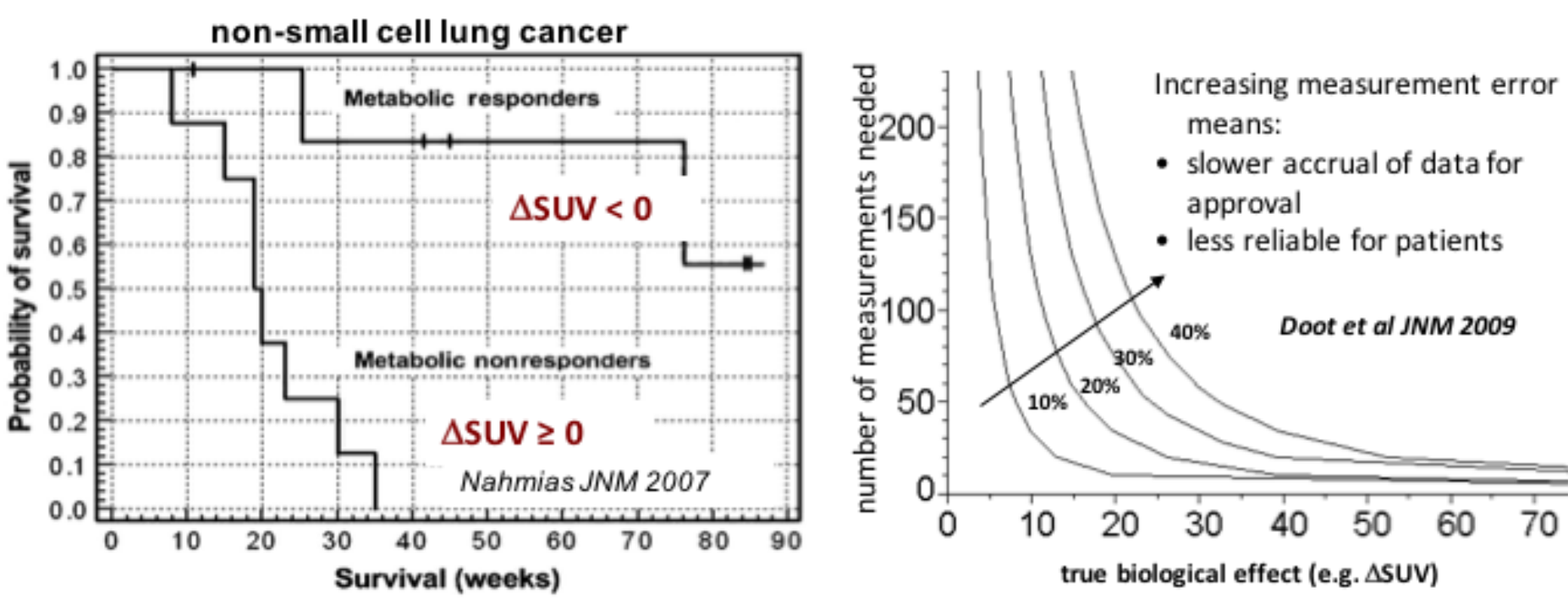# The QIBA FDG-PET/CT Biomarker Committee: An Overview and Status Update
Accelerating the development