

## THE EFFECT OF RADIATION ON DIARRHEA IN CERVICAL CANCER PATIENTS USING 3D-CRT TECHNIQUE AT MRCCC SILOAM SEMANGGI HOSPITAL

Gabreal Injelika Manurip<sup>1</sup>, Yogi Purba Harlis<sup>2</sup>, I Putu Pande Gitawiarsa<sup>1</sup>

<sup>1</sup> AKTEK Radiodiagnostik dan Radioterapi Bali

Jl. Tukad Batanghari VII No. 21, Dauh Puri Klod, Denpasar Selatan, Dauh Puri Klod, West Denpasar, Denpasar City, Bali 80225, Indonesia

<sup>2</sup> Poltekkes Jakarta 2

Jl. Raya Ragunan No.29, RT.6/RW.1, Pasar Minggu, RT.6/RW.1, Jati Padang, Kec. Ps. Minggu, Kota Jakarta Selatan, Daerah Khusus Ibukota Jakarta 12540, Indonesia

Email: [angelmanurip77@gmail.com](mailto:angelmanurip77@gmail.com)

### Abstract

Cervical cancer is one of the most common cancers in women, with radiotherapy being a primary treatment option, including the use of Three-Dimensional Conformal Radiation Therapy (3D-CRT). Although this technique precisely delivers radiation doses to the target area, exposure to surrounding organs often causes gastrointestinal side effects, particularly diarrhea. This study aimed to evaluate the effect of radiation fractionation on the occurrence of diarrhea in cervical cancer patients treated at MRCCC Siloam Semanggi Hospital. A quantitative descriptive design was applied using questionnaires based on a simplified version of CTCAE v5.0, supported by direct observation and interviews. A total of 10 patients participated, resulting in 50 questionnaire entries collected at the 5th, 10th, 15th, 20th, and 25th fractions. The results showed that most patients experienced mild diarrhea starting from the mid-treatment phase (15th fraction), while some showed fluctuating patterns with two peaks (15th and 25th fractions), and others remained stable with mild symptoms. No patients reached grade 3 (severely affecting daily activities). In conclusion, fractionated radiation exposure was associated with the onset of diarrhea, but symptoms were generally mild to moderate. Regular monitoring and nutritional education are essential strategies to minimize gastrointestinal toxicity and maintain patients' quality of life during therapy.

**Keywords:** Radiotherapy, Cervical Cancer, Diarrhea, Fractionation, 3D-CRT

### Introduction

Cervical cancer remains a major global health challenge and is one of the leading causes of cancer-related mortality in women, particularly in low- and middle-income countries where access to screening and vaccination programs is limited. According to GLOBOCAN 2020, cervical cancer ranks as the fourth most common cancer among women worldwide, with approximately 604,000 new cases and 342,000 deaths reported in 2020(1). The burden is particularly heavy in low- and middle-income countries, where limited access to screening and vaccination programs contributes to late-stage diagnosis and poor clinical outcomes. Despite ongoing advancements in preventive strategies such as HPV vaccination and cytology-based or HPV-based screening programs, a significant proportion of women are still diagnosed with locally advanced cervical cancer requiring aggressive treatment modalities, including radiotherapy (2).

Radiotherapy remains the cornerstone of treatment for locally advanced cervical cancer and is often combined with chemotherapy to improve treatment efficacy. Over the past two decades, advances in radiation technology have substantially changed the landscape of cervical cancer management. Conventional two-dimensional radiotherapy has gradually been replaced by three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT), both of which allow more precise dose delivery while sparing surrounding organs at risk (OARs), particularly the bladder, rectum, and small intestine(3–5). Several large clinical series have demonstrated that IMRT improves dose conformity and reduces acute and late gastrointestinal (GI) toxicities compared with 3D-CRT or conventional radiotherapy, which has led to its increasing adoption in modern radiotherapy practice (5–7). Nevertheless, due to limited resources and technical demands, 3D-CRT remains widely applied in many treatment centers, especially in developing countries.(2,8)

