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Photon versus Proton Therapy: Systematic Review of Energy Transfer and Dose Distribution

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ABSTRACT

Radiation therapy is a key part of modern cancer care, and is needed by about half of all people with cancer at some point during their treatment. Photon therapy is the most common modality used today. It is derived from X-rays and gamma rays. It is the most common because it is available and cost effective. Proton therapy, however, is a sophisticated approach using charged particles based on precision. A systematic review was conducted following PRISMA guidelines, by searching for peer-reviewed sources published between 2014 and 2025 to compare the physical and biological characteristics of both modalities, with particular emphasis on energy transfer mechanisms and dose distribution. Results indicate that photon therapy is associated with indirect ionization and an unavoidable exit dose, thus energy is deposited in healthy tissues outside the tumor, increasing the risk of toxicity in normal tissues. Proton therapy on the other hand has a unique Bragg Peak that allows maximum deposition of energy at a specific depth with minimal or no dose beyond the target, thus sparing organs at risk such as the heart and lungs. However, clinical data shows an exception with lower endocrine toxicity with photon therapy than proton therapy in patients with craniopharyngioma (13.7% vs 27.8%). In conclusion, although proton therapy has definite biophysical and dosimetric advantages over photon therapy, treatment selection has to be individualized according to tumor type, anatomical location and biological variability. These findings support evidence-based optimization of radiotherapy by merging physical dose distribution with clinical outcomes.

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INTRODUCTION

The application of ionizing radiation for medical purposes began with the discovery of X-rays by Roentgen in 1895, and the subsequent development of fractionated radiotherapy in the 1920s and 1930s made it a fundamental component of cancer treatment (Paganetti, 2025). Ionizing radiation can be generated from different types of particles and sources, each characterized by distinct energy spectra, interaction probabilities, linear energy transfer

(LET), dose uniformity, dose rates, and methods of delivery (Korns et al., 2023). Currently, cancer is the second leading cause of death globally, and approximately half of all cancer patients require radiation therapy at some point during their treatment (Salem et al., 2024). While photon-based therapies remain the most commonly used method, the introduction of proton beam therapy by Robert Wilson in 1946 introduced a major shift in treatment precision by utilizing the unique physical properties of heavy charged particles (Paganetti, 2025). The first patient was treated with proton therapy in 1954, employing the synchrocyclotron at the University of California, Berkley (Mohan, 2022).

From a physics perspective, the interaction of photons and protons with biological matter differs significantly. Photon-based techniques, including Intensity-Modulated Radiation Therapy and Volumetric-Modulated Arc Therapy, are characterized by an exit dose that deposits energy into healthy tissues beyond the target, thereby increasing the risk of therapy-related toxicities and secondary malignancies (Wang et al., 2024).In contrast, proton therapy exploits the physical Phenomenon of the Bragg Peak, the point at which protons deliver their maximum energy at a precise depth and stop abruptly, resulting in a near-zero dose beyond the tumor (Zhou et al., 2023). This property is particularly advantageous in treating pediatric central nervous system (CNS) cancers (Carbonara et al., 2019). It also minimizes damage to critical organs, such as the heart and lungs, in Non-Small Cell Lung Cancer therapy (Bayasgalan et al., 2021).

Furthermore, modeling studies demonstrate that proton therapy can reduce the anticipated occurrence of radiation-induced secondary cancers by 2 to 15 times compared to photon-based techniques, provided that advanced pencil-beam scanning is used to minimize secondary neutron exposure. However, in clinical follow-up, this percentage is 1.5% and 1.8%, which also has certain causes (Upadhyay et al., 2022). In the future, radiotherapy is expected to advance in multiple directions. As particle therapy continues to develop, it is likely to not only reduce the side effects associated with radiotherapy but also improve its overall effectiveness. Proton therapy is widely used around the world as a key example of particle therapy (Huh & Kim, 2020).

Despite these advantages, several radiobiological and physical challenges persist. Radiobiological, the Relative Biological Effectiveness (RBE) of protons is clinically considered a constant value of 1.1; however, emerging evidence suggests that RBE is not uniform and varies with Linear Energy Transfer (LET), tissue type, and patient-specific factors (McNamara et al., 2020). Physically, range uncertainty remains a significant limitation for protons (Chen et al., 2023). Moreover, proton therapy may lead to exposure to secondary neutrons, which, unlike photon therapy, raises additional safety concerns due to the presence of an exit dose (Hälg & Schneider, 2020). Therefore, reducing radiation exposure to healthy tissues is essential. Advanced techniques such as intensity-modulated photon therapy and proton therapy improve dose conformity but still generate stray radiation, increasing the risk of secondary cancers. Since this exposure is not routinely calculated in clinical practice, risk assessment remains challenging (Newhauser et al., 2018).