of new therapies and improving assessment of response
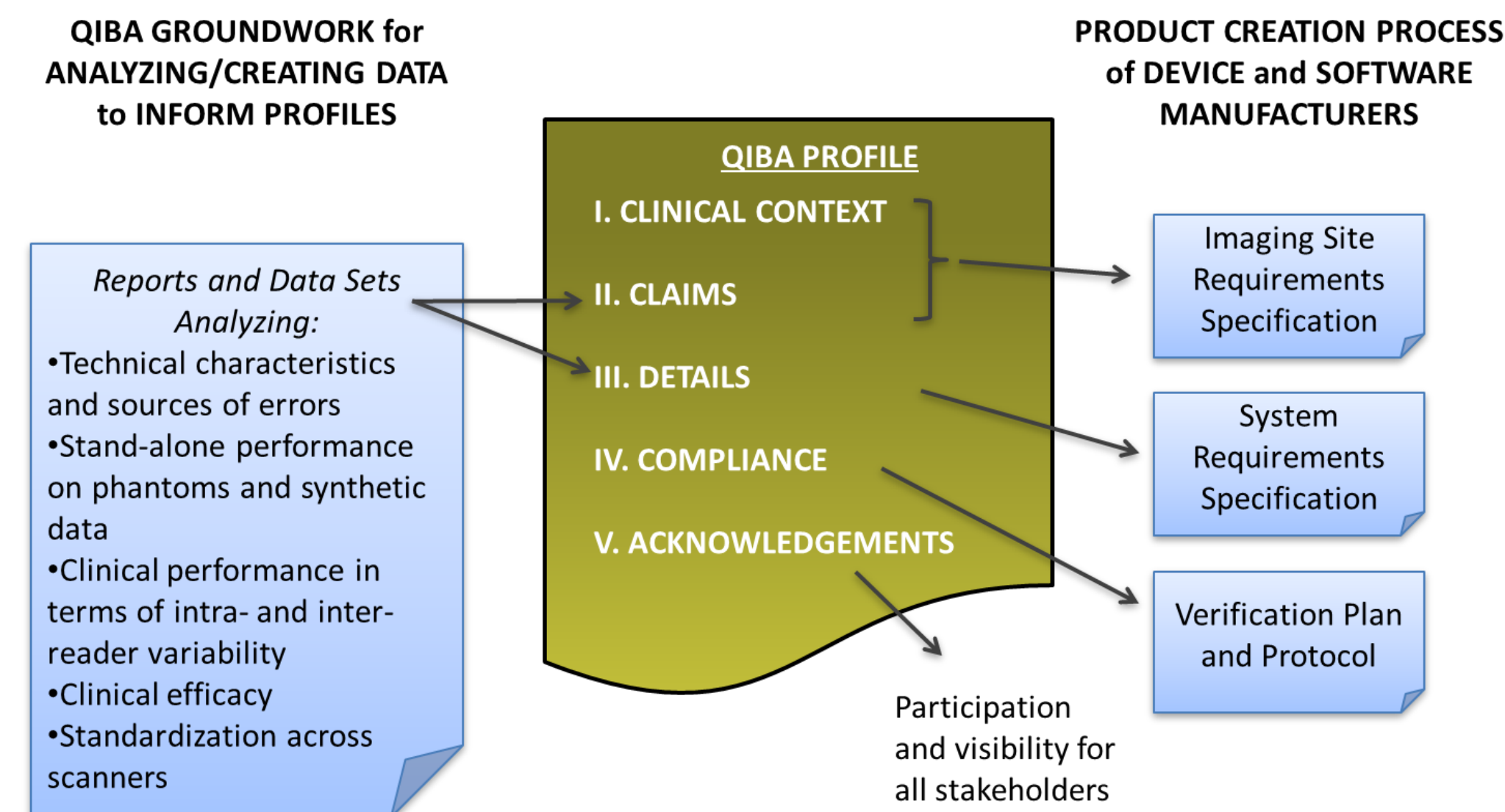
Quantitative Imaging Biomarkers Alliance RSNA

