International Congress on Coagulopathy in Liver Disease

Hemostasis and Thrombosis in Liver Disease: from Bench to Bedside

Castellana Grotte (BA)
8-10 April, 2026

Towards an augmented morphometric approach for vascular liver diseases

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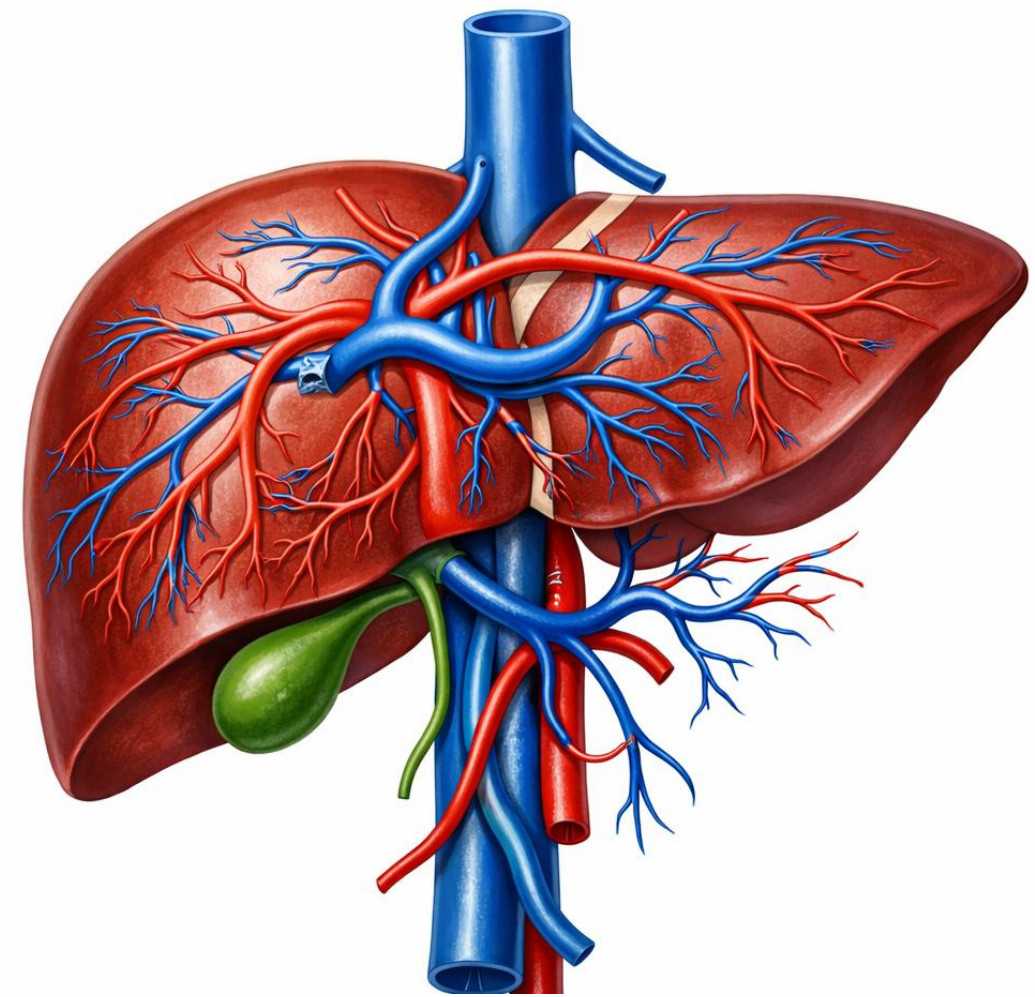
Vascular Liver Diseases

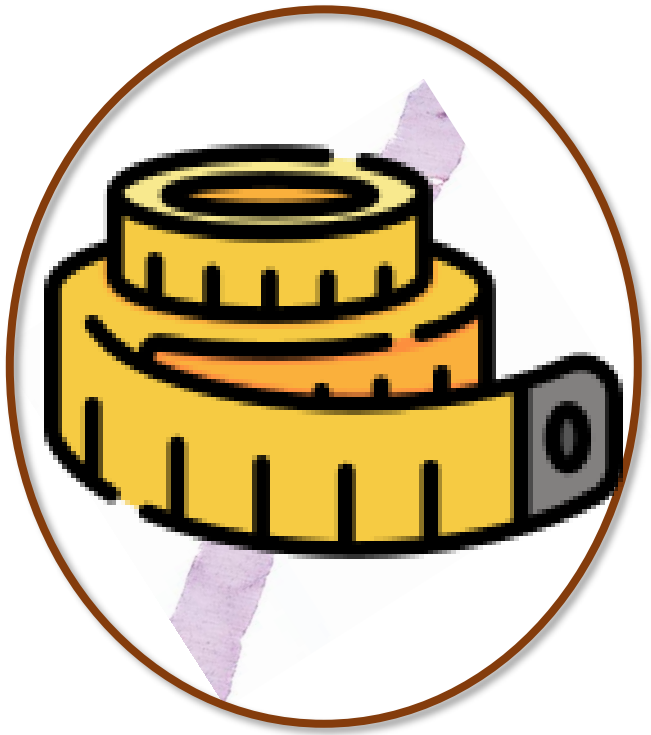


Venous outflow obstruction
Budd-Chiari syndrome
Congestive hepatopathies

Intra-hepatic small vessels
Portal venule (PSVD)
Sinusoids: dilatation, peliosis
Centrilobular vein :SOS/VOD

Portal thrombosis

Histology and Vascular Liver Diseases

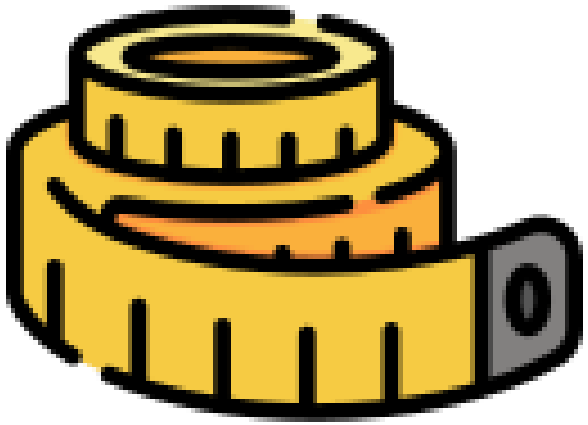


1. **Accurate diagnosis**

→ Describe the elementary lesions
→ Define the pathologic pattern
→ Identify potential associated diseases

2. **Prognostic information**

→ Extent of fibrosis



1. Improve Diagnosis

PSVD: a clinicopathological entity

Biopsy excluding liver cirrhosis

1 **specific** sign of portal hypertension

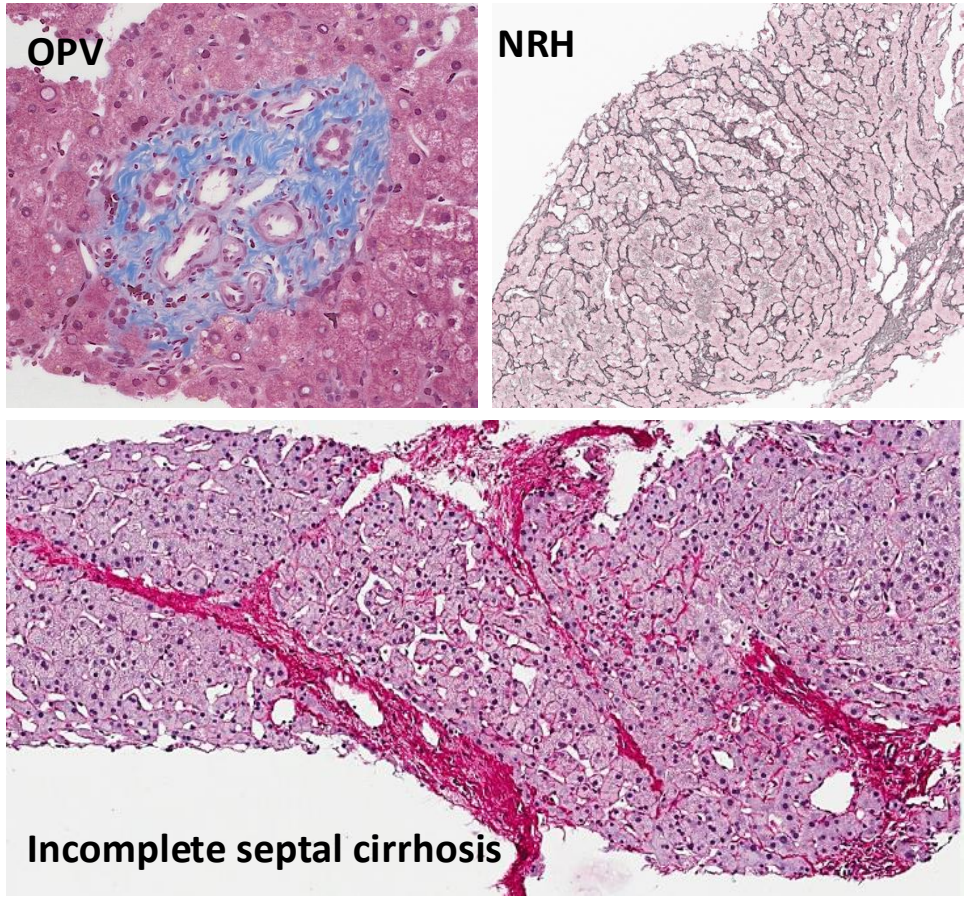
OR

1 **specific** histological lesion for PSVD

OR

1 **non-specific** sign of portal hypertension
+
1 **non-specific** histological lesion of PSVD

Specific signs



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Biopsy excluding liver cirrhosis

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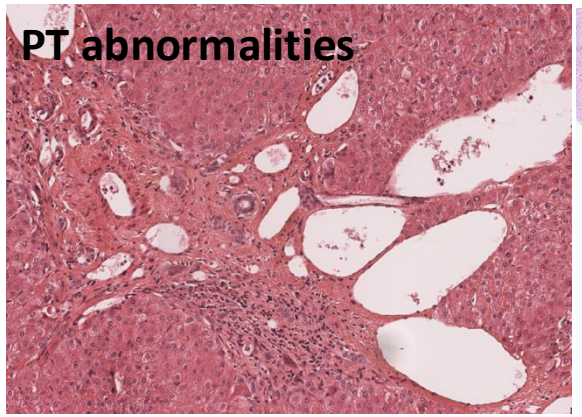
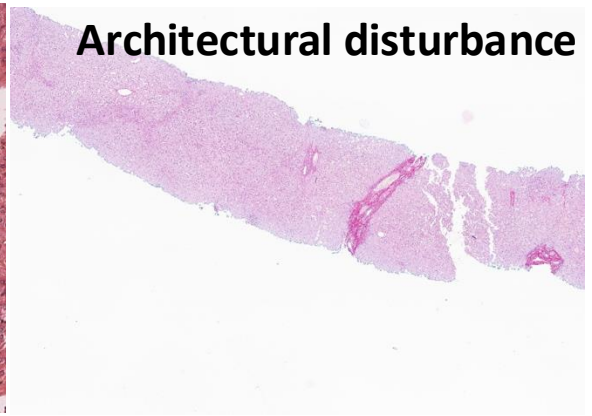
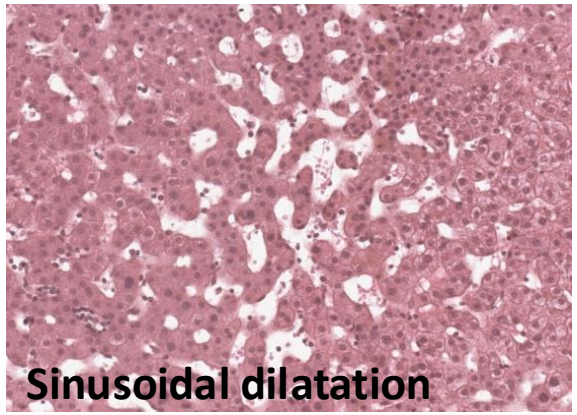
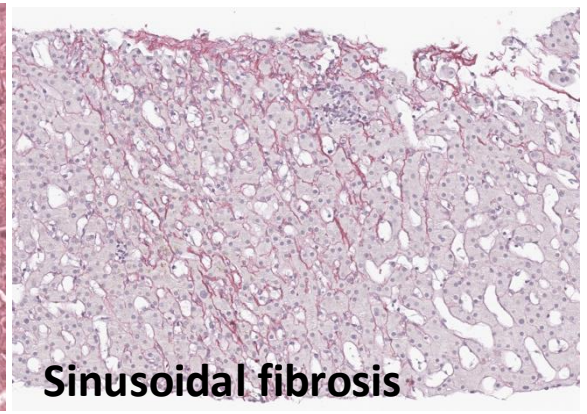
Non specific signs









