Optimal planning strategy among various arc arrangements for prostate stereotactic body radiotherapy with volumetric modulated arc therapy technique

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Background. The aim of this study was to determine the optimal strategy among various arc arrangements in prostate plans of stereotactic body radiotherapy with volumetric modulated arc therapy (SBRT-VMAT).

Patients and Methods. To investigate how arc arrangements affect dosimetric and biological metrics, SBRT-VMAT plans for eighteen patients were generated with arrangements of single-full arc (1FA), single-partial arc (1PA), double-full arc (2FA), and double-partial arc (2PA). All plans were calculated by the Acuros XB calculation algorithm. Dosimetric and radiobiological metrics for target volumes and organs at risk (OARs) were evaluated from dose-volume histograms.

Results. All plans were highly conformal (CI<1.05, CN=0.91) and homogeneous (HI=0.09-0.12) for target volumes. For OARs, there was no difference in the bladder dose, while there was a significant difference in the rectum and both femoral head doses. Plans using 1PA and 2PA showed a strong reduction to the mean rectum dose compared to plans using 1FA and 2FA. Contrastively, the D2% and mean dose in both femoral heads were always lower in plans using 1FA and 2FA. The average tumor control probability and normal tissue complication probability were comparable in plans using all arc arrangements.

Conclusions. The use of 1PA had a more effective delivery time and produced equivalent target coverage with better rectal sparing, although all plans using four arc arrangements showed generally similar for dosimetric and biological metrics. However, the D2% and mean dose in femoral heads increased slightly and remained within the tolerance. Therefore, this study suggests that the use of 1PA is an attractive choice for delivering prostate SBRT-VMAT.

Key words: stereotactic body radiotherapy; volumetric modulated arc therapy; prostate cancer; arc arrangement; dosimetric and biological metrics

Introduction

Prostate cancer is the most common cancer in men, accounting for over one fifth of male cancer diagnoses, with the number of prostate cancer patients rapidly increasing. Various radiotherapy techniques for treating prostate cancer have been considered effective noninvasive treatment options,
especially for elderly patients and those unfit for surgery.1-3

Radiation therapy options for prostate cancer include external beam radiation therapy (EBRT) and brachytherapy. Volumetric modulated arc therapy (VMAT) and intensity-modulated radiation therapy (IMRT) for EBRT is widely used as the standard treatment for prostate cancer. VMAT and IMRT permit dose optimization, in which the dose to the prostate can be increased while reducing toxicities and doses to the rectum and bladder, resulting in improved local control and reduced complications when compared to three-dimensional conformal radiation therapy (3DCRT).4-7 In addition, VMAT can produce equivalent or even better target coverage and normal tissue sparing compared to fixed-field IMRT while taking advantage of more efficient monitor unit (MU) and reducing the delivery times.

The use of SBRT to irradiate primary or metastatic tumors in several anatomical sites is becoming the standard treatment.8-13 SBRT with VMAT (SBRT-VMAT) is a radiotherapy method, which very precisely delivers a high dose of radiation to the target area in either a single dose or a small number of fractions. It is an attractive approach to dose escalation. Recently, researchers using SBRT, including the linear accelerator (Linac) and CyberKnife (CK), have achieved promising results in the treatment of prostate cancer.14-17 To our knowledge, there is very little information regarding the optimal planning for various arc arrangements of prostate SBRT-VMAT.18,19 Moreover, there is no study, which investigates the radiobiological effect of prostate SBRT-VMAT plans.

The aim of this study is to determine the optimal treatment planning approach under the different arc arrangements by analyzing the dosimetric and radiobiological impact in plans for prostate SBRT-VMAT.

Planning strategy for SBRT

Prostate SBRT using VMAT plans were created by the Eclipse™ Treatment Planning System (ver. 11.0.34, Varian Medical Systems). The SABR-VMAT planning system was commissioned for a Truebeam™ Linac (Varian Medical Systems) with a high definition multileaf collimator (HD MLC). Dose distributions were calculated using a 10-MV flattening-filter-free (FFF) beam and the Acuros XB (AXB) dose calculation algorithm with inhomogeneity correction. The calculation grid size was 2.5-mm.

