Analysis of dose distribution in organs at risk in patients with prostate cancer treated with the intensity-modulated radiation therapy and arc technique

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ABSTRACT

This study describes a comparative analysis of treatment plans in 48 patients with prostate cancer treated with ionizing radiation. Each patient was subjected to the intensity-modulated radiation therapy (IMRT) and arc technique. In each treatment plan, the organs at risk were assessed: the urinary bladder, rectum and heads of the femur, as well as the volume of normal tissue. The following features were compared: treatment time, conformity indices for the planning target volume, mean doses and standard deviation in organs at risk, and organ volumes for each particular dose. The treatment period in the arc technique is 13.7% shorter than in the IMRT technique. Comparing the results of the IMRT and arc techniques (arc vs. IMRT), the mean values were 29.21 ± 12.91 Gy versus 28.36 ± 13.79 Gy for the bladder, 20.36 ± 3.16 Gy versus 18.17 ± 5.11 Gy for the right femoral head, and 18.98 ± 3.28 Gy versus 16.67 ± 5.15 Gy for the left femoral head. For the rectum, lower values were obtained after application of the arc technique, not the IMRT technique: 35.84 ± 12.28 Gy versus 35.90 ± 13.05 Gy. The results indicate that the applied therapy has a statistically significant influence on the volume for a particular dose with regard to the urinary bladder. It is advisable to apply the IMRT technique to patients who need the femur heads and urinary bladder protected by exposing them to low irradiation doses.

Key words: Arc technique; intensity-modulated radiation therapy technique; prostate cancer; radiotherapy

Introduction

Prostate cancer is the second most frequently diagnosed neoplastic disease in males in Poland, constituting 13% of neoplasms in 2010. In the last three decades, a five-fold increase has been observed in the number of prostate cancer patients diagnosed in Poland. One of the three methods of treating the growing number of patients affected by this type of cancer is radiotherapy. In recent years, progress in radiotherapy has seen the invention of many modern treatment methods that can efficiently deliver radiation dose to target volumes while protecting healthy tissues and organs.[1-3] Arc[4,5] and intensity-modulated radiation therapy (IMRT)[6] are becoming more popular teleradiotherapy techniques; however, each has its advantages and disadvantages. Hence, the aim of this work was to perform a comparative analysis of treatment plans

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for prostate cancer using the IMRT (five fields) and arc techniques (2 arcs). In this work we present a comparison of doses to organs at risk (OARs) by these two techniques that can be used in assessing the quality of treatment plans. Such a comparison of doses to OARs by two techniques (5 fields IMRT vs. 2 arcs) is not available in the literature in our knowledge.

Methods

A comparative analysis was performed of treatment plans in 48 patients treated with the IMRT and arc techniques in 2014. The plans were done in the Eclipse treatment planning system (Eclipse 10.0, Varian Medical Systems) using AAA calculation algorithm.[7] RapidArc system (Varian) was used for the treatment planning of arc technique. Treatment delivery was done on a Clinac 2300 medical linear accelerator (Varian).

The planning target volume (PTV) included the prostate with seminal vesicles. A margin of 0.9 cm was added to all sides with the exception in the direction of the rectum, where a margin of 0.5 cm was used. The margins were added according to the clinical treatment guidelines and general recommendations.[8,9] The patients were administered a total dose of 70.2 Gy, with fractionated doses of 2.6 Gy each (5 days/week), with the application of photon radiation with a nominal energy of 15 MV. The organs at risk included the urinary bladder, rectum, and heads of the femur (left and right). The volume of healthy tissues located in the pelvis area was also included in the analysis.

Before commencing the treatment procedure, computed tomography was performed on a Siemens Somatom Sensation Open CT-simulator, which was the basis for realization of the treatment plan. During the CT examination and ensuing therapy, the pelvis of the patients was properly immobilized and the patients were instructed to keep their urinary bladder full to provide geometric repeatability.

In the treatment plans where the IMRT technique was applied, five therapeutic fields were used with the following head/collimator/table parameters: 260°/15°/0°, 310°/15°/0°, 50°/345°/0°, 100°/345°/0°, and 180°/0°/0°.[10] In the treatment plans based on the arc technique, two arcs were used with the following collimator/table parameters: clockwise from 181° to 180° and 30°/0° and anti-clockwise from 179° to 180° and 330°/0° [Figure 1].