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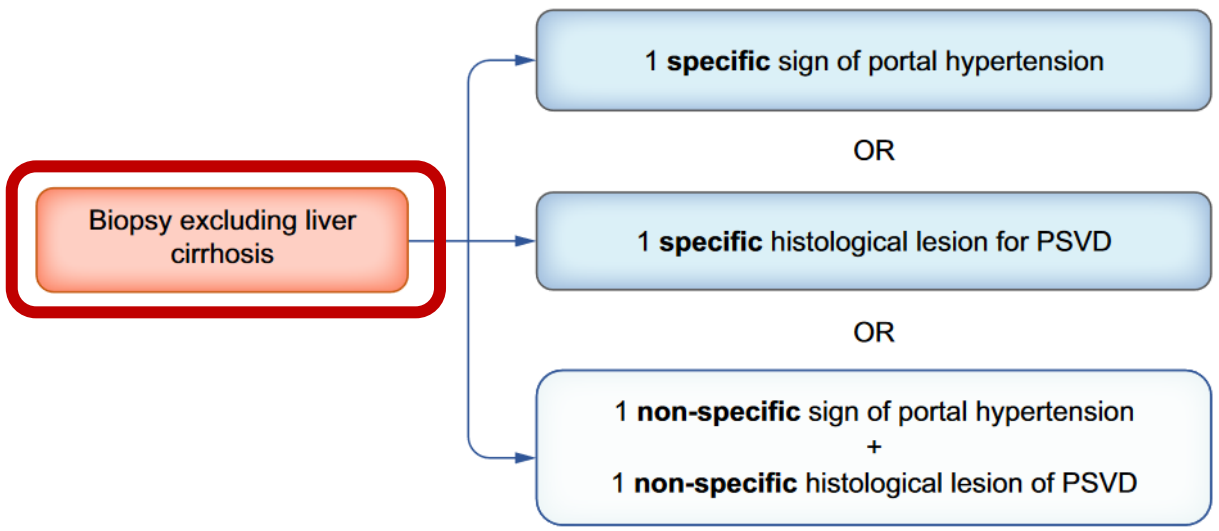
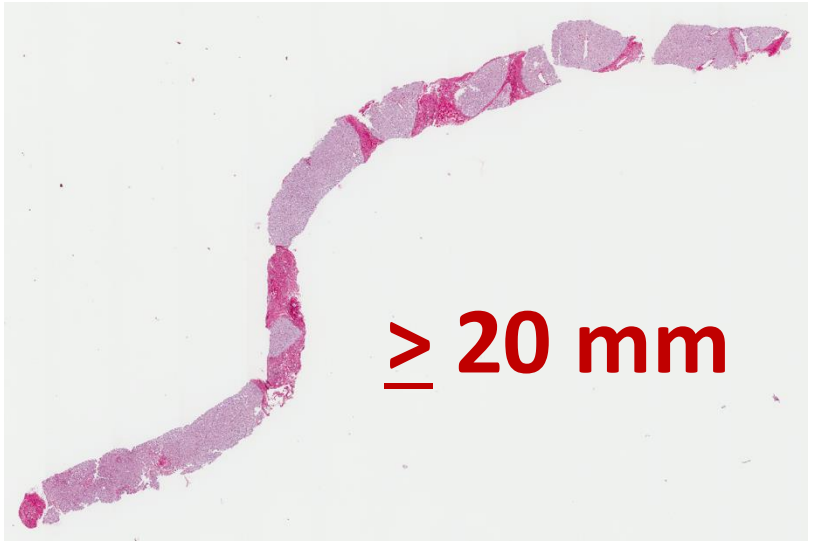
Rule out cirrhosis, Rule in PSVD





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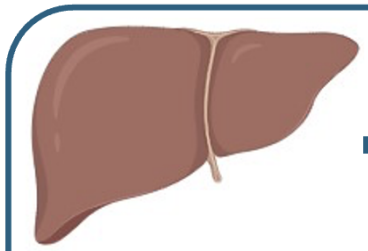
Quality of the biopsy for ruling out cirrhosis



24 liver explants:
- ✓ 12 PSVD
- ✓ 12 cirrhosis

36 000 virtual liver biopsies

Lengths:
5 mm, 10 mm, 15 mm, 20 mm, 25 mm, 5+10 mm, 5+5+5 mm

Staining:
Masson's trichrome
Picrosirius red

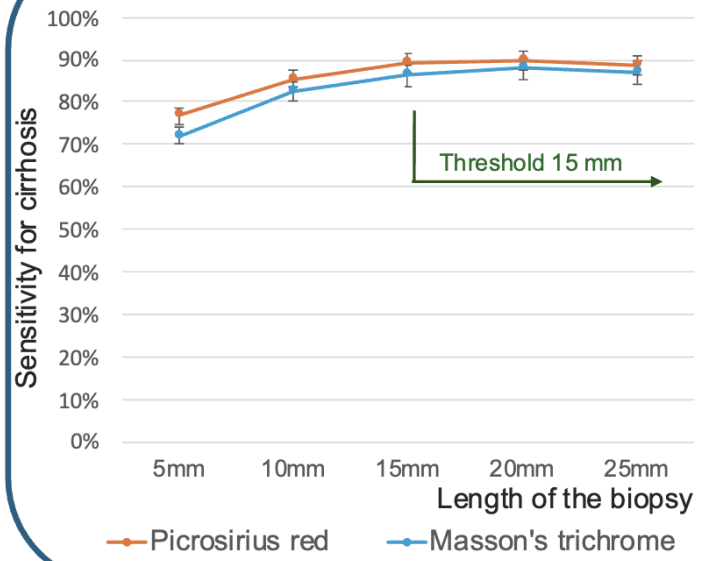
Widths:
1 mm: percutaneous
572 µm: transjugular

Cirrhosis

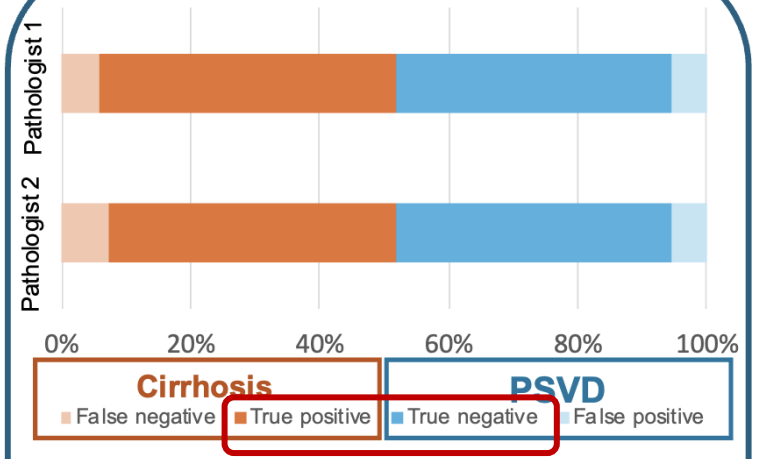
No cirrhosis

Each biopsy assessed by an **expert pathologist**
Validation cohort : 2nd pathologist

Quality criteria of liver biopsy when suspecting PSVD



Sensitivity for cirrhosis: 89%
- plateau from 15 mm
- same with ≥1 **fragment of 10mm**
- picrosirius red > Masson's trichrome
- transjugular route: slightly lower sensitivity than percutaneous but other information



Misclassified when:
- **Cirrhosis:** Laennec 4A; HBV-associated
- **PSVD:** incomplete septal fibrosis

De Broucker C JHEPRep 2025

PSVD: an evolving definition

Biopsy excluding liver cirrhosis

1 **specific** sign of portal hypertension

OR

1 **specific** histological lesion for PSVD

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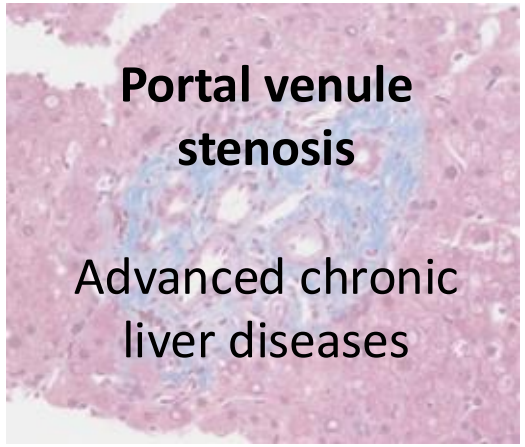
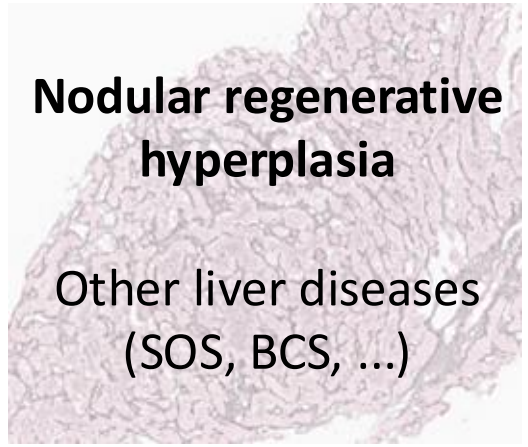
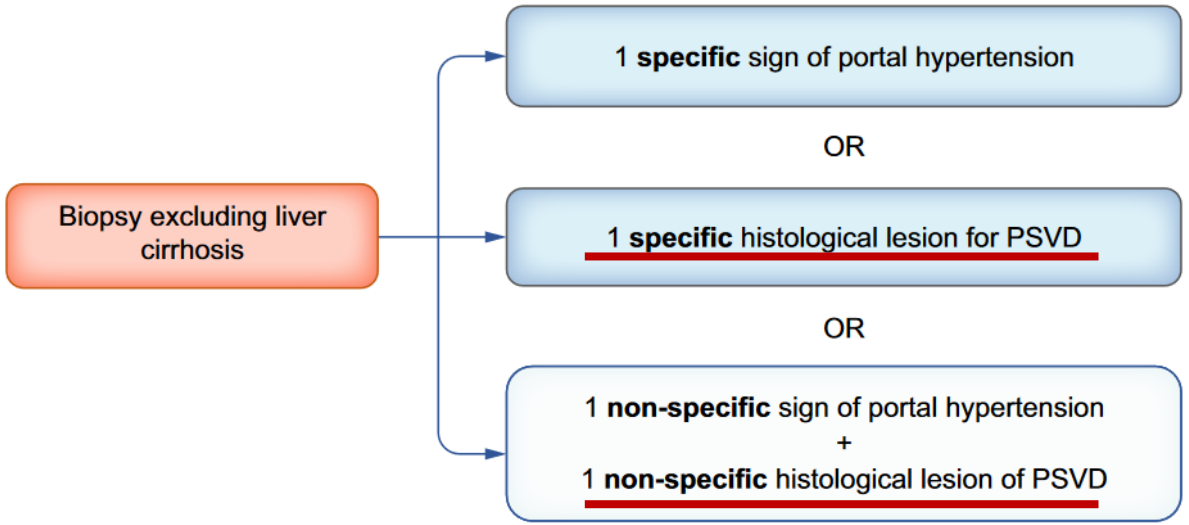
Specific signs ?





PSVD: an evolving definition



European vascular liver diseases network (EURO-VALDI-NET)

- **Move from an expert opinion to an evidence-based analysis**
- Implement a more specific, standardized & reproducible description of histological criteria associated with PSVD

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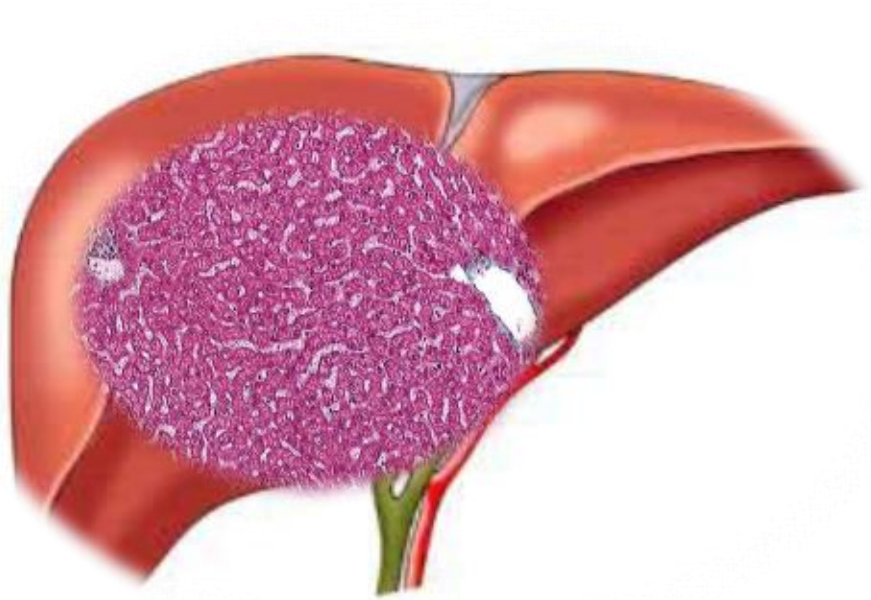
Pathology WG
HOLOGIC

