ATC Principal Investigator's Report
ATC Steering Committee Meeting
Bethesda, MD
November 6, 2007

James A. Purdy, Ph.D.
Department of Radiation Oncology
UC Davis Medical Center
Sacramento, CA, USA

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

New ATC Grant

- The Advanced Technology Consortium (ATC) for Clinical Trials Quality Assurance (QA) is supported by a National Cancer Institute (NCI) U24 grant to Washington University.
- The ATC functions as a “virtual entity” made up of the following clinical trials QA Centers:
  - Image-Guided Therapy QA Center
  - Radiation Therapy Oncology Group (RTOG)
  - Radiological Physics Center (RPC, M.D. Anderson Cancer Center)
  - Quality Assurance Review Center (QARC).

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.

Introduced new acronym for ATC Method 1

QuASA²R: Quality Assurance Submission, Archive, Analysis, and Review System

The ITC developed **QuASA²R** 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.

QuASA²R

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

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

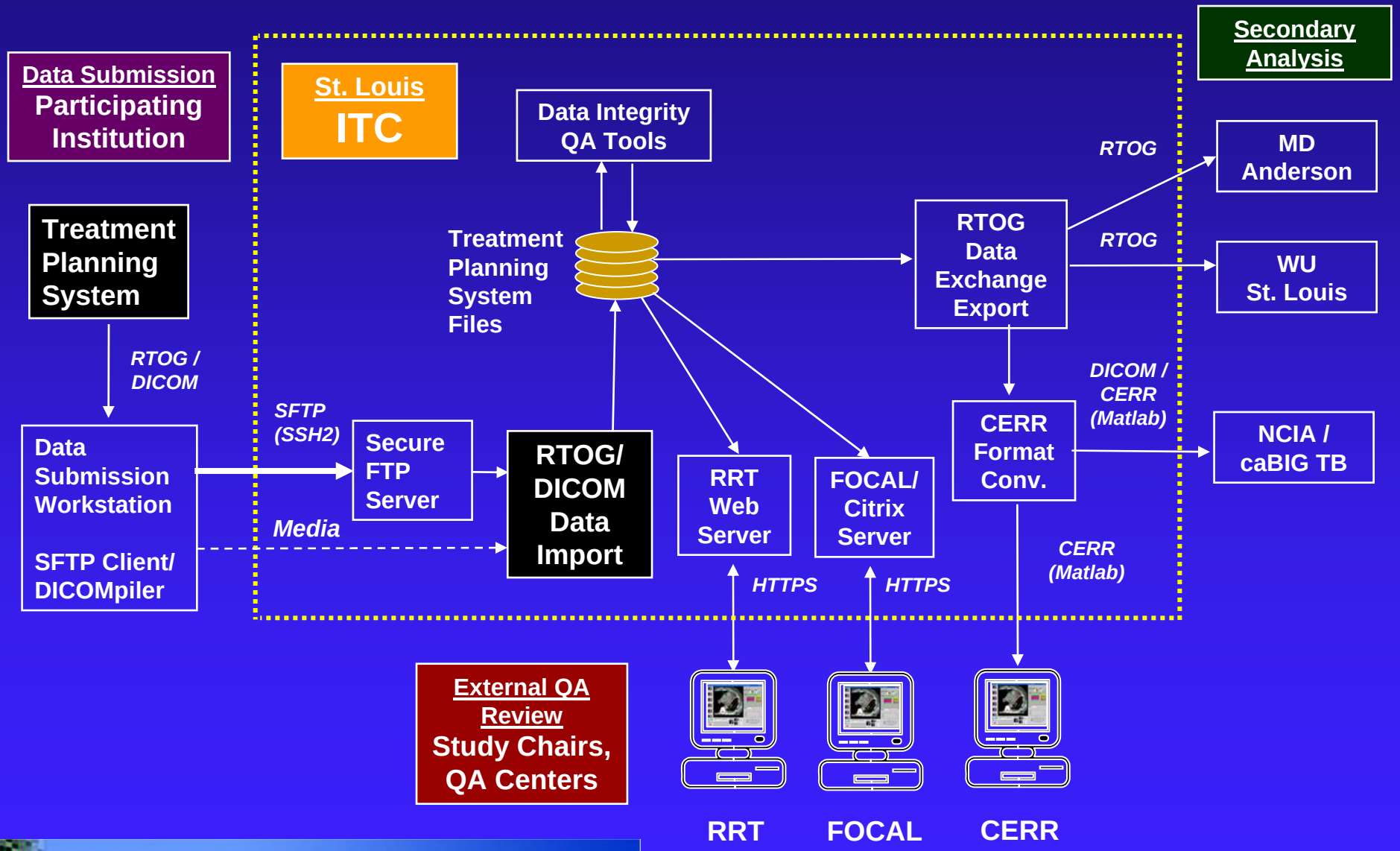
… has enabled the collection, review, and analysis of nearly 6000 protocol case data sets, and

