

Practical Pearls in Diagnosing HCC

Maria Westerhoff, MD

Professor

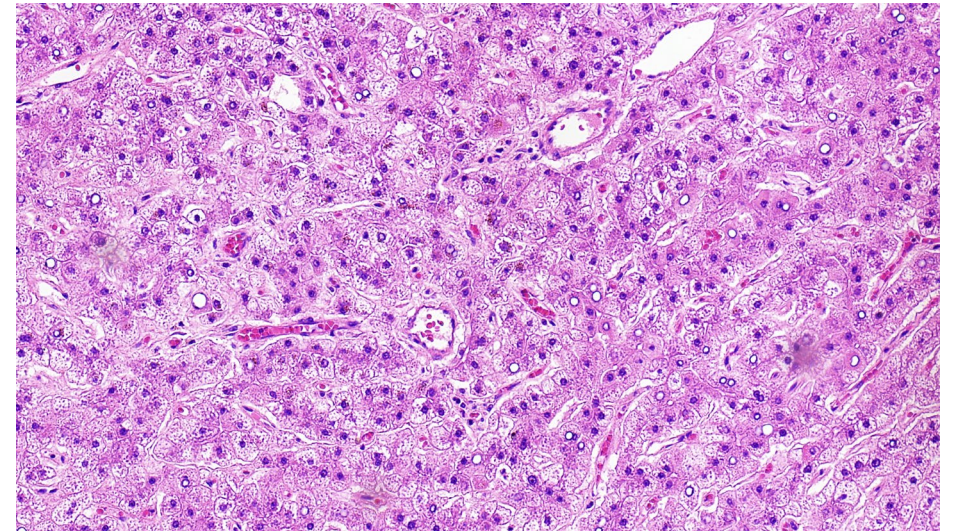
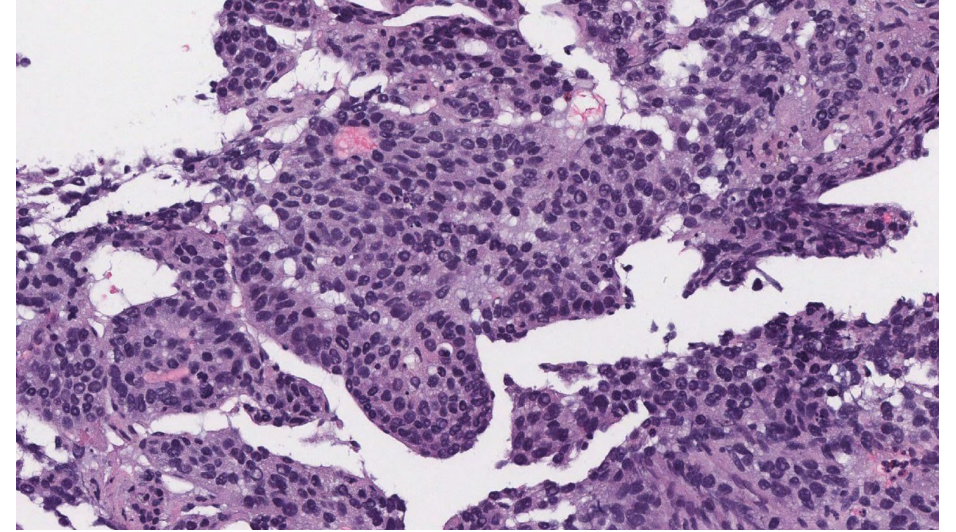
University of Michigan

Why this is Relevant

- Liver biopsy for masses are common surgical pathology specimens
- Metastatic tumors can express hepatocellular markers and mimic HCC histology
- Well differentiated HCC can be extremely difficult to distinguish from benign lesions

Common Issues when Diagnosing an HCC

- **Met or intrahepatic cholangioCA vs. HCC:** You know it's malignant, but not sure it is hepatocytic
- **Benign vs. HCC:** You know it's hepatocytic but can't tell if it is malignant

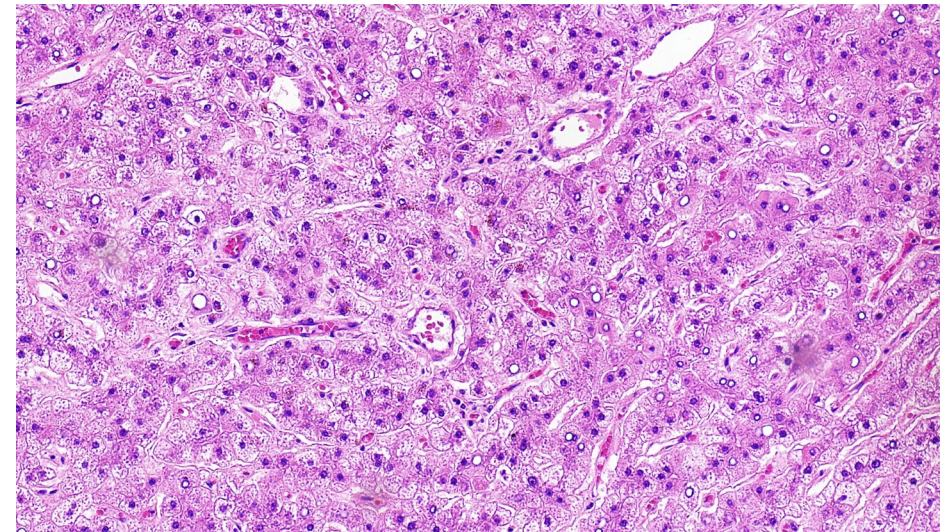
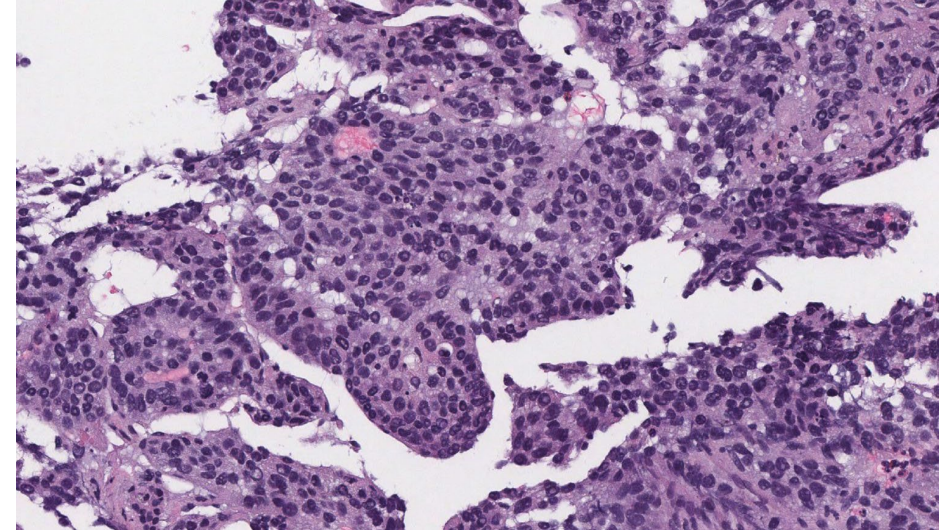


Outline of this Talk

- I. Distinguishing HCC from metastases or iCCA
- II. Distinguishing HCC from benign hepatocellular conditions

Common Issues when Diagnosing an HCC

- **Met or intrahepatic cholangioCA vs. HCC: You know it's malignant, but not sure it is hepatocytic**
 1. Which histologic & IHC features help confirm HCC?
 2. Which tumors mimic HCC histology and which HCC stains can be spuriously positive in mets?
 3. Which stains usually used for mets can be positive in HCC?
- **Benign vs. HCC: You know it's hepatocytic but can't tell if it is malignant**

