A Proposed NCI Clinical Trials Network – Radiotherapy Perspective

Ying Xiao, PhD

Objectives

- Describe NCI's Initiative to revamp the clinical trial system
- Present an overview of a proposed Imaging Radiation Oncology Core (IROC) services Group
- The Information Technology Infrastructure of IROC
- Visions for radiation therapy clinical trial quality assurance

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Revamping the Clinical Trials Systems at NCI

Improve speed & efficiency of development & conduct of trials

- ✓Cancer Trials Support Unit - provide 24/7central registration & collection regulatory documents
- ✓Provide NCI Central IRBs – Adult and Pediatric
- ✓Qualify sites for advanced imaging

Incorporate innovative science and trial design

- ✓NExT – multiple agents under development, with external peer review
- ✓Clinical Assay Development Program (CADP)
- ✓Develop support & funding for non-Group investigators with novel ideas

http://deainfo.nci.nih.gov/advisory/ncab/161_0212/Abrams.pdf

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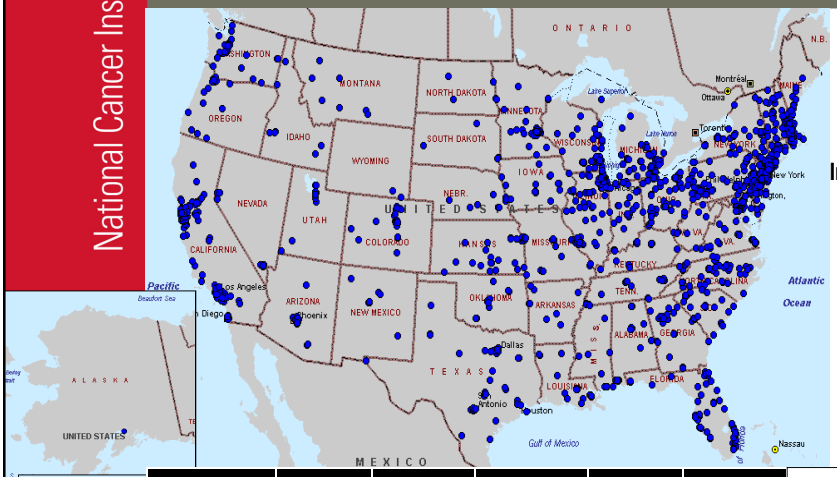
Overview of the Current Program



3,100 Institutions

14,000 Investigators

About 25,000 pts enrolled on tx trials annually

Trials	FY2006	FY2007	FY2008	FY2009	FY2010
All Phases: Treatment Trials	27,667	24,715	25,784	29,285	23,468

Accrual Distribution:
Phase 3: 83.4%
Phase 2: 15.1%
Phase 1/Pilot: 1.5%

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Why Support a Standing, Publicly Funded Clinical Trials Network?

- **Advance science & patient care, especially on important research questions that are not priorities for industry, including evaluating:**
  - Integration of new agents into standard regimens
  - Combinations of novel agents developed by different sponsors
  - Multi-modality regimens (e.g., Surgery, Radiotherapy, IP therapy)
  - Therapies for pediatric cancers, rare cancers, and uncommon presentations of more common cancers
  - Screening, diagnostic, & prevention strategies
  - Optimal duration and dose of drugs & radiotherapy
  - Different treatment approaches already approved for clinical care

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Why Support a Standing, Publicly Funded Clinical Trials Network?

- **Trials oriented toward disease-management, not agent-specific or limited by marketing constraints, with inclusion of research questions related to:**
  - Correlative science
  - Imaging
  - Quality of Life
  - Symptom Management
  - Special Populations (e.g., analyis by sex, age, race/ethnicity)
- **Extensive, direct involvement of entire oncology community in the design, development, & conduct of trials:**
  - Academic center investigators
  - Community & private practice investigators
  - Patient advocates
  - Young investigators in training
  - International collaborators
  - Data-sharing of clinical data & banked biospecimens

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Selected Major Accomplishments of Program: 2005 - 2011

- **Over 30 Practice-Changing Clinical Trials** including therapeutic agents and other modalities, with 4 announced in first 6 months of 2011
  - ACOSOG-Z0011 – Surgery: SLND not inferior to Axillary Dissection in SLN+ BC
  - NCIC-CTG MA.20 – RT: Regional Nodal RT reduces LR & improves DFS in Node+ BC
  - COG-AALL0232 – Pediatrics: High Dose MTX improves EFS in pediatric ALL
  - RTOG-94-08 – Multimodality: Short-term ADT with RT improves OS in prostate cancer
- **Over 10 FDA Indications - New Oncology Agents** (Yr FDA Approval)
  - Bevacizumab – CRC (2006); NSCLC (2006); Renal Cell Cancer (2009)
  - Imatinib mesylate – Pediatric CML (2006); Adjuvant GIST (2008)
  - Nelarabine – T-ALL and T-LBL (2005)
  - Rituximab – Diffuse Large B-cell Lymphoma (2006); Follicular NHL (2006)
  - Trastuzumab - Adjuvant Therapy for Early-stage Her2+ Breast Cancer (2006)
  - Thalidomide – Newly Diagnosed Multiple Myeloma (2006)
  - Anti-GD2 Antibody (ch14.18) in Neuroblastoma (BLA Currently in Preparation)
- **Examples: New Indications Generic Agents** (Yr Publication/Press Release)
  - Daunorubicin in AML (2009); Dexamethasone in Multiple Myeloma (2007)

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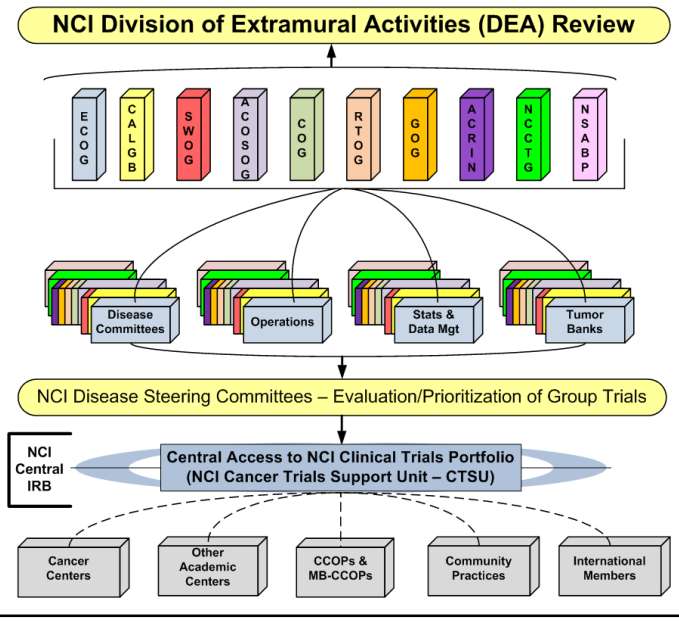
Structure of Program: As of January 2011



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Next Steps in Transforming the System

- New RFA for an Integrated National Clinical Trials Network
- Consolidated Organizational Structure with Funding for 1 Pediatric Group and up to 4 Adult Groups
- Review Criteria with Emphasis on Integration & Collaboration for Overall Scientific Achievement and Operational Efficiency
- Funding Model with Increased Per-Case Reimbursement for "High-Performance" Academic & Community Sites
- Competitive Integrated Translational Science Awards
- Revitalize Cancer Center Role in the Network (U10 awards)

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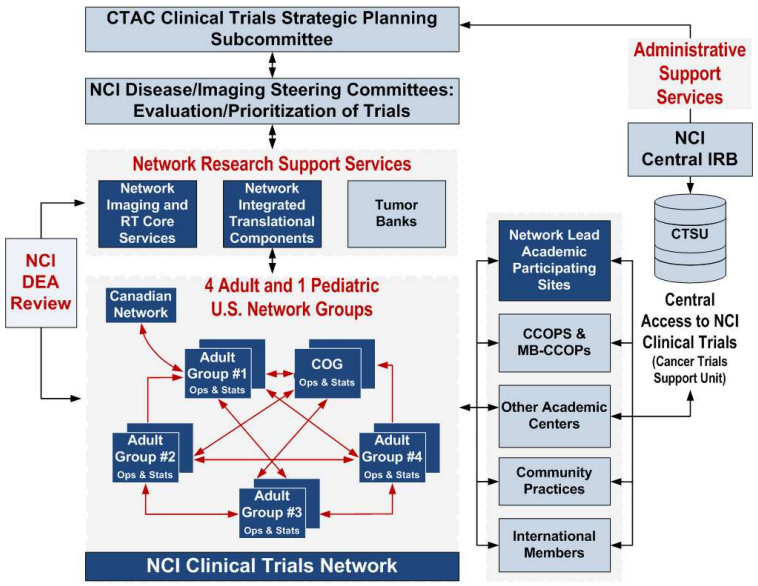
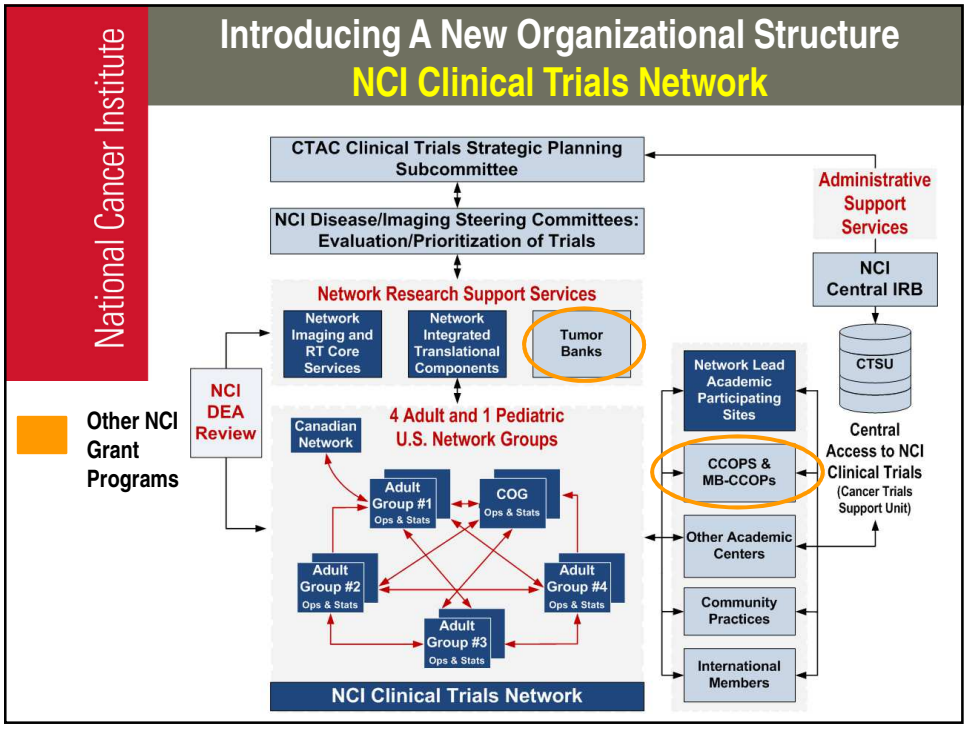
Introducing A New Organizational Structure
NCI Clinical Trials Network



