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The calculation and comparison of integral dose for the rectum, bladder, right and left femur heads in two methods of prostate cancer radiotherapy: S.A.S IMRT vs. 3D CRT

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ABSTRACT

The aim of radiation therapy treatment planning is to achieve an optimal balance between delivering a high dose to target volume and a low dose to healthy tissues. In order to refrain any complications resulting from the dose to the surrounding normal organs, the role of treatment plan has been critically evaluated in term of how large the volume or mass of normal tissues exposed in the radiation. The integral dose, hence, is one of the important guidance for predicting the radiation effects and choosing the treatment plan. The goal of this study is to compare and investigate the integral doses in conformal 3D vs. IMRT plan.

Dosimetric data from five patients of prostate cancer, treated by simultaneous integrated boost IMRT and 3D CRT were evaluated in this prospective study. Target volume and organs at risk were contoured using M.I.R.S Treatment Planning System (Module Integrated Radiotherapy System version 5.0.00). A dose of 80 Gy to the PTV1, 57 Gy to RTV2 and 62 Gy to the PTV3 and 70Gy in 3D CRT and for PTV, was prescribed. For each patient IMRT plans using S.A.S (dynamic Step and Shoot) and 3D CRT with 6, 10 and 18MV energies, were done. To calculate the ID to the normal healthy tissue all the target volumes were achieved. The Integral Dose was calculated as the mean- dose times the volume of the structure.

A total of thirty IMRT and 3D CRT plans were performed for evaluation. The mean ID received by rectum for 3D CRT was almost 1.04% greater than IMRT while in bladder mean value of ID for IMRT is also bigger than 3D CRT approximately about 1.04%. In RFH and LFH the mean values of ID for 3D CRT were almost 1.05% and 1.06% greater than IMRT, respectively. Due to the three PTVs in IMRT the integral dose in target volume has the biggest value comparing with 3D CRT, considerably.

Keywords: Integral dose, IMRT, 3D CRT, radiotherapy, SIB-IMRT

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Introduction

Clinicians are still looking for the optimal planning method of treating prostate cancer with external beam radiation therapy. The role of radical dose radiation therapy has been established in the management of non-metastatic prostate cancer.[1]

Previously, radiation treatment was matched to the height and width of the target volume, meaning that the normal structures were exposed to the beams. Advances in imaging technology have made it feasible to locate and treat the tumor more precisely. In recent years, 3 Dimensional Conformal Radiation Therapy or so called 3D CRT has commonly been used. By using CT or MRI scans we can see the tumor in three dimensions. Therefore, we can design the therapeutic fields that follow the shape of the tumor more closely. So the radiation beam would provide better dose distribution in target volume while avoids healthy tissue as far as possible.

The need for Intensity Modulated Radiation Therapy (IMRT) arised from the requirement to sculpt precise dose distributions which conform in three dimensions to the shape of planning target volumes (PTVs) and which avoid organs at risk (OARs).[2] Nowadays, IMRT has its own place to treatment of variety of cancers. As like 3D CRT, IMRT models the radiation beams to closely fit the region where the tumor is. But it also varies the radiotherapy dose depending on the shape of the target volume. This means that the central part of the target achieves the highest dose of radiotherapy and a surrounding area of tissue obtains lower doses.

IMRT can also create a concave area within the radiotherapy field to avoid organs that would be damaged by the radiotherapy. This is very useful in regions such as the prostate, for example to bring out the rectum or bladder. Hence, IMRT leads to better conformity of dose distribution to the target volume than 3DCRT. The basic principle of IMRT involves irradiation from a number of different directions of beams with nonuniform energy fluences, which have been optimized to deliver a high dose to the target volume and acceptably low dose to the surrounding normal structures.[3] The treatment planning program divides each beam into a large number of beamlets and determines the optimum setting of their energy fluences or beam weights.[3] IMRT increases the volume of normal tissue exposed to some radiation but can reduce the total dose received by critical structures.[4] In addition of mentioned advantages of IMRT over 3D CRT, IMRT can enhance the fluence at margins of the target and compensate the portal boundaries.[5] Another distinct advantage offered by IMRT is that it makes it possible to deliver different doses to different target volumes in a single plan, commonly referred to a Simultaneously Integrated Boos IMRT (SIB IMRT).[5]

