig. 5. Bivariate linear regression models between field length and the mean oesophageal dose and field length and mean lung dose for both original, eso-crop and PTV-crop plans.

lung dose compared to the eso-crop plan ($p < 0.001$) but not when compared to the PTV-crop plan ($p = 0.62$). The eso-crop plan showed no statistically significant decrease in lung V_{5Gy} , compared to the original plan ($p = 0.24$), however, the PTV-crop plan demonstrated a statistically significant dose reduction compared to the original plan ($p < 0.001$). The PTV-crop plan also showed a statistically significant decrease in V_{5Gy} compared to the eso-crop plan ($p = 0.003$).

Average lung V_{20Gy} in the eso-crop plan increased, compared to the

original plan ($p < 0.001$). Lung V_{20Gy} dose for the PTV-crop plan was not statistically different to the original plan ($p = 0.07$).

Impact of field length

Bivariate linear regression is illustrated in Fig. 5.

Field length and mean oesophageal dose presented a strong positive correlation, $R^2 = 0.86$, $R^2 = 0.72$ and $R^2 = 0.74$ for the original, eso-crop

and PTV-crop plans, respectively, with $p < 0.001$ for all three plans.

Linear regression for field length and mean lung dose was $R^2 = 0.67$ for the original plan, $R^2 = 0.69$ for the eso-crop plan and $R^2 = 0.72$ for the PTV-crop plan ($p < 0.001$).

Discussion

Traditionally simple techniques are used to plan emergency RT to MSCC [18]. A single posterior field or anteroposterior-posterioranterior (AP-PA) fields are used aiming at letting the 80% isodose curve cover the ventral part of the vertebra. With VMAT we aim at covering the entire PTV with the 90% isodose curve, which consequently adds significant dose to the oesophagus. However, utilising modulated techniques to treat MSCC has been reported as frequently as 3DCRT approaches in one US based survey [19] and ongoing clinical trials are evaluating the potential for more advanced delivery methods [20].

This study demonstrates the potential of using VMAT technique to achieve oesophageal sparing for MSCC patients without PTV compromise, which has the potential to reduce treatment related toxicity while treating symptoms related to the MSCC. Further OAR sparing can be achieved with some compromise of the PTV without detriment to the CTV coverage. Compromising the PTV target volume may pose a long-term risk of local failure. However, it should be noted that no compromise was made to GTV target volumes. For patients with a short life expectancy of ≤ 6 months, the risk of local failure due to insufficient PTV coverage is low with options such as reirradiation available [7]. In-field recurrence rates have been reported using simple planning techniques of single PA field or APPA [11]. 2-year in-field recurrence rates were 14% for those treated 30 Gy/10#, however the proportion of patients with follow-up ≥ 12 months was only 34% [11].

While VMAT treatment is not a standard approach for palliative patients for many clinics, it could be applied to minimize dose to the oesophagus and other OAR and thereby improving treatment outcomes for these palliative patients. This is especially the case when compared to commonly used techniques such as parallel-opposite pair beams, as the oesophagus is typically located directly in front of the vertebra and thus directly within the beam.

A study investigating dose sparing of the oesophagus for palliative patients has compared standard use of parallel-opposed pair beams with oesophageal-sparing IMRT plans, showing an oesophageal-sparing IMRT plan could reduce the rate of oesophagitis from 13% to 2%, while maintaining a similar dose coverage of the PTV [21]. However, advanced IMRT is more time consuming, compared to VMAT, which may add extra discomfort for palliative patients and increase intra-fraction motion.

For clinics already using the VMAT technique for treating patients with MSCC, this technique could be introduced with a low resource impact, as the average delineation time was shown to be only 8.6 min. One case took 18 min, as the oesophagus was difficult to distinguish from the surrounding tissue.