Dark blue boxes signify NCI DEA reviewed, grant-funded components under this RFA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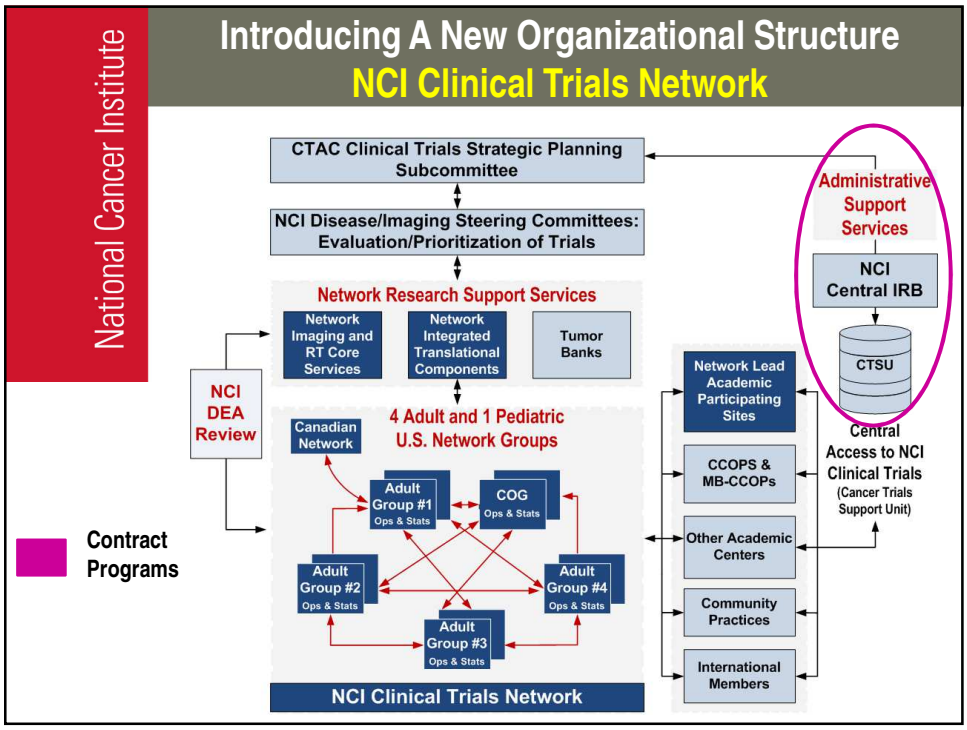
Introducing A New Organizational Structure
NCI Clinical Trials Network
CTAC Clinical Trials Strategic Planning Subcommittee
NCI Disease/Imaging Steering Committees: Evaluation/Prioritization of Trials
Network Research Support Services
Network Imaging and RT Core Services
Network Integrated Translational Components
Tumor Banks
NCI DEA Review
Other NCI Grant Programs
4 Adult and 1 Pediatric U.S. Network Groups
Canadian Network
Adult Group #1
Ops & Stats
COG
Ops & Stats
Adult Group #2
Ops & Stats
Adult Group #4
Ops & Stats
Adult Group #3
Ops & Stats
NCI Clinical Trials Network
Administrative Support Services
NCI Central IRB
CTSU
Central Access to NCI Clinical Trials
(Cancer Trials Support Unit)
Network Lead Academic Participating Sites
CCOPS & MB-CCOPs
Other Academic Centers
Community Practices
International Members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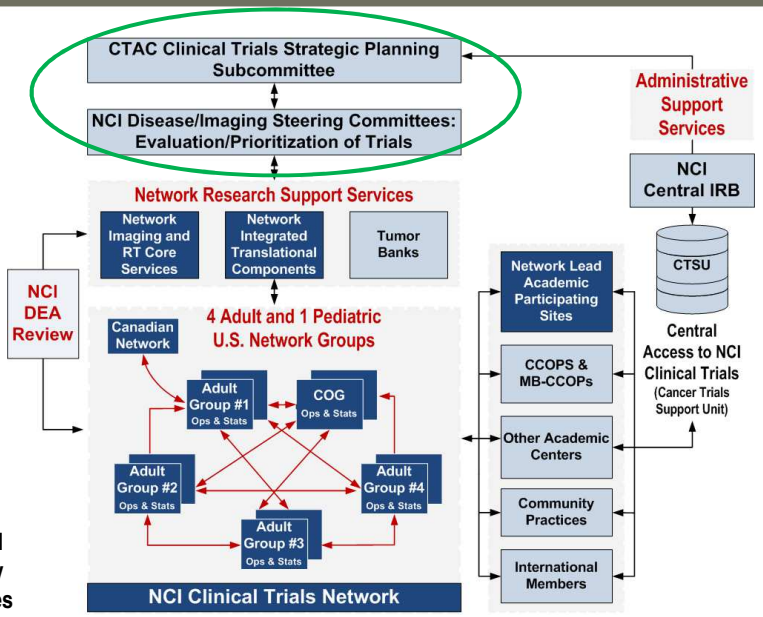

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Rationale for Transforming Current Program:
How Will Consolidated Network System Help?

- **Consolidate infrastructure to gain efficiencies (e.g., IT, Regulatory, Administrative, Tissue Resource Management)**
- **Consolidate Imaging & RT core services to benefit entire Network**
- **Integrate new components into trials to provide value-added research questions (e.g., advanced imaging, translational science)**
- **Integrate new agents into trials**
  - **Ex: Erlotinib, crizotinib, & ipilimumab are being integrated into trials in earlier stages of lung cancer & melanoma treatment requiring screening large populations & combining the agents optimally with surgery, RT, and immunotherapy**
- **Evaluate new agents in molecularly-defined disease subsets**
  - **Ex: Even for common diseases such as breast cancer, # of molecularly-defined patient subsets is increasing & there is a need for trial prioritization evaluating multiple new agents with standard regimens across subsets to avoid duplication & optimize accrual**

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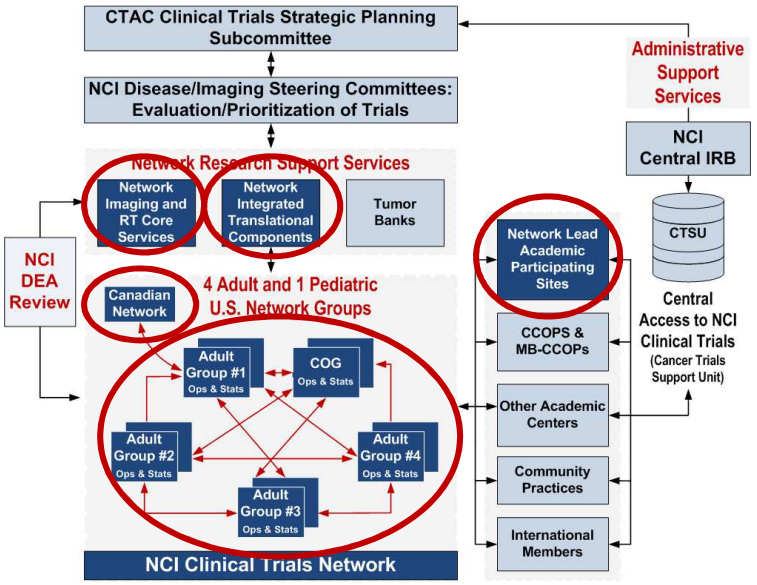
Introducing A New Organizational Structure
NCI Clinical Trials Network



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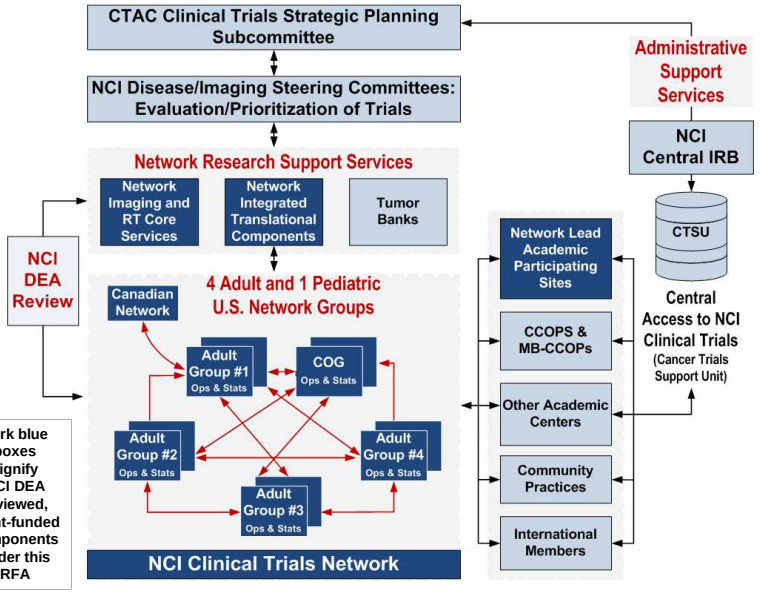

SAM Question 1

We need to support a standing, publicly funded clinical trials network.

