The Radiographer 2008; 55 (3): 13–17

A 3D conformal radiation therapy class solution for dose escalated prostate irradiation

Joshua Runham[1], William McDowall[1], Daniel Bryant[1], Jarad Martin[1, 2]

[1]Cancer Care Services, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia.
[2]St Andrews Cancer Care Centre, Toowoomba, Queensland, Australia.
Correspondence joshua_runham@health.qld.gov.au

Abstract Prostate cancer is a dose responsive neoplasm i.e. the higher the dose of radiation administered, the more likely it is to attain local tumour control. However, high doses without careful conformal treatment planning leads to increased complication rates. This study aims to determine the ideal dosimetric and clinically relevant 3D conformal radiation therapy (3D-CRT) plan for 78 Gy dose escalated prostate treatment.

A pilot study was performed on two patients using computed tomography (CT) images previously acquired to plan their treatment. The planning target volume in one patient encompasses the prostate only (PO) while the other had the prostate and seminal vesicles (PSV) contoured. Three senior radiation therapists and a radiation oncologist evaluated 10 optimised plans and recommended the top three techniques for further investigation. The top three techniques, 5-field (0, 90, 120, 240, 270 gantry angles), 6-field (30, 90, 120, 240, 270, 330 gantry angles) and 8-field (30, 60, 100, 135, 225, 260, 295, 330 gantry angles) were further applied to previously acquired CT images of another three patients, each contoured according to a standardised protocol. The median dose volume histograms (DVH) of the organs at risk (OAR) from five patients were compared to determine the best plan.

The 6-field technique is the best option for dose escalated prostate irradiation. The 8-field technique produced the highest rectal dose while the 5 and 6-field techniques showed little variation ($P = 0.239$). The 6-field technique produced a plan with significantly less dose to the femoral head and neck compared to the 5-field technique ($P = 0.001$).

Keywords: class solution, conformal radiation therapy, dose escalation, prostate

Introduction

It is widely recognised that local tumour control of prostate cancer is increased as the dose received increases[1] and subsequently, prescribed doses to the prostate are being escalated routinely. However, evidence clearly shows that higher prescribed doses and consequently, higher doses to organs at risk (OAR) leads to higher complication rates.[2] Thus, careful conformal treatment is crucial.

External beam irradiation has, historically, provided an adequate means of high dose delivery and now with advancing technology in radiotherapy, subsequent dose escalation demands a growing need to improve dose conformity beyond previously utilised techniques.[3,4,5] As trials such as Randomised Androgen Deprivation and Radiotherapy (RADAR) roll out, and radiation oncology departments explore the means of higher dose delivery, there is still no consensus on a standard technique for dose escalated prostate treatment.[6] This was demonstrated in an extensive literature review and comparison of prostate protocols used in other departments both locally and internationally.

There is extensive evidence in the literature to show that intensity modulated radiation therapy (IMRT) is superior to conformal radiation therapy (CRT).[3,7,8,20] Although this is very rarely disputed, IMRT is not widely available in all centres and can have a large impact on departmental resources. The ultimate consequence of this monopoly of departmental resources is an increase in waiting lists. This means the effectiveness of IMRT needs to be carefully weighed up against its efficiency. Due to resource constraints, only one out of eight radiotherapy centres in Queensland is able to routinely offer IMRT for men with prostate cancer. Even in centres with wider availability this resource needs to be rationed. Consequently, there is a need to investigate whether 3D-CRT (with the use of image guided radiation therapy (IGRT) using fiducial markers), is a viable option for safely escalating reference doses to 78 Gy. It is important to note that IGRT should be considered an integral part of dose escalation as tight dose conformity without accurate tumour localisation is clearly suboptimal.

The objective of this study is to determine the ideal dosimetric and clinically relevant 3D-CRT plan for dose escalated prostate treatment. This includes plans for both prostate only (PO) and prostate plus seminal vesicles (PSV).

