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# Stereotactic Radiotherapy for Localized Prostate Cancer, which is Better CyberKnife or RapidArc?

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### Abstract

Aim: We aim to compare two different stereotactic body radiation therapy (SBRT) techniques, non-isocentric CyberKnife (CK) with isocentric RapidArc (RA), more widely available treatment technique for the treatment of localized prostate cancer.

**Methods:** The study included six patients treated with CK then re-planned with the new version of flattening filter free (FFF) RA and CK. The prescription dose was 36.25 Gy in five fractions. The two SBRT techniques were compared by target coverage, normal tissue sparing, dose distribution parameters and delivery time.

**Results:** The RA technique exhibited comparable PTV coverage and better bladder and rectum sparing at high doses. The conformity and homogeneity indices of the RA were better and statistically significant than the CK plans. Additionally, the RA resulted in statistically significant lower dose regions and faster delivery times than the CK.

**Conclusion:** The good dosimetric distribution and shorter delivery time make the new version of RA an attractive and reasonable alternative SBRT technique for the treatment of localized prostate cancer; however, no intrafractional (real-time) target tracking is possible on the RA, which is available on the CK platform.

Keywords: Stereotactic radiotherapy; RapidArc; CyberKnife

## Introduction

Over recent years, stereotactic body radiotherapy (SBRT) has been increasing in the management of low-and intermediate-risk prostate adenocarcinoma [1]. SBRT is the delivery of either a single dose or a small number of fractions of high-dose, precisely targeted, highly conformal radiation therapy [2]. SBRT improved outcomes may be due to the dose escalation alone, which is widely accepted in prostate adenocarcinoma [3,4]; or as a result of the increased dose per fraction, due to the apparent low  $\alpha/\beta$  ratio of prostatic adenocarcinoma [5,6].

The SBRT, including the CyberKnife technique (CK), has achieved promising clinical results in the treatment of prostate cancer [7-10]. The CK stereotactic radiotherapy system is an accurate image-guided method with intrafractional (real-time) target tracking for delivering radiation to a precisely targeted area using multiple non-isocentric beams with steep surrounding-dose gradients [11]. RapidArc (RA) is volumetric-modulated arc radiotherapy (VMAT) technique that can deliver highly conformal, intensity-modulated radiation doses by a single or multiple rotations of the gantry of the linear accelerator [12].

One of the potential benefits of SBRT is reduced patient visits (4 to 5 fractions) rather than the standard 35 to 40 fractions. A number of small studies and single-centre series have been published showing comparable outcomes with conventional fractionation schedules [13-19]. Most of these studies have used CK treatment. These preliminary studies and case series have led to the development of the PACE study, an international, randomized, phase III study comparing SBRT with both surgery and conventionally fractionated intensity-modulated radiotherapy in two parallel arms [20].

Our study may present an alternative to the CK platform, with the additional benefits of increased availability of gantry-based volumetric systems and possibly shorter delivery times.

# Materials and Methods

### Patients and imaging

Six patients with localized prostate cancer who had recently received hypo-fractionated radical radiotherapy by CK were included in the study. Gold seeds are implanted to prostate by radiologists under transrectal ultrasound guidance (TRUS), and then one week after 1 mm slice thickness CT simulation in a supine position with alpha cradle with bladder and bowel preparation protocol and MR images are acquired. CT scans from the fifth lumbar vertebrae level to below the ischial tuberosities. CT and MR images were transferred to a virtual simulation program to delineate regions of interest (ROIs).

#### Contouring and SBRT treatment plan requirements

The same radiation oncologist delineated the target and the critical structures using CT and MR fusion. The following ROIs were defined: Clinical Tumor Volume (CTV) consisted of the prostate without margin; The CTV was increased by 5 mm to create the planning target volume (PTV) for the RapidArc and by 3 mm for PTV for the CyberKnife. Organs at risk (OARs) that were delineated included the entire rectum; the whole bladder; penile bulb and femoral heads. A treatment plan that delivered 36.25 Gy to the PTVs was attempted in both treatment planning systems. Both modalities were required to achieve these

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Page 2 of 5

criteria as per a combination of studies [7,9,20-25]. Required planning constraints are detailed in Table 1.

