Review Article

Advancing Proton Therapy: A Review of Geant4 Simulation for Enhanced Planning and Optimization in Hadron Therapy

Abstract

Proton therapy is a cancer treatment method that uses high-energy proton beams to target and destroy cancer cells. In recent years, the use of proton therapy in cancer treatment has increased due to its advantages over traditional radiation methods, such as higher accuracy and reduced damage to healthy tissues. For accurate planning and delivery of proton therapy, advanced software tools are needed to model and simulate the interaction between the proton beam and the patient's body. One of these tools is the Monte Carlo simulation software called Geant4, which provides accurate modeling of physical processes during radiation therapy. The purpose of this study is to investigate the effectiveness of the Geant4 toolbox in proton therapy in the conducted research. This review article searched for published articles between 2002 and 2023 in reputable international databases including Scopus, PubMed, Scholar, Google Web of Science, and ScienceDirect. Geant4 simulations are reliable and accurate and can be used to optimize and evaluate the performance of proton therapy systems. Obtaining some data from experiments carried out in the real world is very effective. This makes it easy to know how close the values obtained from simulations are to the behavior of ions in reality.

Keywords: *Computer simulation, proton therapy, radiotherapy, software*

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1. Introduction

Today, radiotherapy is one of the most widely used methods for cancer treatment.[1-6] Tumor irradiation with high-energy photons is one of the common approaches in radiation therapy that may cause damage to healthy tissues along the radiation path. Hadron therapy is an advanced form of cancer treatment that uses charged particles, such as protons and carbon ions, to precisely target and destroy cancerous tumors while minimizing damage to surrounding healthy tissues. Proton therapy delivers high-energy protons that deposit most of their radiation dose at the tumor site, minimizing damage to surrounding tissues. Carbon ion therapy, with its greater biological effectiveness, offers even more precise tumor targeting and a sharper dose fall-off, reducing collateral damage compared to conventional radiation. The treatment process involves careful simulation and planning, followed by the precise delivery of particle beams using sophisticated accelerators. Hadron therapy is particularly beneficial for tumors near critical organs and in complex cases, aiming to improve outcomes and reduce side effects.

In one study, Akbari and Karimian examined how anatomical changes affect radiation dose variations in the prostate and bladder during magnetic resonance imaging-guided carbon-ion radiotherapy (MRgCT) for prostate cancer, highlighting the impact of anatomical variations on dose distributions in this setting.[7] In another study, they evaluated carbon-ion (C-ion) beam deflection and dose perturbation at different depths in a perpendicular magnetic field, relevant for potential magnetic resonance imaging (MRI)-guided carbon therapy development. Their results indicated notable effects at energies above 100 MeV/n in phantoms under a 1.5 T magnetic field.[8] In a third study, they aimed to evaluate the water equivalent ratio variations of various materials encountered in C-ion radiotherapy dosimetry under different magnetic field strengths, simulating conditions relevant to MRgCT scenarios for potential future

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therapeutic applications.[9] These findings contribute to assessing the impact of magnetic fields on C-ion range variations within dosimetric materials commonly used in clinical practice, such as phantoms, detectors, and patient anatomies.

Proton therapy is a subset of hadron therapy, which broadly encompasses the use of protons for cancer treatment. Proton therapy specifically utilizes high-energy protons to target and treat tumors with remarkable precision and effectiveness. The key advantage of proton therapy lies in its ability to deliver the majority of its radiation dose directly to the tumor site while sparing surrounding healthy tissues. Protons deposit most of their energy at a specific depth within tissues known as the Bragg peak, after which there is a rapid decrease in energy delivery, resulting in minimal radiation beyond the tumor. This precise targeting reduces the risk of damage to nearby critical structures and organs, minimizing potential side effects.[10] Proton therapy can be effective in treating cancers that are localized (nonmetastatic) and tumors located in or near sensitive areas such as the brain, heart, and lungs. Currently, the cancers most effectively treated with proton therapy encompass brain cancer, spinal cord tumors, and breast cancer. Matthew Ladra, who serves as the Director of Pediatric Radiation Oncology at Johns Hopkins, Hospital Sibley Memorial Cancer Center, notes that in some pediatric patients, proton therapy can significantly reduce the risk of late radiation-induced side effects.

