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Scientific Paper

Stereotactic radiosurgery of prostate cancer – dose distribution for VMAT and CyberKnife techniques

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Abstract

New capabilities of biomedical accelerators allow for very precise depositing of the radiation dose and imaging verification during the therapy. In addition, computer algorithms calculating dose distributions are taking into account the increasing number of physical effects. Therefore, administration of high dose fractionation, which is consistent with radiobiology used in oncology, becomes safer and safer. Stereotactic radiosurgery (SRS), which is very precise irradiation with high dose fractionation is increasingly widespread use in radiotherapy of prostate cancer. For this purpose different biomedical accelerators are used. The aim of this study is to compare dose distributions for two techniques: VMAT and CyberKnife. Statistical analysis was performed for the two groups of patients treated by VMAT technique (25 patients), and CyberKnife technique (15 patients). The analysis shows that the dose distributions are comparable, both in the treated area (prostate) and in the critical organs (rectum, urinary bladder, femoral heads). The results show that stereotactic radiosurgery of prostate cancer can be carried out on CyberKnife accelerator as well as on the classical accelerator with the use of VMAT technique.

Key words: CyberKnife; VMAT; stereotactic radiosurgery; coefficients of treatment plan evaluation.

Introduction

In recent years, there is an increase in radiotherapy treatment of patients with stereotactic radiosurgery techniques. Why is it happening? From the point of view of radiobiology, the higher the dose the higher the probability of cell destruction; precisely - cell: both, normal and cancer. Treatment planning is therefore employed to minimize the dose in healthy cells and at the same time giving the highest dose in the area of tumor cells. Of course, there must be methods providing such calculated dose to minimize the likelihood of complications and maximize the likelihood of cure. Modern biomedical accelerators enable realization of this objective. In the techniques of stereotactic radiosurgery [1] it is planned to give high dose fractionation, which increases the likelihood of a local cure. However, the higher dose fractionation causes more "load" to critical organs [2]. To minimize the increase of the dose in critical organs should be used the latest techniques of irradiation. Undoubtedly, such techniques in radiotherapy are Volumetric Modulated ArcTcherapy (VMAT), which is realized by means of the classical biomedical accelerator and CyberKnife (CK) - which is implemented by the biomedical accelerator where accelerating (electrons) section is installed on the arm of an industrial robot, which enables directing a beam of radiation from all directions [3,4] (**figure 1**).

Dedicated software, algorithms for dose distribution calculation that include more physical effects of radiation interaction with the environment, along with the technical possibilities of modern accelerators allow the use of increasingly higher fractionation doses, higher compared to the dose of 2 Gy. The technical possibilities of modern radiotherapy, algorithms for dose distribution calculation, imaging methods (both before treatment and during its execution) make it possible to preserve the value of the tolerance dose in critical organs while simultaneously increasing dose in the irradiated volume. Therefore, the therapeutic index is increased [5]. Of course, using such technique of irradiation, we must be sure that we will irradiate the area, which was scheduled for treatment. In the conventionally fractionated irradiation, fractionation doses are much lower (approx. 2 Gy) and the total treatment time is longer, so "minor" shifts during each fraction (in different directions) causes that the average displacement of planned volume with respect to realized is close to zero. It can be assumed that the resolution of the uncertainties of the patient position at the time of a large number of fractions will be decomposed into normal distribution. The situation is different in the case of one or few fractions, that are used in stereotactic technique, which is why it is necessary to verify patient position during each treatment.

Figure 1: Biomedical accelerator [A] for VMAT technique, equipped with a high-resolution multileaf collimator, [B] - CyberKnife equipped with wheel collimators. Both accelerators generates photon radiation (X-6 MV) and are equipped with the X-ray imaging. Despite the technical differences, these accelerators, are perfectly suited to the stereotactic radiosurgery implementation.

In this field, the modern therapeutic devices meet our expectations. Available is kV imaging (kilovolts: 50 - 150 kV), MV (radiation of 3 - 6 MV) and ultrasonography. These devices are an integral part of the accelerator or they are only temporary connected to it, they perform 2D (two-dimensional) and 3D imaging [6,7]. It seems that these are the basic reasons why in recent years we note the increase in the number of stereotactic treatments. Radiotherapists and medical physicists have access to therapeutic apparatus that allow to increase the dose in the tumor volume, while maintaining tolerance dose in critical organs, and ability to perform the imaging verification of the performed therapy. Radiosurgery can be performed by a variety of biomedical accelerators, which use a different geometry of the radiation beams. VMAT technique involves circulation of the radiation source around the patient with the simultaneous adjustment of the shape of the beam field, while the CyberKnife technique uses wheel collimators, the number of radiation beams is much higher than 200, and the shape of the irradiation field does not change during a therapeutic session. Despite the differences, the dose distributions meet the expectations of therapy. Having therapeutic apparatus, which in various ways implement the calculated dose distributions, it is worth to compare these dose distributions performed by different apparatus dedicated for stereotactic treatment.

