# Update on Digital Data Integrity Quality Assurance for Multi-Institutional Advanced Technology Clinical Trials

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## Abstract

**Purpose:** Report on that part of the cooperative group clinical trial quality assurance (QA) review process referred to as *Digital Data Integrity QA (DDIQA)*.

**Method and Materials**: Participants in advanced technology clinical trials supported by the Image-guided Therapy QA Center (ITC) must be able to submit 3D digital datasets (images, contours, and dose distributions) to the ITC. Protocol QA review responsibility has been divided between ITC (DDIQA review) and the cooperative group (CG) for *Protocol Compliance QA Review (PCQA)*. DDIQA consists of review of the completeness of protocol required elements, format, spatial registration, and data corruption. For consistency, structures are renamed and dose volume histograms are recalculated. Data are posted to the web-based *Remote Review Tool (RRT)* a component of the ITC's clinical trial QA system (called QuASA²R) for PCQA review, which includes compliance review of target volume and organ at risk contours as well as review of dose compliance by CG reviewers.

**Results:** ITC has over 14 years experience in receiving/processing over 7000 digital datasets submitted by institutions participating in advanced technology clinical trials. DDIQA metrics show that more than 25 % of submissions are problematic. Problems can be divided into three categories: (1) misunderstanding of protocol requirements, (2) misuse of treatment planning system (TPS) data export feature, and (3) updated TPS software whose data export feature is no longer compliant with QuASA²R requirements. The time and effort required to perform DDIQA and prepare a case for PCQA varies, depending on protocol complexity.

**Conclusion:** DDIQA has proven to be essential for QA of advanced technology clinical trials. Thus, total automation of data submission for rapid QA review of clinical trial datasets is not realistic at this time. Work is currently focused on developing tools that help ITC personnel perform DDIQA more efficiently.

## Introduction

The Image Guided Therapy Quality Assurance (QA) Center (ITC) has been accepting, processing and reviewing digital data submissions for support (QA and analysis) of advanced technology protocols for the past 14 years. For the past 9 years the ITC has been a part of the NIH funded Advanced Technology Consortium (ATC) which consists of national cooperative groups and QA centers. Over 7000 case data sets have been submitted and processed for review. For protocols supported by the ATC, institutions are required to submit the complete 3D treatment planning data set from their treatment planning system. Many of the commercial treatment planning systems in use have implemented digital data export in a standardized format (either DICOM or RTOG data exchange) that can be processed by the ITC and made available to reviewers via a web based Remote Review Tool (RRT) that allows the reviewer to assess the dose volume statistics and structures as planned by the institution and compare these to protocol guidelines. This **Protocol Compliance QA** and analysis requires **Digital Data Integrity QA** by the personnel at the ITC for completeness and integrity of the data. Often data does not come to the ITC in a reviewable form, and the ITC personnel must intervene and investigate issues that need resolution before the data can be processed and reviewed. Thus, at present, the submission and review of digital data is **not yet a totally automated process** and requires human intervention to make possible the review of a large number of the cases that are submitted to the ITC. The QA tools and procedures developed by the ITC have made practical the processing of large amounts of protocol data for review and analysis. Nevertheless, the receipt of reviewable digital data is often an iterative process that requires repeated correspondence with the submitting institution. In addition to insuring the data is reviewable the ITC also prepares the data for review by renaming structures, combining individual fraction groups and deleting non-anatomical/non-protocol structures so that the PI reviewer only needs to review the protocol required structures. Also, DVHs are recalculated so that a database of dose volume statistics with standard structure names exists for QA and analysis of large numbers of cases.

