Imaging as a Biomarker:
Standards for Change Measurements in Therapy
Stakeholder Perspectives
- AAPM, ATC -

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A U.S. Measurement System Workshop
National Institute of Standards and Technology
Gaithersburg, MD, September 14-15, 2006

The American Association of Physicists in Medicine
Stakeholder Perspectives

- AAPM is a scientific, educational, and professional organization of over 5,000+ medical physicists.
- Publications include a scientific journal (***Medical Physics***), technical reports, and symposium proceedings.
- AAPM's mission is to:
  - encourage innovative research and development
  - disseminate scientific and technical information
  - foster the education and professional development of medical physicists
  - promote the highest quality medical services for patients.

AAPM Scientific Organization

Science Council, Imaging Physics Committee (IPC)

- **IPC is a committee of the Science Council and has direct authority and responsibility over all AAPM scientific activities pertaining to diagnostic medical imaging.**
- **IPC is designed to implement and advance the science of imaging physics through its own actions and in consultation with an extensive structure of subcommittees.**
- **IPC has as its core mission the promotion, dissemination and advancement of physical and computational principles as applied to the broad field of medical imaging, computer aided detection and diagnosis, disease screening, technical advancements, and quality assurance.**

AAPM Scientific Organization

Science Council, Therapy Physics Committee (TPC)

- **TPC has direct authority and responsibility over all AAPM scientific activities pertaining to RT physics.**
- **TPC achieves the following broad goals primarily through its Subcommittees, Working Groups, and Task Groups.**
  - Improve accuracy and consistency of RT and other medical interventions through development and publication of scientific, technical and educational documents.
  - Improve therapeutic medical interventions through research in MP and promote scientific research in therapy applications of MP within AAPM.
  - Provide guidance to outside agencies and organizations relative to scientific/clinical interests of AAPM membership.
  - Remain aware of developments from and collaborate with outside organizations.

AAPM Scientific Organization

Science Council, Committees, Subcommittees, Working Groups, Task Groups

AAPM Board

- Science Council
  - Therapy Physics Committee
    - Therapy Imaging Subcommittee
      - Imaging for Treatment Planning WG
        - TG 132: Use of Image Registration and Data Fusion Algorithms and Techniques in RT Treatment Planning
      - Imaging for Treatment Assessment WG
      - Imaging for Treatment Verification WG
        - TG 75: Radiographic imaging doses in RT
        - TG 104: Kilovoltage localization in RT
      - Molecular Imaging in Radiation Oncology WG
      - Imaging for Patient Modeling WG

AAPM has a strong track-record in developing standard-producing documents & working with NIST

Protocols for the determination of absorbed dose from high-energy photon and electron beams

- AAPM SCRAD (PMB 11, 505-520, 1966)
  - NBS coauthor: R. Loevinger
- AAPM SCRAD (PMB 16, 379-396, 1971)
  - NBS coauthor: R. Loevinger
- TG 21 protocol (Med Phys 10, 741-771, 1983)
  - NBS coauthor: R. Loevinger
- TG 51 protocol (Med Phys 26, 1847-1870, 1999)
  - NIST coauthor: B. Coursey

AAPM has a strong track-record in developing standard-producing documents (Imaging)

