Advanced Technology Consortium for Clinical Trials QA Meeting
Held at the RTOG Semi-Annual Meeting in Philadelphia, PA

June 23, 2005

Attending:

ITC
James Purdy, (ATC P.I.)
Walter Bosch
Roxana Haynes
Jeff Michalski (WU)
Bill Straube
S. Vijayakumar (UCD)

RTOG/ACR
Lorraine Quarles
Tom Caldwell
James Galvin (TJU)
Mike Gillin (MDACC)
Vish Iyer
Robert Lustig
Steve King

RPC
Geoff Ibbott
Dave Followill
Jessica Lowenstein

RCET
Jatinder Palta
Vince Frouhar

QARC
T.J. FitzGerald
Marcia Urie

NCI
Jim Deye

Guests
Charles Apgar (ACRIN)
Anthony Levering (ACRIN)
Irene Mahon (ACRIN)
Peter Dixon (NCIC)
Colin Field (NCIC)
Lam Pho (NCIC)
Karen Breitman (Tom Baker CC)
Ken Forster (UT Southwestern)
Ying Xiao (TJU)
Nagata Yasushi (JCOG)
Satoshi Ishikura (JCOG)

MINUTES

1. Dr. Purdy welcomed the attendees and called the meeting to order at approximately 8:00 a.m. All ATC subcontractors were represented by at least one individual.

2. Dr. Deye also welcomed the attendees. He informed the group of the NCI's plans to restructure its cancer clinical trials enterprise. The plan will cost approximately $113M spread over five years. The plan will address four themes: coordination, prioritization/scientific quality, standardization, and operational efficiency. A copy of an article from the Washington Fax providing more details of the plan was given to all ATC participants present. It is clear that this effort will significantly impact ATC and any future IT development efforts must embrace this restructuring plan. Dr. Deye also distributed a copy of CFR 21, Part 11 pertaining to electronic records and electronic signatures and asked if ATC software met these requirements. After some discussion, Dr. Purdy assigned the ATC IT Task Group chaired by Dr. Bosch to review this issue and report back to the ATC at the next teleconference (August or September).

3. Dr. Purdy's P.I. report addressed the following:
   a. The minutes from the June 1, 2005 ATC Teleconference were approved
   b. All remaining *Action Items* from the January 20 ATC meeting were reviewed.
      - Bill Straube/Betty Martin will make a presentation at the AAMD 2005 Annual Meeting (June 26-30, 2005, in San Diego, CA) to review protocol digital data submission and other credentialing requirements for ATC supported protocols.
      - There will be no ATC Booth at the 2005 AAPM Annual Meeting (July 24-28, 2005, in Seattle, WA). Instead, Dr. Purdy will create an ATC Brochure which will be distributed at the MDACC(RPC) Booth **(Action required)**.
      - The ATC Brochure will be updated for the 2005 ASTRO Annual Meeting (October 16-20, 2005, in Denver, CO). **(Action required)** Dr. Purdy has emailed a request to Dr. Deye to obtain permission to distribute the brochure at the NCI Booth as previously done.
      - The issue of RPC brachytherapy software needs and RCET development efforts in this regard were not resolved in this past five month period. It is an agenda item for this meeting.
      - Credentialing requirements for all modalities were reviewed during this six month period and recommendations for changes will be discussed at this meeting.
      - A timeline and methodology for testing/developing ATC Method 2 was agreed on during this past five month period and will be reported on at this meeting.
      - Drs. Bosch, Frouhar and the NCIC group completed the document that clearly describes ATC Methods 1, 2, and 3 and it is now posted on the ATC website.
      - Gray scale PET data from a Siemens and a GE system were successfully submitted to the ITC during this past five month period. Dr. Bosch will report on this at this meeting.
   c. Requests for use of ATC resources by NABTT, UKCCSG, EORTC, and JCOG were reviewed.
      - JCOG has requested ITC support for a second protocol.
      - NABTT: Dr. John Fiveash, M.D., Department of Radiation Oncology, University of Alabama-Birmingham has requested use of ATC Method 1, but has not provided enough details to assess workload by ITC.
      - UKCCSG: Dr. Susan Harden has requested use of ATC Method 1 and possibly Method 2 to support the Phase II Study of Prospective QA by Web-Based Review of Radiotherapy Fields in the Treatment of Standard Risk Medulloblastoma within the HIT-SIOP PNET4 Protocol.
      - EORTC: Dr. Bernard Davis, Univ. Hospital of Zurich is the contact person; no real progress has been made during this past five month period.
   d. Modifications to the ATC Website were discussed.
      - The NCIC link to MA.20 needs work. (Dr. Bosch to work with Colin Field) **(Action required)**
      - Several items need to be updated on the ATC Steering Committee page, particularly timelines for Method 1 at QARC and Method 2 at ITC; meeting presentations, and Tool status report. **(Action required)**
      - The Publication Page needs updating. Dr. Purdy requested all ATC subcontractors to provide him full references of any published manuscript or

