ATC Principal Investigator's Report
ATC Meeting Hosted by QARC
Providence, RI August 1, 2007

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Supported by NIH U24 grant CA81647,
"Advanced Technology QA Center"

Agenda

7:35 AM: Welcome by Local Host (Dr. FitzGerald)
7:35 AM: Project Officer Report (Deye)
7:45 AM: P.I.'s Report (Purdy)

Software Developmental Efforts

8:15 AM: QARC/ATC (Dr. FitzGerald and QARc Staff) Hands-on demonstrations of QARC's informatics technology for clinical trials QA and Review of software development needs/current efforts

9:15 AM: Development of schedule for QuASAR (Quality Assurance Submission, Analysis, and Review) system updates and expansion – (Bosch/Purdy)

9:45 AM: Report on CERR developments in support of ATC (including RPC effort) (Deasy)

10:15 AM: Break

10:30 AM: CALGB Clinical Trials/QARC/ITC/caBIG In Vivo Imaging Workspace efforts (Saltz/FitzGerald/Purdy)

11:00 AM: Exploration of ways in which the ATC effort could become synergistic with the PLUNC effort (Purdy)

11:15 AM: Update on ATC compliant Treatment Planning Systems and IHE-RO Effort (Bosch/Matthews)

11:30 AM: Discussion and recap of software development priorities and time tables (Purdy and all participants)

12:00 PM: Lunch

Agenda

Coordination & Developmental (Credentialing & QA) Efforts

12:45 PM: Dose Calculation Algorithm/Heterogeneity Corrections Clinical Trial issues (Ibbott/Followill)

1:00 PM: RTOG IGRT QA Guidelines; adoption by QARC (Galvin, Michalski, FitzGerald)

1:20 PM: Adaptive Radiation Therapy Clinical Trials Requirements-ATC Developmental Needs (Michalski/FitzGerald)

1:35 PM: Proton Guidelines (Urie/Ibbott)

Service Efforts

1:50 PM: QARC ATC Supported Protocols and QARC Credentialing and QA report

2:05 PM: RTOG/NSABP ATC Supported Protocols
- RPC Credentialing and QA report (Ibbott)
- ITC credentialing and Data Integrity QA Report (Straube)
- RTOG credentialing and Protocol QA Compliance Report (Martin)

2:35 PM: ITC ATC Supported Protocols (Straube/Bosch/Purdy)
- JCOG 0403 Protocol: SBRT
- EORTC ATC Supported Meningioma Protocol
- NABTT ATC Support
- Astra Zeneca

2:50 PM: Open Discussion

3:10 PM: Development of new ATC Priority List (Purdy and all participants)

3:25 PM Next Meetings/Teleconferences (Purdy and all participants)

3:30 PM Adjourn

New *ATC Grant*

The goals as specified in the RFA for our ATC renewal application are to be accomplished through the following ***developmental*, *coordination*, and *service* objectives**:

1. Eliminate duplication of infrastructure developmental efforts and facilitate sharing of QA resources among cooperative groups.
2. Help to insure that appropriate and uniform QA procedures and criteria for advanced technology trials are developed across all cooperative groups.
3. Facilitate/help manage the uniform credentialing of institutions for advanced RT trials.
4. Facilitate/manage digital data protocol submission.
5. Facilitate/manage the QA review of submitted data.
6. Further development of methods for rapid analysis of volumetric treatment planning data.
7. Assist clinical trial Coop. Groups in development of clinical trials including: (a) credentialing requirements; (b) TV definitions; (c) QA procedures; and (d) data submission instructions.
8. Develop, implement, and maintain innovative methods for electronic exchange of digital planning data between institutions participating in clinical trials and between QA Centers.
9. Develop, implement, and maintain innovative web-based software tools to facilitate protocol digital data reviews by Study Chairs, Dosimetry Groups, RPC, and QARC.
10. Develop, implement, and maintain archival treatment planning and QA databases that can be linked with the cooperative groups' clinical outcomes databases.
11. Demonstrate understanding of and ability to achieve compatibility with existing software and electronic health record standards, including caBIG and DICOM RT.

New *ATC Grant*

- Want to explore new approach with Tcons and meetings
  - Face to Face meetings at QA Centers
  - Monthly Tcons for involved QA Centers
  - Perhaps hold Quarterly Tcons for all ATC members?
- We must have a clear understanding of the goals for the ATC grant as opposed to the individual subcontractor (RTOG, RPC, and QARC) grants.

Introduced new acronym for ATC Method 1

The ITC developed **QuASAR** system provides the most advanced medical informatics infrastructure currently in use anywhere in the world to support radiation therapy clinical trials digital data quality assurance.

