A Survey of the ITC Volumetric Treatment Planning Data Archive Supporting RTOG Advanced Technology Clinical Trials

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Abstract

**Purpose:** Survey of volumetric treatment planning (TP) data, linked to outcomes, collected by the Image-guided Therapy QA Center (ITC) in 15 years of facilitating QA review for RTOG multi-institutional advanced technology (AT) clinical trials.

**Materials & Methods:** The ITC as part of the Advanced Technology QA Consortium (ATC) collects volumetric TP data sets linked to outcomes for RTOG Advanced Technology clinical trials. CT images, target-volume/organ-at-risk contours, and 3-D dose distributions exported from commercial TP systems are submitted to the ITC using either DICOM or RTOG Data Exchange format. ITC staff evaluates dataset integrity and completeness, and requests re-submission as needed. Dose-Volume Histograms (DVHs) for required volumes are recalculated from submitted contours and dose distributions. RTOG dosimetrists and study chairs review contours and dose distributions for protocol compliance using ITC’s web-based Remote Review Tool (RRT). Clinical outcomes are reported to RTOG headquarters using protocol-specific forms.

**Results:** The ITC has collected over 5000 complete TP data sets quantifying the relationship between image-based anatomy and planned doses. Disease sites treated in the 10 closed protocols (1800 cases) include prostate, lung, brain, head/neck, and breast. An additional 13 active protocols (>3500 cases) also include liver, cervix, and anus. A sample of data sets available for analysis is listed below. (Doses (Gy) and % volumes are the minimum/maximum/average values.)

- **Prostate** (3DCRT, N=984; PTV D98: 52.2/81.6/75.0, bladder Dmean: 4.9, 75.9, 37.7, rectum Dmean: 12.9, 72.5, 42.7, femoral heads Dmean: 1.8, 49.5, 32.4),
- **Head&Neck** (IMRT, N=64 ; PTV D98: 58.0/73.4/67.6, spinal cord D2: 32.8/44.8/39.6, parotid Dmean: 21.2/50.3/32.4, larynx Dmean: 3.9/57.7/32.9),
- **Lung** (3DCRT, N=158; PTV D98: 50.3/98.2/77.4, spinal cord D2: 0.1/60.1/26.0, esophagus Dmean: 0/63.8/15.9, heart Dmean: 0/45.3/10.5, liver Dmean: 0/19.3/1.2, brachial plexus Dmean: 0/57.7/4.6, lung V20: 5.3/46.6/21.2 %),

The ITC has provided access to these TP protocol data sets for secondary analysis by: (1) export of entire TP data sets as RTOG data exchange files and (2) online data analysis using the RRT. External investigators have used these data for dose escalation trials in prostate (RTOG 9406) and lung cancer (RTOG 9311) and obtained two NIH R01 grants focused on the development of normal tissue complication probability (NTCP) models. Also, online access to RTOG 9406 TP data has been used to analyze erectile dysfunction following 3DCRT for prostate cancer. Using the contour editing feature in the RRT, penile bulb structures, not originally contoured for RTOG 9406, were delineated on these datasets. New DVHs were computed from the stored 3D dose distributions and compared with reported clinical outcomes (impotence). Such an analysis would have required an entirely new study if the volumetric TP data had not been archived in the ITC database.

**Conclusion:** The ITC archive of volumetric images and dosimetry for RTOG Advanced Technology Clinical Trials is a rich resource for developing and testing models of tissue response to ionizing radiation. The value of this archive continues to grow with the incorporation of new data sets from new anatomical sites, and new imaging modalities.

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Data Collection and Quality Assurance for RTOG Advanced Technology Clinical Trials

The Image Guided Therapy QA Center (ITC), as part of the Advanced Technology QA Consortium (ATC), collects volumetric treatment planning (TP) data sets linked to outcomes for RTOG Advanced Technology clinical trials.

