Local Evaluator and Secondary Reader Issues in Oncology Clinical Trials

Ira Smalberg, MD
Tower Imaging Medical Group
ismalberg@yahoo.com

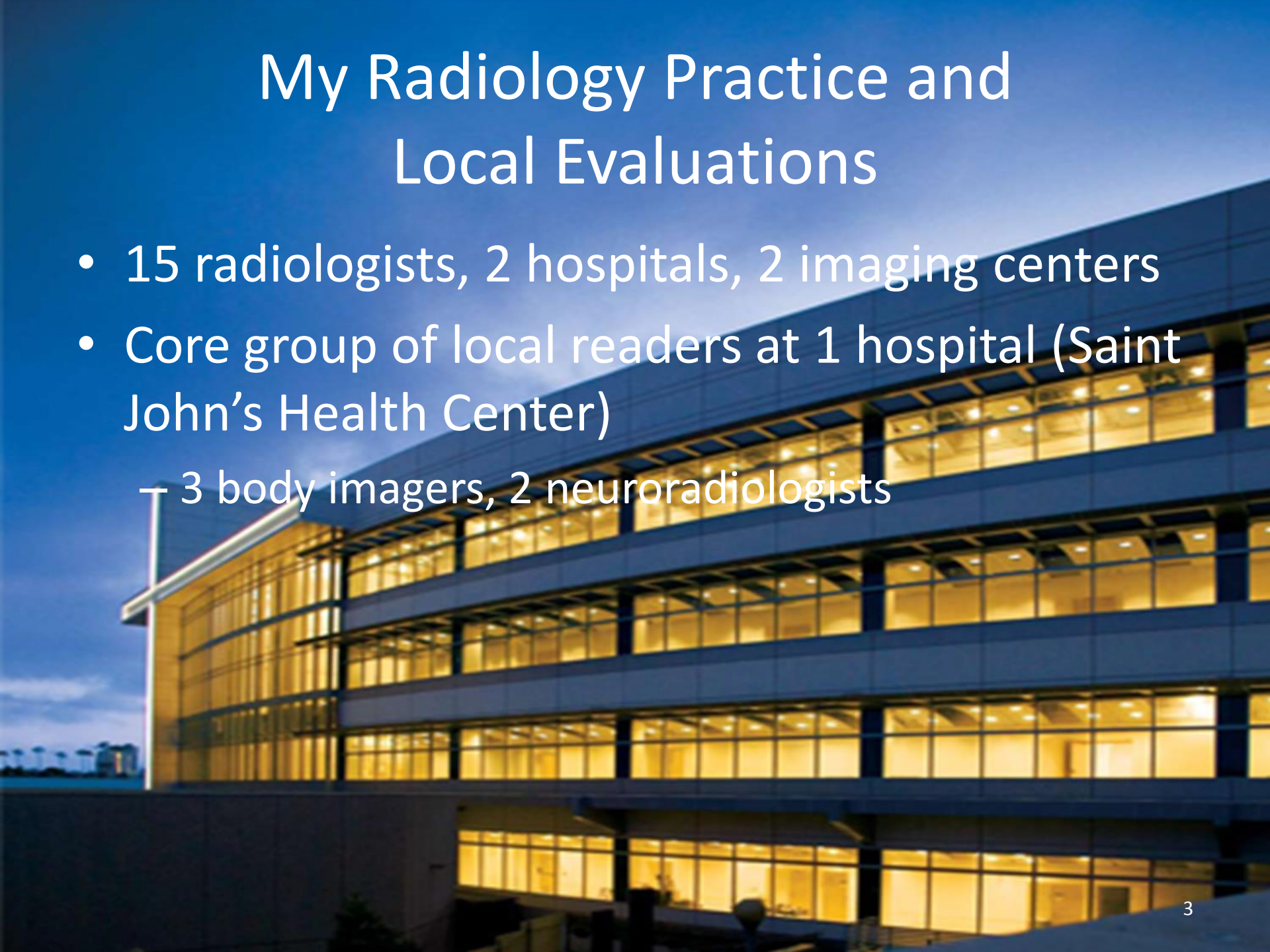
6/27/14
PINTAD

Oncologic Drug Advisory Committee Decision, July 2012

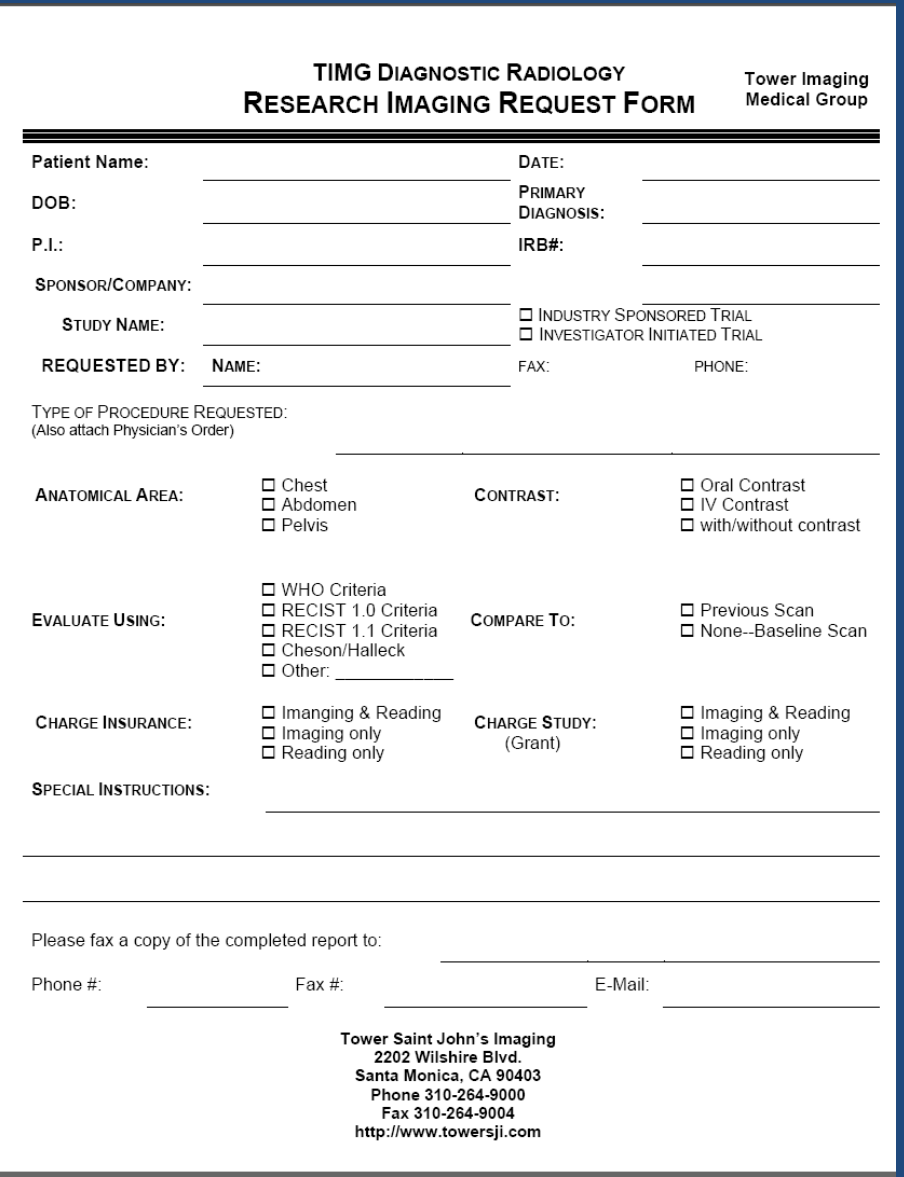
- Permits sponsor companies to rely on investigator RECIST 1.1 assessments, with only a sampling of imaging being subjected to a central review

My Radiology Practice and Local Evaluations

- 15 radiologists, 2 hospitals, 2 imaging centers
- Core group of local readers at 1 hospital (Saint John's Health Center)
  - 3 body imagers, 2 neuroradiologists



How We Do It



TIMG Diagnostic Radiology
Research Imaging Request Form

Tower Imaging Medical Group

Patient Name: _____ **Date:** _____

DOB: _____ **Primary Diagnosis:** _____

P.I.: _____ **IRB#:** _____

Sponsor/Company: _____ _____

Study Name: _____ ☐ Industry Sponsored Trial ☐ Investigator Initiated Trial

REQUESTED BY: **Name:** _____ FAX: _____ PHONE: _____

Type of Procedure Requested:
(Also attach Physician's Order)

