COMPARING FIBROSIS DISTRIBUTION IN LEAN VERSUS OVERWEIGHT/OBESE NASH-CIRRHOSIS PATIENTS USING SHG/TPE MICROSCOPY: AN OBSERVATIONAL ANALYSIS

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INTRODUCTION

- Drug trial for NASH cirrhosis necessitates patients to be classified as F4 by NASH-CRN staging.
- However, F4 classification lacks granularity and a detailed assessment of zonal fibrosis.
- To address this limitation, the approach of Single Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy-based qFibrosis assessment (qF), enables a fully quantitative evaluation.
- The primary goal of this study is to use qF to compare distribution of zonal fibrosis between two distinct patient groups: those with lean body mass (BMI<25) and those who are overweight/obese (BMI≥25).
- The study aims to enhance our understanding of zonal fibrosis patterns in patients with varying BMI statuses, using qF based analysis.

METHODS

- n=133 patients were evaluated from Phase 2b Belapectin NASH cirrhosis drug trials (NCT04365868).
- To assess the liver biopsies, a fully quantitative fibrosis assessment method based on NASH-CRN parameters, known as qF, was employed.
- These patients were divided into distinct groups: the Baseline (BL) category included both lean individuals (n=9) and overweight/obese individuals (n=124), while the End-of-Treatment (EOT) category consisted of lean individuals (n=7) and overweight/obese individuals (n=126).
- The statistical analysis of the data was performed utilizing the Wilcoxon rank sum test.
- To visually represent the findings, heat maps were employed, with any statistically significant differences (p≤0.05) indicated in red.

RESULTS

- At BL, the group exhibited statistically significant periportal fibrosis differences between lean and overweight/obese patients.
- Similar patterns persisted in EOT group, suggesting distinct periportal fibrosis distribution linked to BMI (Figure 1).
- Although the lean group had fewer patients compared to overweight/obese, the consistent observation of significant fibrosis distribution difference in periportal zones in both BL and EOT groups underscores its significance and reproducibility.
- These observations warrant reporting and suggest promising directions for additional exploration, based on BMI categories.

DISCUSSION

- The ability of SHG/TPE based qF analysis to provide consistent differentiation of periportal fibrosis parameters between lean and overweight/obese patients demonstrates its advantage when compared to conventional NASH-CRN staging.
- As seen in Figure 2, there is more periportal fibrosis in the lean patient biopsy (blue circle) as compared to the obese/overweight patient biopsy (white circle) in both the BL and EOT categories.
- Also in Figure 2, in pericentral zone, although there is similar fibrosis in the lean (blue circle) and obese/overweight (white circle) biopsy in BL, the EOT images depict lesser pericentral fibrosis in the obese/overweight patient (white circle) biopsy compared to lean patient (blue circle) biopsy.
- These observations also indicate histopathological variations in zonal fibrosis distribution in NASH cirrhosis, linked to BMI status.
- Larger patient cohorts should be engaged for deeper insights and validation of these initial findings.

CONCLUSION

- The potential utility of the outcomes of this study lies in designing NASH drug trials with tailored fibrosis resolution endpoints, accounting for patients' BMI variations.
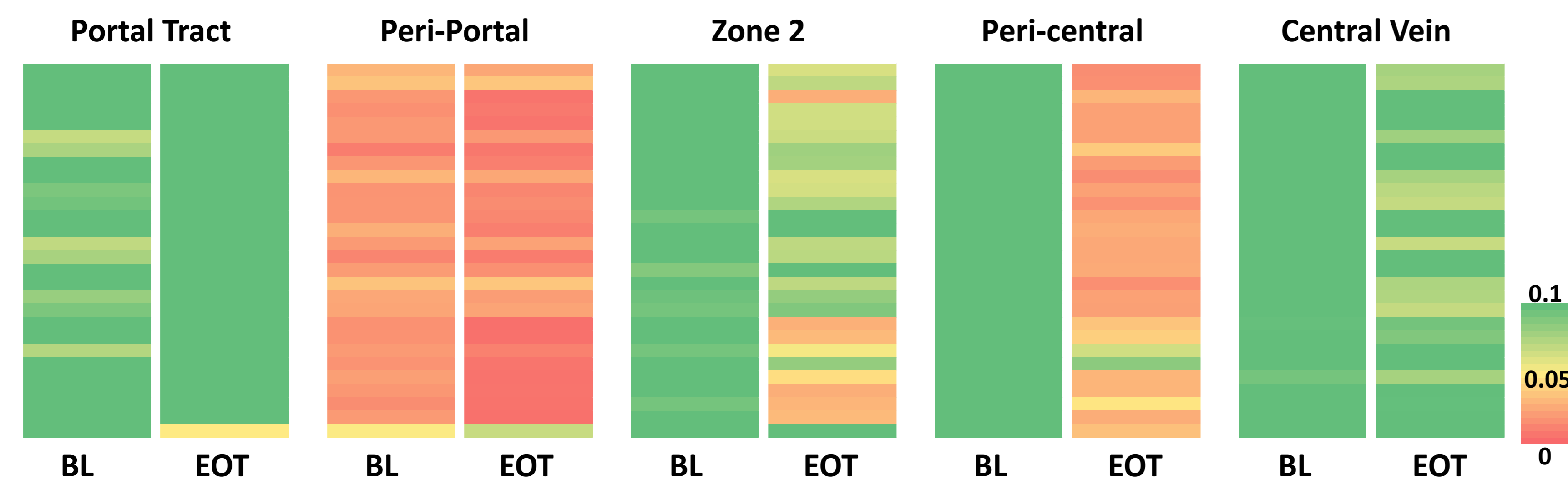
Figure 1. Collagen parameters differ between lean and overweight/obese patients. SHG/TPE microscopy assesses 28 collagen parameters per zone, correlating BL and EOT cohorts via heat map (p≤0.05 in red).
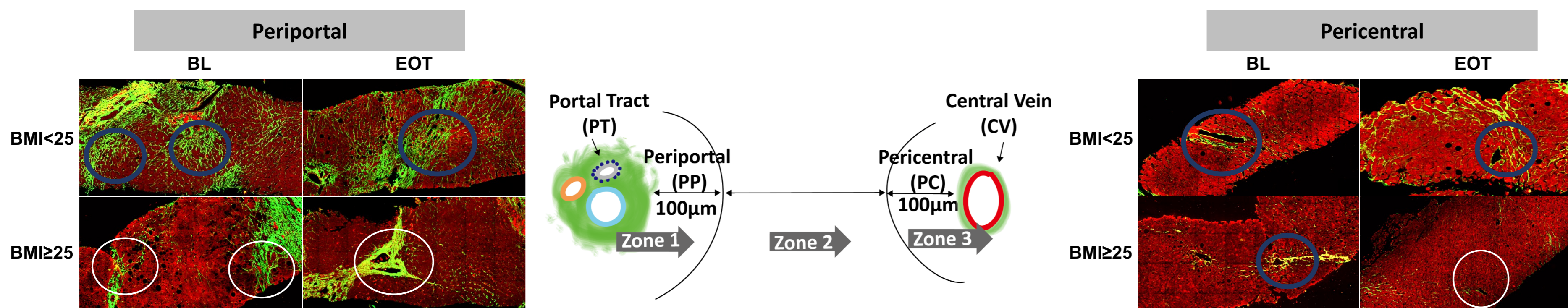
Figure 2. SHG/TPE images in lean versus overweight/obese patients in the periportal and pericentral zones.

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