# QIBA Quarterly

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

**QIBA CONNECTIONS**

Quantitative Imaging Biomarkers Alliance (QIBA)

QIBA Wiki

Contact us
Comments & suggestions welcome.

Daniel C. Sullivan, MD
RSNA Science Advisor

## *QIBA Quarterly* Focuses on Quantitative Imaging

Welcome to *QIBA Quarterly*, an e-newsletter dedicated to providing news and information from the Quantitative Imaging Biomarkers Alliance (QIBA), formed by RSNA in 2007 to unite researchers, healthcare professionals, and industry stakeholders in the advancement of quantitative imaging and the use of biomarkers in clinical trials and practice. *QIBA Quarterly* offers articles, Web links and tools, as well as updates from technical committees and information about opportunities for participation in QIBA activities. You can access the newsletter at RSNA.org/Research/QIBA.

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**IN MY OPINION**

# Radiologists Re-examine Quantitative Imaging

By DANIEL C. SULLIVAN, MD

Radiologists and physicists who have long been interested in the potential for extracting quantitative measurements from medical imaging are re-examining the issue based on changes in response to a variety of forces, including:

1. The evolution toward molecular (personalized) medicine requires quantitative test results.
2. Progression toward evidence-based medicine depends on more quantitative clinical data.
3. Decision-support tools (artificial intelligence) need quantitative input.
4. Pay-for-performance plans need to be based on objective metrics.

In 2008, RSNA convened an ad hoc group of radiologists, physicists, and other stakeholders to make recommendations on educating the radiology community about quantitative imaging and facilitating relevant research. The Toward Quantitative Imaging (TQI) Committee developed the following working definition of quantitative imaging:

> *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). Quantitative imaging includes the development, standardization, and optimization of anatomical, functional and molecular imaging acquisition protocols, data analyses, display methods, and reporting structures. These features permit the validation of accurately and precisely obtained image-derived metrics with anatomically and physiologically relevant parameters including treatment response and outcome and the use of such metrics in research and patient care.*

Recommendations made by the TQI Committee include improving communication with other specialties to facilitate understanding of the clinical settings or problems that would benefit from quantitative imaging results and performing

rigorous clinical trials to show the added value of quantitative metrics.

RSNA is pursuing these goals on several fronts including special programming at the annual meeting, coordination of the Imaging Biomarkers Roundtable and support for the Quantitative Imaging Biomarkers Alliance (QIBA). Increased use of objective, quantitative results from medical imaging studies will improve the appropriateness and consistency of medical care for patients with a diverse array of health problems including cancer, cardiovascular disease, brain disorders, arthritis, and metabolic diseases.

*Daniel C. Sullivan, MD, is a professor in the Department of Radiology at Duke University and serves as RSNA Science Advisor. At Duke he coordinates imaging research, and for RSNA he coordinates a variety of programs related to quantitative imaging and imaging biomarkers.*

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**ANALYSIS: TOOLS & TECHNIQUES**

## Measuring Tumor Volume

By BINSHENG ZHAO, DSc

Using multidetector-row CT (MDCT) to measure tumor volume may be more accurate and sensitive in detecting change in solid tumors than using the standard 1- or 2-diameter measurement. Advances in MDCT allowing thin-slice acquisition where individual image voxels are nearly isotropic have made accurate tumor volume measurement possible.

In order to qualify as a biomarker of novel therapies, this imaging metric for measuring tumor volume must demonstrate a better correlation with therapy-induced biologic activity/clinical outcome than conventional methods. To evaluate volumetric techniques in assessing therapy response and gain acceptance of such techniques in clinical practice, computer assistance is necessary to perform measurements and reduce variability in measured values.

Computer-aided measurement of tumor volume requires automated separation of the tumor from its surrounding background through segmentation. The strategy chosen for segmentation of a specific type of tumor is often influenced by the growing pattern of the tumor and its relationship to surrounding anatomical structures. A simple thresholding algorithm involves an automated determination of a density

value (or Hounsfield unit threshold) that separates the tumor from its background based on density distribution. A region-growing algorithm employs the homogeneity of a certain property of the tumor (density, texture or color) to iteratively group neighboring 2D pixels and 3D voxels into the tumor region. An edge detection and connection algorithm includes calculation of density discontinuity (gradient) followed by connection of edge segments that are likely part of the tumor boundary, using certain constraints to form a closed boundary. A combination of different strategies is often considered to resolve a complex problem.

Although there is no universally accepted algorithm that can properly segment all types of tumors, multiple strategies may be developed for segmenting the same type of tumor. Volume measurement/segmentation algorithms can be affected by factors including image reconstruction filter and slice thickness. For example, an edge-based algorithm may perform better on sharper images reconstructed using high-frequency filters than on smoother images reconstructed using low-frequency filters. Image slice thickness can have a greater effect on size estimations of smaller lesions than on larger ones.

The algorithm itself can also cause measurement variation, which can occur when the operator must manually initiate the software by placing a seed region (or a seed point) inside the lesion to be segmented on a single image or a closed curve of any shape outside the lesion. With information on location and density/densities acquired during the initiation, the algorithm can then automatically identify tumor boundary (in 2D)/surface (in 3D).

Although a number of segmentation algorithms have been developed for lung nodules on CT images, comparing the relative performance of these algorithms is challenging because investigators have developed and tested algorithms using their own, often not comparable, databases.

