Applied Radiation and Isotopes 192 (2023) 110617

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

A dosimetric comparison for SBRT plans of localized prostate cancer between Cyberknife and Varian Truebeam STX device

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ARTICLE INFO

Keywords:
Localized prostate cancer
Volumetric modulated arc therapy (VMAT)
Stereotactic body radiotherapy (SBRT)
CyberKnife (CK)

ABSTRACT

As the Stereotactic Body Radiotherapy (SBRT) approach began to increase in treating patients with localized prostate cancer, it became necessary to investigate which methods used in practice were better. The aim of this study is to perform a dosimetric comparison of the advantages and disadvantages of SBRT treatments for localized prostate cancer delivered by CyberKnife (CK) and Varian Truebeam STX (FF and FFF). Seventeen intermediate and high-risk patients with localized prostate cancer were included in the study. SBRT plans for the CK system and Varian Truebeam STX systems with and without Flattening Filters (Tru-FF and Tru-FFF) were prepared for each patient. Plans prepared for each patient were planned at a fraction dose of 6.7 Gy at 6 MV energy and a target dose of 33.5 Gy in 5 fractions. For all plans, cumulative dose-volume histograms (DVHs) were generated for target volumes and organs at risk (OAR). The maximum doses of PTV (41 Gy) in CK plans are higher than the maximum doses (35 Gy) in VMAT plans prepared with Tru-FF or Tru-FFF beams. The mean dose of the rectal wall (10.06 ± 2.40Gy for CK) is still relatively low compared to other plans (13.46 ± 2.16 Gy for Tru-FF and 13.61 ± 2.32 Gy for Tru-FFF). The bladder wall (14 Gy for CK, 26 Gy for Tru-FF and Tru-FFF) and femoral head (6.8 Gy for CK, 9 Gy for Tru-FF and 9.4 Gy Tru-FFF) doses were also lower for CK plans. The CK plans provide better tumour control due to low doses in critical organs and high target doses than the Tru-FF or Tru-FFF plans. It was observed that CK and VMAT plans for SBRT with 6 MV photon beams provided acceptable results in term of treatment planning criteria such as Conformity Index and Homogeneity Index. It is recommended to use a target tracking system to provide an accurate and reliable SBRT treatment with VMAT and CK techniques.

1. Introduction

Stereotactic Body Radiotherapy (SBRT) gives better results than surgery in treating prostate cancer, which is one of the most common cancer types todays (Serra et al., 2020; Serra et al., 2022; Scobioala et al., 2019a; Scholarworks@gvsu and Puruleski, 2021). SBRT generally provides high dose compliance with treatment fractions of 5 or less. Conventional fractionated Radiotherapy (RT) for prostate cancer typically includes doses of 74–78 Gy delivered in 37–39 fractions. SBRT, with an image-guided system, provides dose accuracy and precision at the target volume for prostate cancer (Serra et al., 2022). Increasing the dose of radiotherapy treatment increases the probability of cure in prostate cancer (Takakusagi et al., 2021; Zilli et al., 2018; Fowler et al., 2013; Parikh and Kishan, 2020). It is known that the safe dose of radiotherapy for prostate cancer depends on the tolerance of the surrounding normal structures (i.e. bladder, rectum and intestine) while providing a high dose to the target. However, the sensitivity of each tissue type to radiation is different. Therefore, in radiotherapy treatments, the dose should be determined precisely enough to treat the tumour and should not cause irreparable damage to normal tissues.

The "α/β" ratio (i.e., cell susceptibility/cell repair) is an essential parameter of the cell-survival linear-quadratic (LQ) model, which

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https://doi.org/10.1016/j.apradiso.2022.110617
Received 16 May 2022; Received in revised form 7 December 2022; Accepted 11 December 2022
Available online 16 December 2022
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describes the sensitivity of each tissue (healthy or tumoural) to changes in the treatment fraction. Prostate cancer cells have a low α/β ratio (i.e., ~1.5 Gy). Critical organs such as the rectum and bladder surrounding the prostate have a higher value (α/β ratio 3–5 Gy) (Fowler et al., 2013; Parikh and Kishan, 2020; Borowicz et al., 2022; Morrison et al., 2019). Therefore, delivering larger doses to the prostate in fewer fractions has led to the preference for hypofractionated therapies, which aim to improve tumour control ratio and reduce late toxicity without increasing the risk of late normal tissue complications (Morrison et al., 2019; Grimm et al., 2011; Teoh et al., 2011).

Various treatment methods used in SBRT of prostate cancer have emerged thanks to scientific developments. While the incidence of prostate cancer is increasing, it is seen that the quality of life decreases with radiotherapy treatments with conventional fractions (e.g. 37–39 fractions). Although conventional Intensity Modulated Radiation Therapy (IMRT) treatments (e g., 37–39 fractions) are successful, studies show that SBRT provides (e.g. five fractions) a significant advantage in terms of reduction of side effects (Grimm et al., 2011; Teoh et al., 2011; Hegazy et al., 2016; Xu et al., 1088). SBRT provides excellent local control for patients unsuitable for surgery or conventional radiotherapy techniques (e.g. IMRT) (Xu et al., 1088; Scobioala et al., 2019b; Chung et al., 2015). The treatments applied with the Volumetric Modulated Arc Therapy (VMAT) technique and the CyberKnife (CK) system draw attention in terms of accessibility. VMAT offers improved target volume coverage compared to conventional radiotherapy techniques and normal tissue coverage using one or two arcs by simultaneously changing the gantry rotation speed, movement of the Multi-Leaf Collimator (MLC) leaves, and dose rate parameters. VMAT also offers shorter treatment delivery times than CK (Holmes et al., 2018; Kothari et al., 2018; Cakir et al., 2019a).

