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Planning study to optimize the dose for low-risk prostate cancer with two IMRT techniques

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SUMMARY

Purpose: The aim of this work is a comparison study of the plan quality betwe en two techniques of a common Intensity Modulated Radiation Therapy (IMRT) was performed to optimize the dose for low risk prostate cancer.

Materials and methods: Based on CT datasets of ten patients with prostate cancer treated at our institution were randomly selected for this study. To optimize the IMRT technique, Two IMRTs configurations, differing for gantry angle direction, were tested for each patient. The first technique (IMRT-S) was used as reference plan utilized a five beams configuration, standard for prostate cancer treatment in our institution, and the second technique (IMRT-OP) combining five plans with five beams for each (25 beams in total), changing beam directions every 7 sessions level (70Gy in 35 fractions) to be irradiated. Plan quality was evaluated by comparing Homogeneity Index (HI), Conformity Index (CI), monitor units (MUs) especially dose volume statistics of the Organs at Risk (OAR) from each technique.

Results: For the same Planning Target Volume (PTV) coverage, the IMRT-OP plans show superior dose homogeneity and conformity in PTV compared to IMRT-S technique. Target coverage was almost similar for both techniques. The sparing of Rectum in terms of 70Gy dose was better in the IMRT-OP technique by 4.9% when compared to the IMRT-S technique. A considerable reduction in 65Gy dose to the Bladder by 3.4% was observed with the IMRT-OP. At the end Remarkable reduction of the dose received at the femoral heads between 36.31% and 53.30% always in favour of the IMRT-OP technique.

Conclusion: Considering the superior quality of the IMRT-OP plan compared to IMRT-S, IMRT-OP may be the preferred modality for centres that don't have VMAT technique for the treatment of prostate cancer, taking into account significant improvements in OARs.

Key words: IMRT, Planning study, Prostate cancer ,HI, CI, OAR

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INTRODUCTION

Prostate cancer is the most common malignant tumour in men. Patients with localized prostate cancer have several treatment options, including prostatectomy, brachytherapy, and External Beam Radiation Therapy (EBRT) [1]. In recent years, Intensity Modulated Radiation Therapy (IMRT) has become the standard of care for delivering external beam radiation therapy, using multiple beams of radiation of different shapes and intensities delivered at a wide range of angles to paint Radiation dose to the tumour, and allows a higher dose of radiation to be delivered to the prostate while reducing the dose to surrounding organs.

IMRT is the approach of delivering non-uniform radiation beam fluencies to produce a uniform dose distribution that maximizes dose to the tumour volume while minimizing dose to normal tissue and critical structures [2]. There are several ways for delivering IMRT. A conventional Multi Leaf Collimator (MLC), originally designed for blocking fields, delivers IMRT by either using multiple field segments (called segmental MLC, SMLC, or "step and shoot" IMRT), which can supply a discrete number of intensities [3], or by having the leaf pairs move across the field at a varying rate (called dynamic MLC, DMLC, or "sliding window" IMRT) to deliver the modulated fields [4]. IMRT can lead to improved conformity of the high dose region to the tumour and requires more accurate delineation of both tumour and normal tissue than conventional radiotherapy. Additional normal tissue often has to be delineated because tissue that is not specified can receive unexpected high doses [5].

Another approach, called Volumetric Modulated Arc Therapy (VMAT), proposed by Otto et al. [6]. VMAT allows for rapid delivery of highly conformal dose distribution. In prostate and Head-and-Neck (HN) VMAT delivered with Varian Rapidarc, literature has shown that double arc plans provide better PTV dose homogeneity than single arc, and at least similar sparing of Organs at Risk (OAR). In addition, the quality of the plane increases when more than two arcs are used, and therefore several entries of the beams, due to the increase in the degrees of freedom [7-8].

