Radiation Oncology Technology Exploration and Quality Assurance in Clinical Trials

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Objectives

• Describe NCI’s Initiative to revamp the clinical trial system
• Present an overview of a proposed Imaging Radiation Oncology Core (IROC) services Group
• Describe the proposed Center for Innovative Radiation Oncology (CIRO) of NRG
• Introduce clinical trial technological exploration and quality assurance science
Overview of the Current Program

- **3,100 Institutions**
- **14,000 Investigators**
- About **25,000 pts enrolled on tx trials annually**

<table>
<thead>
<tr>
<th>Trials</th>
<th>FY2006</th>
<th>FY2007</th>
<th>FY2008</th>
<th>FY2009</th>
<th>FY2010</th>
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</thead>
<tbody>
<tr>
<td>All Phases: Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trials</td>
<td>27,667</td>
<td>24,715</td>
<td>25,784</td>
<td>29,285</td>
<td>23,468</td>
</tr>
</tbody>
</table>

Accrual Distribution:
- Phase 3: 83.4%
- Phase 2: 15.1%
- Phase 1/Pilot: 1.5%
Structure of Program: As of January 2011

NCI Division of Extramural Activities (DEA) Review

- ECOG
- CALGB
- SWOG
- ACOSE
- COG
- RTOG
- GOG
- ACRIN
- NCCTG
- NSABP

Disease Committees
Operations
Stats & Data Mgt
Tumor Banks

NCI Disease Steering Committees – Evaluation/Prioritization of Group Trials

Central Access to NCI Clinical Trials Portfolio (NCI Cancer Trials Support Unit – CTSU)

NCI Central IRB

- Cancer Centers
- Other Academic Centers
- CCOPs & MB-CCOPs
- Community Practices
- International Members
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

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

NCI Clinical Trials Network

4 Adult and 1 Pediatric U.S. Network Groups
- Canadian Network
- Adult Group #1 Ops & Stats
- Adult Group #2 Ops & Stats
- Adult Group #3 Ops & Stats
- Adult Group #4 Ops & Stats
- COG Ops & Stats

Administrative Support Services
- NCI Central IRB
- CTSU

Network Lead Academic Participating Sites
- CCOPS & MB-CCOPs
- Other Academic Centers
- Community Practices
- International Members

Dark blue boxes signify NCI DEA reviewed, grant-funded components under this RFA.
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

ACR IROC Grant
Contact PI, Co-Director RT: D. Followill, Houston; Co-Director Imaging: M.V. Knopp, Ohio

IROC Ohio
PI: M. V Knopp

IROC Houston
PI: D. Followill

IROC Rhode Island
PI: TJ FitzGerald

IROC St Louis
PI: J Michalski

IROC Philadelphia (RT)
PI: J. Galvin

IROC Philadelphia (Imaging)
PI: M. Rosen
IROC’s Five General NCTN Core Services

Site Qualification
Trial Design Support
Credentialing
Data (pre-review) Management
Case Review
Data (post-review) Management

NCTN RT Core Service Operations

Site Qualification
Followill/Galvin

Trial Design Support
Galvin/Fitzgerald

Credentialing
Molineu/Xiao

Data (Pre-rev.) Mgmt
Straube/Ulin

Case Review
Leif/O’Meara/Laurie

Data (Post-rev.) Mgmt
Laurie/O’Meara

Houston QA Center
All IROC QA Centers
Houston-Phil. (RT)
QA Centers
Phil (RT), Rhode Is., St Louis QA Centers
Phil (RT), Rhode Is., Houston QA Centers
Phil (RT), Rhode Is. QA Centers

NCTN Participating Sites
The ACR/IROC Cloud

- OPEN/RSS/Other RAVE
- NCTN Statistics & DM Centers
- NCTN Network Groups
- TRIAD
- Data submission with automatic validation
- Workflow manager; data archive
- Remote application environment
  - Mimvista
  - Velocity
  - MATLAB
  - RTP
  ...

