qFibrosis provides differential changes in different regions of the liver

Addressing the heterogeneity of fibrosis in liver biopsy specimens with qFibrosis – A new paradigm for an old problem

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1 Introduction

- There is clear data showing liver fibrosis predicts liver-related clinical outcomes[1] and a 1-stage fibrosis improvement has been accepted as a reliable end-point in the assessment of non-alcoholic steatohepatitis (NASH).
- But in trials with a 48-week duration, most patients do not change their fibrosis stage according to the CRN system. This is due to either insufficient change in collagen amount or fibrosis distribution. Quantitative assessment of fibrosis has recently been developed for NAFLD patients and qFibrosis (qF),[2] in particular, has been widely used in many NASH clinical trials.
- In these studies, qFibrosis measures many features of collagen fibers such as length, width, intersections and others in a reproducible and fully quantitative manner. In addition, these features can be divided into peri-portal and peri-central zones for sub-analysis.

2 Aim

- qFibrosis can analyse these differential changes which has been shown to provide insights on drug effects. The generalisability in this approach beyond NASH has not been established.
- In this exploratory analysis, a cumulative qFibrosis score was used to identify fibrosis changes in different regions of the liver sections in treated hepatitis C (HCV) subjects who have achieved sustained virological response.

3 Method

- Paired biopsies from 35 patients with Hepatitis C (HCV) assessed to have "no-change" in fibrosis were used in this sub-analysis.
- Using qFibrosis, collagen proportionate area (CPA) of 5 pre-defined fibrosis regions [portal, peri-portal (PP), peri-central (PC), peri-sinusoidal (PS) and bridging] were quantified using second harmonic generation/two photon excitation fluorescence technology (SHG/TPEF).
- CPA values for each region were normalized to a 0 – 1 range with qFibrosis total weighted score (qF-TWS) calculated as a sum of all 5 CPA values.

4 Results

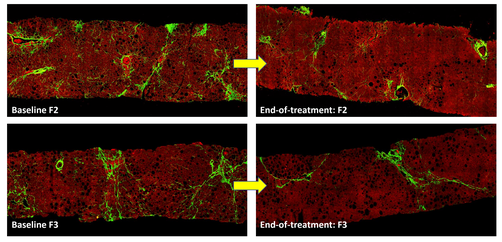

Figure 1: SHG images of 2 cases illustrating intra-stage changes.

(Top row) BL and EOT are both staged F2; (Bottom row) BL and EOT are both staged F3.

- In Figure 1, two examples are shown with no change in fibrosis staging at baseline (BL) and end-of-treatment (EOT) based on conventional CRN staging system.
- Fig. 1, top row: Fibrosis staged F2 at BL and EOT; With qF we observe a significant reduction in peri-sinusoidal fibrosis, with some peri-portal fibrosis reduction.
- Fig. 1, bottom row: Fibrosis staged F3 at BL and EOT; With qF we also observe a significant reduction in peri-sinusoidal fibrosis, with thinning of bridging fibrosis (septa).

4 Results continued

- These cases in Figure 1 demonstrate "intra-stage" changes in fibrosis severity which cannot be captured by conventional staging system.
- Further, the BL F2 sample shows a greater amount of fibrosis compared to the BL F3 sample in Figure 1 i.e., it is important to examine fibrosis changes in different regions of the liver lobule, in addition to the amount of fibrosis.
- Using a radar map to plot these collagen changes provides a more intuitive view of differential changes in fibrosis.

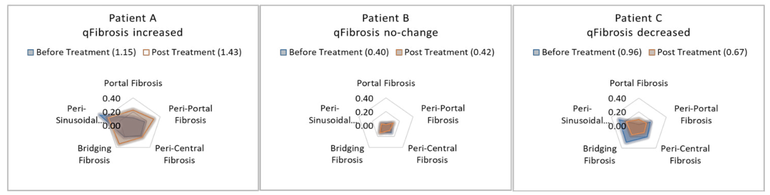

Figure 2: qF-TWS of 3 subjects presented in the format of a radar map. All patients showed no change in fibrosis staging at BL and EOT based on conventional staging system.

- Changes in different regions of the tissue sections and their relationship to overall CPA response of 3 patients from these representative groups is shown in Figure 2.
- We observed differential changes in different regions of the liver, with specific changes in the perisinusoidal region although the conventional fibrosis staging are the same for these 3 patients.

5 Conclusions

- qF-TWS can differentiate subjects with fibrosis progression and regression post-treatment who were determined as no-change by pathologists' assessment.
- The ability of qFibrosis to assess fibrosis heterogeneity on a continuous scale provides the potential of detecting subtle fibrosis changes that cannot be captured by current system. A separate study is planned to establish correlation to clinical outcomes.

6 Acknowledgements

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7 References

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2. Liu F., et al. Hepatology 2020;71:1953–66

8 Contact information

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