In order to reduce de dose for organs at risk, we hypothesized that using different entries (IMRT-OP) of beams (combining 5 plans with 5 beams for each plan) ensure a good plan quality than IMRT-S. In the current study, we found that, when the plan qualities of both modalities were optimized for the best that we

Tab.1. Second optimized technique

	Gantry angles				
Plan 1	0	72	144	216	288
Plan 2	15	87	159	231	303
Plan 3	30	102	174	246	316
Plan 4	45	117	189	261	333
Plan 5	60	132	204	276	348

can achieve, (IMRT-OP) generally had a superior plan quality compared to the standard IMRT-S with 5-beams configuration (see Results section). However, intuitively, increased number of beam directions brings increased intensity modulations and therefore an improvement in IMRT plan quality [9].

In this study, a comparative treatment planning of 2 IMRT techniques was performed. Specifically, we compared the plan quality of IMRT-S (Standard IMRT) to that IMRT-OP (Optimized IMRT) combining 5 plans with 5 beams (Different entries for each combination).

MATERIALS AND METHODS

Ten patients with low risk tumors of the prostate cancer were selected for this retrospective planning comparison. All patients were immobilized in supine position; immobilization was achieved using knee and foot support as immobilization device. CT simulation was performed in 3-mm slices using Siemens Somatom Sensation Open CT (Siemens, Erlangen, Germany).

Planning Target Volume (PTV) and clinical target volume (CTV) are drawn according to the definition given by international commission on radiation units and measurements for one dose level (70Gy in 35 fractions) to be irradiated [10]. A total dose of 70 Gy is delivered to PTV consisting of the gross tumour volume. Clinical treatments were delivered with five fixed-gantry field using the sliding window technique. To optimize the IMRT technique, Two IMRTs configurations, differing for gantry angles direction, were tested for each patient. The first standard technique (IMRT-S) was done by five equally spaced fields (gantry angles: 0°, 72º, 144º, 216º, 288°). In the second optimized technique (IMRT-OP) composed of 5 plans with 5 beams for each as shown in the table 1.

Dose optimization was carried on according to the institution protocol. Dose normalization was set as median dose. OAR's included bladder, rectum, and femoral heads. All plans were generated with 6 MV x-rays delivered with a Varian Clinac DHX 2300. Optimization and calculations were done in the Varian Eclipse treatment planning system (version 10.0.28). As a planning objective for PTV coverage, at least the 95% of the prescribed dose was requested to cover 95% of the target volume. In addition, 107% of the prescribed dose was set as an upper limit on the near-maximum dose D2%, that is the dose to the 'hottest' 2% volume of PTV (D2%<107%) [5].

As for OARs, the main planning objective was to minimise the dose as much as possible while keeping the maximum homogeneity and conformity index of the dose to the PTV. The dose for rectum should be within the following constraints V70Gy≤25%, V60Gy≤45% and V50Gy≤50%. For the bladder, the dose should be V70Gy≤25% and V65Gy≤50% and for the femoral heads V55Gy≤5% and V50Gy≤10% as suggested in the Radiation Therapy Oncology Group (RTOG) [11]. After the completion of treatment planning, plan quality was assessed by analysing the Dose-Volume Histograms (DVH) of PTVs and OARs, and comparing results with the planning objectives and constraints.

The Homogeneity Index (HI) was used to evaluate the homogeneity of the dose in the PTV, as defined by the formula:

HI=(D2%-D98%)/D50%

An HI of zero indicates that the absorbed-dose distribution is almost homogeneous. D50% is suggested as the normalization value [5]. Moreover, the degree of conformity has been evaluated by calculating a radiation Conformity Index (CI) of the dose to the PTV volume, according to ICRU definition [12].

CI=VRI/VTV

Where VRI is the volume of 95% of the prescribed dose and VTV the total volume of the PTV. With this definition, CI=1 corresponds to the ideal conformity. If CI is larger than 1, healthy tissues are irradiated. If CI is less than 1, the target volume is only partially irradiated.

Statistical differences among the dosimetric results of the used techniques were analysed using the paired-sample Wilcoxon's test.

