Journal of Radiotherapy in Practice

Journal of Radiotherapy in Practice 2000
1, 179–189

Original Article

Towards an evidence-based 3D conformal radiotherapy prostate protocol: what is the role of spiral CT?

John Newnham

Clinical Oncology, St George's Hospital, Lincoln, UK

Abstract

Aim: To define the role of spiral CT in evolving an evidence-based 3D Conformal Radiotherapy (CRT) prostate protocol at Lincoln, UK.

Discussion: Tumour doses traditionally prescribed at this centre to the prostate planning target volume (PTV) (64 Gy in 32 fractions) cannot be further escalated without modification of existing technique and may currently be inadequate to obtain the highest probability of local control. Prostate CRT has been demonstrated to be well tolerated with both conventional and escalated doses, however as 3D CRT PTV margins are tightened, prostate position has to be reliably predicted to avoid geographic misses or unacceptable normal tissue toxicity. The question of prostate position variability might be addressed by sequential on-treatment spiral CT scans at this centre. Spiral CT offers specific advantages of speed, small detail conspicuity, and arbitrary axial reconstruction compared to conventional CT with no attached dose penalty. Spiral CT coupled to the next generation of radiotherapy treatment planning systems (RTPs) may soon replace the CT virtual-simulator. There are significant hardware discrepancies between some present generation CT couch tops and linac couch tops. Recently published CT studies that consider prostate position variability may be fundamentally and significantly flawed due to these couch top differences. Due to a paucity of reported evidence regarding immobilisation methods, a spiral CT study is warranted to assess efficacy of immobilization method for an evidence-based prostate protocol. Confirmative spiral CT research at this centre into prostate position variability is required to select adequate margins to form the PTV for an evidence-based 3D CRT prostate protocol. Such a spiral CT study could be integrated with the immobilisation study and may separate or define the correlation (which at present is both unclear and unreported) between pelvic immobilization and prostate position variability. Initial PTV margins defined by expanding the CTV in three dimensions using an ellipsoid with major axes 1.65 times one standard deviation of prostatic displacement reported in initial studies to obtain margins of 0.7 cm laterally, 0.7 cm cranio-caudally and 1.1 cm in the AP direction are presently indicated for this centre's evidence-based prostate protocol.

Conclusion: Spiral CT will provide the essential data set for 3D CRT planning for an evidence-based prostate protocol at Lincoln. Confirmative research using spiral CT is also warranted to assess daily prostate position variability and help define the prostate PTV for an evidence based prostate protocol at this centre.

Keywords

Spiral CT; evidence-based conformal radiotherapy; prostate protocol

Address correspondence to: John Newnham BApSc(Med Rads), Senior Radiographer, Radiotherapy Planning, Clinical Oncology, St George's Hospital, Long Leys Road, Lincoln, Lincs, UK

INTRODUCTION

The technical and clinical context of Lincoln's prostate protocol

The radiotherapy centre at St George's Hospital (Lincoln & Louth NHS Trust, UK) has recently purchased a new CMS Focus 9200 3D radiotherapy planning system (RTP) for clinical use before moving to a purpose-built radiotherapy site at Lincoln County Hospital. A Picker Ultra Z spiral CT scanner is being purchased to augment the existing and retained Sim-CT (Varian Scanvision). This author is responsible for establishing and implementing a spiral CT service, establishing and evolving spiral CT scan protocols and scanning all patients. The aim of this paper is to define the rationale for implementing dose-escalated 3D conformal radiotherapy (3D CRT), thence assess the role of spiral CT in moving towards a local evidence-based 3D CRT prostate protocol through an examination of spiral CT virtual simulation, spiral CT assessment of pelvic immobilization methods and spiral CT assessment of prostate position variability.

Current practice for treating carcinoma of the prostate with external beam radiotherapy

At this centre, all carcinoma of the prostate patients destined for radical external beam radiotherapy are CT scanned for radiotherapy planning using a conventional axial CT scanner and 5/10 mm slice intervals. Prostate planning target volumes (PTVs) are typically planned using a three-field isocentric technique with no conformal beam shaping, in two phases. Phase 1 typically extends to 50 Gy in 25 fractions of 2 Gy, with a PTV of GTV (gross target volume: ICRU definition) of prostate (± seminal vesicles) plus wide margins around CTV_1 and CTV_2 (clinical target volumes 1 & 2 as defined by ICRU). Phase 2 extends to 64 Gy in 32 fractions with reduced but still substantial margins around the GTV using non conformed fields, typically 7 × 7 cm. The size of margins for forthcoming 3D CRT remain to be decided.

Limitations of current practice – towards an evidence-based rationale for 3D CRT

By maximally excluding normal non-target tissue from the PTV, specifically the rectum, 3D CRT theoretically allows dose escalation to the PTV. This should increase tumour control probability[1,2] without increasing the probability of normal tissue complication.[1,3–6] Tumour doses traditionally prescribed at this centre to the prostate PTV (64 Gy in 32 fractions) cannot be further escalated without modifying existing technique and may currently be inadequate to obtain the highest probability of local control.[7–9]

Hanks et al.[10,11] demonstrated that local control of prostatic carcinoma decreases with relatively lower (though still higher than conventional) dose (< 74 Gy, median 72 Gy) and is associated with an increase in subsequent distant metastases when compared to higher dose patients (≥ 74 Gy, median 76 Gy). Analysis of their data (n=286) reinforces the need for the wide adoption of 3D CRT technology allowing safe delivery of higher doses in prostate cancer and provides an evidence-based rationale for implementing prostate 3D CRT at this centre. Pre-treatment prostate specific antigen level (PSA) has been found to be predictive of biochemical no evidence of disease (bNED) at 5 years on both univariate and multivariate analysis[12] and initial results (n=304)[9] indicate that escalating dose from 70–78 Gy most dramatically affects outcome for patients with a PSA level of 10 ng/ml and more specifically for stage T1/T2 disease. Based on 5 year bNED, there appears to be no benefit in escalating dose from 73–78 Gy for T1/T2 patients with PSA ≤ 10ng/ml.[7]

Clinical investigations – is there evidence that 3D CRT is well tolerated?

