Proton versus Photon Radiotherapy Treatment Planning – A Comparative Analysis

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Abstract

Radiotherapy is a salient treatment option that allows clinicians to treat cancerous tissue. This study investigates the efficacy of proton versus photon treatment planning utilising clinical data available from open repositories. MatRad was used to simulate 2 proton therapy and 3 photon therapy treatment plans to deliver a dose of 74 Gy over 37 fractions to the prostate. Clinical objectives and radiobiological parameters were analysed and implemented to ensure patient treatment plans adhere to clinical standards. The results show that proton therapy demonstrated superior dose conformity, specifically when utilising an opposed 45/315 degree beam angle due to the geometry of the beams and proximity to critical structures. However, limitations exist that may affect the reliability of the results including sub-optimal optimisation process, MatRad framework limitations, limited sample size, and limited data diversity. Future studies should consider implementing automated systems to improve contouring accuracy, utilising advanced clinical software to produce reliable treatment plans, investigating mathematical optimisation algorithms, and applying an opposed 45/315 degree beam angle IMPT treatment plan to increasingly diverse prostate patient data sets.

Keywords: radiotherapy, prostate, proton therapy, photon therapy, dose conformity, prostate cancer

1. Introduction

Cancer contributes to a significant number of fatalities per year and is prominent global issue [1]. Fortunately, various treatment options such as radiotherapy are used to treat cancerous tissue and improve the survival rate of patients afflicted with the disease. Radiotherapy is commonly used to destroy cancer cells by distributing high-energy radiation in the range of 4 to 15 MV for photons (X-rays) and 4 to 20 MeV for electrons [2] and has become a vital component of modern cancer treatment, either as a stand-alone treatment method or in combination with other treatment modalities.

Photon therapy is a conventional radiotherapy technique that employs X-rays generated by linear accelerators to deliver a controlled dose of radiation to the tumour site [3]. A state-of-the-art approach for administering high radiation doses using photon beams is Intensity-Modulated Radiation Therapy (IMRT). IMRT achieves precise delivery of radiation that conforms to the tumour's shape by intersecting multiple beams with tailored intensities. This treatment modality relies on the X-ray's ability to penetrate tissue and deposit energy. The dose is precisely modulated utilising varying beam angles to maximize damage to cancer cells while attempting to minimise damage to adjacent, healthy tissue [4].

Proton therapy relies on cyclotrons or synchrotrons to direct and accelerate protons toward cancerous tissue [5]. However, proton radiotherapy differs from conventional radiation therapy by delivering increasingly precise, targeted radiation to cancerous tissue by utilising the unique physical properties of protons. This characteristic is known as the Bragg Peak effect and is a fundamental feature of proton therapy that allows for highly localised radiation delivery [6]. By controlling the depth of the Bragg peak, clinicians can customize treatment plans to match the size, shape, and depth of the target volume while minimizing damage to surrounding organs at risk.

1.1. Aim

This study aims to conduct a comparative evaluation of photon therapy and proton therapy modalities by developing various treatment plans for the prostate. Five theoretical

treatment plans were simulated utilising the MatRad treatment planning software to deliver a dose of 74 Gy over 37 fractions using a parallel opposed Intensity-Modulated Proton Therapy (IMPT) treatment plan, an opposed IMPT treatment plan, a 5-field IMRT treatment plan, a 7-field IMRT treatment plan, and a 9-field IMRT treatment plan. Dosimetric and radiobiological parameters were analysed to determine which treatment option offers superior efficacy by considering the dose delivered to the prostate, bladder, rectum, and the left & right femoral heads.

2. Materials & Methods

All simulations were generated and performed in MatRad v2.10.1 running MATLAB v9.14. All treatment plans were simulated using clinical data available from open repositories. Clinical objectives outlined by eviQ were used as constraints in each treatment plan, ensuring each treatment plan adheres to ideal clinical standards. Figure 1 visualises a section of the MatRad interface used to optimise and implement the parameters used for each treatment plan.