For precise planning and implementation of proton therapy, advanced software tools are needed to model and simulate the interaction between proton beams and the patient's body. One of these tools is the Monte Carlo simulation software called Geant4, developed by European Council for Nuclear Research (CERN). Currently, the most common codes in this field are Geant4 and MCNPX, with Geant4 having an advantage over MCNPX due to its free availability and lack of licensing requirements. In this study, we will investigate the effectiveness of the Geant4 toolkit in proton therapy based on the conducted research.

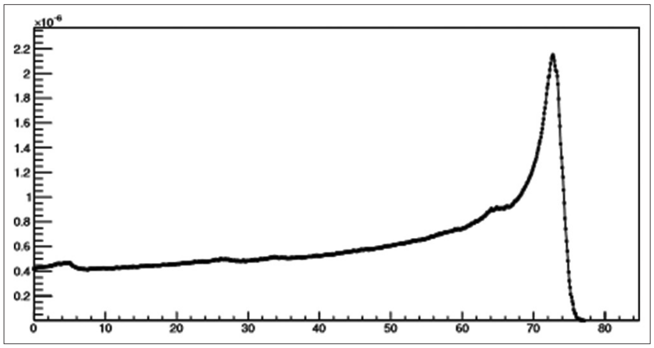

Figure 1:Graph of distributed dose for positioning of the phantom under irradiation of 100 MeV.[8] X-axis is the distance traveled (0–40 mm), and Y-axis is dose (gy×10⁻⁶)

2. Methods

Study type and population

The present research is a review based on the best evidence. Search strategy and approach: A comprehensive search was conducted in reputable international databases including Scopus, PubMed, Scholar, Google Web of Science, and ScienceDirect using predefined keywords. The search terms included "Geant4" and "proton therapy simulation." The extracted articles included 22 ISI articles, 4 PubMed articles, 1 book chapter from CRC Press, and 2 Internet sites.

Inclusion and exclusion criteria

Published articles from 1946 to 2023 were considered for this review.

Charged particle therapy, as a concept, began in the 1950s; hence, it is considered a relatively new concept, and limited information is available. Moreover, companies involved in charged particle therapy are highly secretive about their data. This study aimed to evaluate the accuracy of Geant4 software by examining reputable articles that have evaluated hadron therapy simulations against measured values.

Data extraction

The detailed results obtained from the articles are presented in the "Findings" section, demonstrating that Geant4 simulations are reliable and accurate. They can be utilized for optimization and evaluation of the performance of proton therapy systems.

The concepts and phrases examined in the articles include the following:

2.1 Monte Carlo

The Monte Carlo method is a common approach used in such cases. Monte Carlo methods refer to a numerical technique for solving equations or integrals by utilizing iterative random sampling.[11] It can be described as a solution for a system through microscopic interaction simulations. During the 1930s, Monte Carlo techniques were always about the physics of the target particles, and in

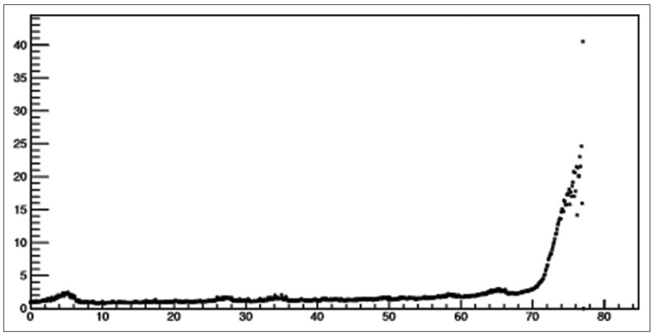

Figure 2: Linear energy transfer for 100 MeV.[8] X-axis is the distance traveled (0–40 mm) and Y axis is the stopping power (MeV/mm)

