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CASE STUDY

Synchronous prostate and rectal adenocarcinomas irradiation utilising volumetric modulated arc therapy

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Abstract

Cases of synchronous prostate and colorectal adenocarcinomas have been sporadically reported. There are case reports on patients with synchronous prostate and rectal cancers treated with external beam radiotherapy alone or combined with high-dose rate brachytherapy boost to the prostate. Here, we illustrate a patient with synchronous prostate and rectal cancers treated using the volumetric arc therapy (VMAT) technique. The patient was treated with radical radiotherapy to 50.4 Gy in 28 fractions to the pelvis, incorporating the involved internal iliac node and the prostate. A boost of 24 Gy in 12 fractions was delivered to the prostate only, using VMAT. Treatment-related toxicities and follow-up prostate-specific antigen and carcinoembryonic antigen were collected for data analysis. At 12 months, the patient achieved complete response for both rectal and prostate cancers without significant treatment-related toxicities.

Introduction

Prostate and colorectal adenocarcinomas are the two most common malignancies in men in developed countries.[1] Therefore, the diagnosis of synchronous prostate and colorectal cancers are not that uncommon. There are several reports of treatment with neoadjuvant chemotherapy and radiotherapy.[2,3] Upfront surgery has been reported as an option to remove both primary malignancies in a single operation.[4] However, perioperative risks, and patients' age and comorbidities will need to be taken into account as colorectal and/or prostate cancer patients tend to be of older age group (above 65 years). Where indicated, patients are treated with neoadjuvant hormonal therapy for prostate cancer prior to irradiation. During radiation, concurrent infusion of 5-fluorouracil (5-FU) chemotherapy was administered as standard for rectal cancer.[5]

In this article, we illustrate a case of a patient with synchronous prostate and rectal cancers treated using the volumetric modulated arc technique (VMAT).

Consent

The patient below has provided consent for his case to be reported and published.

Case Report

A 69-year-old man of good performance status was diagnosed with intermediate-risk prostate adenocarcinoma, cT2b Gleason 4 + 3 = 7 and an initial prostate-specific antigen (PSA) 6.37 μg/L (reference range = 0.0–4.5 μg/L). He reported normal bowel habit and no urinary symptoms. His comorbidities included hypertension, hypercholesterolemia, gastro-oesophageal

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reflux disease and glaucoma. He had received no previous radiotherapy, was not on anticoagulation therapy and had no family history of prostate or colorectal cancer.

Digital rectal examination (DRE) identified prostatomegaly with a palpable nodule in the left lobe, occupying >50% of the lobe with no obvious extracapsular extension. There was no palpable abnormality in the lower rectum. Initial computerised tomography (CT) scan of the abdomen and pelvis, and bone scan showed no evidence of distant metastases.

The initial treatment plan was a 6-month course of neoadjuvant androgen deprivation therapy (ADT) (Lucrin 22.5 mg, 3 monthly) followed by radical external beam radiotherapy to the prostate. Gold seed fiducial markers were inserted into the prostate 4.5 months after commencing ADT.

Two weeks after fiducial marker insertion, the patient continued to experience rectal bleeding. DRE revealed a palpable lesion on the posterior rectal wall, 5 to 6 cm from the anal verge. Subsequent colonoscopy identified a suspicious rectal lesion and biopsy confirmed a moderately differentiated adenocarcinoma. His carcinoembryonic antigen (CEA) was 1.6 U/L (reference range = 0–5.0 U/L).

A magnetic resonance imaging (MRI) scan of the pelvis revealed a malignant rectal stricture at 7 cm from anal verge which extended 4.5 cm superiorly. The tumour extended through the bowel wall into the mesorectal fat. There was an irregular lymph node adjacent to the malignant stricture, suspicious for malignant infiltration. There was also an 8 mm left internal iliac node suspicious for tumour involvement.