Which one of the following is not mentioned as one of the reasons?

a) Multi-modality regimens (e.g., Surgery, Radiotherapy, IP therapy)
b) Optimal duration and dose of drugs & radiotherapy
c) Different treatment approaches not approved for clinical care
d) Therapies for pediatric cancers, rare cancers, and uncommon presentations of more common cancers
e) Combinations of novel agents developed by different sponsors

SAM Question 1 Answer

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b) Optimal duration and dose of drugs & radiotherapy
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d) Therapies for pediatric cancers, rare cancers, and uncommon presentations of more common cancers
e) Combinations of novel agents developed by different sponsors

Correct answer: (c) – Different treatment approaches already approved for clinical care

Reference:
http://deainfo.nci.nih.gov/advisory/ncab/161_0212/Abrams.pdf

SAM Question 2

A consolidated network system helps to better conduct clinical trials.
Which one of the following is not included as one of the rationales?

a) Consolidate Imaging & RT core services to benefit entire Network
b) Consolidate infrastructure to gain efficiencies
c) Evaluate new agents in molecularly-defined disease subsets
d) Reduce cost associated with per case reimbursement
e) Integrate new components into trials to provide value-added research questions (e.g., advanced imaging, translational science)

SAM Question 2 Answer

A consolidated network system helps to better conduct clinical trials.
Which one of the following is not included as one of the rationales?

a) Consolidate Imaging & RT core services to benefit entire Network
b) Consolidate infrastructure to gain efficiencies
c) Evaluate new agents in molecularly-defined disease subsets
d) Reduce cost associated with per case reimbursement
e) Integrate new components into trials to provide value-added research questions (e.g., advanced imaging, translational science)

Correct answer: d) Per case reimbursement will actually increase for some trials for better quality

Reference:
http://deainfo.nci.nih.gov/advisory/ncab/161_0212/Abrams.pdf

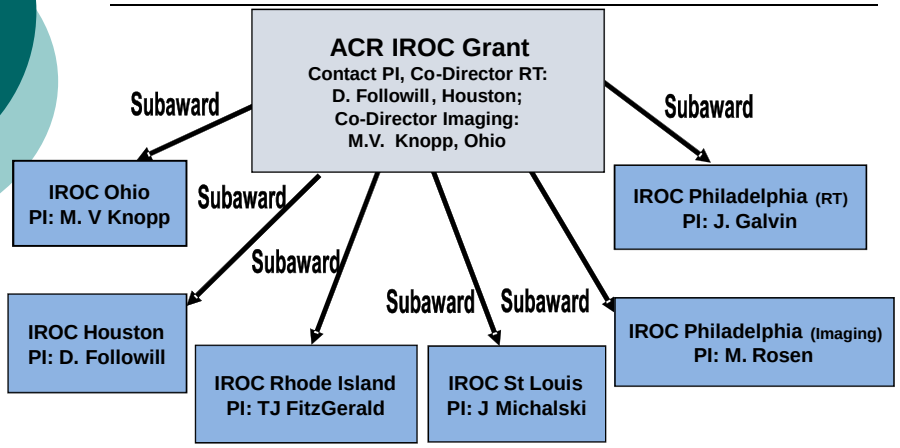
IROC

Imaging and Radiation Oncology Core Group

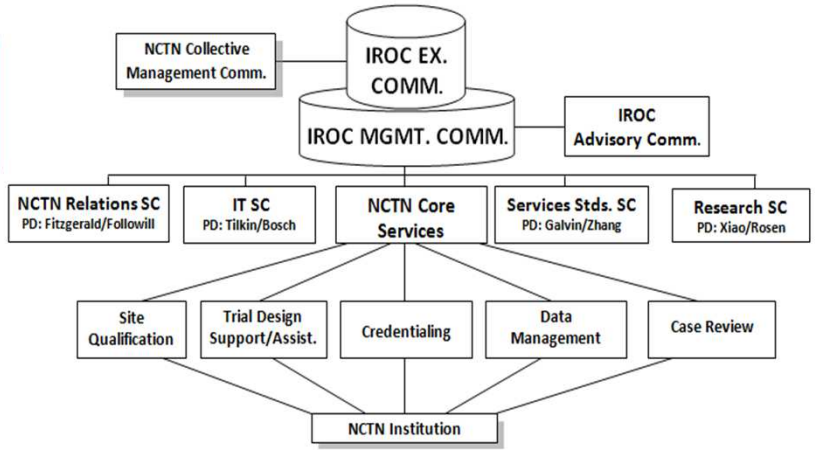
IROC Mission

Provide integrated radiation oncology and diagnostic imaging quality control programs in support of the NCI's NCTN Network thereby assuring high quality data for clinical trials designed to improve the clinical outcomes for cancer patients worldwide

Members of IROC



IROC Leadership Structure



IROC Executive Committee

Co-Directors: Followill/Knopp

IROC Admin: King/O'Meara/Laurie

IROC Management Committee

Six IROC PIs

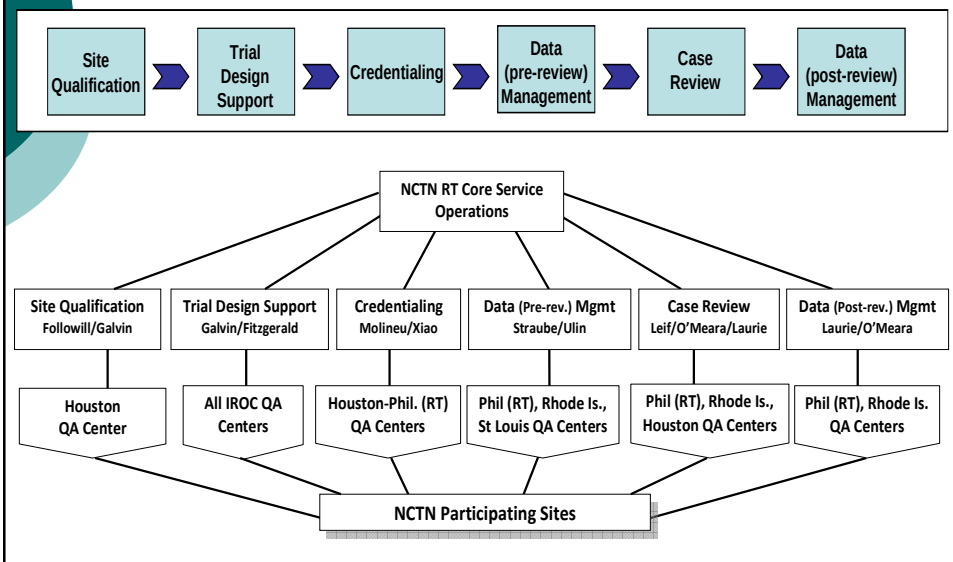
IROC Subcommittee co-chairs

IROC administrators

IROC key staff (RT and imaging)

Purpose: manage IROC QA services/operations to ensure the uniform implementation of IROC core services, prioritization of core services and establish, in collaboration with the NCTN groups, future directions of IROC

IROC's Five General NCTN Core Services



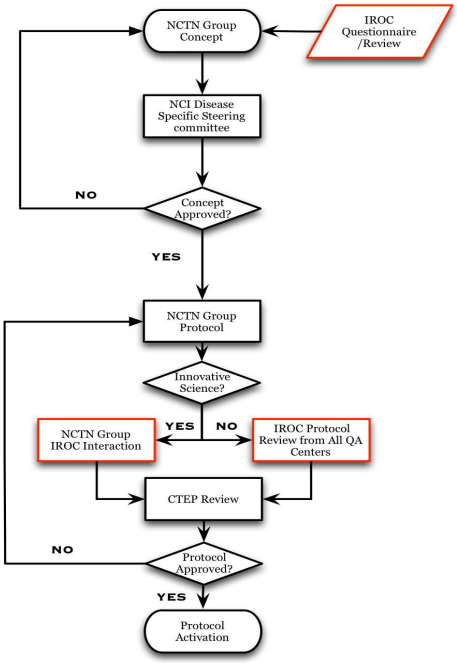
IROC Services to be Provided

1. Site Qualification/Ongoing RT QA
   - Electronic Facility Questionnaire (RT)
   - Ongoing QA
     - Reference beam output audits
     - Verification of TPS data (site visit/virtual visit)
     - Proton Approval
   - Electronic data submission by 1/1/16 by participating sites?