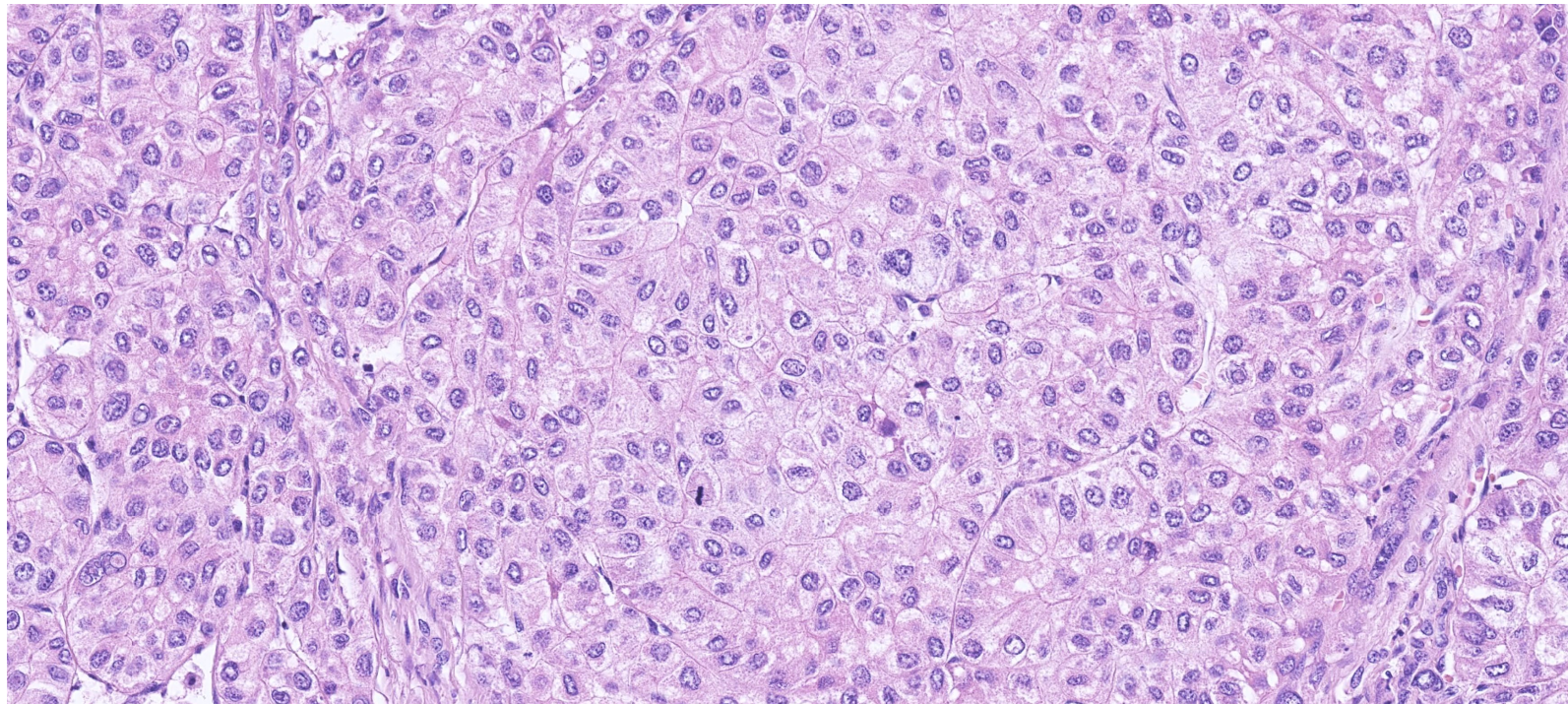
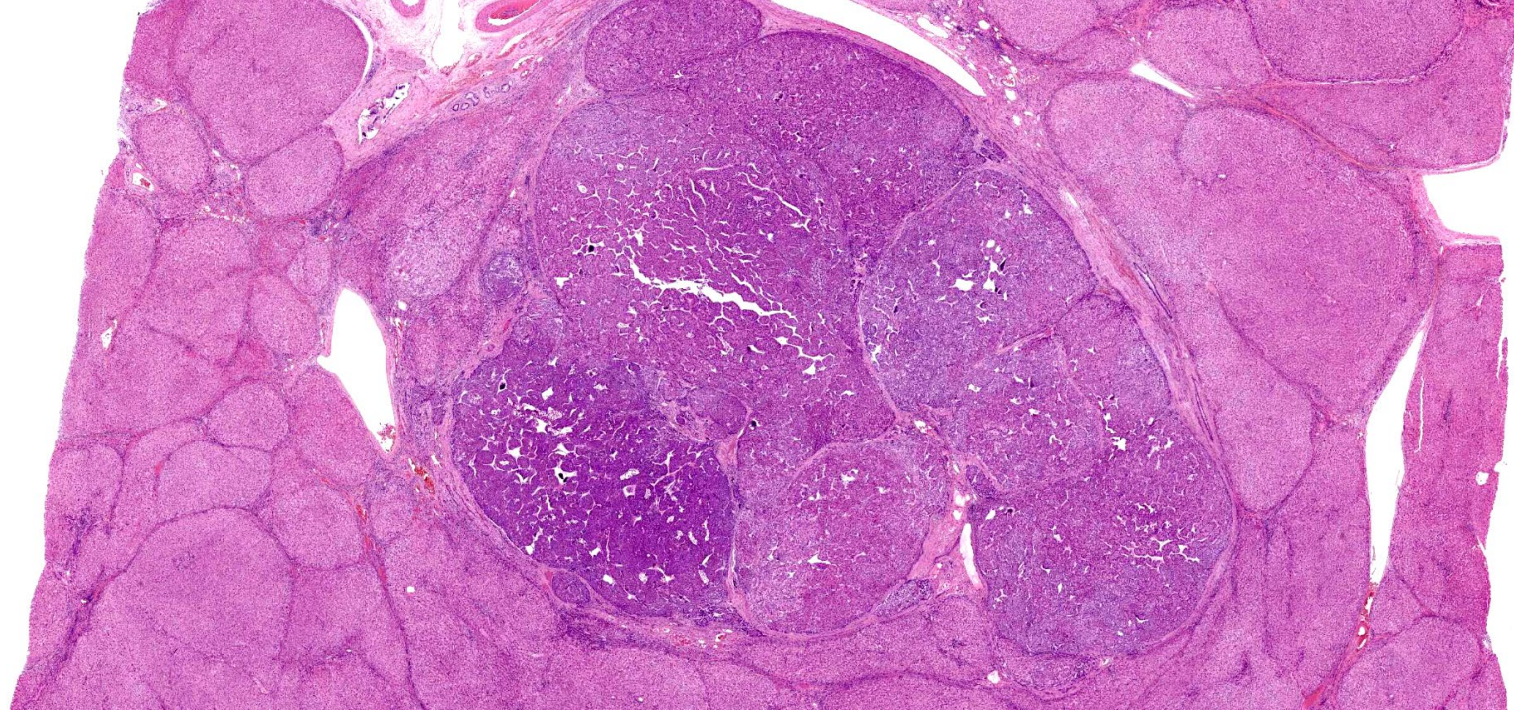


Basics of HCC Histology & Immunohistochemistry

Example of Classic HCC

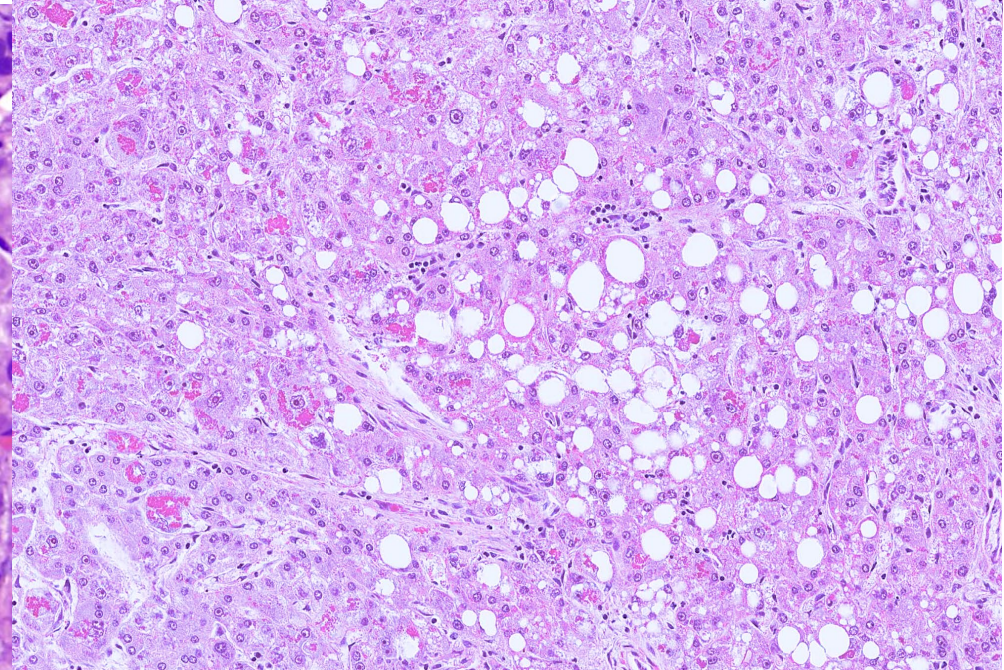
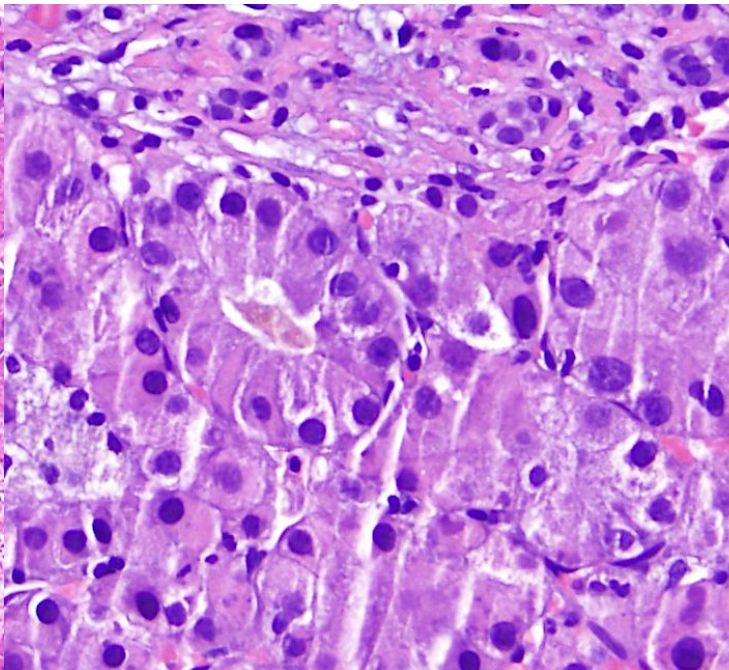
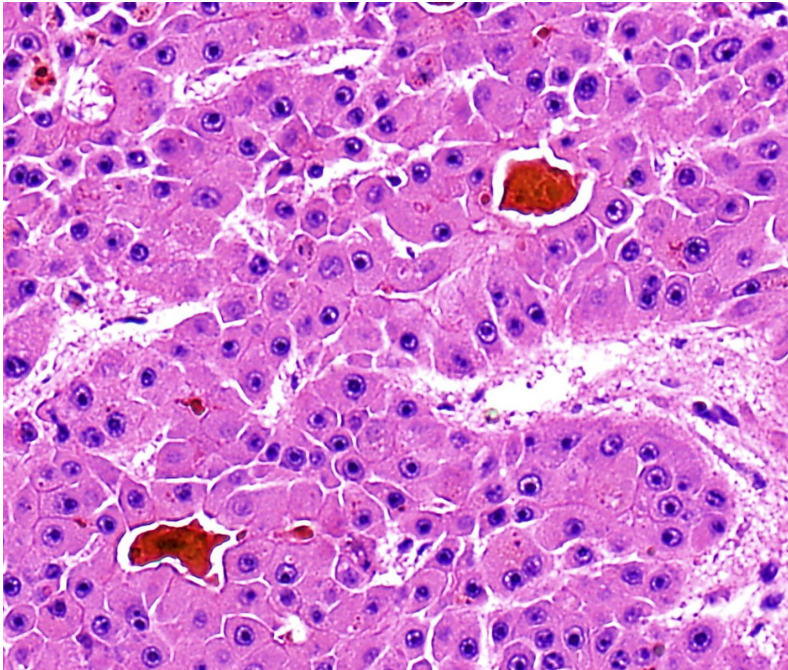
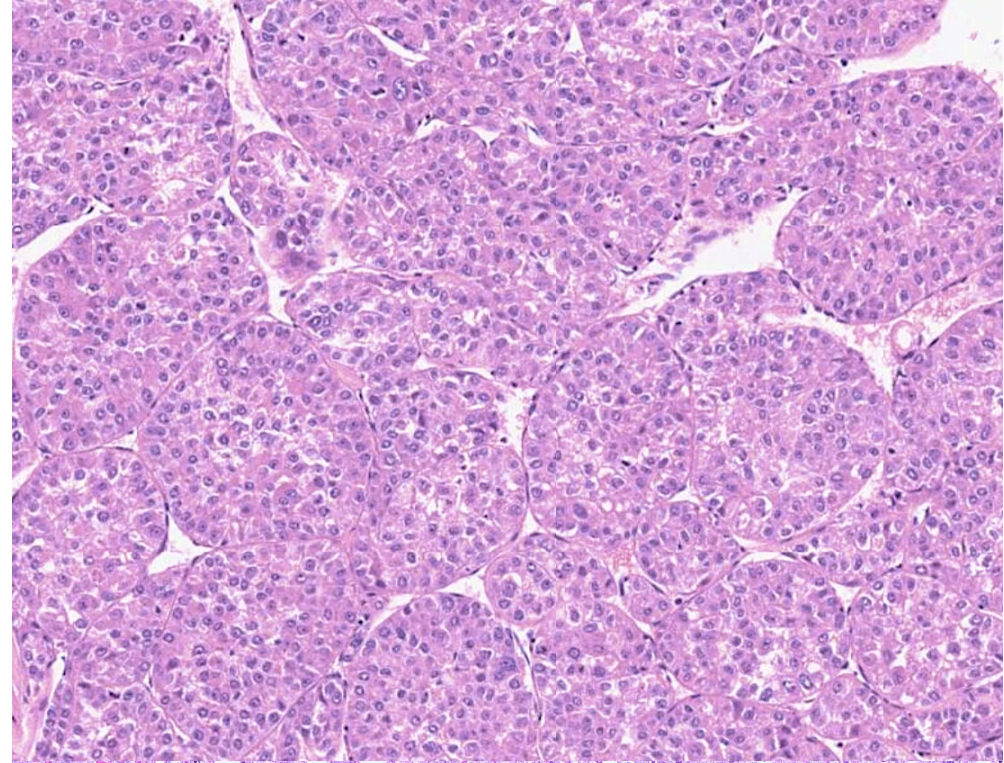
55 Male with
Hepatitis C and
Liver Mass

