Report: Accomplishments of the Advanced Technology Consortium (ATC) toward uniformity, consistency and reciprocity of criteria for participation in NCI sponsored cooperative group clinical trials

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Since its inception, the ATC has made significant accomplishments toward minimizing the efforts required of institutions to participate in the National Cancer Institute (NCI) sponsored cooperative group clinical trials. Without sacrificing the quality of the radiation therapy delivered to trial patients, the ATC has worked to develop uniform credentialing criteria that are consistent across the various study groups, and to have credentialing processes that are recognized among all QA centers and study groups.

One significant accomplishment has been to unify guidelines and forms used by the various quality assurance offices. In 2002 Drs. T.J. Fitzgerald (ATC), M. Roach, and J. Purdy (ATC) were requested by the NCI to develop guidelines for incorporating IMRT techniques into clinical trials. This document served as a template for protocol review of studies permitting IMRT by the radiation research program of the NCI. It articulated specific requirements of the protocols, such as using ICRU (50 and 62) definitions of GTV, CTV, PTV and requiring DVHs of unspecified tissue. Additionally, each institution that intended to participate in these protocols had to demonstrate the ability to plan and deliver an IMRT treatment, i.e. become credentialed. This could be accomplished with a phantom from the RPC **or** a benchmark developed by QARC depending on the requirements of each study group. Satisfactory completion of either was to be recognized as meeting the minimum credentialing requirements of all groups. At that time, it was felt that IMRT for moving targets in inhomogeneous tissue was not sufficiently explored; it therefore prohibited IMRT in thoracic sites. This document pointed to the ATC as the consortium to further refine the guidelines. By 2006, the ATC believed that necessary data and expertise were available to extend IMRT treatments to intra-thoracic lesions. The IMRT guidelines were modified by the ATC to include dose algorithm requirements to account for lung heterogeneity and patient and target localization requirements. These were adopted by the NCI and are currently applicable.

The ATC has also recognized that the number of facilities offering proton radiation therapy is beginning to grow quickly. To assure consistency among the various sites, the NCI asked the ATC to develop appropriate guidelines and credentialing requirements. A detailed questionnaire was developed (adopted by the NCI in May, 2008); the RPC has developed TLD monitoring capability for protons, and site visit criteria are under refinement. Each of these credentialing requirements for proton facilities is accepted by all QA centers and NCI sponsored cooperative groups; 4 of the 5 active proton facilities in the US have successfully completed the questionnaire; all 5 facilities have done the TLD tests, and site visits by the RPC are being scheduled.

To eliminate duplication and reduce the workload placed on the participating institutions, several informational forms have been adopted by all of the ATC QA centers. These forms need be completed only once and the data are shared among the QA centers. These forms include a facility questionnaire for IMRT, a prostate seed implant facility survey, and a prostate seed implant questionnaire. Recent discussions among RTOG, QARC, and the RPC are focused on arriving at IGRT guidelines, data submission requirements and credentialing requirements that will be used by all of the QA centers for all of the study groups as they initiate trials with IGRT components.

Substantial progress has been made by the ATC to create uniform credentialing requirements with reciprocity among the various study groups and QA centers. The first was the development of a common prostate seed implant benchmark (between RTOG and QARC (for ACOSOG)), with common evaluation tools shared between the RPC and QARC. A total of 112 teams of physicists and physicians were credentialed for these studies, 26 by QARC and 86 by the RPC. More recently QARC and the RPC developed 4 common benchmarks which incorporate current 3D planning techniques based on CT scans. An institution can fulfill, with one submission, the needs of the various cooperative groups because the QA centers are sharing these data and results. To date, 97 sites have satisfactorily completed the 3D conformal planning benchmark (required of new sites by most cooperative groups), and 12 and 11 sites, respectively, of the 3D cranial-spinal irradiation and mantle treatment which are required of new COG sites. As the RPC performs on-site dosimetry review visits to participating facilities (47 sites to date), the benchmarks are completed and the data are shared with QARC.

One of the most significant efforts by the ATC has been to ensure that credentialing for participation in trials using IMRT is reciprocal among the QA centers, and hence among the various study groups. The RPC's anthropomorphic phantom designs and dose analyses are recognized by almost all of the study groups including RTOG, COG, GOG, ECOG, SWOG, , NCCTG, ACOSOG, and PBTC for IMRT credentialing. The QARC IMRT benchmark has a similar acceptance. Using the RTOG as an example, each advanced technology protocol specifically states the method of credentialing required for a particular study. In some protocols, either credentialing method is identified as acceptable. An institution can participate in protocols of multiple cooperative groups by satisfactorily fulfilling one of these requirements. Processes are established for notification of the other QA centers when an institution has successfully completed one of these exercises. By September 2008, the RPC has approved more than 459 head and neck IMRT phantom irradiations, 99 prostate IMRT phantom irradiations, and more than 125 QARC benchmarks have been approved.

