RSNA Radiological Society of North America

QIBA Ultrasound Biomarkers Meeting
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Basic Premise For RSNA

- **Extracting objective, quantitative results from imaging studies will improve the value of imaging in clinical practice.**

Why Must Imaging Become More Quantitative?

- ***Molecular medicine (personalized medicine)*** **requires quantitative test results.**
- ***Evidence-based medicine & QA Programs*** **depend on objective data.**
- ***Decision-support tools*** **(CADx, CDSS) need quantitative input.**

"Quantitative imaging …

- ***… is the extraction of quantifiable* features from medical images for the assessment of normal or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal."***

*** Imaging Metrology Workshop: April 3 – 4, 2012**

Biomarker

A characteristic that is objectively measured and evaluated as an indicator of normal biologic or pathogenic processes, or pharmacological responses to a therapeutic intervention.

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From the Metrology Workshop…

- Quantitative imaging biomarker (QIB): an imaging biomarker is quantitative if, when there is only a measurand (variable of interest) or when all factors used to obtain a value of the imaging biomarker other than the measurand are held constant, both 1) the difference between two values of the measurand is meaningful, and 2) there is a clear definition of zero such that the ratio of two values of the measurand is meaningful.
- That is, an imaging biomarker is a QIB if the measurand is a ratio variable as defined by Stevens (1946).

From the Metrology Workshop…

- For example: tumor volume is a QIB because if one tumor has a volume of 0.5 cm^3 and another tumor has a volume of 1.5 cm^3, the following statements have real meaning: 1) the larger tumor is 1.0 cm^3 bigger than the smaller tumor; and 2) the larger tumor is 3 times the size of the smaller tumor.
- For example: PET SUV is a QIB because all factors (i.e., injected dose, body weight, and time of measurement, t) other than the measurand (concentration of radioactivity) for obtaining its value can be held constant. If the SUV (concentration of radioactivity per 1kg body weight and 1 unit of injected dose) at time t is 5 MBq/kg for one tumor and the SUV at the same time t is 10 MBq/kg for another tumor, then the following statements have real meaning: 1) the second tumor has 5 MBq/kg more radioactivity than the first tumor and 2) the second tumor has 2 times as much radioactivity as the first tumor.

Biomarkers

- *"Biomarker is a 'substance', analyte, or otherwise a 'thing'*
  - *Assay methods are needed to measure the biomarker*
  - *Assay method is not the biomarker*
- *One biomarker can have multiple assays that are capable of measuring the biomarker"*

M. Walton, FDA/CDER

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Examples of Imaging Biomarkers

Biomarker	Test	Metric
COPD: Air-tissue ratio	CT scan densitometry	MLD (mean lung density)
Cancer: Tumor burden	CT scan volumetry; MR scan volumetry	Volume
Cancer: Glucose avidity	FDG-PET scan	SUV (standardized uptake value)
Cancer: Vascular permeability	DCE-MRI scan	K_{trans}; IAUC
Brain surgery risk: Proximity to eloquent cortex	fMRI scan brain-mapping	Center and magnitude of cortical activation

FDA Approval Vs. Qualification

Approval (or Clearance) is acknowledgement that, for the stated claim, the drug or device has been shown to have acceptable safety and effectiveness.

Qualification is acknowledgement that, within a stated context of use, the measurement can be relied upon to have a specific interpretation in drug development and regulatory decision-making.

Toward Quantitative Imaging

RSNA Report:

