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Comparison of four 3D conformal treatment techniques to optimise radiotherapy treatment for anal cancer

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Keywords

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Abstract

Introduction: Chemoradiotherapy is the standard of care for anal cancer. Sizeable target volume leads to significant toxicity. We compared four different 3D conformal radiotherapy (3DCRT) techniques with the aim of finding the best technique to achieve the lowest dose to the organs at risk (OAR) without compromising the planning target volume (PTV) coverage. **Methods:** Fifteen computed tomography (CT) data sets from previously treated anal cancer patients (five male and 10 female) were re-contoured according to the Australasian Gastrointestinal Trials Group (AGITG) anal cancer contouring guidelines for N3 disease. Four different 3DCRT plans for each CT data set (standard, V-shape, diamond shape and alternate diamond shape) were generated. Comparisons of the radiation dose to non-rectal bowel (NRB), urinary bladder, genitalia, and femurs were performed. **Results:** V-shape technique achieved significantly lower NRB V40 (mean = 59.6% SD = 11%) than diamond (63.8% SD = 13%), standard (63.8% SD = 11%) and alternate diamond (63.6% SD = 12%) techniques. V-shape technique achieved the lowest mean bladder dose (mean = 45.3 Gy SD = 1.4 Gy). Diamond technique achieved the lowest femur V40 (mean = 32.4%) $P < 0.001$ for all comparisons between diamond and all other techniques. For genitalia V40, diamond technique (mean = 26.4% SD = 20%) and alternate diamond technique (mean = 27.6% SD = 20%) achieved significantly lower dose than V-shape technique (mean = 43.2% SD = 26%) and standard technique (mean = 76.1% SD = 16%) $P < 0.001$ for all comparisons. **Conclusions:** Sophisticated 3DCRT techniques are superior to conventional techniques. Different 3DCRT techniques provide varying levels of dose reduction to OAR, with none of the four techniques investigated capable of reducing dose to all OAR. A combination of techniques may provide the best solution. Further refinement of these techniques should be explored.

Introduction

Chemoradiotherapy has become the standard of care for squamous cell carcinoma of the anal canal, with a cure rate of over 80% and a high rate of sphincter preservation.¹ However, conventional chemoradiotherapy is associated with a high level of acute toxicity and moderate late toxicity.^{2–4} The clinical target volume

(CTV) for anal cancer is sizeable. It extends inferiorly from the anal verge to the level of lumbosacral joint superiorly. The associated acute toxicities from the conventional three- or four-field box technique arising from non-rectal bowel (NRB), bladder, bone, genitalia and skin are substantial, when the primary anal cancer and involved inguinal nodes are treated up to 54 Gy.^{2,4–6} These toxicities during treatment can be severe enough to

warrant a treatment break. While this break often allows the patient to complete their treatment, planned breaks or toxicity-related breaks potentially compromises tumour control.^{7–9}

Three-dimensional conformal radiation therapy (3DCRT) reduces the toxicity from unnecessary radiation exposure to the surrounding normal structures. As the planning target volume (PTV) is not only large but also of non-uniform shape, it is a challenge to achieve an optimal conformal plan that spares organs at risk (OAR) without compromising PTV. The introduction of the Australasian Gastrointestinal Trials Group (AGITG) anal cancer contouring guidelines aims to streamline the contouring of this uncommon cancer.¹⁰

Both intensity modulated radiotherapy (IMRT) and 3DCRT are aimed to improve tumour control and reduce treatment-related toxicity. Although IMRT in anal cancer is gaining acceptance and is being used in parallel with 3DCRT, its superiority awaits confirmation with long-term outcomes of Radiation Therapy Oncology Group (RTOG) trial 0529 and quality of life studies.¹¹ 3DCRT preserves its place with the attractiveness in simplicity. It is a less resource demanding treatment, with room for refinement of its technique and is therefore still in use in departments where IMRT is not able to be routinely used or for patients for whom IMRT is not a viable option.

In this study, we compared four different 3DCRT techniques to explore the optimal conformal plan with the goal to achieve the lowest radiation exposure to the OAR. These treatment techniques were (1) standard, (2) diamond shape, (3) alternate diamond shape and (4) V-shape.

