

Volumetric modulated arc therapy (VMAT) provides the conformality that enables three separate simultaneous pelvic malignancies to be treated radically—a case study

Abstract

Radiotherapy and surgery are both potential modalities for the definitive treatment of pelvic malignancies. Although surgery provides a histological specimen, enabling exact staging, radiotherapy is sometimes preferred as it provides patients the opportunity for organ conservation and therefore perhaps better quality post-treatment survivorship. Our case report details how three separate primary pelvic cancers (prostate, rectal, anal) in one patient were treated simultaneously with definitive radiotherapy. Patient was prescribed 80 Gy in 40 fractions to the planning target volume (PTV) prostate, 54 Gy to PTV anal canal, 45 Gy to the pelvis including PTV rectosigmoid junction and 36 Gy to the PTV inguinal lymph nodes that encompassed clinically negative nodes draining the anus, through the Volumetric Modulated Arc Therapy (VMAT) with 6MV photons. Mean doses to organs at risk (OAR) are 30.01 Gy to the bowel volume, 46.54 Gy to the bladder, 30.42 Gy to the femurs, and 61.84 Gy to the rectum. Radiation doses to the prostate and anal canal are consistent with conventional treatment doses with definitive radiotherapy. The rectal dose was accepted as part of the definitive treatment of rectal cancer following Endoscopic Mucosal Resection (EMR). This could only be achieved through the superior dose conformality of VMAT, maximising the dose given to tumour bearing PTV while minimising the dose to OARs which included normal pelvic structures. All three cancers remained under control at 4 years after treatment, with minimal late toxicity associated with the treatment received. Further RCTs in pelvic malignancies are needed to help clinicians and patients select the best treatments, to improve disease control while maintaining quality of survivorship.

Keywords: radiotherapy, volumetric modulated arc therapy, anal cancer, prostate cancer, rectal cancer, australia, case study

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Abbreviations: RT, radiotherapy; 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity modulated radiotherapy; VMAT, volumetric modulated arc therapy; EBRT, external beam radiotherapy; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; EMR, endoscopic mucosal resection; APR, abdominoperineal resection; SCC, squamous cell carcinoma; OAR, organ at risk; CEA, carcinoembryonic antigen; RTOG, radiation therapy oncology group; PTV, planning target volume; RCT, randomised controlled trial

Introduction

Surgery and radiotherapy (RT) can be competing modalities for the definitive treatment of some pelvic malignancies such as prostate cancer,^{1,2} early (stage IA, IB, IIA) cervical cancer,^{3,4} and early stage bladder cancer.^{5,6} Surgery provides a complete histological diagnosis, which aids exact staging, but involves tissue sacrifice with impact on the quality of survivorship. This is compared with the ability of RT to provide organ conservation. Those who choose surgery may suffer from decision regret.⁷⁻⁹ RT modalities and techniques have evolved over time, enabling better dose conformality. This means more doses to tumours and less to surrounding radiation sensitive normal structures, so more chance of cure for less side effects. Evolution from Three-dimensional Conformal Radiotherapy (3D-CRT) to Intensity

Modulated Radiotherapy (IMRT) and now to Volumetric Modulated Arc Therapy (VMAT) has enabled continuous beam modulation which is delivered in a rotational fashion quickly. Previously delivering therapeutic radical radiation to co-located primaries would be impossible as there would be too much overlap in 3DCRT radiation entrance and exit beams. We present a case where three separate simultaneous pelvic malignancies in the one patient were treated radically. This could only be done with VMAT.

Case study

A fit immunocompetent 74-year old male of Chinese descent was referred for definitive External Beam Radiotherapy (EBRT) for a high-risk, high-grade prostate cancer with Gleason score 4+5 = 9 in all 12 cores tested (Figure 1), and pre-treatment Prostate-specific Antigen (PSA) level elevated at 112mg/ml. Prostate-specific Membrane Antigen (PSMA) scan showed uptake in the prostate with SUV max of 23 in early images, SUV max of 58 in delayed images but no other disease. Co-morbidities included controlled cardiomyopathy, hypercholesterolemia, and Type II diabetes. Staging investigations of pelvic MRI and CT found an incidental polypoid lesion in the lower rectum and suspicious enlargement of the anus. Endoscopic biopsy showed suspicious cells in the rectal lesion and Endoscopic Mucosal Resection (EMR) of a 30mm polypoid lesion

at the rectosigmoid junction confirmed adenocarcinoma with positive margins at the higher portion of the rectum (Figure 2). The anal biopsy showed invasive Squamous Cell Carcinoma (SCC) suspicious for lymphovascular invasion at the anal verge (Figure 3). Definitive surgery for any of these lesions was declined. Injections of androgen deprivation therapy and radiosensitising Capecitabine (Xeloda) were started.