For each of the 48 patients, two treatment plans were generated - one with the arc and the other by the IMRT technique. A comparative analysis was made for the doses to PTV, healthy tissues, and organs at risk. A number of indices were found for determining irradiation area.[11-14] To
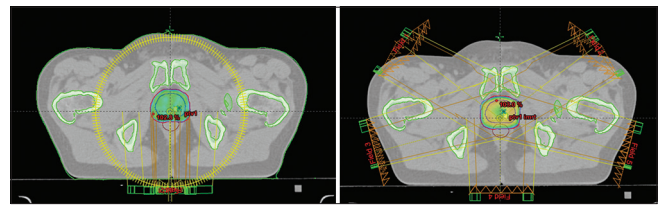

Figure 1: Arc technique – left figure; intensity-modulated radiation therapy technique – right figure

compare PTV values in this study, a conformity index with the following formula was used:[15]

$$CI_{95\%} = V_{95\%}/V_{PTV}$$

where:

$CI_{95\%}$ - conformity index;

$V_{95\%}$ - PTV within 95% isodose;

V_{PTV} - PTV volume

For organs at risk, tolerance doses and volumes are in compliance with internal clinical treatment guidelines. They are presented in Table 1.

No healthy tissues should be irradiated by a dose more than 110% of a prescribed dose.[16]

Mean doses to each OAR were estimated for comparing between techniques.

Statistical analysis
Modern radiotherapeutic methods are similar to each other. Hence, a basic analysis of treatment plans is not sufficient enough to precisely evaluate to what extent organs at risk are exposed to radiation. To make a thorough comparative analysis of the two techniques, standard deviations and dose–volume histograms (DVHs) were interpreted. Statistica 10 software (StatSoft®, Poland) was used for analyses.[17]

Student's t-test
The Student's t-test for independent variables allows a comparison to be made of measurements from two groups. It is used to evaluate the differences between mean values in two groups. The dependent value is a parameter measured in a particular study and its value depends on the selected method. The null hypothesis states that values in both the studied groups are the same. A characteristic feature of the Student's t-test is to emphasize differences in particular cases rather than in differences between mean values for each group.

In this test, $\alpha = 0.05$ was taken as the level of significance. It was assumed that $P < 0.05$ confirms a statistical difference

between the studied measurements. $P \geq 0.05$ indicates that no such differences exist.

Analysis of dose–volume histograms

Histogram analysis was performed using linear models, which allows basic statistical values to be determined and the points in which the two comparable techniques considerably differ from each other to be identified.

The analysis of variance (ANOVA) test was used to conduct a detailed analysis of histograms with repeated measurements.[18-20] The variate test of variances with repeated measurements assesses the impact of the following studied parameters: dose, treatment technique and the relationship between the dose and the treatment technique, and the value of the radiotherapy structure volume (RTSV) ratio. As none of the analyzed variables in this study met the assumption of sphericity, the Greenhouse-Geisser, Huynh-Feldt corrections were used to correct the P values. In all analyses, $\alpha = 0.05$ was adopted as the level of significance. With regard to the study hypothesis, $P < 0.05$ indicates that the studied parameter has an effect on the value of the RTSV ratio, whereas $P \geq 0.05$ indicates that the studied parameter does not have an effect on the value of the RTSV ratio.

The final element of the histogram analysis was a contrast analysis. It is used to assess statistical significance of expected, detailed differences in particular sections of a histogram. *Post hoc* test and the Fisher's least significant difference test (NIR-test) were used to compare irradiation techniques for particular doses. In the NIR-test, the adopted level of significance was $\alpha = 0.05$.

Results

Each of the 48 treatment plans was analyzed with regard to the quality of irradiation of PTV. Precision in dose delivery will probably result in successful therapy and curtail side effects of therapy with ionizing radiation. Table 2 shows the conformity indices for particular treatment techniques.

Irradiation time was also analyzed, as expressed in monitor units (MUs). Table 3 shows a mean value of MUs for one treatment plan realized with the application of the IMRT and arc techniques.

Before conducting a detailed analysis of dose distribution for particular organs, mean doses in particular organs were determined. The results are shown in Table 4.

An essential element of the evaluation of treatment techniques is an analysis of DVHs. Figures 2-6 present the relationship between the dose distribution and the RTSV ratio of an analyzed structure.