The CK is a 6 MV photon beam linear accelerator built on 6 degrees of freedom robotic arm. The wide range of motion follows the irregular edges of the lesion, ensuring high compliance and avoiding OARs due to the different entry points of the treatment areas. Accurate image guidance allows for lowering the limits of uncertainty and minimizing radiation-induced damage to adjacent normal tissues (Serra et al., 2022; Scobioala et al., 2019a; Borowicz et al., 2022). For this, the images of fiducials placed in the prostate in the CK system can be taken with orthogonal X-ray imaging systems throughout the treatment. In addition, excellent biochemical progression-free survival and early toxicity (bladder, rectal, and quality of life) have been reported in prostate radiotherapy compared to similar standard radiation techniques (Morrison et al., 2019; Bijina et al., 2020). After the American Society of Therapeutic Radiology and Oncology (ASTRO) declared in a 2017 publication that the prostate would be an excellent SBRT target, publications showed that CK SBRT has promising results with minimal toxicity for prostate cancer (Kothari et al., 2018).

There are many studies in the literature that make comparisons between CK and VMAT (Serra et al., 2022; Takakusagi et al., 2021; Borowicz et al., 2022). But, as far as we know, there are no comparing studies among CK (6 MV) with VMAT-Flattening Filter Free (6 MV-FFF) and also VMAT-Flattening Filter (6 MV-FF) on the SBRT photon beams plans of localized prostate cancer. In this study, a dosimetric comparison of the advantages and disadvantages of SBRT treatments for localized prostate cancer delivered by CyberKnife (CK) and Varian Truebeam STX (FF and FFF) systems was aimed.

2. Materials and methods

2.1. Patient selection and contouring

Our study was conducted on 17 patients treated in our clinic between 2017 and 2019 with high and medium-risk localized prostate cancer, and the prostate diameter of patients is between 3.5 cm and 6 cm. All study participants signed informed consent, and the Istanbul University Faculty approved the study by the Medicine Clinical Research ethics committee (Protocol Number: 2019/612), Istanbul, Turkey. The study was conducted according to the principles of the Declaration of Helsinki (Assembly, 1996). All patients had fiducial markers placed 7–10 days before the CT scan. An empty rectum and full bladder are necessary to improve prostate imaging and contouring. For this, it is necessary to make an enema. Patients were asked to urinate 30 min before planning tomography and treatment and to drink 500 ml of water. Bladder and rectum preparations (full bladder and empty rectum) were performed before planning tomography and treatment of the patients. For imaging, patients were placed in the supine position, hands-on chest, and feet toward the gantry, using knee support and foot stabilizer, under the clinical protocol. Images of 1 mm section thickness were performed on the Big Bore 4D Philips CT-Simulator device (Philips Healthcare, Cleveland, OH, USA).

Clinical target volumes and critical organs were contoured at once under the guidance of a radiation oncologist to ensure the same conditions in all plans. The prostate volume determined the clinical target volume (CTV), and the planned target volume (PTV) was determined by giving the CTV a margin of 3 mm posteriorly and 5 mm in the other directions. The bladder, bladder wall, rectum, rectal wall, and right and left femoral heads are contoured as OAR. The bladder wall was drawn 2 mm from the bladder and the rectum wall 2 mm from the rectum. The demographic data of the patients and the characteristics of their target and critical organs are given in Table 1.

2.2. Dose constraints for plans

The prescribed dose for each patient is 33.5 Gy. The treatment was carried out with the treatment protocol with a fraction dose of 6.7 Gy in 5 fractions. 95% of PTV is planned to be covered with at least 100% of the therapeutic dose. It was ensured that all critical organs remained below tolerance doses. The maximum dose for the critical organ, the rectum and bladder wall, is 38 Gy, and the maximum dose for 15% of the bladder wall volume is defined as 18.3 Gy[1]. The dose limitations used in the study are shown in Table 2. Dose constraints for OAR are similar to studies in the literature (Serra et al., 2020; Grimm et al., 2011; Seppälä et al., 2017).

2.3. Treatment planning

All treatment plans were approved by the same radiation oncologist, considering dose limitations. The same physicist performed all treatment plans prepared at the maximum dose rate. Treatment planning was performed using two systems: CyberKnife (6 MV) and TrueBeam STx (6 MV-FF and 6 MV-FFF). Although treatment plans were prepared for both systems, all patients were treated only with CK. Details of planning are given below.

2.3.1. SBRT plans with CK plans

Treatment planning was prepared for the CyberKnife system using MultiPlan 3.5.4 (Accuray®, Sunnyvale, USA) treatment plans with 6 MV energy beams. The dose rate is 800 cGy/min (plans referred to as CK plans). The fiducial monitoring method was chosen in CK plans, and at least three fiducials were determined for each patient. CK plans were obtained using non-isocentric beams. Each treatment plan used two collimator apertures ranging from 10 to 40.0 mm. Planning was carried out with the sequential optimization technique. The minimum amount of MU is defined to be 50 MU. Radiation is delivered at a discrete set of Linac positions called nodes. Approximately 75.9 ± 5.7 nodes and 195.7 ± 61.5 beams were used in CK plans.