The primary aim of this study was to determine which of the four planning techniques achieved the lowest percentage of NRB volume that receives 40 Gy (NRB V40). The secondary aims were comparison among different techniques in terms of (1) radiation dose to genitalia (V40), bladder (mean dose) and femoral heads (V40), (2) differences in NRB (V40) and genitalia (V40) between genders and (3) the impact of the depth of the inguinal nodes in NRB (V40) dose.

Methods

This project was reviewed and approved by the research review panel of our institution. Fifteen computed tomography (CT) data sets from patients with anal cancer stage T2–3Nx previously treated with radical chemoradiotherapy in 2008–2010 were randomly selected. Age range was 43–91-years old with a mean of 61. Inclusion criteria included patients with a diagnosed localised squamous cell anal carcinoma who had previously received a course of concurrent chemoradiotherapy with

curative intent. The treatment and simulation set up protocol was unchanged in the study period.

Simulation

The standard protocol for planning CTs was used with scans acquired in a large-bore Philips Brilliance CT scannerTM (Philips Medical Systems, Best, the Netherlands), and axial images taken from iliac crest to 2–5 cm below the perineum with 3 mm × 3 mm slices. Patients were stabilised in a frog leg supine position and asked to have a comfortably full bladder but no specific instruction on bowel preparation was given.

Patients whose bladder volume had less than 80 cm³ of volume when measured on the planning computer system FocalTM (XiO, Elekta AB, Stockholm, Sweden) were excluded.

Contouring

All CT data sets were de-identified. The data sets were re-contoured on a FocalTM (XiO, Elekta AB) workstation by a radiation oncologist (RO) from the Gastrointestinal (GI) unit of the institute according to the AGITG anal cancer contouring guidelines.¹⁰ For this study, all data sets of the patients were assumed to have bilateral inguinal nodal disease stage N3, and they were contoured accordingly.

The gross tumour volume (GTV) of the primary anal cancer was delineated based on pre-treatment CT, magnetic resonance imaging (MRI) or positron emission tomography (PET). In addition, all data sets had bilateral inguinal nodes contoured with a 10 mm added margin as inguinal GTV.

The clinical target volume for 36 Gy (CTV36Gy) included anal GTV, the whole anal canal, internal and external anal sphincters with a 10–20 mm margin, ischiorectal fossa, mesorectum, presacral space, internal and external iliac nodes, obturator nodes, and bilateral inguinal regions. A 10-mm margin was added to any enlarged nodes to account for microscopic invasion, respecting anatomical soft tissue and bone boundaries. For CTV45Gy, the superior extent was reduced to 10-mm inferior to the lower sacroiliac joint, or 10-mm above the most proximal enlarged pelvic node, whichever was most superior. The CTV54Gy included all GTV with a 10 mm added margin.

A 10-mm uniform margin was added to each CTV to generate respective PTVs (PTV36Gy, PTV45Gy and PTV54Gy).

OAR NRB and bladder were contoured by one RO with femoral heads and genitalia contoured by one radiation therapist. Femoral heads were contoured from

the superior border of the femoral head to the inferior border of the ischial tuberosities. NRB was contoured from where rectum ceases at the rectosigmoid junction, to 1.5-cm superior to the pelvic PTV36Gy, wall to wall in loops.¹² Bladder was contoured using the external bladder wall. Genitalia in females had the external vulva contoured, whilst males had the penis and scrotum contoured.

Planning techniques

The four treatment techniques were planned for each data set by the same radiation therapist on a XIO V4.4 (XiO, Elekta AB) planning workstation, using fast superposition algorithm for the photon beams, pencil beam algorithm for the electron beams and 3-mm calculation grid. The total tumour dose was 54 Gy in 1.8 Gy/fraction, with PTV36Gy (Phase 1) receiving 36 Gy, PTV45Gy (Phase 2) receiving 9 Gy and PTV54Gy (Phase 3) receiving 9 Gy. The primary aim of the plans was dose homogeneity across each PTV of -5% to $+7\%$, max dose of 110% in accordance with the International Commission on Radiation Units (ICRU) guidelines and minimise dose to OAR, especially NRB.^{13,14}

The standard technique (as shown in Fig. 1A) consisted of an anterior and posterior (AP/PA) beam for Phase 1 (PTV36Gy) using a mixture of 18 or 6 MV photons dependent on the size of the patient. Phase 2 and 3 (PTV45Gy and PTV54Gy) utilised a three-field technique: a posterior field usually 6 MV and two lateral 18 MV fields to reduce dose to the anterior OAR. Phase

2 and 3 also included anterior electron fields to boost the right and left inguinal nodes, with the electron energy chosen to cover the PTV posteriorly.