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

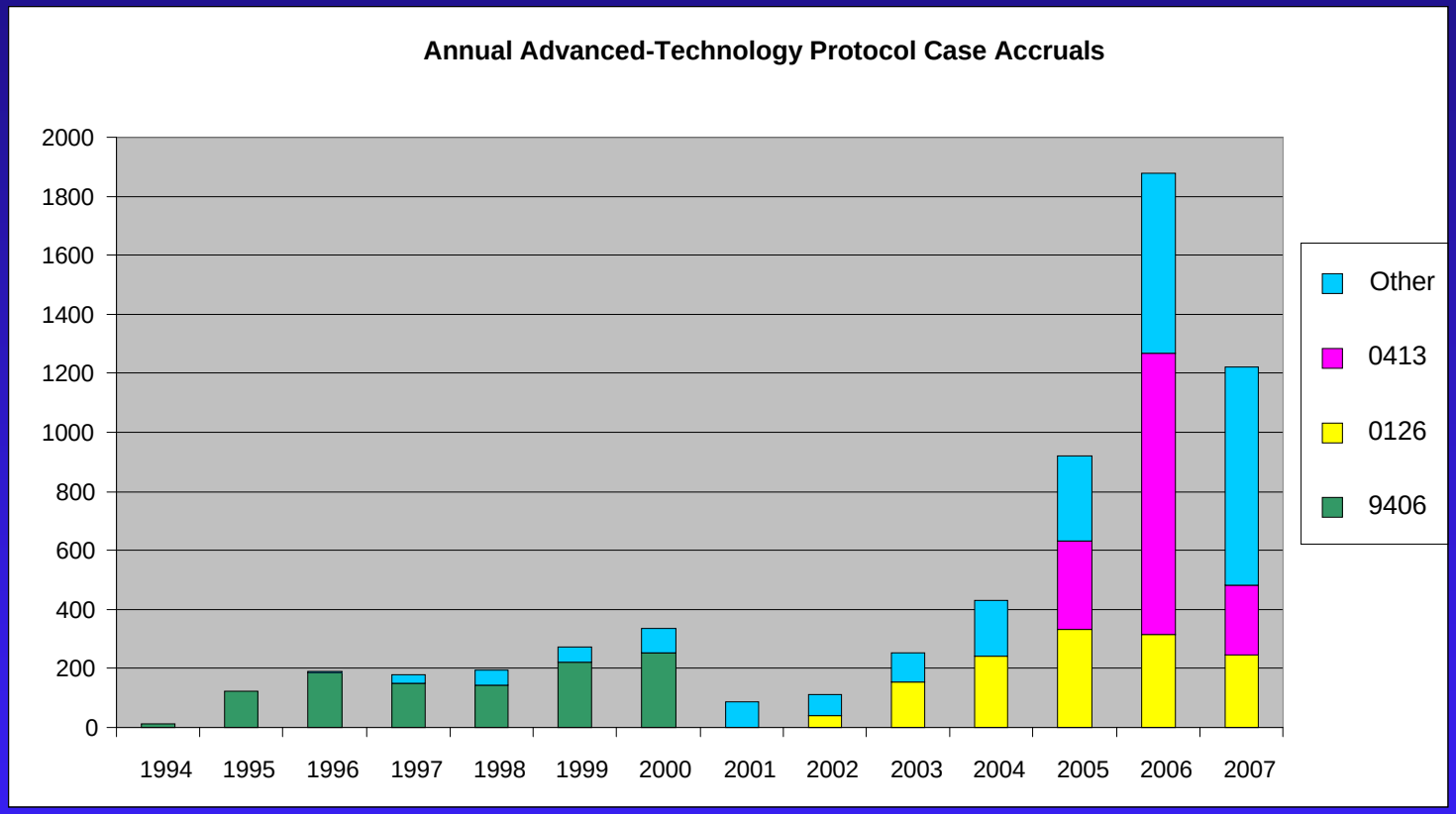
QuASA²R System

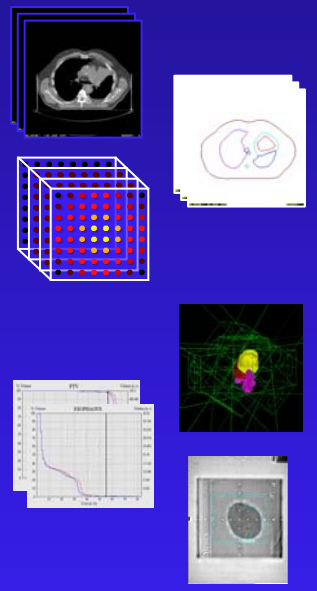
- QuASA²R developed by the ITC through the ATC
- National / International QA resource for RT cooperative protocol groups
- In active production at ITC and QARC
- Supports collection, QA review and analysis of volumetric images and dosimetry
- 13 active protocols, 10 closed protocols (7 cooperative groups/sponsors)

QuASA²R – *Components and Data Flow*



- **<u>Service Objective</u>: August 2007 ATC Mtg:** Nearly 6000 **Complete, Protocol-Case, Volumetric Digital Data Sets Submitted Over 14 Year Period using QuASA²R**





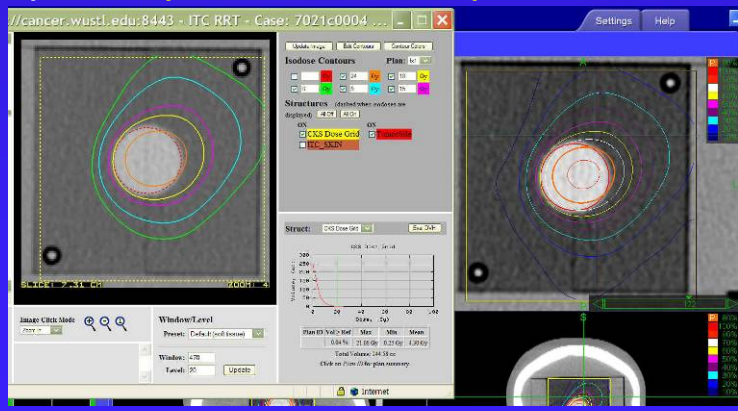
- **9 commercial TPS vendors (18 TPSs) have implemented ATC compliant export capability.**
- **520 institutions able to submit data**

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

- **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)