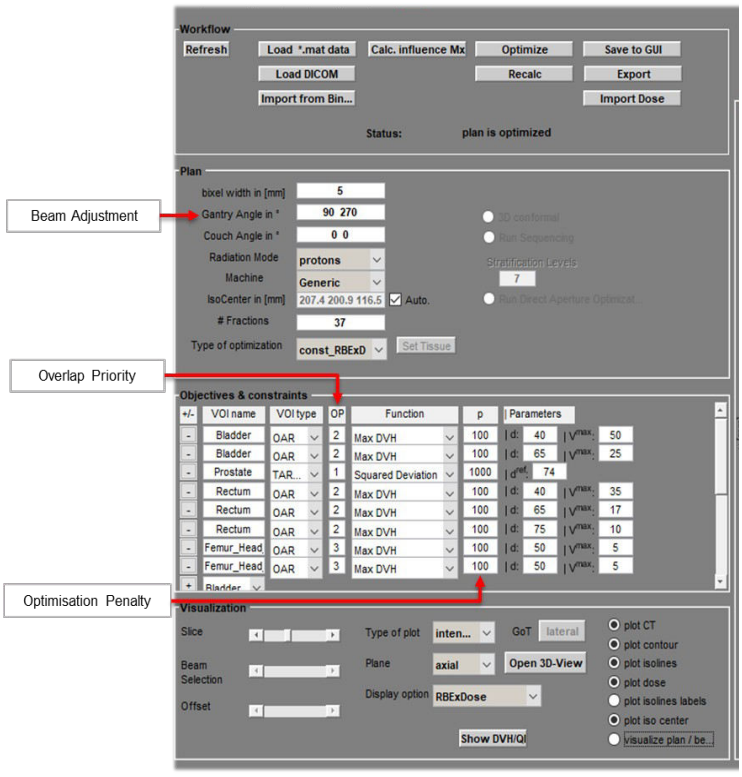


Figure 1: MatRad Interface Used to Implement Parameters Responsible for Proton and Photon Treatment Plan Optimisation Process.

Using existing CT scans of patient prostate data, the patient's external contour was added to the existing prostate structure set using Computational Environment for Radiological Research (CERR). The contoured data set was then used as the base template for the implementation of each treatment plan in the MatRad framework. MatRad's function parameter was set to 'max DVH' for the bladder, rectum, and femoral heads. Clinical objectives for the bladder were set to V40 Gy < 50% & V65 Gy < 25%. Clinical objectives for the rectum were set to V40 Gy < 35%, V65 Gy < 17% & V75 Gy < 10%. Clinical objectives for the left and right femoral heads were set to V50 Gy < 5%. The optimisation penalty for the bladder, rectum and femoral heads was set to 100. The overlap priority for the rectum and bladder was set to 2. The overlap priority for the femoral heads was set to 3. The function parameter for the prostate was set to 'squared deviation' and the dose was set to 74 Gy. The optimisation penalty for the prostate was set to 1000 and the overlap priority was set to 1. A proton therapy treatment plan was then produced using a 90/270 degree parallel opposed beam arrangement over 37 fractions. This process was repeated, producing an additional proton therapy treatment plan, using a 45/315 degree opposed beam arrangement. The clinical objective of V40 Gy < 35% for the rectum was then changed to V35 Gy <35% and 3 photon therapy treatment plans using a 5 field (0º, 72º, 144º, 216º, 288º), 7 field (52º, 102º, 154º, 205º, 257º, 308º, 360º), and 9 field (40º, 80º, 120º, 160º, 200º, 240º, 280º, 320º, 360º) beam arrangement were produced. The Dose Volume Histogram (DVH) and quantitative values for the dose distribution produced for each treatment plan were analysed to ensure ideal clinical objectives outlined by eviQ were achieved and that the maximum dose delivered to the prostate did not exceed 107% of the prescribed dose.

3. Results

3.1 Experimental Uncertainties

As all treatment plans produced are theoretical simulations, the results generated by MatRad show no discrepancies in quantitative values. Each simulation will repeatedly produce the same value. However, uncertainty is considered from all data extrapolated from the Dose Volume Histograms using the convention of maximum error.

