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Original Research Article

Acute enteritis with pelvic SBRT: Influence of bowel delineation methods

Akshay Dinesan, Maneesh Singh, Prachi Mehta, Priyamvada Maitre, Vedang Murthy *

Department of Radiation Oncology, Tata Memorial Hospital and Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Homi Bhabha National Institute (HBNI), Mumbai, India

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ABSTRACT

Purpose: One fourth of the patients receiving SBRT to prostate and pelvis develop mild to moderate acute enteritis. In this study, we aim to study bowel dosimetry for different methods of bowel delineation in patients with and without acute bowel toxicity after whole-pelvic SBRT (WP-SBRT).

Methods and materials: In this prospective study, patients with high-risk prostate cancer treated with WP-SBRT were identified. Patients with acute bowel toxicity (CTCAE v5.0) were included as cases while those without were controls. All the patients had previously received 35–36.25 Gy in 5 fractions to the prostate and 25 Gy in 5 fractions to the pelvis. The bowel was contoured on the planning CT scan using seven different methods, namely- bowel bag (BB), small bowel loop (SB), large bowel loop (LB), combined bowel loop (BL) and bowel loops with margins (BL + 0.5 cm, BL + 1 cm and BL + 1.5 cm). The original clinically used plan was applied to all the contouring methods and dose-volume parameters studied.

Results: A total of 102 patients treated with WP-SBRT were screened and only those with properly documented acute toxicity were included for further analysis. While none of the patients had grade 3 bowel toxicity, 23 (22.5 %) patients had grade 1–2 acute enteritis, and 23 patients without were selected as cases and controls respectively. On visual assessment, the composite dose volume histogram (DVH) were similar for cases and controls for all the delineation methods studied. Objectively, the volume of the bowel structures receiving 7 Gy, 14 Gy, and 25 Gy did not show any statistically significant difference between cases and controls. One in five patients treated with WP-SBRT using bowel bag dose constraints of $V_7 < 1500$ cc, $V_{14} < 500$ cc and $V_{25} < 50$ cc had acute enteritis.

Conclusion: There was no significant difference in planned bowel doses for different bowel delineation methods in patients with prostate cancer treated with WP-SBRT with or without acute bowel toxicity.

Introduction

Stereotactic body radiotherapy or ultra-hypofractionated radiotherapy has emerged as safe and effective treatment for patients with intermediate risk prostate cancer [1,2]. A handful of phase 2 studies have also shown safety and efficacy of SBRT in high-risk prostate cancer patients and randomised evidence is emerging (PRIME, NCT03561961) [3]. The POP-RT trial established prophylactic pelvic radiotherapy, using moderate hypofractionation, as the standard of care in high-risk prostate cancer [4]. The move to whole pelvic SBRT (WP-SBRT) however has been cautious given the concern for bowel toxicity especially with the cranial shift of the superior pelvic contour border to the aortic bifurcation for coverage of the common-iliac nodal region [5,6].

While there is reasonable data for planning dose constraints for organs at risk like bladder, rectum and urethra, bowel constraints have not been adequately reported for pelvic SBRT. The HYTEC organ specific paper for prostate cancer, has included rectal toxicity alone in the bowel domain and there is no mention of constraints for enteritis [7]. In addition, bowel contouring is not yet standardised for SBRT. Historically, bowel bag contouring has remained the common practice for conventional fractionation, owing to the ease of delineation. However, the lack of consensus in bowel delineation for pelvic SBRT is evident from the fact that two large ongoing randomised control trials have different definitions for bowel delineation. The PRIME trial (NCT03561961) has recommended contouring bowel bag while the PACE-NODES trial (NCT05613023) comparing prostate-alone SBRT with prostate and pelvic SBRT in patients of high-risk prostate cancer recommends contouring individual bowel loop.

The lack of consensus in delineation of bowel and the unavailability of bowel constraints are challenges in planning WP-SBRT. Standardised

* Corresponding author at: Tata Memorial Hospital, Dr Ernest Borges Road, Parel, Mumbai, Maharashtra, India.
E-mail address: vmurthy@actrec.gov.in (V. Murthy).