QuASAR

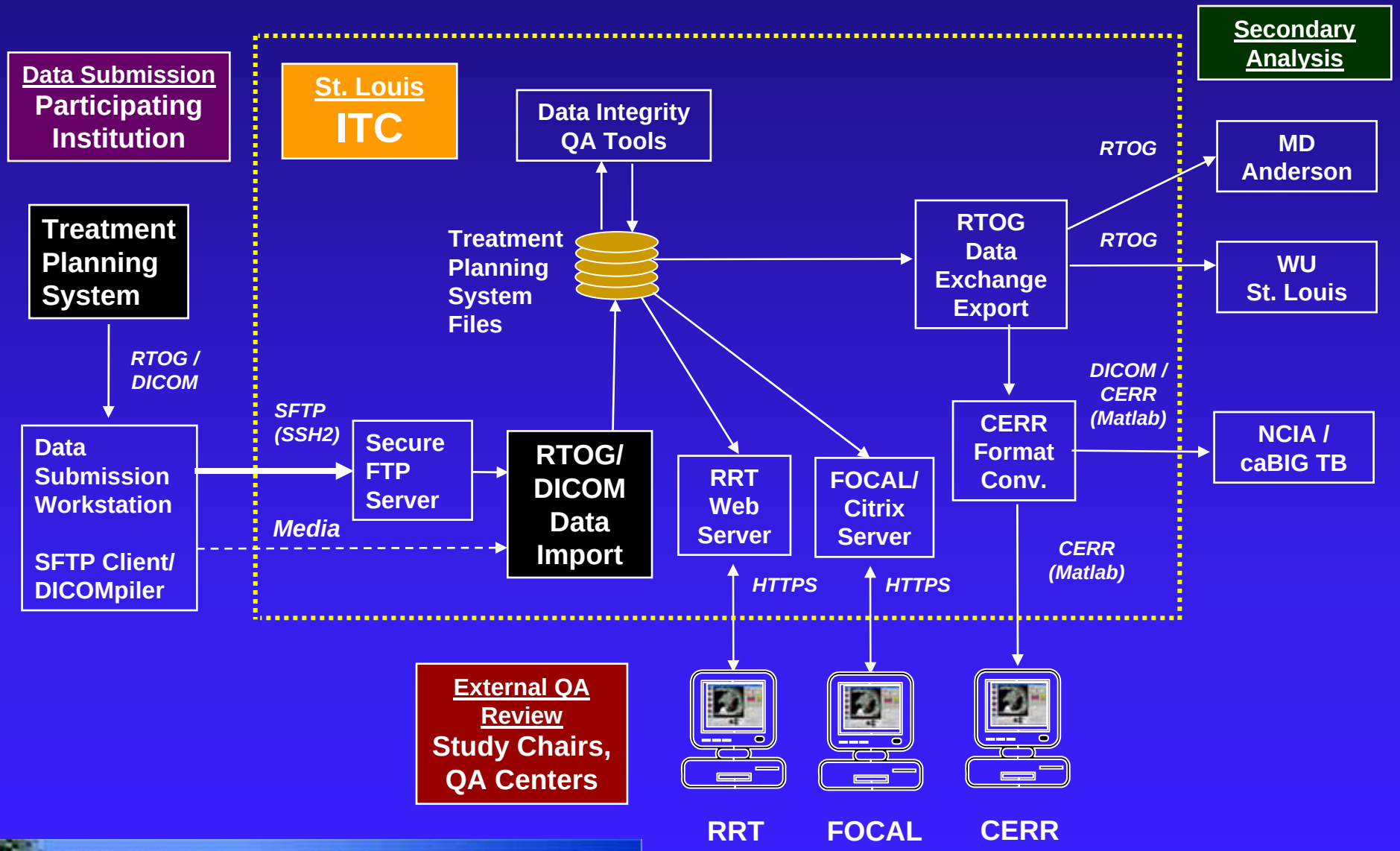
… is based on practical experience in support of clinical trials QA,

… provides secure data submission, analysis, and review of radiation therapy and imaging data,

… has enabled the collection, review, and analysis of >5400 protocol case data sets, and

… will continue to evolve using appropriate information technology to meet the QA needs of RT clinical trials.

QuASAR – *Components and Data Flow*



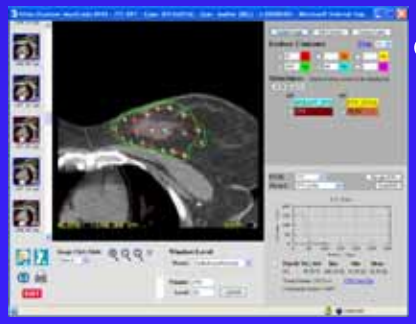
QuASAR – *Adapting and Innovating*

- ATC will make use of Industry systems
  - TeraMedica Evercore
  - IMPAC MOSAIQ
  - *IKOEngelo* (Image segmentation QA)
  - Commercial TPS's
    - CMS
    - Philips Pinnacle
    - Varian Eclipse
    - TomoTherapy HI-ART
- ITC is working with Dr. Joe Deasy and colleagues in WU Bioinformatics & Outcomes Research Division to further the development of CERR to meet ATC needs.
- Will need to develop new thin client applications for distributed case review (RRT)
  - Intuitive user interface
  - Low bandwidth, low latency
  - Minimal configuration requirements

