CHAPTER 1 INTRODUCTION

1.1 Background

Cervical cancer is a significant global health issue and ranks as the fourth most common cancer among women worldwide. The primary etiological factor is the persistent infection with high-risk types of human papillomavirus (HPV), which accounts for nearly all cervical cancer cases (Pandey, 2017). HPV is a sexually transmitted virus with more than an 80% lifetime risk of infection. Although it often presents no symptoms, most sexually active individuals will become infected with HPV at some stage in their lives. The development from HPV infection to cervical cancer is typically slow, often taking several years or even decades. This type of cancer forms in the cells of the cervix, the lower part of the uterus that connects to the upper end of the vagina (Khatun, 2020).

The treatment of cervical cancer has become increasingly important due to its high mortality rate. The standard treatment for cervical cancer includes surgery and chemotherapy. However, surgery can lead to complications such as lymphedema and sexual dysfunction, while chemotherapy often causes systemic side effects that impact overall health and quality of life (Fader, 2018). Moreover, chemotherapy frequently causes widespread side effects, including recurring infections, decreased appetite, and diminished sexual drive, all of which adversely affect overall health and well-being (Abdelhakeem et al., 2024). One effective way to minimize side effects in a cervical cancer treatment is through the use of radiotherapy (Mayadev et al., 2022). Radiotherapu uses radioactive materials or high-energy radiation to kill cancerous tumors and stop their further growth selectively. Its objective is to eradicate cancer cells with minimal harm to the adjacent healthy tissue, thereby improving the patient's overall prognosis (Malafi, 2024). Radiotherapy can be administered through equipment like brachytherapy for internal therapy and Linear Accelerators (LINAC) for external radiation.

LINAC is a modality in radiotherapy that produces ionizing radiation beams by accelerating electrons to generate high-energy X-rays or electrons, which can be precisely directed at tumor tissue. Several radiation techniques used by LINAC include Three-Dimensional Conformal Radiation Therapy (3D-CRT), Intensity Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), and Image Guided Radiation Therapy (IGRT). These techniques heavily rely on the Treatment Planning System (TPS) to visualize the tumor and surrounding healthy tissue, calculate the optimal dose, and minimize damage to tissue outside the target area. The TPS helps to estimate the Equivalent Uniform Dose (EUD) to assess the biological impact of non-uniform radiation dose by expressing it as if the dose were spread evenly across the entire target volume. Since radiation is rarely distributed uniformly inside the treatment area, EUD becomes a key measure in predicting both Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP). TCP reflects how likely the radiation dose is to effectively destroy tumor cells, while NTCP shows the chance of normal tissue around the tumor being affected by the treatment (Pratista and Widita, 2024).

Calculating TCP and NTCP helps assess the radiobiological effects experienced by patients after undergoing radiation therapy. In certain cases, radiation can lead to various side effects in individuals with cervical cancer. Tissues that regenerate rapidly such as the bone marrow, intestines, and bladder tend to be the most sensitive to radiation exposure. Inflammation caused by radiation may affect different organs, leading to conditions like proctocolitis (inflammation of the rectum), enteritis (inflammation of the intestines), and bladder irritation. Other possible complications include ileus (a blockage in the intestines), intestinal perforation, the formation of fistulas (abnormal passages between organs), intestinal or ureteral strictures (narrowing), and hydronephrosis (swelling of the kidneys due to urinary obstruction) (Nadova et al., 2021).

The TCP in glioblastoma brain cancer is estimated using the EUD model while taking into account the influence of cellular repair mechanisms. TCP values are calculated based on different approaches, including cEUD, cEUD-LQ, and rEUD that a modified version of the model that incorporates the effect of cell repair. Among these, the rEUD model tends to produce lower TCP values compared to the others. This decrease happens because the model considers that some tumor cells may survive, having undergone sublethal damage recovery following radiation exposure. (Fatimah and Widita, 2018). Determining the fractionation scheme based on cell repair effects using the EUD model in radiotherapy for glioblastoma patients with the IMRT techniques has shown significant results. The modified rEUD model indicates a very low risk of complications in the organs surrounding the tumor. After NTCP calculations, the best-recommended fractionation scheme is hypofractionation, as it was safe for normal organs around the target while still considering the dose limits received by each organ (Pratista and Widita, 2024).

