Quantification of Fibrotic Changes in Hematoxylin and Eosin-stained Wistar Rat Liver Sections Using Deep Learning

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Objectives

To develop a Deep Learning (DL) algorithm for automated quantification of fibrotic changes in Whole Slide Images (WSI) of Hematoxylin and Eosin (H&E) stained sections from Wistar rat liver.

Introduction

Fibrosis is usually linked to chronic liver parenchymal injury and is considered irreversible. Perpetuation of the fibrotic reaction can lead to end-stage liver disease, cirrhosis, and hepatocellular carcinoma, with a worldwide increase in incidence. Disease models in rodents are utilized to assess efficacy of test compounds being investigated to treat liver fibrosis. Collagen specific histochemical stains such as Masson's Trichrome (MT) or Picrosirius Red (PSR) are commonly used for assessment of fibrosis in rodents. However, these staining techniques add to the cost and turnaround time. We provide a DL-based technique for quantification of fibrosis on H&E-stained liver sections of Wistar rats, a staining technique routinely used in animal studies.

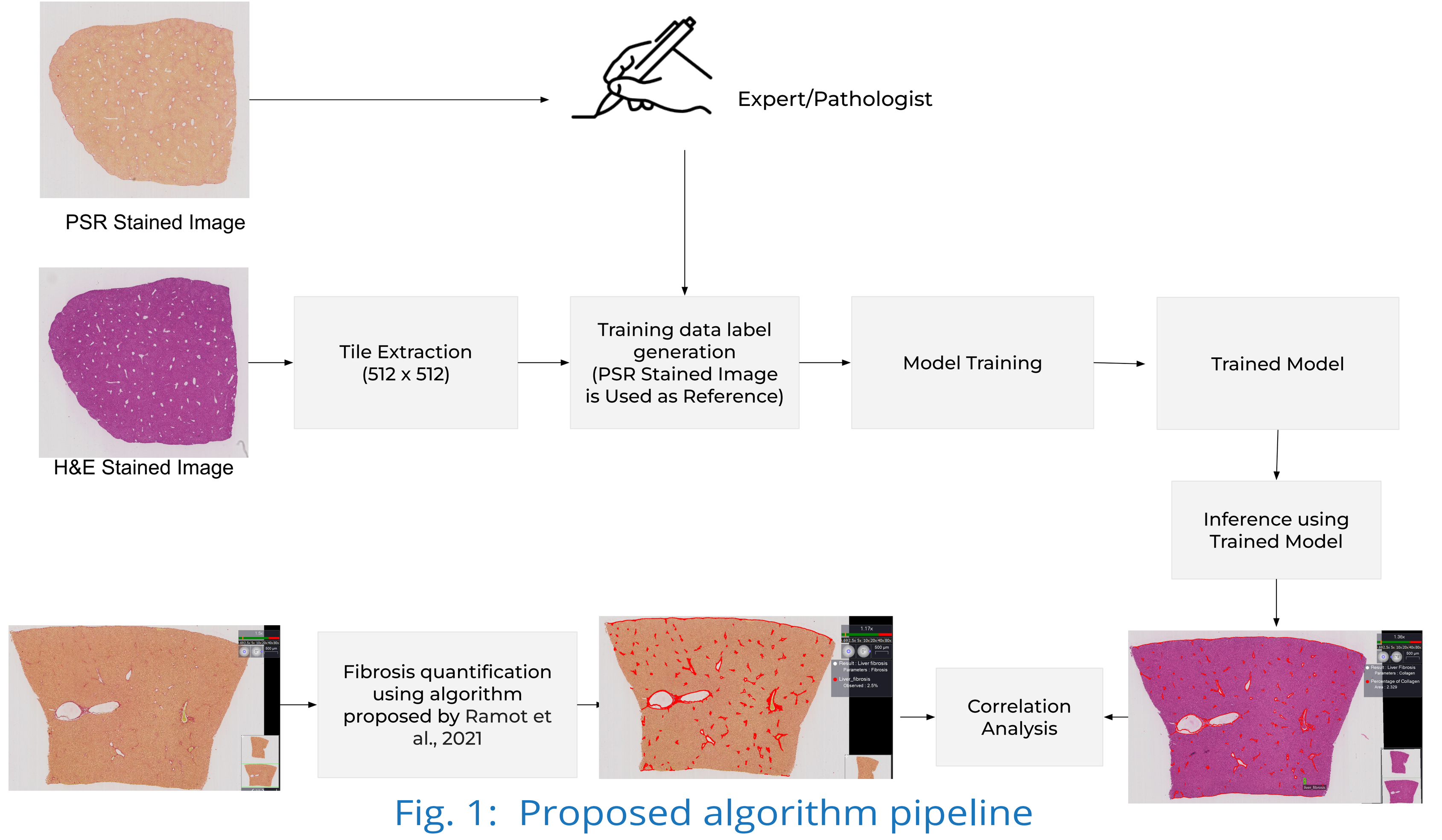

Fig. 1: Proposed algorithm pipeline

Materials and Methods

Training data generation

- 3000 tiles of size 512x512 were extracted from 27 H&E stained WSI at 20x magnification
- Using serial sections stained with PSR, an expert pathologist annotated fibrosis regions in the corresponding sections stained with H&E (Fig. 2)