Method

Previously acquired computed tomography (CT) images of five patients with T1-T2N0M0 prostate carcinoma were used for this study. None of the patients actually received treatment using the plans produced in this dosimetric comparison study.

Simulation

Planning CT data was collected from simulations where a bladder filling/bowel voiding protocol was used and the scans acquired at 3 mm intervals with the patient in a supine position. Standardised headrests and feet stocks were employed for stability and reproducibility.

Table 1: Contouring guidelines.

Structure	Contoured	Limits	Performed by
PTV	1cm uniform margin on CTV except 7 mm post	Whole Structure	RO
Seminal Vesicles	Marked as CTV	1 cm sup of prostate	RO
Rectum	Wall – 3 mm tubular structure	1 cm sup/inf of PTV	RO
Bladder	Wall – 3 mm tubular structure	1 cm sup to sup limit of PTV	RO
Femur	Head and Neck	Inf limit to 1 cm inf of PTV	RT

PTV – Planning Tumour Volume; CTV – Clinical Tumour Volume; Sup – Superior; Inf – Inferior; Post – Posterior RO – Radiation Oncologist; RT – Radiation Therapist

Table 2: Description of field arrangements used in pilot study.

Plan	Description	Gantry angles (°)	Weightings (%)	Wedges
1	4 Fields	0, 90, 180, 270	All Equal	N/A
2	Sunrise	0, 45, 90, 270, 315	15, 10, 25, 25, 15	45^{o}: Thick to Anterior on lateral fields
3	5 Fields with Anterior	0, 90, 120, 240, 270	20, 25, 15, 15, 25	N/A
4	5 Fields Unopposed	18, 90, 162, 234, 306	All Equal	N/A
5	6 Fields	45, 90, 120, 240, 270, 315	10, 25, 15, 15, 25, 10	N/A
6	6 Fields (Steep Anterior Obliques)	30, 90, 120, 240, 270, 330	10, 25, 15, 15, 25, 10	N/A
7	6 Fields Unopposed	30, 90, 162, 234, 306, 270	All Equal	N/A
8	7 Fields	0, 40, 80, 110, 250, 280, 310	All Equal	N/A
9	8 Fields	30, 60, 100, 135, 225, 260, 295, 330	All Equal	N/A
10	Arc	30»130, 230»330	All Equal	N/A

Table 3: Dose volume histogram constraints of organs at risk.

OAR	Tolerance (Gy)
Rectum	V75 <5%
	V70 <25%
	V65 <40%
	V55 <50%
Bladder	V75 <25%
	V70 <35%
	V55 <50%
Femoral head and neck	V55 <0%
	V45 <60%
	V35 <100%

Contouring

The CT data was exported to the Oncentra Masterplan (Nucletron, Version 1.5, AX Veenendaal, The Netherlands) 3D treatment planning system to be contoured. Five consecutive patients with T1-T2N0M0 prostate carcinoma were contoured according to standardised departmental protocols (see Table 1) by a single radiation oncologist (RO) to minimise interobserver variation. The external contour and femoral head and neck were contoured by a single planning radiation therapist (RT) according to the descriptions in Table 1.

Planning

The first two patients formed the basis of the pilot study, where 10 plans (see Table 2) were generated, and a qualitative review performed to determine the three best plans. The additional three patients then had three plans each generated according to these final field arrangements to complete the study.

Beam weighting and multi-leaf collimators (MLC) were used to conform the dose to the PTV. Except for the sunrise technique, no wedges were required in this study. The starting point for beam weightings are described in Table 2 but were altered as required to meet dosimetry criteria.

The PTV dose for all plans was according to ICRU 50/62 criteria. A 100% dose was prescribed to the reference point in the volumetric centre of the PTV. All plans were optimised to ensure dose homogeneity between 95% and 107% of prescribed dose (74.1 Gy–83.46 Gy). Since all plans were similar in this respect, no further data is presented regarding PTV coverage.

