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INDEPENDENT VALIDATION OF SECOND HARMONIC GENERATION/TWO PHOTON EXCITATION IMAGING AND ARTIFICIAL INTELLIGENCE-BASED SNOF INDEX FOR METABOLIC DYSFUNCTION ASSOCIATED STEATOHEPATITIS CIRRHOSIS ASSESSMENT

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INTRODUCTION

- The Septa-Nodule-Fibrosis (SNOF) index was developed using a machine learning approach, aimed at quantifying histological features of cirrhosis in patients with Metabolic dysfunction-Associated Steatohepatitis (MASH) [1]
- The SNOF index incorporates key cirrhosis characteristics such as septa width, length, cellularity, nodule size, area, and fibrosis parameters including the number, length, perimeter, and width of fibres
- Initial studies showed that the SNOF index could predict clinically significant outcomes in MASH cirrhosis such as hepatic venous pressure gradient (HVPG), clinically significant portal hypertension (CSPH), and the presence of varices [1]
- This study seeks to validate the SNOF index in an independent cohort, correlating it with established histopathological staging systems, namely NASH-CRN and Ishak fibrosis staging, to establish its broader utility

AIMS

- To validate the SNOF index in an independent cohort from the BMS Falcon 1 and 2 trials, including patients with early (F3) and advanced (F4) stages of cirrhosis, and assess its correlation with pathologist-based NASH-CRN and Ishak staging
- To evaluate the change in the SNOF index (ΔSNOF) from baseline (BL) to end-of-treatment (EOT) biopsies, and analyse the correlation between SNOF and histological progression, stability, or regression of fibrosis

METHODS

- A total of 598 unstained liver biopsies from the BMS Falcon 1 and 2 trials (NCT03486899, NCT03486912) were analysed, representing patients with both bridging fibrosis and cirrhosis stages (NASH-CRN F3 and F4)
- Spearman correlation was applied to determine the association between the SNOF index and both NASH-CRN and Ishak fibrosis staging systems
- SNOF values at BL and EOT biopsies were compared, with the following categories defined based on the NASH-CRN system of fibrosis staging: Progression (≥1-stage increase in fibrosis), No change (stable fibrosis stage), and Regression (≥1-stage decrease in fibrosis)
- Changes in SNOF value (ΔSNOF) were assessed for each category of Progression, No-change and Regression

RESULTS

- The combined dataset had a mean age of 58.06 years (median 60 years), with 40% male and 60% female participants
- Of the biopsies, 60% were categorized as F3 and 40% as F4 based on NASH-CRN fibrosis staging
- The median NAS scores for the liver biopsies were Steatosis = Grade 1, Ballooning = Grade 2, and Lobular Inflammation = Grade 3
- Strong correlations were observed between the SNOF index and both NASH-CRN (r = 0.604) and Ishak staging (r = 0.65)
- Patients with progressive fibrosis exhibited an increase in SNOF values, while those with stable or regressive fibrosis showed a decrease in SNOF values, with greater decreases in the regression group. These trends were consistent across both NASH-CRN and Ishak staging
- Box-whisker plots illustrate stage-wise cut-offs supported the SNOF index's strong correlation with fibrosis severity and its ability to differentiate between fibrosis stages

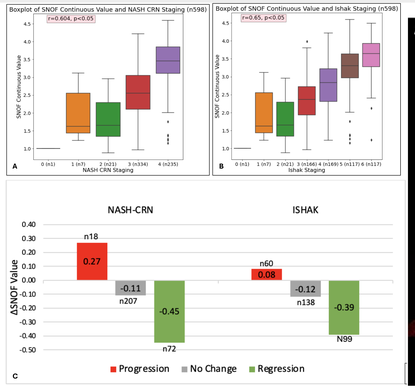

Figure 1: Box and Whisker plot demonstrating correlation of SNOF Index with pathologist-based NASH-CRN staging **[A]** and Ishak staging **[B]** in BMS Falcon 1&2 cohorts (includes Baseline and End-of-treatment samples). **[C]** Change in SNOF (ΔSNOF value) for progression, no-change, and regression cohorts as per NASH-CRN and Ishak fibrosis staging

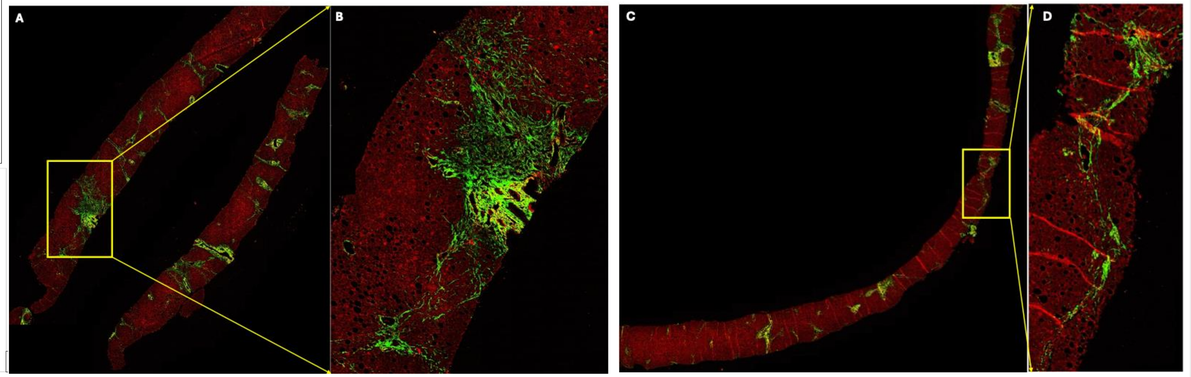

Figure 2. SHG/TPE images illustrating baseline and EOT biopsies. The fibrosis and septal regions are annotated in green, and the hepatocytes are annotated in red. Panel [A] displays the baseline biopsy with a SNOF value of 11.92, accompanied by a zoomed-in view in panel [B] that highlights early fibrous septa. Panel [C] presents the EOT biopsy, showing a reduced SNOF score of 6.01, while panel [D] provides a detailed view of the decreased width and area of the septa, indicating resolution. The NASH-CRN fibrosis stage and Ishak fibrosis score also improved, decreasing from F3 at baseline to F1 at EOT

CONCLUSIONS

- The SNOF index demonstrated a strong correlation with both NASH-CRN and Ishak fibrosis staging systems, providing validation of its applicability as a useful tool to quantify fibrosis features across different patient populations with MASH bridging fibrosis and cirrhosis
- The ability of the SNOF index to track histological changes over time, including fibrosis progression, stability, and regression, makes it a valuable tool for clinical trials assessing treatment efficacy
- Future research should focus on validating the SNOF index in larger, more diverse cohorts, exploring its predictive capabilities in longitudinal studies
- Additionally, linking SNOF to clinical outcomes and identifying cirrhosis from other causes of high liver stiffness, such as congestive hepatopathy, should be considered in future investigations

REFERENCES

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DISCLOSURES

KA, GG, RY, DT are employees of HistoIndex. Rest of the authors declare no relevant disclosures to this publication.

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