

## **FIBROSIS DISTRIBUTION IN LEAN VERSUS OBESE NASH-CIRRHOSIS PATIENTS USING SHG/TPE MICROSCOPY**

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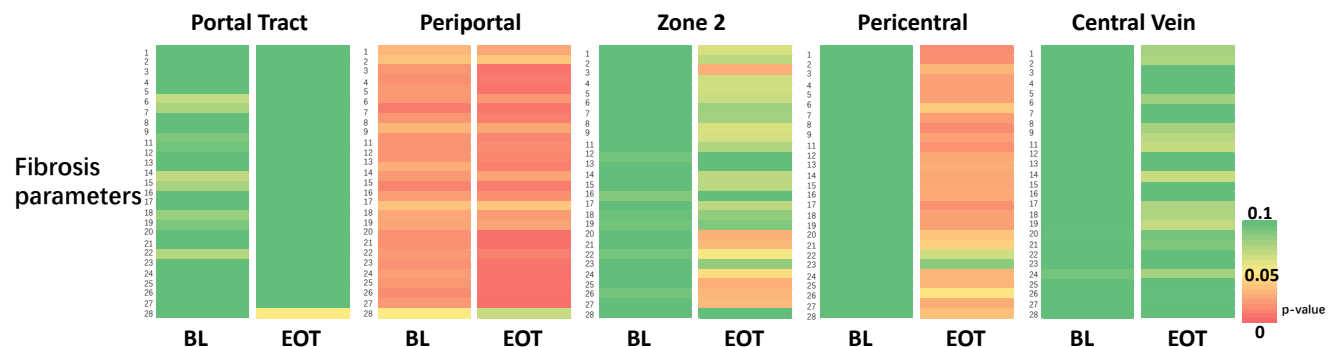
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**Background:** Inclusion criteria for drug trials focusing on Non-Alcoholic Steatohepatitis (NASH) cirrhosis require patients classified fibrosis stage as F4 by pathologists. However, F4 classification lacks comprehensive recording of zonal fibrosis parameters based on NASH Clinical Research Network (CRN). Second Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy-based qFibrosis (qF) offers fully quantitative evaluations. This study compares zonal fibrosis distribution between lean [Body Mass Index (BMI)<25] and overweight/obese (BMI≥25) patients using qF.

**Methods:** 133 patients from Phase 2b Belapectin drug trials (NCT04365868) were included. Paired liver biopsies were evaluated using qF based on NASH-CRN parameters. Patients were categorized into two groups: lean (n=9) and overweight/obese (n=124) in Baseline (BL) group, and lean (n=7) and overweight/obese (n=126) in End-of-Treatment (EOT) group. Statistical analysis by Wilcoxon-rank-sum-test, heat maps employed for visualization.

**Results:** BL group had statistically significant difference in periportal fibrosis parameters between lean and overweight/obese patient (Figure 1). Despite smaller number of patients in lean group compared to overweight/obese group, consistent observation of this significant difference of fibrosis parameters such as fiber length, thickness, etc. in periportal region in BL and EOT groups indicates a possible difference in fibrosis morphology patterns based on BMI.

**Conclusions:** Consistent differences in periportal fibrosis parameters between lean and overweight/obese patients using qF indicates SHG/TPE imaging provides additional information compared to conventional pathologist staging. These findings suggest there could be variations in zonal fibrosis distribution among NASH cirrhosis patients, based on BMI status. Further research with larger patient cohorts would be recommended to expand upon these preliminary observations.



**Figure 1:** Difference of collagen parameters between lean patients versus overweight/obese patients. In SHG/TPE microscopy, 28 fibrosis parameters based on collagen morphology such as fiber length, thickness, etc. are evaluated and quantified in each zone. These were then correlated between BL and EOT cohorts, and the results are shown via heat map with statistical significance ( $p \leq 0.05$ ) depicted in red.

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