CMS Focal®

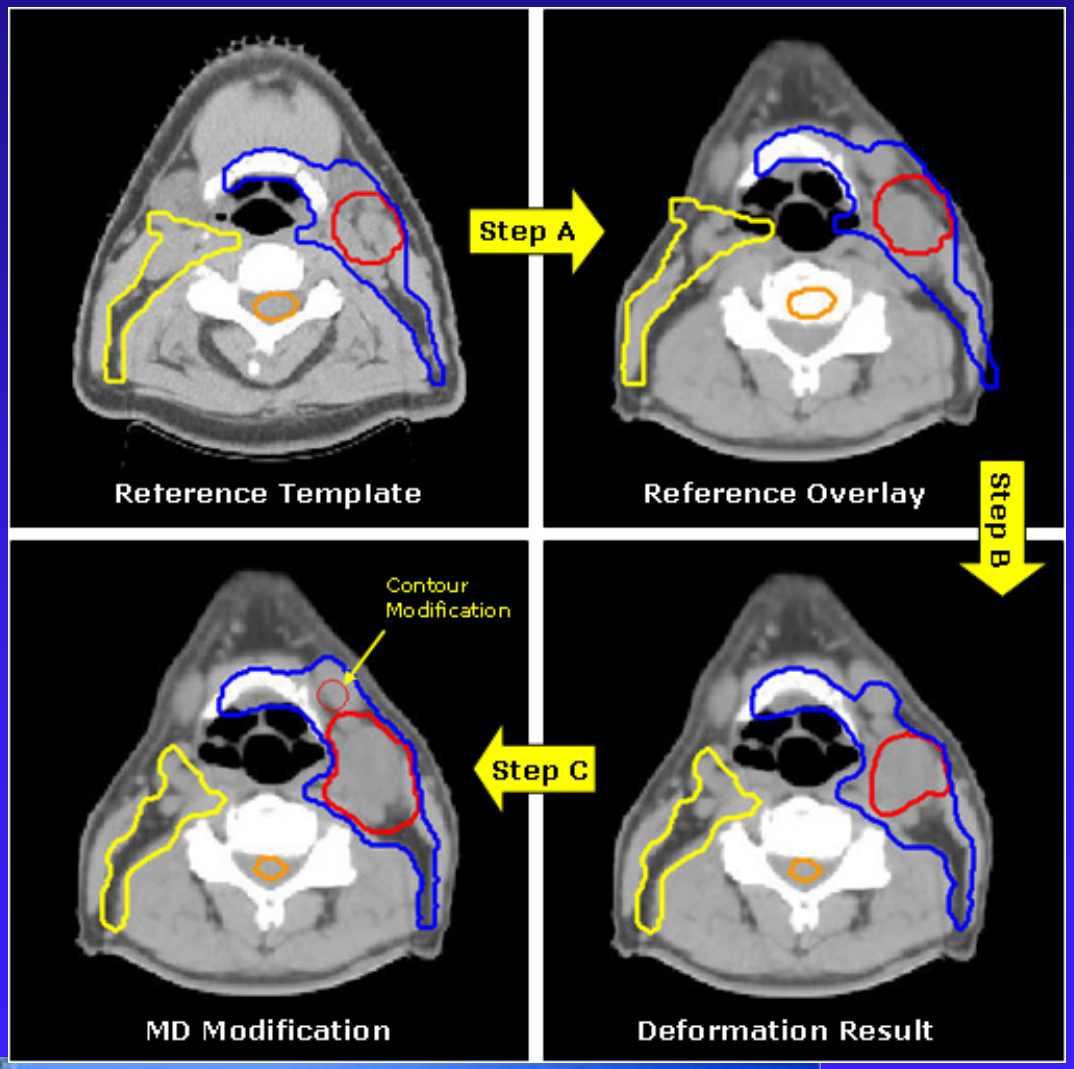
WU CERR

Remote Review Tool



Treatment Planning & Verification → Data Submission → Data Integrity QA → Protocol Compliance Review → Outcomes Analysis

IKOE: A Deformable Image Registration-based System for Computer-Assisted Contouring (K.S. Clifford Chao, M.D., Lei Dong, Ph.D.,…)



How IKOEngelo works..

Step A: Select and overlay disease-specific reference template contours onto the patient's CT images