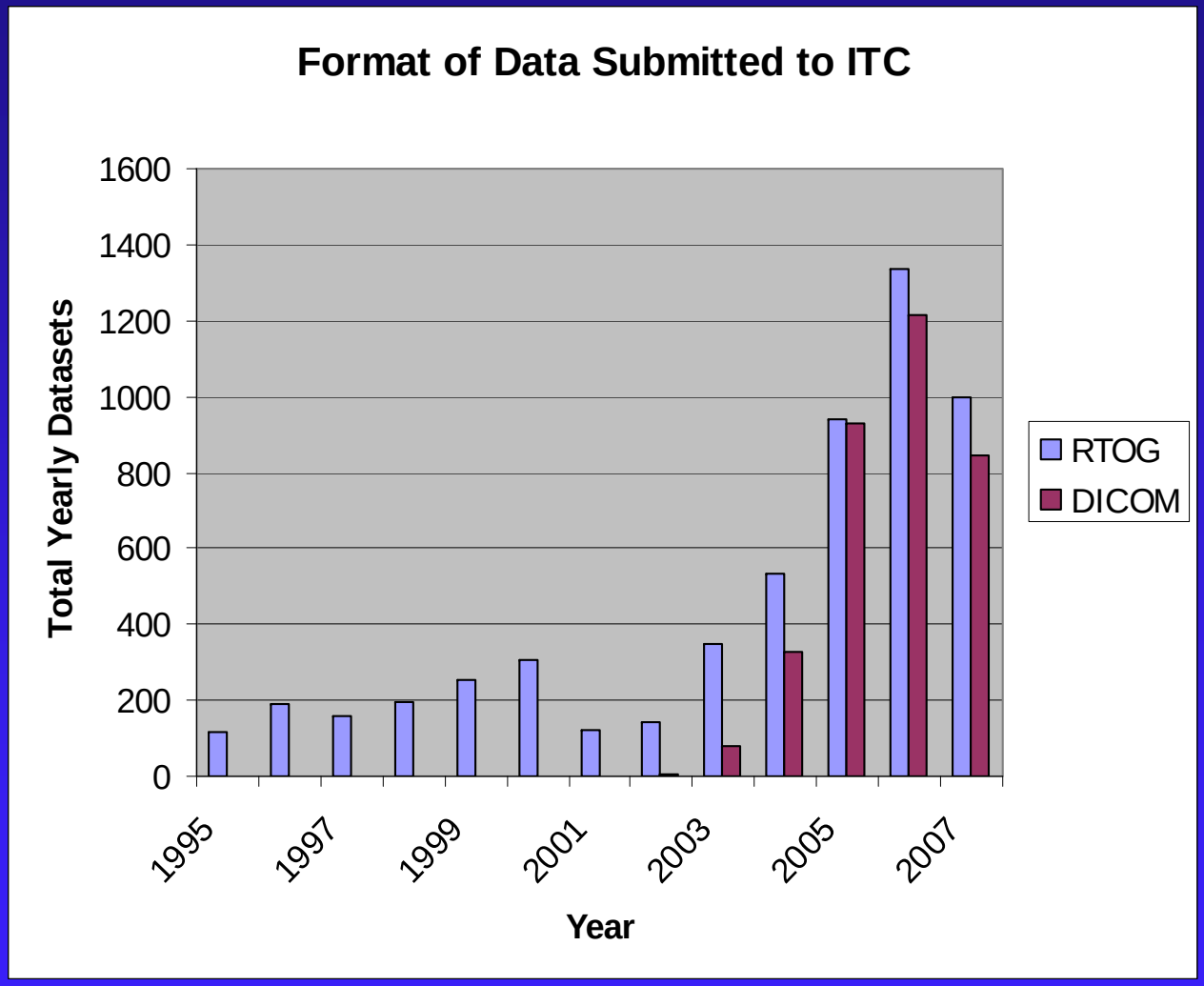
Treatment Planning Systems			Exchange Format	Treatment Modality					
Vendor	System	Version[1]		3DCRT	IMRT	SBRT[2]	Seed Brachy	HDR Brachy	Protons
CMS	Focus/XiO	3.1	R	✓	✓	✓	✓		✓
	XiO	4.3.1	D	✓	✓				
Elekta	RenderPlan 3D		R	✓					
	PrecisePlan	2.01	D	✓	✓	✓			
Nomos	Corvus		R		✓[3]				
Nucletron	Helax TMS		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				✓		

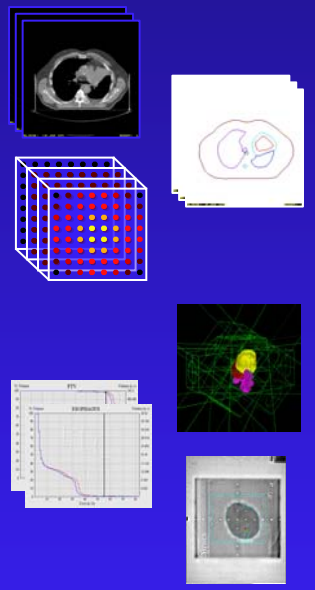
Table of ATC Compliant TP Systems (see http://atc.wustl.edu)



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

ATC(ITC) Digital Data Exchange Development Efforts

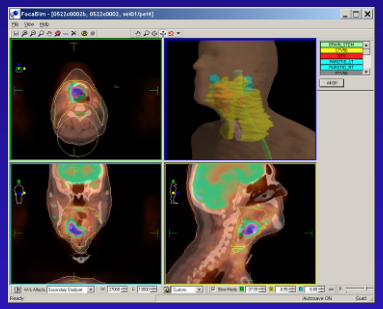




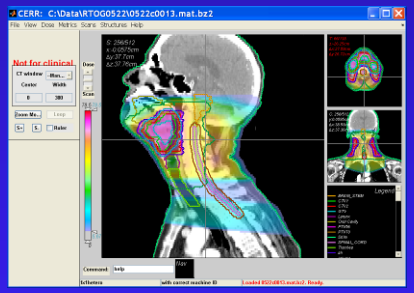
QuASAR – *Adapting and Innovating*

- 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
- Dr. Joe Deasy and colleagues in WU Bioinformatics & Outcomes Research Division are now funded by ATC to further the development of software tools 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

