Radiotherapy and Oncology 111 (2014) 316–320

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

TROP 10.01 BOLART

The outcome of a multi-centre feasibility study of online adaptive radiotherapy for muscle-invasive bladder cancer TROG 10.01 BOLART

Farshad Foroudi a,b,⁎, Daniel Pham a, Aldo Rolfo a, Mathias Bressel a, Colin I. Tang c, Alex Tan d, Sandra Turner e, George Hruby f, Stephen Williams g, Dickon Hayne h, Margot Lehman i, Marketa Skala j, Chakiath C. Jose k, Kumar Gogna l, Tomas Kron a,b

a Peter MacCallum Cancer Centre, Melbourne, Australia; b Sir Peter MacCallum Department of Oncology, University of Melbourne, Australia; c Calvary Mater Newcastle, Newcastle, Australia; d Townsville Cancer Centre, Townsville, Australia; e Westmead Hospital, Sydney, Australia; f Royal Prince Alfred Hospital, Sydney, Australia; g Christchurch Hospital, Christchurch, New Zealand; h Fremantle Hospital, Perth, Australia; i Princess Alexandra Hospital, Brisbane, Australia; j Royal Hobart Hospital, Hobart, Australia; k Auckland Hospital, Auckland, New Zealand; l Mater Centre, Brisbane, Australia

Article history:
Received 12 November 2013
Received in revised form 31 December 2013
Accepted 12 February 2014
Available online 17 April 2014

A R T I C L E  I N F O

Purpose: To assess whether online adaptive radiotherapy for bladder cancer is feasible across multiple Radiation Oncology departments using different imaging, delivery and recording technology.

Materials and methods: A multi-centre feasibility study of online adaptive radiotherapy, using a choice of three "plan of the day", was conducted at 12 departments. Patients with muscle-invasive bladder cancer were included. Departments were activated as part of the pilot study or after site-credentialing visit. There was real-time review of the first two cases from each department.

Results: 54 patients were recruited, with 50 proceeding to radiotherapy. There were 43 males and 7 females with a mean age of 78 years. The tumour stages treated included T1 (1 patient), T2 (35), T3 (10) and T4 (4). One patient died of an unrelated cause during radiotherapy. The three adaptive plans were created before the 10th fraction in all cases. In 8 (16%) of the patients, a conventional plan using a 'standard' CTV to PTV margin of 1.5 cm was used for one or more fractions where the pre-treatment bladder CTV was larger than any of the three adaptive plans. The bladder CTV extended beyond the PTV on post-treatment imaging in 9 (18%) of the 49 patients.

Conclusions: From a technical perspective an online adaptive radiotherapy technique can be instituted in a multi-centre setting. However, without further bladder filling control or imaging, a CTV to PTV margin of 7 mm is insufficient.

© 2014 Elsevier Ireland Ltd. All rights reserved. Radiotherapy and Oncology 111 (2014) 316–320

Muscle-invasive bladder cancer is often treated with a radical cystectomy, although bladder preservation using chemoradiotherapy has comparable outcomes with the advantage that many patients retain their own bladder [1]. The use of concurrent chemotherapy improves outcomes [2] over radiation therapy alone.

Traditionally, radiotherapy for bladder cancer involves irradiation of the entire bladder, with a generous margin to account for variations in bladder position, shape and size [3]. However such volumes lead to unnecessarily high doses to normal tissue for patients whose bladder volume remains small and stable, or conversely, fail to cover the target when the bladder fills significantly. Burridge et al. [4] retrospectively demonstrated the potential of a 'plan of the day' approach for treating bladder cancer, based on three plans created from the planning CT. They were able to show an average small bowel sparing of 31 cm3 compared to non-adaptive techniques [4]. Furthermore, in a comparison of different adaptive radiotherapy strategies for muscle-invasive bladder cancer, the 'plan of the day' technique provided the optimal balance between target coverage and normal tissue sparing [3].

We have previously reported a 'plan of the day' adaptive radiotherapy technique at a single institution which significantly decreased surrounding normal tissue irradiation whilst slightly improving clinical target volume coverage [5]. This process required dedicated radiation therapists, who completed a bladder specific training programme [6]. This included evaluating and matching the Cone Beam CT (CBCT) defined soft tissue position of the bladder prior to each treatment fraction and to choose one of three adaptive plans to apply for treatment on that day.

