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Dosimetric and radiobiological comparison of volumetric modulated arc therapy, high-dose rate brachytherapy, and low-dose rate permanent seeds implant for localized prostate cancer

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ABSTRACT

To investigate the dosimetric and radiobiological differences among volumetric modulated arc therapy (VMAT), high-dose rate (HDR) brachytherapy, and low-dose rate (LDR) permanent seeds implant for localized prostate cancer. A total of 10 patients with localized prostate cancer were selected for this study. VMAT, HDR brachytherapy, and LDR permanent seeds implant plans were created for each patient. For VMAT, planning target volume (PTV) was defined as the clinical target volume plus a margin of 5 mm. Rectum, bladder, urethra, and femoral heads were considered as organs at risk. A 78 Gy in 39 fractions were prescribed for PTV. For HDR and LDR plans, the dose prescription was D_{90} of 34 Gy in 8.5 Gy per fraction, and 145 Gy to clinical target volume, respectively. The dose and dose volume parameters were evaluated for target, organs at risk, and normal tissue. Physical dose was converted to dose based on 2-Gy fractions (equivalent dose in 2 Gy per fraction, EQD_2) for comparison of 3 techniques. HDR and LDR significantly reduced the dose to rectum and bladder compared with VMAT. The D_{mean} (EQD_2) of rectum decreased 22.36 Gy in HDR and 17.01 Gy in LDR from 30.24 Gy in VMAT, respectively. The D_{mean} (EQD_2) of bladder decreased 6.91 Gy in HDR and 2.53 Gy in LDR from 13.46 Gy in VMAT. For the femoral heads and normal tissue, the mean doses were also significantly reduced in both HDR and LDR compared with VMAT. For the urethra, the mean dose (EQD_2) was 80.26, 70.23, and 104.91 Gy in VMAT, HDR, and LDR brachytherapy, respectively. For localized prostate cancer, both HDR and LDR brachytherapy were clearly superior in the sparing of rectum, bladder, femoral heads, and normal tissue compared with VMAT. HDR provided the advantage in sparing of urethra compared with VMAT and LDR.

Introduction

For the low- or intermediate-risk patients with localized prostate cancer, common treatment modalities are radical prostatectomy, external beam radiation therapy (EBRT), and brachytherapy. Many studies have shown that dose escalation improved tumor control.[1-4]

Volumetric modulated arc therapy (VMAT) became more and more popular, and has become one of the standards of care in EBRT for locally advanced prostate cancer, because of the better or equivalent plan quality and higher delivery efficiency compared with fixed gantry intensity modulated radiation therapy (IMRT).[5] As a monotherapy, low-dose rate (LDR) brachytherapy is an established alternative to radical prostatectomy or EBRT for low-risk patients,[1,6,7] with comparable long-term survival and biochemical control, and most favorable toxicity.[7-11] Development of new image-guided techniques with new computer planning systems raised the popularity of LDR brachytherapy. High-dose rate (HDR) brachytherapy initially was introduced as a supplement for EBRT, and proved to be an effective and safe method of treatment.[12,13] With the benefit of freely programmed dwell time and position of the source, HDR brachytherapy was more and more used as monotherapy for the low- and intermediate-risk patients recently,[14-20] as a cost-effective alternative to well-established permanent seed implants.

VMAT, HDR brachytherapy, and LDR brachytherapy techniques are all used in clinical practice, with excellent biochemical control for localized prostate cancer. For the treatment toxicity and quality

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of life, acute and late gastrointestinal and urogenital treatment-related side effects are considered to be generally low for both EBRT and brachytherapy.[21-23] However, VMAT, HDR, and LDR brachytherapy are dramatically different in the dose fractionation scheme, dosimetric, and radiobiological characteristics, with different pattern of the acute and late treatment toxicity. A randomized trial would likely never to be conducted comparing these 3 forms of techniques, a comparative analysis is useful in understanding some of their intrinsic dosimetric and radiobiological differences, to improve the tumor control, gastrointestinal and urogenital toxicity. Another important aspect is the risk of second cancers for the patients treated with irradiation, which increases with increasing integral dose to the organs at risk (OARs) and normal tissue (NT).[24]

The purpose of this study was to investigate the intrinsic dosimetric and radiobiological differences of VMAT, HDR with Iridium-192 (^{192}Ir), and LDR with Iodine-125 (^{125}I) seeds for localized prostate cancer, especially the differences in biological effective dose to the OARs and NT, to improve the tumor control, reduce the gastrointestinal, urogenital toxicity, and the risk of second cancers.

Methods and Materials

Patient characteristics and structure contouring

A total of 10 consecutive patients with low- or intermediate-risk localized prostate carcinoma who had been treated with definitive radiotherapy with 2 arcs VMAT (78 Gy in 39 fractions) were retrospectively selected for this study. The study was approved by the institute review board of our hospital and informed consent was obtained. All patients underwent computed tomography scanning in a supine position with 2.5-mm slice thickness. The image sets were transferred to the Variseed (V8.0, Varian Medical Systems, Palo Alto, CA) treatment planning system for contouring and LDR planning. Afterward all contours together with images were transferred to the Eclipse (V10.0, Varian Medical Systems, Palo Alto, CA) for VMAT and HDR planning.