Realizing the need for evaluating and comparing different computer-aided detection/diagnosis/response assessment algorithms, the National Cancer Institute (NCI) has sponsored several initiatives to establish publically accessible databases, including the Lung Image Database Consortium (LIDC) and Reference Image Database to Evaluate Response to Drug Therapy in Lung Cancer (RIDER). Such a reference database should facilitate development of computer algorithms.

Lastly, it is important to explore the reproducibility of modern CT scanners and advanced tumor measurement tools. This information is needed to distinguish between true tumor changes and measurement variations, which is critical in

determining the cut-off values used to detect biologic tumor changes after therapy. The ultimate goal is to determine as rapidly as possible whether a patient is responding to therapy. Methods that can determine response more accurately and with smaller variations may allow earlier determination of response, allowing clinical trials to enroll fewer subjects or be performed over a shorter period of time.

*Binsheng Zhao, DSc, is associate attending physicist in the Medical Physics and Radiology Departments at Memorial Sloan-Kettering Cancer Center and a member of the QIBA Volumetric CT Technical Committee. As technical director of the Laboratory of Computational Image Analysis, she has been leading algorithm development for computer-aided quantitative assessment of therapy response using volumetric CT.*

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**FOCUS ON**

# Quantitative Imaging Biomarkers Alliance (QIBA)

Imaging biomarkers are increasingly used as primary or secondary endpoints in therapeutic trials. The statistical power, patient safety, efficacy, and efficiency of trials will be increased by characterizing and improving the accuracy and reproducibility (precision) of quantitative results from those imaging biomarkers. Through the work of its technical committees, the Quantitative Imaging Biomarkers Alliance (QIBA) is engaged in understanding and reducing errors where possible so that quantitative results are accurate and reproducible across patients, timepoints, sites, and imaging devices/software from vendors.

QIBA comprises a steering committee, chaired by Daniel C. Sullivan, MD, and technical committees, all of which welcome new participants.

Members include representatives of government agencies, the pharmaceutical industry, vendors, device manufacturers, software developers, clinical research organizations, academic radiologists, radiation oncologists, and medical physicists. The committees meet face to face approximately twice a year including at the RSNA annual meeting. Their ongoing work is conducted via e-mail and regular WebEx conference calls. The work of the technical committees is posted at the QIBA wiki.

## QIBA Technical Committees

**• FDG-PET Technical Committee**
Co-chairs:
Richard Frank, MD, PhD (GE Healthcare)
Alexander (Sandy) McEwan, MB (SNM)
Helen Young, PhD (AstraZeneca)

The FDG-PET/CT Technical Committee aims to foster adoption of pragmatic and cost-effective standards for accurate and reproducible quantitation of tumor metabolism via longitudinal measurements by FDG-PET/CT with clinical relevance and known sigma.

Subcommittee objectives include enabling software version tracking, identifying clinically significant covariates in the quantitation of FDG signal, comparing vendors' computations for quantitation, defining parameters for automated setting of regions of interest and developing a Digital Reference Object (image database) for quality control.

**•DCE-MRI Technical Committee**
Co-chairs:
Gudrun Zahlmann, PhD (Siemens AG)
Michael H. Buonocore, MD, PhD (University of California, Davis)
Jeffrey L. Evelhoch, PhD (Merck)

The DCE-MRI Technical Committee seeks to enable the broad use of DCE-MRI as an imaging biomarker technique by reducing the physical measurement variability associated with the generation and analysis of MR imaging data across scanners from the same or different vendors.

Subcommittees are engaged in defining phantom and generic acquisition protocols for quantitative DCE-MRI and producing synthetic DCE-MRI data appropriate for performing early stage verification of DCE-MRI analysis software.

**•Volumetric CT Technical Committee**
Co-chairs:
Andrew Buckler, MS (Buckler Biomedical LLC)
P. David Mozley, MD (Merck)
Lawrence Schwartz, MD (Memorial Sloan-Kettering Cancer Center)

The Volumetric CT Technical Committee aims to develop the technical capability necessary for imaging vendors to support targeted levels of accuracy and reproducibility for use of volumetric CT as a biomarker in oncologic clinical trials. The committee is developing implementation guidelines—profiles

—through initial groundwork.

Subcommittees are conducting a reader study to estimate intra- and inter-reader bias and variability by examining the level of bias and variance in measuring tumor volumes in patient datasets. The reader study will also determine the minimum detectable level of change that can be achieved when measuring tumors in patient datasets under a “no change” condition, assess the impact of instrumental variability on volumetrics by studying interclinic comparison of CT volumetry, and work toward standards for using volumetric imaging in clinical trials.

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**QI/IMAGING BIOMARKERS IN THE LITERATURE**

## PubMed Search on Imaging and Biomarkers

Each issue of *QIBA Quarterly* will feature a link to a dynamic search in PubMed, the National Library of Medicine's interface to its MEDLINE database. Click here to view a PubMed search on imaging and biomarkers.

Take advantage of the My NCBI feature of PubMed that allows you to save searches and results and includes an option to automatically update and e-mail search results from your saved searches. My NCBI includes additional features for highlighting search terms, storing an e-mail address, filtering search results and setting LinkOut, document delivery service and outside tool preferences.

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