Integral Dose (ID) is the volume integral of the dose deposited in a patient and is equal to the mean dose times the volume irradiated to any dose.[3] The ID is also the area under the curve of a differential absolute-volume histogram.[6] It is often stated that the large number of beamlets and monitor units used in IMRT leads to an increase in ID[7] and that higher-energy photon beams substantially reduce the normal tissue ID (NTID).[9] In contrast, an alternative hypothesis suggests that the total energy deposited in a patient during irradiation (ID) is relatively independent of treatment planning parameters.[6] The aim of this study is to compare the integral dose and also the dose distribution for these two techniques based on the dose–volume histogram (DVH) analysis of the target and critical organs.

Materials and Methods

A. Target contouring

At the onset of study five patients with prostate cancer were selected to be treated with external beam radiation therapy for the future analysis. Planning Computed tomography (CT) images with slice thickness of 3mm was attained for all patients while they fixed in supine form. Target volumes and Organs at Risk (OAR) were contoured using M.I.R.S treatment planning system (Module Integrated Radiotherapy System version 5.0.00) for each kind of treatment. Each treatment plan has the same field's configuration from the aspect of directions and angels as shown in ***table1***:

The clinical linear accelerators (Elekta, Precise model, United kingdom) which produces three range of energies 6, 10, and 18MV and integrated with 80 pairs of leaves (MLCs) was utilized for step and shoot IMRT and 3D CRT for healthy organs sparing.

Table1: the directions and degrees of fields					
Field name	**Field 1**	**Field 2**	**Field 3**	**Field 4**	**Field 5**
Degree	0	72	144	216	288

B. Integral Dose definition

Integral Dose is the total energy absorbed by the body, and computed based on the average organ density, averaged organ dose, and volume as defined in equation as follows:

$$Integral\ Dose=(D.)\bar{}(\rho.)\bar{}V \quad (Gy.Kg)$$ [11]

Where $D\bar{}$ is the averaged dose organ and $\rho\bar{}$ is the averaged organ density, and V is the organ volume.[11] In this study the Integral dose was calculated by following equation:

Integral Dose=Average Dose * Volume (Gy.Lit)

C. Treatment Planning

All patients were treated with both techniques: IMRT and 3D CRT.

In this study for IMRT treatment planning for each beam 11segments was considered and treatments were planned by definition of following regions (***Table 2***) and imposed the doses on PTVs and DVCs (Dose Volume Constraints) for normal tissues as showed in ***table3:***

In this study we considered 80Gy as prescribed dose for PTV1 and other doses were arranged for other PTVs and OARs according to prescribed dose:

For all PTVs, the maximum and minimum doses were measured by prescribed dose time to 102 and 98, respectively.

For the 3D CRT, the CTV (Clinical Target Volume) was the prostate gland and seminal vesicles. The PTV also created by addition of 10 mm margin around CTV and 6mm in the direction of rectum and 70Gy was applied as prescribed dose. Each field has the same dose weight and by use of MLC technology we tried to maintain the healthy organs lower than their tolerance dose, as far as possible. Both of treatments were normalized to isocenter which placed in the center of region including prostate gland and seminal vesicles.

In our study for 3D CRT the whole PTV was set to receive at least 95% (66.50Gy) of the prescribed dose and

Table2: regions definition in IMRT treatment planning	
GTV1	Includes the prostate gland, the base of the seminal vesicles and all gross local extension.
GTV2	GTV2 is not defined.
GTV3	GTV3 includes any lymph nodes identified radiologically as being involved with tumor.
CTV1	GTV1 is grown to directly to create the PTV1 without a defined CTV1.
CTV2	CTV2 includes any seminal vesicle, including the tips, not included in GTV1.
CTV3	CTV3 is the same as GTV3, i.e. no margin is added to GTV3 for microscopic spread.
PTV1	A 10 mm margin is added to the superior, inferior, left, right and anterior directions. Standardly an 8 mm margin is added to the posterior margin
PTV2	CTV2 is grown to create PTV2. A uniform 5 mm margin is added.
PTV3	PTV3 is grown from CTV3. A uniform 5 mm margin is added. This must always be encompassed by PTV2.

in IMRT the mentioned conditions were used to achieve the minimum criteria of 98% of the target volume receives the 95% of the prescribed dose. Therefore, the average dose, the volume of all regions (in both methods) in three ranges of energies (6,10 and 18 MV) were achieved to calculate and compare the integral dose in step and shoot radiation therapy vs. 3 dimensional conformal radiotherapy.