2.3.2. SBRT plans with VMAT (FF and FFF) plans

Firstly, for Truebeam, VMAT plans for 6 MV-FF photon beams were prepared with the Eclipse™ 15.1 (Varian Medical Systems, Palo Alto, USA) planning system. 6 MV-FFF plans are named Tru-FF and the dose rate is 600 cGy/min.

Table 1
Demographic data of the patients participating in the study and the characteristics of their radiotherapy target and critical organs (GS: Gleason Score; PTV: Planned target volume; P.Bulb: Penile Bulb; Sem.ves.: Seminal Vesicles).

Patient No	Clinical Stage	GS	PSA	Risk Level	Age	PTV cc	Prostate volume cc	Rectum volume cc	Bladder volume cc	P. Bulb volume cc	Sem. Ves. volume cc
1	T2BN0M0	3 + 4	4.6	Middle	75	73.70	36.60	123.60	267.90	8.00	15.30
2	T2CN0M0	3 + 4	7.2	Middle	71	110.70	59.70	69.30	269.90	10.50	28.70
3	T3AN0M0	4 + 5	13.0	High	58	65.60	34.00	155.10	930.80	8.20	4.50
4	T2CN0M0	3 + 4	9.6	Middle	62	73.20	38.10	59.10	41.20	7.60	54.20
5	T3AN1M0	4 + 5	16.5	High	79	92.80	49.70	165.70	406.80	10.80	16.80
6	T2BN0M0	3 + 4	16.0	Middle	71	104.20	52.60	62.00	566.80	2.50	10.20
7	T3BN1M1	5 + 5	70.0	High	65	71.20	31.40	47.70	350.00	6.00	8.30
8	T3AN0M0	4 + 4	5.8	High	67	82.60	43.30	90.70	675.90	7.20	12.40
9	T2CN0M0	4 + 3	20.0	High	67	67.10	32.80	48.00	292.90	3.40	9.10
10	T2N1M1	4 + 4	94.5	High	72	80.00	39.50	48.30	343.40	6.10	19.50
11	T3BN1M1	4 + 5	18.0	High	71	84.90	42.50	82.80	322.10	7.30	24.40
12	T2AN0M0	4 + 3	9.0	Middle	72	64.80	31.00	52.60	263.50	11.70	5.50
13	T3AN0M0	4 + 4	7.8	High	75	73.40	39.20	64.40	433.70	4.70	18.30
14	T2CN1M1A	4 + 4	31.0	High	68	74.10	35.30	52.40	652.50	3.20	14.00
15	T2AN0M0	3 + 3	6.7	Middle	73	91.40	51.70	49.70	263.90	6.90	7.80
16	T2CN0M0	3 + 4	6.4	Middle	69	66.70	37.20	71.30	549.20	5.50	35.10
17	T2AN0M0	3 + 4	0.1	Middle	60	70.90	36.20	59.30	246.50	2.50	25.00
Mean					**69 ± 5.2**	**79.25 ± 12.8**	**40.64 ± 7.8**	**76.59 ± 34.9**	**404.53 ± 199.9**	**6.59 ± 2.7**	**18.18 ± 11.9**

Table 2
Dose constraints.

Dose Constraints	PTV	CI	Rectum	Bladder Wall	Femur heads	P.Bulb
	Prescribed dose covering at least %95	≤1.25	D_{max} <38Gy D_{20cc} < 25Gy	D_{max}<38Gy D_{15cc} < 18.3Gy	D_{10cc} < 30Gy	D_{max} <50Gy D_{3cc} < 30Gy

Secondly, for Trubeam, VMAT plans were prepared for 6 MV-FFF photon beams prepared with the Eclipse™ 15.1 planning system. 6 MV plans are named Tru-FFF, with a dose rate of 1400 cGy/min.

Tru-FF and Tru-FFF plans are formed from two 360° iso-arc with collimator angle rotations of 30° and 330°. The rotation movement created was achieved by turning the device 360° clockwise, starting from a 180° gantry angle, then 360° counterclockwise again. In Trubeam (FF and FFF) plans, progressive resolution optimization (PRO) algorithm and inverse planning method were used to determine the most suitable combination of beam weight and MLC shape. Dose limitations were controlled by obtaining Dose Volume Histograms (DVHs) plots for each patient.

Dose distributions and the cumulative DVHs are given in Fig. 1 as an example of CK and Trubeam (FF and FFF) plans.

2.4. Plan evaluation

The Conformity Index (CI) is defined as the ratio of prescription isodose volume (V_{Rx}) to the PTV volume (V_{PTV}). The ideal value of CI is unity, which is generally more significant than one (Borowicz et al., 2022; Cakir et al., 2019b). The CI is described as

$$CI = V_{Rx}/V_{PTV}$$

It is an objective parameter that shows the dose distribution homogeneity in the target volume. According to RTOG, the Homogeneity Index (HI) is defined as the ratio of prescription maximum isodose (Imax) to reference isodose (RI) (Borowicz et al., 2022). The HI is given

$$HI = I_{max} / RI$$

Total MU, CI, HI, and GI of PTV values used in all planning techniques were compared. The doses in the volumes of V20%, V50%, and V95%, together with the mean and maximum doses in the rectum and bladder, were compared (Serra et al., 2020; Bijina et al., 2020). The mean dose of the rectal wall, the mean and maximum dose of the bladder wall, and the dose corresponding to the V15% volume were compared. The V10% and V50% doses of the femoral heads, the maximum dose of the Penile Bulb, and the seminal vesicular mean doses were compared. The DVH graphs and PTV/OAR dose values of the plans obtained according to the dose constraints were evaluated, and the appropriateness of the plans was decided.