abstract that references the ATC U24 CA 081647 as supporting the work. **(Action required)**

e. The Treatment Planning Verification (TPV) database at the ITC and the RTOG Outcomes database in Philadelphia
   - Dr. Sue Tucker (MDACC) was awarded a NCI R01 grant *"Dose-Volume Modeling of Late Rectal and Bladder Injury"* to assess late rectal and bladder toxicity from the results of RTOG 94-06.
   - Joe Deasy (WU) was awarded a NCI R01 grant *"Normal Tissue Complication Modeling for Radiotherapy"* using in part the RTOG 93-11 dataset (113 pts.) to test and refine a post-RT late pneumonitis/fibrosis NTCP model.
   - CMS in St. Louis has requested use of the TPV database; details are still being worked out, but both RTOG and ITC have indicated they are in support of this request. **(Action required)**

f. All subcontractors that have funds remaining from the 2004-05 year should submit carryover budget requests to Dr. Purdy by the end of August. **(Action required)**

g. We have two years remaining on the current ATC grant. While it is a little too early to begin definitive planning for the new grant, Dr. Purdy would appreciate any input from the subcontractors regarding priorities and new initiatives. **(Action required)**

h. A proposal for a NCI sponsored QA Workshop to be held in Washington DC on Sept. 8-9 was reviewed. Co-sponsorship by AAPM, ASTRO, and ACR is being sought. Program Directors are Geoffrey Ibbott, Ph.D. and James A. Purdy, Ph.D. The program would address the broad range of QA concepts and procedures used in modern day radiation therapy, including 3DCRT, IMRT, SRS/SRT, and brachytherapy. The objective is to assess current status of QA requirements and procedures as it is practiced today. This overview and assessment would help set the agenda for further, more detailed and technical, considerations of all aspects of QA in radiotherapy in other venues. Input from those attending this ATC meeting was requested. A final decision on going forth this year in such a short time frame will be made by Drs. Deye, Ibbott, and Purdy later this week. (Note, it was decided to postpone this workshop until 2006)

i. Schedule of ATC conference calls and next meetings
   - Next ATC Teleconference will be August 3, 2005 Note no teleconference in July.
   - Plan for an ATC meeting of at least P.I.s at 2005 COG Semi-Annual meeting scheduled for Dallas, TX in Oct. 25-30, 2005
   - ATC meeting at RTOG Semi-Annual meeting scheduled for January 19, 2006 Fontainebleau Hilton Resort, Miami Beach, FL
   - Plan for ATC Steering Committee Meeting sometime Spring 2006 (Jim Deye to arrange)

4. Dr. Purdy reviewed the ATC Steering Committee response with the group and will develop a response based on the feedback received. **(Action required)**

5. Dr. FitzGerald reported on the status of the efforts of ITC and QARC to implement ATC Method 1 at QARC. Since June 2004, there has been substantial progress:

- Operational Hardware and Software have been installed. DICOM and RTOG format data can be imported into the ATC Method 1 server at QARC using CD media at QARC and FTP submissions via the FTP server at ITC.
- Data imported into the Method 1 server can be reviewed using the Remote Review Tool on any QARC desktop PC.
- A link between the QARC database and the Remote Review Tool has been demonstrated.
- QARC has implemented a mechanism for backup of data using transfer to a Windows system.
- Templates have been created to review volumetric, digital data for three COG protocols and one ACOSOG protocol. Eight institutions have been invited to submit digital treatment planning data on these protocols. To date, 12 case data sets have been submitted. Web pages for these protocols with directions for data submission have been created on the ATC web site.
- The ITC has added capabilities to the Remote Review Tool in response (in part) to requests from QARC: image grayscale presets, image measuring tool, and selection of submitted, re-calculated, or user-calculated DVHs. In addition, QARC physicists and dosimetrists have helped to test these new features.
- QARC personnel have received basic training in the import and review of digital treatment planning data using this system.

