An HE-only workflow for liver fibrosis assessment using HE-predicted collagen

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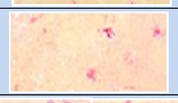
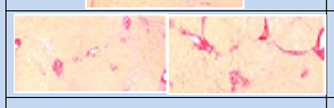
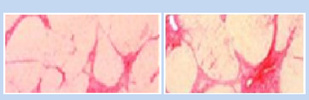
Context and Introduction

- In histology, **HE (Hematoxylin and Eosin)** is the primary tissue stain worldwide.
- **Fibrosis** is a key biomarker in liver diseases.
- To highlight fibrosis, special stains like **HES** (HE with additional saffron), **Sirius Red (SR)** and **Masson's Trichrome (MT)** are used.
- This study aims to **quantify** and **highlight collagen** from **HE** tissue samples **using Deep Learning**. We want to develop an **HE workflow for fibrosis analysis** without the need **for collagen-related stains**.
- This approach is particularly valuable for **low-to-moderate levels of fibrosis** which are only visible at **higher magnification**.

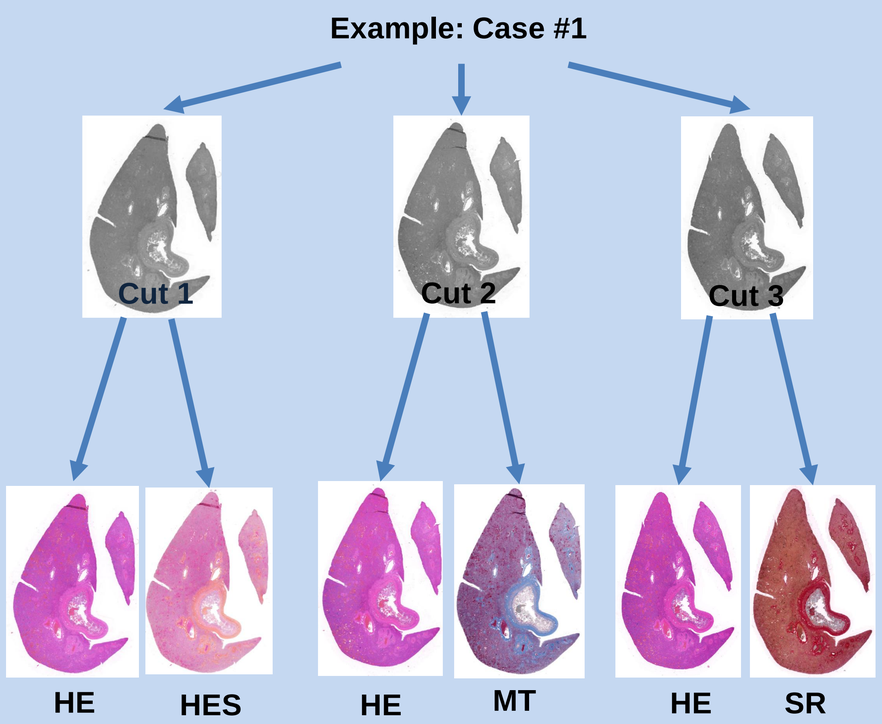
METAVIR[1] Score

Appearence	METAVIR Score	Simple Description
	F0	No fibrosis (normal)
	F1	Fibrosis some portal areas
	F2	Fibrosis most portal areas, some Portal-Portal fibrosis
	F3	Fibrosis portal areas with some marked Portal-Portal fibrosis and some Portal-Central fibrosis
	F4	Cirrhosis (Nodules)

Dataset Acquisition

The dataset was created at the University of Veterinary Medicine Vienna with ethical permission. Every slide was scanned at magnification 40x (0.25 micron/pixel) using a 3Dhistech Panoramic Flash II scanner.

- **11 retrospective animal liver cases**
- **Varying degree of Fibrosis**
- **For each case: HE–HES–MT–SR**
- **Total tissue surface: 10.3 cm2**

