QIBA Newsletter

Quantitative Imaging Biomarkers Alliance RSNA

June 2011 • Volume 3, Number 2

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QIBA MISSION

Improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients and time.

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IN MY OPINION

Imaging CRO Perspective on Quantitative Imaging Measurements

By ERIC S. PERLMAN, MD

Remarkable technologic advancements leading to a deeper understanding of biological processes in human health and disease have reshaped the research and development pathways for diagnostic and therapeutic agents and medical devices. Given the increasing number of potential therapeutic candidates, the need to develop new technologies and strategies to streamline and standardize the process to bring safe and effective therapies to our patients is paramount. Quantitative imaging will play an increasingly important role as an imaging biomarker across multiple imaging modalities and therapeutic areas.

For more than 10 years, following the enactment of the US Food and Drug Administration (FDA) Modernization Act of 1997, the mainstay of industry imaging contract research organization (CRO) work in oncology has been providing and supporting workflow surrounding the use of the Response Evaluation Criteria In Solid Tumors (RECIST) criteria for drug development, primarily in Phase III studies. Processes developed for this use case are relatively common across all vendors, including imaging acquisition manuals, image transfer and anonymization schemes, image analysis tools, electronic data capture solutions and response algorithm derivations. Given the relatively robust nature of CT instrumentation globally in clinical practice, the critical variable in this use case has become the reader - assuming the other quality control processes are followed.

More recently, with improvements in anatomic imaging resolution (e.g. for CT), advances in molecular imaging techniques (e.g., fluorodeoxyglucose [FDG-PET] and dynamic contrast-enhanced MR Imaging [DCE-MRI]) and advanced image processing, attention has focused on quantitative metrics other than linear RECIST

measurements. For anatomic imaging, strategies have concentrated on volumetric analysis rather than uni- or bidimensional measurements. For both anatomic and functional imaging, "groundwork" involves understanding sources of technical variation (e.g., by performing phantom analyses across multiple manufacturers' platforms) and inter/intra-reader variation. A common goal of these activities across all operational process steps is to minimize variability, thereby improving reproducibility of data without loss of accuracy.

The quantitative measurement output (size, contrast agent concentration) is the "raw data" which is central to the quantitative imaging result. There are, however, steps prior to and after the analysis (lesion measurement) step which are equally, if not more, important for achieving confidence in the quantitative metric output. Understanding and minimizing the variance associated with the subject (and subject preparation), the imaging instrumentation, the image acquisition parameters and imaging scientist interactions with advanced analysis tools are all critical path processes.

There are multiple challenges to the development of quantitative imaging standards. For example, FDG-PET/CT is widely used in clinical practice to monitor cancer response. However, there is currently no globally accepted standard for all components of the imaging procedure and response assessment readout which can be implemented across all imaging facilities, for all manufacturers. A Uniform Protocols for Imaging in Clinical Trials (UPICT) protocol* and Quantitative Imaging Biomarkers Alliance (QIBA) Profile** are under development to address these needs. In addition to standard processes, both of these working groups have identified multiple quality control issues which need attention. The facility-centric quality control issues - both for instrumentation and processes - need to be more rigorous for molecular imaging and advanced imaging and image analysis techniques than for CT-based RECIST assessments.

In an imaging CRO, the concept of quantitative imaging - which is critical for imaging biomarkers for clinical trials and eventually clinical practice work - requires attention to standardized prescription and quality control measures for all steps in subject imaging and image interpretation.

- UPICT = Uniform Protocols for Imaging in Clinical Trials
- QIBA = Quantitative Imaging Biomarkers Alliance

Eric S. Perlman, MD, an imaging consultant for clinical trials, is a diagnostic radiologist, internist and nuclear medicine physician who spent 13 years in clinical imaging practice at Princeton Radiology and 10 years at CoreLab Partners (formerly RadPharm), most recently as Chief Scientific Officer. Dr. Perlman is a member of the QIBA FDG-PET Technical Committee and is a core member of the UPICT FDG-PET protocol writing group.

Each issue of QIBA Newsletter features a link to a dynamic search in PubMed, the National Library of Medicine's interface to its MEDLINE database. Link to articles on: "Imaging CRO Perspective on Quantitative Imaging Measurements."

ANALYSIS TOOLS & TECHNIQUES

Predictive Metrics of Quality for Quantitative Imaging

EHSAN SAMEI, PhD, DABR, FAAPM, FSPIE.

