HHS Public Access

Author manuscript

*Phys Med Biol*. Author manuscript; available in PMC 2016 March 10.

Published in final edited form as:

*Phys Med Biol*. 2014 July 21; 59(14): 3749–3759. doi:10.1088/0031-9155/59/14/3749.

# Influence of image slice thickness on rectal dose-response relationships following radiotherapy of prostate cancer

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## Abstract

When pooling retrospective data from different cohorts, slice thicknesses of acquired computed tomography (CT) images used for treatment planning may vary between cohorts. It is, however, not known if varying slice thickness influences derived dose-response relationships. We investigated this for rectal bleeding using dose-volume histograms (DVHs) of the rectum and rectal wall for dose distributions superimposed on images with varying CT slice thicknesses. We used dose and endpoint data from two prostate cancer cohorts treated with 3D-CRT to either 74 Gy (N=159) or 78 Gy (N=159) @ 2 Gy per fraction. The rectum was defined as the whole organ with content, and the morbidity cut-off was Grade ≥2 late rectal bleeding. Rectal walls were defined as 3-mm inner margins added to the rectum. DVHs for simulated slice thicknesses from 3 to 13 mm were compared to DVHs for the originally acquired slice thicknesses at 3 and 5 mm. Volumes, mean, and maximum doses were assessed from the DVHs, and *gEUD* values were calculated. For each organ and each of the simulated slice thicknesses, we performed predictive modeling of late rectal bleeding using the Lyman-Kutcher-Burman (LKB) model. For the most coarse slice thickness, rectal volumes increased (≤18%), whereas maximum and mean doses decreased (≤0.8 Gy and ≤4.2 Gy, respectively). For all *a* values, the *gEUD* for the simulated DVHs were ≤1.9 Gy different than the *gEUD* for the original DVHs. The best-fitting LKB model parameter values with 95% CIs were consistent between all DVHs. In conclusion, we found that the investigated slice thickness variations had minimal impact on rectal dose-response estimations. From the perspective of predictive modeling, our results suggest that variations within 10 mm in

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Presented in part at the European Society for Therapeutic Radiotherapy and Oncology Annual Meeting, April 5–8, 2014, Vienna, Sweden.

***Declaration of interest:*** The authors report no conflicts of interest.

slice thickness between cohorts are unlikely to be a limiting factor when pooling multi-institutional rectal dose data that include slice thickness variations within this range.

## 1. Introduction

Compared with three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated RT is expected to result in fewer patients with severe RT-induced toxicities for particular treatment sites (Teh *et al* 2002, Zelefsky *et al* 2012). However, in the light of this fairly new delivery technique, we still need retrospective data as delivered by 3D-CRT (or even older treatment approaches) to identify dose-response relationships for normal tissue toxicities that may occur many years after RT. One limiting factor in dose-response modeling is that model parameter values typically are estimated from single-institution studies, which has resulted in diverging descriptions of dose-response relationships for similar combinations of critical structures and toxicities. To this end, the pooling of multi-institutional data has been encouraged as one approach to better understand the complexity of relationships between various dose distributions and radiation-induced toxicity (Deasy *et al* 2010). Several sources of uncertainty when pooling data exist and among these, coarse image slice thickness, as used in earlier treatment approaches, is one example. The impact of varying image slice thickness on calculated volumes, as well as on calculated doses, has to some extent been investigated using dose-volume histograms (DVHs) (Butler *et al* 2000, Ebert *et al* 2010, Kirisits *et al* 2007, Prabhakar *et al* 2009, Somigliana *et al* 1996, Weinberg *et al* 2004). Coarse image slice thickness typically introduces larger differences in calculated volumes for small, as compared to large, structures (Ebert *et al* 2010, Kirisits *et al* 2007, Prabhakar *et al* 2009, Weinberg *et al* 2004). However, for calculated doses, differences are typically lower than ±3.5–5% (cf. accuracy required for the absorbed dose to the target) (Ebert *et al* 2010, Kirisits *et al* 2007, Prabhakar *et al* 2009, Weinberg *et al* 2004). Although it is assumed that dose differences of such orders are unlikely to impact dose-response relationships (Butler *et al* 2000, Ebert *et al* 2010), it has, to the best of our knowledge, still not been investigated.

The purpose of this study was to investigate if varying slice thickness influences derived dose-response relationships. We investigated this for rectal bleeding using dose distributions of the rectum and rectal wall in two prostate cancer cohorts treated with 3D-CRT, for which available imaging and dose data allowed for simulations of varying CT slice thicknesses.

