Quantitative Imaging Biomarker Alliance

WHY QIBA: *CT SPECIFICS*

Corporation Visit

Autumn 2010

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Program Director, QIBA

PRINCIPAL LOGISTICAL AND FINANCIAL SUPPORT PROVIDED BY RSNA

Our Team

See speaker notes for full list of individual names

ActiViews Inc.
Amgen
AstraZeneca
Beth Israel Deaconess Medical Center
BioClinica, Inc.
Biomedical Systems
Boston Medical Center
Breast Health Management, Inc
Brigham and Women's Hospital
Bristol-Myers Squibb
Buckler Biomedical LLC
CCS Associates, Inc.
Columbia University
Definiens
Duke University
FDA
GE Healthcare
Glenfield Hospital, UK
Harvard Medical School
Haukeland Univ Hospital
Henry Ford Health System
Imagepace
Intio, Inc.
Iowa Comprehensive Lung Imaging Center
Johns Hopkins University
Kitware, Inc.
Leiden Univ Med Ctr
Lung Cancer Alliance
Mallinckrodt Institute of Radiology
Massachusetts General Hospital
MD Anderson Cancer Center
Median Technologies
Merck
Merge Healthcare
Millennium Pharmaceuticals
MITA (NEMA)
Mount Sinai Hospital
MSKCC
National Jewish Health
NCI NIH Cancer Imaging Program
NIST
Perceptive Informatics, Inc.
Philips Healthcare
RadPharm
Roswell Park Cancer Institute
Rush University Medical Center
Siemens
Stanford University
TeraRecon, Inc.
The Phantom Laboratory, Inc.
Toshiba
University Medical Imaging
University of Alabama at Birmingham
University of British Columbia
University of California, Davis
University of California, Los Angeles
University of Chicago
University of Colorado, Denver
University of Illinois at Chicago (UIC)
University of Iowa
University of Maryland
University of Pennsylvania
University of Pisa
University of Utah
University of Virginia Health System
University of Wisconsin-Madison
VIDA Diagnostics, Inc.
Weill Cornell Medical College

CT has Enjoyed a Proud History of Innovation

1972: Prototype CT
Several hrs per slice acquisition; days for reconstruction

1974: 1st Generation CT
2.5 min/slice

1976: Whole-body CT
5 sec/slice

1989: Helical/Spiral CT
0.3 sec/slice; 40 sec for entire chest (40cm Z-axis)

1998: 4-row MDCT
10 sec for entire chest

2002: 16-row MDCT
8 sec for entire chest

2004: 64-row MDCT
5 sec for entire chest

In a poll of 225 top general internists, CT and MRI were judged to be the most important medical advances in the last 50 years, beating out life-saving therapies such as coronary angioplasty and ACE inhibitors.

Fuchs VR, Sox HC Jr. *Physicians' views of the relative importance of thirty medical innovations*. Health Aff, 2001. 20(5): p. 30-42.

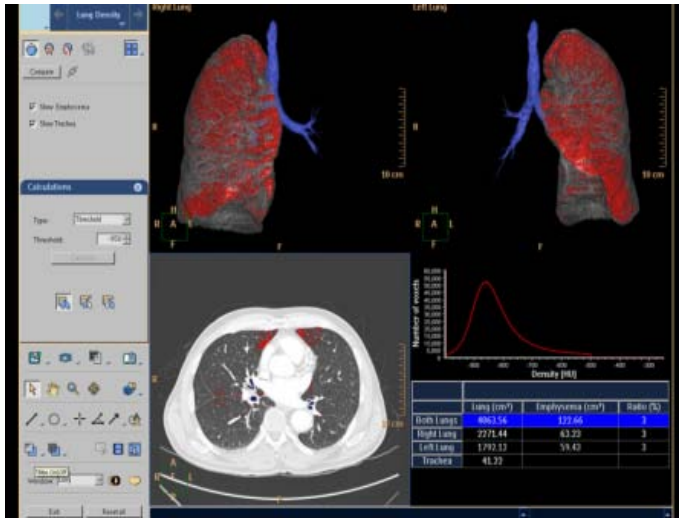
Technology Innovation Continues. Since 2004,

- Spatial Resolution up to 2x higher
- Temporal Resolution over 2x faster
- Artifacts up to 80% less
- Image noise up to 50% less
- Many methods developed for radiation dose reduction
- Multi-energy and spectral CT

Matthew Cham, M.D.
Assistant Professor of Radiology and Medicine, Weill Cornell Medical Center

What's next? Quantitative CT to Measure Disease More Precisely

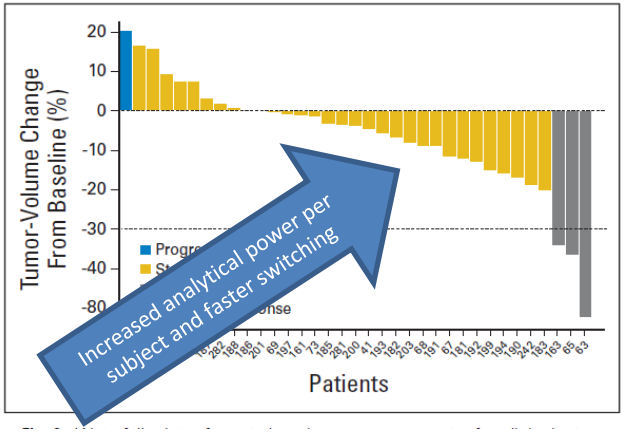
- Technical advances help us move from "qualitative image" to "quantitative image" or measurement
- Measures draw into the clinic as quantitative applications to optimize and personalize patient management
- Examples:
  - longitudinal quantitation of volumetric tumor burden in cancer
  - lung densitometry and airway thickness measurements in chronic obstructive pulmonary disease.



