CHAPTER 1 INTRODUCTION

1.1 Research Background

According to the World Health Organization (WHO), an estimated 20 million new cancer cases and 9.7 million cancer-related deaths occurred in 2022, and the number of new cases is projected to exceed 35 million by 2050 (Bray et al., 2024). One type of cancer that has gained significant attention in the healthcare field is gastric cancer due to its high prevalence and mortality on patient. According to the Global Cancer Observatory (GCO) 2022 data, Gastric cancer ranks fifth in global incidence and mortality, with a total mortality rate of 84.16% in Indonesia (GLOBOCAN, 2022). Due to the nonspecific nature of early symptoms and the infrequent use of routine screening, many patients are diagnosed when gastric cancer has already progressed to an advanced (Guan et al., 2023). Advanced-stage gastric cancer indicates that the cancer has invaded the muscle layer or lymph nodes, with patient survival rates ranging from 20% to 50% (Zhang et al., 2018).

Gastric cancer treatment can be performed through surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy. Most patients are diagnosed at locally advanced stages of the disease, requiring multimodality treatment, in which radiotherapy can be an effective option to relieve symptoms of advanced gastric cancer (Chong and Chau, 2023). Radiotherapy is a cancer treatment method that uses radiation beams (Tsujii et al., 2014). The primary goal of radiotherapy is to destroy cancer cells by damaging the molecular structure of Deoxyribonucleic Acid (DNA) (Lamghari et al., 2023). The most commonly used radiotherapy techniques are conventional (Giselvania et al., 2018). Conventional radiotherapy uses external photon beams, such as X-rays and gamma rays, to destroy cancer cells. However, conventional radiotherapy is less effective for gastric cancer because the radiation dose received by cancer cells is lower compared to modern radiotherapy, such as heavy particle therapy (Liermann et al., 2021).

The most widely used types of heavy charged therapy are proton therapy and carbon ion therapy (Kiseleva et al., 2022). Among these, carbon ions have certain

physical advantages over protons. Carbon ion energy delivers a lower radiation dose upon entering the body and spreads less to surrounding tissues compared to protons (Hoegen-Sabmannshausen et al., 2024). Carbon ion therapy is a form of particle radiotherapy that utilizes carbon ion beams to precisely target and destroy cancer cells (Byun et al., 2023). Due to its greater mass and higher charge +6, carbon ions experience less lateral scattering (Mohamad et al., 2018). This characteristic results from the energy loss of a charged particle increasing as its velocity decreases, resulting in most of its energy being deposited at the target just before the particle stops. This depth dose distribution is known as the Bragg curve, with its peak called the Bragg peak representing the point where radiation energy is concentrated, delivering maximum impact on the cancer (Cherry et al., 2012)

The treatment planning for carbon ion therapy in gastric cancer requires careful consideration due to the stomach's anatomical proximity to multiple critical organs (Song et al., 2023). Treatment Planning System (TPS) is required before therapy to design an optimal dose distribution. The planning process begins with imaging to obtain the shape of the cancer, with the Computed Tomography (CT) being the mostly used imaging technique (Giandola et al., 2023). Contour delineation is performed to define the cancer boundaries, which involves adjusting parameters (such as phantom type, beam energy, dose distribution, irradiation time) (Zarepisheh et al., 2022). Radiotherapy is given in several sessions, a process known as fractionation. This is especially important in carbon therapy, as carbon radiation has strong biological effects and can cause DNA damage that is more difficult to repair. In addition, the way the radiation beam is delivered to the body, such as using Passive Scattering (PS) or Pencil Beam Scanning (PBS) techniques, can also affect how effective the dose is in each session.

TPS generally utilize specialized software to simulate the physical interactions of ions within tissues and integrate these calculations with biological response models. The interactions occurring within the nucleus are probabilistic, and Monte Carlo (MC) code is widely used in treatment planning software to model these interactions probabilities (Park et al., 2021). MC, originally designed for high-energy particle research, has been applied in medical physics to provide highly

accurate computational models for treatment planning and dose distribution analysis (Dedes and Parodi, 2015). MC methods enable comprehensive modeling of the human body by integrating data related to its shape, chemical compotisition, and density (Mutuwong et al., 2024). Commonly used software in the MC method includes Fluktuierende Kaskade (FLUKA), Geometry and Tracking version 4 (GEANT4), Monte Carlo N-Particle (MCNP), and Particle and Heavy Ion Transport code System (PHITS). PHITS is preferred because it demonstrates shorter simulation times and provides distribution dose compared to other particle transport codes such as FLUKA, GEANT4, MCNPX, and MCNP6 (Yang et al., 2017).

