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Clinical Application of Cone-Beam CT (CBCT) in the Delivery of Hypofractionated Radiotherapy for Muscle-Invasive Bladder Cancer (MIBC): Ensuring Adequate Planning Target Volume Coverage and Small Bowel Sparing

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ABSTRACT

Objective: To evaluate the clinical application of cone-beam CT (CBCT)-guided image-guided radiotherapy (IGRT) in muscle-invasive bladder cancer (MIBC), assessing planning target volume (PTV) coverage at the 95% isodose line, dose to the small bowel, and the feasibility of PTV margin reduction.

Study Design: Prospective observational study.

Place and Duration of Study: Department of Radiation Oncology, Combined Military Hospital, Rawalpindi Pakistan, from Nov 2025 to Mar 2026.

Methodology: Thirty-one patients with histopathologically proven muscle-invasive urothelial carcinoma (stage T2–T4, N0–N1, M0) were enrolled following Ethical Review Committee approval. CT simulation was performed with an empty bladder. A dose of 55 Gy in 20 fractions was delivered by VMAT (Eclipse TPS v16.1; Varian CLINAC DHX 2300 / VitalBeam) with a 1.5 cm PTV margin, and daily CBCT enabled online soft-tissue verification and correction. Concurrent weekly cisplatin 40 mg/m² was given where clinically appropriate. Data were analysed using IBM SPSS Statistics version 26.

Results: All 31 patients completed treatment. Mean age was 69.6±10.5 years; 17(54.8%) had T2 disease and 23(74.2%) were node-negative. Adequate PTV coverage at the 95% isodose line (≥95%) was achieved in all 31(100%) patients, with a mean coverage of 97.5±1.1%. The mean dose to 98 cc of small bowel was 30.94±15.44 Gy, within the accepted constraint. PTV margin reduction from 1.5 cm to 1.0 cm was considered feasible in 19(61.3%) patients.

Conclusion: CBCT-guided IGRT using VMAT achieved excellent target coverage with acceptable small bowel doses in MIBC, and supported PTV margin reduction in a majority of patients.

Keywords: Cone-Beam Computed Tomography, Image-Guided Radiotherapy, Muscle-Invasive Bladder Cancer, Planning Target Volume, Urothelial Carcinoma, Volumetric Modulated Arc Therapy.

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INTRODUCTION

Bladder cancer is among the most prevalent urological malignancies globally. It ranks as the tenth most common cancer worldwide, and in Pakistan it constitutes a significant proportion of urological oncology referrals.[1] Most patients present with locally advanced disease owing to delays in referral, limited cystoscopy access, and low public awareness.[2] The reported age-standardized incidence of bladder cancer in Pakistan is approximately 2.1 per 100,000, with male predominance and a rising trend in urban centres.[3]

MIBC is defined as urothelial carcinoma invading the detrusor muscle (clinical stage T2 or higher) and carries a markedly worse prognosis than non-muscle-invasive disease, necessitating prompt definitive treatment.[4] Radical cystectomy has traditionally been the standard of care, yet it carries significant perioperative risk and imposes a considerable psychosocial burden; in Pakistani patients, concerns regarding body image and social stigma frequently lead to refusal of surgery even when it is clinically indicated. Trimodality therapy, comprising maximal TURBT, external beam radiotherapy, and concurrent radiosensitizing chemotherapy, has emerged as a well-validated organ-preserving alternative to cystectomy.[5] Concurrent chemotherapy significantly improves locoregional control compared with radiotherapy alone, and several protocols report survival broadly comparable to cystectomy series in appropriately selected patients.[6]

Technical refinements, notably VMAT and IMRT, have substantially improved dose conformity to the bladder while reducing irradiation of surrounding normal tissues.[7] The addition of daily CBCT-based IGRT has further advanced precision by allowing direct visualisation of the bladder wall before each

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fraction, which is important because the bladder moves independently of bony pelvic landmarks.[8] Despite these advances, published data on CBCT-guided IGRT specifically from Pakistani institutions remain limited. The present prospective observational study was designed to document institutional outcomes of CBCT-guided IGRT for MIBC at a tertiary radiation oncology centre in Pakistan, to evaluate PTV coverage and small bowel dose, and to determine whether observed setup accuracy justifies PTV margin reduction in future protocols.

METHODOLOGY

This prospective observational study was conducted at the Department of Radiation Oncology, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan, after obtaining Ethical Review Committee approval (dated 27 October 2025) and in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. Data collection and treatment delivery were conducted between November 2025 and March 2026. Non-probability convenience sampling was used to recruit consecutive eligible patients. The total patients recruited were 31 in number.