_____ _____ _____

Anatomical Area: ☐ Chest ☐ Abdomen ☐ Pelvis

Contrast: ☐ Oral Contrast ☐ IV Contrast ☐ with/without contrast

Evaluate Using: ☐ WHO Criteria ☐ RECIST 1.0 Criteria ☐ RECIST 1.1 Criteria ☐ Cheson/Halleck ☐ Other: _____

Compare To: ☐ Previous Scan ☐ None--Baseline Scan

Charge Insurance: ☐ Imanging & Reading ☐ Imaging only ☐ Reading only

Charge Study: (Grant) ☐ Imaging & Reading ☐ Imaging only ☐ Reading only

Special Instructions: _____

_____

_____

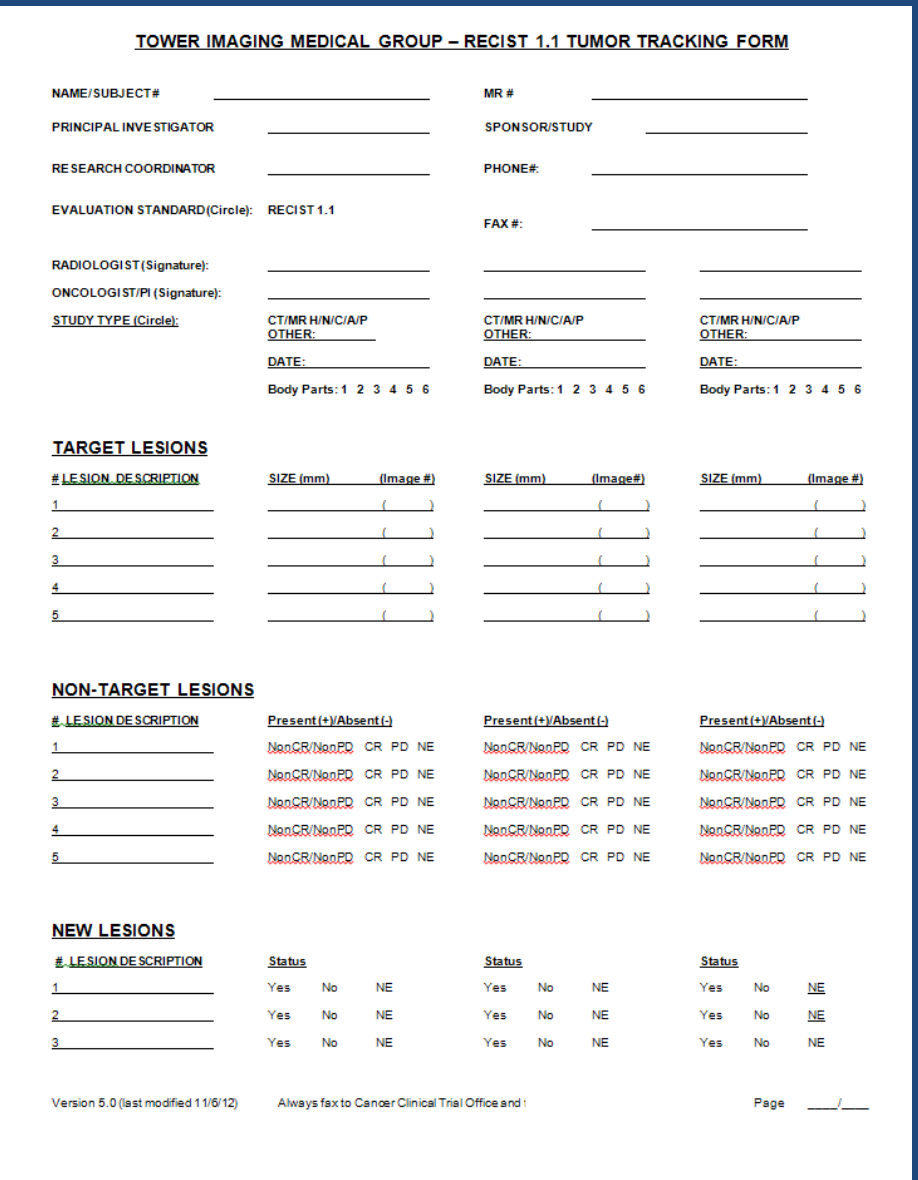
Please fax a copy of the completed report to: _____ _____ _____

Phone #: _____ Fax #: _____ E-Mail: _____

Tower Saint John's Imaging
2202 Wilshire Blvd.
Santa Monica, CA 90403
Phone 310-264-9000
Fax 310-264-9004
http://www.towersji.com