Aim of the study

Comparison of dose distributions for two stereotactic techniques in treatment of prostate cancer: CyberKnife (Accuray) and VMAT (Varian Clinac 23EX). The analysis is based on the coefficients evaluating the dose distributions: Quality of Coverage (RTOG), Conformal Index (COIN), Conformity Index RTOG and RPI [8,9]. We tried to answer the question whether stereotactic radiotherapy, due to the dose distributions, can be implemented on different biomedical accelerators.

Material and Methods

Stereotactic radiotherapy is performed in the Oncology Centre - Maria Sklodowska-Curie Institute in Gliwice since 2001, and since 2010 it is also used in the treatment of prostate cancer. There are two techniques of radiotherapy: VMAT on the accelerator Clinac/ TrueBeam series of Varian Medical Systems (Palo Alto, Ca, USA) and the CyberKnife (CK) of Accuray (USA). The analysis is performed for two groups of patients treated with different protocols on two different biomedical accelerators. High-risk patients (T1 - T3a), who were treated with VMAT technique, received stereotactic BOOST therapy (three fractions in the area of prostate 6.67 Gy / fraction - given in 5-7 days before the start of conventional radiotherapy and 10-14 days after its ending). The total (physical) dose was of 70 Gy [10]. While low-risk patients (T1c-T2a), were treated with the CyberKnife accelerator, were irradiated only radiosurgically, fractional dose of 7.25 Gy in five fractions to a total dose of 36.25 Gy in the 10 days [11]. Since in both schemes total dose and dose fractionation method are different, it was decided to compare the relative doses: VMAT: 6,67 Gy x 3 = 20,01 Gy = 100% and CK: 36,25 Gy = 7,25 Gy x 5 = 100%. It should be noted that the way of defining of therapeutic dose is related to the technique of irradiation, in the case of VMAT: 98% of the planned dose covers at least 95% of the PTV (Planning Target Volume). In both groups the entire volume of the prostate was defined as PTV. In the case of CK: the planned dose is defined on the "isodose", depending on the patient ranging from 75% to 85%. Acceptable dosage (percentage, total, physical) to critical organs (rectum, urinary bladder, and femoral heads) are shown in **table 1**. For dose distribution calculation the AAA algorithm (Eclipse - Varian Medical Systems) [12] and the Ray-Tracking algorithm (MultiPlan – Accuray) [13] were used for VMAT and CyberKnife techniques respectively. **Figure 2** shows typical examples of dose distribution for VMAT and CK technique, from which it appears that therapeutic doses, as well as the doses in the critical organs are comparable.

The way of "preparation" of the patient to the therapeutic session is also different: patients treated with VMAT technique were informed that the bladder has to be "partially" filled, while in the CK group bladder had to be completely filled. There were 25 patients in the group irradiated with VMAT technique and 15 patients in the CK group. These are different groups of actually treated patients, therefore statistical analysis applies to independent groups, and because of the group size - non-parametric tests were used. In order to assess doses in analysed volumes, PTV and critical organs, we used nonparametric Mann-Whitney U test and the level of significance was set at 0.05. In the VMAT technique 1 or 2 full arches were used, in the CK - from 150 to 300 beams. Before the start of the therapeutic session plans made for CK and VMAT techniques were checked dosimetrically; we performed the verification plans on test phantoms and then for both techniques we carried out measurements of the absolute point dose and analysis of fluence maps for VMAT technique. During therapeutic session, imaging verification was performed with use of the kV radiation. For the CK technique two diagonal images were performed before the therapeutic session, in order to correlate the assumed and actual orientation of the patient. Because patients have placed markers (three) in the prostate gland, it is possible to adjust the position of the patient during the therapeutic session. When exposure is activated, the imaging verification is performed by taking kV image in time intervals ranging from 3 to 180 seconds, depending on the mobility of the patient during session. For the VMAT technique two orthogonal images were performed before the irradiation, in order to correlate the assumed and actual orientation of the patient. Upon acceptance of the patient position, CB/CT testing is performed to assess the position of the prostate, rectum, and urinary bladder. This test allows also the evaluation of the rectum and urinary bladder dimensions as compared to the reference conditions (i.e., those for which the dose distribution calculations were performed). After completion of the therapeutic session kV orthogonal images (X-rays) are again performed to evaluate the shift of the patient during session. Log file containing information about the actual movement of the collimator leaves is also stored. CB/CT testing allows to perform the actual contours of organs and dose reconstruction based on the actual motion of the collimator leaves allows to present the actual dose distribution in the irradiated area [14,15]. This analysis is not the subject of this paper, which focuses on the comparison of the physical dose distributions in the two treatment techniques for prostate cancer.

