

Dosimetric Comparison Between Intensity Modulated Radiotherapy and Volumetric-Modulated Arc Therapy Radiotherapy in Hypofractionation Bladder Preservation

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ABSTRACT

Objective: To compare the intensity-modulated radiotherapy (IMRT) 11-field technique to Volumetric-modulated arc therapy (VMAT) for bladder preservation hypofractionated radical radiotherapy in high-risk urothelial bladder cancer cases.

Patients and Methods: A dosimetric analysis of 10 urothelial bladder cancer patients who underwent maximum transurethral bladder resection (TURBT) followed by bladder preservation using hypofractionation. These patients were presented to the radiotherapy department, National Cancer Institute, Cairo, between 2018 and 2020 with radical radiotherapy using the IMRT technique. Two plans were designed for each patient, one using 11-field IMRT and the second using Rapid arc. The two techniques were compared, including the PTV, bowel bag, rectum and both femoral heads, also treatment time.

Results: Comparing different DVHs, the planning target volume (PTV) was adequately covered in both plans, while the 11-field IMRT technique delivered significantly lower monitor unit and treatment time and better homogeneity index and conformity index.

Conclusion: The results of the comparison between IMRT and VMAT show that VMAT is superior to IMRT in terms of homogeneity and conformity and treatment time.

Keywords: Urothelial cancer, bladder preservation, Dosimetric study, IMRT, VMAT

INTRODUCTION

Urothelial bladder cancer is the 10th most common cancer with over 500,000 new cases and 210,000 deaths worldwide in 2020 (1). Approximately 70% of patients are >65 years of age and it is also more common in males (2). Nearly half of cases are associated with a history of smoking, with patients frequently presenting with multiple co-morbidities and frailty (3). Approximately 30% of patients will present with muscle-invasive bladder cancer (MIBC). Surgical management with radical cystectomy (RC) and extended pelvic lymph-node dissection was historically considered to be the gold standard management option. However, this can be associated with morbidity, high post-operative complication rates and often requires a permanent stoma which can affect the patient's quality of life (4).

Bladder preservation or tri-modality therapy (TMT) is an alternative curative treatment for MIBC. Whilst previously offered only to elderly or frail patients, international guidelines now recommend it as a viable option to all suitable patients. It consists of maximal TURBT followed by radiotherapy administered concurrently with radiosensitizers. In some cases, neo-adjuvant chemotherapy is offered to improve outcomes (5), (6). Previous pelvic radiotherapy is the only real contraindication to TMT, although patients with poor bladder function may best be served by RC rather than TMT. Multi-focal disease, carcinoma-in-situ and presence of hydronephrosis were considered contraindications for TMT, although inclusion of these patients in the BC2001 (7) and BCON (8) trials (9) was permitted.

There are no Phase III trials directly comparing surgery and radiotherapy, with the SPARE trial (NCT00867347) finding randomization difficult due to strong pre-conceived clinician and patient preference (10). Outcomes from matched cohorts, population data and a meta-analysis do however give similar results. A meta-analysis comparing outcomes for RC and TMT showed no difference in overall survival, disease-specific survival or progression-free survival with slightly higher early complications in the surgical group. 5-year OS was estimated at 56.2% with RC and 55.0% with TMT (11). Of note, patients tended to be older in the radiotherapy groups. Propensity score analysis from two studies confirmed equivalent disease-specific survival rates (12), (13).

Radiotherapy practice in the UK was reviewed during the COVID-19 pandemic. Whilst radiotherapy across all tumors sites had fallen there has been an increase in bladder radiotherapy by 64.2% (14). It remains to be seen if this trend is maintained as the pandemic is controlled. This review aims to outline current practical aspects of radical radiotherapy and areas of future development.

Throughout much of the world, bladder radiotherapy has been delivered with conventional fractionation of 1.8–2 Gy per fraction. However, in the UK two radiotherapy schedules have commonly been employed, namely 64 Gy in 32# over 6.5 weeks and the hypofractionated regimen of 55 Gy in 20# over 4 weeks. Recently a published meta-analysis comparing the two regimens by combining two large Phase III trials, BC2001 (7) and BCON (8), the hypofractionated regimen is expected to be adopted as standard of care (15). Hypofractionated radiotherapy was found to be superior to 64 Gy in 32 fractions in relation to invasive locoregional control, and non-inferior for overall survival and late bladder and rectum toxicity regardless of choice of radiosensitizers. Although bladder cancer is considered to be rapidly proliferating, it was also thought to hypothetically have a high α/β ratio with a concern that moderate hypofractionation would be less effective and be associated with increased late toxicity. As such the observation that moderate hypofractionation is more effective than conventional fractionation with no additional toxicity was unexpected. This would suggest that the α/β ratio is lower and/or the effect of repopulation more important than predicted. Radiotherapy effectiveness may be reduced after approximately 5 weeks due to tumor repopulation. Shorter fractionations are also more convenient for patients and more cost-effective (16) so the hypofractionated regimen should be adopted as standard of care.