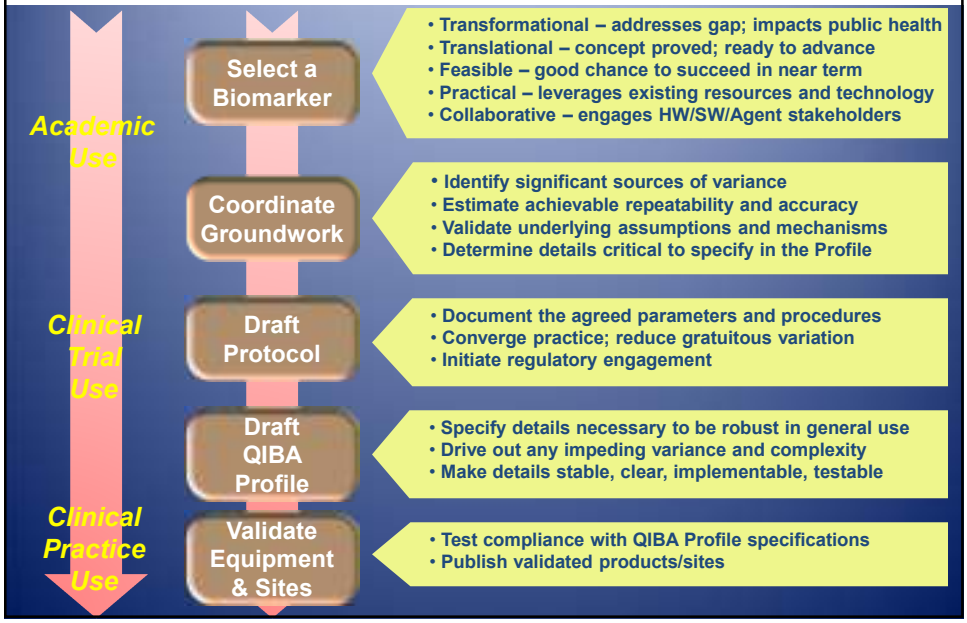
"There are substantial barriers to the widespread use of quantitative measures in clinical radiology – including:

- inherently large number of variables that impede validation of specific metrics,
- diversity of proprietary industry platforms, and
- lack of acceptance by radiologists

Quantitative Imaging Biomarkers Alliance (QIBA) Background

- First meeting: May, 2008
- Mission: Improve value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients, and time.
  - Build "measuring devices" rather than "imaging devices".
  - "Industrialize imaging biomarkers".

QIBA Process – "Industrializing Biomarker Use"



QIBA Goals

- **End goal: Increase use of quantitative imaging methods in clinical practice.**
  - Demonstrating clinical value invokes chicken-and-egg phenomenon: need quantitative tools before their value can be tested in clinical trials and practice.
  - Clinical value also may be dependent on existence of alternative therapies, which in turn may not be developed until there are useful biomarkers.
- **Intermediate goals:**

  1. Help standardize imaging biomarkers for use in clinical trials;

  2. Facilitate FDA-qualification of imaging biomarkers for use in drug development.

Current QIBA Structure

- Steering Committee
- 4 (?) Modality Committees
- 5 Technical Committees
  - Volumetric CT (oncology)
  - CT density (COPD)
  - FDG-PET (oncology)
  - DCE-MRI (oncology)
  - fMRI (seizure disorders)

QIBA Process

- Identify sources of measurement variability
- Collect “groundwork” data
- Write and disseminate “Profiles”.

QIBA Protocols & Profiles

- A Uniform Protocol for Imaging in Clinical Trials (UPICT) Protocol a consensus-derived description of a process to create medical images, and also the use of medical images and the associated underlying quantitative data by providing specifications for reconstruction, post-processing, analysis and interpretation.
- A Profile describes a specific performance Claim and how it can be achieved. It establishes a written standard procedure for obtaining an accurate and reproducible measurement that reflects an imaging biomarker of clinical interest.

QIBA *"Profile"*

A Profile is a document used to record the published data and collaborative work by QIBA participants. The Profile establishes a standard for each biomarker by setting out Claims and Details:

Claims: tell a user what can be accomplished by following the Profile.

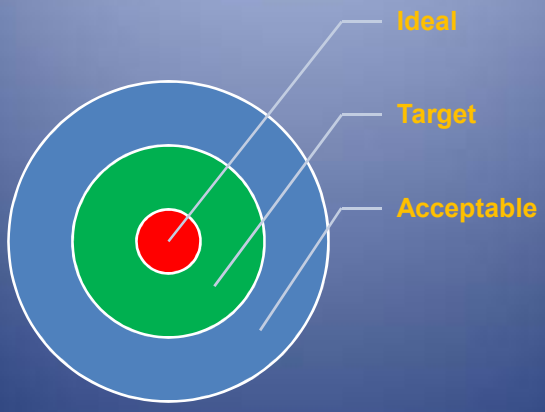
Details:

tell a vendor what must be implemented in their product before they can declare compliance with the Profile;

tell a user what procedures are necessary for the Claims to be achieved.

The process is intended to specify *what* to achieve, not *how* to achieve it.

Tiered Approach To Performance Thresholds Supports Installed Base of Scanners & Guides Future Development



Levels correspond to specifications for parameters that affect measurement variability (e.g., slice thickness, recon algorithm, etc.)

Processes for implementing and revising Profiles

- Public comment
- Field testing
- Compliance assessment
- Future modifications, especially as data from clinical trials and phantom studies come in.

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Thank you

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