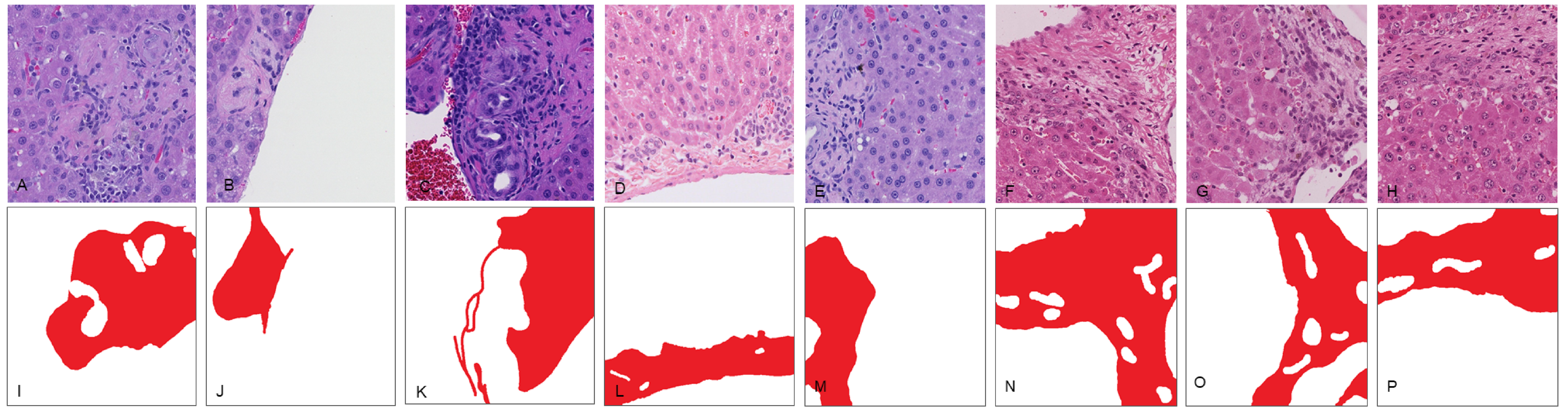

Fig. 2: Original Input Tiles (A to H), Ground Truth Label (I to P)

Model development

- Customized U-Net with Efficient-Net B0 model was trained to identify fibrosis area
- 2100 tiles were used to train the model and the remaining 900 tiles were used for validation.
- The model achieved a F1-score of 91% on the validation set.

Model Validation

- Algorithm was tested on 10 WSI of H&E stained liver sections.
- Quantification results on 100 WSI of H&E stained liver sections were also compared with estimates from serial PSR stained sections
- Estimates on PSR stained sections were obtained using the algorithm proposed in Ramot et al, 2021.

Results

- The algorithm showed a recall of 97.35% and precision of 90.78% in comparison with pathologist annotations.
- The fibrosis quantification results of the current algorithm on H&E stained sections strongly correlated (Pearson correlation coefficient = 0.9237) with fibrotic region quantification in serial sections stained with PSR (Fig. 3 and 4).

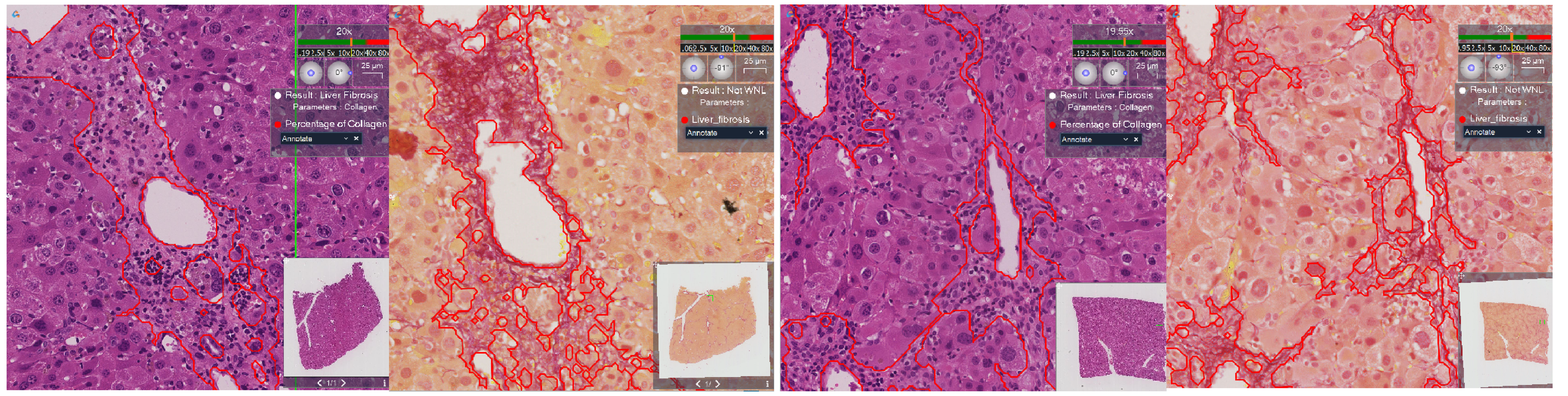

Fig. 3: Fibrosis detection in H&E stained liver WSI in comparison with PSR stained WSI