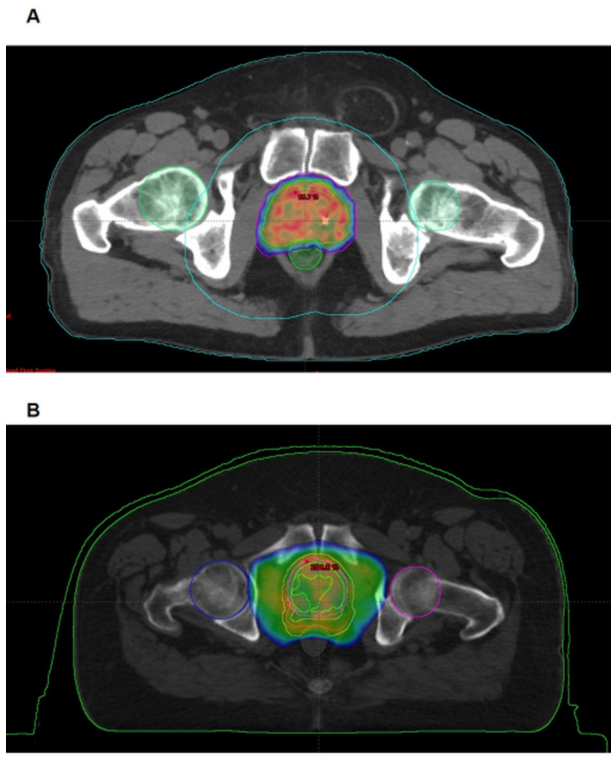

Figure 2: The dose distributions in a plane transverse for CK [A] and VMAT [B] techniques. The doses are shown in relative values, normalized to 100% of a therapeutic dose (planned), the doses values from 80% to 105%: 80% of the dose volume for CK is less than for VMAT technique. The difference between the patient setup is clearly visible: for CK technique patient laid in vacuum mattress while for VMAT technique thermoplastic mask was used for patient stabilization.

Table 1: Volume of critical organs and acceptable doses, which are defined in two irradiation protocols, which correlates with the two treatment techniques. In CK technique total dose (D_{Tot}) is of 36.25 Gy, whereas in the VMAT technique of 70 Gy: 50 Gy, in 2 Gy portions (conventional) and 20 Gy - as a stereotactic BOOST.

Rectum		Bladder		Femoral heads	
VMAT	CK	VMAT	CK	VMAT	CK
$V_{50\%}$-60%D_{tot}	$V_{50\%}$- 50% D_{tot}	$V_{55\%}$-60% D_{tot}	$V_{55\%}$-50%D_{tot}	$V_{45\%}$-57% D_{tot}	$V_{45\%}$-70% D_{tot}
$V_{30\%}$-80%D_{tot}	$V_{20\%}$- 80%D_{tot}	$V_{35\%}$-80% D_{tot}	$V_{25\%}$-80% D_{tot}		
$V_{15\%}$-90%D_{tot}	V_{10}- 90%D_{tot}	$V_{20\%}$-90% D_{tot}	$V_{15\%}$-90% D_{tot}		
$V_{5\%}$-95% D_{tot}	$V_{5\%}$- 100% D_{tot}	$V_{10\%}$-100%D_{tot}	$V_{10\%}$-100% D_{tot}		

Results and Discussion

The first stage of the statistical analysis was evaluation of the defined treatment volumes and critical organs. **Table 2** shows the planning target volume of prostate (PTV) and the volume of anatomical structures. The defined mean value of PTV for CK was 50.93 cm^3, while for VMAT technique - 48.39 cm^3, the differences are not statistically significant. Similarly to the differences between volume of the rectum and femoral heads. However, the difference between the volume of the urinary bladder is statistically significant: 327.76 cm^3 - CK vs. 185.28 cm^3 - VMAT. This difference is linked to the treatment protocol; patients treated with CK technique were informed that the urinary bladder had to be completely filled.