The concept of adaptive radiotherapy for bladder cancer intuitively makes sense and several single institution studies have been reported [5,7–9]. However, the process is complex and successful

⁎ Corresponding author. Address. Division of Radiation Oncology, Peter MacCallum Cancer Institute, St Andrews Place, East Melbourne, Victoria 3002, Australia. E-mail address: farshad.foroudi@petermac.org (F. Foroudi).

http://dx.doi.org/10.1016/j.radonc.2014.02.015
0167-8140/© 2014 Elsevier Ireland Ltd. All rights reserved.
implementation in a single academic institution is not necessarily transferable to the larger variety of centres delivering radiotherapy.

We therefore conducted a multi-centre study of online adaptive radiotherapy, under the auspices of the Trans-Tasman Radiation Oncology Group (TROG), to determine if our online adaptive ‘plan of the day’ technique for treating muscle-invasive bladder cancer was feasible across a variety of centres.

Methods

This study (ANZCTR NCT01142102) was activated at sites following local human ethics review board approval. All Australian and New Zealand facilities which expressed an interest in the trial were sent a facility questionnaire and were included in the trial on a first come first served basis.

Online adaptive “plan of the day” radiotherapy technique

The online adaptive process for the multi-centre study was based on an institutional pilot study [5]. The patients were asked to void immediately prior to entering the CT simulation room. During CT acquisition, patients were positioned supine with pelvic immobilisation. A 3D conformal technique was employed, using a minimum of three fields to deliver 6–18 MV beams, with the majority of dose being given from an anterior and two lateral fields. Intensity modulated radiation therapy was not used due to the increased time required for planning and quality assurance, particularly in view of the need for development of the adaptive plans during the second week of treatment. A variety of planning systems and linear accelerator models were used in the multi-centre study as outlined in Pham et al. [10]. All patients were prescribed 64 Gy in 32 daily fractions over 6½ weeks to the middle of the bladder as defined by the ICRU50 reference point [11]; complete coverage of the PTV by the 95% isodose was required. For each patient, four plans were generated for the entire course of treatment: conventional, small, medium and large. The conventional treatment plan incorporated a 1.5 cm 3D expansion of the CTV (whole bladder) to construct a PTV. The adaptive plans were created from a composite of the planning CT and the first 5 daily on-treatment CBCTs. The small plan was created using a Boolean summation of the two smallest CTVs, as we had previously found that using the single smallest CTV resulted in a plan that was appropriate for treatment in less than 10% of the fractions [12]. Boolean sum, a term in Boolean algebra, is similar to the English language term “or” and would represent any of the included structures in the summation. The large plan was created using a Boolean summation of all the CTVs, and the medium plan used a volume drawn halfway between the smallest CTV and large CTV. A uniform 7 mm margin was then added to create respective PTVs from each of the three adaptive CTVs.

Daily treatment process

Prior to each fraction, 3D volumetric CBCT imaging was used to verify bladder size and position. The treatment schema used a conventional plan with a uniform CTV to PTV margin of 1.5 cm for fractions 1–7. For these first seven fractions, if the imaged bladder was larger than that seen at planning and unable to be encompassed by the PTV, patients were requested to leave the bunker and void before repositioning and rescanning. For fractions 8–32, radiation therapy staff selected from one of the three adaptive plans (small, medium and large). Each of the adaptive plans had been created to ensure coverage of the PTV by the 95% isodose line with the smallest possible margin. If the bladder was larger than the large adaptive plan the patient was requested to void and return for rescanning. If, despite voiding and rescanning the bladder was still larger than the large adaptive plan, the conventional plan was used on that day. The CTV on the conventional plan was determined solely from the planning CT. The time from the pre-treatment CBCT to delivery of the last treatment field each day was retrieved from the Record and Verify systems at each centre to measure the time taken for the entire adaptive process including imaging, plan choice selection and treatment delivery.

Post treatment CBCT scans

Following fractions 10, 15, 20, 25 and 30 a post treatment CBCT was taken for verification purposes, including assessment of intra-fraction bladder filling, organ motion and patient movement.

Radiation therapist training

At least one radiation therapist involved with the daily treatment of each patient was required to have completed training by either a face-to-face workshop-based programme [6] or using customised web-based e-Learning modules [13]. The training workshop and modules included pelvic anatomy, CT, Cone Beam CT, and organ recognition as well as trial-specific information.