The diamond shape technique (Fig. 1B) was described by Vuong et al. in 2003 and consisted of a split field technique where the junction occurs at the cranial extent of the inguinal nodes. Inferior to the junction, the lower technique in Phase 1 and 2 consisted of two anterior obliques and two posterior obliques each covering PTV36Gy and PTV45Gy with concurrent electron beams to the inguinal nodes, with appropriate electron energy required and weighted to cover the PTV by 95% of the dose. The intent of the oblique angled beams was to reduce the dose to the midline structures. Superior to the junction, the technique used AP/PA beams. Phase 3 of this technique is the same as the standard technique using three fields and electrons to boost the inguinal nodes.

The third technique investigated was the alternate diamond shape (Fig. 1C). This technique was adapted from Bui et al.¹⁵ Similar to the diamond shape technique described by Vuong et al.,¹ it uses four opposing oblique fields, forming a diamond configuration to cover the PTV36Gy and PTV45Gy inferiorly, with AP/PA fields to the superior portion of the PTV. Rather than using electron fields to boost the inguinal node area as utilised in the diamond shape technique, the alternate diamond shape technique used two additional, off-axis anterior oblique fields to boost the inguinal PTV to the required dose. Phase 2 and 3 used either the same arrangement as Phase 1, or the three-field arrangement described in both previous techniques.

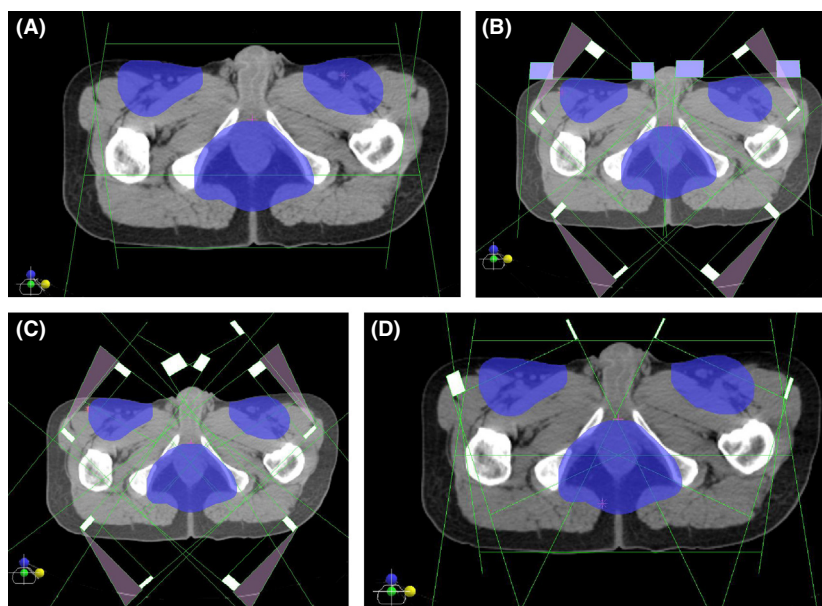


Figure 1. (A) Standard technique. (B) Diamond technique. (C) Alternate diamond technique. (D) V-shape technique.

Table 1. PTV and OAR dosimetry measures.

Dosimetry measure	Definition
PTV36Gy- 95% (%)	The percentage of the PTV36Gy volume covered by 95% of the dose
PTV45Gy- 95% (%)	The percentage of the PTV45Gy volume covered by 95% of the dose
PTV 54Gy -95% (%)	The percentage of the PTV54Gy volume covered by 95% of the dose
NRB V40 (%)	The percentage of NRB that receives 40 Gy
Genitalia V40 (%)	The percentage of genitalia that receives 40 Gy
Mean bladder dose (Gy)	Mean dose to the bladder
Right femur V40 (%)	The percentage of the right femoral head that receives 40 Gy
Left femur V40 (%)	The percentage of the left femoral head that receives 40 Gy

PTV, planning target volume; OAR, organs at risk; NRB, non-rectal bowel.