It is fundamental to this centre's evidence-based prostate protocol that prostate CRT has been demonstrated to be well tolerated with conventional doses of 64.8 Gy,[13,14] and escalated doses of 69 Gy (15) and 78 Gy[8,9] and that conformal 3D CRT significantly reduces acute gastrointestinal effects.[4] 72 Gy delivered as non conformed but reduced fields after 45 Gy (8 × 8 cm thence 6 × 6 cm) is also well tolerated.[16] However, there is varying consensus that 3D CRT allows less rectal volume to be incorporated into the PTV compared to conventional techniques.[8] A recent study (n=266) by Koper et al.[4] found that rectosigmoid toxicity is significantly reduced in patients treated with 3D CRT. Others[17] (n=189) have found that there has been a significant increase in rectal complications when ≥ 30% of the rectum receives

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

≥ 70 Gy. Posterior margins might be reduced or eliminated altogether if daily prostate position could be reliably inferred using spiral CT at this centre. There is some question that CT derived GTVs are larger than MRI derived GTVs:[18–20] using MRI for PTV delineation reduces the amount of irradiated rectal wall. It is interesting to speculate that CT derived GTVs may anatomically already incorporate an inherent CTV1+2 and partial PTV before expansion to these volumes. The use of intravenous contrast has been found to further increase the size of the outlined prostate GTV.[21]

The prostate does not occupy a fixed position within the bony anatomy of the pelvis.[22–29] As prostate PTV doses escalate and 3D CRT requires tighter conformal margins, variation of patient positioning may ultimately lead to either increased toxicity due to more irradiated normal tissue or geographic misses.[30] It is possible that daily prostate and rectal position variability is the underlying cause of the findings of one study (n=266)[31] that prostate 3D CRT did not reduce acute normal tissue toxicity compared to non-conformed radiotherapy, even though rectal volumes were assumed to be reduced using 3D CRT. The question of prostate position variability might be addressed by sequential on-treatment spiral CT scans.

MOVING TOWARDS AN EVIDENCE-BASED 3D CRT PROSTATE PROTOCOL USING CT

The first step at this centre in moving towards a 3D CRT prostate protocol is to gain confidence that conventional tumour doses can be reliably and adequately conformed to a reduced 3D prostate PTV whilst maximally excluding and sparing surrounding normal tissue, thus reducing rectal complications in particular.[4,32] First generation 3 field conformal plans will be produced using current CT data and the new RTP, whilst six field conformal fields could be contemplated for the final field reductions above 50 Gy.[8]

Once installed, the spiral CT will provide the raw data for the planning data set, and can be used to assess variations in prostate position during a course of radiotherapy to confirm (or disprove) that there is a high probability that the GTV and CTV will be adequately encapsulated by the PTV. If the results indicate acceptable levels of accuracy are being achieved, the prostate protocol could be modified by reducing margins around the CTV to allow radiation oncologists to progressively escalate prostate PTV doses in line with supportive findings from the recent literature[7–12,14,15,33] and the ongoing Radiation Therapy Oncology Group (RTOG trial 94–06) 3D CRT prostate dose escalation trial.[34] The first questions to be answered for this evolving evidence-based protocol are therefore:

- How shall the 3D CRT prostate patient be spiral CT simulated and planned?
- Is the prostate set-up reproducible between spiral CT simulation and treatment?
- Is it possible to ascertain the probability that the PTV adequately encapsulates the CTV on a daily basis?

Based on the latter, can PTV margins be reduced (or possibly eliminated) and dose escalated safely?

Research using spiral CT itself may be able to provide data to answer these questions.

ADVANTAGES OF SPIRAL CT OVER CONVENTIONAL NON-SPIRAL CT

Spiral CT is an appropriate modality for CT of the pelvis and prostate in particular.[35–37] Spiral CT is significantly faster than conventional non-spiral CT in both physically scanning the patient[38] and in axial image reconstruction,[37] which now approaches real-time in modern spiral CT systems. As spiral CT acquires a continuous volume of anatomical data, a major advantage of spiral CT over conventional CT is that the centre of a spiral reconstruction can be retrospectively and arbitrarily placed anywhere along the z axis.[37] In addition there is no theoretical limit to the number of slices that can be reconstructed with this arbitrary spacing.[37] It is therefore feasible, and has become normal clinical practice in many centres using spiral CT for diagnostic applications, to set one beam collimation (e.g. 5 mm) and reconstruct axial slices at closer intervals (e.g. 2–3 mm). This retrospective reconstructive ability of spiral CT does not impose the dose penalty associated with conventional CT scanning at thin collimations. Higher dose is produced from the necessity (both in conventional and spiral CT systems) to increase mAs for thin collimations (e.g. 1–3 mm) due to the

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

reduced quanta of photons reaching the CT detectors for such thin collimations. mAs must be sufficiently high to yield an acceptable signal-to-noise ratio to produce a CT image with acceptable low contrast resolution and perceptability for the soft tissues being imaged.

Spiral CT's ability to reconstruct slices at fine intervals reduces the characteristic stair-step appearances seen when using 5–10 mm slices for 3D pelvic anatomy reconstructions,[37] and allows a finer edge definition of the prostate GTV and CTV. Spiral CT's ability to reconstruct slices at arbitrary thin intervals also significantly reduces partial volume effects compared to conventional 8–10mm contiguous slices, thereby improving small detail (or lesion) conspicuity.[37]

Faster spiral scans are also a less daunting prospect for the patient, who may experience multiple on-treatment spiral scans. With appropriate pre-examination oral contrast for bowel opacification and administration of intravenous iodinated contrast media, faster spiral CT scans allow the possibility that the dedicated radiotherapy spiral CT could be used for the diagnostic staging and follow up of cancer patients, thereby easing the pressure on CT resources at some centres, and reducing waiting list times. This author notes that the greatest time spent in spiral CT scanning patients is the time taken to give an adequate explanation of the CT examination to the patient, for the patient to assume the treatment position, and later to get up from the CT couch. This is in contrast to older CTs, where scanning and image reconstruction can take ten minutes or more.