## 2. Methods and materials

### 2.1 Patient cohorts

This study was performed using CT slice thickness data from two prostate cancer cohorts previously treated with 3D-CRT. One of the cohorts included 159 men treated from 2002 to 2006 at Fraser Valley Centre of the British Columbia Cancer Agency (BCCA) in Canada (Liu *et al* 2010). The total dose, using 18 MV photons, was 74 Gy @ 2 Gy per fraction with the dose prescribed to the prostate in either a one-phase (55% of the patients) or the prostate and pelvic lymph nodes in a two-phase boost technique (45% of the patients; 44/46 Gy @ 2 Gy per fraction in the first phase). Treatment planning was originally performed in the

CadPlan or Eclipse treatment planning systems (Varian Medical Systems, Inc., Palo Alto, CA, USA) with their version-dependent dose calculation algorithms. The other cohort also included 159 men. These men were treated at Aarhus University Hospital (AUH) in Aarhus, Denmark from 2005 to 2007 for localized prostate cancer (prostate or prostate and proximal seminal vesicles), to prescribed doses, with 15 MV photon beams, of 78 Gy @ 2 Gy per fraction (Petersen *et al* 2014). Treatment planning had been performed in the Eclipse treatment planning system. For the AUH cohort, the original treatment plans had all been re-calculated with the dose calculation algorithm currently used in the clinic at AUH (AAA, Eclipse v.10.0, Varian Medical Systems, Inc., Palo Alto, CA, USA).

In both cohorts, delineations of the rectum and information on rectal bleeding were available. The rectum was delineated from the recto-sigmoid flexure to the anal canal and was defined as a 'solid' organ including content. For the purpose of this study, DICOM-image and DICOM-RT (Structure set, Dose and Plan) files for all patients were imported into the Computational Environment for Radiotherapy Research for further processing (CERR) (Deasy *et al* 2003). In CERR, we also delineated the rectal wall and defined it as the 3-mm inner margin added to the outer rectum contours. In the BCCA cohort, rectal bleeding had been estimated based on physician assessments at follow-up every six months in the first three years after RT and annually thereafter. The morbidity cut-off used for the BCCA cohort in this study was Grade ≥2 late rectal bleeding (requiring laser coagulations for bleeding) assessed as the maximum-recorded grade at any follow-up. The median follow-up time was 32 months, and rectal bleeding was observed in 12 patients (7.5%) (Liu *et al* 2010, Thor *et al* 2013 in press). Rectal bleeding in the AUH cohort was based on patient-reported information as given by a study-specific questionnaire (Emmertsen *et al* 2012), and Grade ≥2 late rectal bleeding was defined by having noticed blood in stools more than once per month. We randomly sampled 159 men from the original 213 patients in the AUH cohort and performed the sampling so that the rectal bleeding rate corresponded to that of the BCCA cohort (i.e., 12 patients (7.5%)). The median time-to-follow-up for the 159 sampled men was 46 months.

### 2.2 Slice thickness simulations

We used a plug-in to CERR to obtain DVHs for various CT slice thicknesses. In a treatment planning system, DVHs for a given structure is in general obtained from information that can be found in the CT grid. In order to simulate the effect of varying CT slice thicknesses in CERR, we created pseudo CT slices using the information from the originally acquired inter-slice spacing (512×512 pixels). For AUH, the images were acquired by a multi-slice Philips Mx8000 IDT16 CT (slice thickness: 3 mm; in-slice pixel resolution: 0.98×0.98 $mm^2$). For BCCA, images were acquired with a single-slice Philips PQ2000 CT (slice thickness: 5 mm; in-slice pixel resolution: 0.94×0.94 $mm^2$). Dose and structure contours were then interpolated onto these pseudo slices, using linear interpolation to the nearest neighboring voxel, and used to calculate the corresponding DVHs. The original dose grid was 2 mm. Pseudo-slices were created at 3 or 5 mm, depending on the original inter-slice spacing, and at 7, 9, 11 and 13 mm. The DVHs in CERR were then exported with a bin-width of 0.2 Gy and further processed in MATLAB (MATLAB R2012b version 8.0.0.78, The MathWorks Inc., Natick, MA).