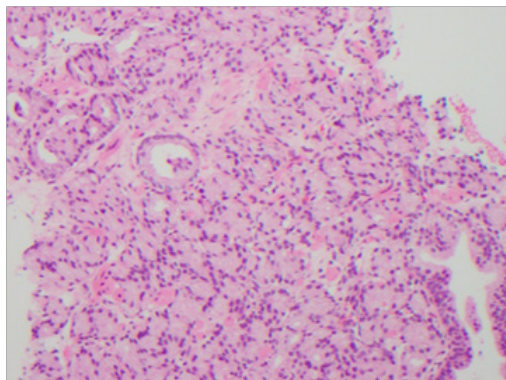
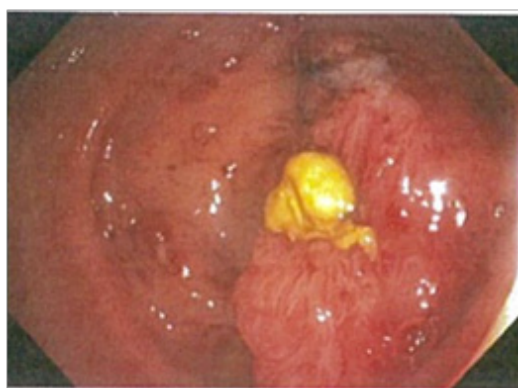
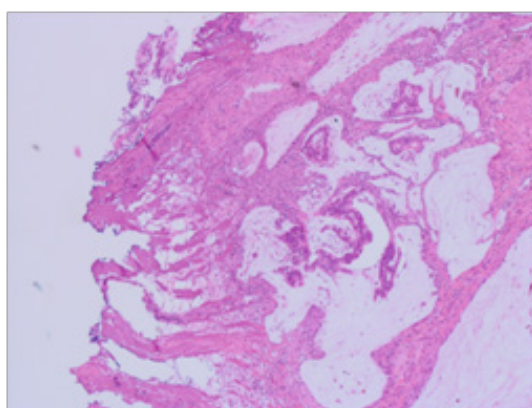


Figure 1 Histology of prostate cancer. Representative section consistent with adenocarcinoma of Grade Group 5 and Gleason Score of 9 (4+5).



A



B

Figure 2 Macroscopic appearance and histology of rectal cancer. (A) Macroscopic appearance of 30mm rectal lesion 12cm from anal verge excised with Endoscopic Mucosal Resection. (B) Histology of rectal adenocarcinoma.

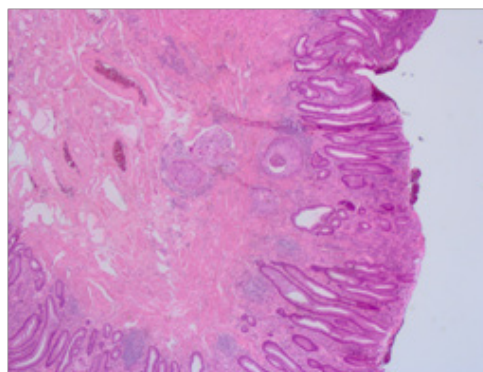
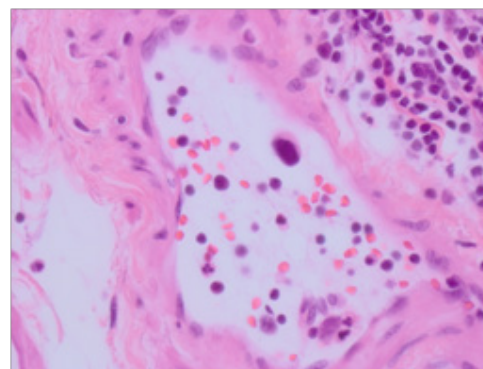


Figure 3 Histology of anal cancer. (A) Small focus of superficially invasive anal squamous cell carcinoma arising within a large area of high-grade squamous intraepithelial lesion. (B) Area suspicious for lymphovascular invasion.