Site activation, credentialing and real time review

Prior to site activation, each site had to complete a facility questionnaire, a benchmarking planning exercise with a clinical case, an on-site image guidance assessment by the study radiation therapist and medical physicist, as well as having a minimum of two radiation therapists completing the workshop or e-Learning modules. The site activation and credentialing process has been outlined in detail by Kron et al. [14]. The first two patients from each participating centre underwent real-time review to ensure that the adaptive plans were developed according to protocol. All patients had end of radiotherapy quality assurance review which involved submission of all planning and treatment data.

Primary endpoint, sample size and statistical analysis

The primary endpoint of feasibility was defined as completion of adaptive treatment without a major protocol deviation. A major protocol deviation was defined as the occurrence of any of the following:

(a) All three adaptive treatment plans were inadequately covering the PTV for more than 10% of treatment fractions, necessitating use of the conventional plan for those fractions. Since the protocol dictated that adaptive treatment plans must be available for fractions 10–32 inclusive, this meant that use of a conventional plan for three or more of these fractions constituted a major protocol deviation.

(b) Three adaptive plans were not created and quality assurance performed in time for the patient’s 10th fraction.

(c) Post treatment imaging demonstrated that the CTV had expanded beyond the PTV chosen in any one of the treatment fractions where post treatment imaging was conducted (usually fractions 10, 15, 20, 25, 30).

The sample size of 50 patients was chosen to allow accrual within 2 years. Allowing for a one-sided error rate of 0.05, if the true feasibility rate is 0.93, then a sample size of 50 patients is sufficient to detect that the true feasibility rate is greater than 0.8 with power of 86%.

Patient demographics, baseline characteristics and treatment details were described using descriptive statistics such as
minimum, maximum, median, mean and standard deviation for quantitative variables, and for qualitative variables as counts and percentages. Each category of major protocol deviation and the overall feasibility of online adaptive radiotherapy were estimated as a proportion with 95% confidence interval using the exact method based on binomial distribution.

Acute toxicities were recorded using Common Terminology Criteria for Adverse Events (CTCAE) version 3. All patients had a baseline record at the time of simulation, weekly toxicity recording during radiotherapy and at 1 and 3 months post treatment.

Results

The study was conducted between August 2010 and March 2013 and all 12 radiotherapy centres recruited at least one participant (maximum 20). Fifty-four participants were recruited. Four participants were excluded as they did not commence radiotherapy for the following reasons: one patient developed a fistula prior to treatment, two patients had non-muscle invasive disease on pathology review, and one patient declined to proceed with radiotherapy. One patient with non-muscle invasive disease (T1) proceeded to complete protocol radiotherapy and was included in the analysis as the focus of this study was on the feasibility of the radiotherapy technique. Table 1 outlines patient, tumour, and chemotherapy details. Note that patients could have involvement of more than one site in the bladder. Patients were on average 78 years old at registration (range 54–88). The median duration of treatment course was 43 days (42–68). One patient died of a cardiovascular event on the day of the fifth fraction leaving 49 patients available for the feasibility analysis.

Table 2 shows the feasibility results, with the adaptive plan creation being possible in all cases. However the two other criteria did not meet our feasibility definition. Fig. 1 indicates the fraction by which all three adaptive radiotherapy plans were created, with 100% created before fraction 10. Twenty-eight patients had a real-time review occurring between fraction 5 and 10. Two cases required resubmission following initial real-time review as proceeding to complete protocol radiotherapy and was included in the analysis as the focus of this study was on the feasibility of the radiotherapy technique. Table 1 outlines patient, tumour, and chemotherapy details. Note that patients could have involvement of more than one site in the bladder. Patients were on average 78 years old at registration (range 54–88). The median duration of treatment course was 43 days (42–68). One patient died of a cardiovascular event on the day of the fifth fraction leaving 49 patients available for the feasibility analysis.

