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Original Research Article

Dosimetric Analysis and Clinical Outcome of Cobalt-60 Based HDR Brachytherapy in Carcinoma Cervix: A Prospective Study

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Abstract

Introduction: Carcinoma cervix is a major health concern in developing countries. High dose rate (HDR) intracavitary brachytherapy (ICBT) following external beam radiotherapy (EBRT) is a crucial part of definitive treatment. The introduction of CT-based image-guided brachytherapy (IGBT) enables improved target coverage and sparing of organs at risk (OARs).

Aim: To evaluate dosimetric parameters, acute toxicities and early clinical response in patients undergoing CT-based HDR brachytherapy using a cobalt-60 (Co-60) source.

Materials and Methods: This prospective observational study included 20 patients with histologically confirmed carcinoma cervix (FIGO 2018 stages IIA–IIIB). All patients received EBRT (50 Gy in 25 fractions) with concurrent weekly cisplatin (40 mg/m²), followed by HDR brachytherapy (7 Gy × 3 weekly fractions). CT-based planning was performed according to American Brachytherapy Society guidelines. Dosimetric parameters including HR-CTV D_{90} and OAR D_{2cc} doses were converted to EQD2. Acute toxicities were graded using CTCAE v5.0 and response was assessed clinically.

Results: The mean HR-CTV D_{90} EQD2 was 84.82 Gy. Mean D_{2cc} doses to bladder, rectum, and sigmoid were 72.93 Gy, 65.62 Gy and 62.06 Gy, respectively, all within recommended tolerance limits. Acute toxicities were predominantly Grade 1–2, with no Grade ≥3 events observed. Complete response was achieved in 90% of patients.

Conclusion: CT-guided HDR brachytherapy using Cobalt-60 is an effective and practical treatment approach for carcinoma cervix. It provides promising results with adequate target coverage with acceptable OAR sparing and minimal acute toxicity.

Keywords: Carcinoma cervix, HDR brachytherapy, Cobalt-60, IGBT, EQD2.

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Introduction

Carcinoma cervix is one of the leading female malignancies worldwide, particularly in low and middle income countries.[1] The standard treatment of locally advanced disease consists of concurrent chemoradiation followed by intracavitary brachytherapy.[2]

Traditionally, conventional brachytherapy planning relied on two-dimensional radiographic anatomical techniques with dose prescription to Point A based on the Manchester system.[3] However, this approach lacked accuracy in representing tumor volume and OAR dose exposure. The introduction of CT/MRI-based image-guided brachytherapy (IGBT) has revolutionized treatment planning by enabling volumetric dose assessment and improved tumor targeting.[1,4] HDR brachytherapy using Co-60 source offers advantages such as shorter treatment duration, outpatient feasibility and cost-effectiveness due to its longer half-life compared to Ir-192.[7,8] This study aims to evaluate dosimetric parameters, acute toxicities and clinical response in patients treated with Cobalt-60 based HDR brachytherapy.

Materials and Methods

This prospective observational study included a total of 20 patients with histopathologically confirmed carcinoma of the cervix. Institutional ethical approval and informed consent from the patient were obtained prior to initiation of the study. All patients were staged according to the FIGO 2018 classification and belonged to stages IIA to IIIB. Only those patients who were planned for initial radical concurrent chemoradiation, had suitable anatomy for intracavitary brachytherapy and had an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or less were included. Patients with a prior history of pelvic irradiation, evidence of distant metastasis or those deemed unfit for anesthesia were excluded from the study.