### 2.3 Slice thickness comparisons

For both organs, the DVHs resulting from various simulated slice thicknesses were compared to the DVHs of the originally acquired slice thicknesses at 3 mm (AUH) and 5 mm (BCCA), the reference DVHs. The volumes, as well as the mean and maximum doses, were assessed. The generalized equivalent uniform dose (*gEUD*) (Niemierko 1999) was also calculated using three different values of the volume dependence parameter *a*: 12.5, 11.1 and 4.3 (corresponding to *n* values of 0.08 (Tucker 2007), 0.09 (Michalski *et al* 2010), and 0.23 (Rancati *et al* 2004), respectively). For each slice thickness, the cohort mean and standard deviation (SD) of the investigated parameters were calculated, and a paired Student's T-test was applied. For the calculated *gEUD*s, we additionally selected a reference sensitivity/specificity cut-off defined as the leftmost corner point of the receiver operating characteristic (ROC) curve. This point corresponds to the *gEUD* threshold for the "best achievable" trade-off between sensitivity and specificity among all plausible cut-off points and thresholds in a ROC curve. Ultimately, we performed predictive normal tissue complication probability (NTCP) modeling in MATLAB with the Lyman-Kutcher-Burman (LKB) model[1] (Kutcher *et al* 1989, Lyman 1985, Niemierko 1999) (Maximum Likelihood method with an exhaustive grid search approach for clinically relevant parameter values ($D_{50}$ in steps of 0.5 Gy; *m* in steps of 0.005; *n* in steps of 0.01) and Profile Likelihood for confidence intervals (CIs) (Schilstra *et al* 2001)). Parameter value comparisons with the reference slice thickness were based on 95% CIs of the estimated best-fitting LKB model parameters.

## 3. Results

Rectal volumes increased with coarser slice thicknesses and ranged from 93 or 95 $cm^3$ to 100 $cm^3$, as compared to 93 or 94 $cm^3$ for the BCCA and AUH cohorts originally acquired slice thicknesses at 5 and 3 mm, respectively (Tables 1 and 2). As illustrated in Figure 1, the largest volume differences compared to the reference volumes were found for the 13-mm simulated slice thickness (AUH: 6.2 $cm^3$, p=0.20; BCCA: 6.9 $cm^3$, p=0.15). In agreement with the rectal volumes, the rectal wall volumes also increased with coarser slice thickness for both cohorts (Tables 1 and 2; Figure 1). On average, the rectal wall volume was approximately half of the corresponding rectal volume for each individual. For the simulated volumes, however, the differences in rectal wall volume were 2 to 3 $cm^3$ larger than differences in rectum volume. Simulations of 9-, 11- and 13-mm slice thicknesses resulted in rectal wall volumes that were significantly larger than the original rectal wall volumes.

For the rectum, the mean dose differed ≤ 1.3 and ≤ 1.3 Gy and the maximum dose ≤ 0.1 and ≤ 0.8 Gy in the BCCA and AUH cohort, respectively. For the AUH cohort, the mean dose extracted from the DVHs resulting from simulations of 11- and 13-mm slice thicknesses were significantly lower than the corresponding dose values assessed from the reference DVHs; for maximum doses, simulations of 9-, 11- and 13-mm slice thicknesses were significantly lower (Table 2). The mean doses assessed from the simulated rectal wall DVHs differed from the corresponding values assessed from the reference DVHs by 2.5 Gy or less

[1]The LKB model has three parameters: $D_{50}$ denoting the dose for a 50% probability of toxicity, *m* describing the steepness of the dose-response curve at $D_{50}$, and *n* denoting the structure volume dependence.

in the BCCA cohort and 4.2 Gy or less in the AUH cohorts. Corresponding values for maximum doses were 0.1 Gy or less in the BCCA cohort and 0.8 Gy or less in the AUH cohort. In the BCCA cohort, significantly lower mean doses were found for 11- and 13-mm slice thicknesses. In the AUH cohort, significantly lower mean doses were found for 7-, 9-, 11- and 13-mm slice thicknesses, and significantly lower maximum doses were found for 9-, 11- and 13-mm slice thicknesses. The combined influence on dose and volume parameters of the rectum and the rectal wall for the investigated slice thicknesses is presented in Figure 2, in which the averaged cumulative DVHs for each cohort are plotted.

Among the investigated $a$ values, the largest differences were found for $a$=4.3 (results for $a$=11.1 and $a$=12.5 not shown). This resulted in *gEUD*s for the simulated rectum and rectal wall DVHs being lower by 0.8 Gy or less and 1.9 Gy or less, respectively, than the *gEUD*s calculated from the originally acquired slice thicknesses at 5 and 3 mm (Tables 1 and 2). For the rectal wall, significantly lower *gEUD*s were seen for 9-, 11- and 13-mm slice thicknesses in both cohorts. Based on the calculated reference sensitivity/specificity cut-off points between the simulated and original DVHs, the difference in threshold *gEUD*s ranged from 0.7 to 5.8%, with the higher percentages seen for the two highest $a$ values (Table 3).