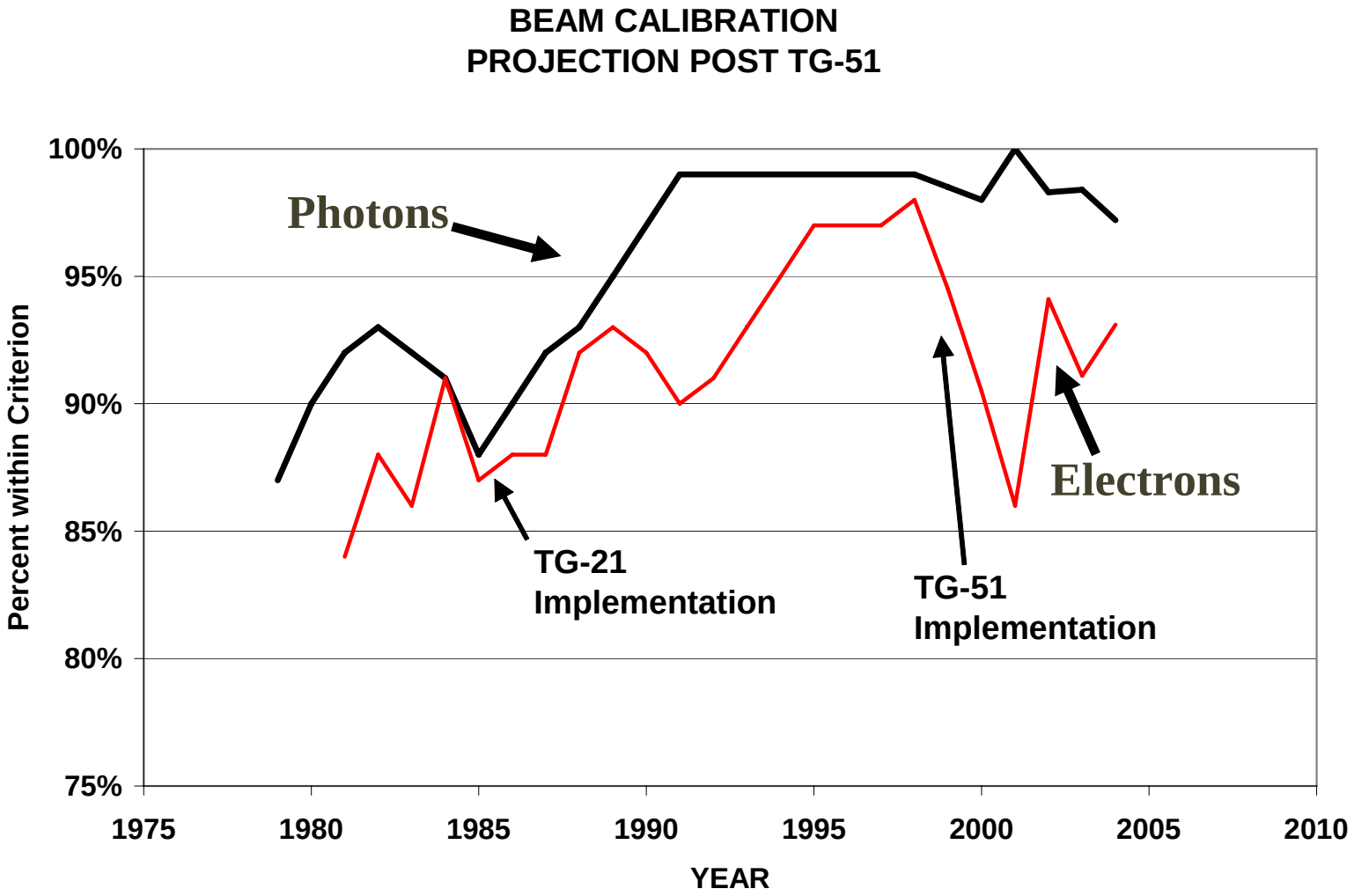
Report No. / ISBN	Title
1 1-888340-04-5	Phantoms for Performance Evaluation and QA of CT Scanners (1977).
15 0-88318-482-6	Performance Evaluation and QA in Digital Subtraction Angiography (1985) Diagnostic X-Ray Imaging Committee/Digital Radiography/ Fluorography TG.
28 0-88318-800-7	QA Methods and Phantoms for Magnetic Resonance Imaging (Reprinted from Medical Physics, Vol. 17, Issue 2) (1990)Nuclear Magnetic Resonance Committee TG #1.
34 1-56396-028-1	Acceptance Testing of Magnetic Resonance Imaging Systems (Reprinted from Medical Physics, Vol. 19, Issue 1) (1992) Nuclear Magnetic Resonance Committee TG #6.
52 1-56396-485-6	Quantitation of SPECT Performance (Reprinted from Medical Physics, Vol. 22, Issue 4) (1995) Nuclear Medicine Committee TG #4.
65 1-888340-22-3	Real-Time B-Mode Ultrasound QC Test Procedures (Reprinted from Medical Physics, Vol. 25, Issue 8) (1998) Ultrasound TG #1.

Radiological Physics Center (RPC)

AAPM Therapy Physics Committee (TPC)

- RPC has been funded by the NCI continuously since 1968 to provide quality auditing of dosimetry practices at institutions participating in NCI cooperative group clinical trials.
- RPC was formed at the urging of radiation physicists through the AAPM, and radiation oncologists through the Committee on Radiation Therapy Studies (CRTS).
- The AAPM Therapy Physics Committee has been, and continues to be, the scientific advisory body to the RPC.

Reference Calibration Discrepancies found during RPC visits



Imaging Physics Center *?*

- There is a clear need for an Imaging Physics Center (funded by the NCI) to provide quality auditing of imaging practices at institutions participating in NCI cooperative group clinical trials.
- The AAPM (Imaging/Therapy Physics Committees) could serve as the scientific advisory body to the Imaging Physics Center.

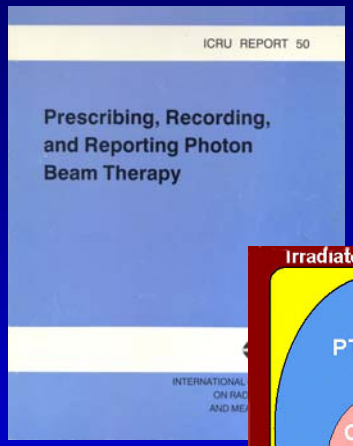
Advanced Technology QA Consortium (ATC)

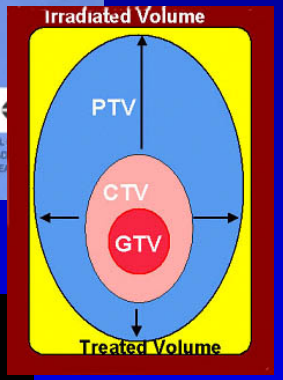
Imaging and IT efforts for RT Clinical Trials as a model... for the role of medical physics for drug therapy response