Trial Concept and Protocol Consultation Key Contact QA Centers

NCTN Group	Radiation Oncology	Imaging
Alliance	Houston	Ohio
COG	Rhode Island	Rhode Island
ECOG/ACRIN	Rhode Island	Philadelphia (I)
NRG Oncology	Philadelphia (RT)	Philadelphia (I)
SWOG	Rhode Island	Ohio

Trial Concept and Protocol Consultation and Assistance



Trial Protocol Assistance

1. Web based assistance (IROC website)
2. Designation of RT, Imaging or RT/Imaging
   - Depending on designation
   - Inclusion of either RT or I assistance phone number or both in protocol
   - Person to talk with

Credentialing

Credentialing is defined as those QA procedures designed to verify ensure that a specific institution, treatment/imaging device, and/or clinician or physicist has the knowledge and capability to meet the protocol specifications prior to being allowed to enter a patient.

Credentialing

Three Tier System

1. Data submission/KA/benchmark/previous patient (electronic)
2. Data submission/KA/benchmark/previous patient/phantom irradiation/IGRT
3. New treatment technology/modality requiring unforeseen QA procedures

Allows:

- Discussion with protocol PI and group to decide on appropriate QA procedures
- Look at Tiers and assign protocol to a specific tier
- Goal is to minimize credentialing requirements for future protocols by grandfathering institutions

IROC Services to be Provided

Patient Case Clinical and Technical Reviews

- **Pre–Treatment** (rapid reviews)
- **On-Treatment** (timely reviews)
- **Post-Treatment** (retrospective review)

IROC will facilitate the logistics and data organization for the clinical reviews. Groups will supply clinicians.

IROC Services to be Provided

Data Management/Secondary Analysis

NCTN DICOM(RT) Archive
(NDA)
+
RAVE

Managed by ACR Core Lab

Accessibility by Group

NCTN Relations Plan

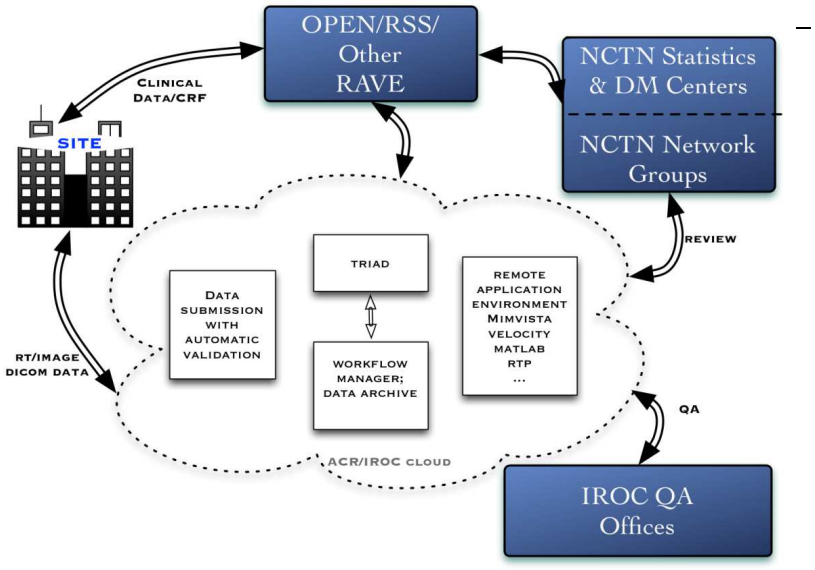
1. IROC Co-Directors are a part of group chairs meetings/calls and NCI/NCTN Collective Management
2. Relationship with each of the 5 group chairs
3. Relationship with group Ops/data/statistics offices
4. Representation on group RT and Imaging committees
5. Assist with innovative RT and Imaging research from Group Centers of Excellence
6. Align IROC IT structure to interact with groups efficiently

Summary

- IROC RT QA centers have decades of experience/ knowledge and infrastructure.
- Protocol review as early as possible is critical to establishing appropriate QA procedures.
- Patient case reviews require IROC and Groups to work together.
- RT and Imaging to work closely together.
- Collaboration and feedback from NCTN Groups is required.
- Groups to have complete accessibility to data.

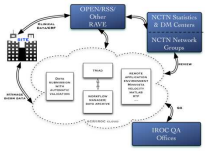
IROC Informatics Infrastructure

The ACR/IROC Cloud



Transfer of Image and Data (TRIAD) System

- End to end complete informatics system
- Designed to transport images and RT treatment data
- Open platform that accommodates third party system integration
- compatible with Health Insurance Portability and Accountability ACT (HIPAA) , and other regulatory requirements
- Interfaces with NCTN tools and services



Required NCTN Tools and Services

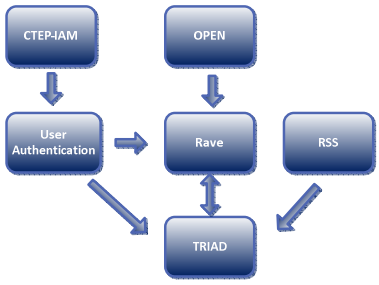
- Common Data elements-the NCTN programs approved sections of the data dictionary in the NCI data standards registry and repository (caDSR);
- NCTN information system for tracking biospecimen collection and from NCTN trials, currently in development
- NCTN Oncology Patient enrollment network (OPEN)
- Regulatory Support Services (RSS) via the Cancer Trials Support Unit (CTSU)
- the NCI Common Terminology Criteria for Adverse Events (CTCAE)
- the Comprehensive Adverse Event and Potential Risks (CAEPR) for agents, if available.

Medidata Rave

- System for capturing, managing and reporting clinical data from Phase 1-3 trials
- Combining electronic data capture (EDC) and
- Clinical data management (CDM)
- Interfaces with other systems

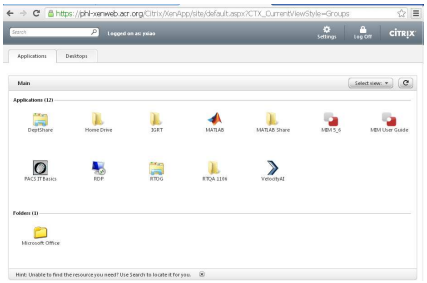
TRIAD Interface with NCTN Program

- User authentication
- List of trials via OPEN and RSS
- Patient list via Rave
- Imaging and RT data submitted and archived with eCRT integration

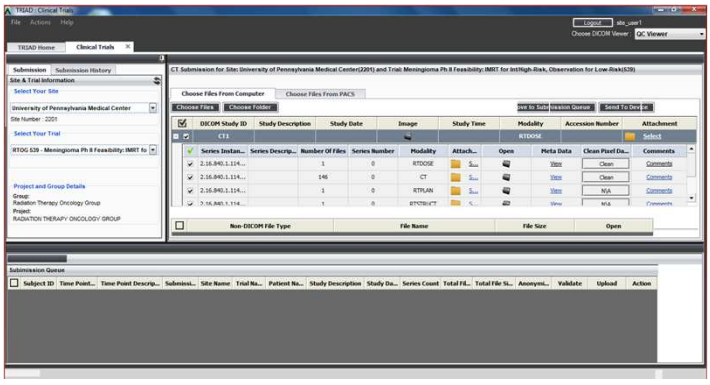


Remote Access

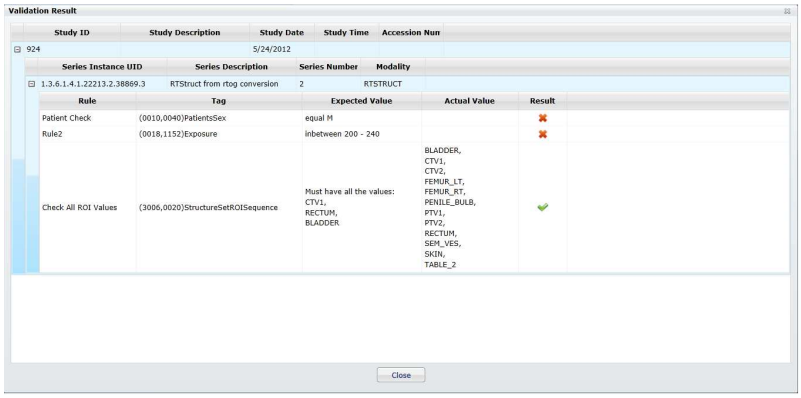
- Citrix XenApp
- Independent Computing Architecture (ICA) Protocol
- High level window display
- Clients support multiple OS



Example: Data Submission via TRIAD



Automated Validation



SAM Question 3

IROC proposes to offer five core services. Which one of the following is not one of them?

a) Site qualification

b) Protocol development

c) Data management

d) Case review

e) Clinical data management

SAM Question 3 Answer

IROC proposes to offer five core services. Which one of the following is not one of them?

a) Site qualification
b) Protocol development
c) Data management
d) Case review
e) Clinical data management

Answer: e) Clinical data management is performed jointly by the operations and statistical center of the network

Reference: http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-12-010.html; http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-12-011.html

SAM Question 4

NCI requires that tools and services provided by NCI be used in clinical trial operations.

Which one of the following is not a NCI provided required system?

a) OPEN
b) Medidata Rave
c) RSS
d) caDSR
e) CAEPR

SAM Question 4 Answer

NCI requires that tools and services provided by NCI be used in clinical trial operations.

