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Volumetric modulated arc therapy in prostate cancer patients with metallic hip prostheses in a UK centre

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ABSTRACT

Aim: This study aimed to investigate whether IMRT using VMAT is a viable and safe solution in dose escalated RT in these patients.

Background: An increasing number of prostate cancer patients are elderly and have hip prostheses. These implants pose challenges in radiotherapy treatment planning. Although intensity modulated radiotherapy (IMRT) is commonly used, there is a lack of clinical studies documenting its efficacy and toxicities in this subgroup of patients.

Materials and methods: The data from 23 patients with hip prostheses and non-metastatic prostate cancer treated with VMAT (volumetric modulated arc therapy) between 2009 and 2011, were retrospectively analyzed. Baseline characteristics, treatment details and outcome data were collected on all patients. The median follow up was 40.9 months. MRI-CT image fusion was performed and the treatment plans were created using RapidArc™ (RA) techniques utilizing 1 or 2 arcs and 10 MV photon beams.

Results: 96% of patients were treated with a dose of 72 Gy/32 fractions over 44 days. 21/23 plans met the PTV targets. The mean homogeneity index was 1.07. 20/23 plans met all OAR constraints (rectum, bladder). Two plans deviated from rectal constraints, four from bladder constraints; all were classed as minor deviations. One patient experienced late grade 3 genitourinary toxicity. Three other patients experienced late grade 2 or lower gastrointestinal toxicity. One patient had biochemical failure and one had a non-prostate cancer related death.

Conclusions: VMAT provides an elegant solution to deliver dose escalated RT in patients with unilateral and bilateral hip replacements with minimal acute and late toxicities.

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1. Background

As the population ages, the number of patients presenting for radiotherapy (RT) with hip prostheses is expected to increase. According to the National Joint Registry, 86,488 hip replacements were done in 2012, a 7% increase from 2011.[1] The incidence of prostate cancer increases markedly from age 50 onwards. Hip replacement surgery is becoming common in these patients who may also have osteoarthritis of the hip. External beam RT is an established treatment option for organ confined prostate cancer, together with radical prostatectomy and active surveillance.[2]

However, treatment planning for patients with metallic prosthesis composed of high Z materials posed challenges. Dose attenuation through a hip prosthesis during pelvic irradiation can be significant, with dose losses having been reported to range between 10% and 64%. This results in inhomogeneous dose distribution in the target volume as well as at the tissue–metal interfaces.[3,4] The prosthesis causes streaking and blurring artefacts in the computed tomography (CT) dataset which prevents accurate contour delineation and alters the image density values required for dose calculation. Moreover, commercial treatment planning systems may not accurately predict doses at these tissue-metallic interfaces and may result in significant dose calculation uncertainties.[5,6]

The Task Group 63 report outlined treatment-planning strategies to overcome these challenges. A commonly used technique is the use of beam portals that avoid the prosthesis in the beam's eye view (BEV).[5] We had previously investigated the feasibility using intensity modulated radiotherapy (IMRT) in patients with hip prosthesis in our institution.[7] Inversely planned IMRT was able to deliver beams that avoided the prosthesis, which generated plans with highly conformal target volumes that spared the bladder and rectum better than corresponding 3D-conformal plans. Other researchers have investigated the use of IMRT in metallic implants as well.[8] Over the last 5 years, the use of volumetric modulated arc therapy (VMAT) systems has gained traction in the field of prostate cancer RT. VMAT system is a rotational IMRT, which allows the simultaneous variation of gantry rotation speed, dose rate, and multi leaf collimator field aperture. It is able to achieve IMRT quality dose distributions with reduction of treatment delivery times and decrement of the number of monitor units.[9] There were dosimetric studies done which demonstrated that arc radiotherapy can be effectively used in this patient group, achieving dose homogeneity despite strict constraints.[10]

2. Aim

Since 2009, we have been treating prostate cancer patients with metallic hips with RapidArc™ (Varian's solution of VMAT) and the aim of this study is to report the radiation technique and clinical data from our experience in treatment of this subgroup. To our best knowledge, this is the only series reporting both dosimetric and clinical outcomes in using VMAT system to deliver RT in patients with metallic hips.

3. Materials and methods

3.1. *Clinical evaluation*

According to literature, a follow up of 3 years is sufficient for the majority of later rectal morbidity to manifest itself.[11] We retrospectively analyzed the clinical records and RT plans of prostate cancer patients with hip replacement treated at our centre from 01/2009 to 05/2011 ($n = 23$), which resulted in a minimum follow up time of 33 months.

