e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(6); 251-256

Original Research Article

Cumulative Equivalent Dose in 2 Gy Fractions (EQD2) to the Target and Organs at Risk Following External Beam Radiotherapy and CT-Guided High-Dose-Rate Intracavitary Brachytherapy in Locally Advanced Carcinoma Cervix: A Prospective Dosimetric Study

Vipul Mehta[1], Manish Kumar Chaturvedi[2], Abhay Jain[3], Rohitashwa Dana[4], Shivani Gupta[5]

[1,3]Assistant Professor, Department of Radiation Oncology, S.M.S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

[2]Assistant Professor, Department of Radiation Oncology, J.L.N. Medical College, Ajmer, Rajasthan, India

[4]Ex. Sr. Professor and Head, Department of Radiation Oncology, S.M.S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

[5]Professor, Department of Radiation Oncology, S.M.S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

Received: 26-04-2026 / Revised: 25-05-2026 / Accepted: 26-06-2026
Corresponding Author: Dr. Manish Kumar Chaturvedi
Conflict of interest: Nil

Abstract:

Background: Locally advanced carcinoma cervix is commonly treated with external beam radiotherapy (EBRT) followed by high-dose-rate (HDR) intracavitary brachytherapy. Accurate estimation of cumulative radiation dose to the target and organs at risk is essential for optimizing tumour control while minimizing treatment-related toxicity.

Aim: This study aimed to evaluate the cumulative equivalent dose in 2 Gy fractions (EQD2) delivered to the target volume and organs at risk following EBRT and CT-guided HDR intracavitary brachytherapy in patients with locally advanced carcinoma cervix.

Materials and Methods: This prospective observational dosimetric study included 22 patients with histopathologically confirmed locally advanced carcinoma cervix, FIGO stage IIB–IIIB. All patients received EBRT to a dose of 50 Gy in 25 fractions, followed by CT-guided HDR intracavitary brachytherapy of 7 Gy per fraction for three fractions. Dose–volume histogram parameters were recorded for the target volume, bladder and rectum. Cumulative EQD2 was calculated using the linear–quadratic model, with an α/β ratio of 10 Gy for the target and 3 Gy for organs at risk.

Results: The mean age of patients was 59.1 ± 7.7 years. Stage IIB disease was present in 59.1% of patients, while 40.9% had stage IIIB disease. The mean target D90 was 8.05 ± 1.59 Gy per brachytherapy fraction. The mean cumulative EQD2 to the target was 86.90 ± 10.11 Gy. The mean cumulative EQD2 to the bladder and rectum, calculated using D2cc, was 93.93 ± 13.41 Gy and 78.39 ± 9.14 Gy, respectively.

Conclusion: CT-guided HDR intracavitary brachytherapy combined with EBRT provided satisfactory target dose coverage and enabled accurate volumetric assessment of organs at risk in patients with locally advanced carcinoma cervix. Cumulative EQD2-based evaluation is a useful method for biologically meaningful dose assessment and treatment optimization. Larger multicentric studies with long-term follow-up are required to correlate cumulative EQD2 with clinical outcomes and late radiation toxicity.

Keywords: Carcinoma cervix, CT-guided brachytherapy, HDR brachytherapy, EQD2, EBRT, dose–volume histogram, organs at risk.

DOI: 10.25258/ijpqa.17.6.45

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Introduction

Carcinoma of the cervix remains a major public health problem and is the fourth most frequently diagnosed cancer among women worldwide. According to GLOBOCAN 2022, an estimated 662,301 new cases and 348,874 deaths due to cervical cancer occurred globally, with nearly 90% of deaths reported from low- and middle-income countries where organized screening and human papillomavirus (HPV) vaccination coverage remain inadequate. [1] India continues to contribute substantially to the global cervical cancer burden, reporting approximately 127,500 new cases and 79,900 deaths in 2022. [2] Despite advances in screening and preventive strategies, a large proportion of Indian women continue to present with locally advanced disease requiring definitive radiotherapy. [3]

Concurrent chemoradiotherapy followed by intracavitary brachytherapy remains the standard treatment for locally advanced carcinoma cervix and has significantly improved local control and survival. [4] Brachytherapy is an indispensable component of radical treatment because it enables delivery of a very high radiation dose to the primary tumour while minimizing irradiation of adjacent normal tissues. Inadequate brachytherapy or failure to achieve optimal tumour dose has been associated with inferior treatment outcomes. [4,5]

