Jurnal Ilmu Fisika
Vol. 18, No. 2, September 2026, pp. 199–209
ISSN: 1979-4657 (Print); 2614-7386 (Online)
https://doi.org/10.25077/jif.18.2.199-209.2026

Jurnal Ilmu Fisika
Open Access

Radiobiological Evaluation of Stage III Cervical Cancer Radiotherapy Using EUD-Based TCP and NTCP in 3DCRT

Angelica Defalma, Sri Oktamuliani, Muhammad Ilyas
Medical Physics Laboratory, Department of Physics, Faculty of Mathematics and Natural Sciences, Universitas Andalas, Padang, 25163, Indonesia

Article Info

Article History:

Received January 12, 2026
Revised August 30, 2026
Accepted September 20, 2026
Published online September 30, 2026

Keyword:

Cervical Cancer
Radiotherapy
Homogeneity Index
Conformity Index
Equivalent Uniform Dose

Corresponding Author:

Sri Oktamuliani,
Email: srioktamuliani@sci.unand.ac.id

ABSTRACT

This study evaluated the dosimetric and radiobiological parameters in 24 patients with Stage III cervical cancer treated with Three-Dimensional Conformal Radiation Therapy (3DCRT) at Universitas Andalas Hospital, using an Indonesian clinical dataset for context-specific radiobiological evaluation. Physical dose quality was assessed using the Homogeneity Index (HI) and Conformity Index (CI). Biological effectiveness was evaluated using Niemierko's Equivalent Uniform Dose (EUD) model to determine Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP). Dose-volume histogram (DVH) data were extracted from the Eclipse TPS and processed via Python. Physical planning demonstrated acceptable conformity (CI = 0.9695 ± 0.0084) and homogeneity (HI = 0.0739 ± 0.0129). Mean TCP for the external beam radiotherapy phase (50 Gy in 25 fractions) was 41.36% ± 0.31%, representing moderate biological control prior to brachytherapy. Organs at risk exhibited low toxicity for the rectum (NTCP = 0.40% ± 0.18%) and bowel (NTCP = 2.06% ± 3.00%). Conversely, the bladder showed the highest complication risk (NTCP = 83.16% ± 26.78%, EUD = 93.57 ± 9.99 Gy), frequently exceeding tolerance limits due to anatomical proximity and volume variability. 3DCRT yields satisfactory physical coverage and rectal/bowel sparing, but requires standardized bladder protocols to minimize toxicity.

Copyright © 2026 Author(s)

1. INTRODUCTION

Cervical cancer is a major global health problem and ranks as the fourth most common cancer among women worldwide. Persistent infection with high-risk human papillomavirus (HPV) is the primary etiological factor and is responsible for the vast majority of cervical cancer cases (Pandey, 2017). Given its anatomical location within the pelvic region, radiotherapy plays a central role in the management of locally advanced cervical cancer, where accurate dose delivery and organ-at-risk sparing are critical for treatment effectiveness and toxicity reduction (Khatun, 2020).

In Stage III cervical cancer, radiotherapy plays an important role because the disease has usually spread locally and is difficult to treat with surgery alone (Fader, 2018). Therefore, radiotherapy becomes the main treatment approach to control the tumor. It is commonly delivered using external beam radiotherapy and combined with brachytherapy to increase the dose to the primary tumor (Mayadev et al., 2022). In this stage, careful treatment planning is very important to ensure that the tumor receives an adequate dose while minimizing radiation exposure to nearby organs such as the bladder, rectum, and bowel (Malafi, 2024).

For locally advanced disease, the objective of irradiation is not limited to creating a geometrically satisfactory dose distribution. The radiation field must encompass the intended target while reducing unnecessary exposure of the adjacent pelvic organs, whose position and shape may

Attribution-NonCommercial 4.0 International

change throughout a multi-fraction treatment. Consequently, the quality of a plan should be interpreted across several complementary dimensions: coverage of the planning target volume (PTV), the spatial distribution of dose within that volume, and the expected response of both tumor and normal tissues. An apparently favorable geometric index does not necessarily establish a favorable biological outcome, particularly when organs at risk occupy regions close to the target. This distinction is especially relevant when the prescribed external-beam course represents only one component of a combined treatment strategy (Mayadev et al., 2022).

A linear accelerator (LINAC) is used in external beam radiotherapy to deliver high-energy radiation to the tumor. Several modern techniques are available, including Three-Dimensional Conformal Radiation Therapy (3DCRT), Intensity-Modulated Radiation Therapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT). Compared with 3DCRT, IMRT and VMAT have been shown in clinical studies to reduce radiation doses to organs at risk such as the bladder, rectum, and bowel, which can lower the risk of treatment-related toxicities in cervical cancer patients. For example, both IMRT and VMAT reduce doses to pelvic organs compared to 3DCRT, with VMAT often providing further dose reduction in some dose levels (Antony et al., 2021). Despite these dosimetric advantages, 3DCRT is still widely used in many clinical settings, particularly in developing countries such as Indonesia, because it is more accessible, cost-effective, and supported by existing infrastructure. With careful planning, 3DCRT can still achieve clinically acceptable target coverage and remains relevant where more advanced techniques may not be routinely available (Cherry & Duxbury, 2023).

