Application of helical tomotherapy in genitourinary malignancies

George Rodrigues, MD,[1,2] Slav Yartsev, PhD,[1,3] Glenn Bauman, MD[1,3]

[1]Department of Radiation Oncology, London Regional Cancer Program, London Health Sciences, London, Ontario, Canada

[2]Department of Epidemiology and Biostatistics, University of Western Ontario, London, Ontario, Canada

[3]Department of Medical Biophysics, University of Western Ontario, London, Ontario, Canada

RODRIGUES G, YARTSEV S, BAUMAN G. Application of helical tomotherapy in genitourinary malignancies. The Canadian Journal of Urology. 2010;17(6):5453-5458.

Introduction: *Helical tomotherapy (HT) is an innovative approach to the delivery of intensity-modulated radiation therapy which combines the imaging elements of helical computed tomography (CT) with megavoltage linear accelerator treatment. The purpose of this report is to describe our experience with the clinical implementation of HT for genitourinary malignancies.*

Materials and methods: *All patients treated with a primary genitourinary malignancy were included in this study cohort. Descriptive statistics for various demographic and treatment-related parameters such as patient age, primary site of disease, site of radiotherapy, goal of treatment, dose/fractionation, immobilization and clinical trial enrolment were calculated.*

Results: *A total of 57 patients diagnosed with a primary genitourinary malignancy were treated on the helical tomotherapy unit during the study period. Median age was 69 years (range 45 to 83 years) and 56 (98.2%) patients were male. Prostate cancer was the most frequently treated genitourinary cancer in this cohort of 57 (94.7%) cases. Ten patients (17.5%) were treated with palliative intent, 46 (80.7%) with radical intent (including full dose prostate bed adjuvant/salvage RT), and one (1.8%) patient was treated in a purely adjuvant manner (high risk postop bladder).*

Conclusions: *HT is a technology that can be utilized in both radical and palliative genitourinary treatment situations in order to deliver precise conformal IMRT therapy with unique localization and critical structure avoidance properties.*

Key Words: helical tomotherapy, genitourinary malignancies

Introduction

The application of various radiation therapy techniques has generally involved targeting macroscopic and microscopic disease with the concurrent avoidance of anatomically adjacent critical structures. The aim of therapy is to achieve the therapeutic goal be it cure, tumor control or palliation with an acceptable level of relevant normal tissue complication probabilities. Recent advancements in imaging and radiation delivery technologies have augmented our ability to optimize the therapeutic ratio between target and normal tissue effects. Specifically, the ability to deliver conformal radiation with intensity-modulated and three-dimensional conformal radiation therapy (IMRT and 3DCRT, respectively) techniques has allowed for significant total dose and dose-per-fraction escalation in a variety of treatment situations while maintaining or reducing the incidence of acute and late side effects. In addition, the advent of image-guided radiation therapy with various technologies including electronic portal imaging, ultrasound, as well as kilovoltage (diagnostic energy) and megavoltage (radiation treatment energy) computed tomography have allowed for increasing confidence in actual treatment delivery and not just in planned treatment dosimetry.[1] This confidence is reflected in the ability to reduce "safety margins" to account for daily uncertainty in patient and tumor position, further enabling the ability to increase dose and reduce acute and late side effects.

The helical tomotherapy (HT) radiation treatment planning and delivery platform is one option to achieve the synergistic therapeutic ratio effects by

Accepted for publication September 2010

Acknowledgement

The authors' would like to acknowledge MaryLu Lacasse for her secretarial support in the preparation of the manuscript. In addition, we acknowledge all the radiation therapists, medical physicists, and other staff who have supported the LRCP tomotherapy program since its inception.

Address correspondence to Dr. George Rodrigues, Department of Radiation Oncology, London Regional Cancer Program, 790 Commissioners Road East, London, ON N6A 4L6 Canada

combining intensity-modulated and image-guided radiation therapy.[2,3] It consists of a 6-MeV linear accelerator mounted on a ring gantry that rotates around a patient who is continually translated through the ring, ultimately leading to helical radiation delivery. The radiation fan beam thickness is user-defined and adjustable from 0.5 cm to 5 cm, and the intensity radiation fluence profile can be dynamically modified using a 64-leaf binary collimator (0.625 cm leaf width at the isocenter) for intensity modulated radiotherapy (IMRT). Computed tomography (CT) detectors on the gantry opposite the linear accelerator allow megavoltage CT (MVCT) imaging primarily for image-guided radiotherapy.[4-6] Treatment planning is achieved by a proprietary inverse planning system (TomoTherapy Inc., Madison, WI, USA).