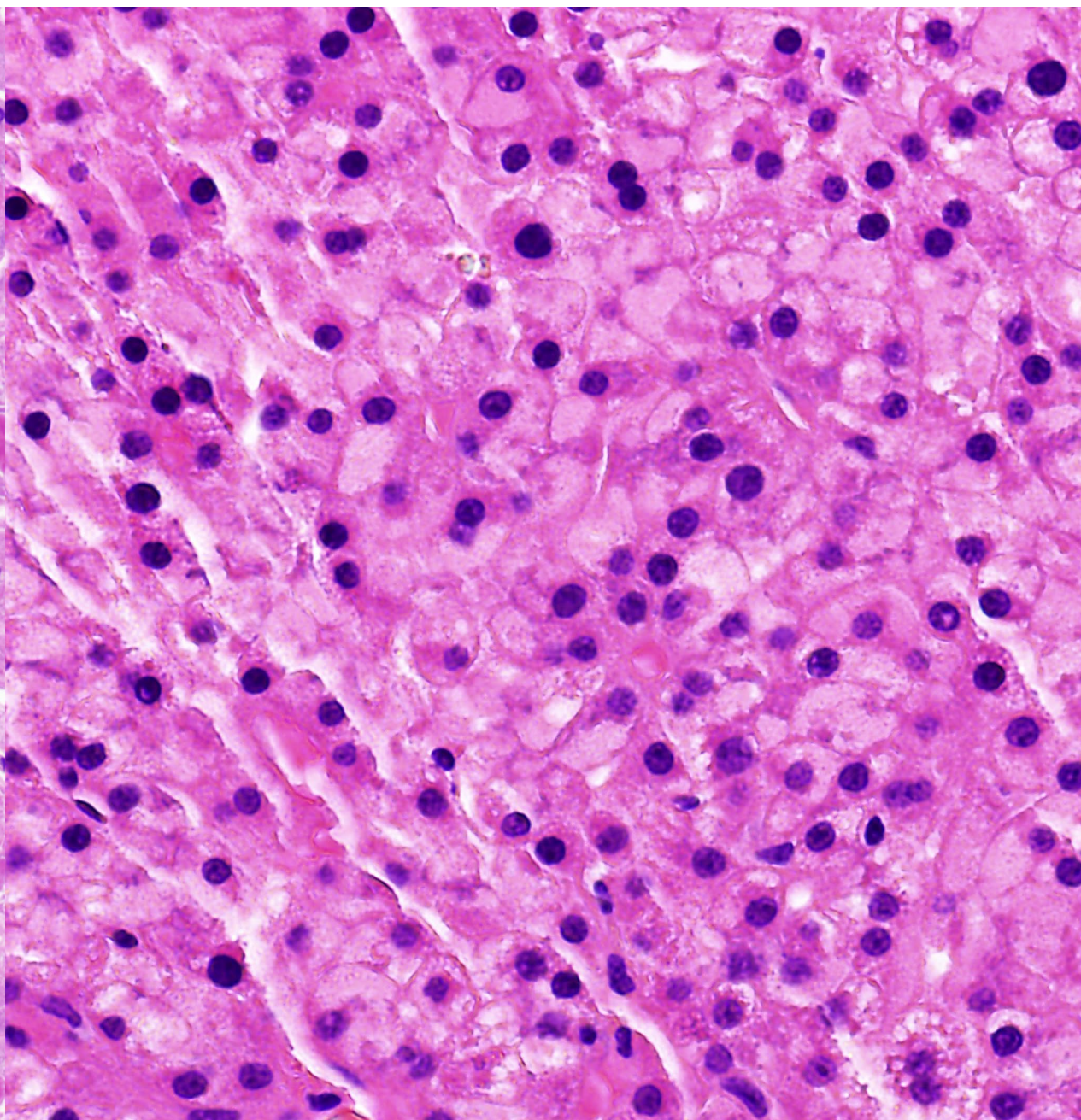
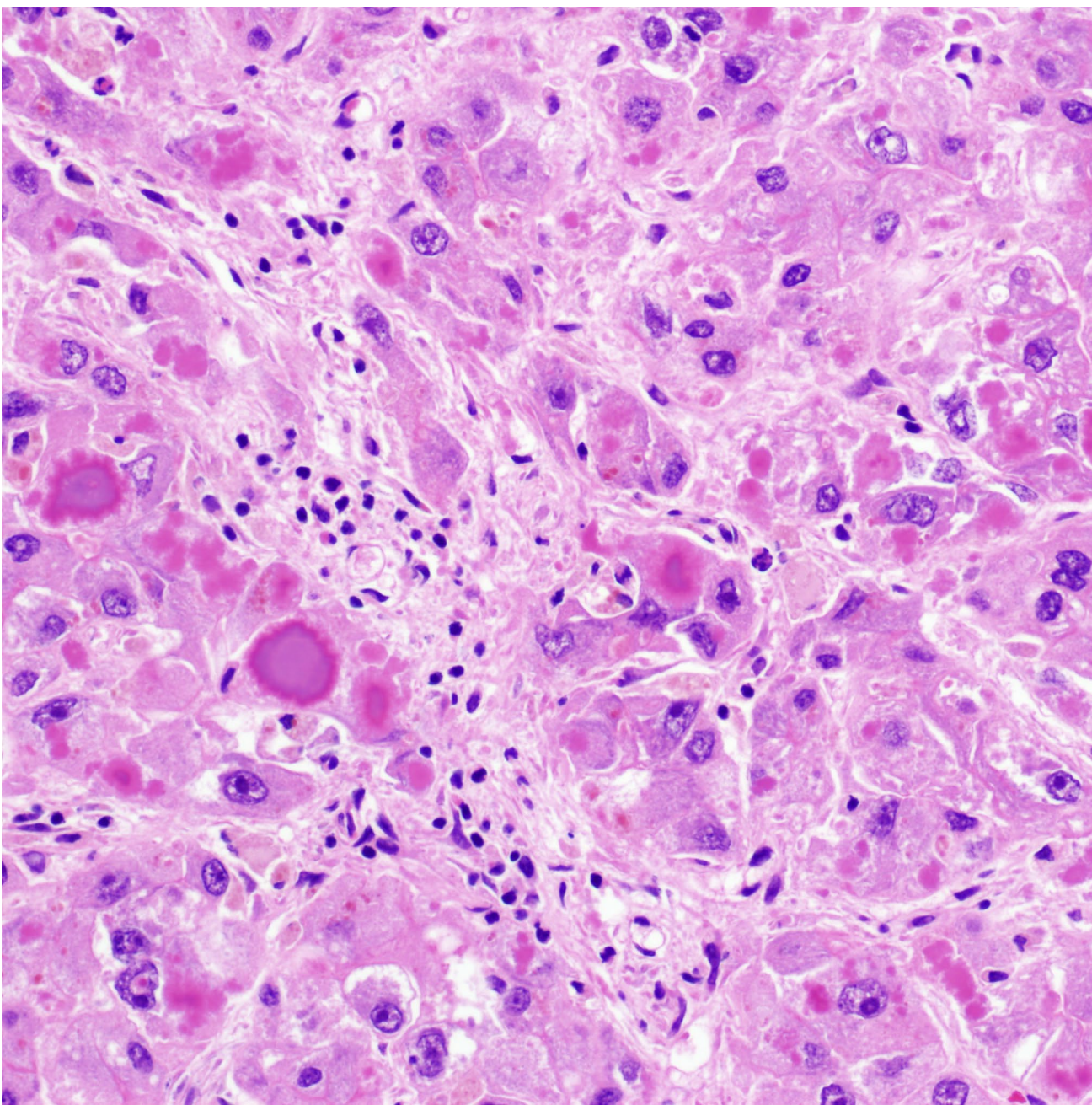
- Classic HCC arises in chronic liver disease
- Polygonal cells with abundant eosinophilic cytoplasm
- Has trabecular or pseudoacinar architecture with thickened hepatic plates (>3 cells), reticulin stain highlights expanded trabeculae or reticulin loss
- Lack of portal tracts in nodule



Histologic Features of HCC

- Polygonal cells, eosinophilic cytoplasm
- Trabecular arrangement
- **Bile formation**, pseudoacinar structures; mucin rules out HCC
- Steatosis, Mallory-Denk bodies