3.2. Data Extrapolation

Table 1 quantifies the dose distribution within the prostate, rectum, bladder, and femoral heads, providing

insight into the radiation delivery characteristics of each treatment modality. Each treatment plan meets ideal clinical constraints outlined by eviQ. However, notable discrepancies can be observed in the dose delivered to the rectum and bladder, with proton therapy showing up to a (24.2 ± 0.5) % reduction in rectal dose. Additionally, the difference in the dose delivered to each volume of interest (VOI) seems to diminish as the number of beams increases when employing various photon therapy treatment options.

Figure 2 visualises the dose distribution within the target volume for each proton and photon IMRT treatment plan. Each treatment option appears to exhibit a high degree of congruence in their respective dose distributions.

Table 1: Dose Received by Prostate, Rectum, Bladder, and Femoral Heads for Parallel Opposed IMPT, Opposed IMPT, 5 Field IMRT, 7 Field IMRT, and 9 Field IMRT Treatment Plans.

Prostate (PTV) 74 Gy (2 Gy per Fraction)	**Parallel Opposed IMPT Proton**	**Opposed IMPT Proton**	**5 Field IMRT Photon**	**7 Field IMRT Photon**	**9 Field IMRT Photon**
$D_{98\%}$ (Gy)	1.94 Gy	1.91 Gy	1.94 Gy	1.95 Gy	1.96 Gy
$D_{2\%}$ (Gy)	2.05 Gy	2.04 Gy	2.02 Gy	2.02 Gy	2.02 Gy
Rectum					
V_{40Gy} <35% (1.08 Gy / Fx)	(15.7 ± 0.5) %	(9.1 ± 0.5) %	(33.3 ± 0.5) %	(30.0 ± 0.5) %	(29.6 ± 0.5) %
V_{65Gy} <17% (1.76 Gy / Fx)	(1.5 ± 0.5) %	(1.3 ± 0.5) %	(6.1 ± 0.5) %	(3.2 ± 0.5) %	(3.1 ± 0.5) %
V_{75Gy} <10% (2.03 Gy / Fx)	(0.0 ± 0.5) %	(0.2 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %
Bladder					
V_{40Gy} <50% (1.08 Gy / Fx)	(5.5 ± 0.5) %	(7.5 ± 0.5) %	(12.0 ± 0.5) %	(12.9 ± 0.5) %	(13.2 ± 0.5) %
V_{65Gy} <25% (1.76 Gy / Fx)	(1.5 ± 0.5) %	(1.9 ± 0.5) %	(4.1 ± 0.5) %	(4.3 ± 0.5) %	(4.3 ± 0.5) %
Femoral Heads					
L V_{50Gy} <5% (1.35 Gy / Fx)	(0.1 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %
R V_{50Gy} <5% (1.35 Gy / Fx)	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %	(0.0 ± 0.5) %