Quantitation – Why and How

Why Quantitation?
Precision Medicine with Imaging

- ❑ *Improve individual patient care*
  - Clinically proven detection and longitudinal quantitation for follow-up
  - Moves imaging from diagnostics and staging to therapy assessment
- ❑ *Accelerate adoption of new molecular diagnostics*
- ❑ *Make clinical trials of new therapies more effective*
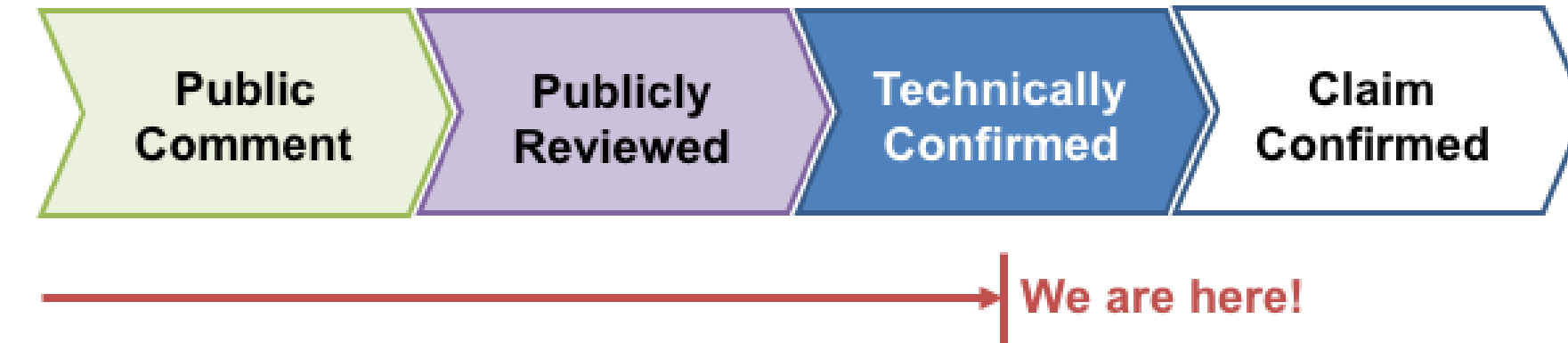- ❑ *All tied to quantitative accuracy*

non-small cell lung cancer

Metabolic responders
$\Delta SUV < 0$
Metabolic nonresponders
$\Delta SUV \geq 0$
Nahmias JNM 2007

Increasing measurement error means:
- slower accrual of data for approval
- less reliable for patients

Doot et al JNM 2009

QIBA Profiles:
Guidance for All Aspects of Quantitation

QIBA GROUNDWORK for ANALYZING/CREATING DATA to INFORM PROFILES

PRODUCT CREATION PROCESS of DEVICE and SOFTWARE MANUFACTURERS

Reports and Data Sets Analyzing:
- Technical characteristics and sources of errors
- Stand-alone performance on phantoms and synthetic data
- Clinical performance in terms of intra- and inter-reader variability
- Clinical efficacy
- Standardization across scanners

QIBA PROFILE
I. CLINICAL CONTEXT
II. CLAIMS
III. DETAILS
IV. COMPLIANCE
V. ACKNOWLEDGEMENTS

- Imaging Site Requirements Specification
- System Requirements Specification
- Verification Plan and Protocol