Results

The volume, average dose and IDs of Body, PTVs, bladder, rectum, Right Femur Head (RFH) and Left Femur Head (LFH) are summarized in ***tables 4, 5, 6, 7and 8***.

Body, Rectum, Bladder, LFH and RFH have the same volume in all patients, while the PTV in 3D CRT is totally different with those in IMRT as shown in ***table1***.

According to the ***table2*** ID of IMRT is about 1.07% higher than 3D CRT for body. Because of the identical volume in body for each case (***Table4***) and also regarding to the integral dose formula, it is obvious that the average dose has the radical role in amount of integral dose. Thus,

Table 3: Dose and DVC definitions			
PTV1	Prescribe dose= 80 Gy	Max Dose=81.6 Gy Min Dose=78.4 Gy	D95 of PTV1≤76.00 Gy D99 of PTV1≤72.00 Gy
PTV2	Prescribe dose= 57 Gy	Max Dose=58.26 Gy Min Dose=55.97 Gy	D95 of PTV2≤54.26 Gy D99 of PTV2≤51.40 Gy
PTV3	Prescribe dose= 62 Gy	Max Dose=64.00 Gy Min Dose=61.54 Gy	
Rectum	D60≤45.71 Gy D30≤74.24 Gy D15≤80.00 Gy D5≤85.68 Gy		
Bladder	D50≤57.12 Gy D25≤68.56 Gy D5≤80.00 Gy		
Right and Left Femur Heads	D50≤62.80 Gy		

Table4: volume of PTVs and OARs									
	The Volume of OARs					3D CRT	IMRT		
	Body(Lit)	Rectum(Lit)	Bladder(Lit)	RFH(Lit)	LFH(Lit)	PTV(Lit)	PTV1(Lit)	PTV2(Lit)	PTV3(Lit)
patient 1	19.533	0.089	0.169	0.169	0.17	0.419	0.309	0.122	0.462
patient 2	15.75	0.074	0.083	0.191	0.189	0.316	0.21	0.123	0.455
patient 3	15.66	0.188	0.165	0.172	0.17	0.388	0.301	0.107	0.57
patient 4	14.857	0.128	0.111	0.175	0.164	0.233	0.175	0.068	0.4
patient 5	16.398	0.172	0.105	0.146	0.144	0.2891	0.165	0.124	0.353

plainly in the regions with equal volume in two treatment ways (Rectum, Bladder, RFH and LFH), the main factor that affected on integral dose is average dose. In Body and with the increasing of energy, the integral dose decreases in both techniques as shown in ***figures1a*** and ***1b***:

For the OARs the following data which are shown in ***tables6*** and *7*, are achieved. In rectum, the mean value of ID for 3D CRT is about 1.04% lesser than IMRT, while in bladder the inverse trend is observed the mean value of ID for 3D CRT is about 1.04% greater than IMRT. As mentioned before, due to the same volume of bladder and rectum, the average dose has the rudiment role. As the other studies shows in IMRT and especially for S.A.S technique, because of increasing in the MU and time of treatment the integral dose goes up, according to the ***table6*** the results of this study show that the integral dose and also the average dose have the equal values, approximately.

In right and left femur head the trend was totally different. In RFH and LFH the integral dose for 3D CRT was about 1.04% and 1.05% higher than IMRT, respectively. On the other hand this finding shows that, in SIB-IMRT right and left femur heads, receive lesser amount of the average dose ***(tables6, 7***). The dose distribution in axial sections is shown in ***Figures 2a***, ***2b***, for 18MV photon beams. These axial sections clearly show the concave PTV dose coverage in SIB-IMRT and 3D CRT.

The Dose Volume Histogram (DVH) was achieved for rectum and bladder in both techniques as shown in ***Figures3a, 3b, 3c*** and ***3d***.

