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VMAT partial arc technique decreases dose to organs at risk in whole pelvic radiotherapy for prostate cancer when compared to full arc VMAT and IMRT

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ABSTRACT

Whole pelvic radiotherapy (WPRT) can sterilize microscopic lymph node metastases in treatment of prostate cancer. WPRT, compared to prostate only radiotherapy (PORT), is associated with increased acute gastrointestinal, and hematological toxicities. To further explore minimizing normal tissue toxicities associated with WPRT in definitive IMRT for prostate cancer, this planning study compared dosimetric differences between static 9-field-IMRT, full arc VMAT, and mixed partial-full arc VMAT techniques. In this retrospective study, 12 prostate cancer patients who met the criteria for WPRT were randomly selected for this study. The initial volume, PTV46, included the prostate, seminal vesicles, and pelvic nodes with margin and was prescribed to 4600 cGy. The cone-down volume, PTV78, included the prostate and proximal seminal vesicles with margin to a total dose of 7800 cGy. For each CT image set, 3 plans were generated for each of the PTVs: an IMRT plan, a full arc (FA) VMAT plan, and a mixed partial-full arc (PFA) VMAT plan, using 6MV photons energy. According to RTOG protocols none of the plans had a major Conformity Index (CI) violation by any of the 3 planning techniques. PFA plan had the best mean CI index of 1.00 and significantly better than IMRT ($p = 0.03$) and FA ($p = 0.007$). For equivalent PTV coverage, the average composite gradient index of the PFA plans was better than the IMRT and the FA plans with values 1.92, 2.03, and 2.01 respectively. The defference was statistically significant between PFA/IMRT and PFA/FA, with p- values of < 0.001. The IMRT plans and the PFA plans provided very similar doses to the rectum, bladder, sigmoid colon, and femoral heads, which were lower than the dose in the FA plans. There was a significant decrease in the mean dose to the rectum from 4524 cGy with the FA to 4182 cGy with the PFA and 4091 cGy with IMRT ($p < 0.001$). The percent of rectum receiving 4000 cGy was also the highest with FA at 66.1% compared to 49.9% (PFA) and 47.5% (IMRT). There was a significant decrease in the mean dose to the bladder from 3922 cGy (FA) to 3551 cGy (PFA) and 3612 cGy (IMRT) ($p < 0.001$). The percent of bladder receiving 4000 cGy was also the highest with FA at 45.4% compared to 36.6% (PFA) and 37.4% (IMRT). The average mean dose to the sigmoid colon decreased from 4177 cGy (FA) to 3893 cGy (PFA) and 3819 cGy (IMRT). The average mean dose to the femoral heads decreased from 2091 cGy (FA) to 2026 cGy (PFA) and 1987 cGy (IMRT). Considering the improvement in plan quality indices recorded in this study including the dose gradient and the dose to organs at risk, mixed partial-full arc plans may be the preferred VMAT treatment technique over full arc plans for prostate cancer treatments that include nodal volumes.

1. Introduction

Worldwide, prostate cancer is the second most common cancer in men and the fourth most commonly occurring cancer overall. It is the second leading cause of cancer death in men in the United States and It was estimated that 34,130 deaths from this disease would have occured in 2021.[1] One of the options in the curative treatment of low and selected intermediate-risk prostate cancer is external beam radiotherapy (EBRT)[2]. For patients at higher risk of nodal involvement, the irradiation of the pelvic lymph nodes may improve outcome by potentially eradicating nodal micrometastases.[3,4] There are several arguments to support the elective treatment of pelvic nodes. For example, surgical lymphadenectomy studies have identified microscopic, radiologically occult, nodal metastases, especially with higher risk tumors.[5] Whole pelvic radiotherapy (WPRT) can potentially sterilize microscopic

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lymph node metastases in treatment of prostate cancer. Update analysis of Radiation Therapy Oncology Group (RTOG) 9413 Trial suggested WPRT may be beneficial when hormonal therapy was given neo-adjuvant and concurrently.[6] Elective nodal irradiation appears to be beneficial in favorable risk prostate cancer in the absence of hormonal therapy.[7] However, although there may be benefits with regards to disease control, the larger volumes irradiated for these patients may result in increased doses to surrounding organ at risk (OAR) including rectum, bladder and small bowel. WPRT, compared to prostate only radiotherapy (PORT), is associated with increased acute gastrointestinal (GI), and hematological toxicities.[8,9] In the largest randomized trials comparing WPRT and PORT, RTOG 9413 used conventional techniques and found significantly increased acute grade 2 GI toxicities by 16.3%. The European GETUG-01 (Groupe d'Etude des Tumeurs Uro-Genitales) Trial used 3-D conformal techniques and found an insignificant 6.9% increase in acute grade 2 or greater GI toxicities. The difference in observed clinical toxicities can largely be attributed to the difference in radiation delivery techniques. Using a 7-field static IMRT technique, Deville *et al.* reported improved toxicity profile with no differences in late GI and GU toxicities between WPRT and PORT, but a significant difference in acute GI toxicity.[10] In a national population study where IMRT was used, Parry *et al.*[11] concluded that including pelvic lymph nodes in radiation fields for high risk or locally advanced prostate cancer was not associated with increased GI or GU toxicity. It is worth noting that the pre-sacral lymph node basin was not part of target volume. RTOG consensus guidelines on pelvic nodal target volumes include pre-sacral nodes.[12] The inclusion of this midline structure increases low dose exposure to bowel and bladder; therefore, it can impact both acute GI and GU toxicities.