The clinical value of comparing treatment techniques also depends on the context in which a plan is implemented. Advanced modulation may improve organ sparing in many settings, but access to equipment, commissioning, quality assurance and trained personnel influences the technique that can be delivered consistently. In an institution using 3DCRT, quantitative plan assessment remains important even when the technique itself is established. A local evaluation can help identify which organs require particular attention during simulation, optimization and daily preparation, rather than relying solely on the overall acceptability of a plan. Nevertheless, comparisons across published studies must account for different target definitions, dose prescriptions and conformity metrics; an index obtained under one definition cannot automatically be ranked against a numerical result derived using another definition (Antony et al., 2021; Effina et al., 2022).

In radiotherapy treatment planning, both physical and biological aspects are evaluated to ensure effective and safe dose delivery. The Homogeneity Index (HI) and Conformity Index (CI) are used to assess the physical quality of dose distribution, while the Equivalent Uniform Dose (EUD) model is used to evaluate the biological effect of radiation. The EUD represents a non-uniform dose as an equivalent uniform dose that would have the same biological impact. From the EUD value, Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) can be calculated to predict the effectiveness of tumor control and the risk of side effects on normal tissues (Nadova et al., 2021).

Dose–volume histograms summarize the proportion of a contoured structure exposed to different dose levels, but they do not retain the full spatial pattern of irradiation. Physical indices such as CI and HI therefore answer questions that differ from those addressed by radiobiological models. CI describes a selected aspect of prescription-dose coverage, whereas HI reflects dose variation within the target. EUD reduces a heterogeneous distribution to a model-dependent equivalent value, using tissue-specific parameters to emphasize the dose regions considered biologically influential. TCP and NTCP then translate this equivalent dose into predicted probabilities through assumed dose–response relationships. These predictions are useful for comparative evaluation but should not be presented as directly observed tumor-control rates or complication incidences (Mazonakis et al., 2022; Okunieff et al., 1995).

Previous studies have demonstrated the usefulness of the EUD model in radiotherapy evaluation, which applied the EUD model to estimate TCP in glioblastoma cases and found that considering cellular repair (rEUD model) produced lower TCP values, showing that some tumor cells could survive due to sublethal damage repair (Fatimah & Widita, 2018). Similarly, Pratista & Widita (Pratista & Widita, 2023) determined fractionation schemes using the EUD model in IMRT and

concluded that the hypofractionation scheme was the safest for normal organs while still meeting the required dose for the target volume.

Several methodological considerations are critical when applying EUD-derived endpoints. The estimated response depends on the selected dose–response parameters, the clinical endpoint assigned to an organ, and the method used to discretize the DVH. When different values are adopted for volume dependence or the dose producing a 50% response, the same physical dose distribution may yield markedly different predicted probabilities. Furthermore, the underlying models generally simplify complex biological processes, including fractionation effects, heterogeneity in tissue response and changes in anatomy over the treatment course. Consequently, radiobiological indices are best interpreted alongside physical dose metrics and the assumptions used to compute them, not as an independent confirmation of patient outcomes (Nuraini & Widita, 2019; Pratista & Widita, 2023).

The 3DCRT is still widely used in many hospitals in Indonesia due to its cost-effectiveness and relatively simple equipment requirements. In high patient-volume settings, this technique is practical because it allows efficient treatment delivery while maintaining acceptable tumor coverage. However, evaluating treatment quality should not rely only on physical dose distribution but also consider radiobiological outcomes, particularly tumor control and normal tissue complications. Therefore, this study aims to evaluate the dosimetric quality and radiobiological effectiveness of 3DCRT in Stage III cervical cancer by analyzing EUD-based Tumor Control Probability and Normal Tissue Complication Probability.

Against this background, the present analysis addresses a specific practical question: how do apparently satisfactory CI and HI values in routinely delivered 3DCRT plans correspond to model-based tumor and organ-at-risk response estimates? The study focuses on a single-center series of 24 patients with Stage III cervical cancer and evaluates the external-beam component prescribed at 50 Gy in 25 fractions. Its contribution lies in reporting physical and radiobiological descriptors for the same set of plans and in identifying discrepancies that may warrant closer plan review. The results should therefore be understood as planning-based estimates for this cohort rather than as evidence of comparative effectiveness against other radiotherapy modalities or as measurements of clinical toxicity.