- CT images, target-volume/organ-at-risk contours, and 3-D dose distributions exported from commercial TP systems are submitted to the ITC using either DICOM or RTOG Data Exchange format.
- ITC staff evaluates *dataset integrity and completeness*, and requests re-submission as needed. Dose-Volume Histograms (DVHs) for required volumes are recalculated from submitted contours and dose distributions.
- RTOG dosimetrists and study chairs review contours and dose distributions for *protocol compliance* using ITC’s web-based Remote Review Tool (see screen images below).
- *Clinical outcomes* are reported to RTOG headquarters using protocol-specific forms.
- Dose-volume statistics, computed at ITC from structure contours and 3D Dose distributions, are analyzed with respect to protocol endpoints by RTOG statisticians.
- Volumetric treatment planning data sets are archived for retrospective analysis.
QuASA²R: Quality Assurance Submission, Archive, Analysis, and Review System

The QuASA²R information infrastructure is used to collect, archive, review and analyze volumetric treatment planning (TP) data sets for RTOG Advanced Technology clinical trials. The components of this system are shown in the diagram below.

- Arrows indicate the flow of data from participating institutions, where data are exported from treatment planning systems using the RTOG Data Exchange or DICOM format.
- At the ITC, submitted data are received and imported to prepare them for Quality Assurance Review.
- The data undergo an analysis process referred to as “Data Integrity QA”.
- The protocol case datasets are made available for external protocol compliance review by study chairs and QA center personnel using both thin- and thick-client applications.
- The system also includes several mechanisms for sharing protocol data for secondary analysis, once the QA process is complete.
RESULTS: Digital DataSubmitted to ITC

Over the past 14 years, more than 5000 complete treatment planning (TP) data sets have been submitted to the ITC by institutions participating in RTOG Advanced-Technology Trials. The chart below shows the annual accrual of protocols cases for these studies.
The ITC QuASA²R Archive includes over 5000 complete TP data sets quantifying the relationship between image-based anatomy and planned doses. Each dataset includes treatment planning CTs, target-volume/organs-at-risk contours, and 3D dose distributions. Treatment plans are available for 3DCRT and brachytherapy seeds.

Disease sites treated on 10 closed protocols (1800 cases) include prostate, lung, brain, head/neck, and breast. 13 active protocols (>3500 cases) also include liver, cervix, and anus. The table below outlines the data acquired for each protocol.
ITC QuASA²R Digital Data Archive

For each protocol case, the following data objects are stored. ITC performs Digital Data Integrity QA to ensure the spatial registration, consistent labeling, and proper scaling of these objects.

- **Volumetric CT images**
  - Define patient coordinate system
  - Protocol-compliant extent and slice spacing

- **Structure Set**
  - Axial slice contours
  - Protocol-compliant names for targets, organs-at-risk
  - PTVs may include organs-at-risk (i.e., a voxel may belong to both a PTV and an OAR)

- **Treatment Plan (3DCRT and Brachy seeds)**
  - Beam geometry and weighting (3DCRT)
  - Source locations and strengths (seed brachytherapy)

- **3-D Dose Distribution**
  - Absolute dose (Gy)
  - Per fraction group
  - Fractionation available from treatment record for most protocols.
RESULTS: Sample Dose Volume Statistics

Collection of volumetric dosimetry data has enabled RTOG investigators to perform quality assurance to maintain the consistency of target volumes and organs at risk, allowing meaningful comparison on dose-volume statistics for advanced-technology trials. Having 3-D geometric data for structures has also made it possible to evaluate the size of margins used in treating patients. Sample dose-volume statistics for several data sets are shown at right.