- Prenegotiated rates
- Research Imaging Request Form
  - Patient, sponsor, and clinical trial demographics
  - Study type and body part(s) to be scanned
  - Assessment method
  - Billing instructions (insurance or study)

Tumor Tracking Forms



TOWER IMAGING MEDICAL GROUP – RECIST 1.1 TUMOR TRACKING FORM

NAME/SUBJECT# _____ MR # _____

PRINCIPAL INVESTIGATOR _____ SPONSOR/STUDY _____

RESEARCH COORDINATOR _____ PHONE#: _____

EVALUATION STANDARD (Circle): RECIST 1.1 FAX #: _____

RADIOLOGIST (Signature): _____ _____ _____

ONCOLOGIST/PI (Signature): _____ _____ _____

STUDY TYPE (Circle): CT/MR H/N/C/A/P OTHER: _____ CT/MR H/N/C/A/P OTHER: _____ CT/MR H/N/C/A/P OTHER: _____

DATE: _____ DATE: _____ DATE: _____

Body Parts: 1 2 3 4 5 6 Body Parts: 1 2 3 4 5 6 Body Parts: 1 2 3 4 5 6

TARGET LESIONS

# LESION DESCRIPTION	SIZE (mm) (Image #)	SIZE (mm) (Image#)	SIZE (mm) (Image #)
1 _____	( )	( )	( )
2 _____	( )	( )	( )
3 _____	( )	( )	( )
4 _____	( )	( )	( )
5 _____	( )	( )	( )

NON-TARGET LESIONS

#. LESION DESCRIPTION	Present (+)/Absent (-)	Present (+)/Absent (-)	Present (+)/Absent (-)
1 _____	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE
2 _____	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE
3 _____	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE
4 _____	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE
5 _____	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE	NonCR/NonPD CR PD NE

NEW LESIONS

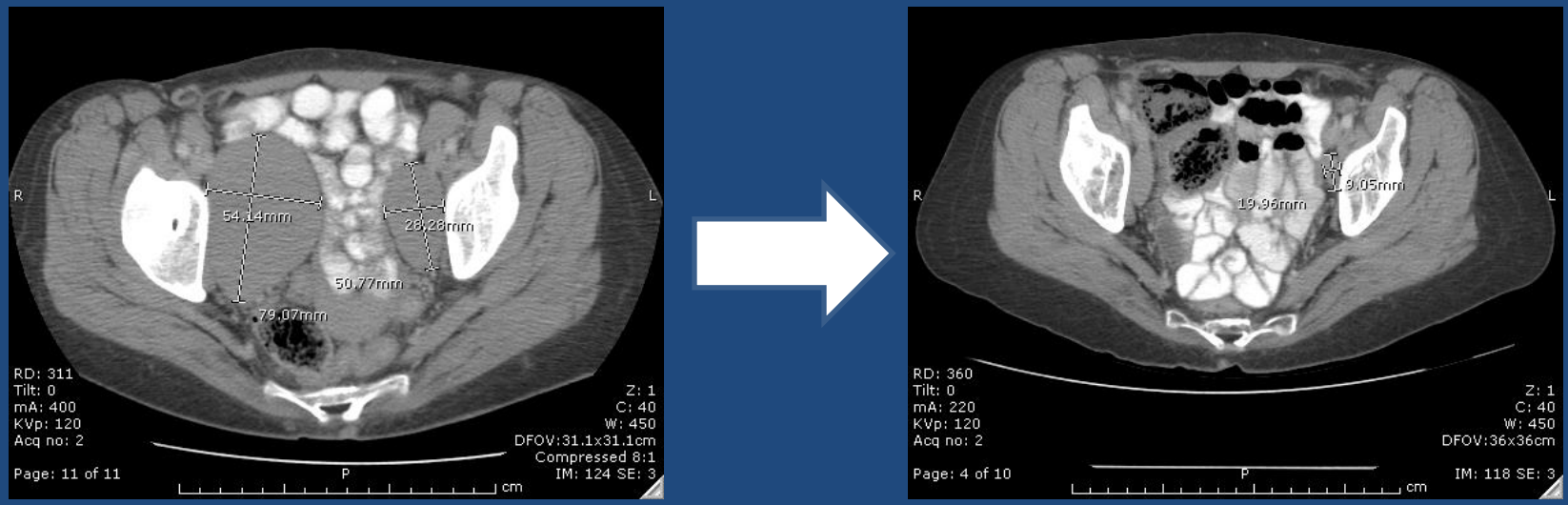
#. LESION DESCRIPTION	Status	Status	Status
1 _____	Yes No NE	Yes No NE	Yes No NE
2 _____	Yes No NE	Yes No NE	Yes No NE
3 _____	Yes No NE	Yes No NE	Yes No NE