Although 1.0 spiral CT pitch (CT couch movement in mm per one CT tube rotation/ CT collimation in mm) was popular in the past,[35–37] 1.5 spiral pitch has been used increasingly in current clinical practice; indeed, 1.4 pitch may itself be optimal for image characteristics.[36] Longitudinal resolution is acceptable with 1.5 pitch coupled to a recent 180 degree high-order cubic-spline interpolation and reconstruction algorithm.

A collimation of 3 or 4 mm, with a 1.5 spiral pitch, and 2 mm slice reconstruction interval is appropriate for this centre – 3 mm slices using axial CT have been acceptable for 3D CRT planning[8,39–41] although 5 mm collimation has also been used.[33,34] Thinner CT collimations than 2 mm are not warranted as axial low-contrast spatial resolution is 2 mm for the new spiral CT. CT slices reconstructed at 1 mm intervals increase the amount of time required by the planner to contour pelvic anatomy and significantly increase the time taken for the radiation oncologist to delineate the GTV on multiple slices spaced at 1 mm. Nevertheless, initial experience at this centre is that the new RTP has sophisticated contouring tools, which significantly speed up the processes of contouring and GTV definition.

Diagnostic spiral CT of the prostate is typically performed with suspended inspiration[31] to reduce mis-registration artefacts caused by gross movement due to breathing during the scan. Gentle, even respiration is practised for radiotherapy planning CT to replicate the patient's treatment condition on the linac. The patient is scanned supine, feet first, with a full bladder to displace small bowel loops anteriorly from the treatment portals. The spiral CT run for prostate planning extends from the ischeal tuberosity to 2 cm above the bladder or the sacroiliac joints to ensure adequate data for 3D reconstruction of both pelvic and target anatomy. This is typically a 120–140 mm spiral, which with a 3 mm collimation and 1.5 spiral pitch equates to 27 gantry revolutions. Coupled to a 1.0 second per revolution scan-time on the Picker Ultra Z, this results in a 27 second spiral. Spiral CTs with lower mA tube ratings require longer scan times (1.5 s) to yield sufficient mAs to produce an image with acceptable low contrast perceptibility and minimal image noise.

In order to maintain the low contrast perceptibility required for radiotherapy contouring and GTV definition, such thin spiral CT collimations require a corresponding increase in mAs compared to traditional 10 mm CT collimations.[37] However, compared to 1.0 pitch, an increase in spiral pitch to 1.5 reduces absorbed dose significantly[42] and may represent the best compromise between thin collimation, radiation dose and optimum image production. Average spiral CT dose to the pelvis (deemed to be approximately 21.9 mGy using the Picker Ultra Z and 1.5 pitch), may not be significant for radiotherapy candidates, given the PTV doses delivered (64,000 mGy and above), and the absorbed scatter doses throughout the pelvis as a

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

whole. The benefit gained from adequately defining the prostate and the rectum, and the possible attendant reduction in the volume of rectum irradiated to 64,000 mGy, is likely to outweigh the probable risk of dose from a repeat or multiple on-treatment spiral CT scans.

VIRTUAL SIMULATION FOR AN EVIDENCE BASED PROSTATE PROTOCOL USING SPIRAL CT DATA IN THE RTP: WILL THE SPIRAL CT-SIM CEASE TO BE?

Virtual simulation[43] allows proposed physical treatment parameters to be practically assessed without the need for the patient to be present. Conway et al.[43] define a 'CT virtual simulator' as a CT scanner coupled to software to emulate a simulator using software tools. At this centre, virtual simulation for the prostate protocol with the new RTP is coincident with external beam planning and conformal field shaping. The RTP at this centre allows multiple windows to be open simultaneously in any combination:

- High resolution CT or MRI axial, coronal or saggittal anatomy images ± beams and/or isodoses.
- 3D wire-frame or solid anatomy ± beams and/or planned isodose distributions in line or solid colour wash format ± subtraction of anatomy as required.
- 3D GTV,CTV,PTV displayed in wire frame or solid format ± beams and/or planned isodose distributions.
- Treatment room view with physical machine parameters graphically displayed.
- BEV (beams eye view) and multileaf collimator generator.
- Multiple DVHs (dose volume histograms).
- DRRs (digitally reconstructed radiographs in simulator, composite, portal, or CT-scout equivalent formats).

This author finds this provides a much better appreciation of gross anatomical relationships/ PTV, CTV, GTV/treatment beam/isodose interactions[40] than the stand-alone anatomical graphical interface of the CT-simulator described by Conway & Robinson in 1997[43] and seen by the author. Moving through anatomy in a 3D or cross sectional fashion in any one window results in a real time translation in the other windows. As these anatomical windows display isodoses, the radiographer is able to assess how closely prescribed tumour dose conforms to the 3D CTV and the level of dose homogeneity across the PTV. Conversely, modifying physical treatment parameters results in real time modifications in the windows open. This RTP thus appears to be embody all that Sherouse et al.[44] envisioned for virtual simulation, and is fundamental for planning in an evidence-based prostate protocol.

Because the CT virtual simulator does not have a full 3D dose calculation engine, repeated transfer of patient data is necessary from the CT-sim computer to RTP and thence backwards and forwards to CT-sim to generate acceptable 3D anatomical displays and BEVs. This is far from ideal in that data corruption possibilities (even with systems supposed to be DICOM-RT compliant) increase with each discrete component in the planning system. The CT-sim is still not all that a planning radiographer could expect a 'virtual simulator' to be. As departments acquire the next generation of RTPs with multiple remote workstations, it is debatable whether the standalone CT-sim has any further place in radiotherapy planning. It also appears that radiographers would be more productively employed in planning than at the CT virtual simulator interface. The author therefore views the dedicated spiral CT unit as another tool (along with MRI) to interface with the core RTP which performs virtual simulation.

