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Intensity-modulated radiotherapy planning for prostate cancer: The evaluation of inter-observer variability and treatment delivery efficiency

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ABSTRACT

Background: The aim of this study was to evaluate inter-observer variability in terms of treatment planning (TP) quality and treatment delivery (TD) efficiency in the setting of IMRT plans and to identify potential optimization objectives that can be implemented in institutional optimization protocols. ***Materials and Methods:*** Four different observers generated IMRT plans for 15 patients with prostate cancer. Plans were evaluated in terms of inter-observer variability considering dosimetric objectives regarding TP quality (using planning target volume (PTV) coverage, conformity index (CI), homogeneity index (HI), organs at risk (OAR) dose constraints and remaining volume at risk (RVR) doses) and regarding TD efficiency (using the mean number of segments, the mean values for total MUs, the mean values for maximum beam MUs and the mean TD time). ***Results:*** Regarding TP quality, there were no clinically significant differences among observers in terms of PTV coverage, CI, HI, OAR dose constraints and RVR doses. Regarding TD efficiency, there were statistically significant differences among observers in terms of the mean number of segments, the mean values for total MUs, the mean values for maximum beam MUs and the mean TD times. ***Conclusions:*** Even for IMRT plans generated according to standardized protocols, TD times significantly differ among planners. The limitation of the number of segments per beam and maximum beam MUs during optimization can lower TD times as well as total MUs and improve TD efficiency. Pre-determined optimization protocols can enable easier transfer of experiences, act as time-savers and result in a more efficient workflow in busy clinics.

INTRODUCTION

Intensity-modulated radiotherapy (IMRT) combines inverse treatment planning (TP) and computer-controlled intensity modulation of the radiation beam to deliver conformal radiotherapy [1]. IMRT is the standard treatment delivery (TD) technique for prostate cancer (Pca), because of its excellent sparing of the surrounding critical structures to reduce genitourinary and gastrointestinal toxicity and the exceptional conformity and homogeneity for planning target volume (PTV) to improve tumor control [2]. Complex IMRT plans result in increased monitor units (MUs) being delivered, prolonged treatment times per fraction and significantly reduced TD efficiency. The increased utilization of IMRT should be accompanied by more efficient TD, without compromising TP quality.

Although TP aims to achieve ideal dosimetric objectives for quality purposes, practitioners should also keep an eye on more efficient TP that translates into more efficient TD in clinical practice. The reasons for more efficient TD are less waiting time with faster TP, improved cost-effectiveness, increased number of patients per treatment machine, shortened treatment durations resulting in better organ motion control and fewer intra-fractional dose uncertainties [3-5]. Muller *et al.* proposed institutional optimization routine to improve TD efficiency without compromising TP quality and have asserted that their approach in this regard following a routine TP procedure can be helpful in daily radiotherapy practice [6].

In addition to conventional IMRT procedures, rotational IMRT paradigms have also been used to reduce TD times using dynamically changing gantry speeds, collimator angles and field shapes [7]. While novel TP systems and software are developed mainly to improve TP quality and shorten TD time, they usually fail to standardize personal preferences. Therefore, TP quality for IMRT applications varies substantially among radiotherapy centers and between planners due to technology available, as well as the planner's personal experience and learning curve [8, 9].

For a department with a heavy patient load, achieving shorter TD times while maintaining adequate (non-inferior and non-compromised) TP quality using TP templates might be a time-saver. Despite acquiring significant experience from the substantial number of patients that have been planned for and treated with modulated rotational approaches, it is essential to evaluate the effects of distinct TP approaches on the achievable TD efficiency. An alternative to conventional fluence-based optimization (FBO, the optimization of fluence maps followed by a leaf sequencing step) is direct aperture optimization (DAO), where the leaf positions and the field weights of multileaf collimator (MLC) apertures are directly optimized to generate plans with equivalent dose distributions with substantially fewer monitor units (MUs) and number of segments [10]. However, the reduction achieved in MUs can differ between planners, even when DAO is used by all of them.