The fourth technique analysed is the V-shape (Fig. 1D). Phase 1 used two anterior oblique beams, an anterior field and a posterior field to cover PTV36Gy. The oblique fields achieve a V-shape dose distribution and provide sparing of dose to midline structures. Phase 2 and 3, for PTV45Gy and PTV54Gy, respectively, used the three-field technique described previously with electrons to boost the inguinal nodes.

Data collection

Organ at risk dosimetry measures (Table 1) were collected for every plan using cumulative dose volume histograms (DVH) from XIO™ and Focal™

Statistical considerations

Power and sample size considerations

Although no formal hypothesis was tested, the following sample size assessment indicates how much precision a sample size of 15 patients yields. Using a matched-pairs t-test, it is possible to detect an effect size of 0.78 with a power of 0.8 allowing for a two-sided alpha value (i.e., risk of type I error) of $P < 0.0005$. This means that to be able to detect a difference between the techniques with probability of 0.8, the mean difference between the techniques would have to be at least 0.78 times the standard deviation of the difference in the pairwise-matched measurements.

Primary and first secondary aims

Repeated measures Analysis of Variance (RM-ANOVA) was used to test for the existence of any overall

differences between the four planning techniques for all PTV and OAR dosimetry measures requiring comparison in Table 1. Greenhouse-Geisser corrected p-values were provided to account for non-sphericity in the data (non-equality of the variances of the differences between pairs of techniques).

Data were tested for significant non-adherence to the assumptions of the repeated measures ANOVA using the Shapiro–Wilks test to test the normality of the residuals.¹⁶ If the Shapiro–Wilks test showed significant departure from normality, as evidenced by a $P < 0.0005$, then the analysis was repeated using a variance stabilising transformation (namely the log transformation). If, even in the presence of such a variance stabilising log transformation, the data still exhibited significant non-adherence to assumptions, then the non-parametric Friedman test was used instead of the RM-ANOVA test.¹⁷ In each case, differences between pairs of techniques were tested using the corresponding pairwise test–matched paired t-tests on either the raw data or log transformed data in the case of RM-ANOVA, and the Wilcoxon test in the case of the Friedman test.

Second and third secondary aims

The comparison of the NRB V40 and the genitalia V40 between the four planning techniques was repeated with males and females considered separately, to determine if there was a technique that was more suited to either group. Data were also grouped into those patients with PTV inguinal node depth >6.5 cm and those with inguinal node depth ≤ 6.5 cm due to the increased difficulty of dose coverage with deeper nodes. The comparison of the NRB V40 between the four planning techniques was repeated for these two sub-groups and considered separately.

For both of these subset analyses, the statistical techniques used were the same as those used to address the primary and first secondary aims above.

Results

The 15 patient samples consisted of five males and 10 females. Four patients with inguinal node depth >6.5 cm and 11 patients with inguinal node depth ≤ 6.5 cm.

Comparison of PTV measures among four techniques showed statistically significant difference for PTV45Gy-95% only ($P = 0.003$) (Table 2A). Pairwise tests were performed for PTV45Gy-95% coverage (Table 2B), which shows the standard technique resulted in a slightly higher percentage coverage (99.1% SD 0.07), and the alternate diamond technique resulted in a slightly lower percentage coverage (98.7% SD 1.1) than the other techniques, resulting in a pairwise difference of $P = 0.002$.

Table 2. Comparison of (A) planning target volume (PTV) dosimetry measures and (B) pairwise differences between planning techniques for which there was a significant overall difference between the planning techniques.

Dosimetry measure	Overall <i>P</i> -value	Test type	Mean values (and SD's) for each planning technique			
			Diamond	Standard	Alternate diamond	V-shape
(A) Comparison of PTV measures						
PTV36Gy- 95% (%)	0.126	RM-ANOVA	99.8 (0.18)	99.8 (0.13)	99.7 (0.23)	99.7 (0.21)
PTV45Gy- 95% (%)	0.003	Friedman	98.9 (0.84)	99.1 (0.70)	98.7 (1.1)	98.9 (0.97)
PTV54Gy- 95% (%)	0.273	Friedman	98.2 (2.4)	98.6 (2.1)	98.0 (2.5)	98.1 (3.2)
<i>P</i> -values for pairwise differences between planning techniques						
Dosimetry measure	Diamond vs. standard	Diamond vs. alternate diamond	Diamond vs. V-shape	Standard vs. alternate diamond	Standard vs. V-shape	Alternate diamond vs. V-shape
(B) Comparison of pairwise difference for PTV45Gy- 95%						
PTV45Gy- 95% (%)	0.031	0.011	0.887	0.002	0.073	0.025

SD, standard deviation; PTV, planning target volume.

