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Research Article

A Treatment Planning Comparison between Intensity Modulated Proton Therapy (IMPT) and Volumetric Modulated Arc Therapy (VMAT) for prostate cancer

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ABSTRACT

Introduction: We made a comparison between IMPT plans and VMAT plans for ten prostate cancer patients with the analysis of dosimetric quantities and EUD for both target volume and OARs. **Methods:** Ten patients planned for VMAT were retrospectively replanned with scanned proton beams. Target and OARs were kept as originally delineated in photon plans with the assumption that the change in dose distribution is acceptable. The prescribed dose to the PTV is 74 Gy using an RBE of 1.1. The optimized VMAT plan of each case was normalized using the PTV coverage value obtained from the optimized IMPT plan. For the PTV and OARs, the dosimetric quantities were analyzed. Moreover, EUD with the exponential parameter α with a 95% confidence level was calculated for both the PTV and OARs. **Results:** For the PTV, all the averaged dose metrics, including the mean dose, the median dose and the maximum dose, the HI and the EUD, in the IMPT plans were statistically ($p \leq 0.05$) better than those in the VMAT plans. The dose to the PTV from IMPT plans ranged from 69.1±4.7 to 79.0±1.1 Gy (RBE), while that from VMAT plans ranged from 68.0 ±2.8 to 81.6 ±1.3 Gy (RBE). The mean dose of 2.6 Gy (RBE) to the body from the IMPT plan was significantly ($p=0.007$) lower than the mean dose of 5.8 Gy (RBE) from the VMAT plans. For all OARs except for the rectum, in the low-to-medium dose region, the volumes receiving low doses in IMPT plans were statistically ($p \leq 0.05$) lower than those in VMAT plans. The IMPT plans show statistically ($p \leq 0.05$) superior dose sparing of the rectum and bladder in comparison to the VMAT plans at the Dmax, Dmean, and V30Gy indices and at all dosimetric indices. **Conclusions:** The results show that the IMPT plans were statistically superior to the VMAT plans for both the PTV and OARs. IMPT plans produced a more homogeneous dose in the PTV. For OARs, the volumes receiving the low doses were statistically lower in IMPT plans than in VMAT plans.

Key words: Intensity Modulated Proton Therapy, Prostate Cancer, Treatment Planning, Volumetric-Modulated Arc Therapy

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INTRODUCTION

Proton therapy has an advantage over photon therapy because of its physical properties. Steep dose gradients outside of the Bragg peak are utilized for increasing the dose to tumors while minimizing irradiation to adjacent normal tissues. In recent years, the number of prostate cancer patients treated with protons has increased [1].

To date, there have been many papers comparing the dose distribution between proton therapy [2–6] and photon therapy, but much controversy still remains [7,8]. These studies mainly compared dose-volume metrics and rarely considered the EUD (equivalent uniform dose) when ranking the plans.

This research aimed to investigate the advantages of the IMPT plan compared to the VMAT plan for prostate cancer. In addition to physical dose quantities as usual, EUD was also calculated to rank the plan according to the criteria of ICRU (International Commission Radiation Units and Measurement) Report 78 and 83. This study did not consider the robustness of the IMPT plans due to the assumption that the change in dose distribution is acceptable [7–13].

Furthermore, the comparison between proton therapy and photon therapy is a necessary preparation for the application of proton therapy in cancer treatment in Vietnam in a few years.

METHODS

Patients and treatment planning

In this retrospective study, ten prostate cancer cases were included. All patients were recruited from TCIA (The Cancer Imaging Archive) [14]. The stage of the cancer patient was not reported in the data. Target and organs at risk volume were kept as originally delineated in photon plans. The aim of this solution was

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to compare the resulting treatment plans. The organs at risk (OARs) included the rectum, bladder, and femur heads.

A total of 74 Gy (RBE) (Relative Biologic Effectiveness) was prescribed to the PTV (Planning Target Volume) with a daily fraction of 2 Gy. The value of 74 Gy was referenced from ICRU 78[15], and the value of 2 Gy is the conventional daily fraction. The RBE of 1.10 recommended by ICRU 78 was used. The dose objectives for the target are presented in Table 1.

The dose constraints for the rectum and bladder were set out by the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) and for femur heads established by the Radiation Therapy Oncology Group (RTOG) (Table 2).

The quantity V_D is the largest volume of a specified VOI (Volume of Interest) that receives a dose more than or equal to the RBE-weighted dose, D_{RBE}. The quantity D_V is the least dose received by a volume, V, of a specified VOI. D_{max} is the maximum dose. In the study, the relative doses were normalized to the prescribed dose. The dose presented in the study is the RBE-weighted dose.