Quantification Increases the Utility and Value of Imaging

Make clinical trials more effective:

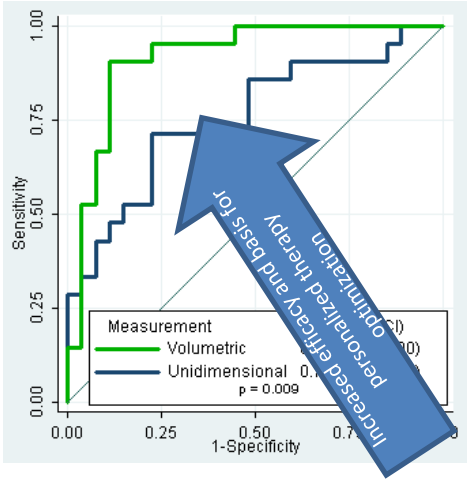
- **Faster** (Window trials—quantitative endpoint); **Cheaper** (Adaptive Bayesian Design, two to three weeks of drug exposure); **Better** (Phantom calibration, standardize method, open source reference tools, defined molecular targets, tailored delivery systems)
- **Tighter** (variance), **lighter** (dose), **standardized** (protocol/profile)



Altorki et al., J Clin Oncol 2010; 28:3131-3137.

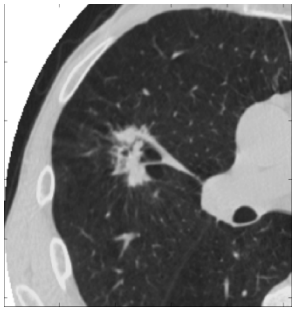
Make care more personalized to patient:

- **Clinically proven** detection and longitudinal quantification for follow-up
- Quantitative CT measures incorporated into **adaptive therapy**
- Moves imaging from diagnostics and staging to **therapy monitoring**

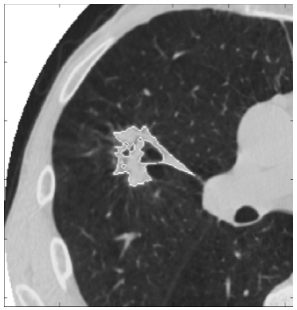


Zhao B, et al. Clin Cancer Res 2010;16:4493 -95

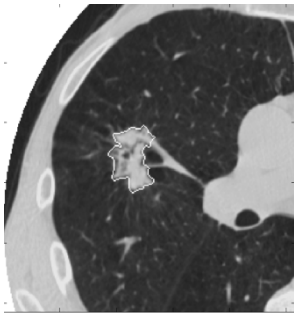
Technical as well as Business Obstacles Impede Realization of the Opportunity



lesion



Reader 1 contour (includes sliver)



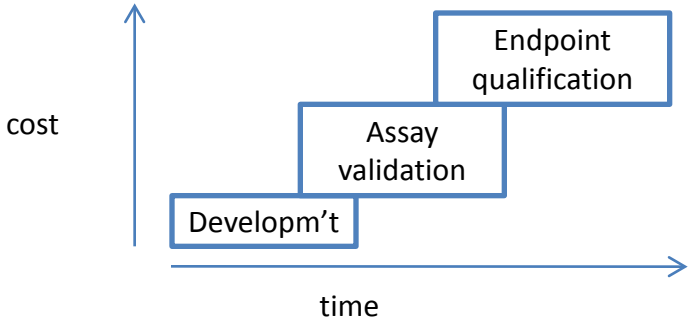
Reader 2 contour (excludes sliver)

- Human perception and machine interface limitation. *Example: even with exquisite images, still uncertainty about what is and isn't part of a lesion with uncertainty in measurements, even with experts.*
- Reference image database with annotations required:
  - Phantom data
  - Clinical studies / trials
  - First users (domain expert)
- Variation across scanner makes and models:
  - DICOM and other standards
  - Different image data quality
  - Different interfaces
  - Different image data acquisition filters
  - Different data representation algorithms and hardware

Efforts by individual manufacturers to qualify quantitative imaging applications:

- *Are more costly, and*
- *Run over longer time periods…*

…than the business model of device and software manufacturers generally support.