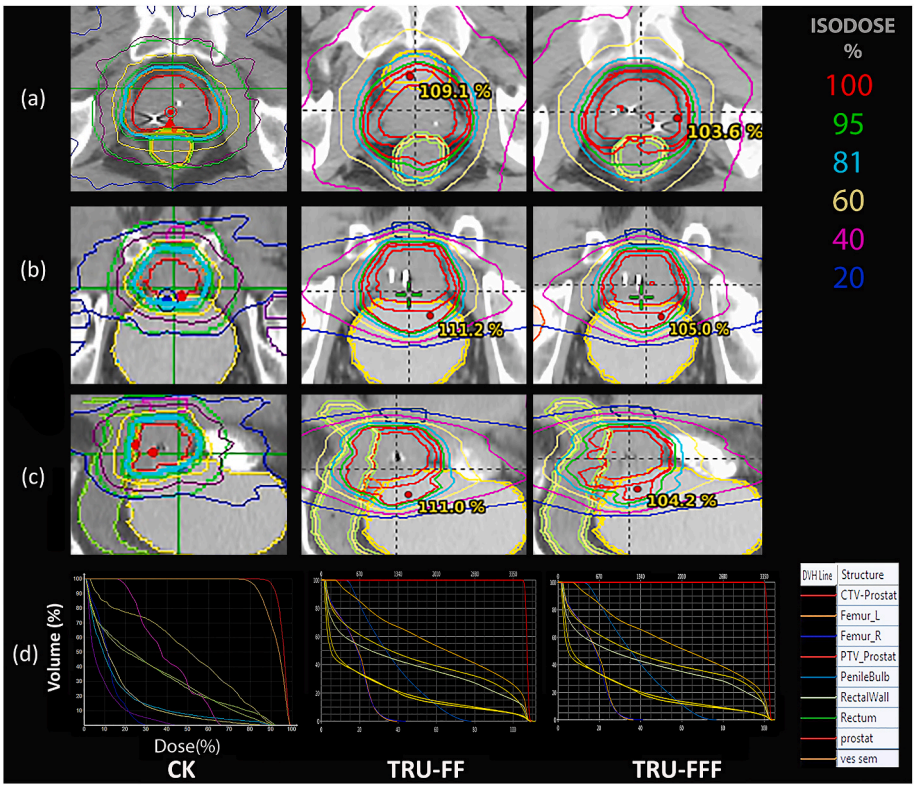


Fig. 1. Dose distributions in different planes for the same patient. (a) transverse, (b) coronal, (c) sagittal slices, and (d) the cumulative DVHs of each technique.

2.5. Quality assurance for treatment plans

In order to accurately deliver very high doses to the target volume with SBRT, some dosimetric testing is required. These tests are essential to prevent errors and worsening from occurring, such as serious normal tissue complications or tumour recurrence. Dosimetric and MU calibrations for CK and Trubeam are made daily. The Gamma Index (GI) was calculated to compare the differences between the measured and calculated dose distributions at the central point.

2.5.1. Quality assurance for CK

A specific QA was performed to measure GI values in CK plans. 30 × 30 cm^2 water-equivalent RW3 plate phantoms (PTW, Freiburg, Germany), calibrated PinPoint ionization chamber with 0.015 cm^3 precision volume (model 31014; PTW, Freiburg, Germany) and PTW Unidos electrometer (PTW, Freiburg, Germany) was used for the measurements. CT images of the RW3 phantom with a slice thickness of 1 mm were acquired, and the images were transferred to MultiPlan version 4.6.1 (Accuray Inc., Sunnyvale, CA, USA) TPS. CK patient plans were transferred to CT images of the RW3 phantom. Then, the dose distributions on the phantom were recalculated at high resolution and recorded. Finally, point dose measurements were made for each plan, and the average value was calculated. Average doses measured by PinPoint were compared with doses calculated by TPS in the precise volume of PinPoint. The percentage difference between the measured and calculated dose was calculated.

2.5.2. Quality assurance for VMAT

In Truebeam system, pre-treatment verification and in-vivo dosimetry can be performed in three dimensions with electronic portal imaging (EPID). In pre-treatment validation, EPID images can be acquired without phantom or patient between the source and detector. In in-vivo dosimetry, on the other hand, data obtained while the patient or phantom is present during treatment is used. In both cases, independent dose validation of therapy can be achieved. Gamma index analysis of each patient's plan on the Trubeam system was performed with the EPID device without any phantoms or patients between the source and the detector. GI values were calculated for all three techniques as recommended in TG AAPM 218, using the criteria of distance (depth and width of the field), $\Delta d = 2$ mm and dose, $\Delta\% = 2\%$. The dose distribution calculated by TPS was used as reference data.

2.6. Statistical analysis

The Wilcoxon Test using SPSS Statistics 22.0 (SPSS Inc., Chicago, IL, USA) was used to determine the statistical significance of better target coverage and better organ preservation between the CK and Trubeam (FF and FFF) plans. CK plan and VMAT plans were compared for target and critical organs by Pairwise comparisons. CK plan and VMAT plans were analyzed, as well as their relations in terms of FF and FFF plans. If $p > 0.05$, there is no statistically significant difference between CK and Tru-FF values, CK and Tru-FFF values, and Tru-FF and Tru-FFF values. If $p < 0.05$, there is a statistically significant difference between CK and Tru-FF values, CK and Tru-FFF values, and Tru-FF and Tru-FFF values.