Table 3A shows the comparison of OAR dosimetry measures for the primary aim of NRB V40 and the first of the secondary aims of genitalia V40, mean bladder dose and V40 for the femurs, across the four planning techniques. Table 3B shows pairwise comparisons between planning techniques for the OAR dosimetry measures. The following conclusions can be drawn from A and B. The V-shape technique achieves significantly lower values of NRB V40 (mean 59.6%) than all other

planning techniques. For the genitalia V40, the diamond technique (mean 26.4%) and the alternate diamond technique (mean 27.6%) achieve significantly lower dose than the V-shape technique (mean 43.2%), which in turn achieves significantly lower dose than the standard technique (mean 76.1%). The V-shape technique achieved the lowest mean bladder doses (mean 45.3 Gy). The diamond technique achieved the lowest femur V40 doses (means 32.3% and 32.4%), being significantly lower than

Table 3. Comparison of (A) OAR dosimetry measures and (B) pairwise differences between planning techniques.

Dosimetry measure	Overall <i>P</i> -value	Test type	Mean values (and SD's) for each planning technique			
			Diamond	Standard	Alternate diamond	V-shape
(A) Comparison of OAR dosimetry measures						
NRB V40 (%)	0.032	RM-ANOVA	63.8 (13)	63.8 (11)	63.6 (12)	59.6 (11)
Genitalia V40 (%)	<0.001	RM-ANOVA	26.4 (20)	76.1 (16)	27.6 (20)	43.2 (26)
Mean bladder dose (Gy)	<0.001	Friedman	48.0 (2.1)	46.2 (2.1)	46.5 (2.7)	45.3 (1.4)
Right femur V40 (%)	<0.001	RM-ANOVA	32.3 (13)	70.8 (17)	58.1 (15)	63.7 (17)
Left femur V40 (%)	<0.001	RM-ANOVA	32.4 (13)	75.0 (16)	54.9 (16)	63.1 (18)
<i>P</i> -values for pairwise differences between planning techniques						
Dosimetry measure	Diamond vs. standard	Diamond vs. alternate diamond	Diamond vs. V-shape	Standard vs. alternate diamond	Standard vs. V-shape	Alternate diamond vs. V-shape
(B) Comparison of pairwise differences between planning techniques						
NRB V40 (%)	0.99	0.841	0.046	0.861	0.005	0.029
Genitalia V40 (%)	<0.001	0.118	0.008	<0.001	<0.001	0.011
Mean bladder dose (Gy)	0.003	<0.001	0.001	0.208	0.018	0.008
Right femur V40 (%)	<0.001	<0.001	<0.001	0.059	<0.001	0.387
Left femur V40 (%)	<0.001	<0.001	<0.001	0.004	0.003	0.116

NRB, non-rectal bowel; V40, percentage of OAR that receives 40 Gy; OAR, organs at risk.

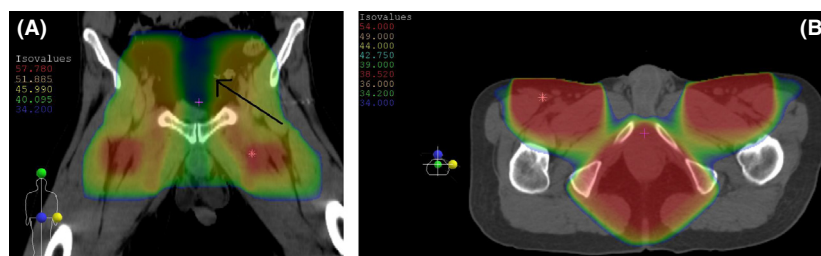


Figure 2. (A) V-Shape technique. Coronal view showing sparing of bladder and NRB with lower dose regions in blue as indicated by arrow. (B) Diamond technique showing dose colourwash of the inferior technique and resultant sparing achieved of genitalia and femurs.

other techniques ($P < 0.001$ for all comparisons). (Fig. 2A and B).

