CHAPTER 1 INTRODUCTION

1.1 Background

Nasopharyngeal carcinoma (NPC) is a type of head and neck cancer that starts in the epithelial cells of the nasopharynx, specifically in the Fossa of Rosenmüller (Su et al., 2024). This cancer has a high incidence worldwide, with around 133,354 cases reported in 2022, leading to a mortality rate of approximately 80,008 deaths (Zhang et al., 2023). In Indonesia, NPC remains a serious health concern, as the country has the second-highest mortality rate globally, with 3,220 deaths recorded in 2019 (Hutajulu et al., 2021). These numbers show that NPC continues to be a major public health issue, highlighting the urgent need for effective treatments to reduce its impact.

Currently, NPC treatment includes chemotherapy, surgery, and radiotherapy, which are chosen based on the stage of the cancer and the patient's condition. In the early stage (Stage I), patients usually receive only radiotherapy. However, in Stage II and higher, chemotherapy is combined with radiotherapy to improve treatment effectiveness (Suryani et al., 2024). Chemotherapy works by killing cancer cells, but it is less effective when used alone and gives better results when combined with other treatments. Surgery is rarely performed because NPC is located close to important nerves and blood vessels, making the procedure risky and potentially causing permanent complications, especially to the eyes and other vital structures (Ratini, 2024). Due to these risks and the limitations of chemotherapy, radiotherapy remains the main treatment for NPC.

Conventional radiotherapy using photons often causes side effects such as dysphagia, xerostomia, hearing loss, optic neuropathy, cognitive impairment and temporal lobe necrosis, as healthy cells also receive the radiation effects (Chen et al., 2019). To overcome these limitations, proton therapy was developed as an alternative that is more precise in killing cancer. Unlike photons that continue to release their energy as depth increases, protons have unique characteristics in their dose distribution. When protons begin to enter the tissue, they release a small amount of energy. Then there is a high energy spike at a certain depth called the Bragg Peak, where this energy spike is utilized to kill cancer cells. With these characteristics, proton therapy can increase the effectiveness of treatment while minimizing the risk of side effects due to radiation exposure to healthy tissue (Weber et al., 2020).

The effectiveness of proton therapy depends on the technique used to deliver the radiation dose to the cancer. Currently, there are two main techniques, namely Passive Scattering (PS) and Pencil Beam Scanning (PBS). The PS technique uses a scatter system and aperture to shape the proton beam to cover the entire target volume, resulting in a more uniform dose distribution. However, this method has limitations in adjusting the dose to complex cancer shapes and has the potential to produce secondary neutrons, which can increase radiation exposure to healthy tissue (Gordon et al., 2021). Meanwhile, the PBS technique directs a very small proton beam (pencil beam) in a controlled scanning pattern, allowing the dose distribution to precisely match the cancer shape. This technique provides better targeting while reducing radiation exposure to surrounding healthy tissue (Mohan et al., 2017). However, in simulations PBS technique is more complex than PS because it requires calculating the dose at each irradiation point while accounting for variations in tissue density, which can affect dose distribution accuracy.

Several studies have compared these two techniques and shown mixed results. For example, research by Rochmatul Ula (2021) analyzing dose distribution in liver cancer using (Particle Heavy Ion Transport System) PHITS version 3.22 showed that PBS is better at providing precise dose distribution, which minimizes radiation exposure to surrounding healthy tissue. The advantages of PBS were also found in research by Handarista (2022) on breast cancer therapy after lumpectomy using PHITS version 3.24. In this research, PBS produced sharp distal fall-off, so that the dose quickly decreased after reaching the target of therapy. This is very important to minimize the adverse effects of radiation on healthy breast tissue and surrounding vital organs.

