QIBA Working Session

Wednesday, November 30, 2011

November 30, 2011 QIBA Session Plenary Session Agenda

3:00 PM Year in Review:

- Status of the Profiles — *Sullivan*
  Schwartz; Zahlmann; Kinahan
- QIBA visits to major device manufacturers — *Sullivan*
- QIBA activities relative to the FDA.
  - Qualification efforts and guidance feedback. — *Buckler*
  - What is QIBA's role in the qualification process? Steering Committee vs. Technical Committee involvement. — *Sullivan*
- Funded Phase I and Phase II QIBA projects: status report
  Zahlmann; Schwartz; Kinahan

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.*
- *It's a long-term process/goal – like "personalized medicine".*

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*
  - *Assay method performance characteristics are important"*

M. Walton, FDA/CDER

4

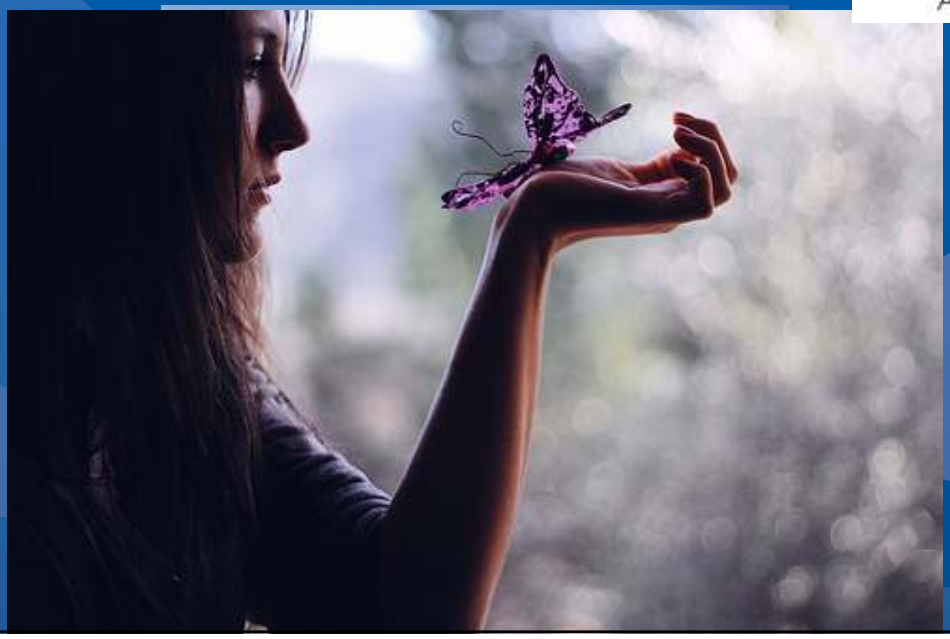
Examples of Imaging Biomarkers

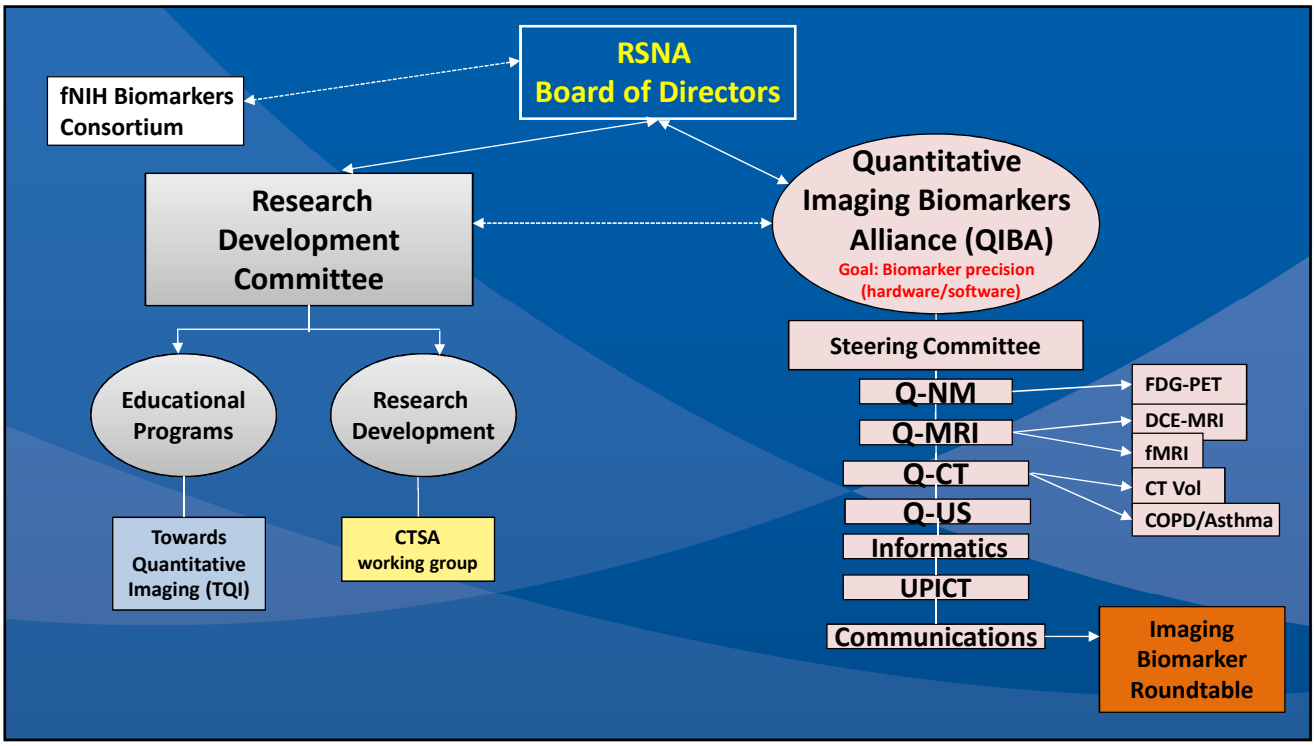
Biomarker	Test	Metric