Table 2 shows the feasibility results, with the adaptive plan creation being possible in all cases. However the two other criteria did not meet our feasibility definition. Fig. 1 indicates the fraction by which all three adaptive radiotherapy plans were created, with 100% created before fraction 10. Twenty-eight patients had a real-time review occurring between fraction 5 and 10. Two cases required resubmission following initial real-time review as creation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning required resubmission following initial real-time review as creation of one of their adaptive plans was not performed per protocol. The study was conducted between August 2010 and March 2013 and all 12 radiotherapy centres recruited at least one participant (maximum 20). Fifty-four participants were recruited. Four participants were excluded as they did not commence radiotherapy for the following reasons: one patient developed a fistula prior to treatment, two patients had non-muscle invasive disease on pathology review, and one patient declined to proceed with radiotherapy. One patient with non-muscle invasive disease (T1) proceeded to complete protocol radiotherapy and was included in the analysis as the focus of this study was on the feasibility of the radiotherapy technique. Table 1 outlines patient, tumour, and chemotherapy details. Note that patients could have involvement of more than one site in the bladder. Patients were on average 78 years old at registration (range 54–88). The median duration of treatment course was 43 days (42–68). One patient died of a cardiovascular event on the day of the fifth fraction leaving 49 patients available for the feasibility analysis.

Table 2 shows the feasibility results, with the adaptive plan creation being possible in all cases. However the two other criteria did not meet our feasibility definition. Fig. 1 indicates the fraction by which all three adaptive radiotherapy plans were created, with 100% created before fraction 10. Twenty-eight patients had a real-time review occurring between fraction 5 and 10. Two cases required resubmission following initial real-time review as creation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable.

Across the whole patient group, the conventional plan was used 4% of the time (49 of 1127 fractions in the adaptive phase) to deliver treatment after fraction 9. The reasons for conventional plan usage varied and included technical issues as well as patient physiology. In 40.8% (20 of 49 fractions) of these instances, the conventional plan was used as a result of technical problems including: malfunction of the CBCT imaging system (n = 5), unavailability of a linear accelerator with CBCT imaging capability (n = 7), or that the adaptive plan not being ready and available for treatment (n = 8). In the remainder (29 of 49 fractions) the conventional plan was used because none of the three adaptive plans encompassed the imaged bladder. Note that patients with conventional plan used two times or less were not included in Table 3 unless the treatment was not feasible for other reasons.

In terms of feasibility, 41 of the evaluable 49 patients were able to complete the adaptive phase of treatment whilst minimising the use of the conventional plan to twice or less. For the remaining 8 patients the conventional plan was used between 3 and 8 times during the adaptive phase. This was due to unavailability of CBCT imaging and 2D planar imaging was used (n = 4) or because no adaptive plan was suitable to cover the imaged bladder (n = 4). This suggests that this plan creation process is not suitable for all patients.

Table 2 shows the feasibility results, with the adaptive plan creation being possible in all cases. However the two other criteria did not meet our feasibility definition. Fig. 1 indicates the fraction by which all three adaptive radiotherapy plans were created, with 100% created before fraction 10. Twenty-eight patients had a real-time review occurring between fraction 5 and 10. Two cases required resubmission following initial real-time review as creation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable. Table 3 depicts the individual participation of one of their adaptive plans was not performed per protocol. At the final review (following resubmission) 99.5% of the planning variables were acceptable.

Post treatment CBCT CTV coverage

We found that in 9 of the 49 participants, the bladder CTV after treatment had expanded beyond the PTV for the chosen plan in at least one of the planned post treatment CBCTs. A total of 14 of the 253 (5.5%) of the post treatment CBCTs showed the bladder to partially be outside the 7 mm PTV margin; this occurred once in six patients; twice in two patients and four times in one patient. One patient’s rapid bladder filling was thought to be a consequence of frusemide taken prior to his morning radiation treatment. Cessation of the drug resulted in excellent subsequent post treatment CBCT coverage. Three patients had pre-chemotherapy hydration prior to treatment, leading to a rapidly expanding bladder. Four patients were judged to have had inappropriate matching of the plan at the pre-treatment stage leading to a suboptimal choice of adaptive plan and hence inadequate target coverage. Table 4 shows the treatment duration for the adaptive fractions at the 12 centres involved in this multi-centre feasibility study.

Acute toxicity

Of the 30 patients that received at least one dose of chemotherapy, 7 (23%) experienced at least one grade 3 acute toxicity using the Common Terminology Criteria for Adverse Events (CTCAE) version 3. As expected different Grade 3 toxicities were seen in patients receiving cisplatin and those having carboplatin, however given the small numbers it is difficult to make comparisons between these two regimens. Of the 19 patients that did not receive chemotherapy,
2 (10%) experienced at least one grade 3 acute toxicity. In total, nine patients (18%) experienced at least one grade 3 acute toxicity. There was no grade 4 acute toxicity.