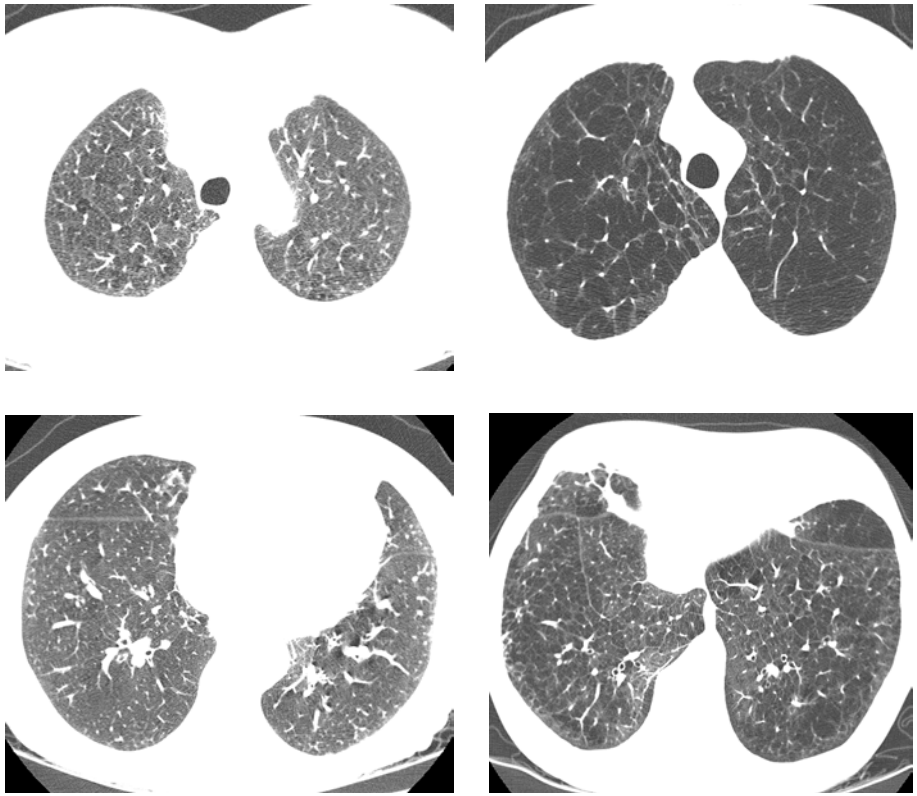
These issues are exacerbated by lack of clarity in regulatory and reimbursement policy which increase the risk while decreasing the incentive

Even when individual companies do these steps, community need for standards required to address multi-vendor reproducibility are not accounted for.

Example Drill Down: COPD is Not One Disease, QCT can be Better than FEV

Two Patients, Similar Obstruction

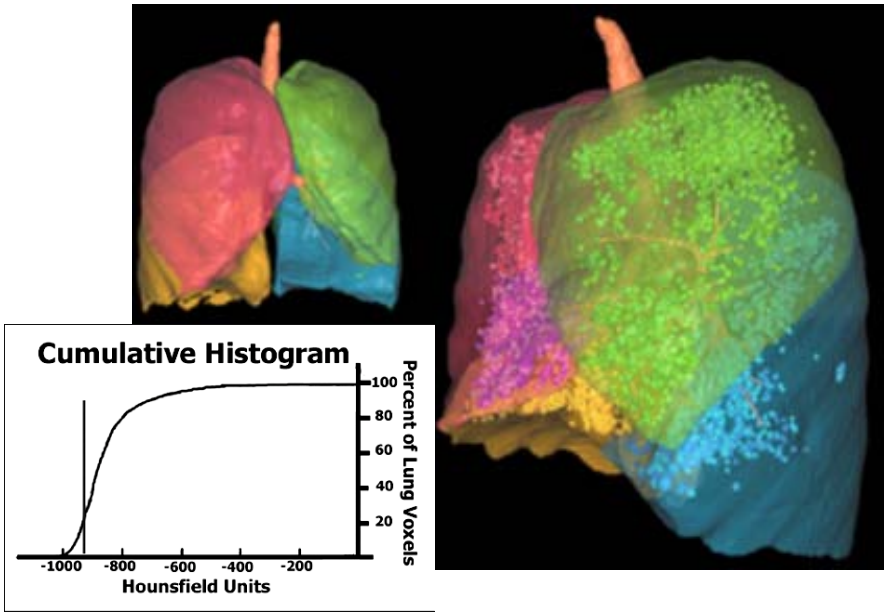
FEV_1 62% predicted **FEV_1 58% predicted**

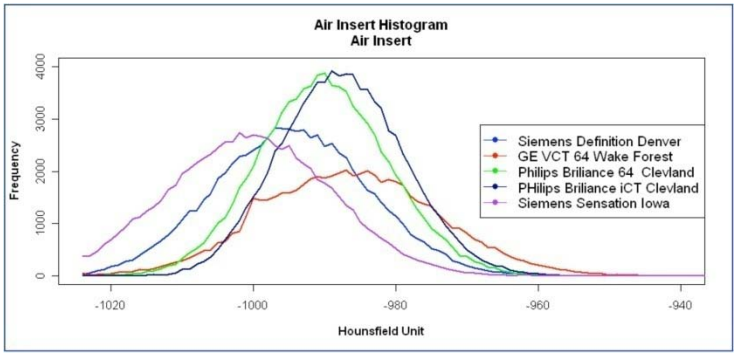


QCT provides sub-phenotypes and facilitates regional analysis

- QCT of emphysema correlates with physiologic evaluation and with histologic evidence of emphysema (Basis: CT Density)
- QCT of air trapping correlates with physiologic evidence of airway obstruction (Basis: CT Density)
- QCT of airway wall thickness correlates with histologic evidence of small airways disease (Basis: CT Spatial Resolution)

Quantitative CT Biomarkers of Emphysema and Air Trapping





MDCT Scanners:

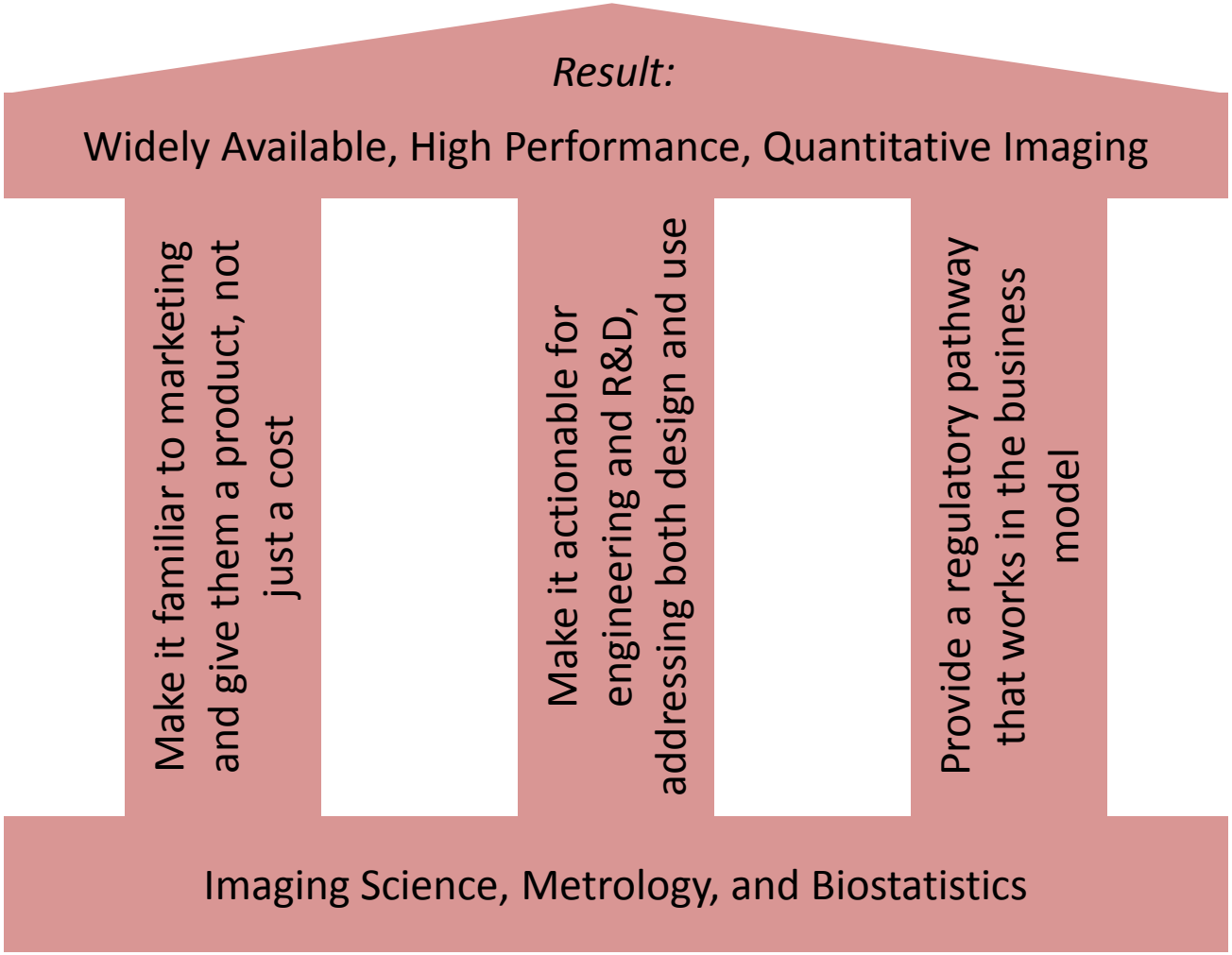
- **Almost global availability.**
- **NIH and industry-based multicenter studies are making use of lung density measures to assess presence, distribution and progression of emphysema and peripheral airways closure.**

However, HU values for air in the trachea and phantoms demonstrate considerable variability between scanner models and manufacturers

What we need to meet the opportunity

- Standardized imaging protocols harmonizing noise as well as spatial and density resolution between scanners.
- Phantoms which stress the quantitative nature of the scanners similarly to in vivo imaging.
- Manufacturer cooperation to standardize lung density measures across scanner models and to assure repeatability of the measures across time.

QIBA Addresses the Obstacles, Enabling Profitable New Products



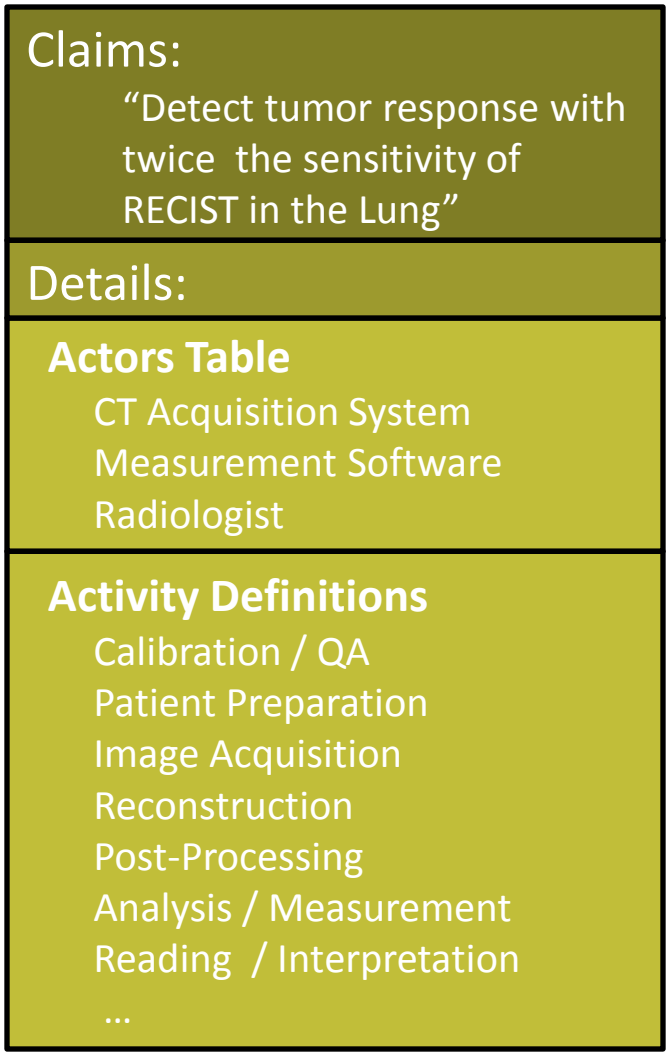
QIBA Profile Content

User Perspective

Will it do what I need?

