

QIBA Musculoskeletal (MSK) Biomarker Committee (BC) Call

Tuesday, April 23, 2019 at 10 AM CT

Call Summary

In attendance

Xiaojuan Li, PhD (Co-Chair)

Thomas Link, MD, PhD (Co-Chair)

Michael Boss, PhD

Angie Botto-van Bemden, PhD

Robert Boutin, MD

Majid Chalian, MD

Ali Guermazi, MD, PhD

Peter Hardy, PhD

Leon Lenchik, MD

Nancy Obuchowski, PhD

Yuxi Pang, PhD

Rob Peters, PhD

Ramya Srinivasan, MD

Cory Wyatt, PhD

RSNA

Joe Koudelik

Susan Stanfa

Moderator: Dr. Link

Review FDA Draft Guidance – Quantitative Imaging (Dr. Botto-van Bemden, Arthritis Foundation)

- “Technical Performance Assessment of Quantitative Imaging in Device Premarket Submissions: Draft Guidance for Industry and Food and Drug Administration Staff” was discussed; specific text was highlighted
- Brief discussion occurred on a couple of concepts in the “Background” section:
 - Relaxometry (T1 or T2 values) in MR
 - Systematic errors and random variation
- III. Scope:
 - “Depending on the intended use of a device, assessment of technical performance alone may not be sufficient and clinical validation may be necessary”
 - “This document is not intended to provide comprehensive guidance on the types of scientific evidence needed to assess the technical performance...”
 - Discussion regarding reproducibility and parameters
 - Using pain for clinical evaluation was deemed a soft and subjective parameter
 - Cartilage structure and change over time may be sufficient
 - MR-based measurements to be defined
- IV. Definitions:
 - It was confirmed that the language in the document does align with QIBA terminology and meaning, as claimed
 - “Bias” (as opposed to “accuracy”) is the proper metrology term that is referred to in QIBA Profiles as the systematic difference between a quantitative imaging value made on the same object and its true value (ground truth)
 - If true value (ground truth) is unknown, then bias cannot be evaluated
 - Phantom usage was identified as a method of establishing ground truth; it was deemed difficult to ascertain in vivo
 - Many QIBA groups use a phantom and longitudinal Claims to measure change between two time points
 - Current clinical validation would involve a longitudinal study of pain, structure & change of cartilage between two time points; a Claim based on change must be identified
- V. Potential Sources of Measurement Error
 - Normal variability vs. true sources of error (variability) need to be identified, including susceptibility artifacts

- In the MSK Profile, potential sources of measurement error (e.g., differences in temperature of the phantom) were discussed and guidance was provided on controlling for variables
- “Patient characteristics” was noted in the FDA paper as a major source of error
- Some sources were not applicable to MSK BC group
- VI. Information to Include in a Premarket Submission
 - B. Technical Performance Assessment was briefly discussed
- The draft guidance document was distributed for comment purposes only (not a final document)
- MSK members were encouraged to submit comments and suggestions based on their perspective and experience within 60 days of publication in the *Federal Register* of the notice; the document was issued on April 19

MSK Profile (Dr. Link)

- Profile review continued, and remaining work was assessed
- There was discussion regarding the longitudinal Claims (no ground truth is known)
- Final results and data from Dr. Li’s Arthritis Foundation study to be presented during ISMRM
 - Another 1 – 2 months is needed before the manuscript will be submitted for publication
 - The Profile is currently based only upon data found in the literature; the Arthritis Foundation study data will strengthen the Profile by providing data from different MRI machines and vendors
 - Dr. Li to present study results on the May 28 MSK BC t-con
 - The MSK BC will be the first QIBA group to include reference values in its Profile; they will be added to Section 3.8: Data Interpretation
- Once Section 4: Assessment Procedures has been finalized, the information will be circulated
- Appendices need to be completed

Discussion on Potential White Papers

- MSK BC may consider identifying where current literature is lacking and what the barriers to using a cross-sectional Claim are
 - Need to identify groundwork necessary to pursue cross-sectional claims
- Discussion regarding publications to which papers should be submitted
 - When work is completed, there should be a better sense of whether to send it to an MR-related publication or a broader journal, like *Radiology*, statistical journals, modality-specific journals like *JMRI*
- Caution to not use other articles as template, as needs differ across biomarkers

OARSI imaging discussion group meeting in Toronto during OARSI 2019 World Congress May 2 – 5

- Reminder that the MSK discussion group meeting is on the Saturday, May 4 at 6 or 6:30pm

Next Call: Tuesday, May 28, 2019 at 10 AM CT [4th Tuesdays of each month]

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