In this study for IMRT 3 PTVs were defined (***table2***) while for 3D CRT there was one PTV. For these four regions the following data were obtained:

Because of different PTVs in SIB-IMRT the inte-

Table5: The average dose and Integral Dose of Body

Energy		Body			
		IMRT		3D CRT	
		D average(Gy)	ID(Lit.Gy)	D average(Gy)	ID(Lit.Gy)
6MV	Patient 1	7.556	147.591	7.692	150.244
	Patient 2	8.101	127.591	7.737	121.858
	Patient 3	10.087	158.031	9.518	149.112
	Patient 4	8.691	129.129	6.764	100.498
	Patient 5	7.851	128.733	8.252	135.32
10MV	Patient 1	7.281	142.231	7.491	146.316
	Patient 2	7.846	123.581	7.406	116.654
	Patient 3	10.195	159.724	9.132	143.071
	Patient 4	8.663	128.708	6.488	96.39
	Patient 5	7.798	127.872	7.9	129.54
18MV	Patient 1	7.076	138.21	7.216	140.946
	Patient 2	7.796	122.8	7.087	111.63
	Patient 3	10.195	159.724	9.132	143.071
	Patient 4	8.663	128.708	6.488	96.39
	Patient 5	7.798	127.872	7.9	129.54

Table6: average dose and integral dose in OARs for IMRT

Energy		Bladder		Rectum		RFH		LFH	
		D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)
6MV	Patient 1	39.998	6.756	56.639	5.041	20.456	3.454	17.346	2.945
	Patient 2	58.48	4.854	51.31	3.825	18.97	3.639	17.78	3.37
	Patient 3	52.04	8.592	48.12	9.076	18.22	3.153	15.32	2.616
	Patient 4	57.44	6.377	47.91	6.149	17.37	3.015	19.42	3.188
	Patient 5	54.22	5.695	46.54	8.023	15.4	2.225	13.71	1.976
10MV	Patient 1	38.95	6.58	54.1	4.815	21.63	3.65	18.33	3.113
	Patient 2	57.56	4.778	50.35	3.753	19.47	3.786	18.4	3.487
	Patient 3	52.79	8.717	48.83	9.21	19.39	3.355	16.44	2.807
	Patient 4	57.82	6.419	48.36	6.206	18.33	3.219	20.48	3.363
	Patient 5	55.04	5.781	47.52	8.193	16.2	2.371	14.62	2.106
18MV	Patient 1	38.7	6.53	53.27	4.741	21.94	3.706	18.75	3.184
	Patient 2	58.15	4.827	51.21	3.818	20.21	3.877	19.11	3.662
	Patient 3	52.35	8.643	48.51	9.15	19.76	3.403	16.76	2.861
	Patient 4	57.51	6.384	48.23	6.19	18.45	3.24	20.45	3.357
	Patient 5	54.23	5.696	46.83	8.073	16.19	2.37	14.72	2.12

Table 7: average dose and integral dose in OARs for IMRT

Energy		Bladder		Rectum		RFH		LFH	
		D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)	D avr (Gy)	ID(Lit.Gy)
6MV	Patient 1	42.44	7.17	63.07	5.614	23.1	3.901	19.95	3.388
	Patient 2	62.01	5.148	55.29	4.122	21.45	4.114	19.62	3.17
	Patient 3	54.13	8.937	43.62	8.226	21.1	3.649	17.19	2.936
	Patient 4	55.1	6.117	37.93	4.868	16.6	2.915	20.39	3.348
	Patient 5	61.38	6.447	48.28	8.324	16.51	2.417	15.45	2.226
10MV	Patient 1	42.29	7.144	62.7	5.581	23.38	3.949	20.27	3.443
	Patient 2	61.91	5.139	54.95	4.097	21.22	4.07	19.67	3.727
	Patient 3	53.95	8.907	43.05	8.119	21.3	3.684	17.59	3.004
	Patient 4	55.3	6.139	37.58	4.823	16.58	2.912	19.91	3.269
	Patient 5	61.21	6.429	47.89	8.256	16.85	2.466	15.94	2.296
18MV	Patient 1	41.75	7.052	61.7	5.492	23.16	3.912	20.11	3.415
	Patient 2	61.48	5.104	54.32	4.05	20.68	3.966	19.37	3.67
	Patient 3	53.33	8.805	42.17	7.954	21.07	3.645	17.57	3.001
	Patient 4	54.83	6.087	36.94	4.742	16.34	2.87	19.28	3.166
	Patient 5	60.55	6.359	47.08	8.116	16.8	2.495	15.97	2.301