Which one of the following is not a NCI provided required system?

a) OPEN
b) Medidata Rave
c) RSS
d) caDSR
e) CAEPR

Answer: b) It is a commercial system not provided by NCI.

Reference:
http://ctep.cancer.gov/investigatorResources/docs/NCTN_Program_Guidelines.pdf

Quality Assurance Science and Vision

Adaptive QA;
Investigation into QA efficiency and efficacy;
collaboration with Imaging QA;
collaboration with NCTN group;

- Evidence based, adaptive quality assurance
  - Implementation of heterogeneity corrected criteria for lung SBRT
  - IGRT review process development, establish criteria
  - IGRT review reporting
  - Techniques to improve contour consistency
- Quality assurance software development, implementation
  - Hausdorff distance/Registration
  - MiMextension, Matlab scripts-e.g.DVH extraction
- Outcome modeling/Secondary analysis
  - Database integration
  - Data analysis methodology
  - Personalized radiotherapy guidance

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Establish Quality Assurance Criteria for Radiotherapy Clinical Trials – for Image Guided Radiotherapy

A Study of Variations Between Image Analysis

Subsets of the comparisons of registration results	Treatment site	Absolute value of difference of registration shifts (mm); mean ± SD (range) LR dimension $\Delta\overrightarrow{LR}$	SI dimension $\Delta\overrightarrow{SI}$	AP dimension $\Delta\overrightarrow{AP}$	Three-dimension $\Delta\overrightarrow{LR}+\Delta\overrightarrow{SI}+\Delta\overrightarrow{AP}$
TomoTherapy vs. the three software systems	Head-and-neck (n = 9)	1.7 ± 1.5 (0.6–5.4)	2.3 ± 1.4 (0.5–4.9)	1.6 ± 1.3 (0.4–3.1)	3.8 ± 1.2 (2.5–6.2)
	Prostate (n = 12)	1.3 ± 1.0 (0.1–3.1)	1.6 ± 1.4 (0.0–5.1)	2.7 ± 2.3 (0.2–6.3)	3.9 ± 2.0 (0.8–6.8)
Elekta vs. the three software systems	Head-and-neck (n = 9)	2.1 ± 1.6 (0.4–5.0)	1.4 ± 0.7 (0.2–2.8)	2.5 ± 0.9 (1.4–4.0)	3.8 ± 1.4 (2.0–6.0)
	Prostate (n = 12)	0.5 ± 0.4 (0.0–1.3)	1.4 ± 0.8 (0.0–2.7)	0.9 ± 0.6 (0.1–1.8)	1.9 ± 0.6 (0.9–2.8)
Varian vs. the three software systems	Head-and-neck (n = 9)	3.6 ± 3.2 (1.2–8.6)	3.3 ± 1.0 (1.6–4.4)	2.6 ± 0.6 (1.1–3.2)	6.1 ± 2.0 (3.4–9.2)
	Prostate (n = 9)	1.3 ± 1.1 (0.2–3.2)	2.6 ± 1.5 (0.5–4.9)	1.5 ± 0.8 (0.5–2.8)	3.5 ± 1.3 (1.1–5.0)
All clinical results vs. the three software systems*	Head-and-neck (n =27)	2.5 ± 2.3 (0.4–8.6)	2.3 ± 1.3 (0.2–4.9)	2.3 ± 1.0 (0.4–4.0)	4.6 ± 1.8 (2.0–9.2)
	Prostate (n = 33)	1.0 ± 0.9 (0.0–3.2)	1.8 ± 1.3 (0.0–5.1)	1.7 ± 1.6 (0.1–6.3)	3.1 ± 1.7 (0.8–6.8)
Complete comparison between each other†	Head-and-neck (n = 54)	2.6 ± 2.1 (0.1–8.6)	1.7 ± 1.3 (0.0–4.9)	1.8 ± 1.1 (0.1–4.0)	4.1 ± 1.9 (1.1–9.2)
	Prostate (n = 66)	1.1 ± 1.0 (0.0–4.6)	2.1 ± 1.7 (0.0–6.6)	2.0 ± 1.8 (0.1–6.9)	3.5 ± 2.0 (0.2–8.3)

Y. Cui (Xiao) et al, Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 1, pp. 305–312, 2011

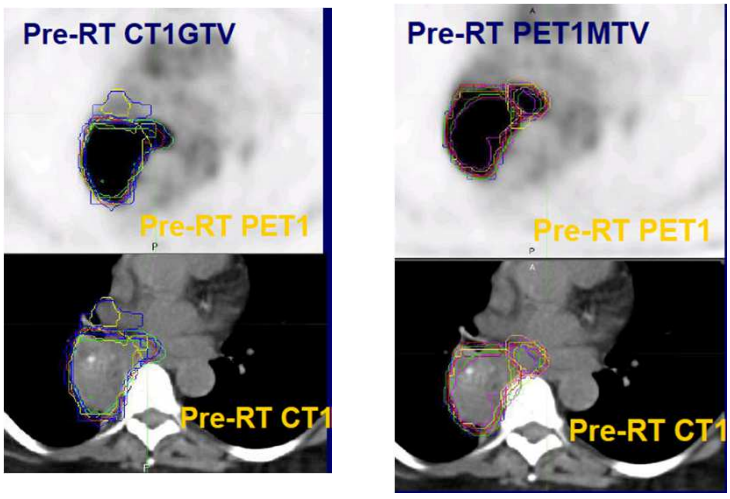
Quality Review for Radiotherapy Clinical Trials – for Image Guided Radiotherapy

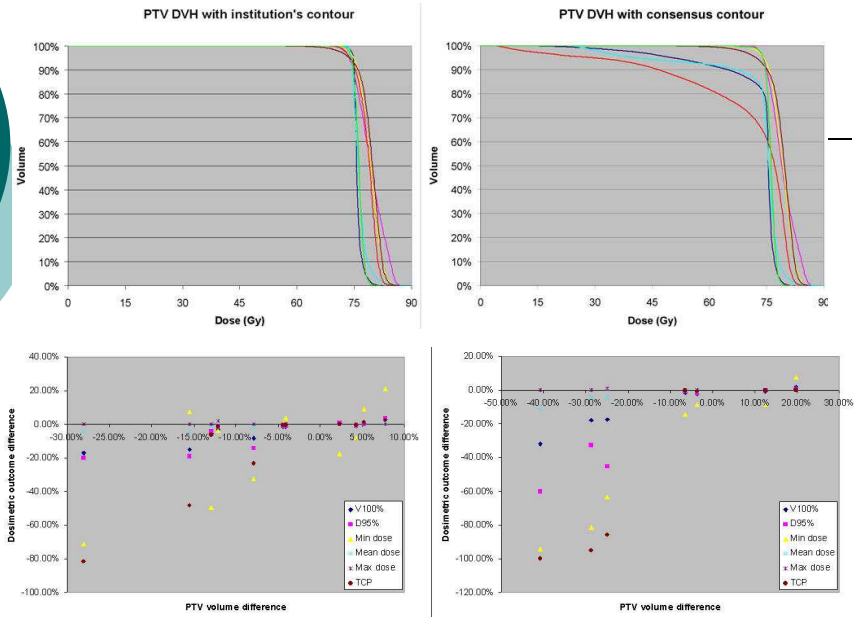
IGRT Credentialing for RTOG Protocols

Protocol # (disease site)	Number of datasets	Absolute value of difference of shifts (mm); mean±SD (range)		
		Left-Right	Superior-Inferior	Anterior-Posterior
0915 (Lung)	71	1.8 ± 1.2 (0.0 - 6.4)	2.0 ± 1.1 (0.0 - 6.9)	2.0 ± 0.9 (0.0 - 5.0)
0813 (Lung)	21	1.7 ± 0.8 (0.1 - 5.1)	2.2 ± 1.0 (0.3 - 5.0)	2.0 ± 1.1 (0.1 - 4.8)
0631 (Spine)	6	0.7 ± 0.6 (0.1 - 1.5)	2.9 ± 3.8 (0.0 - 7.0)	0.4 ± 0.1 (0.1 - 0.9)
0920 (Head&Neck)	35	1.5 ± 1.0 (0.1 - 6.7)	2.5 ± 2.2 (0.0 - 8.2)	1.4 ± 1.1 (0.0 - 7.3)
Overall	133	1.7 ± 1.0 (0.0 - 6.7)	2.2 ± 1.5 (0.0 - 8.2)	1.8 ± 1.0 (0.0 - 7.3)

Y. Cui (Xiao) et al, Implementation of Remote 3D IGRT QA for RTOG Clinical Trials, Int. J. Radiation Oncology Biol. Phys., In Press

Target Defined from Multiple Institutions





Can Use Of An Atlas Decrease Contouring Variability In NSCLC Cases?