This study enhances precise clinical decision-making in cancer radiotherapy by comparing the physical dose distributions and biological properties (LET and RBE) of photon and proton therapies. It highlights key mechanisms, such as the Bragg Peak, to better spare healthy tissues. Overall, it supports evidence-based optimization of modern radiotherapy by integrating radiobiological accuracy with clinical outcomes, cost-effectiveness, accessibility, patient survival, and quality of life.

We present a systematic review comparing the physical and biological properties of photon and proton therapies to facilitate optimal clinical decision. To fulfill the main aim of the research, the specific objectives are:

- To make a comparative analysis of energy transfer and dose distribution characteristics between photon and proton therapy.
- To assess the efficiency of Bragg Peak proton therapy compared with buildup region of photon therapy in tumor coverage and sparing of healthy tissues.
- To evaluate the influence of RBE and secondary neutrons in proton therapy in comparison to the biological outcome of photon therapy.

METHODS AND MATERIALS

This systematic review was conducted in accordance with PRISMA guidelines to ensure a transparent and rigorous study selection process. The study designed to assess the differences in energy transfer mechanisms and dose distribution between photon and proton therapy. Two scientific databases, including PubMed and Science Direct, were systematically searched to ensure comprehensive coverage of the literature. The search was carried out using the following keywords: Photon therapy, Proton therapy, Energy transfer, Dose distribution. The filtering criteria were as follows:

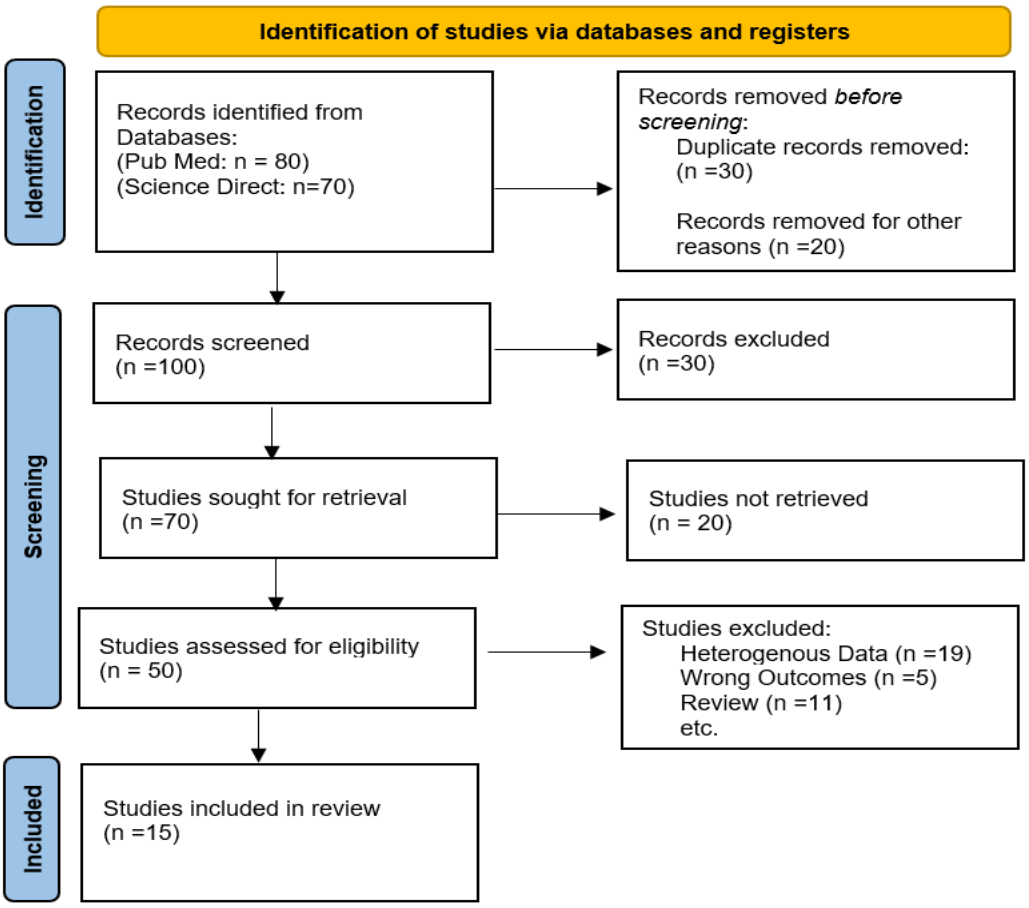
Inclusion criteria: 1- Comprised comparative studies between external beam photon and proton radiotherapy. 2- Published between (2014-2025). 3- Written in English.

