QIBA MRE Biomarker Committee (BC) Call

Monday, April 1, 2019 at 3 PM CT
Call Summary

Participants			**RSNA**
Patricia Cole, PhD, MD (Co-Chair)	Shintari Ichikawa, MD	Suraj Serai, PhD	Joe Koudelik
Richard Ehman, MD (Co-Chair)	M. Rehan Khan, MD	Claude Sirlin, MD	Susan Stanfa
Edward Ashton, PhD	Michael Middleton, MD	Mikio Suga, PhD	
Michael Boss, PhD	Nancy Obuchowski, PhD	Sudhakar Venkatesh, MD	
Anil Chauhan, MD	Kay Pepin, PhD		

Moderator: Dr. Ehman

Review of Previous Call Summary

- The November 20, 2018 call summary from the last MRE BC meeting was approved

Profile Review

- The latest Profile version containing proposed revisions was circulated in advance of this Apr. 1 t-con
- Dr. Ehman reviewed and provided rationale for changes that were made to the Profile
    - Change Log was reviewed:
        - Grammar and text clarifications were provided
        - Latest Profile draft to be retitled to: Stage 2 Consensus Profile
        - Appendices A, B and C were added and vendor-specific scanning protocols in Appendix D were updated
    - Open Issues:
        - Discussion on whether the Profile should contain a requirement that patients need to be scanned on the same MRI scanner with the same software for follow-up exams; inconsistency identified between 3.5.1 and 4.1.3 and needs clarification
        - Consensus that the link to web-based material regarding MR technologist training in 3.5.2 (Figure 1) to be removed; issue was resolved
        - Discussion to continue on whether the proposed limit of 500 pixels per exam (rather than 500 pixels per slice) based on a simulation study performed by MRE BC members should be adopted into the Profile
        - Drs. Obuchowski and Pepin to draft rationale behind the change of the wCV number from 19% to 22% in Appendix B: Background Information for the Claim
        - Appendix C: Conventions and Definitions was added

Region of Interest (ROI) Minimum Size

- In the absence of formal research data, the MRE BC originally deemed the figure of 2,000 pixels (500 x 4 slices) acceptable
    - There was speculation on whether a smaller number would work for clinical trial
    - A repeatability study to examine a large amount of back data to determine where the minimal pixel cut off was proposed, e.g. 500 vs. 700 vs. 900 pixels

- Dr. Middleton gave a presentation on “Assessment of Liver MR Elastography Analyzability,” based on a study he led in collaboration with Liver Imaging Group (UCSD Dept. of Radiology), Gilead Sciences Incorporated and Mayo Clinic (Rochester, MN)

- Purpose: To assess the analyzability criteria of liver MRE used in clinical trials through applying random and concentric pixel removal simulations
- Methods were summarized: cases containing large ROIs were examined and the pixel threshold was adjusted lower while maintaining image quality
- Statistical analysis was performed in MATLAB and was summarized
- UCSD multi-center clinical trials use the following pixels cutoffs:
  - >2000 px total over 4 slices = "analyzable"
  - 700-2000 px total over 4 slices = "marginally analyzable"
  - <700 px total over 4 slices = "not analyzable"

- Discussion:
  - MRE is used as a biomarker for the diagnosis and staging of fibrosis
  - Larger number of pixels increase MRE analyzability regardless of simulation method
  - Range for random method, and range and bias for concentric method both grossly within clinical acceptable limits

- Conclusion: The ranges of simulated liver stiffness for all three pixel cutoffs were small, hence, at a proof-of-concept level, subject to validation in larger cohorts, the MRE liver stiffness analyzability cutoffs were reasonable
- Dr. Middleton provided his recommendations for the Profile:
  - The study found that 2,000 pixels (500 x 4 slices) was unnecessarily high and could be reduced
  - Current Profile wording should be revised to: "total of 500 pixels over all 4 slices (125 pixels per slice)"
  - An additional study was suggested (e.g., trying other techniques/sampling methods)
  - Discussion to continue during an upcoming MRE call

- Experience using the Profile checklist
  - First and second drafts completed by Dr. Pepin
  - Initial feedback by Dr. Khan on practicality/feasibility was circulated prior to the April 1, 2019 MRE BC call
    - The only issue identified was the suggested calculation method for liver stiffness; the majority of radiologists calculate "mean," not "weighted-mean"; some user push-back expected
    - Discussion to be continued during the next MRE call (to be scheduled)

- Discussion on groundwork proposals requested by the Sustainability Implementation Group (SIG), due April 15
  - The SIG is working on a letter to pharma and ICROs to find additional means of financial support (previously provided by NIBIB)
  - The SIG has requested that all QIBA modalities provide up to three groundwork projects that would help advance the current Profiles
  - Examples of projects include: test-retest studies, development of physical phantoms or digital reference objects (DROs), or generation of software (i.e., analysis packages)
  - Guidelines for project concept submissions are as follows:
    - Project descriptions (primary goals and objectives) to be brief in length (~1/2 page; 3 – 4 sentences) and explain benefits to pharmas/ICROs
    - Include name(s) of project PI(s)
    - Amount of requested funding is dependent upon the size of project and should be realistic

        - Projects that would advance Profiles to Stage 3: Technical Confirmation or higher, as well as basic phantom studies required for pre-Stage 1 Profile efforts would be appropriate

    - RSNA staff to circulate the description template and MR CC co-chair contact info
    - Discussion regarding proposed projects from MRE BC members
        - Suggestion for a study to determine agreement between weighted average and straight average ROIs and combine it with the pixel study so that it could benefit pharmaceutical clinical trials
        - Drs. Sirlin and Middleton to work offline and submit a project proposal to further study the minimal ROI pixel values needed for clinical trials and clinical care

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