Impact of sampling size on variability of fibrosis assessment in liver needle biopsies using second harmonic generation/two photon excitation microscopy and artificial intelligence analysis based fibrosis staging

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INTRODUCTION

- The risk of underestimation of histological features increases with smaller biopsies. Prior studies have defined a minimum biopsy size for a reliable assessment of fibrosis by conventional microscopy and informed guidelines for clinical trials in non-alcoholic steatohepatitis (NASH).
- Although digital pathology is increasingly employed in these trials, the impact of the sampling sizes on fibrosis assessment with this technology is poorly defined. We aimed to investigate the effect of sample size on quantification of fibrosis, qFibrosis (qF), and validate its impact on digital pathology readouts.

MATERIALS AND METHODS

- 100 samples (taken from liver resections and explants), 20 each of pathologist-assigned NASH CRN - F0/F1/F2/F3/F4, were evaluated.
- Each sample was subjected to one virtual needle biopsy, fixed width 0.7mm with varying lengths between 5 and 20mm, and fixed length of 15mm with varying widths between 0.5-1.3mm (Figure 1).
- qF stages were determined using Second Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy and artificial intelligence (AI)-based analysis. qF stage was compared with the pathologist assigned fibrosis stage and agreement was evaluated by calculating interobserver Kappa values. The proportion of cases where qF stage was higher or lower than pathologist's stage was calculated.

RESULTS

- Analysis of Kappa values, both unweighted and weighted, showed greater concordance between qF and pathologist assessments as length or width of tissue samples increased (Figure 2).
- For length variability, the Kappa values leveled off at 11mm upwards with asymptote around 15 mm. Highest weighted Kappa value observed was 0.78, consistent with previously published inter-observer Kappa values (Figure 2).

Figure 1. Study flow and methods.

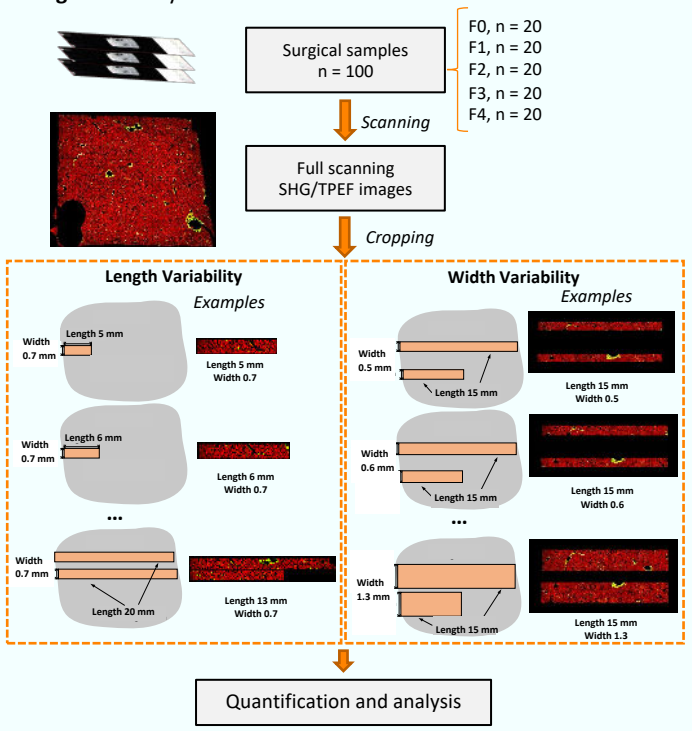


Figure 2: KAPPA between qF stage and pathologist reading for different (A) tissue length and (B) tissue width.

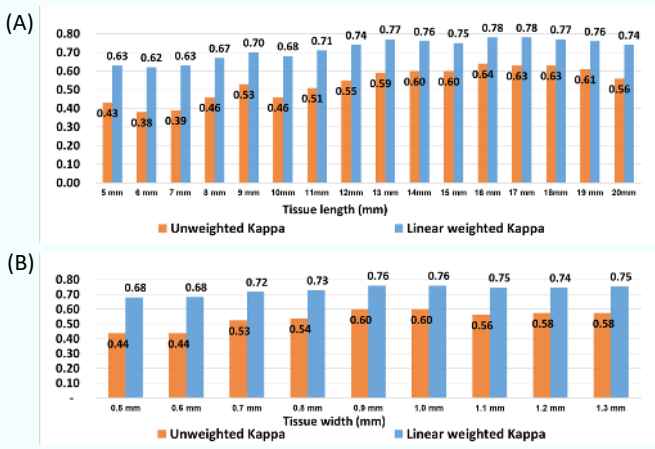
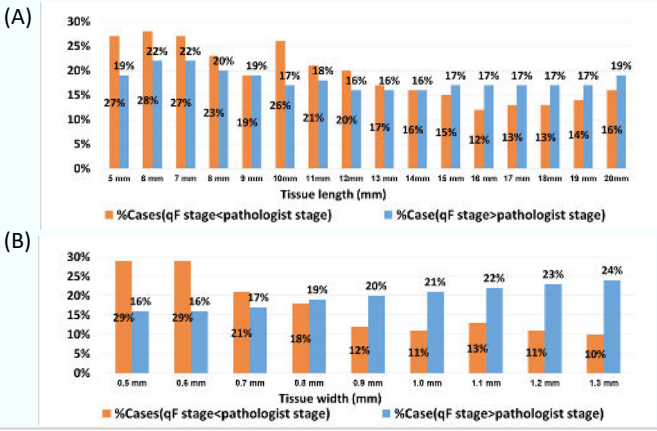


Figure 3: Proportions of cases with qF greater or less than pathologist-assigned stage for different (A) tissue length and (B) tissue width.



RESULTS

- For width variability, the Kappa values leveled off at 0.7mm upwards with asymptote around 0.9 mm, with the highest weighted Kappa value of 0.76 (Figure 2).
- Percentage of cases where qF indicated lower fibrosis stages compared to the pathologist's assessments were greater when tissue length was shorter or tissue width was thinner (Figure 3).

CONCLUSION

- In this systematic investigation, our findings demonstrate that qF tends to underestimate the extent of fibrosis in small biopsy sizes, and a minimum tissue length of 15mm and tissue width of 0.7mm are required for qF to achieve reproducible agreement with pathologist's staging.
- This highlights the importance of considering minimum length and width of liver biopsy when utilizing qF as a clinical diagnostic tool.

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