For HDR and LDR plans, the clinical target volume (CTV) was defined as prostate gland only. For VMAT, the planning target volume (PTV) was contoured by adding a margin of 5 mm to the CTV. The contoured OARs included bladder, rectum (from anus to rectosigmoid junction), femoral heads, and urethra. The NT was defined as the whole body within the skin surface minus the target structures (*i.e.*, PTV for EBRT and CTV for HDR and LDR brachytherapy) and OARs. The whole body was contoured as the entire volume of all slices where the PTV or CTV existed, as well as at an additional 2 cm superior and inferior to the PTV or CTV.

Treatment planning

Individually optimized VMAT, HDR brachytherapy, and LDR permanent seeds implant plans were created for each patient.

Table 1
Dose volume objectives and constraints for VMAT

DVH parameter	%
PTV coverage	D_{95} > 78 Gy
Rectum V_{50}	< 40
Rectum V_{60}	< 25
Rectum V_{65}	< 15
Rectum V_{70}	< 10
Rectum D_{max}	< 78
Bladder V_{30}	< 30
Bladder V_{50}	< 20
Bladder V_{55}	< 15
Bladder V_{70}	< 10
Bladder D_{max}	< 81.9 Gy
Head of femur D_{max}	< 35 Gy
Head of femur V_{30}	< 5

V_N = percentage volume of structures receiving at least N Gy of radiation dose. All doses are given as physical doses.

Table 2
Dose volume optimization objectives and constraints for HDR brachytherapy

DVH parameter	%
CTV D_{90}	≥34 Gy
CTV V_{150}	< 50
Bladder $D_{10\%}$	< 26 Gy
Bladder $D_{1\ cc}$	< 34 Gy
Rectum $D_{10\%}$	< 26 Gy
Rectum $D_{1\ cc}$	< 34 Gy
Urethra $D_{0.1\ cc}$	< 41 Gy

All doses are given as physical doses.

Volumetric modulated arc therapy

A 2 arcs VMAT plan was generated using Eclipse treatment planning system for each patient. The 10-MV photon beams of Varian Trilogy linear accelerator equipped with a Millennium MLC was used. In 39 fractions, 78 Gy was prescribed for PTV, which is clinically used at our institution. The dose prescription was to cover 95% of the PTV with the prescribed dose while considering the OAR constraints (Table 1).

High-dose rate brachytherapy

The dose prescription was 34 Gy (8.5 Gy per fraction) to 90% of the CTV.[19] The treatment plans were generated using Eclipse treatment planning system (Version 10.0, Varian Medical Systems, Palo Alto, CA). In total, 12 to 20 needles were used to optimize the plans. Volume optimization was used to obtain the optimal dose distribution. Peripheral loading was used to ensure good peripheral coverage of the gland, at the same time sparing of urethra and rectum. The optimization objectives and constraints are given in Table 2. The maximum dwell time was set to 30 seconds. The dose shaper feature was used to fine tune the dose distribution.

LDR brachytherapy

The dose prescription was 145 Gy to 90% of the CTV, which is clinically used at our institution. The treatment plans were generated using Variseed treatment planning system (Version 8.0, Varian Medical Systems, Palo Alto, CA). All plans were generated in the preplan module, using loose ^{125}I seeds. The needles were assumed inserted through a perineal template (5-mm grid size) to simulate the routine clinical practice. The planning source strength was 0.508 U (mGym^2/h) (0.40 mCi). Sources were placed around the CTV in accordance with the peripheral implant rule that the dose extended outside the CTV, typically on the order of 3 to 5 mm. Inverse optimization with automatic source placement was used to obtain the optimal dose distribution. The plan objectives were to cover the target volume and minimize dose heterogeneity within the prostate gland, and minimized the dose to the urethra, rectum, and bladder. The optimization objectives and constraints are given in Table 3. The seeds position was fine tuned to obtain the optimal dose distribution.

Dosimetric and radiobiological comparison

The physical dose, dose volume, and biological parameters were evaluated for target, OARs, and NT. Physical dose were converted to biological effective dose based on 2-Gy fractions (equivalent dose in 2 Gy per fraction, EQD_2) for comparison of 3 techniques. EQD_2 was calculated applying the linear-quadratic model. The α/β values used were 1.93 Gy for CTV,[25] 3 Gy for rectum, femoral heads, and the NT,[26,27] and 5 Gy for bladder and urethra.[28]

Eq. (1) was used for VMAT, and HDR brachytherapy, whereas Eq. (2) was used for LDR brachytherapy,[29]

$$EQD_2 = D\cdot\left(\frac{d}{n}+\frac{\alpha}{\beta}\right)/\left(2+\frac{\alpha}{\beta}\right) \quad (1)$$

$$EQD_2 = D\cdot\left(1+\frac{2\cdot D\cdot\beta}{\alpha\cdot\mu\cdot t}\right)\left(1-\frac{1-e^{-\mu\cdot t}}{\mu\cdot t}\right)\left(1+\frac{2\cdot\beta}{\alpha}\right) \quad (2)$$

Table 3
Dose volume optimization objectives and constraints for LDR brachytherapy

DVH parameter	%
CTV D_{90}	145 Gy
CTV V_{150}	< 50
Rectum $D_{1\ cc}$	< 145 Gy
Urethra $D_{0.1\ cc}$	< 217.5 Gy

All doses are given as physical doses.