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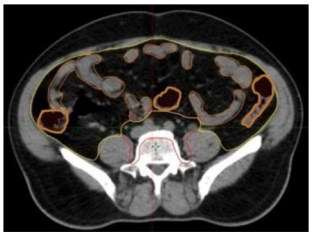
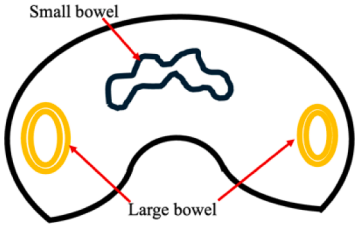
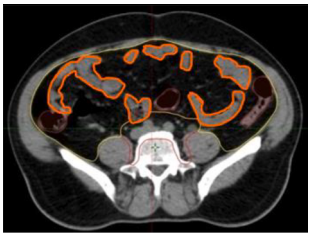
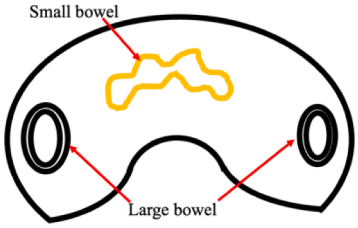
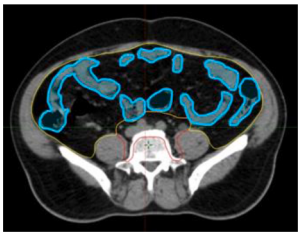
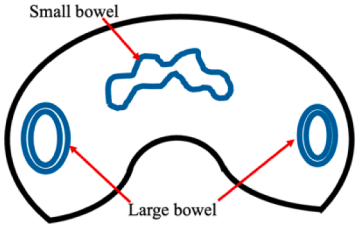
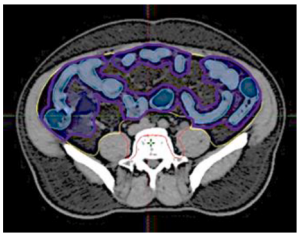
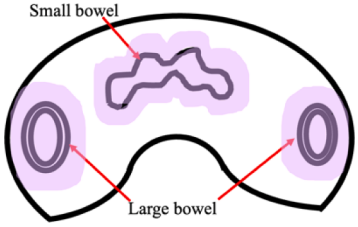
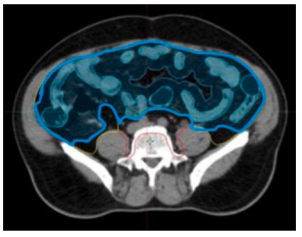
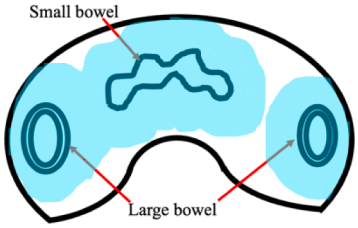
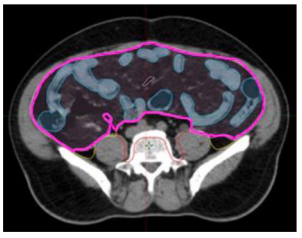
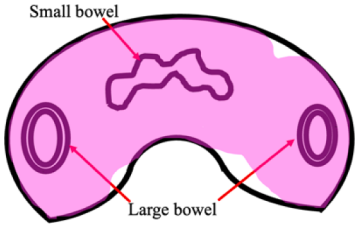
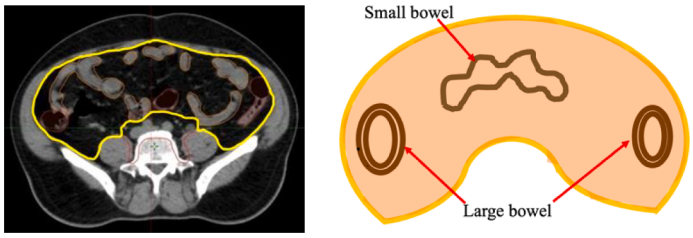
Table 1
Methods of bowel delineation.

Bowel structure	Contouring	Image	
Large bowel loop (LB)	Large bowel loops is contoured caudally from the rectosigmoid junction till 5 cm above the pelvic nodal PTV.		
Small bowel loop (SB)	Small bowel loops alone is contoured caudally from the most inferior small bowel loop till 5 cm above the pelvic nodal PTV.		
Combined bowel loop (BL)	Boolean operation of small and large bowel loop structures is done to generate the combined bowel loop.		
Bowel loop + 0.5 cm (BL + 0.5 cm)	Combined bowel loop is isometrically expanded by 0.5 cm, after which the portion extending beyond bowel bag is cropped out.		
Bowel loop + 1 cm (BL + 1 cm)	Combined bowel loop is isometrically expanded by 1 cm, after which the portion extending beyond bowel bag is cropped out.		
Bowel loop + 1.5 cm (BL + 1.5 cm)	Combined bowel loop is isometrically expanded by 1.5 cm, after which the portion extending beyond bowel bag is cropped out.		