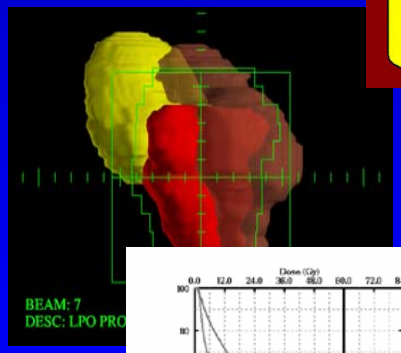
- **ATC dates from April 1992**
  - **Supported by a NCI U24 grant to Washington University and functions as a "virtual entity" made up of the following clinical trials QA Centers:**
    - **Image-Guided Therapy Center (ITC – Washington University in St. Louis and UC Davis)**
    - **Radiological Physics Center (RPC, M.D. Anderson Cancer Center)**
    - **Radiation Therapy Oncology Group (RTOG)**
    - **Quality Assurance Review Center (QARC)**
    - **Resource Center for Emerging Technologies (RCET – Univ. Florida Gainesville)**
  - **facilitates conduct of NCI sponsored advanced technology RT clinical trials requiring digital data submissions.**

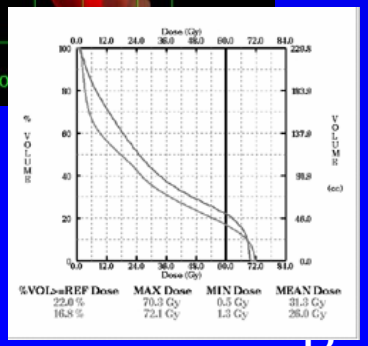
Transitioning From 2DRT to 3DCRT to IMRT to IGRT

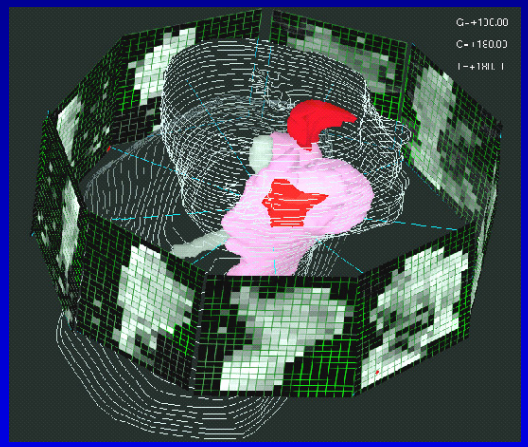
New Paradigms







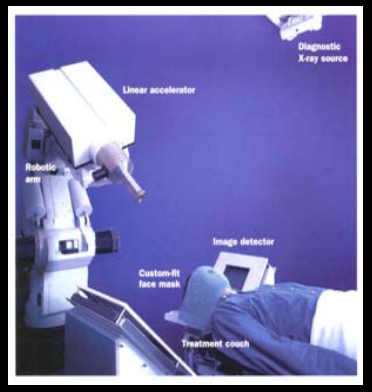




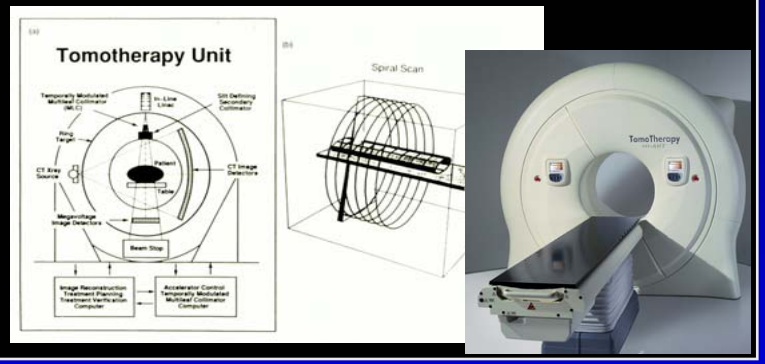
IMRT requires physician to more clearly (quantitatively) define volumes and treatment objectives at beginning of planning process.

Transitioning From 2DRT to 3DCRT to IMRT to IGRT
New Paradigms

- Robotic Pencil Beam IMRT (ACCURAY CyberKnife™) (John Adler, M.D. and group at Stanford)



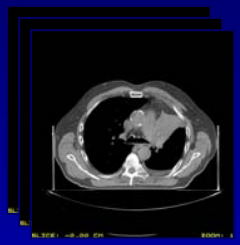
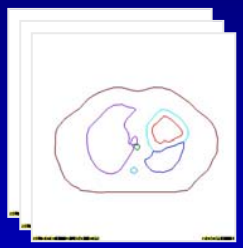
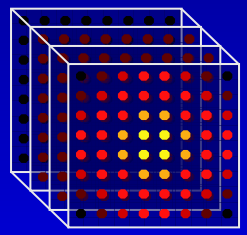
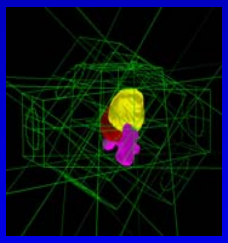
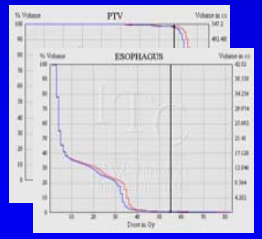
- Mackie, T.R., et al, 1993. Tomotherapy: Med Phys 20, 1709-



