

# QIBA Newsletter



October 2012 • Volume 4, Number 2

---

## In This Issue:

---

### IN MY OPINION

Why FDG-PET is a Useful Biomarker of Tumor Response

By: RICHARD L. WAHL, MD

---

### PUBMED

PubMed Search on *Why FDG-PET is a Useful Biomarker of Tumor Response*

---

### ANALYSIS TOOLS & TECHNIQUES

Challenges in Tackling Quantitative Ultrasound

By: PAUL L. CARSON, PhD

---

### FOCUS ON

QIBA Profile Update

---

### QIBA IN THE LITERATURE

---

## IN MY OPINION

### Why FDG-PET is a Useful Biomarker of Tumor Response

By RICHARD L. WAHL, MD

In oncology there is great interest in using FDG-PET to monitor treatment response across a wide range of cancer types. A large and still increasing body of literature indicates that rapid declines in tumor FDG uptake during many types of treatment are associated with favorable outcomes. Patients whose tumors do not have a major decline in FDG uptake—or a rise in FDG uptake—during treatment are likely to have poorer outcomes.

---

## QIBA MISSION

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

---

## QIBA CONNECTIONS

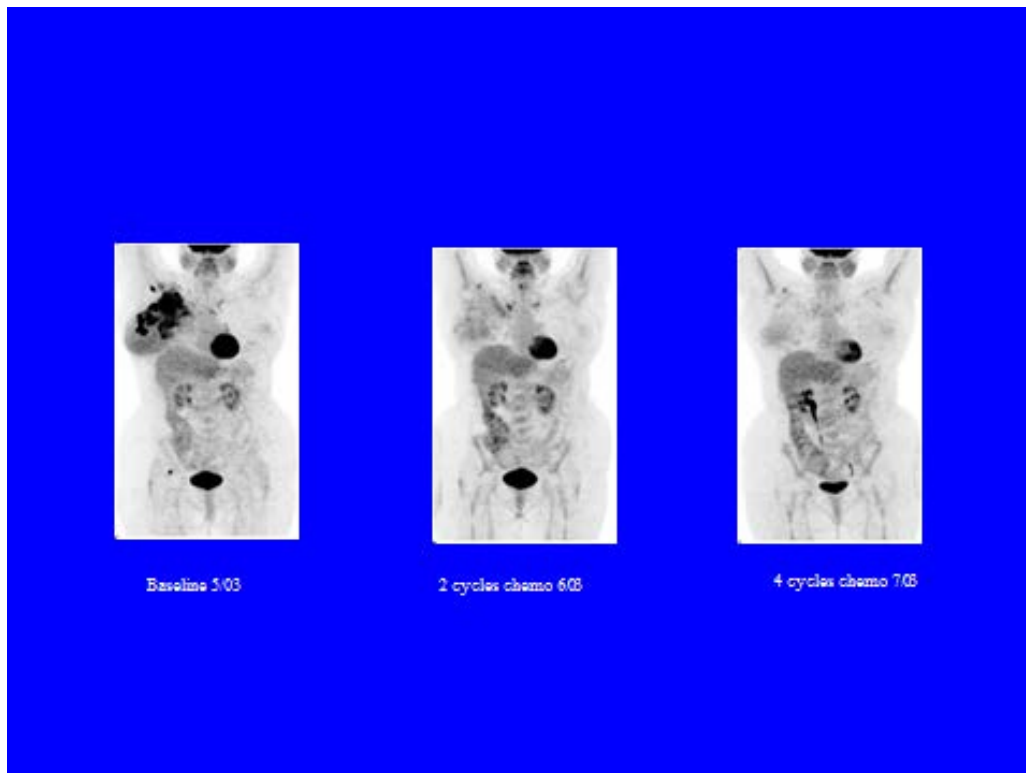
[QIBA Wiki](#)