One attempt for improving the radiotherapy routine by developing IMRT optimization guidelines for intra-departmental use only, is to pay greater attention to optimization based on personal preferences, besides technical parameters. The aim of the present study was to evaluate inter-observer variability in terms of TP quality and TD efficiency in the setting of IMRT plans produced by DAO for PCa and to identify potential optimization objectives that can be implemented in institutional optimization protocols.

MATERIALS AND METHODS

The study design was approved by the Institutional Review Board (IRB) of Kocaeli University (KOU KAEK 2012/85 and supplement 2015/10-19). Following IRB approval, permission for the study was granted by the Hospital Administration. Fifteen patients with localized PCa who received definitive radiotherapy were included in the study. Computed tomography (CT) images and contours previously used for actual treatment planning were retrospectively collected for the study purposes. CT images were de-identified and made available in DICOM format, together with contours, for the observers. Demographics for the patients included in the study were not collected, nor made available to the observers.

Planning computed tomography scanning

The patients were immobilized in a supine position with a full bladder and empty rectum. Using the standard imaging protocol for the Department of Radiation Oncology for patients with prostate cancer, CT images were obtained at a thickness of 0.3 cm.

Delineation of target volumes and organs at risk

Referring to RTOG 0924 protocol [11], clinical tumor volume (CTV) included the prostate and was expanded by 0.6 cm to create PTV. As per RTOG guidelines, the bladder, rectum, bowel bag and femoral heads were delineated as organs at risk (OAR) [12]. The doses delivered to target volumes, OAR and remaining volume at risk (RVR) were prescribed, recorded and reported according to Report 83 by the ICRU.

Dose prescription and treatment planning

Step-and-shoot IMRT plans were generated using Panther TPS (version 5.01, Prowess Inc., Concord, CA). As per RTOG 0924, 75.6 Gy was prescribed for PTV, at 1.8 Gy fractions. Dose constraints for OAR also followed RTOG 0924 [11]. The goal was to deliver 98% of the prescribed dose to PTV, but dose constraints for OAR were given priority over coverage of PTV. Therefore, the goal in the worst-case scenario was to deliver at least 98% of the prescribed dose to CTV and at least 90% of the prescribed dose to PTV.

Plans for the present study were generated by four different observers. Two of them (Observer 1 and Observer 2) had more than five years' experience each in IMRT plans and the remaining observers (Observer 3 and Observer 4) had less than two years'. Each observer independently carried out the plan for each case, blinded to the plans by other observers.

The observers were asked to use a fixed number of (seven) coplanar beams with varying angles. Beam angles were chosen at the observer's discretion, to minimize doses to planning at risk volumes (PRVs) while maximizing PTV coverage. No attempt was made to standardize the optimization method among observers. Optimization objectives such as the segments per beam and the maximum beam MUs were left to the observer's discretion.

Optimization was terminated following the initial achievement of the pre-determined dose constraints for PTV and OAR within a 30-minute limit, to prevent unlimited plan refinement and the resultant unlimited plan complexity.

Dose-volume analysis

Dose-volume histograms (DVHs) were generated for the dose-volume analysis. The maximum dose (D_{max}), the mean dose (D_{mean}) and the minimum dose (D_{min}) for PTV, OAR and the partial volumes of each of these structures receiving a specified dose (VD) were calculated from DVHs.

Plan evaluation and treatment delivery efficiency evaluation

Plans were evaluated in terms of inter-observer variability considering dosimetric objectives regarding TP quality (using PTV coverage, conformity index (CI), homogeneity index (HI), OAR dose constraints and RVR doses) and TP objectives regarding TD efficiency (using the mean number of segments, the mean values for total MUs, the mean values for maximum beam MUs and the mean TD time) [13].

Statistical analysis

Statistical analysis was performed using SPSS for Windows 17.0 (SPSS Inc, Chicago, IL). The one-way analysis of variance (ANOVA) was used to determine whether there were any significant differences between the mean values for the observers. Statistical significance was defined as a p value less than or equal to 0.05.