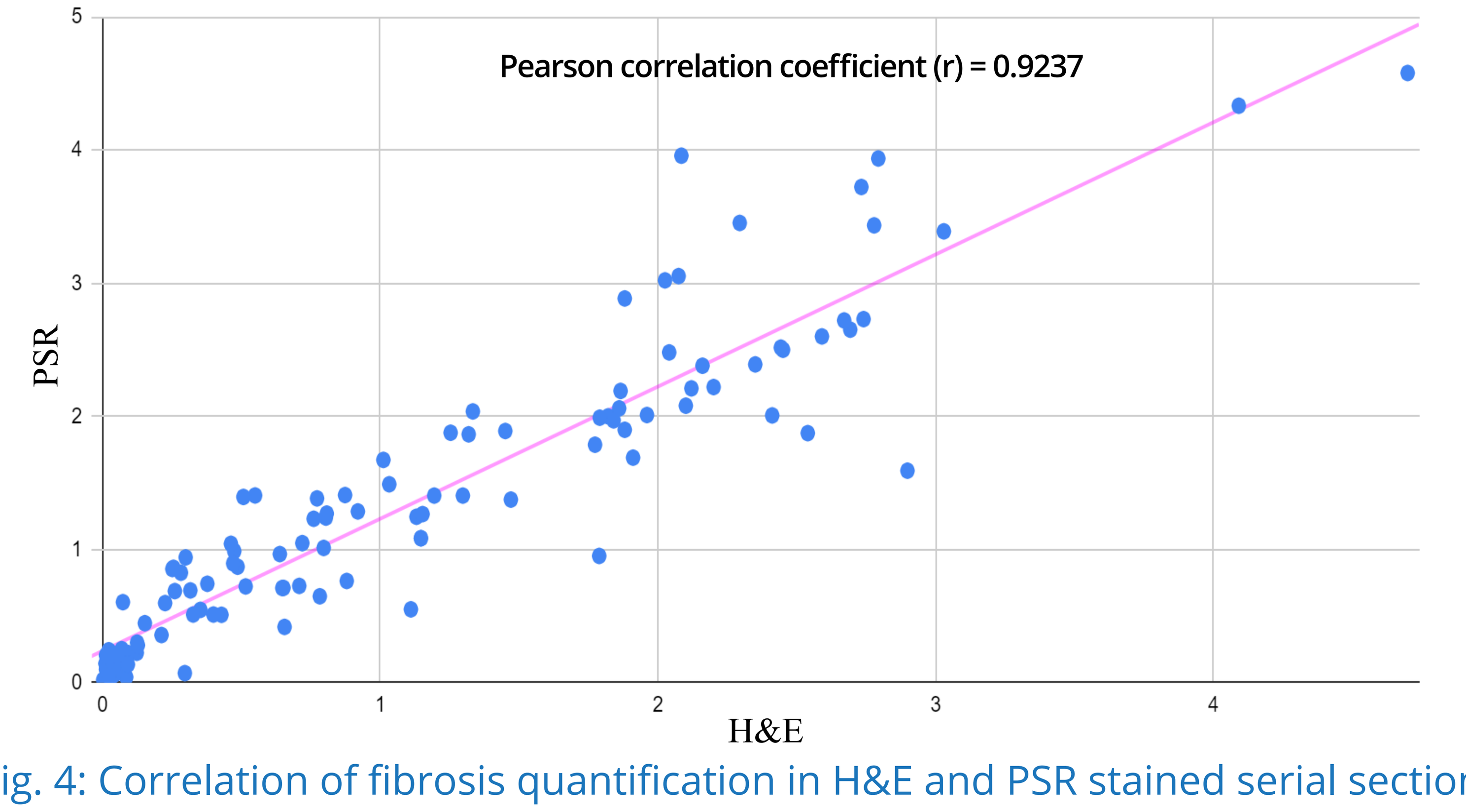

Fig. 4: Correlation of fibrosis quantification in H&E and PSR stained serial sections of liver

Conclusion

The proposed algorithm provides a sensitive and precise method for detecting and quantifying fibrotic alterations in H&E stained sections of Wistar rat liver.

Impact Statement and Way Forward

1. The proposed technique eliminates the requirement for special histochemical stains like PSR for fibrosis quantification in WSI of Wistar rat liver.
2. This method has the potential of routine application in nonclinical efficacy and toxicity studies.

Future works include validating the algorithm on larger data sets from multiple sources.

References

Ramot Y, Deshpande A, Morello V, Michieli P, Shlomov T, Nyska A. Microscope-Based automated quantification of liver fibrosis in mice using a deep learning Algorithm. Toxicol Pathol. 2021;49(5):1126–1133. Doi: 10.1177/01926233211003866