All eligible patients underwent a standardized treatment protocol consisting of external beam radiotherapy (EBRT) followed by high dose rate (HDR) intracavitary brachytherapy. EBRT was delivered to the pelvis to a total dose of 50 Gray in 25 fractions by Intensity Modulated Radiation Therapy (IMRT) technique over a period of 5 weeks, with a daily fraction size of 2 Gray. Concurrent chemotherapy was administered in the form of weekly cisplatin at a dose of 40 mg/m², in accordance with established treatment guidelines for locally advanced cervical cancer.[2]

Following completion of EBRT, patients were advised a rest period of 7 days and then, proceeded to HDR intracavitary brachytherapy. The procedure was performed under appropriate anesthesia and Fletcher Suit Delcos three channel titanium applicator system consisting of a central tandem and pair of ovoids was used in all cases. After applicator placement, patients underwent computed tomography (CT) imaging with a slice thickness of 3 mm for treatment planning. The acquired images were transferred to a dedicated treatment planning system (Multisource HDR Plus, BEBIG by Eckert & Zeigler, Germany) for treatment planning, dosimetric analysis and optimization.

Target volume delineation and organ-at-risk (OAR) contouring were performed in accordance with the recommendations of the GEC-ESTRO working group.[1] The high-risk clinical target volume (HR-CTV) was defined to include the cervix along with any residual gross disease at the time of brachytherapy as shown on Figure 1. Organs at risk including the bladder, rectum and sigmoid colon were contoured on each CT slice to facilitate accurate dose assessment, as shown in Figure 2.

A dose of 7 Gy per fraction to point A was prescribed to the target volume through Manchester system based computer planning and a total of three fractions were delivered at weekly intervals.[30] Treatment planning was individualized for each patient, with optimization of dwell positions and dwell times to achieve pear shaped adequate target coverage as shown in Figure 2, while minimizing dose to surrounding normal tissues. The planning objectives were to ensure that at least 90% of the HR-CTV received the prescribed dose, while keeping OAR doses within recommended tolerance limits as per international guidelines.[2,4]

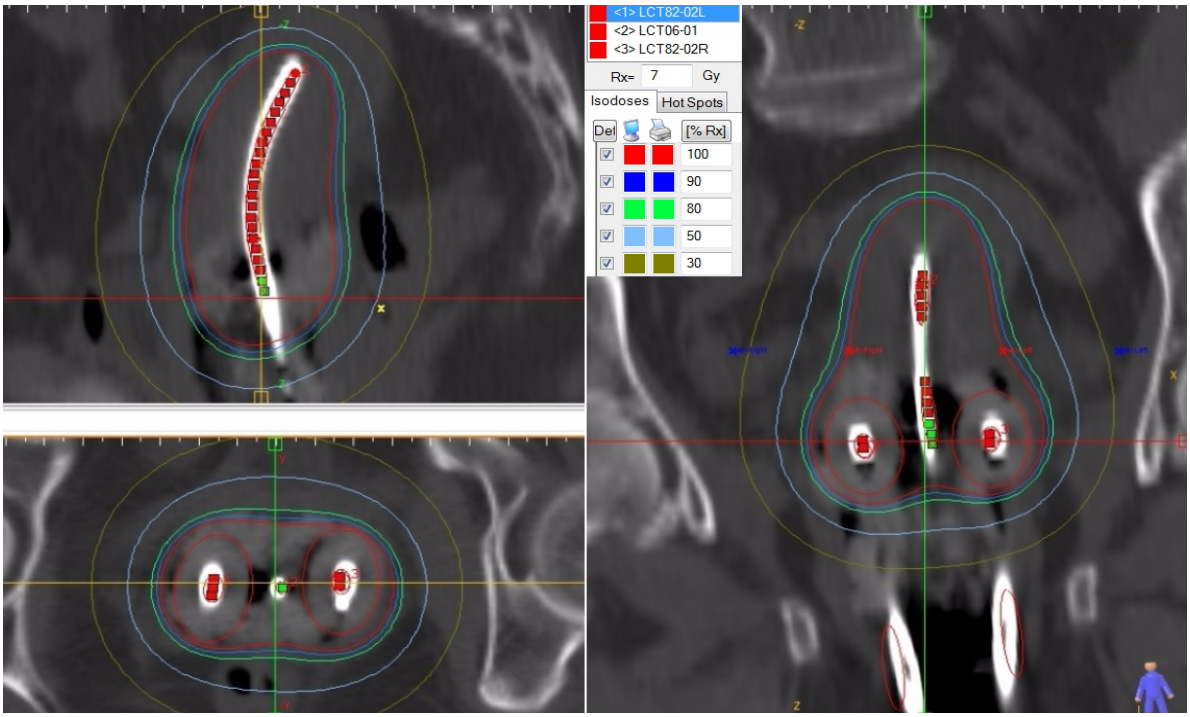

Figure 1: Target delineation and Dose distribution in sagittal, transverse and frontal view

Dosimetric evaluation was carried out using dose-volume histogram (DVH) parameters.