Exclusion criteria: 1- Abstract-only. 2- Non-comparative studies. 3- Articles with incomplete dosimetric data.

All retrieved records were independently screened by two reviewers. After removal of duplicates, studies were first screened based on titles and abstracts, followed by full text eligibility assessment Full-text articles were for acceptability, resulting in (15) scientific sources that fulfilled the selection criteria and were included in the review, consisting of four experimental studies and eleven simulation-based studies. Relevant dosimetric parameters associated to energy deposition and dose distribution were extracted and compiled into comparative tables. Differences between photon and proton therapy were analyzed qualitatively, with particular emphasis on dose conformity, organ-at-risk sparing, and linear energy transfer. Finally, the findings were synthesized to deliver a comprehensive comparison of energy transfer efficiency and dose distribution characteristics between the

two treatment modalities for evaluating their clinical potential. The overall study selection process is summarized in a PRISMA flow diagram shown in the figure below.

Figure 1. *(PRISMA) flowchart of the literature search and study selection process*



FINDINGS

This systematic review critically evaluated empirical and dosimetric data comparing photon and proton radiotherapy, with a focus on energy-transfer mechanisms and dose-distribution characteristics. Particular attention was given to linear energy transfer (LET), Bragg Peak behavior, target dose conformity, and organ-at-risk (OAR) sparing, reflecting key parameters for clinical efficacy and safety.

The literature consistently highlighted three core domains: 1- Energy transfer mechanisms. 2- Dose distribution characteristics and clinical efficacy. 3- Quantitative and qualitative dosimetric data extracted from the included peer-reviewed studies are presented in Tables 1 and 2. These analyses collectively enable a comprehensive evaluation of the relative dosimetric and biophysical advantages of proton versus photon modalities, providing insights into their potential clinical applications.

Table 1*. Overview of Peer-Reviewed Studies Showing Energy Transfer Mechanisms and Dose Distribution Characteristics of Photon and Proton Therapy*

Treatment Type	Energy Transfer Mechanisms	Dose Distribution Characteristics	Key Findings	Study / References
Photon Therapy	Indirectly ionising: Photons transfer energy in two steps. 1- To secondary electrons by interactions such as the photoelectric effect, Compton scattering, and pair production. 2- Then the electrons ionize the medium.	Features a buildup region, where the dose initially rises near the surface, then decreases exponentially with depth.	Widely used, with a predictable depth dose curve.	(Khan & Gibbons, 2014).
Proton Therapy	Direct ionization: Protons gradually lose energy in inelastic The Coulomb interactions with atomic electrons, described by the Bethe–Bloch equation.	Maximum dose at a particular depth, negligible dose beyond Bragg Peak.	It is well suited for conformal therapy, with good dose localization and tissue sparing.	(Newhauser & Zhang, 2015).

From the above information it can be seen, that the physical comparison of photon and proton therapy show clear differences. With photon therapy, the energy is transferred indirectly through secondary electrons. The dose peaks near the surface and decreases with depth. Therefore, the existence of an exit dose in photon therapy introduces additional safety concerns. Proton therapy deposits its energy directly, showing the Bragg Peak. The Bragg Peak is the maximum dose deposition at a certain depth with minimal exit dose beyond the target. This allows for precise dose localization and optimal tissue protection.

Table 2*. Summary of Reviewed Studies Showing Clinical Findings of Photon and Proton Therapy*

Clinical Parameter	Photon Therapy Findings	Proton Therapy Findings	Study/References
Secondary Cancer Risk (Modeling).	Represents the baseline risk due to exit dose.	Expected reduction by a factor of (2-15) using pencil beam scanning.	(Upadhyay et al., 2022).
Secondary Cancer (Clinical Follow-up).	Observed incidence rate of 1.8%.	Observed incidence rate of 1.5%.	(Upadhyay et al., 2022).
Endocrine Toxicity (Craniopharyngioma).	Lower damage rate (13.7%) to the endocrine system.	Higher damage rate (27.8%) superior endocrine spring.	(Pan et al., 2025).
Organ Sparing (Heart& Lungs in NSCLC).	Higher dose bath to non-target organs like heart and spine.	Superior sparing of heart and lungs due to absence of exit dose.	(Bayasgalan et al., 2021).

