Original Article

Assessment of Volumetric-Modulated Arc Therapy for Constant and Variable Dose Rates

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Abstract

Purpose: The aim of this study is to compare the effects of dose rate on volumetric-modulated arc therapy plans to determine optimal dose rates for prostate and head and neck (HN) cases. **Materials and Methods:** Ten prostate and ten HN cases were retrospectively studied. For each case, seven plans were generated: one variable dose rate (VDR) and six constant dose rate (CDR) (100–600 monitor units [MUs]/min) plans. Prescription doses were: 80 Gy to planning target volume (PTV) for the prostate cases, and 70, 60, and 54 Gy to PTV1, PTV2, and PTV3, respectively, for HN cases. Plans were normalized to 95% of the PTV and PTV1, respectively, with the prescription dose. Plans were assessed using Dose-Volume-Histogram metrics, homogeneity index, conformity index, MUs, and delivery time. **Results:** For the prostate cases, significant differences were found for rectum D35 between VDR and all CDR plans, except CDR500. Furthermore, VDR was significantly different than CDR100 and 200 for bladder D50. Delivery time for all CDR plans and MUs for CDR400–600 were significantly higher when compared to VDR. HN cases showed significant differences between VDR and CDR100, 500 and 600 for D2 to the cord and brainstem. Significant differences were found for delivery time and MUs for all CDR plans, except CDR100 for number of MUs. **Conclusion:** The most significant differences were observed in delivery time and number of MUs. All-in-all, the best CDR for prostate cases was found to be 300 MUs/min and 200 or 300 MUs/min for HN cases. However, VDR plans are still the choice in terms of MU efficiency and plan quality.

Keywords: Dose rate, head and neck, prostate, volumetric modulated arc therapy

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Introduction

Volumetric modulated arc therapy (VMAT) has gained popularity in the recent years as it provides dosimetric benefits, reducing monitor units (MUs) and delivery time compared to conventional intensity-modulated radiation therapy (IMRT),[1-3] which has been reported for a wide variety of treatment sites.[4-11] During delivery, the gantry of the linear accelerator (linac) rotates around the patient, whereas the radiation beam is continuously on. Several parameters such as dose rate, multileaf collimator (MLC) aperture shape, gantry rotation speed, and gantry control point spacing could be varied depending on the optimization constraints.[12] The relationship between these VMAT delivery parameters have been extensively studied and reported in several publications.[12-14] Work by Rangaraj *et al*.[12] showed that for a given treatment, gantry speed keeps its maximum value most of the time; and therefore, this parameter does not need to be modulated when dose rate varies between 0 and 600. Their work also showed that optimal dose rate value was 192 MU/min for a prostate plan when all VMAT delivery parameters are allowed to vary. As expected, the shortest treatment time was achieved when constraints on maximum gantry speed, dose rate, and leaf speed were imposed.

Although the variable dose rate (VDR)-based VMAT delivery provides the maximum flexibility and benefit in terms of lower MUs and shorter treatment delivery time, constant dose rate (CDR)-based VMAT delivery may be a viable option for the linacs which cannot vary dose rate. The three treatment planning systems (TPS) that allow VMAT plans to be generated for both constant and VDR delivery are Pinnacle SmartArc module (Philips Medical Systems, Madison, WI, USA),