(*continued on next page*)

Table 1 (*continued*)

Bowel structure	Contouring	Image
Bowel bag (BB)	Bowel bag is contoured starting caudally from the most inferior location of bowel or the rectosigmoid junction (whichever is most inferior) till 5 cm above the superior edge of the pelvic nodal PTV, which was then cropped from the nodal PTV except at places where bowel was seen extending into the nodal PTV.	

contouring, evaluation and reporting of bowel dosimetry are crucial for improving safety of WP-SBRT. To this end, we have analysed the relationship between acute bowel toxicity and the planned bowel dose for different methods of bowel delineation in patients with prostate cancer treated with WP-SBRT.

Methods and materials

In this prospective case-control study approved by the institutional ethics committee (TMC IEC-III, project no. 900880), patients of high-risk prostate cancer who had developed acute bowel toxicity of any grade during or within three months of receiving SBRT to prostate and pelvis were identified as 'cases' from the prospectively maintained institutional database. Our goal was to select patients who could unambiguously serve as cases and controls. This was based on proper documentation of acute enteritis symptoms including carefully differentiating between proctitis (excluded) and enteritis (included) for selecting cases. Upon careful review of 102 patients, we found 23 patients who had well documented acute enteritis (cases), and 25 patients without any symptoms of enteritis. Of these 25 patients, 23 consecutive patients were chosen as controls. None of the patients has infectious or inflammatory bowel disease at baseline assessment. For the purpose of this study, CTCAE v5.0 was used to grade acute bowel toxicity (abdominal pain, abdominal distension, constipation, diarrhoea etc.) recorded during clinical review. Patients with acute rectal toxicity (proctitis) in the absence of bowel toxicity were not included as cases.

Planning CT scan was available for all patients, which was acquired without intravenous and oral contrast in supine position after ensuing bladder protocol and ensuring empty rectum. All the patients had received SBRT to prostate to a dose of 35–36.25 Gy and pelvis to a dose of 25 Gy respectively in 5 fractions delivered every alternate day by volumetric modulated arc therapy (VMAT) using 6MV or 10MV photons. All patients had bowel bag contoured as per institutional protocol. Plans were optimised for the bowel bag as per ALARA (as low as reasonably achievable) principle.

In the present study, planning CT scan was retrieved. For all patients (cases and controls), bowel was contoured using seven different methods as described in Table 1. All the contouring was done by the first author (AD) and verified by a senior radiation oncologist with over 20 years of experience in treating prostate cancer (VM). The original clinically used plan was applied and the dose-volume parameters for different bowel contours were recorded from the Eclipse version15.1 treatment planning system. Mean bowel volume receiving a particular dose was calculated for each bowel structure for the two cohorts and used to generate composite dose volume histogram (DVH) by plotting the dose in x-axis against the mean bowel volume receiving a particular dose (meanV_{xGy}; x = dose) in the y-axis. The DVH was generated for cases and controls for each of the seven method of bowel delineation. Further, the bowel doses for patients with and without acute bowel toxicity were objectively analysed by comparing V_{7Gy}, V_{14Gy} and V_{25Gy} for each of the seven volumes.

Patient demographics were summarized using descriptive statistics. Mann-Whitney *U* test was used to compare V_{7Gy}, V_{14Gy} and V_{25Gy} for each of the seven methods of bowel delineation for patients with and without bowel toxicity. A p-value of less than 0.05 was considered statistically significant.

Table 2
Patient characteristics.

		Case (n = 23)	Control (n = 23)
Median age in years with IQR		68 (62–73)	71 (62–74)
Charlson index	1–2	0	1 (4 %)
	3–4	9 (39 %)	7 (31 %)
	5 or more	14 (61 %)	15 (65 %)
ISUP grade group	GG4 or less	18 (68 %)	16 (70 %)
	GG5	5 (22 %)	7 (30 %)
T stage	T1-T2c	6 (26 %)	6 (26 %)
	T3a-T4	17 (74 %)	17 (74 %)
N stage	N0	9 (39 %)	2 (9 %)
	N1	14 (61 %)	21 (91 %)
M stage	M0	18 (78 %)	19 (83 %)
	M1	5 (22 %)	4 (17 %)
ADT	Medical	21 (91 %)	18 (78 %)
	Surgical	2 (9 %)	5 (22 %)

IQR- Interquartile range, ISUP- International Society of Urological Pathology, GG4- (Gleason) grade group 4, GG5- (Gleason) grade group 5, ADT- androgen deprivation therapy.