Despite these advances, radiation-induced toxicity continues to be a major limitation of therapy. Among these, gastrointestinal complications such as diarrhea, abdominal cramping, and radiation enteritis are the most common and clinically significant (7,9). The severity of these side effects not only impacts patient quality of life but may also compromise treatment compliance and overall therapeutic outcomes (10,11). Acute gastrointestinal toxicity typically arises within weeks of treatment initiation, while late effects, including bowel obstruction, ulceration, or fistula formation, may occur months or years after therapy completion (12).

The pathophysiology of radiation enteritis is multifactorial, involving mucosal injury, vascular endothelial damage, chronic inflammation, fibrosis, and disruption of intestinal microbiota(9,13). Recent mechanistic studies have highlighted that alterations in gut microbiota composition following pelvic radiotherapy can exacerbate mucosal injury and promote chronic inflammation, contributing to persistent or severe gastrointestinal symptoms(9). Additionally, systematic reviews of pelvic radiotherapy outcomes have identified dose–volume parameters of the small bowel as strong predictors of gastrointestinal toxicity, underscoring the critical role of meticulous treatment planning and dose constraints in minimizing complications(13)

Risk stratification models are increasingly being developed to predict which patients are at greater risk of developing acute or late radiation enteritis. For example, nomogram-based approaches have recently been proposed to estimate the probability of  $\geq$  grade 2 acute gastrointestinal toxicity in elderly patients receiving pelvic radiotherapy, further supporting the clinical importance of early detection and proactive management(10). Similarly, studies evaluating tumor volume reduction during treatment have suggested prognostic implications not only for oncologic control but also for normal tissue response, thereby integrating toxicity considerations into overall treatment planning(14)

Several multicenter prospective studies, such as the EMBRACE and EMBRACE II trials, have advanced understanding of clinical outcomes, toxicity profiles, and evidence-based guidelines in gynecologic oncology, demonstrating the critical importance of balancing tumor control with organ preservation(15) Furthermore, single-institution studies continue to provide valuable real-world evidence regarding acute and late gastrointestinal toxicity, informing both local practice and broader clinical recommendations(4,11,12)

In light of these developments, evaluating gastrointestinal complications in patients undergoing 3D-CRT for cervical cancer is of high clinical relevance. Such evaluations not only provide insights into the tolerability and safety of 3D-CRT in resource-limited settings but also establish a foundation for improving treatment planning, patient counseling, and supportive care strategies. Therefore, the present study aims to analyze the incidence and severity of diarrhea and gastrointestinal disturbances in cervical cancer patients treated with 3D-CRT. By focusing on acute gastrointestinal toxicity, this research contributes to optimizing treatment outcomes and quality of life for patients, particularly in clinical environments where advanced IMRT technology is not universally available (8,12,14,15)

This knowledge gap is particularly relevant in Indonesia, where 3D-CRT remains the most widely used technique due to limited access to advanced modalities such as IMRT. Understanding the pattern and severity of gastrointestinal symptoms, especially diarrhea, during treatment fractions is crucial for optimizing supportive care, guiding patient education, and preventing treatment interruptions.

Therefore, the present study was conducted to evaluate the incidence and progression of diarrhea in cervical cancer patients undergoing fractionated radiotherapy with the 3D-CRT technique at MRCCC Siloam Semanggi Hospital. By documenting symptom development across treatment fractions and correlating them with clinical observations, this research aims to generate evidence-based insights for improving patient monitoring, nutritional counseling, and supportive management, thereby enhancing treatment outcomes and quality of life.