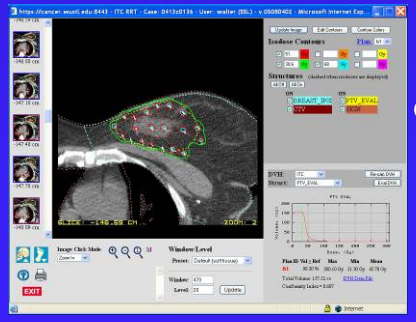
CMS Focal®



WU CERR

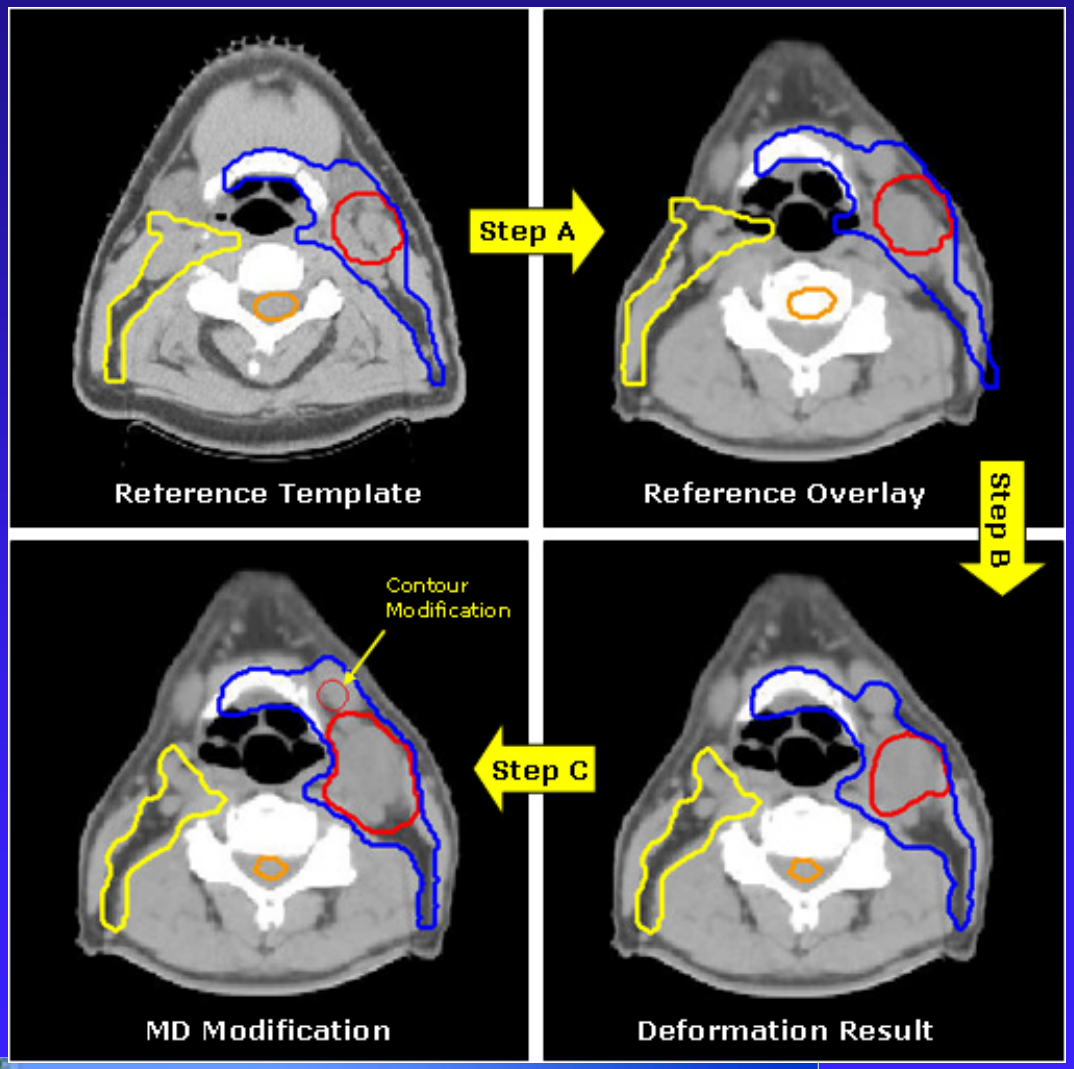


Remote Review Tool



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

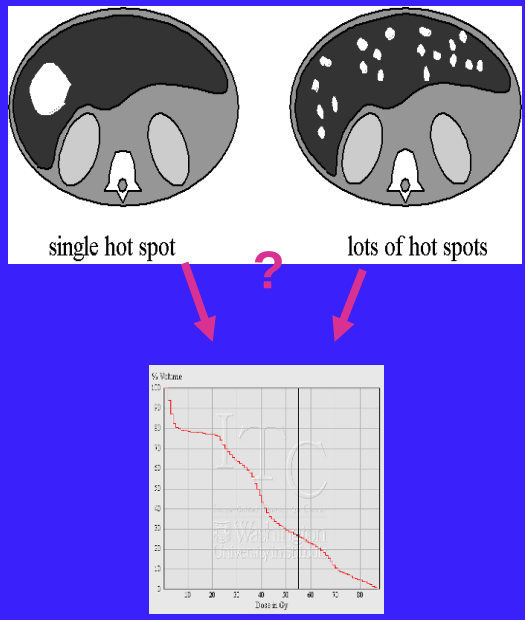
Step C: Physicians modify contours based on clinical judgment

IJROBP 2007 in press

Why Collect Volumetric Data?

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

1. DVHs do not retain spatial information; only aggregate volume of a structure at a given dose is counted.
2. Without vol. 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 vol. 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. DVH statistics do not distinguish between a single, large hot spot and multiple, smaller hot spots.

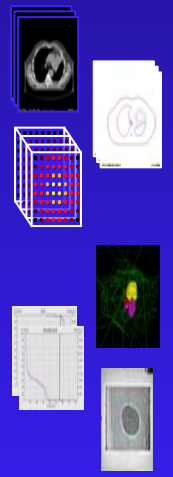
Data Integrity QA Prior to Review for Protocol Compliance

- 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 QuASA²R

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

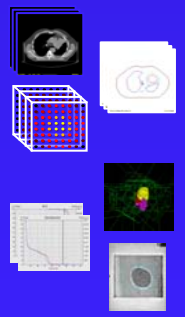
Protocol	# of cases Digitally Submitted	Problems Requiring Human Intervention	% of cases requiring human intervention
0117	27	4	14.8
0126	111	34	30.6
0232	49	4	8.2
0234	3	0	0
0413	159	41	25.8
0415	107	22	20.6
0417	0	0	0
0418	32	5	15.6
0435	1	1	100
0438	3	1	33.3
0521	67	39	58.2
0522	118	19	16.1
0529	15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



Service Objective: Phantom Data Submission for Credentialing - DDIQA

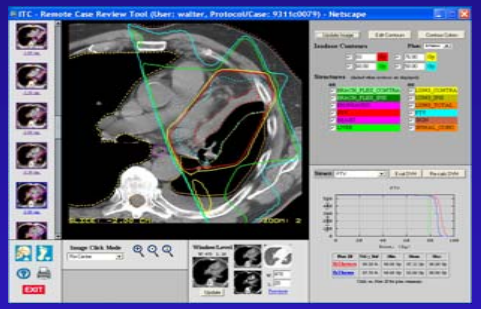
Table 5: Phantom submissions per phantom type and the number of problems encountered that required human intervention by the ITC personnel since March 2006.