the 1940s, Monte Carlo methods saw widespread utilization in the development of weapons of mass destruction such as atomic bombs.[11] However, significant advancements have been made in this field over the past decades. In medical physics, Monte Carlo algorithms work for radiation transport methods. In dosimetry,[1] determining absorbed dose without using numerical methods is not possible.[1] Although significant progress has been made in this field recently, there is still room for improvement. There are numerous unresolved ambiguities, such as how nuclear reactions work.[1] When talking about particle prediction methods, the level of agreement among different models provides confidence, though the quantity of experimental data is insufficient to offer a definitive result on which model or approach is the best.[1] It has been established that Monte Carlo models are an essential tool in design and treatment systems.[1] Monte Carlo models find application at every phase of designing a new hadron. The first and most important Monte Carlo approaches applied for modeling linear accelerators and beam delivery systems, but recently, design and overall protection against harmful radiation in the treatment room have also been crucial. Monte Carlo methods have several advantages over traditional techniques. These advantages include: (1) Monte Carlo techniques can consider patient anatomy employing available information from computed tomography (CT) scans and other methods, (2) Monte Carlo methods have the capability to employ a simulation model that is closer to reality. While traditional methods often use an equivalent water approach for the human body, Monte Carlo methods can use a more realistic model, (3) Monte Carlo methods take into account interactions between particles and nuclei, effectively capturing the behavior of both primary and secondary particles, and (4) different codes are available for individuals interested in simulating heavy proton and ion therapy. The systems most frequently utilized include FLUKA, Geant4, MCNPX, VMCpro, and Shield-Hit. These codes may differ in various aspects, such as accuracy or some systems having a good graphical user interface, while others lack it.[11] Geant4 offers a broad array of functions that go beyond geometry, encompassing collision tracking and the provision of physical models. It allows the simulation of a broad spectrum of differing methods such as hadronic, decay, and electromagnetic, aiming to provide a mimetic simulation of reality for a large variety of different materials, enabling the user to replicate the simulation as realistically as possible. Geant4 is also capable of investigating the behavior of secondary particles (secondary neutrons and gammas) produced in proton therapy.

2.2 Geant4 (geometry and tracking)

The Geant4 simulation toolkit, developed at CERN and released in the early 2000s, is versatile software used to simulate particle interactions with matter using Monte Carlo methods. Originating as a successor to the Geant4 software toolkit, Geant4 is implemented in C++ with an object-oriented approach by the Geant4 collaboration. It accurately models particle interactions, including electromagnetic, hadronic, and nuclear processes, within complex geometries and experimental setups. Geant4 features a comprehensive set of functions beyond geometry, allowing for tracking collisions and providing physical models. Its primary applications span high-energy physics experiments, medical physics simulations (such as proton therapy and imaging techniques), space and astrophysics studies, and nuclear physics research. Continuously developed and maintained by the Geant4 collaboration, the toolkit evolves to meet emerging research needs across diverse scientific domains, enhancing performance and extending its applicability in particle and radiation transport simulations. Simulated particles are moved incrementally, enabling Geant4 to uniformly manage all particles regardless of type, aiming to closely mimic reality for a wide variety of materials and processes.[12] Geant4 plays a crucial role in medical physics, particularly in simulating particle interactions for advanced treatment modalities like proton therapy.

Hadron therapy is a sophisticated functionality available in Geant4 and is incorporated as a standard illustration upon Geant4 installation.[13] In the context of hadron therapy, Geant4 has the following advantages:

1. Simulation of particle interactions: Geant4 accurately simulates how particles interact with human tissues. This is crucial for predicting the dose distribution within a patient's body, ensuring the radiation targets only the tumor with minimal collateral damage
2. Treatment planning optimization: Geant4 aids in optimizing treatment plans. It allows for detailed modeling of patient-specific geometries and tumor characteristics, leading to highly personalized treatment strategies
3. Safety and efficacy: By simulating different scenarios and treatment plans, Geant4 helps in enhancing the safety and efficacy of hadron therapy. It can predict potential risks and side effects, contributing to informed decision-making in treatment planning.