COPD: Air-tissue ratio	CT scan densitometry	MLD (mean lung density)
Cancer: Tumor burden	CT scan volumetry; MR scan volumetry	Volume
Cancer: Glucose avidity	FDG-PET scan	SUV (standardized uptake value)
Cancer: Vascular permeability	DCE-MRI scan	K_{trans}; IAUC
Brain surgery risk: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

QIBA

- 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".

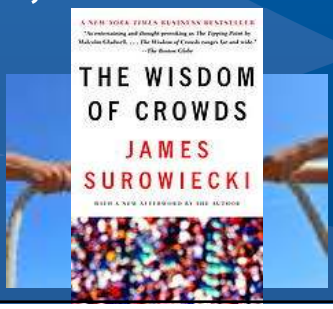
QIBA




RSNA
Board of Directors
fNIH Biomarkers Consortium
Research Development Committee
Quantitative Imaging Biomarkers Alliance (QIBA)
Goal: Biomarker precision (hardware/software)
Steering Committee
Educational Programs
Research Development
Towards Quantitative Imaging (TQI)
CTSA working group
Q-NM
Q-MRI
Q-CT
Q-US
Informatics
UPICT
Communications
FDG-PET
DCE-MRI
fMRI
CT Vol
COPD/Asthma
Imaging Biomarker Roundtable

Tensions

- Stakeholders have different goals, priorities, timelines.
- Different philosophies about desirable versus practical; Idealistic versus realistic.

