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COMPARISON OF VOLUMETRIC ARC MODULATED RADIOTHERAPY AND 3D CONFORMAL RADIOTHERAPY IN PROSTATE BED IRRADIATION

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Summary

Prostate cancer has the highest incidence in male population in Croatia and radiotherapy has been used as a treatment choice for decades. Volumetric modulated arc therapy (VMAT) is a newer radiotherapy technique used at our department for the last year. In our study we performed the estimation of quality improvement achieved by VMAT radiation technique in comparison to 3D CRT for prostate bed irradiation. Conformity Index (CI) and dose delivered to organs at risk (OARs) have been observed. VMAT was superior in achieving more conformal dose. This method was also significantly better at sparing surrounding OARs, especially rectum and femoral heads.

KEYWORDS: *prostate cancer, volumetric modulated arc therapy, 3D conformal radiotherapy*

INTRODUCTION

Prostate cancer is the most common cancer in male population and makes up to 21% of newly diagnosed cases of cancer in males in Croatia(1). Adenocarcinoma is the most common type of prostate cancer. There are several curative treatment options of localized prostate cancer including external beam radiation therapy (EBRT) with or without androgen deprivation therapy (ADT), interstitial brachytherapy and surgery. All of these treatments have specific indications, and each of them has its benefits and possible side effects. The regular determination of prostate specific antigen (PSA) level in follow up after the treatment of prostate cancer is the most important factor in monitoring patient's response to the therapy.

Radiotherapy plays an important role in the treating patients with prostate cancer for decades whether the treatment is curative or palliative. The equipment and techniques of radiotherapy are constantly improving over the time, enabling the more precise tumor treatments with efficient protection of normal tissues.

In the past, the standard of care was two dimensional (2D) radiotherapy and treatment plans were delivered using radiographs and anatomical knowledge. The use of CT scanning for radiotherapy planning and introducing of three dimensional conformal radiotherapy (3D CRT) made it possible to distribute radiation dose shaped like target volume, thus sparing normal tissues. Treatment planning involves contouring the target volume and organs at risk by a radiation oncologist, and manual optimization by a physicist. In order to achieve

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volumetric adaptation, the physicist picks radiation beam parameters including number of beams, beam weights, shapes and directions(2-4).

Further advances in technology have made it possible to develop linear accelerators that are able to deliver higher doses of radiation to target volume. In year 2007, volumetric modulated arc therapy (VMAT) has been introduced as a new rotation based radiation technique. VMAT technology uses a dynamic modulated arc in order to deliver radiation dose which means that rotation of the beam relative to the patient is integrated with delivery of the radiation dose (it is time conserving because the whole target volume is treated at the same time and the rotation does not stop to deliver radiation). It facilitates highly conformal treatment and spares normal tissue around the target by simultaneously coordinating gantry rotation, motion of the multileaf collimator (MLC), and dose rate modulation. Almost every gantry angle is available. VMAT treatment planning differs from planning techniques where physicist manually chooses all beam parameters. This planning method is called inverse planning meaning that dose distribution parameters for target volume and organs at risk are set into the treatment planning software. The computer then uses algorithm that calculates set of photon beam intensities that produce optimal dose distribution(5-12).

So called *salvage radiotherapy* is a radiation treatment that is indicated in case of recurrent prostate cancer after a period of observation following prostatectomy. The recurrence is not yet clinically visible, but determined by the increased prostate specific antigen (PSA) level. Persistent growth of PSA level following prostatectomy may indicate local or metastatic disease. The goal of salvage radiotherapy is to acquire local control of the disease and to prevent or delay occurrence of metastases by the prostate bed irradiation(3,4,6)

The aim of this study was to compare radiotherapy treatment plans for prostate bed irradiation (salvage radiotherapy) using two different techniques: 3D conformal radiotherapy (3D CRT) and volumetric modulated arc radiotherapy (VMAT).

MATERIALS AND METHODS

Fourteen patients (median age 70, in the range 59 to 81 years) undergoing volumetric modulated arc therapy (VMAT) for prostate bed irradiation were included in this study. All patients had biochemically recurrent prostate cancer after prostatectomy, and absence of distant metastases. CT simulation was performed on CT Siemens Somatom Sensation Open with slice thickness of 2 mm. VMAT and 3D CRT treatments were performed using Varian Truebeam linear accelerator with high definition MLC. All patients were treated in the supine position with their feet positioned with FeetSupport™ pad. The patients were instructed to void their bladder and then drink 500 ml of water 30 minutes prior to CT simulation and for each fraction of VMAT treatment according to department internal protocol. Clinical target volume (CTV) and organs at risk (rectum, urinary bladder and femoral heads) were delineated by radiation oncologists. CTV includes prostate bed. Borders of prostate bed delineation according to RTOG are 3-4 cm above the superior edge of pubic symphysis superiorly (includes seminal vesicles), 8-12 mm below vesico-urethral anastomosis (may include slice above penile bulb if vesico-urethral anastomosis is not visible), posterior edge of pubic bone anteriorly, anterior rectal wall (contours may need to be concave around rectum wall in order to include rectoprostatic angles), and levator ani or obturator internus muscles laterally. PTV included CTV plus 8-10 mm uniform margin, and prescribed dose of 66 Gy was applied in 33 daily fractions(2,13-14). Dose to PTV should be between 95% and 107% according to International Commission on Radiological Units and Measurements Reports 50, 62 and 83(15).