As many in this readership would attest, in its first century (1895-1995), medical imaging was primarily developed as a qualitative technique. Imaging devices were often seen as "cameras" used to take "pictures" of the interior of the human body. Radiology correspondingly developed as a subspecialty focused on making sense of what the images exhibit in the context of other related clinical data. The latter, understanding the meaning of the image data in the context of other clinical data, has always been an objective from which radiology has drawn its relevance and significance.

So far, the second century of medical imaging has witnessed notable advancements in technologies enabling images to become more robust and reproducible. A corresponding reduction in variability across all components of imaging systems has provided an opportunity to extract more quantitative information from image data in such a way that the information can contribute to clinical care in a more quantitative way. A quantitative approach to imaging enables one to characterize a medical condition in more definitive ways than a more conventional, interpretive qualitative approach. This offers unprecedented opportunities to quantitatively characterize disease conditions, a cornerstone of evidence-based medicine. Specifically, quantitative imaging enables monitoring the progress of a disease or a treatment regimen across time, making it possible to identify or optimize treatment techniques towards more efficacious, evidence-based and patient-specific treatments.

These worthy goals are only possible if imaging is performed in such a way that quantitative information can be most precisely extracted from image data. Currently imaging systems are primarily designed and used to provide the best interpretive quality and not necessarily the best quantitative quality. Orienting the imaging practice towards quantitative ends requires having relevant figures of merit; one cannot improve something that cannot be measured. In our work at Duke University, the goal is first to identify figures of merit that are explicitly directed towards quantitative precision [1-2]. Implicit in quantification is characterization of specific imaging tasks. Our current work focuses on precision in the estimation of 3D volume of lung tumors in CT exams [3]. Additional imaging tasks under development include quantification of contrast uptake in abdominal CT [4-5], and characterization of chronic obstructive pulmonary disease (COPD) in chest CT.

Drawing from basic imaging properties such as resolution and noise, our objective is to understand how those properties can be related to specific precision by which the targeted tasks are quantified. Explicit to that objective is to define specific imaging parameter settings (or protocols) that can provide the highest figures of metric for quantification while minimizing the radiation dose to the patient, thus minimizing potential risk while enhancing quantitative precision [6].

The research further seeks to benchmark, verify, and validate current measurement methods and test phantoms that are used to characterize imaging performance. Specifically, one goal is to understand how the prediction from these methods and objects speaks to the quantification objective, and how a calibration strategy can be implemented so that the quantitative performance can be benchmarked across devices, protocols, and facilities. A

calibration method can serve as a basis to evaluate the performance of imaging operations that seek to participate in quantitative imaging initiatives.