IMPT planning

The IMPT plans were replanned using LAP (an abbreviation of Laser Accelerated Proton Beam), an extension for the Computational Environment for Radiotherapy Research (CERR)[21,22]. The spot scanning technique was used with discrete energy in the 70-250 MeV range. The range shifter is the last element before the patient with a step of 0.1 cm and could be up to 5 cm. The dose distribution was calculated in a dose grid of 0.977x0.977x5 mm^3 with the pencil beam algorithm accounting for the effects of heterogeneity.

Normally, the beam angles for prostate cancer are 90 degrees and 270 degrees. However, in some cases, the target volume PTV is close to the rectum and the bladder, so these angles are not still suitable. In those cases, the beam angles are changed around these values to minimize the dose delivered to the bladder and rectum as well as satisfy the dose constraints recommended by the QUANTEC[18,19]. The beam angles were chosen individually for each case to protect all the OARs according to the recommendation of the QUANTEC study and RTOG[20]. In this study, two plans consisted of gantry angles of 130 degrees and 230 degrees. The two plans consisted of gantry angles of 80 degrees and 280 degrees. Three plans consisted of gantry angles of 100 degrees and 260 degrees. The remaining three plans consisted of gantry angles of 90 degrees and 270 degrees.

VMAT planning

The VMAT plans were created on the Pinnacle version 16.0.2 treatment planning system with a 3x3x3 mm^3 dose grid using an automated inverse treatment planning algorithm. The dose calculation is based on the collapsed cone convolution superposition algorithm accounting for the heterogeneity of the tissues[23,24]. At the beginning of the optimization process, the AutoPlanning module iteratively performs several optimization cycles to achieve the dosimetric objectives. The dosimetric objectives included the PTV dose objective and OAR dose objectives, which were defined based on the prescription dose for the PTV and the dose constraints for OARs. In the optimization process, the optimizer automatically generates various support structures around the PTV or OAR or overlaps between the PTV and OAR to increase the dose coverage of the PTV and to spare the OARs as much as possible.

For 9 patients, two incomplete arcs were used, with the first arc from 182 degrees to 178 degrees in a clockwise direction and the second arc from 178 degrees to 182 degrees in an anticlockwise direction. For 1 patient, one incomplete arc from 178 degrees to 182 degrees in an anticlockwise direction was applied. Six MV X-rays with a beam spacing of 2 degrees were used for both plans. The optimized VMAT plan of each case was then normalized using the PTV coverage value obtained from the optimized IMPT plan.

Treatment plan evaluation

For PTV, the dosimetric parameters, including the minimum dose Dmin, the maximum dose Dmax, the mean dose Dmean, the median dose Dmedian, conformity index CI, homogeneity index HI and equivalent uniform dose (EUD, based on Niemierko's phenomenological model) recommended and encouraged by ICRU 78 and ICRU 83, were analyzed.

HI[17], CI[16] and EUD[25] are defined in Equations 1, 2 and 3 as follows:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (1)$$

$$CI = \frac{PTV}{TV} \quad (2)$$

TV should be V98%, as suggested by ICRU 83[15].

$$EUD = \left(\sum_t v_i d_i^a\right)^{\frac{1}{a}} = \left(\frac{1}{N}\sum_{i=1}^{n} d_i^a\right)^{\frac{1}{a}} \quad (3)$$

The parameter α is typically positive for healthy organs and negative for target volumes. According to

Table 1: Dose objectives for PTV used for IMPT and VMAT planning

Objectives
V100% > 90%
Inside PTV, V110% ≤ 10%
Dmax of the PTV is not more than 110% of the prescribed dose
More than 110% of the prescribed dose is not allowed outside the PTV
$CI = \frac{PTV}{TV}$ [16] with TV=V98% [17], is infinitely close to 1
$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}}$ [17], is infinitely close to 1

Table 2: Dose constraints for OARs used for IMPT and VMAT planning

Structures	Volume (%)	Dose (Gy)	Max dose (Gy)	Reference
Rectum	<60%	30		QUANTEC study [18]
	<50%	50		
	<35%	60		
	<25%	65		
	<20%	70		
	<15%	75		
Bladder	<60%	50		QUANTEC study [19]
	<50%	65		
	<35%	70		
	<25%	75		
One femur head	<25%	45	50	RTOG 0822 [20]
	<40%	40	50	RTOG 0822 [20]

Niemierko, the EUD was calculated in the uncertainty margins of the 95% confidence level with $\alpha = -10^{+3}_{-5}$ for target volume, $\alpha = 5^{+3}_{-2}$ for the rectum and $\alpha = 7^{+5}_{-3}$ for the bladder.