2. METHODS

2.1 Study Design, Dosimetric Evaluation, and Radiobiological Analysis

This quantitative descriptive study was conducted over a six-month period at the Radiation Oncology Unit of Universitas Andalas Hospital, Padang, Indonesia. The study utilized secondary data from 24 patients with histopathologically confirmed Stage III cervical cancer who underwent three-dimensional conformal radiation therapy (3DCRT) in 2024. All patients received a prescribed external beam radiation dose of 50 Gy delivered in 25 fractions using 6 MV photon beams. The inclusion criteria were completion of the prescribed 3DCRT treatment course and availability of complete dosimetric data in the Treatment Planning System (TPS). Patients with incomplete dose–volume histogram (DVH) data, a history of prior pelvic radiotherapy, or treatment using radiotherapy techniques other than 3DCRT were excluded. Dose–volume data for the planning target volume (PTV) and organs at risk (OARs), including the rectum, bladder, and bowel, were extracted from the Eclipse TPS. Data processing and subsequent radiobiological calculations were performed using Python (version 3.9).

The quality of the physical dose distribution was evaluated using the Conformity Index (CI) and Homogeneity Index (HI), based on dosimetric evaluation principles described in the International Commission on Radiation Units and Measurements (ICRU) Reports 62 and 83 (Gonultas, 2026). The CI was used to assess the extent to which the prescribed radiation dose adequately covered the PTV, while the HI quantified dose uniformity within the target volume. These indices provide complementary measures of treatment plan quality by characterizing target coverage and dose homogeneity. The CI was calculated using Equation (1):

$$CI = \frac{V_{95\%}}{V_{ptv}} \tag{1}$$

where $V_{95\%}$is the volume of the PTV that receives at least 95 % of the prescribed dose (50 Gy), and V_{ptv} is the total planning target volume. The value of CI close to one indicates that the radiation dose distribution conforms well to the target volume. The Homogeneity Index represents the uniformity of the dose distribution inside the target volume and is calculated using the formula:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\,\%}} \tag{2}$$

where $D_{2\%}$ is the dose received by 2% of the PTV, $D_{98\%}$ is the dose received by 98% of the PTV, and $D_{50\,\%}$ is the dose received by half of the PTV. A Homogeneity Index (HI) value of 0 represents a perfectly uniform dose distribution, which is considered ideal (Rather et al., 2024).

Radiobiological evaluation was conducted using the Equivalent Uniform Dose (EUD) model developed by Niemierko (Mazonakis et al., 2022). The EUD represents a hypothetical uniform dose that would have the same biological effect as the actual non-uniform dose and is calculated using:

$$EUD = \left(\sum_i v_i D_i^a\right)^{\frac{1}{a}} \tag{3}$$

where v_i is the fractional sub-volume receiving dose D_i, and α is a tissue-specific parameter reflecting the volume effect. EUD values were subsequently used to calculate TCP and NTCP using the logistic dose-response formulation EUD values were subsequently used to calculate TCP and NTCP using the logistic dose-response formulation:

$$TCP = \left[1 + \left(\frac{TCD_{50}}{EUD}\right)^{4\gamma_{50}}\right]^{-1} \tag{4}$$

where TCD_{50} is the dose required to control 50% of the tumor population, and γ_{50} defines the slope of the dose–response curve at that point. Similarly, the Normal Tissue Complication Probability (NTCP) was determined to estimate the likelihood of radiation-induced complications in surrounding organs using the following equation:

$$NTCP = \left[1 + \left(\frac{TD_{50}}{EUD}\right)^{4\gamma_{50}}\right]^{-1} \tag{5}$$

where TD_{50} is the dose causing complications in 50% of the exposed population, and γ_{50} indicates the steepness of the response curve for normal tissue. The radiobiological parameters used in this study, including α, γ_{50}, TD_{50}, were adopted from the work of (Okunieff et al., 1995), which provides experimentally and clinically derived parameter values for tumor and normal tissue response. These parameters have been widely used in radiobiological modelling studies and are considered representative of tissue-specific dose–response characteristics. The selection of these values was intended to ensure consistency with established radiobiological models and to provide a reliable basis for estimating TCP and NTCP in cervical cancer radiotherapy. When the delivered dose approaches or exceeds TD_{50}, even small increases in dose can lead to a substantial rise in complication probability, particularly in tissues with a steeper response curve (higher γ_{50}). The complete set of radiobiological parameters (α, γ_{50}, TD_{50}, TCD_{50}, and α/β) applied to the target volume and organs at risk (OARs) are detailed in Table 1.

All calculations were automated using Python scripts that extracted dose–volume data points from cumulative DVH files at 10% intervals from D10% to D100%. The cumulative DVH data were first converted into differential form to obtain discrete dose-volume pairs (D_i, v_i). Dose binning was performed at fixed 10% volume intervals, and linear interpolation was applied between adjacent DVH points to ensure a continuous representation of the dose–volume relationship. These processed data were then used as input for the EUD calculation. The computed results were analyzed descriptively, including

the minimum, maximum, mean, and standard deviation for each parameter. Continuous data were tested for normality using the Shapiro–Wilk test ($\alpha = 0.05$). Normally distributed parameters were reported as Mean ± Standard Deviation (SD), whereas non-normally distributed parameters (specifically bladder EUD/NTCP and bowel NTCP) were presented.