Results

A total of 102 patients with high-risk prostate cancer treated with WP-SBRT were screened. Of these, 48 patients had well documented acute bowel toxicity. Twenty-three (22.5 %) patients had grade 1–2 acute enteritis and were included as cases and 23 consecutive patients from the 25 without acute enteritis were included as controls. The two groups were comparable with respect to demographic variables, disease factors and clinical characteristics as summarized in Table 2. All the patients received SBRT to prostate and pelvis delivered on alternate days, over a median duration of 10 days. All patients received long term androgen deprivation therapy (ADT) for a median duration of 24 months. None of the patients in this study had grade 3 or worse acute bowel toxicity. Of the 23 patients with bowel toxicity, 12 (52 %) patients had grade 1 diarrhea, and 11 (48 %) patients had grade 2 diarrhea as per CTCAE v5.0.

The median volume of each bowel structure contour in the ascending order of volume is shown in Fig. 1, with large bowel loop (median volume of 328 cc for cases and 271 cc for controls) being the smallest and bowel bag (median volume of 3088 cc for cases and 2867 cc for controls) being the largest structures. There was no statistically significant difference in the volume of bowel among cases and controls by any of the bowel contouring method. The composite DVH for cases and controls along with the 95 % confidence interval are shown in Fig. 2 **(a-g)**. On visual assessment the DVH were similar for both cases and controls for all the delineation methods studied. Objectively, the volume of the bowel structures receiving 7 Gy, 14 Gy and 25 Gy did not show any statistically significant difference between cases and controls for any of the seven methods of delineation (Table 3). A comparison between