3. Results

3.1. Dosimetric indices for plans

The data obtained from the plans are given in Table 3. Although CI values provided the dose constraints in all three techniques, the CI value of the CK plans was slightly better than the Tru-FF and Tru-FFF plans. On the other hand, Trubeam plans, as rotational techniques, provide a more homogeneous dose distribution when it comes to HI value. We found a 120% difference between the HI of CK (1.25 ± 0.03) and the HI of Trubeam (1.05 ± 0.01 for FF and FFF plans). Serra et al. reported that in CK plans, 125% of the prescription dose is deposited in the inner parts of the tumour (Serra et al., 2022). Besides, CK cannot deliver the dose from the back of the patient due to technical barriers (Borowicz et al., 2022). In these cases, the dose accumulates at a certain point and does not show

Table 3
Dosimetric parameters for all techniques. The results of the p-test among CK, Tru-FF and Tru-FFF are also given in the table. The numbers 1, 2, 3 indicate CK, Tru-FF and Tru-FFF, respectively.

					1/3	1/2	3/2
		CK	Tru-FF	Tru-FFF	p	p	p
CI		1.11 ± 0.06	1.21 ± 0.11	1.18 ± 0.14	0.000	0.000	0.065
HI		1.25 ± 0.03	1.05 ± 0.01	1.05 ± 0.001	0.000	0.000	0.102
Treatment Time (min)		60.71 ± 19.71	2.83 ± 0.17	2.93 ± 0.18	0.000	0.000	0.000
Total MUs		50587.56 ± 15932.49	1648.71 ± 91.36	1772.12 ± 100.14	0.280	0.498	0.000
GI (% ± SD)		100% ± 2%	99.6% ± 0.9%	99.7% ± 0.7%	0.177	0.193	0.163
Target Doses (cGy)							
PTV	**Min Dose**	2953.85 ± 87.83	3214.56 ± 103.92	3215.77 ± 103.58	0.000	0.000	0.758
	Mean Dose	3782.5 ± 232.06	3411.39 ± 1.80	3409.85 ± 7.79	0.004	0.004	0.868
	Max Dose	4198.78 ± 114.24	3508.85 ± 20.65	3512.46 ± 20.15	0.000	0.000	0.193
CTV	**Min Dose**	3401.98 ± 63.75	3322.20 ± 10.31	3313.68 ± 20.16	0.000	0.001	0.035
	Mean Dose	3988.94 ± 82.33	3411.29 ± 3.11	3412.36 ± 9.33	0.000	0.000	0.185
	Max Dose	4198.78 ± 114.24	3500.64 ± 17.38	3505.35 ± 19.79	0.000	0.000	0.149
OAR Doses (cGy)							
Rectum	**V20%**	1949.24 ± 294.78	2930.22 ± 183.13	2938.43 ± 271.36	0.000	0.000	0.039
	V50%	832.12 ± 237.26	1338.07 ± 580.42	1360.31 ± 609.02	0.004	0.005	0.042
	V95%	123.82 ± 80.10	107.20 ± 44.32	114.02 ± 46.34	0.795	0.407	0.000
	Max dose	3799.06 ± 70.82	3503.29 ± 39.67	3516.72 ± 66.82	0.000	0.000	0.246
Rectal wall	**Mean dose**	1005.84 ± 240.47	1346.34 ± 215.55	1361.29 ± 231.75	0.000	0.000	0.044
Bladder	**V20%**	1161.82 ± 319.08	1413.68 ± 461.36	1410.21 ± 450.48	0.009	0.007	0.758
	V50%	524.82 ± 210.55	266.42 ± 232.57	272.09 ± 224.57	0.001	0.001	0.055
	V95%	109.59 ± 98.18	63.38 ± 46.10	87.47 ± 79.59	0.031	0.001	0.004
	Max dose	3772.5 ± 121.81	3716.62 ± 382.07	3666.84 ± 321.98	0.435	0.463	0.028
Bladder Wall	**V15%**	1457.01 ± 468.34	2598.07 ± 577.25	2600.55 ± 580.99	0.002	0.002	0.831
	Mean dose	772.49 ± 202.88	942.09 ± 218.58	944.47 ± 214.58	0.015	0.015	0.177
Left Femur	**V10%**	547.59 ± 199.75	919.04 ± 213.77	960.0 ± 197.97	0.000	0.001	0.000
	V50%	185.35 ± 66.81	569.61 ± 147.78	597.93 ± 148.98	0.000	0.000	0.003
Right Femur	**V10%**	816.12 ± 312.41	893.42 ± 200.61	913.39 ± 190.29	0.210	0.266	0.022
	V50%	405.71 ± 220.87	552.04 ± 149.55	577.46 ± 147.84	0.028	0.028	0.002
P.Bulb	**Max dose**	2521.45 ± 834.58	1959.11 ± 908.35	1809.40 ± 951.12	0.000	0.000	0.831
Sem.Ves.	**Mean Dose**	2081.50 ± 431.60	2285.51 ± 617.71	2340.13 ± 654.52	0.019	0.031	0.868

Note: A p-value <0.05 was considered statistically significant.

a homogeneous distribution. As a result, the HI value has a value higher than 1. These are thought to be the reason why the HI of CK plans is higher than the CK of Truebeam plans in our study.