## Method

This study employed a quantitative descriptive design to evaluate the effect of radiation fractionation on the occurrence of diarrhea in cervical cancer patients. The study population consisted of all cervical cancer patients undergoing external radiotherapy with the Three-Dimensional Conformal Radiation Therapy (3D-CRT) technique at the Radiotherapy Department of MRCCC Siloam Semanggi Hospital. The sample was selected purposively based on inclusion criteria, including cervical cancer patients treated with 3D-CRT, willingness to participate, and ability to complete the questionnaire. A total of 10 patients were included, generating 50 questionnaire entries obtained from five evaluation points at the 5th, 10th, 15th, 20th, and 25th treatment fractions.

The data sources comprised both primary and secondary data. Primary data were collected through questionnaires, direct observation, and short interviews with patients and medical staff. The main instrument was a structured questionnaire developed based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, which was simplified and translated into Indonesian for ease of use. Secondary data were obtained from patients' medical records and radiotherapy treatment planning reports.

Data collection was conducted by administering questionnaires at specific treatment fractions, followed by direct observation and complementary interviews to gather additional information. The collected data were analyzed using descriptive statistics with the assistance of SPSS software to present frequency distributions, percentages, and symptom patterns of diarrhea throughout the course of radiotherapy.

## Results

This study involved 10 cervical cancer patients undergoing external radiotherapy with the 3D-CRT technique at MRCCC Siloam Semanggi Hospital. Each patient completed the questionnaire five times, namely at the 5th, 10th, 15th, 20th, and 25th fractions, resulting in a total of 50 questionnaire entries. The findings are presented in tables and graphs below.

### 3.1 Table

**Table 1 Characteristics of Cervical Cancer Patients at MRCCC Siloam Semanggi Hospital**

| Variable     | Minimum | Maximum | Mean |
|--------------|---------|---------|------|
| Age          | 40      | 69      | 53,4 |
| RT Fractions | 5       | 25      | 15   |

Note: Most patients were aged between 40–69 years with a mean age of 53.4 years. The number of fractions varied, with an average of 15 treatment sessions.

**Table 2 Frequency Distribution of Diarrhea During Radiotherapy**

| Frequency of Diarrhea | Total     | Percentage (%) |
|-----------------------|-----------|----------------|
| Never                 | 15        | 30             |
| Sometimes             | <b>26</b> | <b>52</b>      |
| Often                 | 9         | 18             |

Note: Most patients reported diarrhea sometimes (52%), while 30% never experienced diarrhea and 18% reported it often.

**Table 3 Severity of Diarrhea Among Cervical Cancer Patients**

| Severity of Diarrhea                    | Total     | Percentage (%) |
|---|-----------|----------------|
| Mild (still able to perform activity)   | <b>40</b> | <b>80</b>      |
| Moderate (slightly disturbing activity) | 9         | 18             |
| No complaints                           | 1         | 2              |

Note: The majority of patients (80%) experienced mild diarrhea, 18% had moderate diarrhea, and 2% reported no complaints. No patients experienced severe diarrhea.

**Table 4 Other Gastrointestinal Symptoms Reported by Patients**

| Symptom          | Total     | Percentage (%) |
|------------------|-----------|----------------|
| None             | <b>31</b> | <b>62</b>      |
| Nausea           | 14        | 28             |
| Abdominal cramps | 4         | 8              |
| Bloating         | 1         | 2              |

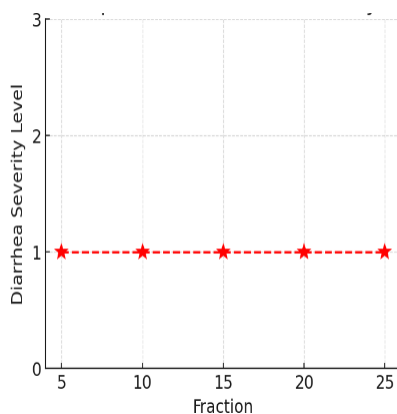
Note: The most common additional symptom was nausea (28%), followed by abdominal cramps (8%) and bloating (2%).