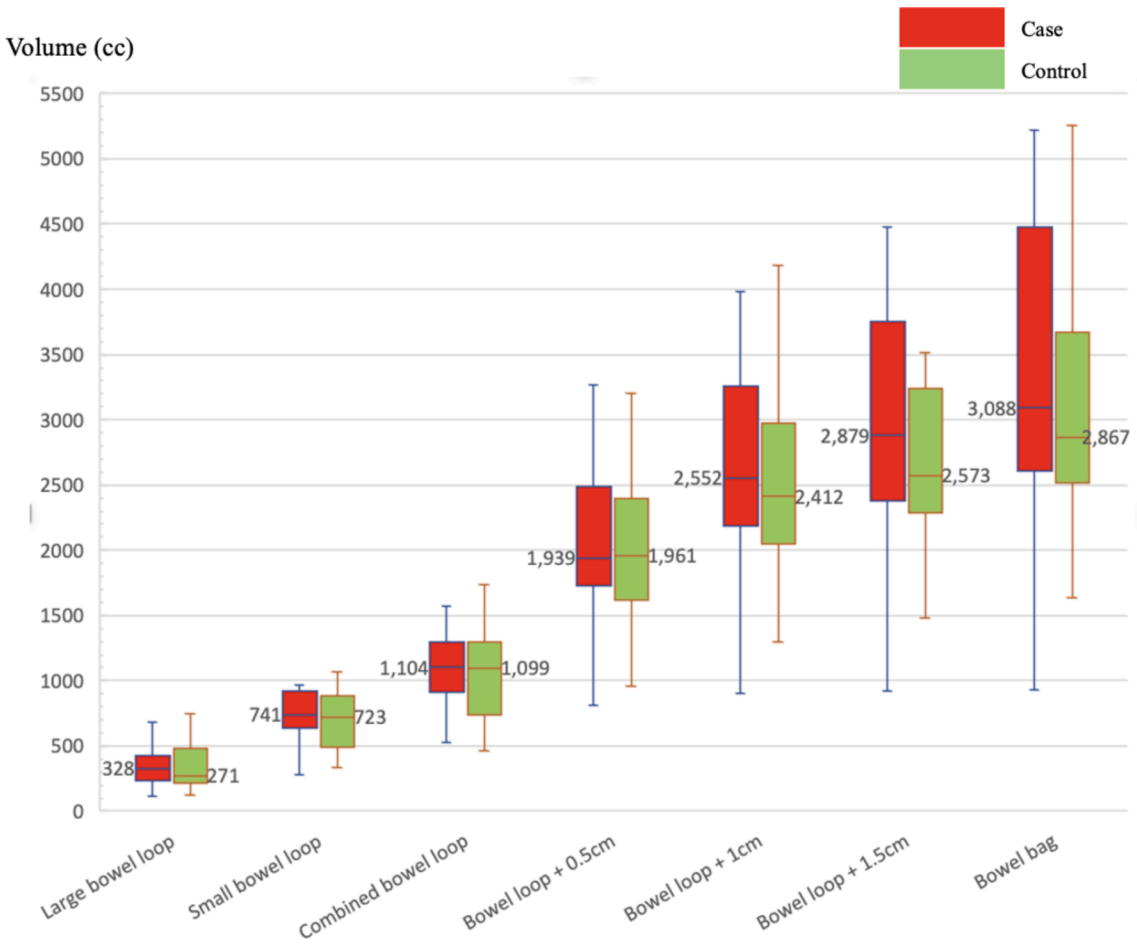


Fig. 1. Box plot showing distribution bowel volumes (in cc) for cases (red) and controls (green) for each of the seven methods of delineation. The median volume of the bowel structure is indicated. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

controls and cases with grade 2 bowel toxicity also showed no statistically significant difference for V_7, V_{14} and V_{25} for any of the bowel delineation method.

Discussion

In the present study, different bowel contouring methods were studied for dosimetric differences in patients with and without acute bowel toxicity after SBRT to prostate and pelvis. We found no difference in planned doses between bowel contours delineated using any of the approaches, including the bowel bag, individual bowel loops, and expanded bowel loops, for patients with and without toxicity.Bowel dosimetry was also not significantly different for patients with no symptoms when compared to those with acute grade 2 enteritis. In practice, bowel bag delineation is simpler and less time consuming compared to contouring individual bowel loops, although most published and ongoing trials of pelvic SBRT in high-risk prostate cancer patients use individual bowel loops contouring. However, the dose constraints to be used for bowel structure in pelvic SBRT remain unclear. Based on our data, with constraints of $V_7 < 1500$ cc, $V_{14} < 500$ cc and $V_{25} < 50$ cc for the bowel bag, about one in five patients had grade 1–2 acute enteritis, with none reporting severe symptoms [8].

The ideal method of contouring bowel as an organ at risk is not clear. The lack of consensus in bowel delineation is highlighted along with the varying approaches followed in existing literature and ongoing WP-SBRT studies (Table 4). The Canadian phase 2 studies on WP-SBRT recommended contouring bowel as large and small bowel loops [9,10,11]. Similarly, the ongoing PACE-NODES trial (NCT05613023), comparing prostate-alone SBRT with WP-SBRT in patients with high-risk prostate cancer, recommends delineation of individual bowel loops [12]. There are, however, certain limitations in contouring individual bowel loops for organ-at-risk delineation. Most of the bowel is intraperitoneal and is held in place by folds of mesentery, resulting in variability in bowel position with mesenteric movement. Additionally, bowel loops may vary in size and shape depending on factors such as dietary patterns and bowel health. As a result, there are multifactorial and unpredictable changes in the bowel position including those arising between simulation and treatment, as well as inter-fraction and intra-fraction variations. In a prospective study of three methods of bowel delineation (bowel loops, bowel loops with 1 cm expansion and bowel bag) only 20 % of the bowel consistently occupied the simulation-position during treatment [13]. This, coupled with the increase in time taken for delineation of individual bowel loops calls into question the utility of individual bowel loop contouring and highlights the need for a bowel delineation method that accounts for internal organ motion and is time efficient.

An alternative and quicker method of delineating bowel loop is the ‘restricted bowel loop contouring’ wherein only the bowel loops within 2–3 cm expansion of the PTV are contoured. Interestingly, in a study by Clarke et al., [14] the time taken to contour bowel was reduced from about an hour with delineation of all individual loops to 15 min with the method of ‘restricted bowel loop contouring’. However, this method will not capture the low dose spill to the bowel loops located away from the target volume.