EBRT has greatly evolved over the past several decades with the improvements of computer hardware and software, as well as technological advances in treatment delivery systems. Advancement in EBRT includes the introduction of intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) that generates more conformal dose distribution. VMAT is an innovative form of IMRT optimization that allows the radiation dose to be efficiently delivered using dynamic modulated arc .[13] Compared with IMRT, the potential advantages of VMAT include a large reduction in monitor units (MU) required to deliver a given fractional dose and a reduction in treatment time.[14-16] Treatment planning studies in the prostate only or in the prostate with seminal vesicles found that VMAT achieved equal or better target coverage and normal tissue sparing over IMRT.[17-19] Few studies have compared IMRT to VMAT for WPRT.[20-23] WPRT encompass larger and more irregularly shaped pelvic target volumes, including the prostate, seminal vesicles, and pelvic lymph nodes and the literature is conflicting.[20-23] Herman Tde L *et al.*[23] reported lower normal tissue doses in VMAT, while maintaining similar target coverage compared to step-and-shoot static field technique. However, articles such as Yoo *et al.*[20] have reported higher normal tissue doses in VMAT when compared against IMRT. The discrepancies between these studies' findings could be due to many different planning variables including the number of IMRT fields, the number of arc fields, beam energy, optimization objectives, and plan normalization.

Table 1
Patient characteristics of the study population.

Variable	Mean	Standard deviation
Age (years)	74.92	8.82
PSA (ng/ml)	65.98	94.35
Gleason Score	8.08	1
Volume-PTV46 (cc)	1076.84	271.75
Volume-PTV78 (cc)	175.87	53.08
Volume-bladder (cc)	337.08	172.13
Volume-rectum (cc)	67.34	16.37
Volume- bowel (cc)	814.4	429.5

To further explore minimizing normal tissue toxicities associated with WPRT in definitive VMAT for prostate cancer, this planning study compared dosimetric differences between static 9-field IMRT, full arc VMAT, and mixed partial-full VMAT techniques.

2. Methods

2.1. Patients

In this retrospective study, 12 prostate cancer patients who were treated at Indiana University (IU) Health, and who met the criteria for WPRT were randomly selected for this study. The patient characteristics are presented in Table 1. This study was approved by IU institutional review board (IRB).

2.2. Plan setup

Patients were simulated according to the departmental prostate cancer CT simulation protocols. The protocol requires patients to be positioned supine with a vacuum cushion immobilization device secured under the knees. The radiotherapy planning CT scan series were acquired using a 16 slice Philips Brilliance Big Bore scanner and the patients were asked to have a full bladder and empty rectum both for simulation and treatment. The CT scans were acquired without intravenous contrast or intraprostatic fiducial markers.

Each patient had an initial and a cone-down planning target volume (PTV). The initial volume, PTV46, included the prostate, seminal vesicles, and pelvic nodes with margin and was prescribed to 4600 cGy. 7 mm margin on the seminal vesicles and 7 mm margin on the prostate were used. The cone-down volume, PTV78, included the prostate and proximal seminal vesicles with margin to a total dose of 7800 cGy. Pelvic nodal CTV was delineated starting at L4-5 junction to include bilateral common iliac, external iliac, internal iliac, presacral and obturator as per RTOG guidelines.[12] Rectum, bladder, bowel, left and right femoral head were contoured as organs at risk (OARs) based on CT images.

For each CT image set with identical target tissue segmentation and organs at risk (OAR) delineation, 3 plans were generated for each of the PTVs: an IMRT plan, a full arc (FA) VMAT plan, and a mixed partial-full arc (PFA) VMAT plan, all using 6 MV photons. The IMRT plans consisted of 9 equally spaced co-planar beams. The FA plans consisted of 2 full, 358 degrees, coplanar arcs with a collimator rotation of *15 degrees and 345 degrees to minimize the contribution of the tongue-and-groove effect to the dose (clockwise rotation from 181 to 179 and counter-clockwise rotation from 179 to 181)*. The field sizes were limited to a 15 cm in the X direction due to leaf travel constraints and to increase dose conformality.[24,25] The PFA plans consisted of 2 partial arcs, and 2 full arcs. The partial arcs were generated by splitting a full arc, with a collimator rotation of 15 degrees, into 2 halves 179 degrees each. The field size of each partial arc was reduced, so that the anterior x jaw on the arcs' lateral projection was limited to 1 cm beyond the beam's central axis. The 2 remaining full arcs had a collimator rotation of 90 degrees and the field sizes were limited so that one arc treated the superior part of the volume and the other arc treated the inferior part of the volume with 2 cm of overlap at the central axis (See Table 2). The isocenter was placed, so that the overlap between the 2 arcs was positioned superior to the PTV78. Plans were generated using 6 MV photon beams from a Varian TrueBeam linear accelerator equipped with a 120 leaf Millennium MLC which has a leaf length of 15 cm at isocenter.

Table 2
Full Arc (FA) and Partial Arc fields: The partial arcs, limits the field size, such that the MLCs aren't able to bridge over wide distances.

Field ID	Field X (cm)	X1(cm)	X2(cm)	Field Y(cm)	Y1(cm)	Y2(cm)	Gantry rotation	Collimator rotation	Couch rotation
Full Arc Sup	12.0	+2.5	+9.5	20.0	+10	+10	181.0CW179.0	90.0	0.0
Full Arc Inf	11.8	+11.8	0.0	20.0	+10.0	+10.0	179.0CCW 181.0	90	0.0
Partial Arc X1	10.2	+9.7	+0.5	23.0	+12.0	+11.0	181.0CW 0.0	15.0	0.0
Partial Arc X2	9.3	+0.5	+8.8	23	+12.0	+11.0	0.0CW 179.0	15.0	0.0

Table 3
Dose specification and dose-volume constraints used for optimization of IMRT and RapidArc VMAT planning for prostate cancer (based on Quantec).