These simulation CT datasets were used to design 2 treatment plans for each patient (VMAT and 3D-CRT). All treatments were planned using treatment planning system (TPS) Eclipse 15.5 (Varian Medical Systems Nederland B.V.). 3D CRT was planned using box technique where contributions of the beams were modified in order to achieve better rectum protection. The primary goal during planning was to achieve equal PTV coverage for both techniques (Homogeneity Index was set to be equal for both 3D CRT and VMAT treatment), and the second goal was to reduce radiation dose delivered to OAR. VMAT treatment planning was performed using two or four arcs, with couch rotation up to 7º and collimator rotation between 330º and 30º. Two rings around PTV were used for optimization, as well as volume of

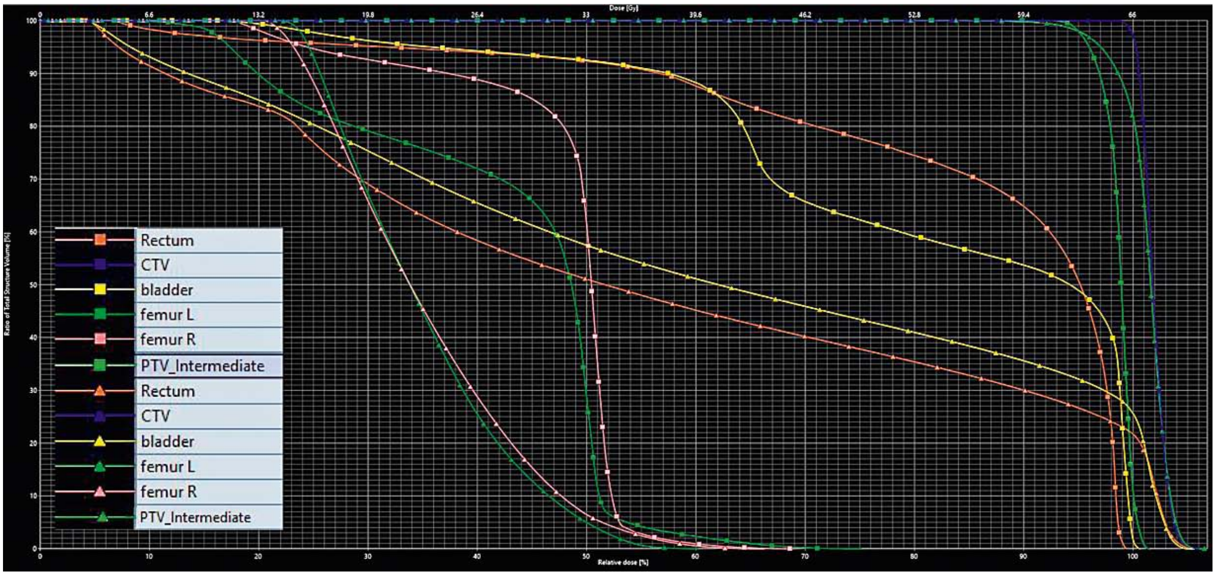

Figure 1. DVH comparison of VMAT and 3D CRT for prostate bed irradiation. VMAT treatment plan lines are shown with squares, and 3D CRT with triangles

rectum without PTV and volume of bladder without PTV. These additional structures were generated in order to reduce dose delivered to OAR.

All VMAT plans were controlled by portal dosimetry using gamma analysis with dose tolerance of 3% and 1 mm. Before every treatment cone beam CT was performed in order to control patient positioning.

One of the most important steps in radiotherapy treatment planning is to evaluate quality of the plan. Radiotherapy plan quality can be assessed using different qualitative and quantitative parameters. The constitutional aspect of plan evaluation is to assess calculated dose distribution which is often based on dose volume histograms (DVH). DVH is unable to show spatial distribution of the radiation dose (16). An example of comparative DVH is shown in Figure 1.