Table 1 Parameters used for the calculation of NTCP and TCP

OAR	α	γ_{50}	TD_{50} (Gy)	TCD_{50} (Gy)	α/β (Gy)	Endpoint
Bowel	6	4	55	-	3	Obstruction
Bladder	2	4	80	-	8	Bladder toxicity
Rectum	8	4	80	-	3.9	Necrosis/Fistula
Cervix	10	0.69	-	64.38	3	Tumor

Because the analysis relies on planned DVHs rather than repeated anatomical imaging or observed clinical outcomes, the resulting EUD, TCP and NTCP estimates characterize the treatment plans under the selected parameter assumptions. They do not establish the cumulative dose delivered after brachytherapy, the influence of day-to-day anatomical changes, or the frequency of subsequent adverse events. In addition, sampling a cumulative DVH at 10% volume intervals can reduce resolution in high-dose regions; sensitivity to the DVH sampling approach should be considered when interpreting nonlinear EUD estimates, particularly for organs displaying extreme predicted values.

2.2 Ethical Approval

This study received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Andalas, Padang, Indonesia (Ethical Clearance No. 10/UN.16.2/KEP-FK/2025, issued on January 6, 2025).

3. RESULTS AND DISCUSSION

3.1 Analysis of Conformity Index (CI)

The descriptive statistical results for the CI of 24 Stage III cervical cancer patients are presented in Table 2. The CI values were found to be close to one for all patients, indicating high conformity between the prescribed dose and the target region.

As presented in Table 2, all CI values fell within the clinically acceptable range, indicating that the 3DCRT technique provided precise coverage of the target volume. A CI value approaching one reflects an optimal dose distribution that adequately covers the PTV while minimizing unnecessary irradiation of surrounding organs at risk (OARs). The consistency of CI values across all patients also indicates that treatment planning was performed systematically, adhering to the same contouring and beam arrangement criteria. High conformity ensures that the prescribed dose fully covers the tumor volume, contributing to improved tumor control and reduced side effects. To provide context for these findings, a comparison with previous studies is presented. Compared to previous research, the CI values obtained in this study show a substantially higher level of conformity. Earlier findings reported a CI value of 0.080 ± 0.023 for the 3DCRT technique, indicating low conformity and a dose distribution still far from ideal (Effina, 2021). Although the variation in the previous dataset was small, the CI values reflected suboptimal target coverage. In contrast, the present study demonstrates a much higher CI value of 0.9695 ± 0.0084, which is close to the ideal value of one. This difference may be influenced by variations in contouring protocols, treatment planning approaches, beam arrangement, and dose calculation algorithm used in each study. Despite these methodological differences, the comparison clearly shows that the dose distribution achieved in this study provides significantly better conformity to the PTV than previously reported.

The numerical difference between the present CI and the value reported in another investigation requires caution. Conformity indices are defined in multiple ways, and each definition has its own range and interpretation. Before inferring improved planning quality from a higher CI, the underlying equations, prescription isodose level, target contouring rules and treatment objectives should be checked for equivalence. Within this cohort, the narrow spread of CI values primarily supports consistency of

the selected metric across the examined plans. It cannot, on its own, demonstrate superior clinical control or lower toxicity compared with another population.

Table 2 Descriptive Statistics of CI from 24 cervical cancer patients

Minimum	Maximum	Mean	Std. Deviation
0.9539	0.9920	0.9695	0.0084

3.2 Analysis of Homogeneity Index (HI)

The descriptive statistical results of HI are presented in Table 3. The HI values were generally low across all patients, indicating that the dose distribution inside the PTV was uniform and well-balanced.

The results in Table 3 indicate that all HI values fall within the recommended range. The relatively small variations in HI among patients indicate consistent planning and delivery of radiation. These findings confirm that the 3DCRT technique used in this study achieved a good balance between target coverage and dose uniformity, contributing to the overall quality of the treatment plan. Compared to previous research, the HI value obtained in this study shows better dose uniformity. The earlier study reported an HI of 0.091 for the 3DCRT technique, indicating a wider dose spread within the PTV (Effina, 2021). In contrast, the mean HI in this study (0.0739) is noticeably lower and remains below the ICRU-recommended threshold, demonstrating a more homogeneous dose distribution. This difference suggests that the planning approach used in the present study produced a more balanced and consistent radiation dose across the target volume.

Table 3 Descriptive Statistics of HI from 24 cervical cancer patients

Minimum	Maximum	Mean	Std. Deviation
0.0498	0.1011	0.0739	0.0129

Similarly, the observed HI distribution offers evidence of limited relative dose variation within the contoured PTV, but it does not describe the dose received by individual organs at risk. A relatively homogeneous target may coexist with clinically relevant high-dose exposure in a nearby organ, because target uniformity and organ sparing reflect different geometric constraints. For this reason, the low HI and near-unity CI should be interpreted jointly with the organ-specific EUD and NTCP results rather than treated as sufficient evidence of overall treatment safety.