Table8: Average dose and integral dose of PTVs for IMRT and 3D CRT

Energy		PTV		PTV 1		PTV 2		PTV 3	
		3D CRT		IMRT		IMRT		IMRT	
		D avrag(Gy)	ID(Lit.Gy)	D avrag(Gy)	ID(Lit.Gy)	D avrag(Gy)	ID(Lit.Gy)	D avrag(Gy)	ID(Lit.Gy)
6MV	Patient 1	69.9	29.286	72.716	22.449	60.992	7.429	67.229	31.072
	Patient 2	69.523	22.021	69.403	14.629	60.928	7.53	63.619	28.985
	Patient 3	69.927	26.917	63.793	19.244	58.264	6.248	59.171	34.033
	Patient 4	69.016	16.096	69.552	12.003	59.587	4.094	64.24	25.721
	Patient 5	70.591	20.414	67.229	11.128	60.457	7.535	63.758	22.537
10MV	Patient 1	70.05	29.346	71.551	22.09	59.724	7.275	66.064	30.533
	Patient 2	69.674	22.069	68.028	14.339	58.815	7.269	62.501	28.476
	Patient 3	69.973	26.935	63.586	19.181	57.955	6.215	59.886	34.444
	Patient 4	69.061	16.106	70.436	12.156	60.313	4.149	64.765	25.931
	Patient 5	70.54	20.401	67.432	11.162	60.689	7.564	64.159	22.679
18MV	Patient 1	69.252	29.122	71.539	22.086	60	7.308	66.034	30.519
	Patient 2	68.89	21.821	69.13	14.572	60.525	7.48	63.616	28.984
	Patient 3	69.408	26.717	63.559	19.173	57.671	6.184	59.775	34.38
	Patient 4	68.224	15.911	70.083	12.095	60.276	4.146	64.457	25.807
	Patient 5	70.033	20.253	66.103	10.942	59.892	7.464	63.232	22.351

gral dose increases. For example for patient 1, 10MV photon beams the total integral dose is: ID of PTV1+ ID of PTV2+ ID of PTV3. In other words in this case the total integral dose of targets volume in SIB-IMRT