A study combines NTCP and TCP based on EUD model with the Simultaneous Integrated Boost (SIB) technique to assess Intensity-Modulated Radiation Therapy (IMRT) and RapidArc dosimetric indices for oropharyngeal cancer. This study evaluated the dose and its effects on the target tumor and adjacent organs such as the brain, spinal cord, and parotid gland. Forty-eight treatment plans for 12 patients, including IMRT (7 and 9 planes) and RapidArc (2 and 3 arcs), were examined. The physical parameters homogeneity index (HI) and conformity index (CI), as well as the radiobiological models Lyman, Kutcher, Burman (LKB) and EUD, were analyzed. The outcomes showed that compared to IMRT, RapidArc (3 arcs) significantly reduced the amount of the organs at risk (OAR) while improving dose homogeneity and compliance. RapidArc has a faster treatment time despite having a more efficient monitoring unit (MU) and nearly the same TCP values for tumor targets compared to IMRT (Dashnamoorthy et al., 2024).

A study of 35 patients utilizing a 6 MV photon beams examined the dosimetry and radiobiological impact of radiation approaches in esophageal squamous cell cancer (ESCC), namely field-in-field (FIF), three-field (3Fs), and four-field box (4Fs). The CI, HI, average dose (Dmean), maximum dose (Dmax), TCP, and V20Gy and V30Gy dosage volumes to the heart and lungs were all assessed, with TCP and NTCP calculated using the Niemierko model. The results demonstrated that the FIF methodology was superior in dose homogeneity, radiation field conformity, and protection of OAR, such as the heart and lungs, with considerable decreases in lung V20Gy and NTCP compared to the 3Fs and 4Fs methods (Rather et al., 2024).

The study evaluates 18 patients who were treated for head and neck cancer. The research team used DVH data to generate TCP and NTCP models for each patient. The EUD was determined for both procedures to determine radiation treatment efficacy. The TCP and NTCP numbers were calculated using mathematical models. IMPT was compared to IMRT based on radiobiological considerations, emphasizing the benefits of sparing OARs and total dose distribution. The study revealed that Intensity-Modulated Proton Therapy (IMPT) resulted in slightly higher TCP values and lower NTCP values compared to IMRT. However, the differences were relatively minimal, making it difficult to draw firm conclusions regarding its clinical superiority. Despite this, IMPT was shown to reduce the maximum dose delivered to critical structures such as the brainstem, parotid glands, and larynx, which could help minimize the risk of treatment-related complications. (Nguyen et al., 2023).

This study introduces a new approach to evaluating the radiobiological effects in patients with stage III cervical cancer treated using 3DCRT technique, which is widely used in hospitals across Indonesia due to its cost-effectiveness and relatively simple equipment requirements. Beyond affordability, 3DCRT offers shorter planning and treatment times, which is advantageous in high-patient-volume settings, and clinical experience shows that it can achieve adequate dose coverage of the tumor while keeping exposure to surrounding organs at risk within acceptable limits. By assessing TCP and NTCP base on EUD model, this research aims to provide a comprehensive evaluation of treatment efficacy. Considering that cervical cancer is one of the leading causes of cancer-related mortality among women in Indonesia, the findings are expected to support clinical decision-making, guide more effective treatment strategies, and serve as a reference for future studies in radiotherapy, particularly in resource-limited settings where 3DCRT remains a practical and effective option.

1.2 Research Objectives

The aims of this research are as follows:

1. To assess the dosimetric evaluation in stage III cervical cancer cases based on the parameters of HI and CI
2. To assess the radiobiological parameters by considering the values of TCP and NTCP using EUD model in stage III cervical cancer cases.

1.3 Research Benefits

The advantages of this study are is provides medical physicists important information for analyze and determine the risk to healthy tissues, as well as the potential for tumor control. It serves as a valuable tool for balancing treatment effectiveness and safety, especially in stage III cervical cancer, based on dosimetric and radiobiological parameters.

1.4 Scope and Limitations of Research

The scope and limitations of this study are outlined as follows

1. The secondary data used in this research were obtained from the Radiation Oncology Unit at Universitas Andalas Hospital.
2. The study involved data from 24 patients diagnosed with stage III cervical cancer who received treatment in 2024.
3. The patient selection was limited to individuals aged between 40 and 70 years.
4. This research focused specifically on the 3DCRT technique using 6 MV photon beams, with a prescribed dose of 50 Gy delivered over 25 treatment fractions.
5. The organs surrounding the cancer that will be analyzed are the bowel, bladder, and rectum.
6. Dose data used for EUD calculations included dose-volume points at $D_{10\%}$, $D_{20\%}$, $D_{30\%}$, $D_{40\%}$, $D_{50\%}$, $D_{60\%}$, $D_{70\%}$, $D_{80\%}$, $D_{90\%}$ and $D_{100\%}$.