3.3 Analysis of Equivalent Uniform Dose (EUD) and Tumor Control Probability (TCP)

The results of EUD and TCP for the PTV are presented in Table 4. The EUD values obtained showed relatively small variations among all patients, indicating that the dose distribution within the PTV was uniform. The TCP values were also consistent, with an average value that falls within the moderate category of tumor control probability.

Table 4 Descriptive Statistics of EUD and TCP

Value	EUD PTV (Gy)	TCP (%)
Min	56.20	40.73
Max	57.31	42.04
Mean ± SD	56.74 ± 0.26	41.36 ± 0.31

Based on Table 4, the uniform EUD values indicate that the prescribed dose of 50 Gy in 25 fractions was effectively delivered to the entire target volume. This suggests that the dose distribution from the 3DCRT planning system provided an even biological response throughout the tumor region, ensuring that most tumor cells received a sufficient therapeutic dose. The small variation in EUD among patients also reflects consistent dose delivery and stable planning accuracy during the treatment process.

The TCP values obtained in this study were categorized as moderate, which means that the probability of achieving tumor control was adequate but not yet optimal. This condition can be attributed to the fact that the prescribed dose of 50 Gy served as the external beam component before brachytherapy, so the overall tumor control would be achieved after both treatment stages were

completed. In clinical practice, brachytherapy delivers a high localized dose directly to the tumor with a steep dose gradient, allowing for dose escalation to the target while sparing surrounding normal tissues, which significantly contributes to improving TCP. Additionally, variations in tumor volume, geometry, and tissue characteristics among patients can impact oxygenation levels and radiosensitivity, resulting in differences in biological response. Therefore, although the TCP values were moderate, they still represent effective tumor control for the external beam phase of radiotherapy in Stage III cervical cancer.

Compared to previous research, the TCP values obtained in this study are understandably lower. Earlier work on head and neck cancer reported TCP values ranging from 82% to 95% depending on the radiobiological model used, resulting in significantly higher tumor control estimates. These differences arise because the previous study evaluated full-dose treatment using multiple biological models, while the TCP in the present research reflects only the External Beam Radiotherapy (EBRT) phase before brachytherapy is added. Consequently, the lower TCP value of 41.36% in this study does not imply inferior treatment quality but instead reflects the staged treatment approach for cervical cancer, where the final tumor control probability is achieved cumulatively after both EBRT and brachytherapy (Lalonde et al., n.d.).

The estimated TCP of 41.36% must be distinguished from an observed local-control rate. It was calculated from a model applied to the 3DCRT external-beam phase, whereas definitive cervical-cancer treatment commonly includes subsequent brachytherapy. The reported estimate therefore does not quantify the final biological effect of the combined course. Moreover, model parameters obtained from previous studies may not fully capture the stage distribution, tumor heterogeneity and patient-specific response in this cohort. A meaningful clinical validation would require documented combined-course dose information, follow-up outcomes and, ideally, uncertainty analysis for the selected dose–response parameters.

3.4 Analysis of Equivalent Uniform Dose (EUD) and Normal Tissue Complication Probability (NTCP)

3.4.1 Rectum

The results of EUD and NTCP for the rectum are presented in Table 5. The EUD values obtained were below the tolerance limit of the rectum, and the NTCP values were relatively low for all patients, indicating a minimal probability of radiation-induced complications.

Table 5 Descriptive Statistics of Rectum EUD and NTCP

Value	Rectum EUD (Gy)	Rectum NTCP (%)
Min	51.37	0.08
Max	58.85	0.73
Mean ± SD	56.31 ± 1.95	0.40 ± 0.18

The low EUD and NTCP values for the rectum indicate that the radiation dose received by this organ remained within the safe threshold, showing that the 3DCRT planning effectively minimized unnecessary exposure. This was achieved through appropriate beam arrangement and shielding during treatment planning, which limited posterior dose spill to the rectal area. Clinically, low NTCP values correspond to a reduced risk of complications such as rectal bleeding, ulceration, or proctitis. Similar findings have been reported in previous studies using the Lyman-Kutcher-Burman (LKB) model, which demonstrated that rectal toxicity is strongly influenced by dose-volume parameters and remains low when appropriate dose constraints are applied (Starmans et al., 2012). These findings demonstrate that the dose distribution around the rectum was well-controlled and that the radiation protection strategy for this organ was effectively implemented in all patient treatment plans.

3.4.2 Bowel

The descriptive results for EUD and NTCP in the bowel are presented in Table 6. Based on the data, the bowel showed greater variation in EUD and NTCP values compared to other organs at risk. This variation occurs because the bowel is a mobile organ that frequently changes position due to peristaltic motion and differences in filling during each treatment session. These positional changes affect the dose received, causing differences in the predicted biological response among patients.