RESULTS

All treatment techniques produced clinically good plans for all the patients. As an example, Figure 1 shows representative axial sections depicting dose distributions obtained with the two planning comparison techniques of dose distribution of IMRT-OP plan with the corresponding IMRT-S, in the three orthogonal planes through the isocenter, for one patient of the sample.

PTV dosimetric evaluations

Tables 2 and 3 provide an overview of the results of PTV coverage, homogeneity, conformity, doses to OARs and plan MU's for the two treatment techniques, the average values were reported for each technique. In the rightmost column, statistically significant differences among technique pairs are reported.

All the treatment plans were evaluated using dose volume histograms (DVHs). In Figure 2, the DVH of PTV for the two irradiation techniques is reported.

In the following, the main results are presented separately for PTV and OAR's. As reported in table 2, no significant

Tab. 2. Dosimetric results for PTV, CI, HI and p value for the sample patients

	Objective	IMRT-S	IMRT-OP	Wilcoxon test (*p*<0.05)
PTV	Prescription at dose median	70Gy	70Gy	--
	$D_{98\%}$ ≥ 95%	97.05 ± 0.91	97.77 ± 0.78	0.05 (none)
	$D_{2\%}$ ≤107%	102.11 ± 0,44	101.94 ± 0.53	0.26 (none)
Homogeneity Index(HI)	0	0.05 ± 0.01	0.04 ± 0.009	0.03
Conformity Index(CI)	1	1.20 ± 0.110	1.14 ± 0.059	0.04
MU	--	517 ± 79.67	513 ± 74.25	0.13 (none)

Tab. 3. Dosimetric results for the OARs and p value for the sample patients

OAR	Objective	IMRT-S	IMRT-OP	Wilcoxon test (*p*<0.05)
Rectum	V70Gy≤25%	56.43 ± 4.77	53.79 ± 5.04	0.02
	V60Gy≤45%	40.73 ± 3.64	39.76 ± 3.25	0.04
	V50Gy≤50%	37.75 ± 3.15	36.99 ± 3.82	0.22 (none)
Bladder	V70Gy≤25%	60.17 ± 4.84	56.90 ± 4.36	0.30 (none)
	V65Gy≤50%	39.24 ± 3.34	37.96 ± 2.79	0.03
Right femoral head	V55Gy≤5%	31.55 ± 2.58	23.66 ± 3.59	0.03
	V50Gy≤10%	29.91 ± 2.71	19.51 ± 3.14	0.01
Left femoral head	V55Gy≤5%	31.42 ± 3.40	23.05 ± 4.37	0.02
	V50Gy≤10%	30.03 ± 3.31	21.13 ± 4.11	0.04

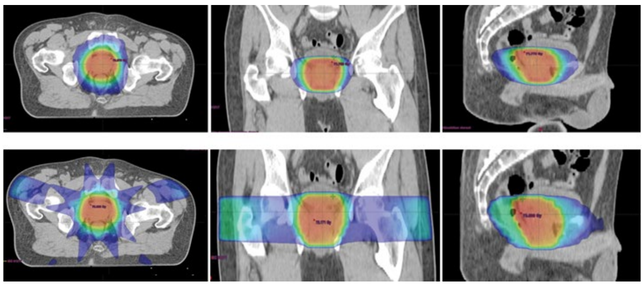

Fig. 1. Dose comparison of IMRT-OP technique (upper) and IMRT-S (lower) in a sample