Participation and visibility for all stakeholders

Transition to a Technically Confirmed Profile

Profile Stages

Public Comment → Publicly Reviewed → Technically Confirmed → Claim Confirmed

We are here!
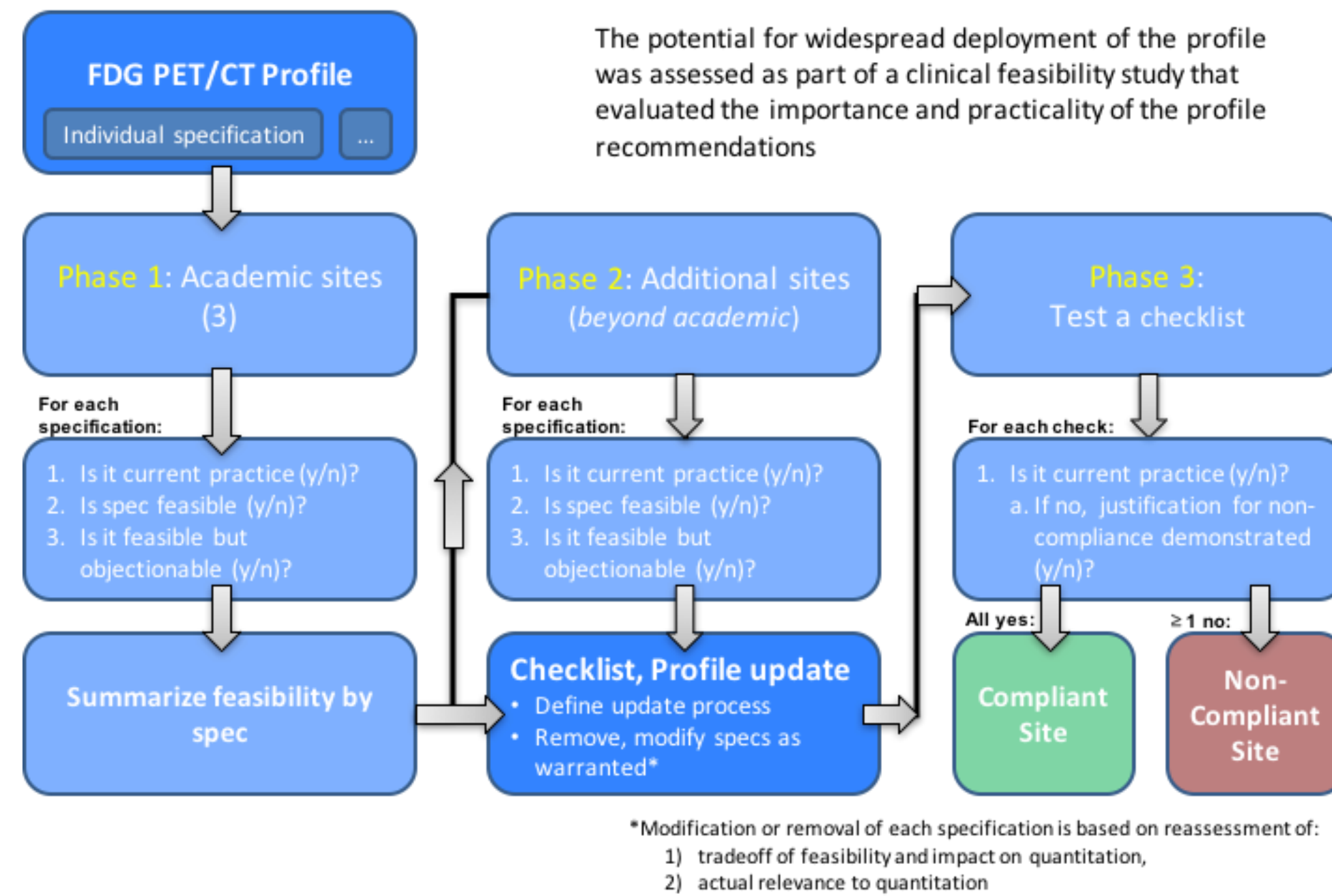
FDG-PET/CT Profile Claim: If Profile criteria are met, then tumor glycolytic activity as reflected by the maximum standardized uptake value (SUVmax) should be measurable from FDG-PET/CT with a within-subject coefficient of variation of 10-12%