1. What is a normal liver ?

A prerequisite to recognize a diseased liver & define thresholds (portal vascular changes)



The Normal Adult Human Liver Biopsy: A Quantitative Reference Standard

ALETA R. CRAWFORD,[1] XI-ZHANG LIN, [2] AND JAMES M. CRAWFORD[1]

TABLE 2. Number of Portal Tracts, Terminal Hepatic Veins, and Solitary Bile Duct Profiles or Cuboidal Strings of Cells per Biopsy

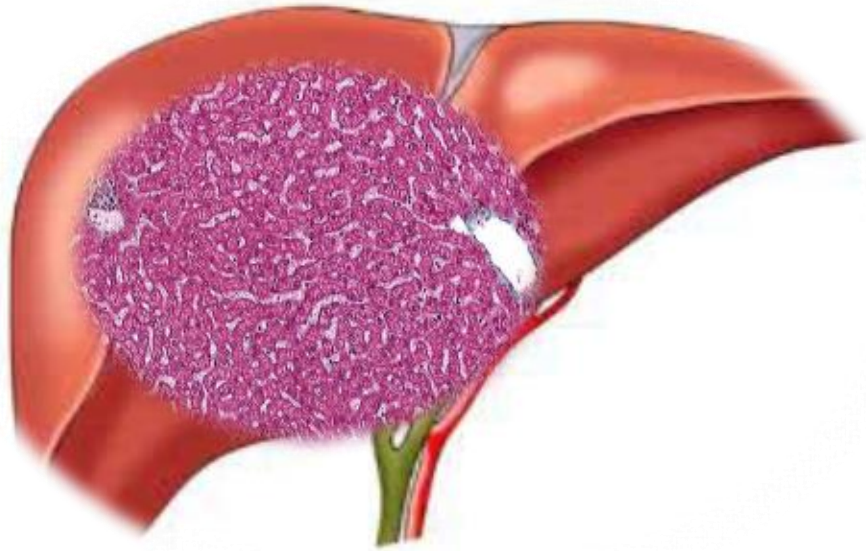
Structure	Average	Total	Range	95% Confidence Interval
Portal tracts	21 ± 10	338	5-38	16-26
Portal triads	11 ± 6	175	3-23	8-14
Portal dyads	8 ± 5	133	1-18	6-11
BD1 + HA	7 ± 5	109	1-17	4-9
BD1 + PV	1 ± 1	14	0-2	0-1
HA + PV	1 ± 1	10	0-2	0-1

Liver biopsy with normal histology (n=16, mean size 18 mm)
Analysis of serial sections (H&E, 15; MT, 10 & retic, 5)

Hepatology 2004

1. What is a normal liver ?

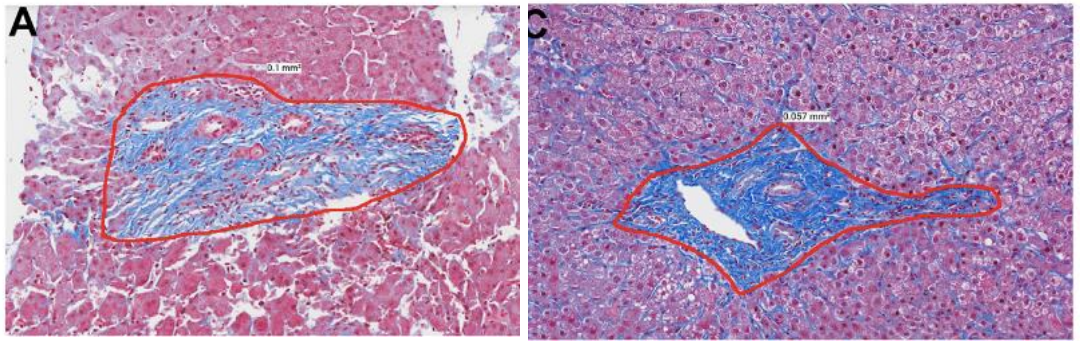
A prerequisite to recognize a diseased liver & define thresholds (portal vascular changes)



Shared Features of Obliterative Portal Venopathy, Normal Liver, and Chronic Liver Disease: A Histologic and Morphometric Analysis

Peizi Li[a], Thomas D. Schiano[b], Swan N. Thung[a], Stephen C. Ward[a], M. Isabel Fiel[a,*]

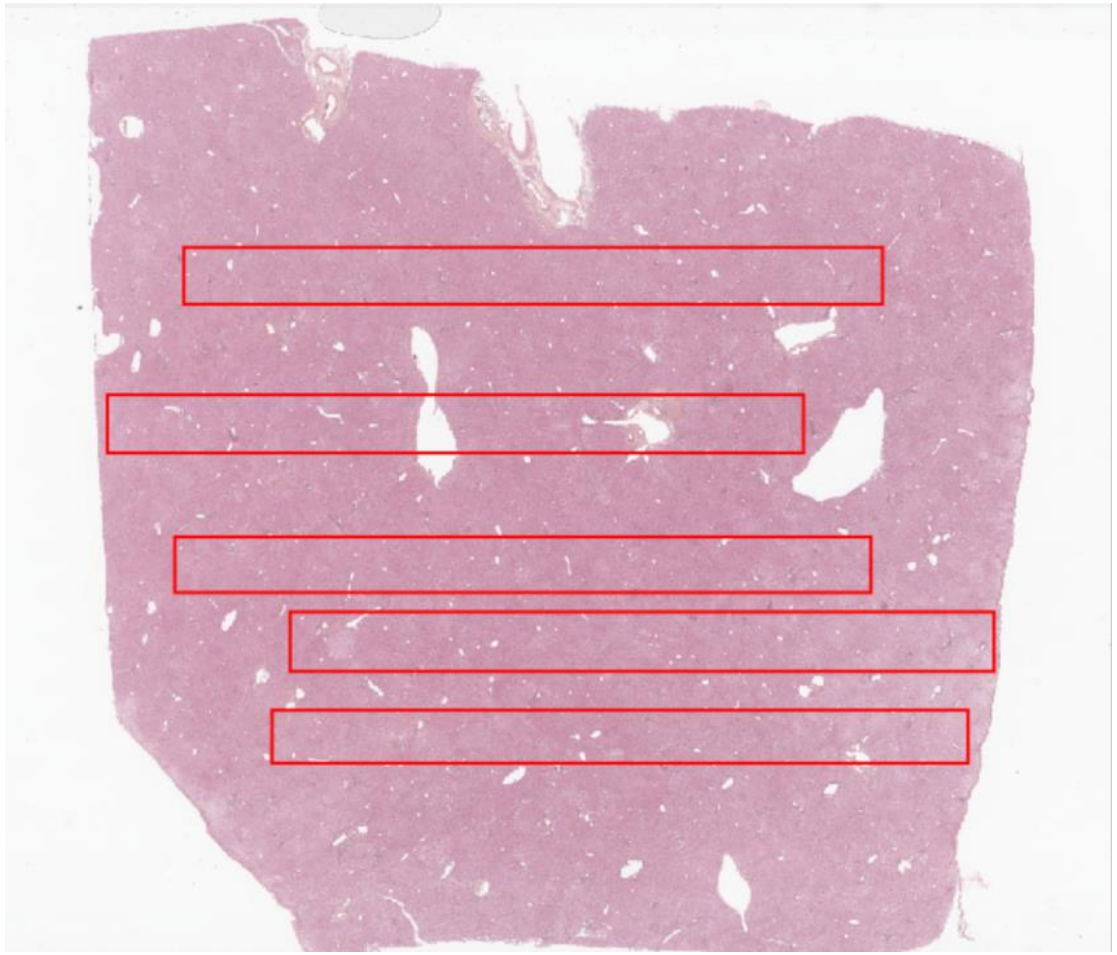
Morphometric analysis of overall PT area (mm^2) and the luminal area of dystrophic portal veins (mm^2)



Liver biopsy [OPV (n=72), Nl liver (n=40) & CLD + OPV (n=40)]
5 portal tracts / biopsy (Masson Trichrome)

Modern Pathol 2025

Morphometric analysis of normal liver



10 Reduced liver grafts
(surgical specimen, 1 WSI / case)
→ 10 WSI

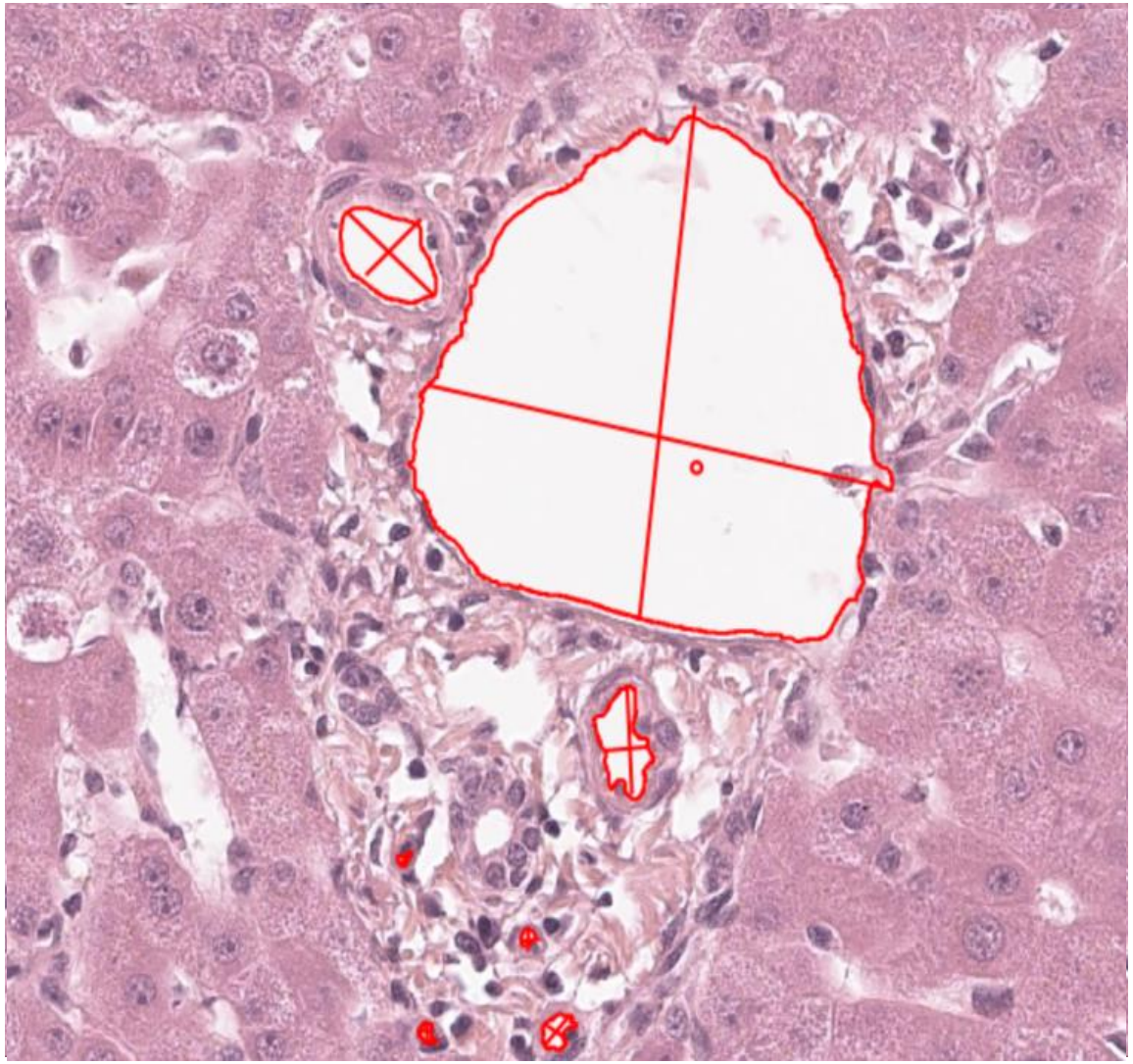
Random generation of "virtual biopsies" from WSI
L = 20 mm, l = 0.9 mm