<table>
<thead>
<tr>
<th>Head &amp; Neck (IMRT, N=64)</th>
<th>Min</th>
<th>Max</th>
<th>Avg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>D_{98}</td>
<td>58.0</td>
<td>73.4</td>
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<tr>
<td>Spinal Cord</td>
<td>D_{mean}</td>
<td>32.8</td>
<td>44.8</td>
</tr>
<tr>
<td>Parotid</td>
<td>D_{mean}</td>
<td>21.2</td>
<td>50.3</td>
</tr>
<tr>
<td>Larynx</td>
<td>D_{mean}</td>
<td>3.9</td>
<td>57.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lung (3DCRT, N=158)</th>
<th>Min</th>
<th>Max</th>
<th>Avg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>D_{98}</td>
<td>50.3</td>
<td>98.2</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>D_{2}</td>
<td>0.1</td>
<td>60.1</td>
</tr>
<tr>
<td>Esophagus</td>
<td>D_{mean}</td>
<td>0.0</td>
<td>63.8</td>
</tr>
<tr>
<td>Heart</td>
<td>D_{mean}</td>
<td>0.0</td>
<td>45.3</td>
</tr>
<tr>
<td>Liver</td>
<td>D_{mean}</td>
<td>0.0</td>
<td>19.3</td>
</tr>
<tr>
<td>Brachial Plexus</td>
<td>D_{mean}</td>
<td>0.0</td>
<td>57.7</td>
</tr>
<tr>
<td>Lung</td>
<td>V_{20}</td>
<td>5.3</td>
<td>46.6</td>
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</table>

<table>
<thead>
<tr>
<th>Prostate (3DCRT, N=984)</th>
<th>Min</th>
<th>Max</th>
<th>Avg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>D_{98}</td>
<td>52.2</td>
<td>81.6</td>
</tr>
<tr>
<td>Bladder</td>
<td>D_{mean}</td>
<td>4.9</td>
<td>75.9</td>
</tr>
<tr>
<td>Rectum</td>
<td>D_{mean}</td>
<td>12.9</td>
<td>72.5</td>
</tr>
<tr>
<td>Femoral Heads</td>
<td>D_{mean}</td>
<td>1.8</td>
<td>49.5</td>
</tr>
</tbody>
</table>
Analysis of Volumetric Dosimetry Data in the ITC Archive

In addition to supporting protocol compliance QA and outcomes analysis for RTOG protocols, the ITC has also provided access to these TP protocol data sets for secondary analysis by: (1) export of entire TP data sets as RTOG data exchange files and (2) online data analysis using the RRT. External investigators have used these data for dose escalation trials in prostate (RTOG 9406) and lung cancer (RTOG 9311) and obtained two NIH R01 grants focused on the development of normal tissue complication probability (NTCP) models. Also, online access to RTOG 9406 TP data has been used to analyze erectile dysfunction following 3DCRT for prostate cancer. Using the contour editing feature in the RRT, penile bulb structures, not originally contoured for RTOG 9406, were delineated on these datasets. New DVHs were computed from the stored 3D dose distributions and compared with reported clinical outcomes (impotence). Such an analysis would have required an entirely new study if the volumetric TP data had not been archived in the ITC database.

As a participant in the Cancer Bio-Informatics Grid (caBIG) In Vivo Imaging Workspace, the ITC has contributed TP data sets from RTOG Protocol 0522 to the National Cancer Imaging Archive (NCIA). Quantitative pre- and post-treatment PET images acquired for these patients on ACRIN Protocol 4500 are also being submitted to the NCIA repository by ACRIN to enable an evaluation of treatment response.
Secondary Analysis: Lung Toxicity (RTOG 9311)

- RTOG 9311 data were analyzed to investigate lung toxicity (radiation pneumonitis) as a function of dose-volume statistics, as well as the spatial coordinates of the gross tumor volume. Multi-institutional RTOG 9311 data were used to test a statistical model derived from single-institution (Washington University) dataset.

- This study showed that models tuned for each subset (WU or RTOG) did not perform well when applied to the other dataset. However, a model derived from the combined data performed well on each data subset. This exercise indicates the advantage in generating robust models based on multi-institutional datasets. [Bradley et al. 2007].

- Such an analysis would have required an entirely new study if the 3D treatment planning data had not been archived in the ITC QuASA²R database.

- The nomogram shown at right (from Bradley et al., 2007) displays the relationship between pneumonitis risk (requiring steroids or more intensive intervention) and the two most significant variables: Mean normal lung dose and relative position within the lung of the center of the high-dose region (0 = most inferior, 1 = most superior).

