SPONSORED BY THE
Federal Ministry of Education and Research

FOCUSED SCORES ENABLE RELIABLE DISCRIMINATION OF SMALL DIFFERENCES IN STEATOSIS

André Homeyer[1], Seddik Hammad[2,3], Lars Ole Schwen[1], Uta Dahmen[4], Henning Höfener[1], Yan Gao[2], Steven Dooley[2], Andrea Schenk[1]

[1] Fraunhofer MEVIS, Bremen [2] Medical Faculty Mannheim, Heidelberg University [3] South Valley University, Qena [4] Jena University Hospital

INTRODUCTION

- Automated image analysis enables quantitative measurement of steatosis in histological images
- Standard scores cannot reliably discriminate small differences due to heterogeneity throughout tissue
- We developed novel, more reliable scores ‘focused’ on steatotic areas

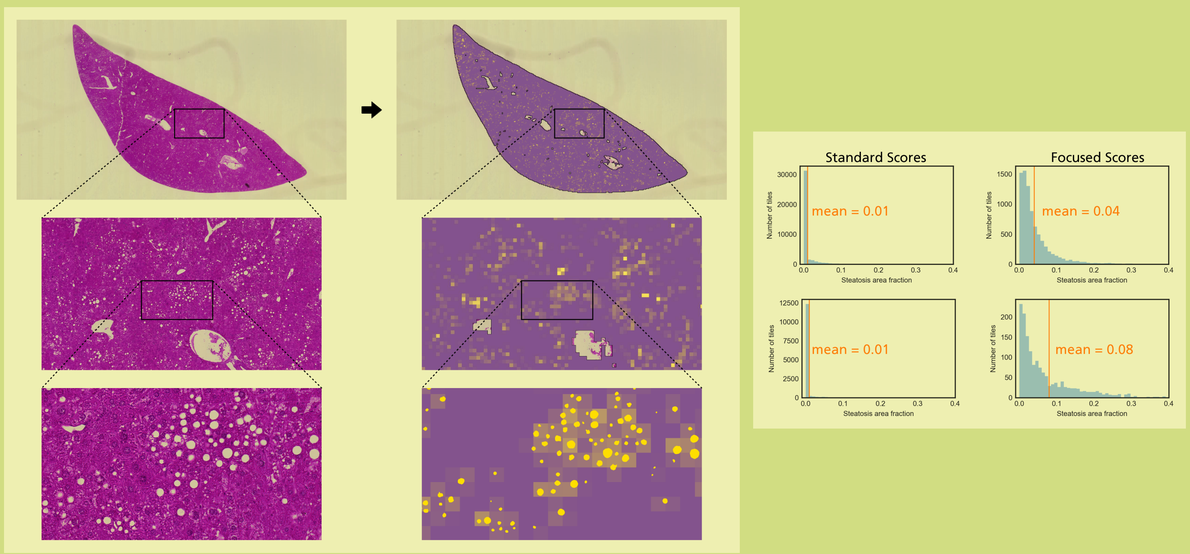

Figure 1. *Left:* Tile-based quantification of steatosis in whole-slide scans. *Right:* Distributions of tile-based steatosis area fractions; the corresponding mean values become discriminative only by focusing on steatotic regions.

MATERIAL AND METHODS

DATASETS

Whole-slide scans (227 nm/pixel) of H&E-stained slides of rodent liver tissue

- A: 4×6 rats fed different diets
- B: 5×6 mice, different periods of STAM treatment [1]
- C: 5×6 consecutive sections of one mouse liver, groups 300 µm apart [3]

FOCUSED SCORES

- Divide image in tiles of size $s \times s$, $s \in 8, \ldots, 128$ µm
- Compute steatosis area fraction (SAF) for each tile
- Compute descriptive statistics (mean, percentiles) over all tiles with nonzero steatosis (SAF $\neq 0$)

PERFORMANCE QUANTIFICATION

- Reliability via intraclass correlation coefficient (ICC; 0: poor, 1: perfect)
- Validity via Kendall’s τ correlation coefficient (0: no, ±1: perfect monotonic correlation); assuming
  - Groups sorted by steatosis level (dataset A)
  - Increase over time (dataset B)
  - (Not applicable for dataset C)

RESULTS: TILE SIZE EVALUATION

Score	Tile size	Statistic/Dataset	ICC/A	ICC/B	ICC/C	τ/A	τ/B
standard	n/a	mean	**0.86**	**0.54**	**0.14**	**0.78**	**0.60**
focused	8 µm	mean	0.84	0.76	0.72	0.79	0.73
focused	16 µm	mean	**0.94**	0.83	0.79	**0.81**	0.76
focused	**32 µm**	mean	**0.92**	**0.86**	**0.83**	**0.81**	**0.82**
focused	64 µm	mean	0.87	0.77	0.67	0.78	0.79
focused	128 µm	mean	0.86	0.62	0.28	0.77	0.70

- Dataset A already discriminated well by standard score
- Substantial improvement by focused mean for datasets B and C
- Tile size 32 µm generally performed best