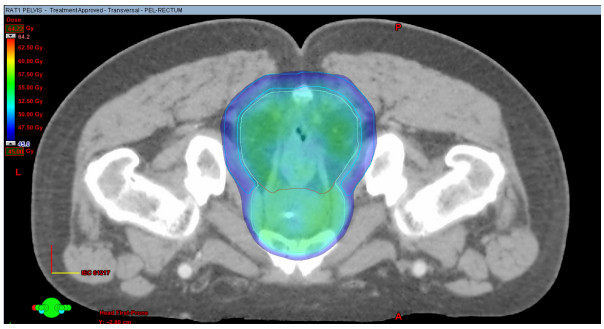
This patient, therefore, had synchronous cT2bN0M0 prostate adenocarcinoma and cT3N1M0 rectal adenocarcinoma.

The patient proceeded with neoadjuvant chemoradiotherapy with continuous 5-FU chemotherapy. Radiotherapy was delivered via two-phase volumetric modulated arc therapy (VMAT) technique. Phase 1 delivered 50.4 Gy in 28 fractions, 5 fractions per week, to the pelvic incorporating the rectum, the involved left internal iliac node and the prostate (Fig. 1). Phase 2 delivered an additional 24 Gy in 12 fractions, 5 fractions per week, to the prostate only.

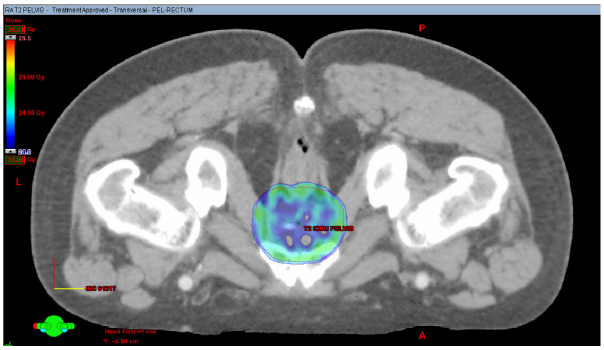
The patient tolerated the treatment well with Common Terminology Criteria for Adverse Events (CTCAE v4.0) grade 1 fatigue, grade 1 skin reaction, and grade 1 cystitis reported.[6]

Six weeks post-radiotherapy, he underwent an abdomino-perineal resection for the rectal cancer. Histopathology confirmed complete pathological response.

Phase 1



Phase 2



Combined phase 1 and 2 plans

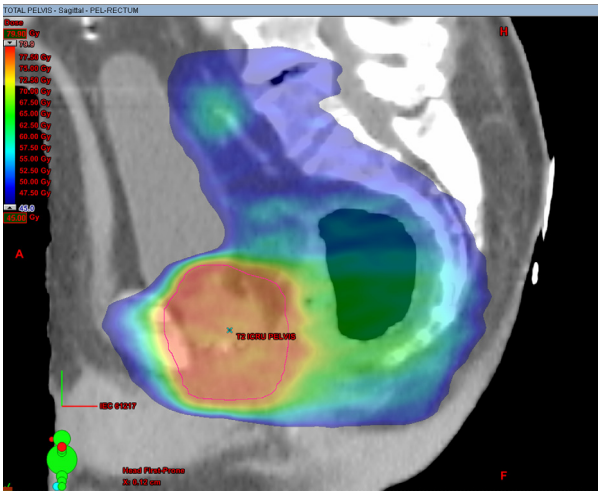


Figure 1. Dose distribution from the treatment planning system from Phase 1, Phase 2 and combined Phases 1 and 2 treatment.

At 6 months follow-up, the patient had a transurethral resection of the prostate (TURP) procedure for prostatism and his prostate chips showed no evidence of malignancy. At 1 year, his PSA and CEA levels were within normal limits, and restaging CT scan showed no evidence of disease recurrence. The patient reported satisfactory bladder and bowel function, and control at 1 year post-irradiation.

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Radiation Therapy Technique

Simulation

The patient was simulated with a comfortably full bladder (using ALCC bladder protocol) with an empty rectum in a prone position on a bellyboard with both arms up. The prone position was selected as to allow for reduction in small bowel irradiation. An evacuated fixation bag was used for head and arm fixation (Civco), and a knee fix was placed under ankles. To ensure reproducibility, the patient was instructed to empty his bladder and consume two cups of water 40 min prior to the scan. This was followed by 1.5 cups of oral contrast 30 min prior to the scan to enable better localisation and contouring of the small bowel. The patient was given dietary instructions to increase his fibre intake to maintain regular bowel function. The simulation CT scan (Toshiba Aquilon LB) was performed with 2 mm slice thickness with intravenous contrast using our department's Surestart IV contrast protocol. No rectal balloon was used and no density overrides for rectal gas. It is the institutional protocol to rescan the patient if there is excessive rectal gas (>50% of prostate volume).