---

## QIBA CONTACT

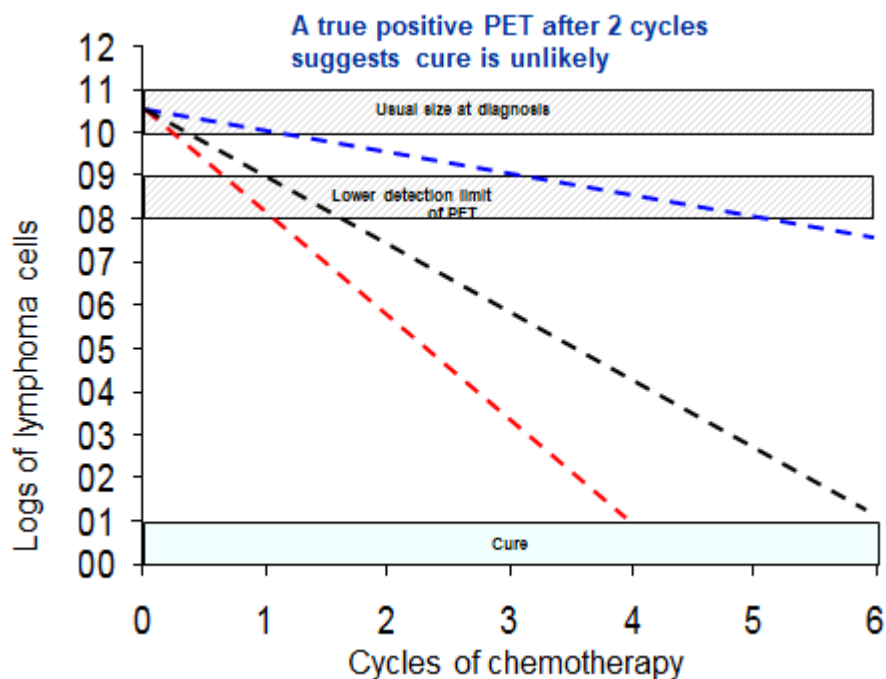
[Contact Us](#)

Daniel C. Sullivan, MD  
RSNA Science Advisor



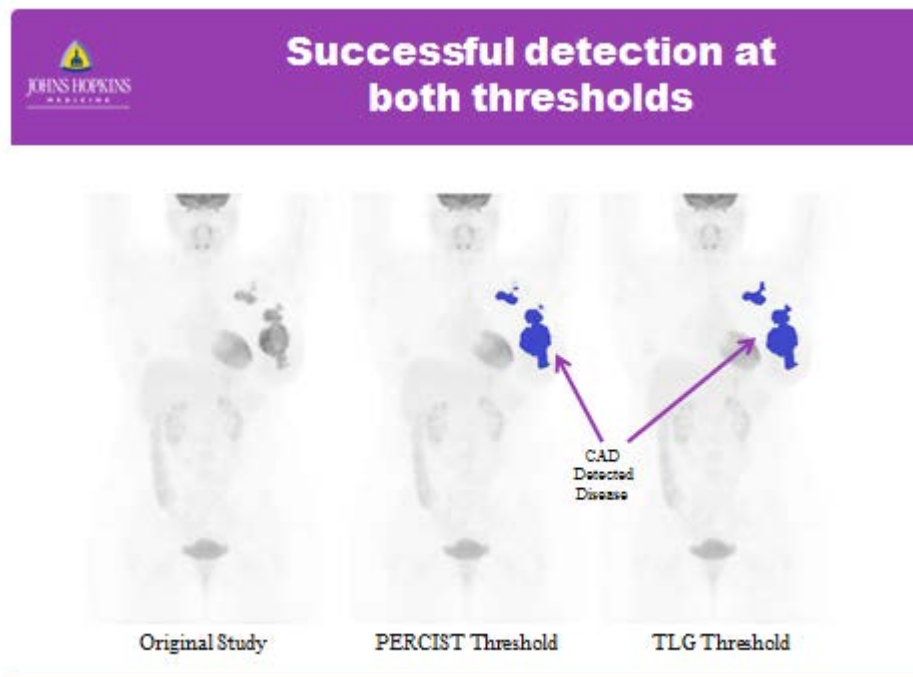
Evidence supports the power of the early FDG-PET assessment. FDG uptake changes during treatment can contribute information regarding outcome that is at least as and sometimes more informative than PET imaging at the end of treatment. Since FDG uptake in tumors is correlated with the number of viable cancer cells in a given tumor, the FDG signal is related to viable cell number. Large drops in tumor FDG uptake are seen in cancers where many cancer cells have been killed by cytotoxic agents.

FDG-PET scans at the end of therapy also indicate, with reasonable certainty, whether a treatment has been effective. A negative PET scan may lead to a clinical decision to observe a patient without additional therapy while a positive PET scan may lead to more treatment, more intense follow up, or biopsy.



Because more cancer therapies are being developed, the historical paradigm of treating a patient for two months with an anti-cancer therapy regimen and then assessing change in tumor size has limitations. This could potentially expose a patient to months of ineffective treatment with attendant side effects, cost, and the lost opportunity to treat with a more effective agent. Early identification of **non**-efficacy of a cancer treatment regimen would be desirable, so that treatments can be changed sooner to agents which may be more likely to be effective. To make such early assessments with high certainty, e.g. after two weeks or so of treatment, it is quite probable that quantification of the PET images will be needed. The need for quantification is likely to be greater when the patient is still undergoing treatment than at the end of treatment when PET is commonly assessed for completeness of response both visually and qualitatively.