Initial clinical implementation of this technology across all tumor sites and treatment intents (i.e. curative versus palliative) has demonstrated that it is a reliable technology that can generally provide treatment dosimetry either comparable with or superior to competing 3DCRT and IMRT techniques.[7,8] Multiple investigations into the image-guided,[6,9-12] dosimetric,[13-16] and clinical[17-19] aspects of this platform as it applies to prostate cancer radiation treatment have been published in the medical literature. The purpose of this report is to describe the experience with this technology in the setting of radical and palliative genitourinary cases treated at our institution since initial clinical implementation. Illustrative examples of the advantages of image-guided intensity-modulated radiation therapy in this setting will also be presented.

Methods and materials

Patient selection

All patients treated on the London Regional Cancer Program (LRCP) helical tomotherapy unit with treatment initiated between September 2004 and December 2007 with a primary genitourinary malignancy regardless of site and stage grouping were included in this study cohort. Institutional Review Board approved clinical trials that were available to this population included the LRCP in-house radical and palliative helical tomotherapy feasibility studies (all primaries eligible), a multi-institutional LRCP coordinated simultaneous in-field brain metastatic disease protocol (all primaries eligible), RTOG 0415 low risk prostate phase III hypofractionated protocol, the OCOG PROFIT intermediate risk prostate phase III hypofractionated protocol, and the Ottawa/LRCP high risk phase III toxicity-reduction protocol.

Helical tomotherapy simulation and planning

Patients were positioned with conventional devices including double leg immobilization, thermoplastic shells, and vacuum immobilization bags, depending on treated anatomic site. Patients were scanned on one of two commercial CT simulators (PQ5000 and Brilliance Big Bore CT; Philips Medical Systems, Cleveland, OH, USA) using 3 mm slice thickness and spacing including the region to be treated plus at least an additional 5 cm of scan length in the superior and inferior directions. Comprehensive contouring of anatomically relevant organs at risk (OAR), as well as the identification of the regions to be treated: gross tumor volume (GTV), clinical tumor volume (CTV), and planning target volume (PTV) was performed on Pinnacle workstation. CT data sets and structures were transferred to the HT planning workstation (TomoTherapy Inc., Madison WI, USA) using the Digital Imaging and Communications in Medicine RT protocol. The tomotherapy planning station resampled the CT data sets to a uniform interslice thickness separation equal to the minimum slice thickness in the planning kilovoltage CT (kVCT) study, typically 3 mm. The HT planning system used an inverse treatment-planning process based on iterative least squares minimization of an objective function, and calculation grid size was selected during the optimization stage (fine, 512 x 512; normal, 256 x 256; coarse, 128 x 128; typically the normal mode was used). Coverage of 95% of the PTV by the prescribed dose was set as the optimization target, and high importance and penalty factors were set for minimum dose coverage of the PTV to ensure adequate tumor coverage. Dose–volume histogram (DVH) points and maximum dose objectives for OAR were set to be slightly more demanding than conventional tolerance doses and were assigned importance and penalty factors more lenient than for the PTV because this was found to result in more efficient optimization. Final dose was calculated using a superposition convolution approach after the optimized plan was approved by the attending physician and physicist.

Helical tomotherapy quality assurance

All HT plans were verified in-phantom using ion chamber and radiographic film and following the dosimetry quality assurance procedure integrated with the HT unit. The patient plan was exported into a phantom anatomy. Treatment of the phantom was followed by film and point dose verification measurements and comparisons with the plan. Measurement points were chosen to lie within the PTV and OAR volumes. Accounting for the finite volume of the ion chamber and positioning variation between the calculation voxel and the ion chamber position, measured values within

5% of the calculated value were deemed acceptable. For the film measurements, radiographic film was placed in sagittal and/or coronal cross-sections of the phantom, exposed, developed, scanned, and compared with the calculated plan. Again, a variation of 5% or less in calculated versus measured dose was deemed acceptable. Before treatment, the attending physician reviewed the HT plan, and the in-phantom results. The case was approved for treatment as long as the HT plan met the assigned planning constraints and the in-phantom dose verification was acceptable.