RT/IMAGE DICOM DATA

ACR/IROC CLOUD

NCTN QA Offices

SITE

Clinical Data/CRF

REVIEW

QA
Example: Data Submission via TRIAD
## Automated Validation

<table>
<thead>
<tr>
<th>Rule</th>
<th>Tag</th>
<th>Expected Value</th>
<th>Actual Value</th>
<th>Result</th>
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<tbody>
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<td>Patient Check</td>
<td>(0010,0040)PatientsSex</td>
<td>equal M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rule2</td>
<td>(0018,1152)Exposure</td>
<td>inbetween 200 - 240</td>
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<td></td>
</tr>
<tr>
<td>Check All ROI Values</td>
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<td>Must have all the values: CTV1, RECTUM, BLADDER</td>
<td>BLADDER, CTV1, CTV2, FEMUR_LT, FEMUR_RT, PENILE_BULB, PTV1, PTV2, RECTUM, SEM_VES, SKIN, TABLE_2</td>
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</table>
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.
NRG Oncology Center for Innovation in Radiation Oncology (CIRO)
Aims of CIRO

1) Promote innovative RT research within the entire NCTN
   • Accelerate the testing of new radiation oncology innovations in NCTN clinical trials in all groups
   • Facilitate the application of innovations across all appropriate protocols

2) Foster intergroup collaboration and protocol harmonization in terms of inclusion and description of RT techniques and delivery devices
   • Reduce timelines for development of new protocols
   • Improve the clarity of NCTN protocols
NRG Committee Structure

Research Strategy Committee

- Concept Prioritization Advisory Committee (CPAC)

- Disease Site Committees
  - Breast
  - Brain
  - Gastrointestinal
  - Colorectal
  - Non-colorectal
  - Genitourinary
  - Gynecologic
  - Ovarian
  - Cervix
  - Uterine Corpus
  - GYN Rare Tumors
  - Head & Neck
  - Lung

- Non-Disease Site Scientific Committees
  - Developmental Therapeutics (DT)
  - Cancer Prevention & Control (CPC)
  - Patient Centered Outcomes Research (PCOR)
  - Translational Science

- Scientific Core Committees
  - Medical Oncology
  - Pathology
  - Radiation Oncology
  - Medical Physics
  - Surgical Oncology
  - Protocol Support
  - Clinical Research Associates
  - Nursing
  - Patient Advocates
  - Special Populations

- Center for Innovation in Radiation Oncology (CIRO)

Protocol Generating Committees

Scientific Interactions
CIRO

1) Radiation Oncology Committee
2) Medical Physics Subcommittee
3) Staff
   Medical Officer
   Technical Officer
   Support Staff
4) Statistical and Data Management Liaison
Medical Physics Committee Membership Structure

- Disease site liaisons
  - Leading member to report @ conference/meeting
- Intergroup, QA core liaisons
  - Leading member to report when requested
- Modality/technology liaisons (Working Group)
  - Leading member to report when requested
- Bio-informatics liaisons (WG)
- Industry liaison(s) (ad hoc guest)
- International liaison(s) (ad hoc guest)
- NCI and Staff liaison(s) (Data Manager, Protocol, Statistics)
  (invited talk on a rotating basis)
Professional Commitment
(Missions, Job Description)

- Interface with disease site committees as liaisons
  - Cover disease site conferences and face-to-face meetings
- Interface with intergroup, QA core and NCI
- Serve as Physicist PI on protocols
  - Overall protocol design and development
  - Specific responsibility for technical RT aspects and QA considerations
- General Responsibilities
  - Prospective identification of physics/QA objectives in new trials
  - Aid in creation of RT clinical Trials protocol templates
- Interface with Vendors of Technologies as needed
- Monthly conference
- Bi-annual NRG face-to-face meetings
SDMC Collaborations

• Support design and implementation of innovative radiation oncology technologies
• Pursuit of innovative prospective designs to evaluate radiation therapy quality assurance (RTQA) as part of clinical trials
• Collaborate on predictive model building for radiotherapy and quality assurance
Quality Assurance Science and Vision

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

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