5 virtual biopsies / WSI

→ 50 virtual biopsies

A Sayadi, Pathology fellow

Methods

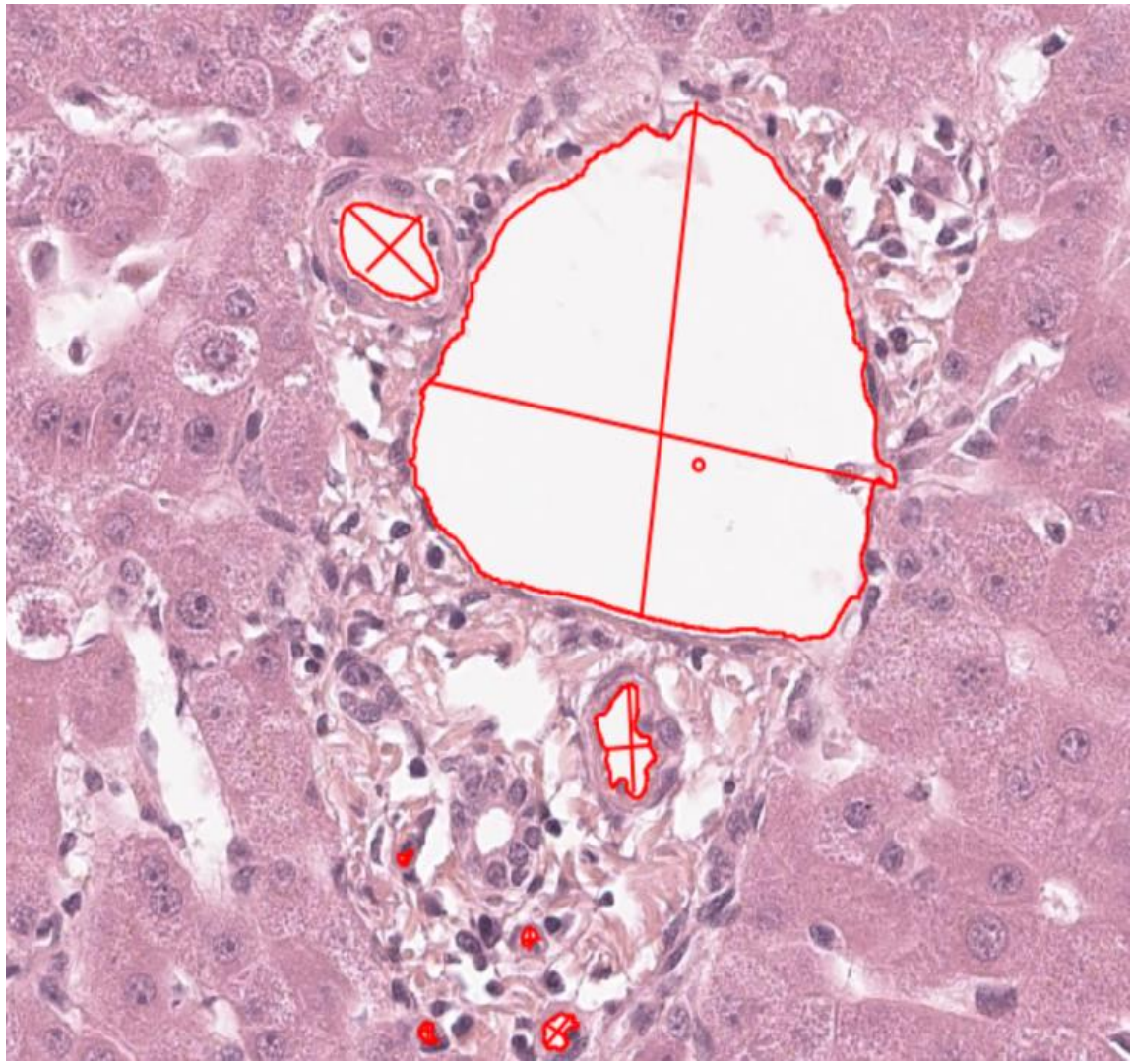


Measurements : QuPath

- Number of portal tracts (including dyads)
- Number of hepatic arteries (HA), bile ducts (BD) & portal veins (PV) / portal tract
- Area (μm^2), largest and smallest axis (μm) of HA & PV

A Sayadi, Pathology fellow

Results (Portal venules)



Characteristic	N = 50[1]	95% CI[2]	[Q2.5 - Q97.5]
PT without PV (%)	19.1	[20.6;28.6]	[0.0 - 48.4]

Characteristic	N = 292[1]	[Q2.5 - Q97.5]
PV axis / Artery axis (longitudinal, µm)	6.9	[1.9 - 22.8]
PV axis / Artery axis (orthogonal, µm)	6.3	[1.0 - 20.5]

[1] Median

[2] CI = Confidence Interval

Portal venule stenosis : threshold according to the axis

PV ⩽ 2 HA (longest/longitudinal axis)

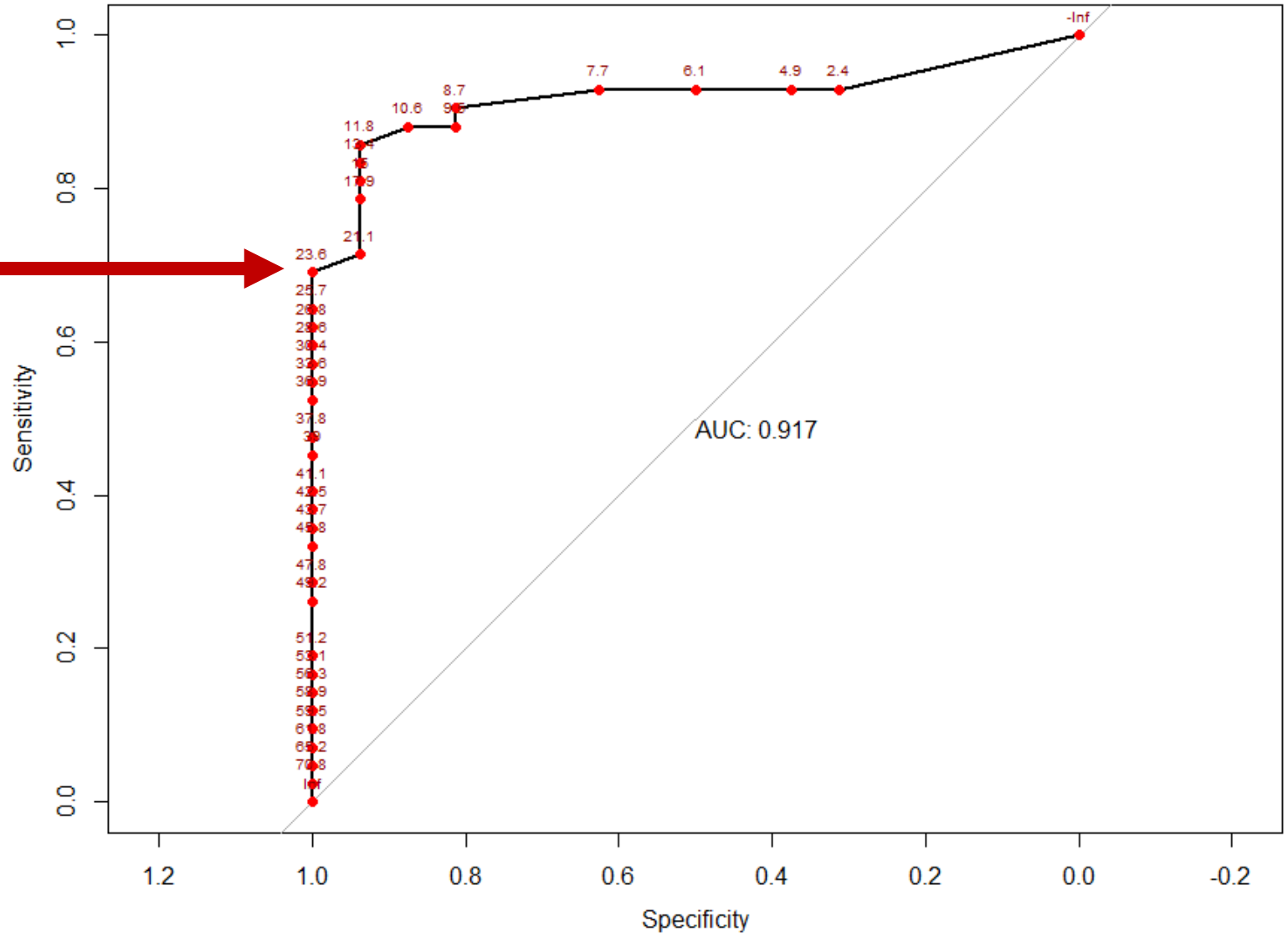
PV ⩽ HA (smallest/orthogonal axis)

Threshold for PV stenosis – PSVD *vs* normal liver

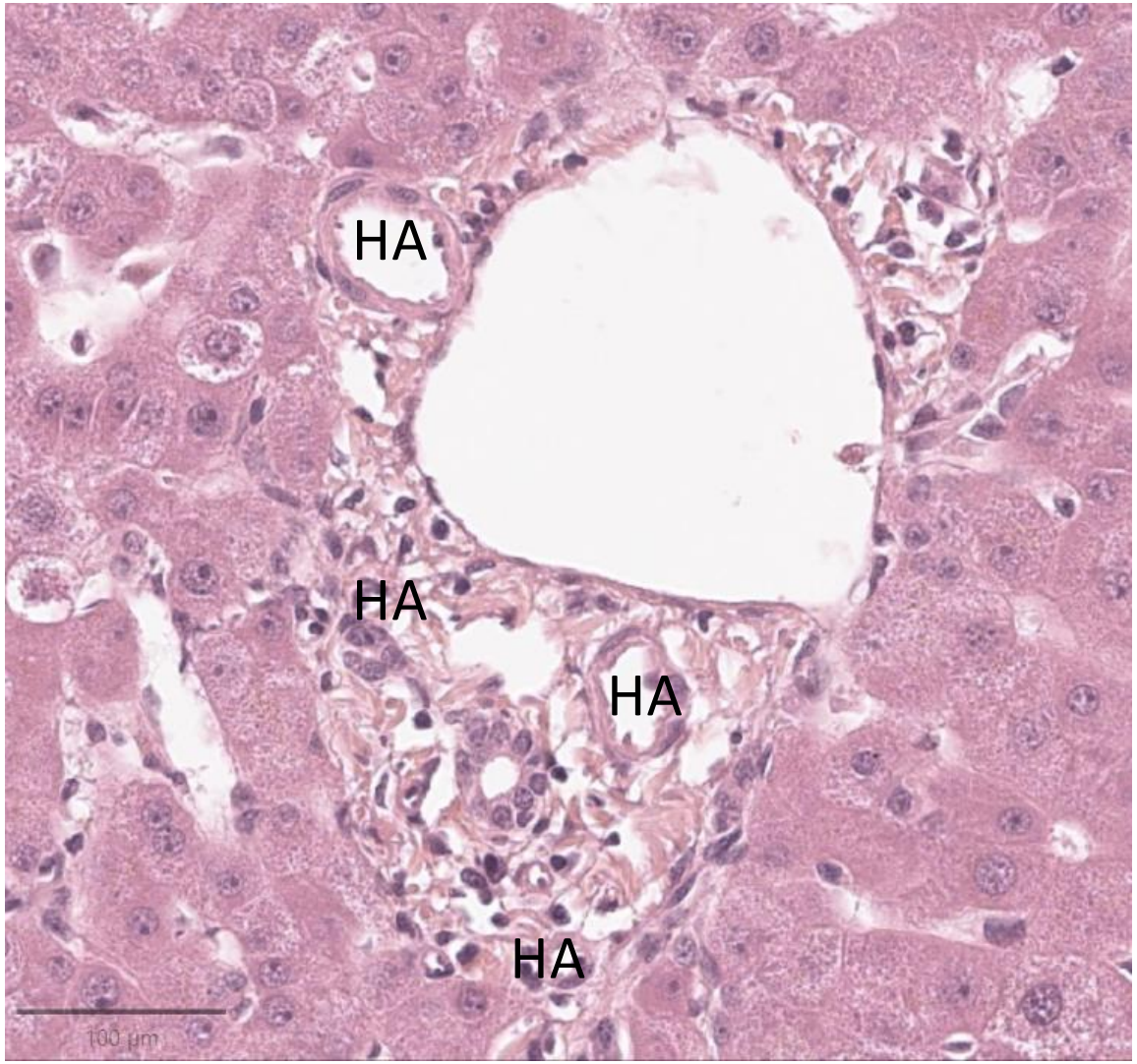
=> How many portal tracts should be involved for a PSVD diagnosis?