Training and support continues via weekly teleconferences between QARC and ITC personnel. Work is ongoing on the following tasks:

- Establishment of an FTP server at QARC to receive data from submitting institutions.
- Establishment and documentation of data handling and QA procedures for digital treatment planning data at QARC.
- Incorporation of minor enhancements to ITC tools to improve support for QARC data review procedures.
- Building local expertise in data import and review process at QARC and identifying FTE support for the anticipated volume of data.

6. Dr. Bosch reported on the status of implementing ATC Method 2 at ITC. ITC has completed testing of RCET software version 2.3 (WebSys client/server, Rapid Image Viewer applet, and WebSys Administration Tools).
   - The current test cycle has been performed on the POLARIS server at ITC by Mr. Sean O'Leary. The test data set used for testing has consisted for DICOM and RTOG format data from ATC Compliant and Vendor Complete, commercial treatment planning systems, which were check using ATC Method 1 to ensure all objects could be reviewed. The POLARIS server has been disconnected from internet access during testing to assure stability of the software.
   - A time table of the testing procedures was presented indicating the dates for software installation, functional testing, as well as, upload/download/comparison testing on the server.
   - Several improvements implemented on the WebSys system were noted along with suggestions to improve the usability of this system.

- A list of specific findings was presented. Outstanding issues include failure of the WebSys client to recognize some DICOM objects, failure to create a new protocol case when an existing case with the same Case ID (in another protocol) exists, improper handling of certain DICOM objects encoded using Explicit-VR transfer syntax, inability to scan RTOG files with filename extensions, multiple grayscale control problems in the Rapid Image Viewer applet, and failure to completely delete case records from the database using the web-based server administration tools.
- Test results have been sent to RCET with further specific information to be communicated via teleconference during the week of June 27, 2005. Internet access to the POLARIS server is to be restored to allow RCET to install updated (version 2.4) server software. Once this update is complete, testing will recommence at ITC.

7. Drs. Frouhar and Palta demonstrated some of the administration tools they had implemented in support of the of Method 2 implementation at ITC. ITC acknowledged that these tools are very helpful in their ongoing efforts to implement Method 2 at the ITC.

8. Colin Field gave a presentation on the status of implementing ATC Method 3 at NCIC. He reported that significant progress had been made since the Jan-05 ATC meeting as shown by the outline below:
   a. Meetings were held as needed (Weekly ROQAC MA.20, every 6th week ROQAC, Semi-annual NCIC CTG, and Conference calls with RCET & ATC as needed)
   b. Completed testing of NCIC CTG Test Server
   c. Moved software to Production Server for user testing
   d. User Documentation completed (MA.20 submission manual, MA.20 reviewers manual, NetSys Installation and configuration manual, FAQ)
   e. Released NCIC CTG Data Warehouse for MA.20 clinical use on May 30, 2005 (letter). Colin asked that we please excuse their oversight for not explicitly thanking RCET, ATC, and NCI-US.
   f. They have decided that all MA.20 centers need to be re-credentialed (3 have been and 5 are in progress).
   g. Thus far, 10 cases have been submitted for rapid or final review
   h. The following goals have been set (July to December, 2005)
      - Perform rapid reviews for credentialed institutions
      - Perform final reviews for credentialed institutions
      - Educate submitting institutions (hands-on assistance with credentialing, CARO presentation in September)
      - Credential more institutions (Canadian institutions, top accruing centers to MA.20 from the US and Australia)
      - Develop distributed and redundant personnel infrastructure to perform (1) technical dry run reviews and 92) clinical dry run reviews
      - Initiate Pilot Project to re-evaluate submission of DICOM-RT and RTOG data objects to NCIC CTG Data Warehouse (Method 2.b)
      - Select NCIC CTG protocol to use as test of 3D data sets using RCET technology
      - Develop QA goals for NCIC CTG for next 5 years (e.g. ‘Vision Statement’)