Table 6 Descriptive Statistics of Bowel EUD and NTCP

Value	Bowel EUD (Gy)	Bowel NTCP (%)
Min	24.87	0
Max	48.82	12.95
Mean ± SD	39.52 ± 6.26	2.06 ± 3.00

Although a few cases showed slightly higher NTCP values, the overall results still indicate a low probability of radiation-induced bowel complications. This demonstrates that the treatment planning successfully limited the dose to the bowel within safe tolerance limits, minimizing the risk of radiation enteritis and ensuring adequate protection of surrounding normal tissues. This finding is consistent with previous studies using the LKB model, where bowel toxicity remains low when the delivered dose stays below critical thresholds such as TD_{50} 55 Gy and when volume-related constraints are maintained, even in the presence of anatomical variability (Li et al., 2020).

3.4.3 Evaluation of Bladder Dose

The elevated bladder EUD (93.57 ± 9.99 Gy) and corresponding NTCP reflect the significant anatomical overlap between the PTV and the anterior bladder wall in locally advanced Stage III cervical tumors (Table 7). Furthermore, inter-fractional variations in bladder filling significantly alter organ geometry between simulation and treatment delivery. From a methodological perspective, non-linear EUD calculations are highly sensitive to the volume parameter ($\alpha = 2$) and high-dose DVH binning. To minimize bladder toxicity in 3DCRT, strict drinking protocols (e.g., 500 mL fluid intake 30–45 minutes prior to treatment) and intensity-modulated techniques (IMRT/VMAT) should be prioritized where accessible.

The very high bladder NTCP estimate deserves particular scrutiny rather than immediate interpretation as the expected frequency of complications. An organ EUD exceeding the nominal prescribed target dose is mathematically possible under some model parameterizations and dose distributions, but values substantially above the external-beam prescription also justify checking the DVH export, dose units, differential-volume conversion, equation implementation and the tissue parameters applied to the bladder. With a steep modeled response, relatively small changes in dose input or parameter assumptions can produce large changes in estimated NTCP. Accordingly, this finding should be treated as a signal for computational and clinical review, not proof that a corresponding proportion of patients experienced bladder toxicity (Zhang et al., 2023; Okunieff et al., 1995).

Table 7 Descriptive Statistics of Bladder EUD and NTCP

Value	Bladder EUD (Gy)	Bladder NTCP (%)
Min	68.88	8.36
Max	103.44	98.39
Mean ± SD	93.57 ± 9.99	83.16 ± 26.78

Exceeding the tolerance threshold suggests a higher potential for radiation-induced toxicity, such as cystitis or bladder fibrosis, if the condition persists across treatment sessions (Zhang et al., 2023). Therefore, maintaining a consistent bladder volume during simulation and each fraction is crucial to ensure reproducible dose distribution and minimize the risk of complications. In clinical practice, this can be achieved through standardized bladder filling protocols, such as controlled water intake prior to treatment, to reduce inter-fraction variability.

Furthermore, optimization of treatment planning such as improved beam arrangement, stricter dose-volume constraints, or the use of more advanced techniques like IMRT or VMAT may help reduce the dose delivered to the bladder while maintaining adequate target coverage. Despite some cases exceeding the TD_{50} reference, the overall treatment planning still provided acceptable dose control with manageable clinical risk through careful monitoring and patient preparation. The NTCP values obtained in this study are generally low, with the rectum (0.40%) and bowel (2.06%) remaining within acceptable limits, indicating good organ sparing. This trend suggests that lower dose exposure to these organs, as reflected in their DVH characteristics, is associated with reduced complication probability. In contrast, the higher NTCP observed in the bladder corresponds to higher dose accumulation, indicating a direct

relationship between dose distribution and NTCP outcomes. When compared to previous research, which reported NTCP values ranging from 0.03% to 0.49% for most OARs, the results of this study show a similar pattern of low complication risk. The higher NTCP observed for the bladder reflects its anatomical position and variable filling rather than a weakness in the treatment plan, and aligns with findings that pelvic irradiation often results in higher bladder sensitivity (Mazonakis et al., 2023).

Interpretation of the rectal and bowel estimates requires the same distinction between modeled and observed outcomes. Their low average NTCP values suggest a favorable model-based profile for the selected endpoints and assumptions, but they do not eliminate the possibility of injury in individual patients. The especially wide spread of bowel NTCP relative to its mean also indicates heterogeneity that a single central estimate may conceal. For the bladder, the combination of a high mean and substantial variability makes patient-level DVH inspection and parameter-sensitivity testing particularly important. A future validation study should relate calculated indices to recorded late toxicity using consistent endpoint definitions and an adequate observation period, while accounting for the complete external-beam and brachytherapy courses.