- Note that the importance of the position of the high dose region could not have been probed without the complete CT-based dataset.
RTOG 9406 data have been analyzed by Dr. Sue Tucker and colleagues to investigate rectal toxicity. The ITC has provided access to TP data for this protocol, and RTOG has provided clinical staging and outcome data for secondary analysis. Dr. Tucker was successful in obtaining an NIH R01 grant investigating the use of these data sets for developing normal tissue complication probability (NTCP) models. Results of this analysis are being presented at this meeting.
Secondary Analysis: GU Toxicity (RTOG 9406)

- RTOG 9406 data were analyzed to investigate GU toxicity (impotence) as a function of dose to Penile Bulb, a structure not originally delineated in the RTOG 9406 data. Online access to the RTOG 9406 TP data sets was provided to Dr. Mack Roach for an investigation of erectile dysfunction following 3D conformal RT for prostate cancer. Using the contour editing feature in the ITC Remote Review Tool, Dr. Roach retrospectively delineated penile bulb structures in RTOG 9406 datasets and new DVHs were computed from the 3D dose distributions archived for these patients and compared with reported clinical outcomes (impotence) [Roach 2004].

- This study showed that patients whose median penile dose was >52.5 Gy had a greater risk of impotence compared with those receiving <52.5 Gy ($p < 0.039$) and concluded that dose to the bulb of the penis seems to be associated with the risk of radiation-induced impotence. Such an analysis would have required an entirely new study if the volumetric TP data had not been archived in the ITC QuASA²R database.

- Figure at right shows an example of one case included in this study. Isodose lines for 6000, 5250, 4500, and 3500 cGy moving outward are shown. Penile bulb is also shown with a dotted line in the lower three panels.

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Discussion: Why Collect Volumetric Data?

The substantial effort required to acquire volumetric images and dosimetry data invites the question, “Why not just collect DVHs?”

1. The effect of radiation may vary depending on location within an organ (cf. panel 9). However, DVHs do not retain spatial information; only the aggregate volume of a structure at a given dose is counted.

2. Without volumetric data, it is not possible to detect and correct contouring inconsistencies.

3. Without volumetric data, it is not possible to compute dose statistics for volumes other than those in submitted DVHs.

4. Without volumetric data, it is difficult or impossible to determine which structures are included or excluded in a DVH (e.g., “LUNG – PTV” versus “LUNG – GTV”).

5. DVHs calculated using different commercial treatment planning systems have been shown to be inconsistent (Straube, et. al., Med Phys, 2005).

Different dose distributions throughout an organ may lead to different expectations of toxicity for some organs. However, DVH statistics do not distinguish between a single, large hot spot and multiple, smaller hot spots.
Summary and Conclusions

• The ITC QuASA²R archive has supported data integrity QA and protocol compliance QA for RTOG Advanced Technology Clinical Trials, enabling the acquisition of more than 5000 complete treatment planning datasets, evaluated for data integrity and protocol compliance, for outcomes analysis in these studies.

• The ITC archive has enabled secondary analysis of RTOG data sets by several investigators. Such investigations would have required new studies if the volumetric TP data had not been archived in the ITC database.

• Anonymized RTOG 0522 data are being made available to the National Cancer Imaging Archive with quantitative pre- and post-treatment PET images (from ACRIN) to enable a functional-imaging-based evaluation of treatment response.

• It is our intent to make anonymized data from other protocols available for secondary analysis via the NCI Cancer Bio-Informatics Grid (caBIG).

• The ITC QuASA²R archive of volumetric images and dosimetry for RTOG Advanced Technology Clinical Trials is a rich resource for developing and testing models of tissue response to ionizing radiation. The value of this archive continues to grow with the incorporation of new data sets from new anatomical sites and new imaging modalities.

• Investigators wishing to request access to ATC data sets should download Guidelines for Requests for ATC Data by Investigators on the ATC website Resources page (http://atc.wustl.edu/resources).
References and Acknowledgements


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