IMRT has been previously compared with VMAT in various types of cancer. Several studies have suggested that VMAT produces highly conformal dose distributions, achieves accurate dosimetric delivery and reduces treatment time.

1. PATIENTS AND METHODS

Ten patient's urothelial bladder cancer who candidate for bladder preservation or refusing surgery presented to the radiotherapy department at National Cancer Institute, Cairo, between 2018 and 2020 and received hypofractionated radiotherapy using the IMRT technique. All patients were scanned using a CT simulator in a supine position with immobilization by knee and ankle rest support after rectal preparation using a laxative enema and empty bladder. CT scan slices with a thickness of 2.5 mm were obtained from the top of L1 to 2 cm below the ischial tuberosities. The CT images were automatically transferred to an Eclipse planning workstation, where the CTV and relevant organs-at-risk (OARs) were delineated.

RADIOTHERAPY TREATMENT PLAN

- 1) CT simulation and preparation • Computed tomography scans were obtained for all patients undergoing RT with 3-mm slices. All patients were prepared with an empty bladder and empty rectum. The scan was done in supine position; 3 radiopaque markers were placed using a laser localizer device to ensure positional consistency. These predetermined landmark locations served as the standard point for comparison. 2) Targets: • Gross Target Volume (CTV b) = Whole empty bladder.
- 2) Clinical Target volume (CTVn) = pelvic lymph node regions at risk which were the presacral nodes and the bilateral distal common iliac, external iliac, internal iliac, and obturator nodes.

The CTVn was created by adding 7 mm to GTVn with trimming so as not to extend outside the true pelvis, nor into muscle or bone. The CTVn was cropped out of bowel.

- the presacral nodes extended from L5-S1 to the top of S3 and included 1.0-1.5 cm of tissue anterior to the sacrum and between the vessel contours. ○ the iliac nodes derived by contouring the common iliac, external and internal iliac vessels starting superiorly at L5-S1. To better visualize the pelvic vasculature, IV contrast was recommended but not required since some patients may have renal insufficiency.
- The external iliac vessels were contoured inferiorly to the top of the femoral heads, and the internal iliac vessels were contoured inferiorly until they were no longer visible on the CT scan or exit through the true pelvis via the greater sciatic notch. The iliac nodes were created by expanding the iliac vessels by 7 mm in the anterior, posterior and lateral dimensions, but not the superior and inferior dimensions.
- the obturator nodes encompassed 1.0 cm width of tissue medial to the obturator internus muscles extending from the anterior border of the ilium to the posterior border of the ilium. The obturator nodes were contoured starting superiorly where the internal and external iliac vessel contours stop and extend inferiorly to the top of the symphysis pubis.

- Prostate electively was included in CTV45 and is included in CTV55 if involved with tumor.
- Planning Target Volume (PTV 45) = PTV was created by adding 7 mm CTV n. • PTV55 = bladder with 2 cm margin.

3) Organs at Risk:

- Rectum >> the rectum contour included the rectum and anal canal and was contoured on every slice from the recto-sigmoid junction superiorly to the level of the ischial tuberosities inferiorly.
- Bowel>>contours of the bowel contour included the entire small bowel, cecum, ascending, transverse, and sigmoid colon in one bowel bag contour. Superiorly, the bowel contour started 3 cm above the superior extent of the CTVn. Inferiorly, the contour discontinued on the CT slice where no portion of bowel is visible.

The contours included the volume surrounding loops of bowel out to the edge of the peritoneum as bowel may occupy this space at any time during the course of treatment.

- Both Femoral heads till lesser trochanter.

4) Dose constrains:

PTV

D95% is 100% of the prescribed dose, acceptable deviation of 95%•D2% ≤ 107 % of the planned absorbed dose according ICRU Report 83(Gregoire & Mackie, 2011).

Dose constrains were modified from RTOG 0126 trial which corrected to a daily fraction of 2.75-3 Gy using linear quadratic formula and used in hypofractionation protocol for prostate cancer (hypofractionation protocols were restricted to bladder only and not including pelvic LN). (Moore et al.,2015). for prostate cancer (hypofractionation protocols were restricted to bladder only and not including pelvic LN). (Moore et al.,2015).

➤ Rectum V48and V52<35%

➤ Both femoral heads: Dmax 45 Gy

➤ Bowel bag V45<195CC.

Treatment Planning

Two plans were generated for each patient, one using the 11-field IMRT and the other using single 360° Rapid Arc. The two techniques were compared using dose volume histogram (DVH) analysis of the PTV, bowel bag, rectum, and pelvic bone marrow. Both treatment plans were performed using the Eclipse treatment planning system (TPS) using 5 mm leaf width and 6 MV photon energy. Statistical analysis simple t-test was used to compare mean values ± SD for different DVH parameters between the two treatment techniques, with a p-value ≤ 0.05 considered statistically significant.

