Clinical Oncology xxx (2016) 1–8

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Real-time Image-guided Adaptive-predictive Prostate Radiotherapy using Rectal Diameter as a Predictor of Motion

R. Oates [*†], A. Brown [‡], A. Tan [‡§], F. Foroudi [¶], M. Lim Joon [¶], M. Schneider [†], A. Herschtal [||**], T. Kron [**††]

[*] Radiation Therapy Services, Peter MacCallum Cancer Centre, Bendigo, Victoria, Australia
[†] Medical Imaging & Radiation Sciences, Monash University, Melbourne, Victoria, Australia
[‡] Radiation Oncology, Townsville Cancer Centre, Townsville, Queensland, Australia
[§] College of Medicine and Dentistry, James Cook University, Queensland, Australia
[¶] Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia
[||] Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia
[**] Sir Peter MacCallum Department of Oncology, The University of Melbourne, Parkville, Victoria, Australia
[††] Physical Sciences, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

Received 21 December 2015; received in revised form 13 September 2016; accepted 19 September 2016

Abstract

Aims: To investigate a relationship between maximum rectal diameter (MRD) on pre-treatment cone beam computed tomography (CBCT) and intra-fraction prostate motion, in the context of an adaptive image-guided radiotherapy (IGRT) method.
Materials and methods: The MRD was measured on 2125 CBCTs from 55 retrospective patient datasets and related to prostate displacement from intra-fraction imaging. A linear regression model was developed to determine a threshold MRD associated with a high probability of small prostate displacement. Standard and reduced adaptive margin plans were created to compare rectum and bladder normal tissue complication probability (NTCP) with each method.
Results: A per-protocol analysis carried out on 1910 fractions from 51 patients showed with 90% confidence that for a MRD $\leq$ 3 cm, prostate displacement will be $\leq$5 mm and that for a MRD $\leq$ 3.5 cm, prostate displacement will be $\leq$5.5 mm. In the first scenario, if adaptive therapy was used instead of standard therapy, median reductions in NTCP for rectum and bladder were 0.5% (from 9.5% to 9%) and 1.3% (from 6.6% to 5.3%), respectively. In the second scenario, the NTCP for rectum and bladder would have median reductions of 1.1% and 2.6%, respectively.
Conclusions: We have identified a potential method for adaptive prostate IGRT based upon predicting small prostate intra-fraction motion by measuring MRD on pre-treatment CBCT.

Key words: Adaptive; IGRT; NTCP; prostate cancer; radiotherapy

Introduction

Radiotherapy dose escalation for prostate cancer offers improved biochemical control, but may also lead to increasing toxicity, which is concerning for patients with long-term survival prospects [1]. Prostate cancer radiotherapy clinical target volumes most commonly include the prostate with or without the seminal vesicles. The rectum, bladder and penile bulb are organs at risk in immediate proximity to the prostate and are partially included in the planning target volume (PTV). Minimising PTV margins where possible would reduce the risk of toxicity and potentially allow safe dose escalation.

Historic inter-fraction and intra-fraction prostate motion data are commonly used to calculate PTV margins. These data take into account random treatment errors for all treatment fractions, many of which will not be present for each fraction. Two key components of prostate intra-fraction motion are the filling of the rectum and the duration of the treatment. Cine-magnetic resonance imaging has shown that patients who present with an empty rectum may be at much lower risk of intra-fraction prostate motion compared

Author for correspondence: R. Oates, PO Box 126, Bendigo, Victoria 3552, Australia. Tel: +61-3-5454-9234; Fax: +61-3-5454-9289.
E-mail address: richard.oates@petermac.org (R. Oates).

http://dx.doi.org/10.1016/j.clon.2016.09.019
0936-6555/

with patients who present with a full rectum [2,3]. Several studies have also shown that the longer the fraction duration, the greater the risk of prostate motion [3–5].

To reduce the effect of random errors during prostate radiotherapy, intra-fraction monitoring using methods such as radiofrequency transponders, stereoscopic kV systems and using on-board imaging, may allow reductions of margins down to 5 mm or less [6–8]. Greatly reducing treatment times with volumetric modulated arc therapy (VMAT) and flattening filter free modes may also reduce the probability of intra-fraction motion [5]. For those without access to new technologies, alternative methods to reduce margins could be investigated.