The primary parameters analysis included HR-CTV D90 (dose received by 90% of the target volume) and D2cc values for the bladder, rectum and sigmoid colon representing the minimum dose received by the most exposed 2 cubic centimeters of these organs.

All dose parameters were converted into equivalent dose in 2 Gy fractions (EQD2) using the linear-quadratic model to allow comparison with standard dose constraints.[4]

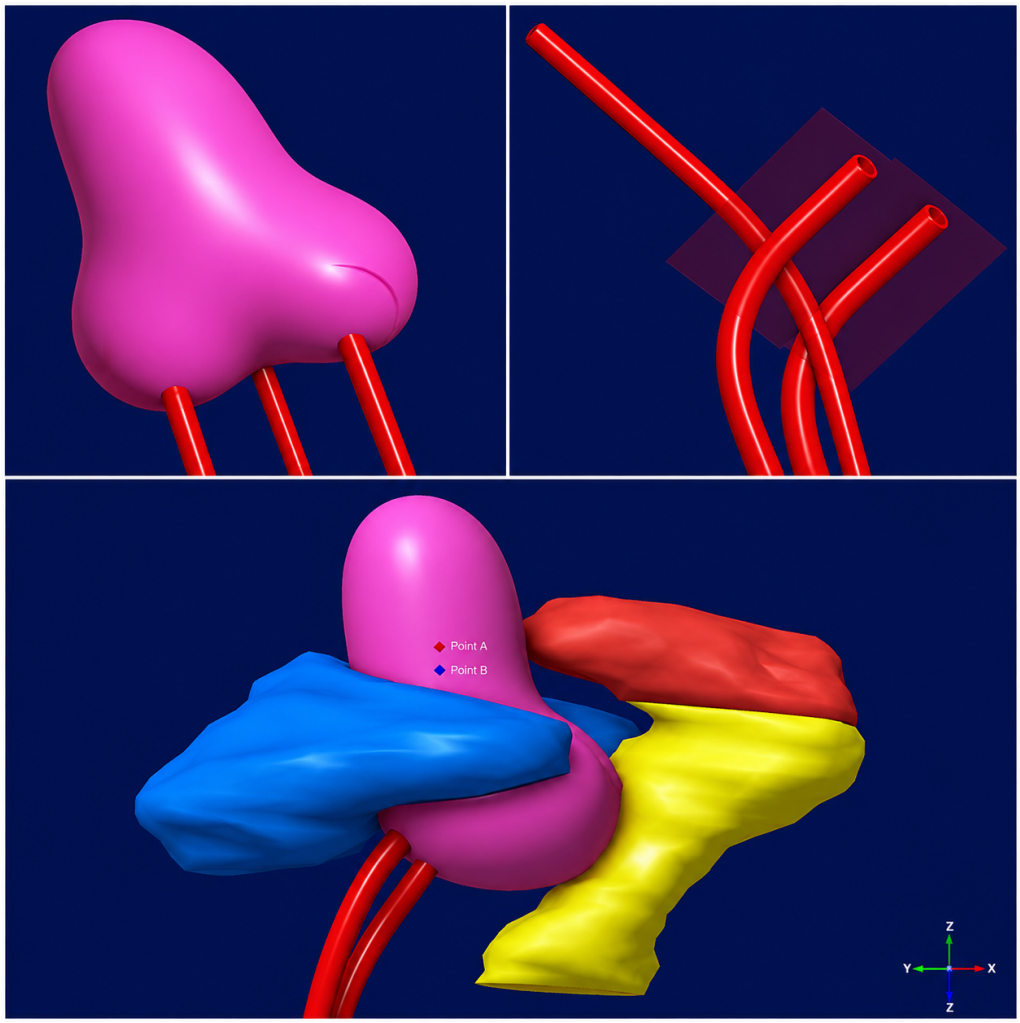

Figure 2: Pear shaped dose distribution (pink), three channel applicator position and organs at risk in sagittal view. (Urinary Bladder – blue, Rectum – yellow, sigmoid - red)

