Effect of a Hydrogel Spacer on Achievable Rectal DVH for IMRT in Prostate Cancer

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Disclosure

• Augmenix, Inc. - Core Laboratory Service Contract
  – W. Bosch
  – J. Michalski
  – W. Straube

• Augmenix Clinical Trial Support
  – N. Mariados – minor investment in Augmenix, Inc.
  – J. Sylvester – consulting for Augmenix, Inc.
  – D. Shah
  – S. Kurtzman
  – S. Zimberg
Background

- Implanted tissue spacers show promise in reducing radiation dose to organs at risk and/or permitting dose escalation to target volumes.
- The dosimetric effect of an absorbable hydrogel peri-rectal spacer for reducing rectal dose during treatment of prostate cancer was evaluated in a randomized trial by comparing plan dosimetry.
  - Pre- and post-implant plans in the same patient
  - Implanted and control subjects
- Significant reduction in rectal dose was demonstrated despite inherent variations in plan optimization.
Purpose

The purpose of this analysis was to confirm the reduction in rectal dose shown in the pivotal trial. A validated prostate DVH prediction model, trained with high-quality clinical prostate plans, was used to compute achievable DVHs based on patient geometry for datasets planned with and without tissue spacer.
Hydrogel Spacer

- Imaging and treatment planning for men undergoing IMRT for localized stage T1-T2 prostate cancer was performed both before and after hydrogel spacer implantation between the prostate and anterior rectum.

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
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<tbody>
<tr>
<td>Average peri-rectal space</td>
<td>1.6 ± 2.2 mm</td>
<td>11.8 ± 4.8 mm</td>
</tr>
</tbody>
</table>
Treatment Planning and QA

• Each patient had two sets of images (CT, MR) and two treatment plans.
• MR images were rigidly registered to planning CTs to assist in segmentation of prostate and seminal vesicles, rectum, bladder, and penile bulb.
• Pre- and post-implant plans were independently optimized to deliver 79.2 Gy to the CTV and to satisfy dose-volume constraints for rectum, bladder, and penile bulb.
• Re-contouring of prostate, rectum and bladder by core lab physicians and evaluation of submitted plan dosimetry were used to assure consistency of pre- and post-implant plans.
DVH Model

A Knowledge-Based Planning approach was used to predict achievable DVHs based on patient geometry.

1. OAR voxels are grouped into “bands” based on their minimum distance to the target volume.

2. For each band of OAR voxels, a sub-DVH is computed using a model with parameters fit to a clinical training set.

3. Sub-DVHs are combined to produce the predicted DVH for the OAR.

Predicted DVHs

- Predicted DVHs represent achievable, well-optimized plans.
- Clinical plans varied from slightly better to somewhat less well-optimized.
Results

- Predicted DVHs were computed for pre- and post-implant datasets for 101 peri-rectal spacer patients at five clinical sites.
- Predicted rectal volumes receiving at least $x$ Gy ($V_x$) were consistent with clinical $V_x$ for both pre- and post-implant treatment plans.
- Spearman rank correlation coefficients comparing clinical and predicted $V_x$ values were all significantly positive ($p<0.0001$)
Reduction in Rectal V60, V70

- For each patient, the difference between pre-implant and post-implant rectal Vx was computed.
- Predicted DVHs confirm clinical reduction of V60 and V70 with hydrogel spacer.
- Spearman correlations comparing pre- and post-implant differences in V60 and V70 were significantly positive (p<0.0001).

<table>
<thead>
<tr>
<th></th>
<th>V60pre – V60post</th>
<th>V70pre – V70post</th>
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<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td>6.4 ± 4.3 cc</td>
<td>5.0 ± 2.9 cc</td>
</tr>
<tr>
<td><strong>Predicted</strong></td>
<td>5.6 ± 3.7 cc</td>
<td>4.2 ± 2.6 cc</td>
</tr>
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</table>
Results by Treating Site

- Agreement between predicted and clinical DVH values was better for some sites than others and appears to reflect the degree of plan optimization.
- Best correlation between clinical and predicted DVHs was for sites with mean clinical V70 < mean predicted V70.

Spearman correlation coefficients between clinical and predicted V70

<table>
<thead>
<tr>
<th>Site</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>0.640</td>
<td>0.818</td>
<td>0.588</td>
<td>0.926</td>
<td>0.956</td>
</tr>
<tr>
<td>Post</td>
<td>0.754</td>
<td>0.887</td>
<td>0.897</td>
<td>0.974</td>
<td>0.982</td>
</tr>
<tr>
<td>Pre-Post</td>
<td>0.754</td>
<td>0.871</td>
<td>0.600</td>
<td>0.959</td>
<td>0.981</td>
</tr>
</tbody>
</table>
Discussion: DVH Comparison

• DVHs are used to measure the efficacy of the peri-rectal spacer in reducing rectal dose.
• DVHs are also affected by
  – Plan optimization (planning technique)
  – Segmentation (extent of rectal contour)
• A knowledge-based planning approach was used to predict achievable DVHs based on patient geometry.
• Use of absolute DVH metrics mitigates variability due to differences in segmentation.
Conclusion

- A knowledge-based planning DVH model was used to obtain a consistent, objective assessment of the dosimetric benefit of a hydrogel peri-rectal spacer for prostate IMRT.
- Predicted DVHs showed reductions in V60 and V70 consistent with results of the regulatory trial in this subset of patients.
- An indication of differences in the quality of treatment planning was seen in the degree of agreement between clinical and predicted DVHs.
- A reduction in rectal dose was seen even for less well-optimized plans.
- DVH prediction models, such as the one used in this analysis, may prove useful in assessing plan quality in multi-institution trials.
Thank you.