

Second Harmonic Generation (SHG) microscopy : a novel automated method for quantification of hepatic steatosis in chronic liver disease

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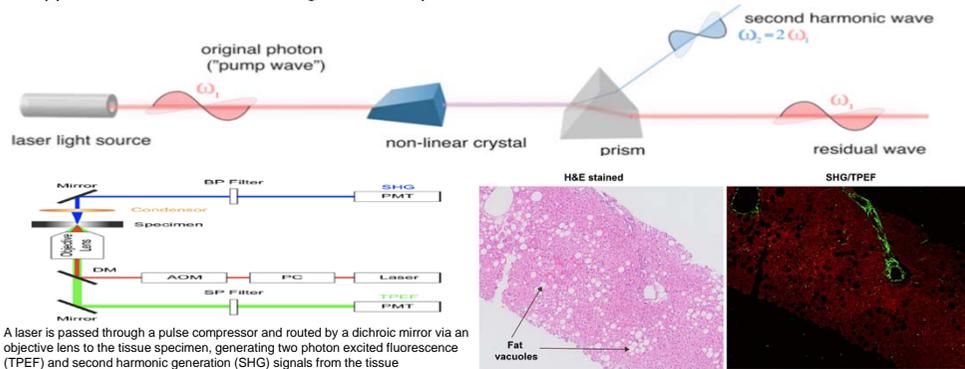
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Background

Non Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease globally and with the increasing obesity epidemic worldwide, NAFLD often coexists with other liver diseases such as chronic hepatitis B (CHB). NAFLD can manifest in a spectrum of phenotypes, and histological assessment remains the current “gold standard” for characterizing NAFLD. However, the semiquantitative nature and potential human subjective variability may limit accuracy. SHG microscopy is a novel technology using multiphoton microscopy with optical imaging techniques that has been validated to quantify fibrosis across a range of liver diseases. Separately, we created an automated algorithm based on signature SHG parameters that reflect hepatic steatosis (HS) on liver histology. We explored the utility and application of SHG for the diagnosis and quantification of HS.

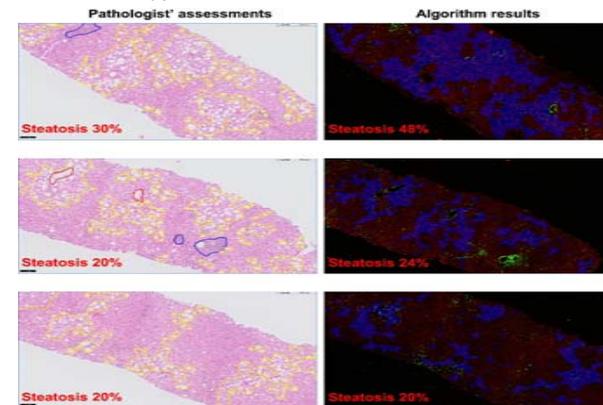


Methods

SHG microscopy analysis using Genesis™ (HistoIndex, Singapore) was applied on 86 archived liver biopsy samples. Separately, 3 individual expert liver histopathologists quantified HS on a continuous scale. Correlation between the 3 individual histopathologists was assessed for inter-observer variability. Reliability was correlated between the mean score of the 3 histopathologists and SHG assessment. Clinical information including demographics, anthropometry, medical history, biochemical and histological variables were obtained from electronic medical records. Data analysis was performed using SPSS.

Results

The mean age of the cohort was 51.3 ± 10.4 years (range 23.0 to 69.0 years) with 58.1% male preponderance and 83.7% Chinese ethnicity. The mean BMI was 29.7 ± 6.8 (range 17.6 to 50.5) kg/m². Patients with NAFLD, CHB and CHB-NAFLD comprised 50.0%, 18.6% and 31.4% of the cohort respectively. 44.4% of the cohort had advanced (stage 3-4) fibrosis. There was minimal inter-observer variability between the 3 liver histopathologists, with an intraclass correlation of 0.924 (95% CI 0.894-0.947; $p < 0.001$). Similarly, there was good correlation between the histopathologists and automated SHG microscopy assessment of HS with Pearson correlation of 0.934: $p < 0.001$.



Conclusion

SHG is a reliable and novel method for automated quantitative assessment of HS across CHB, NAFLD and CHB-NAFLD, which can potentially aid the histopathologists in providing more sensitivity and standardization. At the same time, it can also augment efficiency and throughput in clinical practice and trial settings.

Disclosures:

Chang PE, Goh BBG, Leow WQ, Lim KH and Tan CK have no financial disclosures to declare. Dean Tai is the Managing Director and Chief Scientific Officer of HistoIndex Pte Ltd.