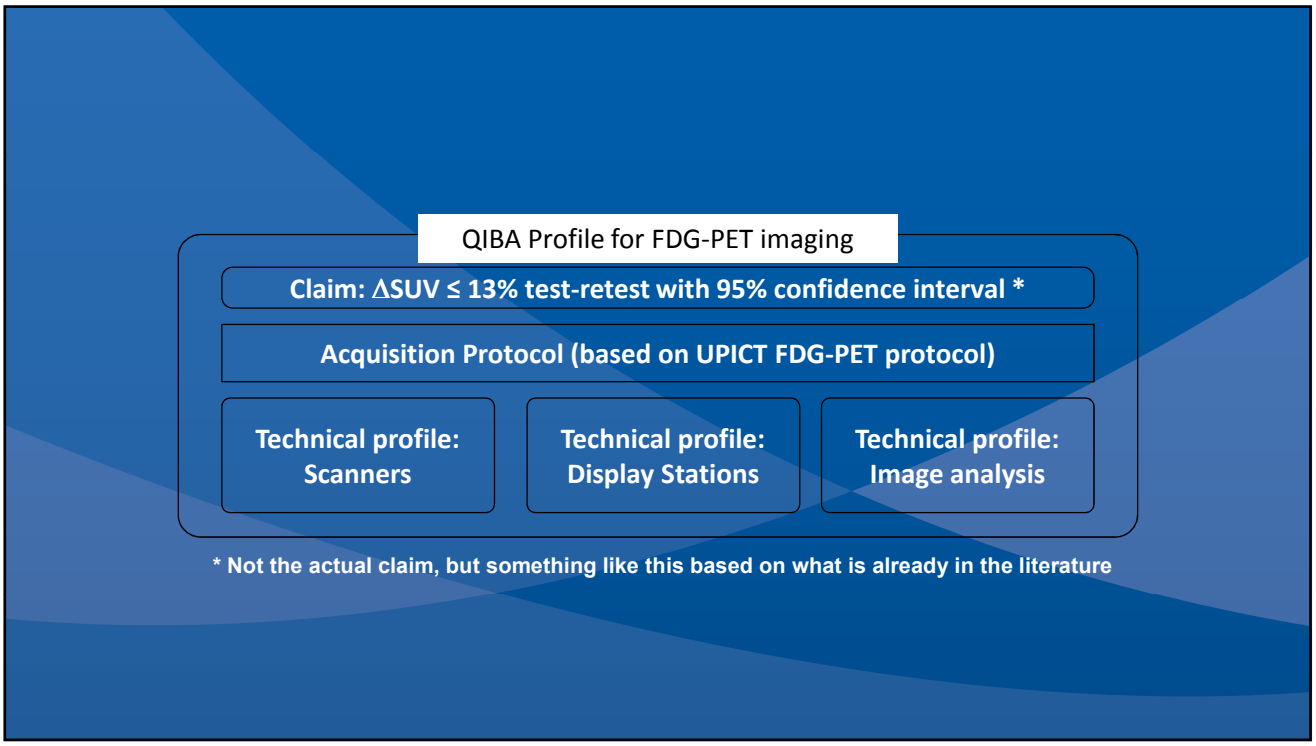


QIBA Protocols & Profiles

- 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.

Status of the Profiles

- CT Volumetry: L. Schwartz
- DCE-MRI: G. Zahlmann
- FDG-PET: P. Kinahan
- COPD/Asthma
- fMRI



QIBA visits to major device manufacturers

DATE	VENDOR	LOCATION	PARTICIPANTS
10/26/2010	General Electric CT NM MR	Milwaukee, WI	Bresolin Buckler Sullivan Kinahan McNitt-Gray Jackson (T) Gupta
02/23/2011	Philips MR	Cleveland, OH	Bresolin Buckler Miller Sullivan Jackson (T)
03/02/2011	Siemens NM	Knoxville, TN	Bresolin Buckler Sullivan Kinahan (T)
04/20/2011	Toshiba CT, NM, MR	Vernon Hills, IL	Bresolin Buckler Sullivan Jackson(T) McNitt-Gray(T) Kinahan (T) O'Donnell

QIBA activities relative to the FDA.

Qualification efforts and guidance feedback.
Buckler

What is QIBA's role in the qualification process? Steering Committee vs. Technical Committee involvement.