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Raystation (RaySearch Laboratories, Stockholm, Sweden), and Oncentra MasterPlan (Nucletron B. V., Veenendaal, the Netherlands). On the other hand, Eclipse (Varian, Palo Alto, CA) does not have constant dose rate option. Recently published work by Yu *et al*.[15] compared CDR-based, VDR-based VMAT plans with multicriteria optimization (MCO) VMAT plans in nasopharyngeal cancer patients using Raystation TPS. In their comparison, they selected 400 MU/min as its CDR, yet did not mention rationale to selecting such value. Their study found that CDR plans achieved similar target coverage, dose homogeneity, and target conformity compared to VDR-and MCO-VMAT plans, with some inferiority in target coverage but superior in dose homogeneity. In addition, the brainstem dose was higher in comparison, but found to be within clinical tolerance. A work by McGarry *et al*.[11] compared CDR and VDR plans to IMRT in prostate cancer and found that dose homogeneity and conformity were not significantly different in any of the three. In this study, the CDR level was not specified, but "selected" from values ranging from 100 to 600 MU/min. The results showed significantly higher MUs for CDR compared to IMRT, yet delivery time was significantly shorter. A more recent study by Hatanaka *et al*.[16] compared IMRT, VDR, and CDR for 28 prostate cases, in which they found that IMRT had a larger number of MUs and longer treatment time compared to VDR and CDR, but optimization time was longest for CDR. They also found that bladder volume, if >100 cm^3, was a good index to determine the feasibility of using CDR to meet bladder dose constraints. Again, constant dose rate was not specified for this study. Fei *et al*.[17] used an iterative algorithm to heuristically optimize both dose rate and gantry speed to obtain CDR for five prostate and two head and neck (HN) cases. The study compared the CDR plans to VDR and IMRT and concluded that CDR plans are comparable to VDR when longer treatment times are allowed but results in higher MU values.

To accurately use CDR, an optimum dose rate level needs to be determined. Although other studies have provided a comparison of CDR-to VDR-based plans, the constant dose rate value was arbitrarily chosen for all of these studies. In this work, we provide a systematic study to compare different constant dose rate to VDR based VMAT treatment plans for prostate and HN cases.

Materials and Methods

Volumetric modulated arc therapy optimization

Pinnacle's SmartArc module (research v. 9.100, Philips Medical Systems, Madison, WI) was used for the optimization and generation of VMAT plans. A detailed description of SmartArc module was published by Bzdusek *et al*.[18] and will be summarized here for completeness. First, a set of segments spaced by 24° is generated for a user-defined defined dynamic arc which consists of arc length, couch, and collimator angles. Second, the fluence maps are converted to MLC segments following an intensity modulation optimization performed on the fluence maps for the segments generated in the first step. The MLC segments are then filtered and redistributed around the arc to achieve the final arc spacing. The final MLC segments are optimized using direct machine parameter optimization to satisfy dose volume objectives, gantry and leaf speed, and dose rate constraints. Pencil beam calculation algorithm is used during the optimization. The final dose calculation is done using superposition/convolution algorithm, and finally, segment weight optimization is performed to remove potential errors due to use of pencil beam algorithm during the optimization. One of the dynamic arc specific constraints utilized during machine parameter optimization is the dose rate. The dose rate can be set to "constant" for the entire arc or "variable" for the optimization of the individual control point dose rates in the current version of Pinnacle TPS. As Bzdusek *et al*. pointed out,[18] the gantry speed was constrained to a fixed value in Pinnacle's SmartArc module since allowing the gantry speed to vary during the optimization did not provide significant improvement. Varian linac with 6 MV and 18 MV photons and 120 leaf Millennium MLC (Varian Medical Systems, Palo Alto, CA) was used for the planning and delivery of the VMAT plans.

Volumetric modulated arc therapy treatment planning

Ten prostate and ten HN cases were selected and utilized for this study. All cases were previously treated with either conventional step-and-shoot IMRT or VMAT techniques and contoured for the corresponding planning target volumes (PTVs) and organs at risk (OARs). For the prostate cases, the OARs included bladder, rectum, right and left femurs, and bowel. The HN OARs were brainstem, spinal cord, parotids, mandible, oral cavity, larynx, and esophagus. The optimization objectives for all structures used for the VMAT optimization are listed in Tables 1 and 2. Prescription dose for the prostate cases was 80 Gy in 40 fractions to the PTV. HN cases were planned with a simultaneous integrated boost to three targets: PTV1, PTV2, and PTV3. The corresponding prescription doses were 70, 60, and 54 Gy, respectively, delivered in 33 fractions. Plans were normalized such that 95% of the prostate PTV and HN PTV1 received 100% of the prescription dose in each plan correspondingly.