- Establish guidelines to access NCIC CTG Data Warehouse for non-NCIC sponsored trials
- Develop grant application with ATC/RCET to provide continued support and development of infrastructure & operating procedures (hardware, software, personnel) at NCIC CTG.

i. The NCIC group summarized their experience thus far with ATC Method 3:
   - Installation of the RCET infrastructure is not yet plug and play. Other groups should be made aware that dedicated resources must be provided:
     – 0.5 FTE systems support staff
     – Hardware/software cost to-date: ~$50,000 CAD
   - Better documentation and SOPs will facilitate distribution of RCET system to other groups.
   - NCIC CTG is too reliant on volunteers (Liz Elliot, Lam Pho, Sonia Schellenberger, Wendy Parulekar, Colin Field)
   - Outstanding Items – RCET / NetSys
     - Remove, or password protect, log files which contain confidential information
     - Add user verification during NetSys download
     - Addition of appropriate MA.20 dataset to NetSys download for training
     - Problem with Case ID not being unique across NCIC protocols – temporary solution DR_CALM0007. Other protocols will reuse case #.
     - Use version 3 of the rapid review tool - done

9. Dr. Ibbott led a discussion on brachytherapy software needs at RPC. He pointed out that the RCET BrachySys program did not meet the RPC's new evolved needs in this area. Also, he reminded the group that he had negotiated a proposal from Varian to provide RPC a complete Eclipse EX system at the cost of the hardware, installation and 1st year service contract at a cost of approximately $9500, but that he does not have such funds budgeted in RPC's ATC subcontract to cover this amount. Dr. Palta pointed out that a planning system did not solve all the needs of RPC in terms of digital data submission, web-based review, and archival into a common ATC database He presented a slide showing a proposed configuration that addressed these issues. Dr. Purdy indicated he would speak to Varian at the upcoming meeting to discuss Varian donating this equipment. He also asked RCET and RPC to continue to discuss this issue, particularly the proposed RCET configuration, and see if consensus on RCET developmental efforts can be reached (based on the assumption that Varian would donate an Eclipse system). **(Action required)**

10. Dr. Ishikura gave a presentation updating the group on the JCOG 0403 Protocol (a phase II study of SBRT in patients with T1N0M0 NSCLC). He thanked the ITC for their support in digital data submission and processing for his QA review using the Remote Review Tool. Thus far, 26 cases have been submitted. ITC indicated that the workload to support this effort was not great because the data are being submitted to the ITC from a single central group (Dr. Ishikura's). Dr. Ishikura requested similar support for a second protocol that would start next year. The ITC agreed that it could handle this second protocol and approval was given to proceed.

11. Dr. Purdy led the discussion of the review of ATC credentialing requirements for 3DCRT Protocols which are as follows:
    (1) Facility Questionnaire describing institutional personnel, equipment, and treatment techniques must be downloaded from the ATC web site and submitted to the ITC.
    (2) A Dry Run (Benchmark) Test: Contact the ITC (itc@castor.wustl.edu) and request an FTP account for digital data submission. A complete patient data set as specified by the treatment protocol must be submitted to the ITC to demonstrate compliance with 3D technical requirements (see Dry Run Guidelines at http://atc.wustl.edu/protocols/).

    After discussion, it was agreed to eliminate some hardcopy data (isodoses) used by ITC to check digital data integrity.

12. Dr. Palta led the discussion of ATC credentialing requirements for IMRT Protocols. He presented a revision of the current *NCI Guidelines for the Use of Intensity-Modulated Radiation Therapy in Clinical Trials.* Current ATC credentialing requirements for IMRT protocols requiring digital submission are as follows:
    (1) Facility Questionnaire describing institutional personnel, equipment, and treatment techniques must be downloaded from the ATC web site and submitted to the ITC.
    (2) A Dry Run (Benchmark) Test: Contact the ITC (itc@castor.wustl.edu) and request an FTP account for digital data submission. A complete patient data set as specified by the treatment protocol must be submitted to the ITC to demonstrate compliance with 3D technical requirements (see Dry Run Guidelines at http://atc.wustl.edu/protocols/).
    (3) Phantom test with RPC or IMRT Benchmark depending on cooperative group and/or protocol.