Patients had histologically confirmed, T1 to T3 prostate cancer adenocarcinoma evaluated by history, examination, serum prostate specific antigen (PSA) and magnetic resonance imaging (MRI) of the pelvis prior to treatment. All were treated with radical intent. Androgen deprivation therapy (ADT) consisting of LHRH analogue administration 3 months prior to RT initiation was primarily offered to patients with adverse risk features (PSA > 10, cT3, and/or Gleason ≥7). The D'Amico risk classification was used to define risk groups.

3.2. *CT simulation and contouring*

Patients were given enemas and followed a drinking protocol. CT scanning was performed with the patient in the supine position with full bladder, immobilized using ankle stocks and knee support. CT images were acquired with 3 mm spacing using a Philips Brilliance wide bore CT scanner. Additionally, an MRI scan optimized for RT planning was performed using a Philips Intera 1.5 Tesla scanner.[12] The MRI scan was fused with the planning CT in order to assist in contouring the prostate, seminal vesicles (SV), rectum, bladder and prostheses on axial slices of the CT. The high dose clinical target volume (CTV) was defined as: i) Prostate only for the low risk group ii) Prostate and base of the SV for intermediate and high risk groups. CTV was expanded 5 mm isometrically to form the planning target volume (PTV). The high dose PTV was prescribed 72 Gy/32# or 74 Gy/37#. Additional dose levels 64 Gy/32 and 50 Gy/32# were prescribed for treatment to the whole SV and pelvic lymph nodes, respectively, at physician's decision. Organs at risk (OARs) evaluated in this study were the bladder (from base to dome), rectum (from anus to recto-sigmoid flexure) and small bowels (for pelvic treatment only).

3.3. *Radiotherapy planning and optimization*

Plans were created with the Varian Eclipse TPS, version 8.9 (Varian Medical Systems, Palo Alto, CA). Either single or double arc plans were created depending on the difficulty of the individual case. For single arc plans, a clockwise arc from 180.1° to 179.9° with collimator rotation 45° was used, and for double arc plans, the second arc was a counterclockwise arc with a complement collimator angle of 315°. A beam energy of 10 MV was used for all arcs. The BEV graphics in the TPS were used to determine the arc avoidance sectors that would prevent the radiation beams from entering through the left and right prostheses. The isocentre was placed in the centre of the PTV. All plans were inversely optimized using the Varian Eclipse Progressive Resolution Optimizer (version 8.9.08) with

Table 1 – Dose constraints to rectum and bladder based on CHHIP trial.[12]

Dose for 74 Gy/37#	Dose for 72 Gy/32#	% of total dose	Relative max volume (%)
Rectum			
50.3	47.6	68	60
60.0	56.7	81	50
65.1	61.6	88	30
70.3	66.5	95	15
74	72	100	3
Bladder			
50.3	47.6	68	60
60	56.7	81	25
74	72	100	5

an objective of achieving at least 95% of the PTV receiving the prescription dose of 72 Gy in 32 fractions while keeping the dose to OARs below the planning constraints. The dose for all optimized plans was calculated using the Varian Anisotropic Analytical Algorithm (AAA), version 8.9.08, using a 2.5 mm dose calculation grid.

The dose volume histograms (DVH) were generated in the Eclipse TPS for evaluation and reviewed by the oncologist. Minimum PTV coverage was ≥95% and maximum coverage was ≤105%. Homogeneity index defined as the ratio of volume of dose at 5% of the PTV (D5%) to the volume of dose at 95% of PTV (D95%) was calculated. Target doses of OARS were generated and our predefined institutional target doses of the constraints which are based on CHHIP trial[13] are listed in Table 1. The plans were approved if all the constraints were met or where there were only minor deviations (within 5% of the target doses). An example of dose distribution of VMAT is shown in Fig. 1.

Patients were treated with Varian 2100C RapidArc™ linear accelerators and set up accuracy was verified with anterior and lateral kilovoltage X-ray imaging.

3.4. *Clinical assessment*

Patients were monitored weekly during treatment and seen within 1 month after RT completion. They were reviewed every 3–6 months until 36 months post RT and then annually after. Acute treatment related toxicities (defined as <3 months post RT) and late toxicities were scored according to the Radiation Therapy Oncology Group (RTOG) late radiation morbidity scoring scheme version 9.[14] Every symptom was counted even if it occurred only on one single occasion. Serum PSA was checked at each visit and biochemical recurrence was defined according to the ASTRO Phoenix criteria.