For each patient case, VMAT plans were generated with six different dose rates of CDR: 100, 200, 300, 400, 500, and 600 MUs/min, and one plan with VDR with minimum

Table 1: Prostate cases organs at risk constraints

Organ	Dose (Gy)
Bladder	
25%	65
50%	40
Rectum	
17%	65
35%	40
Bowel	
150 cc	40
Femurs	
Maximum	50

and maximum dose rate set to 0 and 600 MUs/min. Gantry speed was variable, with a maximum of 6 degrees/second. According to Bzdusek *et al*. whether gantry speed is variable or fixed, it does not affect plan outcome.[18] All the cases had two coplanar full arcs and 4° gantry spacing resolution and 0.46 cm/deg leaf motion constraint for best plan quality and complexity balance as reported by Mihaylov *et al*.[14] Orthogonal collimator angles arrangement of 45° were used for the prostate plans which had consisted of one full arc. Two full overlapping arcs were used for the HN plans with collimator angles of 45° and 135° to provide possible complementing segments due to MLC geometrical limitations. Maximum gantry speed and MLC leaf speed for all plans were of 6 deg/s and 2 cm/s, respectively. Photon energy for prostate was 18MV and 6 MV for HN cases. All parameters were set for Varian 21EX machine.

Table 2: Head and neck cases organs at risk constraints

Organ	Dose (Gy)
Brainstem	
Maximum (D2%)	50
Cord	
Maximum (D2%)	40
Mandible	
20%	60
Oral cavity	
30%	45
Parotids	
50%	25
Mean	26
Larynx	
50%	45
Esophagus	
30%	45

D2 is used as a surrogate for D_{max}

Volumetric modulated arc therapy plan assessment

Plans were compared using dose volume histogram (DVH) parameters such as dose to 2% of the volume (D2), dose to 30% of the volume (D30), dose to 50% of the volume (D50), homogeneity index (HI) of targets, conformity index (CI), dose to organs at risk (OARs), MUs, and delivery time. D2 was used as a surrogate for the maximum dose. The HI was calculated using the expression[19]: HI = [(D2-D95)/Dprescription] × 100, where D2 is the dose to 2% of the PTV, D95 is the dose to 95% of the PTV, and Dprescription is the prescribed dose. The CI was calculated using the Radiation Therapy Oncology Group definition: CI = PIV / TV, where PIV is the prescription isodose volume and TV is the target volume. The delivery time obtained is the estimated delivery time calculated by the TPS taking into account all the parameters of the plan.

The comparisons between different plans were made relative to the VDR plans, which was used as benchmark reference, using the Wilcoxon signed-rank test.[20] The average values of the DVH indices were found to be statistically significant if $P \leq 0.05$.

Results

Prostate cases

All CDR plans resulted in equivalent dose-to-target coverage as the VDR plans. Table 3 shows mean dose and standard deviation values for average dose to target and OARs. Significant difference was found for the dose to bladder D50 for CDR100 (39.02 ± 8.19 Gy) and CDR200 (39.52 ± 8.40 Gy) with respect to VDR (36.37 ± 10.68 Gy). The results for dose to 35% of rectum showed significant difference between

Table 3: Mean values and standard deviation for variable dose rate and the six constant dose rate plans for the ten prostate cases