Over the nearly decade of the ATC existence, the technology used in radiation therapy has changed dramatically. Radiation therapy planning and treatment delivery are far more complex, and the entire discipline has become totally dependent on computers and computer networks. Retrospective analysis of the patient data from trials employing advanced technologies requires that the data be submitted and stored electronically, and hence electronic data exchange has been a major focus of the ATC as briefly reviewed in the following paragraph.

The ITC maintains the RTOG Data Exchange format specification and the ATC DICOM Conformance Statement to specify requirements for protocol case digital data submission. The ITC has hosted a series of RTOG/DICOM Implementers' Workshops (1995, 1999, 2001, 2002,

2003, and 2004) to help vendors implement ATC compliant digital data export capabilities. ITC (primarily Dr. John Matthews) has interacted (and continues to interact) with multiple TPS developers to help expose several problems in interpretation and/or implementation of the vendor's data export feature. Vendors submit DICOM or RTOG Data Exchange datasets to ITC via SFTP/media. ITC imports these datasets (and makes them available for web-based review by the vendor to evaluate correctness of data transfer using ITC's Remote Review Tool (RRT). Screen captures are emailed to vendors for RT Plan validation. Examples of problems seen include CT/Structure/Dose mis-registration and DVH-calculation discrepancies. Once the software is released by the vendor and a clinical user successfully submits a digital data set, the system is eligible for listing as ATC Compliant on the ATC website. To date, 11 TPS vendors (20 different planning systems), including the vast majority of popular commercial systems, have been designated as ATC-compliant regarding RTOG and/or DICOM export software. This electronic data export credentialing is accepted by all the QA centers and the ability of QA centers to take advantage of these data has been shared among the ATC members. Thus far, the ITC has received electronic data from nearly 600 institutions for 36 different protocols (15 closed and 21 open as of Oct. 1, 2008.

The ITC is an active participant (primarily Dr. Bosch) in the DICOM standards process, having served on WG-7 (Radiotherapy Objects), which is currently working on development of next-generation DICOM RT objects, and WG-18 (Clinical Trials), regarding the Clinical Trials ID, de-identification profile. In addition, the ATC became an Organizational Member of the International Integrating the Healthcare Enterprise (IHE) as of March, 2008, and remains fully committed to supporting the mission and vision of IHE in Radiation Oncology (IHE-RO). The ATC (primarily through Dr. Bosch) is an active participant in the IHE-RO Technical Committee. The ATC has facilitated distribution of IHE-RO Test Data and Test Tools via ITC Secure FTP server and has participated in all IHE-RO Connectathon Test Committees (most recent held in Houston on Jul 31 – Aug 5, 2008).

In 2005 the ITC installed the Remote Review Tool software at QARC, which allows web review of 3D treatment plans and structures, and established a secure FTP site at QARC for submission of the RTP data. 3D data submission to QARC is therefore identical to the process for RTOG and the ITC (for RPC), except for the different sFTP addresses. In addition, specific ATC workstations were installed at the RPC and the RTOG that had direct connections to the server located at the ITC. Institutions familiar with one can use the same process for other cooperative groups. As of September 2008, 82 institutions had sFTP accounts at QARC and nearly 600 institutions had accounts with the ITC. Another data analysis toolbox, the Computational Environment for Radiotherapy Research (CERR) has been developed by Dr. J. Deasy's group at Washington University. This tool shows great promise and the ITC, RPC, QARC and RTOG are either actively using it or exploring how they may use it in their day to day activities of performing QA for the clinical trial patient data submitted. Being written in open source code, Dr. Ken Ulin at QARC has made significant improvements to the original software with respect to the needs of QA centers. Capabilities such as the ability to import additional plans to an existing study (for subsequent phases of treatment or modified plans), the ability to perform a dose summation of multiple (>2) dose distributions, and the ability to easily and simply display beam parameters have significantly augmented CERR's usefulness for QARC. Nearly 500 digital RT cases at QARC are currently linked to this viewer. These developments are being incorporated into the ongoing upgrades of CERR, with plans for RPC and RTOG to use this

software for review of digitally submitted plans. The RPC has also contracted with the CERR group to generate specific routines that will allow the RPC to perform its phantom analyses in a more comprehensive manner and more efficiently. So far 300 phantom irradiations have been analyzed using the CERR tool. This CERR group became part of the ATC consortium in the most recent grant cycle and is expected to play a very active role in assisting the QA centers to use common analysis tools, whether for patients or phantoms.

Another IT related accomplishment is the creation of the ATC website (http://atc.wustl.edu/), from which ATC information can be obtained and links to all the QA centers are provided. The ATC members provide mutual links to common forms and credentialing information, with only one center keeping each document (preventing different versions in different places). There is a flow of constant communication between the various QA centers to ensure that the forms, credentialing requirements and other trial requirements posted on the websites is current.