Acute treatment-related toxicities were assessed on a weekly basis during the course of treatment and were graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.[9] Patients were assessed for acute toxicities on monthly follow up visits for a minimum period of 6 months. Particular attention was given to gastrointestinal and genitourinary toxicities.

Early clinical response to treatment was evaluated after completion of therapy through detailed per-vaginal and per-speculum examination at monthly intervals for a period of 6 months. Patients were categorized as having achieved complete response (CR) or partial response (PR) based on clinical findings. Statistical analysis was performed using descriptive methods. Continuous variables were summarized using mean, standard deviation and range and the results were interpreted accordingly.

Results

A total of 20 patients with histopathologically confirmed carcinoma cervix were included in the study. The age of the patients ranged from 40 to 59 years. The majority of patients presented with locally advanced stage disease, with stage IIIB constituting 50% of the cohort, followed by stage IIB in 40% of patients, reflecting the typical presentation pattern seen in developing countries.

Dosimetric Outcomes: Dosimetric analysis demonstrated adequate target coverage in all patients. The mean high-risk clinical target volume

(HR-CTV) D90, expressed as equivalent dose in 2 Gy fractions (EQD2) was 84.82 Gy, with a range of 81–89 Gy.

Notably, all patients achieved an HR-CTV D90 of ≥80 Gy, which is in accordance with recommended therapeutic thresholds and has been associated with improved local control rates in previous studies.[2,5]

Target Coverage: With respect to organs at risk (OARs), the mean D2cc doses were well within acceptable tolerance limits. The mean bladder D2cc was 72.93 Gy, which is below the recommended constraint of <90 Gy.[2] Similarly, the mean rectum D2cc and sigmoid D2cc were 65.62 Gy and 62.06 Gy, respectively, both within the recommended limits of <75 Gy.[4] These findings indicate effective sparing of normal tissues while maintaining adequate target dose coverage.

Range of doses (EQD2Gy) received during ICBT:

- HR-CTV D_{90} - 31 to 39 (mean 34.8)
- Bladder D_{2cc} - 15.1 to 29.6 (mean 23.8)
- Rectum D_{2cc} - 8.5 to 20.6 (mean 15.9)
- Sigmoid D_{2cc} - 1.5 to 20.2 (mean 11.04)

Table 1: Cumulative Dose (EQD2Gy) by EBRT plus ICBT to Target Volume and Organs at Risk

Parameter	Mean (± SD) EQD2 (Gy)	Recommended Limit
HR-CTV D_{90}	84.82(± 2.45)	80-90[2]
Bladder D_{2cc}	72.93(± 2.96)	<90[2]
Rectum D_{2cc}	65.62(± 2.97)	<75[4]
Sigmoid D_{2cc}	62.06(± 2.91)	<75[4]

All doses to the organs at risk were within tolerance limits.