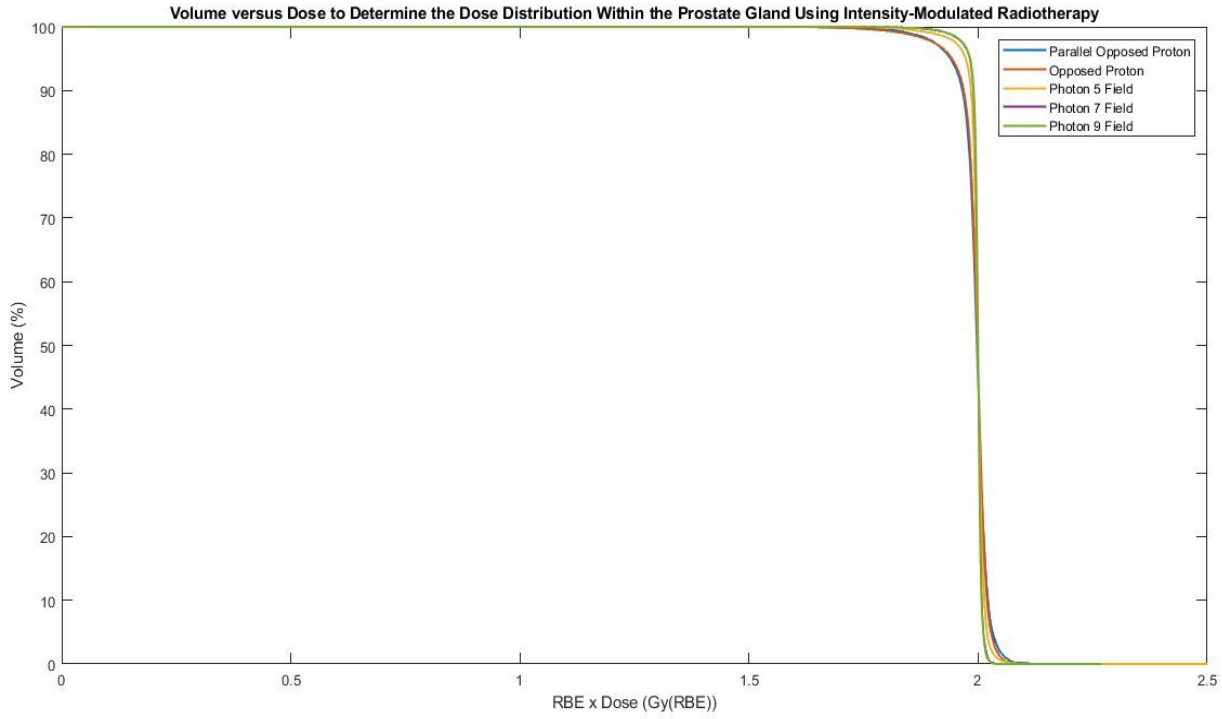


Figure 2: Dose Delivered to Target Volume for Parallel Opposed Proton, Opposed Proton, Photon 5 Field, Photon 7 Field, and Photon 9 Field Radiotherapy Treatment Plans.

Figure 3 shows that the radiation delivered to the bladder and rectum is increased when using photon 5 field, photon 7 field, and photon 9 field treatment options and that both opposed and parallel opposed proton therapy treatment modalities deliver a lower incidence of bladder and rectal damage. However, employing a 45/315 degree beam configuration results in significantly reduced rectal damage compared to all other tested beam arrangements.

The impact on the femoral heads differs from the rectum and bladder. Figure 4 shows that utilising a parallel opposed proton therapy beam arrangement increases the dose received by the left and right femur. However, an opposed 45/315 degree beam arrangement remains the optimal option to reduce the dose delivered to the femoral heads, as it seems to deliver minimal radiation to the volume of interest.

3.3 Quantitative Analysis

Quantitative measures such as mean dose and dose uniformity were examined to validate visual observations. The results suggest that the dose distributions for proton therapy and photon therapy are comparable, with no notable discrepancies observed in the results. However, a slight improvement in dose uniformity seems to occur as the number of beams increases.

To quantify dose uniformity, the homogeneity index was calculated using:

$$HI = \frac{D_5}{D_{95}}$$

Where:

D_5 = Dose received by 5% of the target volume.

D_{95} = Dose received by 95% of the target volume.

