Feasibility of Using Deep-learning-based Techniques for Liver Couinaud Segmentation and Proton Density Fat Fraction (PDFF) Estimation - a Pilot Analysis

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Disclosures

**MSM:** Pfizer stockholder; consultant to Median, Novo Nordisk, and Kowa

**UCSD:** clinical, laboratory service, and other agreements and contracts with pharmaceutical companies, CROs, and MR scanner manufacturers.
Background

- MRI-PDFF is a non-invasive biomarker of hepatic steatosis\textsuperscript{1,2,3}
- We know there is geographic variation of MRI-PDFF across the liver\textsuperscript{4}
- Typical analysis involves assessing PDFF values in each of the nine Couinaud segments and reporting a mean value for the entire liver
- ROI placement to assess PDFF assessment requires an experienced analyst, so there is a need for an automated analysis methodology
- Improved analysis methods would also help us better understand variability in the liver

Purpose

- Demonstrate feasibility of using semi-automated deep-learning and imaging analysis techniques to:
  
a. segment the entire liver
  
b. outline the individual Couinaud segments
  
c. exclude major vessels and bile ducts
  
d. explore segmental PDFF variability across the liver
Methods

- **Study design:** Retrospective pilot feasibility analysis
- **Subject selection:** Convenience sample of 27 adults from the NASH CRN FLINT trial\(^5\)
- **Images:** Source and parametric map MRI-PDFF images
- **Reference analysis:** PDFF values determined using conventional methods
- **Semi-automated analysis:**
  - Whole liver segmentation - existing deep-learning tool
  - Couinaud segment annotation - combined analyst-driven technique
- **Statistics:** ICCs; Regression and Bland-Altman plots

Conventional PDFF analysis

- Nine (or fewer) round ROIs were manually placed on source images in each of the 9 Couinaud segments by a data analyst, avoiding major vessels and bile ducts, artifact, lesions, other organs, and the edges of the liver
- ROIs transferred to parametric PDFF maps; PDFF values recorded
- Segmental average PDFF values calculated as mean of 9 PDFFs in that segment
- Whole liver PDFF value calculated as mean of PDFFs of all 9 segments
- Segmental PDFF standard deviations calculated as standard deviation of the 9 PDFF values in that segment
- These values provided the reference values for this analysis
Liver segmentation

- Automated whole liver segmentation - previously-developed convolutional neural network- (CNN)-based tool developed by Dr. Wang⁶

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⁶. Wang et al, abstract entitled "A convolutional neural network-based automated hepatic-fat quantification method in nonalcoholic fatty liver disease, ISMRM Artificial Intelligence Workshop, 2018"
Details of CNN-based methods

- A total of 280 MRI-PDFF exams were identified from datasets from prior studies performed at UCSD\(^6\)
- 240 exams were used for sequential testing and 40 exams were used for validation
- Iterative testing was performed on sequential subsets of the 240-exam test dataset, with validation against the to final 40 cases performed at each iteration, until a target minimum Dice score of 0.80 was obtained
- Final DICE scores ranged from 0.88 to 0.96, mean of 0.93

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6. Wang et al, ISMRM Workshop abstract 2018
Manual annotation of major vessels and falciform ligament to enable drawing of planes between segments (IVC, MHV, RHV shown here)
Annotation of vessels and ducts

- Major branches of major vessels and ducts manually outlined by data analyst
Delineation of Couinaud segments
Segmental and whole liver PDFF

- Python-based custom image analysis tool created by Dr. Wang
- Based on annotated 'points' placed in each major vessel and duct, and on the falciform ligament; and on corrected whole-liver tissue-segmentation created using the CNN-based tool; and on identified major vessels and ducts, Dr. Kang used a custom image analysis tool to:
  a) separate the liver into segments
  b) Subtract the identified major vessels and ducts
  c) Calculate mean PDFF per identified segment
  d) Calculate the mean PDFF per subject
  e) Calculate the PDFF standard deviation of each identified segment
Results

- 27 adult cases analyzed from the FLINT study
- Mean whole-liver PDFF was 16.7% (range: 5.6 to 30.1%); mean whole liver SD was ±4.5% (range: ±2.9 to ±5.8%)
- Segment 8 showed the highest mean PDFF (17.4%) and segment 2 the lowest (15.7%)
- Segment 4b showed the highest mean SD (5.6%) and segment 7 the lowest mean SD (3.5%)
- ICC of whole liver mean PDFF for (automated map PDFF) versus (manual ROI placement method for PDFF) = 0.994 (95% CI: 0.986, 0.997)
Regression: CNN vs. Manual ROIs

27 data points, whole-liver results

\[ y = 0.9971x - 0.0805 \]
Bland-Altman: CNN vs. Manual ROIs

27 data points, whole-liver results

Mean bias = -0.13%; p = 0.082
95% LOA (-0.86%, 0.60%)
SD = 0.37
Discussion - future directions

- Additional cycles of CNN learning with validation in independent datasets to include vessel segmentation
- Expansion to full FLINT and CyNCh datasets
- Comparison to histologic steatosis
- Analysis of confounders
- A new biomarker, or just a more efficient biomarker?
- Use in future studies
Thank you

Note: Corrections were made to slides 7, 8, and 12 on 21 May 2018 (after the presentation) to the references to the abstract by, and to the contributions from Dr. Wang.