>25% of portal tracts with PV stenosis

=> Sp 100% (PSVD vs normal)



Results (Hepatic arteries)



Characteristic	N = 50[1]	[Q2.5 - Q97.5]
Total arteries by biopsy	10.0	[5.0 - 25.0]
Mean PA per PT	1.2	[0.7 - 2.5]
PT with >3 arteries	0.0	[0.0 - 3.0]
Total BD by biopsy	12.5	[6.2 - 23.8]
Mean BD per PT	1.5	[1.0 - 2.5]
PT with >3 BD	0.0	[0.0 - 2.0]
PA/BD ratio	0.8	[0.4 - 1.6]

[1] Median

Hyperarterialized PT : threshold

HA > 3 / PT

A Sayadi, Pathology fellow

2. New histological criteria for PSVD

1. Exploratory cohort of patients with PSVD (n=42), & normal liver (n=16)
Histological review by 9 pathologists (COST)

2. Study cohort of 218 patients with PSVD (n=88), normal liver (n=41) & chronic liver diseases (n=89)
Histological review by COST pathologists

3. External validation
Histological review by 9 other pathologists

Histological grid
(features associated with PSVD)

- ✓ Nb PT and nb of PT with portal abnormalities (PV stenosis, muscularized PV, herniated/dilated PV, hyperarterialized/vascularized PT)
- ✓ Sinusoidal dilatation & fibrosis (Y/N)
- ✓ Regenerative changes / RNH (Y/N)
- ✓ Portal fibrosis & bridging (Y/N)
- ✓ Centrilobular vein changes (Y/N)

Identify major & minor histological criteria associated with PSVD

Statistical analysis

- Elementary lesions

→ considered present when > 50% of readers saw the lesion

- Thresholds for selection of histological criteria

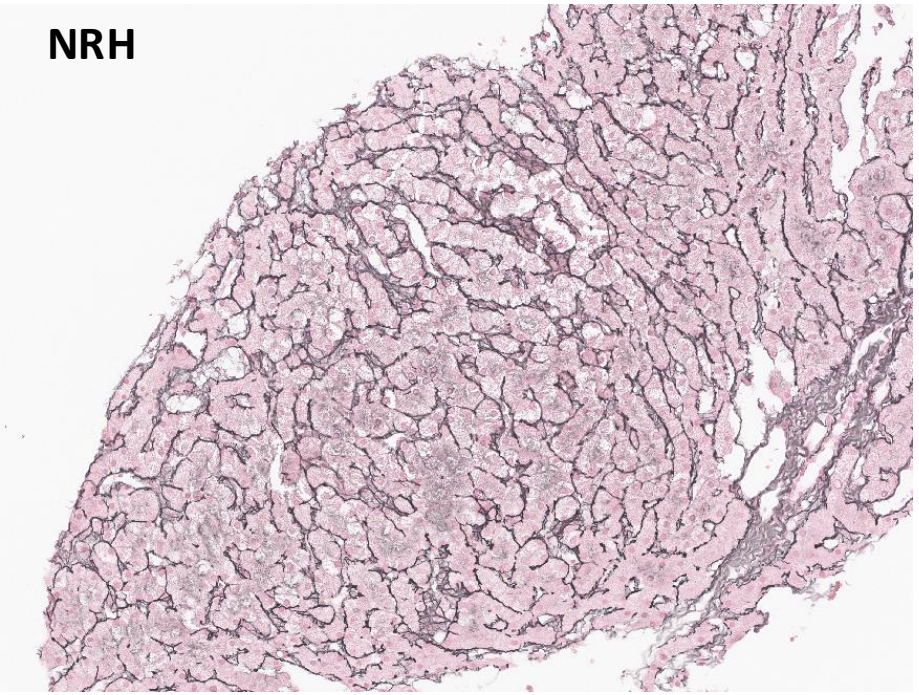
→ **Major criteria**: Spe > 0.95 & sens > 0.10

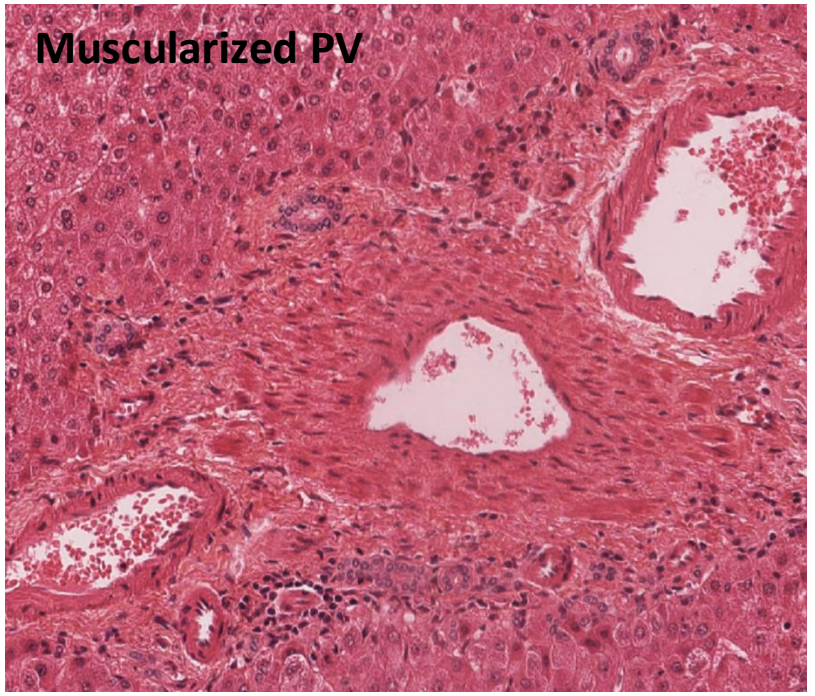
→ **Minor criteria**: Spe 0.80-0.94 & sens > 0.10
(in biopsies without major criteria)

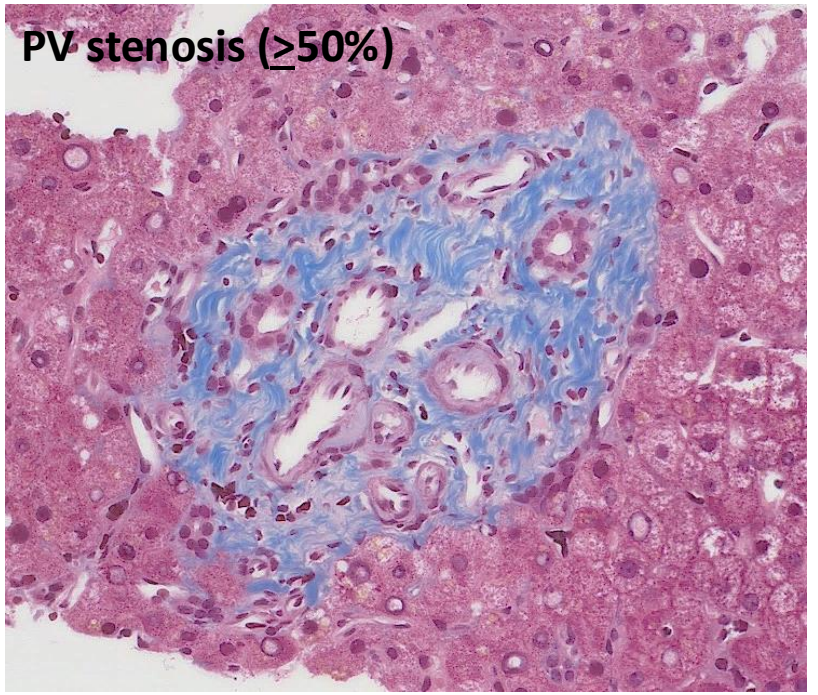
Major criteria	Sensitivity	Specificity	N	TP	TN	FP	FN
NRH	0.193	**1.000**	218	17	130	0	71
Muscularized portal venule	0.148	**1.000**	218	13	130	0	75
Portal venule stenosis > 50 % of portal tracts	0.205	**0.992**	218	18	129	1	70

Minor criteria	Sensitivity	Specificity	N	TP	TN	FP	FN
Regenerative changes	0.532	**0.845**	176	25	109	20	22
Abnormal distribution of vascular structures	0.511	**0.837**	176	24	108	21	23
Portal venule stenosis 25-49% of PT	0.319	**0.915**	176	15	118	11	32

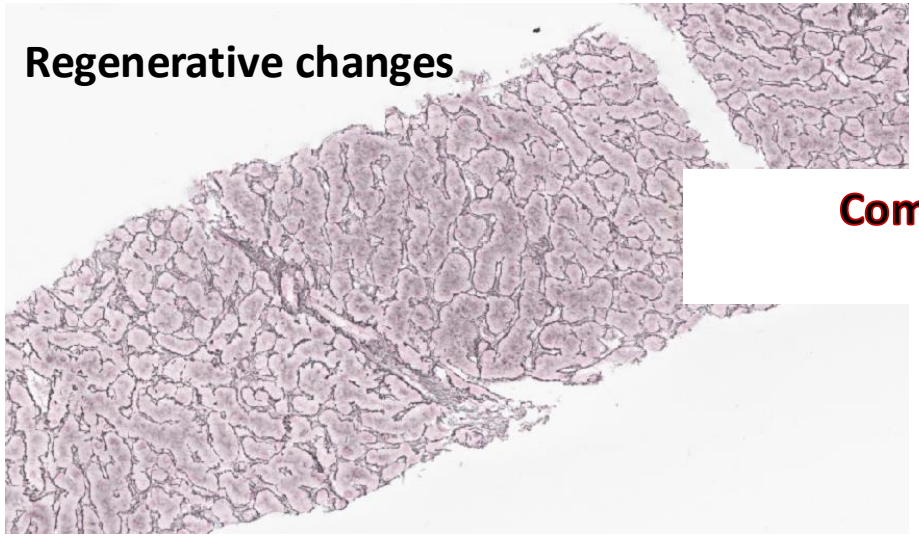
Major criteria

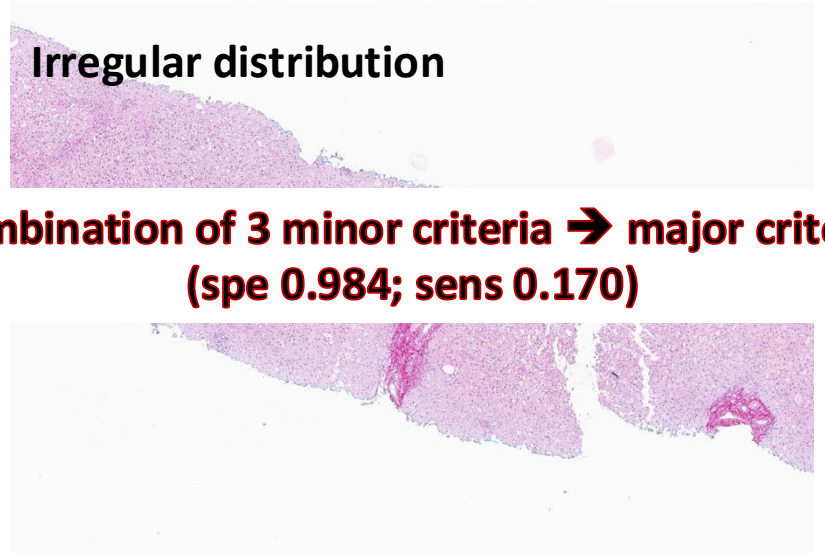


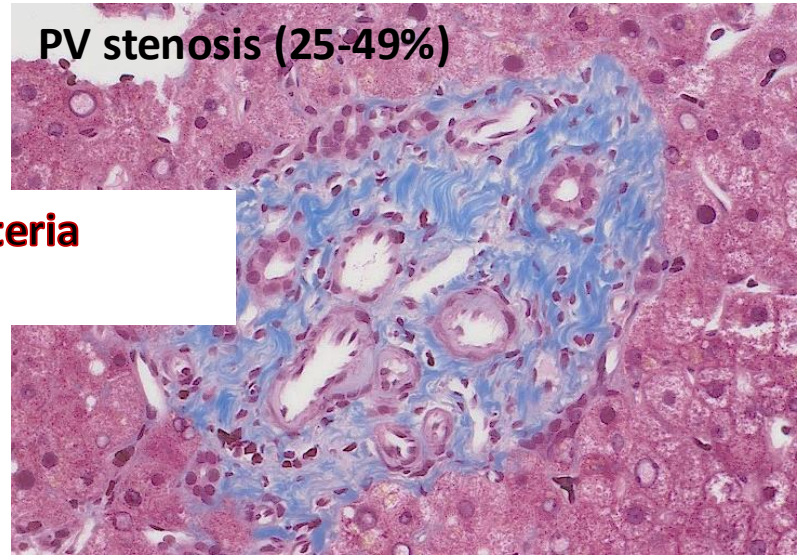




Minor criteria



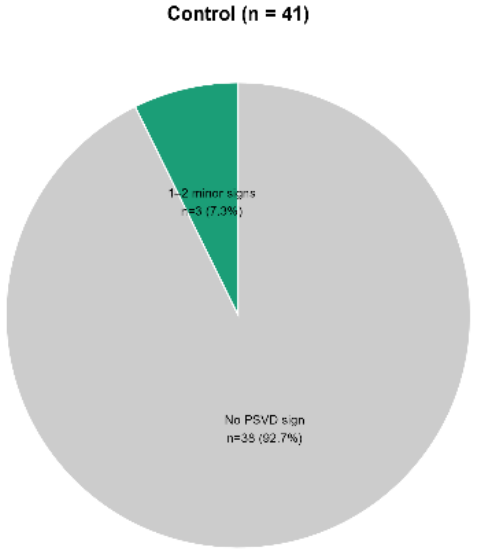




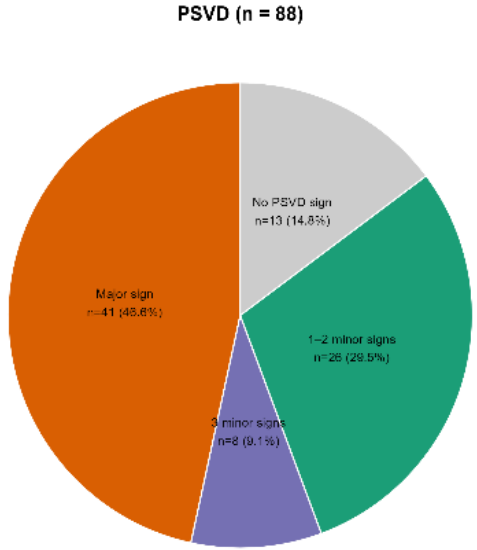
Combination of 3 minor criteria → major criteria
(spe 0.984; sens 0.170)