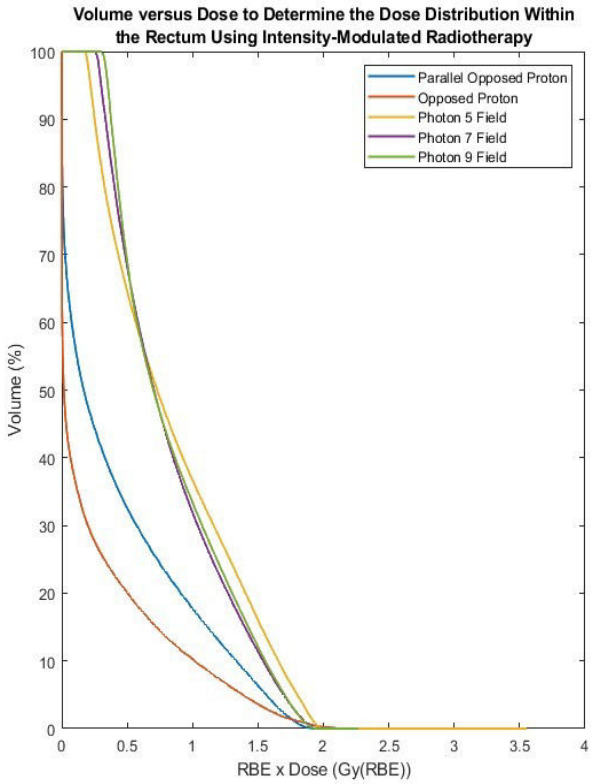
Example calculations using data acquired from opposed IMPT proton therapy are shown below.

$$HI = \frac{D_5}{D_{95}}$$

$$HI = \frac{2.02}{1.94}$$

$$HI = 1.04$$

The homogeneity index and mean dose values for the target volume for each treatment plan are documented in Table 2.



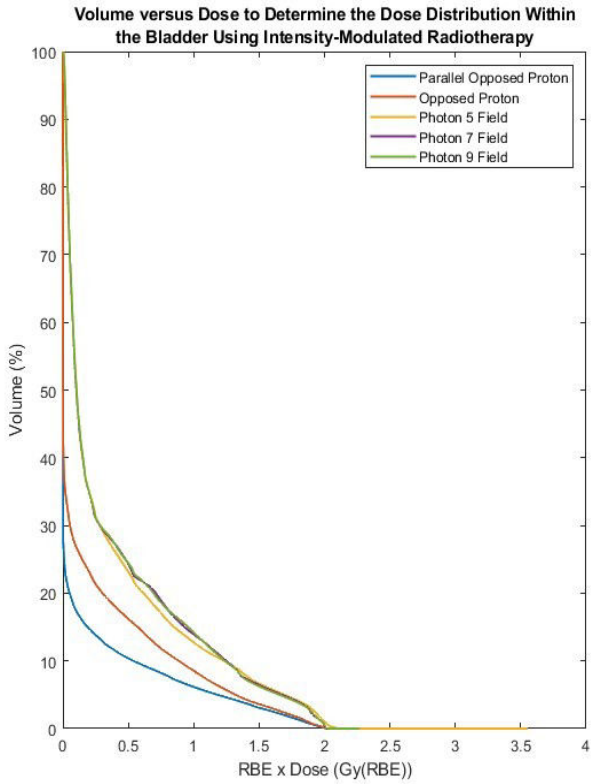
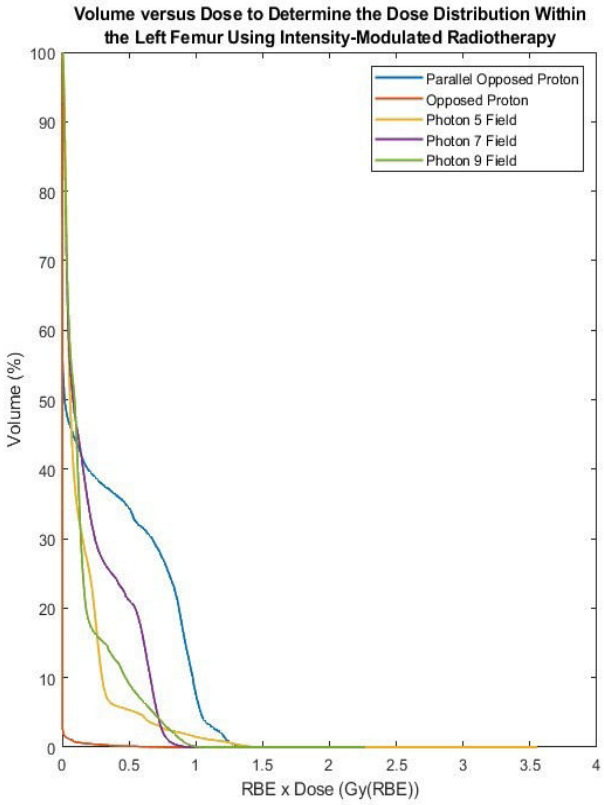


Figure 3: Dose Delivered to Rectum & Bladder for Parallel Opposed Proton, Opposed Proton, Photon 5 Field, Photon 7 Field, and Photon 9 Field Radiotherapy Treatment Plans.



