Evaluation and comparing rectum and bladder's clinical complications in pelvis radiotherapy in order to treat prostate cancer by using custom block and MLC for three- dimensional conformal radiotherapy

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ABSTRACT

Ionization radiation caused to incidence of complications in the exposed organs. In prostate radiotherapy, rectum and bladder have been radiated unwantedly and indicated some complications during and after treatment. The purpose of present study is to consider and to compare clinical complications of rectum and bladder in custom block and MLC for 3- D conformal radiotherapy, in order to determine if both treatments differ with respect to creating radiation protection, subsequently in the incidence of complications. In this respect, 72 patients with prostate cancer classified into two arms, above 60 years without the history of previous radiotherapy, hormone therapy and surgery, were selected randomly in October 2014. In one arm, patients were treated with block 3- D conformal radiotherapy, and in second arm with MLC outbound technique for 3- D radiotherapy. Rectal and bladder clinical complications were recorded before, during (at the end of 10 treatment sessions), 3 and 6 months after treatment then compared based on tables (RTOG/ LENT).Obtained results showed that patients had a significant difference in such complications as urinary frequency after 10 treatment sessions, 3 months after treatment ($p<0.02$ and $p<0.04$, respectively) Also, patients had a significant difference in regard to dysuria at the end of treatment ($p<0.02$). In both arms, patients had a significant difference in constipation after 30 sessions also at the end of treatment ($p<0.02$, $p<0.02$, respectively).In comparing different grades of complications based on RTOG/ LENT tables, it was not observed a significant difference between patients' complications in both arms.

Keywords: clinical complications; conformal radiotherapy; prostate cancer.

INTRODUCTION

Three- dimensional conformal radiotherapies (3-D CRT) are alternatives rapidly conventional procedures to treat prostate cancer. The purpose of using CT scans and computer designing with more focus on target volume, subsequently, transmitting more radiation to tumor. Today, MLC for 3-D CRT replaced custom block 3D CRT in order to treat prostate cancer. There are three strategies using from MLC, inbound, outbound and cross bound, depending on the location of the treatment, treatment technic and sensitivity surrounding vital structures used.

In considering the effect of dose on volume, and the incidence of delayed rectal complications by 3- D CRT, it was found that the more dose in rectal volume, the more delayed rectal complications, however, the most apparent complication was rectal bleeding[1-4]. During some reports, it was observed that dosage above 70Gy to treat prostate cancer with intermediate and high risk, their PSA level, before treatment was more than PSA>10 mg/ ml, plays a significant role in treatment, but a dosage less than 70Gy is problematic for such patients [5]. Among other studies, we could refer to study of comparing 3- D CRT to conventional radiotherapy in the treatment of prostate cancer in 3 and 6 months following up, it was not observed a significant difference among acute and delayed complications [6].

Also, increasing rectal bleeding in treatment fields resulted in reducing delayed complications of 2-4 grades [7]. 3- D CRT allow higher radiation dosages to treat prostate cancer, however, it was shown that delayed rectal bleeding is occurred in a special threshold of dosage volume proportion [8]. In this study, we attempted to consider and compare clinical complications of rectum and bladder in patients with prostate cancer irradiated by custom block and MLC in outbound technique for 3- D CRT.

MATERIALS AND METHODS

72 patients with prostate cancer above 60 years by G4-G9 grades were selected in two 36 members' arms. Patients CT scans and MRIs were fused by using treatment planning software; the GTV, CTV and PTV were prepared under the supervision of physician. All patients provided written informed consent for participation.

GTV: grow tumor volume.
CTV: clinical tumor volume.
PTV: planning tumor volume.
Patients in first arm were treated by custom block and in second arm, by MLC in outbound technique. Both arms were treated by linear accelerator apparatus. Dosage of every fraction was 1.8- 2 Gy and total dosage was in the range of 64-74Gy. Patients were 5 days in week and 2 days were rested. Data related to patients complications before, during (at the end of 10 sessions), after treatment (3-6 month) were collected and registered. Complications were compared, tables and diagrams prepared. Finally, they were compared based on RTOG/ LENT tables.

STATISTICAL ANALYSIS

In order to compare patients' complications in two treatment arms, Mann- Whitney, Fisher and χ^2 were used.

