COMPARISON OF DOSE STATS FOR BLADDER WALL AND RECTUM WALL VS. WHOLE ORGANS FOR VMAT PROSTATE RT

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DISCLOSURE

In relation to this presentation, I declare no conflicts of interest
LEARNER OUTCOMES

1) Walled vs. solid structure contours for hollow organs

2) 2D (slice-by-slice) vs 3D cropping tools for generating walled structure contours

3) Correlations between dose statistics for walled and solid rectum and bladder, and how this can be used to translate dose constraints between walled and solid structures

INTRODUCTION

- 2003: Cégep de Ste-Foy (Québec, Canada), 2003
- 2003: Radiation therapist at the Cross Cancer Institute, Edmonton
- 2008: Started as dosimetrist
- 2011: CMD certification
HYPOFRACTIONATED RT FOR INTERMEDIATE RISK PROSTATE CA

- Edmonton: Standard of care fractionation for IR prostate CA = 78 Gy/39
  - Originally 4f technique, then 7f IMRT, now 1 or 2 arc VMAT

- 2007: joined hypofractionated OCOG (Ontario Clinical Oncology Group) trial - PROFIT: PROstate Fractionated Irradiation Trial.

PROFIT

- PROFIT trial: can a shorter course of RT safely replace 78/39 for IR prostate cancer?

- Study regimen = 60 Gy/20 fractions
  - Reduces patient visits by 19
  - Benefits patient
  - Reduces linac workload
WALL STRUCTURES

- PROFIT constraints specified to the rectal wall and to the bladder wall
- Wall structures are intuitive for hollow organs like the rectum and the bladder
  - Dose given inside the walls may not be radiobiologically significant
- Downsides:
  - Wall structures sampling can be very small
  - DVHs may not be as accurate
  - Common dose constraints are set for full structures

CREATION OF WALL STRUCTURE

- 2007: contouring tools let us create wall structures in a 2D manner
  - Dosimetrist would manually create a 3 mm wall on each transverse slice
2D WALL

- 2D wall structure as created from transverse slice only
- Creates “chopping” effect (red arrows)

3D WALL

- Today: contouring tools can create wall structure automatically with true 3D expansion
18MM WALLED STRUCTURES

- The PROFIT trial asks that the wall structures are limited to 18 mm sup and inf to the CTV.

PROFIT RESULTS

- PROFIT: hypofractionated RT (60 Gy / 20 f) was not inferior to conventional RT
  - 5-year disease-free survival = 85% (both arms)
  - No significant differences in GU or GI toxicity
- Hypofractionated RT is more convenient and should be considered for IR prostate ca

*Catton et. al., Journal of Clinical Oncology (2017)*
NEW STANDARD OF CARE

- 2017: After positive results from the trial, hypofractionated regimen would become a standard of care for IR prostate Ca at our institution.

- This is the only occasion we use wall structures and structures limited to a certain extent.
PROJECT PURPOSE

• Statistical relationship: walled vs. full structure for both the bladder and the rectum?
  • (when using VMAT for IR prostate ca.)

• Correlation affected by using 2D or 3D contouring?

• Affected if the structure is fully contoured or limited to a specified extent?
  • (18 mm sup/inf as per trial)
  • Affected by hypofractionated regimen or a standard fractionated regimen?

SIMILAR PAST PROJECT

• Garcia-Vicente & al. (2005):
  • correlation between rectum and rectum wall DVH with 3D-CRT
  • Argued that wall structure not needed for about 90% of cases

• This work: extends similar analysis:
  • Both rectum and bladder wall
  • Using VMAT (not 3D CRT)
COLLECTION OF DATA

- 10 cases
- 2 plans/case:
  - 60 Gy / 20 f
  - 78 Gy / 39 f
- Varian Eclipse v.13.6
- 0.25 cm calculation grid size
- Acuros_13623
- VMAT, 2 arcs
- Normalization: 100% of the total dose to cover 95% of the PTV
- Clinical protocol created to collect accurate data