One consequence of optimising the dose off the oesophagus, was the increased dose into the lungs, increasing the risk of pneumonitis. Radiation pneumonitis is a serious complication, which in grave cases may lead to death [22]. Both dose and irradiated lung volume play a large role in developing radiation pneumonitis, where most studies validate the mean lung dose and V_{20Gy} as parameters correlated to an increase in radiation pneumonitis [22]. Investigations have showed that changing the dose constrains to the lungs from only including the standard V_{20Gy} to $<40\%$ of the lung volume to also including an added dose constrain of V_{5Gy} to $\leq 60\%$ reduced the fatal radiation pneumonitis from 17% to 4% of the included patients [23]. Radiation pneumonitis may also be a risk factor worth considering for patients irradiated for MSCC at the level of the oesophagus and therefore it is relevant to investigate how reducing and optimising on the dose delivered to the oesophagus for VMAT for MSCC affects the dose to the lung volume.

To evaluate the impact of oesophageal sparing on lung dose, this

study included dose measures of lungs, without adding any dose sparing or optimisation of the lungs, as this would increase the treatment planning complexity and duration.

Without optimising lung dose, a localised area is receiving an increased dose, it is unclear how this will affect the patients undergoing radiotherapy for MSCC. One previous study in palliative lung cancer treatment investigated the total lung volume receiving 5 Gy in an interest in keeping this volume $\leq 60\%$ [23], which showed that the introduction of a V_{5Gy} significantly reduced the incidence of lethal pneumonitis. In this study V_{5Gy} dose metric was not part of the optimisation for original or new plans. However, both eso-crop and PTV-crop plans demonstrated lower V_{5Gy} , compared to the original plans.

When looking at the dose range for lung values, there is a great variety in range, with a portion of the included patients receiving a larger dose to the lungs. As illustrated in Fig. 5, this is depending on the length of the treatment field and number of irradiated vertebrae. Further data are required to quantify how this affects clinical outcomes and risk of adverse effects.

The advantage of oesophageal dose optimisation varied for each patient with patients where the oesophagus did not overlap with the target volumes being most likely to have increased oesophageal sparing. Furthermore, as illustrated in Fig. 5, patients with a longer treatment field were likely to have an increased oesophageal dose, which may indicate that these patients will experience an increased advantage of dose reduction to the oesophagus.

In our study, the large difference in the optimised $D_{2\%}$ oesophageal doses is due to the area of oesophageal PTV overlap. As target volume coverage usually is prioritised above OAR sparing, the oesophagus receiving a high dose can only be reduced by 3.3 Gy, following the traditional guidelines of PTV margin. However, if prioritising the oesophagus as an important OAR above the PTV target volume, it is possible to reduce the average maximum dose by 10.1 Gy.

Compromising the PTV for palliative patients receiving thoracic radiotherapy to reduce dose to OARs, to achieve the clinical objective of symptom relief over local control has been suggested previously [21] and the results of this study also suggest potential clinical benefits for MSCC patients. This research study provides treatment plan evaluations of the feasibility of planning and further investigating the possibility of partial PTV compromise to achieve a better dose sparing of the oesophagus. However, more research, both retrospective and prospective phase 3 clinical trials are needed to fully evaluate the clinical relevance of both OAR sparing and PTV compromise, as well as assessing the risk of local failure, before this could be implemented or recommended as clinical standard practice. Furthermore, the consequences of dose optimisation to one OAR on other relevant structures such as the lungs and heart require further investigation. Clinical data are needed to assess how balancing OAR and PTV dose distribution affects relevant clinical outcomes for the MSCC population, prior to clinical implementation of this technique. A phase 3, randomized trial is currently recruiting to evaluate these questions [24].