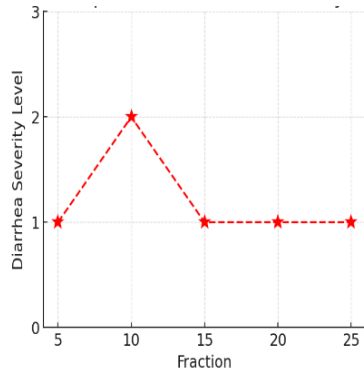
**Table 5 Impact of Diarrhea on Patient Activities**

| Impact on Daily Activities | Total     | Percentage (%) |
|----------------------------|-----------|----------------|
| No disturbance             | <b>41</b> | <b>82</b>      |
| Slightly disturbing        | 9         | 18             |

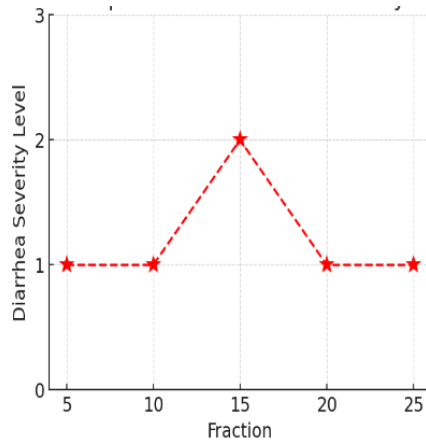
Note: Most patients (82%) reported that diarrhea did not interfere with their daily activities, while 18% felt slightly disturbed.

### 3.2 Graphics/Images

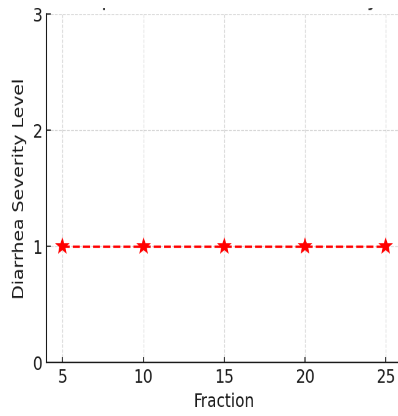
**Graph.1 Development of Diarrhea Severity in Patient P1**



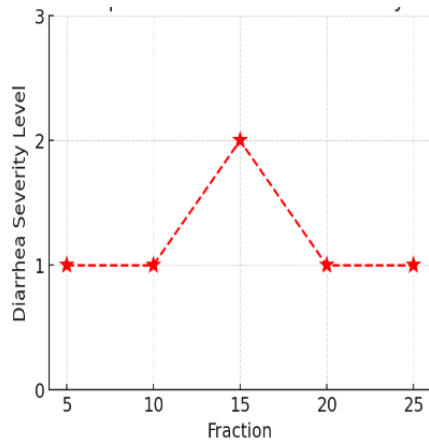
**Graph.2 Development of Diarrhea Severity in Patient P2**



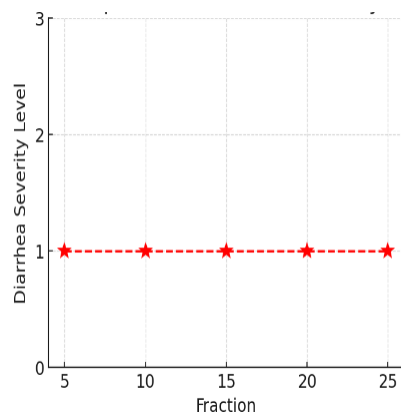
**Graph.3 Development of Diarrhea Severity in Patient P3**



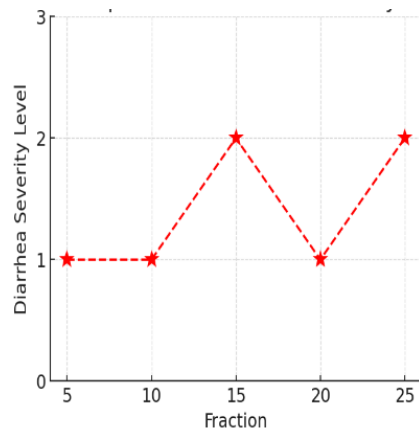
**Graph.4 Development of Diarrhea Severity in Patient P4**