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**

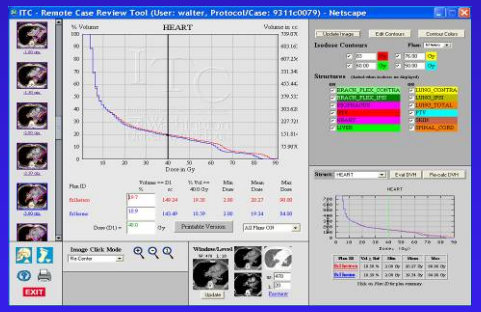


Protocol Compliance Review

- **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**



RRT structure contour, iso-dose display



RRT dose-volume analysis display

RTOG Protocols Contributing to the QuASA²R Archive

Site	Protocol		Open	Data sets*	Rx dose	Organs at Risk
Brain	9803	Brain 3DCRT	N	195		Brain_stem Cerebellum Cerebrum Optic_chiasm Optic_nerve Spinal_cord
Breast	0319	Partial breast 3DCRT	N	53	38.5 Gy	Breast Heart Lung Thyroid
	0413	Partial breast	Y	1315	34 Gy (Brachy) or 38.5 Gy (3DCRT)	Breast Heart Lung Thyroid
GI	0529	Anal canal IMRT	Y	28	54 Gy	Femurs Genitals Iliac_crest Large_bowel Small_bowel
	0438	Liver SBRT	Y	8		Kidney Liver Small_bowel Spinal_cord Stomach
GU	9406	Prostate 3D	N	1062		Bladder Femurs Penile_bulb* Rectum
	0126	Prostate 3D/IMRT	Y	1166	70.2 - 79.2 Gy	Bladder Femurs Penile_bulb Rectum
	0232	Prostate seeds	Y	267	Brachy seeds +/- EBRT (45Gy)	Rectum Urethra
	0415	Prostate hypofractionated	Y	187	73.8 Gy (conv.) or 70 Gy (hypo-frac)	Bladder Femurs Penile_bulb Rectum
	0521	Prostate IMRT	Y	163	72 Gy	Bladder Femurs Penile_bulb Rectum
	0321	Prostate HDR	N	122		Bladder Rectum Urethra
GYN	0418	Cervix IMRT	Y	71	50.4 Gy	Bladder Femurs Rectum Sacrum Small_bowel
H/N	0022	Oropharynx 3DCRT/IMRT	N	68	66 Gy	Brain_stem Larynx Mandible Parotids Spinal_cord Submandib_glands
	0225	Nasopharynx 3DCRT/IMRT	N	65	70 Gy	Brain Brain_stem Larynx Lens Mandible Optic_nerve Optic_chiasm Orbit Parotitds Pituitary Spinal_cord Temporal_lobe TMJ Tongue
	0234	Head/Neck IMRT	Y	79		Spinal_cord
	0435	Head/Neck Palifermin	Y	8	70 Gy	Brachial_plexus Brain_stem Larynx Parotids Spinal_cord
	0522	Head/Neck 3DCRT/IMRT, PET	Y	223	70 Gy	Brachial_plexus Brain_stem Larynx Parotids Spinal_cord
Lung	9311	Lung 3DCRT	N	177		Brachial_plexus Esophagus Heart Liver Lung Spinal_cord
	0117	Lung 3DCRT	Y	57	70 - 75.25 Gy	Esophagus Heart Liver Lung Spinal_cord
	0236	Lung SBRT	N	52		Brachial_plexus Bronchial_tree Esophagus Heart Lung Spinal_cord Trachea
	0515	Lung PET/CT target delineation	Y	9		Carina Heart Liver Lung Spinal_cord

* Data sets include: CT images, Structure Contours, 3D Dose Distributions, and Plans (3DCRT, Brachy seeds)

ITC QuASA²R Archive includes over 5000 complete TP data sets quantifying the relationship between image-based anatomy and planned doses. Each dataset includes planning CTs, target-volume/organs-at-risk contours, and 3D dose distributions. Plans are available for 3DCRT and brachy. seeds.

Sample Dose Volume Statistics

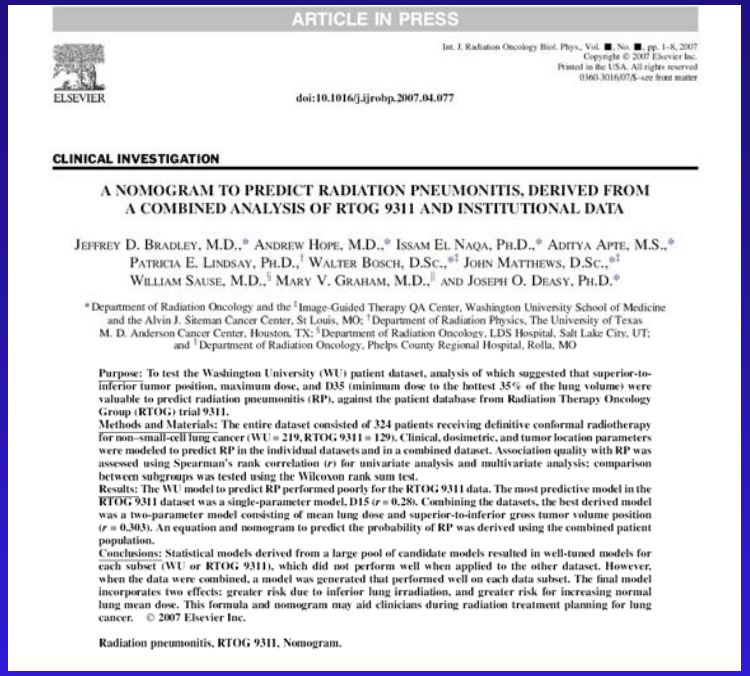
- Collection of volumetric dosimetry data has enabled RTOG investigators to perform QA to maintain the consistency of target volumes and organs at risk, allowing meaningful comparison on dose-volume statistics for advanced-technology trials.
- Having 3-D geometric data for structures has also made it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

Head & Neck (IMRT, N=64)		Min	Max	Avg	
PTV	D_{98}	58.0	73.4	67.6	Gy
Spinal Cord	D_{mean}	32.8	44.8	39.6	Gy
Parotid	D_{mean}	21.2	50.3	32.4	Gy
Larynx	D_{mean}	3.9	57.7	32.9	Gy
Lung (3DCRT, N=158)		**Min**	**Max**	**Avg**	
PTV	D_{98}	50.3	98.2	77.4	Gy
Spinal Cord	D_2	0.1	60.1	26.0	Gy
Esophagus	D_{mean}	0.0	63.8	15.9	Gy
Heart	D_{mean}	0.0	45.3	10.5	Gy
Liver	D_{mean}	0.0	19.3	1.2	Gy
Brachial Plexus	D_{mean}	0.0	57.7	4.6	Gy
Lung	V_{20}	5.3	46.6	21.2	%
Prostate (3DCRT, N=984)		**Min**	**Max**	**Avg**	
PTV	D_{98}	52.2	81.6	75.0	Gy
Bladder	D_{mean}	4.9	75.9	37.7	Gy
Rectum	D_{mean}	12.9	72.5	42.7	Gy
Femoral Heads	D_{mean}	1.8	49.5	32.4	Gy

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.

