QIBA Proton Density Fat Fraction Biomarker Committee (PDFF BC) Update Call
Thursday, March 1, 2018 at 3 PM (CT)

Call Summary

Participants

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

RSNA

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

RSNA Staff attempt to identify and capture all committee members participating on WebEx calls. However, if multiple callers join simultaneously or call in without logging on to the WebEx, identification is not possible. Call participants are welcome to contact RSNA staff at QIBA@RSNA.org if their attendance is not reflected on the call summaries.