VMAT plan preparation

The planning CT image dataset (2 mm slice thickness) was imported into the Eclipse (Varian Medical Systems, Palo Alta, California) Contouring workspace, and the departmental RapidArc (RA) Prostate Two Phase protocol template was assigned.

The target volumes (gross tumour volume, GTV; clinical tumour volume, CTV) were defined (Table 1), with the aid of diagnostic staging CT and MRI scans.

Table 1. Target volumes.

Volumes	Dose (Gy)	Targets
GTV Phase 1	50.4	Rectal tumour, prostate, metastatic iliac node
GTV Phase 2	24.4	Prostate
CTV Phase 1	45	GTV phase 1 + mesorectum, presacral space, external and internal iliac nodes and obturator nodes
CTV Phase 1	50.4 Gy	1. Rectal tumour + mesorectum and presacral space on corresponding rectal tumour CT slices + 1 cm superior and inferior margin 2. Prostate and seminal vesicles 3. Metastatic iliac node + 1 cm margin
CTV Phase 2	74.4	Prostate and seminal vesicles

A 10 mm margin in all directions was added onto the respective CTVs to create planning target volumes (PTVs), except posterior margin from prostate, which was expanded by 7 mm.

Organs at risk (OARs) were contoured including the small bowel, large bowel, bladder, external genitalia and bilateral femurs. The body was contoured with the bellyboard included to ensure it was accounted for in the dosimetry, couch bars out were added as structures.

RapidArc versions of the target volumes and critical structures were created. RapidArc PTVs are expanded copies of the delineated target volumes expanded by 1 mm in the X and Z planes, and by 2 mm in the Y plane. RapidArc Rectum and RapidArc Bladder were created by cropping the original structure and then modifying the copy using the Boolean (crop) tool to exclude them from the RapidArc PTVs allowing a 2 mm margin. The RapidArc versions of critical structures are only used to generate an optimal distribution, and not for final DVH dose reporting.

The planning was done on Varian Eclipse Version 8.6 using the Varian AAA Version 8.615 dose calculation algorithm, calculated on a 2 mm grid. The plan was created using inverse planning with no plan normalisation. The plan template imported one arc field and additional arcs were added when the radiation therapist determined that one arc could not achieve an acceptable distribution. Two arcs were chosen for this case as the PTV volumes were not particularly wide and had no sudden geometrical variations in the superior to interior planes. Arc fields were labelled by the direction of the arc. The isocentre was adjusted in the anterior and posterior direction to mid-PTV to improve PTV coverage for the full arc rotation. The width of the primary collimators for arcs was kept to 15 cm (*X*-axis) to allow for full multileaf collimators interdigitation to optimise beam modulation and the length was 22.5 cm (*Y*-axis).

VMAT was delivered with collimator rotations ranging between 25° and 45° allowing more flexibility for modulation and minimises interleaf transmission. For each beam, the collimators were fitted to target structure with a 5 mm margin to ensure the collimators full coverage of all PTV structures. In this case, the PTVs could not be covered for the full arc and therefore two arcs were chosen. Coverage was confirmed by viewing the movie loop of the arc in the beams eye view (BEV) and adjusting the collimators as required.

Optimisation

The optimisation objectives are summarised in Tables 2 and 3.

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Table 2. Phase 1 optimisation objectives.

	Objective	Dose (Gy)	Volume (%)	Priority
Femurs	Upper	28	0	60
Uninvolved bladder	Upper 1	20	50	70
	Upper 2	32	10	90
	Upper 3	41.5	0	90
Small bowel	Upper	30	0	50
PTV45	Upper	47	0	150
	Lower	45	100	150
PTV 50.4	Upper	52.4	0	150
	Lower	50.4	100	150

Table 3. Phase 2 optimisation objectives.