The SBRT-VMAT plans were set up with four arc arrangements such as single-full arc (181° to 179°; 1FA), single-partial arc (240° to 120°; 1PA), double-full arcs (181° to 179° and 179° to 181°; 2FA), and double-partial arcs (240° to 120° and 120° to 240°; 2PA). The arc arrangements for SBRT-VMAT plans are presented in Figure 1 A to D. The collimator rotation angles were 30°.

The prescription dose was 42.7 Gy and was administered in seven fractions. Compared to 78 Gy in 39 fractions, which is the standard prostate fractionation, this delivers a higher biologically effective dose (BED) to the prostate (216.3 Gy vs. 182.0 Gy; α/β 1.2 Gy) but an equivalent dose to late responding tissues (129.5 Gy vs. 130.0 Gy; α/β 3.0 Gy). For all cases, a minimum of 95% of the prescription dose (40.6 Gy) was assigned to cover 95% of the PTV (V₉₅ ≥ 95%). No OAR constraints for
prostate SBRT have yet been reported. Therefore, we used the modified constraints for the OARs derived from those reported by Murray et al.\textsuperscript{22} that were suitable for our planning study. The OAR constraints for this planning study are listed in Table 1.

### Evaluation of dosimetric and biological parameters

The mean, maximum, and minimum doses for PTV were measured from cumulative dose-volume histograms (DVH) of plans using four arc arrangements for all patients. In order to investigate the target coverage, V\textsubscript{100\%} for CTV and PTV were evaluated.

The conformity index (CI) was defined as follows:

\[
CI = \frac{V_{RI}}{TV}
\]

The ideal conformity is defined as CI = 1. A value of CI > 1 indicated that healthy tissue has been irradiated.\textsuperscript{23} The conformation number (CN) takes into consideration the irradiation of healthy tissue. It is the product of two fractions, TV\textsubscript{RI}/TV and TV\textsubscript{RI}/V\textsubscript{RI}, where TV is the volume of the PTV, TV\textsubscript{RI} is the volume of the PTV covered by the reference isodose line, and V\textsubscript{RI} is the volume enclosed by the reference isodose line. TV\textsubscript{RI}/TV is the quality of the target coverage and TV\textsubscript{RI}/V\textsubscript{RI} is the volume of healthy tissue irradiated with the reference isodose (95% of prescribed dose) or more.\textsuperscript{24}

The dose homogeneity index (HI) was determined as follows:

\[
HI = \frac{(D_{5\%} - D_{95\%})}{D_{50\%}}
\]

where D\textsubscript{5\%} is the maximum dose received by 5% of PTV, D\textsubscript{95\%} is the minimum dose received by 95% of PTV, and D\textsubscript{50\%} is the dose received by 50% of PTV. A lower HI represents a more homogeneous plan, because D\textsubscript{5\%} and D\textsubscript{95\%} were surrogate markers of maximum dose and minimum dose in the PTV, respectively.

The near-to-maximum dose (D\textsubscript{2\%}) and mean dose for the OARs were evaluated. In addition, we conducted a detailed analysis of the rectum and bladder volumes that received at least 95% (V\textsubscript{95\%}), 80% (V\textsubscript{80\%}), 50% (V\textsubscript{50\%}), and 20% (V\textsubscript{20\%}) of the prescription dose; these values represent very high, high, intermediate, and low doses, respectively. In addition, total monitor units (MUs) were compared in each plan between single arc and double arc arrangements.