However, different results were found in research by Dwi Fianto (2022) which analyzed dose distribution in medulloblastoma cancer using PHITS version

3.24. In this research, the PS technique was better at producing a more homogeneous dose distribution. This technique allows a wider and more even dose coverage, which is very important in the treatment of brain cancer to avoid cold spots (areas with too low dose) that can increase the risk of recurrence. Similar results were also found in research by Nofi Santika (2023) on liver cancer therapy using PHITS version 3.20, The PS technique in this research is more suitable for large size targets due to its more even dose spread and its ability to maintain homogeneity of dose distribution, especially in large cancer volumes. Therefore, the effectiveness of PBS and PS is highly dependent on the characteristics of the cancer which has different characteristics such as anatomical location, volume, diameter, as well as the range of energy required based on the depth of the cancer in the tissue. Therefore, the selection of the optimal proton therapy technique should be based on the characteristics of the cancer and conducted according to the Treatment Planning System (TPS).

One of the major factors in a TPS is optimizing the dose distribution to effectively destroy cancer cells while minimizing radiation exposure to Organs at Risk (OAR). Besides dose distribution, other factors such as irradiation homogeneity, therapy time efficiency, radiation direction, and energy range used are also important in selecting the most suitable technique for NPC. To ensure accurate dose distribution calculations, a simulation method is needed that can represent the complex interactions between radiation particles and biological tissues. One method that is often used is the Monte Carlo (MC) method, in proton therapy this method has an important role because in addition to considering electromagnetic interactions. Monte Carlo can also calculate the effects of nuclear interactions, such as non-elastic collisions and multiple scattering, which significantly affect the dose distribution in the patient's body (Paganetti, 2014). Application of this method requires specialized software, such as Fluctuierende Kaskade (FLUKA), Geometry and Tracking version 4 (GEANT4), Monte Carlo N-Particle (MCNP), and PHITS. Among this software, PHITS was chosen for its ability to simulate the interaction of various types of particles in a wide energy range as well as its efficiency in radiation dose calculations in medical applications

(Furuta and Sato, 2021). In addition, a previous research comparing this specialized software showed that PHITS has a faster calculation time while still maintaining an accurate depth-dose curve compared to other simulation programs (Yang et al., 2017).

Previous studies have compared the PBS and PS techniques in various types of cancer, such as breast cancer and medulloblastoma. However, no research has specifically analyzed the effectiveness of these two techniques for NPC. NPC has distinct characteristics compared to breast and medulloblastoma cancers, particularly in terms of dose distribution, which is influenced by factors such as cancer location, volume, surrounding healthy tissue, and depth within the tissue. These differences mean that the dose distribution and irradiation strategy for NPC require a more tailored approach. Additionally, there has been no research using the latest version of PHITS to simulate dose distribution specifically for NPC. Based on that, this research aims to analyze and compare the PBS and PS techniques in proton therapy for dose optimization in NPC using the latest version of the PHITS simulation, PHITS 3.341.

1.2 Research Purpose

The aim of this research is to:

1. Analyze and compare the total irradiation time to achieve the optimal dose between PBS and PS techniques in proton therapy.
2. Analyze and compare the equivalent dose distribution received by cancer targets and OAR to determine the optimal dose between PBS and PS techniques in proton therapy

1.3 Research Benefit

This research is expected to contribute to the advancement of radiotherapy, particularly in proton therapy planning for nasopharyngeal cancer. By utilizing PHITS version 3.341 simulations, this research aims to determine the more effective and safety irradiation technique between Pencil Beam Scanning (PBS) and

Passive Scattering (PS) in enhancing the optimal dose in cancer while minimizing radiation exposure to OAR.

1.4 Research Scope and Limitations

The scope and limitations of this research are as follows:

1. The simulation software used in this research is PHITS version 3.341.
2. The type of nasopharyngeal cancer analyzed is Non-Keratinizing Carcinoma (NKC) stage II, which has a cancer volume of 3 cm^3 and does not show signs of metastasis.
3. The cancer is modeled with a spherical shape, where the Gross Tumor Volume (GTV) has a radius of 0.89 cm, the distance from GTV to Clinical Target Volume (CTV) is 0.5 cm, and the distance from CTV to Planning Target Volume (PTV) is also 0.5 cm.
4. The OARs that will be analyzed in this research include the skin, tongue, salivary glands, eyes, and teeth.