	Objective	Dose (Gy)	Volume (%)	Priority
Femurs	Upper	11	0	60
Uninvolved bladder	Upper	2	32	70
	Upper	10	5	90
	Upper	18	0	90
Small bowel	Upper	15	0	50
PTV 74.4	Upper	26	0	150
	Lower	24	100	150

Pre-treatment quality assurance

Before the patient's first fraction, the plan underwent quality assurance testing using the department's procedures to test for delivery accuracy. This involved delivering the treatment onto a phantom, and measuring the dose distribution and dose to a point in this phantom. These results were then compared to those calculated by the treatment planning system and the plan was considered accurate (within experimental limitations) as the pre-set tolerances were met. The patient plan then proceeded to treatment.

The ArcCHECK (Sun Nuclear Corporation, Melbourne, Florida) phantom is routinely used to measure dose distribution and dose to a point for VMAT treatment plans. For the dose distribution comparison, the commonly used gamma analysis method[7,8] was carried out using a threshold setting of 10% and a tolerance of greater than 95% of the diodes passing per field with 3% or 3 mm.[9] For the dose to a point comparison, a dose difference of less than 3% is considered a pass.[10] These tolerances are base on those set for intensity modulated radiation therapy (IMRT) as VMAT modulation is similar to IMRT.

The plan for Phase 1 was within tolerance with a composite pass rate of 99.5% (99.2% counterclockwise, CCW, rotation and 98.8% for clockwise, CW, rotation) and dose to a point difference of 1.0%. Phase 2 was also within tolerance with a composite pass of 99.3% (99.5% CCW and 99.1% CW).

Treatment delivery

The patient was treated in the simulated position. Treatment position was verified using daily kilovoltage (kV) imaging. Daily kV images were matched to the bony anatomy and although prostate fiducial markers were outlined, they were not used in Phase 1 of treatment as they were not a good surrogate for the rectal and nodal volumes. The fiducial markers were used for daily kV matching during Phase 2 of treatment.

Discussion

Colonias et al.[3] described the utilisation of IMRT technique in a case to deliver irradiation to the prostate and rectum with the intent of avoiding prostatectomy and preserving sphincter function, while limiting acute and chronic toxicity. The patient described about the grade 2 enteritis, experienced during treatment and for 4 weeks post-treatment requiring the use of anti-diarrhoeal medication. He subsequently underwent low anterior resection and colonic J-pouch. He remained disease-free at 14 months with good sphincter function.

Qiu et al.[2] reported a case series of 4 patients with synchronous prostate and rectal cancers treated with neoadjuvant chemoradiation to the pelvis to 45–50 Gy with concurrent 5-FU, followed by caesium-131 (Cs-131) brachytherapy boost to the prostate to 80–90 Gy. All patients subsequently underwent low anterior resection with diverting loop ileostomy. Of 4 patients, two patients developed faecal incontinence (grade 1 and 2) and one patient had erectile dysfunction and high stoma output. The latter patient did not have a reversal of his ileostomy due to grade 3 gastrointestinal toxicity post-operatively with high stomal output and subsequent recurrent anastomotic strictures requiring balloon dilatation. At 24–53 month follow-up post-treatment, one patient has hormone refractory metastatic prostate cancer and another patient has rising CEA.

VMAT was chosen in this case as it offers highly conformal dose delivery, achieving similar target coverage as IMRT but with better organ-at-risk sparing especially to the rectum and femoral heads as previously demonstrated by Crowe et al.[11] In this case, VMAT achieved all the objectives of radiation therapy treatment and provided the opportunity to treat this volume in a single arc as opposed to IMRT which requires multiple beams targeting multiple treatment volumes to spare organs at risks (Fig. 2). The ability to modulate gantry angle, collimation and dose rate to treat this complex volume makes this technique more superior than IMRT.[12] Previous studies at the ALCC for prostate and anus cases have indicated that VMAT can achieve

