Proton-Density Fat Fraction Biomarker Committee Progress Report 2017

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Organizational Structure Update

Dr. Claude Sirlin (University of California at San Diego, CA) announced at the June 1st Biomarker Committee meeting, that he had stepped down as co-chair. Dr. Takeshi Yokoo (UT Southwestern, Dallas, TX) was appointed to replace Dr. Sirlin and joined Dr. Scott Reeder (University of Wisconsin at Madison, WI) to co-chair the Committee. We would like to thank Dr. Sirlin for his leadership during his term.

On May 17-18th, 2017, Dr. Reeder and Dr. Yokoo attended QIBA Annual Meeting at Alexandria, VA.

Profile Development Status

Initial drafting of the PDFF profile began in July 2017, led by a core profile writing group of 7 members. Each part of the profile document template was assigned to one or two core writing members. The initial draft of the profile segments was turned in by Sept. 2017. Segments are currently being combined into a single master document.

Informed by groundwork publications and summarized in recent meta-analysis (see "groundwork project status/update", right), the draft profile claims are:

Clinical Context

PDFF by Magnetic Resonance Imaging (MRI) can be used to quantify the hepatic fat content for diagnosis, severity grading, disease monitoring, or treatment response assessment on a per-subject basis, in those with suspected or known hepatic steatosis (a.k.a. fatty liver) of any etiology.

Claim 1 (cross-sectional)

For a measured PDFF of X, a 95% confidence interval for the true PDFF value is X ± 5%.

Claim 2 (longitudinal)

A measured change in PDFF of ±5% or more indicates that a true change has occurred with ≥95% confidence.

Claim 3 (longitudinal)

For a measured change in PDFF of X%, a 95% confidence interval for the true change is [X-5%, X+5%].

Profile Development Status (cont'd)

The following open issues are actively discussed at monthly teleconferences:

- Conformance procedures – see below
- Standardization of patient/subject preparation
- Standardization of PDFF reporting procedures
- Compilation of manufacturer/model specific protocol recommendations

We aim to complete drafting and release the document for public comment in Q1 2018.

Conformance Procedure Update

Open issues for conformance procedures for linearity, bias, repeatability, and reproducibility:

❑ For technical development and validation (e.g. manufacturer), require:

- Phantom-only or "phantom + human" study?
- Accept equivalence test against other validated PDFF methods?
- Recommend MR spectroscopy as reference standard for human study?
- Require human repeatability study

❑ For a new performance site (clinical care or clinical research):

- A phantom-only study sufficient for linearity and bias?
- Methods to assess repeatability in human subjects?
  1. How many subjects needed?
  2. Range of PDFF?

❑ PDFF phantoms

- Required features (e.g. PDFF range, relaxation parameters)?
- Recommend/require certain design and construction?
- Standardize across sites?
- Ensure availability at all potential sites

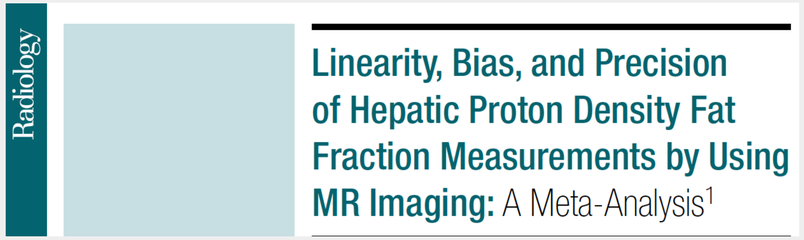
Profile Impact / Implications

The profile is intended to provide a performance benchmark for:

- New MRI-based PDFF pulse sequence and/or reconstruction product development and validation by industry (e.g., scanner manufacturers) or nonprofit organizations (e.g., research institutions).
- Performance sites participating in multicenter research studies
- New imaging centers starting MRI PDFF clinical service
- Reference for quality assessment, quality control, and troubleshooting

Groundwork Project Status/Update

The PDFF Biomarker Committee has recently published a meta-analysis of 23 liver PDFF groundwork studies that evaluated MRI-PDFF linearity, bias, repeatability and reproducibility.



Yokoo T, Serai SD, Pirasteh A, Bashir MR, Hamilton G, Hernando D, Hu HH, Hetterich H, Kühn JP, Kukuk GM, Loomba R, Middleton MS, Obuchowski NA, Song JS, Tang A, Wu X, Reeder SB, Sirlin CB; RSNA-QIBA Proton Density Fat Fraction Committee. Radiology. 2017 Sep 11:170550. [Epub ahead of print] PMID: 28892458

The meta-analysis of approximately 17,000 MRI-PDFF measurements in ~2,000 subjects concluded that "*MR imaging-PDFF has excellent linearity, bias, and precision across different field strengths, imager manufacturers, and reconstruction methods.*"

The estimated 95% limits of agreement between MRI and MR spectroscopy (reference) was ±4%, and 95% confidence interval for reproducibility was ±4%. These estimates were used to inform the profile claims.

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