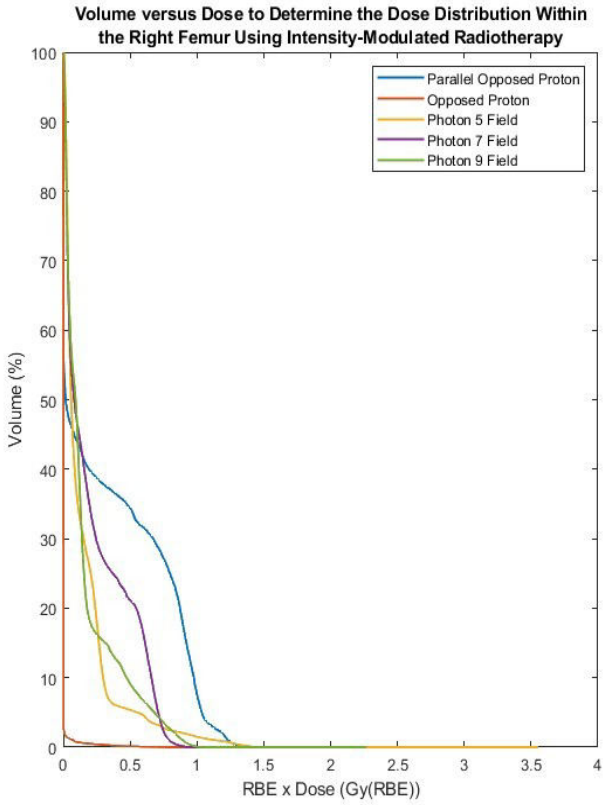


Figure 4: Dose Delivered to Left and Right Femur for Parallel Opposed Proton, Opposed Proton, Photon 5 Field, Photon 7 Field, and Photon 9 Field Radiotherapy Treatment Plans

Table 2: Mean Dose and Homogeneity Index Calculated for Parallel Opposed Proton, Opposed Proton, Photon 5 Field, Photon 7 Field, and Photon 9 Field Treatment Plans.

	Parallel Opposed IMRT Proton	Opposed IMRT Proton	5 Field IMRT Photon	7 Field IMRT Photon	9 Field IMRT Photon
Mean Dose	1.99 Gy	1.99 Gy	2.00 Gy	2.00 Gy	2.00 Gy
Homogeneity Index	1.04	1.04	1.03	1.02	1.02

4. Discussion

This study utilised MatRad to develop five treatment plans for a single prostate patient. Each treatment plan meets ideal clinical objectives documented by eviQ. This was accomplished by implementing various radiobiological parameters and optimising the beam intensity and orientation of two proton therapy and three photon therapy treatment plans. Results suggest that both proton and photon treatment modalities exhibit similar target dose distributions. Although, notable discrepancies can be observed in the dose conformity between the two
treatment methods, with proton therapy delivering markedly less radiation to the rectum and bladder.

However, the reliability of the results may be influenced by several factors.

Proton therapy seems to administer an increasingly conformal treatment, depicted by the 24.2% reduction in rectal dose when administering an opposed 45/315 degree beam arrangement. The notable reduction in rectal dose may be influenced by the unique beam arrangement that bypasses the left and right femoral heads as well as a large proportion of the rectum. The precision of both parallel opposed and opposed IMPT treatment options offer significant advantages in dose conformity relative to each photon therapy treatment plan produced, potentially due to the Bragg Peak effect [6]. This makes proton therapy an effective treatment option for tumours located in close proximity to critical structures such as optical nerves and potentially reduces long-term side effects [7]. However, proton therapy is associated with higher treatment costs and limited availability and must be considered when developing and administering patient-specific treatment plans [5].