Previous studies have primarily conducted simulations in carbon ion therapy. Nurfatthan (2019) researched dose distribution in carbon ion radiotherapy has been carried out by several researchers with various approaches. In this research used the PHITS program to analyze the dose and time of irradiation in lung cancer with Passive Scattering (PS) techniques. the results showed that the (Organ At-Risk) OAR dose was still below the threshold. Then Ahsan (2021), have a similar study on Non-Small Cell Lung Cancer (NSCLC) using carbon ion therapy through PHITS based simulations. This study successfully analyzed the optimum therapy energy, the dose received by OAR, and irradiation time using the PS technique. However, both studies have certain limitations. The limitation is the lack of variation in beam delivery techniques, as they only focus on PS without considering other techniques, such as Pencil Beam Scanning (PBS), which offer better dose conformity and target coverage.

Chuong et al., (2018) conducted a study comparing PS and PBS techniques in carbon ion therapy for liver cancer using a case study method. The results showed that the PBS technique improved target coverage and reduced radiation dose to several organs near the cancer, such as the duodenum, small intestine, stomach, and spine, in treating advanced pancreatic cancer. However, PBS increased the dose to the liver and lowered the dose to deeper healthy tissues. The main advantage of PBS is its better dose conformality, making it more effective for irregularly shaped cancer. Then Asadi et al., (2022), a simulation study using water phantoms was

conducted to analyze system energy parameters based on depth dose data in the energy range of (120–235) MeV and to compare the performance of PS and PBS. The results showed that proton therapy with PBS provides a more precise dose distribution and reduces exposure to healthy tissues compared to PS. However, these studies mainly focus on advanced liver and pancreatic cancer cases, and simulations using water phantoms do not fully represent the complexity of human biological tissue, which may affect the accuracy of dose distribution predictions in clinical settings.

Based on previous studies, this research aims to compare PS and PBS techniques in carbon ion therapy for gastric cancer through simulations using PHITS and a human phantom model. This research also considers the role of fractionation to evaluate which technique provides the most optimal dose distribution. Considering the limited clinical data available on carbon ion therapy for gastric cancer, this study is expected to offer a more accurate representation of dose delivery and contribute to a better understanding of treatment effectiveness, particularly in protecting nearby healthy tissues.

1.2 Research Purpose

The purpose of this research is to:

1. Determine the total fractionation time to achieve the prescription dose.
2. Determine the optimal dose distribution of carbon ion therapy using PS and PBS irradiation techniques, by examining the dose distribution based on equivalent dose values for cancer and OAR.

1.3 Research Benefits

Study aims to provide benefits for medical physicists, radiation oncologists, and researchers in the field of particle radiation therapy by comparing the passive scattering and pencil beam scanning techniques for dose optimization in carbon ion therapy for gastric cancer, to observe the differences in dose distribution received by the cancer and the OAR. determining a more effective and safer irradiation

technique, as well as offering additional considerations in planning particle-based therapy for gastric cancer.

1.4 Research Scope

The scope and limitations of this study are as follows:

1. The simulated cancer is an adenocarcinoma modeled as an elliptical cylinder with a volume of 39.10 cm^3, based on imaging results from (Yu et al., 2022).
2. The phantom used in this simulation is the ONRL-MIRD phantom.
3. The observed parameters include the absorber dose, and equivalent dose received by the cancer volume and the OAR with technique passive scattering and pencil beam scanning.
4. The simulated OAR includes the skin, kidneys, liver, spine, heart, lungs, and pancreas.
5. The irradiation was performed from the Anterior Posterior (AP).
6. Irradiation using techniques PS and PBS.
7. The simulation uses software PHITS Version 3.341.
8. The prescription dose is based on clinical guidelines, such as 54 Gy (RBE) according to (Zhang et al., 2021)