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PDF - Biomarker of Hepatic Steatosis

Proton-density fat fraction (PDDF) is a quantitative imaging biomarker (QB) of hepatic triglyceride concentration that can be measured using magnetic resonance imaging (MRI) or spectroscopy (MRS). PDDF is a fundamental property of tissue and represents the ratio of MR-visible triglyceride protons to the sum of triglyceride and water protons. As the only standardized QB for hepatic steatosis, PDDF holds promise for multi-center research studies and in clinical practice. Compelling published data indicate that MRI-PDDF has high linearity and negligible bias against MRS as the reference, as well as excellent test-test reliability. In comparison there are limited data on the performance of PDDF in multi-center or clinical settings where individuals may undergo MRS-PDDF measurements on different scanners of different vendors, field strengths, and possibly using different reconstruction algorithms.

Working Criteria for PDDF by MRI

PDDF-linearity bias study: liver "fat fraction" imaging AND spectroscopy "magnetic resonance" NOT Review [Publication Type]

Fig 1 (right) shows excellent linearity of MRI-PDDF across entire observed MRS-PDDF range of 0.0 - 46.2%. The regression intercept did not deviate significantly from 0. The regression slope was<1, but this deviation was 1.3% (by OR=0.025) is unlikely to be significant clinically or in clinical practice. Fig 2 (below) demonstrates that MRI agreed closely with MRS in PDDF measurements, with negligible mean bias. Overall agreements were between approximately ±4%. The vendor, field strength and reconstruction algorithms had small (mostly <2%) impact in bias.

Materials and Methods

A PubMed literature search was performed for primary research articles using the following inclusion criteria:

For linearity/bias study: liver "fat fraction" imaging AND spectroscopy "magnetic resonance" NOT Review [Publication Type]

For precision study: liver "fat fraction" imaging (preferably OR reproducibility or reliability study) "magnetic resonance" NOT Review [Publication Type]

Abstracts, then the full paper, were screened using the following exclusion criteria: secondary analysis of previously published data; not meeting criteria for PDDF; not in vivo human study; no MRS-PDDF (i.e. not-long TR multi-TE SE sequence, for linearity/bias study); no repeated PDDF measurements (for precision study). The authors of the articles meeting all inclusion/exclusion criteria were invited to submit detailed data and reconstruction methods.

For each subject’s MRI PDDF measurements, the following data were recorded in a pooled database:

• Field strength: 1.5 or 3.0T
• Vendor: GE, Siemens, or Philips
• Reconstruction: Magnitude, complex, or hybrid
• Exam number: Repeated exam setup (coil, calibration, etc.)
• Acquisition number: Repeated acquisition with identical exam setup
• Original Index: Region of interest (ROI) label in the liver
• MRI-PDDF (%): Average PDDF within an ROI
• MRS-PDDF (%): Co-localized to MRI ROI, if available

Fig 3 (right) shows excellent precision of MRI-PDDF across the observed PDDF range with repeatability coefficient of 2.9%. Repeatability coefficient incorporates additional sources of variability (field strength, vendor, reconstruction, and exam-setup effects) was 4.3%.

Conclusion

This interim meta-analysis of liver MRI-PDDF data from multiple published studies demonstrated excellent linearity, negligible bias, and high precision across different field strengths, vendors, and reconstruction algorithms.

References


Fig 1: Linearity

slope = 0.959 [0.967, 0.962]
R2 = 0.919
N subjects = 1470
N obs = 2849
N studies = 18

Fig 2: Bias

Fixed Effects Analysis (relative bias to PDDF)
Vendor: GE (base): Siemens ±0.148; Philips ±2.268
Field: 1.5T (base): 1.5T ±0.148
Recon: Mag (base): Complex ±0.360 Hybrid ±1.124

Fig 3: Precision (per-single at ROI)
Repeatability Coefficient (RDC): ±0.821
Repeatability Coefficient (RDC): ±0.821

Per-subject average MRI-PDDF (%)

N subjects = 1645
N obs = 14,305
N studies = 17

Random Effects SD Estimates
Field strength effects
Vendor effects
Exam setup effects

0.024
0.345
0.208

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