OPTIMIZATION DETAILS

- Used NTO (normal tissue objective)
- Used Automatic sparing of normal tissue
- Started with these priorities and adjusted if needed:
  - NTO 150
  - OAR 80
  - PTV 120
CONTOURING

- Prostate, Seminal vesicles, CTV & PTV
- Femurs
- Bladder, bladder 18 mm, bladder wall, bladder wall 3D, bladder wall full 2D, bladder wall full 3D
- Rectum, rectum 18 mm, rectum wall, rectum wall 3D, rectum wall full 2D, rectum wall full 3D
- ‘Opt’ structures

PRESENTATION OF DATA

- 3 different scenarios to analyze:
  - 1) Standard fractionation with standard contouring, using Lawton’s constraints
  - 2) PROFIT hypofractionation dose with the full length contouring of the OAR
  - 3) PROFIT hypofractionation with the contouring of OAR limited to 18 mm sup-inf the CTV (exactly as per PROFIT)
STATISTICS

• What statistical question do we need to answer?

How are walled structure and solid structure dose statistics related?

STATISTICS

• Example: V50Gy, Dmax, etc.
• Correlation – interdependence of two variables
  • Eg. Dmax (wall) vs. Dmax (solid)

Strongly correlated data

Poorly correlated data
CORRELATION

- Correlation may be linear or non-linear
- Different tests may be used to generate a correlation coefficient

![Linear correlation](image1)
![Non-linear correlation (monotonic)](image2)

CORRELATION COEFFICIENT

- Pearson’s correlation: goodness of linear fit
- Spearman’s correlation: “non-parametric rank-order” test

![Pearson = 1.0
Spearman = 1.0](image3)
![Pearson = 0.85
Spearman = 1.0](image4)
CORRELATION COEFFICIENT

• Pearson’s correlation requires a set of assumptions of the data to be made

• Spearman’s is more widely applicable, and in our case (n = 10), is the appropriate test

TEST FOR SIGNIFICANCE

• Is our Spearman coefficient statistically different than zero (ie. data not correlated)?

• Generate p-value
  • Percent chance that a random data set of equal size could generate equivalent correlation (or stronger)
TEST FOR SIGNIFICANCE

• Statistical analysis performed by faculty biostatistician (S. Ghosh)
• Calculations used SPSS statistics software (v. 19)

SCENARIO 1: 78 GY/39 FRACTIONS

• Lawtons' Constraints:
  • Rectum: V50Gy ≤ 50%, V70Gy ≤ 20%
  • Bladder: V55Gy ≤ 50%, V70Gy ≤ 30%

• Data collected:
  • Rectum wall 2D, Rectum wall 3D & Rectum:
    D50, D20, V50Gy, V70Gy, Mean, Max
  • Bladder wall 2D, Bladder wall 3D & Bladder:
    D30, D50, V70Gy, V55Gy, Mean, Max
RESULTS SCENARIO 1:
2D WALL RECTUM V50GY

RESULTS SCENARIO 1:
3D WALL RECTUM V50GY
RESULTS SCENARIO 1: 2D WALL BLADDER V55GY

- Wall Structure V55 (%)
- Solid Structure V55 (%)

Spearman R = 0.833
2 tailed p = 0.003

RESULTS SCENARIO 1: 3D WALL BLADDER V55GY

- Wall Structure V55 (%)
- Solid Structure V55 (%)

Spearman R = 0.988
2 tailed p = <0.001
RESULTS SCENARIO 1: 3D WALL BLADDER MAX

<table>
<thead>
<tr>
<th>Wall Structure Dmax (cGy)</th>
<th>Solid Structure Dmax (cGy)</th>
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<tbody>
<tr>
<td>8200</td>
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</table>

Bladder Dmax
Linear (Bladder Dmax)

Spearman R = 0.673
2 tailed p = 0.033

RESULTS FOR CONVENTIONAL FRACTIONATION REGIMEN (78 GY/39):

• All points generally strong correlation
  • Spearman’s R > 0.80 (p < 0.01)

• Exception = bladder Max dose: medium correlation
  • Spearman’s R = 0.67 (p = 0.03)

• 3D wall correlation to the full structure is better than the 2D wall.

