# QIBA Musculoskeletal (MSK) Biomarker Committee (BC) Call

Tuesday, January 26, 2021 at 10 a.m. CT

*Call Summary*

| **In attendance** | | | **RSNA** |
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| *Xiaojuan Li, PhD (Co-chair)* | Majid Chalian, MD | Kecheng Liu, PhD, MBA | Joe Koudelik |
| *Thomas Link, MD, PhD (Co-Chair)* | Ruud de Boer, PhD | Annelise Malkus, PhD | Susan Stanfa |
| Michael Boss, PhD | Maggie Fung, MEng | Nancy Obuchowski, PhD | |
| Angie Botto-van Bemden, PhD | Ali Guermazi, MD, PhD | Yuxi Pang, PhD | |
| Robert Boutin, MD | Peter Hardy, PhD | Cory Wyatt, PhD | |
| John Carrino, MD, MPH | Jason Kim, PhD | | |

## Update on Special Report for *Radiology* Manuscript (Dr. Chalian)

- The manuscript has received major revisions by *Radiology* and the authors are currently working on the revisions.
- As soon as the paper is published, it will be added to the QIBA EndNote literature collection

## Multisite/multivendor grant and phantom development (Dr. Li)

- Dr. Li received R01 funding to perform a multi-center standardization study, which will help advance the Profile through technical and claim confirmation
- Dr. Li has been working with Drs. Mirowski (Verellium, LLC) and Keenan (NIST) on phantom development
    - The mechanical design of a new MSK phantom has been completed
    - The team is working on finalizing the vial solution and the timeline for phantom delivery will be shared with MSK BC members

## MSK Profile – Review Public Comments (Dr. Link)

- The public comment period closed on October 29, 2020, and MSK BC members have been using the **MSK public comment resolution Google Sheet** to document how feedback is addressed
- Forty-one of the 113 comments received have already been addressed on previous calls

*Comments from Frank W. Roemer, MD (University of Erlangen-Nuremberg)*

- Section 3.7: Image Data Analysis - commenter agreed that the segmentation to be overlaid to T1ρ and T2 maps is ideal, but in reality, this is a very challenging task that needs co-registration particularly as the 3D GRE images have much higher resolution/thinner slices compared to the T2 or T1ρ images
    - Suggestion to exchange “shall” for “ideally”
    - The MSK BC recommends DESS/MENSA; MAPSS should not be used for segmentation
- Section 3.7 (Figure 2) - The image marking for lateral femur will be redrawn
- Section 3.8: Image Data Interpretation (Figure 4) – an issue was noted re: normative values grouped for KL0 and 1; suggestion to present and aim at displaying KL0 and 1 as separate entities
    - The MSK BC clarified that the figure refers to WORMS 0 and 1, not KL 0 and 1
- Section 4.1.3: Assessment Procedure - Imaging Analysis: suggestion to explore additional data extraction beyond T2 and T1ρ values
    - MSK BC to consider whether to include texture analysis of cartilage T2 maps and will add references and additional discussion of problems

*Comments from Gregory Chang, MD (NYU Langone and former ISMRM MSK Study Group Chair)*

- Section 3.7.1: Image Data Analysis (Discussion) - suggestion to accommodate a variety of Profile user types by providing a short list of software that can perform image analysis
    - MSK BC stated that a product for cartilage segmentation is not currently available from manufacturers and will note this in this discussion section; additional information and studies will also be included
    - The Profile will be modified once manufacturers provide this as a commercial product
- Section 3.6. Image Data Acquisition Discussion – suggestion to add a recommendation for the number of echoes
    - For reproducible measurement of mono-exponential decay components, a minimum of four echoes will be recommended
    - While reproducibility for mono-exponential fitting would be good with four echoes, more echoes may provide in-depth information about cartilage degradation (e.g., providing more information about fast decaying components by using bi-exponential fitting) and introduce longer acquisition time
    - Optimized number of echoes and optimized echo spacing for specific questions are active areas of research
- Section 3.2: Installation - rheumatologists and orthopedists may be unaware that even different model 3T scanners from the same vendor could demonstrate variation in measurements, and noting this was suggested
    - MSK BC will also specify that variability occurs in the following situations as well: same vendor and field strength scanners, different models from the same vendor, and same model but different machines

*Comments from Flavia M. Cicuttini, MSc, MBBS, FRACP, PhD (Monash University and OARSI board member)*

- The document contains a good general approach and guidelines; however, it may need to be acknowledged that if there is the need to examine change, groups who do work on the same machine, using a standard protocol and measurement approach may be able to assess the state of the cartilage and detect clinically significant changes using modifications of the approach presented
    - MSK BC noted that the Claim is longitudinal, and the existing Profile discussion will be expanded to include modified approaches
- Section 2: Clinical Context and Claims (Important Considerations and Limitations) – The Claim requires focus on subjects with less severe cartilage loss; it was noted that a Kellgren-Lawrence (KL) score of 2 can be associated with significant (advanced) cartilage loss and evidence needs to be provided that the Claim is valid in the setting of KL2
    - OAI data are available and studies that demonstrate cartilage damage in KL2 will be cited (references need to be added in the discussion section)
- Section 2 (Discussion) - if cartilage composition changes size beyond 11-14% limits, one can be 95% confident there has been a true change in the cartilage composition
    - Clarification needed re: the difference between identifying true change in an individual compared to average change that may be detected across two groups, e.g., in a clinical trial
    - A biostatistician would be needed, and the clinical trial issue will be addressed re: detection of smaller changes; Dr. Obuchowski provided clarification

*Comments from Samuel A. Einstein, PhD (York Hospital)*

- Section 2: Clinical Context and Claims (Important Considerations and Limitations) - the studies supporting the Claims are based on phantoms and a few healthy volunteers (data in references are limited), yet the Claims seem to be applied to the clinic
    - Larger studies are underway, e.g., the multisite/multivendor and phantom development funded by the R01 grant; the data justifying these Claims in a clinical setting will be incorporated into the Profile

- Section 3.2: Installation - additional requirements needed for hardware specifications such as for the RF amplifier and gradient performance
    - No specific requirements are necessary because it varies from scanner to scanner and the proposed T1rho and T2 sequence lack additional requirements beyond the current standard clinical MR scanners
    - If the sequence runs on a scanner there is no need to specify RF and gradient details
- Section 3.3.1: Periodic QA (Discussion) - partial pressure of oxygen changes have a significant effect on T2 if bacteria start growing in the agarose when stored at room temperature
    - This was deemed a viable concern, which will be acknowledged in the Profile
    - Dr. Li to request input from Dr. Keenan (NIST) and Dr. Mirowski (Verellium) for a detailed response; the R01 grant proposed to check the phantom stability during the study period
    - Dr. Boss (former NIST staff) concurred that was unaware of any agarose phantoms that do not eventually degrade
        - It was also noted that NIST had very limited experience with agarose, typically using other (more stable) fill solutions with 5-year estimated stability
        - The phantoms developed during his tenure were not intended for long-term storage
- 3.3.2: Periodic QA (Specification Table) – suggestion to add ACR definition of MR scientist as a potential physicist qualification; “physicist” will appear in place of “MRI scientist” in the Stage 2: Consensus Profile draft
- Dr. Einstein’s comments will continue being addressed during the February 23 MSK BC Meeting

**Next Call:** Tuesday, February 23, 2021 at 10 a.m. CT [4th Tuesdays of each month]

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