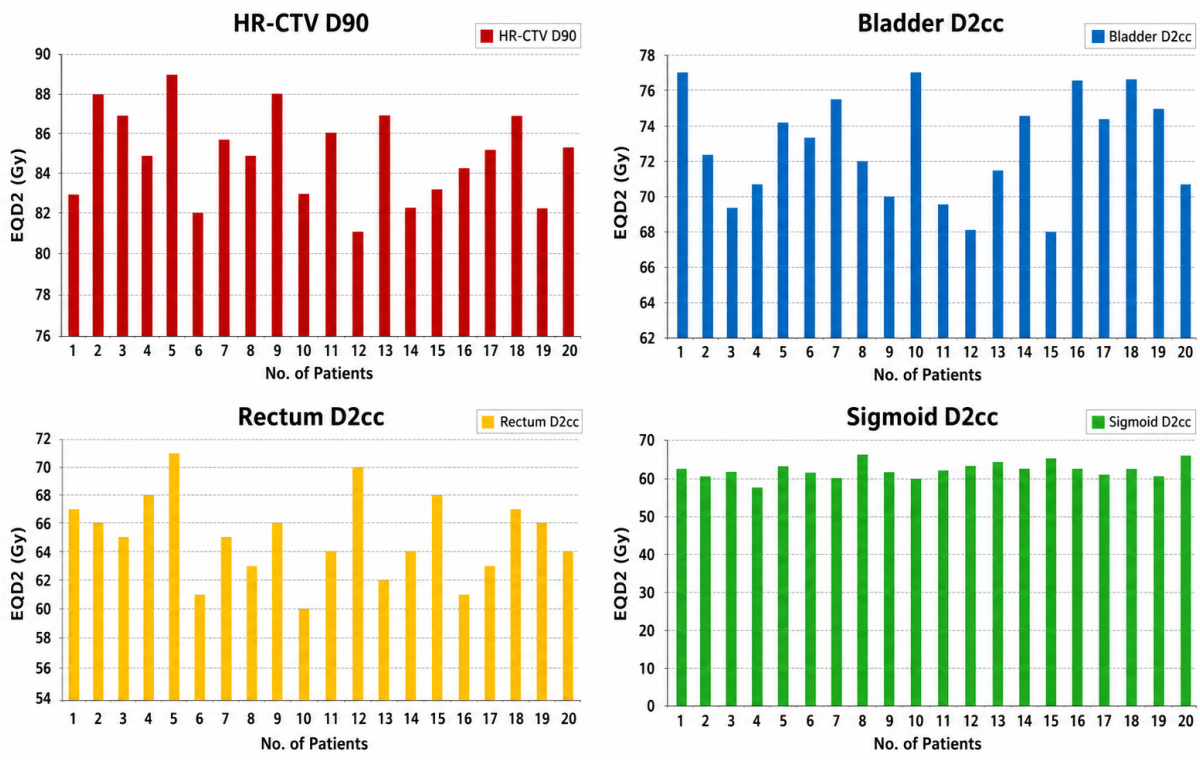

Figure 3: Cumulative Doses to Clinical Target Volume (HR-CTV D_{90}) and Equivalent dose (EQD2) of 2 cc volume (D_{2cc}) to OARs

Toxicity Profile: The treatment was well tolerated, with only mild acute toxicities observed. Grade 1 vaginitis was the most common adverse effect, occurring in 35% (n=7) of patients. Gastrointestinal toxicity was minimal, with Grade 1 diarrhea observed in 10% (n=2) of patients and Grade 2 diarrhea in another 10% (n=2). No patients experienced Grade 3 or Grade 4 toxicities, highlighting the safety of CT-based image-guided HDR brachytherapy.

Genitourinary toxicity was nominal as well, as 20 % (n=4) patients experienced Grade 1 urinary symptoms, while only 5% (n=1) patient suffered from Grade 2 cystitis. 30% (n=6) patients complained of non-specific, mild, intermittent

lower abdominal pain, whereas, 15% (n=3) patients reported fatigue while undergoing treatment.

Clinical Outcome: Clinical response evaluation demonstrated a high rate of tumor control. After completion of treatment, patients were kept on close follow up at monthly intervals for a minimum period of 6 months, with imaging done at an interval of 3 months. After 6 months of close observation, complete response (CR) was achieved in 90% (n=18) of patients, while the remaining 10% (n=2) patients exhibited partial response (PR). These outcomes are comparable with previously published studies evaluating HDR brachytherapy in cervical cancer, which have reported similar response rates.[5,6]

Discussion

The present prospective study evaluated the dosimetric parameters, acute toxicity profile, and early clinical outcomes of CT-guided high-dose-rate (HDR) intracavitary brachytherapy using a cobalt-60 (Co-60) linear source in patients with locally advanced cervical cancer treated with definitive concurrent chemoradiotherapy. The study demonstrated excellent target coverage with a mean cumulative HR-CTV D90 of 84.82 Gy EQD2 while maintaining bladder, rectum, and sigmoid D2cc doses within internationally recommended tolerance limits.