Pilot study

From investigations reported in the literature[4,9,10,11] and protocols from six radiation oncology departments, 10 potential plans (see Table 2) were accumulated for inclusion. It was deemed more efficient to perform a pilot study on two separate sets of CT images with PO and PSV structures included in the PTV. These 10 different field arrangements were optimised for a 78 Gy reference dose according to the ICRU Report 50 and 62 guidelines[12,13] and OAR dose constraints were adhered to as described in Table 3.

Qualitative analysis

Three senior planning RTs and one RO with an interest in genitourinary oncology ranked the DVHs of the 10 plans for the initial two patients based on (in descending priority): PTV coverage (≥ 74.1Gy), rectal dose constraints (V75 Gy, V70 Gy, V65 Gy, V55 Gy), bladder dose constraints (V75 Gy, V70 Gy, V55 Gy) and femoral head and neck dose constraints (V55 Gy, V45 Gy, V35 Gy).

Based on the DVH evaluation of each OAR, the following techniques were unanimously chosen to be the top three techniques: (The numbers in brackets indicate the gantry angles used).

- 5-field technique (0, 90, 120, 240, 270)
- 6-field technique (Steep anterior obliques) (30, 90, 120, 240, 270, 330)
- 8-field technique (30, 60, 100, 135, 225, 260, 295, 330).

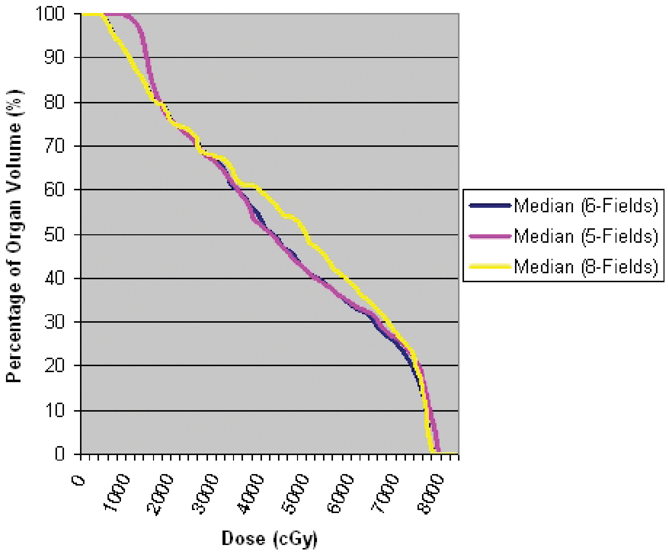

Figure 1: Rectal DVH.

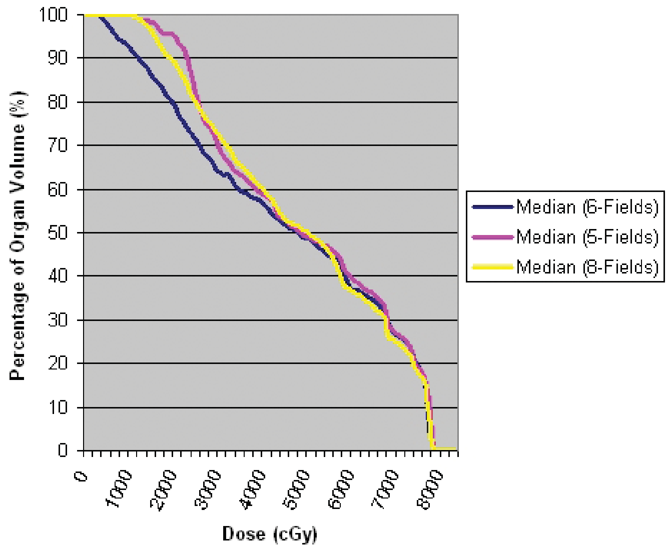

Figure 2: Bladder DVH.