The above information indicates that clinical comparisons of photon and proton therapies show different secondary cancer risk, endocrine toxicity, and organ sparing. There is a baseline risk of secondary cancer from exit dose in photon therapy with a clinical incidence of 1.8% vs 1.5% for proton therapy. Modeled studies suggest that the use of pencil-beam scanning in proton therapy could reduce secondary cancer risk by 2-15-fold as compared to photon therapy. There are some exceptions, such as in craniopharyngioma patients, where photon therapy has shown to be more effective in reducing the endocrine toxicity 13.7% of endocrine damage was in photon therapy and 27.8% in proton therapy. Photon therapy for Non-Small Cell Lung Cancer can lead to higher doses of radiation to nearby non-target organs such as the heart and spine. Proton therapy, on the other hand, allows better sparing of the heart and lungs because of minimal exit dose.

In conclusion, the findings suggest that proton therapy offers biophysical and dosimetric benefits that might translate into enhanced efficacy and safety of treatment in comparison with photon therapy. But there are also some exceptions like in patients with craniopharyngioma.

Photon Interaction Mechanisms with Matter

When an X-ray or gamma-ray photon beam passes through a material, interactions occur between the photons and the atoms of the medium, resulting in energy transfer to the material. The first stage of energy deposition occurs through interactions that release electrons from the atoms of the absorbing medium. These energetic electrons subsequently deposit their energy along their trajectories by causing atomic ionization and excitation. When the absorbing medium is human tissues, the deposited energy may be sufficient to damage cellular components and potentially impair cell reproductive capacity. However, most of the absorbed energy is ultimately dissipated as heat, producing minimal biological effects. Ionizing photons interact with atoms mainly through three fundamental mechanisms: the Photoelectric effect, Compton scattering, and Pair production, each of which results in the generation of high-energy secondary electrons (Khan & Gibbons, 2014). The photoelectric effect, first observed by Hertz, occurs when a photon is absorbed by an atom, causing one of the atom's bound electrons to be ejected (Jho et al., 2023).

Compton scattering occurs when a high-energy photon collides with an electron, transferring part of its energy to the electron, causing the electron to recoil, and increasing the photon's wavelength (Zhu, 2023). This phenomenon has significant applications in clinical practices, particularly in radiation therapy (Khalaf & Kaminer, 2023). Furthermore, pair production occurs when the energy of a photon surpasses the required threshold (1.022Mev) (Khan & Gibbons, 2014). It is worth noting that Gamma-rays have greater penetrating power than particles or electrons from decays. They easily penetrate human tissue (Belyaev & Ross, 2021).

Photon Energy Transfer and Dose Distribution

Effective radiotherapy requires accurate radiation dose monitoring to improve outcomes and limit side effects. Because different tissues possess distinct physical and chemical properties, radiation interacts differently with each tissue type. Moreover, photon fluence calculations are complex, making it challenging to determine absorbed dose. However, for uncharged radiation such as photons, KERMA (kinetic energy released in the medium) can be considered equal to the absorbed dose under conditions of electronic equilibrium and when bremsstrahlung losses are negligible (Shamsabadi et al., 2024). KERMA is the ratio of the total initial kinetic energy of charged particles (electrons and positrons) liberated by photons to the mass of the material in which they are produced(Khan & Gibbons, 2014).

$$K = \frac{dE_{tr}}{dm} \qquad (1)$$

The (KERMA) unit is $\frac{jol}{kg} = Gray$.

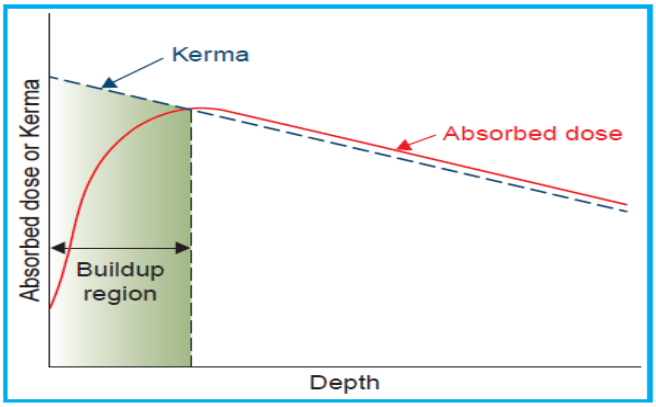


Figure 2. Schematic diagram illustrating absorbed dose and (KERMA) versus depth (Khan & Gibbons, 2014)

The dose quantifies radiation from all ionizing particles, charged or uncharged, for all materials and energies. It reflects the biologically significant effects produced by ionizing radiation. The current definition of dose is the ratio of the mean energy imparted by ionizing radiation, $d\bar{\epsilon}$ to the mass of the material, dm. The unit for absorbed dose is the gray (Gy).