Version 5.0 (last modified 11/6/12) Always fax to Cancer Clinical Trial Office and Page ____/____

- RECIST 1.1, Cheson/Halleck
- Indicate target, nontarget, new lesions
- Completed concurrent with transcribed clinical dictation with all lesions also tracked in clinical report
- Faxed TTF to research site and to our billing office
- Scanned TTF into PACS and save hard copy on file

How We Do It

- Lymphoma/Leukemia Imaging Conference
  - Biweekly review of all radiology for patients with the oncology clinical trial teams
- Point person



Other Local Evaluator Models

- Separate clinical and research reads
  - One radiologist vs. dedicated group of select radiologists
  - Tracked lesions do not necessarily match up to those discussed in clinical report

Local Evaluation Struggles

- Overwhelmed by daily clinical work and/or clinical trial work
- Basic workflow issues
  - Identifying clinical trial patients
  - Billing mechanisms
- Lack of interest by (busy) radiologists
- Lack of confidence in the radiology department
  - Clinical trial teams turn away studies
  - Poor imaging reports
  - Need for outsourcing of research reads
- Academic turf issues between subspecialty radiologists
- Poor communication with radiology department
  - Protocol approval and review?
  - Investigator meeting attendance by local radiologist(s)?

Quantitative Imaging in Oncology Patients: Part 1, Radiology Practice Patterns at Major U.S. Cancer Centers

(Tracy A. Jaffe, Nicholas W. Wickersham and Daniel C. Sullivan; AJR 2010)

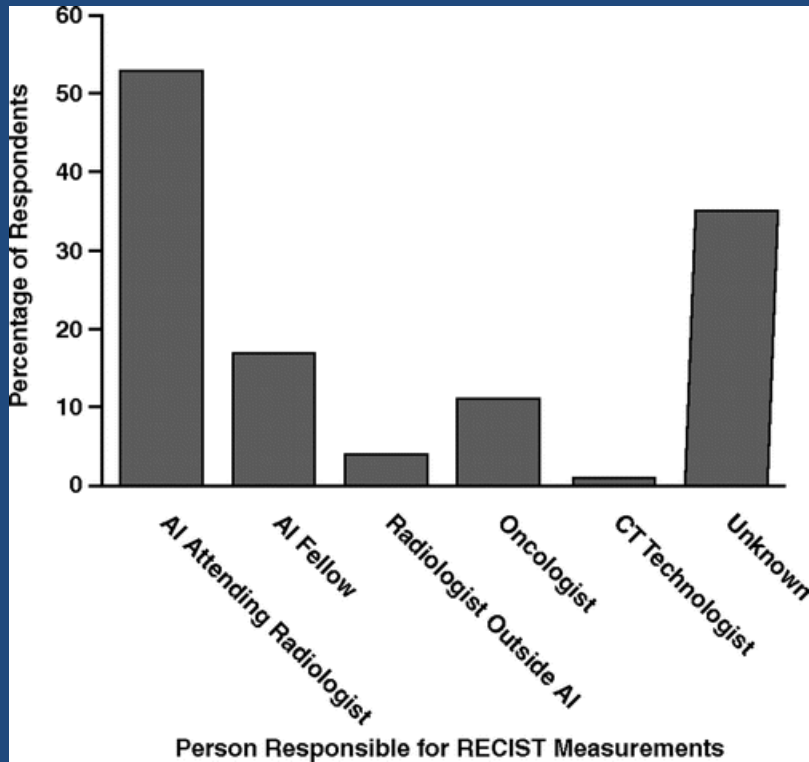
- E-mail survey
- 565 abdominal imaging radiologists at 55 US NCI-funded cancer centers
- 52% response rate

Survey Findings: General

- Centralized committee or a process for approval of industry-sponsored clinical trials?
  - 42% Yes
  - 30% No
  - 28% Unsure
- Familiarity with RECIST?
  - 82% Yes
  - 69% actually knew difference between target and nontarget lesion definitions
  - 48% participated in RECIST measurements for clinical trials
- Funding for RECIST measurements
  - 22% Yes
  - 31% No
  - 47% Unsure