- 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].



ARTICLE IN PRESS

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–8, 2007

0360-3016/07/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2007.04.077

CLINICAL INVESTIGATION

A NOMOGRAM TO PREDICT RADIATION PNEUMONITIS, DERIVED FROM A COMBINED ANALYSIS OF RTOG 9311 AND INSTITUTIONAL DATA

JEFFREY D. BRADLEY, M.D.,* ANDREW HOPE, M.D.,* ISSAM EL NAQA, PH.D.,* ADITYA APTE, M.S.,*
PATRICIA E. LINDSAY, PH.D.,† WALTER BOSCH, D.SC.,*‡ JOHN MATTHEWS, D.SC.,*‡
WILLIAM SAUSE, M.D.,§ MARY V. GRAHAM, M.D.,‖ AND JOSEPH O. DEASY, PH.D.*

*Department of Radiation Oncology and the ‡Image-Guided Therapy QA Center, Washington University School of Medicine and the Alvin J. Siteman Cancer Center, St Louis, MO; †Department of Radiation Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX; §Department of Radiation Oncology, LDS Hospital, Salt Lake City, UT; and ‖Department of Radiation Oncology, Phelps County Regional Hospital, Rolla, MO

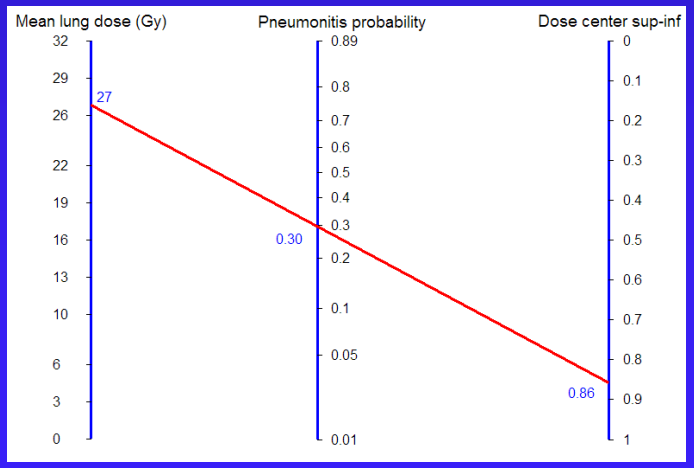
Purpose: To test the Washington University (WU) patient dataset, analysis of which suggested that superior-to-inferior tumor position, maximum dose, and D35 (minimum dose to the hottest 35% of the lung volume) were valuable to predict radiation pneumonitis (RP), against the patient database from Radiation Therapy Oncology Group (RTOG) trial 9311.

Methods and Materials: The entire dataset consisted of 324 patients receiving definitive conformal radiotherapy for non–small-cell lung cancer (WU = 219, RTOG 9311 = 129). Clinical, dosimetric, and tumor location parameters were modeled to predict RP in the individual datasets and in a combined dataset. Association quality with RP was assessed using Spearman's rank correlation (r) for univariate analysis and multivariate analysis; comparison between subgroups was tested using the Wilcoxon rank sum test.

Results: The WU model to predict RP performed poorly for the RTOG 9311 data. The most predictive model in the RTOG 9311 dataset was a single-parameter model, D15 ($r = 0.28$). Combining the datasets, the best derived model was a two-parameter model consisting of mean lung dose and superior-to-inferior gross tumor volume position ($r = 0.303$). An equation and nomogram to predict the probability of RP was derived using the combined patient population.

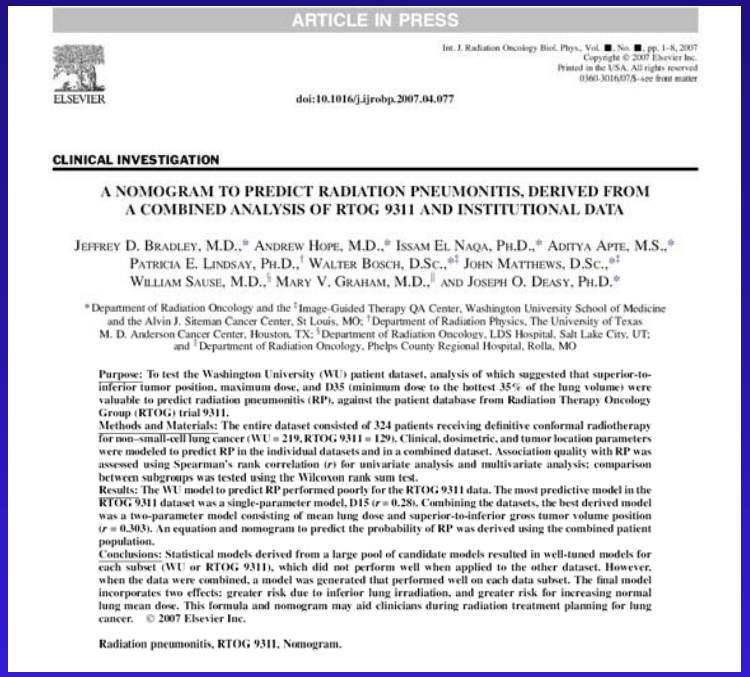
Conclusions: Statistical models derived from a large pool of candidate models resulted in well-tuned models for each subset (WU or RTOG 9311), which did not perform well when applied to the other dataset. However, when the data were combined, a model was generated that performed well on each data subset. The final model incorporates two effects: greater risk due to inferior lung irradiation, and greater risk for increasing normal lung mean dose. This formula and nomogram may aid clinicians during radiation treatment planning for lung cancer.

Radiation pneumonitis, RTOG 9311, Nomogram.



Secondary Analysis: Lung Toxicity (RTOG 9311)

- 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.