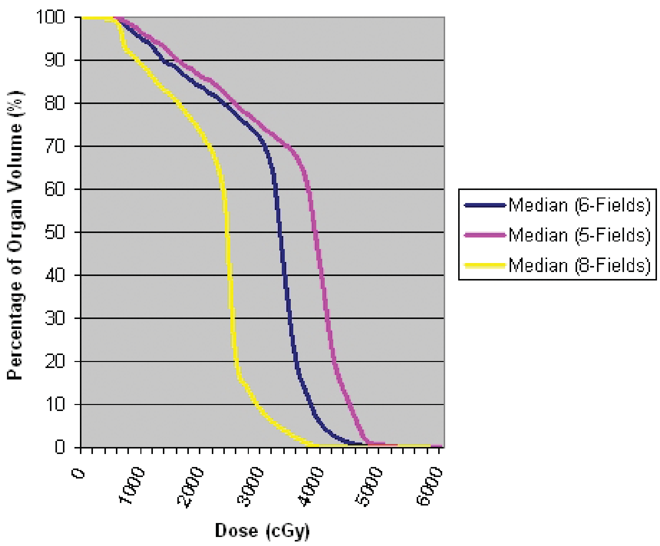

Figure 3: RT Femur DVH.

Quantitative analysis

These three plans were then optimised to the remaining three patients. With these plans now complete for all five patients, the DVH data for each OAR was exported to Microsoft Excel® 2003 (Microsoft, Seattle, USA) for graphical presentation and statistical analysis. This DVH binned data needed to be normalised into 100cGy increments for each patient so a true comparison could be made. From this, a median DVH value for each OAR was calculated (see Figures 1–3).

The median DVHs for each OAR allowed an easy comparison of each of the field arrangements. A statistical analysis at the dose constraint intervals was done as a quantitative review using pairwise comparisons. These were made using a two-sample study t-test with a significance level of $P < 0.05$ taken as statistically significant (see Tables 4a, b, c).

Results

The rectum and bladder DVHs in Figures 1 and 2, show little difference between the 5- and 6-field arrangements. A t-test analysis of the 5-field and 6-field techniques further show that the volume of rectum and bladder receiving a specific dose as indicated in Table 4a are not statistically significant. The 8-field arrangement on the other hand is eliminated as an option for dose escalation because it produces the greatest dose to the primary dose restricting organ, the rectum, and differs significantly to the 5-field ($P = 0.0001$) and 6-field ($P = 0.0003$) techniques at V55 Gy or the volume of rectum receiving 55 Gy (see Figure 1 and Table 4 b, Table 4 c). A 6-field technique is preferred over a 5-field technique because of the decreased femoral head and neck dose (see Figure 3). In fact, this is statistically significant at 35 Gy ($P = 0.001$) and 45 Gy ($P = 0.006$) (see Table 4a).

Discussion

Plan evaluation

Conformal planning is a very subjective process with the end result based on many variables including; observer dependence, patient dependence and OAR dependence. Consequently, the best plan is only the interpretation of an individual planner and their understanding of the RO's prescription. This study has tried to standardise the way in which each plan was optimised but accepts that variation in optimisation will occur as the plans still need to be clinically relevant.

The small variation found between the 5- and 6-field arrangements reveals that the concept of a class solution is becoming irrelevant in the world of conformal radiation therapy. More and more, plans are required to be tailor made to meet higher reference doses while maintaining strict OAR tolerances. The idea that one treatment technique is ideal for each situation is no longer a reality. However, an evidence-based starting point is a necessity in the interest of efficiency and standardisation within a radiation oncology department. Still, if both plans are similar what other considerations can be used to distinguish between the plans? The 5-field technique has some other advantages in that the anterior and lateral portals can be used for isocentre checks. The 6-field technique would require an anterior field created for the purpose of checking the isocentre and not to be used for treatment. Therefore, a 5-field technique can be deemed more efficient to plan and treat with the reduced number of fields.

The justification of the viable use of both the 5- and 6-field techniques made from these results when tempered with a flexible planning approach will ensure quality dosimetry and ultimately, the most achievable positive outcome for the patient.

Table 4a: Two sample t-test of 5-field and 6-field beam arrangements for selected dose constraints.