Step B: Deform reference template contours to fit the patient's anatomy

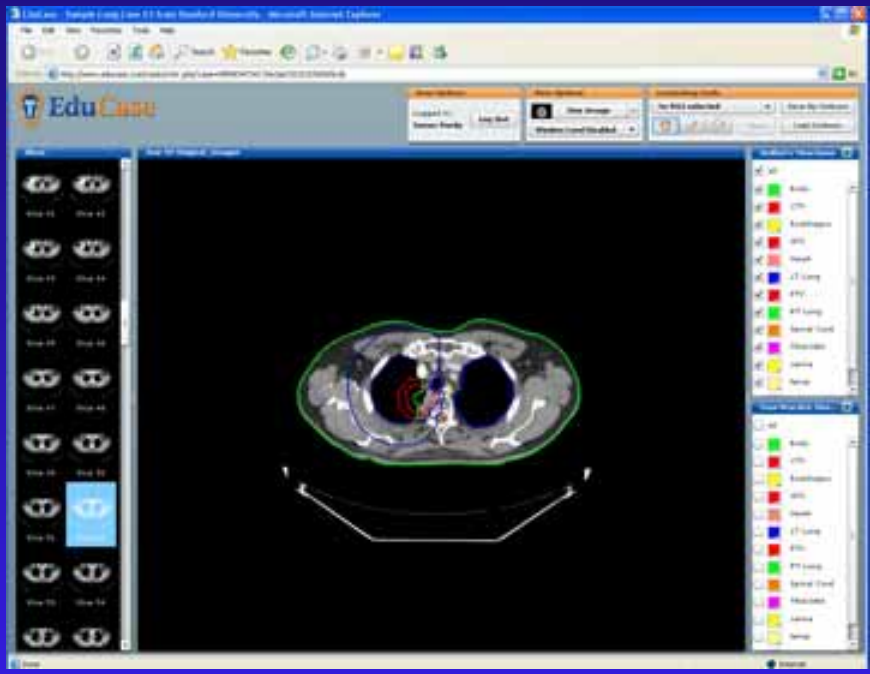
Step C: Physicians modify contours based on clinical judgment

IJROBP 2007 in press

EduCase (Art Boyer, Ph.D. and Scott Kaylor, M.S.)

RadOnc eLearning Center, LLC - EduCase

- EduCase lets you share IMRT cases with the world. EduCase users can upload their IMRT cases and view them online with complete image sets and contoured structures. These cases can be viewed from any computer in any location with a standard web browser.
  - **Share:** EduCase is an IMRT case repository created by the community. You can upload your own interesting cases to share with others. All members of the EduCase community can discuss cases and exchange knowledge. You can use EduCase to send an interesting case to a colleague and discuss the case online.
  - **Teach:** You can upload cases to create a rich teaching file for your residents. Your residents will be able to access the cases and practice contouring from both work and home. You can review the contours that your residents have saved and address any problems you find with their contouring methods.



- **Learn:** Use EduCase to learn contouring techniques. You can practice your own contouring while viewing a case, and compare your contours with the original contours that were used for treatment. There's no better way to learn contouring than straight from the experts themselves. You can save your contours and have them reviewed by a mentor or colleague.

New *ATC Grant*

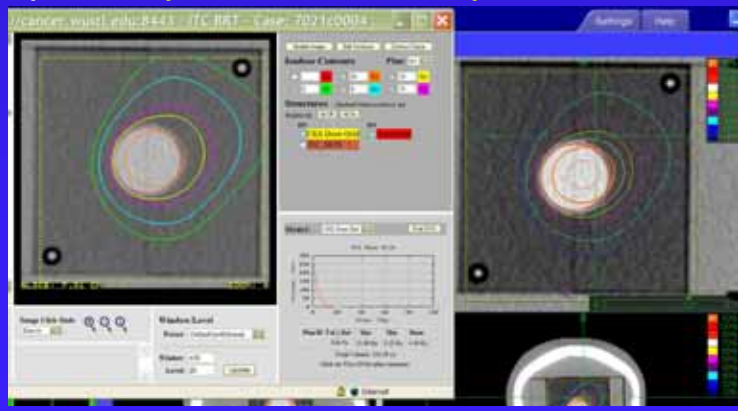
- Explore ways in which ATC effort can become synergistic with other NIH informatics efforts:
  - Quality Research in Radiation Oncology (QRRO: Frank Wilson, Jean Owen)
  - R01CA8615: PLanUNC (P.I. Ed Chaney) regarding possible collaborations regarding use of within QuASAR system. Main focus is on validation of a convolution/superposition algorithm, and implementation of a multi-image handling tool for ART/IGRT. Implementing multiple standard and cutting-edge registration and segmentation techniques.
  - R01CA116743: (P.I. George Xu, Rensselaer Polytechnic Institute, Troy, NY) Patient Modeling and Organ Dose Calculations Using Monte Carlo Methods

ATC(ITC) Digital Data Exchange Development Efforts will continue to be mission vritical: :

- **Maintain requirements for clinical trials data submissions**
  - RTOG Data Exchange Format Spec.
  - ATC DICOM Conformance Statement
- **Assistance to TP vendors**
  - Hosted 6 Digital Data Exchange and DICOM Technical Workshops (1995–2004) for TP vendors
  - Assist individual TPS manufacturers in implementing ATC compliant export capabilities
  - Organize 2004 ATC/AAPM/NEMA DICOM Demonstration
  - Participated in DICOM WG-18 (Clinical Trials)
  - Actively involved in IHE-RO Initiative (DICOM interoperability) and DICOM WG-7 (development of next-generation DICOM RT Objects)