In proton therapy, Geant4 is used to accurately model the passage of high-energy protons through various tissues and organs of the human body. This simulation capability allows medical physicists and researchers to predict the behavior of protons as they deposit energy along their path, enabling precise targeting of tumors while minimizing damage to surrounding healthy tissues. Geant4 incorporates sophisticated physics models to simulate interactions such as proton scattering, nuclear reactions, and energy deposition, considering the unique physical properties of protons and their biological effects on tissues. Through Geant4 simulations, medical physicists can optimize treatment planning, assess dose distributions, and study the impact of different beam parameters on treatment outcomes.

In addition, Geant4 is instrumental in developing and evaluating novel techniques within proton therapy, such as range verification methods and treatment delivery optimizations, ultimately contributing to the advancement and refinement of this cutting-edge cancer treatment technology. The accuracy and versatility of Geant4 in simulating particle interactions make it an indispensable tool for enhancing the effectiveness and safety of proton therapy and other radiation-based treatments in medical physics.

The traditional challenges in proton therapy planning include managing range uncertainty due to tissue density variations, addressing tissue heterogeneity to optimize dose distributions and minimize healthy tissue exposure, implementing effective motion management strategies to account for patient movement during treatment, navigating the complexity of treatment planning with proton beams to achieve desired dose distributions while ensuring patient safety, conducting rigorous quality assurance to verify treatment plans and delivery systems, and fostering interdisciplinary collaboration among medical physicists, radiation oncologists, dosimetrists, and other experts to optimize treatment strategies. Overcoming these challenges requires ongoing advancements in technology, treatment techniques, and collaborative approaches to enhance the accuracy, safety, and efficacy of proton therapy for cancer treatment.

Geant4 simulations play a vital role in addressing the challenges of optimizing proton therapy planning. First, Geant4 accurately models the interaction of high-energy protons with tissues, offering insights into range uncertainties due to tissue density variations and aiding in optimizing treatment plans for precise dose delivery to target volumes while minimizing exposure to healthy tissues. Second, Geant4 assists in motion management by simulating patient movements such as respiratory motion, enabling the development and evaluation of motion compensation techniques such as gating or tracking to enhance treatment accuracy. Third, Geant4 navigates the complexities of treatment planning by simulating dose distributions and beam characteristics, optimizing beam angles, energies, and modulation techniques for desired dose distributions and patient safety. In addition, Geant4 contributes to quality assurance by verifying treatment plans through simulated dose calculations, ensuring reliability and accuracy before patient treatment. Geant4 also facilitates interdisciplinary collaboration among medical experts by providing a common platform for visualizing and analyzing treatment plans based on accurate simulation data, enabling collaborative optimization of treatment strategies. Overall, Geant4's contributions significantly enhance the accuracy, safety, and efficacy of proton therapy in cancer treatment.

2.3 Bragg peak

A Bragg curve illustrates how the dose is distributed as particles traverse a medium. Analyzing this curve allows the identification of the Bragg peak, which manifests at the termination of the particle's range, notably evident with charged protons.[14,15]

2.4 Spread-out Bragg peak

By employing diverse beam-shaping devices such as energy absorbers or modulators, it becomes possible to create a spread-out Bragg peak (SOBP). Essentially, the SOBP can be viewed as an elongation of the Bragg peak. Combining Bragg peaks from multiple beams facilitates the generation of a wider SOBP, enabling a homogeneous dose distribution within the target volume.[15]

2.5 Linear energy transfer

Linear energy transfer refers to the energy that an ionizing particle delivers to a target in relation to the distance it covers during its travel.[16] This concept delineates how radiation interacts with matter. It is a naturally positive value and is contingent on the particle type, particle energy, and the target material.[16]

2.6 ROOT

ROOT is a software tool developed by Cern, designed for the analysis of extensive datasets. Geant4, predominantly coded in C++, follows an object-oriented approach while also incorporating additional languages such as Python. The integration of ROOT with Geant4 proves advantageous, given that ROOT scripts can seamlessly integrate into Geant4 code, streamlining the data analysis process.[17]

2.7 Detector and phantom geometry

The typical phantom utilized in this hadron therapy illustration is a water phantom. This choice is primarily due to the fact that a water phantom accurately mimics the composition of the human body, ensuring precise simulation outcomes.