Sullivan

FDG-PET Biomarker Qualification Review Team (BQRT)

- Briefing document submitted Spring, 2011
- Meeting with FDA BQRT June 17, 2011
- Key issues in FDA response:
  - Prefer that we be more specific regarding variant of SUV being considered
  - Request systematic consideration of errors for lesion size, instrumentation factors, and calibration
  - Require RCT designs to establish degree to which SUV captures treatment effect; CALGB Lymphoma trial design is of this type, ACRIN 6678 is not an RCT

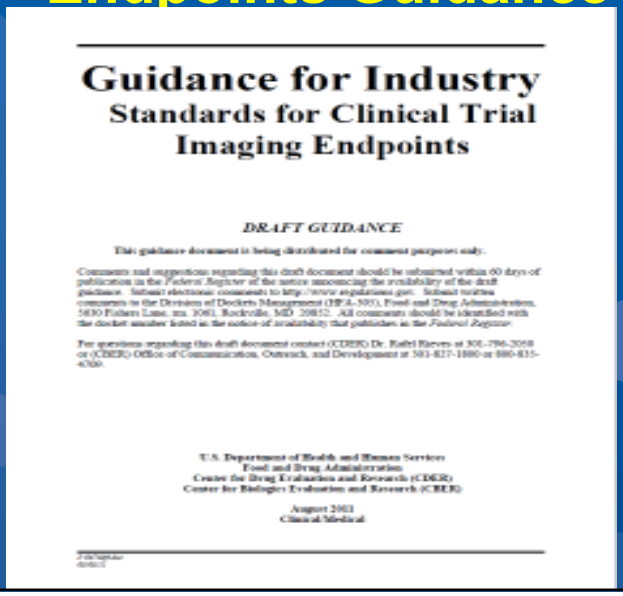
CT Volumetry Biomarker Qualification Review Team (BQRT)

- Briefing document submitted June, 2011
- Meeting with FDA BQRT Aug. 31, 2011
- Key issues in FDA response:
  - Prefer that we tie to clinical benefit (rather than compare to unidimensional assessments)
  - Prefer that context for use be more specific
  - Prefer that thresholds not be trial dependant
  - Encourage use in early phase trials

Biomarker Qualification Review Teams (BQRT)

- Current Status/Plans:
  - Template for the full data package that merges qualification guidance has been composed
  - Study reports for QIBA groundwork may be submitted as they are completed
  - Pharma company donations of trial data may enable retrospective re-analysis
  - Responses to FDA issues being considered to determine scale of effort going forward, including whether prospective RCTs will be needed and how limits of generalizability may be determined

QIBA Response to FDA Imaging Endpoints Guidance



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 Havers 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 2003
Clinical/Medical

QIBA Response to FDA Imaging Endpoints Guidance

- Comments were solicited from QIBA participants, collated, and submitted to FDA Oct. 15, 2011
- Matrix was developed to map QIBA Protocol/Profile issues to FDA guidance. Submitted to FDA with comments Oct. 15, 2011
- QIBA members communicated with Pharma Imaging Group on their response, and participated in the PIG "Limited Duration Key Issue Team"

QIBA activities relative to the FDA.

Qualification efforts and guidance feedback.

Buckler

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Sullivan

QIBA MR Projects

Title	Budget	PI
DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution	$60,347	E. Jackson, MDACC
Software Development for Analysis of QIBA DCE-MRI Phantom Data	$29,975	E. Ashton, VirtualScopics
Digital Reference Object for DCE-MRI analysis software verification	$57,763	D Barboriak, Duke Univ
Test-Retest Evaluation of Repeatability of Tumor K^{trans} Assessment in Human Subjects	$175,000	M. Rosen, ACRIN
Quantitative measures of fMRI reproducibility for pre-surgical planning	$33,423	J. Voyvodic, Duke Univ
Quantitative measures of fMRI reproducibility for pre-surgical planning	$19,411	E. DeYoe, Medical College of Wisc
Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility	$29,376	J. Pillai, Hopkins
Total: (NIBIB: HHSN268201000050C)	$405,295	