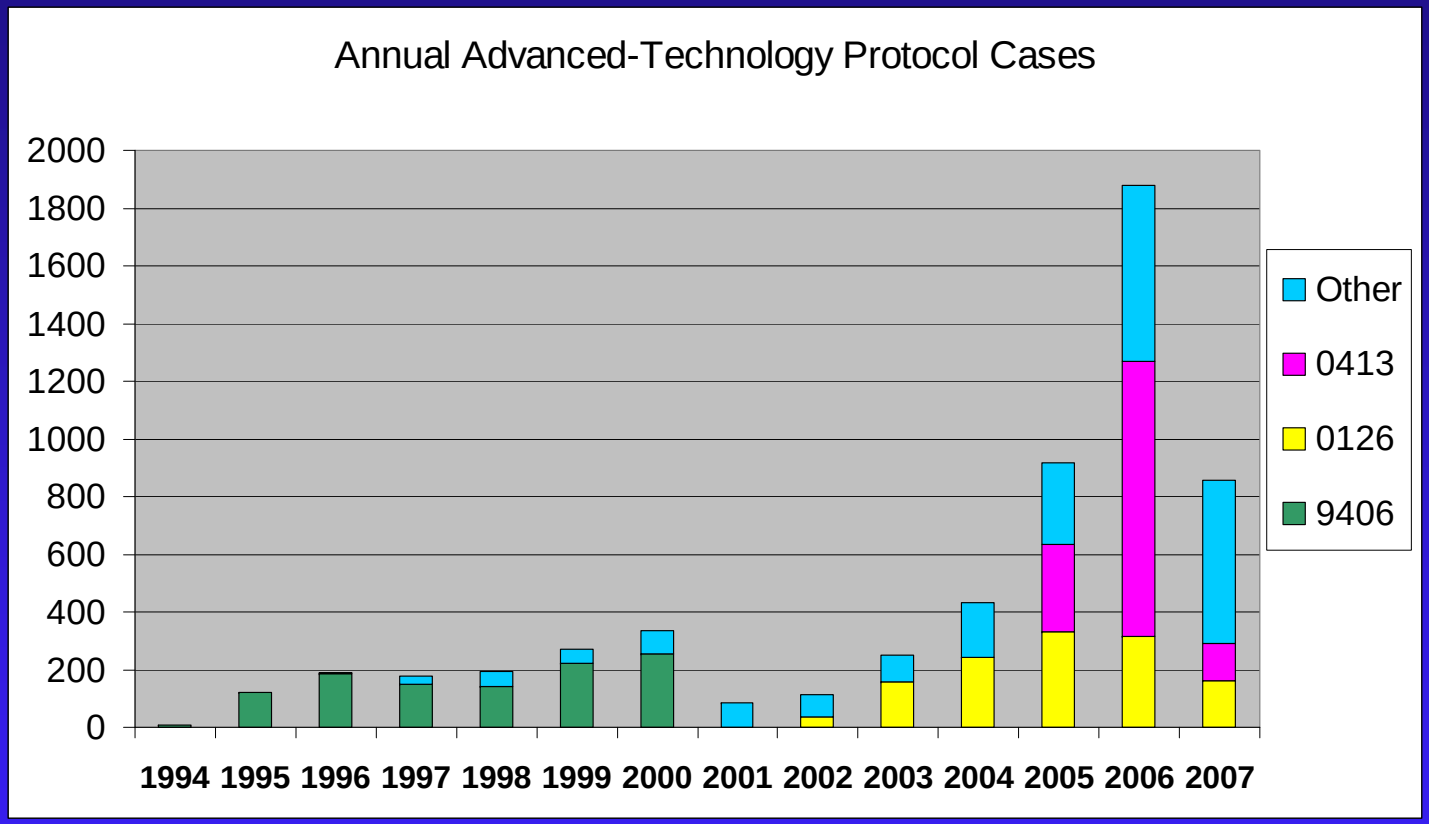
Treatment Planning Systems			Exchange Format	Treatment Modality					
Vendor	System	Version[1]		3DCRT	IMRT	SBRT[2]	Seed Brachy	HDR Brachy	Protons
CMS	Focus/XiO	3.1	R	✓	✓	✓	✓		✓
	XiO	4.3.1	D	✓	✓				
Elekta	RenderPlan 3D		R	✓					
	PrecisePlan	2.01	D	✓	✓	✓			
Nomos	Corvus		R		✓[3]				
Nucletron	Helax TMS		R	✓	✓				
	TheraPlan Plus		R	✓					
	Oncentra MasterPlan	1.5	D	✓	✓				
	PLATO RTS	2.62	D	✓					
	PLATO BPS	14.2.6	D					✓	
Philips	Pinnacle[3]		R	✓	✓	✓			
	AcqPlan	4.9	R	✓					
Rosses Medical	Strata Suite CTPlan	4.0	R				✓		
RTek	PIPER	2.1.2	R				✓		
TomoTherapy	Hi-ART	3.0[4]	D		✓				
Varian	BrachyVision	6.5 (Build 7.1.67)	D					✓	
	Eclipse	7.1	D	✓	✓	✓			✓
	VariSeed	7.1	D				✓		