ARTICLE IN PRESS

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–8, 2007

0360-3016/07/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2007.04.077

CLINICAL INVESTIGATION

A NOMOGRAM TO PREDICT RADIATION PNEUMONITIS, DERIVED FROM A COMBINED ANALYSIS OF RTOG 9311 AND INSTITUTIONAL DATA

JEFFREY D. BRADLEY, M.D.,* ANDREW HOPE, M.D.,* ISSAM EL NAQA, PH.D.,* ADITYA APTE, M.S.,*
PATRICIA E. LINDSAY, PH.D.,† WALTER BOSCH, D.SC.,*‡ JOHN MATTHEWS, D.SC.,*‡
WILLIAM SAUSE, M.D.,§ MARY V. GRAHAM, M.D.,‖ AND JOSEPH O. DEASY, PH.D.*

*Department of Radiation Oncology and the ‡Image-Guided Therapy QA Center, Washington University School of Medicine and the Alvin J. Siteman Cancer Center, St Louis, MO; †Department of Radiation Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX; §Department of Radiation Oncology, LDS Hospital, Salt Lake City, UT; and ‖Department of Radiation Oncology, Phelps County Regional Hospital, Rolla, MO

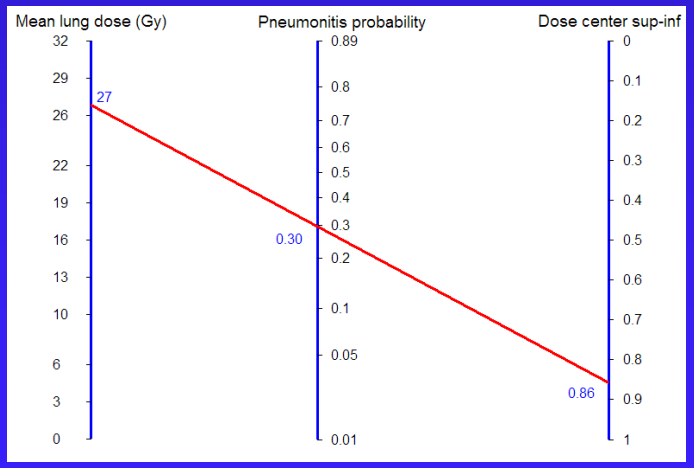
Purpose: To test the Washington University (WU) patient dataset, analysis of which suggested that superior-to-inferior tumor position, maximum dose, and D35 (minimum dose to the hottest 35% of the lung volume) were valuable to predict radiation pneumonitis (RP), against the patient database from Radiation Therapy Oncology Group (RTOG) trial 9311.

Methods and Materials: The entire dataset consisted of 324 patients receiving definitive conformal radiotherapy for non–small-cell lung cancer (WU = 219, RTOG 9311 = 129). Clinical, dosimetric, and tumor location parameters were modeled to predict RP in the individual datasets and in a combined dataset. Association quality with RP was assessed using Spearman's rank correlation (r) for univariate analysis and multivariate analysis; comparison between subgroups was tested using the Wilcoxon rank sum test.

Results: The WU model to predict RP performed poorly for the RTOG 9311 data. The most predictive model in the RTOG 9311 dataset was a single-parameter model, D15 ($r = 0.28$). Combining the datasets, the best derived model was a two-parameter model consisting of mean lung dose and superior-to-inferior gross tumor volume position ($r = 0.303$). An equation and nomogram to predict the probability of RP was derived using the combined patient population.

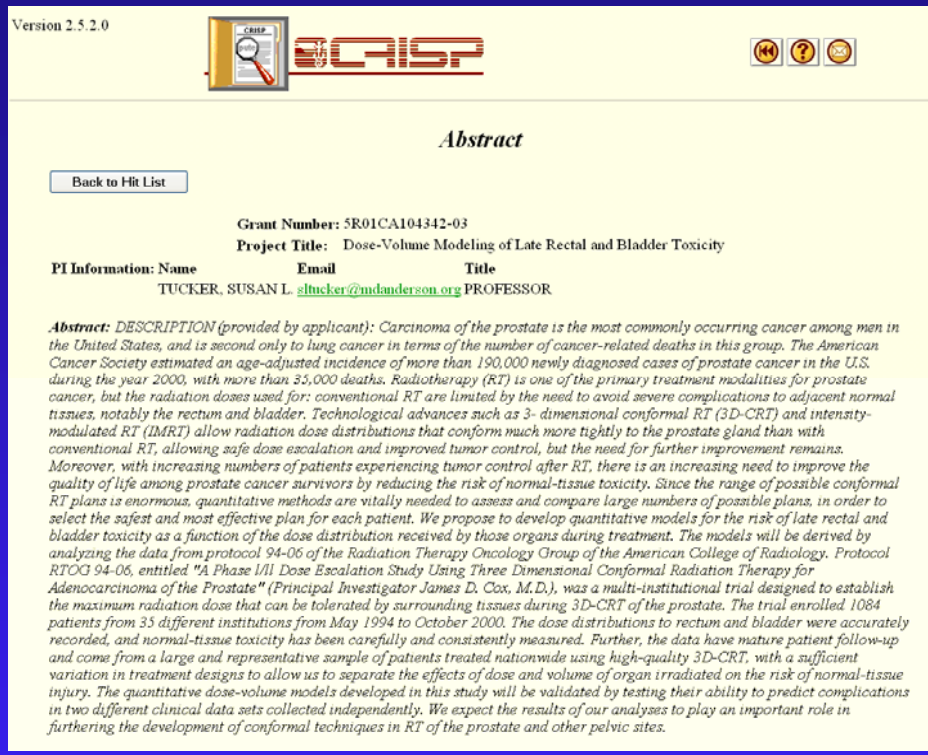
Conclusions: Statistical models derived from a large pool of candidate models resulted in well-tuned models for each subset (WU or RTOG 9311), which did not perform well when applied to the other dataset. However, when the data were combined, a model was generated that performed well on each data subset. The final model incorporates two effects: greater risk due to inferior lung irradiation, and greater risk for increasing normal lung mean dose. This formula and nomogram may aid clinicians during radiation treatment planning for lung cancer.

Radiation pneumonitis, RTOG 9311, Nomogram.



Secondary Analysis: GI Toxicity (RTOG 9406)

- 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 [See CRISP abstract at right].
- Results of this analysis were presented at ASTRO Annual Mtg.



