Clinical Oncology xxx (2014) 1–9

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Comparison of Margins, Integral Dose and Interfraction Target Coverage with Image-guided Radiotherapy Compared with Non-image-guided Radiotherapy for Bladder Cancer

F. Foroudi [*] [†], D. Pham [‡], M. Bressel [§], N. Hardcastle [¶], S. Gill [*] [†], T. Kron [†] [¶]

[*] *Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Center, Melbourne, Victoria, Australia*
[†] *Sir Peter MacCallum Department of Oncology, University of Melbourne, Victoria, Australia*
[‡] *Radiation Therapy Services, Peter MacCallum Cancer Center, Melbourne, Victoria, Australia*
[§] *Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Center, Melbourne, Victoria, Australia*
[¶] *Physical Sciences, Peter MacCallum Cancer Center, Melbourne, Victoria, Australia*

Received 25 September 2013; received in revised form 12 February 2014; accepted 25 February 2014

Abstract

Aims: To measure the difference in cumulative doses received by the bladder (target) and integral doses with different clinical target volume (CTV) to planning target volume (PTV) margins, comparing set-up to skin tattoos versus image-guided radiotherapy to bone or soft tissue.
Materials and methods: Four plans were generated on each planning computed tomography dataset using the CTV with 5, 10, 15, 20 mm PTV margins using a three-dimensional conformal four-field technique. Set-up data based on skin, bone and soft tissue to the bladder on pre-treatment cone beam computed tomography (CBCT) were recorded. In total, 316 CBCTs were evaluable from 10 bladder cancer patients. Each CBCT was fused to the planning computed tomography dataset using the isocentre corresponding to each of the three pre-treatment matching conditions. The target was contoured on each CBCT and called the CTV of the day and the plan was re-calculated to determine the dose to this.
Results: The mean D95 with CTV to PTV margins of 5, 10, 15 and 20 mm for skin set-up was 89.4, 93.0, 97.2, 98.6; for bone 88.8, 92.6, 96.7, 98.6; and for soft tissue 96.3, 98.6, 98.7, 99.5. With soft-tissue matching, the mean (standard deviation) volume of normal tissue receiving 5 Gy with 5, 10, 15 and 20 mm margins was 3899 (1022), 4561 (1142), 5663 (1304) and 6315 (1426) in cm^3.
Conclusion: Soft-tissue matching results in superior target coverage and a reduced integral dose to the surrounding tissues. With soft-tissue matching, increasing CTV to PTV margins progressively beyond 5 mm results in modest improvement in CTV coverage, but a large increase in integral dose.

Key words: Bladder cancer; dose accumulation; image-guided radiotherapy; margins; radiation dose

Introduction

The bladder is a dynamic soft-tissue organ, the size and shape of which can vary according to urine filling. Its position can also vary according to its size as well as the extent of rectal filling. Due to the bladder being highly deformable, it is advantageous to have repeated imaging, methods for calculating the delivered dose at each fraction and a technique for computing the cumulative dose distribution to assess the delivered bladder doses [1].

Meijer *et al.* [2] used dose warping techniques to compare a library of six generated simultaneous in-field boost intensity-modulated radiotherapy (IMRT) plans with a conventional single plan. This was conducted in a single patient who showed substantial differences in bladder filling at planning computed tomography scanning as well as during radiation treatment [2]. In this patient they found that differences in dose distribution were mainly induced by non-uniform and out-of-plane stretching of the bladder wall [2]. Thus, the bladder seems to be an ideal organ for adaptive radiotherapy with daily positioning based on the bladder soft tissue.

Examining adaptive radiotherapy, Burridge *et al.* [3] retrospectively analysed 5, 10 and 15 mm clinical target

Author for correspondence: F. Foroudi, Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Institute, St Andrews Place, East Melbourne, Victoria 3002, Australia. Tel: +61-3-9656-1111; Fax: +61-3-9656-1424.
E-mail address: farshad.foroudi@petermac.org (F. Foroudi).

0936-6555/$36.00 © 2014 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.clon.2014.03.007

volume (CTV) to planning target volume (PTV) expansion in the superior direction and in their geometrical analysis they found that the volume of small bowel irradiated could be reduced by daily cone beam computed tomography (CBCT) and soft-tissue matching. Webster *et al.* [4] compared different adaptive bladder cancer radiotherapy techniques and found that a plan of the day provided the optimal balance between target coverage and normal tissue sparing.