For the rectum and bladder, the mean dose, the EUD (defined in equation 3), and the relative volumes that received the dose limits of 30 Gy, 50 Gy, 60 Gy, 65 Gy, 70 Gy, and 75 Gy (for rectum) (QUANTEC [18]), 50 Gy, 65 Gy, 70 Gy, and 75 Gy (for bladder) (QUANTEC [19]) were compared. For the femur head, the maximum dose and the relative volume receiving dose limits of doses of 40 Gy and 45 Gy were analyzed.

The Wilcoxon matched-pairs signed-rank test was used to determine any significant differences ($p \leq 0.05$) between the planned PTV doses and the planned OAR doses for the two techniques.

In addition, Pearson's correlation coefficient r was calculated to measure the strength of linear dependence between the two same dosimetric quantities of the two techniques for both the PTV and OARs. The value of r is presented in Table 3.

RESULTS

PTV

For VMAT plans, at least 95% of the PTV receiving the prescription dose from proton plans was used for dose-volume normalization in the VMAT plans for the corresponding cases.

From Table 4, most of the averaged dosimetric quantities of PTV of IMPT plans, except for the minimum dose and the CI, were statistically ($p \leq 0.05$) better than those of VMAT plans. In the IMPT plans, the minimum dose, the maximum dose, the mean dose and the median dose are closer to the prescribed dose than those in the VMAT plans. As a consequence, the HI value is lower in the IMPT plans, indicating that the dose in the PTV in IMPT plans is more homogeneous than that in the VMAT plans. The same level of isodose 95% coverage, CI equal to 0.93, was achieved in both IMPT plans and VMAT plans.

In addition, the calculated Pearson's correlation coefficients (**Figure 1**) showed that the linear relationship between the Dmean, Dmedian and HI of the PTV from the IMPT plans and those from the VMAT plans was moderate. It also showed a weak linear relationship between Dmin from IMPT plans and that from

Table 3: The value of Pearson's correlation r

r	Correlation
$0 < \|r\| \leq 1$	Strong
$0.5 < \|r\| \leq 0.75$	Moderate
$0.25 < \|r\| \leq 0.5$	Weak
$0 < \|r\| \leq 0.25$	Very weak

Table 4: The averaged dosimetric quantities to the PTV for the IMPT plans and VMAT plans for ten prostate cancer patients.

	VMAT Mean ±SD Gy(RBE)	IMPT Mean ±SD Gy(RBE)	p value (≤0.05)
Minimum dose (Gy)	68.0 ±2.8	69.1±4.7	0.575
Maximum dose (Gy)	81.6 ±1.3	79.0±1.1	0.007
Mean dose (Gy)	77.2 ±1.0	76.2±1.1	0.012
Median dose (Gy)	77.3 ±1.0	76.3±1.1	0.018
V100%	97.6%	97.6%	1
CI	0.93±0.1	0.93±0.1	1
HI	0.07±0.02	0.04±0.01	0.005

