CHAPTER 1 INTRODUCTION

1.1 Background

Brain cancer cases have always increased through the years. Brain cancer is cells growing abnormally in the brain. According to World Cancer Research Fund International, the amount of brain cancer in 2022 reached 321,731 people (WCRF, 2024). Glioblastoma (GBM) is a cancer that grows in central nervous system, specifically in spinal cord. The life expectancy patients have to live longer than three years only 3-5% (Karkon-Shayan et al., 2023). GBM make up approximately 80% of all Central Nervous System (CNS) tumors. However, current treatment options are often ineffective due to factors such as the Blood-Brain Barrier (BBB), tumor heterogeneity, an immunosuppressive Tumor Micro Environment (TME), as well as the disease's poor prognosis and high recurrence rate (Nedaeinia et al., 2025).

In cancer treatment, there are various types of treatment, including immunotherapy, hormone therapy, hyperthermia, photodynamic therapy, blood stem cell transplant, surgery, targeted therapy, chemotherapy, surgery, and radiotherapy (Nedaeinia et al., 2025). The current standard of care, known as the Stupp protocol, consists of maximal surgical resection followed by fractionated radiotherapy at a total dose of 60 Gy delivered in 30 fractions, combined with concurrent and adjuvant temozolomide (TMZ) chemotherapy. This regimen yields a median overall survival of approximately 14.6 months, which increases to 21.7 months for the patients.

There are two types of radiotherapy, external radiotherapy and internal radiotherapy. External radiotherapy means that the radiation comes from the machine located outside of the patient's body, while internal radiotherapy is the radiotherapy that delivers radiation sources directly to the cancer. There are advantages to external radiotherapy, it kills the cancer cell that surgery cannot reach, minimize cancer size, high safety for the patient, provide unpainful treatment

for the patient, decreases cancer symptoms, increases the patient's quality of life, and stimulates the body to develop immune response to the cancer.

Radiotherapy uses particles to kill the cancer cell. Some machines for external beam radiotherapy are accelerators, Linear Accelerator (LINAC), and Cobalt-60 teletherapy (Mahendra et al., 2025). An accelerator is a machine that produces and accelerates charged particle beams. When particles accelerate, they have greater velocity and produce greater energy to kill the cancer cells. The well-known accelerators are microtrons, betatrons, and cyclotrons. Linear accelerators (LINAC) are accelerators with straight trajectories that accelerate electrons to kinetic energies from 4 to 25 MeV. Cobalt-60 teletherapy is a teletherapy machine that uses Cobalt-60 as the radiation source.

Intensity Modulated Radiation Therapy (IMRT) is one of the irradiation techniques in radiotherapy that allows the dose of radiation to be precisely modulated according to the 3D shape of the cancer by modulating the intensity of the beam of radiation in several small volumes. Husni et al., 2021 have done research about the comparison between radiotherapy techniques that have been used in Indonesia, such as 3D-CRT and IMRT. This research states that the IMRT technique is more efficient for cancer treatment, specifically for breast cancer. Before irradiating the patient, treatment planning is carried out, called the Treatment Planning System (TPS), that used to measure the dose distribution, energy, beam angle, and type of irradiation technique. The TPS method that is commonly used in hospitals is the Anisotropic Analytical Algorithm (AAA), which considers variations in tissue density. At the time of irradiation, patients are prone to receiving scattered radiation outside the target area, which can cause secondary cancers (Acun et al., 2014).

To ensure the accuracy of dose delivery and mitigate potential errors, such as those in out-of-field absorbed dose, the verification of the TPS is essential. The necessity for radiotherapy plan verification stems from the potential inaccuracies of dose calculation algorithms within the TPS, particularly under complex clinical conditions. The out-of-the-field region absorbed four times lower doses than the Planning Target Volume (PTV), it has been proven that there are scattered doses

during the radiation treatment. In treatment planning several factors need to be considered such as the Organ at Risk (OAR) which is an organ that has sensitivity to radiation so the dose received by the organ during irradiation must be taken into account. Planning Target Volume (PTV) is a consideration of the combined effect of all possible geometric variations so that the radiation dose is right on target (Benedict, 2004).