## Methods And Materials

The ITC has been receiving digital data for advanced technology protocols for 14 years utilizing the Quality Assurance Submission, Analysis, Archive, and Review (QuASA²R) system. Figure 1 shows a flow diagram which illustrates the path of the data from submission to review. Data are converted by the institution's treatment planning system to either DICOM or RTOG data exchange files which are then sent to the ITC via Secure FTP or Media. The ITC reviews the digital data at the time of receipt to ensure that it is complete and ready to be processed so that it can be reviewed by the sponsoring study group using the ATC's RRT. Once the digital data integrity review is complete and the data are deemed ready for processing, the data are extracted into a proprietary file format using tools developed by the ITC. Included in this processing is the renaming of structures (Figure 3) to a standard naming convention that allows the recalculation of DVHs and the later analysis of dose volume statistics among subjects in a clinical trial. A significant portion of the data submissions are incomplete or cannot be processed or reviewed for a number of reasons. These problems require human intervention to request resubmission of the data or to resolve issues with the data before it can be made available for review. Tables 1 and 2 show the rate of problems that are encountered on a daily basis. Table 1 shows this data for protocol cases submitted and Table 2 shows this data for digital data submission of the treatment planning data submitted for Radiologic Physics Center (RPC) phantoms used to credential institutions for various advanced technology protocols.

### Categories of Submission Problems

Over the years several issues have been seen consistently which require intervention by the ITC personnel.

1. Misuse of Treatment planning system data export capabilities.
2. Missing protocol required elements or mistakes in protocol understanding.
3. Error in use of digital transfer software
4. New release of treatment planning system with inability to correctly submit ATC compliant data.

Problems in categories 1,2, and 3 are seen on a daily basis. Category 4 occurs much less frequently, but is much more complicated to resolve because it requires software changes by the vendor.

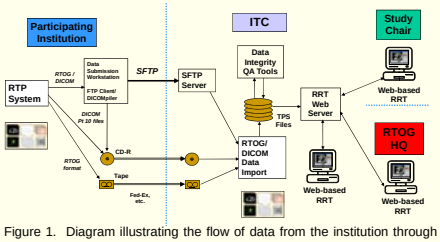


Figure 1. Diagram illustrating the flow of data from the institution through the ITC to the reviewers. The ITC performs digital data integrity QA to ensure that the data are reviewable.

## Results

| Disease Site | Number of cases Digitally Submitted | Problems Requiring Human Intervention | % Cases Requiring Human Intervention |
|---|---|---|---|
| Lung | 61 | 20 | 33 |
| Prostate 3D/IMRT | 1140 | 250 | 22 |
| Prostate Seed | 183 | 23 | 13 |
| Partial Breast | 1083 | 281 | 26 |
| Liver SBRT | 10 | 2 | 20 |
| Prostate 3D/IMRT with Nodal Volumes | 378 | 181 | 48 |
| H&N IMRT | 591 | 160 | 27 |
| Pelvic IMRT | 206 | 46 | 22 |
| **TOTAL** | **3652** | **963** | **26** |

Table 1. March 10, 2006- May 30, 2008 - Protocol Case Digital data submissions per protocol type and the number of problems encountered that required human intervention by ITC personnel.

| Phantom | # of Submissions | Problems Requiring Human Intervention | % Cases Requiring Human Intervention |
|---|---|---|---|
| H&N | 362 | 77 | 26 |
| Pelvis | 89 | 31 | 35 |
| Lung | 65 | 25 | 38 |
| Liver | 15 | 4 | 27 |
| **TOTAL** | **531** | **154** | **29** |

Table 2. RPC Phantom submissions per phantom type and the number of problems encountered that required human intervention by ITC personnel for March 10, 2006 – May 30, 2008

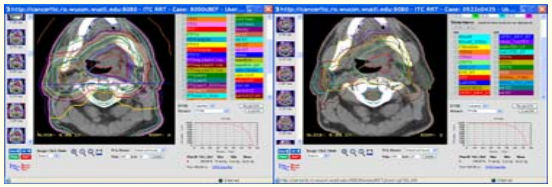

Figure 2. Images demonstrating a H&N IMRT case before (Left) the case is prepared by experienced ITC personnel for review and after the case is ready for review (Right). Many contours used for optimization are extraneous in the review process and can be removed. Protocol-required structures are renamed to standard names. The PI physician reviewer only views the anatomical structures necessary to review protocol compliance. Before DDIQA this case had 51 structures. After DDIQA this case had only 24 structures all of which represent protocol-required anatomy and targets