Features that Support Diagnosis of HCC

| | HCC |
|---|------------------|
| Cirrhosis | Yes |
| Alpha fetoprotein levels | Increased in 60% |
| Bile formation | Yes |
| Steatosis | Yes |
| Eosinophilic cytoplasm, polygonal cells | Yes |
| Trabecular architecture | Yes |
| Mallory-Denk bodies | Yes |
| Combo of + IHC: Arg-1, HepPar-1, glypican 3 | Yes |

Features that Support Diagnosis of HCC

| | HCC | Other tumors |
|---|------------------|---|
| Cirrhosis | Yes | Unlikely (<2%); iCCA may arise in cirrhosis |
| Alpha fetoprotein levels | Increased in 60% | Germ cell tumors |
| Bile formation | Yes | Hepatoid adenoCA |
| Steatosis | Yes | Angiomyolipoma (fat outside the cells) |
| Eosinophilic cytoplasm, polygonal cells | Yes | Neuroendocrine tumors, iCCA, acinar, AML |
| Trabecular architecture | Yes | NET, adrenal, renal, acinar cell CA |
| Mallory-Denk bodies | Yes | iCCA – eosinophilic globules |
| Combo of + IHC: Arg-1, HepPar-1, glypican 3 | Yes | Hepatoid adenoCA |

USEFUL MARKERS FOR DIAGNOSING HCC

| Marker | Staining Pattern | Positive Staining | Reported Sensitivity in HCC (%) |
|-------------|---------------------------------|---|--|
| HepPar-1 | Cytoplasmic | Liver: normal and neoplastic | WD: 91–100 PD: 22–81 ^{6,12,13,24,30,56} |
| ARG-1 | Cytoplasmic/nuclear | Liver: normal and neoplastic | WD: 94–100 PD: 44–100 ^{6,12,13,24,30,56} |
| BSEP | Any (predominantly canalicular) | Liver: normal and neoplastic | WD: 92–100 PD: 45–78 ^{13,24,30} |
| pCEA | Canalicular | Liver: canalicular pattern is specific Nonliver: noncanalicular patterns | WD: 82–92 PD: 54–78 ^{24,30} |
| CD10 | Canalicular | Liver: canalicular pattern is specific Nonliver: noncanalicular patterns | WD: 72 PD: 67 ³⁰ |
| GPC-3 | Cytoplasmic/ membranous | Benign liver: negative HCC: positive <ul style="list-style-type: none"> • Including scirrhous subtype • May be negative in fibrolamellar subtype | WD: 50–76 PD: 67–100 ^{24,30,40,58,67} |
| Albumin ISH | Dotlike signal | Liver: normal and neoplastic <ul style="list-style-type: none"> • Often including cholangiocarcinoma | WD: 100 PD: 99 ⁵⁶ |

| GENERAL RULE OF THUMB: | HCC | Metastatic adenoCA |
|--|-----|--------------------|
| Albumin-ISH | + | – |
| Combination of positive ARG-1, Hep Par-1, Glyp-3 | + | – |
| Combo of CK7, CK20, MOC31 | – | + |

Using a Combination of Immunohistochemical Markers to Support HCC

| Differentiation | Arginase-1, No. (%) | Glypican-3, No. (%) | Hep Par-1, No. (%) |
|--------------------|---------------------|---------------------|--------------------|
| Well, n = 13 | 13 (100) | 2 (15) | 13 (100) |
| Moderately, n = 41 | 40 (98) | 24 (58) | 34 (83) |
| Poorly, n = 35 | 34 (88) | 29 (74) | 12 (30) |

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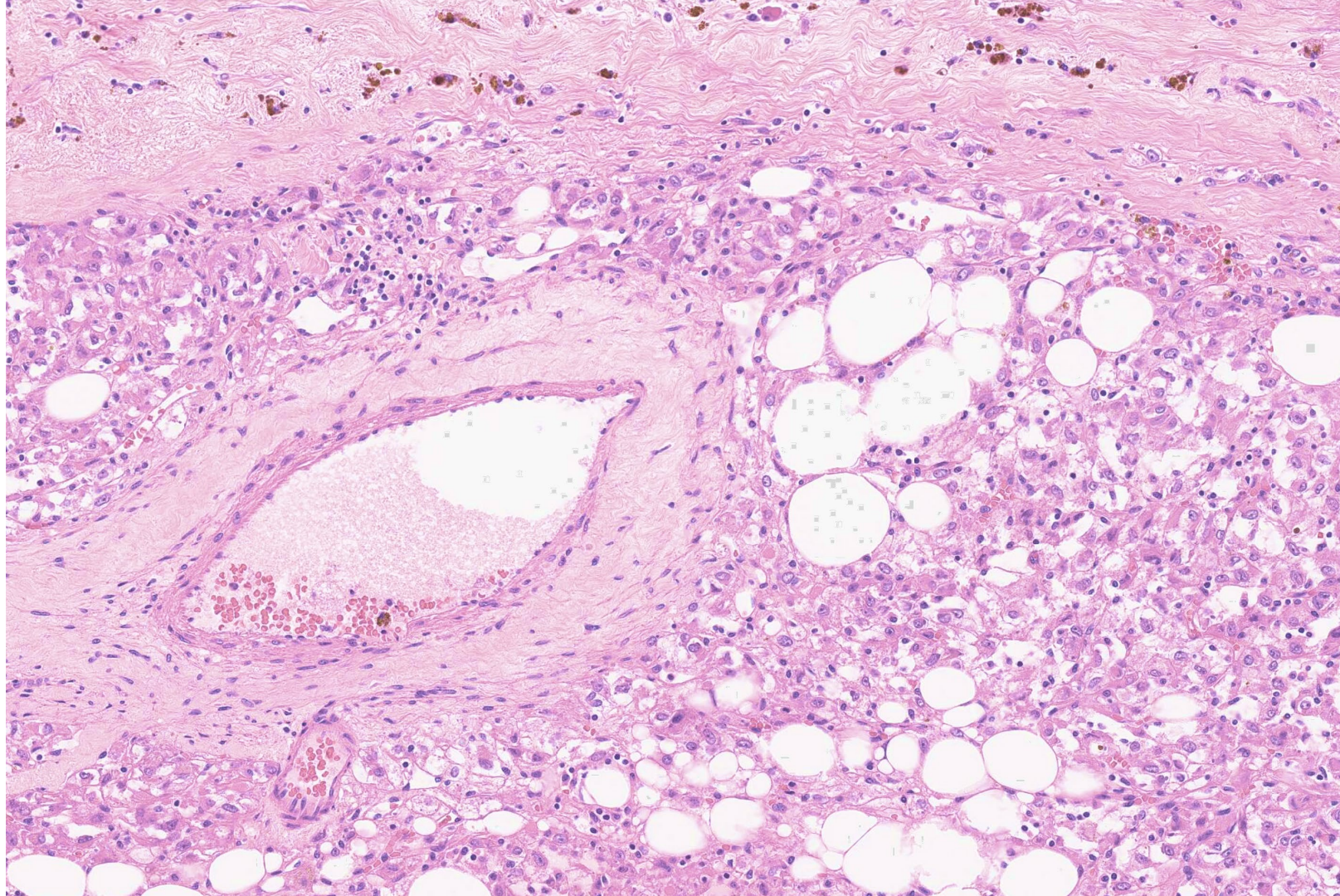
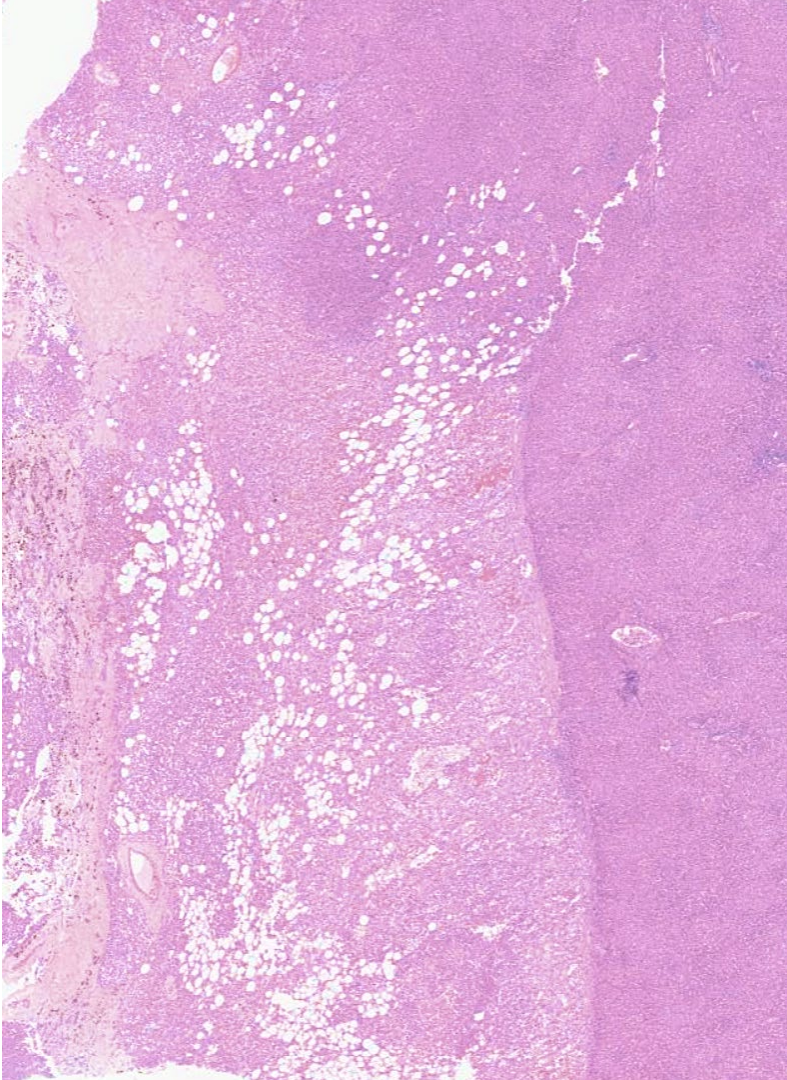
| Differentiation | Hep Par-1 ⁺ and/or Glypican-3 ⁺ , No. (%) | | Hep Par-1 ⁺ and/or Arginase-1 ⁺ , No. (%) | | Glypican-3 ⁺ and/or Arginase-1 ⁺ , No. (%) | |
|-------------------------|---|----------|---|----------|--|----------|
| Tumor cells staining, % | ≥5 | ≥50 | ≥5 | ≥50 | ≥5 | ≥50 |
| Well, n = 13 | 13 (100) | 13 (100) | 13 (100) | 13 (100) | 13 (100) | 13 (100) |
| Moderately, n = 41 | 41 (100) | 40 (98) | 41 (100) | 40 (98) | 41 (100) | 41 (100) |
| Poorly, n = 39 | 36 (97) | 34 (87) | 37 (97) | 34 (88) | 39 (100) | 37 (95) |

Abbreviation: Hep Par-1, hepatocyte paraffin antigen 1.