## **Treatment planning**

**RapidArc:** Eclipse treatment planning system (Varian Medical Systems, Inc., Palo Alto, CA) was used along with the analytical anisotropic algorithm (AAA, Version 11.031) dose calculation algorithm. For RA optimization, progressive resolution optimizer (PRO) Version 11.031 was used. All plans generated using True Beam LINACS with 120 leaf millennium multileaf collimator and kV imaging, 2 full arcs one clockwise and the other counterclockwise, with collimator angles  $\pm$  20° from 0° and a couch angle of 0°, SRS Arc mode, 6 MV Flattening Free Filter (FFF) beam energy, and maximum dose rate of 1400 MU/min. Both arcs had the same isocenter, located at the center of the PTV.

**CyberKnife:** Inverse planning was carried out using the sequential optimization algorithm using MULTIPLAN v. 5.1 for delivery on a CyberKnife G4 v10.1 (only the IRIS collimators was used) which is capable of delivering 800 MUs/Min. The planning approach was to use a Prostate-path (allows 114 Nodes and 5° of pitch correction), 2 shells (i.e., 2 mm to control the conformity to the PTV and 40 mm to control the dose spillage), and the range of MUs per beam per fraction was 50-150. The PTV was prescribed to an isodose line of (78% to 80%) and a maximum of conformity index (CI) 1.24 was achieved. The PTV was at least covered by 99.2% of dose or more. The range of beam numbers was 100-150.

## **Plan evaluation statistics**

**Target volume coverage:** The percentages of the PTV that received 95% of the prescription dose, PTV mean, median and maximum were compared between the CK and RA plans.

**Dosimetric parameters:** The normalized conformity index (nCI) was calculated as:

CI=VRI/TV

But homogeneity index equation as follows:

# HI=I<sub>max</sub>/RI

Where, VRI: Volume of prescribed dose for PTV; TV: Total volume of PTV; I<sub>mm</sub>: Maximum dose and RI: Prescribed dose of PTV [26].

The percentages of the rectum and urinary bladder that received 18 Gy (V18), 28 Gy and the volume (cm<sup>3</sup>) that received 36 Gy (V36) of the prescription dose were compared. The dose regions (V10, V20, V30 and V36) were evaluated based on the body volume received 10, 20, 30 and 36 Gy of the prescription dose for each group.

#### Treatment time

The on-couch time for the patient will be added to the overall beam-on time for the RapidArc treatments, in our hospital the imaging and registration time is on average 3 min to 4 min (CBCT 1 min, reconstruction and registration in three planes 2 min to 3 min).

#### Statistical analysis

The dosimetric endpoints of the target volumes, normal organs, CI, HI and delivery time were analyzed using the non-parametric (small sample size) Wilcoxon signed rank test (SPSS, V19, USA), a probability value of <0.05 considered to be statistically significant (two tailed).

# Results

## Target volume coverage

All dose constraints regarding PTV coverage were similarly achieved by both plans except the maximal doses generated by the RA plans were statistically significant lower than those of the CK plans (p value 0.028).

#### **Comparison of dosimetric parameters**

The median of Conformity and homogeneity indices of RA plans had a statistically significant higher degree of conformity than the CK plans (p values 0.027 and 0.026) (Table 2).

## Normal tissue sparing

We analyzed the volume dose parameters of the rectum and

PTV Rectum	Minimum dose received by PTV	≥ 34.4 Gy 95% of prescription dose				
	V18<50% V28<20% V36<1 cm³					
Bladder	V18<40% V36<10cm³					
Femoral heads	Maximum point dose	30 Gy				
Penile bulb	Maximum point dose	No more than 100% of prescription dose				

Table 1: Dose planning constraints.

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6	
	RA	СК	RA	CK	RA	CK	RA	CK	RA	CK	RA	CK
Prostate volume (cm <sup>3</sup> )	160		95		45		79		96		63	
PTV volume (cm <sup>3</sup> )	264	211	174	134	95	78	159	99	178	152	120	71
PTV34.4 (95%)	99	99.2	99.3	99.4	99.5	99.5	99.3	99.5	99.7	99.4	99.4	99.5
PTV Mean (Gy)	36.8	30.5	36.3	38.2	36.3	40.5	36.3	39.9	36.3	40.6	36.3	39.6
Mean (%)	102	84	100	105.4	100	112	100	110	100	112	100	109
PTVmax (Gy)	39	45.9	38	38.2	39.4	46.5	39.3	45.9	38.3	45.9	37.9	45.3
max (%)	108	127	105	127	109	128	108	127	106	127	105	125
nCl	1.07	1.17	1.1	1.14	1.06	1.22	0.95	1.24	1.04	1.20	1.05	1.22
н	1.08	1.27	1.05	1.27	1.09	1.28	1.08	1.27	1.06	1.27	1.04	1.25

CK: CyberKnife; RA: RapidArc; PTV: Planning target volume; PTVmax: Maximum dose to PTV; nCl: Normalized conformity index; HI: Homogeneity index.