What/who do I need to get started?

What do I have to do (procedures, training, performance targets) to achieve the Claims?



Vendor View

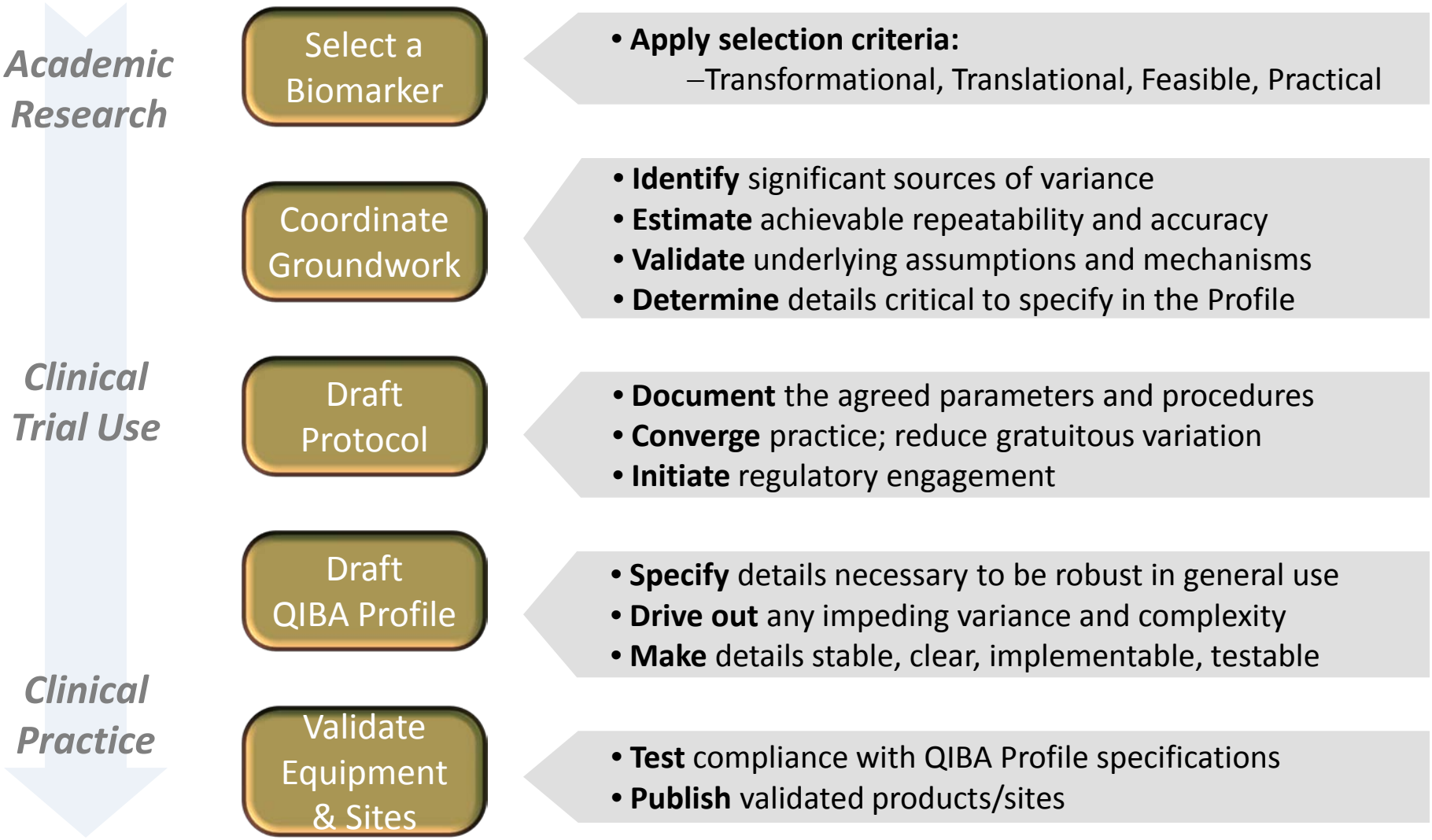
Why do you want me to do this?

Which of my products are affected?