Results of comparison of NRB V40 and genitalia V40 for the male and female subsets appear in Table 4. The NRB V40 dose was smallest for the V-shape technique for both male and female patients, but was not statistically significant. For both female and male patients, the diamond and alternate diamond techniques achieved lower doses to the genitalia V40 than the V-shape and the standard techniques. In Table 5, the comparison of NRB V40 for patients both with and without inguinal node depth >6.5 cm appears. This shows that for patients with inguinal node depth >6.5 cm, the V-shape technique achieved lower NRB V40 doses than any other techniques. For patients with inguinal node depth ≤ 6.5 cm, there was no significant difference in NRB V40 between the four techniques.

Discussion

The radiotherapy treatment fields for anal canal cancer encompass many OAR, which make achieving an optimal plan particularly challenging. However, as the bladder and NRB are organs that are in the superior half of the field,

and the femurs and genitalia are in the lower half of the treatment field, it is feasible to use different arrangements of beams to treat the superior and inferior portions of the PTV. We found that the best technique to reduce dose to the bladder and NRB was the V-shape whilst the diamond shape gave the least dose to the femurs and genitalia. One plan alone could not reduce dose to all OAR.

The OAR dosimetry endpoints of this study were pre-determined before commencement of the study. Treatment breaks are often necessary in anal carcinoma patients due to the acute toxicities that occur to the OAR in the treatment area.^{8,18} To reduce treatment breaks, it is necessary to reduce dose to these organs.¹ Although the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) report has given recommended dose/volume limits for some OAR that are relevant to anal cancer, the exact dose response relationships for genitalia or bladder remains unclear.^{19–21} So the dose constraints used have been a mix of clinically proven ones^{1,12} and ones derived from experience and results in the literature.^{2,22} With so many OAR in close proximity to the PTV, there is great difficulty in achieving the recommended dose constraints when treating anal cancer.

Table 4. Comparison of non-rectal bowel (NRB) V40 and Genitalia V40 across planning techniques for the five male and 10 female patients.

Dosimetry Measure	RM-ANOVA <i>P</i> -value	Friedman test <i>P</i> -value	Mean values (and SD's) for each planning technique			
			Diamond	Standard	Alternate diamond	V-shape
(A) Male						
NRB V40 (%)	0.361	0.733	63.2 (14)	64.0 (9.0)	63.0 (14)	58.7 (9.4)
Genitalia V40 (%)	0.001	0.003	9.72 (14)	61.0 (20)	10.2 (12)	29.1 (27)
(B) Female						
NRB V40 (%)	0.095	0.733	64.0 (14)	63.7 (12)	63.8 (12)	60.1 (12)
Genitalia V40 (%)	<0.001	0.003	34.7 (17)	83.7 (7.3)	36.3 (17)	50.3 (24)

Results of comparisons of important dosimetry measurements between planning techniques. Although all tests satisfied the conditions for a parametric analysis (RM-ANOVA), due to the small sample sizes, the results of the non-parametric Friedman test are provided for confirmation. (*P*-values tend to be somewhat larger, reflecting the decreased power associated with non-parametric tests). NRB, non-rectal bowel; V40, percentage of OAR that receives 40 Gy; OAR, organs at risk.

Table 5. Comparison of non-rectal bowel (NRB) V40 across planning techniques for patients both with and without inguinal node depth >6.5 cm.

Sub-group	RM-ANOVA <i>P</i> -value	Friedman test <i>P</i> -value	Mean values (and SD's) for each planning technique			
			Diamond	Standard	Alternate diamond	V-shape
Inguinal node depth >6.5 cm	0.022	0.044	72.8 (6.9)	71.2 (8.9)	70.8 (8.8)	63.1 (9.2)
Inguinal node depth ≤6.5 cm	0.368	0.629	60.4 (14)	61.1 (11)	60.9 (13)	58.4 (11)

Results of comparisons of important dosimetry measurements between planning techniques. Although all tests satisfied the conditions for a parametric analysis (RM-ANOVA), due to the small sample sizes, the results of the non-parametric Friedman test are provided for confirmation. (*P*-values tend to be somewhat larger, reflecting the decreased power associated with non-parametric tests.)