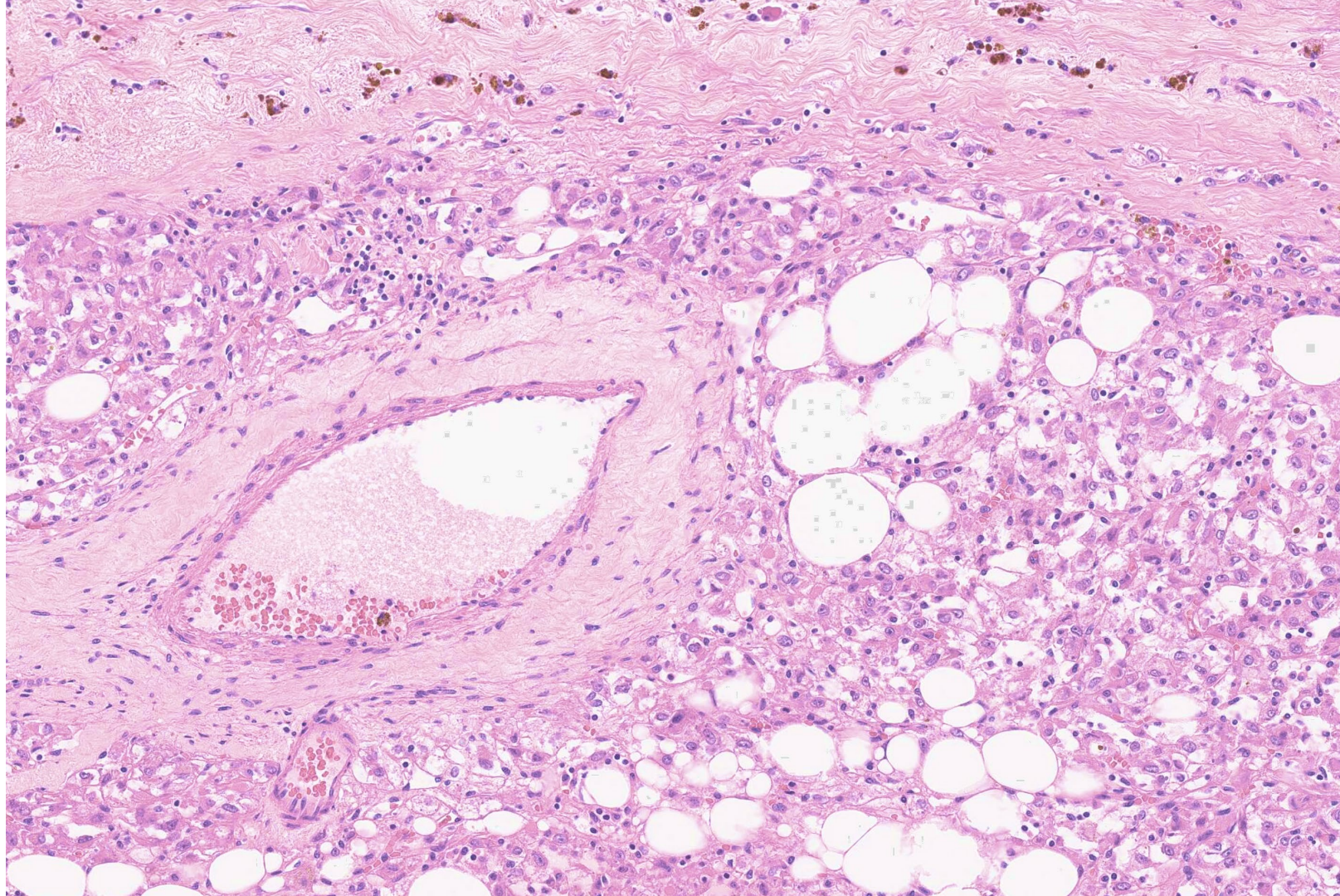
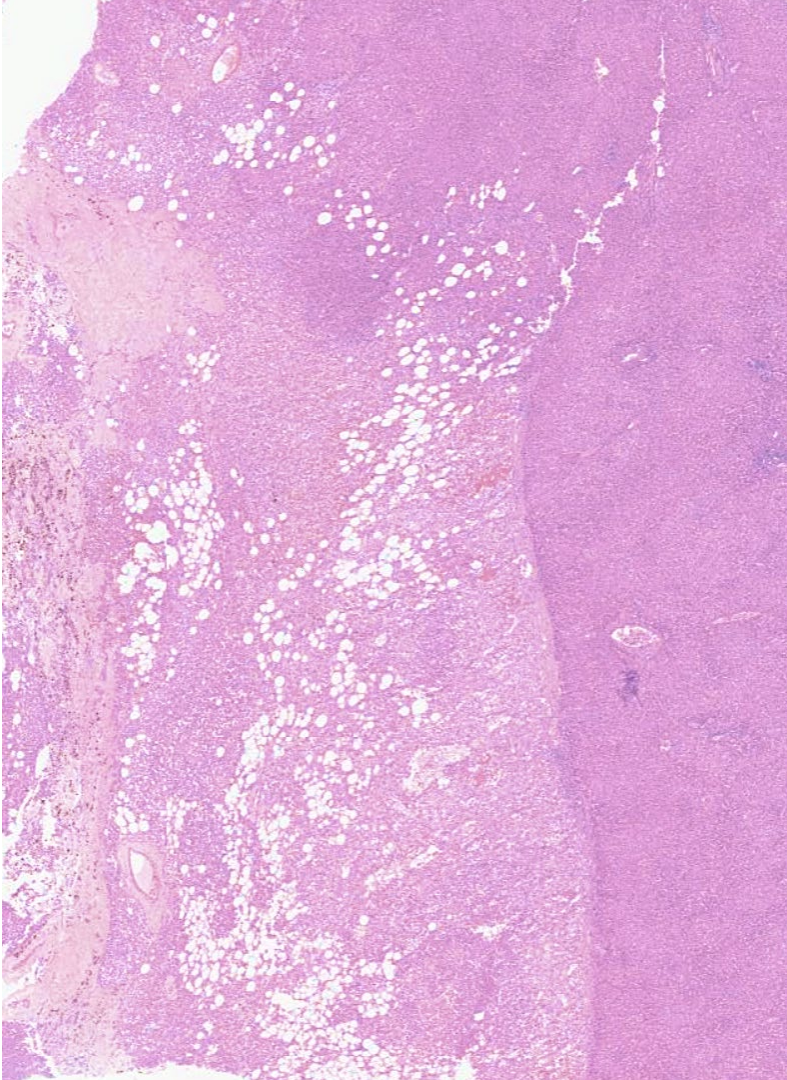
Tumors that Can Mimic HCC