In a previous planning study comparing bowel delineation strategies, the bowel bag, as opposed to bowel segment and expanded bowel

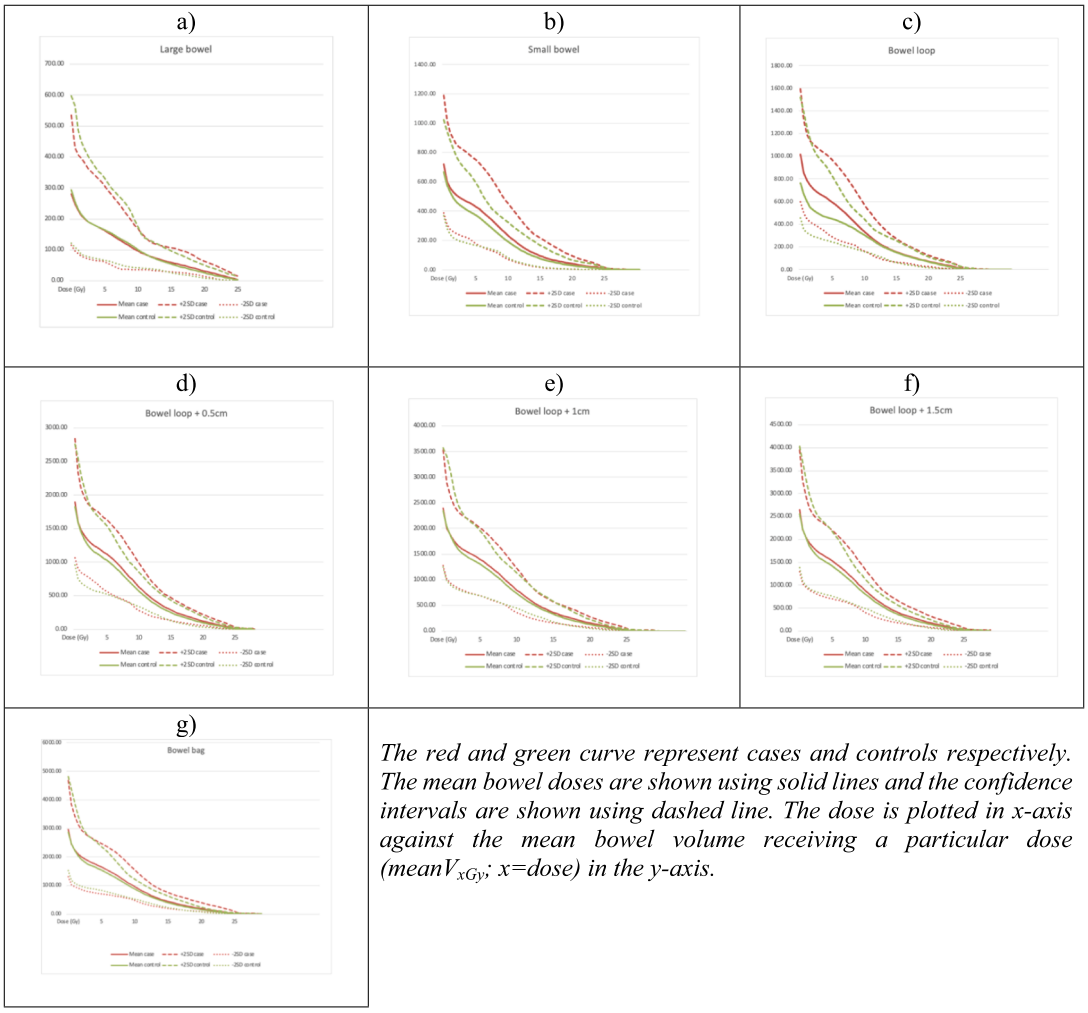


Fig. 2. Composite dose volume histogram (cDVH) showing plot of mean bowel dose with 95 % confidence interval. The red and green curve represent cases and controls respectively. The mean bowel doses are shown using solid lines and the confidence intervals are shown using dashed line. The dose is plotted in x-axis against the mean bowel volume receiving a particular dose (meanV_{xGy}; x = dose) in the y-axis. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
V_7, V_{14} and V_{25} along with mean and 95% confidence interval for cases and controls for each of the seven methods of bowel delineation.