Parameters	Mean±SD	Mean (correlation)					
	VDR	CDR100	CDR200	CDR300	CDR400	CDR500	CDR600
PTV							
$D_{2\%}$ (Gy)	86.07±1.35	86.24±1.99	86.51±1.73	86.36±1.87	86.16±1.69	86.54±1.53	86.71±1.74
$D_{95\%}$ (Gy)	79.95±0.13	79.91±0.11	79.85±0.16	79.86±0.06	79.90±0.08	79.89±0.09	79.89±0.06
Bladder							
$D_{2\%}$ (Gy)	84.68±2.07	84.82±2.38	84.98±2.24	84.76±2.56	84.65±2.39	84.93±2.31	85.23±2.55
$D_{25\%}$ (Gy)	62.05±11.34	63.17±9.25	63.75±9.30	62.93±9.58	63.47±9.18	63.34±9.30	63.62±9.71
$D_{50\%}$ (Gy)	36.37±10.68	39.02±8.19*	39.52±8.40*	38.18±9.45	38.37±9.36	38.00±9.30	37.60±9.44
Rectum							
$D_{2\%}$ (Gy)	81.93±3.06	81.56±3.70	81.57±3.53	81.68±3.67	81.71±3.22	81.91±3.62	82.19±3.82
$D_{17\%}$ (Gy)	61.28±11.03	62.40±11.19	62.43±9.95	61.75±10.92	61.75±10.68	61.74±10.91	62.10±11.03
$D_{35\%}$ (Gy)	39.11±11.08	41.74±8.77*	41.88±8.79*	40.54±10.28*	40.44±10.27*	40.37±10.18	40.64±10.20*
Right femur							
$D_{2\%}$ (Gy)	28.23±8.82	31.35±6.60*	32.36±7.99*	31.25±7.41*	30.28±7.85*	30.41±8.51*	62.68±8.56*
Left femur							
$D_{2\%}$ (Gy)	28.38±9.05	33.32±8.76*	32.50±9.80*	32.44±9.60*	32.54±9.90*	33.31±10.58*	34.62±10.43*

Underlined values show the closest mean dose to the benchmark VDR. Values in table need to be underlined. *Significant difference with respect to VDR. VDR: Variable dose rate, SD: Standard deviation, PTV: Planning target volume, CDR: Constant dose rate

VDR (39.11 ± 11.08 Gy) and all CDR plans, except CDR 500 (40.37 ± 10.18 Gy). Both femurs had significantly lower dose with the VDR plan compared to all CDR plans [cf. Table 3]. All other OAR parameters were not significantly different between any CDR and VDR plans. The results showed a significant difference in HI between VDR and CDR100, CDR200, CDR500, and CDR600, with average values of 7.65 ± 1.69, 7.91 ± 2.46, 8.32 ± 2.20, 8.31 ± 1.93 and 8.52 ± 2.16, respectively. Average values of HI and CI are illustrated on Figure 1. Significant difference was found in CI between all CDR plans and VDR. MUs were significantly higher for CDR400, 500 and 600 compared to VDR. In addition, all CDR plans were significantly higher in delivery time compared to VDR. Figure 2 shows the average number of MUs and delivery time for each dose rate plan.

Head and neck cases

Plans were normalized to achieve target coverage for PTV1 of 70 Gy. Dose to 95% of PTV2 and PTV3 deviated from the prescription dose of 60 and 54 Gy, respectively, by <2% for PTV2 and 2.3% for PTV3, which was not significant. Table 4 shows average dose indices for the HN cases. It can be observed that for CDR200 and 300, the least number of significant differences for dose indices was found with respect to VDR. The only two values significantly higher for CDR200 were max dose to PTV2 and to brainstem. For CDR300, PTV2 D2 and mandible D2 were significantly higher compared to VDR. The HI for PTV1 was significantly better for VDR compared to CDR400, 500, and 600. PTV2 showed a significantly HI for CDR300, 400, and 600 and for PTV3 in plans CDR300, 400, 500, and 600. Figure 3 illustrates the increasing trend of the HI and CI as the dose rate increases. CI was significantly higher for CDR200–600 compared to VDR. All CDR plans were significantly different than VDR when comparing delivery time. The difference in MUs was significant for all CDR plans, except CDR100, compared to VDR. Figure 4 illustrates the mean values for MUs and delivery time for each dose rate plan.