3. Results

In this section, we discuss the details in two parts: (1) The history of substituting photons with protons and, (2) studies that have investigated proton therapy using Geant4 simulations and compared the simulated data with experimental data. For the first part, we trace back to the 1940s when Robert Wilson pioneered the transition from using photons to protons in cancer treatment. The initial therapeutic applications commenced during the 1950s.[18] Moreover, the treatments were performed at nuclear physics research facilities utilizing nondedicated accelerators. At that time, the number of body members accessible for treatment was limited because the accelerators did not have sufficient power to penetrate protons into deeper tissue layers.[18] However, with advancements in accelerator technology and progress in medical imaging and computing in the late 1970s, physicians were allowed to employ proton therapy more extensively in common treatments.[18]

It was not until sometimes later that the first clinics acquired proton therapy facilities, until the early 1990s.[11] The first case was constructed in Loma Linda in 2018 in the United States, where today more than 50 proton therapy centers are operational.[18] The subsequent phase in the progression of particle therapy was the shift toward carbon and other heavy ions,[18] which are better substitutes for protons as they provide better local control for highly invasive tumors with lower and delayed toxicity[18] and improve the patient's quality of life. By 2018, globally, over 120,000 cancer patients received postcancer treatment with hadron therapy, and from this total of 120,000 cases, 20,000 were specifically treated using carbon ions.[18] In ion therapy, the majority of the dose accumulates toward the end of the particle's range. Hence, the dose reaching healthy tissue along the beam line is lower compared to the utilization of conventional photons, even as an equivalent dose reaches the tumor.[19] By applying particle therapy in treatment, less radiation can be used, resulting in an increase in the radiation dose to the tumor with a lower proportion of the dose distributed in healthy tissue. This primary benefit sets particle therapy apart from traditional X-rays. Nevertheless, only a small fraction of radiotherapy patients, around 8.0%, undergo treatment using protons, carbon ions, or other high-mass particles.[19] In the next section, studies on proton therapy using Geant4 simulations and the comparison of simulation results with experimental data will be discussed. Silva *et al*.[20] conducted a study in 2020 comparing systematically important parameters for proton imaging with Geant4 simulation under various physics conditions. They analyzed the energy, angles, and proton coordinates at the point of exiting the absorber. They concluded that precision in simulating the output energy in modern proton imaging devices is crucial and fundamental for medical purposes. Within proton imaging, the resolution of density (contrast) relies on the output energy and its associated uncertainty. Musa *et al*.[21] in 2019 compared experimental SOBP for proton beams with simulated SOBP using gamma index criteria to validate the Monte Carlo model. According to this study, a 98% gamma passing rate demonstrated satisfactory agreement between measurement values and simulations. Paganetti *et al*.[22] in a 2000 study introduced calibration methods for a treatment planning system using proton beams through Geant4 simulation software. Their study presented the calibration process and the construction of target models for proton beam simulation. In addition, Geant4 simulation results were compared with experimental data using MCNPX radiation transport software. The results demonstrate that Geant4 software is a powerful tool for proton therapy treatment planning and can be fully utilized for designing and optimizing proton therapy systems. In another study in 2005, a Geant4-based simulation for a proton radiation system was presented to validate dose distribution by Aso *et al*.[23] This simulation illustrated the radiation and therapeutic systems operational at the Hyogo Ion Beam Medical Center. The radiation system encompassed a lateral beam spreading mechanism and a range modulation system, enabling a three-dimensional dose dispersion. Simulations were conducted for proton beams utilizing the isocentric rotational nozzle for therapeutic energies of 150, 190, and 230 MeV. The simulated distributions were then compared with the measured dose distributions obtained using a water phantom positioned at the isocenter. This simulation setup mimics the practical aspects of administering radiation to the patient. The simulations pertaining to the proton range, focusing on crucial materials within the beamline and lateral field uniformity, were duly validated. In addition, the simulated dose distributions, based on Geant4, were corroborated through Bragg peak and double peak Bragg measurements. This validation demonstrates good agreement between simulations and measurements. Daftari[24] compared lateral dose distributions in proton therapy using Geant4 in 2005. The article investigates the Geant4 simulated calculations compared to experimental results for lateral dose distribution in proton therapy. The simulation results of Geant4 for the lateral dose in proton therapy were compared with experimental results for proton energies of MeV 60 and MeV 70. In addition, simulation results for lateral dose in treatment planning for protons with MeV 180 and MeV 190 energies were compared with measured data. The results indicate that Geant4 simulations for calculating lateral dose in proton therapy are done with high accuracy and are usable for improving proton therapy systems. In another study by Chang[25] in 2006, published in the Medical Physics journal, a Monte Carlo simulation system based on Geant4 for proton radiation therapy was developed. The simulation system was designed using a very precise description of the physics and geometry of proton beams. To validate the simulation system, two types of experiments were conducted in proton therapy techniques. First, the accuracy of the simulation system was examined by comparing the simulation results with experimental results. Second, to investigate the dose deposition inside the tissue, the signal-to-noise ratio in CT images used in proton therapy planning was measured. The results demonstrate that the proposed simulation system can agree well with the measured values in experiments. In a validation and clinical dose computation study conducted by Guatelli[13] in 2010, the accuracy of Monte Carlo simulations using Geant4 tools for proton therapy applications was investigated. They performed dose calculations using different proton therapy models, including superficial dosimetry and breast cancer treatment and compared the results with experimental data. In the case of the superficial dosimetry model, the comparison of calculated superficial dose values with experimental data showed a computational error of about 3%. On the other hand, for the breast cancer treatment model, the comparison of three-dimensional dose with experimental data indicated a computational error of about 1%. Finally, the authors stated that Geant4 simulations are reliable and accurate, suitable for optimizing and evaluating the performance of proton therapy systems. Mairani[26] presented their research results in 2014, utilizing Geant4 simulations in proton therapy, covering single-point scanning to active beam delivery. The authors compared Monte Carlo simulations using Geant4 toolbox for various proton therapy delivery systems with measurements from different experimental setups. The authors demonstrated that Geant4 can accurately simulate the distribution of proton radiation dose for a range of delivery systems and can be used for optimizing and evaluating the performance of proton therapy systems. The article emphasizes the importance of accurate Monte Carlo simulations in proton therapy and the potential benefits of using Geant4 for this purpose. In 2019, Ekelund[11] at the Nuclear Physics group of KTH Royal Institute of Technology in Sweden performed several simulations in proton and carbon therapy with different codes. By varying the most fundamental parameters, such as beam energy or particle type, variations in dose distribution, range, and the appearance of the Bragg peak were investigated. The impact of parameter changes was observed in the comparison of results in the Dose.out file. Simulations were performed for energies ranging from 60 to 260 megavolts with increments of 10 megavolts per run, resulting in a total of 21 simulations. Dose.out files were saved for each simulation. Let.out files were saved for energies of 60, 100, 140, 180, 220, and 260 MeV. Analysis was conducted on the Dose.out and Let.out files for 100 MeV and 180 MeV energies. Dose.out and Let.out for 100 MeV are presented in Figures 1 and 2, respectively.