Digitally reconstructed radiographs (DRRs) drawn from the RTP at this centre will be initially used for pre-treatment sim-CT verification of 3D CRT prostate treatment plans, though Valecenti et al.[45] (n=75) conclude that when virtual simulation is available, verification of 3D CRT plans may be eliminated for prostate 3D CRT, due to the adequacy of portal imaging to verify planned treatment accuracy.

IS PATIENT POSITION AT SPIRAL CT SUFFICIENTLY REPRODUCIBLE FOR AN EVIDENCE-BASED PROSTATE PROTOCOL?

An evidence-based prostate protocol should be based on a set-up that is consistently reproducible: if a daily prostate patient set-up is only partly or

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

inconsistently reproducible compared to the CT set-up there should be no expectation that the isocentre of the 3D CRT PTV position will be as virtually simulated. Yet, of the 6 spiral CT manufacturers who tendered for the spiral CT for Lincoln and Louth's new radiotherapy centre, only one at present provides a CT couch top functionally identical to linac treatment couches. Other manufacturers who tendered still rely on inserting a plank of material, secured with varying fixation methods, into the traditionally concave patient scanning cradle of the diagnostic CT in an attempt to replicate the flat linac treatment couch. So pivotal is this issue of reproducibility and couch tops that some radiotherapy units may decide to buy a particular spiral CT on the basis of reproducible radiotherapy-specific couch specification rather than fundamental spiral CT hardware and software specification. The possibility therefore exists that such an acquisition may be less well matched to tender specifications for core spiral CT hardware, image production and post-processing than other CT units under consideration. This centre is investigating the use of a concave diagnostic cradle that can be inserted on the flat topped CT couch when required for diagnostic staging scans.

In the most disturbing recent examples of CT couch inserts for radiotherapy planning observed by the author (UK, Australia, USA and France) the couch insert is levelled using a bubble ruler to ensure alignment of the insert. This method allows the couch insert to be tilted to one side or the other by several millimetres yet still appear visually aligned. Alternatively, the insert may move by several millimetres (or more) as the patient assumes the treatment position or when the radiographer levels the patient up. This may be significant because, as shall be demonstrated in this paper, 3D CRT prostate margins and prostate position variability are necessarily being defined in millimetres.

The discrepancy between couch tops begs the question whether or not recently published CT studies, which consider prostate position variability,[3,22,27,39,41,46–49] are fundamentally or significantly flawed due to couch top differences. Until these differences can be quantified, and perhaps until authors specify what type of hardware and what type of couch top they used in their studies, the clinical impact and relevance of differing couch tops may be difficult to assess.

Whilst agreeing with Rosenman et al.[50] that in many circumstances diagnostic CT images should be coregistered with CT planning scans and then used for PTV definition, differences in inherent patient position due to varying couch tops at diagnostic CT scanning (pelvic patient in concave diagnostic cradle) and radiotherapy CT scanning (flat top) potentially weakens their conclusion that co-registration is an essential part of 3D CRT without adding the rider that it is essential to assess CT hardware and incorporate known systematic error introduced into the planning data set.

IS A SPIRAL CT STUDY WARRANTED ON THE EFFICACY OF PELVIC IMMOBILISATION DEVICES USED IN AN EVIDENCE-BASED PROSTATE PROTOCOL?

An evidence-based prostate protocol should consider immobilisation as a possible means to ensure that the PTV adequately encapsulates the CTV. As stated, the prostate is a mobile organ. Though pelvic immobilization is practised as a matter of course at the centres associated with the studies below, only **one** recent large scale study[30] has been done to justify using immobilisation devices for prostate 3D CRT, and this study relied on portal imaging for assessment of immobilisation efficacy and not CT, which the author considers is more accurate in defining the prostate, a soft tissue organ. The literature mentions a wide range of immobilisation devices used in studies:

- Mid lumbar/thoracic to mid thigh posterior-only foam Alpha cradles.[30,39,41,51,52]
- Mid lumbar to below the knees foam Alpha cradles.[30]
- Mid thorax to feet prone Alpha foam cradles.[33]
- Leg immobiliser below the knees.[24,30]
- Aquaplast abdomen and pelvis cast to mid thigh with Alpha cradle to lower legs and feet.[30]
- VacFix bags.[49]
- Pelvis-only anteriorly encasing thermoplastic cradles.[52]
- No immobilisation device – lateral simulation tattoos alone.[3,19,22,48,53]

There is no consensus in the literature that any one form of immobilisation is warranted, beneficial or

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

preferred over any other. Three views emerge, though the question remains whether immobilisation of the pelvis produces a corresponding and significant immobilisation of the prostate?

IMPROVEMENT WITH IMMOBILISATION

Lattanzi et al.[39] (n=6) contend that daily set-up variation was markedly improved with the use of the Alpha cradle secured to a 1.25 cm thick polystyrene board with 16 × 16 cm square removed posteriorly to facilitate treating of the posterior field. Average daily set-up error as assessed through sequential port films was 3.3 mm immobilised as compared to 8 mm unimmobilised. However, due to differing populations (both sample numbers are small, were at different centres and were measured seven years apart) and differing error assessment methods it may be unrealistic to compare these two populations. Further confirmative research using sequential CT image coregistration in a sophisticated RTP or dedicated image-merging software and matched populations of immobilised vs. unimmobilised patients would be required to support Latanzi et al's contentions regarding efficacy of immobilisation method. Mubata et al.[49] in a portal imaging study (n=24) contend that VacFix bags (n=12) reduced translational anatomy shifts and maintained pelvic orientation more than no immobilization (95% of VacFix patients had a pelvic rotation of less than 2°, compared to 86% of patients with no immobilisation). Though this is encouraging, maintaining bony pelvic orientation is no guarantee that the prostate is adequately encapsulated by the PTV irradiated.