Table 3. Comparison of contouring consistency in Case3 with that in Case1 and Case2

Quantity / Case	PTV		Esophagus		Heart		Brachial Plexus	
	MSD* (mm)	Dice†	MSD (mm)	Dice	MSD (mm)	Dice	MSD (mm)	Dice
Case1 (n = 11)	2.55	92.4%	2.16	77.3%	4.45	86.4%	16.27	28.9%
Case2 (n = 7)	4.56	86.4%	2.65	75.8%	3.85	86.8%	19.85	31.3%
Case3 (n = 10)	3.09	88.6%	1.69	83.7%	2.25	93.3%	8.23	34.9%

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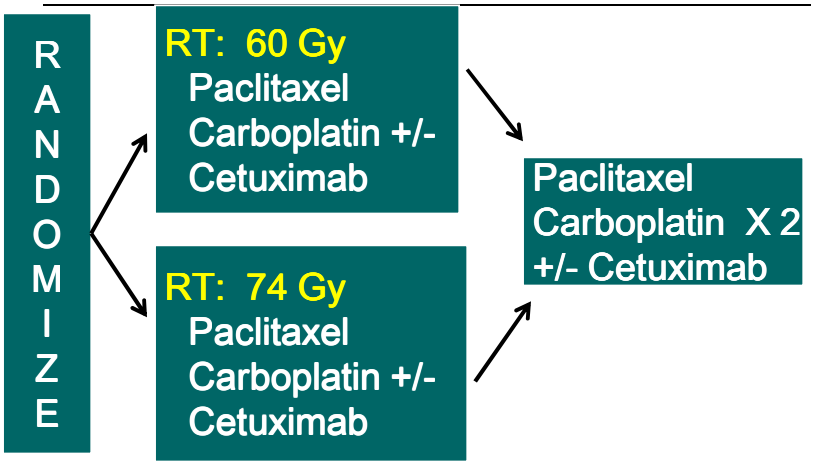
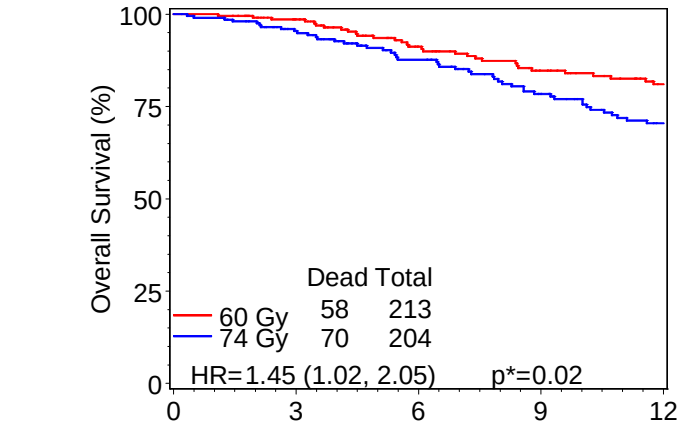
RTOG 0617, NCCTG N0628,CALGB 30609
Conventional vs. High Dose RT



Overall Survival



Patients at Risk					
60 Gy	213	190	149	124	104
74 Gy	204	175	137	116	93

*One-sided p-value, left tail

- Evidence based, adaptive quality assurance
  - Implementation of heterogeneity corrected criteria for lung SBRT
  - IGRT review process development, establish criteria
  - IGRT review reporting
  - Techniques to improve contour consistency
- Quality assurance software development, implementation
  - Hausdorff distance/Registration
  - MiMextension, Matlab scripts-e.g.DVH extraction
- Outcome modeling/Secondary analysis
  - Database integration
  - Data analysis methodology
  - Personalized radiotherapy guidance

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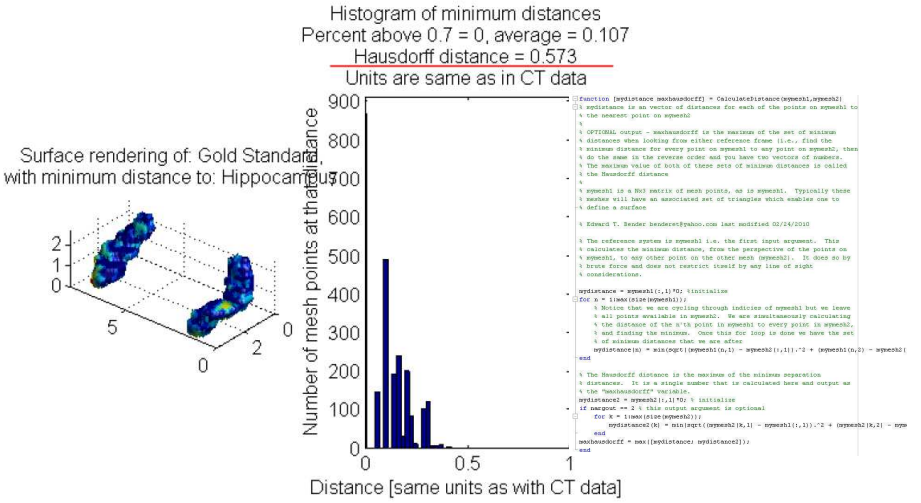
Quantitative Contour Evaluation – Hausdorff Distance



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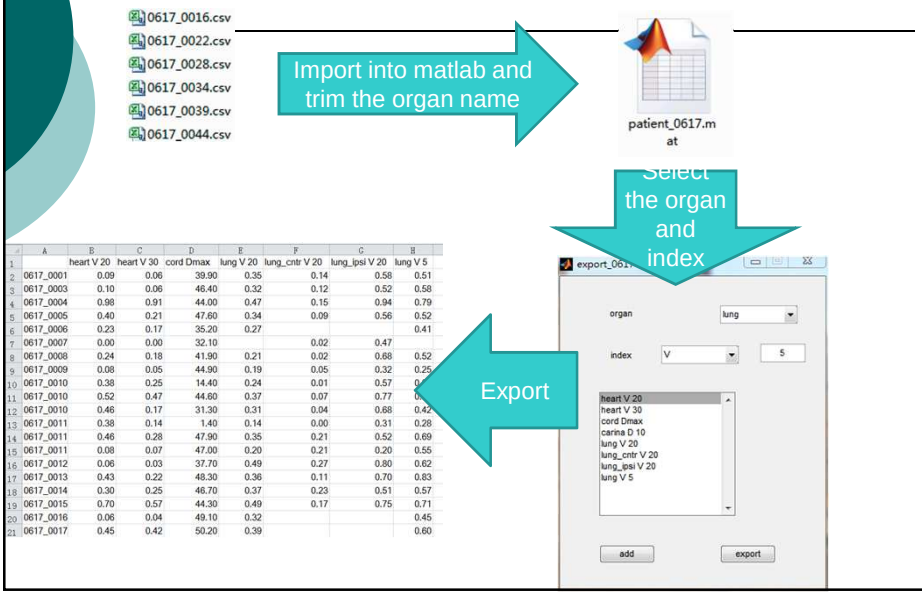
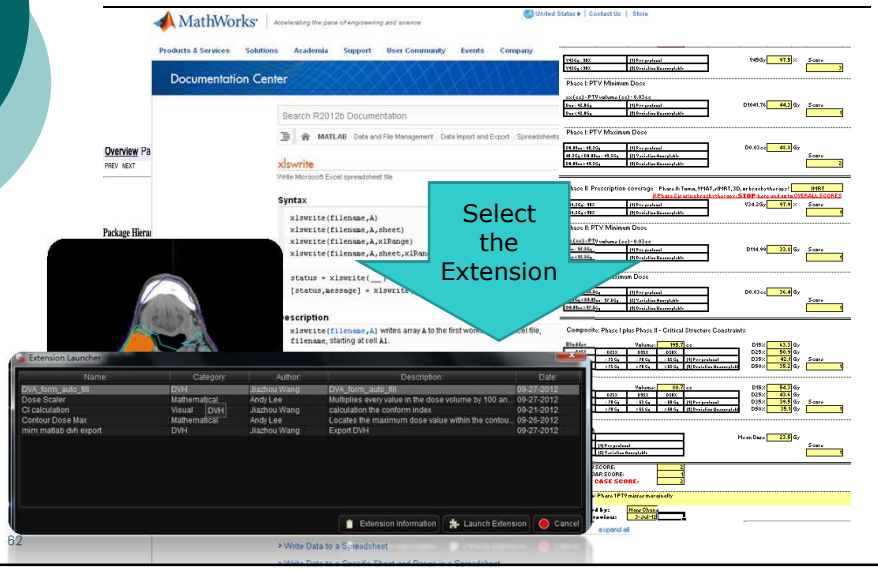
DVH Parameters Extraction



	heart V 20	heart V 30	cord Dmax	lung V 20	lung_cntr V 20	lung_ipsi V 20	lung V 5
0617_0001	0.09	0.06	39.90	0.35	0.14	0.58	0.51
0617_0003	0.10	0.06	46.40	0.32	0.12	0.52	0.58
0617_0004	0.98	0.91	44.00	0.47	0.15	0.94	0.79
0617_0005	0.40	0.21	47.60	0.34	0.09	0.56	0.52
0617_0006	0.23	0.17	35.20	0.27			0.41
0617_0007	0.00	0.00	32.10		0.02	0.47	
0617_0008	0.24	0.18	41.90	0.21	0.02	0.68	0.52
0617_0009	0.08	0.05	44.90	0.19	0.05	0.32	0.25
0617_0010	0.38	0.25	14.40	0.24	0.01	0.57	0.4
0617_0010	0.52	0.47	44.60	0.37	0.07	0.77	0.6
0617_0010	0.46	0.17	31.30	0.31	0.04	0.68	0.42
0617_0011	0.38	0.14	1.40	0.14	0.00	0.31	0.28
0617_0011	0.46	0.28	47.90	0.35	0.21	0.52	0.69
0617_0011	0.08	0.07	47.00	0.20	0.21	0.20	0.55
0617_0012	0.06	0.03	37.70	0.49	0.27	0.80	0.62
0617_0013	0.43	0.22	48.30	0.36	0.11	0.70	0.83
0617_0014	0.30	0.25	46.70	0.37	0.23	0.51	0.57
0617_0015	0.70	0.57	44.30	0.49	0.17	0.75	0.71
0617_0016	0.06	0.04	49.10	0.32			0.45
0617_0017	0.45	0.42	50.20	0.39			0.60

Application Extension – Automatic Report



- Evidence based, adaptive quality assurance
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  - Personalized radiotherapy guidance

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SAM Question 5

From the investigation into different image registration systems, we observed intrinsic registration uncertainties among the systems themselves.