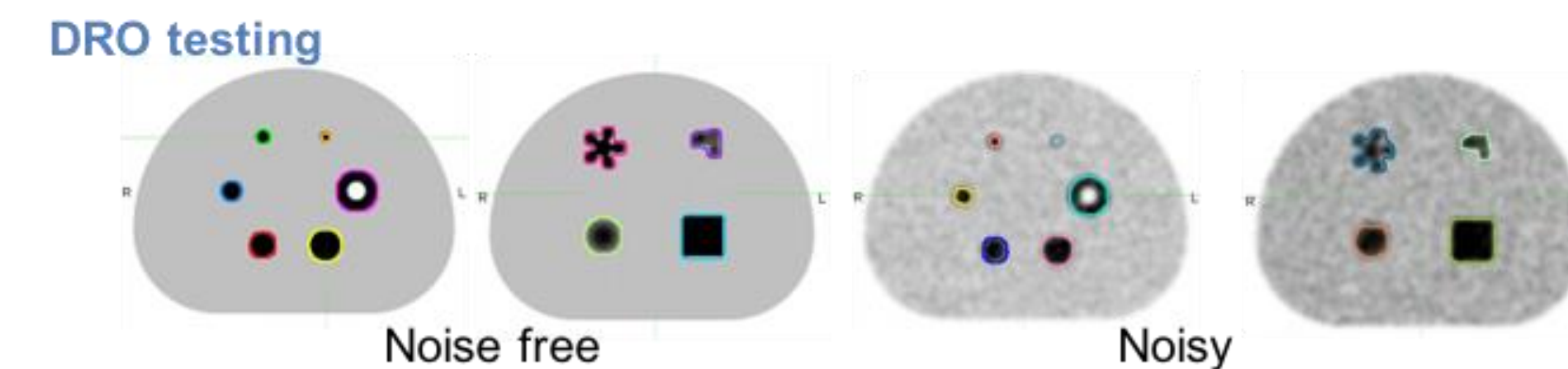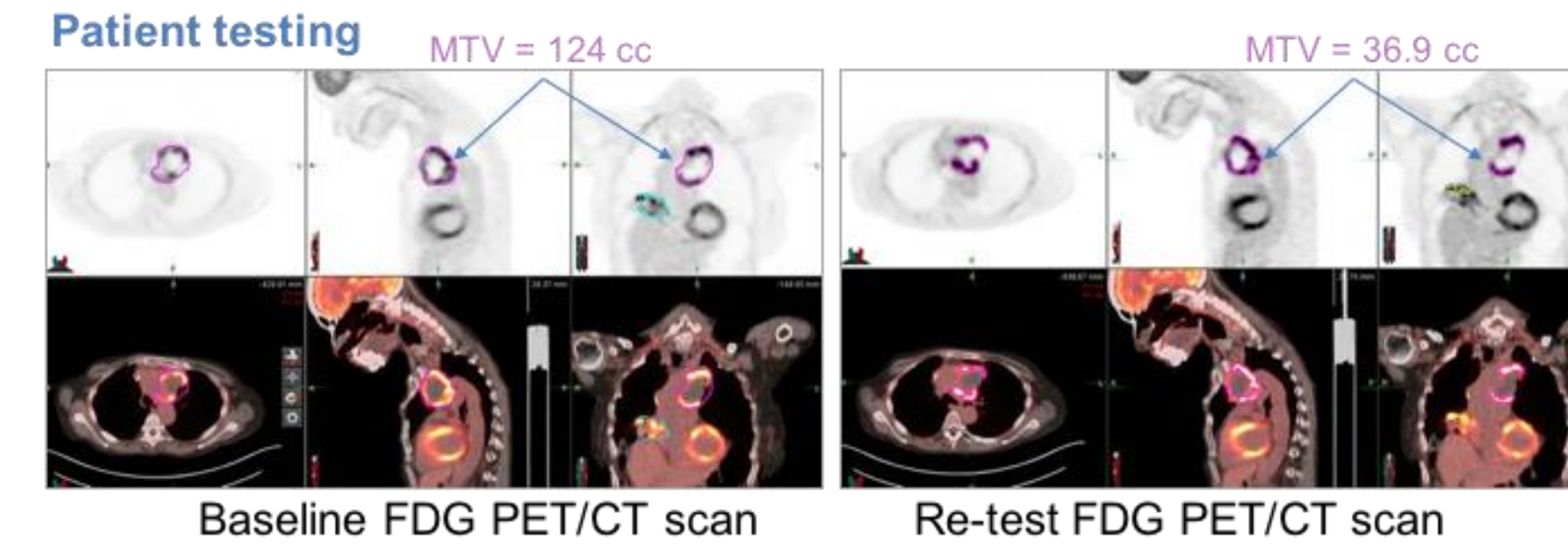| Stage	Description
Public Comment	The Profile describes key factors that affect the claim and has proposed recommended procedures that address the factors
Publicly Reviewed	Each issue raised during Public Comment is formally addressed
Technically Confirmed	Profile details have been implemented in more than one facility using a **Field Test** (described below) and each individual actors (systems and persons) successfully met the specifications
Claim Confirmed	Overall performance was determined and claim was achieved

FDG PET/CT Profile Field Test Groundwork Project

The potential for widespread deployment of the profile was assessed as part of a clinical feasibility study that evaluated the importance and practicality of the profile recommendations

FDG PET/CT Profile
Individual specification

Phase 1: Academic sites (3)

For each specification:
1. Is it current practice (y/n)?
2. Is spec feasible (y/n)?
3. Is it feasible but objectionable (y/n)?