Table 1: Dose constraints for each organ at risk

Structure	Dose constrains (%)
Rectum	V65Gy<17
	V35Gy<50
Bladder	V65Gy<25
	V40Gy<50
Femoral head	V50Gy<10

Table 2: Conformity index for each technique

Technique	Conformity index±SD	P
IMRT	0.977±0.012	0.067
Arc	0.982±0.012	

SD: Standard deviation, IMRT: Intensity-modulated radiation therapy

Table 3: Number of monitor units for each technique

Technique	Monitor units±SD	P
IMRT	671.8±96.6	0.000
Arc	579.5±126.6	

SD: Standard deviation, IMRT: Intensity-modulated radiation therapy

Table 4: Mean dose and standard deviation in organ at risk

	Mean dose±SD (Gy)		P
	IMRT	Arc	
Bladder	28.36±13.79	29.21±12.91	0.130
Rectum	35.90±13.05	35.84±12.28	0.806
Right femoral head	18.17±5.11	20.36±3.16	0.083
Left femoral head	16.67±5.15	18.98±3.28	0.265
Healthy Tissues	3.77±6.36	3.71±5.89	0.208

IMRT: Intensity-modulated radiation therapy, SD: Standard deviation

The ANOVA of particular values of RTSV for organs at risk, carried out with the application of the ANOVA Test, determined which factors influencing RTSV were statistically significant. Such factors were assumed to include a treatment technique and a dose. Another significant parameter in this analysis is the interaction between the treatment technique and dose, which will enable us to know the statistical influence of any of the above factors on the RTSV value to be determined. Table 5 shows the final result of the ANOVA for organs at risk.

The ANOVA shown in Table 5 confirmed the presence of an interaction between treatment technique and dose. Hence, it is justifiable to compare RTSV values in particular doses for the studied treatment techniques. A detailed analysis of the RTSV with the use of the Fisher's least significant difference is shown in Table 6, as well as a comparison of the differences in RTSV values according to dose with percentage RTSV values for the IMRT technique (ΔRTSV).
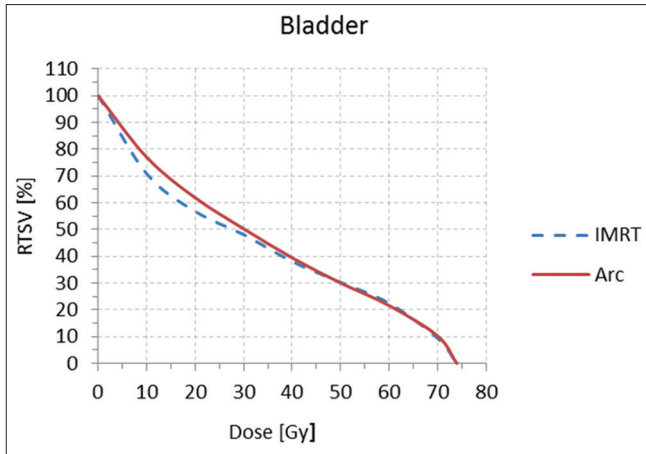
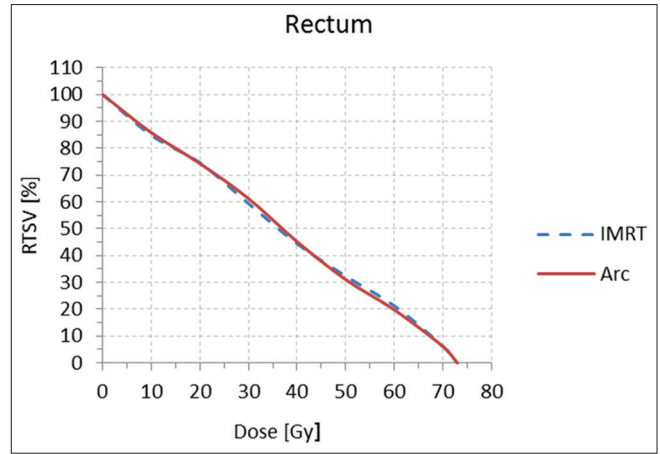Figure 2: Mean dose–volume histogram for bladder

