

EVALUATING IMPACT OF WEIGHT CHANGES ON HISTOLOGICAL PATTERNS OF LIVER FIBROSIS IN MASH: IMPLICATIONS FOR SPATIAL INTERROGATION

Nicholas Syn^{1,2}, En Ying Tan³, Joo Wei Ethan Quek⁴, Daniel Huang³, Jonathan Lee³, KUTBUDDIN AKBARY⁵, Yayun Ren⁵, Cheng Han Ng³, Aileen Wee^{1,4}, Gwyneth Soon¹, Nur Halisah Binte Jumat³, Yock Young Dan³, Mark Dhinesh Muthiah³

1. Department of Pathology, National University Health System, Singapore
2. Division of Biomedical Informatics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
3. Division of Gastroenterology and Hepatology, Department of Medicine, National University Hospital (NUH), Singapore, Singapore
4. Yong Loo Lin School of Medicine, National University of Singapore, Singapore
5. HistoIndex Pte Ltd, Singapore, Singapore

INTRODUCTION

- Metabolic dysfunction associated steatohepatitis (MASH) is a severe form of Metabolic dysfunction associated steatotic liver disease (MASLD) characterized by hepatic steatosis, inflammation, hepatocyte injury, and fibrosis, which can progress to cirrhosis and hepatocellular carcinoma
- The progression of MASH-related fibrosis and the potential for its regression are influenced by metabolic factors, with weight loss being a key therapeutic target
- However, the mechanisms underlying fibrosis regression, especially in response to bariatric surgery, remain poorly understood
- Previous studies have shown that weight loss achieved through bariatric surgery correlates with histological improvements in fibrosis. However, spatial patterns of fibrosis regression and progression within the liver lobule have not been fully explored
- This study uses Second Harmonic Generation/Two Photon Excitation (SHG/TPE) imaging and AI analysis based qFibrosis to assess the correlation of weight changes with liver fibrosis spatial distribution within the liver lobule in pre-bariatric surgery patients' liver biopsies

AIMS

- To evaluate the correlation of pre-surgery weight changes on spatial patterns of liver fibrosis in bariatric surgery patients' liver biopsies using qFibrosis
- To identify distinct regions of the liver with fibrosis distribution patterns, correlating these processes with pre-surgery weight dynamics (loss or gain)

METHODS

- Study Population: Sixty-nine bariatric surgery patients with a histological diagnosis of MASH were included
- The cohort was divided into two groups based on weight dynamics in the six months preceding surgery: those with weight loss (n=60) and those with weight gain (n=8)
- Patients were placed on a Very Low-Calorie Diet (VLCD) prior to surgery. Weight change was calculated as a percentage relative to baseline weight
- Core liver biopsies were taken during surgery and analysed using SHG/TPE imaging combined with AI-assisted quantification of collagen parameters (qFibrosis) [1]. This technique enables detailed analysis of collagen morphology, with specific attention to key fibrotic zones (central, pericentral, portal, periportal, perisinusoidal, chicken wire fibrosis) defined by the NASH-CRN system. Each zone is quantified by 28 collagen morphometric parameters and presented as a continuous value
- Statistical Analysis: Spearman correlation was employed to evaluate the relationship between weight change and qFibrosis-derived collagen morphological parameters in different liver zones

RESULTS

- Negative correlations were found between the percentage of weight loss and several key collagen parameters measured through qFibrosis
- Chicken wire fibrosis ($r = -0.4$), pericentral fibrosis ($r = -0.42$), and overall hepatic fibrosis ($r = -0.49$) all demonstrated marked reductions in collagen content and fibre density with increased weight loss
- In zone 2 fibrosis, a weaker but still notable correlation was observed ($r = -0.32$)
- These results suggest that pre-surgery weight loss has a strong correlation with fibrosis distribution in specific regions, with chicken wire fibrosis being seen lesser in these group of patients
- In contrast, patients who gained weight before surgery showed positive correlations between weight gain and increases in collagen parameters in these regions
- Weight gain was associated with increased fibrosis in the same zones that showed regression with weight loss, especially in the chicken wire and pericentral regions of the liver

CONCLUSIONS

- This study demonstrates that relative weight loss prior to bariatric surgery is significantly associated with reduced overall hepatic fibrosis, with the most pronounced effects observed in zones of chicken wire fibrosis
- The findings highlight the importance of different liver zones, particularly the chicken wire zone, in responding to weight loss, suggesting that specific areas of the liver could be more susceptible to fibrosis regression with metabolic interventions
- The correlation between weight loss and fibrosis reduction emphasizes the role of weight management as a key therapeutic approach in MASH
- Identifying these spatial patterns of fibrosis regression could improve our ability to predict responders and non-responders to weight loss interventions, helping to refine patient selection for therapies targeting fibrosis resolution
- These insights pave the way for precision medicine approaches in treatment of MASH, allowing for more targeted therapies based on the spatial characteristics of fibrosis within the liver lobule