For both organs and cohorts, the best-fitting LKB model parameter values estimated from the simulated DVHs were similar to those estimated from the DVHs assessed from the originally acquired slice thicknesses. For the rectum, differences in LKB parameters $D_{50}$, $m$ and $n$ were within 4 Gy, 0.03 and 0.01, respectively, and for the rectal wall, within 8 Gy, 0.04 and 0.02, respectively. A very large overlap was seen between both the 68% (not shown) and 95% CIs for all investigated combinations of slice thicknesses and structures in both cohorts (Tables 1 and 2).

## 4. Discussion

Until now, dose-response relationship estimations following RT have typically relied on single-institution data. To overcome statistical issues relating to small sample sizes and to explore the validity of previously proposed parameter estimates, multi-institutional data pooling has been advocated (Deasy *et al* 2010). Image slice thickness has been suggested as one potentially contributing source of uncertainty in the multi-institutional data pooling scenario (Ebert *et al* 2010, Kirisits *et al* 2007, Weinberg *et al* 2004), but no study has investigated potential effects on dose-volume response relationships. In the current study, we investigated this for the rectum and found that rectal DVHs assessed from CT slice thicknesses in the range of 3 mm to 13 mm resulted in the same best-fit LKB model parameters for rectal bleeding in prostate cancer patients treated with 3D-CRT.

Previous studies have focused on the influence of varying image slice thickness on structure volumes. In those studies, dose variations have typically been quantified with respect to selected portions of the DVH. Those studies were also limited to small changes in investigated slice thickness (Ebert *et al* 2010, Kirisits *et al* 2007) or mainly concerned large structures (Weinberg *et al* 2004). It has been demonstrated that coarse image inter-slice spacing has larger effects on small volumes (<100–200 $cm^3$) than on large volumes, with respect to structure volume and dose (Ebert *et al* 2010, Prabhakar *et al* 2009, Weinberg *et al*

2004). The rectum and rectal wall volumes for the originally acquired slice thicknesses in the study presented here were small, on average 93 to 94 $cm^3$ and 45 to 50 $cm^3$, respectively. We therefore hypothesized that the volume and dose differences, as induced by various slice thicknesses for structures of such volumes, could be “large enough” to have an impact on the dose-volume response relationships for rectal bleeding. Indeed, for the rectal wall, we found significantly larger volumes and significantly smaller values in the investigated dose parameters for the coarser slice thicknesses, as compared to the corresponding values from the originally acquired slice thicknesses for both cohorts. However, although we took into account intra-institutional and cohort-specific characteristics, used the entire DVH, investigated a broad range of slice thicknesses and in addition, restricted our analyses to small structures, we found no clinically meaningful differences in the *gEUD* thresholds or best-fitting LKB model parameter values for rectal bleeding in any of the cohorts.

A couple of things must be kept in mind with respect to the interpretation and generalizability of our results. Firstly, we cannot speculate if dose grid resolutions, volume reconstruction or dose calculation algorithms that are different from those used in our study would have influenced the simulations and thereby, our results. Secondly, we applied the same slice thicknesses to the entire patient cohort and made comparisons between extreme variations. The more realistic scenario would involve pooling randomly distributed slice thicknesses between cohorts (Kim *et al* 2004), potentially leading to smaller volume and dose differences than reported here and subsequently, no probable impact on model parameter values. Finally, our analyses were restricted to the volume parameter values previously reported for rectal toxicity; investigating a broader set of volume parameters was beyond the scope of this work. On the other hand, strengths of this study are that we investigated varying slice thickness in two independent cohorts and for two structures, and we found similar results between cohorts, even though the investigated endpoint was assessed in two different ways (physician-assessed or patient-reported). A final comment is that the relative magnitude of the uncertainties associated with slice thickness differences will in general be small compared with other major sources of error such as inter- and intra-observer delineation variability, dose calculation differences across treatment planning systems as well as setup error and organ motion.

## 5. Conclusion

From the perspective of predictive modeling, our results suggest that variations within 10 mm in image slice thickness between cohorts have minimal impact on rectal dose response estimations and are unlikely to be a limiting factor when pooling multi-institutional rectal dose data.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

We thank all the patients who participated in the two studies, as well as the staff at BCCA and AUH who were involved in patient care and data collection. The Varian Corporation, the Swedish Cancer Society, the Assar Gabrielsson Foundation, the King Gustav V Jubilee Clinic Cancer Research Foundation, Tore Nilssons Foundation for Medical Research and the Syskonen Svenssons Foundation for Medical Research are also gratefully acknowledged, as well as the helpful comments from our anonymous reviewers.

