QIBA Proton Density Fat Fraction Biomarker Committee (PDFF BC) Call

Thursday, January 7, 2021 at 3 p.m. (CT)

Call Summary

Participants			**RSNA**
Takeshi Yokoo, MD, PhD (Co-chair)	Thomas Chenevert, PhD	Nancy Obuchowski, PhD	Joe Koudelik
Scott Reeder, MD, PhD (Co-chair)	Gavin Hamilton, PhD	Jonathan Riek, PhD	Susan Stanfa
Mustafa Bashir, MD	Diego Hernando, PhD	Manohar Roda, MD	
Jean Brittain, PhD			

Review of Previous Call Summary

- The 11.05.2020 call summary was approved as presented

Discussion focused on Conformance Procedures in the "Open Issues" section of the Profile

- PDFF BC feedback provided since the November 5th meeting was reviewed
- Conformance testing will be required for vendors developing a new PDFF technique
    - Conformance requirement details based on the round-robin study still needed in the Profile
- For PDFF products that have been vetted by the vendors, the users will not be required to repeat conformance testing, as long as the pulse sequences are used according to the vendor's specifications, unless otherwise recommended by PDFF BC
- Conformance testing to include linearity and bias testing using a validated triglyceride based PDFF phantom, covering a typical range of PDFF values (PDFF=0 is required; ≥5 vials minimum up to 40% or above)
    - It was noted that if biochemical analysis is needed to measure PDFF in the tissue in order to prove linearity and bias, more consideration re: whether a phantom should be required is needed
    - If a clinical trial uses a phantom as part of QA, techniques intended to work in human subjects also need to work in a phantom
    - Concern that the technique is being forced to conform to a requirement based on a method that requires validation
    - It was noted that the Calimetrix phantom could work with some techniques, but not all
    - Conformance testing could be done with an external reference standard
    - The method must work with the user's reference scanner
    - It was determined that bias testing would be done against an independent non-MR reference standard of triglyceride and water hydrogen (proton) concentration (per Dr. Hu's paper), which may include biopsy with biochemical extraction analysis and known fat fraction values calculated based on proton-density (i.e., PDFF), rather than some other fat fraction values such as volume- or weight-based
        - Referenced: Hu HH, Li Y, Nagy TR, Goran MI, Nayak KS. **Quantification of Absolute Fat Mass by Magnetic Resonance Imaging: A Validation Study against Chemical Analysis**. (PMID: 23204926)
    - It was discussed that if a manufacturer conducts conformance testing, a clear reporting of the method is needed to ensure that a standard user will have the same results if they follow the same procedure, i.e., validation studies must be transparent and described in a manner that is reproducible
- Conformance testing to include a repeatability study in human subjects
    - If repeatability coefficient is set too low, a very large sample size would be needed; suggestion to increase it to 5%
    - Per Dr. Obuchowski, sample size of the test-retest study should be at least 35 to be sufficient such that the upper bound of the 95% confidence interval of the repeatability coefficient (PMID: 29298603)

- Dr. Yokoo to rerun his data analysis to determine the upper bound of the 95% confidence interval

- Other recons (R2*, B0, IP, OP, W, F) and how they are used, to be discussed during an upcoming meeting
- Discussion re: how PDFF reporting should be done
  - Representative sections of the liver
  - Multiple ROIs or areas of segmentation in both lobes, avoiding vessels, bile ducts, lesions, or artifacts
  - ROIs to be co-registered as much as possible in longitudinal studies
  - Minimum of two ROIs, including at least one in the left lobe and one in the right, with a minimum size of 4cm^2
  - Segmentation of the liver still requires general guidelines
  - Median has been deemed acceptable; discussion on this to be continued during upcoming call

Next QIBA PDFF BC call: Thursday, February 4, 2021 at 3 p.m. (CT)

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