### Table 1. Dose volume constraints adopted for planning study

| Volume | Rectum | Bladder | Femoral heads |
|--------|--------|---------|--------------|
| V\textsubscript{42.7 Gy (100\%)} | < 5% | V\textsubscript{42.7 Gy (100\%)} | < 10% |
| V\textsubscript{38.4 Gy (80\%)} | < 15% | V\textsubscript{34.7 Gy (87\%)} | < 25% |
| V\textsubscript{33.0 Gy (75\%)} | < 35% | V\textsubscript{29.9 Gy (70\%)} | < 50% |
| V\textsubscript{28.0 Gy (65\%)} | < 45% |
| V\textsubscript{24.8 Gy (58\%)} | < 70% |
| V\textsubscript{20.0 Gy (47\%)} | < 80% |

D\textsubscript{max} = the maximum dose; V\textsubscript{xx Gy} = the volume receiving dose of xx Gy (x% of the prescription dose)

For the radiobiological model evaluation, we utilized the MATLAB program to calculate the Niemierko’s equivalent uniform dose (EUD)-based tumor control probability (TCP) and normal tissue complication probability (NTCP).\textsuperscript{25,26} According to Niemierko’s phenomenological model, the EUD is defined as follows:

\[
EUD = \left( \sum_{i} (V_i E Q D_i^\alpha) \right)^{\frac{1}{\alpha}}
\]

where \(\alpha\) is a tissue-specific parameter describing the volume effect, and \(E Q D_i^\alpha\) is the partial tumor volume, which receives dose D in Gy. For tumors, \(\alpha\) takes negative values; for serial-like structures, \(\alpha\) takes large positive values; and for parallel-like structures, \(\alpha\) takes values close to 1.

The prostate TCP was calculated with Niemierko’s EUD-based TCP. The equation is defined as follows:

\[
TCP = \frac{1}{1 + \left( \frac{TCD_{50}}{EUD} \right)^{\gamma_{50}}}
\]

where \(TCD_{50}\) is the tumor dose to control 50% of the tumors when the tumor is homogeneously irradiated, and the \(\gamma_{50}\) is the slope of dose response at a TCP of 50%. NTCP for OARs were calculated using Niemierko’s EUD-based NTCP with the following equation:

\[
NTCP = \frac{1}{1 + \left( \frac{T D_{50}}{EUD} \right)^{\gamma_{50}}}
\]

where \(T D_{50}\) is the tolerance dose for a 50% complication rate at a specific time interval (e.g., 5 years in the Emami et al. normal tissue tolerance data) when the whole organ of interest is homogenously irradiated. The \(\gamma_{50}\) is specific to the normal structure of interest and describes the slope of the dose-response curve.

Table 2 lists parameters used to calculate Niemierko’s EUD-based TCP and NTCP. These
of the four arc arrangements of all patients were very similar as shown in Table 3 and Figure 3A. In four arc arrangements, the volume of the CTVs that received 100% of prescription dose was greater than 97.6% (range 96.7–98.4%), which indicated very good coverage the CTV in the VMAT plan. All plans were highly conformal with CI < 1.05 and CN = 0.91, and the doses were homogeneous (HI = 0.09±0.12).

The doses to bladder tissue showed no difference among all arc arrangements. However, there were significant differences in the doses of the rectum, left and right femoral head (Table 4, Figure 3A, C, D, E). Compared to 1FA and 2FA, 1PA and 2PA arrangements resulted in a significant reduction of the mean dose (V50%) of the rectum. These arc arrangements resulted in a significant increase in the near-to-maximum dose D2% and mean dose of the left and right femoral head.

Table 5 summarizes the MUs and delivery time for the prostate SBRT plans using the four arc arrangements. The average MU was 1575 ± 63, 1607 ± 56, 1646 ± 97, and 1660 ± 98 for plan using 1FA, 1PA, 2FA, and 2PA, respectively. Plans using 1FA required lower MUs than those using other arc arrangements. The average delivery time was 1.01 ± 0.02, 0.69 ± 0.01, 2.00 ± 0.01, and 1.36 ± 0.02 for 1FA, 1PA, 2FA, and 2PA, respectively. The ratio of delivery time was 1.46, 2.90, and 1.97 for 1FA, 2FA, and 2PA compared to 1PA.

The average TCP of prostate tumors and the average NTCP of OARs in the four arc arrangement plans are shown in Table 6. TCP and NTCP values were comparable for all arc arrangements.