Rectum: *P*-value		Bladder: *P*-value		Fem Head and Neck: *P*-value	
V55	0.239	V55	0.244	V35	0.001*
V65	0.476	V70	0.241	V45	0.006*
V70	0.975	V75	0.158	V55	0.332
V75	0.311				

*Statistically significant at *P*-value <0.05

Table 4b: Two sample t-test of 5-field and 8-field beam arrangements for selected dose constraints.

Rectum: *P*-value		Bladder: *P*-value		Fem Head and Neck: *P*-value	
V55	0.0001*	V55	0.239	V35	0.001*
V65	0.102	V70	0.260	V45	0.008*
V70	0.580	V75	0.636	V55	0.332
V75	0.398				

*Statistically significant at *P*-value <0.05

Table 4c: Two sample t-test of 6-field and 8-field beam arrangements for selected dose constraints.

Rectum: *P*-value		Bladder: *P*-value		Femur Head and Neck: *P*-value	
V55	0.0003*	V55	0.549	V35	0.011*
V65	0.374	V70	0.457	V45	0.137
V70	0.374	V75	0.504	V55	0.374
V75	0.374				

*Statistically significant at *P*-value <0.05

Dose constraints

The best plan is also very dependent on prioritisation of critical structure importance. The rectum is by far, the most dose limiting structure[2,6,14] for prostate irradiation. Theoretically, the advantage of using a multi-field technique is to introduce as much dose from the lateral fields as possible. The lateral fields provide the best capacity to spare the rectum but are limited by the given femoral head and neck tolerance. The other fields are then required to complete the dose to the reference point (RP) while avoiding the femoral head and necks and also limiting dose to the rectum. Our study demonstrates that a 6-field technique provides significantly less femoral head and neck dose than a 5-field technique (see Figure 3 and Table 4a). The 8-field technique is not recommended for clinical use because compared to the 5-field and 6-field techniques it contributes the greatest dose to the rectum. It is clear that OAR doses directly dictate the treatment technique choice. This highlights the importance of a clear protocol for OAR contouring and acceptable DVH restrictions.[6] As essential as this requirement is, it is complicated by the limited evidence of bladder and femur tolerances.[6]

Observations

The post oblique fields used in the 5- and 6-field arrangement (30^0 below horizontal) allow the dose to be delivered to the reference point while limiting dose to the OARs. During treatment on the Elekta Precise™ treatment units, these fields will often require the treatment couch C-Arms and carbon fibre to be moved out of the field. This decreases the efficiency of the treatment unit, introduces a manual handling problem and potentially moves the patient in relation to the set isocentre. Solid carbon fibre treatment tops may remove this dilemma but even some of these still have metal reinforcements that may attenuate the treatment fields. These observations, however, should not influence the choice of technique recommended here as dose conformity and limiting dose to OARs supersede these issues.

Interobserver variation in CTV and PTV delineation has a large effect on the dosimetric outcome of a plan.[15] The co-registration of CT and other imaging techniques like MRI may allow for a more accurate localisation of the target tissue which, in clinical practice yields smaller radiation volumes with an expected decrease in toxicity.[4] Regular use of MRI to enhance CTV and PTV delineation would greatly increase the conformity and consequently the effectiveness of the 6-field technique to spare critical tissue while ensuring adequate PTV coverage.

The patients included in this study underwent a bladder filling/bowel voiding program before planning and during treatment. Current evidence demonstrates the effect of prostate movement due to bladder and rectal distension and the advantages of reproducing internal organ motion.[16,17,18,19] It was evident that the size and position of the rectum was more favourable when compared with other prostate patients not on the bowel/bladder prep protocol.

In the pilot study, a 5-field technique (0, 45, 90, 270, 315 gantry angles) also known as 'sunrise' was eliminated in the ranking process. A more recent review of protocols from other departments has revealed the adoption of this technique for prostate dose escalation. This technique also eliminates the problem encountered with the carbon fibre and the post oblique fields previously mentioned. As benchmarking is a fundamental part of evaluating a change in protocol, it was thought prudent to reassess this arrangement in relation to the end results of this project. It was concluded that although the rectal DVHs for the 'sunrise' technique were comparable, the dose delivered to the femoral head and necks were considerably increased. Thus, its original exclusion as a class solution is justified and further supports the evidence that the 6-field technique is the most acceptable technique for dose escalation.