Helical tomotherapy image-guidance

Daily megavoltage CT (MVCT) studies were acquired for registration with the planning kVCT studies for daily image-guided patient setup. For the MVCT studies, images were acquired with a beam slice thickness of 0.5 cm, interslice spacing of 6 mm, nominal beam energy of 3.5 MV, using "coarse" mode (helical pitch factor of 2.4: 12 mm couch increment per 10 s gantry rotation), and a 40 cm field of view. The images thus acquired were reconstructed with a pixel matrix of 512 x 512. Automated image registration using bone and soft tissue presets was followed by manual refinement (x, y, z, and rotational adjustments) of the registration. The attending physician and therapists reviewed the final registration in the sagittal, coronal, and axial plans and made manual adjustments as necessary for optimal alignment for the first fraction. Beyond the first fraction physicians were contacted if pretreatment MVCT indicated shifts outside the identified thresholds, if difficulty was experienced obtaining a satisfactory co-registration, or if significant changes in cross-sectional anatomy were noted; otherwise the therapists made positioning corrections independently.

Analysis

Descriptive statistics for various demographic and treatment-related parameters such as patient age, primary site of disease, site of radiotherapy, goal of treatment, dose/fractionation, and clinical trial enrollment were calculated. Mean and standard deviation for immobilization data relating to x, y, z, and overall vector MVCT based patient shifts were calculated. Due to the heterogeneity of this population, clinical outcome data such as toxicity and local control will not be presented in this report.

Results

A total of 255 patients were treated on the helical tomotherapy unit between September 2004 and December 2007. Of these, 57 (22.4%) patients were diagnosed with a primary genitourinary malignancy. Of this genitourinary cohort, median age was 69 years (range 45 to 83 years) and 56 (98.2%) patients were male. Prostate cancer was the most frequently treated genitourinary cancer in this cohort in 54 of 57 (94.7%) cases. Two patients with bladder cancer and one patient with primary renal cancer were also included in this cohort.

Ten patients (17.5%) were treated with palliative intent, 46 (80.7%) with radical intent (including full dose prostate bed adjuvant/salvage RT), and one (1.8%) patient was treated in a purely adjuvant manner (high risk postop bladder). Of the ten patients treated with palliative intent, three patients were treated to the prostate, three to the spine, and one each to the brain, skull, hip, and prostate with pelvic/para-aortic nodes. Palliative radiation dose was 30 Gy in 10 fractions in eight patients with one patient receiving 45 Gy in 10 fractions and one patient 25 Gy in 10 fractions.

Forty of 46 (87%) radical patients were treated to the prostate only with standard radiation doses including 70 Gy/ 35 fractions (n = 2), 73 Gy/35 fractions (n = 15), 73.8 Gy in 41 fractions (n = 2), and 78 Gy in 39 fractions (n = 7) as well as hypofractionated doses such as 60 Gy in 20 fractions (n = 9) and 70 Gy in 28 fractions (n = 5). Three patients were treated to the prostate bed (66 Gy in 33 fractions), one patient to the prostate bed with pelvic nodal coverage, one patient with intact prostate with simultaneous pelvic nodal coverage and one postoperative margin and node positive bladder case (45 Gy in 25 fractions to pelvis).

Thirty-six of 57 (63%) patients were treated on a clinical trial. Thirteen patients were enrolled in the in-house radical and palliative helical tomotherapy feasibility clinical trials.[7] Fifteen patients were enrolled in the intermediate risk Canadian PROFIT study randomizing between dose-escalated radiation (78 Gy in 39 fractions) versus dose-per-fraction escalated (60 Gy in 20 fractions) radiotherapy. Six patients were enrolled in the RTOG low risk randomized controlled trial assessing standard radiotherapy (73.8 Gy in 41 fractions) versus hypofractionated radiotherapy (70 Gy in 28 fractions). Two further patients were enrolled on clinical trials assessing simultaneous in field boost radiotherapy to oligometastatic disease to the brain and a University of Ottawa led high risk prostate cancer trial assessing three-dimensional conformal radiation therapy versus helical tomotherapy.