The principal focus of treatment must remain on avoiding geographic miss of the target volume, the potential for which is increased with tight margins, which has been shown in other pelvic malignancies [5]. Geometric margins for interfraction bladder motion have been previously reported using different set-up methods [6] as well as effects of image-guided adaptive radiotherapy [7]. However, dosimetric coverage of the target and dose reduction to surround pelvic normal tissues with differing margins and set-up methods has not been previously reported. Although adaptive radiotherapy provides more conformal dose coverage of the target, image-guided radiotherapy (IGRT) alone is more widely available and would still be expected to provide better coverage of the target than the standard set-up to skin tattoo marks alone. The aim of this study was to compare bladder IGRT (bone and soft tissue) and set-up to skin tattoo marks to determine the incremental benefit of IGRT, for centres where adaptive radiotherapy for bladder cancer is not yet available. To this aim, the margins required for dosimetric coverage of the planning CTV using daily positioning based on either conventional skin tattoo marks, IGRT employing either bony landmarks or the soft tissue centre of the bladder were measured. As larger PTV margins probably result in better target coverage in all cases, we compared margins against the integral dose delivered to normal tissue, to assess the trade-off between the margin and dose delivered to normal tissue.

Materials and Methods

Patient Selection

Accrual to the study started after institutional research ethics board approval was granted. Eligible patients had muscle invasive bladder cancer, were suitable for radical radiotherapy and provided informed consent to enter an adaptive radiotherapy protocol. Details of the protocol have been previously published [7]. The first 10 patients treated on that protocol were selected for analysis in this study. Accrual occurred at our main site and one satellite centre with the same treatment equipment (Varian Trilogy/21iX Linear accelerator with CBCT, Varian Medical Systems, Palo Alto, CA, USA). Patients were excluded if they had previous pelvic radiotherapy, unilateral or bilateral hip prostheses or evidence of nodal or distant metastatic disease. The study was conducted between November 2007 and December 2008 and accrued 27 patients with muscle invasive transitional cell carcinoma of the bladder (T2-T4N0M0). All patients were advised to void before treatment in order to have an empty bladder. Each patient underwent a course of treatment delivering 64 Gy to the whole bladder over 32 treatments using daily pre-treatment CBCT soft-tissue imaging.

Clinical Target Volume Delineation and Plan Generation

For each patient, a planning computed tomography scan was used to delineate the bladder CTV. Patients were advised to empty their bladder before planning simulation. Data were import into the Eclipse™ treatment planning system (v8.9, Varian Medical Systems) for plan generation. A single radiation oncologist (FF) delineated the bladder organ in order for four PTVs to be generated using CTV expansions of 5, 10, 15 and 20 mm.

A single dosimetric planner (DP) generated plans for each PTV using a four-field box technique. 18 MV beams were used to prescribe a dose of 64 Gy using 0.5 cm multileaf collimator leaves to conform to the PTV. The dose was normalised to the ICRU point ensuring coverage was within ±5% of the prescription dose. The dose was calculated on a 2.5 mm calculation grid using the Analytical Anisotropic Algorithm (v8.9).

The daily pre-treatment CBCT data for each patient were imported into the planning system to determine daily bladder CTV coverage and position. In total, 320 CBCT were taken. However, due to CBCT reconstruction problems, four datasets were lost and unable to be used for analysis. A single radiation oncologist (FF) delineated the bladder CTV from each CBCT dataset for dosimetric analysis. The CTV consisted of the bladder and tumour extension where applicable, without elective nodal coverage.

Image Guidance Correction

For each patient, the pre-treatment CBCT data were used to determine, for each fraction, the bladder position if treatment had been set-up according to (1) an external skin tattoo; (2) internal bony anatomy; or (3) the centre of the bladder target. The skin set-up position was taken directly from the shift recorded on our record and verification system. Internal bone was derived from the manual matching made on our treatment planning system. Data recorded from the MOSAIQ™ (Elekta AB, Stockholm, Sweden) record and verification system as well as manual registration tools on Eclipse™ were used to determine the isocentre shifts for each of the image guidance conditions. As auto-registration on the planning system used rotation to match the datasets, manual matching was carried out in the orthogonal planes to mimic online matching in the three orthogonal planes. Soft-tissue registration was based on bladder centroid registration. The centre of the bladder in the anterior/posterior, superior/inferior and left/right was measured and used to align the bladder CTV from each CBCT to the planning computed tomography bladder volume. In this study we used the outlined CBCT CTV to determine centroid registration. However, in clinical practice, registration to the bladder centre can be carried out in the online environment using planning CTV structures to match the imaged bladder with even coverage all around [7,8]. For each patient, a

Please cite this article in press as: Foroudi F, et al., Comparison of Margins, Integral Dose and Interfraction Target Coverage with Image-guided Radiotherapy Compared with Non-image-guided Radiotherapy for Bladder Cancer, Clinical Oncology (2014), http://dx.doi.org/10.1016/j.clon.2014.03.007