• When D values compared to corresponding V values, both showed a 2 tailed p value <0.001.
SCENARIO 1: V70 BLADDER

- Dmax correlation was not strong.
- Use V70 as Dmax alternative
- 3D wall contouring more correlated than 2D (R = 0.969 vs R = 0.759)

SCENARIO 2: DOSE AS PER PROFIT (60GY/20), STANDARD CONTOURING (STRUCTURE FULL LENGTH)

- Focus on 3D wall structures

- PROFIT dose constraints are
  
  Rectum wall \[ D_{30} \leq 46 \text{Gy} \] \[ D_{50} \leq 37 \text{ Gy} \]
  Bladder wall \[ D_{30} \leq 46 \text{Gy} \] \[ D_{50} \leq 37 \text{ Gy} \]
RESULTS SCENARIO 2:
3D RECTUM WALL D30

![Graph showing the relationship between Wall Structure 3D D30 and Solid Structure D30. The graph includes a linear regression line and a Spearman correlation coefficient of 0.964, with a 2-tailed p-value < 0.001.]

RESULTS SCENARIO 2:
3D RECTUM WALL MAX DOSE

![Graph showing the relationship between Wall Structure 3D Dmax and Solid Structure Dmax. The graph includes a linear regression line and a Spearman correlation coefficient of 0.976, with a 2-tailed p-value < 0.001.]

RESULTS SCENARIO 2:
3D BLADDER WALL D30

![Graph showing the relationship between Wall Structure 3D D30 (cGy) and Solid Structure D30 (cGy). The graph includes data points and a linear trend line. Spearman R = 0.976, 2-tailed p < 0.001.]

RESULTS SCENARIO 2:
3D BLADDER WALL MAX DOSE

![Graph showing the relationship between Wall Structure 3D Dmax (cGy) and Solid Structure Dmax (cGy). The graph includes data points and a linear trend line. Spearman R = 0.681, 2-tailed p = 0.030.]

RESULTS HYPOFRACTIONATED
WE LEARN …

• Strong correlations between 3D wall and solid structure dose statistics
  • Similar result to standard fractionation
  • Bladder max dose is an exception

• Bladder wall contour is necessary to know true max dose to organ

SCENARIO 3: DOSE AND CONTOURING AS PER PROFIT

• 60 Gy / 20 fractions

• Same dose constraints as before

• Contouring: Bladder & rectum walls: only extend 18 mm sup and inf from CTV

• Concentrates the information where it matters the most
RESULTS SCENARIO 3: 3D RECTUM WALL D30

Spearman R = 0.939
2 tailed p=<0.001

RESULTS SCENARIO 3: 3D BLADDER WALL D30

Spearman R = 0.564
2 tailed p=0.090
RESULTS HYPOFRACTIONATED, LIMITED EXTENT CONTOURING

- Correlations are still strong for the rectum wall, as with previous scenarios (high R, low p)

- Correlations are poor for the bladder wall
  - D30 BW R=0.564  p= 0.090
  - D50 BW R=0.612  p= 0.060

- 3D 18 mm bladder wall potentially most clinically relevant OAR
  - bladder area where the most toxicity is expected
  - low correlation: to accurately assess dose here, it needs to be contoured

TRANSLATING FULL STRUCTURE CONSTRAINTS TO WALL CONSTRAINTS

- Example: How does V55 Gy (full) = ? (wall)
- Good correlation does NOT mean full = structure

- If linear, can use \( y = mx + b \) formula
  - \( m \) = slope, \( b \) = intercept
  - (generate using best-fit)