$$D = \frac{d\bar{\varepsilon}}{dm} \qquad (2)$$

In radiation therapy, direct dose measurement in patients is rarely possible. Instead, dose distribution is generally estimated using phantoms made of tissue-equivalent materials. Water phantoms are commonly used because they closely mimic the absorption and scattering properties of soft tissues, are widely available, and provide reproducible results. However, practical challenges arise when using water phantoms with detectors such as ionization chambers, as these devices can be affected by water unless specifically designed to resist it. Solid phantoms are often used as alternatives. In both patients and phantoms, the absorbed dose varies with depth, influenced by Beam characteristics (energy, field size,

source-to-surface distance, and collimation). An important procedure in the dose calculation process is establishing the dose variation with depth along the central axis of the beam. The central axis dose distribution can be characterized by normalizing the dose at a depth d, with compared to the dose at reference depth d_0. Clinically, the peak radiation dose along the central axis is often reported as (Khan & Gibbons, 2014). These measurements form the basis for planning and verifying patient treatment to ensure accurate and safe radiation delivery. When the percentage depth dose has been determined, the dose absorbed at a given depth and the dose at the reference depth are determined. So, the formulas are as follows:

$$P = \frac{D_d}{D_{d_0}} \times 100\% \tag{3}$$

$$D_{\max} = \frac{D_d}{P} \times 100\% \tag{4}$$

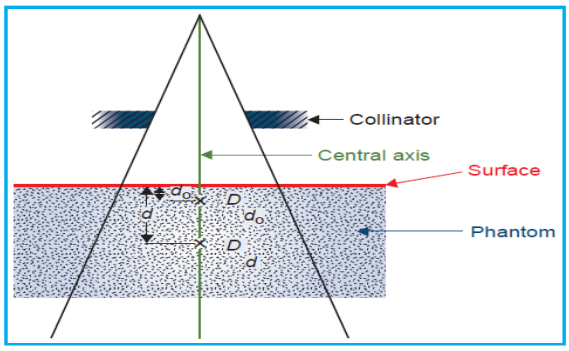


Figure3*. Explains the percentage depth dose (Khan & Gibbons, 2014)*

Protons Interaction Mechanisms with Matter

At the outset, we briefly review the principal mechanisms by which protons interact with matter and their significance. Figure 4 shows the different ways a proton can interact with an atom or its nucleus, including Coulomb interaction with electrons, Coulomb interactions with the nucleus, nuclear reactions, and Bremsstrahlung. As a first approximation, protons continuously lose their kinetic energy through successive inelastic Coulomb interactions with atomic electrons. Most protons travel approximately along straight paths because their rest mass is 1836 times greater than that of an electron. In contrast, a proton passing close to an atomic nucleus undergoes elastic scattering due to Coulomb repulsion and is deflected by the extremely large mass of the nucleus; it deviates from its initial path. Inelastic nuclear interactions between protons and atomic nuclei occur infrequently; however, they have a profound effect on an individual. During a nuclear interaction, when the incident proton penetrates the nucleus, the reaction may result in the emission of a proton, a deuteron (^{2}H), a triton (^{3}H), a heavy ion, or one or more neutrons. Finally, the emission of Bremsstrahlung radiation by protons is theoretically possible, although it occurs with very low probability; at the energies used in proton therapy, this effect is negligible (Newhauser & Zhang, 2015).