3.2. Dose Volume Histograms and statistical analysis

The mean and maximum doses to the PTV and the CTV were significantly higher ($p < 0.000$) in CK plans compared to the plans of other techniques. The V20% doses to the rectum were significantly lower ($p < 0.000$) in CK plans. In contrast, the maximum doses delivered to the rectum were significantly higher ($p < 0.000$) in the CK plans compared to the plans of other techniques, and the mean doses delivered to the rectal wall were significantly lower ($p < 0.000$). The maximum doses to the bladder were significantly lower in the Tru-FF plans compared to the Tru-FF plans ($p < 0.028$). The V50% doses applied to the left and right femur were significantly lower in the CK planes compared to the plans of the other techniques ($p < 0.028$; <0.000, respectively). The maximum doses to the penile bulb were significantly lower ($p < 0.000$) in Tru-FFF plans compared to the CK plans. The mean doses to the seminal vesicle were significantly lower ($p < 0.031$) in CK plans compared to the Tru-FF plans. These values and other limitation data are shown in Table 3.

3.2. Treatment times and MUs

Treatment times were examined as irradiation time only. This period does not include preparation and the hospitalization time of the patient. Accordingly, it can be seen from Table 3 that the treatment time of the CK treatments is considerably longer than the Tru-FF and Tru-FFF treatments ($p \ll 0.05$). When Tru-FF and Tru-FFF plans were compared in terms of treatment time, Tru-FF treatments were statistically shorter ($p \ll 0.05$).

When the total MUs are evaluated, it is seen that the MU value of the CK plans is considerably higher than the MU values of the Tru-FF and Tru-FFF plans. When Tru-FF and Tru-FFF plans are compared, it is seen that Tru-FF plans complete the treatment with less MU in Table 3.

3.4. Delivery quality assurance

Fig. 2 includes the GI analysis of the Tru-FF plan of one patient. The planned dose shows the dose distribution calculated by TPS. The portal dose shows the dose distribution obtained with the EPID system. The blended dose shows the comparison of two different methods. This figure shows the mean values for GI calculated for two types of criteria: (i) distance (depth and width of the field), $\Delta d = 2$ mm, and (ii) dose, $\Delta\% = 2\%$. Acceptance criteria for GI values were >95%. GI values (for %2/2 mm criterion) were 100% ± 2%, 99.6% ± 0.9% and 99.7% ± 0.7% for CK, Tru-FF and Tru-FFF, respectively. The values are given in Table 3.

6. Discussion

SBRT plan is an effective treatment option for low- and intermediate-risk prostate cancer in terms of efficacy, safety, patient quality of life, and side effects (Serra et al., 2022). Some studies indicate that five-fraction SBRT therapy achieves tumour control probabilities of 90–95% in patients with low- and intermediate-risk prostate cancer (Serra et al., 2022; Parikh and Kishan, 2020). SBRT therapy in low-risk prostate cancer patients shows clinical outcomes similar to radical prostatectomy in terms of survival and quality of life (Serra et al., 2022).

In addition, studies are still ongoing to confirm that higher doses in high-risk prostate cancer patients will increase the likelihood of tumour control (Serra et al., 2022).

It is interesting to explore whether rotational approaches such as VMAT or robotic approaches such as CK can provide a better SBRT treatment. Although VMAT and CK techniques have different parameters (such as collimator and dose rate) and different dose algorithms,

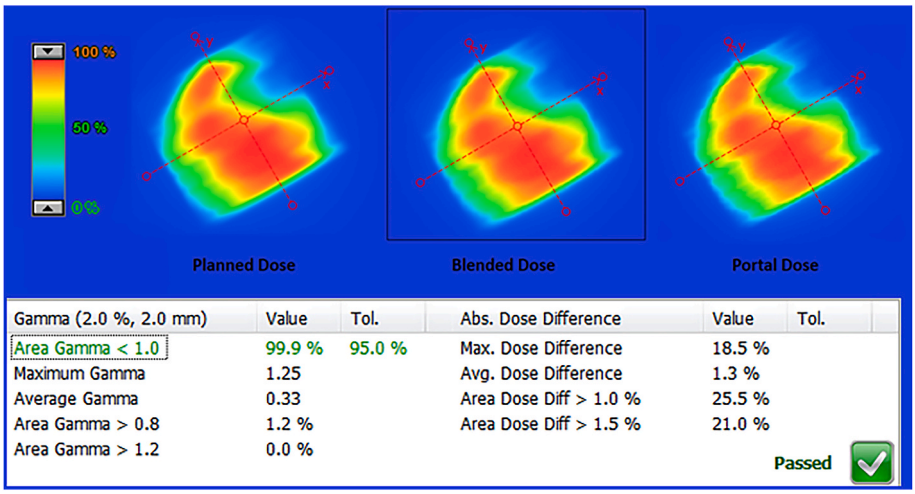


Fig. 2. An example from the Tru-FF plan for GI analysis.

comparing is helpful. In this retrospective study, the dosimetric comparison of Cyberknife and Trubeam devices (Tru-FF and Tru-FFF) and the treatment plans obtained in the treatment of prostate cancer were evaluated in terms of tumour coverage and protection of OARs.