RESULTS

Based on the evaluation of dosimetric objectives regarding TP quality, there were no clinically significant differences among observers in terms of PTV coverage (figure 1a), CI, HI, OAR dose constraints (figure 1b and figure 1c) and RVR doses (figure 1d). Each of the observers provided treatment plans that were acceptable in daily clinical practice. Further, none of the observers provided treatment plans of significantly superior quality, compared to those of the other observers (table 1).

Based on the evaluation of TP objectives regarding TD efficiency, there were statistically significant differences among observers in terms of the mean number of segments ($p<0.001$), the mean values for total MUs ($p<0.001$), the mean values for maximum beam MUs ($p<0.001$) and the mean TD times ($p<0.001$) (table 2). Personal preferences such as lowering the number of segments and the MUs per beam effectively reduced TD times.

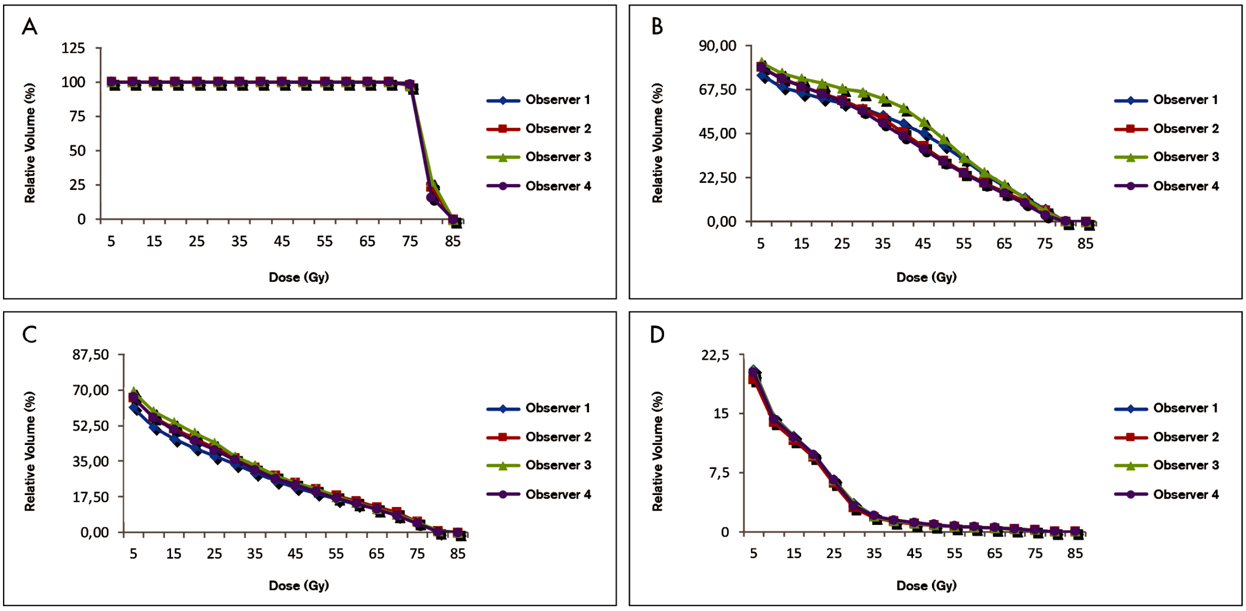

Figure 1. Dose volume histograms (DVHs) for four observers (Observer 1 in blue, Observer 2 in red, Observer 3 in green and Observer 4 in black) demonstrating **(a)** planning target volume (PTV) coverage, **(b)** rectum organ at risk (OAR) doses, **(c)** bladder

Table 1. Dose-volume analysis of dosimetric objectives (planning target volume (PTV) coverage, conformity index (CI), homogeneity index (HI), organs at risk (OAR) dose constraints and remaining volume at risk (RVR) doses for four observers.