4. Results

The patient characteristics are presented in Table 2. The mean follow up time was 40.9 months (30–54 months). Late toxicity with a minimum follow up time of 33 months was available for only 22 patients, because of one non-prostate related death. No patients were lost to follow up. Only 1 patient had biochemical recurrence after 43 months post RT; his disease was initially staged as T3a, Gleason 8 and PSA of 19.1.

Table 2 – Patient characteristics.

Mean age (range), years	76 (65–84)
Item	Number of patients (%)
Hip replacement	
Bilateral	11 (48)
Single	12 (52)
D'Amico risk group	
Low risk	1 (4)
Moderate risk	6 (26)
High risk	15 (65)
Androgen deprivation therapy (ADT)	
None	2 (9)
Short course (<6 months)	14 (61)
Long course	7 (30)

4.1. *Acute and late toxicities*

In Table 3, the grades of the pre-treatment symptoms and acute and late toxicities are shown.

7 patients (30%) showed pretreatment GU symptoms of ≥G1 and 1 (4%) patient experienced G1 rectal bleeding prior to RT. The bleeding was caused by the prostate biopsy and complicated by his being on warfarin.

Acute G2 GU toxicity was found in 7 patients (30%), while there were no G2 GI toxicities. We found that at the end of 1 month post RT, there were 7 patients (30%) requiring alpha-blockers for control of their GU symptoms, compared to 4 (17%) pre-treatment. Majority of the patients with GU toxicities experienced frequency, urgency and bladder spasms. No patients had hematuria. 3 patients (13%) who had G1 GI toxicity reported increased bowel frequency. The RT plan was reviewed and no abnormalities were found.

1 patient (4%) demonstrated late grade ≥ 2 GU toxicity. This patient experienced late G3 morbidity with haemorrhagic cystitis. He was later found to have radiation induced bladder neck ulceration 2 years post RT. He did not have any GI complaints. 2 patients (9%) demonstrated late grade ≥ 2 GI toxicity. Both experienced proctitis and one also reported rectal bleeding.

4.2. *Dosimetry*

Most patients (65%) had MRI-CT fusion; those that did not either had a contraindication (pacemaker) or it was the physician's decision. 7 patients (30%) were planned with double arcs, 5 of whom had bilateral hip replacements, as optimization targets were met only by using 2 arcs. Most of the high-dose PTV was defined as prostate and the base of SV as 22 (96%) patients had moderate or high risk disease. 22 patients (96%) were prescribed a total dose of 72 Gy in 32# to the PTV. 1 patient was prescribed to 74 Gy in 37#. 21 (91%) plans met the required PTV target doses. 2 plans had acceptable minor deviations with minimum PTV dose of 90% and 94% (<95%). The mean homogeneity index (ratio of D5% to D95%) was 1.07.

For the rectum, 21 plans (91%) met the required dose constraints. The medium dose region of 2 plans (V68%) exceeded the maximum vol. of 60%. For the bladder, there were 19 plans that met the required dose constraints. The high dose region (V81%) of 4 plans exceeded the maximum volume of 25%.

