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EVALUATION OF THE CONSISTENCY AND HETEROGENEITY OF FIBROSIS ASSESSMENT IN ADJACENT VIRTUAL LIVER NEEDLE BIOPSIES USING AI-BASED QFIBROSIS

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BACKGROUND

- Liver fibrosis serves as a key prognostic indicator in patients with metabolic dysfunction-associated steatohepatitis (MASH) and is a key surrogate endpoint in MASH clinical trials.
- Despite the increasing application of digital pathology in these trials, which offers quantitative and reproducible assessments of fibrosis dynamics, the impact of needle positioning and serial sectioning on fibrosis assessment remains inadequately addressed
- This study evaluates the consistency and heterogeneity of fibrosis assessment in adjacent virtual liver needle biopsies using Second Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy with artificial intelligence (AI)-based qFibrosis (qF) assessment.

METHOD

- SHG/TPE microscopy scanned 100 liver samples taken from liver resections or explants in the SteatoSITE cohort, spanning NASH-CRN stages F0 to F4.
- Two adjacent virtual needle biopsies (VNBs) were extracted from each image, each measuring 0.9 mm in width and 15 mm in length. (Figure 1 and Figure 2)
- qF assessment was performed independently for each VNB, focusing on fibrosis areas within 5 liver zones: portal tract (PT), periportal (PP), Midzonal (MD), pericentral (PC) and central vein (CV).

RESULTS

Figure 1. Study flow and methods.

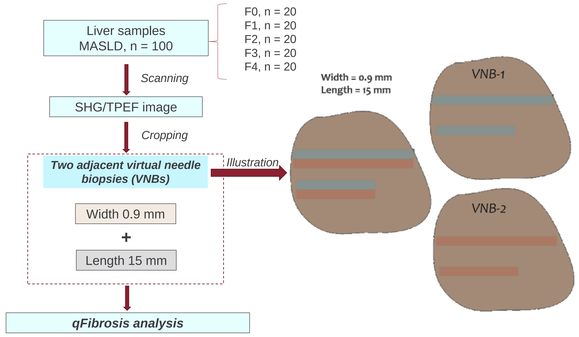


Figure 2. Examples of SHG/TPEF images for the two adjacent virtual needle biopsies.

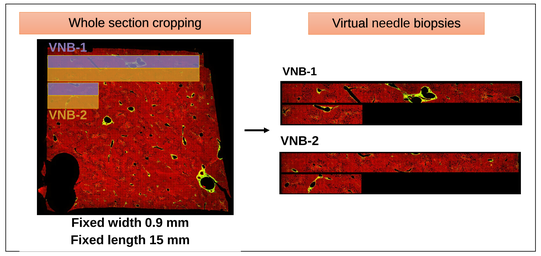
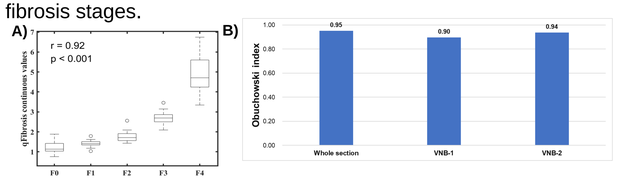


Figure 3: **A)** qFibrosis concordance with NASH CRN fibrosis stages of whole explant or resection block using Spearman's correlation. B) Obuchowski index of qFibrosis continuous value for NASH CRN fibrosis stages.



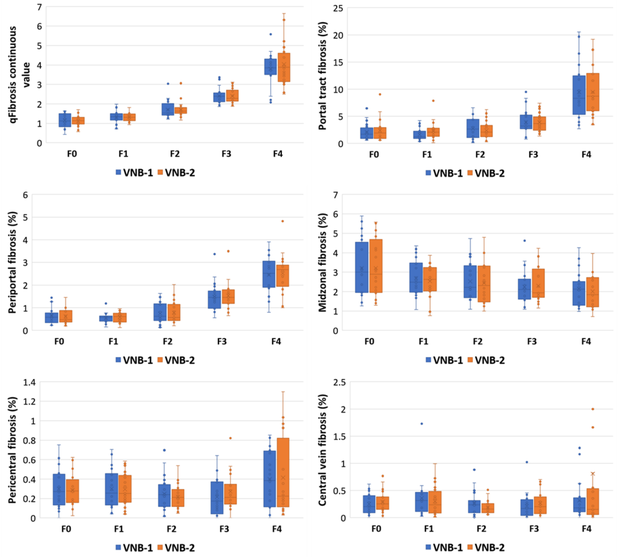
- qFibrosis assessment of whole explant or resection block showed excellent concordance with NASH-CRN stages (r = 0.92; p < 0.001). The qF assessments of both VNBs correlated strongly with NASH-CRN stages, achieving Obuchowski indices of 0.90 and 0.94, respectively. (Figure 3)
- There was substantial agreement between the two VNBs' qF stages (linear weighted kappa=0.71).
- 61 samples showed identical qF stages across the adjacent VNBs, with only 1 sample displaying a 2-point discrepancy.

Table 1: Relative differences of qFibrosis continuous value and zonal fibrosis between VNB-1 and VNB-2.

	Median	Lower quartile	Upper quartile
qFibrosis continuous value	2.79%	-11.54%	13.48%
Overall fibrosis	1.87%	-10.16%	16.40%
Portal tract fibrosis	9.47%	-23.51%	66.71%
Periportal fibrosis	0.12%	-13.05%	23.13%
Midzonal fibrosis	-3.54%	-15.80%	13.95%
Pericentral fibrosis	-0.95%	-36.77%	84.35%
Central vein fibrosis	4.91%	-60.33%	99.10%

- Statistical analysis (Wilcoxon signed rank test) confirmed no significant differences in the continuous qF values between the adjacent VNBs, with a median difference of 3% (interquartile range: -12% to 13%). (Table 1)

Figure 4: Boxplot of qFibrosis continuous value and zonal fibrosis for VNB-1 and VNB-2 for different NASH-CRN fibrosis stages.



- Zonal fibrosis differences were also non-significant (p>0.05) (Figure 4).Among the zones, PP and MD fibrosis showed the smallest variations - median difference of 0% (-13%, 23%) and -4% (-16%, 14%), respectively. CV fibrosis showed the greatest variability, with a median difference of 5% (-60%, 99%). (Table 1)

CONCLUSIONS

- This systematic analysis confirms that adjacent VNBs are sufficiently reliable for fibrosis assessment using SHG/TPE microscopy.
- The high consistency observed in fibrosis evaluations across adjacent VNBs supports the reliability of qF as a method for quantitative fibrosis assessment in clinical trials.

CONTACT INFORMATION

All authors participated in the development of this poster and approved the final poster for presentation.

CONTACT INFORMATION

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