Discussion

Much has been published regarding the use of VMAT in prostate cancer, but little regarding the use of SBRT using VMAT for prostate cancer. Most of the previous studies for prostate SBRT employed the CK technique. The CK technique is an

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**TABLE 2. Parameters used to calculated Niemierko’s EUD-based TCP and NTCP**

| Tissue   | 100%dpf (Gy) | Fraction (#) | α    | β    | TDD50 (Gy) | TCD50 (Gy) | dpf (Gy) | α/β |
|----------|--------------|--------------|------|------|------------|------------|----------|-----|
| Prostate | 6.1          | 7            | -10  | 1.0  | 28.34      | 2          | 1.20     |     |
| Rectum   | 6.1          | 7            | 8.33 | 4    | 80         | 2          | 3.90     |     |
| Bladder  | 6.1          | 7            | 2    | 4    | 80         | 2          | 8.00     |     |
| Femur    | 6.1          | 7            | 4    | 4    | 65         | 2          | 0.85     |     |

α/β = Alpha-beta ratio; 100%dpf = 100% dose per fraction; dpf = Parameters’ source data’s dose per fraction.
accurate image guided method for delivering radiation to a precisely targeted area using multiple nonisocentric beams with steep surrounding dose gradient.\textsuperscript{16} In the previous study reported by Chow and Jiang,\textsuperscript{19} the dosimetry and radiobiological model variation was investigated in prostate VMAT plans using the single- and double-full arc technique. The authors reported that the double-arc technique could lower the dose-volume criteria of the rectum and bladder but increase the rectal NTCP. In addition to the study above, we included the single and double-partial arc (1PA and 2PA), which avoided irradiation of the rectum for the optimal prostate SBRT-VMAT plan. This study focused on arc arrangements as a key preparatory step in facilitating clinical planning studies.

The prostate SBRT-VMAT plans for all arc arrangements generated conformal dose distributions for target volumes (PTV and CTV). We found that the dose distributions in the anterior and posterior direction were lower when the partial arc arrangements (1PA and 2PA) were used instead of the full arc (1FA and 2FA). In contrast, the dose distributions in the left and right direction for full arc arrangements were lower than those of the partial arc (Figure 2). This was due to the application of arc angles, which avoided the direct irradiation of the rectum.

With respect to the dose to the OARs, the effect of the dose difference on bladder tissue was negligible for the different arc arrangements. The differences between the partial and full arc arrangements were observed in several dose-volume criteria (e.g., $V_{20\%}$ and $V_{5\%}$) and were slightly lower in plans using the partial arc arrangements than the full arc arrangements. For the rectum, the partial arc arrangements showed relatively strong reductions of the mean dose compared to the full arc arrangements while all plans using four arc arrangements showed no dramatic differences in the high and low doses. For the left and right femoral head in Table 3, Figures 3D,E, we found that the $D_{\text{mean}}$ and mean dose were always lower when the full arc arrangements were used compared to the partial arc arrangements. We also observed better sparing in the right femoral head compared to the left femoral head.

The clinical delivery time of prostate SBRT-VMAT plans using the one arc arrangements (1FA and 1PA) was approximately half compared to that of the two arc arrangements (2FA and 2PA). The reduced delivery time by using one arc arrangements has the potential to decrease the effects of intrafractional motion because prostate motion is