Discussion

In this work, six different constant dose rate plans have been compared to find the optimum dose rate for prostate and HN cases when VDR is not available. Differences in OAR sparing were for the most part not significantly different between CDR and VDR with few exceptions. Similar results were reported for nasopharyngeal cancer, in which 12 previously treated patients were used for comparison between VDR, MCO, and CDR of 400 MU/min, results of this study showed no significant dosimetric differences between MCO, CDR and VDR plans.[15]

It has been previously demonstrated that VDR VMAT is superior than CDR in terms of delivery time and number of MUs,[15,21,22] yet with significantly lower delivery time than IMRT.[11] This study demonstrated consistent increase of MUs as the constant dose rate increased. In prostate cases, the number of MUs was significantly different than VDR for dose rates

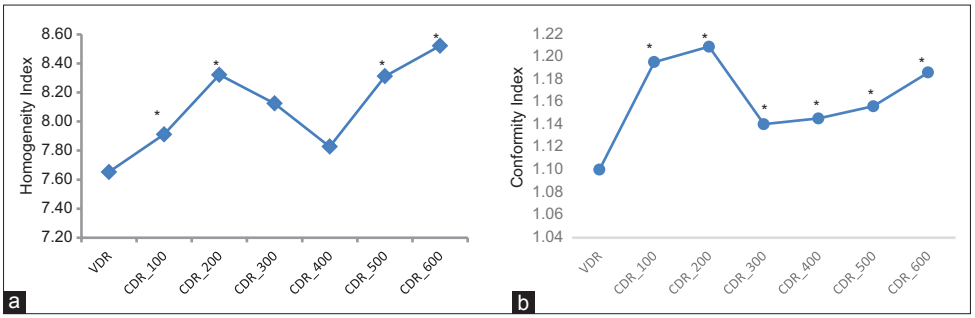

Figure 1: (a) Average planning target volume homogeneity index – a value approaching zero means higher planning target volume dose homogeneity. The asterisks denote significant difference between the corresponding constant dose rate plan's homogeneity index with respect to the variable dose rate value. (b) Average planning target volume conformity index – a value close to one means better conformity of the dose to the planning target volume

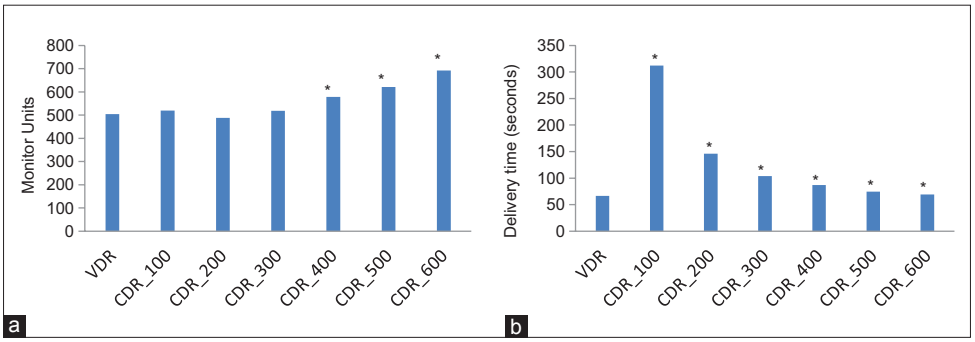

Figure 2: Prostate cases average (a) monitor units and (b) delivery time for each dose rate plan. Asterisk denotes significant difference with respect to variable dose rate

Table 4: Comparison between variable dose rate and the six constant dose rate plans for various parameters for the five head and neck cases