Future directions

The results from this study will allow consolidation of an evidence based protocol for dose escalated irradiation with external beams. This will allow an efficient planning and treatment process that will provide increased benefit for both the department and ultimately, the patient. With input from this department's ROs and the senior RTs, we expect to implement a protocol that encourages the use of either the 5- or 6-field technique.

Based on both the evidence of this project and the current literature,[16,17,18,19] bladder and bowel prep is warranted to be included in a departments' prostate protocol. Guidelines reported by the Faculty of Radiation Oncology Genito-Urinary Group (FROGG)[6] and the RADAR trial[21] recommend the use of standard contouring guidelines for all structures. The advantages of utilising these guidelines have already been outlined and thus, need to be included in the updated protocol.

IGRT allows accurate verification of isocentre localisation and has been identified as the preferred method (where available) of field placement for dose escalated prostate treatment.[6,22,23,24] It is important to note that IGRT or the use fiducial markers should be considered an integral part of dose escalation as tight dose conformity without accurate daily tumour localisation is illogical.

Conclusion

As demonstrated by the results, the 6-field arrangement is recommended for dose escalated prostate irradiation. However, there is little variation between the 5- and 6-field techniques and so; the 5-field arrangement can also be considered an acceptable plan as it has some other clinical advantages. With the use of fiducial markers or IGRT, dose escalation with 3D-CRT is viable up to 78 Gy.

References

1 Pollack A, Zagars GK, Starkschall G, Antolak JA, Lee JJ, Huang E, *et al*. Prostate cancer radiation dose response: results of the M D Anderson phase III randomized trial. *Int J Rad Oncol Biol Phys* 2002; 53: 1097–105.

2 Peeters ST, Lebesque JV, Heemsbergen WD, van Putten WL, Slot A, Dielwart MF, *et al.* Localized volume effects for late rectal and anal toxicity after radiotherapy for prostate cancer. *Int J Rad Oncol, Biol, Phys* 2006 15; 64: 1151–61.

3 Oh CE, Antes K, Darby M, Song S, Starkschall G. Comparison of 2D conventional, 3D conformal, and intensity-modulated treatment planning techniques for patients with prostate cancer with regard to target-dose homogeneity and dose to critical, uninvolved structures. *Med Dosimet* 1999; 24: 255–63.

4 Bogers JA, van der Maazen RW, Visser AG. Conformal photon-beam radiotherapy of prostate carcinoma. *Eur Urol* 2002; 41: 515–22.

5 Morris DE, Emami B, Mauch PM, Konski AA, Tao ML, Ng AK, *et al.* Evidence-based review of three-dimensional conformal radiotherapy for localized prostate cancer: an ASTRO outcomes initiative. *Int J Rad Oncol, Biol, Phys* 2005; 62: 3–19.

6 Skala M, Berry M, Duchesne G, Gogna K, Tai KH, Turner S, *et al*. Australian and New Zealand three-dimensional conformal radiation therapy consensus guidelines for prostate cancer. *Australas Radiol* 2004; 48: 493–501.

7 Luxton G, Hancock SL, Boyer AL. Dosimetry and radiobiologic model comparison of IMRT and 3D conformal radiotherapy in treatment of carcinoma of the prostate. *Int J Rad Oncol, Biol, Phys* 2004; 59: 267–84.

8 Zelefsky MJ, Fuks Z, Happersett L, Lee HJ, Ling CC, Burman CM, *et al.* Clinical experience with intensity modulated radiation therapy (IMRT) in prostate cancer. *Radiotherap Oncol* 2000; 55: 241–9.