These favourable dosimetric outcomes translated into a 90% complete clinical response with only Grade 1–2 acute toxicities and no Grade ≥3 adverse events. Collectively, these findings indicate that CT-guided Co-60 HDR brachytherapy is a feasible and effective treatment strategy capable of achieving high-quality image-guided brachytherapy outcomes, particularly in centres where MRI-guided adaptive brachytherapy is not routinely available.

Image-guided adaptive brachytherapy (IGABT) has transformed the management of locally advanced cervical cancer by replacing conventional point-based prescription with individualized volumetric treatment planning. The GEC-ESTRO Working Group established HR-CTV D90 as the principal parameter for target dose evaluation and D2cc of the bladder, rectum, and sigmoid as standard dose-volume metrics for organs at risk (OARs). These recommendations have been adopted internationally because volumetric planning facilitates optimization, thus improving tumour coverage while reducing treatment-related morbidity compared with conventional two-dimensional brachytherapy.[1,4,10-12] Adequate HR-CTV dose escalation remains one of the strongest predictors of local control after definitive chemoradiotherapy. Recent GEC-ESTRO, IBS-GEC ESTRO and American Brachytherapy Society (ABS) guidelines recommend a cumulative HR-CTV D90 EQD2 of 80–90 Gy, where achieving or exceeding the dose of 85 Gy does not violate the OAR constraints.[11,12] In the current study, the mean cumulative HR-CTV D90 EQD2 of 84.82 Gy was well within the recommended therapeutic limits, demonstrating successful dose escalation while maintaining acceptable normal tissue doses.

Our findings are in accordance with the landmark EMBRACE-I study, in which MRI-guided adaptive brachytherapy achieved a median HR-CTV D90 EQD2 of approximately 85 Gy and achieved five-year local control rates exceeding 92% with low rates of severe late toxicity.[5] Although MRI remains the reference standard because of its superior soft-tissue delineation, the present results indicates the importance of carefully performed CT-guided planning in achieving dosimetric objectives similar to those reported in large international collaborative studies. This observation is particularly relevant in developing countries, where routine MRI-guided brachytherapy is often limited by cost, infrastructure, and scheduling constraints.

The HR-CTV dose observed in the present study is also consistent with the RetroEMBRACE analysis, which demonstrated a clear dose–response relationship between HR-CTV D90 and local tumour control. Patients receiving cumulative HR-CTV EQD2 doses above 85 Gy experienced significantly lower local recurrence than those receiving lower doses, emphasizing the importance of adequate target dose escalation during brachytherapy treatment.[13]

Newer findings from EMBRACE-I have further shown that insufficient HR-CTV coverage is an independent predictor of local failure despite modern chemoradiotherapy, suggesting the vital role of optimized brachytherapy treatment in cervical cancer management.[5] The EMBRACE II protocol based on the results of EMBRACE-I and Retro EMBRACE analyses by validating advanced dose–volume prescription strategies, standardized contouring, and adaptive planning techniques, provides the current benchmark for image-guided adaptive brachytherapy in locally advanced cervical cancer.[14]

Recent developments in CT-guided image-guided brachytherapy further support the clinical relevance of the present findings. Despite to its lower soft-tissue delineation of CT as compared to MRI and possible overestimation of residual tumour volume, standardized contouring recommendations published by IBS-GEC ESTRO have substantially improved target delineation and treatment accuracy.[12] CT-based planning with accurate applicator reconstruction and individualized dwell time optimization, when combined with meticulous

clinical examination, can provide clinically acceptable target coverage while maintaining OAR doses within safe limits. Recent Asian reports by Li et al and Suzumura et al, have demonstrated cumulative HR-CTV D90 EQD2 values ranging from 82 to 87 Gy with favourable local control and acceptable toxicity, findings that closely reflect the observations in the present study.[16-18]

