qFibrosis-Based Collagen Microarchitecture Profiling Identifies Recurrence-Associated Fibrotic Signatures in HCC Biopsies

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INTRODUCTION

- HCC develops within a complex fibrotic and stromal microenvironment that influences tumor progression, treatment response and recurrence risk.
- Conventional fibrosis staging systems provide limited spatial and quantitative characterization of collagen remodelling within HCC-associated liver tissue.
- qFibrosis is an AI-based SHG/TPEF quantitative histopathology platform enabling detailed collagen features and microarchitectural profiling across anatomically distinct tissue zones.

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AIM

This study evaluated whether region-specific qFibrosis collagen parameters assessed in peri-tumoral liver tissue are associated with early vs. late HCC recurrence after surgical resection, and whether these associations differ by underlying cirrhosis status.

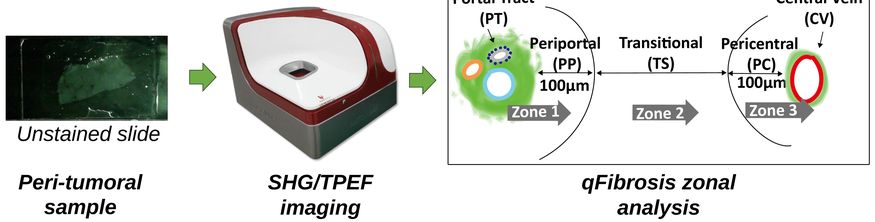
METHOD

PATIENTS:

- 85 HCC patients surgically resected at NCKUH, Taiwan
  - Cirrhotic: n=40 (HBV=26, HCV=14);
  - Non-cirrhotic: n=45 (HBV=40, HCV=5).
- RECURRENCE GROUPS:
  - Early: DFS <1 year (n=30);
  - Late: DFS >=1 year (n=55).

qFIBROSIS ANALYSIS:

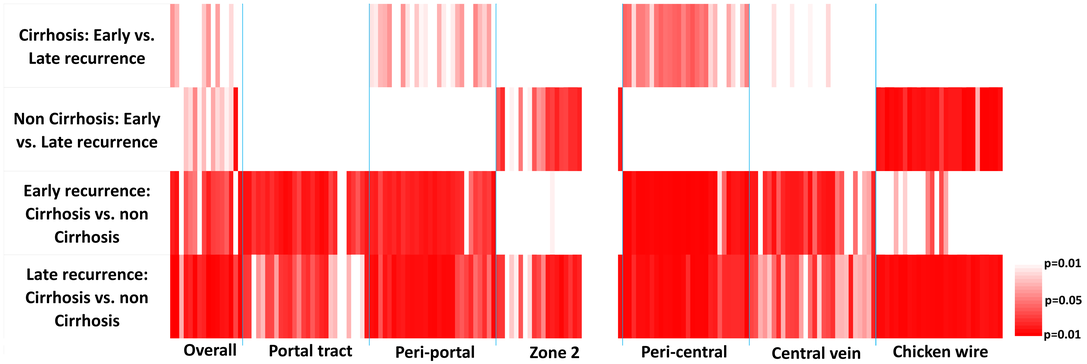
- Peri-tumoral liver samples analyzed across 7 hepatic lobule regions: Overall, Portal tract, Peri-portal, Zone 2, Peri-central, Central vein, Chicken-wire.
- 184 collagen parameters quantified per sample.



Peri-tumoral sample ***SHG/TPEF imaging*** ***qFibrosis zonal analysis***

RESULTS

- Early recurrence in non-cirrhotic: higher qFibrosis in Zone 2 and chicken-wire regions.
- Early recurrence in cirrhotic: high pericentral qFibrosis parameters.
- Recurrence-associated patterns differ by cirrhosis status.



Region-specific collagen microarchitecture profiling. *Upper 2 heat maps compares collagen parameters between early and late recurrence HCC biopsies from cirrhotic and non-cirrhotic patients. Lower 2 heat maps compares collagen parameters in cirrhotic vs. non-cirrhotic biopsies within early and late recurrence groups. Darker red signals indicate statistically significant increases in qFibrosis parameters. Wilcoxon rank sum test; p<0.05 significant.*

CONCLUSIONS

- qFibrosis-based collagen morphometry identifies distinct spatial fibrosis patterns associated with early HCC recurrence in cirrhotic and non-cirrhotic liver backgrounds.
- Region-specific ECM alterations may reflect biologically distinct tumor-stroma interactions and recurrence mechanisms across different HCC backgrounds.
- Quantitative spatial fibrosis profiling using qFibrosis may provide clinically relevant prognostic information beyond conventional fibrosis staging and support biomarker-driven patient stratification in HCC clinical trials.