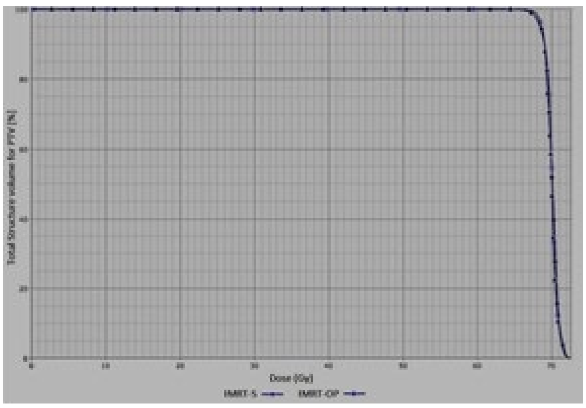

Fig. 2. DVH of PTV in the sample patients for the two investigated techniques

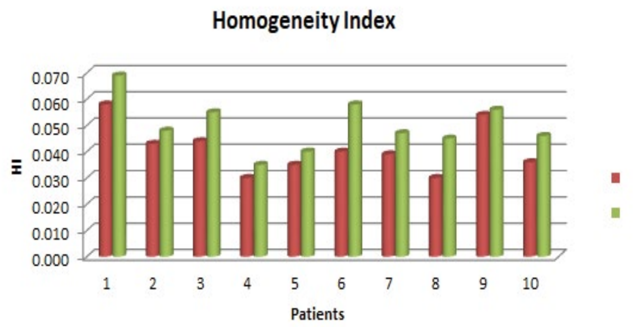

Fig. 3. Homogeneity Index (HI) of the two techniques for each sample patient

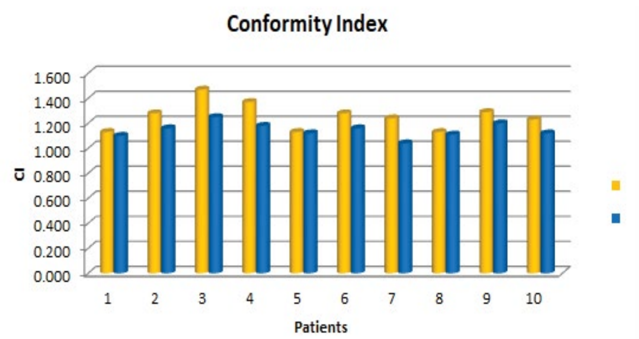

Fig. 4. Conformity Index (CI) of the two techniques for each sample patient

differences difference is observed for the PTV when comparing D98% (97.77 ± 0.78 versus 97.05 ± 0.91 Gy, p=0.05) and D2% (101.94 ± 0.53 versus 102.11 ± 0.44 Gy, p=0.26) obtained with the 2 techniques. Similarly, no significant difference was found for MUs.

For HI, the results were achieved in IMRT-OP and IMRT-S with (0.04 ± 0.009) and (0.05 ± 0.01), respectively, however, the difference between IMRT-OP and IMRT-S is statistically significant with p=0.03. As for CI a significant difference with p=0.04 was found in favour the IMRT-OP than IMRT-S and the results are as follows (1.14 ± 0.059) and (1.20 ± 0.110).

Figure 3 and 4 show the HI and CI of the plans obtained with the 2 techniques for all sample patients.

Organs at Risk (OAR's)

In Figure 5 the DVHs of rectum, bladder and femoral heads for the two irradiation techniques are reported respectively.

Rectum: The dose delivered to the rectum (Table 2) satisfied its constraint for the two considered techniques. For this OAR, IMRT-OP technique shows a significantly lowest value for V70Gy and V60Gy. The sparing of the rectum in terms of 70Gy and 60Gy doses is better in the IMRT-OP technique by 4.9% and 2.4% when compared to IMRT-S technique. No significant difference was found between the two techniques for V50Gy.

Bladder: All plans were able to achieve the objective of the Bladder and IMRT-OP proved to be better in terms of sparing. (Table 3). No statistically significant difference was found for V70Gy, and a considerable reduction by 3.4% was observed with IMRT-OP when compared to the IMRT-S technique in terms of 65Gy as the dose.

Right and Left femoral heads: Femoral heads were adequately spared by both techniques (Table 3). IMRT-OP technique showed significant differences value for V55Gy and for V50Gy. A considerable reduction for left and right femoral heads by 33.34% and 36.31% was observed in constraint dose V55Gy and for V50Gy, there are 53.30% , 42.12% in favour of IMRT-OP.