In terms of set-up accuracy for the 40 patients treated to the prostate alone with available set-up data, mean absolute patient shifts were 2.6 mm (SD 2.0 mm), 1.5 mm (SD 1.2 mm), and 2.4 mm (SD 1.4 mm) for the anterior-posterior, lateral, and superior-inferior directions, respectively. Overall vector shifts were a mean magnitude of 4.4 mm (SD 2.1 mm).

A prostate image-guidance example (TomoTherapy MVCT with corresponding CT Simulation KVCT) of a patient with bilateral hip prostheses is illustrated in Figure 1. The MVCT images have fewer artifacts than the corresponding KVCT images due to the fact that megavoltage radiation has minimal reliance on the photoelectric effect in its interactions with matter (leads to less scattering events). The registration of the images in order to generate couch shifts was performed, in part, by assessment of a checkerboard fusion of the MVCT and KVCT images, Figure 2. Examples of various interesting or challenging clinical scenarios are also presented to illustrate the ability of image-guided intensity-modulated radiation therapy to accurately

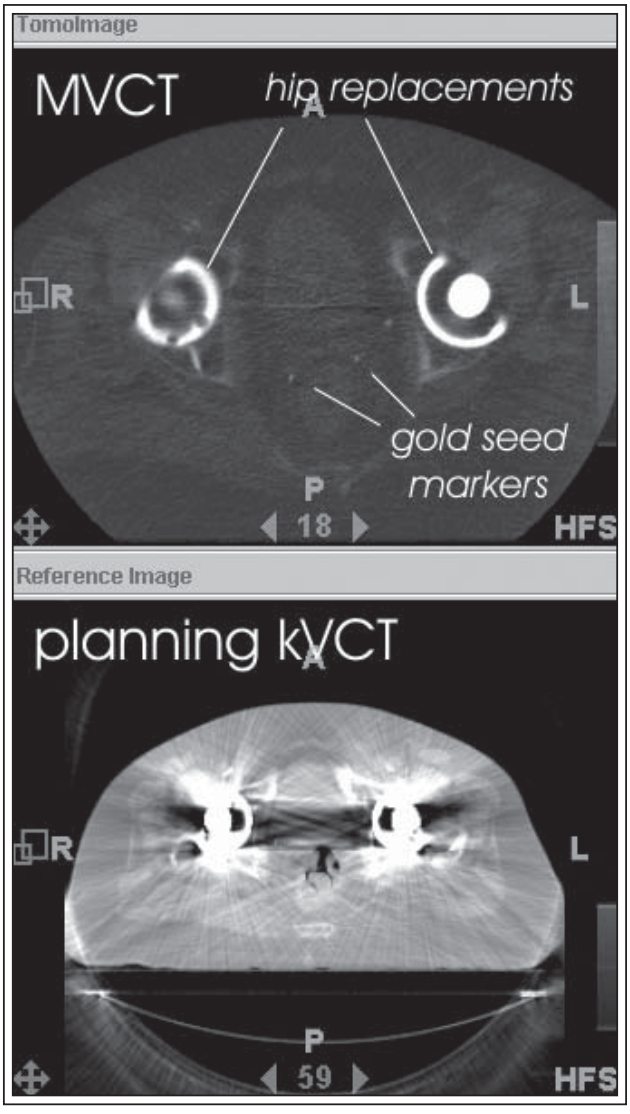

Figure 1. Example of megavoltage (MVCT) TomoTherapy and kilovoltage (KVCT) CT simulation imaging on a prostate cancer patient with bilateral hip prostheses.

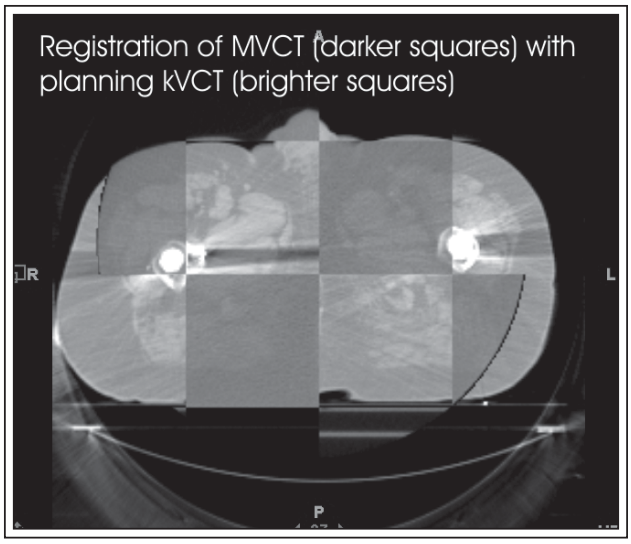

Figure 2. Checkerboard fusion imaging of prostate cancer patient with bilateral hip prostheses in order to calculate daily couch shift.