External validation* of minor & major criteria associated with PSVD

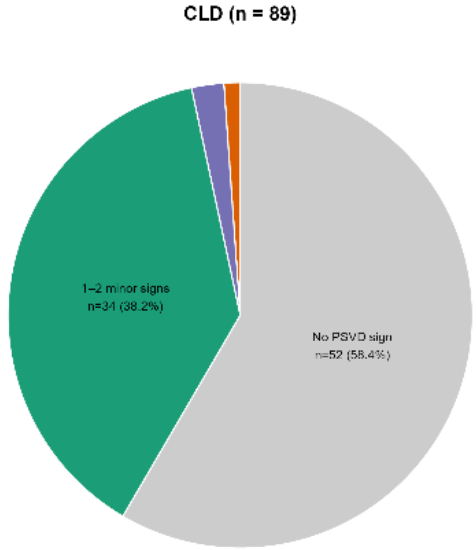
Major criteria	Sensitivity	Specificity
Any major	0.478	**0.99**
3 minor	0.104	**0.99**
Any major OR 3 minor	0.552	**0.99**



Major signs never seen in controls

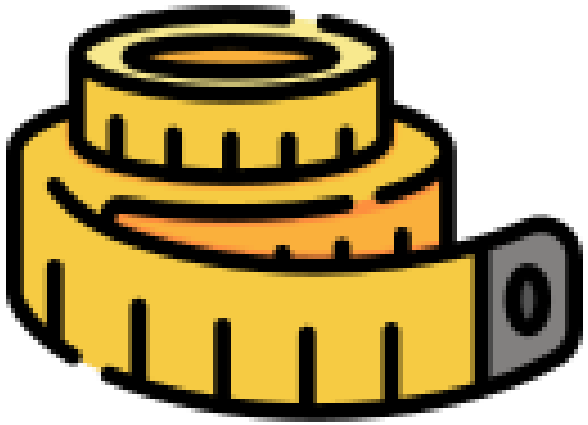


Absence of signs (major or minor) in 14.8%



Major OR 3 minor signs seen in 2%

* M Guindi, D Kleiner, R Saxena & S Kakar (USA), L Freitas & V Alves (Brasil), K Harada (Japan), P Das (India)



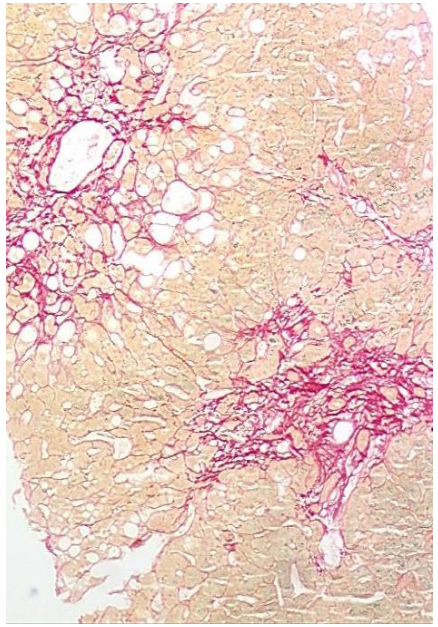
2. Provide prognostic information

Liver fibrosis
The ultimate step of chronic liver damage

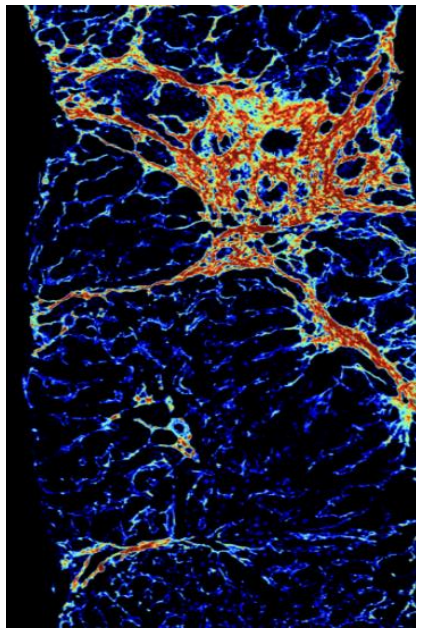
- **Prognostic factor** in various etiologies
- Dynamic and reversible process
- Heterogeneous distribution throughout the liver
- Assessed using 1/2 quantitative staging systems specific to etiology
- **Quantitative assessment is needed for ↗ *granularity* and ↘ *interobserver variability***

AI-digital pathology
Morphometric assessment using dedicated tools

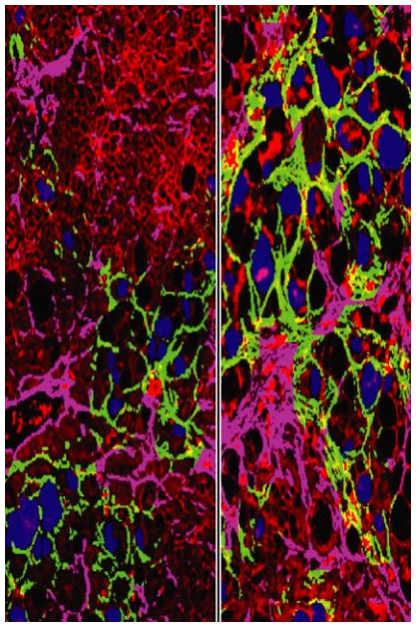
→ Accurate & objective quantification on a continuous scale
→ Qualitative analysis ($\neq$ *phenotypes of fibrosis*)



Sirius red
Masson trichrome

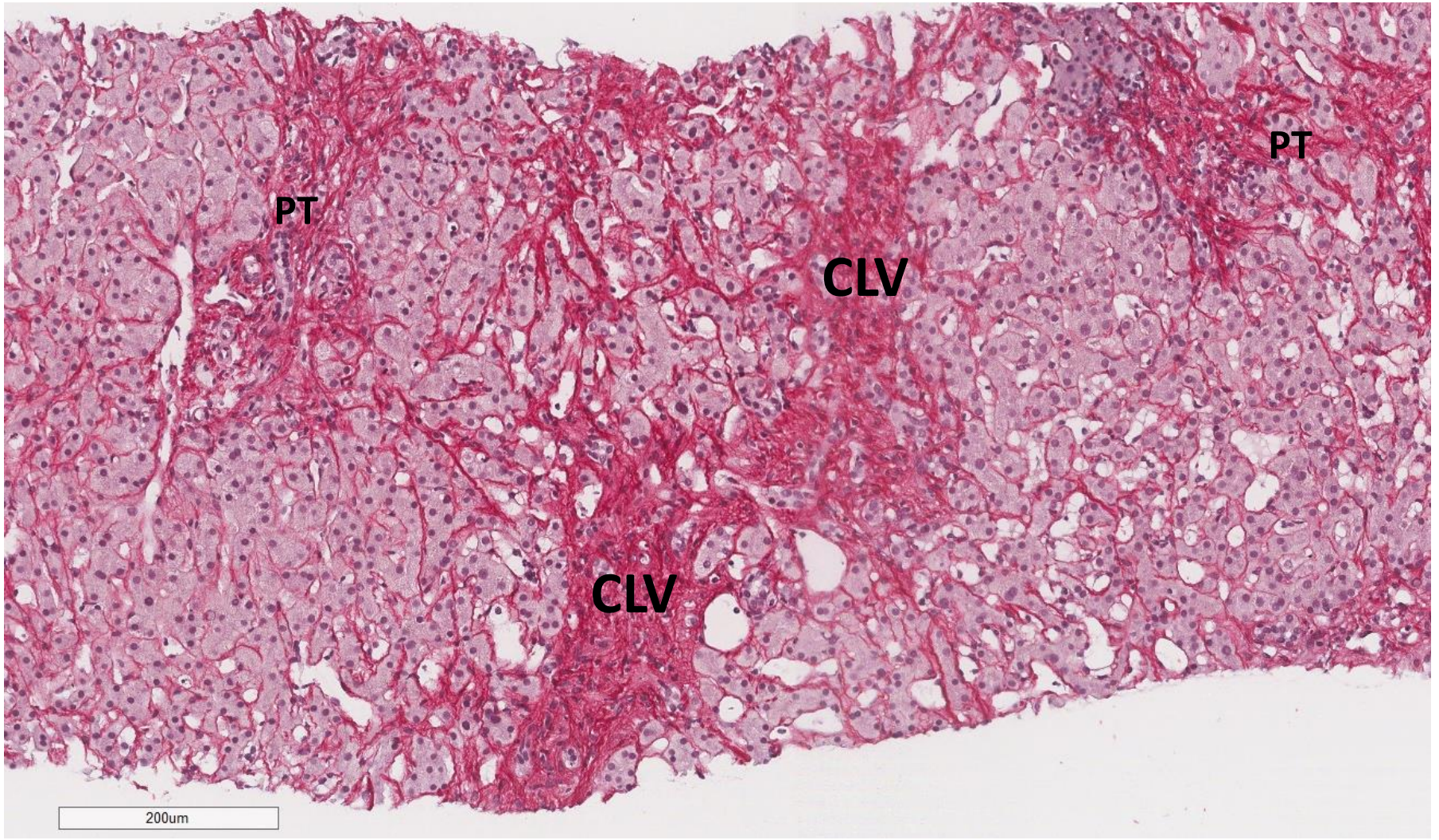


Fibrosis (Pharmanest®)



qFIS
(SHG, HistoIndex®)

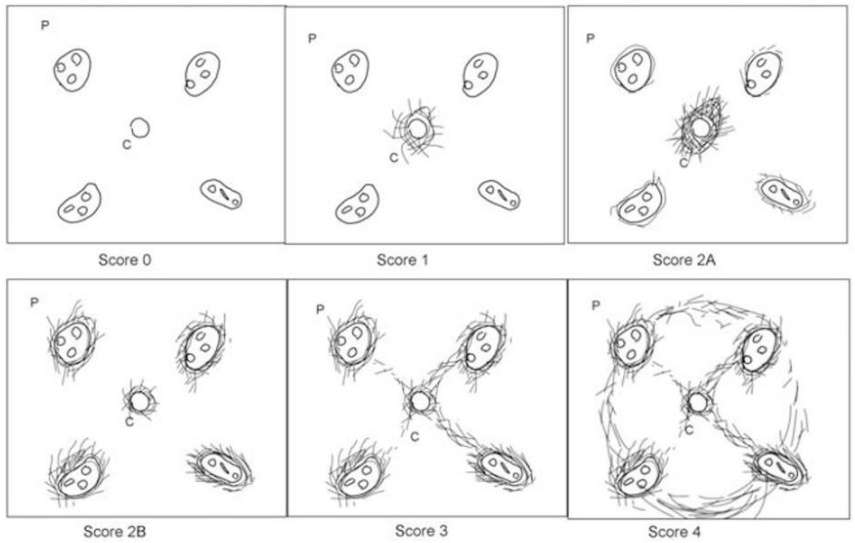
« Vascular » pattern of liver fibrosis
Venous obstruction outflow

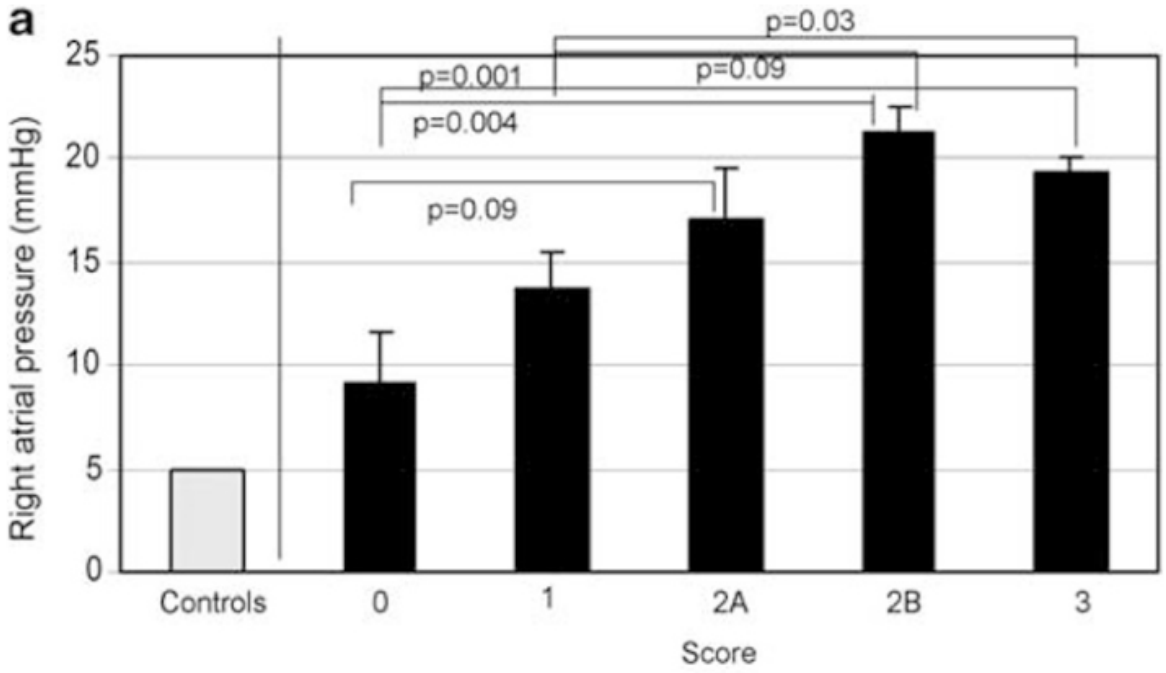


Congestive hepatic fibrosis score: a novel histologic assessment of clinical severity