Rigorous standards and quality control are necessary to precisely quantify PET imaging of cancer with FDG. The QIBA approach has helped focus practitioners of FDG-PET on a more standardized imaging approach. Standardized methods, such as those of the UPICT 1.0 and the FDG-PET/CT Profile 1.0 and with more robust analytical approaches such as the PERCIST 1.0, are now being used.



Quantitative FDG-PET/CT at baseline and soon after treatment is emerging as a potent quantitative, non-invasive method to phenotype tumors and observe the effects of a specific treatment. Efficacy or non-efficacy can be predicted by early scans with increasing certainty. With this approach, cancer treatments that aren't working could be changed to more effective therapies that could potentially be implemented sooner than with traditional anatomic imaging approaches. Resources would not be wasted on expensive treatments with a low probability of efficacy, but money and effort could be applied to using the right treatment in the right patient.

Whether the SUV peak, SUV max, metabolic tumor volume or total lesion glycolysis is the most important parameter to assess remains under study, as does the optimal cut-off thresholds for therapeutic non-efficacy for specific cancers and treatments. While much work remains, there is worldwide interest in using PET with FDG to promptly assess treatment efficacy in a wide range of cancer types and treatments. The QIBA approach—which extends from consistent dose calibration to scanner specifics, to software, patient selection and physician expertise—applies rigor and consistency to these increasingly quantitative imaging approaches. With these paradigms, cancer treatment will be changed so that each patient is assured that the drug predicted to help battle their disease is actually working. This can be assured by sequential, quantitative, FDG-PET providing non-invasive phenotyping of cancers and their response to therapy.

*Richard L. Wahl, MD, is the director of nuclear medicine at Johns Hopkins University School of Medicine in Baltimore, Md., and vice-chairman of radiology for technology and new business development. He is a professor of radiology and oncology as well as the first Henry N. Wagner, Jr. Professor of Nuclear Medicine. His scientific interests focus on cancer imaging and therapy with targeted radiopharmaceuticals. Dr. Wahl pioneered the use of [18-F] FDG for tumor imaging with PET. He and his colleagues developed the SUV-lean body mass, quantitative PET treatment response approaches and the PERCIST criteria for treatment response in PET.*



*He is one of the inventors of radio-immunotherapy of lymphoma with anti CD20 antibodies and of patient individualized dosimetry based on whole body clearance rates. Dr. Wahl has written/edited five major textbooks and authored more than 350 peer-reviewed publications. He has lectured throughout the world and has been honored with multiple professional awards and named lectureships including being named the "most influential radiology researcher" in 2005 in the "Minnie" awards.*

### **PubMed Search on: "Why FDG-PET is a Useful Biomarker of Tumor Response"**

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: "Why FDG-PET is a Useful Biomarker of Tumor Response" [here](#).

### **ANALYSIS TOOLS & TECHNIQUES**

#### **Challenges in Tackling Quantitative Ultrasound**

By: PAUL L. CARSON, PhD

Eighteen key researchers, physicians, and/or industry representatives in ultrasound and QIBA and RSNA leaders attended a two-hour meeting at the 2011 RSNA Annual Meeting in Chicago to establish a Quantitative Ultrasound Biomarker Committee within QIBA. After explaining the QIBA process, leaders in each of six possible quantitative ultrasound imaging modes spoke briefly on how a mode might serve as the target for QIBA profile development.

*Possible target areas for a QIBA biomarker and speakers were:*

- |   |  |
|---|--|
| • Elastography – Related Measures                           | Timothy J. Hall, PhD, Ellen B. Mendelson, MD |
| • Measures with Contrast Agents                             | Robert F. Mattrey, MD, James Jago, PhD       |
| • Pressure Measurement with Contrast Agents                 | Flemming Forsberg, PhD                       |
| • Quantitative Frequency Dependent Imaging from Backscatter | Timothy J. Hall, PhD                         |
| • Volume Flow and Other Doppler Measures                    | J. Brian Fowlkes, PhD                        |
| • Pulse Echo Volumetrics                                    | Brian S. Garra, MD                           |

Following this meeting, a newly formed organizing committee arranged a planning meeting in March 2012 prior to the American Institute of Ultrasound in Medicine meeting in Phoenix, to select one high-priority area for a QIBA effort to improve ultrasound's quantitative reproducibility and fidelity to reference standards. Speakers on the narrowed field of four contending topics are in Table 1. Many of their presentations are available publicly in the [QIBA Wiki](#), or specifically the [Ultrasound Wiki](#).

