QIBA Newsletter

Quantitative Imaging Biomarkers Alliance RSNA

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In This Issue:
IN MY OPINION

ANALYSIS TOOLS & TECHNIQUES

QIBA EDUCATION
QIBA and QI/Imaging Biomarkers in the Literature

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

QIBA CONNECTIONS
QIBA Wiki

QIBA CONTACT
Contact Us

Timothy J. Hall, PhD
QIBA Chair

In My Opinion

FDA's Final Guidance on Quantitative Imaging in Radiological Device Submissions

By NICHOLAS PETRICK, PhD
Center for Devices and Radiological Health, U.S. Food and Drug Administration

The U.S. Food and Drug Administration's Center for Devices and Radiological Health (FDA/CDRH) released the final guidance document "Technical Performance Assessment of Quantitative Imaging in Radiological Device Premarket Submissions" on June 16, 2022 [1].

QIBA's substantial and sustained efforts in developing methods, data, and Profiles for characterizing quantitative imaging (QI) functions and reducing their variability when implemented was critical in developing the groundwork necessary for the QI guidance effort.

This QI Guidance document represents FDA's current thinking by providing recommendations for manufacturers on information to include in premarket submissions for radiological devices that include QI functions. The guidance does not bind device manufactures, FDA, or the public such that manufacturers are free to use alternative approaches that satisfy the requirements of the applicable statutes and regulations for their device.

The guidance document is applicable to all devices that generate QI values across a wide range of radiological imaging modalities, intended uses, levels of automation and algorithms, but is not intended to provide comprehensive information on all submission requirements. Recognizing that QI functions have a broad range of intended uses, this guidance provides a general framework for developing and communicating appropriate technical performance information.

The guidance starts by discussing the scope of the document and then provides some basic QI-related definitions based on the work of QIBA and FDA-NIH Biomarker Working Group [2-4]. Importantly, the FDA distinguishes between a QI value and a QI function where a QI function is

defined as a medical device or a component or part of a medical device that produces QI values. This allows the guidance to distinguish between a general QI value and a specific medical device (or component) implementing a QI function. Sources of measurement error are discussed at a high level with sources of error coming from variations in patient characteristics, image acquisition, and image processing highlighted.

The main focus of the QI guidance is describing the information to include in submissions for describing the QI function, technical performance assessment and device labeling. The technical description of QI function(s) should be at a sufficient level of detail including details on the input data, image acceptance activities, level of user interaction necessary and the information presented to the user about the derived values.

The technical performance assessment should be based on performance specifications that correspond to the claims and uncertainty of the QI function with any supporting performance data demonstrating that the QI function meets these predefined specifications.

A key point is that uncertainty should be included in the performance specifications and ideally assessed under conditions that reflect the intended use of the device whether using phantoms or clinical image data. The guidance then describes basic labeling information to include in a submission. It makes clear that the labeling must satisfy any applicable requirements for the premarket submission type and should include sufficient information for the end user to obtain, understand, and interpret the QI values provided.

Finally, the guidance includes a set of basic example cases based on a manual, semi-automated, and fully automated hypothetical vessel stenosis measurement function to help illustrate how the validation and labeling for a QI function can vary for different designs and outputs.

The QI guidance represents the agency’s first step in providing manufacturers details on the type of information to include in premarket device submissions for radiological QI functions and is available to manufacturers, researchers, FDA reviewers, and the public to help them in

understanding FDA's current thinking around the technical assessment of these important medical image analysis tools.

References

1. U.S. Food and Drug Administration, *Technical Performance Assessment of Quantitative Imaging in Radiological Device Premarket Submissions - Guidance for Industry and FDA Staff, in FDA Guidance Document*. 2022, U.S. Food and Drug Administration: Silver Spring, MD.
2. Kessler, L.G., et al., *The emerging science of quantitative imaging biomarkers terminology and definitions for scientific studies and regulatory submissions*. Stat Methods Med Res, 2015. **24**(1): p. 9-26.
3. Sullivan, D.C., et al., *Metrology Standards for Quantitative Imaging Biomarkers*. Radiology, 2015. **277**(3): p. 813-25.
4. FDA-NIH Biomarker Working Group. *BEST (Biomarkers, EndpointS, and other Tools) resource*. 2016; Available from: http://www.ncbi.nlm.nih.gov/books/NBK326791/.

