Reducing Variability in Rectal Cancer Target Volume Delineation - An Education Intervention

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Authors: J. Doughton¹, H. Foley¹, S. Morrison¹, A. Plank², M. Fay³, J. Martin²; ¹Woolloongabba/AU, ²Toowomba/AU, ³Brisbane/AU
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Purpose

Radiotherapy (RT) has proven efficacy in locally advanced rectal cancer [1]. Optimisation of this established treatment competes with newer therapies for research resources. Variation in plan quality is a common problem, with the radiation oncology community still developing validated methods for its assessment [2,3].

It is apparent that target delineation practice can still be significantly improved in a range of tumour sites [4,5]. In the TROG 02.02 HeadStart trial of head and neck cancer treatment, the quality of the RT delivered had a confounding effect on overall survival rates [6,7]. RT plans that were initially in accordance with protocol resulted in a 20% improvement in 2 year survival compared with plans with major deficiencies.

Clinical trials now frequently feature contouring atlases and a credentialing phase with the aim of reducing contour variation - improving the quality of plans. The investigators in the Radiation Therapy Oncology Group (RTOG 0529) trial of dose-painted IMRT for anal canal carcinoma found that 81% of plans submitted for rapid turnaround quality assurance (QA) required re-contouring [8,9]. The main problem areas were the mesorectal, presacral and inguinal subsites. The RTOG group has published an atlas for contouring anorectal cancer with the aim of addressing this finding [10]. This atlas takes into account previous work in incorporating reported locoregional patterns of failure into the CTV [11].

With these issues in mind, we examine the effectiveness of a structured educational intervention on standardising target delineation. Furthermore, our study provides a snapshot of current target delineation practice for rectal cancer in the community setting.
Methods and Materials

*Primary goal:* Assess the value of an education intervention through a measured reduction in interobserver variability and greater conformity with atlas guidelines.

*Trial design:* A prospective non-randomised study evaluating the efficacy of an educational intervention on CTV delineation in locally advanced rectal cancer.

*Participants:* Radiation oncologists and radiation oncology trainees from 4 sites in South East Queensland, Australia, were invited to participate.

*Intervention:* The RTOG atlas for conformal RT or IMRT treatment was presented as an aid to target delineation [10].

*Ethics:* Exemption from full ethics review was obtained (HREC/10/QRBW/321) under the provisions for auditing activities.

*Schema:* See Fig. 1 below.
Case details

- The tumour was located 3 cm from the anal verge and required long-course neoadjuvant chemoradiotherapy. See Fig. 2 on page 7, Fig. 3 on page 7 and Fig. 4 on page 8.

A gross tumour volume (GTV) was developed by the investigators in collaboration with an expert lower gastrointestinal tract radiologist.

- A reference (Ref) CTV (equivalent to a CTV 45 Gy pelvic volume was created by the investigators as per the RTOG atlas.
• All participants were blinded to each other’s work, and in the case of the Post-CTV, they were also blinded to their Pre-CTV volumes.
• The questionnaire was adapted from previously published work [12].

**Education Intervention**

• The education intervention consisted of a didactic presentation outlining the issues of locoregional failure, oncological and radiological anatomy, the advantages of a contouring atlas and a review of the RTOG atlas for target delineation in anorectal cancer [10].
• The session went for 25-40 minutes, allowing discussion during and after the presentation.
• The presentation and atlas article were also available to participants afterward.

**Analysis**

All structure sets were downloaded to the Eclipse TPS (Varian, Palo Alto, California, version 8.6.17).

**How was conformity measured?** The conformation number (CN) was used to measure conformity. It is a concordance index demonstrating conformity with an "ideal" volume [13,14]. The maximal CN is 1, where there is perfect agreement between the Ref CTV and the participant CTV, with lower values showing a progressively greater deviance from the ideal. It compares both volumetric and positional variation. Conformation number was used in order for our data to be comparable with a similar study [12]. This was measured by:

\[
CN = \frac{OV^2}{(\text{Ref CTV Volume} \times \text{Participant CTV Volume})}
\]

where:

CN = Conformation Number. Participant CTV compared to Ref CTV

OV = Overlap Volume. This was the overlap of Ref CTV and Participant CTV volumes as measured using Boolean operators.