Table 1 Proposed scoring system for congestive hepatic fibrosis

	Congestive hepatic fibrosis score
0	No fibrosis
1	Central zone fibrosis
2A	Central zone and mild portal fibrosis, with accentuation at central zone
2B	At least moderate portal fibrosis and central zone fibrosis, with accentuation at portal zone
3	Bridging fibrosis
4	Cirrhosis



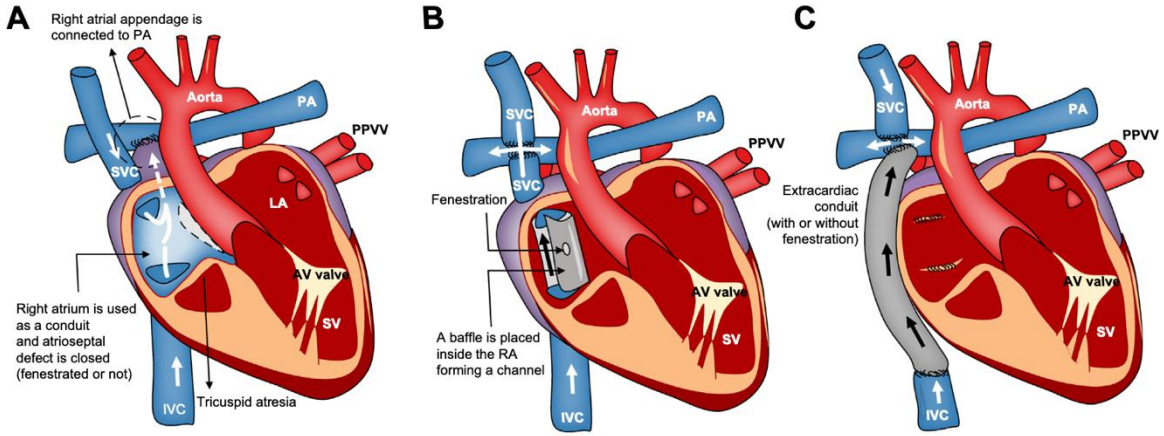


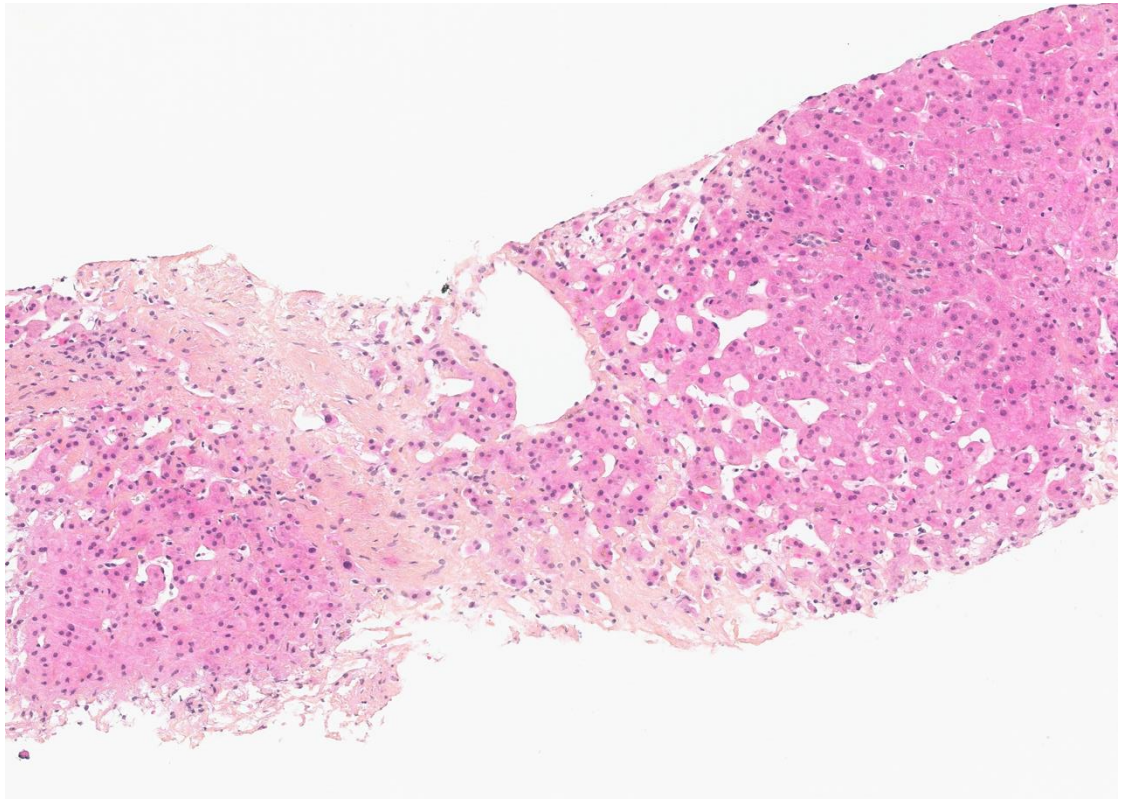
Dai DF Modern Pathol 2016

EASL-ERN position paper on liver involvement in patients with Fontan-type circulation

Luis Téllez[1,2], Audrey Payancé[3,4], Eric Tjwa[5], María Jesús del Cerro[6,7], Lars Idorn[8], Stanislav Ovroutski[9], Ruth De Bruyne[10,†], Henkjan J. Verkade[11,†], Fabrizio De Rita[12], Charlotte de Lange[13], Annalisa Angelini[14], Valérie Paradis[15,16], Pierre Emmanuel Rautou[17,18,†], Juan Carlos García-Pagán[19,20,*]

Fontan circulation is the result of connecting the systemic veins directly to pulmonary arteries (avoiding the right ventricule)





Prevalence and characterization of fibrosis in surveillance liver biopsies of patients with Fontan circulation☆,☆☆

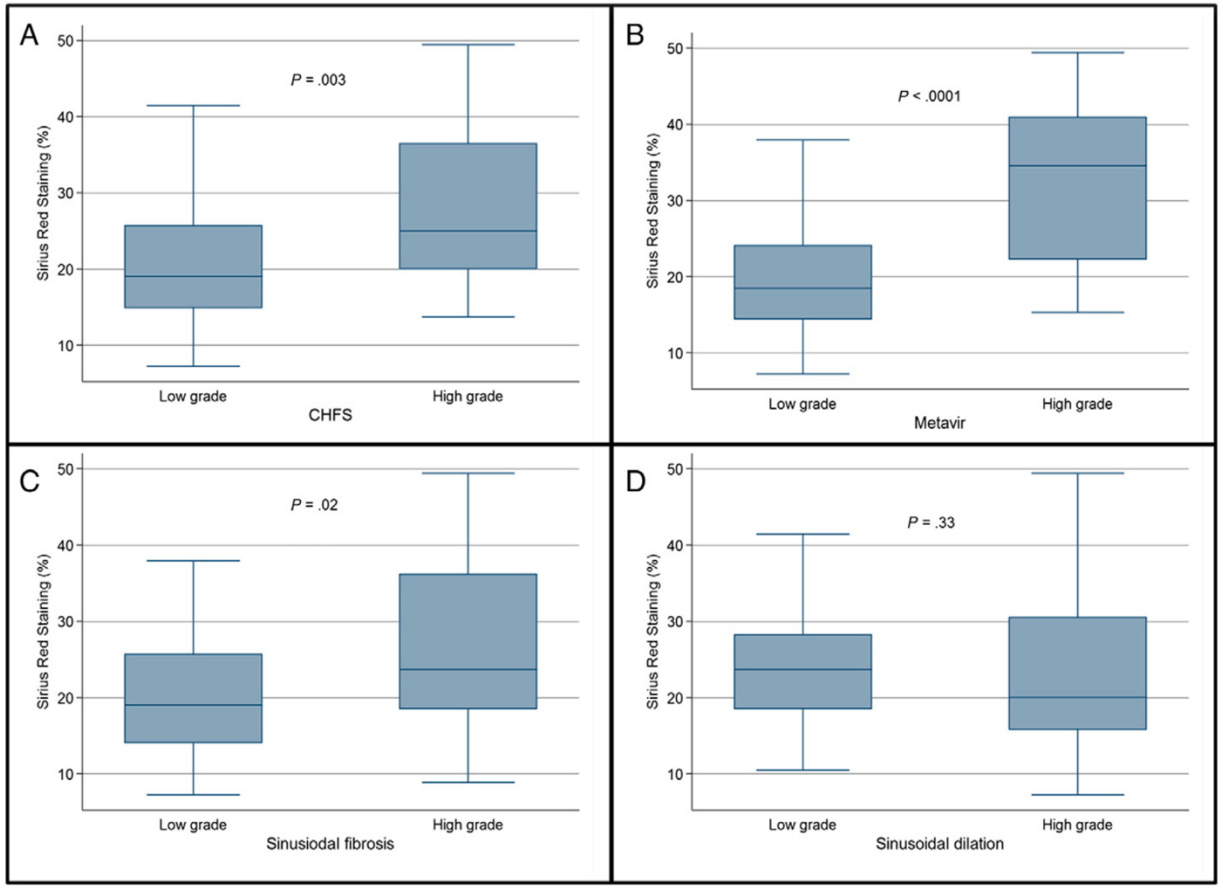
Retrospective analysis of 74 liver biopsies

➢ **½ quantitative scoring systems**
METAVIR, congestive hepatic fibrosis, sinusoidal fibrosis & sinusoidal dilation scores

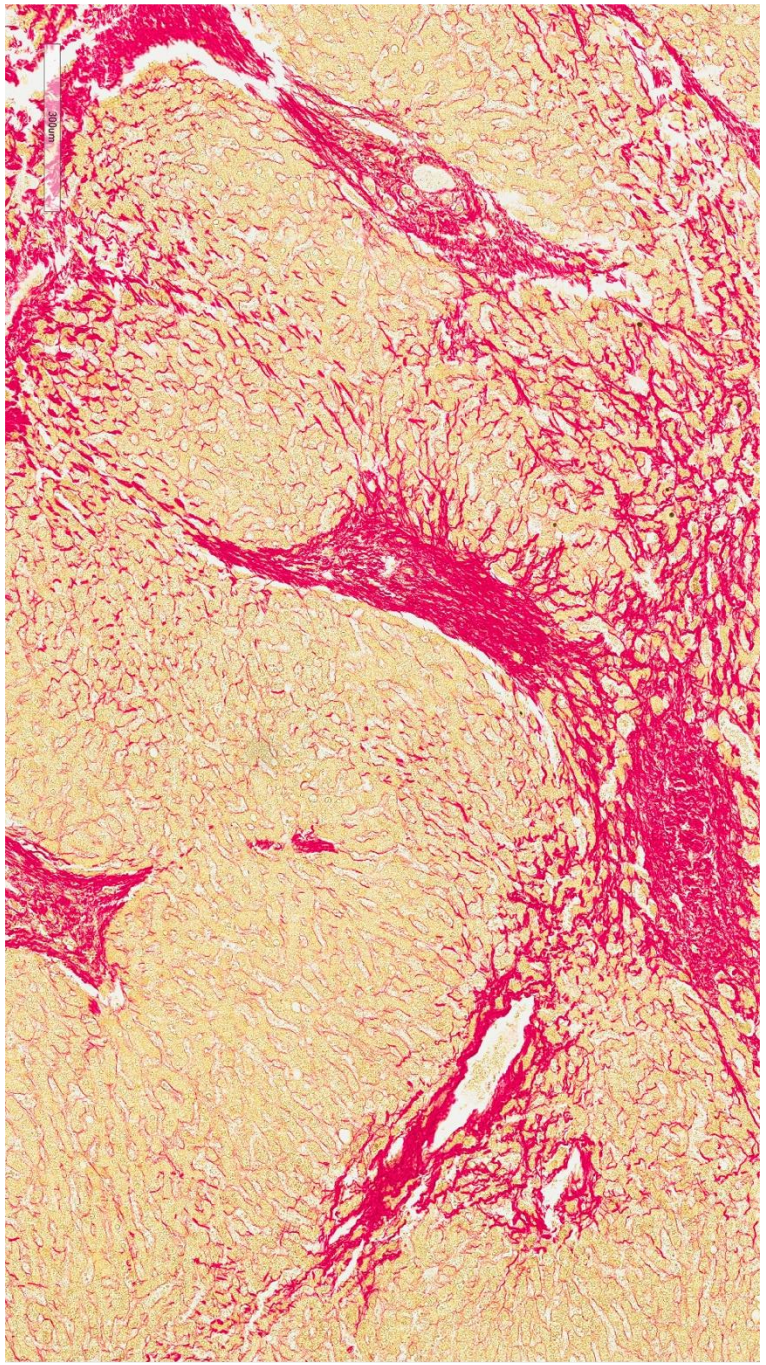
→ Centrilobular & perisinusoidal fibrosis (100%, Bridging & cirrhosis according to CHFS in 39.2%)
→ Portal fibrosis (93.2%, METAVIR F3-F4 in 36.2%)