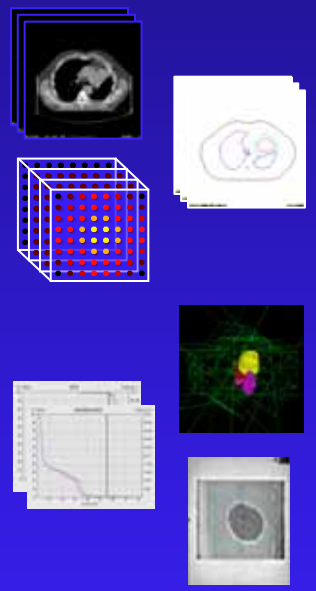
Table of ATC Compliant TP Systems (see http://atc.wustl.edu)



Screen capture showing comparison of RRT (left) and CyberKnife iso-dose displays

- **<u>Service Objective</u>: August 2007 ATC Mtg: 5823 Complete, Protocol-Case, Volumetric Digital Data Sets Submitted Over 13 Year Period using QuASAR**





- **9 commercial TPS vendors (18 TPSs) have implemented ATC compliant export capability.**
- **520 institutions able to submit data**

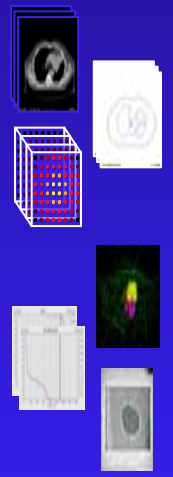
Data Integrity QA Prior to Review for Protocol Compliance

- Experience shows approximately 25% of data sets received require some intervention to be reviewable.
- Data QA Concerns
  - Completeness
    - Are required objects present & interpretable?
  - Identification
    - Are case, plan, structure IDs consistent?
  - Consistency
    - Are images, structures, doses spatially registered?
    - Are doses properly scaled?
    - Are DVHs calculated in a consistent manner?

Service Objective: Digital Data Integrity QA for protocol cases using QuASAR

Table 2: 2007 - Protocol Case Digital data submissions per protocol and the number of problems encountered that required human intervention by the ITC personnel.

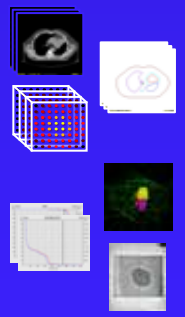
Protocol	# of cases Digitally Submitted	Problems Requiring Human Intervention	% of cases requiring human intervention
0117	27	4	14.8
0126	111	34	30.6
0232	49	4	8.2
0234	3	0	0
0413	159	41	25.8
0415	107	22	20.6
0417	0	0	0
0418	32	5	15.6
0435	1	1	100
0438	3	1	33.3
0521	67	39	58.2
0522	118	19	16.1
0529	15	3	20
TOTAL	**692**	**173**	**25**



Service Objective: Protocol Data Submission for Credentialing - DDIQA

Table 4: 2007 - Credentialing submissions per protocol and the number of problems encountered that required human intervention by the ITC personnel.

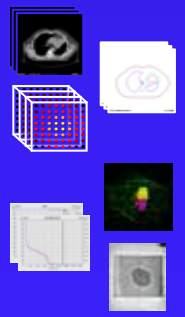
Protocol	# of cases Digitally Submitted	Problems Requiring Human Intervention	% of cases requiring human intervention
0117			0
0126	10	5	50
0232	13	1	7.7
0413	83	29	34.9
0415	3	0	0
0435	1	0	0
0521	3	0	0
0522	39	12	30.8
TOTAL	**152**	**47**	**30.9**



Service Objective: Phantom Data Submission for Credentialing - DDIQA

Table 5: Phantom submissions per phantom type and the number of problems encountered that required human intervention by the ITC personnel since March 2006.

Phantom	# of Submissions	Problems Requiring Human Intervention	% of cases requiring human intervention
H&N	164	42	26
Pelvis	46	18	39
Lung	14	7	50
Liver	3	0	0
TOTAL	**227**	**73**	**32**



Protocol Compliance Review

- Protocol compliance review consists of:
  - review of target volume and organ at risk contours compliance by the specific Protocol Study Chair (SC) (QA Center designees) using QuASAR's web-based *Remote Review Tool (RRT)*; and
  - review of protocol dose prescription and dose heterogeneity compliance using the RRT.
  - Timeliness of review can be problematic

ATC(ITC) Support of NABTT Clinical Trials

- NABTT (ATC is working with Dr. John Fiveash, M.D., Department of Radiation Oncology, Univ. of Alabama Birmingham)
  - There will be 9-10 NABTT institutions participating in these studies.
  - Protocols are Phase I/II with maximum of 90-100 cases.
  - Plan is to review approx. 30-50% of protocol cases (all IMRT and first case for 3DCRT)
  - Credentialing involves planning a benchmark case and submitting data (same benchmark for all protocols)
  - QA for currently active study (NABTT 0603) to be done by J. Fiveash and Bob Lustig. ATC will identify this protocol as N0603.