Parameters	VDR (mean)	Mean (correlation)					
		CDR100	CDR200	CDR300	CDR400	CDR500	CDR600
PTV1							
$D_{2\%}$ (Gy)	75.09±1.18	74.85±1.46	74.96±0.87	75.27±0.82	76.50±1.82*	77.26±1.98*	77.58±1.89*
$D_{95\%}$ (Gy)	69.92±0.08	69.92±0.07	69.95±0.09	69.96±0.09	69.96±0.19	69.94±0.25	69.94±0.19
PTV2							
$D_{2\%}$ (Gy)	70.59±0.85	70.66±0.70	70.93±1.12*	71.37±1.10*	72.20±1.52*	72.97±2.04*	73.97±2.95*
$D_{95\%}$ (Gy)	60.95±1.02	61.01±1.09	61.10±0.98	61.00±0.46	60.55±1.12*	61.20±3.26	60.16±0.94*
PTV3							
$D_{2\%}$ (Gy)	61.93±3.03	61.90±3.17	62.13±3.26	62.53±2.50	63.58±3.04*	64.56±3.40*	65.30±4.00*
$D_{95\%}$ (Gy)	54.99±1.09	54.80±1.04	54.86±1.10	54.31±0.71	53.99±1.05*	53.32±2.42*	52.90±3.95*
Brainstem							
$D_{2\%}$ (Gy)	40.79±5.12	42.88±5.41*	42.89±6.29*	42.75±7.00	42.61±5.87	43.28±4.96	45.11±6.98*
Cord							
$D_{2\%}$ (Gy)	35.05±4.68	38.92±9.58*	35.65±4.75	35.93±2.78	36.92±2.52	38.14±1.11*	38.51±5.54*
Mandible							
$D_{20\%}$ (Gy)	55.00±7.18	56.55±6.55	56.42±6.79	57.64±6.21*	58.95±4.88*	60.05±4.77*	60.35±6.53*
Oral cavity							
$D_{30\%}$ (Gy)	34.18±14.37	35.07±14.46	35.82±14.30	35.73±14.87	37.68±14.42*	37.45±14.40*	37.05±14.78*
Right parotid							
$D_{50\%}$ (Gy)	25.75±6.97	26.89±8.57	27.45±8.93	27.57±8.64	27.03±8.52	26.80±9.08	26.97±8.45
Left parotid							
$D_{50\%}$ (Gy)	22.82±5.81	23.38±4.63	23.31±4.34	23.34±4.34	23.35±4.14	23.56±4.11	23.63±3.86
Larynx							
$D_{50\%}$ (Gy)	38.97±3.29	39.54±3.58	39.58±3.42	39.08±3.81	39.08±4.40	39.04±4.39	39.51±5.51
Esophagus							
$D_{30\%}$ (Gy)	33.82±8.57	34.57±7.73	34.49±8.02	33.71±8.26	34.61±7.64	34.80±7.42	37.26±8.86

Underlined values show the closest mean dose to the benchmark VDR. Values in table need to be underlined. *Statistically significant difference with respect to VDR. VDR: Variable dose rate, PTV: Planning target volume, CDR: Constant dose rate

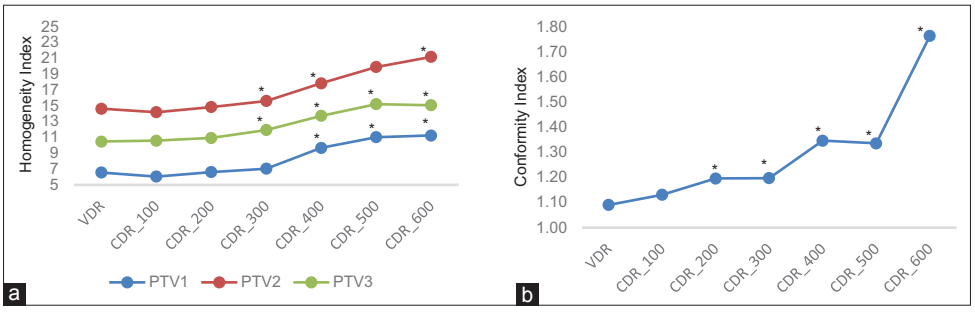

Figure 3: Head and neck cases (a) average planning target volume 1, planning target volume 2, and planning target volume 3 homogeneity index – a value approaching zero means higher target dose homogeneity. (b) Average planning target volume 1 conformity index – a value close to one means better conformity of the dose to the target. Asterisks denote statistically significant difference with respect to the variable dose rate plan