**Discussion**

We have previously reported a single institution pilot study using a similar plan of the day adaptive technique for muscle-invasive bladder cancer [5]. Now in this multi-centre study of the technique we found that the technical aspects of the plan creation were possible. However in 9 of the 49 participants (18%) at least one post-treatment CBCT indicated that the bladder had filled beyond the PTV during the course of treatment delivery. However, in total, this accounted for only 14 of the 253 (5.5%) post treatment scans. As this was assessed after completion of treatment delivery it clearly represents a ‘worst case scenario’ since the bladder was likely to have been within the PTV earlier on during the treatment delivery. It is also noteworthy that the 3D conformal delivery required in the trial would be relatively forgiving of a geographic PTV miss. For centres using 3D-CRT technique a 1.0 cm CTV to PTV margin would seem to be relatively safe in particular as any cold-spots would occur at the edges of the PTV. However appropriate choice of margins will become even more critical in the future when IMRT with highly conformal dose distributions would be used. Furthermore, the increased time required to deliver treatment with IMRT will influence the margin required to account for intra-fraction bladder filling.

Staff feedback and further training may minimise the occurrence of suboptimal plan selection during the adaptive phase of treatment. Similarly the hydration required prior to chemotherapy delivery can increase the degree of diuresis and the rapidity of bladder filling. Addressing this may be as simple as changing the treatment time to prior to chemotherapy, or using the conventional plan to account for faster bladder filling on chemotherapy days.

Assuming a spherical bladder with an average radius of 3 cm (bladder volume 113 cc) a margin reduction from 1.5 to 0.7 cm would result in a substantial PTV reduction of 45%. However, for some individuals a 7 mm CTV to PTV margin may be insufficient to account for intra-fraction bladder filling. There may be possible

<table>
<thead>
<tr>
<th>Centre</th>
<th>n</th>
<th>Min</th>
<th>1st quartile</th>
<th>Mean</th>
<th>Median</th>
<th>3rd quartile</th>
<th>Max</th>
<th>Standard deviation</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>4.9</td>
<td>5.5</td>
<td>6.2</td>
<td>6.0</td>
<td>6.7</td>
<td>8.8</td>
<td>0.9</td>
<td>(5.8–6.5)</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>7.1</td>
<td>8.5</td>
<td>10.2</td>
<td>10.0</td>
<td>11.0</td>
<td>16.0</td>
<td>2.2</td>
<td>(9.6–10.9)</td>
</tr>
<tr>
<td>C</td>
<td>2</td>
<td>4.0</td>
<td>6.0</td>
<td>7.3</td>
<td>7.0</td>
<td>8.0</td>
<td>12.0</td>
<td>1.8</td>
<td>(6.8–7.9)</td>
</tr>
<tr>
<td>D</td>
<td>8</td>
<td>3.0</td>
<td>6.0</td>
<td>8.2</td>
<td>7.0</td>
<td>9.0</td>
<td>31.0</td>
<td>4.4</td>
<td>(7.5–8.8)</td>
</tr>
<tr>
<td>E</td>
<td>1</td>
<td>7.0</td>
<td>8.0</td>
<td>10.3</td>
<td>9.0</td>
<td>10.5</td>
<td>26.0</td>
<td>4.1</td>
<td>(8.6–12.1)</td>
</tr>
<tr>
<td>F</td>
<td>1</td>
<td>4.0</td>
<td>4.0</td>
<td>4.6</td>
<td>5.0</td>
<td>5.0</td>
<td>6.0</td>
<td>0.6</td>
<td>(4.4–4.9)</td>
</tr>
<tr>
<td>G</td>
<td>20</td>
<td>5.0</td>
<td>8.0</td>
<td>10.3</td>
<td>10.0</td>
<td>12.0</td>
<td>38.0</td>
<td>3.0</td>
<td>(10.0–10.5)</td>
</tr>
<tr>
<td>H</td>
<td>2</td>
<td>4.4</td>
<td>7.7</td>
<td>9.9</td>
<td>10.0</td>
<td>11.5</td>
<td>15.0</td>
<td>2.5</td>
<td>(9.2–10.7)</td>
</tr>
<tr>
<td>I</td>
<td>4</td>
<td>5.7</td>
<td>8.7</td>
<td>10.4</td>
<td>10.0</td>
<td>11.9</td>
<td>20.3</td>
<td>2.6</td>
<td>(9.9–10.9)</td>
</tr>
<tr>
<td>J</td>
<td>4</td>
<td>6.0</td>
<td>11.0</td>
<td>13.8</td>
<td>14.0</td>
<td>17.0</td>
<td>21.0</td>
<td>3.9</td>
<td>(13.0–14.6)</td>
</tr>
<tr>
<td>K</td>
<td>1</td>
<td>7.0</td>
<td>9.0</td>
<td>10.5</td>
<td>10.0</td>
<td>12.0</td>
<td>16.0</td>
<td>2.1</td>
<td>(9.6–11.4)</td>
</tr>
<tr>
<td>L</td>
<td>3</td>
<td>2.6</td>
<td>6.3</td>
<td>7.7</td>
<td>7.4</td>
<td>9.5</td>
<td>15.8</td>
<td>2.7</td>
<td>(7.1–8.4)</td>
</tr>
</tbody>
</table>
strategies to modify this at the adaptive planning stages such using asymmetrical margins with larger superior and anterior margins. In 8 of 49 participants, the conventional plan was used more than twice during the adaptive phase of treatment. More than half of this group of patients had a conventional plan used due to the unavailability of CBCT imaging. Online adaptive planning requires daily CBCT image verification and in departments that have access to only one CBCT imaging system, back up treatment relies on 2D planar imaging and reverting to the use of the conventional treatment plan. In some patients the adaptive plans did not adequately encompass the imaged bladder. Bladder infection and the inability to void may also lead to use of the conventional plan. In one patient the bladder volumes from CBCTs obtained during the first week of treatment were not representative of the volume seen in the remaining treatment fractions, and required replanning. A successful adaptive protocol hinges on patients understanding the importance of having an empty bladder and ensuring complete voiding directly prior to radiotherapy. Even in the cases where the conventional plan had to be used, the soft tissue positioning and 1.5 cm CTV to PTV margin, is likely to result in reduced bowel irradiation compared to non-image guided treatments. In a small number of patients, while we found technical aspects of adaptive radiotherapy were possible; unfortunately their bladder physiology did not respect the protocol requirements.