PTV	95% PTV received 99% of the prescription dose
	≤3% PTV received >107% of prescription dose
	≤3% PTV received <93% of prescription dose
Rectum	V75 Gy ≤15%
	V70 Gy ≤20%
	V65 Gy ≤25%
	V60 Gy ≤35%
	V50 Gy ≤50%
Bladder	V80 Gy ≤15%
	V75 Gy ≤25%
	V70 Gy ≤35%
	V65 Gy ≤50%
Femoral Heads	V50 Gy ≤50%

2.3. Optimization, calculation, normalization, and evaluation

All plans were generated using Varian's Eclipse Treatment Planning Software version 13.7. VMAT plans used the Varian RapidArc technology. Optimization was performed using the Photon Optimizer (PO) and dose was calculated using Anisotropic Analytical Algorithm (AAA) both version 13.7. A 2 mm calculation grid was used. As recommended by the third Physics ESTRO workshop[26] to avoid inter-planning variability biased planning, plans for each technique used the same planning objectives template with automatic optimization and automatic intermediate dose. All plans were normalized so that 95% of the PTV received 99% of the prescription (see Table 3). Dose constraints for the OAR were based on Quantec publication (Table 3). The composite plans were evaluated based on dose-volume statistics for OAR and plan quality. D1cc was used as a more representative surrogate for maximum dose.

2.4. Plan quality

Plan quality is an important part of treatment plan evaluation. Isodose distributions were generated on computed tomography (CT) image sets of 12 patients. In order to objectively quantify the quality of a dose distribution in a target irradiation, derived DVH dose metrics have been proposed. These metrics include homogeneity, conformity and gradient indices.[26,27] Various definitions of these indices have been proposed in the literature.[27] However, we used the version as defined by RTOG as they have been shown to suffice for routine clinical treatment plan evaluation if a dose distribution is available for visual inspection.[28]

$$CI_{RTOG} = V_{RI}/TV \quad (1)$$

Where where *VRI* is reference isodose volume, and *TV* is target volume.

$$HI_{RTOG} = Imax/RI \quad (2)$$

where *I max* is maximum isodose in the target, and *RI* is reference isodose

$$GI(R50\%) = Volume\ of\ 50\%\ isodose\ line/volume\ of\ prescription\ isodose\ line \quad (3)$$

Where, GI = Gradient index

The normal tissue integral dose (NTID) is the radiation delivered to the whole patient body was defined as the product of the mean dose and the volume of normal tissue, this is expressed in equation 4:

$$NTID[Gy \cdot L] = D_{Mean-NT}[Gy] \cdot V[L], \quad (4)$$

where $D_{Mean-NT}$ [Gy] is the mean dose delivered to volume V [L] (where L – liter).[29] Normal tissue is defined as the whole body within the skin surface minus the PTV.

2.5. Statistical analysis

To compare the results between the different treatment plans, a two tailed paired student t- test was used. The data was checked to see if it was not a normal distribution by evaluating the skewness and kurtosis. A p-value of < 0.05 was considered to indicate significance.

3. Results

The average age for the group was 74.92 ± 8.8 years ranging from 65 to 91 years. The mean PSA was 65.9 ± 94.4 and range was 4 to 313. The mean volume of PTV46 and PTV78 were 1076.8 ± 271.7 cc and 175.9 ± 53.1 cc respectively. Thus, PTV46 represented a relatively large and complicated target, whereas PTV78 represented a relatively small and simple target in this study. The average volume of bladder, rectum and small bowel were 337.08 ± 172.1 cc, 67.34 ± 16.4 cc and 814 ± 429.5 cc respectively. The NTID was 313 ± 106 Gy-L, 310 ± 101 Gy-L and 305.9 ± 105 Gy-L for IMRT, FA and PFA respectively.

3.1. Plan quality

Plan quality evaluation is presented in Table 4. The definition of CI by RTOG (Eq. 1) is easy to interpret. A CI equal to 1 corresponds to ideal scenario. A CI greater than 1 indicates that the irradiated volume is greater than the target volume and includes healthy tissues. If the CI is less than 1, the target volume is only partially covered by prescription dose.[27] According to RTOG guidelines, if the conformity index is situated between 1 and 2, treatment is considered to comply with the treatment plan; an index between 2 and 2.5, or 0.9 and 1, is considered to be a minor violation, and an index less than 0.9 or more than 2.5 is considered to be a major violation.[27] None of the plans had a major CI violation by any of the 3 techniques. PFA plan had the best mean CI index of 1.00 and significantly better than IMRT ($p = .03$) and FA ($p = .007$).

Similarly, RTOG recommends that if the homogeneity index (HI) (Eq. 2) is <2, treatment is considered to comply with the protocol. If this index is between 2 and 2.5, the protocol violation is considered to be minor, but when the index exceeds 2.5, the protocol violation is considered to be major, but may nevertheless be considered to be acceptable[27]. None of the plans had any HI violation by any of the 3 techniques (HI < 2). PFA and IMRT plans had similar HI ($p = .3$) but significantly better than FA, $p = .001$ and $p = .002$ for FA compare to IMRT and FPA respectively.