9 Bedford JL, Khoo VS, Oldham M, Dearnaley DP, Webb S. A comparison of coplanar four-field techniques for conformal radiotherapy of the prostate. *Radiotherap Oncol* 1999; 51: 225–35.

10 Khoo VS, Bedford JL, Webb S, Dearnaley DP. Class solutions for conformal external beam prostate radiotherapy. *Int J Rad Oncol, Biol, Phys* 2003; 55: 1109–20.

11 Neal AJ, Oldham M, Dearnaley DP. Comparison of treatment techniques for conformal radiotherapy of the prostate using dose-volume histograms and normal tissue complication probabilities. *Radiotherap Oncol* 1995; 37: 29–34.

12 ICRU Report 50: Prescribing, recording and reporting photon beam therapy. International Commission on Radiation Units and Measurements. 1993.

13 Wambersie A LT. ICRU Report 62: prescribing, recording and reporting photom beam therapy (Supplement to ICRU Report 50).

14 Fiorino C, Cozzarini C, Vavassori V, Sanguineti G, Bianchi C, Cattaneo GM, *et al*. Relationships between DVHs and late rectal bleeding after radiotherapy for prostate cancer: analysis of a large group of patients pooled from three institutions. *Radiotherap Oncol* 2002; 64: 1–12.

15 Lee YK, Bollet M, Charles-Edwards G, Flower MA, Leach MO, McNair H, *et al*. Radiotherapy treatment planning of prostate cancer using magnetic resonance imaging alone. *Radiotherap Oncol* 2003; 66: 203–16.

16 Pinkawa M, Asadpour B, Gagel B, Piroth MD, Holy R, Eble MJ. Prostate position variability and dose-volume histograms in radiotherapy for prostate cancer with full and empty bladder. *Int J Rad Oncol, Biol, Phys* 2006; 1; 64: 856–61.

17 Pinkawa M, Fischedick K, Asadpour B, Gagel B, Piroth MD, Eble MJ. Low-grade toxicity after conformal radiation therapy for prostate cancer--impact of bladder volume. *Int J Rad Oncol, Biol, Phys* 2006; 64: 835–41.

18 Roeske JC, Forman JD, Mesina CF, He T, Pelizzari CA, Fontenla E, *et al.* Evaluation of changes in the size and location of the prostate, seminal vesicles, bladder, and rectum during a course of external beam radiation therapy. *Int J Rad Oncol Biol Phys* 1995; 33: 1321–9.

19 Ghilezan MJ, Jaffray DA, Siewerdsen JH, Van Herk M, Shetty A, Sharpe MB, et al. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). *Int J Rad Oncol Biol Phys* 2005; 62: 406–17.

20 Skala M, Holloway L, Bailey M, Kneebone A. Australia-wide comparison of intensity modulated radiation therapy prostate plans. *Australas Radiol* 2005; 49: 222–9.

21 Incorporated T-TROG. A Randomised Trial Investigating the Effect on Biochemical (PSA) Contol and Survival of Different Durations of Adjuvant Androgen Deprivation in Association with Definitive Radiation Treatment for Localised Carcinoma of the Prostate 2004. Available online at: www.trog.com.au [verified November 2008].

22 Schaly B, Bauman GS, Song W, Battista JJ, Van Dyk J. Dosimetric impact of image-guided 3D conformal radiation therapy of prostate cancer. *Phys Med Biol* 2005; 50: 3083–101.

23 Schiffner DC, Gottschalk AR, Lometti M, Aubin M, Pouliot J, Speight J, *et al*. Daily electronic portal imaging of implanted gold seed fiducials in patients undergoing radiotherapy after radical prostatectomy. *Int J Rad Oncol Biol Phys* 2007; 67: 610–9.

24 Skala M, Rosewall T, Dawson L, Divanbeigi L, Lockwood G, Thomas C, *et al*. Patient-assessed late toxicity rates and principal component analysis after image-guided radiation therapy for prostate cancer. *Int J Rad Oncol Biol Phys* 2007; 68: 690–8.