One of the dose distribution parameters evaluated during the acceptance of the treatment plan is the value of the minimum dose in the irradiated volume (PTV). Because of the way of defining the dose in CK technique, the average minimum dose is 87%, while in the VMAT technique is 96.59%, the difference is statistically significant (**table 3**). It should be noted that the way of defining of the therapeutic dose is associated with a possibility of obtaining an acceptable dose distribution. The standard deviation in CK technique is two times higher than in the VMAT technique; 3.54 (CK) vs 1.62 (VMAT), the difference is statistically significant. This means that dose homogeneity in the VMAT is greater than in CK technique. The second, no less important parameter for the assessment of the plan and the dose distribution is the value of the maximum dose to the critical organs. Performed calculations show that they are comparable for the two treatment techniques, the differences between them are not statistically significant. This is a very interesting result, especially since the volume of the urinary bladder in the CK technique is almost twice higher than in the VMAT technique. Despite this, the maximum dose in this organ is similar for both techniques. One could think how would look the dose distribution in CK technique, if the patients were irradiated with "medium-filled" urinary bladder, as is recommended in the treatment with VMAT technique.

Taking into account the minimum dose in PTV, it can be concluded that for the VMAT technique, it is higher in this area and the standard deviation is lower than for the CyberKnife technique (differences are statistically significant). By contrast, the maximum doses in critical organs are comparable, the differences between them are not statistically significant. The average value of the dose throughout the irradiated area is 5.05% for VMAT and 5.33% for CK technique ($p = 0.0743$). Based on the performed analysis it can be concluded that in spite of different protocols, irradiation and methods of patient preparation, dose distributions are comparable and acceptable, meet the requirements of treatment protocols. Particularly important are the maximum doses in the critical organs. Therefore, we also carried out the analysis evaluating what percentage volume of PTV, urinary bladder and rectum is covered by a therapeutic dose. The results are shown in **table 4**. The performed analysis shows that in the CK technique more than 95% of the planning target volume (PTV) received a therapeutic dose, while in the VMAT technique only 75% (statistical significance $p < 0.05$). However, almost 7% of the urinary bladder receive therapeutic dose using the CyberKnife technique while only 4% with the VMAT technique (the difference is not statistically significant $p = 0.0653$). Even bigger is the difference between the volumes of the rectum, respectively nearly 5% for CK and only 0.5% for VMAT technique (in this case the difference is statistically significant, $p < 0.05$). These results are not surprising if we go back to the way of defining of the therapeutic dose in both treatment techniques. Undoubtedly defining of dose on the isodose of 80% in the CyberKnife technique causes that "almost" entire planning target volume is covered by the therapeutic dose, but the maximum dose is much higher than for VMAT technique, as a consequence, larger volumes of critical organs are given a therapeutic dose.

Table 2: The average values of the volume of critical organs and PTV in both irradiation techniques and the "p" coefficient evaluating statistical significance.

	PTV [ccm]	Bladder [ccm]	Rectum [ccm]	Femoral heads [ccm]	
				right	left
VMAT	48.39	185.28	87.28	67.03	66.97
CK	50.93	327.76	71.14	67.78	66.51
p	0.7751	**0.0022**	0.2604	0.8294	0.9020

Table 3: Minimum doses in PTV and maximum doses in critical organs for both analyzed techniques. Statically significant differences exist for the minimum doses and standard deviations between CK and VMAT techniques.

	Dose [%] minimum	Standard deviation	Dose [%] maximum			
	PTV	PTV	Bladder	Rectum	Femoral head	
					left	right
VMAT	96.59	1.62	107.02	103.63	33.28	33.09
CK	86.60	3.54	108.56	105.03	35.92	38.40
p	**< 0.05**	**< 0.05**	0.2603	0.3223	0.4147	0.1316

Table 4: Volume (percentage) of the prostate and critical organs, which are covered by a therapeutic dose.

	% CTV covered by a therapeutic dose	% volume of bladder covered by a therapeutic dose	% volume of rectum covered by a therapeutic dose
VMAT	75.37	3.98	0.56
CK	95.37	6.92	4.86
p	**< 0.05**	0.0653	**< 0.05**

Table 5. The values of coefficients evaluating the dose distributions.