Conventional brachytherapy planning was based on two-dimensional orthogonal radiographs using Point A for dose prescription and ICRU bladder and rectal reference points for organ-at-risk dose estimation. [6] However, point-based dosimetry does not accurately reflect the actual three-dimensional dose distribution within the tumour and surrounding organs at risk. The development of computed tomography (CT)-guided image-based brachytherapy has enabled accurate target delineation, volumetric assessment of organs at risk and optimization of dose distribution using dose–volume histogram (DVH) parameters. [7,8] CT-guided brachytherapy has become a practical alternative in centres where MRI-guided brachytherapy is not routinely available and has demonstrated improved target coverage with more reliable assessment of doses to the bladder and rectum. [9,10]

Modern image-guided brachytherapy recommends reporting dose using volumetric parameters rather than conventional reference points. The dose received by 90% of the high-risk clinical target volume (D90) is considered the principal parameter for target dose assessment, whereas the minimum dose to the most irradiated 2 cm^3 (D2cc) of the bladder and rectum is regarded as the most clinically relevant predictor of late toxicity. [11,12] Since treatment of carcinoma cervix consists of both external beam radiotherapy (EBRT) and high-dose-rate (HDR) brachytherapy delivered using different fractionation schedules, cumulative biological dose is best expressed as the equivalent dose in 2 Gy fractions (EQD2) using the linear-quadratic model. This approach permits meaningful summation of EBRT and brachytherapy doses and facilitates comparison with internationally accepted dose constraints. [12,13]

Although CT-guided HDR brachytherapy is increasingly practiced in Indian tertiary care centres, published evidence regarding cumulative EQD2 to the target and organs at risk remains limited. Evaluation of cumulative EQD2 using patient-specific DVH parameters is essential for optimizing tumour dose while maintaining acceptable doses to the bladder and rectum. Therefore, the present study was undertaken to evaluate the cumulative equivalent dose in 2 Gy fractions (EQD2) delivered to the target volume and organs at risk following external beam radiotherapy and CT-guided HDR intracavitary brachytherapy in patients with locally advanced carcinoma cervix.

Materials and Methods

This prospective observational dosimetric study was conducted in the Department of Radiation Oncology, Sawai Man Singh (SMS) Medical College and Attached Hospitals, Jaipur, Rajasthan, a tertiary care teaching hospital. Twenty-two patients with histopathologically confirmed locally advanced carcinoma cervix (FIGO stage IIB–IIIB) who completed the prescribed course of radical radiotherapy were included in the study. Patients with distant metastasis, incomplete treatment, or incomplete dosimetric records were excluded.

The study protocol was approved by the Institutional Ethics Committee of SMS Medical College and Associated Group of Hospitals, Jaipur. Written informed consent was obtained from all participants before enrolment, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

All patients received external beam radiotherapy (EBRT) to a total dose of 50 Gy in 25 fractions (2 Gy per fraction, five fractions per week), followed by CT-guided treatment planning for high-dose-rate (HDR) intracavitary brachytherapy, delivering 7 Gy per fraction in three fractions over a period of 3 weeks.

Following applicator insertion, computed tomography (CT) simulation was performed with the applicator in situ. CT images were transferred to the treatment planning system for contouring and dosimetric evaluation. The target volume and organs at risk (bladder and rectum) were delineated on CT images, and three-dimensional treatment planning was performed. Dose–volume histogram (DVH) parameters including D90, D95 and D100 for the target volume and D0.1cc, D0.2cc, D1cc, D2cc and D5cc for the bladder and rectum were recorded. ICRU bladder and rectal reference point doses were also documented.

The cumulative equivalent dose in 2-Gy fractions (EQD2) was calculated by combining the EBRT dose with the HDR brachytherapy dose using the linear–quadratic model. An α/β ratio of 10 Gy was used for target dose calculations, whereas an α/β ratio of 3 Gy was used for organs at risk. Target cumulative EQD2 was calculated using D90, while bladder and rectal cumulative EQD2 were calculated using D2cc dose–volume parameters.

Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables are presented as mean ± standard deviation (SD) and range, whereas categorical variables are expressed as frequencies and percentages. Descriptive statistics were used to summarise patient characteristics, target dose–volume parameters, organ-at-risk doses and cumulative EQD2 values.

Results

A total of 22 patients with histopathologically confirmed locally advanced carcinoma cervix were included in this prospective dosimetric study. All patients completed external beam radiotherapy (EBRT) to a dose of 50 Gy in 25 fractions, followed by CT-guided treatment planning for high-dose-rate (HDR) intracavitary brachytherapy, delivering 7 Gy per fraction in three fractions over a period of 3 weeks. All patients were available for dosimetric evaluation.

Patient Characteristics: The baseline demographic and clinical characteristics of the study population are presented in Table 1. The mean age of the patients was 59.1 ± 7.7 years (range, 46–70 years). Twelve patients (54.5%) were younger than 60 years, while 10 patients (45.5%) were aged 60 years or above. According to the FIGO 2018 staging system, 13 patients (59.1%) had stage IIB disease and nine patients (40.9%) had stage IIIB disease. Squamous cell carcinoma was the histopathological diagnosis in all patients.