Survey Findings: Performing RECIST Measurements

- 6% noted that oncologists approach specific radiologists for RECIST measurements
- 41% noted the process was an ad hoc issue for each new protocol
- 41% did not know

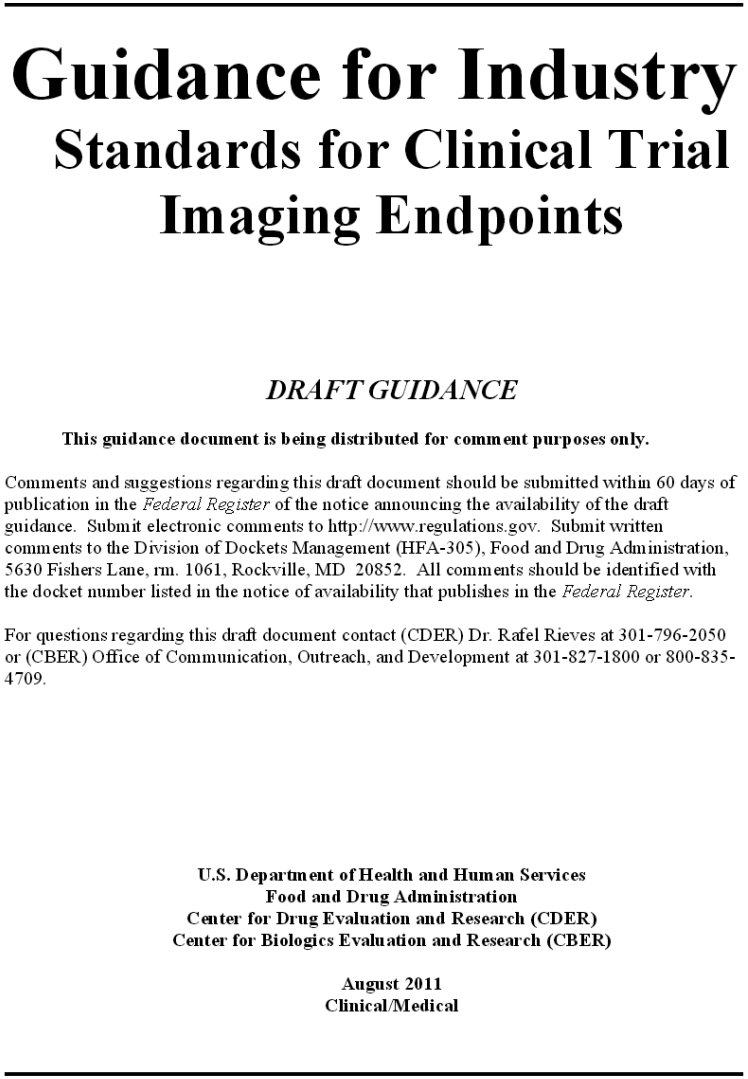


Benefits of Quality Local Evaluation

- Added value to our interpretations
  - Clinical interpretation may be of no use to research team needing quantification of results
- Active part of multidisciplinary research team
- Supports our hospital's research mission
- Adds prestige to our radiology practice
- Makes administrators happy
- Secures our hospital contract

Do You Want to Support Imaging In Oncology Clinical Trials?

- Oncologists and Administrators: “Yes!!”
- Radiologists: “Yes, but…”



Guidance for Industry

Standards for Clinical Trial Imaging Endpoints

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Dr. Rafel Rieves at 301-796-2050 or (CBER) Office of Communication, Outreach, and Development at 301-827-1800 or 800-835-4709.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

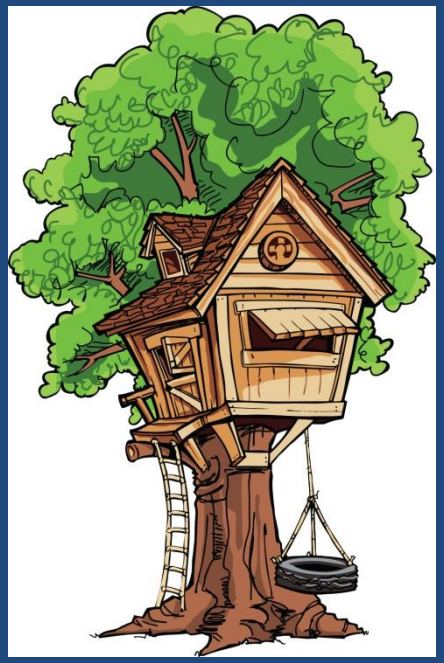
August 2011
Clinical/Medical

I:\9676dft.doc
08/08/11

- Reader Selection
- Reader Fatigue
- Site Qualifications

FDA Guidance (Draft): Reader Selection

- How do you become a member of the club if you are not already in the club?
- Documented specific knowledge, experience, and successful prior past performance as a central reviewer