The third parameter in plan evaluation is the gradient index (GI) and is a measure of the steep dose gradient outside the target volume. Therefore, the GI plays a significant role in addition to the conformity index. The dose falloff outside target volume is very important in SRS as a measure of plan quality, especially a predictor of complications. Gradient indices have been proposed to compare treatment plans of equal conformity. For equivalent PTV coverage, the average composite gradient index of the PFA plans was better than the IMRT and the FA plans with values 1.92, 2.03, and 2.01 respectively. The difference was statistically significant between PFA/IMRT and PFA/FA, with p- values of < 0.001.

3.2. Organs at risk

Table 5 provides a summary of all investigated parameters with the data presented as the mean +/- standard deviation. The graphical presentation of the doses to the OAR are presented in Figs. 1 and 2 The IMRT plans and the PFA plans provided very similar doses to the rectum, bladder, sigmoid colon, and femoral heads, which were lower than the dose in the FA plans. The average mean dose to the rectum decreased from 4524 cGy with the FA to 4182 cGy with the PFA and 4091cGy with IMRT. The percent of rectum receiving 4000 cGy was also the highest with FA at 66.1% compared to 49.9% (PFA) and 47.5% (IMRT). The average mean dose to the bladder decreased from 3922 cGy (FA) to 3551 cGy (PFA) and 3612 cGy (IMRT). The percent of bladder receiving 4000 cGy was also the highest with FA at 45.4% compared to 36.6% (PFA) and 37.4% (IMRT). The average mean dose to the sigmoid colon decreased from 4177 cGy (FA) to 3893 cGy (PFA) and 3819 cGy (IMRT). The average mean dose to the femoral heads decreased from 2091 cGy (FA) to 2026 cGy (PFA) and 1987 cGy (IMRT).

Table 4
Plan quality evaluation for the 3 planning techniques; IMRT, VMAT (2 Full Arcs- FA) and VMAT (2 Full arcs and 2 Partial arcs- PFA). CI = conformity index, HI = homogeneity Index, GI = gradient index, NTID = normal tissue integral dose, MU = monitor unit, SD - standard deviation.

	IMRT		FA		PFA		*p*-value		
	Mean	SD	mean	SD	Mean	SD	IMRT/FA	FA/PFA	IMRT/PFA
CI PTV 78	1.02	0.04	1.05	0.04	1.00	0.03	0.055	.007	0.025
CI PTV 46	1.50	0.17	1.49	0.16	1.43	0.14	0.658	.000	0.000
HI	1.07	0.01	1.09	0.01	1.07	0.01	0.001	.002	0.339
GI PTV 78	2.03	0.37	2.01	0.35	1.92	0.33	0.32	.001	0.0001
GI PTV 46	3.81	0.58	3.64	0.32	3.63	0.48	0.11	.90	0.0006
NTID (Gy-L)	313.0	106.3	310.2	101.6	305.9	105.4	0.176	.039	0.000
MU	2829.5	220.51	1267.79	129.32	1818.82	201.89	0.000	.000	0.000

Table 5
Dosimetric comparison of organs at risk doses for the 3 planning techniques: IMRT, VMAT (2 Full Arcs -FA) and VMAT (2 Full arcs and 2 Partial arcs-PFA) plans. D1cc, dose received by 1 cc volume of the organ, Vxx, % volume receiving xx Gy, F.H Rt= Right femoral head, F.H. Lt= left femora l head, p- values from t- test.