- \( y \) = wall tolerance
- \( x \) = solid tolerance

\[
y = 0.95x + 0.06
\]
EXAMPLE

• Linear fit equation $y = 0.95x + 0.06$
• $Y = V_{55}$ Gy wall tolerance (%)
• $X = V_{55}$ Gy solid bladder tolerance (%)
  • Lawton assumes $V_{55} < 50$

• Insert into equation gives:
  $V_{55,\text{wall}} < 54$

EXAMPLE

• Other conventional solid structure constrains can be translated
• Examples from this work:

<table>
<thead>
<tr>
<th></th>
<th>Lawton Constraint</th>
<th>Translated Constraint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full Structure</td>
<td>3D Wall Structure</td>
</tr>
<tr>
<td>Rectum</td>
<td>$V_{50}$ Gy</td>
<td>$&lt; 50%$</td>
</tr>
<tr>
<td></td>
<td>$V_{70}$ Gy</td>
<td>$&lt; 20%$</td>
</tr>
<tr>
<td>Bladder</td>
<td>$V_{55}$ Gy</td>
<td>$&lt; 50%$</td>
</tr>
<tr>
<td></td>
<td>$V_{70}$ Gy</td>
<td>$&lt; 30%$</td>
</tr>
</tbody>
</table>
EXAMPLE 2: RECTAL WALL D30

- Linear fit equation $y = 1.09x + 153$
- $y = D30\%$ wall tolerance (cGy)
- $x = D30\%$ solid rectum tolerance (cGy)
  - PROFIT Study: $D30\% < 4600$ cGy

- Rearrange for $x$:
  $x = (y - 153)/1.09$

Solid $D30 < 4080$ cGy

EXAMPLE 2

- Convert wall constraints from PROFIT to equivalent solid constraints
- Rectum examples (poor bladder correlation)

<table>
<thead>
<tr>
<th></th>
<th>PROFIT Constraint</th>
<th>Translated Constraint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wall Structure (18 mm S-I of CTV)</td>
<td>Solid Structure</td>
<td></td>
</tr>
<tr>
<td>Rectum $D30$ (cGy)</td>
<td>$&lt; 4600$ cGy</td>
<td>$&lt; 4080$ cGy</td>
</tr>
<tr>
<td>Rectum $D50$ (cGy)</td>
<td>$&lt; 3700$ cGy</td>
<td>$&lt; 3470$ cGy</td>
</tr>
</tbody>
</table>
BUT!

• Pearson’s: goodness of linear fit
• Spearman’s correlation: “rank-order” test

![Graphs showing Pearson and Spearman correlations]

CAREFUL!

• Pearson correlation high for many constraints
  • Need more cases to justify statistics

• If not linearly correlated (p > 0.05):
  • Direct translation may be difficult
  • Look to trial results for new tolerances?
CONCLUSIONS FROM PROJECT.
USING VMAT FOR IR PROSTATE CA:

• Strong statistical relationship between rectum wall and rectum, for all 3 scenarios.

• Strong statistical relationship between bladder wall and bladder, for conventional fractionation and hypofractionation with regular extent contouring.

• 3D contouring is much more correlated than 2D

• Fractionation scheme doesn’t affect correlation

• D based values or V based values don’t affect correlation

• Extent of contouring affects the correlation between bladder wall and bladder
POSSIBLE CHANGE OF PRACTICE

• Rectum wall structure for hypofractionated regimen could be replaced by rectum using translated dose constraint

• Bladder wall structure is required to know true max dose

FUTURE WORK

• Increase case number

• Confirm validity of translated constraints
RECOMMENDATIONS

• Bladder wall contouring should be considered for assessing toxicity in clinical trials

• Walled structures: use high resolution contours and small calc grid (0.125 cm)

• If using wall structure, 3D contouring is the more accurate way.

ACKNOWLEDGEMENTS

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  • L. Kellogg, MRT(T), CMD
QUESTIONS? COMMENTS?

Ouf!!! I'm Done!
THANKS!

BIBLIOGRAPHY