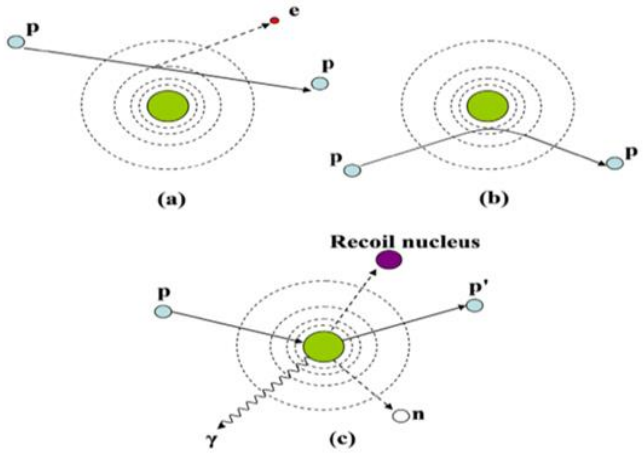


***Figure 4**. Illustrates the main mechanisms of proton interaction in matter (Newhauser & Zhang, 2015)*

Proton Energy Transfer and Dose Distribution

Protons are heavy, positively charged subatomic particles. When they pass through matter, Protons steadily lose energy as they interact with nearby atomic electrons and nuclei. Stopping power, which represents the rate of energy loss per unit path length, increases as the proton slows. This process results in the proton depositing a significant amount of energy just before coming to rest. As a result, the proton dose deposition reaches its peak at the distal end of the proton range, producing the Bragg Peak, as shown in Figure 5. A unique property of protons is that once they stop, they deposit almost negligible radiation dose past the Bragg Peak. The point along the proton path where it comes to rest and forms the Bragg Peak depends on its initial energy. In clinical proton therapy, the proton energy can be continuously adjusted as the beam enters the patient's body, ensuring that the radiation reaches the tumor while minimizing exposure to nearby healthy tissues. (Chhabra et al., 2016).