    After discussion, it was agreed to maintain the above requirements.

13. Dr. Ibbott led the discussion of ATC credentialing requirements for Brachytherapy Protocols which are as follows:
    (1) Questionnaires (QA Knowledge Assessment Questionnaire; Facility Questionnaire)
    (2) Benchmark plans (similar for LDR, HDR prostate brachy; new CT-based plans for breast, to be developed for other protocols)
    (3) Initial case review (Alternative to benchmark for RTOG GYN protocols)
    (4) Electronic review (when protocol requires; facilitates benchmark review).

    After discussion, it was agreed to maintain the above requirements.

14. Dr. Galvin led the discussion of ATC credentialing requirements for SBRT Protocols which are as follows
    (1) Facility Questionnaire describing institutional personnel, equipment, and treatment techniques must be downloaded from the ATC web site and submitted to the ITC.
    (2) A Dry Run (Benchmark) Test: Contact the ITC (itc@castor.wustl.edu) and request an FTP account for digital data submission. A complete patient data set as specified by the treatment protocol must be submitted to the ITC to demonstrate compliance with 3D technical requirements (see Dry Run Guidelines at http://atc.wustl.edu/protocols/).
    (3) Phantom test with RPC.

(4) Immobilization/Localization and Respiration Control Systems Test with RTOG (Dr. Galvin)

After discussion, it was agreed to maintain the above requirements.

15. Dr. Galvin led the discussion regarding establishing ATC credentialing requirements for the use of IMRT for intra-thoracic treatments, in which significant heterogeneities are encountered and tumor mobility is likely. This is clearly an important issue and one that ATC needs to start work on as soon as possible. Dr. Purdy asked Dr. Palta as chair of the ATC IMRT TG to reconvene the task group and work with Drs. Jim Galvin and Ken Forrester to draft proposed credentialing requirements. **(Action required)** The issue of TomoTherapy Hi-ART and Cyber-Knife systems was also discussed but no specific recommendations were made. At this time, neither of these systems has distributed ATC compliant software for digital submission.

16. Anthony Levering provided a brief description of the ACRIN / PET Core Lab technical capabilities. The RTOG 0522 Protocol was discussed. This protocol will utilize ACRIN to capture quantitative digital PET data. It also has been modified to greatly encourage digital submission of the RT objects to the ITC. (Drs. Bosch and Levering to investigate what effort it would take to download the PET data (gray scale only with normalization) to ITC. **(Action required)**

17. ATC support of NSABP B-39 / RTOG 0413 is going well. No major issues were reported by RPC, ITC, or RTOG. Already 70 institutions are credentialed and an additional equally large number of institutions are going through the credentialing process.

18. Drs. Palta and Frouhar made a presentation demonstrating RCET's data mining software tools. Thus far the work is fairly preliminary, but does look very interesting.

19. Dr. Bosch gave a brief presentation updating the group on the IHE effort. At this time this effort appears minimal for ATC and reports will be strictly FYI.

20. Dr. Purdy led the discussion on problems that have been reported regarding the inconsistency in the definition of the target volumes in RTOG 0225. It was agreed that a task group would be formed (Dr. Michalski Chair, Dr. Lee, Dr. Garden, TBN M.D., Dr. Xia, Dr. Galvin, Dr. Purdy) to correct the written definitions. **(Action required)**

21. Dr. Galvin led the discussion on RTOG developing protocols and concepts that are requesting ATC support.
    - RTOG 0415: Phase III study of Hypofractionated 3D-CRT/IMRT versus Conventionally Fractionated 3D-CRT/IMRT in Patients Treated for Favorable-Risk Prostate Cancer
    - RTOG 0417: Phase II Study of Iressa in Combination with Definitive RT and Cisplatin