Reducing the dose as much as possible to OAR is the aim of 3D conformal treatment planning, as for this group of patients in particular, it can have an impact on reduced toxicities, treatment breaks and increased local regional control (LRC).¹¹

NRB is one OAR that does have defined dose/volume limits, and associated toxicity of severe enteritis if dose constraints are not met.^{2,20} Therefore, dose received by the NRB was used as the primary objective when analysing the data produced in this study, as it is known that if toxicity is reduced to this organ this in turn may result in fewer treatment breaks and higher rates of LRC.

Addressing the primary objective, results indicate that the V-shape achieved lower mean NRB V40 than the standard (mean values 59.6% vs. 63.8%). Both the diamond shape and the alternate diamond shape had higher NRB V40 values than the standard.

NRB V40 was further investigated and the data sets split into two different groups of depth of the inguinal node PTV, as deeper node depth makes it more difficult to achieve dose coverage and can lead to a higher NRB dose. For patients with depth >6.5 cm (*n* = 4) the V-shape achieved lower NRB V40 doses than any other technique as shown in Table 5, however, for patients with depth <6.5 cm (*n* = 11), there was no significant difference between the four techniques analysed.

Whilst overall the V-shape achieves the best NRB V40, results demonstrate it is superior to the other three plans when the depth of the inguinal PTV is >6.5 cm. As only four out of the 15 patient data sets had inguinal PTVs with a depth greater than 6.5 cm, these results are not conclusive for all patients. However, they do give a clear indication that the V-shape may benefit this group of patients, but further investigation with a larger sample would be required to confirm this.

There could therefore be an argument that for patients whose inguinal node PTV depth is ≤6.5 cm, AP/PA would be suitable to use for the superior portion of the PTV. However, the other benefit to the V-shape is the lower mean bladder dose it achieved when compared

with the other three plans, which is not related at all to the depth of the inguinal node PTV.

Other proven dose toxicity data that exists for this group of patients is dose to femurs and the relationship with bone fractures.^{4,23} The diamond shape delivered the significantly lowest dose to the femurs. This is extremely important as by reducing the dose to this OAR, the risk of late toxicities would also reduce. The diamond shape, along with the alternate diamond technique also delivered the least dose to the genitalia. Whilst we do not have evidence from clinical trials of the dose acceptable for genitalia, from clinical experience of the skin reactions that occur in this area, any reduction of dose will only benefit the patient.

This study found that different arrangements of beams in the superior and inferior portions of the PTV would reduce dose to OAR. As the diamond shape technique utilised an AP/PA field arrangement for the superior portion of the PTV, replacing this with the V-shape beam arrangement would further reduce dose to OAR. A potential future study will be to compare this 'best fit' 3DCRT plan with IMRT in terms of radiation dose to OAR.

The limitations of this study are low patient numbers, an uneven mix of male to female cases and varying depths of inguinal nodes. However, for departments electing to treat with 3DCRT, or needing to due to the patient or tumour size, it does provide valuable information on the benefits of the differing techniques.

Conclusion

Sophisticated 3DCRT techniques are superior to 'simple' conventional techniques. Different 3DCRT techniques provide varying levels of dose reduction to OAR, with none of the four techniques investigated capable of reducing dose to all OAR. A combination of the diamond shape and V-shape techniques may provide the best solution. Further refinement of these techniques should be explored.

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Conflict of Interest

The authors declare no conflict of interest.