ATC(ITC) Support of NABTT Clinical Trials

- Case will be uploaded to ATC website for review. This will occur after boost has been planned and will approximately occur at the time the patient has completed treatment. Treating radiation oncologist will communicate via email with NABTT central office that case has been uploaded. It is the responsibility of the treating physician to upload IMRT cases as the central office will not know if IMRT or 3D was used to plan the case.
- Email will be sent to protocol Rad. Oncology PI by central office that case has been uploaded and is ready for review. ITC will be cc'd on this email (itc@castor.wustl.edu) as well so that that they are aware the dataset has been submitted and is ready to be processed for QA. If a case is from the Radiation Oncology PI's institution, the email will also be sent to Drs. Fiveash and Shaw to provide peer review.
- ITC will process the data and provide Digital Data integrity QA on the data. Once the data are ready for review the central office will be notified and they will notify the Radiation Oncology PI.
- Radiation Oncology PI will logon and review cases at least monthly. Email report of reviewed cases and outcomes will be sent to NABTT central office with cc to Drs Shaw and Fiveash and ITC.
- Central office will compare theoretical audit list to actual audited list quarterly and send email to Drs. Fiveash and Shaw. Theoretical audit list includes all patients that are the first enrolled patients by each institution on each protocol. Additional patients treated with IMRT will also be uploaded for reviewed.
- Drs. Fiveash and Shaw will maintain a spreadsheet with credentialing and audit results for all trials. Results will be reviewed at the NABTT meeting.

ATC(ITC) Support of EORTC Clinical Trials

- ATC(ITC) is working with the EORTC to provide data integrity QA for the upcoming EORTC Protocol 22042 “Adjuvant postoperative high-dose radiotherapy for atypical and malignant meningioma: a Phase-II and registration study”.
- Testing of data submission (using SFTP) and review (using RRT) are currently underway.
- Waiting on signed agreement regarding protection of patient data.

ATC(ITC) Support of JCOG Clinical Trials

- Institutions participating in protocol JCOG 0403 submit digital data representing CT images, structure sets, treatment plans, 3D dose distributions, and DVHs to Dr. Satoshi Ishikura, Director of the Radiotherapy Support Center, Tokyo, JAPAN, who then forwards these data to ITC in St. Louis for processing.
- Data are reviewed by Dr. Ishikura or his delegate using the ITC Remote Review Tool.
- Currently, 14 institutions are eligible to enroll patients and capable of digital data submission on JCOG 0403; 125 patients are registered to study.

ATC(ITC) Support of AstraZeneca Clinical Trial

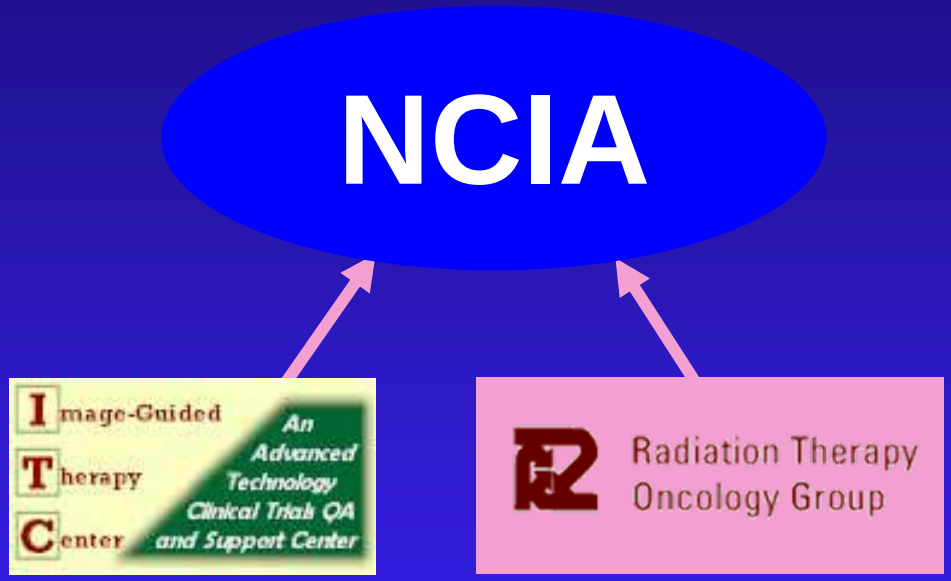
- ITC support of the AstraZeneca H&N protocol has begun.
  - Three institutions credentialed
  - 8 case studies have been submitted and reviewed

ATC is working with caBIG/NCIA

- ATC is one of the funded participants in the caBIG In Vivo Imaging Workspace.
  - ATC members (ITC, RTOG, QARC) and ACRIN are actively participating in the Testbed Special Interest Group (SIG).
  - Exploring project with Ohio State Univ., QARC, ITC, and CALGB
  - Working with OSU on RSNA demonstration project “Application of caGrid® Middleware to Facilitate Quality Assurance for Advanced Technology Radiation Therapy Clinical Trials”
    - Volumetric CT images, target-volume/organ-at-risk (TV/OAR) contours, treatment plans, and 3D dose distributions submitted by study participants converted to Matlab format using CERR.
    - CERR datasets are then used for distributed protocol compliance review of image segmentation and dosimetry.
    - To facilitate distributed review of the CERR datasets, a secure grid-based infrastructure is used for distribution of data sets and collection of reports