QIBA CT Projects

Title	Budget	PI
Inter-scanner/inter-clinic comparison of reader nodule sizing in CT imaging of a phantom	$25,000	C. Fenimore, NIST M. McNitt-Gray, UCLA D. Clunie, CoreLab Partners
Assessing Measurement Variability of Lung Lesions in Patient Data Sets	$40,420	M. McNitt-Gray, UCLA D. Clunie, CoreLab Partners
Validation of volumetric CT as biomarker for predicting patient survival	$108,366	B. Zhao, Columbia NY
Development of assessment and predictive metrics for quantitative imaging in chest CT	$75,000	B. Chen, E. Samei, Duke Univ
Comparative Study of Algorithms for the Measurement of the Volume of Lung Lesions: Assessing the Effects of Software Algorithms on Measurement Variability	$35,500	G. Kim, UCLA
Quantifying variability in measurement of pulmonary nodule (solid, part-solid and ground glass) volume, longest diameter and CT attenuation resulting from differences in reconstruction thickness, reconstruction plane, and reconstruction algorithm.	$42,070	K. Garg, D. Miller, A. Scherzinger, U of Colorado, Denver
Impact of Dose Saving Protocols on Quantitative CT Biomarkers of COPD and Asthma	$49,754	S. Fain, Wisconsin
Total: (NIBIB: HHSN268201000050C)	$392,734	

QIBA PET Projects

Title	Budget	PI
Meta-analysis to analyze the robustness of FDG SUV changes as a response marker, post and during systemic and multimodality therapy, for various types of solid extracerebral tumors.	$73,000	O. Hoekstra, University of the Netherlands
QIBA FDG-PET/CT Digital Reference Object Project	$68,240	P. Kinahan, U Washington
Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes	$57,500	R. Wahl, Johns Hopkins
Personnel Support for FDG-PET Profile Completion	$16,000	E. Perlman, PAG
Evaluation of the Variability in Determination of Quantitative PET Parameters of Treatment Response Across Performance Sites and Readers	$55,000 $45,000	R. Wahl, Hopkins Analysis sites
Evaluation of FDG-PET SUV Covariates, Metrics and Response Criteria	$34,000	J. Yap, Dana Farber
Integration of Retrospective Reviews of 2-3 Groupings of Clinical Trial Datasets (This includes the current Hoekstra proposal) Will utilize the PERCIST analysis	$50,000	O. Hoekstra, Netherlands
Total: (NIBIB: HHSN268201000050C)	$398,740	

November 30, 2011 QIBA Session Plenary Session Agenda

- 3:35 PM Going Forward:
  - Updates on Profiles vs. protocols — *Sullivan*
  - Processes for implementing and revising Profiles — *O'Donnell*
    - Public comment
    - Field testing
    - Compliance assessment
    - Future modifications, especially as data from clinical trials and phantom studies come in.
  - QI Task Force report — *Miller*
    - Future QI biomarkers for development. — *Sullivan*
      - Possibility of DW-MR
      - Possibility of a QIBA effort in ultrasound
    - Succession planning.

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.