	Quality of coverage RTOG	Conformity index RTOG	COnformal Index (COIN)	RPI
VMAT	0.9659	1.2843	0.4312	0.7086
CK	1.0093	1.8934	0.7696	0.5935
p	0.1743	0.6837	**< 0.05**	**< 0.05**

Because the values of the minimum doses in PTV and maximum in critical organs should not be the only parameters that determine the acceptance of the treatment plan, or its rejection as not meeting the therapeutic objectives, therefore the next step of the dose distribution comparison was to calculate coefficients, which in the literature are dedicated to this type of purposes. Applied and calculated coefficients: Quality of Coverage, Conformity Index, Conformal Index (COIN) and RPI, results are presented in **table 5**.

Coefficients: Coverage of Quality and Conformity Index did not show differences between the analyzed techniques. It should be added that these coefficients take into account only distributions of the doses in the PTV (treated prostate gland). The other two include distributions of the doses in the PTV and OaR's (Organs at Risk). If they are equal to 1 it means, that per-formed dose distribution plan meets our expectations, the closer to 0, the treatment plan increasingly diverges from our assumptions. Therefore, COIN indicates better compliance of calculated plan with our assumptions for CK technique, whereas the RPI - vice versa - for the VMAT technique. This is due to the fact that in calculation of COIN value the dose distribution in the PTV is "more important" than dose in the critical organs. For the CK technique 96% of the PTV receives planned dose, while only 75% for the VMAT technique. In the case of RPI coefficient dose distributions in PTV and critical organs are compared, but their weight are equal, and that means that a greater number of critical organs, than the areas of irradiation, determines the value of this coefficient. Since the doses in the rectum and urinary bladder are smaller in the case of VMAT than in the CK technique, therefore the RPI coefficient indicates the distributions of doses in VMAT technique as closer to our objectives.

Irradiation of patients using IMRT, VMAT, CK, and TT techniques is increasingly reported in the literature [16-22]. Despite the technological differences related to the geometry of generated beams: the changing shape of the beam field vs circular tubes, the dose distributions we obtain as a result of the calculations are very comparable, of course, for "small" cancerous changes.

Stereotactic radiotherapy, radiosurgery in patients with prostate cancer (due to the volume) can be implemented using a variety of therapeutic devices: VMAT, CyberKnife or TomoTherapy. Protocol of preparing patients for the therapy also may vary with, e.g. filling of the urinary bladder, method of immobilization such as thermoplastic mask or vacuum mattress. We raised a question whether dose distributions that are calculated for two different groups of patients treated with VMAT technique and CyberKnife are comparable. The results are consistent with the literature [23,24], which relate to the comparison of dose distributions in various techniques. The applied coefficients of treatment plan evaluation, Quality of Coverage, Conformity Index, Conformal Index and Radiation Planning Index, also indicate that both treatment techniques are acceptable. Please note, however, that the comparisons relate only to the "physical" dose distributions, radiobiological values and the duration of treatment, which in both schemes is different, are not taken into account. Another important issue is how to define the therapeutic dose and the value of the therapeutic dose. Since both techniques, due to the distributions of doses are equivalent, it is worth recalling what are the differences between them at the level of implementation, in particular in the verification of treatment. In CK technique we have the opportunity to take verification pictures (kV) during the therapeutic session and correcting improper orientation of the patient. In VMAT technique, we have the opportunity to take pictures (kV) verifying the position before starting the radiation exposure, it is possible to perform CB/CT tests - it allows to assess the shifts in the location and dimension of critical organs and the prostate gland. In accelerators of a new type (TrueBeam) it is also possible to take pictures kV in the course of radiotherapy. Finally, there is possibility to read information related to the implementation of radiation and the reconstruction of the actual position of organs. Performed calculations show that perhaps the dose distribution in the PTV, for the CK technique, could be more homogeneous if the patients being prepared for the radiotherapy were informed that the bladder must be "empty" as in the case of patients irradiated with VMAT technique.

Conclusions

Calculations of the dose distributions in SRS radiotherapy for VMAT and CK techniques shows, that stereotactic radiosurgery of prostate cancer can be carried out on CyberKnife accelerator as well as on the classical accelerator with the use of VMAT technique. Both treatment techniques meets the therapeutic objectives and can be used alternatively for radiotherapy of prostate cancer. It should be remembered, however, that the way of defining the dose for both analyzed techniques is different, this means that any comparison can be made only after bringing the values of planned therapeutic doses to a common denominator.

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