	IMRT		FA		PFA		*p*-value		
	Mean	SD	Mean	SD	Mean	SD	IMRT/FA	FA/PFA	IMRT/PFA
Target									
CTVn (cGy)	5388	336	5463	308	5369	321	0.001	0.000	0.045
CTVp (cGy)	8027	45	8134	41	8052	30	0.000	0.000	0.002
PTV46 (cGy)	5703	299	5759	266	5697	292	0.005	0.001	0.412
PTV78 (cGy)	7999	34	8091	40	8021	22	0.000	0.000	0.002
Rectum									
Dmean (cGy)	4091	463	4524	437	4185	426	0.000	0.000	0.092
Dmax (cGy)	7883.0	562.6	8086.7	364.6	8030.5	412.3	0.008	0.127	0.013
D1cc (cGy)	7436.5	1011.1	7639.3	746.9	7518.0	919.4	0.036	0.096	0.048
V75	7.7%	4%	8.4%	4%	8.1%	4%	0.036	0.215	0.029
V70	11.8%	5%	12.9%	6%	12.0%	5%	0.013	0.016	0.537
V65	15.6%	6%	17.3%	7%	15.7%	6%	0.003	0.003	0.827
V50	29.1%	8%	37.1%	9%	29.8%	8%	0.000	0.000	0.491
V40	47.5%	13%	66.1%	14%	50.0%	11%	0.000	0.000	0.183
Bladder									
Dmean (cGy)	3612	517	3922	522	3551	504	0.000	0.000	0.080
Dmax (cGy)	8215.1	286	8191.3	333	8134.9	460	0.714	0.270	0.446
D1cc (cGy)	7866.0	646	7871.2	769	7786.6	835	0.901	0.009	0.220
V75	7.2%	5%	6.7%	4%	6.1%	4%	0.223	0.015	0.029
V70	9.5%	6%	9.0%	5%	8.2%	5%	0.175	0.003	0.027
V65	11.9%	7%	11.3%	6%	10.4%	5%	0.145	0.002	0.015
V50	21.0%	9%	23.1%	8%	20.1%	8%	0.003	0.000	0.002
V40	37.4%	9%	45.4%	9%	36.5%	9%	0.000	0.000	0.195
Sigmoid									
Dmean (cGy)	3819	549	4177	532	3893	562	0.002	0.000	0.266
Dmax (cGy)	6234	1292	6206	1369	6062	1336	0.734	0.030	0.096
D1cc (cGy)	5575	781	5569	715	5338	645	0.931	0.001	0.005
V70	1.2%	4%	0.8%	3%	0.6%	2%	0.328	0.289	0.314
V45	41.2%	19%	60.5%	18%	43.6%	20%	0.001	0.000	0.516
Bowel									
Dmean (cGy)	1948	764	1950	785	1937	778	0.895	0.536	0.473
Dmax (cGy)	5052	493	5092	420	5005	394	0.490	0.002	0.394
D1cc (cGy)	4797	502	4829	512	4784	455	0.635	0.166	0.760
V45 (cc)	33.3	29.2	33.9	26.2	32.6	27.6	0.791	0.389	0.433
F.H. Rt									
Dmean (cGy)	1925	273	2090	324	2005	331	0.003	0.004	0.067
Dmax (cGy)	5216	472	5083	889	4750	959	0.402	0.001	0.021
D1cc (cGy)	4793	466	4584	784	4233	827	0.108	0.001	0.001
V50	0.9%	2%	0.6%	1%	0.4%	1%	0.103	0.083	0.082
V40	7.5%	5%	5.5%	5%	3.7%	5%	0.001	0.005	0.000
F.H. Lt									
Dmean (cGy)	2050	212	2091	221	2058	193	0.505	0.256	0.882
Dmax (cGy)	5230	353	5148	523	5072	613	0.423	0.349	0.259
D1cc (cGy)	4755.45	400	4628	476	4545	524	0.101	0.237	0.028
V50	0.4%	1%	0.7%	2%	0.5%	1%	0.104	0.083	0.082
V40	6.6%	5%	5.8%	6%	4.7%	5%	0.308	0.138	0.048
Illiac Crest									
Dmean (cGy)	2264	348	2186	339	2170	340	0.004	0.555	0.0006
V40	10.0%	2.7%	8.7%	2.8%	8.5%	2.4%	0.0095	0.708	0.0057

The PFA plans and the FA plans provided lower doses to the iliac crests compared to the IMRT plans. The average mean dose was lowest with PFA at 2170 cGy, slightly higher with FA at 2186 cGy, and highest for IMRT at 2264 cGy. The dose to the bowel and penile bulb was lower in the PFA plans than both IMRT plans and FA plans. The volume of bowel receiving 4000 cGy was 30.9 cc with PFA, 33.3 cc with IMRT, and 33.9 cc with FA. The average mean dose to the penile bulb was 2986 cGy with PFA, 3288 cGy with IMRT, and 3245 cGy with FA.

Another important variable in treatment plan evaluation is Normal Tissue integral dose (NTID), which is the average dose to non-target tissue. The NTID was calculated as in equation 4 and the results are presented in Table 4. VMAT resulted in decrease in NTID and PFA had the lowest mean NTID.

4. Discussion

The target volume for low-risk prostate patients is confined to the prostate and may extend to include part of the seminal vesicles for intermediate-risk patients. Treatment plans for these relatively small and regularly shaped targets can easily be designed to deliver a therapeutic dose to the target while limiting the dose to normal structures such as bladder and rectum.[21] Studies looking at low-risk prostate cases found that VMAT provides improved target coverage and OAR sparing compared with a 5-field IMRT[17] and produces comparable dose–volume histogram (DVH) indices to Helical tomotherapy (HT).[30] For intermediate-risk cases, VMAT offers some improvements in plan quality[18,31] and treatment efficiency over IMRT Zhang, Happersett *et al.* 2010.[21]

Few studies have evaluated VMAT technique in high-risk groups.[21] High-risk prostate patients present a more challenging planning task because of both the larger target volumes required and the separate dose targets. Target volumes for higher risk cases can include the prostate, seminal vesicles, and pelvic lymph nodes (LN), resulting in targets that are large, irregularly shaped, and surrounded to a significant extent by normal tissues. Thus, it is more difficult to achieve adequate dose coverage while maintaining acceptable OAR dose levels.

As pointed out in the introduction, the studies comparing VMAT and IMRT have resulted in conflicting results. The discrepancies between these studies' findings could be attributed to many different