- 2002: Elekta Synergy™ research platform installed.
- 2004: Varian Trilogy
- 2004: Siemens ARTÍSTE, (Integrated Dose-Guided)

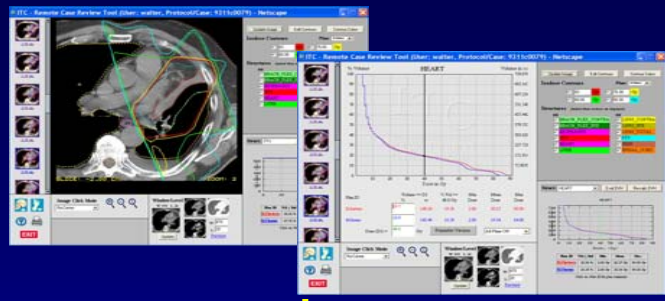
Data Objects for Imaged-Based RT Clinical Trials
New Paradigms

- **Data Objects**
  - Volumetric, digital images
  - Contours of volumes
  - 3-D dose distributions
  - Treatment verification images
  - Treatment plan
  - DVHs
- **Challenges**
  - Defining basic technical/clinical QA criteria necessary for protocol participation.
  - Develop mechanism for participant electronic data submission
    - Heterogeneous treatment planning systems
    - Proprietary data formats
  - Develop QA program for protocol compliance review.

Typical Data Set per Patient ~ 100 MB

ITC Clinical Trials Remote Review System (*ATC Method 1*, in use for all RTOG ATC-supported protocols.)



Worldwide
Participating Institution

St. Louis
ITC

Worldwide
Study Chair

RTP System

RTOG / DICOM

Data Submission Workstation

FTP Client/ DICOMpiler

SFTP

SFTP Server

Data Integrity QA Tools

RRT Web Server

TPS Files

Web-based RRT

DICOM Pt 10 files

CD-R

RTOG format

Tape

Fed-Ex, etc.