Tuğrul, 2021 demonstrated that significant discrepancies between algorithms arise when using small radiation fields and in regions with high tissue density variations, such as at the interface between bone and soft tissue. This underscores the need for validation using a more accurate method like Monte Carlo (MC) simulation. The research found that while the MC algorithm in Monaco TPS showed near-perfect results, the Collapse Cone (CC) algorithm produced significant errors, especially at the interfaces between different tissues, such as underdosing when transitioning from lung to water or water to bone. This demonstrates that algorithm accuracy is critical, as simpler algorithms can be unreliable in complex treatments like Stereotactic Body Radiation Therapy (SBRT) involving small fields and tissue inhomogeneities.

Altuwayrish et al., 2022 conducted research comparing dosimetric calculations between the PRIMO MC code and the Eclipse TPS for brain cancer radiotherapy. Their study was performed in a two-stage process. First, the PRIMO simulation of a Varian Clinac 600C linac was validated against physical measurements, showing 98% agreement. Second, treatment plans for five brain cancer patients designed in Eclipse were recalculated in the validated PRIMO environment to compare key dosimetric parameters for the PTV and OAR. The results showed good agreement, with an average of 94% agreement between PRIMO and Eclipse for the patient cases, confirming that PRIMO is an accurate tool for evaluating treatment plans generated by a commercial TPS.

Robert et al., 2025 confirmed that PRIMO simulation can effectively validate both experimental beam data and 3D dose distributions from a TPS. Their quantitative comparison relies on gamma index analysis, where high passing rates (above 95%) with criteria such as 2%/2 mm for Percentage Depth Dose (PDD) and

3%/3 mm for beam profiles confirm the validity of both the simulation model and the treatment plan.

This study aims to compare the dose distribution in the Eclipse Treatment Planning System (TPS) using the Anisotropic Analytical Algorithm (AAA) with the Monte Carlo method in PRIMO software for patients diagnosed with glioblastoma. Unlike the research conducted by Altuwayrish et al. (2022), which used a Clinac 600C LINAC, this study will employ a Clinax CX LINAC and using patients' DICOM data with glioblastoma diagnoses.

1.2 Research Objectives

This study aims to compare the dose distribution calculated by Monte Carlo method in PRIMO software with that generated by the Eclipse Treatment Planning System (TPS) using the Analytical Anisotropic Algorithm (AAA) for patients diagnosed with glioblastoma. Specifically, the comparison includes dosimetric parameters such as D_{min}, D_{max}, D_{mean}, $D_{98\%}$, $D_{95\%}$, $D_{50\%}$ and $D_{2\%}$. This comparison is necessary because the AAA algorithm, while widely used in clinical practice, has known limitations in accurately modeling dose deposition in heterogeneous regions and high-dose gradient areas, such as the interfaces between skull bone and brain tissue. These limitations may lead to discrepancies in dose calculation, particularly in the penumbra region and at tissue interfaces, which could affect the accuracy of treatment plan evaluation.

1.3 Research Benefit

This study provides benefits in three areas:

1. Academically, it contributes evidence regarding the dosimetric differences between AAA in Eclipse TPS and Monte Carlo simulation in PRIMO for glioblastoma radiotherapy, demonstrating that AAA systematically overestimates treatment plan conformity compared to Monte Carlo,

particularly at field edges and penumbra regions where tissue density variations are significant.

2. Clinically, the findings highlight the importance of independent dose verification in glioblastoma treatment planning. The identification of dose discrepancies between AAA and Monte Carlo in critical organs at risk, particularly the brainstem and optic nerves, provides relevant information for radiation oncologists and medical physicists in evaluating treatment plans.
3. Methodologically, this study demonstrates the feasibility of using PRIMO as an independent secondary dose verification tool for glioblastoma IMRT treatment plans, with the validated linac model achieving a gamma passing rate of 98.9%. The study also provides practical insights into the challenges of performing Monte Carlo-based plan verification when MLC type incompatibility exists between the clinical system and the simulation software.

1.4 Research Scope

To avoid expanding the object of study, the problem limitation is focused on the following matters:

1. The type of cancer reviewed is glioblastoma cancer with total data of four patients (DICOM) using 6 MV photon energy of LINAC with type Clinac-CX and treated with IMRT.
2. Due to the unavailability of MLC80 in PRIMO software, treatment plan parameters were manually entered and the MLC type was substituted with MLC120 for the purposes of simulation.
3. The data will be analyzed, including the Dose Volume Histogram (DVH), Heterogeneity Index (HI), and Conformity Index (CI).
4. Data simulatation will be using PRIMO Monte Carlo software 0.3.(32-64).1880.