Version 2.5.2.0

CRISP

Abstract

Back to Hit List

Grant Number: 5R01CA104342-03
Project Title: Dose-Volume Modeling of Late Rectal and Bladder Toxicity

PI Information: Name	Email	Title
TUCKER, SUSAN L.	sltucker@mdanderson.org	PROFESSOR

Abstract: *DESCRIPTION (provided by applicant): Carcinoma of the prostate is the most commonly occurring cancer among men in the United States, and is second only to lung cancer in terms of the number of cancer-related deaths in this group. The American Cancer Society estimated an age-adjusted incidence of more than 190,000 newly diagnosed cases of prostate cancer in the U.S. during the year 2000, with more than 35,000 deaths. Radiotherapy (RT) is one of the primary treatment modalities for prostate cancer, but the radiation doses used for: conventional RT are limited by the need to avoid severe complications to adjacent normal tissues, notably the rectum and bladder. Technological advances such as 3- dimensional conformal RT (3D-CRT) and intensity-modulated RT (IMRT) allow radiation dose distributions that conform much more tightly to the prostate gland than with conventional RT, allowing safe dose escalation and improved tumor control, but the need for further improvement remains. Moreover, with increasing numbers of patients experiencing tumor control after RT, there is an increasing need to improve the quality of life among prostate cancer survivors by reducing the risk of normal-tissue toxicity. Since the range of possible conformal RT plans is enormous, quantitative methods are vitally needed to assess and compare large numbers of possible plans, in order to select the safest and most effective plan for each patient. We propose to develop quantitative models for the risk of late rectal and bladder toxicity as a function of the dose distribution received by those organs during treatment. The models will be derived by analyzing the data from protocol 94-06 of the Radiation Therapy Oncology Group of the American College of Radiology. Protocol RTOG 94-06, entitled "A Phase I/II Dose Escalation Study Using Three Dimensional Conformal Radiation Therapy for Adenocarcinoma of the Prostate" (Principal Investigator James D. Cox, M.D.), was a multi-institutional trial designed to establish the maximum radiation dose that can be tolerated by surrounding tissues during 3D-CRT of the prostate. The trial enrolled 1084 patients from 35 different institutions from May 1994 to October 2000. The dose distributions to rectum and bladder were accurately recorded, and normal-tissue toxicity has been carefully and consistently measured. Further, the data have mature patient follow-up and come from a large and representative sample of patients treated nationwide using high-quality 3D-CRT, with a sufficient variation in treatment designs to allow us to separate the effects of dose and volume of organ irradiated on the risk of normal-tissue injury. The quantitative dose-volume models developed in this study will be validated by testing their ability to predict complications in two different clinical data sets collected independently. We expect the results of our analyses to play an important role in furthering the development of conformal techniques in RT of the prostate and other pelvic sites.*

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].
- 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 ($p \leq 0.039$) and concluded that dose to the bulb of the penis seems to be associated with the risk of radiation-induced impotence.

Int. J. Radiation Oncology Biol. Phys., Vol. 60, No. 5, pp. 1351–1356, 2004

0360-3016/04/$-see front matter
doi:10.1016/j.ijrobp.2004.05.026

CLINICAL INVESTIGATION — Prostate

PENILE BULB DOSE AND IMPOTENCE AFTER THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY FOR PROSTATE CANCER ON RTOG 9406: FINDINGS FROM A PROSPECTIVE, MULTI-INSTITUTIONAL, PHASE I/II DOSE-ESCALATION STUDY

MACK ROACH, M.D.,* KATHRYN WINTER, PH.D.,† JEFFREY M. MICHALSKI, M.D.,‡ JAMES D. COX, M.D.,§ JAMES A. PURDY, PH.D.,‖ WALTER BOSCH, D.SC.,‖ XIAO LIN, M.D.,‖ AND WILLIAM S. SHIPLEY, M.D.¶

*University of California San Francisco, San Francisco, CA; †Radiation Therapy Oncology Group, Philadelphia, PA; ‡Washington University, St. Louis, MO; §3D Quality Assurance Center at Washington University St. Louis, MO; ‖The University of Texas M. D. Anderson Cancer Center, Houston, TX; ¶Massachusetts General Hospital, Boston MA

Purpose: To assess the relationship between the dose to the bulb of the penis and the risk of impotence in men treated on Radiation Therapy Oncology Group (RTOG) 9406.
Methods and Materials: Men enrolled on a Phase I/II dose-escalation study, RTOG 9406, who were reported to be potent at entry and evaluable ($n = 158$) were selected for inclusion. Follow-up evaluations were scheduled every 3, 4, and 6 months for the first, second, and the third through fifth years, then annually. At each follow-up visit an assessment of potency status was made. Penile structures were defined by a single observer blinded to the potency status, using Web-based, on-line software. The dosimetry for penile structures was calculated at the Quality Assurance Center at Washington University and provided to RTOG Statistical Headquarters to determine whether there was a relationship between dose and impotence.
Results: Patients whose median penile dose was ≥52.5 Gy had a greater risk of impotence compared with those receiving <52.5 Gy ($p = 0.039$). In a multivariate analysis neither age, the dose to the prostate, nor the use of hormonal therapy correlated with the risk of impotence.
Conclusions: Dose to the bulb of the penis seems to be associated with the risk of radiation-induced impotence.

Prostate cancer, Three-dimensional conformal radiotherapy, Impotence.

Figure 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.

ATC(ITC) Support of NABTT Clinical Trials

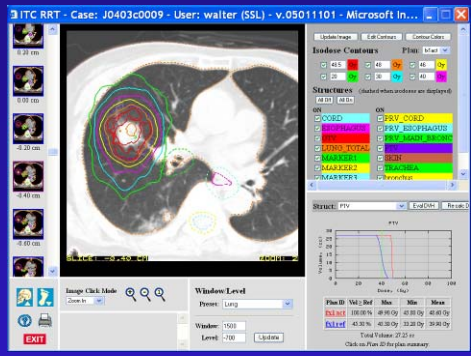
- NABTT (ATC is working with Dr. John Fiveash, M.D., Department of Radiation Oncology, Univ. of Alabama Birmingham)
  - There will be 9-10 NABTT institutions participating in these studies.
  - Protocols are Phase I/II with maximum of 90-100 cases.
  - Plan is to review approx. 30-50% of protocol cases (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 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

Challenges/Opportunities: ATC Supported Trials

- Continue to update QuASA^{2}R 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