FDA Guidance (Draft) : Reader Fatigue

- Doing “double duty” if an independent contractor
  - Perform reads after-hours or on days off from a full-time clinical/academic radiology position
- Sponsor and imaging core lab deadline pressures
  - Weeks → Same day
    - Same day eligibility reads
    - Confirmation of progression reads

Insurance for Readers?

- Do readers need to be licensed as a physician in states where they are rendering “research reports”?
  - Individual state rules and regulations regarding state licensure and what constitutes the practice of medicine vary.
- Do reader interpretations constitute establishing a doctor-patient relationship?
  - If yes, then readers have a duty to the patient/subject to adhere to the standard of medical care.
  - Probably readers can be sued (but not likely).
- Would imaging core labs and/or sponsors (and/or employers) cover you if you were sued?
  - “Hold harmless” clause in the contract?
  - Cost of defending the allegation

FDA Guidance (Draft): Site Qualifications

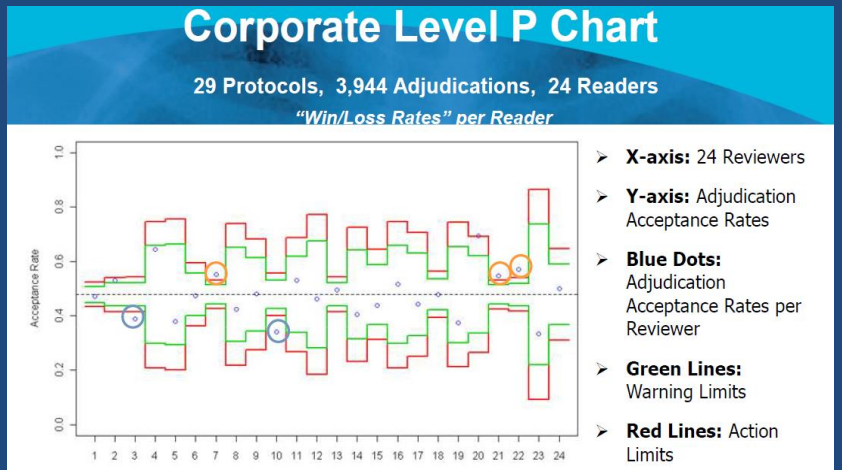
- Emphasizes technical imaging capabilities
- Does not discuss qualifications of the local radiologists or other evaluators at the site
  - Area to address in future

Training and Performance Metrics: Local Readers

- Assumes the reader is a radiologist (but not always the case!)
- Much lower bar, may just need to be a warm body in a smaller group
  - Highly variable education and training within and across sites
- Suspect little or no ongoing metrics beyond radiologist or monitor reading the report(s) at follow up time points

Training and Performance Metrics: Central Readers

- Much higher bar, specific experience and training, CV reviewed by ICL and sponsor
- 2 reader/1 adjudicator and other adjudication paradigms
- P charts
- Personal communication
- Getting asked to be a reader on future studies
- Review and discussion of training and adjudication cases
  - Reinforce study rules
  - Calibrate reading philosophies