Adaptive techniques for bladder cancer are potentially complicated by intra-fraction bladder filling. Murthy et al. [7], using helical tomotherapy CT images pre and post treatment found that 16% of patients no longer had their bladder contained within the treated area at the end of treatment. Foroudi et al. [15] demonstrated that when taking into account patient motion, bladder centroid motion, and bladder filling, the required margins to cover intra-fraction changes from pre-treatment CBCT to post-treatment CBCT in the superior, inferior, right, left, anterior, and posterior were 1.25 cm (range, 1.19–1.50 cm), 0.67 cm (range, 0.58–1.12 cm), 0.74 cm (range, 0.59–0.94 cm), 0.73 cm (range, 0.51–1.00 cm), 1.20 cm (range, 0.85–1.32 cm), and 0.86 cm (range, 0.73–0.99), respectively. Asymmetrical margins with larger anterior and superior margins may therefore improve coverage in future adaptive protocols.

Conclusions

In the clinical trial setting our feasibility criteria were based on our own institution’s pilot data. While they could not be met similarly in a multi-centre setting, technical implementation was possible as all centres were activated and were able to recruit at least one patient into the trial. All 49 patients who underwent adaptive planning successfully completed radiotherapy treatment. The CTV to PTV margin was inadequate in some cases due to fluid load or medication use which resulted in rapid bladder filling. Several centres reverted to planar imaging and use of the conventional plan when CBCT was unavailable; however with further investment into 3D imaging technology, this may become less of an issue.

Conflict of interest statement

None of the authors have any relationships with people or organisations which may appropriately influence this study.

Acknowledgements

Funded by an Australian NHMRC Project Grant 628527 and New Zealand Cancer Society Grant 11134. Appreciate input of the other members of the trial management committee: David Connah (Consumer), A/Professor Jeremy Millar (Radiation Oncologist), Professor Gillian Duchesne (Radiation Oncologist), Ms. Sandra Younie (Health Economist), Dr. Keen Hun Tai (Radiation Oncologist), and Dr. Leanne Tyrie (Radiation Oncologist).

References