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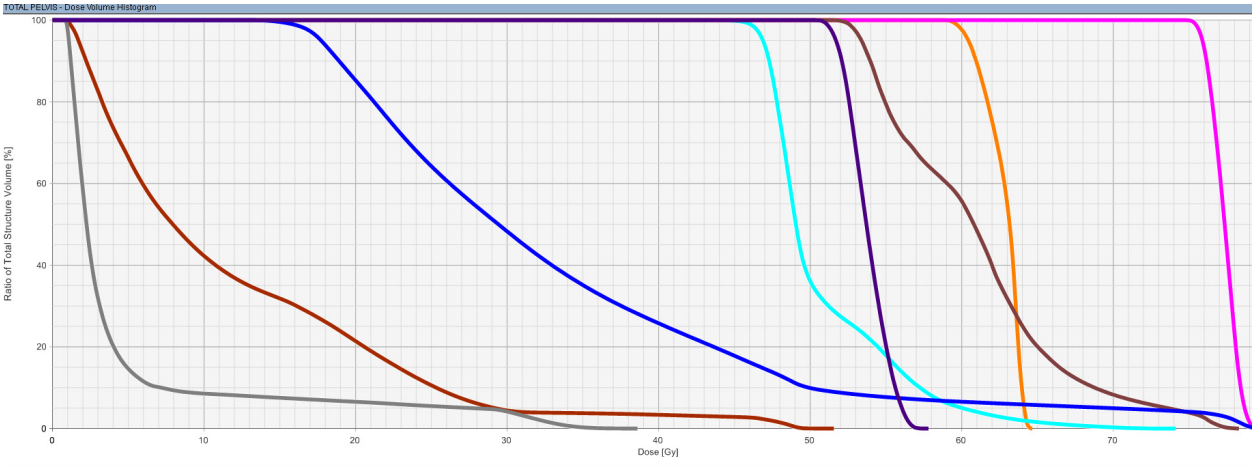

Figure 2. Dose–volume histogram from combined Phases 1 and 2 treatments.

comparable and often superior plans to IMRT, this is more apparent when more PTV volumes are introduced.[13] VMAT has a shorter treatment delivery time[14,15], which is an important consideration particularly for a patient lying on a bellyboard.

In addition, the patient presented with PR bleeding post-fiducial marker insertion, which can be a relatively common complication of the procedure. Gill et al.[16] reported that 11% of patients had rectal bleeding lasting more than 2 weeks (most with grade 1 and 2 toxicity), post-fiducial markers insertion under transrectal ultrasound guidance. Given that rectal bleeding is a well documented and common complication of fiducial markers insertion, the decision to either observe or further investigate may be difficult.

In a study by Sharp et al.[17], routine colonoscopy prior to brachytherapy diagnosed asymptomatic colorectal carcinoma in 3.2% of patients while 44% of patients required a biopsy or polypectomy during colonoscopy. Post-brachytherapy, 2% of unscreened patients developed colorectal carcinoma within a mean time of 73.2 months.

Furthermore, rectal toxicity was less prevalent and less severe in men who had screening colonoscopy prior to brachytherapy compared to those who had not had screening colonoscopy.[17] This finding may be due to decreased likelihood of malignant transformation in those who had a screening colonoscopy with polypectomy. Hence, Sharp et al.[17] has recommended routine screening colonoscopy for all patients prior to radiotherapy for prostate cancer if they have not had one in the preceding 3 years.

Although rectal bleeding is a common complication of fiducial markers insertion in the short term, it warrants further investigation. We recommend that DRE examination be indicated for all patients with rectal bleeding. As illustrated in our case, a brief PR examination revealed a palpable mass. However, if the culprit is of more proximal anatomical location, DRE examination may not be revealing. Hence, it would be reasonable to recommend colonoscopy to investigate all unusual rectal bleeding post-fiducial markers insertion. Furthermore, this may justify observation for patients if rectal bleeding develops during or in the short term after radiotherapy; preventing biopsies of the irradiated rectum.

Conclusion

To our knowledge, this is the first report of using VMAT technology in treating synchronous prostate and rectal adenocarcinomas. In our case, the patient achieved complete remission of both carcinomas at 1 year post-treatment with minimal toxicity. In addition, we recommend that DRE examination be indicated for all patients presenting with rectal bleeding.

Conflict of Interest

The authors declare no conflict of interest.

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