DISCUSSION

The major advantage of IMRT is the ability to decrease the dose to critical structures, which in turn has been demonstrated to decrease the adverse effects of RT [13-14]. However, compared with 3D-CRT, both IMRT and VMAT result in improved dose distributions compared with 3D-CRT, delivering less dose to normal tissues and maintaining a high dose to the target volume [15].

The aim of this study was to compare the performance of IMRT-OP technique (combining sessions) and a five-field IMRT (IMRT-S) for treatment of prostate cancer with one dose level. IMRT-OP was resulted as the “good technique”, as it was able to globally satisfy the dose volume constraints set for both target coverage/homogeneity and OAR sparing, compared with IMRT-S technique as showed in figure 1. It was found by Enzhuo et al. that when more gantry angles were added to the IMRT plans, the VMAT plan quality was still consistently better until the number of beams in IMRT reached 12-16 beams. At this point, which varied among the patients examined, the IMRT plan quality became similar to or slightly better than that of VMAT [16-17]. Beyond this point, the plan quality of IMRT does not improve noticeably further even if more beams are used. This indicates that, for prostate cancer, the plan quality of VMAT is a limit to which the plan quality of IMRT converges as increasing numbers of beams are used [9] and can reduce hot spots in the PTV where the sum of plans for IMRT-OP compensates for areas of suboptimal dose.

The effect of the number of beams on plan quality has been previously studied by Pirzkall et al. [17], who found that less than 9 beams may result in increased dose in regions far away from the target [18]. Our study showed that the radiation dose to the bladder was found to be better in terms of savings for IMRT-OP. However, the percentage of rectal volume receiving more than 65 Gy and 40 Gy was consistently lower in IMRT-OP than in IMRT-S, and our comparison concludes that the combination of 5 plans with 5 beams for each by changing the beams directions every 7 sessions are able to give the same or better quality for treatment of prostate cancer such as VMAT in one dose-level irradiation. Also, the analysis performed by Cozzi et al. leads to the conclusion that VMAT can reduce the peripheral dose from about 8% at 5 cm to about 30% at 15cm from the PTV surface as shown in the figure 1 [16]. As for the doses to the specific organs at risk, significant differences are observed on average in our study between the IMRT-S and IMRT-OP plans. These differences are in favour of the IMRT-OP plans. Regarding the number of MUs, the IMRT uses a greater number of MU per treatment, which lead to greater interleaf scatter dose and has therefore led to concern about an increased risk of induction of second malignancy [19], and the risk of a second malignancy after RT is dependent, not only on the scatter dose and MUs, but also on the volume of normal tissue receiving low-dose RT [20], and this is our goal in this study using the IMRT-OP technique (combining 5 plans with 5 beams for each, changing the beam directions every 7 sessions) which will lead to reduce the dose to the normal structure, and therefore decrease the probability of secondary malignancies. The main disadvantage of the IMRT-OP planning technique is the increased time required for creating the IMRT plans, as we have to create a new plan after each 7 sessions. But it has many advantages of using IMRT-OP are a physical limit to dose homogeneity for IMRT-S arising from limited leaf speed and the limited number of control points. Also, the IMRT-OP adds more freedom for possible leaf positions. Each plan required only a single optimization session and the same number of optimization steps, independent of the amount of interactive change of the optimization objectives [21].

A final note will be devoted to experimental verification of the accuracy of IMRT delivery against calculation estimates. These activities are mandatory before any clinical activation of a new technique and IMRT must be properly verified.

CONCLUSION

We have demonstrated that the IMRT-OP technique generates significantly superior plans compared to the 5-beam clinical IMRT plans (IMRT-S) used at our institution. Despite of the disadvantage of increased time for creating IMRT-OP plans, and taking in to account the organs at risk protection and plan quality, IMRT-OP may be a good modality for treating prostate cancer.

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