treat targets adjacent to sensitive critical structures. Figure 3 provides visual examples of radical or adjuvant helical tomotherapy treatment prostate cancer with various treatment volumes including the prostate,

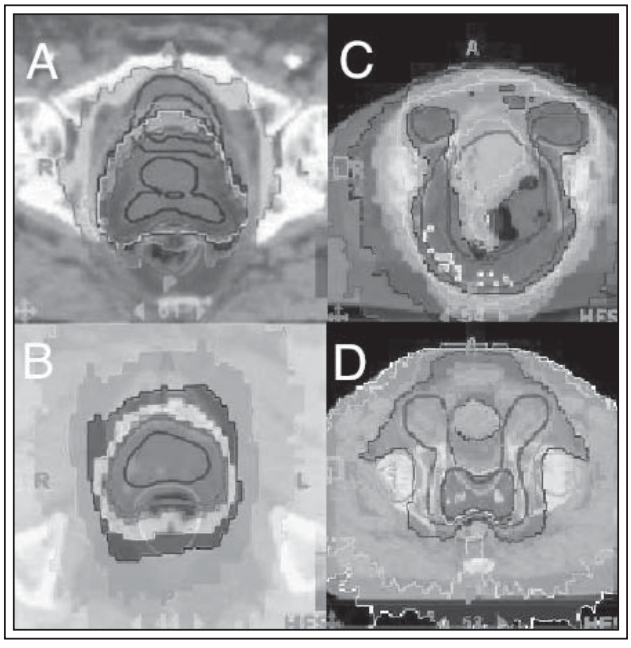

Figure 3. Examples of radically planned genitourinary helical tomotherapy cases. a) Intermediate risk prostate cancer. b) Post-prostectomy prostate bed. c) Post-cystectomy margin positive bladder cancer. d) High risk post-prostatectomy prostate bed and pelvic lymph nodes.

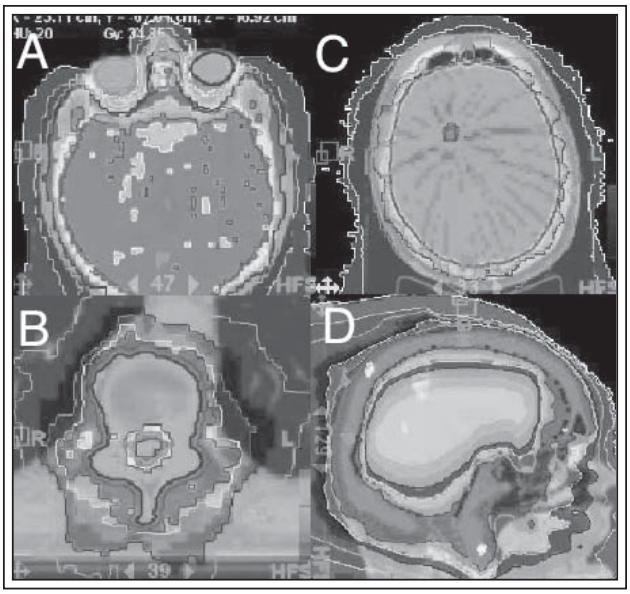

Figure 4. Examples of palliatively planned genitourinary helical tomotherapy cases. a) Whole brain. b) Thoracic spine. c) Whole brain plus stereotactic brain metastasis boost. d) Whole skull.

prostate bed, seminal vesicles, and pelvic lymph nodes. Figure 4 demonstrates the application of helical tomotherapy in the treatment of palliative disease in whole brain, stereotactic brain metastases, spine, and skull. All clinical examples demonstrate the ability of helical tomotherapy to plan (and deliver) highly conformal normal tissue-avoidance radiotherapy.