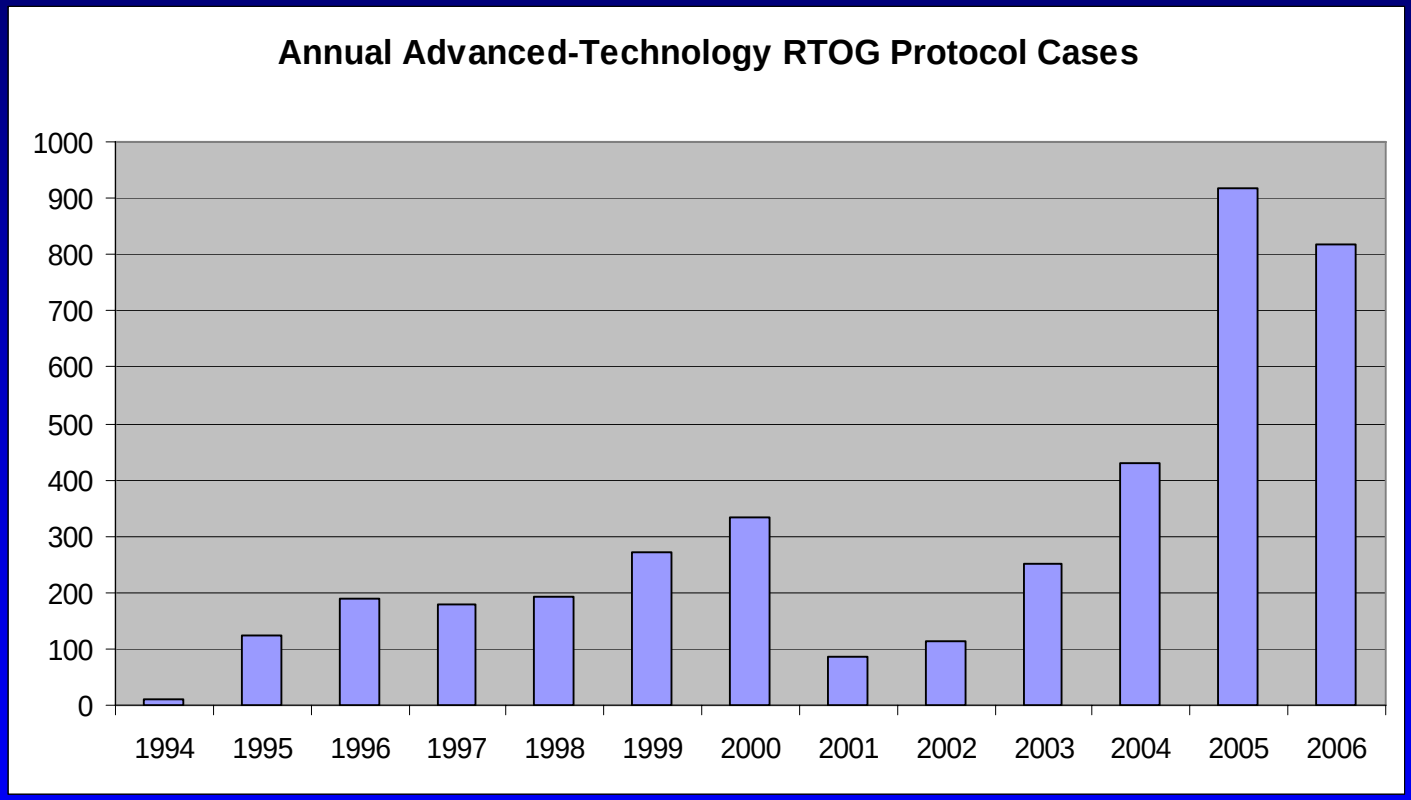
RTOG/ DICOM Data Import

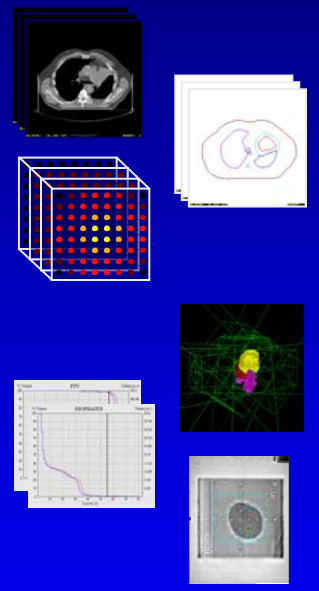
Philadelphia
RTOG HQ

Web-based RRT

Web-based RRT

- **Sept. 1, 2006 ATC Mtg: 4208 Complete, Protocol-Case, Digital Data Sets Submitted to ITC Over 12 Year Period**

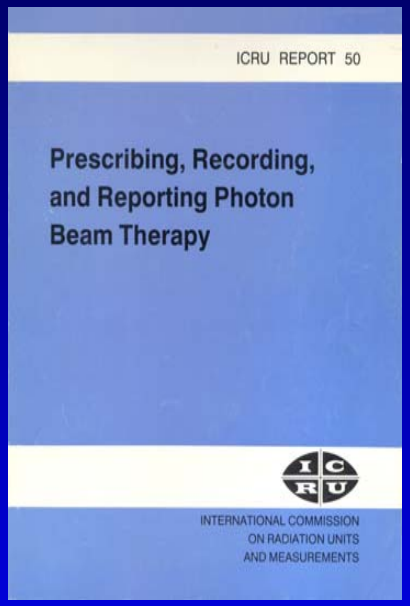


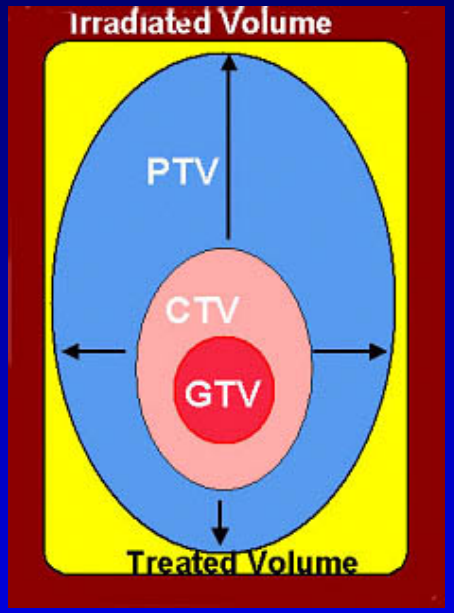


- **15 commercial TPS vendors have implemented export capability**
- **426 institutions able to submit data to ITC in St. Louis**

Accurate Specification of Target Volume
- Key issue in 3DCRT/ IMRT/ IGRT -

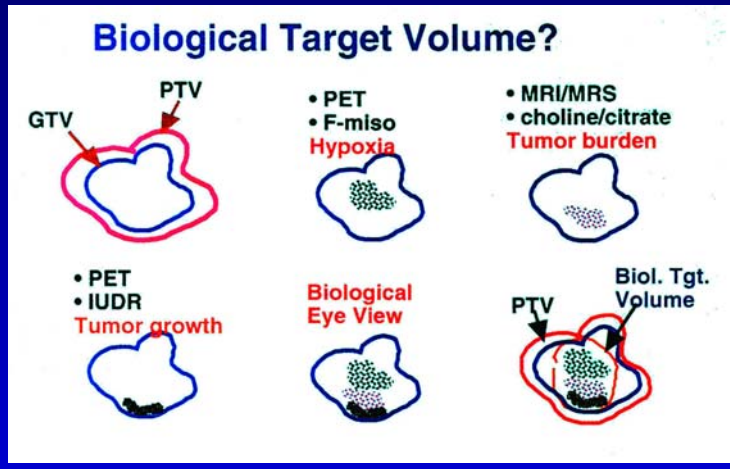
- Volumes of known tumor, i.e., Gross Tumor Volume (GTV),
- Volumes of suspected microscopic spread, i.e., Clinical Target Volume (CTV)
- Marginal volume necessary to account for setup variations and organ and patient motion, i.e., Planning Target Volume (PTV).