Homogeneity Index (HI) is the ratio between volume of PTV that receives 95%-107% (11) of dose and total volume of PTV:

$$HI\left(95\%-107\%\right)=\frac{V_{PTV(95\%-107\%)}}{V_{PTV}}$$

HI of 1 represents the ideal uniform dose within a target volume.

Conformity Index was calculated as a ratio of volume treated at a given isodose (95%) to the treated volume:

$$CI=\left(\frac{V_{PTV(95\%)}}{V_{PTV}}\right)x\left(\frac{V_{PTV(95\%)}}{V_{Isodose(95\%)}}\right)$$

where $V_{PTV(95\%)}$ is volume of PTV that gets 95% or more of the radiation dose, $V_{Isodose\ 95\%}$ is volume of tissue that gets 95% or more of the dose, and V_{PTV} is total volume of PTV. This index is less than 1 in most clinical cases. A value of 1 indicates that none of the 95% dose is delivered to normal tissue surrounding the target volume(16).

The priority of treatment planning is to define target volume dose and constraints to OARs. OAR dosage constraints are based on clinical studies of the acceptable toxicity of radiation dose delivered to a certain organ. Dosage constraints protocol for prostate bed irradiation used in our department is shown in Table 1(2,17,18).

Table 1.

Dosage constraints protocol for OARs according to QUANTEC (17-18)

	Dose (Gy)	Volume (%)
Rectum	50 60 65	50 35 25
Bladder	65	50
Femoral head	50	50

Table 2.
*VMAT and 3D CRT plan comparison (statistically significant values **bolded**)*

	3D CRT	VMAT	p-value
$V_{Isodose\ 95\%}$ ($cm^{3)}$)	407,4 ± 116,3	324,3 ± 82,1	**0,04**
$V_{PTV\ 95\%}$ ($cm^{3)}$)	306,9 ± 81,6	306,6 ± 81,5	0,99
Conformity Index	0,73 ± 0,04	0,91 ± 0,02	**<0,0001**
Rectum V40 Gy (%)	71,9 ± 16,1	37,2 ± 12,9	**<0,0001**
Rectum V50 Gy (%)	53,9 ± 18,7	30,1 ± 10,9	**0,0004**
Rectum V60 Gy (%)	43,6 ± 17,8	22,5 ± 8,6	**0,0005**
Rectum V66 Gy (%)	7,2 ± 10,2	6,8 ± 6,7	0,9
Rectum D_{mean} (Gy)	49,0 ± 7,0	33,8 ± 8,5	**<0,0001**
Bladder V40Gy (%)	83,4 ± 25,1	60,3 ± 23,2	**0,02**
Bladder V50Gy (%)	69,3 ± 26,5	54,9 ± 23,3	0,14
Bladder V60Gy (%)	62,2 ± 25,7	48,8 ± 23,0	0,16
Bladder V66 Gy (%)	22,6 ± 22,7	21,6 ± 23,6	0,91
Bladder D_{mean} (Gy)	53,2 ± 13,8	44,3 ± 14,1	0,1
Femoral head left D_{mean} (Gy)	24,1 ± 5,0	13,0 ± 5,3	**<0,0001**
Femoral head left D_{max} (Gy)	41,0 ± 8,9	29,8 ± 7,2	**0,0011**
Femoral head right D_{mean} (Gy)	26,0 ± 4,3	12,1 ± 5,3	**<0,0001**
Femoral head right D_{max} (Gy)	40,3 ± 8,3	29,0 ± 6,6	0,0005

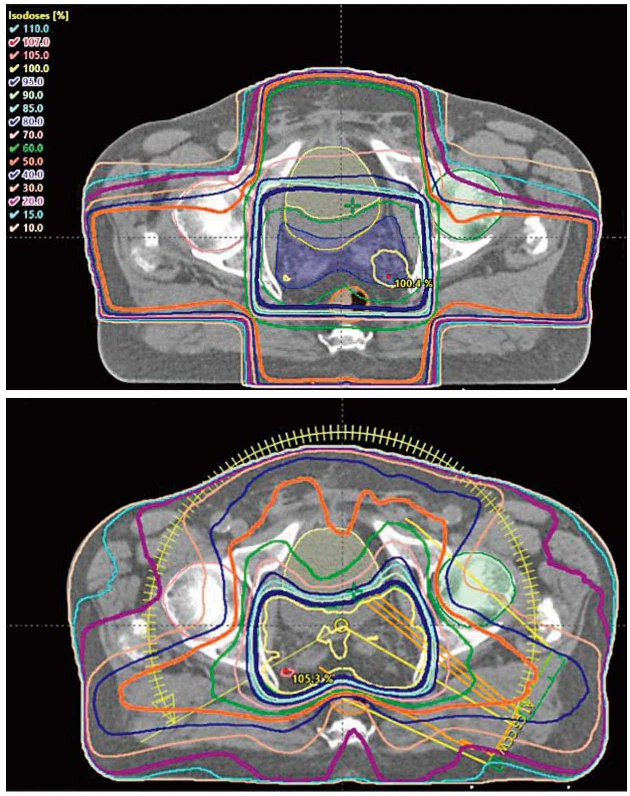

Figure 2. Comparison of isodose lines in VMAT (lower image) and 3D CRT (upper image)

Statistical analysis was performed using the student t-test, and p-value below 0,05 was considered statistically significant.