Treatment modalities other than VMAT can be considered in patients with MSCC depending on symptoms, severity, prognosis and other clinical parameters influencing treatment choice and technical availability. The SC24 trial included patients with spinal metastasis and pain, which were randomized to stereotactic body radiotherapy (SBRT) or conventional radiotherapy. Half of patients had epidural disease and 2% in the SBRT arm had high grade of compression [25]. This suggest that some patients with symptomatic spine metastasis can be treated with SBRT techniques that allows dosimetric constraints of any nearby OAR. On the other hand, the PROMPTS study showed that patients with asymptomatic MSCC from prostate cancer can safely avoid radiotherapy and thereby toxicity of esophagitis [26]. The use of MR-LINAC based treatment could be a way to improve efficacy of palliative radiotherapy with scan, plan and treat approach without the need of a planning CT [27]. This would also allow oesophageal avoidance with online adaptation, however compromises to the PTV would still be required with

this approach.

Conclusions

This data demonstrates the possibility of reducing both mean and maximum oesophageal dose for patients with MSCC using single arc VMAT, with an increased delineation time of 8.6 min and without adding to treatment delivery time.

The PTV compromising technique was superior in both oesophageal and lung dose reduction, however, the clinical relevance of PTV dose compromise has yet to be established.

Oesophageal dose optimisation in thoracic MSCC may reduce the patient experienced toxicity, but also results in altered lung dose metrics, if not considered in the plan optimisation. Clinical data are needed to assess how balancing OAR and PTV dose distribution affects relevant clinical outcomes for the MSCC population, prior to clinical implementation of this technique.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Sarah Barrett holds a research grant from Varian Medical Systems, not related to this research. Morten Hiul Suppli and Gitte Persson work in departments which hold research agreements with Varian Medical Systems which are unrelated to this research.