NO IMPROVEMENT WITH IMMOBILISATION

Antolak et al.[46] contend that immobilisation devices (n=17) did not appear to reduce set-up errors. Song et al.[30] found in a comparison of no immobilisation (n=20), Alpha cradles mid femora (n=8), Alpha cradles mid tibia (n=10), Styrofoam leg immobiliser alone (n=14), and Aquaplast plus Alpha cradle (n=10) that there was no significant reduction in probability of overall patient movement with any of the immobilisation devices compared to no immobilisation. Song et al. concluded that no immobilisation method was effective in reducing movement in obese patients. It is perhaps pertinent to note that Song et al. found that obese patients and patients with a pelvic girth greater than 105 cm had a higher probability of movement in Alpha cradles (+66%, p=<0.05) than without and that there was no evidence to support the general assumptions that unimmobilised obese patients moved more than unimmobilised normal ones for pelvic irradiation.

No comment on rationale for chosen immobilisation method

Several pelvic studies[3,41,47,51] do not comment on the rationale behind the decision to use a certain type of immobilisation. Van den Broek et al.[52] comment that after difficulties with the Alpha cradle (patient positioning difficulties and cradle breakage) they transferred to thermoplastic cradle, though they believed a better immobilisation device than their present thermoplastic cradles, perhaps longer thermoplastic sheets, was required to reduce variation in longitudinal displacement of the PTV. These cradles continue to undergo trials at this centre using sim-CT and portal imaging.

Based on clinical experience, this author notes that anteriorly encasing thermoplastic cradles pose additional technical problems. Thermoplastic cradles must tie up to patient bony pelvis anatomy, yet lateral tattoos are tied in with alignment marks drawn on the cradles. The tattoos (on both verification and treatment) may be displaced as the skin catches or pulls in different directions at cradle application, especially with patients of larger habitus (this may tie in with Song et al's analysis). When aligning lateral tattoos to the cradle marks, it appears that the simulator or treatment radiographer may sometimes only move skin and not achieve any significant adjustment of bony anatomy. For these reasons, ongoing portal imaging studies conducted by colleagues at this centre may shed some light on the reproducibility of these cradles regarding alignment of pelvic bony anatomy.

Can spiral CT assessment help define which form of immobilisation (if any) is warranted for an evidence based prostate protocol?

Based on the above discussion, the paucity of CT assessment of efficacy of immobilisation methods, and the inherent controversy of immobilisation vs

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

no immobilisation, a spiral CT study at this centre on efficacy of immobilisation method is warranted. Two initial trial arms into which all prospective radiotherapy prostate patients would be randomised are proposed: thermoplastic cradles vs. no immobilisation (based on Song et al's observations). Initial spiral CT could be used as the benchmark and DRRs produced for simulator and linac portal verification using fiducial or chamfer matching technique.[19] Better still, patients undergoing weekly sequential spiral scans for prostate position (discussed below) could be assessed for efficacy of immobilisation method. Merged sequential spiral CT scans into an RTP or other dedicated software capable of such merge and displacement measurement gives directly comparable data sets with greater soft tissue detail than merged linac portal images[54] even with multiple match points using fiducial or chamfer matching techniques. Until a study with a large number of recruited patients is reported, it appears that optimal immobilisation technique and patient positioning for prostate are yet to be determined.[30]

SPIRAL CT ASSESSMENT OF PROSTATE POSITION VARIABILITY

General considerations regarding prostatic displacement

There appears to be good agreement amongst multiple observers[55] in defining the prostate PTV. To select adequate margins to form the PTV for an evidence-based 3D CRT prostate protocol, it is important to quantify the uncertainty in the internal motion of the prostate and seminal vesicles.[41] There is no data to support the contention that uncertainty in internal motion of the prostate and seminal vesicles depends on or correlates with uncertainty in patient position set-up.[41] This finding may tie in with previous comments on the demonstrated lack of inherent benefits of immobilisation methods. It is further assumed that the positions of organs on the pre-treatment CT scan represent the mean positions of these organs during a course of therapy. Yet Antolak et al.[46] found that both bladder and rectal volumes decreased between the pre-treatment CT scan and first on-treatment CT scan at 2 weeks, but were then constant for all on-treatment CT scans repeated every two weeks. Similarly, Zelefsky et al.[33] found that prostatic displacement during a course of radiotherapy is more pronounced amongst patients who have large rectal and bladder volumes on initial planning scans. Both of these findings imply there may be a systematic error in planning prostate 3D CRT. This author contends that an early on-treatment spiral CT scan should be contemplated at this centre to confirm these pertinent findings of Antolak et al.[46] and Zelefsky et al.,[33] both of whom further found that prostate mobility is not significantly correlated with bladder volume, but correlates significantly with rectal volume. It may be pertinent to speculate further that differing diets between individuals might significantly produce differences in rectal filling and distension, and thereby lead to more or less pronounced and significant prostatic displacement. This may be another indication for pursuing regional confirmative CT research into prostate position variability.

Specific measurements of prostatic displacement

Using transverse, coronal and saggittal projections, Antolak et al.[46] also report that the mobility of the CTV (prostate and seminal vesicles) was characterised by a one sample standard deviation of 0.09 cm left to right (**laterally**) 0.36 cm cranio-caudally (**sup-inf.**) and 0.41 cm **anterio-posteriorly**. Nevertheless, individual displacements are extremely variable ranging from 0.03 to 1.5 cm.[46] This data fits in the middle range of previously published data on prostate CTV mobility.[3,22,24,26–29,54,56] Along the lateral axis, all data indicates that the prostate is fairly immobile with a standard deviation of 0.1 cm. Along the anterior-posterior axis five studies report a variability of 0.4 cm,[25,26,28,46] though two studies quote smaller deviations of 0.2 cm[22,24] and two studies quote 0.5 cm.[29,56] Along the cranio-caudal axis standard displacements are more variable ranging from 0.17 cm to 0.51 cm. Beard et al.[47] found that prostate motion could not be predicted by evaluating simply measured parameters from a double CT scan sequence.