Our data has shown intra-fraction motion of greater than 5 mm in only 4.7% of fractions [4], so identifying fractions with reduced motion is one possibility. Adaptive radiotherapy offers methods to reduce PTV margins when conditions are appropriate. Previous studies have outlined offline [9–11], hybrid [12,13] and online protocols [14–19] for adaptive prostate radiotherapy. None of these has predicted daily prostate motion based on cone beam computed tomography (CBCT) rectal presentation.

This study investigated the relationship between rectal diameter on pre-treatment CBCT as a predictor of small intra-fraction prostate motion, which could be used in an adaptive image-guided radiotherapy (IGRT) protocol. We also investigated other predictors of prostate motion, such as the presence of bowel gas within treatment fields or superior to the treated volume at CBCT. We assessed the image quality of CBCT and its effect on the adaptive method.

Materials and Methods

Dataset Selection

This study used retrospective datasets from 55 consecutive patients treated at the Townsville Cancer Centre between July 2011 and August 2012 with daily CBCT imaging before treatment and megavoltage electronic portal images (EPI) acquired during treatment delivery, which allowed analysis of intra-fraction prostate motion. We received ethics approval from the Townsville Hospital and Health Service Human Research Ethics Committee and the Peter MacCallum Cancer Centre Ethics Committee. Eligible patients were 50 years of age or older, who received prostate three-dimensional conformal radiotherapy (3DCRT) to a dose of 74–78 Gy in 37–39 fractions. All had biopsy-proven prostate adenocarcinoma TNM stages T1–T3b, three prostate gold seed fiducial marker implants and were Eastern Cooperative Oncology Group (ECOG) performance status 0-2. All patients were treated supine on Elekta XVI linacs (Elekta, Stockholm, Sweden), with CIVCO kneefix and feetfix (CIVCO Medical Solutions, Coralville, USA) indexed to the treatment couch.

Cone Beam Computed Tomography Assessment

All CBCTs were assessed by one observer (RO). Planning computed tomography was carried out with 2 mm slices and CBCTs were reconstructed with 2 mm slices. CBCT data were fused with the planning data on FOCAL v4.62 (Elekta) at a corrected position for the fiducial markers. Each CBCT rectum was contoured on the planning computed tomography for the length of the rectum planning contour. The maximum rectal diameter (MRD) was measured according to methods outlined previously [20]. The presence of rectal gas within the treatment fields and superior to the treated volume was contoured and the number of bubbles and volumes were recorded. We considered there to be no gas for volumes less than 1 cm^3.

Image Quality

To assess the usability of CBCT images, image quality was subjectively graded by one observer (RO) as optimal, adequate or inadequate. Scans were considered optimal if there was minimal artefact and structures were easily identifiable, adequate if there was mild–moderate artefact and structures were sufficiently identifiable to achieve study aims and inadequate when severe artefact precluded rapid structure identification.

Motion Assessment

Each fraction consisted of five treatment fields – left, left anterior–oblique, anterior, right anterior–oblique and right. EPIs were recorded at six time points during left and right field delivery and three time points during the shorter duration anterior field. Pre-treatment daily matches were carried out by a variety of clinical radiation therapists. All two-dimensional image matches were carried out by one investigator (AB). Images from each field provided two-dimensional displacements relative to the pre-treatment CBCT fiducial marker alignment in two directions: lateral fields provided anterior–posterior and superior–inferior displacements, whereas the anterior field provided superior–inferior and left–right displacements. We combined the prostate displacements measured in various directions and at various time points during a treatment fraction into a single overall measure of prostate displacement per fraction.

To do this, we denoted the measured prostate displacement at a given time point t_t (within a given fraction and patient) in the anterior–posterior, superior–inferior and left–right directions as $d_{AP,t}$, $d_{SI,t}$ and $d_{LR,t}$ respectively. For each time point we then calculated the two-dimensional prostate displacement d_t by adding the two available one-dimensional displacements in quadrature as follows.

$$\textit{For the left and right fields}: d_t = \sqrt{d_{AP,t}^2 + d_{SI,t}^2}$$

$$\textit{For the anterior field}: d_t = \sqrt{d_{LR,t}^2 + d_{SI,t}^2}$$

We calculated the mean d_t over the available time points for each field, and took the largest of the three resulting means as the maximum projection-detectable prostate displacement for the given fraction.

Please cite this article in press as: Oates R, et al., Real-time Image-guided Adaptive-predictive Prostate Radiotherapy using Rectal Diameter as a Predictor of Motion, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.09.019