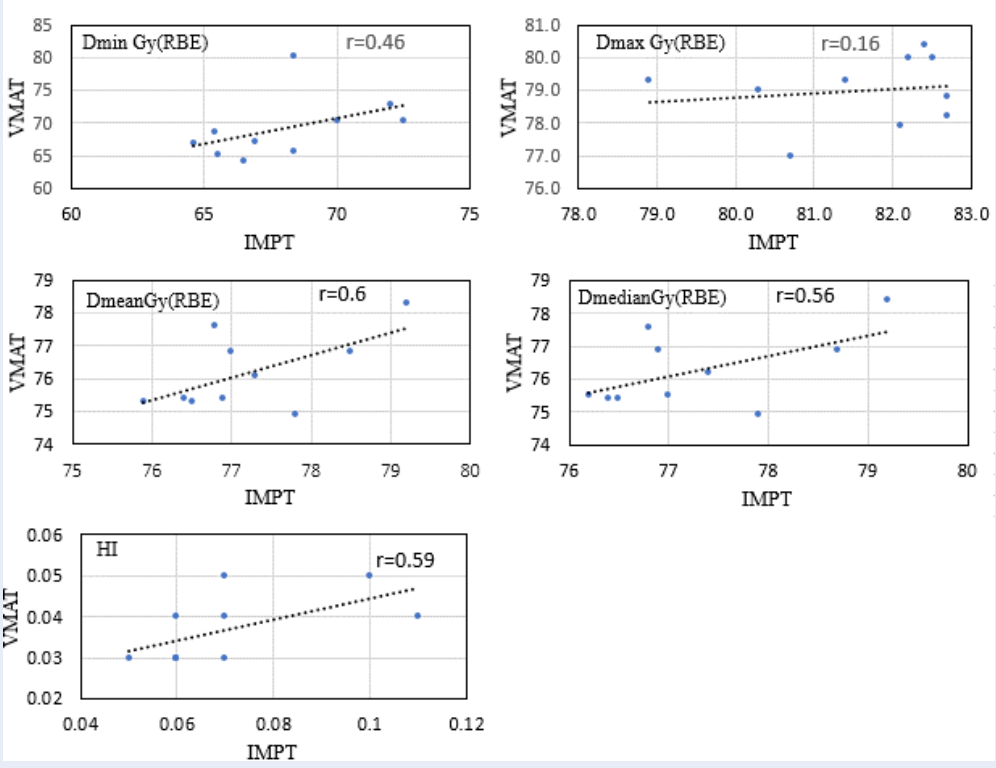

Figure 1: The Pearson's correlation coefficient between the two same dosimetric quantities of PTV from two techniques IMPT and VMAT.

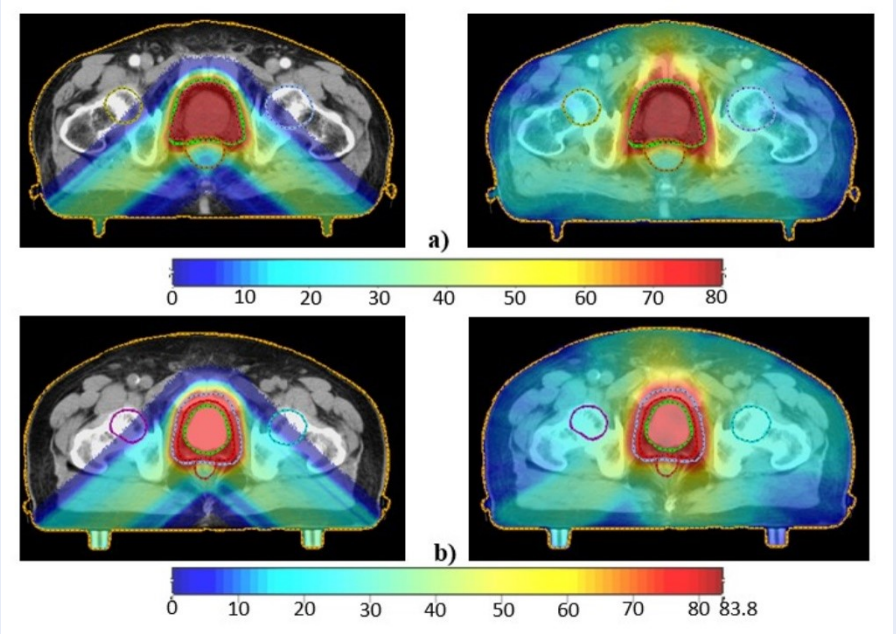

Figure 2: **The dose distributions in the transverse planes in the IMPT plans (left) and VMAT plans (right) of patient 1 (a) and patient 2 (b). The unit is Gy (RBE).**