Tinger et al. (n=51)[41] who employed weekly CT scans of the pelvis, found mean displacements of the prostate of 0 mm (SD = ±0.9 mm) along the lateral axis, 0.5 cm (SD = ±2.6 mm) in the anterior-posterior axis, and 1.5 mm (SD= ±3.9 mm) in the cranio-caudal axis. An interesting

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

observation made by Lattanzi et al.[39] is that prostate motion after 50 Gy is significantly less than previously reported: this may reflect radiation-induced early physiologic changes which restrict prostate motion as dose accrues.

Antolak et al.[23,46] choose 95% as the probability that a point on the edge of the CTV would be enclosed by the PTV and therefore expanded the CTV in three dimensions using an ellipsoid with major axes 1.65 times one sample standard deviation of the data from their study to obtain margins of 0.7 cm laterally, 0.7 cm cranio-caudally (sup.-inf.) and 1.1 cm in the AP direction. These margins accord well with Tinger et al's[41] CTV margins of 0.7 to 1.1 cm designed to encompass measured uncertainties of the centre of the prostate volume with a probability of 95%. Similarly, Antolak et al's CTV margins accords well with Dawson et al's proposition[48] that borders around the CTV required for 95% certainty are 5.6 mm, 10.3 mm and 12.4 mm respectively.

The margins proposed by Antolak et al. are therefore indicated for this centre's prostate protocol and compare favourably with the margins of 0.5 to 1.0 cm specified in the current RTOG 94–06 dose escalation protocol for prostate radiotherapy. However, Antolak et al.[23,46] point out that the prime considerations when defining the PTV are minimum dose to the CTV and avoidance of organs at risk when drawing beam portals.

Thus, though data in the above studies are consistent with each other, given that individual displacements reported are quite variable, this author contends that it is essential to perform confirmative spiral CT research at this centre into prostate position variability, lest there be unrecognised possibilities of significant geographic missing and underdosing of the prostate. Such a spiral CT study could be integrated with the immobilisation study and may separate or define the correlation (which at present is both unclear and unreported) between pelvic immobilisation and prostate position variability.

The question remains whether more frequent on-treatment spiral CT scans are inherently better than fewer. Considering Beard et al's[47] reservations about two on-treatment scans, and Antolak et al's measurements[46] and analysis, spiral CT scans would be indicated at least once every 2 weeks and may be justified once a week. As dose accrues, physiologic changes may 'tether' the prostate and reduce overall movement[39] thus reducing the need for very frequent spiral CT scans above 50 Gy: confirmative research now being performed on this matter would be highly illuminating.

CONCLUSION

Spiral CT will provide the essential data set for 3D CRT planning for an evidence based prostate protocol at Lincoln. Spiral CT offers significant advantages over non-spiral CT in terms of increased speed (and therefore patient comfort and compliance), reduced dose for fine collimations, improved small detail and lesion conspicuity, and arbitrary slice reconstruction interval with no dose penalty attached. Spiral CT coupled to the next generation of RTPs may soon replace the CT virtual-simulator. If positional reproducibility is to be maintained for an evidence-based protocol, spiral CT couches should ideally exactly replicate linac treatment couches, and any studies done using CT couch inserts should be viewed with caution. The author makes the following recommendations:

- Spiral CT on-treatment scans are indicated weekly or every two weeks for dose escalated patients to define the prostate PTV for dose escalation and 3D CRT.
- At least one on-treatment spiral CT scan is indicated to identify and reduce systematic error in prostate planning.
- A prospective spiral CT study is warranted to assess efficacy of immobilisation method for prostate 3D CRT.

Dose escalation produces significant improvement in outcome for T1/T2 ca prostate patients with lower PSA levels, but it appears likely that the best therapeutic outcomes will only arise from a 3D CRT technique that has a high probability of adequately encapsulating the prostate PTV. At this time, sequential spiral CT scans are indicated to define a 3D CRT technique and provide further evidence of individual prostate position variability which would then define technique for individual patients. Sequential spiral CT is indicated to assess whether prostate position variability is constant throughout a course of radiotherapy both as a function of the individual, or for populations as a

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

whole, or whether prostate position variability decreases as dose accrues. Such evidence from ongoing CT based studies may change current PTV definition and may make it possible to significantly reduce posterior margins, thus sparing more rectal volume and reducing radiation-induced complications and morbidity, whilst still adequately encapsulating the prostate CTV.