Nicholas Petrick, PhD

Nicholas Petrick, PhD, is deputy director for the Division of Imaging, Diagnostics and Software Reliability at the U.S. Food and Drug Administration, Center for Devices and Radiological Health and is a member of the FDA Senior Biomedical Research Service. Dr. Petrick's QIBA activities include serving as FDA representative to the Steering Committee and a member of the CT Modality Committee. His research interests include machine learning algorithms for medical imaging and digital health, quantitative imaging and assessment methodology development.

Analysis Tools and Techniques

European Imaging Biomarkers Alliance (EIBALL) - Biomarkers Inventory

By AAD van der LUGT, MD, PhD

In 2015, the European Society of Radiology (ESR) formed the European Imaging Biomarkers Alliance (EIBALL) as the European counterpart of QIBA. Historically, medical imaging has been evaluated for presence or absence of disease. In the last decades, we have seen an increase in quantitative information extracted from medical imaging. First, in the preclinical and clinical research domain, in which imaging markers have been used as a proxy for biological markers. In a later phase measurement, these imaging biomarkers have slowly been translated to the clinical domain.

It has become clear that measurement of imaging biomarkers is influenced by many technological and biological parameters, resulting in tremendous variation, which makes the use of these biomarkers in research problematic and in clinical practice very challenging. QIBA and EIBALL have both been formed to tackle this problem and to promote the path towards harmonisation in image acquisition and analysis but also towards more consensus in the methodology in evaluating the accuracy of the measurements.

Nevertheless, EIBALL feels that the problems and potential solutions are not yet widely known within our community. As QIBA has already developed a solid structure for the development of biomarker profiles, EIBALL has chosen to support this program by stimulating European experts to participate in the different biomarker committees.

In addition, EIBALL sees a clear role for itself in creating more awareness within the European Imaging community for imaging biomarkers. To this end, we publish position papers and organize educational sessions at ESR and subspecialty societies. A specific task we have executed for several years is the development of a biomarkers inventory.

Biomarkers Inventory

The biomarkers inventory is designed to provide a reference for clinicians and researchers such that these biomarkers can be incorporated into clinical trials and to start building an evidence base.

The inventory is subdivided across the different organ systems and includes both oncological and non-oncological biomarkers. At the start, a template has been drafted indicating the information needed for the inventory. Crucial information is the name of the biomarkers, units of measurement, acquisition modality, data acquisition requirements, how the measurement is performed (manual measurement or drawing a region of interest, or with an automated algorithm), indication for use (diagnostic, predictive, treatment evaluation), status (established or in development) and the available evidence.

The inventory has been developed by EIBALL committee members in close collaboration with the European subspecialty societies. For example, the list of cardiovascular biomarkers was developed with the European Society of Cardiovascular Radiology. In most cases, the subspecialty society involved several members of their research committee in the listing of relevant biomarkers and the collection of evidence. In the oncological imaging domain, EIBALL has sought a collaboration with the European Organisation for Research and Treatment of Cancer (EORTC). The final list was approved by the EIBALL subcommittee and subsequently published on the website.

The current inventory contains an overview of breast, liver, pancreatic, prostate, kidney, gynaecological, paediatric, and cardiovascular imaging biomarkers. It has a focus on CT and MRI-based biomarkers. We have plans to gradually expand the inventory with new topics and biomarkers extracted from other imaging modalities. It remains challenging to update the inventory regularly with new insights and evidence. Finally, we hope to crosslink to existing QIBA biomarker Profiles.

In 2022, EIBALL started to promote the biomarkers inventory in order to enable the use in clinical trials and to further support the evidence of those imaging biomarkers for its final use in clinical care.

The EIBALL committee is open to remarks, comments, suggestions, and support to improve the quality and use of the biomarkers inventory.