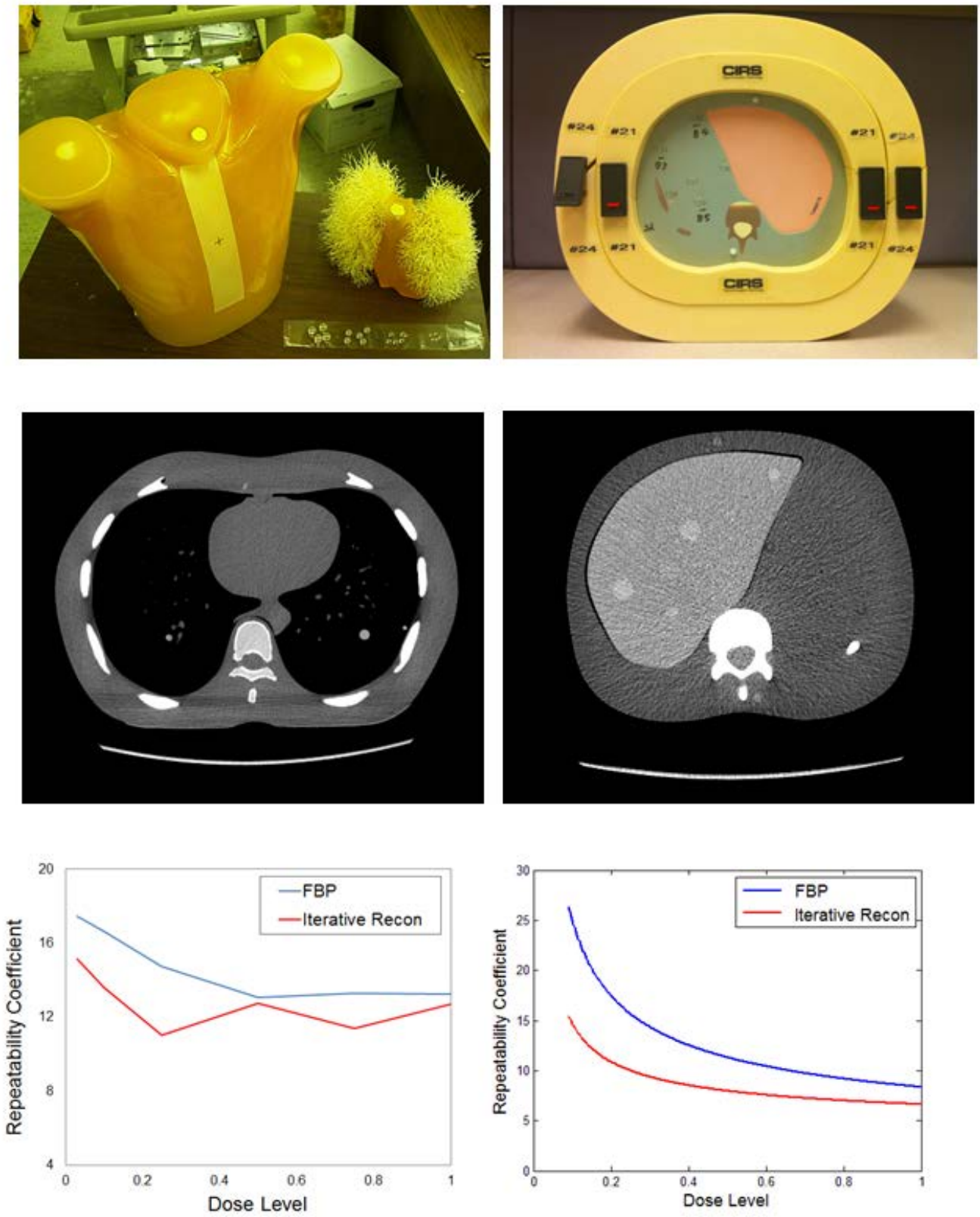

Figure: Example of phantoms used at Duke University to characterize quantification of lung nodule volumes (*top-left*) and abdominal contrast uptake (*top-right*). Typical images are correspondingly shown (*middle row*), while the precision by which those tasks can be performed is shown correspondingly as a function of dose level and reconstruction technique (*bottom row*).

References:

[1] Quantitative Imaging in Breast Tomosynthesis and CT: Comparison of Detection and Estimation Task Performance. *Medical Physics*, 2010; 37(6): 2627-2637. Richard S, et al.

[2] Quantitative Breast Tomosynthesis: from Detectability to Estimability. *Medical Physics*, 2010: 37(12): 6157-6165. Richard S, et al.

[3] Quantitative CT: Technique Dependency of Volume Assessment for Pulmonary Nodules. SPIE International Symposium on Medical Imaging, San Diego, CA, February 2010, Proc. SPIE Medical Imaging 7622: 76222W, 2010. Chen B, et al.

[4] Precision of Hepatic CT Image Quantifications: A Comparative Study of Conventional (FBP) and Iterative Reconstruction Algorithms (ASiR and MBiR). SPIE International Symposium on Medical Imaging, Orlando, FL, February 2011, Proc. SPIE Medical Imaging 7961, 2011. Chen B, et al.

[5] A New Iodinated Liver Phantom for the Quantitative Evaluation of Advanced CT Acquisition and Reconstruction Techniques. SPIE International Symposium on Medical Imaging, Orlando, FL, February 2011, Proc. SPIE Medical Imaging 7961, 2011. Chen B, et al.

[6] Predictive Models for Observer Performance in CT: Applications in Protocol Optimization. SPIE International Symposium on Medical Imaging, Orlando, FL, February 2011, Proc. SPIE Medical Imaging 7961, 2011. Richard S, et al.

Ehsan Samei, PhD, is a professor of radiology, medical physics, biomedical engineering, and physics, and the director of Carl E. Ravin Advanced Imaging Laboratories at Duke University in Durham, N.C. He is a member of the QIBA Volumetric CT Technical Committee. Dr. Samei's current research interests include quantitative imaging, molecular x-ray imaging, and theoretical and experimental methods in medical image formation, analysis, assessment, display, and perception.

QIBA AND QI/ IMAGING BIOMARKERS IN THE LITERATURE

This list of references showcases articles that mention QIBA, quantitative imaging, or quantitative imaging biomarkers.

QIBA in the Literature

In most cases, these are articles published by QIBA members, or relate to a research project undertaken by QIBA members that may have received special recognition. New submissions are welcome and may be directed to QIBA@rsna.org