Additional Activities

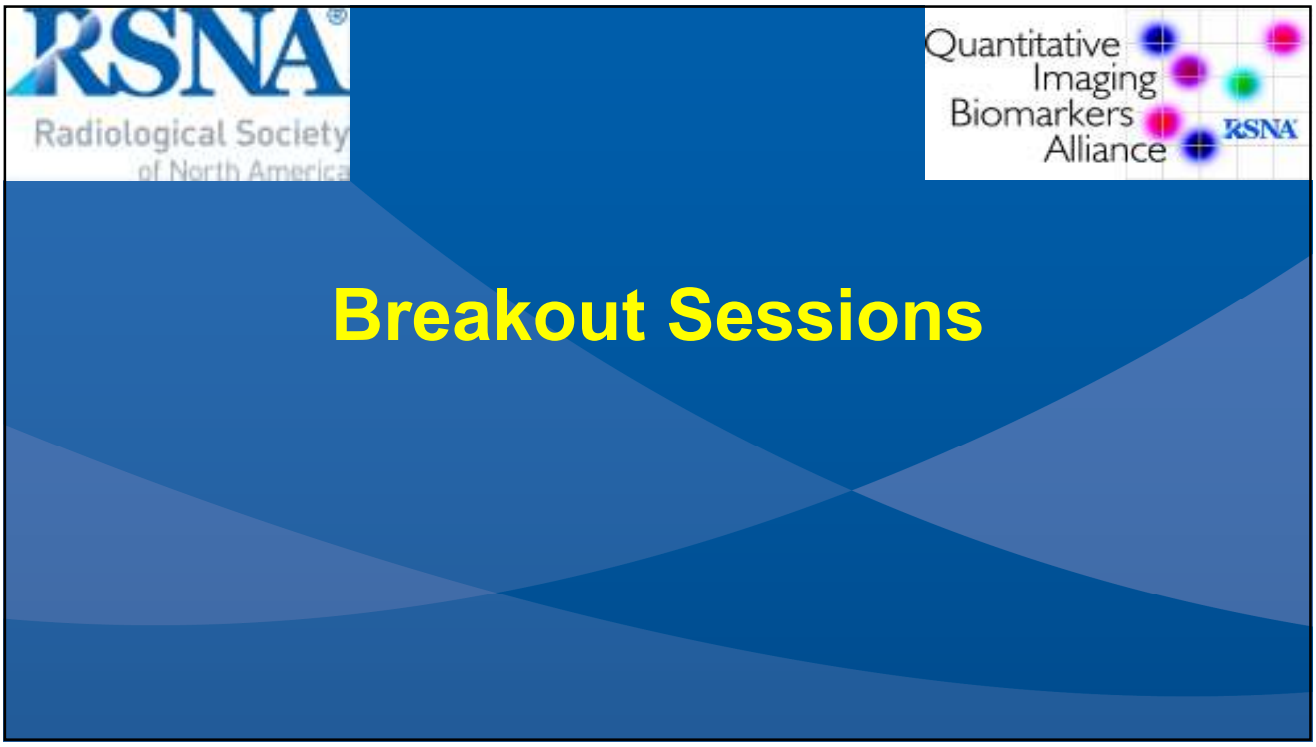
- Informatics task force: K. Andriole, Chair
- Metrology Workshop: N. Obuchowski, D. Raunig, L. Kessler, Co-Chairs. A. Dima, C. Gatsonis, M. Kondratovich, K. Myers, A. Reeves, Planning committee members
  - Agenda topics: 1. Statistical terms; 2. Technical performance of an imaging assay; 3. Algorithm comparison.

QI Task Force report

- Empaneled by RSNA BOD in Dec. 2010, to evaluate current RSNA programs in quantitative imaging and imaging biomarkers, and make recommendations to the BOD about program priorities, future directions, governance structures, and models for sustainability.
- 18 members representing academia, governmental agencies, private practice, and industry—pharmaceutical, equipment manufacturers and software.
- Monthly conference calls and one day-long, in-person meeting in May, 2011.
- Strongly endorsed the importance of quantitative imaging and imaging biomarkers to the future of radiology, as well as on-going RSNA support of the programs, particularly QIBA.

QI Task Force report

- Suggested some simplification of the program structures, including "mainstreaming" of Toward Quantitative Imaging and the CTSA Imaging Working Group, and co-scheduling the Imaging Biomarkers Roundtable with other meetings.
- Recommended pursuit of strategies to accelerate the development of new profiles and protocols.
- Recommended prioritization of biomarkers that have immediate applications to clinical practice in addition to drug development and validation.
- Stressed the need for attention to leadership sustainability and succession planning to ensure the continued viability of the programs.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of North America
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Breakout Sessions