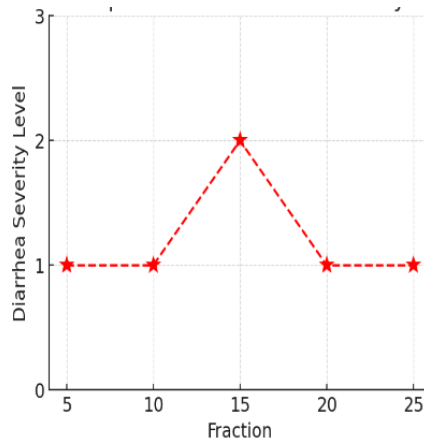
**Graph.5 Development of Diarrhea Severity in Patient P5**



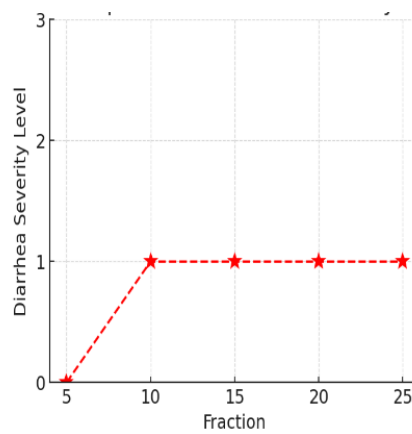
**Graph.6 Development of Diarrhea Severity in Patient P6**



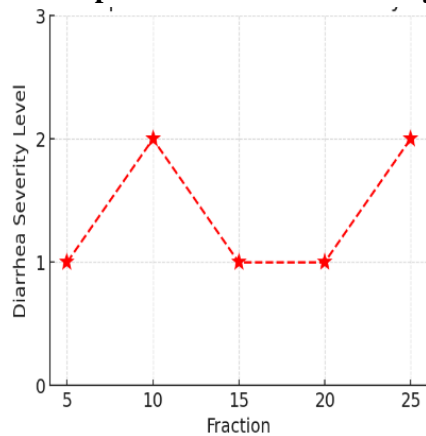
**Graph.7 Development of Diarrhea Severity in Patient P7**



**Graph.8 Development of Diarrhea Severity in Patient P8**



**Graph.9 Development of Diarrhea Severity in Patient P9**



**Graph.10 Development of Diarrhea Severity in Patient P10**

## Discussion

The findings of this study indicate that most cervical cancer patients undergoing external radiotherapy with the 3D-CRT technique experienced mild to moderate diarrhea, with no patients reaching a severe grade. This aligns with the characteristics of acute gastrointestinal side effects, which typically emerge during the second to third weeks of radiotherapy. In particular, the graphical analysis of symptom progression showed that the majority of patients reached their peak diarrhea severity at the 15th fraction, consistent with literature describing the onset of acute gastrointestinal toxicity. Andreyev

(2015) reported that approximately 70% of cervical cancer patients experienced changes in bowel habits during radiotherapy, with diarrhea and increased frequency of defecation being the most common symptoms.

Several patients in this study exhibited fluctuating patterns with two symptom peaks, namely at the 15th and 25th fractions. This phenomenon may be explained by the cumulative effect of radiation dose on the intestinal mucosa, leading to progressive epithelial damage. Kidd et al. (2020) reported that patients receiving pelvic radiation with conventional techniques were more likely to experience recurrent symptoms compared to those treated with IMRT. This suggests that the limitations of 3D-CRT in minimizing radiation exposure to surrounding organs, particularly the rectum and small intestine, contribute to the fluctuating pattern observed in some patients.

