AI digital pathology using qFibrosis reveals heterogeneity of fibrosis regression in hepatitis B and C patients with SVR

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INTRODUCTION

Liver fibrosis is a dynamic process and complex fibrosis patterns comprising progressive and regressive features have been observed, particularly in post-intervention samples. Conventional staging systems are static assessments of fibrosis and lack granularity to delineate the heterogeneity of fibrosis features in pre- and post-treatment biopsies, resulting in a less than adequate evaluation of fibrosis regression.

AIM

The aim of this study is to understand the fibrosis dynamics and its relation to evaluating post-treated viral cases by employing second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy which provides a reproducible and quantitative analysis for fibrosis features.

METHOD

158 paired Hepatitis B (n=100) and C patients(n=58) biopsies from pre- and post- treatment were were examined. All Hepatitis B (HBV) patients achieved sustained virologic response (SVR) after 78 weeks treatment. Hepatitis C (HCV) cases achieved SVR after 24 weeks treatment. Liver fibrosis (qFibrosis) were quantitated using SHG/TPEF microscopy and the changes in the collagen proportionate area (CPA) were assessed quantitatively according to hepatic regions, including portal tract (PT), per-portal (PP), zone 2 (Z2), peri-central (PC), and central vein (CV).

RESULTS

For biopsies showing stages F5/6, all post-treatment cases revealed significantly less CPA (11 – 70%) across all regions as compared to the pre-treatment, suggesting fibrosis significantly reduction, such as septal thinning in the post-treatment cases despite being staged as F5/6 according to the Ishak system. For the F3/4 cohort, a similar CPA were observed, except in the PC and CV regions where more CPA (9 – 14%) was observed in the post-treatment cases at 24 weeks. This suggest a 24 weeks' timeframe was insufficient to resolve some portal-central bridging. In the F0/1/2 cohort, less CPA (9 – 42%) across all regions observed at 78 weeks treatment and more CPA (30 – 42%) at the PP and Z2 regions were observed at 24 weeks treatment, suggest fibrous expansion of portal areas remained.

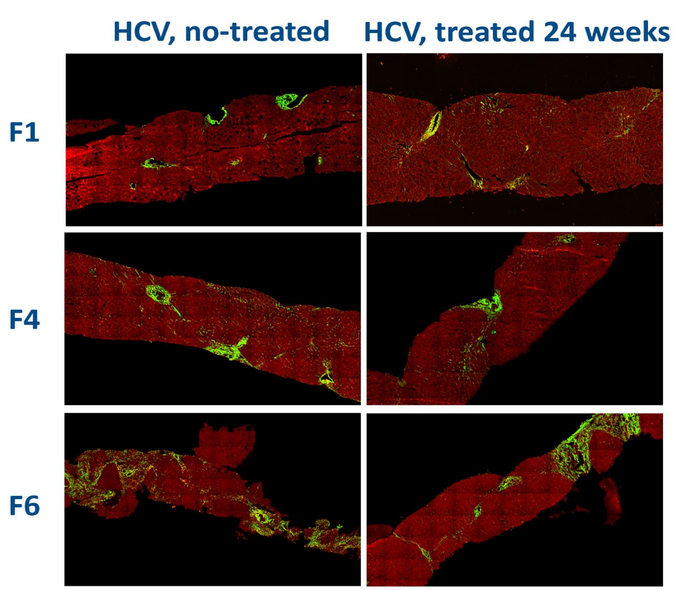

Figure. Example images from SHG/TPEF microscopy in various Ishak stages (F1, F4 and F6) between pre- and post-treatment HCV patient samples. .

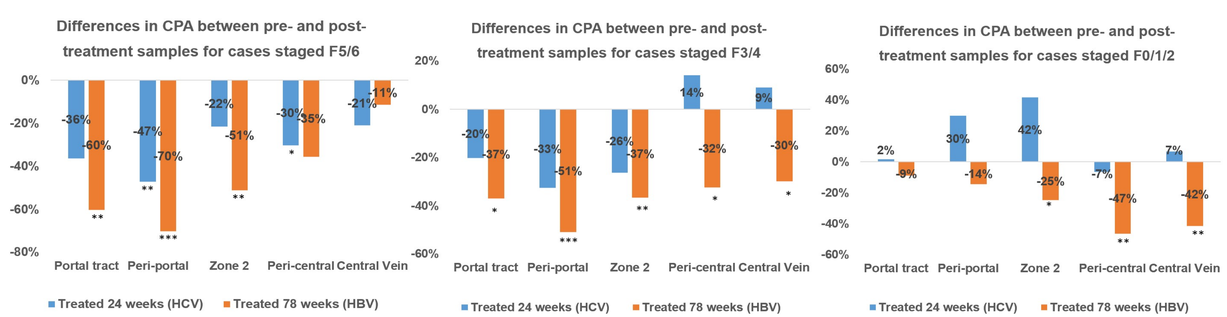

Figure. Difference in CPA between pre- and post-treatment samples

CONCLUSIONS

Following successful anti-viral treatments, the pre- and post-treatment biopsies provide quantitative evidence for the heterogeneity of fibrosis features even within the same fibrosis stages. Quantitative qFibrosis approach has the potential to provide new insights in the dynamics of fibrosis regression for hepatitis cases, as early as 24 weeks after SVR.

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