Tumors that Can Mimic HCC Histologically

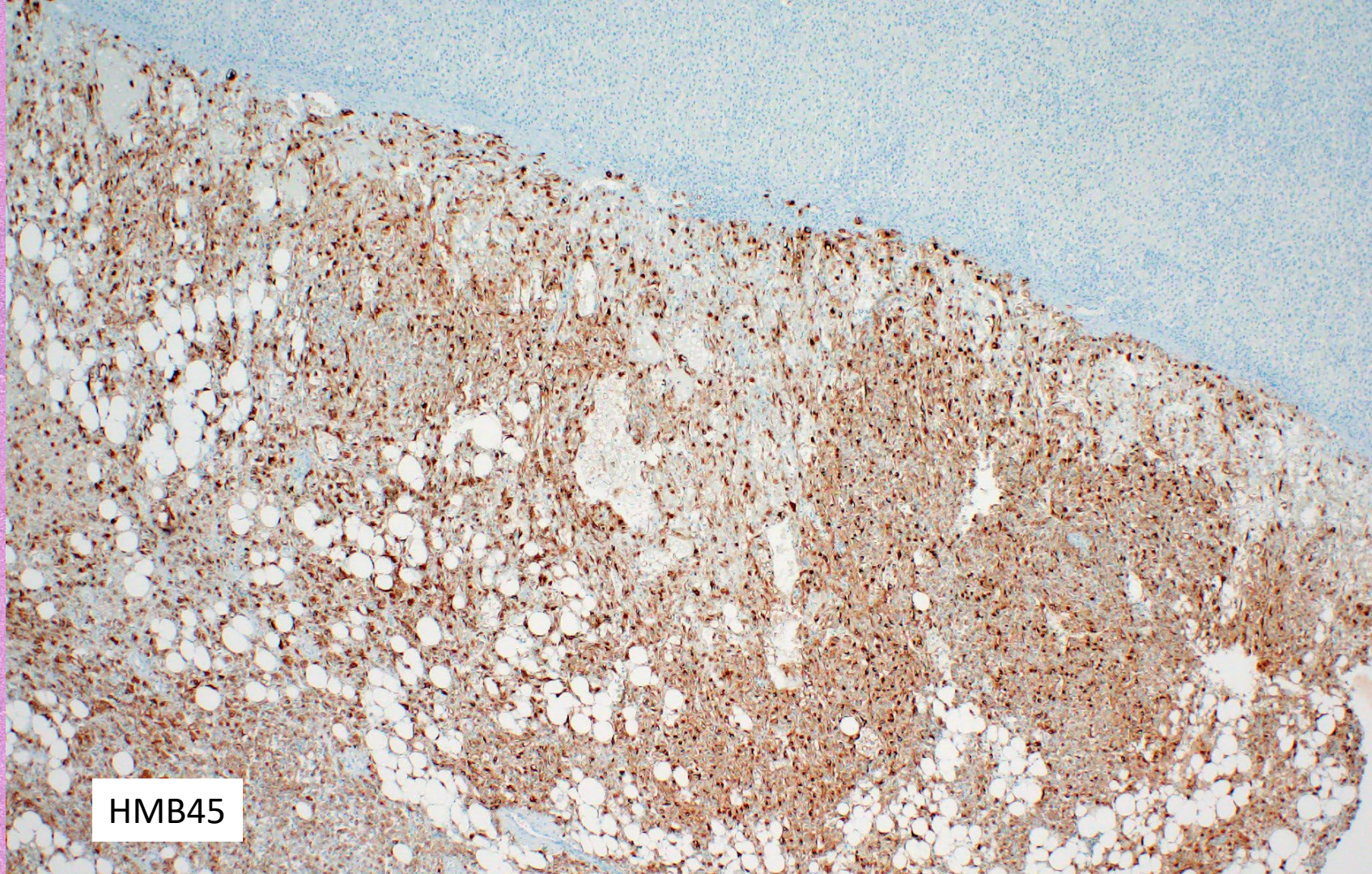
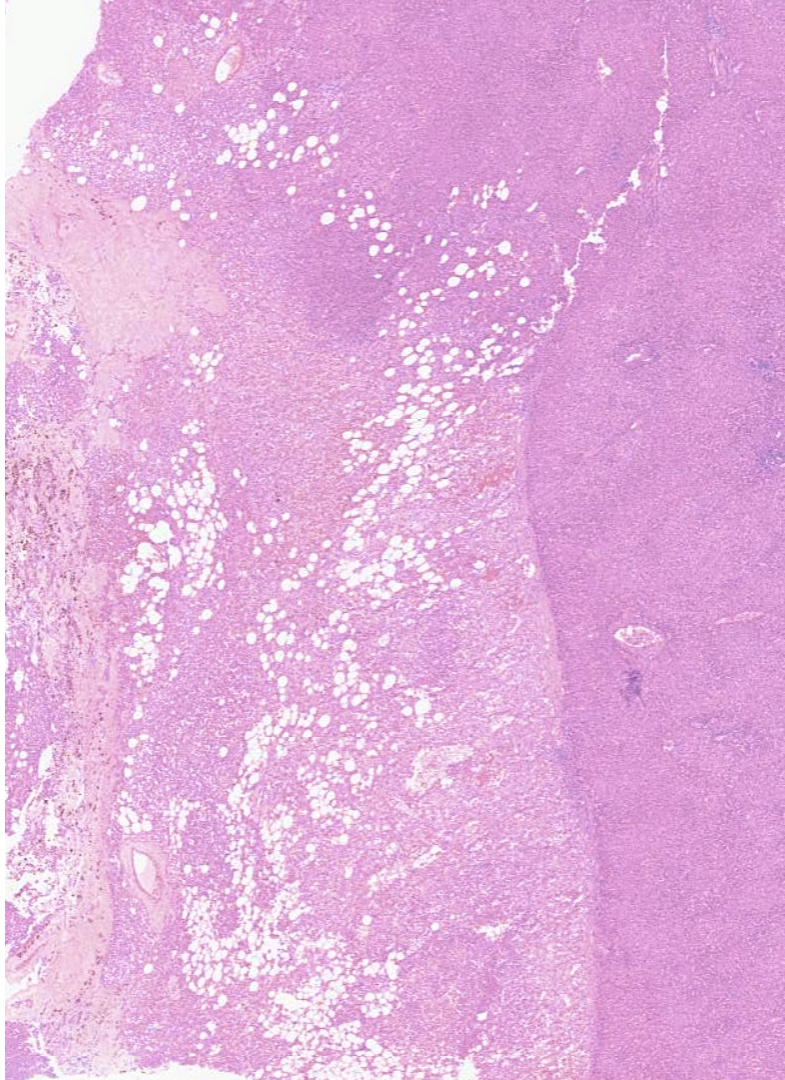
34 F with liver mass



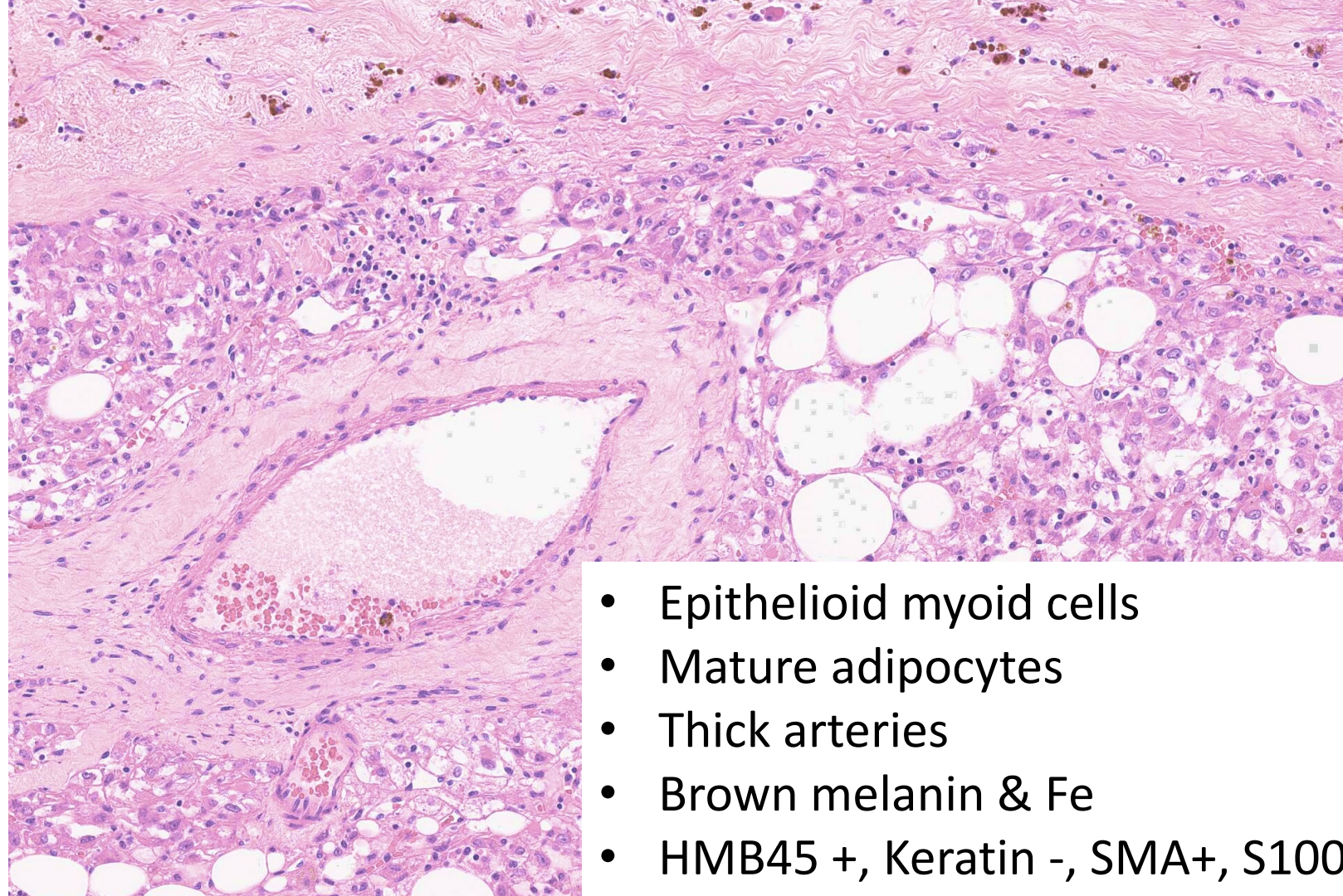
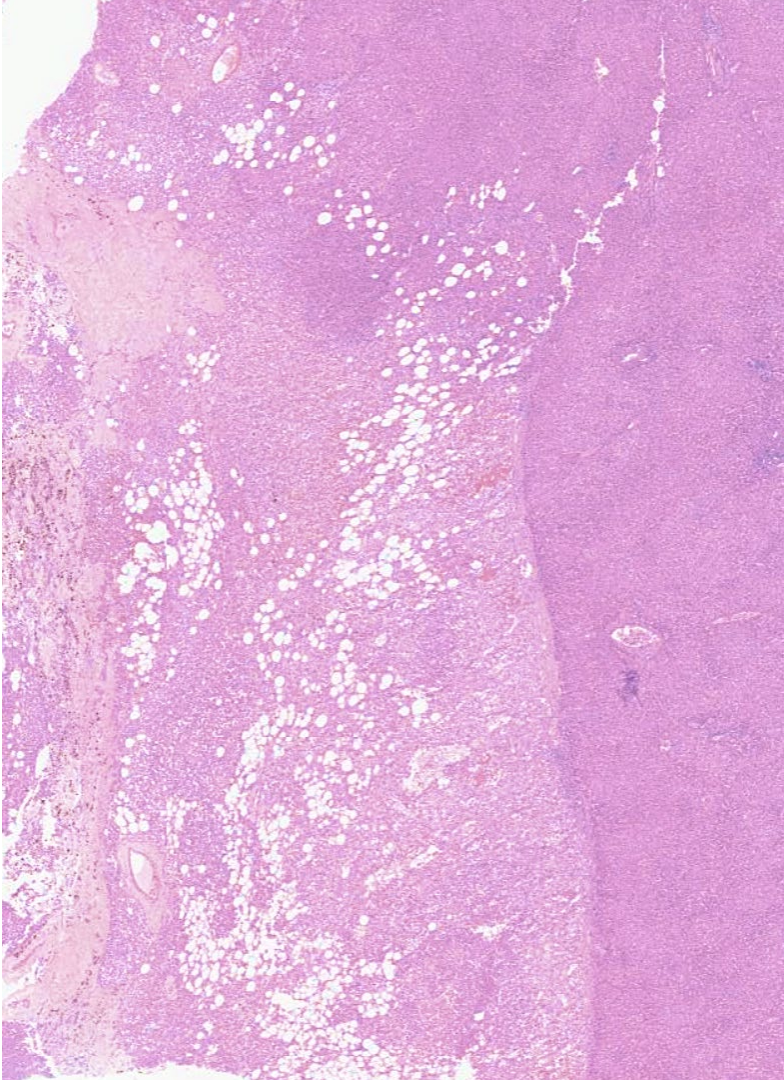
In HCC, the Fat Droplet is INSIDE the cell