Table 2: Target dose results.

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bladder. All requirements were comparable in both groups; however, the CK plans achieved a superior sparing of the rectum and bladder in the low dose region (V18 and 28 for rectum and V18 for bladder) but statistically insignificant (p values 0.3, 0.2 and 0.4), while the RA plans exhibited a lower percentage of rectal and bladder volumes that received 100% of the prescription dose compared with the CK plans but statistically insignificant (p values 0.17 and 0.11). The femoral heads and penile bulb received lower doses with RA. The body V35 was the

same for both groups, whereas body V10, V20, V30 was all lower with RA in all cases with p values of 0.04, 0.03 and 0.06 respectively (Table 3).

# **Treatment time**

Across all five fractions of radiation treatment, the estimated delivery time of the RA (beam on 2.4 min, CBCT 1 min, reconstruction and registration in three planes 2 min) is faster than the CK (Mean and Median 5.4, 5.4 *vs* 34.3, 34.5 min) with significance (p value 0.028). The details are shown in Table 4.

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6	
	RA	СК	RA	СК	RA	СК	RA	СК	RA	СК	RA	СК
Rectum												
V18 Gy (%)	41.3	46.8	45.9	35.8	39.5	43.1	46.1	31.6	37.9	41.4	47.6	41.2
V28 Gy (%)	18.5	17.9	16.3	15.4	14.8	20.8	17.2	16.8	16.5	11.3	22.6	15.5
V36 Gy (cm <sup>3</sup> ) (%)	1.4	0.70	0.01	0.30	0.05	1.7	0.01	0.81	0.01	0.34	0.03	0.40
Bladder												
V18 Gy (%)	37.7	35.4	37.3	36	10.6	13.3	33.6	36	33.7	36	85.2	17.2
V36 Gy (cm³) (%)	7.2	7.3	0.3	5.2	1.5	6.88	0.8	1.37	0.01	3.6	1.05	0.20
Penile bulb									^			
Max dose (Gy)	30.6	30.5	36.7	34.9	38.4	38.6	39.3	31.7	38	37.2	36.5	36.7
Max dose (%)	84.4	84.1	101.2	96.3	106	106.5	108.4	87.5	105	102.6	100.7	101
RFH												
Max (Gy)	18.6	25	12.6	20	14.9	11.6	10.9	19.3	16.8	25.7	11.3	17.7
LFH												
Max (Gy)	18.5	26.7	11.7	18.6	13.5	12.5	18.9	15.1	17.2	22	10	14.5
Body									^			
Volume (cm <sup>3</sup> )	23469		46767		29441		32226		21826		24312	
V10 Gy (%)	10.6	11.9	4.3	7.4	3.9	4.3	5.7	6	7.4	9.7	5.5	5.3
V20 Gy (%)	3	3	1.2	1.9	1	1.1	1.3	1.4	2	2.7	1.3	1.4
V30 Gy (%)	1.5	1.4	0.5	0.9	0.5	0.5	0.7	0.6	1.1	1.3	0.7	0.6
V35 Gy (%)	1.1	1	0.4	0.6	0.3	0.3	0.5	0.4	0.8	0.9	0.5	0.3
Time (min)	5.4	33	5.4	34	5.4	35	5.4	35	5.4	38	5.4	31

RFH: Right Femur Head; LFH: Left Femur Head.

# Table 3: Organs at risk dose and treatment time results.

		RA		P value	
	Mean	Median	Mean	Median	
PTV95%	99.4	99.4	99.4	99.5	0.49
PTVmax	107	106.7	127	126.6	0.028
PTV mean	100	100	105	110	0.34
nCl	1.05	1.06	1.2	1.21	0.027
н	1.1	1.07	1.27	1.27	0.026
Rectum					
V18 Gy (%)	43.1	43.6	40	41.3	0.35
V28 Gy (%)	17.7	16.9	16.3	16.5	0.25
V36 Gy (cm³) (%)	0.25	0.02	0.71	0.54	0.173
Baldder					
V18 Gy (%)	39.7	35.5	27.3	30.8	0.46
V36 Gy (cm³) (%)	1.8	0.93	4.1	4.4	0.116
Penile bulb max Gy (%)	101	103	96.3	99	0.173
Femur head max Gy (%)					
Right	14.2	13.8	20	19.6	0.046
Left	15	15.4	18.2	16.9	0.116
Body					
V10 (%)	6.23	5.6	7.4	6.7	0.046
V20 (%)	1.63	1.3	1.9	1.65	0.038
V30 (%)	0.83	0.7	0.9	0.75	0.68
V36 (%)	0.6	0.5	0.6	0.5	0.78
Time	2.4	2.4	34.3	34.5	0.028

Table 4: Statistical results of both plans.