The uncertainty is approximately?

a) 0.5 mm
b) 1 mm
c) 2 mm
d) 3 mm
e) 5 mm

SAM Question 5 Answer

From the investigation into different image registration systems, we observed intrinsic registration uncertainties among the systems themselves.

The uncertainty is approximately?

a) 0.5 mm
b) 1 mm
c) 2 mm
d) 3 mm
e) 5 mm

Answer: c)

Reference: Y. Cui (Xiao) et al, Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 1, pp. 305–312, 2011

Rapid Learning CAT (Computer Assisted Theragnostics)

MAASTRO/RTOG-ACR/Fudan Collaboration

- A Federated Approach as An Alternative to NBIA?

Challenges to share data

[..] the problem is not really technical [...]. Rather, the problems are ethical, political, and administrative. Lancet Oncol 2011;12:933

1. Administrative (time)
2. Political (value, authorship)
3. Ethical (privacy)

4. Technical

CAT approach

CAT is a research project in which

we develop an IT infrastructure -> *technical*

to make radiotherapy centers

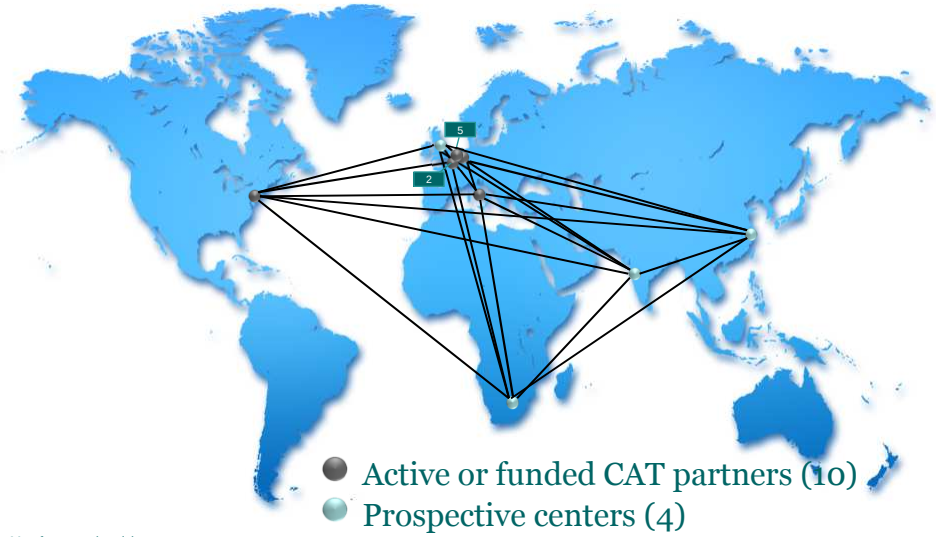
semantic interoperable (SIOp*) -> *administrative*

while the data stays inside your hospital -> *ethical*

under your full control -> *political*

* SIOp level 3 = Machine Readable ->Data in common syntax and with common meaning

Network 11/2011

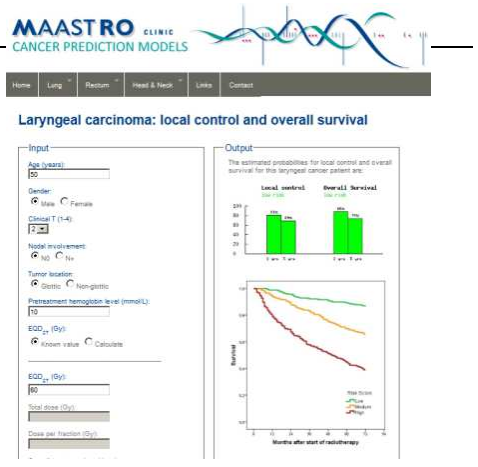


- Active or funded CAT partners (10)
- Prospective centers (4)

Map from cgadvertising.com

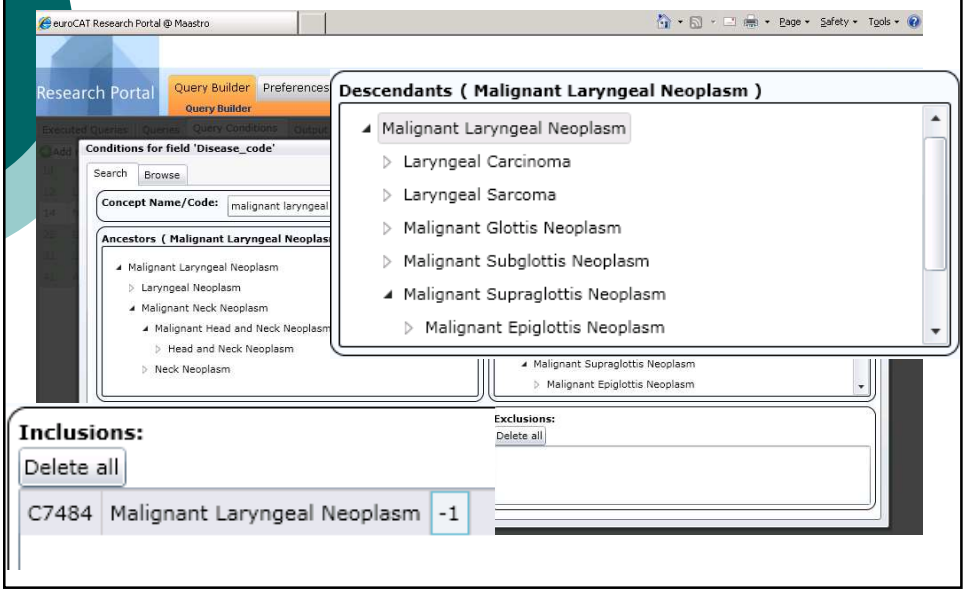
Laryngeal carcinoma model

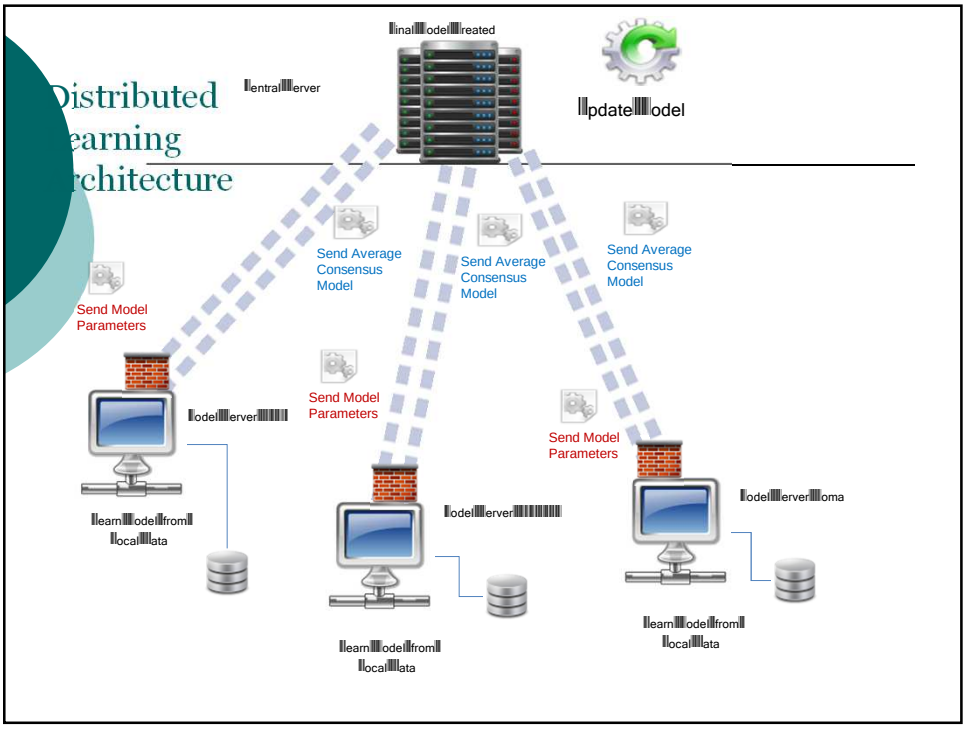
- 994 MAASTRO patients
- 1990-2005
- www.predictcancer.org
- Input parameters
  - Age
  - Hemoglobin
  - T-stage
  - EDQ2T (Gy)
  - Gender
  - N+
  - Tumor location
- Output parameters
  - Overall survival