RESULTS

Table 1.The frequency and percentage of urinary Frequency in participants with regard to hospital, during follow up

Arm	urinary Frequency	Pre-treatment		Acute complication										Delayed complication	
				After 10 sessions		After 20 sessions		After 30 sessions		At the end of treatment		3 months after treatment complication		6 months after treatment complication	
		frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage
Block	yes	12	33.3	10	27.8	20	55.6	20	55.6	18	50	4	11.1	2	5.6
	No	24	66.7	26	72.2	16	44.4	16	44.4	18	50	32	88.9	34	94.4
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
MLC	yes	18	50	20	55.6	17	47.3	18	50	20	55.6	11	30.6	5	13.9
	No	18	50	16	44.4	19	52.7	18	50	16	44.4	25	69.4	31	86.1
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
significant level		NS		P< 0.02		NS		NS		NS		P< 0.04		NS	

By using χ^2 test, it was determined that the percentage of patients with urinary frequency after 10 sessions in both arms had a significant difference (27.8% against 55.6%) ($p<0.02$); it was the same after 3 months of treatment (11.1% against 30.6%), ($p<0.04$).

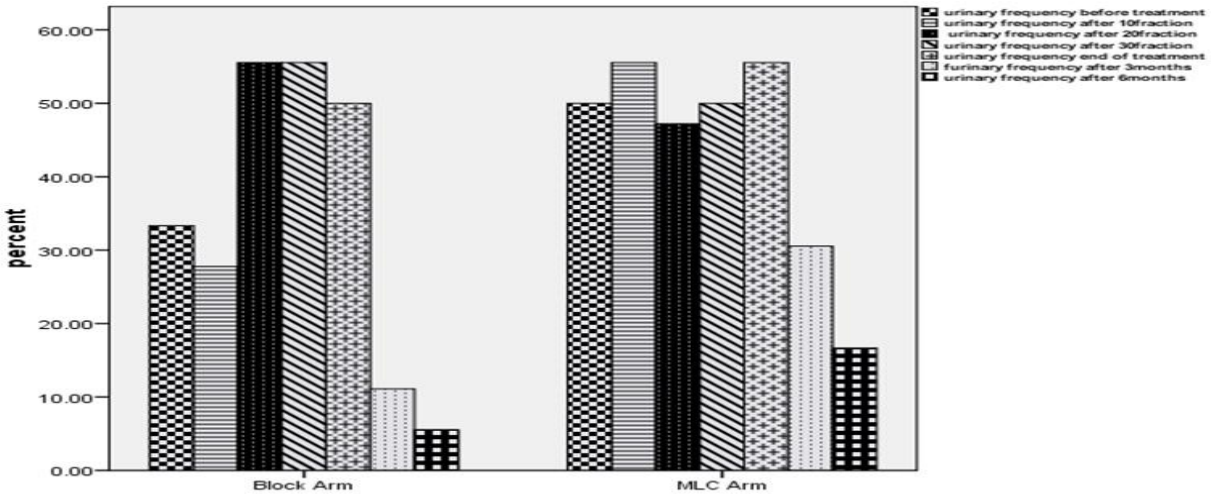

Figure 1. Percentage of urinary frequency.

Table 2.the frequency and percentage of dysuria in participants with regard to arm, during follow up

Arm	dysuria	Pre-treatment		Acute complication										Delayed complication	
				After 10 sessions		After 20 sessions		After 30 sessions		At the end of treatment		3 months after treatment complication		6 months after treatment complication	
		frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage
Block	yes	4	11.1	12	33.3	7	19.4	13	36.1	16	44.4	10	27.8	2	5.6
	No	32	88.9	24	66.7	29	80.6	23	63.9	20	55.6	26	72.2	34	94.4
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
MLC	yes	3	8.3	8	22.2	10	27.8	7	19.4	7	19.4	4	11.1	4	11.1
	No	33	91.7	28	77.8	26	72.2	29	80.6	29	80.6	32	88.9	32	88.9
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
significant level		NS		NS		NS		NS		P< 0.02		NS		NS	

By using χ^2 test, it was determined that the percentage of patients with dysuria during the end of treatment had a significant difference (44.4% against 19.4%), ($p< 0.02$).