RT planning, with target volume encompassing the anal region, prostate, rectosigmoid junction and pelvic and inguinal lymphatics, was performed. Patient was prescribed 80 Gy in 40 fractions to the planning target volume (PTV) prostate, 54 Gy to the PTV anal canal, 45 Gy to the PTV pelvis including rectosigmoid junction and 36 Gy to the PTV inguinal lymph nodes that included clinically negative draining anal nodes, through VMAT with 6MV photons. Mean dose to organs at risk (OARs) are 30.01 Gy to the bowel, 46.54 Gy to the bladder, 30.42 Gy to the femurs, and 61.84 Gy to the rectum. Radiation doses to the prostate and anal canal are consistent with conventional treatment doses with definitive radiotherapy. As patient refused Abdominoperineal Resection (APR) as initial definitive surgical treatment, the rectal radiotherapy dose was accepted as part of the definitive treatment of rectal cancer following EMR. Patient was agreeable to having salvage APR in the event that radical treatment of rectal cancer fails to achieve control of disease. Table 1 summarises the dose to each Planning Target Volume (PTV) and OAR. Figure 3 shows the cross-sectional dosimetry on the axial and midline sagittal scan. Figure 4 summarises the doses to tumour and OAR volumes through a Dose-Volume histogram. Radiotherapy to the prescription dose was completed on time. There were no acute toxicities that delayed treatment. To date, 4 years following RT completion, the patient has no late toxicities. His Prostate-specific Antigen (0.26 ng/ml) and Carcinoembryonic Antigen (3.0 ng/ml) levels remain within normal limits.

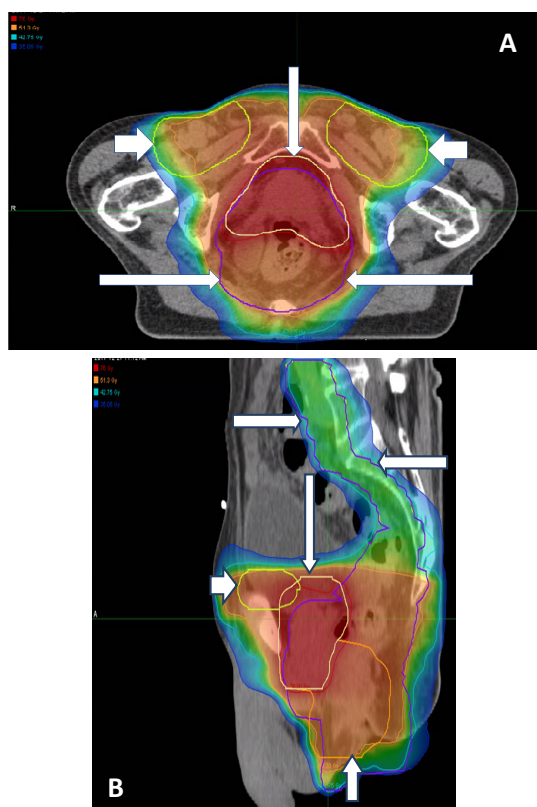


Figure 4 Cross-sectional dosimetry on axial (A) and midline sagittal (B) Scan. Short horizontal arrows— PTV1 (Regional lymph nodes) – 36Gy; Long horizontal arrows – PTV2 (Pelvis) – 45Gy; Short vertical arrows – PTV3 (Anal Canal)— 54Gy; Long vertical arrows – PTV4 (Prostate)— 80Gy.

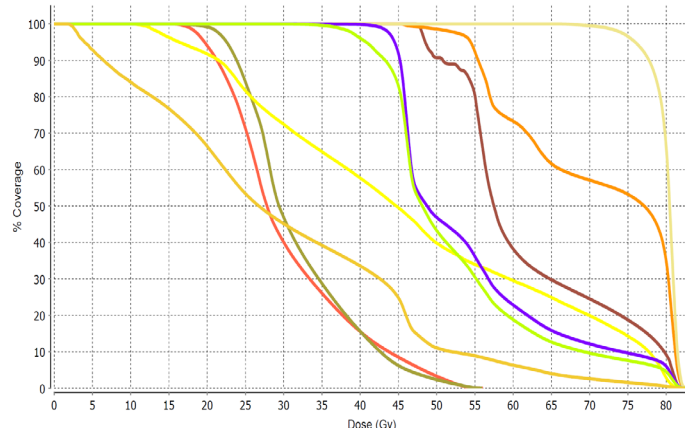


Figure 5 Dose Volume histogram with summary of doses to tumour and organ at risk (OAR) volumes. Short horizontal arrows – PTV1 – 36Gy; Long horizontal arrows – PTV2 – 45Gy; Short vertical arrows – PTV3 – 54Gy; Long vertical arrows – PTV4 – 80Gy; Green Triangle – Bowels; Black Triangle – Femurs; Red Triangle – Bladder; Brown Triangle – Rectum.

Discussion

We present a case where three separate simultaneous pelvic malignancies in the one patient were treated radically with VMAT.