- RTOG 0418: Phase II Study of Intensity Modulated Radiation Therapy (IMRT) to the Pelvis +/- Chemotherapy for Post-Operative Patients with Either Endometrial or Cervical Carcinoma
- RTOG 0435: Phase III Study Unresectable H&N; IMRT/3D-CRT
- Chemo in Locally Advanced Cervical Cancer, Optional Brachy/CT
- RTOG 0438: Phase I Trial of Highly Conformal Radiation Therapy for Patients with Unresectable Hepatobiliary Cancer and Liver Metastases
- RTOG 0521: Phase III study of Androgen Suppression (AS) and Radiation Therapy (RT) vs. AS and RT followed by Chemotherapy with Docetaxel and Prednisone for Localized, High-Risk Prostate Cancer
- RTOG 0529: Phase II Study Trial Evaluating Capecitabline, Cisplatin and IMRT (plus Cetuximab) in Carcinoma of the Anal Canal

Concepts

- Phase III Study Hypofractionated Intensity Modulated Radiation Therapy (IMRT) with Incorporated Boost for early Stage Breast Cancer (Gary M. Freedman, M.D.)
- Phase III Study Trial of Moderate Dose IMRT + Chemotherapy versus Conventional Dose IMRT for Resected Intermediate Risk Head and Neck Cancer (Mitchell Machtay, M.D.)
- Phase I/II Study Trial of FDG-PET/CT Guided Intensity Modulated Radiation of Oropharyngeal Cancer (Dian Wang, M.D., Ph.D.)
- Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) for Patient with Operable Early Stage Non-Small Cell Lung Cancer (Robert D. Timmerman, M.D.)

This is clearly a significant workload for the ITC, RPC, and RTOG HQ Dosimetrists and will require prioritization based on present staffing. The exact number of patients required for these studies will need to be determined. Each group will need to assess the workload required per study/per patient accrued. This will be a topic for several of the RTOG/ITC/RPC Teleconferences scheduled this summer and we will report back to the full ATC. **(Action required)**

22. Dr. Purdy led the discussion reviewing the ATC Priority List. It was decided to separate the list into a service priority list and a developmental list. A proposed draft is listed below. Please provide feedback to Dr. Purdy by the end of July. **(Action required)**

Service Priorities

1. Provide daily operational support for ongoing ATC facilitated protocols (RTOG, NSABP, JCOG, see ATC website for protocol details) - [Service for ATC supported protocols is given highest priority; ask that response be given within three day period]
   a. Facilitate digital data submissions
   b. Evaluate/approve institution's credentialing tests for each specific protocol
   c. Facilitate/perform QA reviews of submitted digital data sets
   d. Maintain QA and treatment planning databases

2. Provide support to NCIC in their use of ATC Method 3 technology.
3. Interface with RTP vendors and foster implementation of ATC compliant DICOM export capability.
   a. ITC assistance to vendors for DICOM and/or RTOG Data Exchange implementation
   b. ATC representation in NEMA/DICOM Working Group 7
   d. ATC representation in IHE initiative
4. Provide expertise in the areas of protocol design, credentialing, monitoring, and analysis for new clinical trials that utilize advanced technologies and require digital data submission (e.g., NSABP B-39/RTOG 0413). The effort includes the following:
   a. Credentialing tests and criteria (and periodic review of existing requirements/criteria)
   b. Phantoms
   c. QA procedures, documents, and criteria
   d. ATC web page/links
   e. TPV and QA databases
5. Facilitate outcome analysis and data mining for ATC supported closed protocols.

Developmental Priorities

1. Implement ATC Method 1 technology at QARC and increase use of this technology by other cooperative groups, i.e., COG, SWOG, and CALGB. (See current time line for this work).
2. Develop, test, and implement ATC Method 2b technology at NCIC. (See current time line for this work).
3. Develop, test, and implement ATC Method 2a technology at ITC. (See current time line for this work).
4. Develop/implement brachytherapy QA software to facilitate RPC support of clinical trials. (See current time line for this work).
5. QA of protocols requiring multi-modality imaging (PET, MRI, Image fusion)
6. Publications

23. Drs. Deye and Purdy thanked all for their participation, with particular thanks to RTOG staff for their efforts in arranging the meeting facilities. The meeting adjourned at approximately 5:00 pm.

Respectfully submitted July 7, 2005
James A. Purdy, Ph.D.
ATC Principal Investigator