DVH analysis in this study revealed that although the mean dose to organs at risk (OARs) was generally below tolerance thresholds, one case of bladder overdose and several cases of rectal doses approaching the upper limit were observed. This finding is consistent with Ren et al. (2023), who demonstrated that gastrointestinal toxicity may still occur even when OAR doses remain within safe limits, particularly when influenced by factors such as anatomical variations or organ motion during therapy. These findings underscore the importance of individualized treatment planning using patient-specific DVH data to reduce the risk of toxicity.

In addition to technical factors, the results also suggest the influence of non-technical factors such as dietary compliance and individual sensitivity. Some patients with relatively low rectal doses still experienced moderate diarrhea, indicating the contribution of factors beyond treatment planning. Mangoni et al. (2016) emphasized that adherence to a low-fiber diet and adequate hydration are critical in reducing the incidence of diarrhea among pelvic radiotherapy patients.

Another important finding of this study is that none of the patients developed severe diarrhea (grade 3), suggesting that symptoms generally remained within the mild to moderate range. This provides evidence that although 3D-CRT has limitations compared to more advanced techniques such as IMRT or VMAT, it remains a reasonably safe option, particularly when supported by proper clinical monitoring and nutritional counseling. Therefore, this study supports previous literature indicating that 3D-CRT is still relevant in facilities with limited technological availability, but must be complemented with additional strategies to minimize the risk of gastrointestinal side effects.

## **Conclusion**

This study confirms that external radiotherapy using the 3D-CRT technique in cervical cancer patients may result in gastrointestinal side effects, particularly diarrhea, with severity levels that generally remain within the mild to moderate range. This demonstrates that even though the treatment planning protocol adhered to international standards and the prescribed doses to the planning target volume were within recommended limits, symptoms can still occur in certain patients. Such findings underscore the limitations of 3D-CRT in adequately sparing adjacent pelvic organs, especially the rectum and small intestine, which continue to represent critical challenges in clinical practice. In this regard, the primary objective of the study, namely to evaluate the influence of fractionated radiation on the occurrence of diarrhea in cervical cancer patients treated with 3D-CRT, has been achieved, while also providing insights into the distinct pattern of symptom development, particularly the peak occurring in the middle phase of treatment.

The observed symptom trajectory, with a predominant peak at the 15th fraction and fluctuations in a subset of patients towards the end of treatment, indicates that the biological response is shaped not only by technical aspects of irradiation but also by individual patient conditions. This reinforces the notion that non-technical factors, including anatomical variability, organ motion, and dietary compliance, play a decisive role in symptom manifestation. The variability of patterns enriches the

understanding that patient response to radiation is multifactorial and requires a comprehensive approach that extends beyond dose parameters alone.

Analysis of the DVH further highlighted that, while most organs at risk received mean doses within tolerance thresholds, there were instances where the bladder exceeded safety limits and several rectal doses approached the upper margin. These findings emphasize the necessity of adopting more precise planning strategies that can better protect surrounding structures. In essence, this study demonstrates not only the symptomatic outcomes of treatment but also the critical importance of patient-specific DVH evaluation as an integral component of clinical radiotherapy practice.

The conclusion that may be drawn is that 3D-CRT remains a viable option in centers with limited technological resources, provided it is complemented with adequate nutritional counseling, close clinical monitoring, and the possibility of adjusting planning protocols according to individual characteristics. This aligns with the broader movement towards personalized medicine, in which patient-specific adaptations are expected to reduce the risk of side effects while improving overall quality of life.

The implications of this research point toward the need for future studies that incorporate more advanced techniques such as IMRT and VMAT, both of which have been theoretically and empirically shown to improve dose sparing of adjacent organs without compromising tumor coverage. By involving larger patient populations, subsequent studies will be able to provide more objective comparisons of the relative strengths of 3D-CRT, IMRT, and VMAT in terms of tumor control as well as toxicity profiles. In this way, the present study contributes not only to the understanding of gastrointestinal toxicity in 3D-CRT but also sets a foundation for the advancement of radiotherapy toward more precise, adaptive, and patient-centered approaches.

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