above 400 MU/min. On the other hand, HN cases showed, on average, lower MUs for CDR100 and higher MUs for dose rates above 200 MUs/min. Delivery time was significantly different than VDR (120.40 ± 0.70 s average) for all CDR plans for HN cases, with the highest value for CDR100 (274.80 ± 43.95 s average). A study by Tang *et al*. reported that delivery time was minimally different between VDR and CDR for HN cases,[23] yet it failed to mention what dose rate was used for CDR, which can lead to significant variations as it has been shown in this study. Prostate cases resulted in significant higher delivery time only for all CDR plans compared to VDR, but the number of MUs was significantly higher for CDR400, 500, and 600. Therefore, when determining the best dose rate for delivery, CDR100 can be rejected since the average delivery time was twice as long compared to CDR200 and 300 and about five times longer than VDR.

Taking into account all dosimetric parameters for prostate cases, the ideal dose rate would be CDR300, as the quality of these plans were the closest to VDR plans and the least

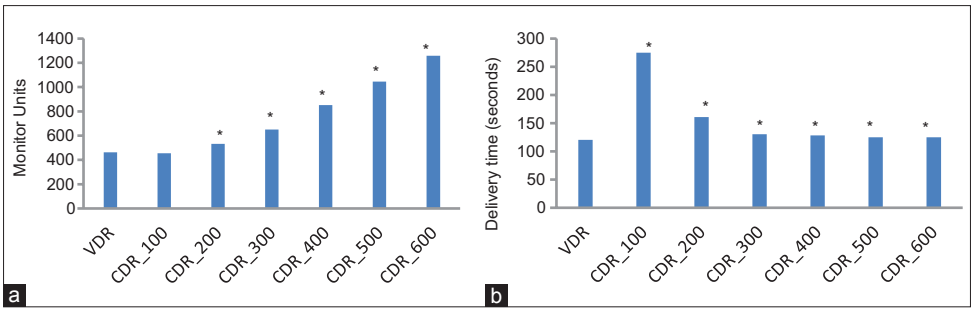

Figure 4: Head and neck cases average (a) monitor units and (b) delivery time for each dose rate plan. Asterisk denotes statistically significant difference with respect to variable dose rate

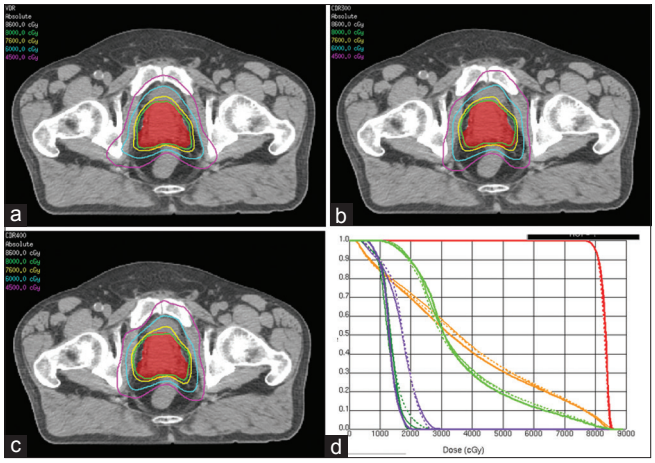

Figure 5: Axial view of isodose lines for prostate patient 9 for variable dose rate (a), constant dose rate 300 (b) and constant dose rate 400 (c) plans. (d) The corresponding dose-volume-histogram with variable dose rate shown in solid thick line, constant dose rate 300 in dashed line and constant dose rate 400 in thin line.Volume of interest is shown as follows: planning target volume (red), bladder (orange), rectum (light green), right femur (purple), and left femur (dark green)