References

- [1] Böhm P, Huber J. The surgical treatment of bony metastases of the spine and limbs. *J Bone Joint Surg Br* 2002;84-B(4):521–9.
- [2] George R, Sundararaj JJ, Govindaraj R, Chacko AG, Tharyan P. Interventions for the treatment of metastatic extradural spinal cord compression in adults. *Cochrane Database Syst Rev* 2015;2018(7). <https://doi.org/10.1002/14651858.CD006716.pub3>.
- [3] Loblaw DA, Laperriere NJ. Emergency treatment of malignant extradural spinal cord compression: an evidence-based guideline. *J Clin Oncol* 1998;16(4):1613–24.
- [4] Drudge-Coates L, Rajbabu K. Diagnosis and management of malignant spinal cord compression: part 1. *Int J Palliat Nurs* 2008;14(3):110–6.
- [5] Hoskin PJ, Grover A, Bhana R. Metastatic spinal cord compression: radiotherapy outcome and dose fractionation. *Radiother Oncol* 2003;68(2):175–80.
- [6] Maranzano E, Latini P. Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: final results from a prospective trial. *Int J Radiat Oncol Biol Phys* 1995;32(4):959–67.
- [7] Oldenburger E, Brown S, Willmann J, van der Velden JM, Spatek M, van der Linden YM, et al. ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases. *Radiother Oncol* 2022;173:240–53.
- [8] Rades D, Fehlauer F, Schulte R, Veninga T, Stalpers LJA, Basic H, et al. Prognostic factors for local control and survival after radiotherapy of metastatic spinal cord compression. *J Clin Oncol* 2006;24(21):3388–93.
- [9] Joiner, M.C. and A. van der Kogel, *Basic Clinical Radiobiology (5th ed.)*. 5th ed. 2018: CRC Press.
- [10] Maranzano E, Bellavita R, Rossi R, De Angelis V, Frattegiani A, Bagnoli 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):3358–65.
- [11] Rades D, Stalpers LJA, Veninga T, Schulte R, Hoskin PJ, Obralic N, et al. Evaluation of five radiation schedules and prognostic factors for metastatic spinal cord compression. *J Clin Oncol* 2005;23(15):3366–75.
- [12] Kong F, Quint L, Machtay M. RTOG 1106 - Atlas for Organs at Risk (OARs) in Thoracic Radiation Therapy.
- [13] Gram V, Fog LS, Hemer M, Pappot H, Aznar MC, Suppli MH, et al. Patient reported upper gastro-intestinal symptoms associated with fractionated image-guided conformal radiotherapy for metastatic spinal cord compression. *Tech Innov Patient Support Radiat Oncol* 2020;13:1–5.
- [14] Pursley J, Damato AL, Czerminska MA, Margalit DN, Sher DJ, Tishler RB. A comparative study of standard intensity-modulated radiotherapy and RapidArc planning techniques for ipsilateral and bilateral head and neck irradiation. *Med Dosim* 2017;42(1):31–6.
- [15] Anamalayil SJ, et al. Effects of full-neck volumetric-modulated arc therapy vs split-field intensity-modulated head and neck radiation therapy on low neck targets and structures. *Br J Radiol* 2016;89(1062):20160009.
- [16] Chen H, Wang H, Gu H, Shao Y, Cai X, Fu X, et al. Study for reducing lung dose of upper thoracic esophageal cancer radiotherapy by auto-planning: volumetric-modulated arc therapy vs intensity-modulated radiation therapy. *Med Dosim* 2018; 43(3):243–50.
- [17] Tamaki T, et al. 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*, 2018; 59(5): 639-648.
- [18] Logan JK, Jiang J, Shih Y-C, Lei X, Xu Y, Hoffman KE, et al. Trends in Radiation for Bone Metastasis During a Period of Multiple National Quality Improvement Initiatives. *J Oncol Pract* 2019;15(4):e356–68.
- [19] Gutt R, Malhotra S, Jolly S, Moganaki D, Cheuk AV, Fosmire H, et al. Management of metastatic spinal cord compression among Veterans Health Administration radiation oncologists. *Ann Palliat Med* 2018;7(2):234–41.
- [20] Rades D, Hansen O, Jensen LH, Dziggel L, Staackmann C, Doemer C, et al. Radiotherapy for metastatic spinal cord compression with increased radiation doses (RAMSES-01): a prospective multicenter study. *BMC Cancer* 2019;19(1). <https://doi.org/10.1186/s12885-019-6390-x>.
- [21] Granton PV, Palma DA, Louie AV. Intentional avoidance of the esophagus using intensity modulated radiation therapy to reduce dysphagia after palliative thoracic radiation. *Radiat Oncol* 2017;12(1):27.
- [22] Jain V, Berman A. Radiation Pneumonitis: Old Problem. *New Tricks Cancers (Basel)* 2018;10(7):222. <https://doi.org/10.3390/cancers10070222>.
- [23] Khalil AA, Hoffmann L, Moeller DS, Farr KP, Knap MM. New dose constraint reduces radiation-induced fatal pneumonitis in locally advanced non-small cell lung cancer patients treated with intensity-modulated radiotherapy. *Acta Oncol* 2015;54(9):1343–9.
- [24] ESO-SPARE: Esophagus Sparring Radiotherapy for Thoracic and Cervical Metastatic Spinal Cord Compression. (ESO-SPARE). 2021; Available from: <https://clinicaltrials.gov/ct2/show/NCT05109819>.
- [25] Sahgal A, Myrehaug SD, Siva S, Masucci GL, Maralani PJ, Brundage M, et al. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial. *Lancet Oncol* 2021;22(7):1023–33.
- [26] Dearnaley D, Hinder V, Hijab A, Horan G, Srihari N, Rich P, et al. Observation versus screening spinal MRI and pre-emptive treatment for spinal cord compression in patients with castration-resistant prostate cancer and spinal metastases in the UK (PROMPTS): an open-label, randomised, controlled, phase 3 trial. *Lancet Oncol* 2022;23(4):501–13.
- [27] Benson R, Clough A, Nelder C, Pitt E, Portner R, Vassiliou M, et al. Evaluation of the palliative radiotherapy pathway in a single institute: Can an MR Linac improve efficiency? *J Med Imaging Radiation Sci* 2022;53(2):S44–50.