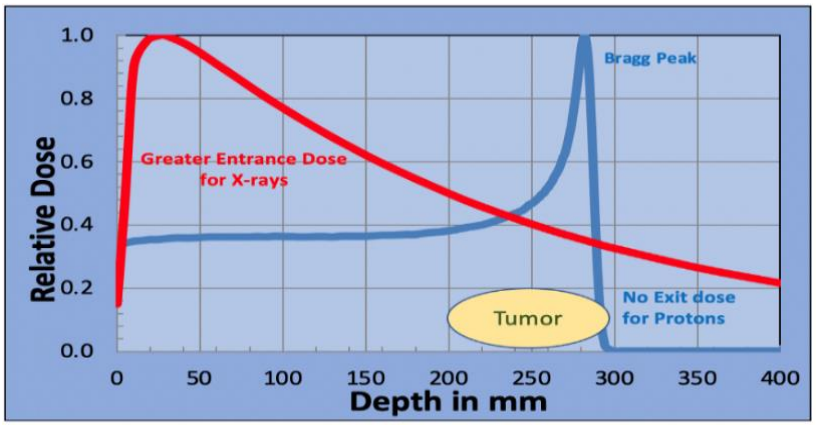


***Figure 5.** Shows the Bragg Peak of proton therapy and the buildup region of photon therapy (Maughan, 2022)*

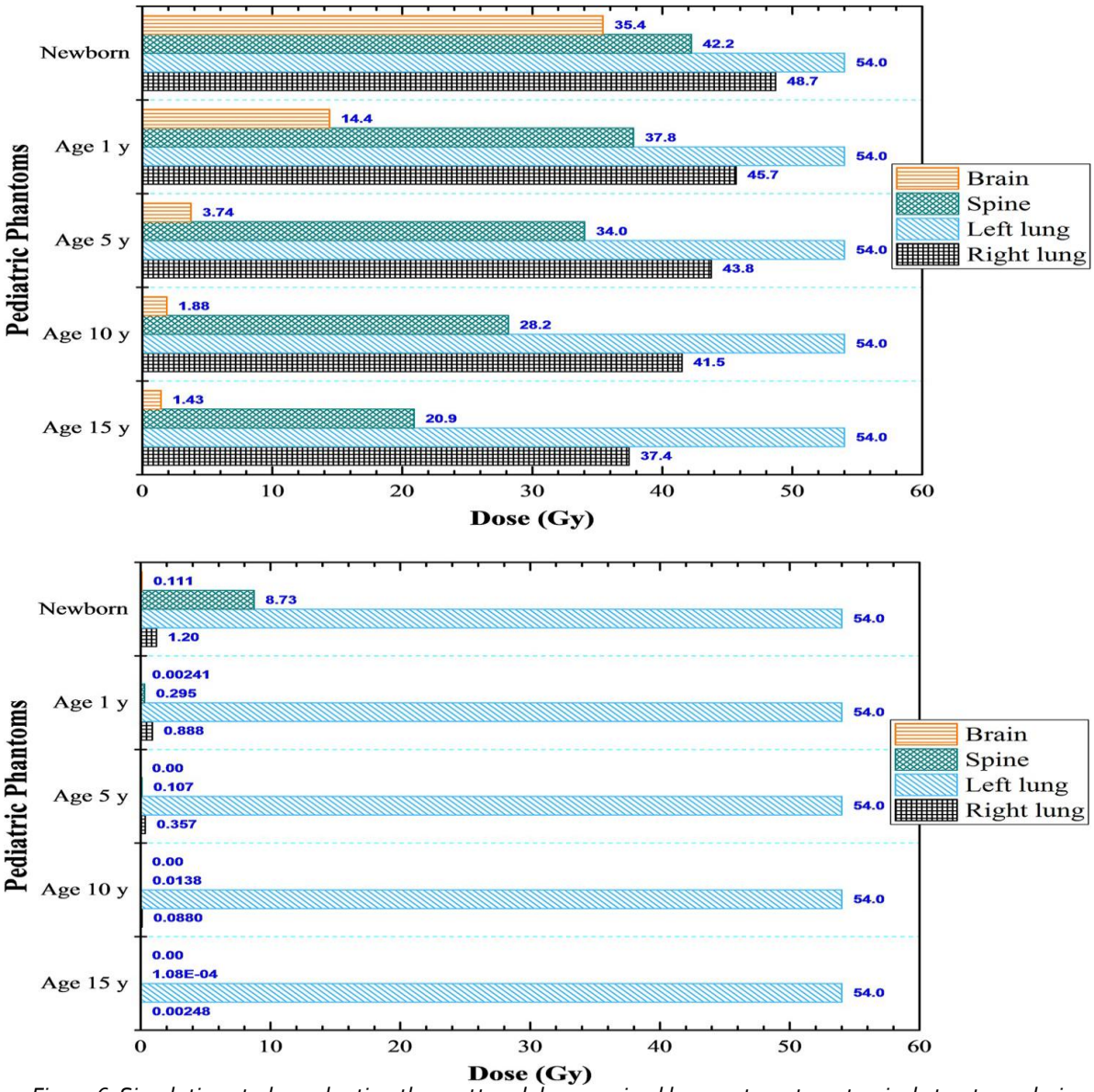


Figure 6. Simulation study evaluating the scattered dose received by non-target anatomical structures during CHART (continuous hyper-fractionated accelerated radiotherapy) for left-lung cancer, using both (6MV) linear accelerator and proton beams (Shahmohammadi Beni et al., 2021)

Stopping Power of Massive Charged Particles in a Medium

The stopping power of a medium is the average energy loss per unit distance of charged particles traveling through it. This quantity is independent of the particle mass, but depends on the square of the particle's atomic number, the particle velocity in the medium and the density of the material through which the particle passes. Many researchers have theoretically evaluated the energy loss in matter, but the first classical derivation of this was given by Hans Bethe who developed a mathematical expression for the calculation of energy loss in a medium. Later, Felix Bloch improved upon this formula to arrive at the stopping-power expression for a charged particle passing through a medium. The full form of this equation is as follows (Mohammed, 2024).

$$-\frac{dE}{dx}=\left(\frac{e^2}{4\pi\varepsilon_0}\right)^2\left(\frac{4\pi Nz^2Z\rho}{m_ec^2\beta^2A}\right)\left[\ln\left(\frac{2m_ec^2\beta^2}{I}\right)-\ln\left(1-\beta^2\right)-\beta^2\right] \quad (5)$$

As the classical radius of the electron (*re*) is expressed by: $r_e=\frac{e^2}{4\pi\varepsilon_0 m_ec^2}=2.818\cdot10^{-13}cm$

$$-\frac{dE}{\rho dx}=\left(4\pi Nr_e{}^2m_ec^2\right)\left(\frac{z^2}{\beta^2}\right)\left(\frac{Z}{A}\right)\left[\ln\left(\frac{2m_ec^2\beta^2}{I}\right)-\ln\left(1-\beta^2\right)-\beta^2\right] \quad (6)$$

Where: $\frac{dE}{dx}$ stopping power, ρ density of material, $\frac{dE}{\rho dx}$ mass stopping power, N_A Avogadro number ($6.022\cdot10^{23}mol^{-1}$), m_e electron mass, C light's velocity, m_eC^2 rest energy for the electrons (0.511 MeV), *z* atomic number of the incident particle, *Z* atomic number of material, A atomic mass of material, *I* mean excitation energy, β represents the ratio of the particle's velocity to the speed of light in a vacuum. Since $\left(4\pi Nr_e{}^2m_ec^2\right)=(0.307075\text{mol}^{-1}cm^2)$ then:

$$-\frac{dE}{\rho dx}=\left(0.307075\right)\left(\frac{z^2}{\beta^2}\right)\left(\frac{Z}{A}\right)\left[\ln\left(\frac{1.022\cdot10^6\beta^2}{I}\right)-\ln\left(1-\beta^2\right)-\beta^2\right] \quad (7)$$

DISCUSSION

This review systematically analyzed the differences in energy transfer and dose distribution between photon and proton therapies. The results confirm the hypothesis that the physical properties provided by heavy charged particles offer a considerable benefit in therapy precision compared to traditional X-ray-based modalities. The most consistent outcomes were the identification of the location of maximum energy deposition in proton therapy, which allows for maximum dose deposition at a specific depth followed by an abrupt stop, and the presence of an unavoidable exit dose in photon therapy. Collectively, these results indicate that while both modalities are essential cornerstones of cancer management, proton therapy's unique depth dose profile facilitates superior sparing of healthy tissues distal to the tumor.