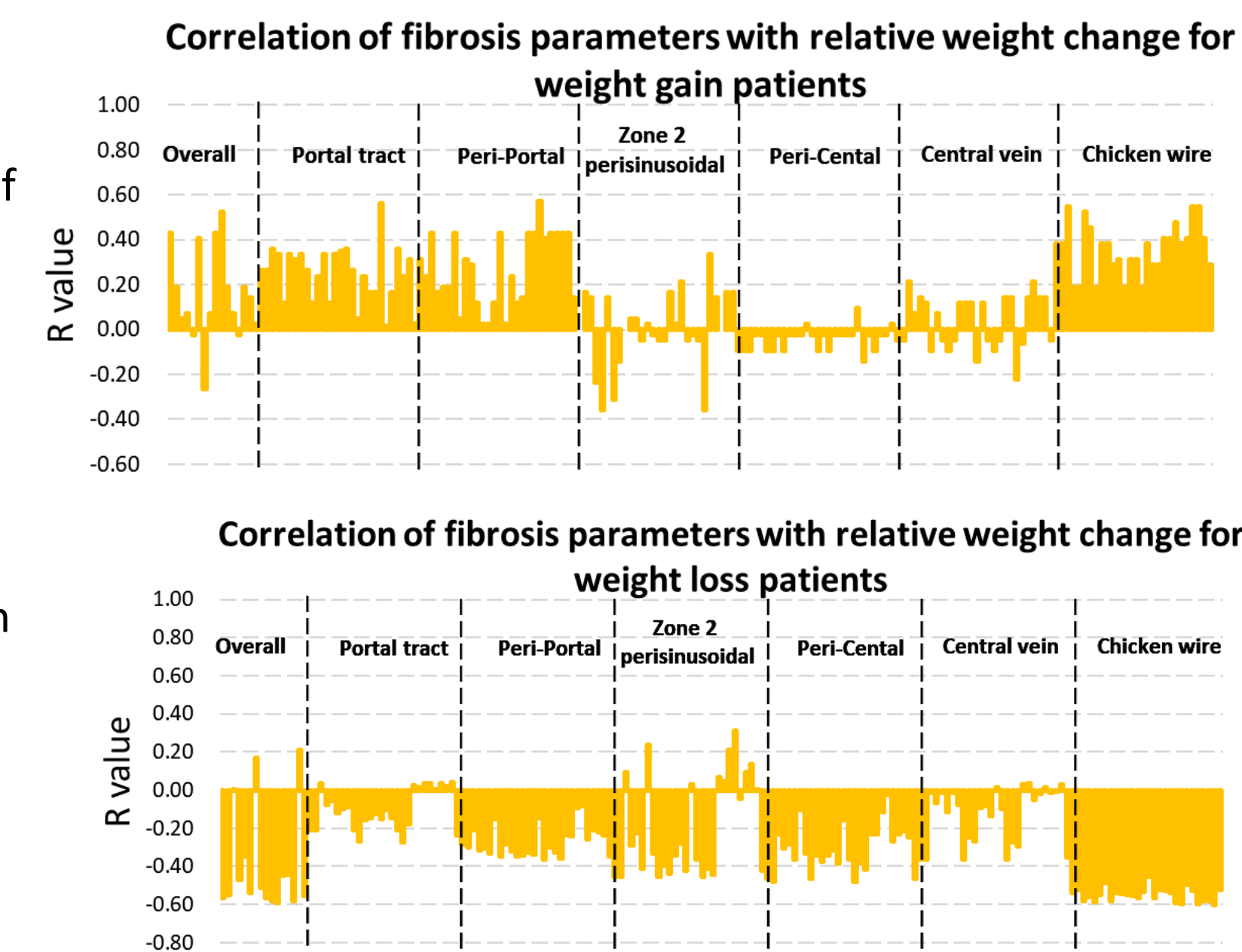


Figure 1: Demonstrates the correlations between qF parameters, based on zonal classification as per the NASH-CRN system, with pre-surgery weight loss and weight gain. [A] Shows the correlation of qF-based parameters with weight loss and weight gain, categorized according to the NASH-CRN zonal system