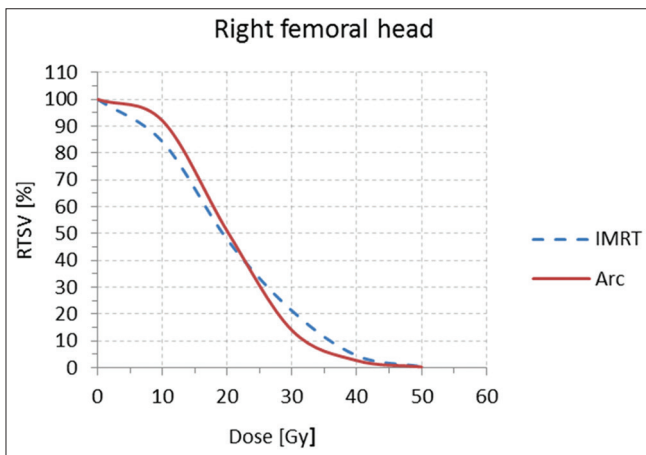
Figure 3: Mean dose–volume histogram for rectum

Figure 4: Mean dose–volume histogram for the right femoral head
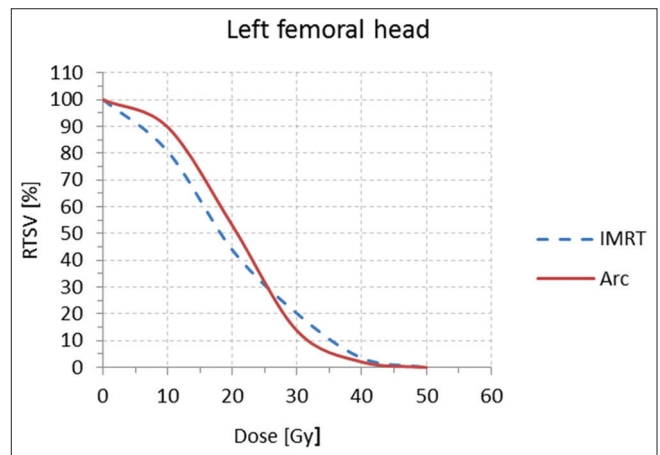

Figure 5: Mean dose–volume histogram for the left femoral head

Table 5: Analysis of variance values for radiotherapy structure volume-treatment technique and dose

	P				
	Bladder	Rectum	Right femoral head	Left femoral head	Healthy tissues
Technique	0.000	0.869	0.852	0.165	0.000
Dose	0.000	0.000	0.000	0.000	0.000
Interaction between technique-dose	0.000	0.001	0.000	0.000	0.000

Discussion

To make a comparative analysis of treatment plans performed with the application of various techniques, one condition must be fulfilled, i.e., the PTVs in each technique must be equally irradiated. To compare the intensity of irradiation, the conformity index was analyzed. The analysis of these indices shown in Table 2 confirms no statistical significance between the obtained values ($P > 0.05$), which in turn, indicates no differences between the plans with regards to the dose coverage of PTV. However, it remains unclear as to what extent the structures located close to the PTV are irradiated.

A statistically significant difference can be seen between the techniques with regard to irradiation time [Table 3]. The treatment time expressed in MUs is 13.7% shorter in the arc technique than in the IMRT technique. In addition, the operator does not need to enter the therapy room to trigger another arc in the arc technique. Unfortunately, the total treatment period is much longer for the IMRT technique as the person setting the next radiation field must be present, which has a great impact on the number of patients treated. The fact that the treatment period in the arc technique is considerably shorter positively contributes to the accuracy of the therapy and increase in patient's comfort.

An analysis of Table 4 confirms that the mean standard deviation is higher for each studied structure for the IMRT technique than the arc technique. The higher value of the standard deviation confirms a greater difference between the dose and the mean value and thus, a greater difference in the distribution in the studied structure. Unfortunately, the analysis of standard deviations does not indicate the size of the dose to which the whole structure is exposed. To identify slight differences, more parameters of treatment plans should be analyzed.