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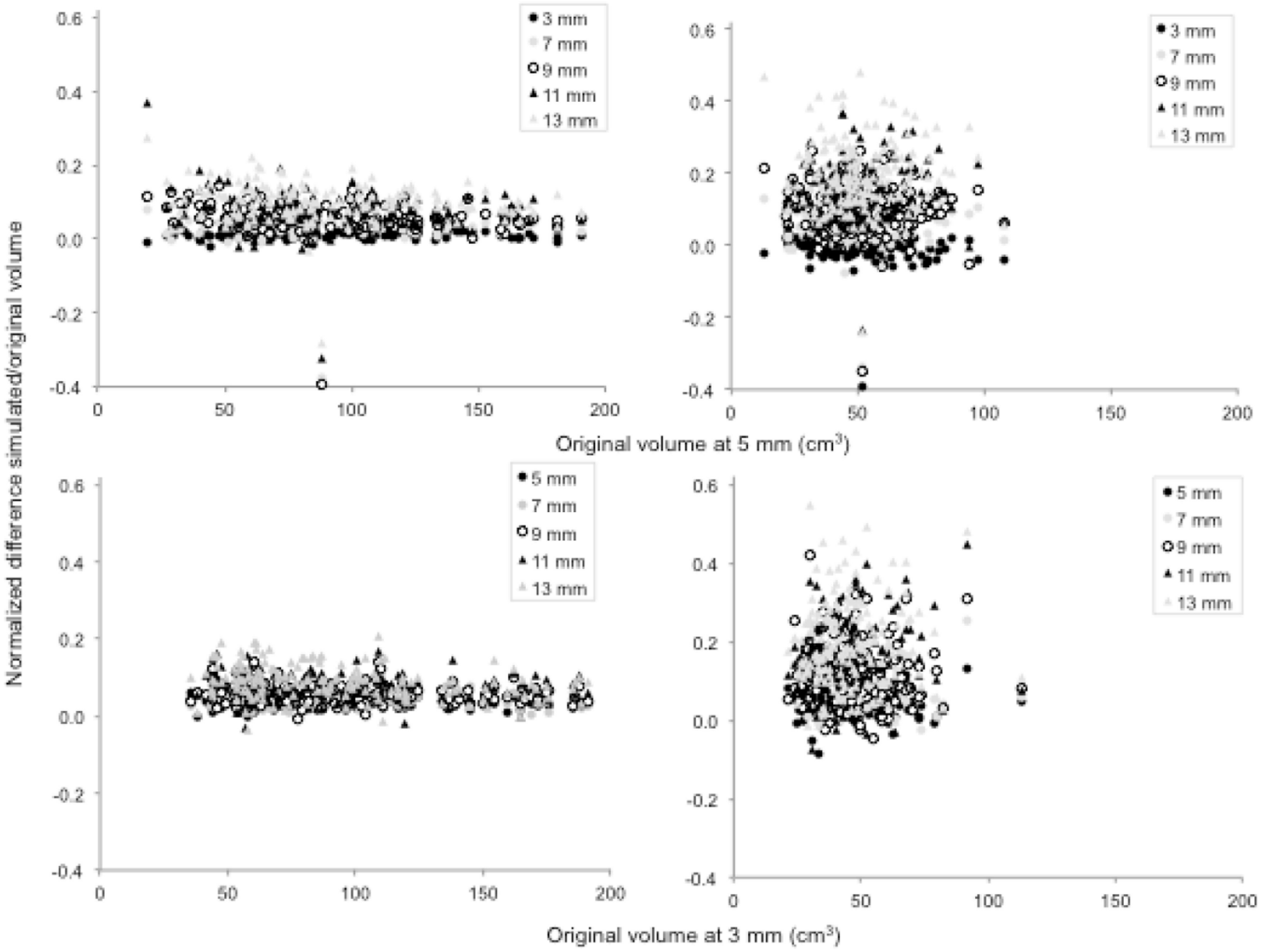


**Figure 1.**

The normalized difference between the simulated and original rectal volumes (rectum: left; rectal wall: right) plotted as a function of the original rectal volumes for the BCCA cohort (upper panel) and the AUH cohort (lower panel), respectively. *Note: The x-axis for the rectum volumes (left panel) has been scaled such that three and four data points have been excluded from the BCCA and AUH cohort, respectively*.