Summarize feasibility by spec

Phase 2: Additional sites (*beyond academic*)

For each specification:
1. Is it current practice (y/n)?
2. Is spec feasible (y/n)?
3. Is it feasible but objectionable (y/n)?

Checklist, Profile update
- Define update process
- Remove, modify specs as warranted*

Phase 3: Test a checklist

For each check:
1. Is it current practice (y/n)?
   a. If no, justification for non-compliance demonstrated (y/n)?

All yes: Compliant Site
≥ 1 no: Non-Compliant Site

*Modification or removal of each specification is based on reassessment of:
1) tradeoff of feasibility and impact on quantitation,
2) actual relevance to quantitation
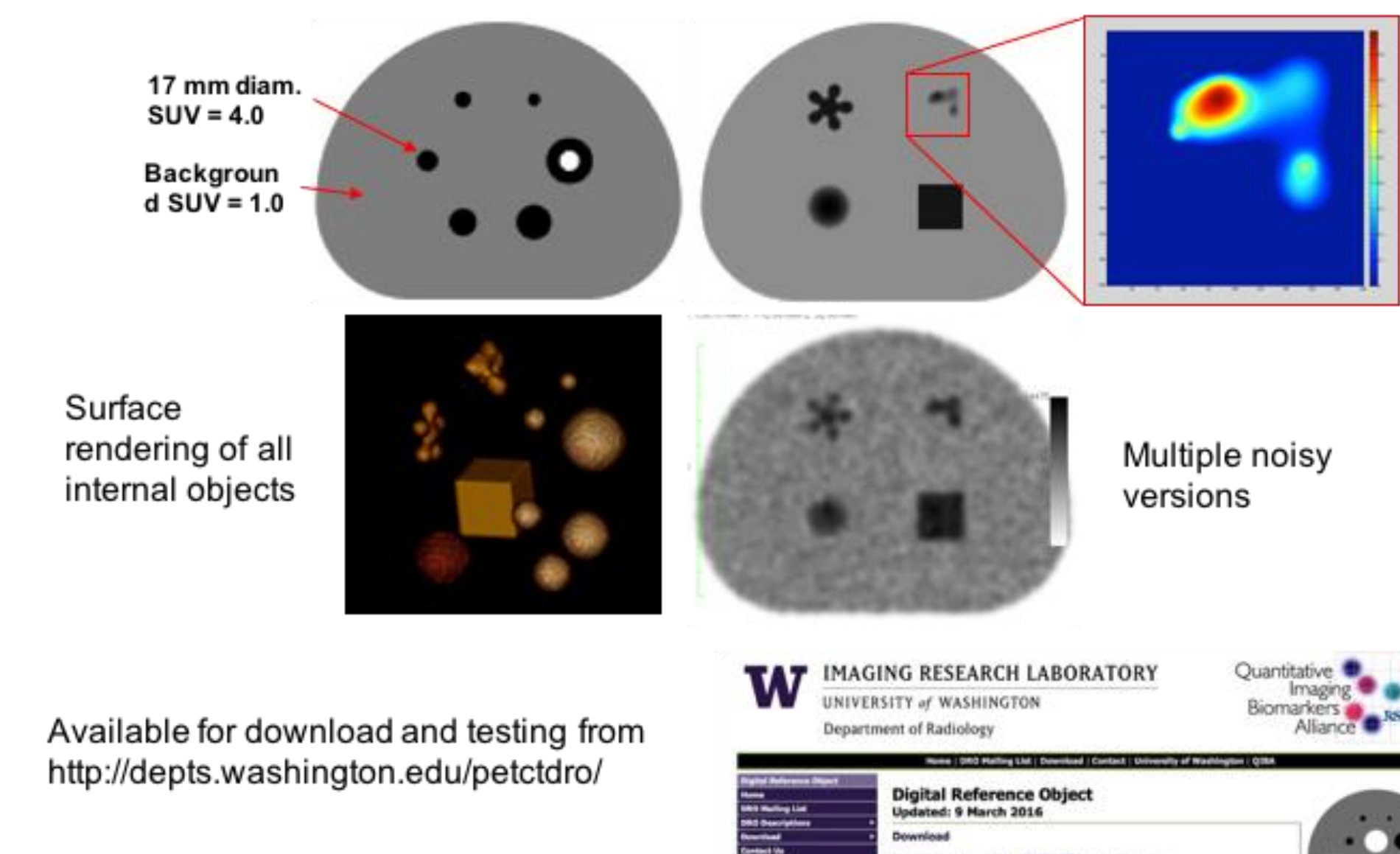