Discussion

Many recent innovations in radiation treatment planning, treatment delivery and treatment confirmation have been developed to deliver accurate and precise treatment to cancer patients in a variety of treatment scenarios. Various IMRT solutions that currently are in clinical use include: linear accelerator-based "step and shoot" and dynamic multileaf collimator treatment, serial tomotherapy, helical tomotherapy, arc-based techniques, and robotic assisted therapies. Similarly, image-guided technologies have utilized various technologies including: photographic film, gold plated fiducial markers, electronic portal imaging, kilovoltage and megavoltage cone beam CT, and megavoltage helical tomotherapy imaging. Recent advances in optical and radiotransmitter based tumor imaging/tracking may provide further degrees of freedom in the image-guided treatment of moving targets. Helical tomotherapy combines intensity-modulated radiation therapy with image-guidance technology to accurately and precisely deliver highly conformal radiotherapy with the goal of improving the therapeutic ratio.

The concept of a helical tomotherapy unit was first reported in the medical literature in 1993.[12] In this paper, various components of the modern helical tomotherapy was described including: the use of a binary multileaf collimator to generate an intensity modulated radiation fan beam, megavoltage detectors for both imaging and dose verification purposes, and a ring gantry system by which the imaging and treatment functions could occur around the patient in a helical fashion. Various benchtop and clinical prototypes were created and tested in order to explore the engineering, dosimetric, and clinical issues related to this new form of radiation therapy. Three identical clinical prototypes were created and commissioned at the University of Wisconsin, Cross Cancer Institute (Edmonton), and the London Regional Cancer Program in 2002-2003. Initial investigations into this technology revolved around the dosimetric, MVCT imaging, and clinical implementation of this technology;[7,13,15,16,20] however, more recently new investigations into the use of adaptive radiation therapy (ART) have been described.[1,5] ART involves the use of deformable registration of daily MVCT images with the planning CT in conjunction with dose reconstruction to generate delivered radiation dose. With this information, clinicians can reoptimize the radiation treatment by means of replanning radiation therapy to correct overdosage of critical structures and any underdosage of relevant tumor targets that may occur. Other investigations into the image guidance procedures[4,6,9-11,20,21] and dose distribution optimization/comparisons[13-16] have further defined the properties of the tomotherapy unit.

Initial clinical implementation of helical tomotherapy has been described in two reports.[7,8] Bauman et al reported on 60 patients enrolled in two prospective studies assessing both palliative and radical treatment scenarios for any primary tumor or metastatic site.[7] Helical tomotherapy plans were felt to be equivalent or superior in 95% of cases and a target versus normal tissue tradeoff was involved in the other 5% of cases. Imaging and treatment time was 27 minutes (range, 16 to 91 minutes) on average and the majority of patients were pleased with the treatment process. Sterzing et al in their report of the first 150 patients treated at their tomotherapy site confirmed that total imaging and treatment time was on average 24.8 minutes. They were able to implement helical tomotherapy into their department in a variety of treatment scenarios to achieve highly conformal radiotherapy delivery. Clinical reports also detail the short term toxicity results

of definitive prostate and prostate bed radiotherapy with helical tomotherapy.[17-19] Additionally two phase I/II clinical trials have reported on the feasibility of delivering hypofractionated radiotherapy in the high-risk prostate cancer setting.[21,22] While our experience reported here has been primarily in the treatment of prostate cancer, the application of daily image guided IMRT to other primary tumors where tumor motion or OAR sparing to allow high dose therapy is under investigation.

In conclusion, we have demonstrated the range of clinical applications of helical tomotherapy in the setting of radical and palliative genitourinary malignancy radiation treatment. In radical therapy, helical tomotherapy can be utilized to deliver high dose or dose-per-fraction to the target of interest while maintain safe levels of normal tissue irradiation. In palliative malignancies, the goal would usually be that of normal tissue dose reduction in order to spare patients unneeded toxicity; however, high dose palliative stereotactic applications also exist that can benefit from the image-guidance and conformal delivery properties of helical tomotherapy. □