In 2020, utilizing Geant4 and FLUKA codes, a SNYDER head phantom encompassing skin, skull, brain, and tumor components was simulated by Hashemi *et al*.[27] The brain tumor, resembling brain tissue and shaped like a sphere with a radius of 1 cm, was placed 1.5 cm below the skin. The results demonstrate that by modulating the initial Bragg peaks associated with 85.76 mega electron volt proton energy and their corresponding weights, an SOBP can be obtained, covering the tumor volume longitudinally and laterally. The proton absorbed dose within the skin, skull, tumor, and brain tissues for 85.76 mega electron volt proton energy was calculated. It was found that 99.99% of the total dose is absorbed within the tumor volume. The flux and absorbed dose of secondary neutrons and photons, prominent secondary particles resulting from nonelastic nuclear reactions of protons in distinct tissues, were computed. The absorbed dose resulting from protons, secondary neutrons, and secondary photons within tumor, skin, skull, and brain tissues was also calculated. Notably, over 99% of the total dose was absorbed within the tumor. Furthermore, the irradiation of the tumor was achieved in three dimensions, whereas minimal absorbed dose was received by healthy tissues. Sangwan and Kumar[28] in 2021 successfully simulated Bragg peaks for proton beams with energies of 62, 130, 170, 200, and 240 MeV for treatment planning for hadron therapy employing the Geant4 simulation toolkit. A comparison of the simulated Bragg peaks for energies of 130–240 MeV shows that with increasing energy, the particle range can be increased, allowing for clinical treatment of deep-seated tumors. The outcomes of the computational analysis from the predesigned Geant4 are in good agreement with the expected Bragg peak production, confirming the reliability of the Geant4 code. Since 2023, the possibility of performing radiobiological experiments has been provided at the Delft Proton Therapy Center in The Netherlands by Groenendijk *et al*.[29] To fully exploit this resource, the Geant4 simulation platform has been introduced to the research and development line to investigate, plan, and optimize in this field. The Geant4 platform has been developed to simulate both pencil beam and scattered field in parallel. Three different sets of experimental proton data with energies of 70, 150, and 240 MeV for pencil beams in air and depth-dose profile in water have been used to train an asymmetric Gaussian pencil beam model from a proton source using a Kapton vacuum pipe output window. The stability of the Geant4 platform was then evaluated using three independent experimental datasets in both pencil beam states at 120 and MeV 200 energies and in the scattered field state at 150 MeV energy. The results demonstrate a high level of agreement between the developed Geant4 platform and the experimental data, revealing a high level of agreement in investigating main physical parameters, including beam spot size, range coverage, initial energy spread, dose depth distribution, and field uniformity. These results at intermediate energies indicated that the developed simulation platform is capable of reproducing the characteristics of the research beamline, thus enabling simulation-based planning and optimization of future radiobiological studies at the Holland Delft Proton Therapy Center.