As seen in Table 3, CK plans have better dose compliance to PTV than VMAT plans in terms of CI values. Similarly, the study of Seppala et al. (Assembly, 1996), in which 4 SBRT techniques (CK, IMRT, VMAT-Varian and VMAT-Elekta) were compared, reported similar CI values (1.11; 1.02; 1.10 and 1.12 respectively) for the four techniques. Borowicz et al. (2022) compared CK, VMAT, and IMRT plan in their study, and the CI values (1.17, 1.25, and 1.07, respectively) were close to one. On the other hand, Serra et al. (2022) performed a dosimetric comparison between the CK and VMAT-FFF plans as the SBRT technique in their study with 10 prostate cancer patients. They reported that CI values for VMAT plans (1.01 ± 0.02) proved a better dose conformation to PTV than CK plans' (1.09 ± 0.04) in their study. In our study, unlike the literature, VMAT plans with flattening filter beams were also evaluated. When evaluated in terms of the Flattening Filter, it is seen that Tru-FFF plans provide a better conformity index than Tru-FF plans. Also, the CI values of the Tru-FFF plans were found to be better than the CI values of the CK plans. However, in terms of CIs, the difference between the literature and our study is around 10% and is not a significant difference in terms of plan evaluation. The better CI is thought to be due to the rapid decrease in the dose gradient in FFF beams.

On the other hand, HI and GI values in CK plans are slightly worse than in VMAT plans. Borowicz et al. (2022) stated that the high HI value in CK plans (1.25 ± 0.03) was because VMAT/IMRT plans (respectively 1.07 ± 0.01/1.04 ± 0.01) were isocentric and CK plans were non-isocentric. Serra et al. (2022) reported that HI values were higher in CK plans (1.24 ± 0.03) than in VMAT-FFF plans (1.2 ± 0.02) and GI values were similar for both plans (24 ± 8 for CK and 22 ± 8 for VMAT-FFF). On the other hand, we determined that Tru-FF (1.05 ± 0.01 for HI and 99.63% ± 0.92 for GI) and Tru-FFF (1.05 ± 0.01 for HI and 99.73% ± 0.74 for GI) plans did not make a statistically significant difference in HI and GI values. As a result of GI analysis in our study, it is seen that all three treatments give excellent results, and as seen in Table 3, no statistically significant difference was found between them.

When evaluated in target doses, PTV doses were significantly higher in CK plans than in Tru –FF and Tru –FFF plans. Similarly, in the study of Seppala et al. (Seppälä et al., 2017), it was seen that the target doses of CK plans (37.8 ± 0.4Gy) were higher than other plans (36.2 ± 0.4; 36.5 ± 0.3 and 36.6 ± 0.4 Gy for IMRT, VMAT-Varian and VMAT-Elekta respectively). In Irazola et al. study, it was stated that tumour doses should be increased for good tumour control (Irazola et al., 2019). Takakusagi et al. (2021) compared volumetric-modulated arc therapy (VMAT) radiation plans between conventional VMAT with flattening filter (cFF-VMAT) and flattening filter-free VMAT (FFF-VMAT) for localized prostate cancer. They reported that the doses of PTV D98 (about 66.2Gy) were similar in comparing FF-VMAT and FFF-VMAT plans. Chung et al. (2015) reported that from a dosimetric perspective, prostate SBRT plans using 6 and 10 MV FFF beams were similar to those created with 6 and 10 MV FF beams. They reported that Dmean values of PTV are 44.4 ± 0.2, 44.4 ± 0.2 Gy for 6 MV FF and FFF and also 44.0 ± 0.3 44.2 ± 0.2 Gy for 10 MV FF and FFF. Also, Tru –FF and Tru –FFF plans were compared in terms of PTV doses (Dmax, Dmean, Dmin) in our study, and no statistically significant difference was found ($p > 0.05$). This similarity can be explained by the loss of importance of the filter effect in small-area irradiation (Chung et al., 2015).

Although the Dmax<38 Gy criterion for the rectum was met in all three plans, doses corresponding to 20% and 50% of the rectum in the CK plans were statistically significantly lower than the Tru-FF and Tru-FFF plans, as seen in Table 3. In the study of Seppala et al. (Assembly, 1996), the D50% doses of the rectum are 12.5 ± 2.9, 11.0 ± 2.9, 10.0 ± 3.5 and 11.6 ± 2.2 for CK, IMRT, VMAT-Varian and VMAT-Elekta respectively. In this case, the lowest value is for VMAT-Varian. similar to our study, in the study of Serra et al. (2022), the D50% dose of the rectum was found to be lower in CK plans than in VMAT plans. On the other hand, in other studies (Takakusagi et al., 2021; Chung et al., 2015), no statistically significant difference was found between FF and FFF plans. Similarly, Dmean for the rectal wall in CK plans was significantly lower than the Tru-FF and Tru-FFF plans ($p > 0.00$), as seen in Table 3. Serra et al. (2022) reported similar values with Dmax (37Gy) for the rectal wall. It was observed that FF beams provided better protection than FFF beams in the rectum and rectal wall irradiation ($p < 0.05$). No other comparisons were found between FF and FFF for the rectal wall.

In CyberKnife, most beams are transmitted from the front; therefore, it is impossible to avoid the bladder while simultaneously providing good target coverage and rectal dose sparing effect. Our study found that the maximum doses of the bladder were close to each other in all plans. However, the bladder wall dose is the lowest in CK plans. Serra et al. (2022) reported similar results in CK and VMAT plans for the bladder and bladder wall dose values. The dose corresponding to 50%, 95% and the maximum dose of the bladder, another vital critical organ in prostate irradiation, was found to be significantly lower in the Tru-FF plan compared to the Tru-FFF plan, as seen in Table 3. Nevertheless, Chung et al. (2015) and Takakusagi et al. (2021) reported similar dose values in VMAT-FF and FFF plans for the mean dose values of the bladder.