Table 1: Baseline demographic and clinical characteristics of the study population (N = 22)

Characteristic	Value
Age (years), mean ± SD	59.1 ± 7.7
Age range (years)	46–70
Age <60 years	12 (54.5%)
Age ≥60 years	10 (45.5%)
FIGO stage IIB	13 (59.1%)
FIGO stage IIIB	9 (40.9%)
Histopathology (Squamous cell carcinoma)	22 (100%)

Target Dose–Volume Parameters: Target dose coverage was evaluated using dose–volume histogram (DVH) parameters derived from CT-based treatment planning. The mean dose delivered to 90% of the target volume (D90) was 8.05 ± 1.59 Gy (range, 5.0–10.4 Gy). The corresponding mean D95 and D100 were 7.19 ± 1.43 Gy (range, 4.7–9.3 Gy) and 4.79 ± 0.93 Gy (range, 2.7–5.9 Gy) respectively.

Table 2: Target dose–volume histogram parameters

Parameter	Mean ± SD (Gy)	Minimum	Maximum
D90	8.05 ± 1.59	5.00	10.40
D95	7.19 ± 1.43	4.70	9.30
D100	4.79 ± 0.93	2.70	5.90

Dose–Volume Parameters of Organs at Risk: The dose–volume parameters for the bladder and rectum obtained from CT-based treatment planning are summarized in Table 3.

For the bladder, the mean doses to the most irradiated 0.1 cc, 0.2 cc, 1 cc, 2 cc and 5 cc volumes were 11.44 ± 2.18 Gy, 10.67 ± 2.08 Gy, 8.84 ± 1.75 Gy, 7.10 ± 1.46 Gy and 6.13 ± 1.15 Gy respectively. The mean ICRU bladder reference point dose was 5.19 ± 1.18 Gy.

For the rectum, the mean doses to the most irradiated 0.1 cc, 0.2 cc, 1 cc, 2 cc and 5 cc volumes were 7.48 ± 1.54 Gy, 7.17 ± 1.47 Gy, 6.28 ± 1.23 Gy, 5.47 ± 1.03 Gy and 4.70 ± 1.08 Gy respectively. The mean ICRU rectal reference point dose was 5.03 ± 1.24 Gy.

Table 3: Dose–volume histogram parameters of organs at risk

Dose parameter	Bladder (Mean ± SD, Gy)	Rectum (Mean ± SD, Gy)
ICRU reference point	5.19 ± 1.18	5.03 ± 1.24
D0.1cc	11.44 ± 2.18	7.48 ± 1.54
D0.2cc	10.67 ± 2.08	7.17 ± 1.47
D1cc	8.84 ± 1.75	6.28 ± 1.23
D2cc	7.10 ± 1.46	5.47 ± 1.03
D5cc	6.13 ± 1.15	4.70 ± 1.08

Cumulative Equivalent Dose in 2-Gy Fractions (EQD2): Cumulative equivalent dose in 2-Gy fractions (EQD2) was calculated by combining the EBRT dose with the HDR brachytherapy dose using the linear–quadratic model. Target EQD2 was determined using D90, while bladder and rectal EQD2 were calculated using D2cc dose–volume parameters.

The mean cumulative EQD2 to the target (D90) was 86.90 ± 10.11 Gy, with values ranging from 68.75 to 103.04 Gy. The mean cumulative EQD2 to the bladder (D2cc) was 93.93 ± 13.41 Gy (range, 80.62–119.94 Gy), whereas the mean cumulative EQD2 to the rectum (D2cc) was 78.39 ± 9.14 Gy (range, 66.80–96.18 Gy).

Table 4: Cumulative equivalent dose in 2-Gy fractions (EQD2) to the target and organs at risk

Structure	Dose Metric	Mean ± SD (Gy EQD2)	Minimum	Maximum
Target	D90	86.90 ± 10.11	68.75	103.04
Bladder	D2cc	93.93 ± 13.41	80.62	119.94
Rectum	D2cc	78.39 ± 9.14	66.80	96.18

Discussion

The present prospective observational dosimetric study evaluated the cumulative equivalent dose in 2 Gy fractions (EQD2) delivered to the target volume and organs at risk following external beam radiotherapy (EBRT) and CT-guided high-dose-rate (HDR) intracavitary brachytherapy in patients with locally advanced carcinoma cervix. The study demonstrated satisfactory target dose coverage with a mean D90 of 8.05 ± 1.59 Gy per brachytherapy fraction and a mean cumulative EQD2 of 86.90 ± 10.11 Gy. The mean cumulative EQD2 to the bladder and rectum was 93.93 ± 13.41 Gy and 78.39 ± 9.14 Gy, respectively, reflecting the cumulative biological dose received by the organs at risk during the complete course of treatment.