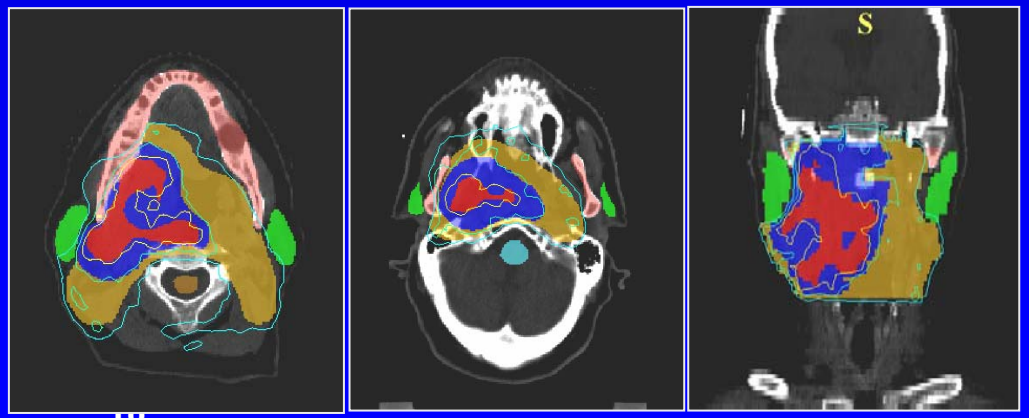


Accurate Specification of Target Volume
- Key issue in 3DCRT/ IMRT/ IGRT –
Future Directions

- Ling, et al. IJROBP 47(3): 551- 560, 2000: ***Toward Multidimensional Radiotherapy (MD-CRT): Biological Imaging and Biological Conformality***

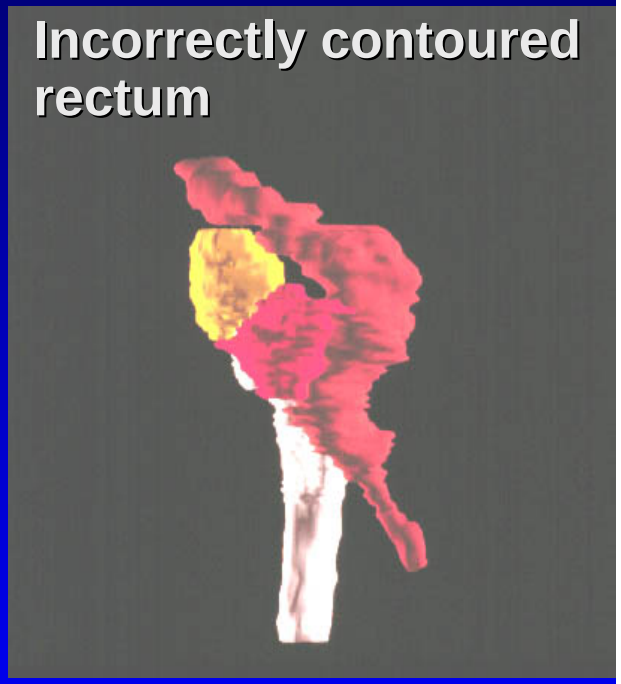


- Chao et al. IJROBP. 49(4):1171-1182, 2001: ***A Novel Approach to Overcome Hypoxic Tumor Resistance: Cu-ATSM-Guided IMRT.***



Accurate Specification of Organ at Risk Volume - key issue in 3DCRT/IMRT/IGRT -

- Organs at risk are defined as critical normal tissues, such as the spinal cord or rectum, whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose.



- Need consistent definition (e,g, RTOG specifies the rectum starting from the anus (at the level of the ischial tuberosities) for a length of 15 cm or when the rectosignoid flexure is identified.

ATC - RTOG Protocol Requirements

New Paradigms

- ICRU 50 Volume Descriptions
- Dose prescription (including organ-at-risk dose tolerance specification)
- Digital data submission required
- QA
  - Credentialing
    - Facility Questionnaire
    - Dry-run Test
    - Phantom Test
  - Data Integrity QA
  - Protocol Compliance QA

ATC - RTOG Protocol Credentialing

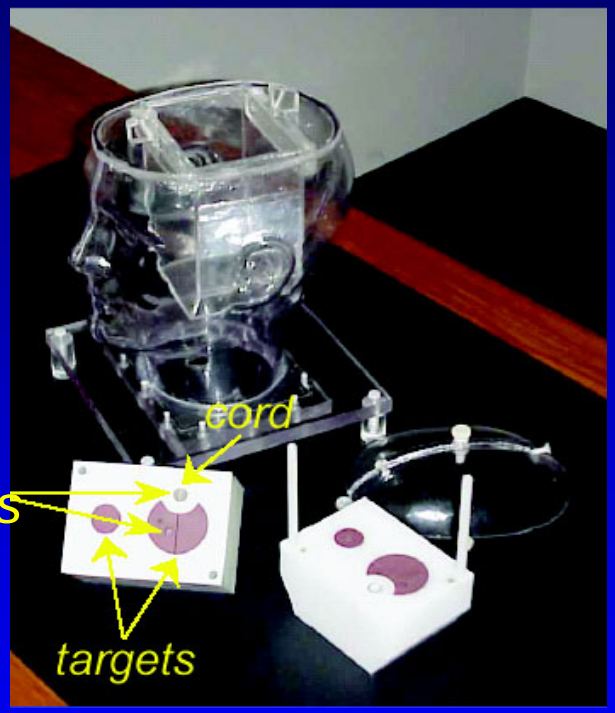
ITC Benchmark ("Dry Run") Test (0022)