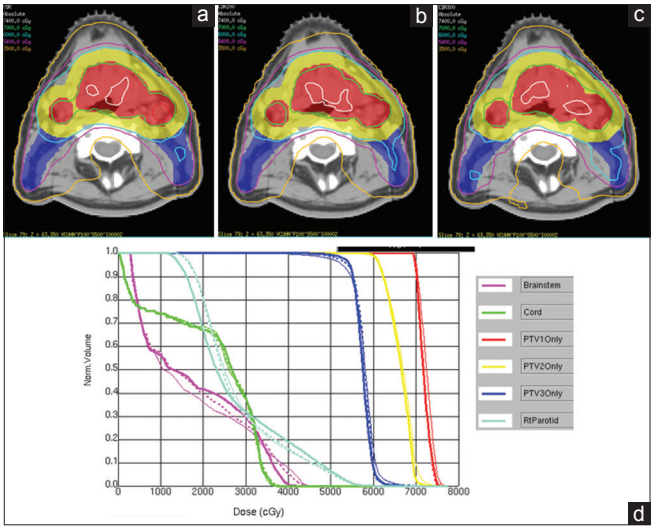

Figure 6: Axial isodose line display for the head and neck patient 10 for variable dose rate (a), constant dose rate 200 (b), and constant dose rate 300 (c) plans. (d) The corresponding dose-volume-histogram with variable dose rate shown in solid thick line, constant dose rate 200 in dashed line and constant dose rate 300 in thin line

variable between patients for most of the OAR constraints. On average, the delivery time was comparable to VDR, but MUs were higher, yet not significantly different than VDR [cf. Figure 2]. A higher delivery time may lead to more uncertainty in positioning, yet the largest difference between CDR300 and VDR was 54 seconds for patient 3. Dose rate of 300 MUs/min is in-line with what is observed in the clinic even when linacs with VDR are used. Figure 5 illustrates the dose distribution of a VDR plan with CDR300 and 400 with the corresponding DVH for patient 9. It can be observed that the largest differences between VDR and the CDR plans for this patient occurred in the lower dose range for the femurs, but for the set dose constraints, slight dose variation occurred.

The same analysis was performed for HN cases, where high-dose rates (CDR500 and CDR600) lead to higher MUs and higher between-patient variations and on average resulted in a higher deviation from VDR. From Table 4, it can be concluded that the CDR plans with the least differences with respect to VDR were the low-dose-rate plans (CDR100–300), but delivery time was higher for CDR100 with respect to CDR 200 and 300 [cf. Figure 4]. Taking into account all the parameters, the best dose rate for HN plans would be either 200 or 300 Mus/min. Even though the delivery time would be longer for CDR than VDR, the largest difference observed was about 1 minute, which should not translate to motion issues during delivery. Figure 6 illustrates the dose distribution of patient 10 and the DVH for plans VDR, CDR200, and 300. The results also showed that the HI and CI for the three PTVs increased as dose rate increased, further emphasizing the dose rate should be kept in the mid-range.

Conclusions

Six constant dose rate VMAT plans were compared to a benchmark VDR plan to find the optimal constant dose rate for linacs incapable of delivering VDR VMAT. Constant dose rate plans met most dose constraints for OARs when comparing to VDR plans a few dose parameters were significantly different. The observed differences in the number of MUs and delivery time were significant. The best constant dose rates for prostate was found to be 300 MUs/min and either 200 or 300 MUs/min

for HN cases. The results showed that these dose rates resulted in lowest differences between CDR and VDR VMAT plans.

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Conflicts of interest

There are no conflicts of interest.

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