### TABLE 3. Dosimetric results for target volumes in prostate SABR-VMAT plans using four arc arrangements

| Arc Arrangement | Avg ±SD (range) |
|-----------------|-----------------|
| **PTV coverage** |                 |
| $D_{\text{mean}}$ (Gy) | 44.3±0.2 (44.2-44.6) |
| $D_{\text{max}}$ (Gy) | 48.9±0.8 (47.8-49.8) |
| $D_{\text{min}}$ (Gy) | 33.0±0.4 (32.4-33.2) |
| $D_{2\%}$ (Gy) | 44.6±0.3 (44.2-45.0) |
| $D_{5\%}$ (Gy) | 46.1±0.2 (45.9-46.3) |
| $D_{95\%}$ (Gy) | 41.5±0.3 (41.1-41.8) |
| $V_{100\%}$ (%) | 87.5±1.9 (85.1-90.2) |
| **CTV coverage** |                 |
| $D_{\text{mean}}$ (Gy) | 44.5±0.4 (44.4-44.8) |
| $D_{\text{max}}$ (Gy) | 48.4±0.8 (47.9-49.8) |
| $D_{\text{min}}$ (Gy) | 33.0±0.4 (32.4-33.2) |
| $D_{2\%}$ (Gy) | 44.5±0.3 (44.2-45.0) |
| $D_{5\%}$ (Gy) | 46.1±0.2 (45.9-46.3) |
| $D_{95\%}$ (Gy) | 41.5±0.3 (41.1-41.8) |
| $V_{100\%}$ (%) | 87.5±1.9 (85.1-90.2) |

Avg = average; $D_{\text{min}}$ = the dose received at least 5% volume; $SD$ = the standard deviation; $V_{100\%}$ = the volume received at least 95% volume; $D_{\text{max}}$ = the maximum dose; $D_{\text{mean}}$ = the mean dose; $D_{2\%}$ = the dose received at least 2% volume; $D_{5\%}$ = the dose received at least 5% volume; $D_{95\%}$ = the dose received at least 95% volume; $V_{100\%}$ = the volume received 100% of prescription dose.

![FIGURE 2. An example of the dose distributions achieved with (A) one full arc (1FA), (B) one partial arc (1PA), (C) two full arcs (2PA), and (D) two partial arcs (2PA) arrangement in prostate SBRT-VMAT for the same patient.]
TABLE 4. Dosimetric results for organs at risk in prostate SBRT-VMAT plans using four arc arrangements

| Organs of risk       | Avg. SD (range) |
|----------------------|-----------------|
|                      | IFA             | 1FA             | 2FA             | 2PA             |
| Rectum D_{mean} (Gy)| 25.2±1.7        | 23.3±2.0        | 23.6±1.8        | 23.4±1.9        |
|                      | (23.1-27.2)     | (21.4-25.8)     | (21.3-26.0)     | (21.3-26.4)     |
| Rectum D_{5\%} (Gy) | 44.2±0.3        | 44.6±0.4        | 44.1±0.4        | 44.5±0.2        |
|                      | (43.7-44.5)     | (44.0-45.1)     | (43.8-44.7)     | (44.3-44.9)     |
| Rectum V_{100\%} (%)| 9.0±1.4         | 10.1±1.3        | 8.3±1.3         | 9.8±1.5         |
|                      | (6.6-10.3)      | (8.1-11.5)      | (7.0-10.2)      | (7.6-11.6)      |
| Rectum V_{5\%} (%)  | 19.1±3.0        | 19.7±3.2        | 18.0±2.8        | 19.4±3.4        |
|                      | (15.1-23.2)     | (15.2-23.8)     | (15.2-21.9)     | (14.8-24.3)     |
| Rectum V_{2\%} (%)  | 71.0±8.8        | 53.9±9.4        | 60.0±11.1       | 54.1±9.0        |
|                      | (61.1-80.1)     | (41.9-63.7)     | (46.9-77.4)     | (42.5-66.7)     |
| Rectum V empt (%)    | 90.2±2.5        | 90.0±2.7        | 89.6±3.0        | 90.0±2.8        |
|                      | (87.7-93.4)     | (87.1-94.1)     | (85.6-93.5)     | (87.3-94.0)     |
| Bladder V_{50\%} (%)| 10.8±0.9        | 18.7±7.1        | 18.5±6.1        | 18.3±6.9        |
|                      | (13.4-31.1)     | (13.2-31.0)     | (15.7-29.0)     | (12.9-30.4)     |
| Bladder V empt (%)   | 45.6±0.2        | 45.6±0.2        | 45.6±0.3        | 45.6±0.4        |
|                      | (45.5-45.6)     | (45.3-45.9)     | (45.0-45.8)     | (45.3-46.4)     |
| Bladder V empt (%)   | 54.4±1.7        | 52.5±1.6        | 54.1±1.7        | 52.1±1.6        |
|                      | (37.2-79.1)     | (36.4-76.5)     | (37.0-79.4)     | (36.2-76.1)     |
| Left femoral head D_{mean} (Gy) | 12.8±1.8 | 18.7±2.3 | 17.2±2.4 | 13.9±1.4 |
|                      | (10.5-15.1)     | (16.9-22.7)     | (9.3-14.9)      | (11.7-15.3)     |
| Left femoral head D_{2\%} (Gy) | 19.7±2.2 | 23.5±4.4 | 18.3±3.0 | 20.1±2.0 |
|                      | (16.9-21.8)     | (15.6-21.6)     | (13.4-20.7)     | (16.7-21.8)     |
| Right femoral head D_{mean} (Gy) | 10.8±0.9 | 13.3±2.5 | 12.4±1.7 | 13.2±2.1 |
|                      | (9.2-11.5)      | (9.2-15.5)      | (10.5-14.2)     | (10.7-16.5)     |
| Right femoral head D_{2\%} (Gy) | 16.4±1.2 | 20.6±3.7 | 18.1±1.9 | 19.7±2.3 |
|                      | (14.3-18.0)     | (14.3-23.6)     | (15.8-20.1)     | (16.2-22.5)     |