Aad van der Lugt, MD, PhD

Aad van der Lugt is chair and professor of Radiology & Nuclear Medicine at the Erasmus MC, University Medical Center Rotterdam, the Netherlands. His research focuses on vascular imaging (CTA/MRA) with emphasis on the characterization of atherosclerotic disease in the carotid artery with ultrasound, CT, and MRI and on acute stroke treatment. He has been co-PI of the MR CLEAN trial, a landmark study that changes the treatment of ischemic stroke worldwide. He is cofounder of the European Population Imaging Infrastructure. He is the delegate for the Netherlands on the Euro-Bioimaging Board, member of the research Committee of the European Society of Radiology and chair of the European Imaging Biomarkers Alliance (EIBALL), a subcommittee of the European Society of Radiology.

The Academy and QIBA Announce Inaugural Fellowship Recipients:

Aligned missions enable unique opportunity for collaboration.

Pictured from left to right: *Drs. Caroline Chung, Timothy J. Hall, Shanshan Jiang, Ashwin Parihar, and Gudrun Zahlmann during the 2022 Quantitative Imaging Symposium: Sponsored by QIBA*

Photo Credit: *Oscar Einzig, Oscar & Associates, official photographer for RSNA 2022*

The Quantitative Imaging Biomarkers Alliance (QIBA) and the Academy for Radiology & Biomedical Imaging Research have announced the recipients of the inaugural Academy Council of Early Career Investigators in Imaging

(CECI^2) QIBA Fellowship: Shanshan Jiang, MD, PhD, and Ashwin Singh Parihar, MD.

This fellowship will offer these early career investigators the opportunity to engage with some of our communities' experts in the field of quantitative imaging and will provide them an opportunity to receive mentorship from QIBA authorities, learn from and contribute to the activities of a specific Biomarker Committee, and help build a social media presence to raise awareness of QIBA.

Dr. Jiang is a member of the CECI^2 Class of 2020-21 and an assistant professor of radiology at Johns Hopkins University in Baltimore. Her research focuses on developing and applying novel MRI methodologies to neurological diseases.

Dr. Parihar is a member of the CECI^2 Class of 2022 and an instructor in radiology at the Mallinckrodt Institute of Radiology at the Washington University School of Medicine in St. Louis. His research focuses on theranostics, nuclear medicine, and oncologic imaging.

This fellowship opportunity was specifically extended to members of the Academy's CECI^2 Council, which was formed in 2014 to recognize the achievements of researchers who are in the early phases of their careers and engage them in advocacy for research funding.

Questions about CECI^2 can be directed to Casey Cappelletti, ccappelletti@acadrad.org.

For More Information:

Learn more about QIBA.

Learn more about The Academy.

Learn more about the Academy's CECI^2 Council.

Announcement from the European Imaging Biomarkers Alliance (EIBALL)

As discussed in Dr. van der Lugt's article, the ESR EIBALL Subcommittee Biomarkers Inventory is designed to provide a reference for researchers and trialists so that these biomarkers can be incorporated into clinical trials.

This inventory (provided with help from QIBA, ESCR, ESGAR, ESHNR, ESMEMB, ESPR, ESUR and EUSOBI) provides evidence for biomarker use in radiological trials.

EIBALL subcommittee members {partnered with QIBA representatives on the EIBALL Subcommittee} deployed the inventory working with specialist European societies to refine input and expand the resource. Workshops and webinars on biomarkers will be held in the coming year and a dedicated session is planned for the European Congress of Radiology 2023.

QIBA Acknowledgments Page

QIBA gratefully acknowledges all volunteers who have helped advance quantitative imaging throughout the medical community. We recognize those that have made significant contributions over the past year, especially in areas of Profile development, implementation, metrology and various advisory roles. Please click to see the list of 2022 QIBA Acknowledgements. Thank you for your contributions!

QIBA Activities

QIBA Biomarker Committees are open to all interested persons. Meeting summaries, the *QIBA Newsletter* and other documents are available on the

QIBA website RSNA.org/QIBA and wiki http://qibawiki.rsna.org/.

QIBA Resources:

- About QIBA
- QIBA Webpage
- QIBA Wiki
- QIBA Biomarker Committees
- QIBA Organization Chart
- QIBA LinkedIn page
- QIBA Twitter page
- QIBA Videos

Please contact qiba@rsna.org for more information. We welcome your participation.

QIBA and QI/Imaging Biomarkers in the Literature

Please note that the list of references has been migrated to EndNote. To obtain access to the RSNA EndNote citations, please send an email request to: qiba@rsna.org.

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