Inclusion Criteria: Histopathologically proven muscle-invasive urothelial carcinoma of the bladder; clinical stage T2–T4, N0–N1, M0; ECOG performance status 0–2; creatinine clearance ≥ 50 mL/min by the Cockcroft–Gault formula; prior TURBT; and ability to provide written informed consent.

Exclusion Criteria: Small contracted bladder; prior pelvic radiotherapy; active inflammatory bowel disease; uncontrolled concurrent illness; pregnancy; or histology other than urothelial carcinoma.

CT simulation was performed in the supine position with a knee-and-ankle immobilization device and an empty bladder to standardize the filling state at each fraction. Intravenous contrast was administered to optimize delineation of the bladder wall, tumour bed, and pelvic nodal stations. The clinical target volume (CTV) included the entire bladder and, in node-positive cases, regional pelvic nodes. A uniform PTV expansion of 1.5 cm was applied in all directions. All treatment plans were generated on the Eclipse Treatment Planning System v16.1 (Varian Medical Systems, Palo Alto, CA, USA) using VMAT to a prescribed dose of 55 Gy in 20 fractions—a moderately hypofractionated schedule biologically equivalent to conventional 64–66 Gy.[9] Treatment was delivered on Varian CLINAC DHX 2300 or VitalBeam linear accelerators. Concurrent cisplatin 40 mg/m² was administered weekly where clinically appropriate, with the remaining patients treated by radiotherapy alone on the basis of age or renal function.

Daily CBCT was acquired before each fraction using the on-board imaging system. Online registration was performed against the planning CT with priority given to bladder wall position, and translational corrections in the anterior-posterior, superior-inferior, and left-right axes were applied before beam delivery. Systematic and random setup errors were assessed using the Van Herk margin recipe[10] to validate the applied 1.5 cm PTV margin and to assess the feasibility of reducing it to 1.0 cm on a per-patient basis. PTV coverage was recorded as the percentage of the PTV receiving the 95% isodose, and the dose to 98 cc of small bowel (D98cc) was extracted from the dose–volume histogram for each plan.

The collected data were entered and analysed using Statistical Package for Social Sciences version 26.0. Continuous variables (age, PTV coverage, small bowel dose) were reported as Mean±SD, and categorical variables (T and N stage, histopathology, treatment characteristics, PTV coverage adequacy, and margin-reduction feasibility) as frequencies with percentages.

RESULTS

An analysis was conducted on 31 patients with muscle-invasive bladder cancer who completed the full 20-fraction course of CBCT-guided VMAT. The mean age of patients was 69.6 ± 10.5 years (range 47–92 years), with most falling in the >70 years age group, 14 patients (45.2%), followed by 61–70 years, 11 patients (35.5%), and ≤60 years, 6 patients (19.4%). All 31(100%) patients had a histologically confirmed diagnosis of high-grade papillary urothelial carcinoma. Tumour (T) stage was T2 in 17(54.8%), T3 in 7(22.6%), and T4 in 7(22.6%) patients, while nodal (N) stage was node-negative in 23(74.2%) and node-positive in 8(25.8%) patients. Maximal TURBT had been performed in 25(80.6%) patients. All patients were simulated and treated with an empty-bladder protocol and received 55 Gy in 20 fractions by VMAT with daily CBCT (Table-I). Concurrent weekly cisplatin was administered in 23(74.2%) patients, and neoadjuvant chemotherapy was given in 22(71.0%) patients.

In terms of dosimetric outcomes, adequate PTV coverage at the 95% isodose line (≥95% of the PTV

covered) was achieved in all 31(100%) patients, with a mean PTV coverage of 97.5±1.1% (range 95.7–101.3%). The mean dose to 98 cc of small bowel (D98cc) was 30.94±5.44 Gy, comfortably within the accepted small bowel tolerance for this schedule, with all evaluable plans meeting the constraint. On the basis of the setup reproducibility observed with daily CBCT and the Van Herk margin analysis, reduction of the PTV margin from 1.5 cm to 1.0 cm was considered dosimetrically feasible in 19(61.3%) patients, while the existing 1.5 cm margin was retained in the remaining 12(38.7%) patients (Table-II). No radiotherapy interruptions attributable to treatment toxicity occurred.