RESULTS: PERCENTILE EVALUATION

Score	Tile size	Statistic/Dataset	ICC/A	ICC/B	ICC/C	τ/A	τ/B
focused	32 µm	mean	0.92	0.86	0.83	**0.81**	0.82
focused	32 µm	10th perc.	0.81	0.75	0.28	0.75	0.74
		⋮					
focused	32 µm	50th perc.	0.88	0.84	0.91	**0.80**	0.83
focused	32 µm	60th perc.	0.89	0.85	**0.94**	**0.80**	0.84
focused	32 µm	**70th perc.**	**0.91**	**0.87**	**0.93**	**0.80**	**0.86**
focused	32 µm	80th perc.	**0.93**	**0.88**	**0.85**	0.81	**0.86**
focused	32 µm	90th perc.	**0.94**	**0.87**	0.72	0.81	0.84

- 32 µm tile size fixed from above
- Focused high percentiles performed better than focused mean or lower percentiles
- 70th percentile generally performed best

RESULTS: RELIABLE DISCRIMINATION

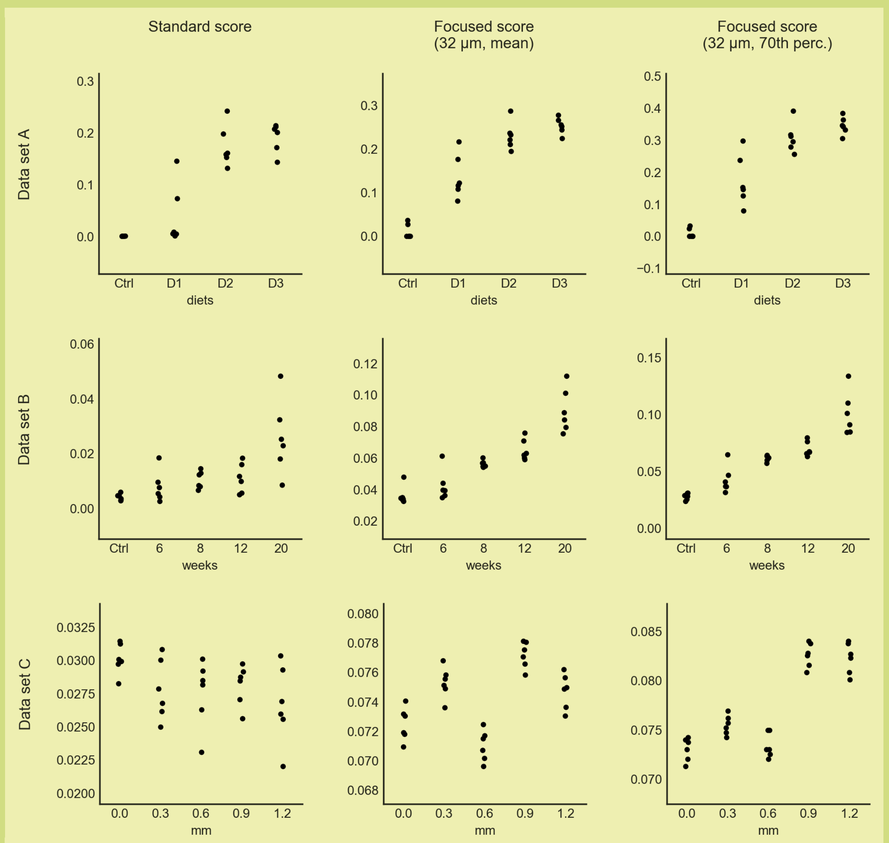

Figure 2. In the standard steatosis score (mean steatosis area fraction), different groups of specimens with small inter-group differences *(left column)* are hard to tell apart. In contrast, the focused mean *(middle)* and focused 70th percentile *(right column)* reliably discriminates between the different groups.

DISCUSSION & CONCLUSIONS

- Hotspot analysis focuses on regions with phenomenon of interest
- Tile size needs to match structures of interest and their heterogeneity
- High percentile enhances focus on phenomenon of interest and excludes inevitable artifacts

REFERENCES

[1] M. Fujii et al., *A murine model for non-alcoholic steatohepatitis showing evidence of association between diabetes and hepatocellular carcinoma*, Medical Molecular Morphology **46** (2013), no. 3, 141–152. DOI 10.1007/s00795-013-0016-1

[2] A. Homeyer, S. Hammad, L. O. Schwen, U. Dahmen, H. Höfener, Y. Gao, S. Dooley, and A. Schenk, *Focused scores enable reliable discrimination of small differences in steatosis*, Diagnostic Pathology **13** (2018), no. 76, 1–9. DOI 10.1186/s13000-018-0753-5

[3] L. O. Schwen, A. Homeyer, M. Schwier, U. Dahmen, O. Dirsch, A. Schenk, L. Kuepfer, T. Preusser, and A. Schenk, *Zonated quantification of steatosis in an entire mouse liver*, Computers in Biology and Medicine **73** (2016), 108–118. DOI 10.1016/j.compbiomed.2016.04.004

CONTACT

André Homeyer ‹andre.homeyer@mevis.fraunhofer.de›
Ole Schwen ‹ole.schwen@mevis.fraunhofer.de›