Study summary Findings from the current research, when compared with prior literature, show overlap in some areas but notably diverge elsewhere. There is agreement in the literature that a fundamental physical difference between photon and proton therapies is that photons have an exit dose they cannot avoid delivering to normal tissues beyond the target volume while protons use the Bragg Peak to deposit their maximum energy at depth, after which they stop abruptly. And sources have shown that this property leads to improved sparing of these key organs, such as the heart and lungs, in patients with non-small cell cancer (Bayasgalan et al., 2021). However, differences do exist relative to clinical and biological assumptions; whereas modeling predicts improvements in secondary cancer risk for proton therapy compared with photon therapy from 2- to over 15-fold, clinical follow-up data are

margin narrow (1.5% for protons vs 1.8% for photons)(Upadhyay et al., 2022). Furthermore, some sources highlight specific clinical exceptions where photon therapy remains superior, such as in the treatment of craniopharyngioma, where photons resulted in a lower endocrine damage rate of 13.7% compared to 27.8% for protons (Pan et al., 2025). Moreover, although clinical protocols usually adopt a fixed Relative Biological Effectiveness (RBE) of 1.1 for protons, numerous studies indicate that (RBE) can vary depending on Linear Energy Transfer (LET) and the type of tissue involved (McNamara et al., 2020).

The limitations of this research on photon and proton therapies involve several challenges that complicate a definitive comparison of their efficacy. A unique gap exists between theoretical models, foreseeing 2 to 15-fold secondary malignancy risk advances with protons and clinical follow-up information displaying an opposed gap of 1.5% for photons versus protons 1.8%. Alternatively, clinical exceptions also exist in which photon therapy appears to achieve better results; for example, in craniopharyngioma patients for whom photons resulted in significantly less endocrine toxicity (13.7%) than protons (27.8%). Finally, the study is methodologically restricted to English-language comparative studies published between (2014-20125), potentially excluding relevant new or non-English data. To address the existing gaps in radiotherapy research, future investigations must transition from theoretical modeling to longitudinal clinical studies that prioritize biological accuracy and real-time technological precision.

In summary, this review highlights that proton therapy offers clear biophysical and dosimetric benefits over conventional photon therapy, mainly due to the Bragg Peak, which eliminates the exit dose. Evidence consistently shows better protection of vital organs, such as the heart and lungs, though real outcomes do not fully match theoretical predictions of a large reduction in secondary cancers. However, remaining uncertainties (e.g. variable RBE) and observed exceptions in craniopharyngioma patients necessitate more specific tailoring of radiotherapy for the individual to optimize both clinical outcome and physical/ mental morbidity outcomes.

CONCLUSION

The findings of this systematic review emphasized that the choice between photon and proton therapies is determined by fundamental differences in their energy-transfer mechanisms and resulting dose distributions. Photon therapy, while being the most commonly used approach, is limited by its indirect ionization and the presence of an exit dose that inevitably exposes healthy tissues beyond the tumor. This exposure contributes to a baseline risk of secondary malignancies and a higher dose bath to critical organs in complex cases like lung cancer. Conversely, proton therapy offers a significant physical advantage through the Bragg Peak, allowing maximum energy deposition at the target depth and nearly zero beyond that point. This precision makes proton therapy a superior choice for patients in the pediatric age group and those with tumors in proximity to vital tissues, such as the heart and spine, significantly reducing the potential for long-term toxicities. However, clinical data

also indicates that proton therapy is not a universal solution; for example, photon therapy remains more effective in sparing the endocrine system in patients with craniopharyngioma. In summary, while proton therapy demonstrates clear dosimetric superiority in many clinical scenarios, treatment selection must be highly individualized. Future advancements in radiotherapy should focus on resolving current uncertainties regarding the Relative Biological Effectiveness (RBE) and secondary neutron exposure to further optimize patient outcomes. Ultimately, integrating physical precision with specific clinical evidence will ensure the highest quality of life and survival for cancer patients.

Authors Contribution

- ✓ Musa Khan Khpalwak designed the study and oversaw its implementation.
- ✓ Ehsanullah Saqib conducted the investigation and performed the data analysis.
- ✓ Noor Mohammad Azizi wrote the manuscript with input from all authors.
- ✓ Each author carefully evaluated and approved the final manuscript.

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Conflict of Interest Statement

The authors report no competing interests related to this review.

Data Availability Statement

Relevant data for this study are available from the corresponding author upon request.

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