Table 6: Analysis of dose–volume histogram – the Fisher's least significant difference test (NIR-test)

	Dose (Gy)	RTSV (%) (mean value)		P test NIR	$|\Delta RTSV|$ (%)
		IMRT	Arc		
Bladder	10	70.87±3.14	77.02±3.08	0.000	8.68
	20	56.83±3.21	61.91±3.36	0.000	8.93
	30	48.17±2.97	50.34±3.22	0.000	4.50
	40	38.75±2.45	39.49±2.64	0.013	1.91
	50	30.32±2.00	30.08±2.15	0.658	0.79
	60	22.51±1.64	21.66±1.69	0.121	3.78
	70	9.46±1.03	10.33±1.01	0.117	9.20
Rectum	10	85.01±1.56	86.08±1.65	0.090	1.26
	20	74.67±1.87	74.45±2.00	0.722	0.29
	30	59.42±1.90	61.25±2.36	0.004	3.08
	40	44.44±1.48	45.13±1.86	0.277	1.55
	50	32.36±1.19	31.04±1.30	0.038	4.08
	60	21.27±0.99	19.80±1.06	0.020	6.91
	70	6.19±1.68	6.14±0.65	0.941	0.81
Right femoral head	10	84.22±2.76	92.22±1.57	0.001	9.50
	20	47.77±3.55	50.89±4.59	0.179	6.53
	30	21.86±2.96	13.96±3.58	0.001	36.14
	40	4.56±1.31	2.74±1.39	0.432	39.91
Left femoral head	10	80.65±3.17	89.70±2.13	0.000	11.22
	20	43.85±3.57	52.99±4.59	0.000	20.84
	30	20.11±2.56	13.67±3.23	0.005	32.02
	40	3.55±0.94	2.10±0.72	0.519	40.85
Healthy tissues	10	10.46±1.83	12.44±2.11	0.000	18.93
	20	6.50±1.13	5.01±1.22	0.000	22.92
	30	3.53±0.71	2.25±0.72	0.000	36.26
	40	1.49±0.37	1.13±0.37	0.000	24.16
	50	0.69±0.17	0.57±0.15	0.084	17.39
	60	0.34±0.09	0.28±0.08	0.413	17.64

RTSV: Radiotherapy structure volume-treatment, IMRT: Intensity-modulated radiation therapy, NIR: Fisher's least significant difference test
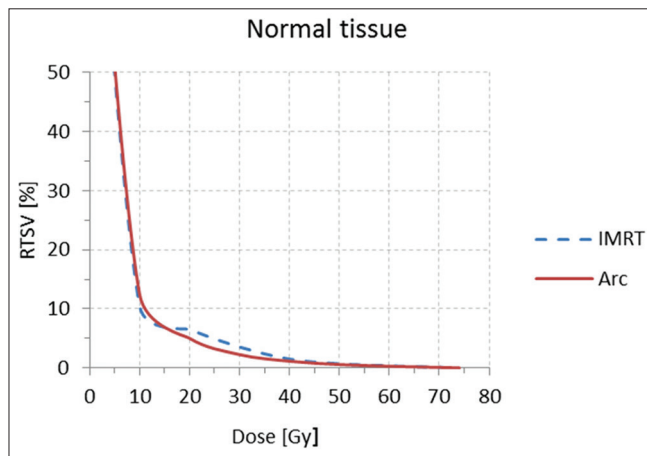

Figure 6: Mean dose–volume histogram for normal tissue

In the first stage, the mean dose planned for the OAR was determined on the basis of an analysis of dose distribution in the volume of the studied structure. The analysis presented in Table 4 demonstrates that the larger differences in the mean dose are observed for the heads of the right (12.0%) and left (13.9%) femur. A higher mean value can be observed in the arc technique. A difference in mean doses is also noticeable for the urinary bladder, wherein the mean value is 3% higher in the arc technique than the IMRT technique. For the rectum, the difference in the mean doses is lower than 0.5%. It is worth emphasizing that all the values shown in Table 4 are not statistically significant, which confirms the fact that the mean dose in the volume is not a reliable parameter to compare plans where differences in dose distribution are scarcely noticeable. Hence, it is necessary to conduct a detailed analysis of the dose, depending on the volume of the studied structure.

The urinary bladder is an organ which requires special attention during radiotherapy. By following suitable bladder protocol, it is possible to daily reproduce same level of bladder fill as that observed in the treatment plan. The RTSV value for the urinary bladder, in the range of 0–40 Gy, is lower in the IMRT technique than in the arc technique. For doses above 40 Gy, the difference between these two techniques is small and it remains within the margin of error. The results of the Fisher's least significant difference test [Table 6] indicate that the RTSV values for the urinary bladder are significant up to a dose of 40 Gy, while these values are not significant above 40 Gy.