An important highlight of the current study is the uniformity of treatment delivery. All the patients were planned with a similar treatment schedule and received external beam radiotherapy by IMRT technique to a dose of 50 Gy in 25 fractions with concurrent weekly cisplatin, followed by intracavitary HDR brachytherapy boost in three fractions with dose of 7 Gy using a standardized CT-based planning protocol. All the patients completed the overall treatment within 60 days. This treatment uniformity minimizes any confounding arising due to variations in external beam dose, chemotherapy or brachytherapy fractionation and strengthens the interpretation that the favourable dosimetric outcomes primarily resulted from optimized image-guided planning. Furthermore, individualized dose optimization based on dose-volume histogram (DVH) parameters ensured excellent HR-CTV coverage while respecting established OAR constraints, reflecting current principles of modern adaptive brachytherapy.

Overall, the target dose achieved in this study is consistent with contemporary international recommendations and compares favourably with outcomes reported from both MRI guided adaptive brachytherapy and modern CT guided techniques. These findings support the evidence that CT guided HDR brachytherapy, when performed according to standardized contouring guidelines and rigorous quality assurance protocols, represents a practical and effective alternative in institutions where MRI-guided adaptive brachytherapy cannot be routinely implemented.

Although, adequate target dose escalation is essential to achieve therapeutic goals and durable local control, minimizing radiation exposure to surrounding normal tissues is equally important in optimizing the therapeutic ratio. The transition from point-based dosimetry to volumetric image-guided brachytherapy has enabled more accurate assessment of doses delivered to organs at risk (OARs) and D2cc of the bladder, rectum and sigmoid colon are regarded as the standard dosimetric parameters because of their strong correlation with radiation-induced morbidity. [1,4,10-12] In the present study, the mean cumulative bladder D2cc EQD2 was 72.93 Gy, well below the recommended tolerance limit of 90 Gy EQD2. Similarly, the cumulative rectal and sigmoid D2cc EQD2 values were 65.62 Gy and 62.06 Gy, respectively, remaining comfortably within internationally accepted dose constraints. These favourable results reflect careful applicator placement, standardized CT-based contouring, and individualized dwell-time and dwell position optimization, and consistent adherence to modern image-guided planning principles. Comparable OAR doses have been reported in EMBRACE-I and subsequent multicentre studies, where compliance with volumetric dose constraints was associated with excellent tumour control and a low incidence of severe gastrointestinal and genitourinary toxicity.[5,13] Dose-response analyses from the EMBRACE collaboration have further demonstrated that increasing rectal and bladder D2cc is associated with a higher probability of late radiation morbidity, thereby validating the currently accepted dose constraints used in clinical practice.[19,20]

The favourable OAR dosimetry observed in this study translated into encouraging early clinical outcomes. Complete clinical response was achieved in 90% of patients, while the remaining patients demonstrated partial response during first 3 months of post-treatment assessment. Although longer follow-up is required to determine long-term local control and survival, this response rate is comparable with contemporary image-guided brachytherapy series reporting complete response rates between 85% and 95% following definitive chemoradiotherapy.[5,16,21] These findings reaffirm that successful tumour control depends not only on the imaging modality but also on accurate target delineation, optimal applicator geometry, individualized treatment planning, and maintenance of overall treatment time.

Acute treatment-related toxicity was minimal, with only Grade 1–2 gastrointestinal, genitourinary, and vaginal toxicities observed, and no Grade 3 or higher adverse events. Mild vaginitis was the most frequent complication and was successfully managed conservatively. The absence of severe acute toxicity is consistent with the favourable dose-volume parameters achieved in this cohort and supports the effectiveness of CT-guided treatment optimization. Similar toxicity profiles have been reported in EMBRACE-I and recent systematic reviews comparing three-dimensional image-guided brachytherapy with conventional two-dimensional techniques, which consistently demonstrate reductions in severe treatment-related morbidity following volumetric planning.[20,22]