2. Results

ICRU 83 recommends reporting V95% and D2%. D95% is the minimum absorbed dose that covers 95% of the volume of the PTV.D2% is the near maximum dose as a replacement for the “maximum absorbed dose.

The D95% of the PTV received at least 95% of the prescribed dose in both plans in both PTVs with no significant difference (p= 0.18 for PTV 55 and 0.87 for PTV 45). D2% was less than 107% of the prescribed dose in both plans in both PTV 55 and PTV 45 with no significant difference (p=0.08 and 0.46 respectively). Regarding Dmax of both femoral head, no significant difference between two plans (p=.085 and 0.3).

The V45 of the bowel were higher in the VMAT plan than IMRT but results no significant (p=0.56).

The V48 and V52 of the rectum were non-significant between two plans (p=0.51 and 0.64).

Based our data, the HI values were obtained for the IMRT technique of 1.081 and for the VMAT technique of 1.061 with the t-test (p value = 0.018 which differed statistically significantly. This shows that HI scores using the VMAT technique show better homogeneity when compared to the IMRT technique. Meanwhile, the CI value for the IMRT technique was 0.519 while the VMAT technique was 0.641. The results of the t- test p-value = 0.263 showed no significant difference. This shows that the VMAT technique conforms more than the IMRT technique because it produces a greater CI value. Because VMAT is more conformable, this technique is expected to be able to minimize the absorbed dose to the organs at risk.

VMAT showed shorter time for treatment and less monitor unites needed for treatment (p<0.05).

Table 1: Results of comparison between two plans

Structure	Dosimetric Parameter	IMRT	VMAT	P-value
		Mean \pm SD	Mean \pm SD	
PTV_55Gy	D95% (Gy)	54.58 \pm 0.65	54.47 \pm 0.55	0.18
	D2% (Gy)	57.06 \pm 1.34	57.93 \pm 2.62	0.08
PTV_45Gy	D95 % (Gy)	44.57 \pm 1.16	44.60 \pm 1.05	0.87
	D2% (Gy)	45.11 \pm 2.07	45.41 \pm 1.84	0.46
Bowel bag	V45Gy	94.51 \pm 48.17	109.73 \pm 64.26	0.56
Right femoral head	Dmax (Gy)	41.80 \pm 5.15	42.16 \pm 2.95	0.85
Left femoral head	Dmax (Gy)	40.4 \pm 4.88	51.32 \pm 30.87	0.3
Rectum	V48Gy (%)	13.9 \pm 12.49	17.93 \pm 14.04	0.51
	V52Gy (%)	10.06 \pm 10.17	12.43 \pm 11.74	0.64
CI	CI	0.519 \pm .04	0.634 \pm 0.09	0.263
HI	HI	1.081 \pm .03	1.061 \pm .02	0.018
	MU	1746.2 \pm 120.48	1217.1 \pm 225.87	< 0.05
	Time (min)	2.91 \pm 0.20	2.03 \pm 0.38	< 0.05

3. Discussion

VMAT has demonstrated efficiency in delivering prescribed doses while minimizing exposure to surrounding healthy tissues. Studies have shown that VMAT plans can achieve slightly better Planning Target Volume (PTV) coverage compared to IMRT. For instance, VMAT plans resulted in a PTV coverage of 98.885%, while IMRT plans achieved 98.594%, indicating a marginal but notable improvement. Our results are comparable to the published data (17).

Regarding treatment efficiency, VMAT offers significant advantages. Studies have reported that VMAT requires fewer monitor units and shorter delivery times than IMRT. For example, VMAT plans required 18.6% fewer monitor units and reduced delivery times, with average 'beam-on' times of 1.30 minutes, compared to 4.52 minutes for IMRT plans. In our study treatment time 2.9 minutes for IMAT and 2.03 minutes for VMAT (18).

Studies have demonstrated that VMAT plans result in improved conformity indices, which indicates a more precise dose distribution around the target volume. Our results showed better conformity in IMRT vs. VMAT (19).

VMAT may provide slightly significant homogeneity index which potentially leading to improved treatment outcomes. (20)

While IMRT allows for meticulous planning and delivery, ensuring that high doses are confined to the tumor, studies have shown that VMAT and IMRT plans may reduce volumes of the small intestine and Dmax of both femori but more with VMAT. Our study shows no significant between to techniques.

4. Conclusions

From the present study, we concluded that both VMAT and IMRT are advanced radiation therapy techniques with their respective strengths. Emerging evidence suggests that VMAT may provide better homogeneity in dose distribution within the PTV, potentially leading to improved treatment outcomes. Also decrease treatment time and monitor unites However, the choice between VMAT and IMRT should be individualized, considering various dosimetric parameters, clinical objectives, and patient-specific factors.

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