Imaging in NCI’s Phase II and III Trials

Lalitha K. Shankar, MD, PhD, Chief, Clinical Trials Branch Cancer Imaging Program National Cancer Institute QIBA Annual Meeting May 2013

Imaging Tools For Cancer Management – Current Approach

• Screening
• Diagnosis
• Staging
• Restaging
• Surveillance
Evaluating patients based on biologic characteristics of the primary tumor and metastases for personalized care

- Prognostic Markers
- Predictive Markers
- Assessing therapeutic response
- Focused surveillance/screening

**Imaging Tools For Cancer Management: Preferred Approach**

- Metabolism – FDG
- Proliferation – FLT, FDG, Diffusion MR
- Metastasis – FDG, Ferumoxytol
- Angiogenesis – DCE-MRI
- Hypoxia – FMISO, Cu-64 ATSM
- Receptor Imaging – FES, FDHT, In-Octreotide

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Qualification of an Imaging Biomarker

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Key issues in imaging tool assessment: Phase II

• Preliminary efficacy
• Reproducibility
• Tissue correlation

In the context of patient management with standard treatment:

• prognostic capabilities
• predictive capabilities
• assessment of treatment response
Issues:

- Variability of signal –
  - Within a histology
  - Within a patient on different days (without therapeutic intervention)
  - With different scanners from the same manufacturer
  - With scanners from different manufacturers
  - With different therapeutic interventions

Standardization

Early Clinical Evaluations

- PAR-11-216: Early Phase Clinical Trials in Imaging and IGI
- CTEP-CIP Phase II N01 Consortia for evaluation of novel treatments (7 contracts including 22 NCI Cancer Centers)
- ACRIN’s Experimental Imaging Scientific Committee studies
Biomarker, Imaging, & Quality of Life Studies Funding Program (BIQSFP)

Eligible trial types for BIQSFP funding are:

- Trials conducted by CG’s and CCOP Research Bases.
- Phase 3 treatment trials with integral or integrated biomarker or imaging studies, and/or quality of life studies.
- Phase 3 cancer prevention and QOL clinical trials with integral or integrated biomarker or imaging studies, and/or QOL studies.
- Large (≥100 patients), randomized phase 2 treatment trials with integral or integrated biomarker or imaging studies.
- For CEA, the parent concept must be a randomized phase 3 clinical trial with a comparator arm.

Criteria for Review of Biomarker and Imaging Studies:

- The strength of the preliminary data for both test utility and performance characteristics including cutpoints.
- The potential of the test to change practice and have high impact on patient care (e.g. the impact of the test itself or the change of therapy indicated by the results of the trial).
- The ability of the test to yield well defined and validated interpretations that will guide decision-making.
- The extent of standardization of the tests as to be transferable to the non-research setting.
- The adequacy of the process for specimen collection or image acquisition including feasibility data.
- A description of potential cost-sharing approaches that can be developed with entities that would eventually commercialize the test.
Imaging Biomarker Development

The process of developing a qualified imaging biomarker to a surrogate marker is an international partnership between the public and private sectors.

A surrogate marker is one that is intended to serve as a substitute for a clinically meaningful endpoint - for example PFS.

Functional Activity Vs. Clinical Predictivity

- Larger Phase II and III multicenter studies via the NCI cooperative groups and EORTC
- To establish impact in:
  - Prognosis (e.g. FDG, FMISO)
  - Selection of appropriate therapy (e.g. FES)
  - Assessment of therapeutic response (e.g. DCE MRI)
- Regulatory Approval: does the agent/modality impact a clinically (or biologically) meaningful endpoint: how a person feels, functions or survives (effect size is a moving target)
- Clinical Practice: reimbursement by IIIrd party payers (CMMS, Blues, HMOs)
Collaborations for Assessment of Imaging Tools

- NCI-FDA (Tracer development pathways)
- NCI-CMS
- NCI-EORTC
- Response Assessment – collaboration with EORTC and Pharma
  - RECIST 1.1
  - FDG – ongoing evaluation
- QIBA
- Biomarkers Consortia

Prequalification of Imaging Capabilities in Cancer Centers

- CIP program in collaboration with ACRIN and ACR for qualification of all NCI Comprehensive Cancer Centers to perform:
  - PET CT (static and dynamic)
  - DCE MR
  - Volumetrics
    - Across all major scanner manufacturers
    - For brain and body imaging

*SOPs available online: [http://www.acrin.org/CORELABS/NCICQIEQUALIFICATIONPROGRAM.aspx](http://www.acrin.org/CORELABS/NCICQIEQUALIFICATIONPROGRAM.aspx)
CQIE: Program Proposal

- Purpose: to establish a resource of ‘trial ready’ sites within the NCI Cancer Centers Program that are capable of conducting clinical trials in which there is an integral molecular and/or functional advanced imaging endpoint.