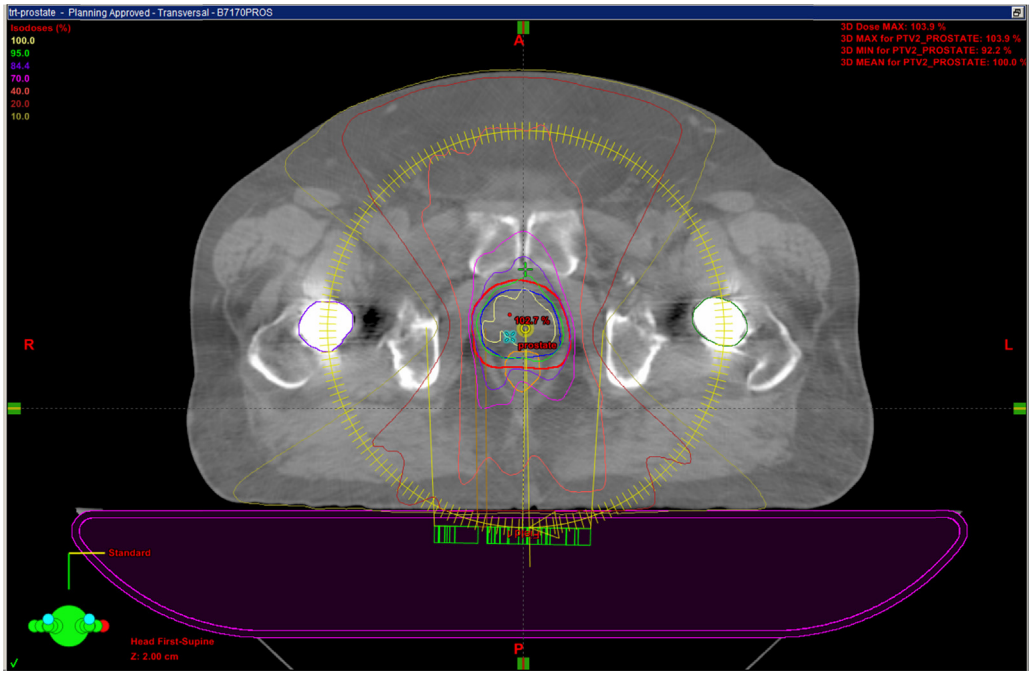

Fig. 1 – Cross sectional image of CT image on TPS demonstrating the dose distribution of VMAT.

Table 3 – Pretreatment complaints, acute and late toxicities according to the RTOG scoring scheme.

Item	Number of patients (%)				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Pretreatment					
Genitourinary (GU)	16 (70)	3 (13)	4 (17)	0	0
Gastrointestinal (GI)	22 (96)	1 (4)	0	0	0
Acute toxicity					
GU	12 (52)	4 (17)	7 (30)	0	0
GI	20 (87)	3 (13)	0	0	0
Late toxicity					
GU	19 (83)	3 (13)	0	1 (4)	0
GI	19 (83)	2 (9)	2 (9)	0	0

However, these were minor deviations deemed acceptable to the treating physicians. Table 4 summarized the dosimetric results of OARs.

5. Discussion

Techniques in RT for localized prostate cancer have changed significantly over the past decade. Level 1 evidence supports RT dose escalation for localized prostate cancer patients of all risk groups. This has led to a shift towards increasing advanced, more conformal RT techniques. VMAT, because of the physical advantages, is increasingly preferred over other IMRT delivery systems in some centres. In our experience, it provides a superior solution in planning the treatment of patients with metallic hip implants, due to the need to avoid using lateral beams, compared to other IMRT delivery techniques.

Table 4 – Dosimetric results of rectum and bladder.

Parameter (%)	Mean values (%), range	
	Rectum	Bladder
V68%	46.9 (36–66)	26.5 (9–49)
V81%	24.8 (11–43)	15.7 (6–30)
V95%	3.8 (0–8)	–
V100%	0 (0–1)	0 (0–2)

There is a lack of published data on toxicity rates in patients treated with VMAT. To our knowledge, there are none on patients in the hip replacement group. There is a series reporting incidence of acute GI and GU toxicities in patients with localized prostate cancer treated with arc therapy. Like ours, they did not have any G4 acute toxicity observed.[15] From the data of randomized trials on dose escalated IMRT, the late GU toxicity (grade 2) rates range from 7% to 21.8%. The late GI toxicity (grade 2) range from 6% to 17.3%.[16–18] Our own study reflects similar rates. There is a series reporting that VMAT appears to be associated with a reduced acute GI and GU toxicity when compared to IMRT.[19] Our study also reflects low acute GU and GI toxicity (≥grade 2) of 30% and 0%, respectively.

Despite the dosimetric problems posed by the presence of high Z materials in the dataset, the majority of planning objectives (91%) were met with acceptably few minor deviations. Conformity of treatment, not explicitly considered a planning objective, was also acceptable. DVH analysis of OARs also showed that most plans did meet our institutional constraints, which can be considered stricter as they are based on the treatment of patients without hip prostheses.

This report is limited by its retrospective nature and the lack of an equivalent control group from our centre. We await more numbers and greater follow up duration. Although our patients had a median follow up time of 41 months and all patients had minimum follow up time of at least 33 months, continued scoring of toxicity is needed, because an increase of GU complications had been reported after 3 years.[20]

6. Conclusion

VMAT provides an elegant solution in delivery of dose escalated radiotherapy to non-metastatic prostate cancer patients with hip prostheses. The acute and late GU and GI toxicities are low and comparable to modern IMRT series after a minimum follow up of 33 months.

Conflict of interest

None declared.

Financial disclosure

None declared.

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