HMB45

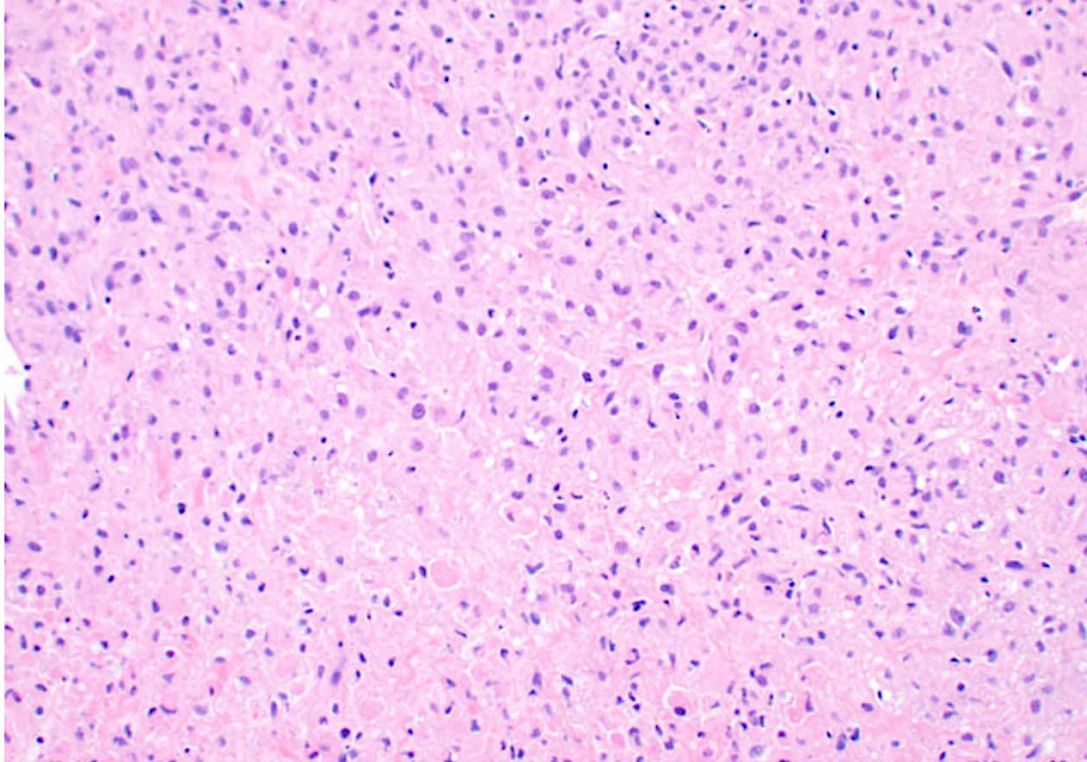


Angiomyolipoma

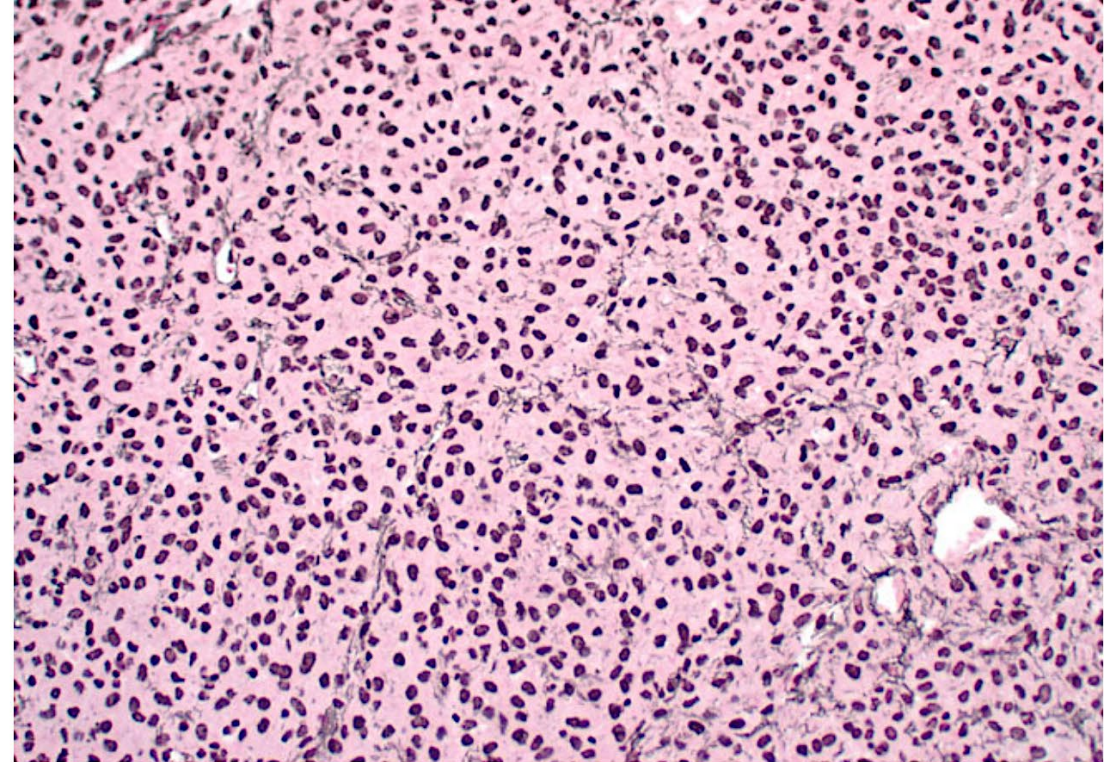


- Epithelioid myoid cells
- Mature adipocytes
- Thick arteries
- Brown melanin & Fe
- HMB45 +, Keratin -, SMA+, S100-

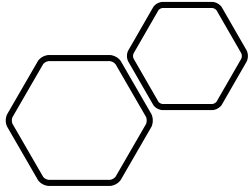
Fat-poor AML can Mimic HCC



Epithelioid smooth muscle cells
have eosinophilic cytoplasm like HCC

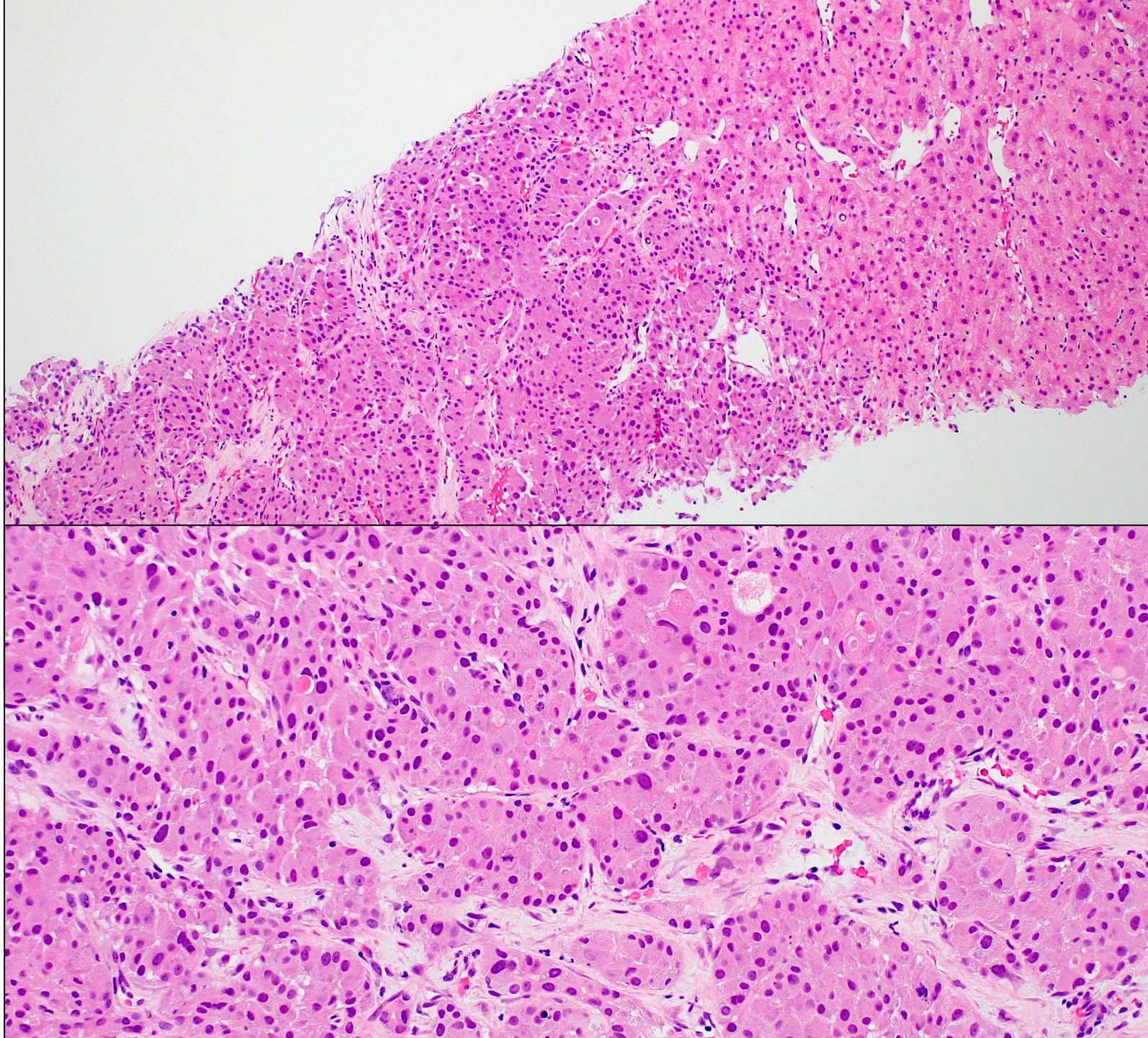


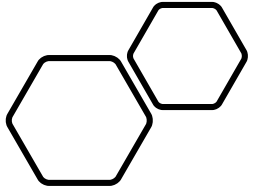
Reticulin 'loss' or appearance of
Trabecular expansion