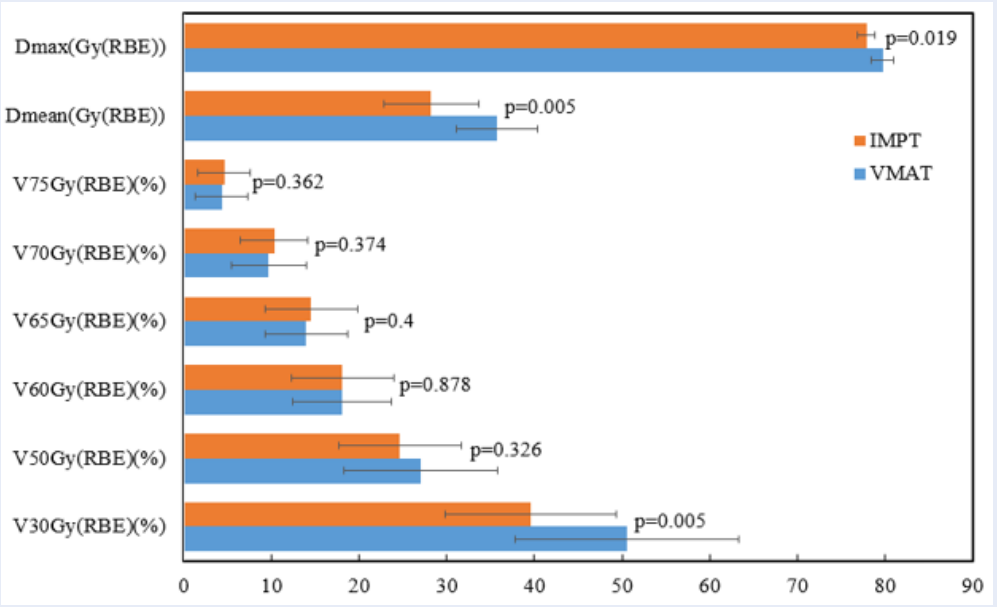

Figure 3: **Averaged relative volumes of rectum at dose constrains (Table 1) for the IMPT plans and VMAT plans.**

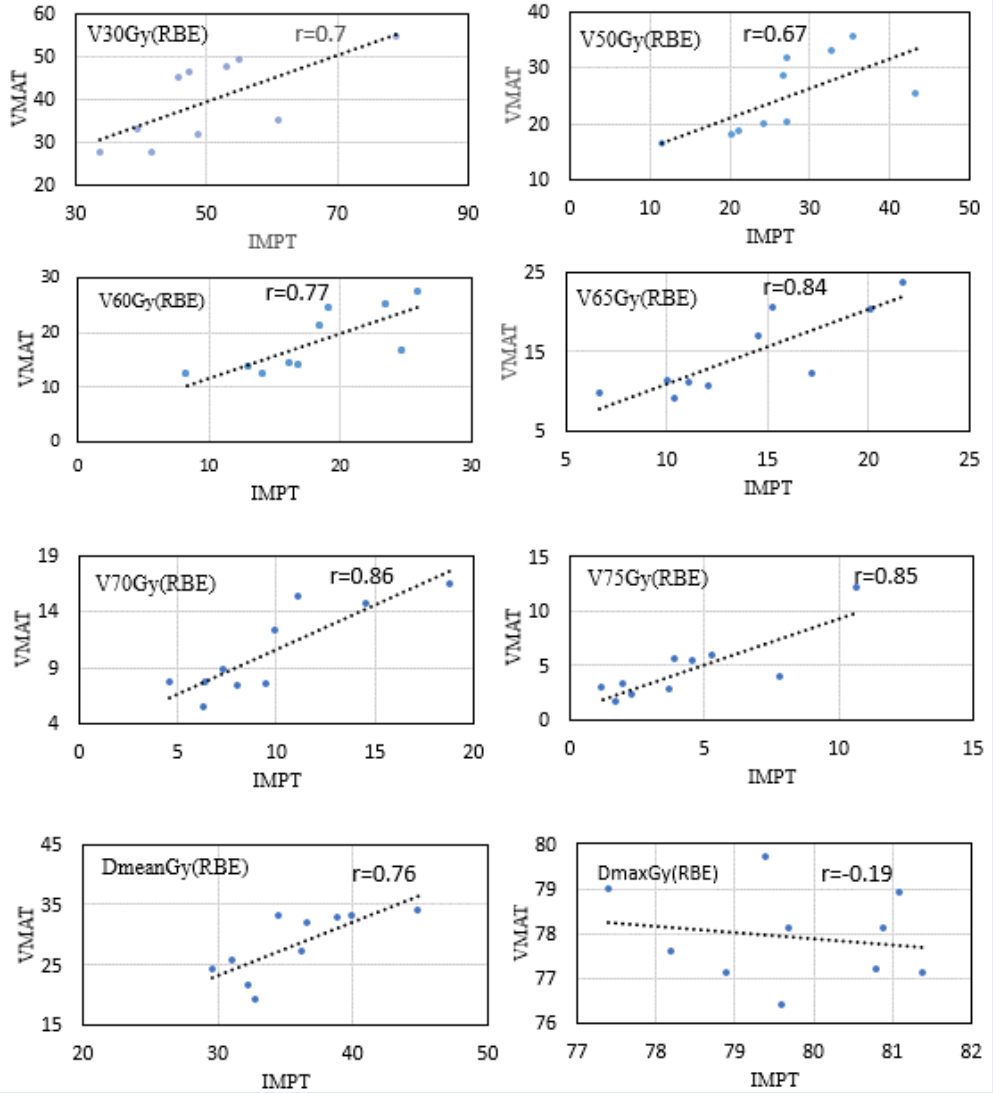

Figure 4: **The Pearson's correlation coefficient between the two same dosimetric quantities of rectum from two techniques IMPT and VMAT.**

VMAT plans. For Dmax, the linear relationship is very weak.