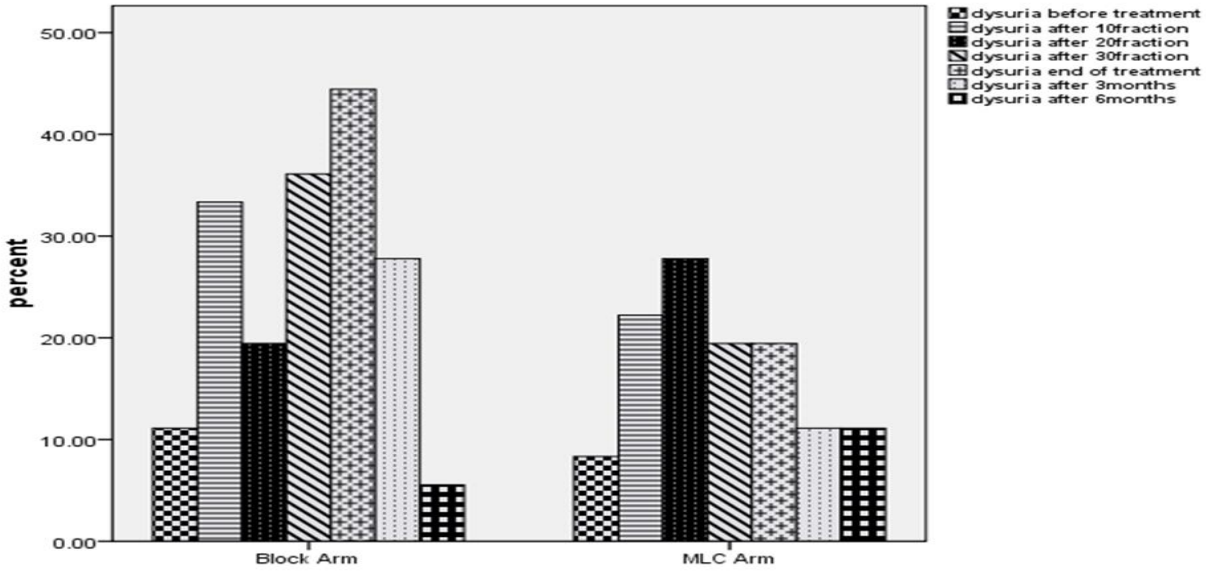

Figure 2.percentage of dysuria in participants in both Arms.

Table 3.frequency and percentage of constipation in participants with regard to arm during follow up.

Arm	constipation	Pre-treatment		Acute complication										Delayed complication	
				After 10 sessions		After 20 sessions		After 30 sessions		At the end of treatment		3 months after treatment complication		6 months after treatment complication	
		frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage
Block	yes	0	0	1	2.8	1	2.8	2	5.6	4	11.1	2	5.6	3	8.3
	No	36	100	35	97.2	35	97.2	34	94.4	32	88.9	34	94.4	33	91.7
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
MLC	yes	0	0	3	8.3	5	13.9	10	27.8	13	36.1	4	11.1	3	8.3
	No	36	100	33	91.7	31	86.1	26	72.2	23	63.9	32	88.9	33	91.7
	total	36	100	36	100	36	100	36	100	36	100	36	100	36	100
significant level		NS		NS		NS		P <0/02		P <0/02		NS		NS	

By using Fisher test, it was determined that the percentage of patients with constipation after 30 sessions had a significant difference in both arms (5.6% against 27.8%), ($p<0.02$). It was the same at the end of treatment (11.1% against 31.6%), ($p<0.02$).

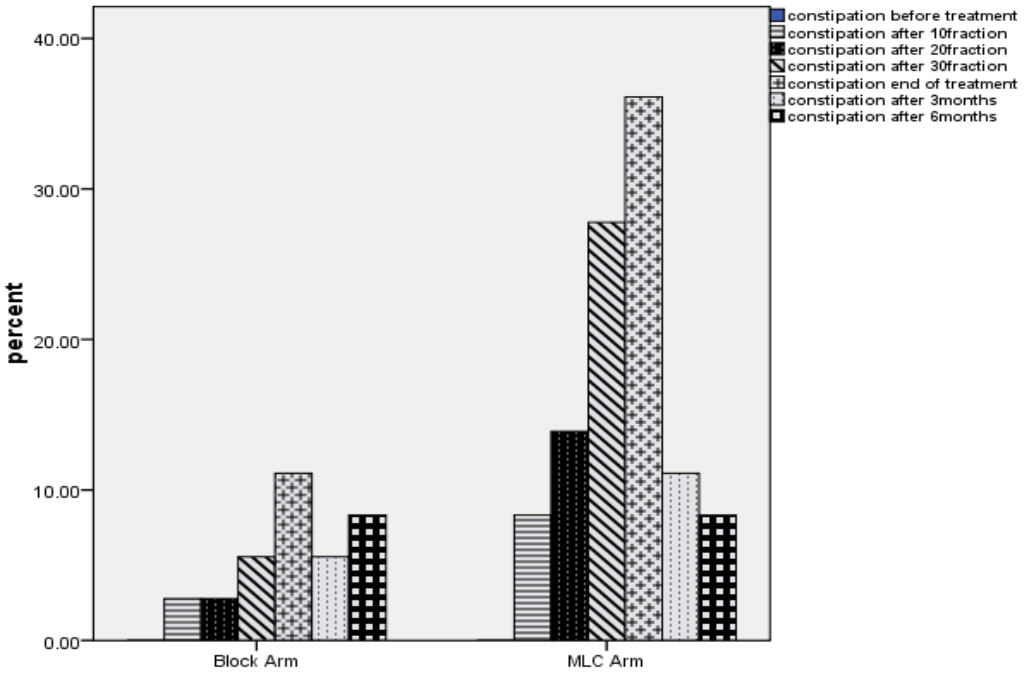

Figure 3 Percentage of constipation in participants in both arms

Table 4.distribution and comparison of acute rectal complication grades in participants in both arms, based on RTOG table