CQIE: Objectives

- Qualify 59 Cancer Centers by end of July 2011
- Annual requalification of qualified centers through 2014
- Publish qualification procedures for further dissemination
- Promote qualified centers
CQIE Program Development

- Leverage existing ACRIN qualification procedures
- Engage experts from the imaging community: ACRIN, AAPM, SNM, QIBA/RSNA
- Resource ACR Accreditation Program
- Acquire phantoms and develop required documents
- Pilot qualification procedure at 1 site

Technical Qualification

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Courtesy Mitch Schnall, MD, PhD
Results to date

- Fully Qualified NCI Cancer Centers
- Published qualification instructions and a list of qualified sites
- SOPs shared with research groups in Europe – CRUK, EORTC and Asia
- Identified numerous equipment issues (non-DICOM, no dynamic PET capability, faulty cable connector, etc)
- Stimulated scientific debate (eg: appropriate CT QC measures, optimal phantom)
- Created interest among other research groups and industry

Courtesy Mitch Schnall, MD, PhD

EORTC Imaging Group
EORTC Imaging Group

- NCI-EORTC collaboration in clinical imaging
- Standardizing imaging readouts for use in multicenter trials: The EORTC, EANM, EARL Quantitative PET Imaging accreditation program
- Web-based analysis for multiple readers: the EORTC Imaging Platform
  - EORTC Imaging Group N DeSouza et al. EJC Volume 10, Issue 1, Pages 82-87, March 2012

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NCI's Clinical Imaging Steering Committee
Vision for the Imaging Steering Committee

- Establish a forum for the extramural imaging and oncology communities to provide strategic input to NCI regarding our significant investment in imaging activities in clinical trials.
  - Prioritize research activities and clinical trials
  - Improve efficiencies in treatment trials

Needs Assessment:

- Prioritization of activities in imaging as they relate to NCI’s strategic goal and objectives
- Robust extramural imaging representation in review of concepts with imaging aims (primary or secondary)
- Enhanced integration of imagers with oncologic expertise in the process of idea generation at the task force level
Functions of CISC

• Blended steering committee with the functionality of:
  – Investigative Disease Steering Committee
  – Scientific Steering Committee
• Will provide a “ready resource” of imagers to provide desired input to the other steering committees and their taskforces

Goals of CISC

Construct a National plan
  – Develop strategic priorities to efficiently use imaging as an enabling technology for cancer research and management.
  – Conduct clinical trials planning meetings focused on oncologic disease applications across imaging modalities.
Goals of CISC

• Improve clinical trial outcomes & increase predictive value of early phase trials
  – Accelerated validation of high priority agents that apply to registration
  – Develop imaging technology/methods for tumor systems biology and customized treatments.

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Goals of CISC

• Provide a forum for extramural imagers and oncologists to improve imaging science involvement in the NCI-Disease Steering Committee processes
  – Establish a ready pool of reliable, accountable and diverse imaging experts
  – Allow efficient investment of time and effort, better engagement and concentration of expertise
  – Environment for imaging scientists and oncologist to explore imaging science across pathways and targets

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Membership of CISC

- Two co-chairs (Dr. Steve Larson and Dr. Neil Rofsky)
- Representatives from ACRIN, CTEP- Coop Groups, SPORE’s, CCOP’s, Cancer Centers
- Liaisons from other NCI-Dz SC’s/TF’s
- Subject experts, e.g., molecular, anatomic and functional imaging, oncologists, pathologists, patient advocates, clinical community oncologists, biostatisticians, clinical trial methodologists

Concept Review

There is no duplicative review
Functional Activity Vs. Clinical Predictivity

- Larger Phase II and III multicenter studies via the NCI cooperative groups and EORTC
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Resources for Imaging Activities within the Cooperative Group Network

For efficient assessment of promising imaging agents and modalities and their role in the development of therapeutic strategies and cancer management:
- Processes for Qualification of Cancer Centers (CQIE) for Advanced Imaging (PET and MR)
- Development of a national distribution system for investigational imaging agents
- Biomarker, imaging, and quality of life studies funding program (BIQSFP)
- Imaging and Radiation Therapy Core for the NCTN
- Clinical Imaging Steering Committee (CISC)
Collaborations for Assessment of Imaging Tools

- NCI-FDA (Tracer development pathways)
- NCI-CMS
- NCI-EORTC
- Response Assessment – collaboration with EORTC and Pharma
  - RECIST 1.1
  - FDG – ongoing evaluation
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Thank you!