OARs

Figure 2 shows that in the IMPT plans, fewer normal tissues were irradiated compared to the VMAT plans. The mean dose of 2.6 Gy (RBE) to the body from the IMPT plan was significantly (p=0.007) lower than the mean dose of 5.8 Gy (RBE) from the VMAT plans. The result is similar for the max dose, 78.8 Gy (RBE) from IMPT plans compared to 81.6 Gy (RBE) from VMAT plans.

From **Figure 3** , the IMPT plans show statistically ($p \leq 0.05$) superior dose sparing of the rectum in comparison to the VMAT plans at the Dmax, Dmean and V30Gy indices. The IMPT plans were statistically ($p > 0.05$) equal between the VMAT plans and IMPT plans at V50 Gy, V60 Gy, V65 Gy, V70 Gy and V75 Gy.

The Pearson's correlation coefficients in **Figure 4** show the strong (V60 Gy, V65 Gy, V70 Gy, V75 Gy and Dmean) or moderate (V30 Gy and V50 Gy) linear relationship between VMAT plans and IMPT plans for the rectum. For Dmax, the linear relationship between the two techniques is very weak.

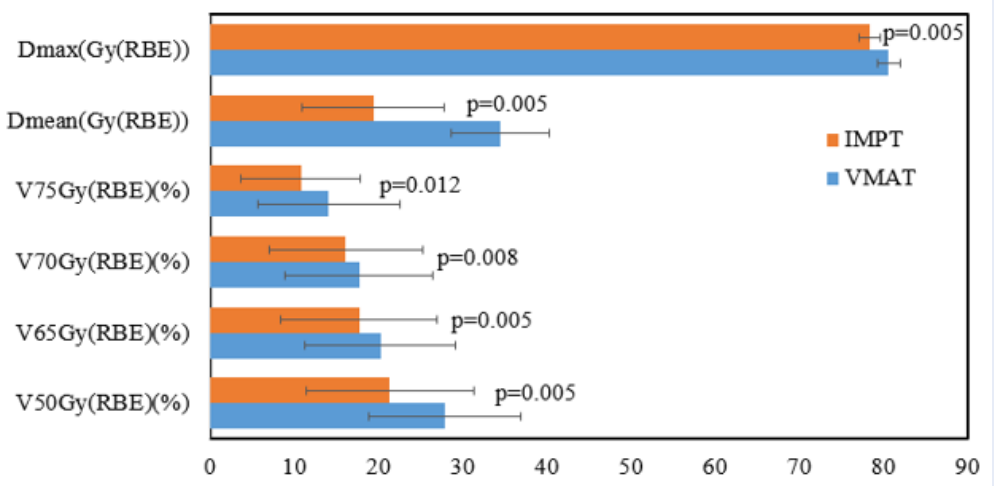

Figure 5: **Averaged relative volumes of bladder at dose constrains (Table 1) in the IMPT plans and VMAT plans.**