RT has been proven to be a definitive treatment modality for prostate cancer,¹⁰ while concurrent chemoradiation is the mainstay treatment for anal SCCs following the Nigro Trial.¹¹ However, the role of RT in rectal cancer treatment is less clearly defined. Endoscopic resection alone is not considered adequate treatment, with the standard surgical treatment being transabdominal surgery such as low anterior resection or abdominoperineal resection.¹² For prostate cancer, the Australian and New Zealand Faculty of Radiation Oncology Genito-urinary Group recommended dose escalation to 78–80 Gy, as it has been shown to improve tumour control, resulting in improved biochemical failure free survival when compared with conventional radiotherapy doses (68–70.2 Gy) in all risk groups.¹³ A minimum dose of 45 Gy is the currently recommended for radical treatment of anal SCC.¹⁴ Due to heterogeneity of results seen with higher boost doses of radiation up to 70 Gy, conventional doses between 50.4 to 59.4 Gy are acceptable reserving doses at the higher end of the spectrum for bulkier anal disease.^{15–17} Nonetheless, higher RT doses to primary tumours inadvertently resulted in greater indirect exposure of radiotherapy doses to OAR,^{18,19} causing acute and late genitourinary and gastrointestinal toxicities.

VMAT enabled our patient to receive the recommended dose to each PTV as per current guidelines, while keeping the dose to OARs within the limits of dose constraints as outlined in Table 1. The patient is alive and well with no evidence of disease 4 years later. Late rectal and bladder toxicity was minimal at Grade 0–1, as per Radiation Therapy Oncology Group (RTOG) Toxicity Criteria.²⁰ Only the superior conformality of VMAT could deliver this. What is needed for this result is adequate dose for loco-regional control for all three cancers, but the dose to OAR is below that associated with late toxicity. It could be argued that the patient was radiation sensitive and that is why all three cancers were cured. However, if that were the case, OAR tissue would also be radiosensitive and late RT effects would be expected. It also should be acknowledged that good endoscopic resection of the rectal lesion in this patient enabled RT to definitively treat the microscopic residual disease. This highlights the potential for pre-radiotherapy surgical debulking as a treatment option for early rectal cancer with curative intent.

This patient declined definitive surgery for any lesions. Patients are driving what treatment they will get based on quality of life. For example, patients may choose to have radiotherapy to allow less intense surgical treatment which may facilitate sphincter-conservation²¹ and bladder-sparing surgeries²² when treating rectal cancer and bladder cancer respectively. RT preserves normal tissue leading to perhaps higher quality survivorship for the same oncological outcomes as surgery.

Conclusion

Perhaps combined modality treatments will be the best, with surgery for debulking allowing a lower RT dose to be used. This combined modality treatment has been successfully implemented in the treatment of breast cancer with radiotherapy after a breast-conserving surgery.^{23,24} Randomised Controlled Trials (RCTs) are also currently being undertaken to establish the use of transoral surgery and lower dose post-operative radiotherapy to minimise treatment toxicity in Human Papilloma Virus-associated oropharyngeal squamous cell carcinoma.^{25–27} RCTs in pelvic malignancies are needed to help clinicians and patients to select the best treatments, which are tailored to the patients' individual cases.

Table I Dose-volume distributions and constraints for target volume and organs at risk in prostate, rectal, anal cancer radiotherapy. *Radiation dose constraints to OAR are in accordance to RTOG recommendations

Target volume	Dose distribution	Prescribed dose
PTV1 – Inguinal Lymph Nodes (2804.15ml)	Max Dose: 83.03Gy Mean Dose: 52.48Gy	36 Gy
PTV2 – Pelvis including Rectosigmoid Junction(2040.09ml)	Max Dose: 83.03Gy Mean Dose: 54.13Gy	45 Gy
PTV3 - Anal Canal (361.42ml)	Max Dose: 83.03Gy Mean Dose: 70.63Gy	54 Gy
PTV4 - Prostate (189.49ml)	Max Dose: 83.03Gy Mean Dose: 79.93Gy	80 Gy
Organ-At-Risk (OAR)	Dose Constraints*	
	V65 Gy < 50%	
Bladder (234.64ml)	V70 Gy < 35%	
	V75 Gy < 25%	
	V80 Gy < 15%	
	V60 Gy < 35%	
Rectum (41.36ml)	V65 Gy < 25%	
	V70 Gy < 20%	
	V75 Gy < 15%	
Bowel (1830.39ml)	V45 Gy < 30%	
Femur (138.76ml)	V50 Gy < 5%	

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Conflicts/disclosures

Authors declare that there is no conflict of interest.

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