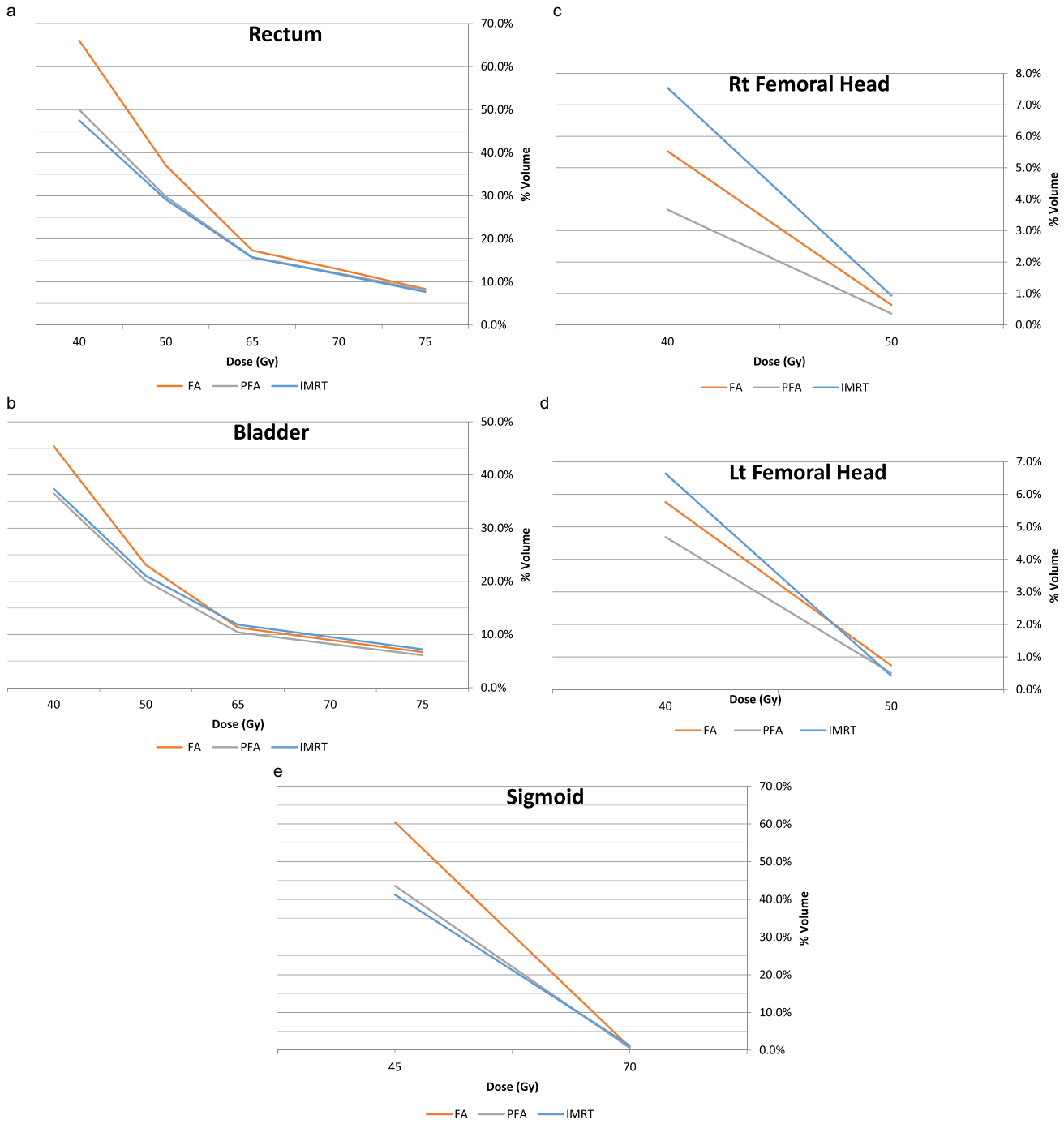

Fig 1. Dosimetric comparison of organs at risk doses as a function of volume of IMRT, VMAT (2 Full Arcs-FA) and VMAT (2 Full arcs and 2 Partial arcs-PFA) plans: (a) Rectum, (b) Bladder, (e) sigmoid, (c) Right Femoral Head and (d) left Femoral Head. (Color version of figure is available online.)

planning variables including the number of IMRT fields, the number of arc fields, beam energy, optimization objectives, and plan normalization. For IMRT techniques, increases in the number of IMRT beams have been associated with dose distribution equivalent to VMAT, with plateau effect at 9 beams.[32,33] The effect of beam energy has been addressed in multiple studies and the consensus is that beam energy has limited effect on plan quality.[34,35] So, in this study we limited our study to 6 MV. Plan optimization and normalization and plan algorithm are significant[35] contributors to plan quality. In our study, plan normalization and optimization (see Table 2) was standardized across the 3 plans. So, the only variable in this study was the number of arcs (Table 3). Multiple-arc prostate VMAT have been reported to have a better dosimetric result than the single-arc at a cost of increased delivery time, MU, and spread of low doses.[31,36]

4.1. Plan quality

Radiation therapy plan quality can be defined as the clinical suitability of the delivered dose distribution that can be realistically expected from a treatment planning.[26] Plan evaluation is mainly characterized through some indices of plan quality such as dose metrics, plan robustness and plan complexity. Homogeneity index (HI), conformity index (CI) and gradient index (GI) were the