➢ **Quantitative analysis**
% collagen deposition (CD)

→ ↗ Mean % CD (24% *vs* 2.6% in controls, p=.001)
→ Higher % CD associated with stages 3 & 4 [CHFS, METAVIR & sinusoidal fibrosis]



Surrey LF Human Pathol 2016



Case Control Study

Correlation analysis of collagen proportionate area in Budd-Chiari syndrome: A preliminary clinicopathological study

- Nine patients (5F, 4M, median age 29 y) with BCS undergoing TIPS
  - The median CPA level and correlation of CPA and prognosis of TIPS
- Results
  - Median CPA 23.07% (0%-40.2%)
  - Significant correlation of CPA with history of gastrointestinal bleeding (p = 0.005), alanine aminotransferase (p = 0.038) & prothrombin time (p = 0.044)
  - No significant correlation with shunt dysfunction (2/9) or hepatic encephalopathy (1/9) after TIPS

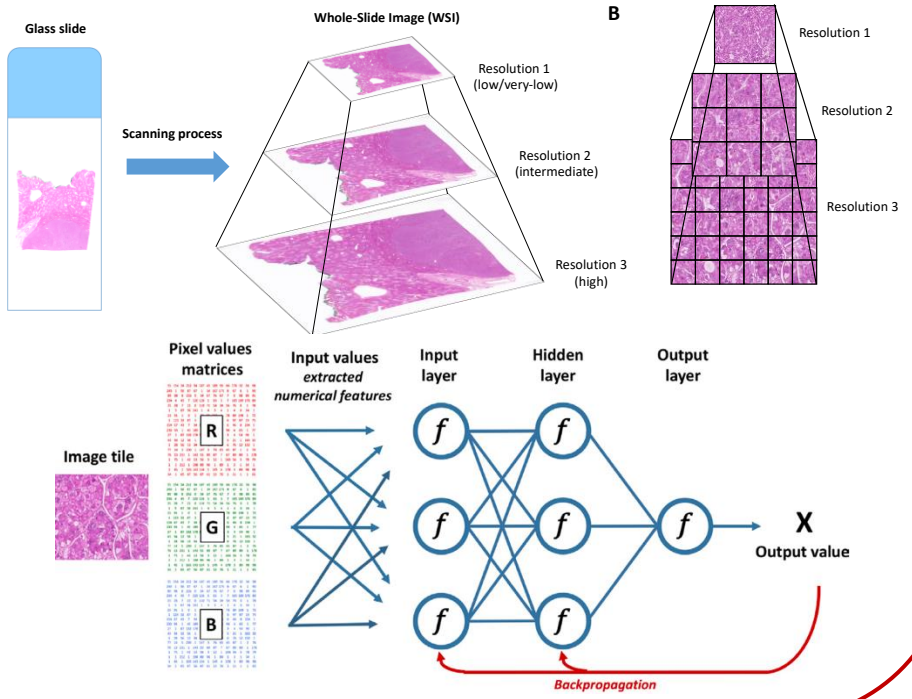
He FL World J of Clinical Cases 2019

AI-Digital Pathology

AI Digital Pathology: A complex process

Digital slide / WSI

- **WSI** : multiple images obtained @ ≠ magnifications
- **Tessellation** : WSI → smaller image patches (tiles 224x224 – 512x512 pixels)



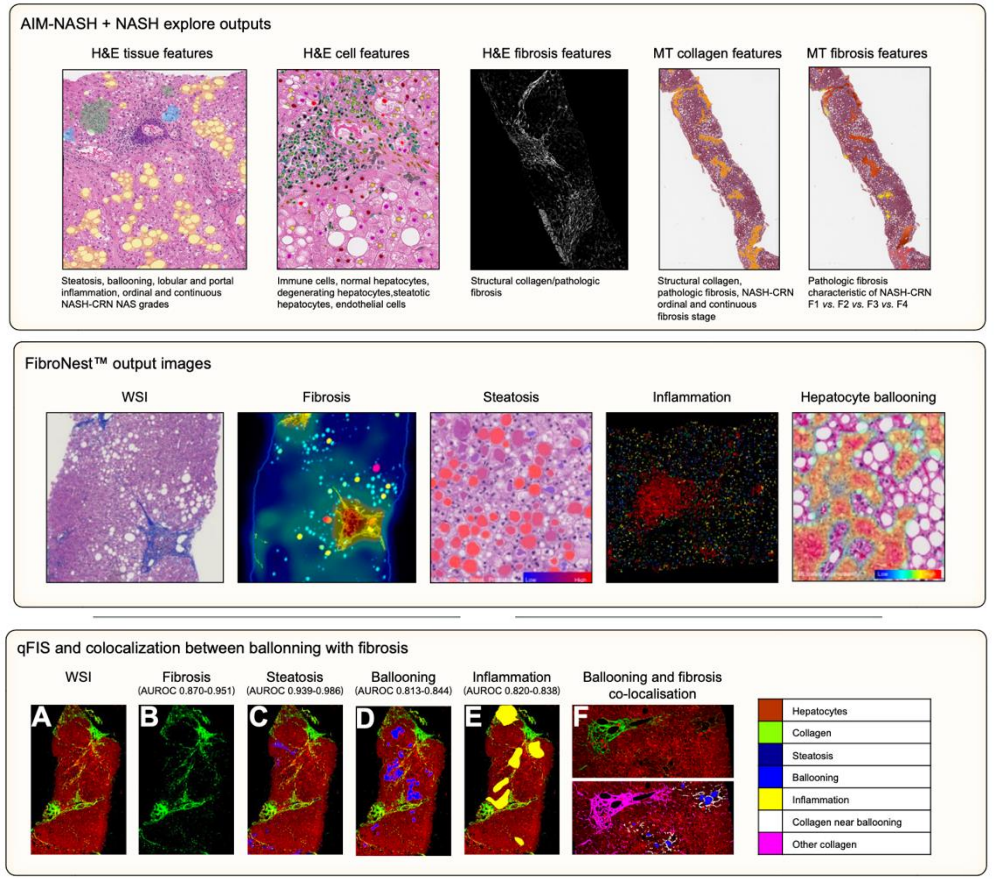
Calderaro J et al Gut 2020

AI-Digital Pathology: An opportunity

Augmented pathology

- ↗ granularity of histological features
- Objective & quantitative assessment of histological criteria
- Uncover subtle histopathological patterns imperceptible to the human eye
- Predict molecular signatures, prognosis, response to treatment, …

Artificial intelligence-assisted digital pathology for non-alcoholic steatohepatitis: current status and future directions



Ratziu V J Hepatol 2023

AI-Digital Pathology: An opportunity

Augmented pathology

- ↗ granularity of histological features
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- Uncover subtle histopathological patterns imperceptible to the human eye
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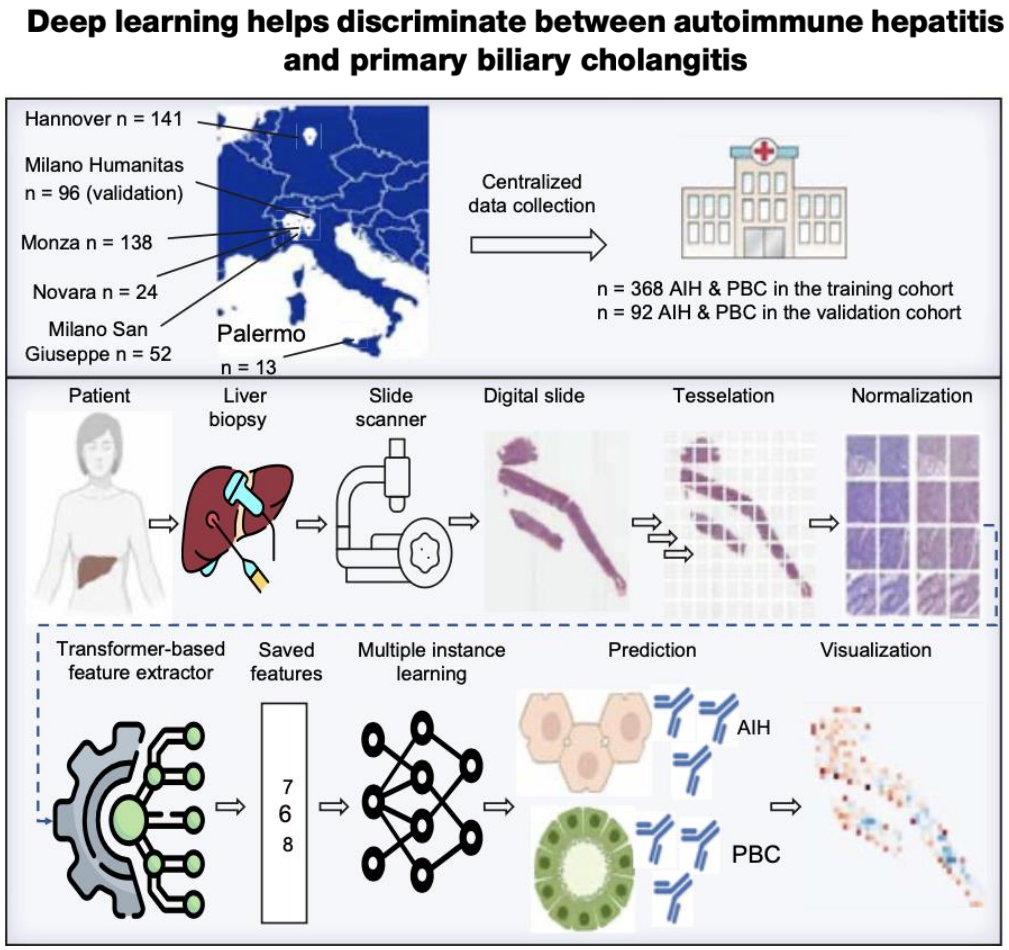

External validation (AUC=0.78 to 0.86)

Gerussi A JHEP Rep 2024

Deep-Learning approaches for improved understanding of porto-sinusoidal vascular disorder (PSVD) histology

Collaborating groups

- Laura ZIGUTYTE, Jakob KATHER (Else Kroener Fresenius Center for Digital Health, Medical Faculty Carl Gustav Carus, Technical University Dresden, Dresden, Germany)

- Thomas SORZ, Georg SEMMLER, Bernhard SCHEINER, Thomas REIBERGER (Division of Gastroenterology and Hepatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria)

- Juan-Carlos GARCIA-PAGAN, Virginia HERNÁNDEZ-GEA, Asunción OJEDA, Carla FUSTER (Hepatic Hemodynamic Unit, Liver Unit and Pathology Department, Hospital Clínic Barcelona, Barcelona, Spain)

- Pierre-Emmanuel RAUTOU, Valerie PARADIS (Hôpital Beaujon, Service d'Hépatologie, Clichy, France)

Conclusions

- Vascular liver diseases & Histology→ Diagnostic and prognostic features

- **Morphometry & AI-Digital Pathology → Augmented pathology**

  - Provide a automatic quantitative assessment of morphological features
    →↘ subjectivity & variability of readers

  - Assist pathologists
    → Bring expertise to less experienced ones & Alleviate time-consuming tasks

  - **An opportunity, not the Holly grail !**

https://fhu-mosaic.com/

CENTRE DE RECHERCHE SUR L'INFLAMMATION

FHU MOSAIC

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AP-HP. Nord Université de Paris

Team « From Micro to Macro in Cancer Development »

Pathology Dpt

Beaujon hospital

- Pathology (V Paradis)
  - Radiology (M Ronot)
- Liver Surgery (M Lesurtel)
  - Hepatology (PE Rautou)
- Liver oncology (M Bouattour)

TQRCG

PSVD Atlas

iMAP

Université Paris Cité

LA LIGUE CONTRE LE CANCER

AFEF

Fondation pour la recherche sur le cancer

arc

INSTITUT NATIONAL DU CANCER

Région îledeFrance

Paris PSVD meeting (Dec 2025)