References

1. Mackie TR, Kapatoes J, Ruchala K et al. Image guidance for precise conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2003;56(1):89-105.
2. Mackie TR. History of tomotherapy. *Phys Med Biol* 2006;51(13): R427-R453.
3. Mackie TR, Balog J, Ruchala K et al. Tomotherapy. *Semin Radiat Oncol* 1999;9(1):108-117.
4. Drabik DM, MacKenzie MA, Fallone GB. Quantifying appropriate PTV setup margins: analysis of patient setup fidelity and intrafraction motion using post-treatment megavoltage computed tomography scans. *Int J Radiat Oncol Biol Phys* 2007;68(4):1222-1228.
5. Lu W, Olivera GH, Chen Q et al. Deformable registration of the planning image (kVCT) and the daily images (MVCT) for adaptive radiation therapy. *Phys Med Biol* 2006;51(17):4357-4374.
6. Shah AP, Langen KM, Ruchala KJ, Cox A, Kupelian PA, Meeks SL. Patient dose from megavoltage computed tomography imaging. *Int J Radiat Oncol Biol Phys* 2008;70(5):1579-1587.
7. Bauman G, Yartsev S, Rodrigues G et al. A prospective evaluation of helical tomotherapy. *Int J Radiat Oncol Biol Phys* 2007; 68(2):632-641.
8. Sterzing F, Schubert K, Sroka-Perez G, Kalz J, Debus J, Herfarth K. Helical tomotherapy. Experiences of the first 150 patients in Heidelberg. *Strahlenther Onkol* 2008;184(1):8-14.
9. Fiorino C, Di Muzio N, Broggi S et al. Evidence of limited motion of the prostate by carefully emptying the rectum as assessed by daily MVCT image guidance with helical tomotherapy. *Int J Radiat Oncol Biol Phys* 2008;71(2):611-617.
10. Kupelian PA, Lee C, Langen KM et al. Evaluation of image-guidance strategies in the treatment of localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2008;70(4):1151-1157.
11. Langen KM, Zhang Y, Andrews RD et al. Initial experience with megavoltage (MV) CT guidance for daily prostate alignments. *Int J Radiat Oncol Biol Phys* 2005;62(5):1517-1524.
12. Mackie TR, Holmes T, Swerdloff S et al. Tomotherapy: a new concept for the delivery of dynamic conformal radiotherapy. *Med Phys* 1993;20(6):1709-1719.
13. Grigorov G, Kron T, Wong E, Chen J, Sollazzo J, Rodrigues G. Optimization of helical tomotherapy treatment plans for prostate cancer. *Phys Med Biol* 2003;48(13):1933-1943.
14. Hong TS, Tomé WA, Jaradat H, Raisbeck BM, Ritter MA. Pelvic nodal dose escalation with prostate hypofractionation using conformal avoidance defined (H-CAD) intensity modulated radiation therapy. *Acta Oncol* 2006;45(6):717-727.
15. Rodrigues G, Yartsev S, Chen J et al. A comparison of prostate IMRT and helical tomotherapy class solutions. *Radiother Oncol* 2006;80(3):374-377.
16. Rodrigues G, Yartsev S, Chen J et al. A comparison of prostate IMRT and helical tomotherapy class solutions. *Radiother Oncol* 2006; 80(3):374-377.
17. Cheng JC, Schultheiss TE, Nguyen KH, Wong JY. Acute toxicity in definitive versus postprostatectomy image-guided radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 2008; 71(2):351-357.
18. Cozzarini C, Fiorino C, Di Muzio N et al. Significant reduction of acute toxicity following pelvic irradiation with helical tomotherapy in patients with localized prostate cancer. *Radiother Oncol* 2007;84(2):164-170.
19. Keiler L, Dobbins D, Kulasekere R, Einstein D. Tomotherapy for prostate adenocarcinoma: a report on acute toxicity. *Radiother Oncol* 2007;84(2):171-176.
20. Song WY, Chiu B, Bauman GS et al. Prostate contouring uncertainty in megavoltage computed tomography images acquired with a helical tomotherapy unit during image-guided radiation therapy. *Int J Radiat Oncol Biol Phys* 2006;65(2):595-607.
21. Pervez N, Small C, MacKenzie M et al. Acute toxicity in high-risk prostate cancer patients treated with androgen suppression and hypofractionated intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2010;76(1):57-64.
22. Di Muzio N, Fiorino C, Cozzarini C et al. Phase I-II study of hypofractionated simultaneous integrated boost with tomotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 2009; 74(2):392-398.