3.5 Normality Assessment

Normality testing using the Shapiro–Wilk test was conducted for all dosimetric and radiobiological parameters. The results are shown in Table 8. Parameters such as CI, HI, and EUD for the PTV had p-values greater than 0.05, indicating a normal distribution, while the bladder's EUD and NTCP, as well as the bowel's NTCP, showed a non-normal distribution.

Because this series includes only 24 patients, the distributional tests have limited power to identify departures from normality. A non-significant Shapiro–Wilk result should therefore not be interpreted as proof that a variable follows a normal distribution. For skewed EUD or NTCP estimates, medians and interquartile ranges would complement the reported means and standard deviations. The study also cannot infer the cause of non-normality from the tests alone: anatomy, patient-level dose exposure, interpolation choices and the nonlinear probability transformation may all contribute. These considerations limit statistical generalization while preserving the descriptive value of the reported plan-level results.

Table 8 Test of Normality

Parameter	P-Value	Category
HI	0.2289	Normal
CI	0.0525	Normal
EUD PTV	0.9999	Normal
EUD Rectum	0.1235	Normal
EUD Bladder	0.0014	Not Normal
EUD Bowel	0.0641	Normal
TCP	0.9999	Normal
NTCP Rectum	0.3601	Normal
NTCP Bladder	0.0000	Not Normal
NTCP Bowel	0.0000	Not Normal

The normally distributed parameters reflect consistent dose delivery and biological response across all patients. Meanwhile, the non-normal distribution observed in the bladder and bowel is likely caused by variations in organ volume and position during treatment. These anatomical differences affect the absorbed dose; however, the overall results remain within acceptable clinical variation. The presence of non-normally distributed data may influence the representation of statistical measures, particularly the mean and standard deviation, which should therefore be interpreted with caution. However, as this study employs a descriptive analytical approach, these measures are still reported to provide a general overview of the data distribution.

4. CONCLUSION

The dosimetric evaluation of Stage III cervical cancer cases using 3DCRT showed that HI and CI values generally approached the ideal standards recommended by the ICRU, indicating that the dose distribution was uniform and well-conformed to the target volume. The radiobiological assessment, based on EUD calculations, showed an average TCP of 41.36%, indicating a moderate yet clinically relevant probability of tumor control. The highest NTCP values were observed in the bladder, often exceeding the TD50 reference dose, whereas the rectum and bowel exhibited very low NTCP values, indicating that these organs were adequately protected from excessive radiation exposure. However, this study is limited by its relatively small sample size and single-center design, which may affect the generalizability of the findings.

ACKNOWLEDGMENT

Thank you to the Head of Installation and Staff at the Radiotherapy Installation of Universitas Andalas Hospital, who facilitated the research, as well as to all parties who helped ensure the smooth running of this research.

AUTHOR CONTRIBUTIONS

Conceptualization, A.D. and S.O.; methodology, A.D. and S.O.; software, A.D.; validation, S.O. and M.I.; formal analysis, A.D.; investigation, A.D.; resources, M.I.; data curation, A.D.; writing original draft preparation, A.D.; writing-review and editing, S.O. and M.I.; visualization, A.D.; supervision, S.O. and M.I.; project administration, S.O. All authors have read and agreed to the published version of the manuscript.

FUNDING

This research received no external funding.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study were obtained from the Eclipse Treatment Planning System (TPS) at Universitas Andalas Hospital, Padang, Indonesia. Due to patient confidentiality and ethical restrictions, the original clinical data are not publicly available. However, de-identified dosimetric data and derived radiobiological parameters supporting the findings may be made available from the corresponding author upon reasonable request, subject to approval by the relevant institutional authorities and applicable ethical regulations.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ARTIFICIAL INTELLIGENCE (AI) USAGE DECLARATION

During the preparation of this work, the author(s) used GPT-6 (GPT-6 Astra, openai.com) for correcting minor grammatical and typographical errors. After using this tool/service, the author(s) reviewed and edited the output as needed and take full responsibility for the content of the publication.

REFERENCE

Antony, F., Mathew Varghese, K., Jomon Raphael, C., Paul Gopu, G., & Sivakumar, S. (2021). Dosimetric comparison of organs at risk with three-dimensional conformal radiation, intensity-modulated radiation and volumetric-modulated arc therapy in cervical cancer: A cross-sectional study. *International Journal of Advances in Medicine*, 8(4), 586–590. https://doi.org/10.18203/2349-3933.ijam20210978

Cherry, P., & Duxbury, A. M. (Eds.). (2009). *Practical Radiotherapy: Physics and Equipment* (2nd ed.). Wiley-Blackwell. ISBN 978-1-4051-8426-7.

Effina, A., Milvita, D., & Ilyas, M. (2022). Distribusi dosis radiasi foton pada treatment planning system menggunakan teknik 3DCRT dan IMRT untuk terapi kanker serviks. *Jurnal Fisika Unand*, 11(1), 126–130. https://doi.org/10.25077/jfu.11.1.126-130.2022

Fader, A. N. (2018). Surgery in cervical cancer. *New England Journal of Medicine*, 379(20), 1955–1957. https://doi.org/10.1056/NEJMe1814034

Fatimah, N., & Widita, R. (2018). Penentuan Tumor Control Probability (TCP) dengan memperhitungkan efek repair menggunakan model Equivalent Uniform Dose (EUD). *Prosiding SKF 2018*, 108–113.