Other Recent and Current Groundwork Projects

Test-Retest Measurements of Metabolic Tumor Volume

Primary goal: establish the biologic repeatability of FDG PET metabolic tumor volume (MTV) and total lesion glycolysis (TLG) using the arm C data of ACRIN 6678 and MERCK data

Patient testing
MTV = 124 cc   MTV = 36.9 cc

Baseline FDG PET/CT scan   Re-test FDG PET/CT scan
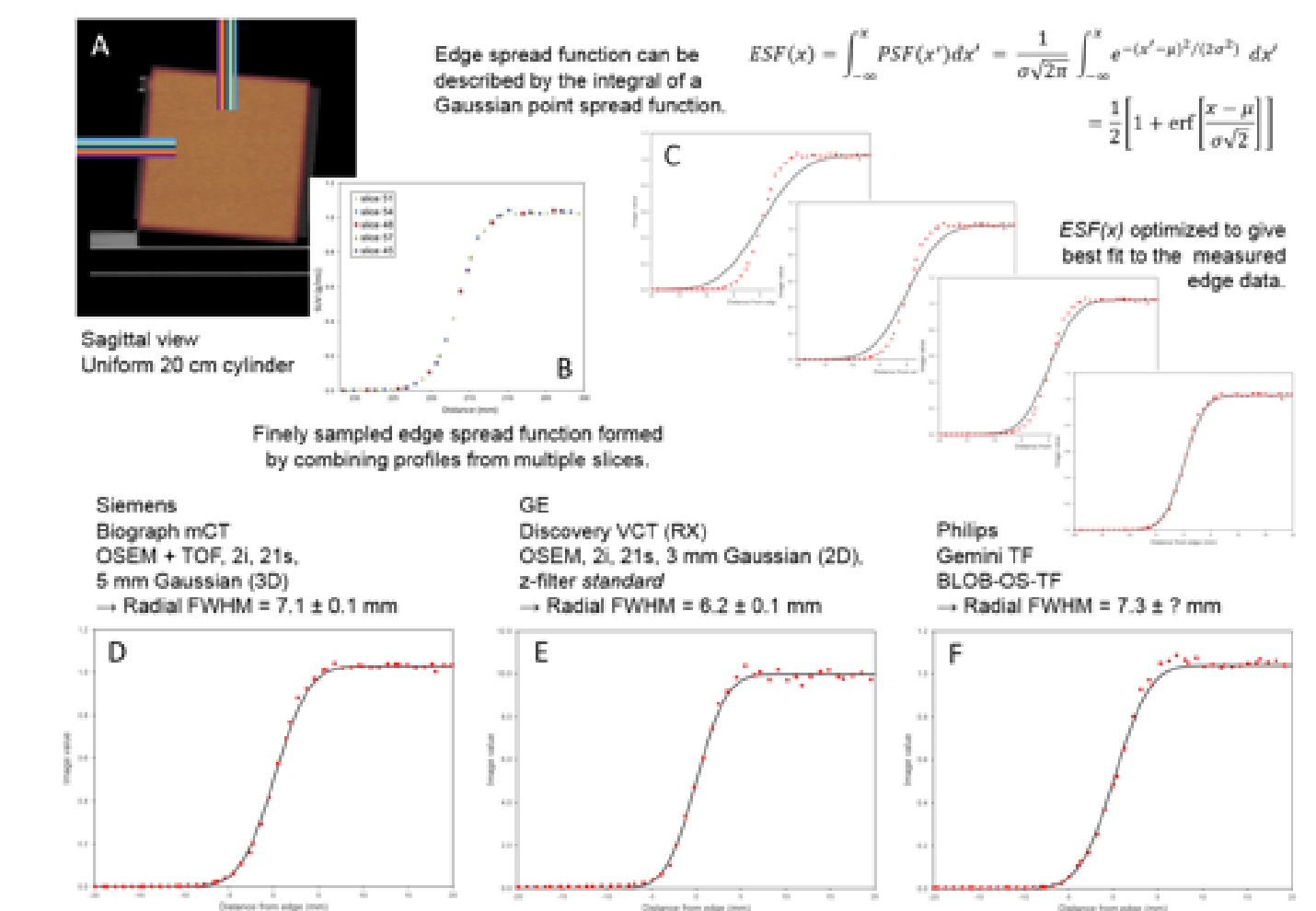
DRO testing