Geant4 simulations contribute significantly to the advancement of radiation therapy by enabling more precise, personalized, and safer treatment protocols through accurate dose calculations, optimization of treatment planning, validation of treatment plans, risk assessment, innovation in therapy techniques, as well as education and training. Geant4 plays a pivotal role in improving patient outcomes and quality of care in radiation oncology.

4. Discussion

The concept of hadron therapy emerged in the 1950s and is therefore considered a relatively new concept with limited available information. Companies engaged in hadron therapy tend to be discreet and cautious in sharing their data. Hence, confirming whether the data collected through simulations are under any circumstances similar to the values obtained in real hadron therapy is challenging. The lack of data may be due to the scarcity of clinics that perform hadron therapy. The question arises as to why the number of hadron therapy clinics is low and why a small number of patients are treated with charged particles. Two factors include the lack of established clinical data and the range of uncertainties associated with proton and heavy ion use. Nevertheless, the primary obstacle remains the substantial expenses of establishing new charged particle therapy centers involved.[10] Facilities that make proton therapy more expensive than ion therapy, called combined centers, have made proton therapy the most expensive. For precise planning and proton therapy delivery, advanced software tools for modeling and simulating the interaction between proton radiation and the patient's body are required. The user should acknowledge that the effectiveness of hadron therapy may be influenced by a restricted understanding of the nuclear reactions involved, especially fundamental nuclear reactions, as it can be problematic. In addition, the user must have sufficient training to use advanced simulation software to perform accurate simulations. Although published research in this area is scarce for the reasons mentioned, the studies presented in this article demonstrate that the Geant4 toolkit has great potential for proton therapy simulations. With the reasons stated below, it can be said that Geant4 is promising.

Geant4 simulations contribute significantly to enhancing precision and safety in hadron therapy through the following key aspects: (1) providing insights into particle interactions, (2) optimizing treatment planning, (3) assessing safety risks, (4) fostering research and development, and (5) facilitating education and training. These simulations empower clinicians and researchers to deliver more targeted, effective, and safer cancer treatments using proton therapy and carbon ion therapy.