References

- Vuong T, Devic S, Belliveau P, Muanza T, Hegyi G. Contribution of conformal therapy in the treatment of anal cancer carcinoma with combined chemotherapy and radiotherapy: results of a Phase II study. *Int J Radiat Oncol Biol Phys* 2003; **56**: 823–31.
- Menkarios C, Azria D, Laliberté B, et al. Optimal organ-sparing intensity-modulated radiation therapy (IMRT) regimen for the treatment of locally advanced anal canal carcinoma: a comparison of conventional and IMRT plans. *Radiat Oncol* 2007; **2**: 41.
- Cummings B, Keane T, Thomas G, Harwood A, Rider W. Results and toxicity of the treatment of anal canal carcinoma by radiation therapy or radiation therapy and chemotherapy. *Cancer* 1984; **54**: 2062–8.
- Tomaszewski J, Link E, Leong T, et al. Twenty-Five year experience with radical chemoradiation for anal cancer. *Int J Radiat Oncol Biol Phys* 2012; **83**: 552–8.
- Ortholan C, Resbeut M, Hannoun-Levi JM, et al. Anal canal cancer: management of inguinal nodes and benefit of prophylactic inguinal irradiation (CORS-03 Study). *Int J Radiat Oncol Biol Phys* 2012; **82**: 1988–95.
- Matthews J, Burmeister B, Borg M, et al. T1-2 anal carcinoma requires elective inguinal radiation treatment – The results of Trans Tasman Radiation Oncology Group study TROG 99.02. *Radiother Oncol* 2011; **98**:93–8.
- Weber D, Kurtz J, Allal A. The impact of gap duration on local control in anal carcinoma treated by split-course radiotherapy and concomitant chemotherapy. *Int J Radiat Oncol Biol Phys* 2001; **50**: 675–80.
- Bartelink H, Roelofsen F, Eschwege F, et al. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. *J Clin Oncol* 1997; **15**: 2040–9.
- John M, Pajak T, Flam M, et al. Dose escalation in chemoradiation for anal cancer: preliminary results of RTOG 92-08. *Cancer J Sci Am* 1996; **2**: 205–11.
- Ng M, Leong T, Chander S, et al. Australasian Gastrointestinal Trials Group (AGITG) contouring atlas and planning guidelines for intensity-modulated radiotherapy in anal cancer. *Int J Radiat Oncol Biol Phys* 2012; **83**: 1455–62.
- Kachnic L, Winter K, Myerson R, et al. RTOG 0529: a Phase 2 evaluation of dose-painted intensity modulated radiation therapy in combination with 5-Fluorouracil and Mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal. *Int J Radiat Oncol Biol Phys* 2013; **86**: 27–33.
- Devisetty K, Mell L, Salama J, et al. A multi-institutional acute gastrointestinal toxicity analysis of anal cancer patients treated with concurrent intensity-modulated radiation therapy (IMRT) and chemotherapy. *Radiother Oncol* 2009; **93**: 298–301.
- International Commission on Radiation Units and Measurements: Prescribing, recording and reporting photon beam therapy. In ICRU Report, 50. ICRU Publications, Bethesda, MD, 1993.
- International Commission on Radiation Units and Measurements: Prescribing, recording and reporting photon beam therapy (Supplement to ICRU report 50). In ICRU Report, 62. ICRU Publications, Bethesda, MD, 2000.
- Bui T, Harvey J, Brown E, Scott M, Haines T, Davidson K. Conformal external beam radiotherapy in the treatment of anal canal carcinoma: a retrospective study of a genital organ sparing technique. *J Med Imaging Radiat Oncol* 2009; **53**: 396–404.
- Shapiro S, Wilk M. An analysis of variance test for normality (Complete Samples). *Biometrika* 1965; **52**: 591–611.
- Friedman M. The use of ranks to avoid the assumption of normality implicit in the analysis of variance. *J Am Stat Assoc* 1937; **32**: 675–701.
- Allal A, Mermillod B, Roth A, Marti MC, Kurtz J. The impact of treatment factors on local control in T2–T3 anal carcinomas treated by radiotherapy with or without chemotherapy. *Cancer* 1997; **79**: 2329–35.
- QUANTEC report. *Int J Radiat Oncol Biol Phys* 2010; **76** (Suppl.): S1–160.
- Kavanagh B, Pan C, Dawson L, et al. Radiation dose–volume effects in the stomach and small bowel. *Int J Radiat Oncol Biol Phys* 2010; **76**(Suppl.): S101–7.
- Viswanathan A, Yorke E, Marks L, Eifel P, Shipley W. Radiation dose–volume effects of the urinary bladder bowel. *Int J Radiat Oncol Biol Phys* 2010; **76**(Suppl.): S116–22.
- Mell L, Schomas D, Salama J, et al. Association between bone marrow dosimetric parameters and acute hematologic toxicity in anal cancer patients treated with concurrent chemotherapy and intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2008; **70**: 1431–7.
- Myerson R, Outlaw E, Chang A, et al. Radiotherapy for epidermoid carcinoma of the anus: thirty years' experience. *Int J Radiat Oncol Biol Phys* 2009; **75**: 428–35.