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

Thursday, March 1, 2018 at 3 PM (CT)

Call Summary

Participants			**RSNA**
Scott Reeder, MD, PhD (Co-chair)	Gavin Hamilton, PhD	Nancy Obuchowski, PhD	Joe Koudelik
Takeshi Yokoo, MD, PhD (Co-chair)	Michael Middleton, MD	Elif Sikoglu, PhD	Susan Stanfa
Mustafa Bashir, MD			

Review of Previous Call Summary

- The 02.01.2018 call summary was approved as presented

Profile

- We discussed what would be needed for a new PDFF MRI method to demonstrate QIBA-conformance in terms of variability and bias
    - To demonstrate QIBA conformance to the Longitudinal Claim in the PDFF Profile, test-retest repeatability measurements in human subjects would be needed to confirm that variability is within a defined, acceptable range, with 95% confidence
    - The "acceptable range" of repeatability coefficient should be similar to what was shown in meta-analysis; details to be discussed
    - Bias is more complicated than variability; if there were a perfect reference standard for PDFF, a cross-sectional bias Claim could be made
        - We discussed the use of spectroscopy (MRS) or previously-validated MRI methods to demonstrate Profile conformance
        - Simulations by Dr. Obuchowski showed that if the reference standard contain variability (i.e. imperfect reference standard, like MRS or previously-validated MRI), there is an unacceptably high probability of misclassifying new PDFF methods as Profile-conformant
        - Developing a new standardized physical phantom to demonstrate conformance may be sufficient; more discussion is needed regarding such a reference standard

Repeatability

- In vivo conformance tests for repeatability needs to include sufficient number of patients across the range of clinically-relevant PDFF range (from 0% to approx. 30%)
    - Conformance test needs to demonstrate that the standard deviation is constant across the full range of clinically-relevant PDFF values – i.e. conformance limited to PDFF 0-5% range is not acceptable
    - Dr. Obuchowski to provide guidance for study design and sample size determination

Bias

- Fat-water phantoms with known PDFF values using phantom-specific recon protocol should be required but may not be sufficient
    - We discussed whether human testing for bias conformance is needed or phantom only is sufficient.
    - Some members felt strongly that some sort of human testing is needed in addition to phantom
    - An acceptable clinical "reference standard" such as in vivo spectroscopy or previously-validated MRI (an imperfect reference standard, but may be an acceptable reference standard for bias)?
    - MR spectroscopy or previously-validated MRI may have bias from true PDFF because it is an experimental instrument; it is an imperfect reference standard
    - When an imperfect reference standard is used as a bias reference standard, the percent of errors in determining QIBA conformance is too high (see above comments re Simulation results)
    - Therefore, the group is inclined to use phantom for formal bias conformance testing, and use spectroscopy or previously-validated MRI to test linearity in vivo. We can require the new PDFF technique to have a linear correlation coefficient above certain value against spectroscopy or previously-validated MRI.

Standard Reference Object for Bias (i.e. Phantom)

- Would need to conduct additional, round-robin multivendor study to determine bias (acquisition and reconstruction for each scanner needed), with vendor-specific recons
- Phantoms may help identify imaging sites that implement the Profile correctly, i.e., conformant sites
- Specs for phantom development to be provided
- Suggestion to collaborate with Calimetrix, as it has the only commercial fat phantom on the market
    - Discussion on how to fund the Calimetrix phantom
    - Discussion of how to address possible conflict of interest for Dr. Reeder (Co-founder of Calimetrix)
    - Disclaimer will be drafted to acknowledge conflict of interest and explain how the issue will be navigated, i.e.:
        - Some boundary between Dr. Reeder and this project needed
        - Data cannot be housed at the University of Wisconsin-Madison
        - Data may be stored and analyzed by an independent party
- Dr. Reeder to discuss this possible collaboration with Calimetrix colleagues
- Additional discussion needed regarding the range of fat fractions for phantoms

- Drs. Yokoo and Obuchowski to collaborate on the statistical issues on the repeatability and linearity testing

Next call: Thursday, April 5, 2018 at 3 PM CT

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