Photon therapy remains a well-established and effective treatment modality [8]. However, the treatment method seems to hold the potential to deliver increased radiation to organs at risk, possibly due to the exit dose associated with the delivery method [9]. A slight improvement in dose uniformity seems to occur as the number of beams increases, suggesting that augmenting the beam count may contribute to an increasingly homogeneous distribution of radiation within the target volume. While this increase in dose uniformity was evident, it is essential to emphasize that the magnitude of improvement was relatively small and may not have substantial clinical implications. The dose uniformity in each proton therapy treatment plan may be influenced by the parameters utilised in the development of each treatment module. Increasing the prescribed dose may affect dose uniformity for protons. However, due to time constraints and limitations of the MatRad framework, the optimisation of various parameters remains incomplete. Additionally, the dose delivered to the target volume seems to produce diminishing returns when increasing the beam count. Future studies should aim to observe the impact that each incremental beam count has on the dose distributed to the prostate, bladder, rectum, and the left & right femoral heads.

Although the results strongly suggest proton therapy offers increased precision and tumour control, several additional factors may influence the accuracy and reliability of the results. The limited sample size of 5 treatment plans restricts the ability to perform various quantitative measures and statistical analyses. Increasing the sample size and subjecting the collected data to statistical analysis may

produce increasingly reliable and statistically significant results.

Additional errors may be produced in the comparison between proton and photon treatment modalities due to the possibility of an unfair evaluation. It is essential to consider that all proton and photon treatment plans produced may not be optimized to their full potential, due to the limitations of the MatRad framework utilised during the investigation [10]. Implementing an automated system to explore various radiobiological parameters and utilising advanced software such as Raystation to produce treatment plans has the potential to enhance optimization, leading to increasingly robust results. Future studies should additionally consider the relative biological effectiveness of protons versus photons at varying dose ranges to determine optimal treatment efficiency for disparate clinical cases.

MatRad employs a default algorithm for optimising treatment plans [10]. Although this algorithm is suitable for research purposes, it's important to note that the choice of the mathematical optimisation algorithm that is implemented can influence the quality of the treatment plans. Exploring alternative optimisation algorithms using increasingly advanced optimisation tools or software may improve the reliability of the results.

Manually contouring CT scans may produce varying outcomes. Future studies should reduce potential contouring variability by implementing quality control checks or using advanced software tools that offer automated contouring options.

Developing and comparing treatment plans on single patient data may restrict the accuracy and reliability of the results. Extrapolating data from an increasingly diverse patient data set that considers various cancer types, tumour locations, and tumour sizes may provide an increasingly comprehensive understanding of the relative effectiveness of both treatment modalities across several clinical scenarios.

5. Conclusion

This study successfully produced two proton therapy and 3 photon therapy treatment plans that achieve ideal clinical constraints. Both treatment modalities distribute similar target dose distributions. However, various factors may have influenced the reliability of the results such as the limitations of the MatRad framework, a limited sample size, manually contouring CT scans, and sub-optimal optimisation techniques. Results suggest that proton therapy offers an increasingly conformal delivery method and that employing the use of an opposed 45/315 degree beam angle IMPT treatment plan may be the optimal choice when treating prostate cancer due to the geometry of the incident beams relative to the critical structures surrounding the prostate. However, the choice between these modalities relies on clinical considerations including tumour size and shape, the spatial relationship to critical structures, and cost and availability constraints. Future studies should consider increasingly reliable optimisation processes, automated contouring options, increasing sample size and diversity, investigating the mathematical underpinnings of the MatRad framework, and applying an opposed 45/315 degree beam angle IMPT treatment plan to various diverse prostate patient data sets. By reducing radiation exposure on healthy tissue, we can enhance the effectiveness of treatment options while potentially minimising adverse side effects, improving clinical outcomes and potentially revolutionising the way we treat cancer.

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