Dosimetric Objectives	Observers			
	Observer 1 Mean ± SD	Observer 2 Mean ± SD	Observer 3 Mean ± SD	Observer 4Mean ± SD
PTV				
D_{mean}(Gy)	78.6 ± 0.3	78.8 ± 0.6	78.9 ± 0.3	78.3 ± 0.9
D_{max} (Gy)	81.1 ± 0.7	81.6 ± 1.3	82.2 ± 0.6	82.1 ± 1.2
D_{min} (Gy)	72.9 ± 0.7	72.3 ± 0.5	73.0 ± 0.2	72.6 ± 0.9
CI	0.954 ± 0.002	0.955 ± 0.004	0.953 ± 0.002	0.958 ± 0.011
HI	0.073 ± 0.009	0.079 ± 0.016	0.084 ± 0.006	0.075 ± 0.016
Bladder				
D_{mean} (Gy)	23.6 ± 9.5	25.6 ± 9.5	26.3 ± 9.3	25.0 ± 10.4
D_{max} (Gy)	79.6 ± 1.1	80.2 ± 1.6	81.1 ± 0.7	80.8 ± 1.6
Rectum				
D_{mean} (Gy)	36.0 ± 5.4	34.9 ± 4.4	39.6 ± 3.5	34.2 ± 5.3
D_{max} (Gy)	79.8 ± 0.6	79.6 ± 0.8	79.9 ± 0.8	78.5 ± 1.1
RVR				
D_{mean} (Gy)	4.5 ± 0.7	4.6 ± 0.7	4.8 ± 0.7	4.8 ± 0.7
D_{max} (Gy)	80.7 ± 0.6	81.3 ± 1.2	81.9 ± 0.5	81.7 ± 1.3

Table 2. Analysis of planning objectives (the mean number of segments, the mean values for total monitor units (MUs), the mean values for maximum beam MUs and the mean treatment delivery times) for four observers.

Planning Objectives	Observers				p value
	Observer 1 Mean ± SD	Observer 2 Mean ± SD	Observer 3 Mean ± SD	Observer 4 Mean ± SD	
Number of segments	36 ± 2	43 ± 9	49 ± 2	63 ± 0	< 0.001
Total MUs	317 ± 19	339 ± 39	392 ± 29	366 ± 14	< 0.001
Maximum beam MUs	43 ± 3	45 ± 4	61 ± 6	47 ± 13	< 0.001
Treatment delivery time (seconds)	383 ± 13	443 ± 67	489 ± 16	585 ± 3	< 0.001

DISCUSSION

TD efficiency is as an important output of the planning process. It should not be overlooked for a clear emphasis on TP quality, since inter-observer variations are to be expected, based on the experience level of the planners. Despite universal recommendations for beam arrangements in IMRT planning, there are inherent variations among departments due to the range of TPSs, calculation algorithms, dose- prescribing methods, documented planning and optimization protocols. In a study across 141 oncology centers, Duhmke et al. found treatment failure to be significantly influenced by the quality of RT planning, mostly resulting from inadequate beam arrangements [14]. Departmental protocols regarding institutional experiences and patient diversity can control for inter-observer variations and maintain a high standard for TP quality, while avoiding overly complex IMRT plans. Therefore, planning and optimization templates developed by experienced planners are time-savers.

In this study, the authors aimed to evaluate the variation between observers in terms of TD efficiency, while using the same TPS and adhering to the same TP quality measures in a department with a heavy patient load. The main reason for the considerable variation between observers in terms of TD efficiency was that the optimization step was left at the observer's discretion for minor adjustments, with only major TP goals set. The degree of freedom for optimization objectives needs clearer identification. In a study using a fixed number of beams and a fixed number of gantry angles, it has been shown that the greater the number of segments lead to the better the plan in terms of dose distribution, but only at the expense of increased delivery time [3].

DAO [15, 16] is an inverse planning approach, where the leaf positions and relative weights of segments are optimized, instead of the relative weights of pencil beams. With DAO, the planners have control over the complexity of TP, by specifying the maximum number of segments per beam angle. This can simplify IMRT TP without compromising the plan quality and boost TD efficiency. Although differences between DAO and FBO were previously reported, inter-observer variability in TP has not been explicitly documented. The flexibility provided for the planners to incorporate the number of segments per beam angle and the maximum number of MUs per beam angle as optimization parameters (considering that these are not clearly stated in institutional planning guidelines), can result in treatment plans with similar quality with similar TD efficiency. Accordingly, the optimization formulations in common use for DAO can be modified to have the number of MUs appear as a constraint rather than as an objective, if a reliable bound, which will be case dependent, is known [17]. The present study aimed at evaluating the variations among observers collaborating in the same clinic in terms of TD efficiency, in the setting of IMRT plans produced by DAO. Plans were sought to be kept as uncomplicated as possible yet fulfilling the pre-arranged dose constraints for PTV and OAR. The number of fields per beam angle was preset to seven to reflect an institutional standard and for easier plan comparisons, while all the remaining parameters were at the observer's discretion, barring dosimetric losses.