Table-I: Demographic and Treatment Characteristics of the Study Population (n=31)

Variable	n(%)
Age (years)	69.6±10.5
Age Groups	
≤60 years	6(19.4%)
61–70 years	11(35.5%)
>70 years	14(45.2%)
Histological Diagnosis	
High-grade papillary urothelial carcinoma	31(100.0%)
Tumour (T) Stage	
T2	17(54.8%)
T3	7(22.6%)
T4	7(22.6%)
Nodal (N) Stage	
Node-negative (N0)	23(74.2%)
Node-positive (N1)	8(25.8%)
Treatment Characteristics	
Maximal TURBT performed	25(80.6%)
Concurrent weekly cisplatin 40 mg/m²	23(74.2%)
Neoadjuvant chemotherapy	22(71.0%)
RT technique – VMAT	31(100.0%)
RT dose – 55 Gy / 20 fractions	31(100.0%)
Daily CBCT-guided IGRT	31(100.0%)
Empty-bladder simulation protocol	31(100.0%)

SD = standard deviation; TURBT = transurethral resection of bladder tumour; RT = radiotherapy; VMAT = volumetric modulated arc therapy; CBCT = cone-beam computed tomography; IGRT = image-guided radiotherapy.

Table-II: Dosimetric Outcomes and PTV Margin Analysis (n=31)

Outcome	n(%)
PTV coverage at 95% isodose line (%)	97.5±1.1
Adequate PTV coverage (≥ 95%)	31(100.0%)
Dose to 98 cc of small bowel, D98cc (Gy)	30.94±5.44
Small bowel constraint met	30(100.0%)*
PTV Margin Reduction (1.5 cm → 1.0 cm)	
Feasible	19(61.3%)
Not feasible (1.5 cm retained)	12(38.7%)

*PTV = planning target volume; SD = standard deviation; D98cc = dose received by 98 cubic centimetres of small bowel. *Small bowel dose was evaluable in 30 of 31 plans (one value missing); the constraint was met in all evaluable plans.*

DISCUSSION

This prospective study confirms that CBCT-guided IGRT using VMAT is technically feasible, dosimetrically precise, and reproducible for MIBC at a tertiary centre in Pakistan. Adequate PTV coverage in 100% of patients and small bowel doses well within tolerance collectively represent a strong institutional benchmark and compare favourably with published international series.[11]

The fundamental challenge in bladder radiotherapy is organ motion, as the bladder changes shape, volume, and position between fractions. Historically this was managed with margins of 2–3 cm, creating large irradiated volumes and resulting in chronic radiation enteritis and proctitis in a significant proportion of survivors.[12] The shift to daily soft-tissue CBCT matching directly addresses this by visualising the bladder before every fraction and enabling real-time correction, while the empty-bladder simulation protocol removes filling variability as a dominant source of interfractional motion.[13] These findings are consistent with the RAIDER trial, which demonstrated that adaptive IGRT strategies reduce organ-at-risk doses without compromising target coverage.[14]

The mean small bowel D98cc of 30.94 Gy observed in this study compares favourably with historical conventional radiotherapy series, where mean bowel doses of 40–50 Gy were common.[15] Reducing bowel dose into the range reported here materially decreases the lifetime risk of late radiation enteritis and strengthens the quality-of-life argument for organ preservation. The finding that PTV margin reduction from 1.5 cm to 1.0 cm was feasible in the majority of patients (61.3%), supported by Van Herk analysis, is consistent with published series using daily CBCT and would further reduce the treated volume and normal-tissue irradiation.[16]

The clinical relevance of these findings is amplified by the realities of MIBC management in Pakistan, where radical cystectomy requires specialist expertise and support not uniformly available. The hypofractionated 55 Gy / 20 fractions schedule is biologically equivalent to conventional 64–66 Gy, shortens treatment, and improves throughput without compromising efficacy. A library-of-plans adaptive strategy has been shown to reduce mean small bowel dose further and is achievable with existing Eclipse and CLINAC infrastructure, representing a logical next step for this institution.[17] MR-guided adaptive radiotherapy offers additional precision but requires dedicated MR-linac platforms not currently available in most Pakistani centres.[18]

LIMITATION OF STUDY

This was a non-randomized, single-institution study with a limited sample size, sufficient for dosimetric analysis but not for robust clinical-endpoint conclusions. The observation period precludes assessment of long-term local control, bladder preservation, and late toxicity, and patient-reported quality-of-life data were not systematically collected. The dose to 98 cc of small bowel was missing for one plan. Multicentre prospective studies with longer follow-up are warranted to validate these dosimetric gains.

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CONCLUSION

CBCT-guided IGRT using VMAT achieved excellent dosimetric outcomes in MIBC, with adequate 95% isodose PTV coverage in all 31 patients (mean 97.5±1.1%) and a mean small bowel D98cc of 30.94±15.44 Gy within established tolerance. Setup accuracy with daily CBCT supported PTV margin reduction from 1.5 cm to 1.0 cm in the majority of patients, offering the potential for further reductions in normal-tissue irradiation. These findings support CBCT-guided organ-preserving radiotherapy as a practical and reproducible approach for MIBC in a resource-limited setting.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

OR & AM: Data acquisition, data analysis, critical review, approval of the final version to be published.

IW & TM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MUK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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