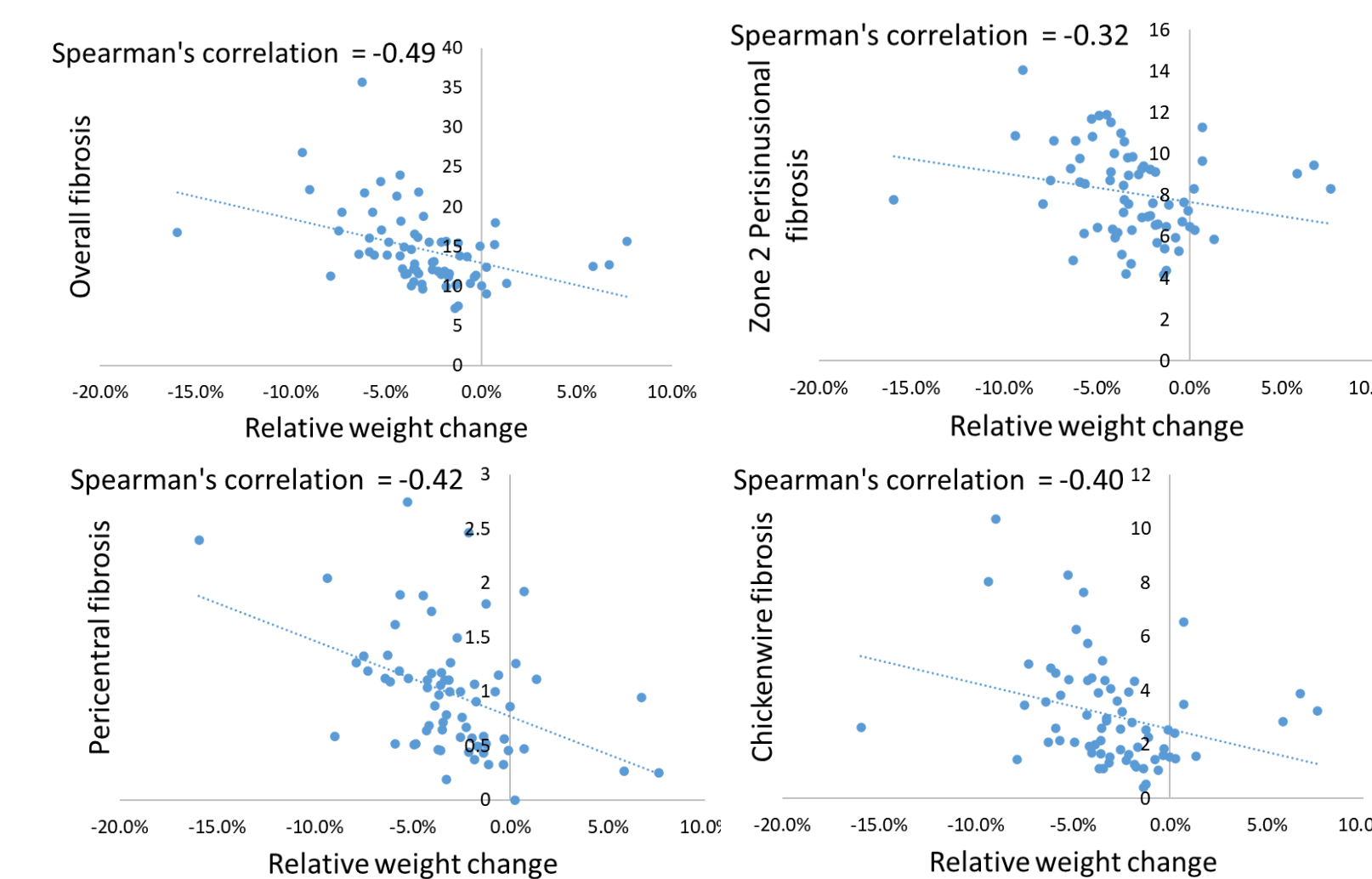


Figure 1: Demonstrates the correlations between qF parameters, based on zonal classification as per the NASH-CRN system, with pre-surgery weight loss and weight gain. [B] Presents scatter plots and correlations of relative weight change with individual zonal qF parameters, highlighting those with high r-values