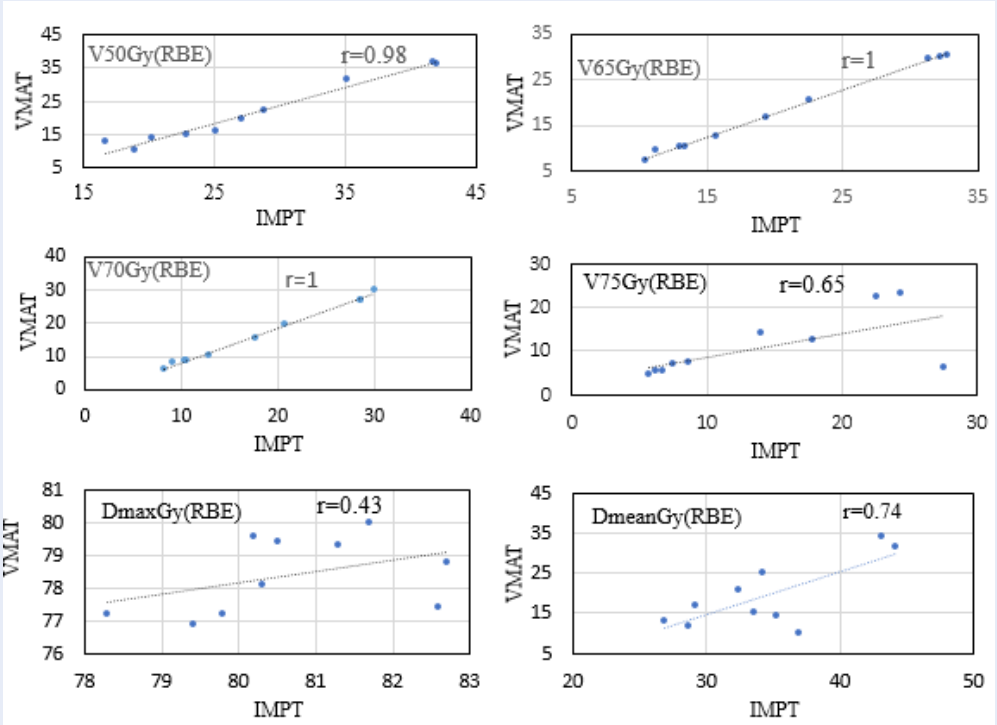

Figure 6: **The Pearson's correlation coefficient between the two same dosimetric quantities of bladder from two techniques IMPT and VMAT.**

From **Figure 5** , the IMPT plans show statistically ($p \leq 0.05$) superior dose sparing of the bladder in comparison to the VMAT plans at all dosimetric indices.
Pearson's correlation coefficients showed a strong (V50 Gy, V65 Gy, V70 Gy) or moderate (V75 Gy and Dmean) linear relationship between VMAT plans and IMPT plans for the rectum (**Figure 6**). Similar to the result of dose sparing of the rectum, for Dmax, the linear relationship between the two techniques is weak.
From Table 5, the IMPT plans show statistically ($p > 0.05$) equal dose sparing of both femur heads in comparison to the VMAT plans at the Dmax and Dmean indices.

EUD analysis

From Table 6 , the IMPT plans show a statistically ($p \leq 0.05$) lower EUD of PTV, closer to the dose requirement (74 Gy), in comparison to the VMAT plans. The IMPT plans also show statistically ($p \leq 0.05$) lower EUD to the baldder. For the rectum, the IMPT plans show statistically ($p \leq 0.05$) equal EUD in comparison to the VMAT plans.
Table 6 shows that the results from EUD have the same trend as the results from the dose distribution to each struct.

DISCUSSION

The same PTV coverage in the IMPT plans and VMAT plans of the corresponding case was applied in the study. In the treatment planning process, we changed the gantry angles to optimize the IMPT plans. In comparison with VMAT plans, IMPT plans produced plans with better dosimetric quality.
IMPT planning could produce a dose to the PTV with better dose homogeneity than VMAT planning. The results of the averaged minimum dose, the averaged maximum dose, the averaged mean dose and the averaged median dose proved that the dose to IMPT plans was closer to the prescribed dose compared to that in VMAT plans. The reduction in the maximum dose to the PTV was expected to translate the reduction in the maximum dose to the rectum and the bladder. Consequently, the results showed that the averaged maximum dose of the bladder was lower in the IMPT plans. These results were similar to the results found by Angelia Tran et al.[3], Suresh Rana et al.[26] and Sergiu Scobioala et al.[27] while comparing the same struct.
IMPT plans succeeded in significantly reducing the dose to normal tissues due to only two beams used in IMPT plans compared to many small beams used in VMAT plans. Overall, for OARs, including the bladder and both femurs, the volumes being irradiated at dose limits are lower in IMPT plans. The most beneficial in the IMPT plan is only a small volume of OARs being irradiated in the low-to-medium dose region. The volume of the bladder being irradiated was reduced in both the high dose and the low dose regions. For the rectum, the volume being irradiated was reduced in the low-dose region and was comparable in the medium- to high-dose region. These results were obtained from the characteristics of the depth dose curve of the proton beam. Moreover, the dose to which structure is better also depends on the priority in protecting the OARs.
The results showed that there were strong relationships between the IMPT technique and VMAT technique for most dosimetric quantities, except for the maximum dose and minimum dose. These results implied that with the same patient and the same user, the high dose-volume in VMAT plans met the high dose-volume in the IMPT plans.
The EUDs of the bladder in IMPT plans were also lower than those in VMAT plans with the exponential parameter α with a confidence level of 95%. The research pointed out the typical advantages of IMPT plans when compared with VMAT plans. The limitation of the research is that the plan robustness of IMPT plans should be analyzed specifically.