RTOG 9406 NCIA Dataset Project

Proposed addition of 3DOG/RTOG 9406 treatment planning and outcomes data set to the National Cancer Imaging Archive



- **Treatment Planning Data**
  - **DICOM RT**
  - **CERR**
- **Histories, Staging, and Outcomes Data**
  - **Forms**
  - **CDEs**

ATC (ITC, RTOG) Posters/Presentations at 2007 ASTRO Annual Meeting

- A Survey of the ITC Volumetric Treatment Planning Data Archive Supporting RTOG Advanced Technology Clinical Trials: W. R. Bosch, W. L. Straube, J. W. Matthews, J. M. Michalski, J. O. Deasy, B. Young, E. O'Meara, W. J. Curran, J. D. Cox, J. A. Purdy.
- Dosimetric Evaluation of Heterogeneity Corrections for RTOG 0236: Hypofractionated Radiotherapy of Inoperable Stage I/II Non-Small Cell Lung Cancer: Y. Xiao, W. L. Straube, W. R. Bosch, R. D. Timmerman, J. Galvin.
- Dose-volume analyses of grade $\geq$ 2 late rectal toxicity among patients treated on protocol RTOG 94-06: S.L.Tucker, L. Dong, W.R. Bosch, J. Michalski, K. Winter, R. Mohan, Kuban, M.R. Cheung, A.K. Lee, J.D. Cox
- Fit of a Generalized Lyman Normal-tissue Complication Probability (NTCP) Model to Grade > 2 Late Rectal Toxicity Data from Patients Treated on Protocol RTOG 94-06: S. L. Tucker, L. Dong, W. R. Bosch, J. Michalski, K. Winter, A. K. Lee, M. R.Cheung, D. A. Kuban, J. D. Cox, R. Mohan
- Variation in the Definition of Clinical Target Volumes for Postoperative Conformal Radiation Therapy of Prostate Cancer: J. M. Michalski, C. Lawton, I. El-Naqa, M. A. Ritter, T. Pisansky, C. N. Catton, R. K. Valicenti, M. J. Seider, H. M. Sandler, W. Bosch.

ATC Workshop (Special Interest Session) held at 2007 AAMD Annual Meeting

- Held as breakout session from main program
- First session involved Eclipse (8:30 - 9:30); second session involved Pinnacle (10:00-11:00); third session involved Rahd and Nucletron (11:00-12:30)
- Bill Straube presented an overview of ATC and digital data submission to the groups prior to each session and then vendors demonstrated TPS digital data submission UI's.
- All Vendors brought equipment to demonstrate their submission.
- All vendors plan on putting together information for the ATC website.
- ATC should plan to do another workshop at the next AAMD Annual meeting to be held in New Orleans.

DATA REQUESTS
ATC Supported Clinical Trials

- 06/13/07 - Andrew Jackson Ph.D., Department of Medical Physics, Memorial Sloan Kettering Cancer Center.
  - From the ATC-ITC, we request (for each patient treated under RTOG 9311) Dose Volume Histograms (% volume, absolute dose – calculated with tissue inhomogeneity corrections) for paired lungs only or for the two lungs separately and the paired lungs if available, together with the absolute volumes of these structures.
  - From the ATC-RTOG, we request each patient's RTOG acute and late lung complication grade, time of diagnosis of complication and follow-up time, adjuvant chemotherapy status (yes/no) from patients treated under RTOG 9311.

DATA REQUESTS
ATC Supported Clinical Trials

- 06/14/07 - Lyndon S. Hibbard, PhD, CMS Research, CMS, Inc., St. Louis, MO,
  - From the ATC-ITC, we request data in the RTOG Protocol 9406 (“A Phase I/II Dose Escalation Study … Adenocarcinoma of the Prostate”). We are particularly interested in the CT images and anatomy structure contours to develop programs to automatically segment the prostate (GTV) and critical organs.

Challenges/Opportunities: ATC Supported Trials

- Continue to update QuASAR without disrupting support of ongoing clinical trials;
- Developing a more formal mechanism for evaluating how well ATC is meeting its ***developmental*, *coordination*, and *service*** objectives**;**
- Multi-modality imaging (PET, MRI, MRS) target definition (data import) and subsequent image fusion QA;
- IGRT data submission and QA (EPID, daily MV and kV Cone beam CT, Helical Tomotherapy MV CT, US,…);
- QA review of the accuracy and quality of the institution's motion management methodology;
- Heterogeneous dose calculations (QA evaluation criteria);
- Outcome analysis tools (e.g., for protocols such as lung in which the dose data archived have either poor or no dose heterogeneity corrections;
- Proton beam therapy;
- ATC compliant data export for stereotactic specialized treatment systems (e.g., Elekta Gamma Knife);
- New processes such as adaptive radiation therapy (need deformable registration QA tools)
- Data sharing

Challenges/Opportunities: ATC Supported Trials

- NCI (Dr. Deye) to appoint independent Evaluation Committee (EC)
- NCI (Dr. Deye) to appoint new ATC Steering Committee
- Agree on dates for next ATC meeting (at ITC?)