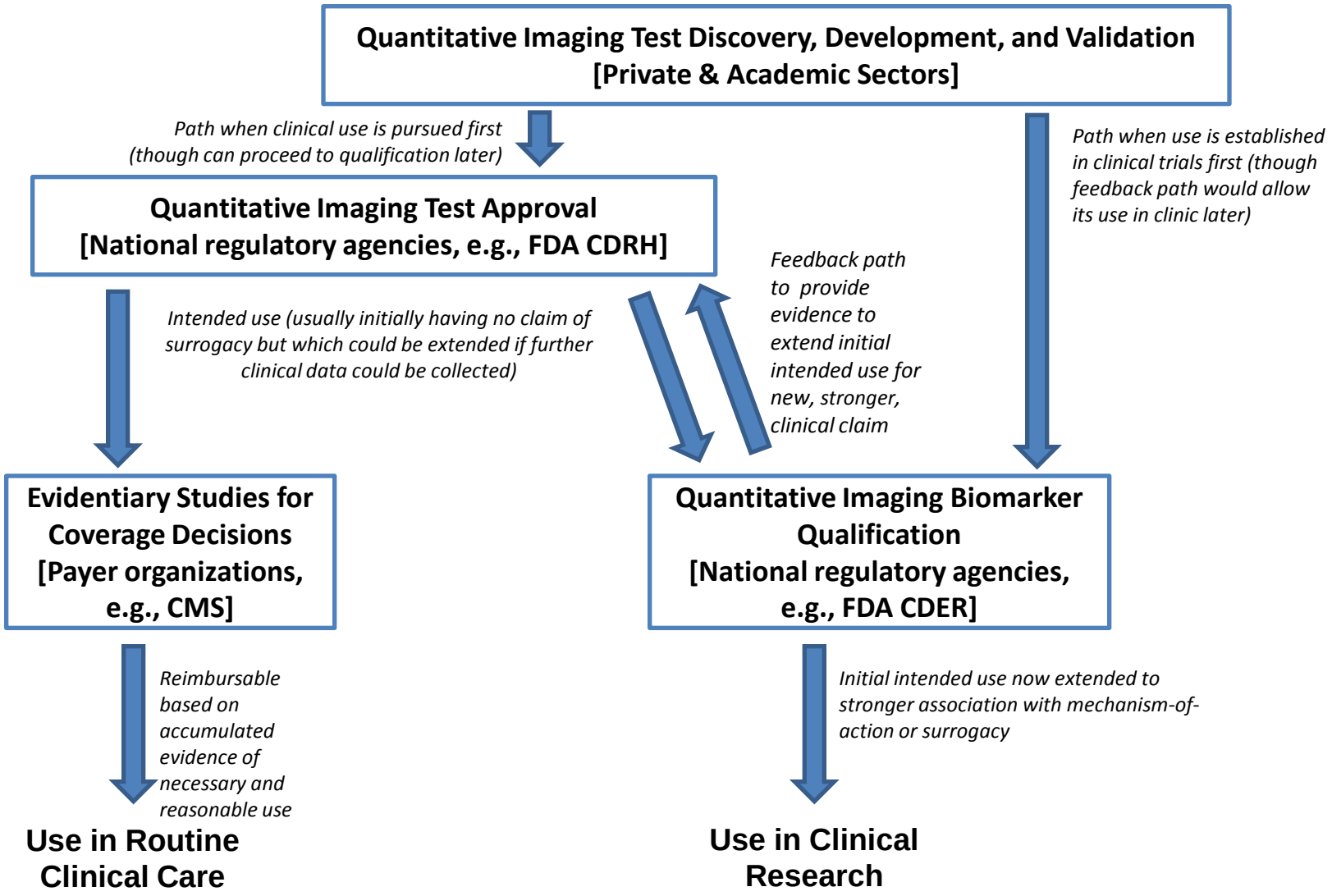
What do I have to implement; (features, capabilities, performance targets)

How will I be tested?