An important feature of the present study is the exclusive use of a cobalt-60 HDR source. Although iridium-192 remains the most commonly used radionuclide for HDR brachytherapy, contemporary planning and clinical studies have demonstrated negligible clinically relevant differences between Co-60 and Ir-192 with respect

to target coverage, dose conformity, and OAR sparing when modern three-dimensional treatment planning is employed.[23,24] The primary advantage of Co-60 being a significantly longer physical half-life (5.27 years versus approximately 74 days for Ir-192), results in less frequent source replacement, lower operational costs and reduced interruptions in treatment. These advantages are particularly relevant in resource constrained healthcare systems, where financial limitations often restrict access to advanced radiotherapy technologies. Consequently, international agencies and professional societies recognize Co-60 HDR brachytherapy as an acceptable alternative to Ir-192, when adhered to standard image-guided planning protocols and rigorous quality assurance procedures.[25,26,27]

The observations of the present study have important implications for routine clinical practice, particularly in developing countries. Although MRI-guided adaptive brachytherapy remains the reference standard because of its superior soft-tissue visualization and widespread implementation, still it continues to be limited by infrastructure, cost and availability. Recent consensus recommendations acknowledge that CT based image guided brachytherapy, when performed adhering to standardized contouring protocols and integrated with thorough clinical examination, represents a practical and clinically effective alternative.[5,28] The favourable dosimetric profile and early clinical outcomes observed in the present study further support this approach and demonstrate that high-quality brachytherapy can be delivered without routine MRI availability.

The prospective design of the study allowed systematic collection of dosimetric analysis, toxicity evaluation and response assessment data using predefined assessment criteria. All patients received a uniform treatment protocol consisting of external beam radiotherapy with concurrent weekly cisplatin followed by CT-guided HDR intracavitary brachytherapy using an identical fractionation schedule and similar overall treatment time, thereby minimizing treatment heterogeneity. Furthermore, HR-CTV and OARs were contoured according to internationally accepted recommendations, all doses were reported as EQD2 values and acute toxicities were graded using CTCAE version 5.0, facilitating comparison with contemporary international literature.[9] The relatively small sample size and single centre design limit the generalizability of these findings. The six month follow up period precludes assessment of long-term local control, disease free survival, overall survival and late gastrointestinal or genitourinary toxicity, which remain critical endpoints in cervical cancer management. In addition, the absence of a direct MRI-guided comparison prevents evaluation of potential differences in target delineation and dosimetric accuracy. Finally, patient's quality of life outcomes were not evaluated and should be incorporated into future prospective studies.

Future research should focus on larger multicentre studies with longer follow up to validate these findings and establish long term oncological outcomes. Comparative evaluations of CT-guided and MRI-guided adaptive brachytherapy within similar patient populations would further clarify their relative clinical effectiveness. Emerging technologies, including hybrid intracavitary-interstitial brachytherapy, artificial intelligence assisted auto segmentation, deformable image registration and adaptive treatment planning, may further improve target delineation, treatment precision and workflow efficiency in cervical cancer brachytherapy.[29-31]

Hence, this prospective study demonstrates that CT-guided Co-60 HDR intracavitary brachytherapy provides excellent target coverage while maintaining bladder, rectum, and sigmoid doses within internationally accepted tolerance limits. The favourable dosimetric profile was associated with a high complete clinical response rate and minimal acute toxicity, supporting the safety and effectiveness of this approach. Although longer followup and larger multicentre studies are required, the present findings indicate that CT-guided Co-60 HDR brachytherapy is a clinically effective, cost-efficient, and practical treatment strategy for locally advanced cervical cancer, particularly in resource-limited settings where routine MRI-guided adaptive brachytherapy is not feasible.

Conclusion

Intracavitary brachytheraphy boost after definitive concurrent chemoradiation is an effective and practical treatment approach strategy for locally advanced carcinoma cervix. CT-based image-guided HDR brachytherapy using Co-60 source achieves dosimetric outcomes comparable to international standards, with excellent early clinical response and minimal toxicity. These results are consistent with the established guidelines by GEC-ESTRO, ABS and EMBRACE studies, reinforcing the role of image guided brachytherapy as the standard of care in modern radiation oncology.

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