Introduction & Aim

The gold standard for assessment of liver fibrosis and steatosis is using MASH biopsies, though there has often been concern that the disease may present differently in different liver lobes (particularly in early stages). This concern is magnified when using quantitative or AI based digital pathology techniques, as depending on the algorithm, small changes in structure (e.g. the presence of veins) can have large impacts on results. Additionally, when using a digital pathology analysis technique, the computational costs and time are magnified greatly with increased biopsy size.

The goal of this study is to analyze the phenotypic fibrosis scores generated by our FibroNest™ Digital Pathology platform on subsections of wedge-shaped biopsies (large biopsies from liver transplants) and investigate how the results may vary within the wedge.

Method

- 17 Wedge Liver Biopsies were sections into smaller portions which were analyzed and graded using the FibroNest System.
- FibroNest™, a cloud-based image analysis platform, was used to quantify the fibrosis phenotype including 32 traits for collagen deposition, fiber morphometry, and architecture (measures the organization and buildup of complex fibers).
- Principal quantitative fibrosis traits (up to 315 qFTs) are automatically detected and combined into a Phenotypic Fibrosis Composite Score (Ph-FCS).
- A standard set of Pre-Defined qFTs were used for standardized comparison.
- Each sub portion of the wedge generated its own Ph-FCS. These were then compared to determine both absolute and relative change within a biopsy.

Results

Of the 17 wedge biopsies, only 3 of the Ph-FCS biomarkers had a Coefficient of Variation (CoV) equal to or greater than 10%. Average CoV (N=17) is 7.2% and Median CoV (N=17) is 8.0%.

![Intra-Biopsy Ph-FCS Coefficient of Variation (CoV)](image)

Fig. 1: Box and Whisker illustrating the variance that in the scores within different portions of a wedge biopsy. The lowest CoV is 2% and the highest is 11%. The vast majority (14/17) of the biopsies have variations below 10%. 2 are 10% exactly, and one is 11%.

![Ph-FCS Values](image)

Figure 2. Representative images of the biopsies with Ph-FCS for each sub portion. Figure A is the Wedge with the most extreme CoV (11%) while figure B has a more average CoV (6%). It can be observed that Wedge ‘A’ has a unique pattern of Fibrosis present in only one of the sub sections. While Wedge ‘B’ also has a feature that only appears in one of the subsections it is no where near as large. This indicates that provided that a ‘unique event’ is avoided, sub sectioning a wedge biopsy is completely valid.

Conclusions

- Using large wedge liver biopsies from pre-cirrhotic MASH patients, we establish that the intra-liver Coefficient of Variability of the Ph-FCS fibrosis Digital Biomarker is between 8% and 10%.
- We are actively searching for a rare and retrospective cohort of Pre-cirrhotic MASH patients with multiple liver biopsies to confirm this assessment.