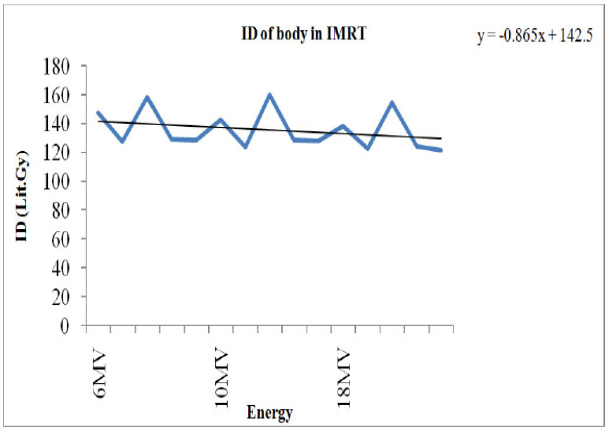


Fig1a: The trend of ID in Body for IMRT

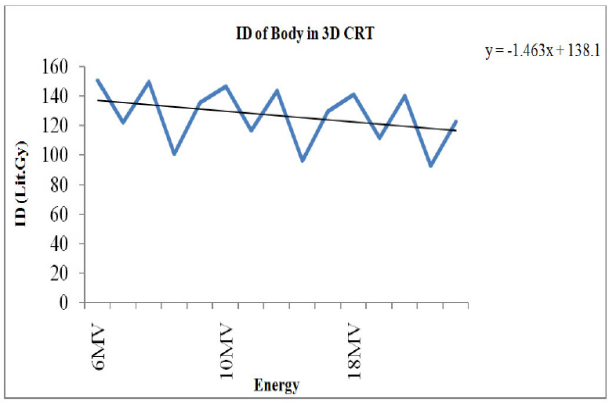


Fig1b: The trend of ID in Body for 3D CRT

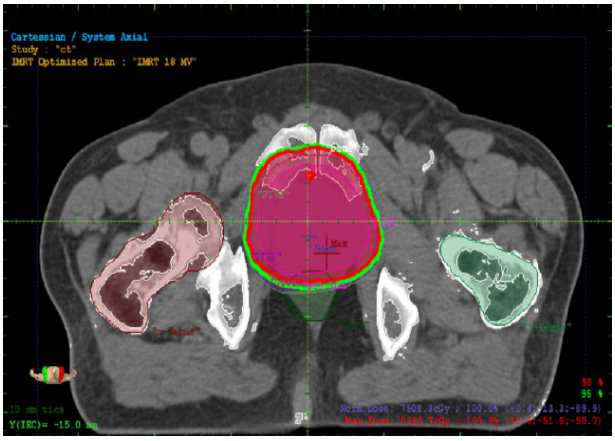


Fig 2a: Axial section dose distribution in IMRT

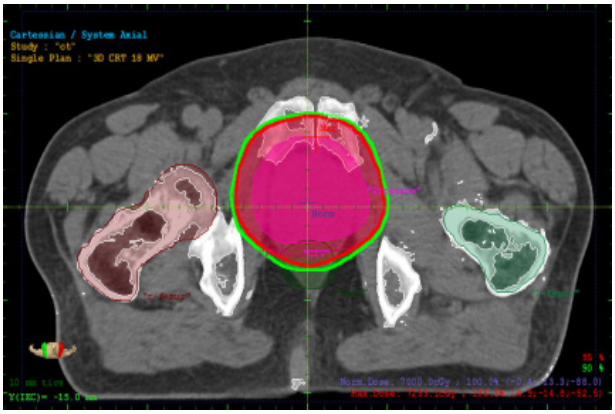


Fig 2b: Axial section dose distribution in 3D CRT

is (22.09+7.275+30.533)59.898 (Lit.Gy) while for 3D CRT the integral dose of PTV would be 29.346 (Lit.Gy). Therefore, according to table8 the integral dose in SIB-IMRT is higher than 3D CRT. In both of treatment modalities and for both studied cases the integral dose decreases with increasing energies, ***Figure4***.

Discussion

Commonly, both IMRT and 3DCRT techniques lead to the same outcomes regarding PTV coverage. In this study both plans was assessed by using the following criteria: 95% of prescribe dose must delivered to 95% of PTV for 3D CRT and also 95% of prescribe dose should delivered to98% of target volume for IMRT Fig2a, 2b. Integral dose or total cumulative dose to normal untreated tissues is higher in IMRT as compared to conventional treatment.[12, 13] Compared to conformal prostate radiotherapy IMRT provided better normal tissue sparing and further reduction of rectal toxicity and late effects. The inverse-planned IMRT further reduce hotspots, because of beam modulation during optimization compared to 3DCRT.[14]

The monitor unit for IMRT is 6-8 times more than 3DCRT is a concern.[5] This shows that the integral dose would also be higher. This result is consistent with Pirzkall et al who studied that the Integral dose for IMRT is higher than conventional treatment.[13] In this study the Integral doses for IMRT is almost equal to 3DCRT for normal tissues, (***table 6and 7***). The equality of ID for OARs is probably emanated from multiple prescribed doses for each PTV used in IMRT therefore during optimization healthy tissues received the same average dose. According to the table8, ID of PTVs in SIB- IMRT is higher than 3D CRT. In general, high integral dose maybe attributed to secondary malignancies for patients with a low risk for systemic relapse that after treatment.