References

1. Emami B, Lyman J, Brown A, et al. Tolerance of normal tissue to therapeutic irradiation (Abstr.). Int J Radiat Oncol Biol Phys 1991; 21: 109–122
2. Leibel SA, Ling CC, Kutcher GJ, Mohan R, Cordon-Cordo C, Fuks Z . The biological basis for conformal three-dimensional radiotherapy defined. Int J Radiat Oncol Biol Phys 1991; 21: 805–811.
3. Bergström P, Löfroth PO, Widmark A. High precision conformal radiotherapy (HPCRT) of prostate cancer – a new technique for exact positioning of the prostate at the time of treatment. Int J Radiat Oncol Biol Phys 1998; 305–311.
4. Koper PCM, Stroom JC, van Putten WLJ, et al Acute morbidity reduction using 3D CRT for prostate carcinoma: a randomized study. Int J Radiat Oncol Biol Phys 1999; 43(4): 727–734.
5. Roach M 3rd, Pickett B, Weil M, Verhey L. The critical volume tolerance method for estimating limits of dose escalation during three-dimensional conformal radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys 1996; 35(5): 1019–1025.
6. Vijayakumar S, Chen GTY. Implementation of three dimensional conformal radiation therapy: prospects, opportunities and challenges. Int J Radiat Oncol Biol Phys 1995; 33(5): 979–983.
7. Hanks GE, Hanlon AL, Pinnover WH, Horwitz. Dose response for favourable and unfavourable subgroups of the classic pretreatment PSA groups. Int J Radiat Oncol Biol Phys 1999; 43(5)s1: 198.
8. Pollack A, Zagars GK, Starkshall G, Childress CH, Kopplin S, Boyer AL, Rosen II. Conventional vs. conformal radiotherapy for prostate cancer: preliminary results of dosimetry and acute toxicity. Int J Radiat Oncol Biol Phys 1997; 34(3): 555–564.
9. Pollack A, Zagars GK, Smith LG, Antolak JA, Rosen II. Preliminary results of a randomized dose-escalation study comparing 70 Gy to 78 Gy for the treatment of prostate cancer. Int J Radiat Oncol Biol Phys 1999; 45(3) S1: 4.
10. Hanks GE, Schultheis T, Hanlon A, Hunt M, Lee W, Epstein B, Coia L. Optimization of confomral radiation treatment of prostate cancer: report of a dose escalation study. Int J Radiat Oncol Biol Phys 1997; 37(2): 543–550.
11. Hanks GE, Hanlon AL, Horwitz, et al A relationship of local prostate dose and subsequent metastasis with 3D CRT in prostate cancer. (Abstr.) Int J Radiat Oncol Biol Phys 1998; 42(Suppl. 1): 143.
12. Wurtzer JC, Hanlon A, Horowitz E, Pinover W, Hanks G. Analysis of bNED control and factors predicting outcome in non-palpable (Clinical stage 1c) adenocarcinoma of the prostate treated with 3D conformal external beam radiation therapy (Abstr.) Int J Radiat Oncol Biol Phys 1998; 42(Suppl. 1): 144.
13. Lilleby W, Fossa SD, Waehre HR, Lsen DG. Long-term morbidity and quality of life in patients with localized prostate cancer undergoing definitive radiotherapy or radical prostatectomy. Int J Radiat Oncol Biol Phys 1999; 43(4): 735–743.
14. Zelefsky MJ, Ashkenasy E, Kelsen S, Leibel SA. Tolerance and early outcome results of postprostatectomy three dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 1997; 39(2): 327–333.
15. Fukunaga Johnson N, Sandler HM, et al Results of 3D conformal radiotherapy in the treatment of localized prostate cancer. Int J Radiat Oncol Biol Phys 1997; 38(2): 311–317.
16. Liu L, Glickman AS, Coachman N, et al Low acute gastrointestinal and genitourinary toxicities in whole pelvic irradiation of prostate cancer. Int J Radiat Oncol Biol Phys 1999; 43(4): 735–743.
17. Storey MR, Pollack A, Zagars GZ, Smith LG, Antolak JA, Rosen II. Complications from dose escalation in prostate cancer: preliminary results of a randomized trial. Int J Radiat Oncol Biol Phys 45(3)S1: 47.
18. Kagawa K, Lee WR, Shultheiss TE, Hunt MA, Shaer AH, Hanks GE. Initial clinical assessment of CT-MRI image fusion software in localization of the prostate for 3D conformal radiation therapy. Int J Radiat Oncol Biol Phys 1998; 38(2): 319–325.
19. Rasch C, Barillot I, Remeijer P, Touw A, van Herk M, Lebesque JV. Definition of the prostate in CT and MRI: a multi-observer study. Int J Radiat Oncol Biol Phys 1999; 43(1): 57–66.
20. Roach M, Faillace Akazawa P, Malfatti C, Holland J, Hricak H. Prostate volumes defined by magnetic resonance imaging and computerized tomographic scans for three dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 1996; 35(5): 1011–1018.
21. Zhou SM, Bentel GC, Lee CG, Ansher MS. Differences in gross target volumes on contrast vs noncontrast CT scans ultilized for conformal radiation therapy treatment planning for prostate cancer. Int J Radiat Oncol Biol Phys 1998; 42(1): 73–78.
22. Althof VG, Hoekstra CJ, te Loo HJ. Variation in prostate position relative to adjacent bony anatomy. Int J Radiat Oncol Biol Phys 1996; 34(3): 709–715.
23. Antolak J, Rosen II. Planning target volumes in radiotherapy: how much margin is needed? Int J Radiat Oncol Biol Phys 1999; 44(5): 1165–1170.
24. Balter J, Sandler HM, Lam K, Bree RL, Lichter AS, Ten Haken RK. Measurement of prostate motion over the course of routine radiotherapy using implanted markers. Int J Radiat Oncol Biol Phys 1995; 31: 113–118.
25. Crook JM, Raymon Y, Salhani D, Yang H, Esche B. Prostate motion during standard radiotherapy as assessed by fiducial markers. Rad Oncol 1995; 37(1): 35–42.
26. vanHerk M, Bruse A, Kroes APG, Shouman T, Touw A, Lebesque JV. Quantification of organ motion during conformal radiotherapy of the prostate by three dimensional image registration. Int J Radiat Oncol Biol Phys 1995; 33(5): 1311–1320.
27. Melian E, Mageras GS, Fuks Z, Leibel SA, Niehaus SA, Lorant H. Variation in prostate position quantitation and implications

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press

for three-dimensional conformal treatment planning. Int J Radiat Oncol Biol Phys 1998; 38(1): 73–81.