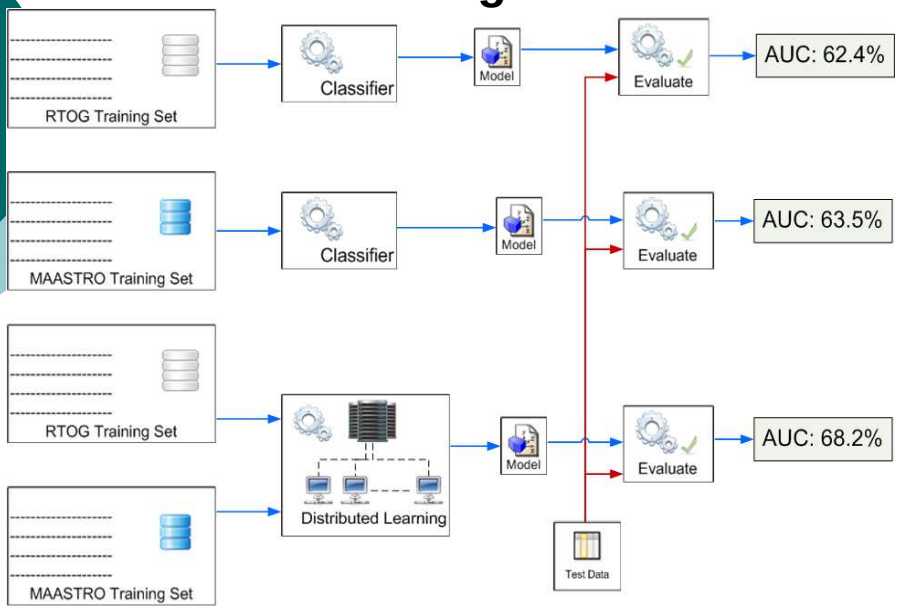
www.predictcancer.org

Larynx Query





Distributed Learning Results



Cox Regression Model

- Inputs
  - gender
  - Hemoglobin value
  - ARM
  - Age
  - EQD2T
  - Disease
  - T staging
  - N staging
- P value
  - 0.418
  - 0.000
  - 0.633
  - 0.000
  - 0.000
  - 0.000
  - 0.000
  - 0.003

Performance of our cox model

- ROC analyze: AUC=0.71
- Compare to the MAASTRO

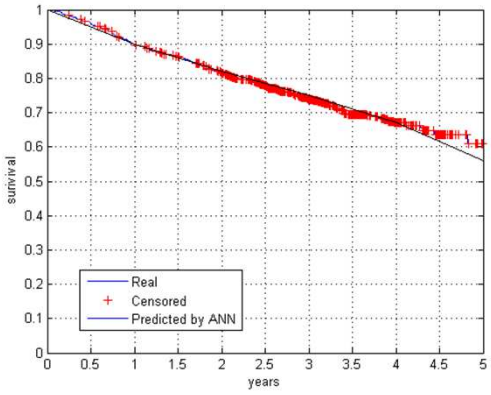
	Survival	
	Model based on multiple variables	Model based on TNM
MAASTRO (n = 994)	0.73	0.62
(95% CI)	(0.70–0.77)	(0.58–0.63)
Leuven (n = 109)	0.68	0.70*
(95% CI)	(0.50–0.82)	(0.45–0.81)
VU Amsterdam (n = 178)	0.74	0.65
(95% CI)	(0.69–0.87)	(0.57–0.75)
NKI/AVL Amsterdam (n = 205)	0.71	0.57
(95% CI)	(0.60–0.82)	(0.52–0.69)
Manchester (n = 403)	0.76	0.63
(95% CI)	(0.72–0.81)	(0.58–0.69)
Pooled external datasets	0.71	0.60
	(0.70–0.76)	(0.57–0.62)

Artificial Neural Networks

- Inputs
  - gender
  - Hemoglobin value
  - ARM
  - Age
  - EQD2T
  - Disease
  - Tstage
  - Nstage

Performance of our Artificial Neural Networks model

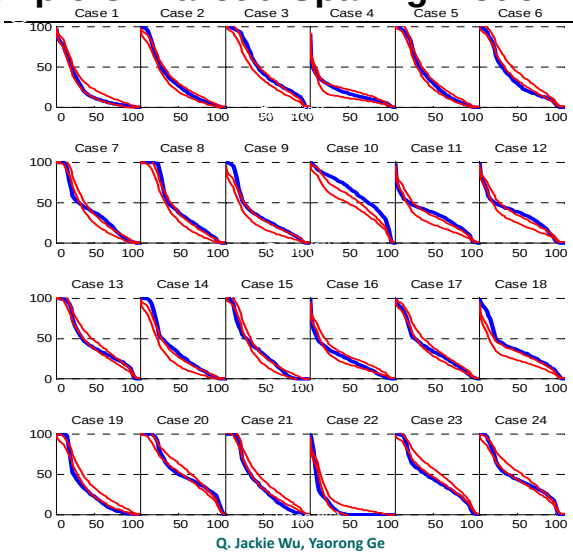
- ROC analyze: AUC=0.75



Investigations in Progress

- Include image information
- Include QA parameters
- Use Support Vector Machine (SVM)
- Optimize model parameters

Establishing knowledge-based models for IMRT planning quality evaluation Example Of Parotid Sparing Modeling

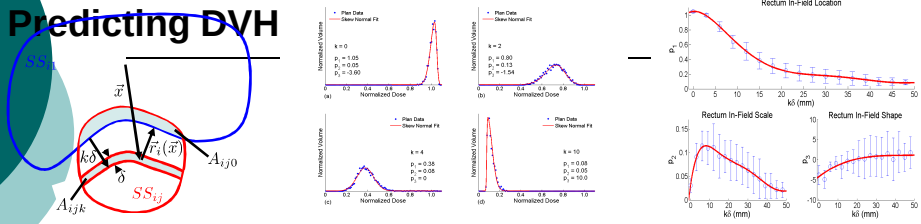


— Actual Plan DVH

— Modeled Lower and Upper Bound of DVH

Q. Jackie Wu, Yaorong Ge

Experience-based dose volume histogram prediction in IMRT: A new QC paradigm Predicting DVH



$$V'_{ij} = \sum_{k=0}^{\infty} \chi_{ijk}$$

$$\Phi(p_1, p_2, p_3; D) = \frac{1}{\pi p_2} e^{-\frac{(D-p_1)^2}{2p_2^2}} \int_0^{p_3(D-p_1)/p2} e^{-\frac{t^2}{2}} dt$$

$$\bar{p}_{jkq} = \frac{1}{N} \sum_{i=1}^{N} p_{ijq} \rightarrow p_{jq}(k)$$

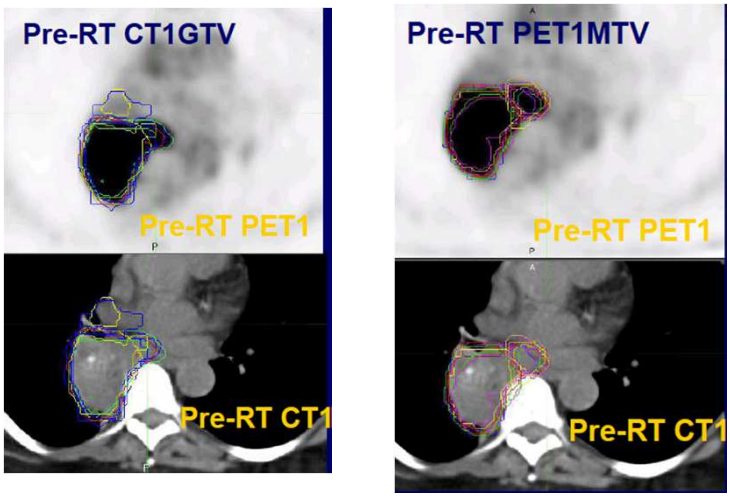
- With universal fitting function and parameter fits $p_{jq}(k)$, which are derived from all N training patients, we have the desired result:

$$V'_{ij,pred} = \sum_{k=0}^{N} \Phi\left[p_{j1}(k), p_{j2}(k), p_{j3}(k); D\right] \cdot V(A_{ijk})$$

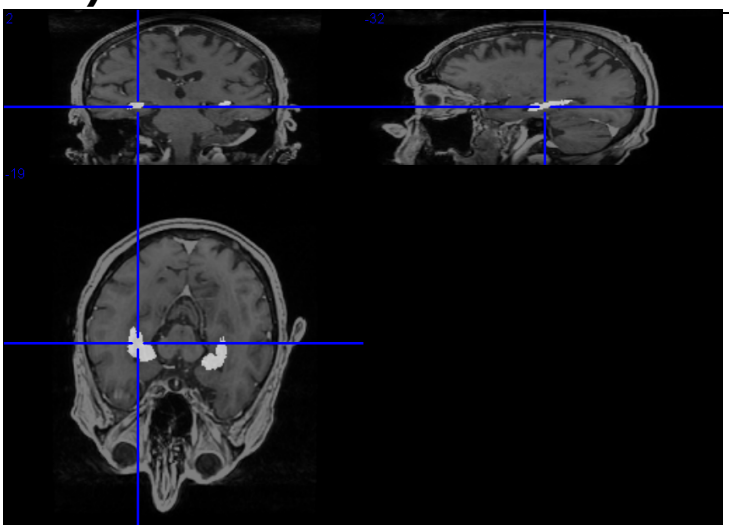
- This equation takes as input geometric variables and the derived fitting parameters and outputs a predicted DVH for an organ based only on the input structure set SS_{ij}

Kevin L. Moore, Ph.D., DABR

Target Defined from Multiple Institutions, Incorporating Imaging QA



Auto-Segmentation of Hippocampus (0933)



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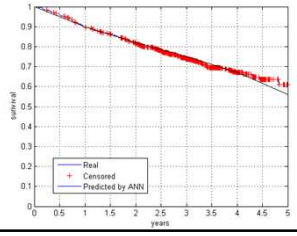
Extension of CAT

- Include image information
- Include QA parameters
- Use Support Vector Machine
- Optimize model parameters

ROC analyze: AUC=0.75 from
Artificial Neural Network model



Future Quality Assurance

- Perspective QA trials, independently or as part of a clinical trial, with adaptive statistical design
- Retrospective QA data analysis for efficacy and efficiency

Thank You