Noise free   Noisy

Metabolic Tumor Volume Digital Reference Object (DRO)

- A synthetic DICOM object for testing software computations of metabolic tumor volume
- Based on the NEMA NU-2 Image Quality phantom

17 mm diam.
SUV = 4.0
Background SUV = 1.0

Surface rendering of all internal objects

Multiple noisy versions

IMAGING RESEARCH LABORATORY
UNIVERSITY of WASHINGTON
Department of Radiology

Digital Reference Object
Updated: 9 March 2015

Available for download and testing from
http://depts.washington.edu/petctdro/

A Procedure to Facilitate Greater Standardization of PET Spatial Resolution

- Allows standardization of protocols across multiple sites and manufacturers
- Uses standard phantoms to measure the edge spread function (ESF), which can be converted to FWHM to characterize resolution and thus quantitation

Edge spread function can be described by the integral of a Gaussian point spread function.

$$ESF(x) = \int_{-\infty}^{x} PSF(x')dx' = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{x} e^{-(x'-\mu)^2/(2\sigma^2)} dx'$$

ESF(x) optimized to give best fit to the measured edge data.

Sagittal view
Biograph mCT
Uniform 20 cm cylinder

Finely sampled edge spread function formed by combining profiles from multiple slices.

Siemens
Biograph mCT
OSEM + TOF, 2i, 21s,
5 mm Gaussian (3D)
→ Radial FWHM = 7.1 ± 0.1 mm

GE
Discovery VCT (RX)
OSEM, 2i, 21s, 3 mm Gaussian (2D),
z-filter standard
→ Radial FWHM = 6.2 ± 0.1 mm

Philips
Gemini TF
BLOB-OS-TF
→ Radial FWHM = 7.3 ± ? mm

What We're Doing
and How You Can Participate

Specific accomplishments and plan

- ✓ Collection of recommendations for quantitative PET
- ✓ Presentation (joint with FNIH) to FDA for Biomarker Status
- ✓ NIBIB grant applications to fund operations
- ✓ Year 1 -4 research projects accomplished
- ✓ Year 5 research project funding- progress
- ✓ FDG-PET/CT Profile published and publically reviewed
- ✓ Collaboration with UPICT on Protocols
- ✓ Amyloid Writing Group established, Draft profile approaching completion
- ✓ PET Amyloid Profile Writing Group working for 2 years and became an Affiliate of Global Alzheimer's Association Interactive Network
- ✓ SPECT Profile Writing Group initiated
- ✓ Completed Phase II Profile testing of PET/CT FDG profile.
- ✓ Implementation of Profiles
- ✓ Clinical use of Profile

Organization Standing Activities

- ✓ QIBA Monthly Steering Committee meeting
- ✓ Profile telephone conferences: Alternating weekly for FDG profile, Amyloid profile, and SPECT profile writing groups
- ✓ Bi-annual QIBA meetings, and updates at RSNA
- ✓ Working visits with vendors
- ✓ Special task force meetings – as necessary
- ✓ Profile testing
- ✓ Profile Implementation (by QIBA and vendors)

For more information, visit
http://qibawiki.rsna.org