Contour		Volume in cc		p value
		Case (n = 23)	Control (n = 23)	
Large bowel loop	V_7	142 (115–169)	147 (115–179)	0.85
	V_{14}	67 (56–79)	64 (53–76)	0.67
	V_{25}	6 (4–9)	4 (2–7)	0.22
Small bowel loop	V_7	379 (316–442)	322 (278–367)	0.09
	V_{14}	124 (94–154)	102 (79–124)	0.31
	V_{25}	11 (7–15)	7 (4–10)	0.15
Combined bowel loop	V_7	524 (454–593)	469 (407–531)	0.44
	V_{14}	192 (160–225)	165 (140–191)	0.29
	V_{25}	17 (12–22)	12 (7–16)	0.11
Bowel loop + 0.5 cm	V_7	992 (877–1108)	905 (802–1004)	0.32
	V_{14}	361 (308–414)	320 (276–364)	0.23
	V_{25}	23 (16–29)	15 (10–20)	0.10
Bowel loop + 1 cm	V_7	1245 (1094–1396)	1152 (1025–1278)	0.39
	V_{14}	459 (394–525)	418 (362–474)	0.29
	V_{25}	27 (18–36)	18 (13–24)	0.16
Bowel loop + 1.5 cm	V_7	1362 (1188–1536)	1250 (1114–1385)	0.41
	V_{14}	509 (435–583)	460 (405–515)	0.27
	V_{25}	30 (19–41)	20 (13–26)	0.16
Bowel bag	V_7	1469 (1266–1672)	1361 (1204–1519)	0.40
	V_{14}	557 (471–643)	509 (447–570)	0.46
	V_{25}	36 (18–53)	22 (16–29)	0.24

Table 4
Summary of bowel constraints used for pelvis SBRT in prostate cancer.

Study	Target	Prescription dose	Contour	Bowel constraint used
SATURN [9]	Prostate Pelvis	40 Gy/5#/ 5 weeks 25 Gy/5#/ 5 weeks	Small and Large Bowel loops	$V_{25} < 20$ cc, $V_{30} < 2$cc, $D_{max} < 38$ Gy
FASTR [10]	Prostate Pelvis	40 Gy/5#/ 5 weeks 25 Gy/5#/ 5 weeks	Small and Large Bowel loops	$V_{25} < 190$ cc, $V_{27.5} < 2$cc
SPARE [11]	Prostate Prostate + Pelvis	HDRBT boost 15–19 Gy 25 Gy/5#/ 5 weeks	Small and Large Bowel loops	$V_{25} < 20$ cc
PACE NODES (NCT05613023)[12]	Prostate Pelvis	36.25 Gy/5#/ 2 weeks 25 Gy/5#/ 2 weeks	Bowel loop	$V_{18.1} < 5$cc, $V_{30} < 1$cc
PRIME (NCT03561961) [3]	Prostate Pelvis	36.25 Gy/5#/ 2 weeks 25 Gy/5#/ 2 weeks	Bowel bag	$V_{25} < 80$ cc
HOPE [15]	Prostate Prostate + Pelvis	HDRBT boost 15 Gy 25 Gy/5#	Not specified	$V_{25} < 40$ cc, $D_{1cc} \leq 26$ cc

HDRBT- High dose rate brachytherapy.

segment (BS + 1 cm), had dual advantages: avoiding underestimation of low-dose spill to the bowel and accounting for bowel motion. The authors noted that a failure to account for bowel motion in the bowel segment contour led to a 10 % underestimation of the bowel receiving high dose spill [13]. This study recommends bowel bag contouring as a simple and practical solution for bowel delineation.

Bowel contouring in the ongoing PRIME trial (NCT03561961), comparing whole-pelvic moderately hypofractionated RT versus SBRT in patients with high-risk prostate cancer, has included the entire bowel bag for all patients [3]. Compared to drawing individual bowel loops, contouring bowel bag is easier (shorter learning curve, decreased inter-observer variations), quicker (better resource optimisation), and most importantly, always encompasses all the bowel loops (accounting for simulation-to-treatment changes, inter-fraction and intra-fraction bowel movement). While being robust, the ease and higher reproducibility of bowel bag delineation could lead to the added opportunity of standardising the bowel constraints for WP-SBRT.