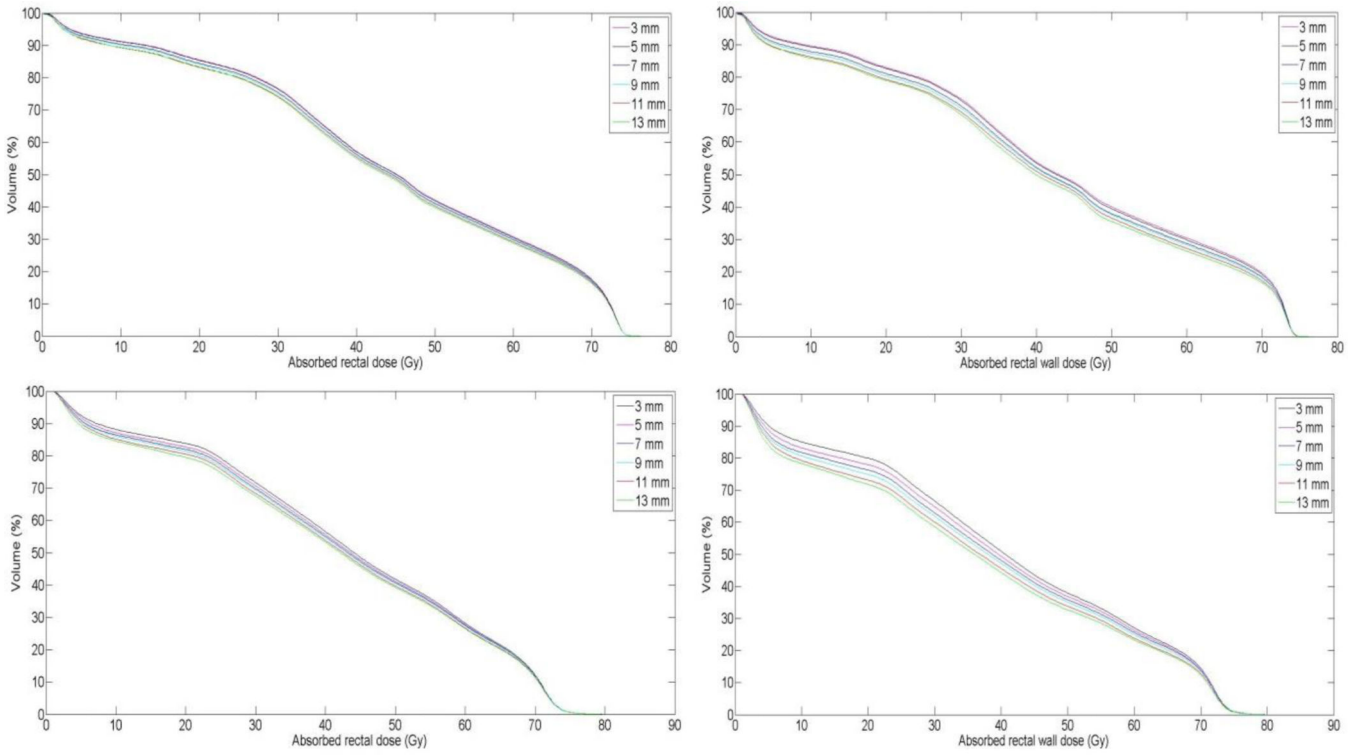


**Figure 2.**

Averaged cumulative DVHs over the rectum (left) and the rectal wall (right) for the BCCA cohort (upper two figures) and AUH cohort (bottom two figures). The DVHs from the originally acquired slice thicknesses in 5 and 3 mm, respectively, are shown in black.

*Phys Med Biol*. Author manuscript; available in PMC 2016 March 10.

**Table 1**

Averaged values from the BCCA cohort for volume, maximum dose, mean dose, *gEUD*, and the best-fitting LKB model parameters obtained from simulations of various slice thicknesses for the rectum and rectal wall.