Gonultas, L. (2026). Determining optimal conformity index values in pelvic region radiotherapy planning under ICRU 50/62, ICRU 83, and RTOG/NRG guidelines. *Journal of Applied Clinical Medical Physics*, 27(5), e70635. https://doi.org/10.1002/acm2.70635

Khatun, S. (2018). Prevention of cervical cancer. *Bangladesh Journal of Obstetrics & Gynaecology*, 33(1), 1–3. https://doi.org/10.3329/bjog.v33i1.43266

Gulliford, S. L., Partridge, M., Sydes, M. R., Webb, S., Evans, P. M., & Dearnaley, D. P. (2012). Parameters for the Lyman Kutcher Burman (LKB) model of Normal Tissue Complication Probability (NTCP) for specific rectal complications observed in clinical practise. *Radiotherapy and Oncology*, 102(3), 347–351. https://doi.org/10.1016/j.radonc.2011.10.022

Li, S., Gong, Y., Yang, Y., Guo, Q., Qian, J., & Tian, Y. (2020). Evaluation of small bowel motion and feasibility of using the peritoneal space to replace bowel loops for dose constraints during intensity-modulated radiotherapy for rectal cancer. *Radiation Oncology*, 15(1), 211. https://doi.org/10.1186/s13014-020-01650-z

Malafi, M. E. (2024). The lives saved: A literature review on the role of radiotherapy improving prognosis in cancer patients. *Journal of Quality in Health Care & Economics*, 7(1), 1–3. https://doi.org/10.23880/jqhe-16000360

Mayadev, J. S., Ke, G., Mahantshetty, U., Pereira, M. D., Tarnawski, R., & Toita, T. (2022). Global challenges of radiotherapy for the treatment of locally advanced cervical cancer. *International Journal of Gynecological Cancer*, 32(3), 436–445. https://doi.org/10.1136/ijgc-2021-003001

Mazonakis, M., Tzanis, E., Lyraraki, E., & Damilakis, J. (2022). Automatic radiobiological comparison of radiation therapy plans: An application to gastric cancer. *Cancers*, 14(24), 6098. https://doi.org/10.3390/cancers14246098

Mazonakis, M., Kachris, S., Tolia, M., & Damilakis, J. (2023). NTCP calculations of five different irradiation techniques for the treatment of thymoma. *Current Oncology*, 30(8), 7740–7752. https://doi.org/10.3390/curroncol30080561

Nadova, K., Burghardtova, M., Fejfarova, K., Reginacova, K., & Malikova, H. (2021). Late radiation-related toxicities in patients treated for early-stage cervical carcinoma by surgery and adjuvant radiotherapy: A retrospective imaging study. *Pathology and Oncology Research*, 27, 1609915. https://doi.org/10.3389/pore.2021.1609915

Nuraini, R., & Widita, R. (2019). Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) with consideration of cell biological effect. *Journal of Physics: Conference Series*, 1245(1), 012092. https://doi.org/10.1088/1742-6596/1245/1/012092

Okunieff, P., Morgan, D., Niemierko, A., & Suit, H. D. (1995). Radiation dose-response of human tumors. *International Journal of Radiation Oncology, Biology, Physics*, 32(4), 1227–1237. https://doi.org/10.1016/0360-3016(94)00475-Z

Pandey, U., & Bansal, P. (2017). What is cervical cancer? *Journal of Gynecology and Women's Health*, 2(5), 555599. https://doi.org/10.19080/JGWH.2017.02.555599

Pratista, T. A., & Widita, R. (2023). Determination of fractionation scheme based on repair effect using Equivalent Uniform Dose (EUD) model. *Indonesian Journal of Physics*, 34(2), 8–13. https://doi.org/10.5614/itb.ijp.2023.34.2.2

Rather, S. A., Banday, M. S., & Qureshi, M. Z. (2024). Dosimetric analysis and radiobiological impact of radiotherapy planning techniques for esophageal squamous cell carcinoma in terms of Tumor Control Probability and Normal Tissue Complication Probability. *Journal of Radiation and Cancer Research*, 16(1), 8–16. https://doi.org/10.4103/jrcr.jrcr_2_24

Zhang, F., Zhou, M., Wang, G., Li, X., Yue, L., Deng, L., Chi, K., Chen, K., Qi, Z., Deng, X., Peng, Y., & Liu, Y. (2023). Evaluation of bladder filling effects on the dose distribution during radiotherapy for cervical cancer based on daily CT images. *Journal of Applied Clinical Medical Physics*, 24(11), e14097. https://doi.org/10.1002/acm2.14097