Primary outcome was measured by the ratio of "average Post-CN" / "average Pre-CN" for each matched pair. A confidence interval not crossing 1 would be considered statistically significant.
Visual analysis allowed identification of particular aspects of the CTVs which might commonly lead to disagreement and/or improvement following education [11,12]. Table 1 on page 9 in the sidebar indicates the observation criteria.

Statistics

McNemar’s test was used for analysis of these categorical values. Based on approximately 80% of plans needing to be re-contoured in the RTOG 0529 trial [9], 24 contouring participants would detect a 50% change in the number of doctors whose contouring was in agreement with the atlas after intervention, with a power of 0.8 and p-value=0.05 (two-tailed).
Fig. 2: a) Images of the selected case with GTV and Reference CTV shown. Lower pelvis.

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Fig. 3: b) Images of the selected case with GTV and Reference CTV shown. Mid pelvis.

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Fig. 4: c) Upper pelvis.

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<table>
<thead>
<tr>
<th>Anatomical Subsite</th>
<th>Criteria for adherence to atlas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranial extent</td>
<td>Within 2 slices (6 mm) of the reference contour. Atlas = at the division of the common iliac vessels into internal and external iliac vessels.</td>
</tr>
<tr>
<td>Pre-sacrum</td>
<td>At least 1 cm anterior to the sacrum in the cranial aspect of the CTV</td>
</tr>
<tr>
<td>Mesorectum</td>
<td>Completely covered to rectosigmoid junction and down to levator ani muscles. Complete coverage circumferentially.</td>
</tr>
<tr>
<td>Lateral pelvic wall</td>
<td>Delineation of internal iliac vessels and the posterior portion of obturator vessels (close to entry into obturator canal – as per reference contour). Does not include delineation of the external iliac vessels. Does not include pelvic sidewall muscles or bone.</td>
</tr>
<tr>
<td>Bladder</td>
<td>Anterior CTV extends at least 1 cm into posterior wall.</td>
</tr>
<tr>
<td>Caudal extent</td>
<td>2cm below GTV. Expands beyond levator ani muscles into ischiorectal fossa by a few millimetres only (approximately 5-8 mm).</td>
</tr>
</tbody>
</table>

**Table 1:** Criteria for visual analysis of participant CTVs.

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Results

Of 40 doctors invited, 29 participated in the study. There were 24 valid Pre and Post data sets (matched pairs) suitable for analysis.

Volumetric Analysis

Reference CTV volume was 764 cc.

Average Pre-CTV volume was 795 cc.

Average Post-CTV volume was 741 cc for Post-CTV (7% smaller).

Conformity

The average conformation number improved after the intervention, from 0.63 to 0.68 (p=0.001). There was also less interobserver variability, with a narrower range and less CN outliers as seen in Fig. 5 on page 19.

The ratio of Pre and Post CTV CNs for each matched pair was obtained. The frequency of these ratios is displayed in Fig. 6 on page 19. The average of these ratios was 1.09 (95% confidence interval 1.04-1.16; p-value (two-sided) = 0.001). This indicates an improvement in conformity of target delineation after the education intervention.

Visual analysis

Results for visual analysis are reported in Table 2 on page 20. There was a small improvement in each subsite except for the lateral pelvic subsite. Axial views of pre- and post-intervention contours from participants are depicted below (Figures 7-12). The red contour is the reference CTV.
Fig. 7: Pre-intervention CTVs -3.6cm axial slice.

References: Princess Alexandra Hospital - Woolloongabba/AU
Mesorectum - good improvement in coverage of the mesorectum, the most problematic area in the RTOG 0529 trial, with a 21% improvement in participants’ concordance with atlas guidelines.
Fig. 10: Post CTVs +1.5cm axial slice.

References: Princess Alexandra Hospital - Woolloongabba/AU
Fig. 11: Pre CTVs +3.6cm axial slice.
References: Princess Alexandra Hospital - Woolloongabba/AU

Fig. 12: Post CTVs +3.6cm axial slice.
References: Princess Alexandra Hospital - Woolloongabba/AU
Fig. 13: Pre CTVs sagittal slice.