ODAC Ruling and Local Evaluators

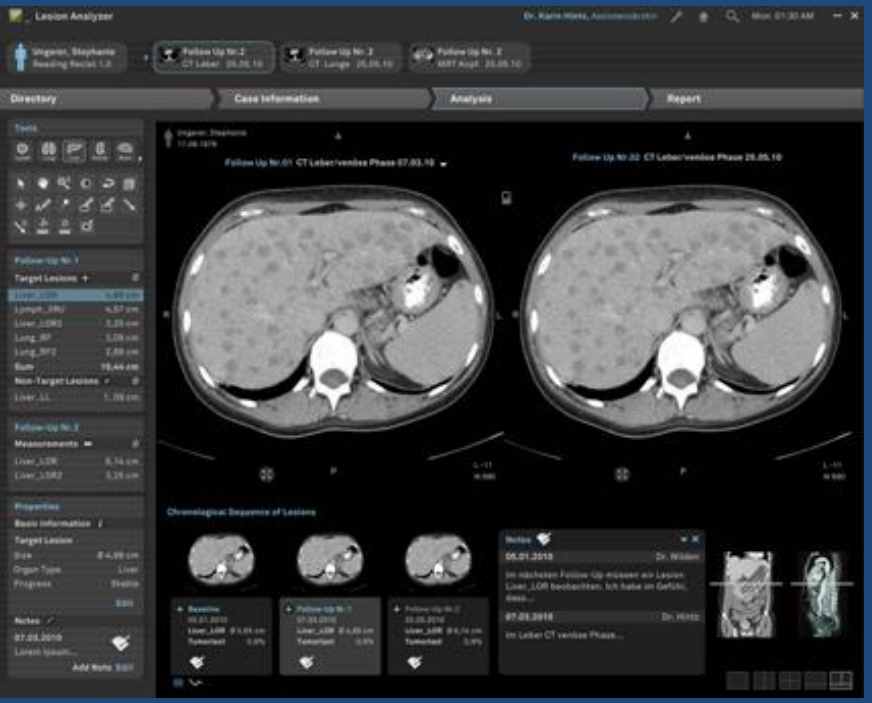
- An immense, increased responsibility for LE's to "get it right" the first time!

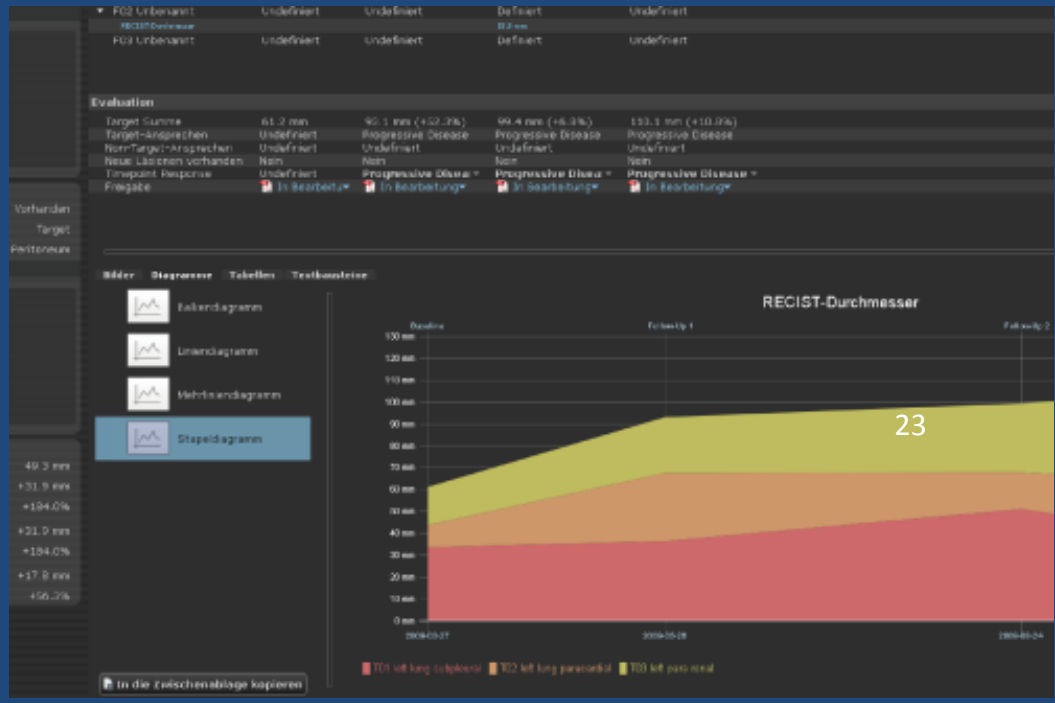
Future Goals for Local Radiology Sites

- Heighten radiology awareness of pending and active clinical trials
- Prospectively review and approve clinical trials
- Set appropriate budgeting and fees
- Streamline workflows
- Standardize procedures for imaging assessment and reporting, including performance metrics
- Improve collaboration and communication with clinical trial teams and PI's
  - Academic credit
- Requires time, effort, and support from local administrators and sponsors
- Enhanced technology
  - EDC
  - Research PACS

Future Goals: Enhanced Technology

- Electronic Data Capture
- Research PACS





Thank you!!

Local Evaluator and Secondary Reader Issues in Oncology Clinical Trials

Ira Smalberg, MD
Tower Imaging Medical Group
ismalberg@yahoo.com

6/27/14
PINTAD