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# Page 4 of 5

# Discussion

Stereotactic body radiotherapy (SBRT) using CK has recently emerged as an alternative technique to deliver hypofractionated radiotherapy to the prostate, comparable in many respects to high dose rate (HDR) brachytherapy, but with a noninvasive approach [7,13,15,17,27-29].

Almost all the literature on prostate SBRT delivers these treatments on CyberKnife but there is increasing interest in using conventional LINACS to deliver SBRT. In our study we tried to find out a reasonable alternative to CK especially with the new versions of RA. We compared the two methods of SBRT delivery available to us at our institution-CyberKnife (using Multiplan planning software) and RapidArc (arc therapy using Varian LINACS). We used the criteria regarding to the prescription dose, dose constraints and CTV to PTV margin depending on many studies [7,9,17,20-33].

CyberKnife system incorporates near real-time tracking of the prostate which allows smaller margins to be used, as it tracks and corrects for intra-fraction motion so if intra-fraction motion could be tracked and corrected during arc-therapy on a conventional LINAC, then the dosimetry is likely to be at least as good as CK. However, without intra-fraction motion control, a margin of 2 mm to 3 mm is likely to be needed to account for intrafraction motion after initial setup to gold markers [34]. Alternatively, if new flattening filter free (FFF) LINACS can deliver these plans in much shorter times, then intra-fraction motion may be less important, although transient, significant excursions of prostate position are still possible [35] and this was implicated in our study, by using RA with FFF.

In our study, the dose constraints regarding PTV coverage were achieved by both planning techniques. The conformity and homogeneity indices of the RA plans were better than the CK plans and statistically significant (p values 0.027 and 0.026). The constraints on the rectum and bladder were well achieved by both planning techniques. Additionally, the RA plans resulted in lower body dose regions (V10, V20, V30 were all lower with RA in all cases with p values of 0.04, 0.03 and 0.06 respectively but V35 was the same for both groups), lower statistically significant monitor units, and faster statistically significant delivery times (mean 2.4 min) than the CK plans (34.3 mean min).

Tree et al. [36] have shown that RA and CK can produce clinically acceptable plans where comparing the new versions of CK and RA treatments, the results showed a higher conformity and a lesser low-dose region of the RA when compared to the CK, with a similar target coverage and normal tissue sparing, even under different PTV margins. The mean estimated delivery time for treatments was 39 min for CK and 3 min for RA. These differences were the result of the different nature of the CK and RA systems.

Macdougall et al. [37] have shown that there is no discernible dosimetric advantage to choosing CyberKnife over RapidArc for SBRT delivery in prostate cancer. All dose constraints regarding PTV coverage were achieved by both planning platforms. The nCI was consistently better with RapidArc. The constraints on the rectum and bladder were well achieved by both planning platforms. The body V35 was consistently lower with CyberKnife, whereas body V10, V20, V30 were all lower with RapidArc in all cases. The mean estimated delivery time for treatments was 39 min for CyberKnife and 3 min for RapidArc.

Lin et al. [38] have shown that RA plans were shown to have a greater potential than CK plans in creating conformal dose distributions and in



Figure 1: Displayed the CK & RA isodose lines of one patient (axial, sagittal, coronal & 3D view).

reducing treatment times. The RA plans consistently exhibited superior PTV coverage and better rectum sparing at low doses in the both groups. The conformity and homogeneity indices of the RA plans were better than the CK plans. Additionally, the RA plans resulted in fewer low-dose regions, lower MUs, and faster delivery times than the CK plans. Currently, RA has become one of the SBRT options for localized prostate cancer treatments at their institution (Figure 1).

#### Conclusion

There is no dosimetric advantage for choosing CK over RA for SBRT delivery in prostate cancer. Given the significant benefits of RA in terms of availability and delivery time, make the new version of RA reasonable alternative SBRT technique for the treatment of localized prostate cancer; however, no intrafractional (real-time) target tracking is possible on the RA, which is available on the CK platform.

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