Avg. = average; D_{mean} = the dose received at least 5% volume; D_{mean} = the mean dose; D_{5\%} = the dose received at least 5% volume; D_{2\%} = the dose received at least 95% volume; SD = the standard deviation; V empt (%) = the volume received 100% of prescription dose.

TABLE 5. Average monitor unit and delivery time for prostate SBRT-VMAT plans using four arc arrangements

| Beams    | 1FA (Mean±SD) | 1FA (Mean±SD) | 2FA (Mean±SD) | 2FA (Mean±SD) |
|----------|---------------|---------------|---------------|---------------|
| MU       | 1575±63       | 1627±56       | 1646±97       | 1600±98       |
| Delivery time (min) | 1.0±0.02 | 0.6±0.01 | 2.0±0.01 | 1.3±0.02 |

TABLE 6. TCP of prostate tumor and NTCP of OARs for four arc arrangement plans

| Beams | 1FA (Mean±SD) | 1FA (Mean±SD) | 2FA (Mean±SD) | 2FA (Mean±SD) |
|-------|---------------|---------------|---------------|---------------|
| TCP (%)| 93.35±0.08    | 99.28±0.06    | 93.32±0.08    | 93.36±0.08    |
| NTCP (%)| 0.44±0.23    | 0.61±0.21    | 0.40±0.23    | 0.56±0.22    |
| Rectum | 0.01±0.02    | 0.01±0.03    | 0.00±0.01    | 0.00±0.02    |
| Bladder | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    |
| LT Femur | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    |
| RT Femur | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    | 0.00±0.00    |

Conclusions

Prostate SBRT-VMAT plans using four arc (1FA, 1PA, 2FA, and 2PA) arrangements offered high conformity for target volumes. This study demonstrated that prostate SBRT-VMAT using 1PA (240°...
to 120°) showed reasonably fast delivery time and produced equivalent target coverage and better rectum sparing, although the near-to-maximum dose and mean dose of the left and right femoral heads increased slightly. However, the doses in both femoral heads remained well within the clinical normal tissue tolerance. For evaluating the radiobiological metrics, all plans using four arc arrangements produced comparable TCP for prostate tumors and NTCP for OARs. Therefore, it was concluded that the use of IPA was an attractive choice for treating prostate cancer using SBRT-VMAT.

Author Contribution

Conception and design of the study: JBC TSS. Coordination of the study: SWK JSK JWL. Case selection, radiation treatment planning, and analysis: KYE CHS JSK JYK JBC. Manuscript preparation: JBC SWK. Manuscript revision and editing: JBC JSK IAK TSS. Manuscript approval: all authors.

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