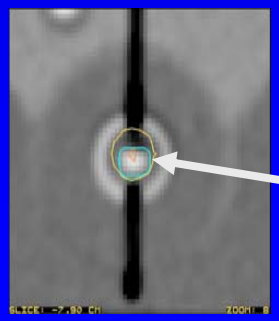
- **18 institutions passed the Dry-Run requirement**
  - 1 institution achieved no deviation
  - 17 institutions achieved minor deviation
- **Parotid sparing**
  - 13 institutions achieved no deviation
  - 5 institutions achieved minor deviation
- **Number of submissions it took to meet credentialing guidelines**
  - 1 submission: 6 institutions
  - 2 submissions: 9 institutions
  - 3 submissions: 3 institutions

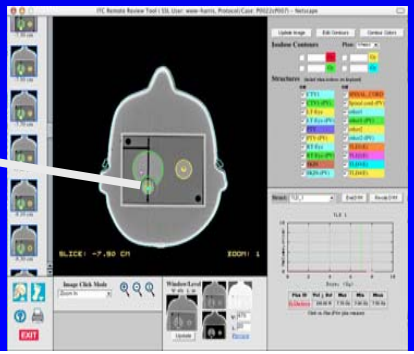
ATC - RTOG Protocol Credentialing

RPC IMRT Phantom Test (0022, 0225)

Phantom	H&N
Irradiations	217
Pass	146
Fail	57
Under analysis /at institution	12
Unevaluable	12
Year introduced	2001







34% failed on first attempt

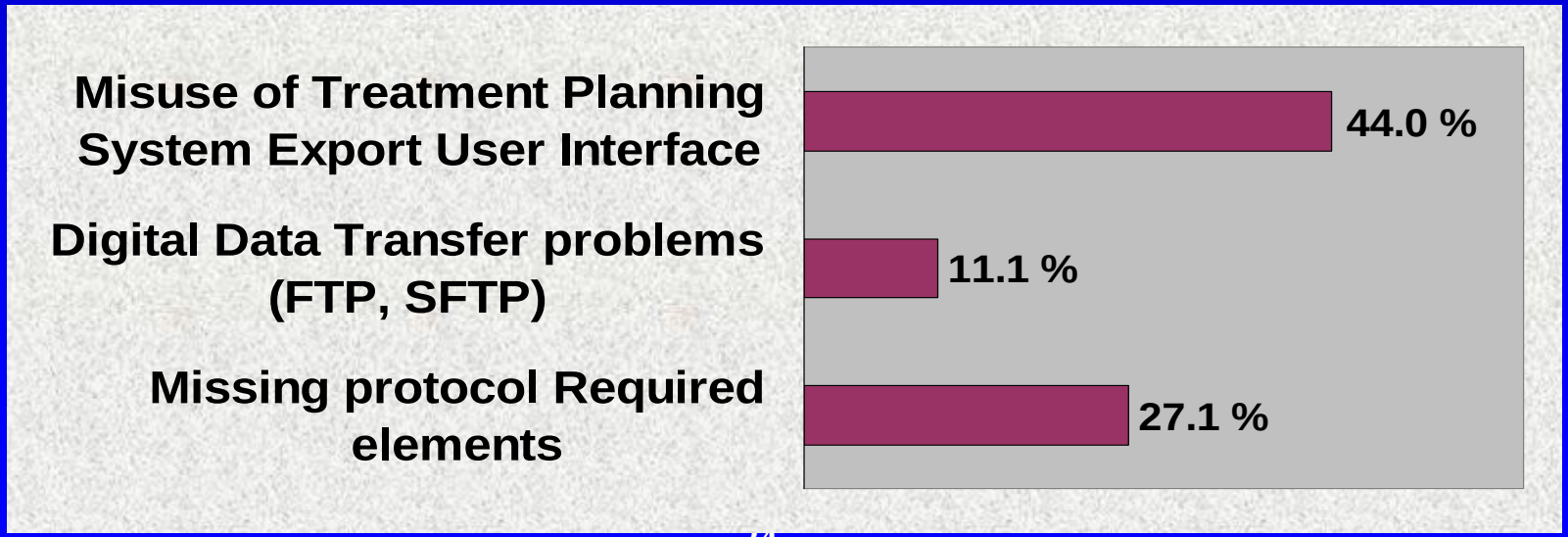
ATC - RTOG Protocol QA Data Integrity QA
(*Categories of Submission Problems)*