Acute rectal complication		G0	G1	G2	G3	G4	total
Block Arm	frequency	14	15	6	1	0	36
	percentage	38.9	41.6	16.7	2.8	0	100
MLC Arm	frequency	14	16	5	1	0	36
	percentage	38.9	44.4	13.9	2.8	0	100
significant level		NS	NS	NS	NS	NS	-

Mann- Whitney test didn't show a significant difference in the grades of acute rectal complications in both arms.

Table 5. Distribution and comparison of acute bladder complications grades in participants in both arms, based on RTOG table.

Acute bladder complication		**G0**	**G1**	**G2**	**G3**	**G4**	**total**
Block Arm	frequency	2	16	16	2	0	36
	percentage	5.6	44.4	44.4	5.6	0	100
MLC Arm	frequency	9	10	16	1	0	36
	percentage	25	27.8	44.4	2.8	0	100
significant level		NS	NS	NS	NS	NS	-

By using Mann- Whitney, it was determined that, based on RTOG table, acute bladder complication grades had no significant effect in both arms.

Table 6.distribution and comparison of delayed rectal complications in participants in both arms, based on LENT table.

Acute rectal complication		G0	G1	G2	G3	G4	total
Block Arm	frequency	32	3	1	0	0	36
	percentage	88.9	8.3	2.8	0	0	100
MLC Arm	frequency	29	4	2	1	0	36
	percentage	8.5	11.1	5.6	2.8	0	100
significant level		NS	NS	NS	NS	NS	-

Mann- Whitney test didn't show any significant difference in the delayed rectal complication grades among patients in both arms.

Table 7.distribution and comparison of delayed bladder complication in participants in both arms, based on LENT table.

Acute bladder complication		G0	G1	G2	G3	G4	total
Arm 1	frequency	31	2	1	2	0	36
	percentage	86	5.6	2.8	5.6	0	100
Arm 2	frequency	26	4	1	5	0	36
	percentage	72.2	11.1	2.8	13.9	0	100
significant level		NS	NS	NS	NS	NS	-

Mann- Whitney test didn't show any significant difference in various grades of delayed bladder complication among patients in both arms.

Table 8.Dose-Volume Histogram

ritical structure	Rectum(prostate cancer)							
	Custom block Arm							
Total dose	74 Gy	72 Gy	68 Gy	70 Gy	65 Gy	64 Gy	76 Gy	73 Gy
Mean Dose	41.51Gy	51.57Gy	48.5Gy	47Gy	40.87Gy	37GY	48.12GY	48.22Gy
Volume	V40	V40	V40	V40	V40	V40	V40	V40
Dose/Volume	<46.8%	<70%	<54%	<55%	<45%	<30%	<75%	<57%
Volume	V50	V50	V50	V50	V50	V50	V50	V50
Dose/Volume	<47%	<70%	<47%	<46%	<36%	<23%	<36%	<43%
Volume	V60	V60	V60	V60	V60	V60	V60	V60
Dose/Volume	<21%	<42%	<15%	<14%	<11%	<13%	<19%	<27%
Volume	V65	V65	V65	V65	V65	V65	V65	V65
Dose/Volume	<16%	<35%	<12%	<11%	<9%	<10%	<14%	<22%
Volume	V70	V70	V70	V70	V70	V70	V70	V70
Dose/Volume	<11%	<17%	<8%	<7%	<5%	<4%	<9%	<17%