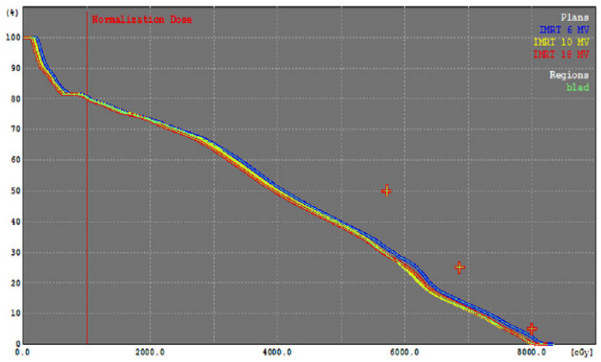


Fig 3a: DVHs of bladder in IMRT

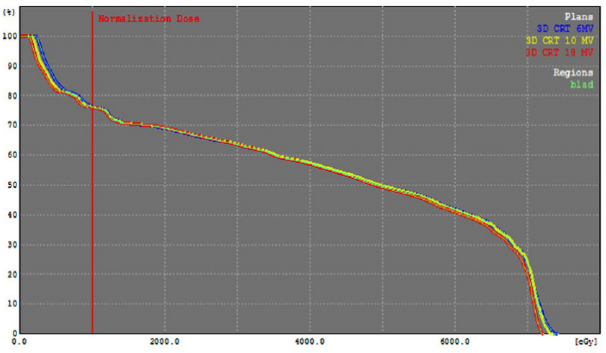


Fig 3b: DVHs of bladder in 3D CRT

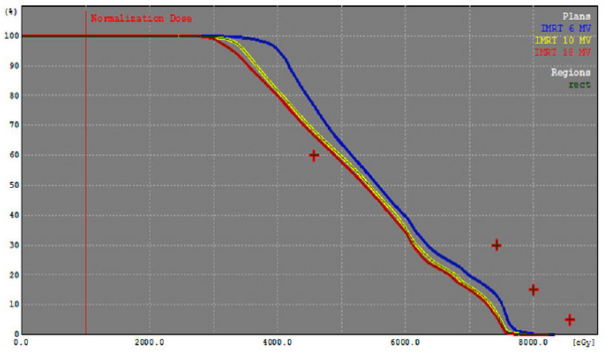


Fig 3c: DVHs of rectum in IMRT

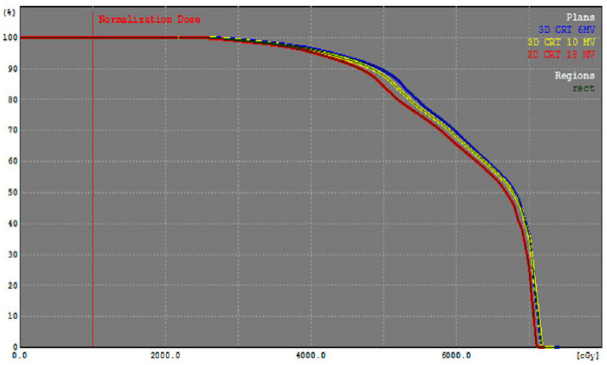
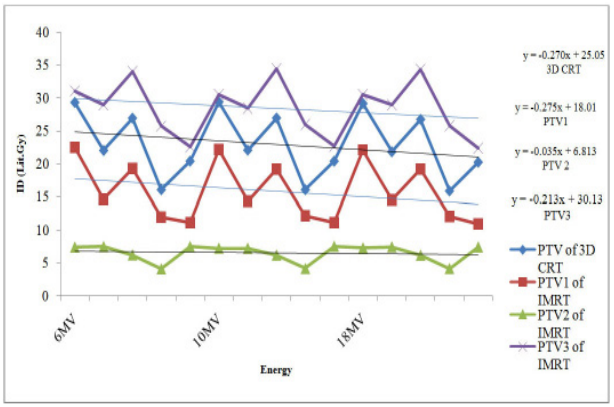


Fig 3d: DVHs of rectum in 3D CRT



Fugure4: The trend of ID in both techniques for PTVs

Conclusion

In general, Multiple-field radiation leads to decrease the volume receiving high radiation dose and increase the volume receiving low-dose radiation. Therefore, theoretically, there may be an increased risk of second malignancies. However, this can be rather difficult to interpret when we apply it to modern radiation techniques in which multiple radiation fields are used.3 There is little difference between 3DCRT and SIB- IMRT, for three ranges of energies 6, 10 and 18MV, in the ID to the rectum, bladder, RFH and LFH. The little difference in ID in these organs originated from the identical average dose in both treatment planning. This means that in SIB-IMRT regarding to the several dose to target volume and increased amount of prescribed dose (80Gy) vs. 3D CRT (70Gy), the healthy tissue received the same dose as like conformal RT and it is the worthy benefit, while the target volumes in this method attained highest dose and the results of treatment became better, obviously. Both treatments have the good results in prostate cancer treatment but according to our results the SIB-IMRT should better results of treatment regarding to the integral concept.

The data provide evidence that it is necessary to consider the integral dose as one of the important factors for choosing the treatment plan, especially for the prostate cancer treatment.

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