CONCLUSIONS

This study compares IMPT plans and VMAT plans. The results show that the doses to both the PTV and OARs are statistically ($p \leq 0.05$) improved in IMPT plans. The dose to the PTV in the IMPT plans was closer to the prescribed dose than that in the VMAT plans. The dose to the PTV from IMPT plans ranged from 69.1 ± 4.7 to 79.0 ± 1.1 Gy (RBE). The dose to the PTV from VMAT plans ranged from 68.0 ± 2.8 to 81.6 ± 1.3 Gy (RBE). IMPT plans succeeded in significantly reducing the dose to both OARs and other normal tissues in the low-to-medium dose region. The mean dose of 2.6 Gy (RBE) to the body from the IMPT plan is significantly lower than the mean dose of 5.8 Gy (RBE) from the VMAT plans. The IMPT plans show statistically superior dose sparing of the rectum and bladder in comparison to the VMAT plans at the Dmax, Dmean, and V30Gy indices and at all dosimetric indices. The results from the study pointed out that the IMPT technique should be preferred in the treatment of prostate cancer.

ABREVIATIONS

EUD: equivalent uniform dose
IMPT: intensity-modulated proton therapy
VMAT: Volumetric Modulated Arc Therapy

Table 5: The averaged maximum doses and the averaged mean doses to both femurs

OARs	Maximu dose			Mean dose			
	Mean ±SD Gy(RBE	Mean ±SD Gy(RBE	p value (≤0.05)	Mean ±SD Gy(RBE		IMPT Mean ±SD Gy(RBE)	p value (≤0.05)
	VMAT	IMPT		VMAT			
Right femur head	41.5±5.'	38.5±6.	0.203	17.9±3.4	13.8±8.0	0.169	
Left femur head	42.4±5.'	40.2±8.	0.508	19.1±4.4	14.8±8.4	0.415	

Table 6: The averaged EUD to the PTV, rectum and bladder

The exponent α (95% confidence level)	VMAT Mean ±SD Gy(RBE)	IMPT Mean ±SD Gy(RBE)	p value (≤0.05)
PTV			
-15	77.0±1.3	76.3±1.1	0.046
-10	77.1±1.1	76.3±1.1	0.016
+7	77.4±1.0	76.3±1.1	0.011
Rectum			
12	64.2±5.0	64.1±4.3	0.799
7	58.6±7.2	58.7±6.4	0.878
4	52.0±9.9	51.6±9.0	0.477
The exponent α (95% confidence level)	VMAT Mean ±SD Gy(RBE)	IMPT Mean ±SD Gy(RBE)	p value (≤0.05)
Bladder			
	62.3±3.2	60.2±3.2	0.005
	56.3±3.8	53.7±4.7	0.005
	48.8±4.1	43.9±6.1	0.005

ICRU: International Commission Radiation Units and Measurement
TCIA: The Cancer Imaging Archive
OARs: Organs At Risk:
RBE: Relative biological effectiveness
QUANTEC: Quantitative Analyses of Normal Tissue Effects in the Clinic
RTOG: Radiation Therapy Oncology Group
PTV: Planning Target Volume
LAP: Laser accelerated proton beam
CERR: Computational Environment for Radiotherapy Research

AUTHORS' CONTRIBUTIONS

Thu T. C. Nguyen, Xuan T. Le contributed in treatment planning, acquisition of data, interpretation of data. Thu T. C. Nguyen made the final correction for the manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

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Phí xuất bản: Miễn phí
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Lập chỉ mục (Indexed): Google Scholar, Scilit

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Tỉ lệ chấp nhận đăng 2021: 65%
Phí xuất bản: Miễn phí
Thời gian phản biện: 45 ngày
Lập chỉ mục (Indexed): Google Scholar, Scilit

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Ngôn ngữ bài báo: Tiếng Việt
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Phí xuất bản: Miễn thu phí đối với tác giả là CBVC của ĐHKHXHNV, ĐHQG-HCM; Tác giả khác: 500.000 VNĐ/bài
Thời gian phản biện: 75 ngày
Lập chỉ mục (Indexed): Google Scholar, Scilit

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Ngôn ngữ bài báo: Tiếng Việt và tiếng Anh
Tỉ lệ chấp nhận đăng 2021: 87%
Phí xuất bản: liên hệ tòa soạn
Thời gian phản biện: 45 ngày
Lập chỉ mục (Indexed): Google Scholar, Scilit

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Ngôn ngữ bài báo: Tiếng Việt
Tỉ lệ chấp nhận đăng 2021: 70%
Phí xuất bản: Miễn phí
Thời gian phản biện: 30 ngày
Lập chỉ mục (Indexed): Google Scholar, Scilit

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