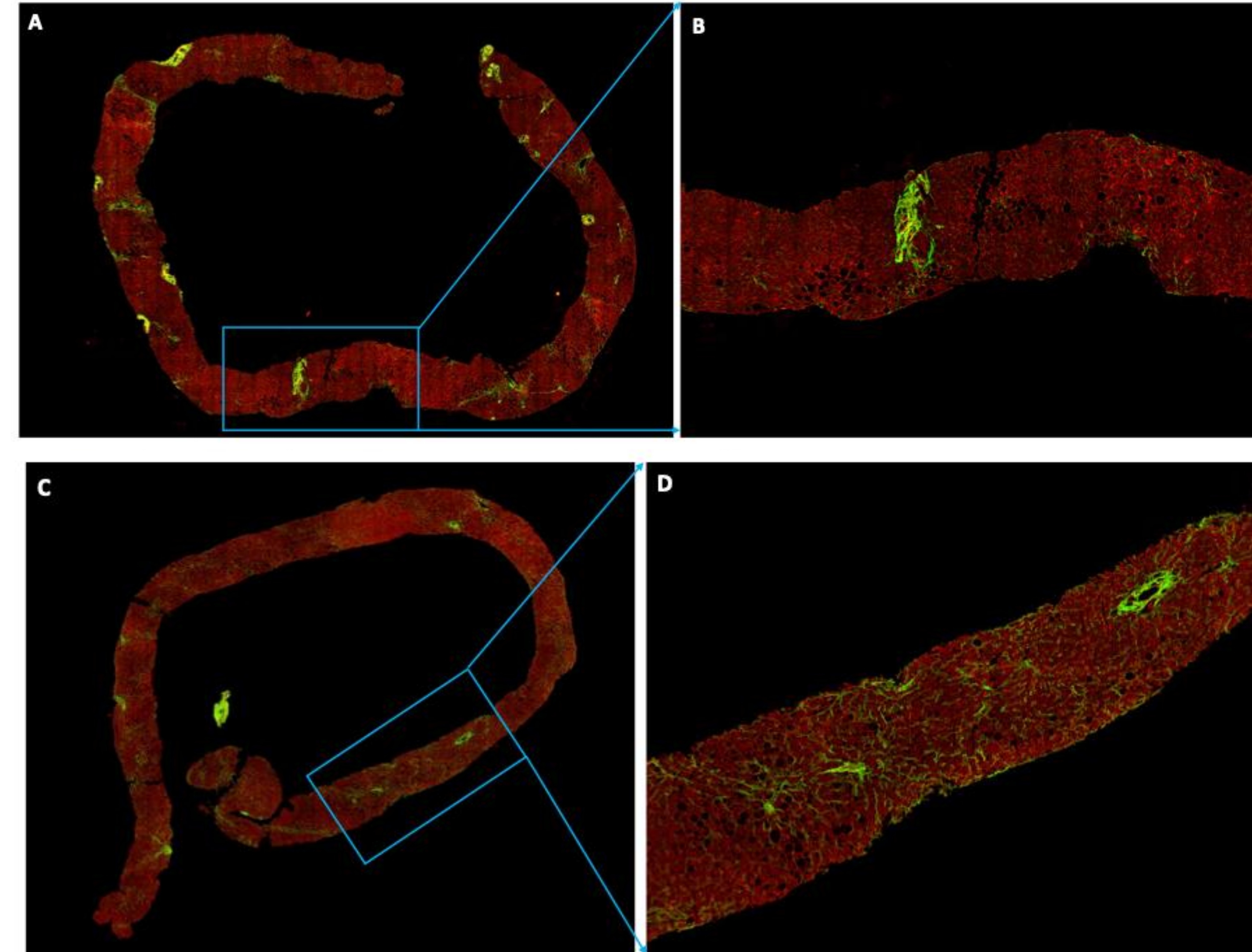


Figure 2: SHG/TPE images of liver biopsies from patients with pre-surgery weight loss and weight gain on VLCD. Fibrosis is annotated in green, and hepatocytes in red. [A] and [B] depict liver biopsies from a patient with 4.1% relative weight loss prior to bariatric surgery. The qFibrosis values for chicken wire fibrosis and pericentral regions are 1.92 and 0.69, respectively. [A] shows overall reduced chicken wire fibrosis in the biopsy, while [B] provides a closer view, illustrating the reduced amount of chicken wire fibrosis. [C] and [D] show liver biopsies from a patient with 6.7% relative weight gain before surgery. The qFibrosis values for chicken wire fibrosis and pericentral regions are 3.86 and 0.95, respectively, indicating more fibrosis in these regions than in the weight loss case. [C] shows more extensive chicken wire fibrosis throughout the biopsy, and [D] is a zoomed-in view showing a higher distribution of chicken wire fibrosis in this patient

REFERENCES

1. Liu F, Goh GBB, Tiniakos D, et al. qFIBS: An Automated Technique for Quantitative Evaluation of Fibrosis, Inflammation, Ballooning, and Steatosis in Patients With Nonalcoholic Steatohepatitis. *Hepatology* (2020), 71: 1953-1966

DISCLOSURES: KA, YR are employees of HistoIndex. Rest of the authors declare no conflicts of interest relevant to this publication

ACKNOWLEDGEMENTS

We would like to acknowledge the assistance of Galvin Gan at HistoIndex in providing the appropriate images for this poster

CONTACT INFORMATION

Mark Muthiah: mark_muthiah@nuhs.edu.sg
Kutbuddin Akbary: akbary.kutbuddin@histoindex.com