RESULTS AND DISCUSSION

Comparison of DVH (shown in Figure 1) was used in order to graphically compare 3D CRT and VMAT. We can observe that PTV curves for both techniques are similar because HI was set to be equal for both techniques. It is also important to emphasize that OAR curves decrease in lower doses using VMAT treatment planning than with 3D CRT. This means that higher doses of radiation are delivered to larger volume of OARs with 3D CRT.

Conformity Index, volume of rectum and bladder that receive 40 Gy, 50 Gy, 60 Gy and 66 Gy, mean dose delivered to rectum, bladder and femoral heads, and maximum dose femoral heads receive are values used to compare these two treatment techniques. Conformity index was calculated with the foremost mentioned formula(4,16).

As compared to 3D CRT, Conformity Index for VMAT was significantly better. Mean CI for VMAT was 0,91 (±0,02) and for 3D CRT 0,73 (±0.04) with p-value <0,0001. Hence, larger volume of tissue outside of PTV is receiving 95% of the prescribed dose using 3D CRT. This can be observed in Figure 2 where isodose line distribution is shown for both techniques. Medium and high doses isodose lines are distributed to lower risk tissues, thus sparing OARs. Low dose isodose line in VMAT shows more homogenous dose distribution.

A significant statistical difference was found using VMAT technique in terms of reducing the volume of rectum that receives 40 Gy (p<0,0001), 50 Gy (p=0,0004), 60 Gy (p=0,0005), and mean dose delivered to rectum (p<0,0001) with VMAT technique compared to 3D CRT (mean values shown in Table 2). Regarding the bladder, VMAT was able to significantly reduce volume that receives 40 Gy (p=0,02). VMAT was superior in reducing the mean (p<0,0001 for both sides) and maximum dose (p=0,0005 - right, p=0,0011 - left) delivered to femoral heads. These results are in the concordance to previous data(3,4,5,7). Analysis of the volume of rectum and bladder that receive prescribed dose of 66 Gy showed no statistical difference with both techniques. Mean values of V66 for both rectum and bladder are similar due to the fact that portions of rectum and bladder are included in PTV. Analysis of volume of bladder that received 50 Gy and 60 Gy and mean dose delivered to bladder showed no statistically significant difference. These values can be explained by multiple factors, but it is reasonable to assume it is caused by the low number of participants in the study. It is necessary to increase number of participants in order to clarify this situation.

Target coverage and sparing of the normal tissue should be a fundamental factor in selection of the treatment(4). A statistically significant difference between the two techniques was observed in 10 out of 15 parameters. Considering all variables from Table 2, VMAT achieves better overall protection of OARs and other tissues surrounding the target volume compared to 3D CRT.

CONCLUSION

It was possible to compare VMAT and 3D CRT for prostate bed irradiation. This study shows that VMAT achieves superior conformity index, thus reducing radiation dose to tissue surrounding the target volume. Furthermore, VMAT significantly reduced dose delivered to rectum, femoral heads and bladder. VMAT should be the treatment of choice for prostate bed irradiation in our department for the patients with recurrent prostate cancer after prostatectomy.

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Sažetak

USPOREDBA VOLUMETRIJSKI MODULIRANE LUČNE RADIOTERAPIJE I 3D KONFORMALNE RADIOTERAPIJE LEŽIŠTA PROSTATE

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Rak prostate ima najvišu stopu incidencije u muškoj populaciji u Hrvatskoj, a radioterapija se desetljećima koristi kao terapijski izbor. Volumetrijski modulirana lučna terapija (VMAT) je novija tehnika radioterapije koja se u zadnjih godinu dana koristi u našoj ustanovi. U ovom radu uspoređivali smo VMAT s 3D konformalnom radioterapijom (3D CRT) kod provođenja zračenja ležišta prostate. Promatrane vrijednosti bile su indeks konformalnosti i doza zračenja na organe od rizika (OAR). VMAT-om su dobivene bolje vrijednosti indeksa konformalnosti. Ova metoda također je značajno bolja u poštedi organa od rizika, posebice rektuma i glavica femura.

KLJUČNE RIJEČI: *rak prostate, volumetrijski modulirana lučna terapija, 3D konformalna radioterapija*