While preparing treatment plans, every effort is made to protect the rectum against the application of overdoses, as these might be harmful for the patient. The distribution of doses in the rectum is similar in the two treatment techniques [Figure 3]. A significant difference was observed in the RTSV value only for doses 30, 50, and 60 Gy [Table 6]. However, it should be pointed out that the *P* value was 12.5 times smaller than 0.05 for a dose of 30 Gy; the other *P* values were smaller about 0.012 for 50 Gy and 0.03 for 60 Gy, but these differences cannot be considered significant.

A lower RTSV value was observed for doses up to 20 Gy for the heads of the right and left femur examined with the IMRT technique. For doses above 20 Gy, this tendency is reversed. For the head of the right femur, a significant difference in the RTSV value was observed for doses of 10 and 30 Gy, whereas for the head of the left femur, significant differences were noted for doses ranging from 10 to 30 Gy. The results shown in Table 6 confirm the most noticeable differences in RTSV values between the two treatment techniques. For particular doses, the difference in RTSV value with regard to the heads of the right and left femur ranges from 10% to 40%.

We also analyzed the doses to healthy tissues located around the PTV. Here, lower RTSV values were observed for doses up to 10 Gy after the IMRT technique. Above 10 Gy, the RTSV value was lower for the arc technique. Significant differences between the techniques can be observed up to a dose of 40 Gy. In the arc technique, a greater volume of healthy tissues receives a lower dose in comparison to the IMRT technique.

The ANOVA test provided interesting observations [Table 5]. It showed that the applied technique has a significant influence on the RTSV value of the urinary bladder and volume of healthy tissues, however no such a relationship was observed with regard to other organs at risk. The value of RTSV depends on the applied dose and this regularity is observed in each studied structure. The ANOVA test confirms that in each studied organ, there is a characteristic interaction between the applied technique and irradiation dose. Hence, for some ranges of doses, the applied technique contributes to a change in the RTSV value and the change is dose-dependent.

There are many publications that describe differences between IMRT and arc technique in prostate cancer.[2,21-29] Table 7 shows the mean doses or volume structure in OAR in publication which describes the treatment planning with two arcs or five fields in IMRT. The results of mean doses or volume structure in OAR in these plans are similar to results obtained in this work. The differences in the results are from dose prescription in PTV or optimization parameters. We did not find publications which compared

treatment plans using two arcs and five fields IMRT technique.

Conclusions

The IMRT and arc techniques are commonly followed techniques in the treatment of patients with ionizing radiation. They are equivalent techniques, which we confirmed in our study. Both the techniques allow an advanced procedure of modeling distribution to be applied in patients and they both effectively irradiate PTV, which is the most required condition for their clinical application. The arc technique required a shorter irradiation period than the IMRT technique. The analysis of exposure of organs at risk to radiation confirmed the greatest differences in the heads of the femur and in the urinary bladder for doses below 20 Gy and 40 Gy. The IMRT technique outperforms the arc technique with regard to the exposure of healthy tissues to radiation for low doses (<10 Gy). To protect the heads of the femur and the urinary bladder, it is advisable to apply the IMRT technique at low radiation doses.

Table 7: Summary of mean doses and volume structure in organ at risk in intensity-modulated radiation therapy and arc techniques in various treatment planning

	IMRT	Arc
Yoo *et al.*[25]*		
Bladder (Gy)	39.8	41.3
Rectum (Gy)	35.3	37.5
Small bowel (Gy)	17.8	19.2
Wolff *et al.*[30]*		
Rectum (Gy)	34.9	38.8
Guckenberger *et al.*[26]*		
Rectum (%)		
V70Gy	4.1	8.1
V40Gy	22.8	22.0
Bladder (%)		
V70Gy	7.3	6.8
V40Gy	30.0	26.5
Zhang *et al.*[22]**		
Rectum (Gy)	49.7	49.7
Bladder (Gy)	46.1	45.1
Ost *et al.*[24]**		
Rectum (%)		
V70Gy	14.0	9.0
V40Gy	70.0	43.0
Bladder (%)		
V70Gy	8.6	7.5
V40Gy	40.3	30.1
Femoral head (%)		
V20Gy	80.0	50.0
V30Gy	49.0	20.0
V40Gy	11.0	4.0

*7 fields IMRT-2 arches, **5 fields IMRT-1 arches. IMRT: Intensity-modulated radiation therapy

Conflicts of interest

There are no conflicts of interest.

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