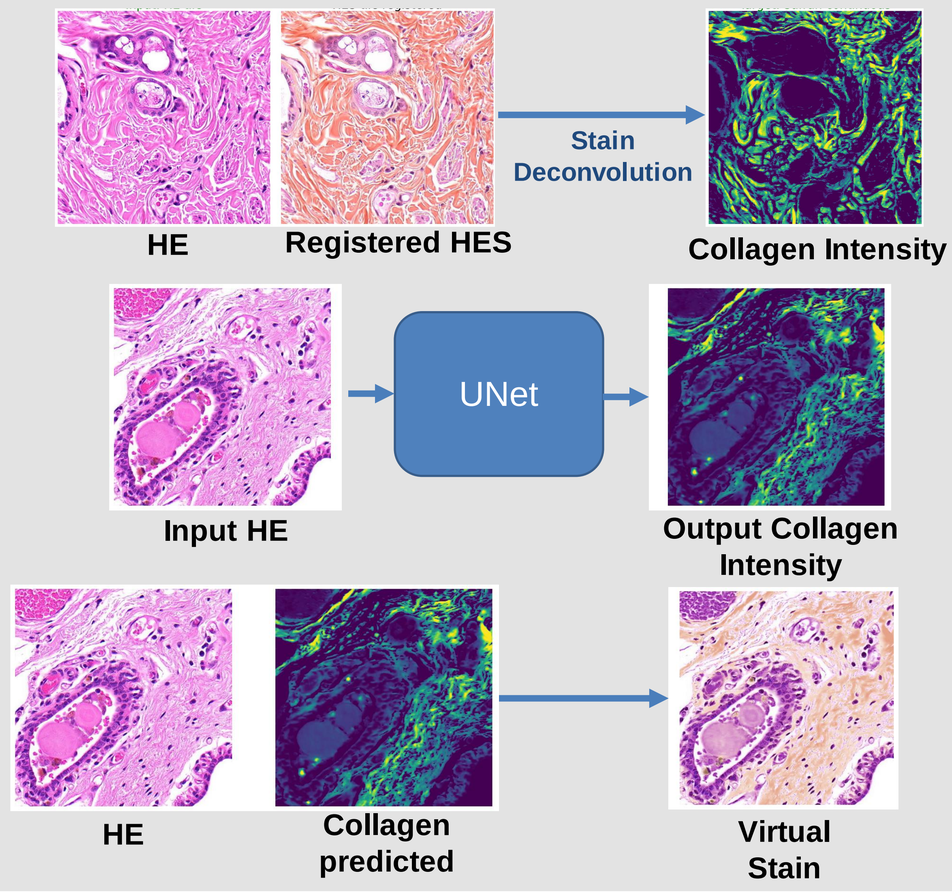


Method

Step 1: Target Extraction: We **registered** restained HE and HES slides, and we extracted for each HE tile the associated **pixel-wise Saffron intensities** using **Stain Deconvolution**

Step 2: Deep Learning We train a **UNet**[2] to predict the Saffron intensities from HE tiles at magnification 20x.

Step 3: Virtual Staining We defined a **simple reconstruction method** based on stain convolution to get **virtual HES** from the **HE image and the predictions**.



Results

Figure 1 – Quantitative Evaluation protocole
Pearson correlations are computed between **the predicted collagen** intensity and **the real stain intensities** (extracted via stain deconvolution). **Our model was trained using HES images** and was evaluated on the three different stainings.

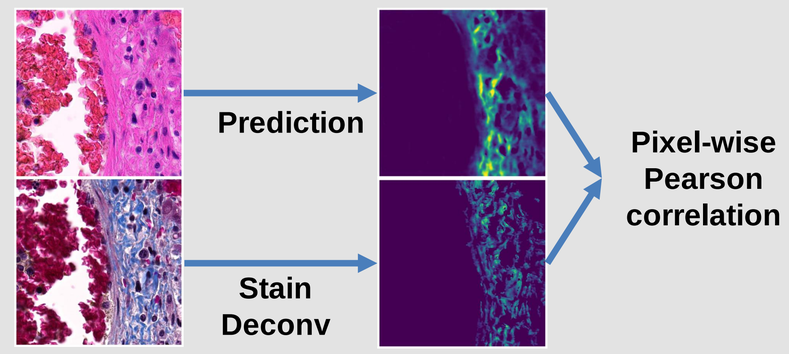


Table 1 – Pixel-wise correlation
Pearson correlation obtained with the **quantitative evaluation protocole**. We got better correlation with HES because our model was trained on this staining.

	HES	Sirius Red	Masson's Trichrome
Pearson correlation with predictions	0,87	0,71	0,78

Figure 2 – Qualitative Evaluation protocole
Each **pathologist** graded the **METAVIR** score on the **virtually stained slide** and **the real MT slide** with a **two weeks washout time**.
We computed the **agreement** between the two scores.

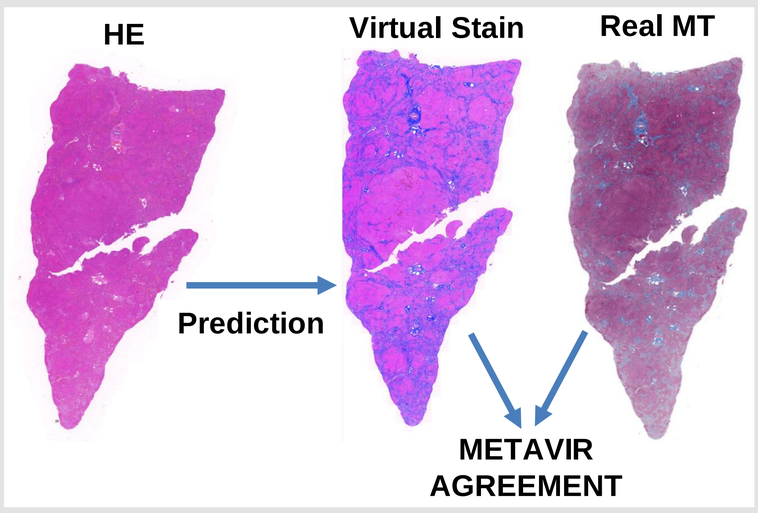


Table 2 – METAVIR Agreement
METAVIR agreement obtained with the **qualitative evaluation protocole**.
METAVIR Distribution: 1 F0, 4 F1, 2 F2, 2 F3, 2 F4
Unique Error: F0 predicted as F1 on synthetic slide

	Pathologist 1	Pathologist 2
METAVIR Agreement Rate (Real vs Virtual)	10 / 11	11 /11

References, Collaborators & Partners.

35th European Congress of Pathology, 9-13 September, Dublin
[1] Intraobserver and interobserver variations in liver biopsy interpretation in patients with chronic hepatitis C., 1994 METAVIR Study Group
[2] U-net: Convolutional networks for biomedical image segmentation, Ronneberger, Olaf and Fischer, Philipp and Brox, Thomas, International Conference on Medical

Conclusion

- We proposed a method that allows to **predict accurately pixel-wise fibrosis intensities from HE** images, allowing to quantify the fibrosis **at high magnification**.
- We showed that this method can generate virtually stained slides from HE images that highlight fibrosis content allowing the pathologist to grade the METAVIR almost exactly like on a real Masson's Trichrome slide.
- This study paves the way for future product development allowing to reduce the need for special stains in fibrosis detection.

Link to related article