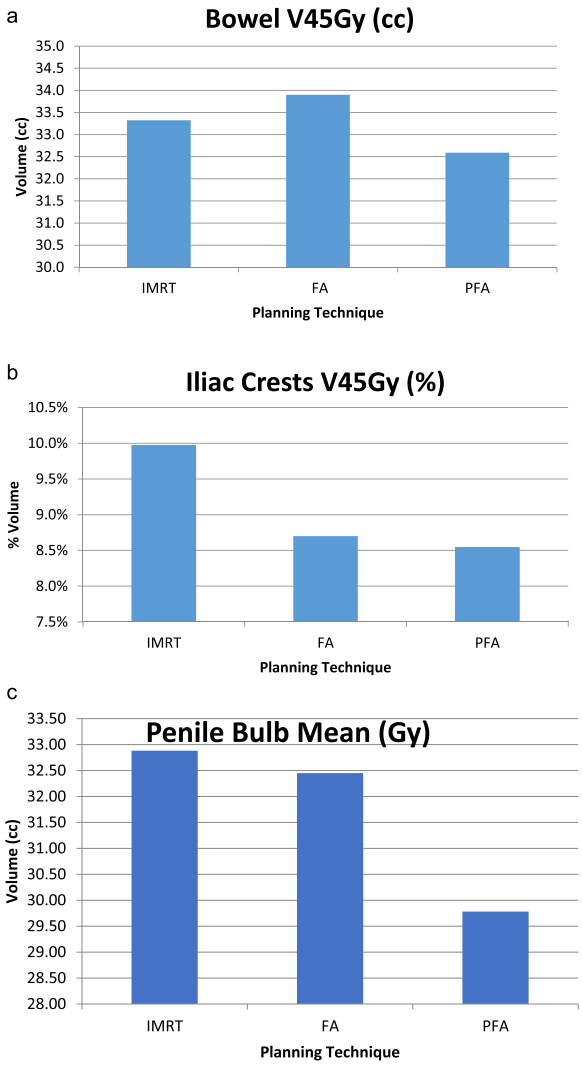

Fig. 2. Dosimetric comparison of organs at risk doses as a function of volume of IMRT, VMAT (2 Full Arcs- FA) and VMAT (2 Full arcs and 2 Partial arcs -PFA) plans: (a) Bowel, (b) Iliac Crest and (c) Penile bulb. (Color version of figure is available online.)

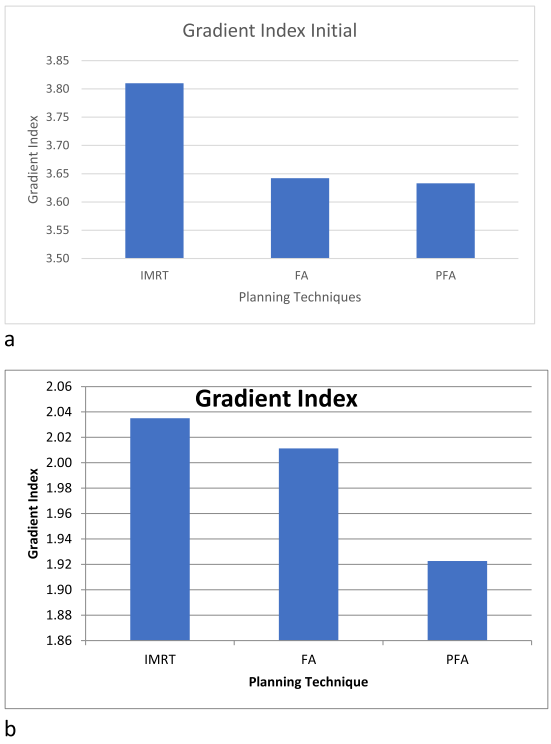

Fig. 3. Gradient Index for 3 planning techniques (a) Initial plan- PTV46 and (b) boost plan PTV78.

derived DVH dose metrics that were reported in this study. In this study, we found that the dose distributions evaluated using plan quality indices for IMRT and VMAT plans (FA, and PFA) were clinically acceptable according to current RTOG requirements. However the CI, HI and GI were significantly better for PFA than FA VMAT plans.

A steep dose fall off is important in order to decrease toxicity in tissues surrounding the target, especially in treatment involving high doses per fraction and this is quantified using dose gradient index.[37] This is very critical for prostate cancer treatment where the rectum and bladder are very close to the target. In our study the PFA showed a significant dose fall off compared to IMRT and FA.

Plan complexity can significantly impact plan quality, since increased delivery complexity (e.g., MLC modulation, dose rate changes, gantry speed) increases the possibility of delivery uncertainties. It is not trivial to determine if a given complexity is appropriate, or optimal, for a specific plan.[38] Proposed plan complexity metrics are based on many parameters, from MLC speeds and segment opening to fluence map complexity. Most do not correlate well with dose delivery measurements. Often the total monitor units (MU) per delivered Gy for a specific plan is used as a benchmark to identify plans with higher complexity than usual. We did not quantify plan complexity in this study.

4.2. OAR

When the PTV includes the prostate, seminal vesicles and lymph nodes as the case for WPRT, IMRT has been reported to perform better in dose sparing for bladder, rectum and small bowel than VMAT.[20] There is a need and clinical significance in looking for planning techniques like PFA presented here that produce lower OAR dose, in order to reduce toxicity or side effects. Fig. 1, clearly demonstrates the superiority of the PFA over FA in OAR sparing.

This reduction in OAR dose using the PFA technique was achieved at the expense of increased plan complexity. Increasing the plan by 2 additional arcs resulted in more MU. There was a 43% increase in MU from FA to PFA plans. However, the PFA MUs are still notably lower than the MU for IMRT. Also adding 2 more arcs will result in increased total treatment time which has the drawback of potential intrafraction motion. Studies have shown that for prostate cancer treatment, intrafraction motion increases with treatment time.[39] Also, there is the question of planning efficiency – calculation time, ease of optimization. One would expect that the PFA takes more planning time, even though templates can be created to generate the plan automatically. Finally, increasing number of arcs and MUs increases the leakage as modulation increases and smaller MLC openings are used.

4.3. NTID

Modern techniques such as IMRT and VMAT enable better dose sculpting and safe delivery of high total doses to the PTV while sparing OAR and adjacent healthy tissue. However, multifield approaches, used in these techniques produce large volumes of low dose inside the patient body. Dose in normal tissue may also increase the risk of secondary malignancies.[40] Radiation-induced

secondary malignancies are an infrequent but probable complication of radiation therapy.[41,42] There are several factors that can impact secondary cancer risk. These factors include: age at irradiation, type of irradiated tissue, irradiated volume, treatment technique and previous irradiation.[43] NTID has become an important variable when evaluating treatment plans from different techniques when other indices are similar because of the clinical risk of secondary malignancies.