| BCCA cohort Slice thickness (mm) | Structure | Volume ± SD ($cm^3$) | Max dose ± SD (Gy) | Mean dose ± SD (Gy) | *gEUD* (*a*=4.3) ± SD (Gy) | $D_{50}$ (95%CI) | *LKB* *m* (95%CI) | *n* (95%CI) |
|---|---|---|---|---|---|---|---|---|
| 3 | Rectum | 92.9 ± 41.4 | 74.0 ± 0.6 | 44.7 ± 9.0 | 55.4 ± 4.0 | 78.5 (69.0, >200) | 0.12 (0.04, 0.64) | 0.07 (0.01, >1.0) |
| | Rectal wall | 49.9 ± 15.4 | 74.0 ± 0.6 | 43.5 ± 8.8 | 55.5 ± 3.6 | 80.0 (70.0, 140) | 0.12 (0.04, 0.54) | 0.06 (0.02, >1.0) |
| 5 *(Ref.)* | Rectum | 92.9 ± 41.6 | 74.0 ± 0.6 | 44.6 ± 9.0 | 55.3 ± 4.0 | 78.5 (69.0, >200) | 0.12 (0.04, 0.64) | 0.07 (0.01, >1.0) |
| | Rectal wall | 51.1 ± 16.0 | 74.0 ± 0.6 | 43.2 ± 8.9 | 55.3 ± 3.6 | 78.0 (70.0, 140) | 0.12 (0.04, 0.54) | 0.08 (0.02, >1.0) |
| 7 | Rectum | 92.9 ± 41.6 | 73.9 ± 0.6 | 44.1 ± 9.1 | 55.1 ± 4.0 | 78.0 (69.0, >200) | 0.11 (0.04, 0.64) | 0.06 (0.01, >1.0) |
| | Rectal wall | 53.6 ± 17.0* | 73.9 ± 0.6 | 42.3 ± 9.1 | 54.8 ± 3.7 | 80.0 (70.0, 140) | 0.12 (0.04, 0.54) | 0.06 (0.02, >1.0) |
| 9 | Rectum | 96.2 ± 42.7 | 73.9 ± 0.6 | 43.9 ± 9.2 | 55.0 ± 4.0 | 82.5 (69.5, >200) | 0.15 (0.04, 0.65) | 0.07 (0.01, >1.0) |
| | Rectal wall | 55.3 ± 17.4* | 73.9 ± 0.6 | 41.9 ± 9.4 | 54.6 ± 3.8* | 86.0 (76.0, 140) | 0.16 (0.06, 0.56) | 0.06 (0.02, >1.0) |
| 11 | Rectum | 97.1 ± 43.3 | 73.9 ± 0.6 | 43.5 ± 9.2 | 54.8 ± 4.0 | 82.0 (69.5, >200) | 0.14 (0.04, 0.66) | 0.06 (0.01, >1.0) |
| | Rectal wall | 57.4 ± 18.7* | 73.9 ± 0.6 | 41.2 ± 9.6* | 54.3 ± 3.8* | 82.0 (74.0, 140) | 0.14 (0.04, 0.56) | 0.06 (0.02, >1.0) |
| 13 | Rectum | 99.8 ± 44.4 | 73.9 ± 0.6 | 43.3 ± 9.3 | 54.6 ± 4.2 | 78.5 (69.0, >200) | 0.12 (0.03, 0.65) | 0.06 (0.01, >1.0) |
| | Rectal wall | 60.0 ± 19.7* | 73.9 ± 0.6 | 40.7 ± 9.8* | 53.8 ± 4.0* | 82.0 (74.0, 140) | 0.14 (0.04, 0.54) | 0.06 (0.02, >1.0) |

* $p \leq 0.05$

Note: All comparisons were performed relative to the DVH of the originally acquired slice thickness at 5 mm.

*Phys Med Biol*. Author manuscript; available in PMC 2016 March 10.

**Table 2**

Averaged values from the AUH cohort for volume, maximum dose, mean dose, *gEUD*, and the best-fitting LKB model parameters obtained from simulations of various slice thicknesses for the rectum and rectal wall.