**Table 1**  
**Speakers, Topics and Summaries, Phoenix Planning Meeting**

Elastography Measures	Timothy J. Hall, PhD David Cosgrove, MD
Measures with Contrast Agents	Paul Dayton, PhD Kenneth Hoyt, PhD Nicolas Rognin, MSc, PhD
Morphometrics	Brian S. Garra, MD Thomas R. Nelson, PhD
Volume Flow / Doppler	Jonathan Rubin, MD, PhD Michelle L. Robbin, MD, MS

**Table 2**  
**Ballot employed in first votes**

<b>2012 QIBA Ultrasound Quantitative Biomarker Planning Meeting Score Sheet March 29, 2012</b> Using a scale of 1-4, where 4 is the highest; please enter a non-repeated score for each biomarker in each of the five criteria (I-V).	Elastography	Volume Flow / Doppler	Morphometrics	Contrast Agents
<b>I. Transformational</b> Addresses a significant medical biomarker need ...				
<b>II. Translational</b> — will likely result in significant improvement in the development, approval, or delivery of care to patients. The following characteristics are desirable: ...				
<b>III. Feasible</b> — ... end goals can likely be achieved in a specific timeframe (3 years) and likely to produce the expected outcomes...				
<b>IV. Practical</b> — leverages preexisting resources... wherever possible; warrants access to RSNA resources and support.				
<b>V. Collaborative</b> — would uniquely benefit from the multi-stakeholder composition and approach of QIBA and could be feasibly executed under its policies ...				

Before substantial comparative discussion by the entire group, a vote was taken in which all participants ranked each measurement area by the criteria on the ballot in Table 2. The expectation was to continue with increasingly deep discussion in a Delphi-like process until one topic was selected. The spread was greatest in the first ballot in which one topic was eliminated. It then became apparent that all of the proposed measures, including the eliminated morphometry, were thought of as nearly equally appropriate for QIBA efforts. By the end of the meeting a reasonable preference was expressed for elastography in the form of shear wave speed, or elastic modulus estimated therefrom. The choice of medical problem was not clearly defined, though discrimination of fatty and fibrous liver infiltration and breast cancer diagnosis were the two most prominent applications discussed. The need in liver is quite strong, as the current diagnostic standard in the U.S. is quite invasive (Figure 1).

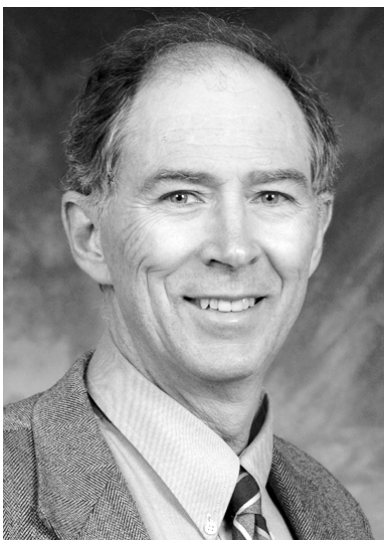


**Figure 1**

Invasive liver fibrosis/fat assessment is expensive, unsuited for longitudinal monitoring, and has limited sampling.

It was clear throughout the discussions that all of the six original topics are exciting areas of research and clinical development and nearly all are ready for a QIBA-type effort. A QIBA Shear Wave Speed Ultrasound Technical Committee (SWS-US-TC) was formed, led by co-chairs Brian Garra, MD, Andrzej Milkowski, MS, and Timothy Hall, PhD. The current 70 members in this open committee are listed on the Wiki. They have formed three subcommittees and bold goals are being discussed for greatly reducing cross-platform variability in SWS measurements in the liver.

*Paul L. Carson, PhD, is a collegiate professor of basic radiological sciences (BRS), Department of Radiology, a professor of biomedical engineering, and member of applied physics at the University of Michigan. Dr. Carson's research and clinical support interests include quantitative imaging, medical ultrasound (functional imaging, equipment performance, safety, new or improved diagnostic and therapeutic instrumentation and applications including microbubble creation and drug delivery in body fluids in vivo), multimodality breast imaging and therapy including combined-X-ray tomosynthesis / ultrasound / photoacoustics and microwave / ultrasound systems. He serves as QIBA Scientific Coordinator.*



## FOCUS ON

### QIBA Profiles now available for Implementation!

Profiles developed by the PDF-MRI and CT Volumetry Technical Committees have been released for implementation and are accessible on the [QIBA webpage](#) of the RSNA website.

Implementation instructions and the feedback form [may be found here](#).

## 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](mailto:QIBA@rsna.org)