Though priority was given to TP quality in the present study, observers were expected to use their expertise to experiment with parameters that were not specifically addressed in the planning guidelines (such as the number of segments per beam angle) to come up with treatment plans that were both as close to the ideal scenario as possible and also efficient in terms of TD. Therefore, this study aimed to search for optimization parameters that could result in better TD efficiency without compromising TP quality. In a study evaluating plans produced by DAO with limited number of segments allowed per beam direction, Jiang et al. found that five segments per beam angle were sufficient for many cases, with no need to use more than nine segments per beam angle [18]. Hence, uncomplicated plans in the study referred to at most nine apertures per beam angle. The pre-arranged dose constraints for PTV and OAR were attained by all observers and the measures of TP quality were very similar. Still, there was a significant difference among the observers in terms of TD efficiency, resulting in a significant difference in TD times. The number of segments per beam (mostly 5 for Observer 1) and maximum beam MUs (mostly less than 45 for Observer 1) appeared to be the optimization parameters resulting in non-inferior TP quality with better TD efficiency. Since Observer 1 was one of the most experienced observers in IMRT, this finding supports Everitt et al., who claimed that while pre-determined guidelines and dose constraints ensured upholding of planning standards, they should not override the autonomy and ability of skilled planners to optimize beam angles, number of fields and number of segments [9].

Since highly complex plans are associated with an increased level of dosimetric uncertainty, plan complexity should be balanced with optimal dosimetry. Dosimetric uncertainties, coupled with the increased pressure on limited resources, will lead to less-than-optimal treatment plans when very small fields, low MUs per segment and high overall MUs are used. It is important to reduce the complexity of beamlet-based IMRT plans as much as possible, since excessively complex plans deliver unnecessarily high MUs. It is also desirable to reduce the discrepancy between the optimal treatment solution and the deliverable treatment solution following segmentation [18]. Further, the increase in MUs will lead to higher head leakage, larger scatter and possibly increased radiation-induced malignancies [19, 20]. Based on a linear risk estimate, the risk of radiation-induced malignancies is decreased by a factor of two with DAO, compared to conventional optimization. By using DAO, the risk of radiation-induced malignancies can be kept at the 3D-CRT level, without further compromising plan quality. A limitation of the present study is that the authors did not evaluate the potential clinical relevance of the lower MUs or the lower head leakage through dosimetric measurements. A better way to generalize the results of the present study can be the comparison of TP quality vis-a-vis TD efficiency over the entire spectrum of patients treated in the department, possibly reflecting any clinical relevance.

CONCLUSIONS

In the present study, the observers with the longest experience in IMRT planning (Observer 1 and Observer 2) produced plans with significantly lower mean number of segments, lower mean values for total MUs, lower mean values for maximum beam MUs and lower TD times. These findings indicate that even for IMRT plans generated according to standardized protocols, TD times significantly differ among planners. However, the limitation of the number of segments per beam and maximum beam MUs during optimization can lower TD times as well as total MUs. Therefore, attempts to reduce TD times without compromising TP quality should improve TD efficiency. Pre-determined optimization protocols can enable easier transfer of experiences, act as time-savers and result in a more efficient workflow in busy clinics. Lowering total MUs for TP can lower the integral doses, further enhancing TD efficiency. Long-term clinical follow-up could facilitate the identification of the possible reduction of risks concerning radiation-induced malignancies.

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***Author contribution**:* EYE and HSE designed the study, performed statistical analysis and prepared the manuscript. A.K, MCŞ, AK and BT performed treatment planning and reviewed the manuscript.

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