Image-guided brachytherapy has become the standard approach for treatment planning in carcinoma cervix because it enables accurate delineation of the target and surrounding normal tissues and facilitates volumetric dose assessment using dose–volume histogram (DVH) parameters. [7,8] Unlike conventional point-based dosimetry, volumetric parameters such as D90 for the target and D2cc for organs at risk provide a more reliable estimate of tumour dose coverage and radiation exposure to normal tissues. [11,12] In the present study, the mean target D90 of 8.05 Gy per fraction translated into a cumulative EQD2 of 86.90 Gy, indicating adequate biological dose delivery to the target. This observation is consistent with the recommendations of GEC-ESTRO and the American Brachytherapy Society, which advocate the use of D90 as the principal dosimetric parameter for assessment of target coverage in image-guided brachytherapy. [8,11]

The bladder remains one of the most important dose-limiting organs during intracavitary brachytherapy. In the present study, the mean bladder D2cc per fraction was 7.10 Gy, corresponding to a cumulative EQD2 of 93.93 Gy. Similar studies by Patil et al. demonstrated that volumetric bladder doses obtained using CT-based planning differed considerably from conventional ICRU point doses, highlighting the superiority of volumetric dose assessment for estimating the actual dose received by the bladder.[10] Likewise, Ling et al. reported that CT-assisted treatment planning improved visualization of bladder dose distribution compared with conventional radiographic techniques. [6] These findings support the routine use of CT-based volumetric parameters for bladder dose evaluation during HDR brachytherapy.

The rectum is another critical organ at risk because excessive radiation exposure is associated with late gastrointestinal toxicity. In the present study, the mean rectal D2cc per fraction was 5.47 Gy, resulting in a cumulative EQD2 of 78.39 Gy. Similar observations have been reported by Fellner et al., who demonstrated improved assessment of rectal dose using CT-based treatment planning compared with conventional radiographic planning. [9] Patil et al. also observed that volumetric rectal dose parameters provided a better estimate of radiation exposure than ICRU reference point measurements. [10] These findings emphasize the importance of volumetric dose assessment for minimizing rectal toxicity while maintaining adequate target coverage.

An important strength of the present study is the use of cumulative EQD2 rather than physical dose alone. Because definitive treatment of carcinoma cervix combines EBRT and HDR brachytherapy using different fractionation schedules, reporting cumulative EQD2 provides a biologically relevant estimate of the total dose delivered to the target and organs at risk. The linear-quadratic model permits summation of doses from different treatment components and facilitates comparison with internationally accepted dose constraints and image-guided brachytherapy recommendations. Contemporary evidence continues to support cumulative EQD2-based reporting as an integral component of image-guided adaptive brachytherapy for treatment optimization and outcome evaluation. [8,11,13-15] The present study therefore provides clinically meaningful dosimetric data that may assist in optimization of treatment planning and evaluation of dose constraints in routine clinical practice.

The findings of the present study should be interpreted in light of certain limitations. The study was conducted at a single tertiary care centre with a relatively small sample size of 22 patients, which may limit the generalizability of the findings. In addition, the study was confined to dosimetric evaluation and did not assess long-term clinical outcomes such as local tumour control, survival or late radiation toxicity. Future studies with larger patient cohorts and longer follow-up are required to correlate cumulative EQD2 with treatment outcomes and radiation-related complications.

Despite these limitations, the present study provides valuable evidence regarding cumulative EQD2 following EBRT and CT-guided HDR intracavitary brachytherapy in patients with locally advanced carcinoma cervix. The use of CT-based treatment planning and DVH-derived parameters enabled comprehensive assessment of target dose coverage and organ-at-risk doses, thereby supporting the continued adoption of image-guided brachytherapy in routine clinical practice.

Conclusion

CT-guided high-dose-rate (HDR) intracavitary brachytherapy, when integrated with external beam radiotherapy (EBRT), enabled comprehensive volumetric dosimetric evaluation of the target volume and organs at risk in patients with locally advanced carcinoma cervix. The use of cumulative equivalent dose in 2 Gy fractions (EQD2) provided a biologically meaningful assessment of the total radiation dose delivered during the complete course of treatment. In the present study, satisfactory target dose coverage was achieved while cumulative doses to the bladder and rectum were quantified using clinically relevant dose–volume parameters. These findings support the role of CT-guided image-based brachytherapy and cumulative EQD2 in optimizing treatment planning and facilitating comprehensive dosimetric evaluation of target coverage and organ-at-risk exposure. Future multicentric studies with larger patient cohorts and long-term clinical follow-up are required to validate these findings and establish the relationship between cumulative EQD2, tumour control, treatment outcomes and late radiation-induced toxicity.

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