When evaluated in terms of femur doses, in our study, the doses corresponding to 10% and 50% of the left femur in CK plans were the lowest ($p \ll 0.05$). Serra et al. (2022) reported similar maximum dose

values (15Gy) for the femoral heads for CK and VMAT plans. In the case of using FF beams, the femur doses in the Tru-FF plans were found to be lower than the Tru-FFF plans in our study. Chung et al. (2015) reported similar dose values for the femoral heads for VMAT-FF and VMAT-FFF plans. The maximum dose of the penile bulb, vital for erectile dysfunction, was found to be the lowest in Tru-FFF plans ($p \ll 0.05$) in our study. These results suggest CK plans are accompanied by less collateral effects in critical organs at risk. Similarly, Serra et al. (2022) reported that the dose of the penile bulb was lower in CK plans(8Gy) than in VMAT plans (34Gy) in their study.

Placing fiducial on the prostate tissue to determine the location of the prostate more accurately is a preferred method in CK plans. However, this method is not preferred in VMAT plans because it requires an invasive procedure and additional cost. Instead, control is provided by kV-CBCT. Bladder and rectum fullness can not always be adjusted at the same level, and these additional times spent preparing the patient cause the treatment time to prolong and this process to be tiring for the patient. Each patient's anatomy can play an essential role in determining the superiority of a particular technique. Thanks to the real-time target tracking system in CK treatments, lower doses are provided in the patient's bladder wall, rectum and femur.

There is a big difference between CK treatments and Tru-FF and Tru-FFF treatments in terms of treatment time in our study. The CK plans try to irradiate the target from many different points. This irradiation causes the device to make many movements and prolongs the treatment time. In their study, Serra et al.2 treated a hypo fractionated VMAT-FFF with the Clarity ultrasound probe. They stated that VMAT-FFF plans have become an attractive and reasonable alternative SBRT technique for localized prostate cancer due to the shorter treatment time. They mentioned that when operating in FFF mode, the radiation beam would be expected to increase the dose rate and consequent reduction in treatment delivery times. Also, Takakusagi et al. (2021) showed that FFF-VMAT plans had a shorter treatment time. Therefore, Linac-based systems provide benefits in terms of treatment time. Since the intrafraction movement of the prostate is time-dependent, VMAT plans with the shortest irradiation times are more advantageous than CK.

Since the prostate is a mobile organ, correct placement is essential for the treatment to continue correctly. Thanks to the reference markers in the CK plans, images are taken throughout the treatment without any preliminary preparation. If the match is achieved, the treatment continues. However, in VMAT treatments, it is necessary to ensure the patient's bladder fullness and rectal cleansing at the beginning of the treatment. After these preparations, a single image is taken and is not retaken until the treatment is finished. Although this procedure provides a shorter duration of VMAT treatment, it raises some doubts about the accuracy of organ placement in 2–3 min treatment time. Although the prolonged treatment period may affect the immobility of the patient, thanks to the fiducial tracking system, CK treats the target with accuracy and precision. Nonetheless, short treatment time seems to be advantageous in the preference of VMAT plans as an SBRT technique, it can turn into a significant disadvantage in devices without a target tracking system. Therefore, it is recommended to make a good decision before choosing CK, Tru-FF, or Tru-FFF plans to treat patients who can not stay in the same position for a long time.

Finally, our study included more patients than the literature in the dosimetric comparison of CK, Tru-FF and Tru-FFF plans. This study did not include seminal vesicles with the prostate as the only target. We also discussed an essential criterion for planning by including the flattening filter effect. We compared doses at target volume and OAR volume. Our study shows that treatment planning algorithms are effective in the treatment and user experience is among the influential parameters. In cases where the tumour tracking system is not used in VMAT plans, the target volume should be carefully contoured. Otherwise, the tumour dose will be low and may cause serious radiobiological effects. It is predicted that CK plans with their complex algorithm, which supply high target doses and low OAR doses, will create common side effects and prolonged survival in line with the expectation of radiotherapy.

7. Conclusion

As a result of this retrospective study, it was seen that both CK and VMAT plans provided acceptable results in the treatment of SBRT in patients with localized prostate cancer. It was determined that there was no statistically significant difference in terms of CI, HI, GI, treatment time, PTV doses and, OAR doses between the plans prepared with Tru-FF and Tru-FFF beams in VMAT plans. Even if the total preparation times (for patient preparation for CT imaging, simulation and treatment planning) required for both treatment modalities are almost equal, it was observed that VMAT plans could be used easily in patients who could not stay for a long time due to the short duration of VMAT treatment. It is recommended to use a target tracking system to provide an accurate and reliable SBRT treatment with VMAT and CK techniques. However, the advantage of CK plans is that they achieve low doses in critical organs such as the rectum wall, bladder wall, and femoral head while achieving high doses in the target volume. This is due to its technical superiority in determining tumour location. If the patient does not have a long-term hospitalization problem, CK plans should be preferred because the target is high and OAR doses are low. In this way, it is expected that side effects will decrease and survival time will increase.

Source of support

None.

CRediT authorship contribution statement

Ahmet Murat Şenişik: Resources, Methodology, Investigation, Data curation. **Murat Okutan:** Writing – review & editing, Writing – original draft, Supervision, Resources, Investigation, Conceptualization. **Aydın Çakir:** Resources, Investigation, Data curation, Conceptualization. **Ayça Iribaş Çelik:** Investigation, Conceptualization. **Esra Kaytan Sağlam:** Supervision, Methodology, Investigation, Data curation, Conceptualization. **Görkem Çevikbaş:** Validation, Methodology. **Bayram Demir:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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