Development of an Optimal Continuous Pediatric Fibrosis Score to Assess Severity and Progression of Fibrosis in NAFLD

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ABSTRACT

- Histological staging of NAFLD is essential to determine severity and progression to NASH.
- Fibrosis a key manifestation of progression, assessed by current standardized categorical staging as F0-F4.
- Pediatric histology demonstrates a different pattern and quality of fibrosis in a significant subset of children, not found in adults.
- Pathologists are thus limited by categorical limitations to quantify and qualitate the variations and complexities between the distinct types of steatohepatitis and progression of disease.
- This study presents the utility of an automated morphometric image analysis method of label-free two-photon images to score fibrosis in liver biopsies as a continuous measure.

OBJECTIVES

To develop a continuous pediatric Fibrosis Score for the assessment of fibrosis development in pediatric NASH.

METHODS

- Pediatric fatty liver biopsy slides (N=90) were read by pathologists for standard fibrosis staging.
- Unstained slides from the same scored biopsies were imaged with Genesis2008 2PE and Second Harmonic Generation (SHG) images.
- Image analysis using cloud-based computational methods (FibroNest©, PharmaNest, USA) exploited the SHG images to quantify multiple traits of the collagen phenotype.
- Statistical analysis with ANOVA was conducted to compare pathology staging F0(29), F1(43), F2(10) and F3(7), with calculated composite scores.

RESULTS - Analysis

F0-F1c Progression Scoring (3 phenotypic traits help differentiate F0 from F1c)

Phenotypic Composite Scores correlate with NASH-CRN fibrosis Scoring

CONCLUSIONS

- A continuous pFS calculated by phenotypic image analysis of unstained pediatric liver biopsies correlates with histological staging.
- Development of this automation/technology should permit quantitation of linear changes in fibrosis that may assist in limiting time commitments or sample sizes in clinical trials.
- Demonstrate meaningful continuums in progression/regression.
- This methodology also has the potential to distinguish the two NASH subtypes.
- Classify F0 from F1c, mitigating current limitations of pathology.