28. Roeske JC, Forman JD, Mesina CF, et al Evaluation of changes in size and location of the prostate, seminal vesicles, bladder and rectum during a course of external beam radiotherapy. Int J Radiat Oncol Biol Phys 1995; 33(5): 1132–1329.
29. Vigneault E, Pouiliot J, Lavierdiere J, Roy J, Dorion M. Electronic portal imaging detetction of radioopaque markers for the evaluation of prostate position during megavoltage irradiation – clinical study. Int J Radiat Oncol Biol Phys 1997; 37(1): 213–221.
30. Song PY, Washington M, Vaida F, et al A comparison of four patient immobilization devices in the treatment of prostate cancer patients with three dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 1996; 34(1): 213–219.
31. Tait DM, Nahum AE, Meyer LC, et al Acute toxicity in pelvic radiotherapy, a randomised trial of conformal versus conventional treatment. Rad Oncol 1997; 42(2): 121–136.
32. Sandler HM, McLaughlin W, Ten Haken RK, Addison H, Forman J, Lichter A. Three dimensional conformal radiotherpay for the treatment of prostate cancer: low risk of chronic rectal morbidity observed in a large series of patients. Int J Radiat Oncol Biol Phys 1995: 33(4): 797–801.
33. Zelefsky MJ, Crean D, Magera GS. Quantification and predictors of prostate position variability in 50 patients evaluated with multiple CT scans during conformal radiotherapy. Rad Oncol 1999; 50(2): 225–234.
34. Pailiwal BR, Ritter MA, McNutt TR, Mackie TR, Thomadsen BR, Purdy JA, Kinsella TJ. A solid water pelvic phantom and prostate phantom for imaging, volume rendering, treatment planning, and dosimetry for an RTOG multi-institutional 3-D dose escalation study. Int J Radiat Oncol Biol Phys 1998; 42(1): 205–211.
35. Blanck C. Understanding Spiral Scanning. Philadelphia: Lippincott, Williams & Wilkins, 1998
36. Fishman EK, Jeffrey RB. Spiral CT: Principles, Techniques and Clinical Applications. 1998. London: Raven P Lippincott, 1998
37. Silverman PM. Spiral (Spiral) Computed Tomography: A Practical Approach to Clinical Protocols. 1998. London: Lippincott, Williams & Wilkins.
38. Herts BR, Perl J, Seney C, Lieber ML, Davros WJ, Baker ME. Comparison of examination times between CT scanners: are the newer scanners faster? Am J Roent 1998; 170(1): 13–18.
39. Lattanzi J, McNeely S, Hanlon A, et al Daily CT localization for correcting portal errors in the treatment of prostate cancer. Int J Radiat Oncol Biol Phys 1999; 41(5): 1079–1086.
40. Pelizzari CA, Grzeszczuk R, Chen GTY, et al Volumetric visualization of anatomy for treatment planning. Int J Radiat Oncol Biol Phys 1996; 34(1): 205–11.
41. Tinger A, Michalski JM, Chend A, et al A critical evaluation of the planning target volume for 3-D conformal radiotherapy of prostate cancer. Int J Radiat Oncol Biol Phys 1998; 42(1): 213–221.
42. McNitty G, Cagon CH, Solberg TD, Chetty I. Radiation dose in spiral CT: The relative effects of collimation and pitch. Med Phys 1999; 26(3): 409–414.
43. Conway J, Robinson MH. CT virtual simulation. Brit J Radiol 1997; 70 (S1): 106–118.
44. Sherouse GW, Moscher CE, Novins K, Rosenman J, Chaney EL. Virtual simulation: concept and implementation. In: The Use of Computers in Radiation Therapy (Eds: Bruinvis, et al.). Amsterdam: Elsevier, 1987.
45. Valecenti RK, Waterman FM, Croce RJ, Corn B, Suntharalingam N. Efficient CT simulation of the four field technique for conformal radiotherapy of prostate carcinoma. Int J Radiat Oncol Biol Phys 1997; 37(4): 953–957.
46. Antolak JA, Rosen IA, Childress CH, Zagars GK, Pollack A. Prostate target volume variations during a course of radiotherapy. Int J Radiat Oncol Biol Phys 1998; 42(3): 661–672.
47. Beard CJ, Kijewski P, Bussiere M, et al Analysis of prostate and seminal vesicle motion: implications for treatment planning. Int J Radiat Oncol Biol Phys 1996; 34(2): 451–458.
48. Dawson LA, Mah K, Franssen E, Morton G . Target position variability throughout prostate radiotherapy. Int J Radiat Oncol Biol Phys 1998; 42(5): 1155–1161.
49. Mubata CD, Bidmead AM, Ellingham LM, Thompson V, Dearnley DP. Portal imaging protocol for radical dose-escalated radiotherapy treatment of prostate cancer. Int J Radiat Oncol Biol Phys 1998; 40(1): 221–231.
50. Rosenman JG, Miller EP, Tracton G, Cullip TJ. Image registration: an essential part of radiation therapy treatment planning. Int J Radiat Oncol Biol Phys 1998; 40(1): 197–205.
51. Sharma R, Duclos M, Chuba PJ, Shamsa F, Forman JD. Enhancement of prostate volume definition with intravesical contrast. A dosimetric evaluation. Int J Radiat Oncol Biol Phys 1997; 38(3): 575–582.
52. Van den Broek S, Vandensteene N, Salamon E. From conventional to conformal radiotherapy for the prostate: a practical dosimetric and technical approach. Varian Users Meeting, 27 April 1998 proceeds: 96–99.
53. Morganti AG, Valentini V, Mantello G, Mattiucci GC, Luzi S, Leone M, Cellini N. Cost- and time-sparing simplified conformal therapy for prostate cancer: is it feasible. Int J Radiat Oncol Biol Phys 1998; 42(1): 65–71.
54. Hanley J, Lumley MA, Mageras GS, et al Measurement of patient positioning errors in three-dimensional conformal radiotherapy of the prostate. Int J Radiat Oncol Biol Phys 1997; 37(2): 435–444.
55. Valicenti RK, Sweet JW, Hauck WW, et al Variation of the clinical target volume definition in three-dimensional conformal radiation therapy for prostate cancer. Int J Radiat Oncol Biol Phys 1999; 44(4): 931–935.
56. Rudat V, Shraube P, Oetzel D, Zierhut D, Flentje M, Wannenmacher M. Combined error of patient positioning variability and prostate motion uncertainty in 3D conformal radiotherapy of localized prostate cancer. Int J Radiat Oncol Biol Phys 1996; 35(5): 1027–1034.

https://doi.org/10.1017/S1460396999000291 Published online by Cambridge University Press