Slosarek *et al.*[40] found that when using different methods (VMAT, IMRT, Helical Tomotherapy and cyberknife (CK)) of treatment delivery. very similar amounts of dose were deposited to the treated volume but the mean NTID was statistically significantly different. In our study, NTID decreased by 0.9% from IMRT to FA and 2.8% from IMRT to PFA. The difference between IMRT and PFA was statistically significant ($p < 0.001$). Yoo *et al.*[20] reported that 7% to 8% greater integral dose in VMAT than in IMRT which is not confirmed in our study. Similar to our study, Palma *et al.*[17] noted larger integral doses with IMRT than with VMAT for prostate cancer. Integral dose is related not only to the delivered MUs but also to other complicated factors such as corresponding aperture sizes and shapes, target volumes and shapes. The study by Haciislamoglu[44] revealed that for WPRT, VMAT did not increase the predicted risk when compared to IMRT, despite the VMAT plans resulting in distributing lower dose over a larger volume of normal tissue than IMRT.

4.4. Plan field width

Although VMAT enhances radiotherapy by increasing tumor volume conformity, there are mechanical limitations. The MLC leaves in the Varian linear accelerator travel on a carriage that allows a maximum x-jaw extent of 15 cm. Overextension when using VMAT reduces the modulation level and results in poor target dose distribution and OAR sparing.[24,45] Unlike IMRT, which allows carriage shifts to provide coverage for large PTVs, VMAT requires a single carriage position due to the constant motion of the gantry. According to Huang *et al.*[24] when the field size is set to <15 cm, anywhere inside the field can be modulated by both sides of the MLC to achieve better optimization results. When the field size is >15 cm, some areas in the field can only be reached by 1 side of the MLC, prohibiting adequate modulation.

Our study evaluated the impact of using half field width in the treatment planning of large, complicated target like in WPRT. Our results confirm that for Varian Linac, VMAT plan quality is dependent on the field width. PFA VMAT with the help of reduced field width shows a clear advantage for the irradiation of whole pelvis. Ugurlu found similar results for nasopharyngeal carcinoma patients, where half field plans showed similar target coverage to full fields plans but reduced OAR doses.[46] Another study by Rossi *et al.* demonstrated that one full and 2 half arcs tended to have better PTV coverage for complicated targets in patients with anorectal carcinoma or vulvar cancer than 2 full arcs.[47]

4.5. Elekta versus Varian

The MLC design can impact the coverage and Varian and Elekta have different designs. The Elekta Versa HD Agility head has no backup jaws and one hundred sixty 5 mm (projected width at isocenter) multileaf collimators (MLCs) travel up to 3 cm/s over the full 40×40 cm2 field-of-view.The MLC carriage can travel at 3.5 cm/s for a maximum MLC leaf speed of 6.5 cm/s .[48] The Elekta MLC has no 15 cm field size limitation that has been discussed for Varian Linac. Reports by Fontenot *et al.*[22] and Peters *et al.*[49] using Elekta machines have reported different results. Using Elekta Infinity radiotherapy accelerator, Fontenot reported that for prostatic irradiation with seminal vesicle and/or lymph node involvement, Single-arc VMAT plans were dosimetrically equivalent to fixed-beam IMRT plans with significantly improved delivery efficiency.

Similarly, a study by Peter *et al.* for Elekta Synergy demonstrated that for prostate cases with LN, the sparing of the OARs for both single and double arc plans were not different compared to IMRT.[49]

4.6. Limitations of dosimetry planning studies

It is known that the patient anatomy and tumor location may not be the same among different patients. Hence, the treatment planning results of 1 case may not be exactly applicable to another case. There are various influencing parameters in the treatment planning that can cause the results of one study to contradict the other one. For example, treatment planning system itself varies from one vendor to another, and this can lead to different planning results. The type of dose calculation engine to calculate the prostate plans can give different IMRT and VMAT results.[50] The experience of the treatment planning personnel and planner biases can impact the plans. The experienced and skillful planners can generate superior treatment plans compare to inexperienced planners.[51] Technique evolution and software upgrades can have an impact on the dosimetric plan. Taking VMAT for example, one can have an option of using one arc, 2 arcs, 3 arcs, etc. Rana *et al*[52] and other researchers have demonstrated that single arc technique can produce different results when compared to double arc technique. Again, the partial single arc technique using avoidance sectors could produce better results by reducing rectal and bladder dose as demonstrated by Rana *et al.*[52] Reduction of rectal and bladder dose can reduce the normal tissue toxicities, thus improving the quality of life of prostate cancer patients.

As one evaluates different plans, one has also acknowledge the fact that, the dose distribution delivered to the patient depends not only on the planned dose distribution but also on the robustness and complexity of the treatment plan.

5. Conclusions

Considering the improvement of the plan quality indices recorded in this study including the dose gradient and the dose to organs at risk, mixed partial-full arc plans may be the preferred VMAT treatment technique over full arc plans for prostate cancer treatments that include nodal volumes. When static field IMRT is compared to full arc VMAT, IMRT provides lower doses, similar to the mixed partial-full arc plans, for rectum, bladder, sigmoid, and bowel doses. However, IMRT also has higher gradient index, penile bulb dose, and iliac crest mean dose.

Authors Contribution

All authors were involved in the preparation of the manuscript. All authors reviewed and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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