- **Thus far over 4000 protocol data sets submitted to ITC.**
- **Type problems seen include:**
  1. Misuse of TPS data export capabilities.
  2. Missing protocol required elements (or mistakes in protocol understanding).
  3. Error in use of digital transfer software (FTP, SFTP).
  4. New release of TPS software with inability to correctly submit ATC compliant data.
- **Categories 1,2,3 problems seen on a daily basis.**
- **Category 4 occurs much less frequently, but is much more complicated to resolve because it requires software changes by the TPS vendor.**

ATC - RTOG Protocol QA

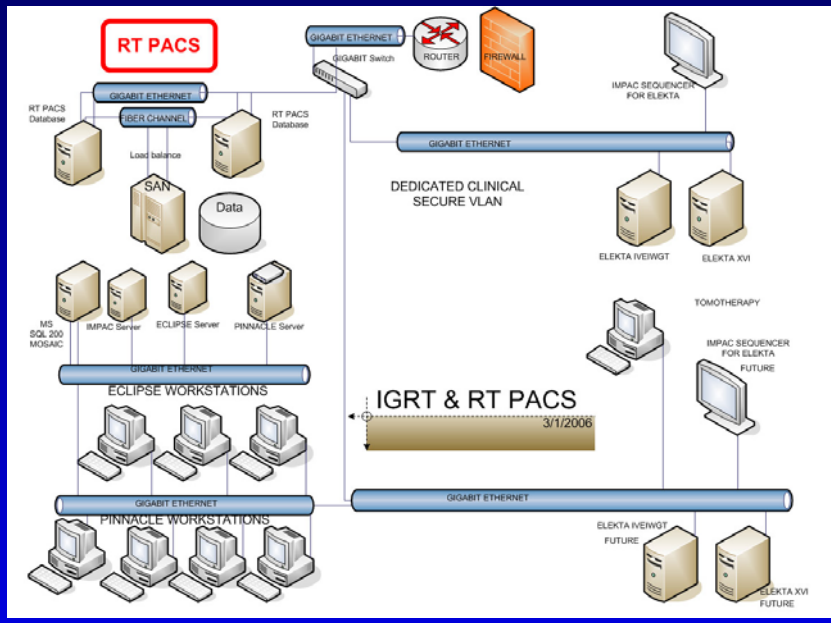
ITC Digital Data Integrity QA – Problem Rate By Type of Error

- Thus far over 4000 protocol data sets submitted to ITC.
- Overall 27% of cases submitted require human intervention by the ITC due to data submission errors.
- Chart below shows rate of specific error categories that are seen on a daily basis.
- 44% of these errors are caused by a misuse of TPS export user interface.



Key Challenges
Radiation Oncology PACS

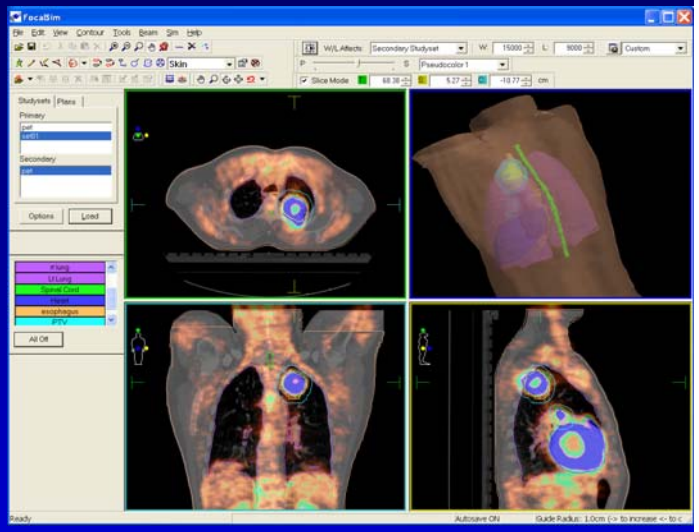
- Radiation oncology department digital data storage needs increase dramatically with the use of IGRT.
- IGRT clearly points to need for a new type informatics infrastructure for radiation oncology, i.e. something similar is some ways (but uniquely different in other ways) to a diagnostic PACS.



- For lack of a better term, we are using the term radiation oncology PACS, (RO-PACS), but realize that the “P” is not appropriate as multiple type of data need to be archived, and data types, data/work flow, and software tool issues must be addressed.

Key Challenges for ATC Supported Clinical Trials

- New Imaging Modalities: PET (Quantitative), Image fusion QA.
- Adaptive Radiotherapy, Image-Guided Therapy (Cone beam CT, Helical Tomotherapy)
  - Daily Confirmation and Adjustment using On-Board Imaging (EPID, Cone Beam CT)
  - Multiple treatment plans/large volume of data
- 4-D CT
  - Large data sets (several 100 MB)



SUMMARY AND CONCLUSIONS

- Radiation therapy is rapidly becoming more and more dependent on imaging data.
- AAPM (medical physicists) has(have) played a key role in standardizing dose delivered, RT nomenclature, QA, etc. in 3DCRT/IMRT/IGRT clinical trials.
- ATC has been a pioneer in the development of electronic data exchange and QA software/databases for advanced technology RT clinical trials.
- AAPM (medical physicists) and ATC can play a similar role in helping develop standards and the needed informatics infrastructure to further develop imaging to measure therapy response.