MLC Arm								
Total dose	**74 Gy**	**72 Gy**	**68 Gy**	**70 Gy**	**65 Gy**	**64 Gy**	**63 Gy**	**66 Gy**
Mean Dose	**43.7 Gy**	**54.15 Gy**	**51 Gy**	**51 Gy**	**42 Gy**	**37 Gy**	**36 Gy**	**39 Gy**
Volume	V40	V40	V40	V40	V40	V40	V40	V40
Dose/Volume	<51%	<74%	<58 %	<58%	<50 %	<33%	<65%	<67%
Volume	V50	V50	V50	V50	V50	V50	V50	V50
Dose/Volume	<48%	<74%	<54 %	<51%	<42 %	<30%	<48%	<56%
Volume	V60	V60	V60	V60	V60	V60	V60	V60
Dose/Volume	<25%	<44%	<21 %	<18%	<15 %	<14%	<23%	<42%
Volume	V65	V65	V65	V65	V65	V65	V65	V65
Dose/Volume	<16%	<41%	<15 %	<14%	<13 %	<12%	<15%	<14%
Volume	V70	V70	V70	V70	V70	V70	V70	V70
Dose/Volume	<14%	<19%	<10 %	<11%	<9%	<6%	<10%	8%

Critical structure	**Bladder(prostate cancer)**							
Costum Block Arm								
Total dose	74 Gy	72 Gy	68 Gy	70 Gy	65 Gy	64 Gy	76 Gy	73 Gy
Mean Dose	49 Gy	46 Gy	45 Gy	45 Gy	39 Gy	40 Gy	64 Gy	55 Gy
Volume	V40	V40	V40	V40	V40	V40	V40	V40
Dose/Volume	<73%	<71%	<70%	<70%	<63%	<63%	<75%	<69%
Volume	V65	V65	V65	V65	V65	V65	V65	V65
Dose/Volume	<23%	<8%	<8%	<8.5%	<9%	<11%	<30%	<29%
Volume	V70	V70	V70	V70	V70	V70	V70	V70
Dose/Volume	<14%	<10.5 %	<6%	<5%	<7%	<8.5%	<15.5%	<11.5%
MLC Arm								
Total dose	74 Gy	72 Gy	68 Gy	70 Gy	65 Gy	64 Gy	63 Gy	66 Gy
Mean Dose	52 Gy	50 Gy	47 Gy	50 Gy	42 Gy	43 Gy	41 Gy	45 Gy
Volume	V40	V40	V40	V40	V40	V40	V40	V40
Dose/Volume	<74%	<73%	<63%	<66%	<64%	<64%	<64%	<57%
Volume	V65	V65	V65	V65	V65	V65	V65	V65
Dose/Volume	<25.5%	<12%	<11%	<10%	<12%	<15%	<10.5%	<13%
Volume	V70	V70	V70	V70	V70	V70	V70	V70
Dose/Volume	<17%	<11%	<10%	<8%	<10%	<10.5 %	<9%	<10%

DISCUSSION

Acute radiotherapy complications have affected patients' life quality significantly. Acute digestive complications would occur during or soon after treatment with such signs as pain and irritation, bleeding, constipation, diarrhea, mucus effusion, excrement urgency and distress [9, 10]. In addition to imposing care costs, acute radiotherapy reactions resulted in subsequent late complications [11]. Crock et .al research (2001) showed that, among 202 patients with prostate cancer, totally 25% and 11% had mild and acute complications, respectively [12]. Talarli et.al (2006) has studied dosage uptake by critical organs in patients treated with Block and MLC

3- D CRT. Finally, it was shown that dosage uptake by bladder, rectum and femur by MLC method was more than custom block [13]. Robert lee et.al (1996) in one investigation on 257 patients with prostate cancer treated with 3-D CRT has considered the effect of dosage volume in the incidence of delayed rectal complications. 18 patients showed 2-3 grades complications. The most prevalent complications were anal bleeding [2]. This research, by considering and comparing acute and delayed rectal and bladder complications among patients in 1 and 2 arm showed that patients had a significant difference in urinary frequency complication after 10 sessions (27.8% against 55.6%), ($p<0.02$), also, 3 months after the completion of treatment (11.1% against 30.6%) ($p<0.04$). By comparison of patients in both arms, it was determined that they had a significant difference in dysuria after completion of treatment (44.4% against 19.4%) ($p <0.02$). Comparison of patients in regard to constipation complication in both arms showed that, after 30 sessions, they had significant difference (5.6% against 27.8%), ($p<0.02$). After completion, they had significant difference (11.1% against 36.1%), ($p< 0.02$). Sexual dysfunction were seen in trifle of patients in both groups which may caused by irradiation of penile bulb.

Anal non-bleeding and reduced bladder complications after 6 month of termination of radiotherapy course, probably, results from small volume irradiation exposed to 70 Gy of absorbed dose.

CONCLUSION

In summary, here we showed early (Acute) complications produced by multileafs method is more than custom block method, but in the comparison of grades of complications based on RTOG/LENT tables, it was not observed a significant difference. Answering this question needs complementary study that, of both treatment methods, which one is preferable in regard to incidence of less clinical complication in rectum and bladder.

"The authors declare no conflict of interest"

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