The present work has certain limitations including those inherent to small dosimetric studies. However, to the best of our knowledge this is the first study analysing bowel contouring and bowel dosimetry in patients with prostate cancer treated with WP-SBRT. The validity of these results for late bowel toxicity is not known. Most cases had mild bowel symptoms of abdominal distention, abdominal pain or altered bowel habits which may be related to dietary or infectious etiology rather than radiation. The doses to different bowel structures were recorded on plans originally optimized for the bowel bag; though replanning for each contouring method would have been ideal, we decided against this dosimetric exercise based on (i) the negligible difference in previous dosimetric replanning studies [13], and (ii) the close volumetric agreement between each delineation method for patients with and without toxicity in the present study. While bowel bag delineation is much easier and faster when compared to individual bowel loops, quantification of the time taken to contour would have provided objective data.

Conclusion

The planned doses to bowel contours delineated using different methods such as the bowel bag, individual bowel loops, or expanded bowel loops were not found to have any statistically significant difference for patients with or without acute enteritis after WP-SBRT. Using bowel bag dose constraints of $V_7 < 1500$ cc, $V_{14} < 500$ cc and $V_{25} < 50$ cc, about 20 % patients treated with WP-SBRT are estimated to have acute Grade I-II enteritis. The findings of this study may help inform bowel contouring practice and standardise bowel bag dose constraints for broader clinical implementation in patients with prostate cancer undergoing WP-SBRT.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] van As N, et al. Phase 3 trial of stereotactic body radiotherapy in localized prostate cancer. N Engl J Med 2024;391:1413–25.
[2] Widmark A, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. Lancet 2019;394:385–95.
[3] Murthy V, et al. Study protocol of a randomised controlled trial of prostate radiotherapy in high-risk and node-positive disease comparing moderate and extreme hypofractionation (PRIME TRIAL). BMJ Open 2020;10 (NCT03561961).
[4] Murthy V, et al. Prostate-only versus whole-pelvic radiation therapy in high-risk and very high-risk prostate cancer (POP-RT): outcomes from phase III randomized controlled trial. JCO 2021;39:1234–42.
[5] Spratt DE, et al. Patterns of lymph node failure after dose-escalated radiotherapy: implications for extended pelvic lymph node coverage. Eur Urol 2017;71:37–43.
[6] Meerleer GD, et al. Elective nodal radiotherapy in prostate cancer. Lancet Oncol 2021;22:e348–57.
[7] Wang K, et al. Prostate stereotactic body radiation therapy: an overview of toxicity and dose response. Internat J Radiat Oncol Biol Phys 2021;110:237–48.
[8] Murthy V, et al. Acute and late adverse effects of prostate-only or pelvic stereotactic radiation therapy in prostate cancer: a comparative study. Internat J Radiat Oncol Biol Phys 2022;114:275–82.
[9] Musunuru HB, et al. Phase 1-2 study of stereotactic ablative radiotherapy including regional lymph node irradiation in patients with high-risk prostate cancer (SATURN): early toxicity and quality of life. Internat J Radiat Oncol Biol Phys 2018;102:1438–47.
[10] Bauman G, et al. A phase 1/2 trial of brief androgen suppression and stereotactic radiation therapy (FASTR) for high-risk prostate cancer. Internat J Radiat Oncol Biol Phys 2015;92:856–62.
[11] Musunuru HB, et al. Stereotactic pelvic radiotherapy with HDR boost for dose escalation in intermediate and high-risk prostate cancer (SPARE): Efficacy, toxicity and quality of life. Radiother Oncol 2021;161:40–6.
[12] As, N. van et al. PACE-NODES protocol. A phase III randomised trial of 5 fraction prostate SBRT versus 5 fraction prostate and pelvic nodal SBRT. https://www.icr.ac.uk/media/docs/default-source/default-document-library/pace-nodes-protocol-v3-0_17-04-24.pdf?sfvrsn=fa633b69_0. (NCT05613023).
[13] Sanguineti G, Little M, Endres EJ, Sormani MP, Parker BC. Comparison of three strategies to delineate the bowel for whole pelvis IMRT of prostate cancer. Radiother Oncol 2008;88:95–101.
[14] Clarke E, Howells R, Beasley M, Murray L. Restricted bowel loop contouring: Improving efficiency in radiotherapy contouring for abdomino-pelvic Stereotactic Ablative Radiotherapy (SABR). Clin Transl Radiat Oncol 2020;24:60–4.
[15] Mendez LC, et al. Is hypofractionated whole pelvis radiotherapy (WPRT) as well tolerated as conventionally fractionated WPRT in prostate cancer patients? The HOPE Trial. BMC Cancer 2020;20:978.