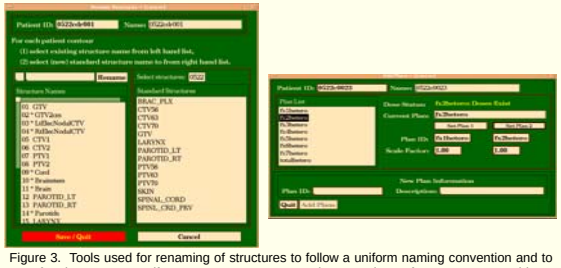

Figure 3. Tools used for renaming of structures to follow a uniform naming convention and to sum fraction groups. Uniform structure names permit comparison of DVHs among subjects enrolled on a clinical trial protocol. While standard structure names for each of the ATC-supported protocols are posted on the ATC website (http://atc.wustl.edu), submitted data often differ from the standard. Correct interpretation of submitted structure names may require visualization of contours, especially for head and neck cases (Figure 2). Maintaining the fractionation scheme for a given patient is important for later analysis, however, dose volume statistics need to be analyzed for the total dose delivered to the patient in order to correctly correlate these data with clinical outcomes.

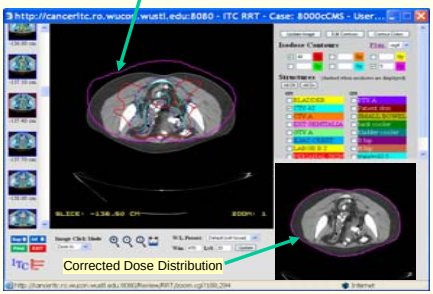


Figure 4. Submission illustrating an incorrect DICOM submission due to incorrect implementation by the Vendor. In this case the patient was planned Head First Prone, but the dose was exported as Head First Supine. This caused a misregistration of the dose relative to the patient anatomy. This particular case was a rapid review case meaning that the case had to be reviewed for protocol compliance by the protocol PI before the patient could start treatment. ITC personnel were able to catch this problem during DDIQA, and also make an adjustment to the dose registration so that the case could be reviewed in the time period allotted for rapid reviews (3 business days). Extensive comparisons of screen captures of isodoses provided by the institution to the corrected digital data were done to make sure the digital data represented the way the patient was planned.

## Discussion

- Our previous report of Digital Data Integrity QA (DDIQA) for 2480 cases showed that the rate of intervention by experienced personnel required to collect reviewable data was 27% (*Straube, et al., Digital Data Integrity QA for Multi-Institutional Clinical Trials. Presented at the 49th Annual Meeting of the AAPM*). This report of over 3600 clinical trial cases and over 500 RPC phantom digital data submissions shows that the intervention is still needed between 25 and 30% of the time.
- It may not be necessary to collect all of this information, simply to perform protocol compliance QA for a particular case. In fact current practice with some cooperative groups does not require the complete 3D data set to be submitted in digital format. To permit data analyses beyond those defined in the protocol, however, it is essential to build a rich, high-quality data base of volumetric treatment planning information in addition to ensuring the quality of treatments for protocol accruals (*Bosch et al., A Survey of the ITC Volumetric Treatment Planning Data Archive Supporting RTOG Advanced Technology Clinical Trials, presented at the 2007 49th Annual Meeting of ASTRO*). To ensure the quality of this database, we have also facilitated the review of every submitted protocol case by a PI reviewer.
- The sometimes complicated process of preparing the data by renaming contours, eliminating non-anatomical/non-protocol structures is done not only to simplify the review of cases by PI reviewers, but also to ensure uniformity in structure naming in recalculated DVHs.

## Conclusions

- The processing of digital data for the review of advanced technology clinical trials is currently only semi automated, and **not yet a totally automated** process.
- A focused review of the data collected over the past 2 years shows that approximately 26% of the protocol case data and 29% of phantom data submitted requires human intervention in order to obtain complete, reviewable digital data (Table 1 and Table 2).
- Procedures and tools developed by the ITC have made possible the collection of a large volume of data for these studies, the preparation of these data for Protocol compliance QA (Figures 2 and 3), and the creation of a large archive of treatment planning data for these cases for later data mining.
- The most common sources of problems in digital data submission are the following:
  - Errors in the use of digital data submission software on the treatment planning device.
  - Errors in the understanding of the required protocol elements.
  - Errors in the use of FTP and SFTP software.
  - Errors in the ATC compliant DICOM export of the treatment planning system (Figure 4).