| AUH cohort Slice thickness (mm) | Structure | Volume ± SD ($cm^3$) | Max dose ± SD (Gy) | Mean dose ± SD (Gy) | *gEUD* (*a*=4.3) ± SD (Gy) | *D50* (95%CI) | *LKB* *m* (95%Cl) | *n* (95%Cl) |
|---|---|---|---|---|---|---|---|---|
| 3 (*Ref.*) | Rectum | 93.9 ± 42.4 | 75.9 ± 1.6 | 43.1 ± 7.0 | 54.2 ± 3.9 | 76.0 (70.0, 140) | 0.06 (0.04, 0.52) | 0.02 (0.02, > 1.0) |
| | Rectal wall | 44.9 ± 14.6 | 75.8 ± 1.6 | 40.9 ± 6.7 | 53.9 ± 3.5 | 74.0 (66.0, 140) | 0.06 (0.04, 0.54) | 0.04 (0.02, >1.0) |
| 5 | Rectum | 95.3 ± 43.0 | 75.6 ± 1.6 | 42.5 ± 7.0 | 54.0 ± 3.9 | 76.0 (70.0, 140) | 0.06 (0.04, 0.52) | 0.02 (0.02, >1.0) |
| | Rectal wall | 46.3 ± 15.0 | 75.5 ± 1.7 | 39.9 ± 6.9 | 53.5 ± 3.6 | 74.0 (64.0, 140) | 0.06 (0.04, 0.54) | 0.06 (0.02, >1.0) |
| 7 | Rectum | 96.5 ± 43.3 | 75.6 ± 1.6 | 42.1 ±7.0 | 53.9 ± 3.9 | 76.0 (70.0, 140) | 0.06 (0.04, 0.54) | 0.02 (0.02, >1.0) |
| | Rectal wall | 47.8 ± 16.1 | 75.5 ± 1.6 | 39.1 ± 6.9* | 53.2 ± 3.6 | 76.0 (66.0, 140) | 0.8 (0.04, 0.56) | 0.04 (0.02, >1.0) |
| 9 | Rectum | 97.5 ± 43.6 | 75.4 ± 1.6* | 41.9 ± 7.0 | 53.7 ± 4.0 | 76.0 (70.0, 140) | 0.06 (0.04, 0.52) | 0.02 (0.02, >1.0) |
| | Rectal wall | 49.3 ± 16.4* | 75.4 ± 1.6* | 38.4 ± 7.2* | 52.9 ± 3.7* | 76.0 (66.0, 140) | 0.08 (0.04, 0.54) | 0.04 (0.02, >1.0) |
| 11 | Rectum | 98.9 ± 44.6 | 75.2 ± 1.6* | 41.4 ± 6.9* | 53.5 ± 3.9 | 76.0 (72.0, 140) | 0.06 (0.04, 0.52) | 0.02 (0.02, >1.0) |
| | Rectal wall | 51.2 ± 17.9* | 75.1 ± 1.6* | 37.4 ± 7.0* | 52.4 ± 3.6* | 82.0 (68.0, 140) | 0.10 (0.04, 0.56) | 0.02 (0.02, >1.0) |
| 13 | Rectum | 100.1 ± 44.4 | 75.1 ± 1.6* | 41.8 ± 6.8* | 53.4 ± 3.9 | 76.0 (68.0, 140) | 0.06 (0.04, 0.52) | 0.02 (0.02, >1.0) |
| | Rectal wall | 53.0 ±18.0* | 75.0 ± 1.7* | 36.7 ± 7.1* | 52.0 ± 3.7* | 76.0 (64.0, 140) | 0.10 (0.04, 0.54) | 0.06 (0.02, >1.0) |

*$p \leq 0.05$

Note: All comparisons were performed relative to the DVH of the originally acquired slice thickness at 3 mm.

**Table 3**

*gEUD* at ROC cut-off points corresponding to the leftmost corner point of the ROC curve for various slice thicknesses in the BCCA and AUH cohorts.

| | Slice thickness (mm) | *a* | 3 | 5 | 7 | 9 | 11 | 13 | Δ | % |
|---|---|---|---|---|---|---|---|---|---|---|
| Rectum | *BCCA cohort* | 12.5 | 64.4 | 64.3 | 64.6 | 66.1 | 63.5 | 63.8 | 2.6 | 4.0 |
| | | 11.1 | 63.7 | 63.6 | 63.5 | 65.5 | 61.9 | 62.8 | 3.5 | 5.6 |
| | | 4.3 | 56.4 | 56.4 | 56.1 | 53.3 | 53.9 | 53.1 | 3.3 | 5.8 |
| | *AUH cohort* | 12.5 | 62.1 | 62.0 | 62.2 | 62.2 | 61.8 | 62.0 | 0.4 | 0.7 |
| | | 11.1 | 61.3 | 61.5 | 62.0 | 61.3 | 61.2 | 61.0 | 1.0 | 1.6 |
| | | 4.3 | 54.9 | 54.8 | 54.8 | 54.8 | 54.3 | 54.0 | 0.9 | 1.6 |
| Rectal wall | *BCCA cohort* | 12.5 | 64.6 | 64.5 | 64.1 | 63.8 | 63.5 | 63.3 | 1.2 | 1.9 |
| | | 11.1 | 64.1 | 63.6 | 63.3 | 63.1 | 62.5 | 63.3 | 1.6 | 2.5 |
| | | 4.3 | 55.9 | 55.9 | 55.2 | 55.1 | 54.3 | 53.1 | 2.8 | 5.0 |
| | *AUH cohort* | 12.5 | 63.2 | 63.2 | 62.8 | 63.2 | 62.7 | 62.4 | 0.8 | 1.3 |
| | | 11.1 | 62.3 | 62.2 | 62.2 | 62.2 | 61.9 | 61.5 | 0.8 | 1.2 |
| | | 4.3 | 54.5 | 54.0 | 53.8 | 53.8 | 52.9 | 52.2 | 2.3 | 4.2 |

Δ denotes the maximum difference in *gEUD* between all slice thickness for a particular *n*-value, % denotes Δ normalized to the *gEUD* of the original slice thickness (5 mm in BCCA and 3 mm in AUH)