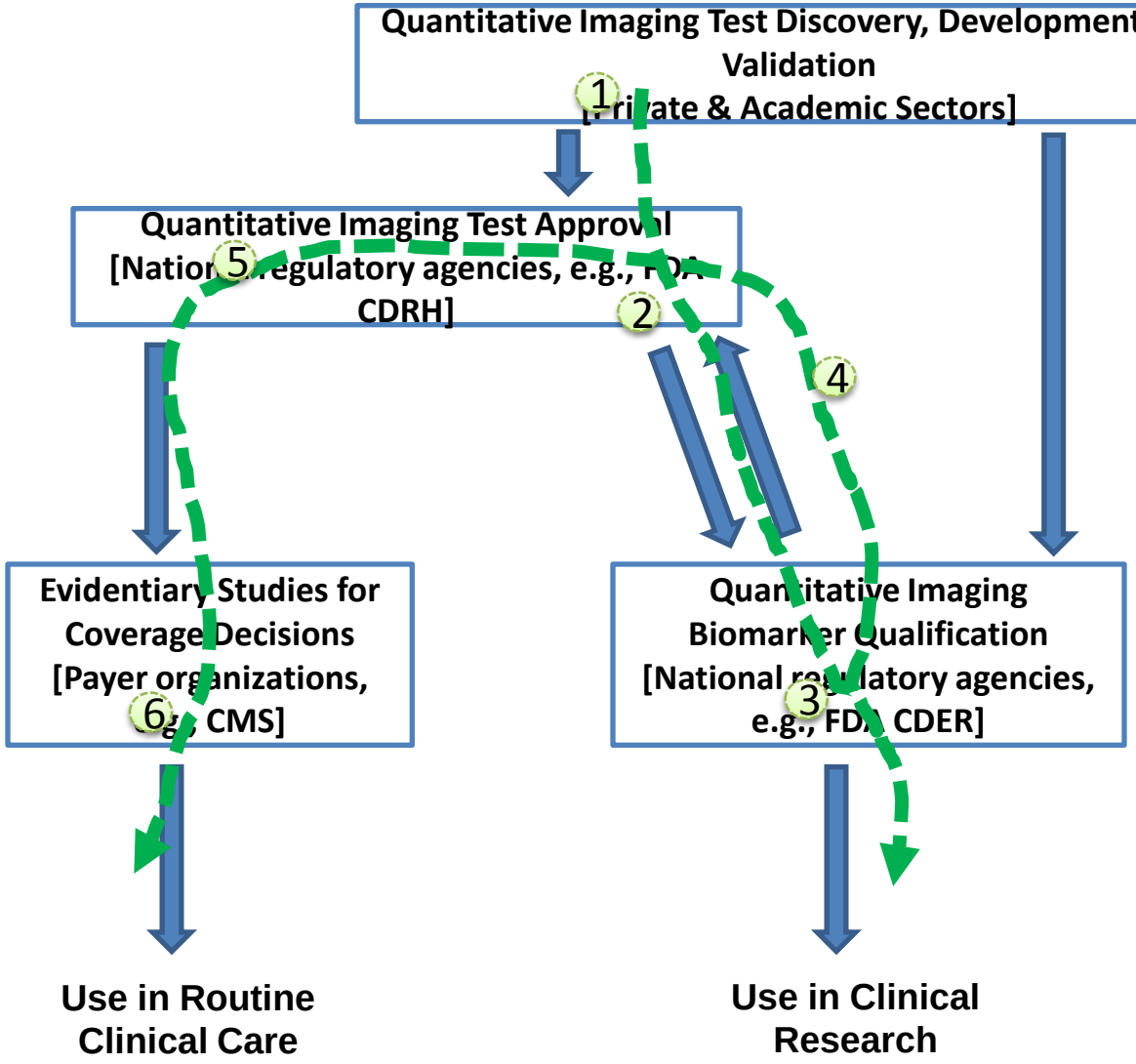
QIBA "Industrializes" QI



QIBA is an Active Sponsor in Regulatory Pathways that Leverage Collaboration

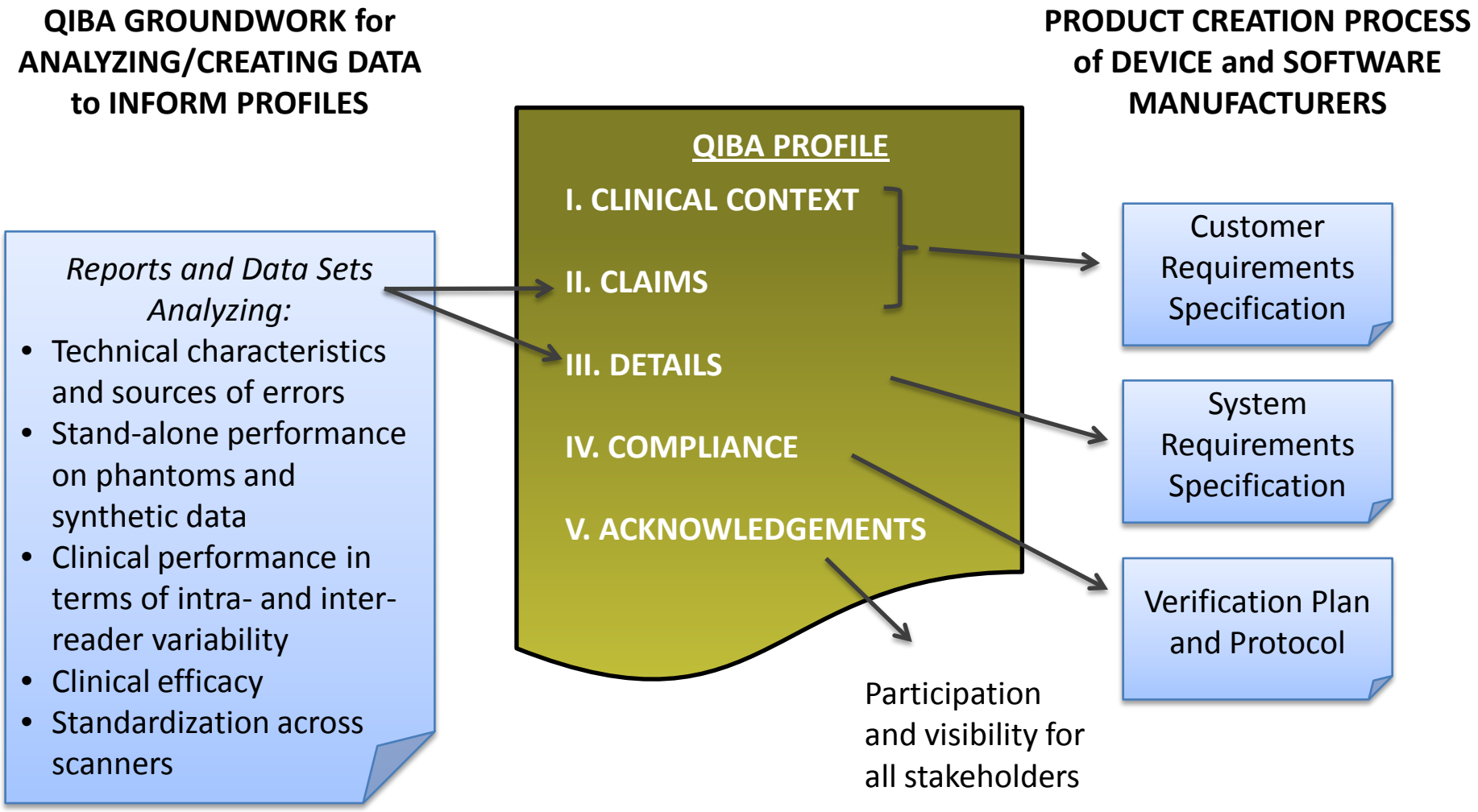


Example Drill Down: How Pathways may be Applied to Advance Volumetric CT

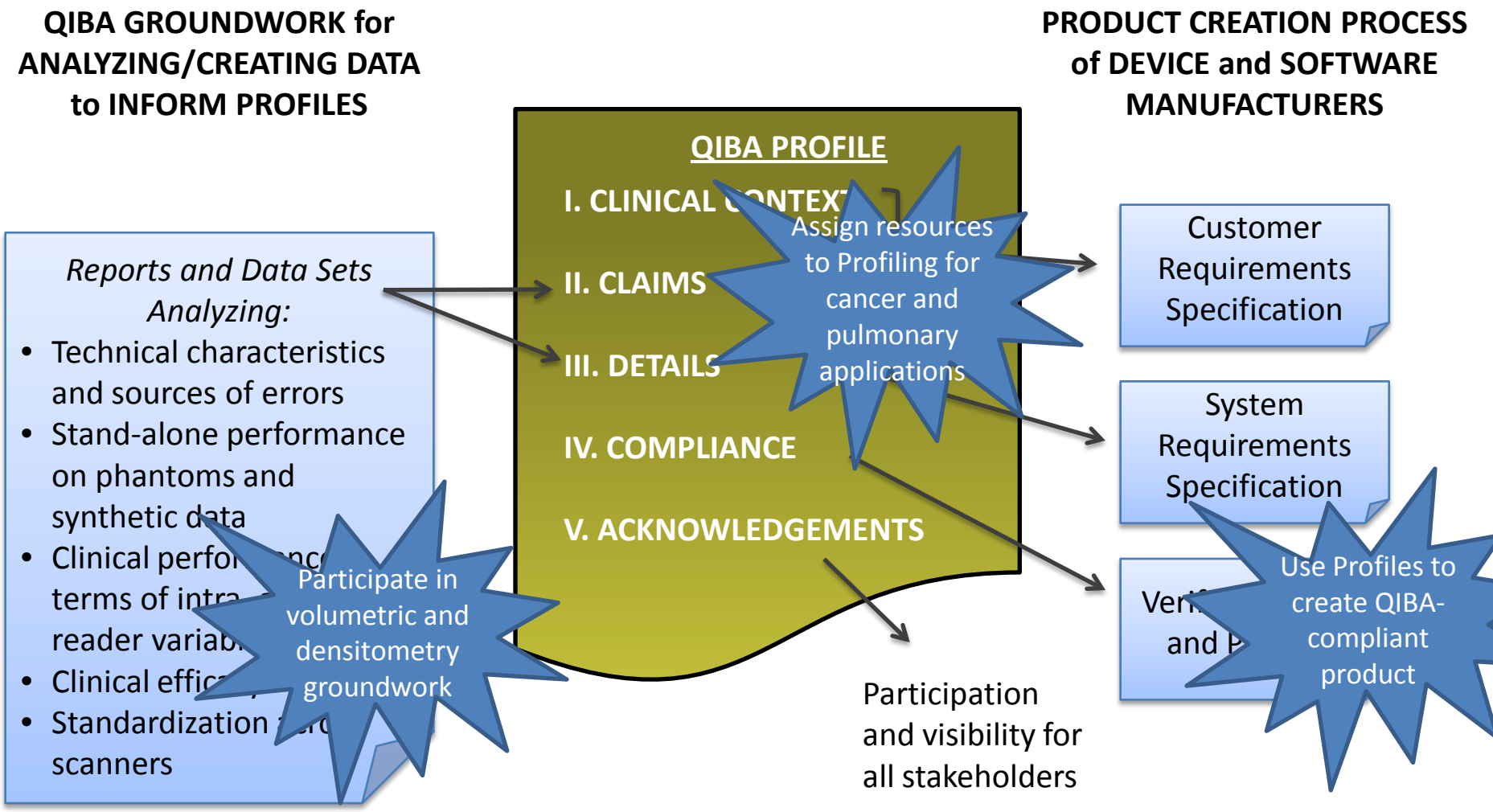


1. Vendors have developed, and are refining, volumetric CT (vCT) applications.
2. Many of these solutions have been approved by CDRH, but with weak intended use (no explicit connection with biology or response).
3. A sponsoring collaborative would make a connection to response by qualifying the class of devices for clinical research in an indicated disease setting.
4. These “qualification data” would be available to be contributory as evidence for individual device sponsors as they re-register their products (if they are already a compliant implementation) or re-engineer them (to become compliant).
5. Given the availability of these data, individual vendors can pursue approval for their vCT products, but now with stronger claims as established in the qualification activity.
6. The qualification data collected would provide the scientific basis for reimbursement.

QIBA Leverages Resources and Bridges Perspectives Across Communities



Our Offer – and our Request – is to Increase your Engagement with Us



To be specific, for volumetric analysis and densitometry, we are requesting:

- Assist with collaborative groundwork activities:
  - Participate in experimental studies for characterizing performance.
  - Review requests and provide feedback on standardizing acquisition system characteristics.
- Apply engineering resources to help refine QIBA profiles:
  - Assist with the engineering analysis being performed to arrive at requirement levels and functional specifications.
  - Assist with the writing of QIBA profile claims.
- Prepare for future product development and marketing:
  - Review QIBA profiles and current product performance claims.
  - Perform QIBA studies and internally validate QIBA compliance.
  - Obtain approval to claim QIBA compliance.

We can't do it alone, you can't do it alone. We need to do it together.

- Utilization of imaging grows as it is used for monitoring response and adapting therapy.
- Technical as well as business obstacles impede commercialization.
- QIBA addresses these obstacles, accounting for individual stakeholder value propositions.
- The commercialization model is similar to IHE, including relationship to product creation process.
- Collaborative resources in precompetitive model address the science and provide critical mass as well as cost sharing for regulatory data collection.
- We invite you to join us in making the critical step of defining Profiles.
- New products compliant with the outputs of this process will fuel a virtuous cycle of innovation in this next generation of imaging, rewarding all participants.