References: Princess Alexandra Hospital - Woolloongabba/AU
Fig. 14: Post CTVs sagittal slice.

References: Princess Alexandra Hospital - Woolloongabba/AU

Cranial extent - about half the CTVs were higher or lower than the Ref CTV by greater than 2 slices (6 mm). The Pre data had 8/24 incorrect and the post data had 3/24 incorrect. Sagittal views of CTVs are shown above (fig. 13-14) and coronal views in the side bar (Fig. 15 on page 21, Fig. 16 on page 21).

Caudal extent - greatest disagreement with reference CTV. Even after the intervention, 19/24 still varied in comparison with the Ref CTV.
Post-hoc analysis showed a slight improvement in the number of sites marked as incorrect, from a mean Pre error count of 3.2 to a mean Post error count of 2.7, scored out of 6 subsites. This was not statistically significant (Wilcoxon signed ranks test: p=0.18).

**Suggestions from the survey**

- Further clarification of anatomy of obturator vessels.
- Using mesorectum and levator ani muscles as references for target delineation was helpful.
- More case examples on CT voluming for lesions at high, mid or low rectal sites.
- Greater exposure to imaging anatomy, MRI interpretation and cases with patients planned in the supine position (as per local practice).
- Local agreement to extent of inferior coverage for low rectal tumours. (NB. Local guidelines differ from the RTOG atlas.)
Fig. 5: Box plot of conformation number (CN) distribution (n=24) before and after intervention, showing mean trend. Dark solid lines represent the median CN, the boxes display the interquartile range (middle 50% of observations), the dots are outliers, and the lines are a measure of data spread. CN is expressed as a percentage in the y axis (CN x 100).

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Fig. 6: Frequency distribution of ratios of (CN Post) / (CN Pre) for each participant (n=24). The higher the ratio, expressed as a percentage in this graph, the greater the improvement in similarity between the participant’s CTV compared to the reference ("gold standard") CTV volume. CN = Conformation Number.

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Table 2: Visual analysis of how well subsites were covered by participant CTVs, compared with the atlas and reference contour. An improvement between Pre and Post CTVs is seen. "Yes" = sufficiently covered. "No" = insufficiently covered.

<table>
<thead>
<tr>
<th>Subsite</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranial extent as per atlas</td>
<td>yes 11</td>
<td>no 13</td>
</tr>
<tr>
<td></td>
<td>yes 12</td>
<td>no 12</td>
</tr>
<tr>
<td>Presacral space as per atlas</td>
<td>yes 19</td>
<td>no 5</td>
</tr>
<tr>
<td></td>
<td>yes 20</td>
<td>no 4</td>
</tr>
<tr>
<td>Mesorectum completely covered</td>
<td>yes 16</td>
<td>no 8</td>
</tr>
<tr>
<td></td>
<td>yes 21</td>
<td>no 3</td>
</tr>
<tr>
<td>Anterior CTV 1 cm into posterior bladder wall</td>
<td>yes 9</td>
<td>no 15</td>
</tr>
<tr>
<td></td>
<td>yes 14</td>
<td>no 10</td>
</tr>
<tr>
<td>Lateral subsite as per atlas</td>
<td>yes 10</td>
<td>no 14</td>
</tr>
<tr>
<td></td>
<td>yes 8</td>
<td>no 16</td>
</tr>
<tr>
<td>Caudal region as per atlas</td>
<td>yes 4</td>
<td>no 20</td>
</tr>
<tr>
<td></td>
<td>yes 5</td>
<td>no 19</td>
</tr>
</tbody>
</table>

Fig. 15: Pre CTVs coronal slice.

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Fig. 16: Post CTVs coronal slice.

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Conclusion

An improvement in quality of target delineation is required in the context of a change to conformal CT planning and IMRT techniques amongst most centres. This study shows that an educational intervention is able to significantly impact on the consistency of contouring. Visual analysis of problem subsites is useful in auditing practice and in informing further educational needs. A focus on the importance of circumferential coverage of the mesorectum and lymph node sites at risk (pre-sacral and obturator) is suggested for further educational interventions and guideline development.
References