Geant4 simulations enable the development of more personalized and effective treatment plans for patients undergoing proton therapy. By accurately modeling how high-energy protons interact with individual patient anatomy, including tissue density variations and biological responses, Geant4 allows medical physicists to customize treatment parameters based on specific patient characteristics. These simulations predict the range and distribution of radiation doses within the body, enabling the optimization of beam delivery parameters such as angles, energies, and modulation techniques to maximize tumor dose while minimizing exposure to healthy tissues. Geant4 simulations also assess the impact of patient motion, such as respiratory movements, on treatment accuracy and enable the evaluation of motion management techniques such as gating or tracking to ensure precise beam alignment with target volumes throughout treatment. This personalized approach facilitated by Geant4 contributes to improved treatment effectiveness and patient outcomes in proton therapy, advancing the field of personalized medicine by tailoring treatment plans to individual patient needs and characteristics.

Future technological advancements in Geant4 simulations for proton therapy have the potential to revolutionize cancer treatment by enhancing precision, efficiency, and customization. One critical area of development involves refining tissue modeling and biological response within Geant4 to enable more accurate predictions of proton interactions tailored to individual patient anatomy and biology, facilitating the creation of personalized treatment plans that optimize dose delivery based on specific tissue characteristics and lead to improved treatment outcomes with reduced side effects. Another significant advancement is the integration of advanced imaging techniques directly into Geant4 simulations, enabling more accurate and patient-specific treatment planning that allows clinicians to adapt treatment plans in real time based on intratreatment imaging feedback. This integration enhances tumor targeting and reduces damage to healthy tissues, improving overall treatment efficacy and patient outcomes. In addition, the integration of machine learning and artificial intelligence within Geant4 could automate treatment optimization processes, predict treatment outcomes, and generate adaptive strategies based on extensive patient data, further optimizing Geant4 simulations to individualize treatment approaches and maximize therapeutic benefits for patients. These advancements, coupled with improvements in computing power and simulation algorithms, hold the potential to transform proton therapy into a personalized, precise, and adaptive cancer treatment modality. Ongoing research efforts are also focusing on integrating Geant4 simulations more deeply into the clinical workflow, exploring enhanced algorithms for more accurate dose calculations, real-time simulation capabilities to adjust treatments in response to tumor changes, and integrating imaging data (such as MRI or CT scans) into simulations to enhance accuracy and effectiveness.

Despite its advantages, incorporating Geant4 simulations into routine clinical practice faces several challenges. One challenge is the high computational resources required for detailed simulations, which can be a limiting factor in some clinical settings. Another challenge is the complexity of the software, which demands specialized knowledge and necessitates proper training for medical physicists to effectively utilize Geant4. Finally, continual development is necessary as technology and understanding of cancer treatment evolve, requiring ongoing updates and improvements in Geant4 simulations.

Looking ahead, several challenges will need to be addressed for the widespread adoption and advancement of Geant4 simulations in proton therapy. First, the increasing computational demands associated with detailed and patient-specific simulations could strain resources, particularly for smaller clinics or institutions with limited access to high-performance computing. Addressing this challenge will require innovative solutions to manage costs and improve accessibility, such as collaborative initiatives or cloud-based computing platforms. Second, cost considerations related to implementing and maintaining advanced simulation technologies could pose barriers to accessibility, especially in regions with limited financial resources. Streamlining costs through open-source development and shared resources may help promote broader adoption of Geant4 simulations. In addition, ensuring user-friendliness and usability of Geant4 software for clinicians and medical physicists will be crucial for effective integration into clinical workflows. Developing intuitive interfaces and comprehensive training programs can facilitate the use of Geant4 in treatment planning and decision-making. Finally, regulatory considerations and standards for utilizing simulation data in treatment protocols will need to be established to ensure patient safety and compliance. Overcoming these challenges will require collaborative efforts across stakeholders to drive innovation, affordability, and standardization in the application of Geant4 simulations for proton therapy.

The future of Geant4 in hadron therapy looks promising, with ongoing research and development aimed at making simulations faster, more accurate, and user-friendly. These advancements could lead to more widespread adoption of this technology in cancer treatment, ultimately contributing to more effective and personalized therapy strategies.

5. Conclusion

Based on published research, Geant4 simulations appear promising and accurate for optimizing and evaluating the performance of proton therapy systems. In addition, the future of Geant4 in hadron therapy looks bright, with ongoing research and development aimed at making simulations faster and more accurate.

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Conflicts of interest

There are no conflicts of interest.

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