Tumors that Mimic HCC Histologically

- 61 year old male with pancreas mass, also with liver mass

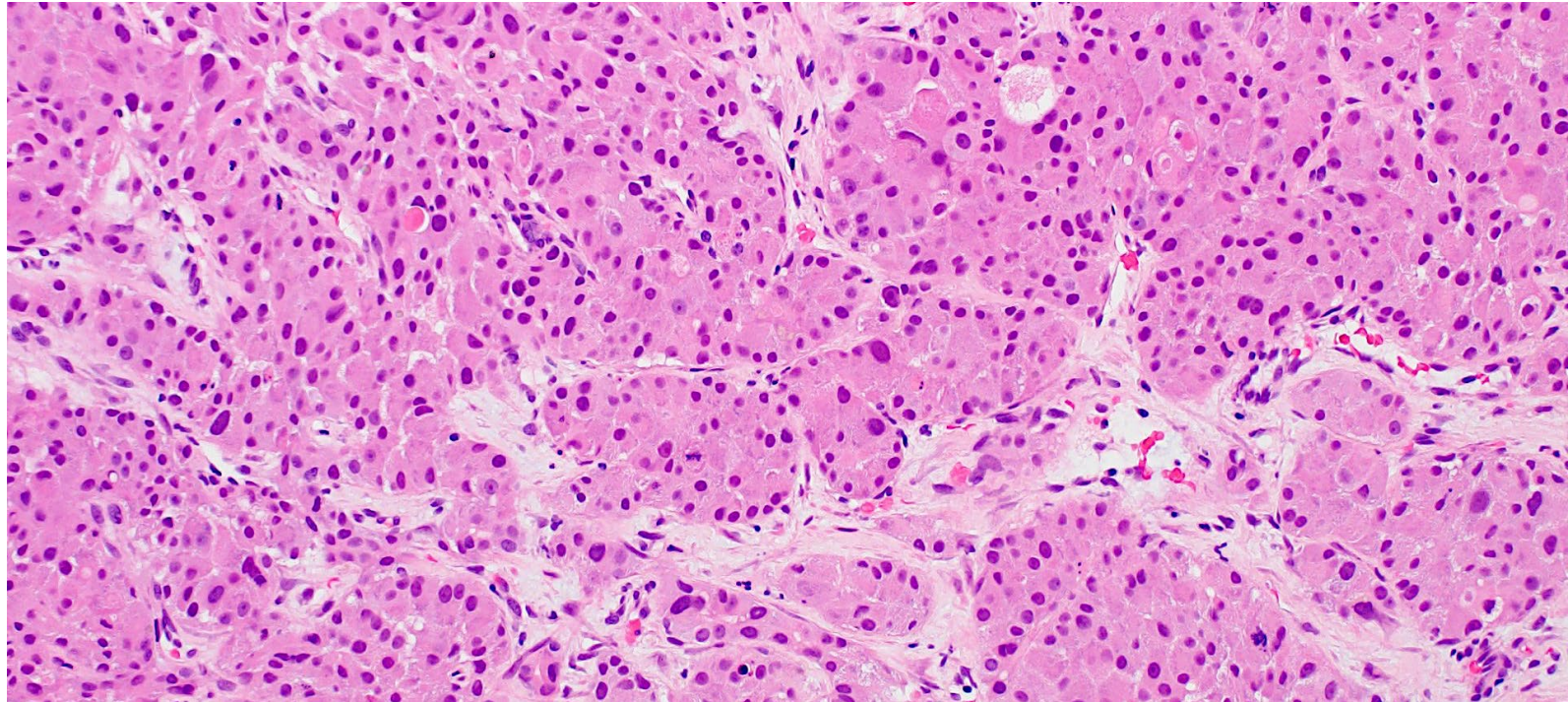
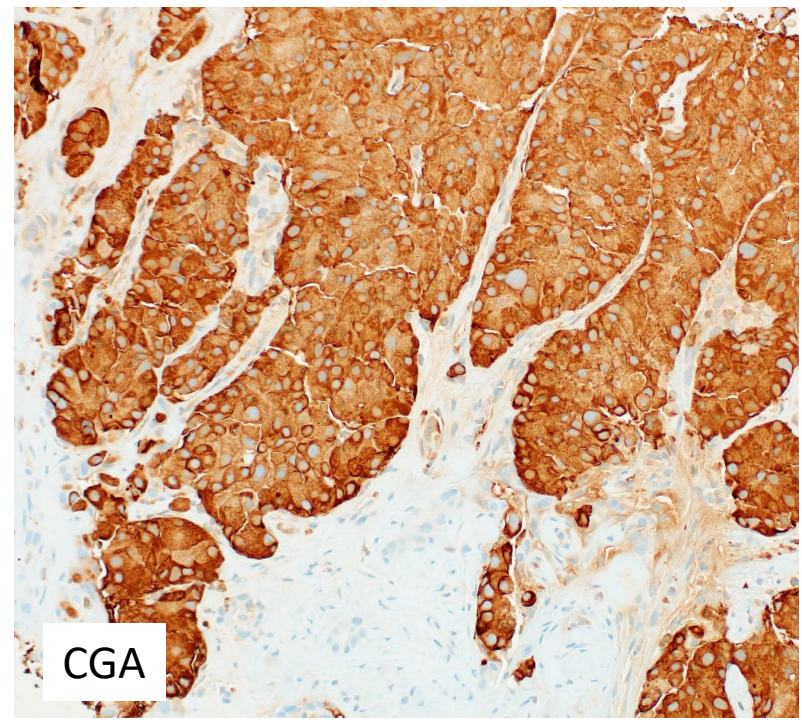
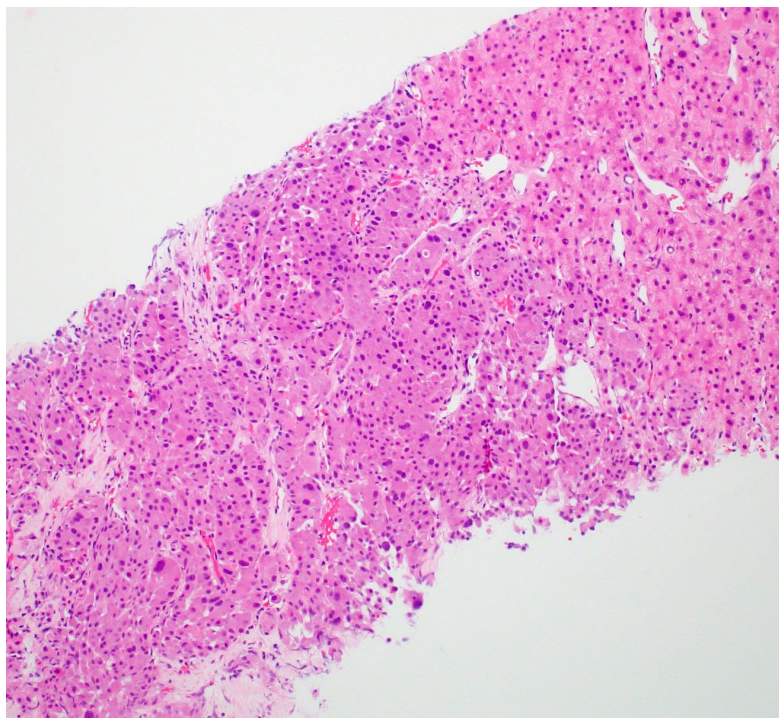


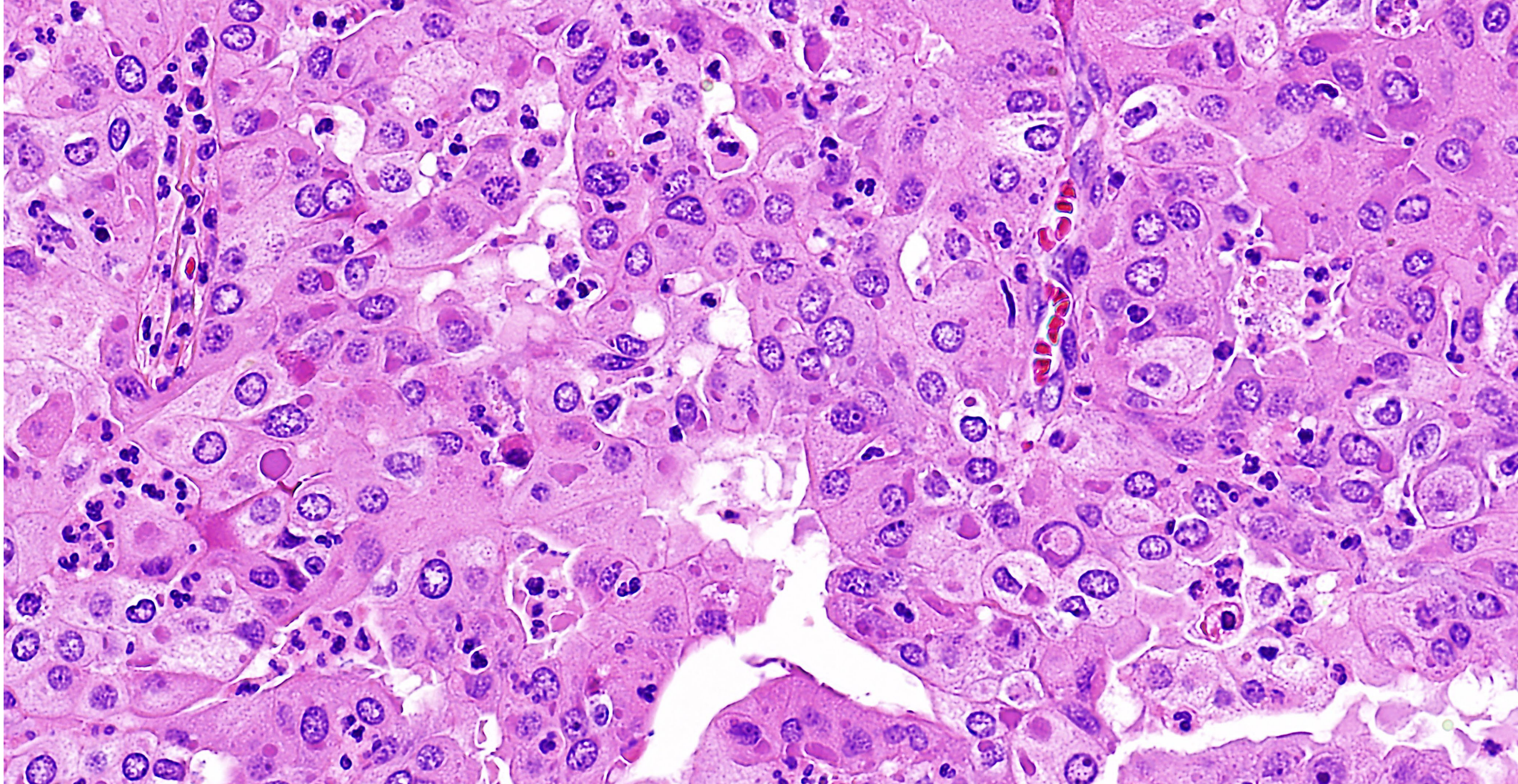


Tumors that Mimic HCC Histologically

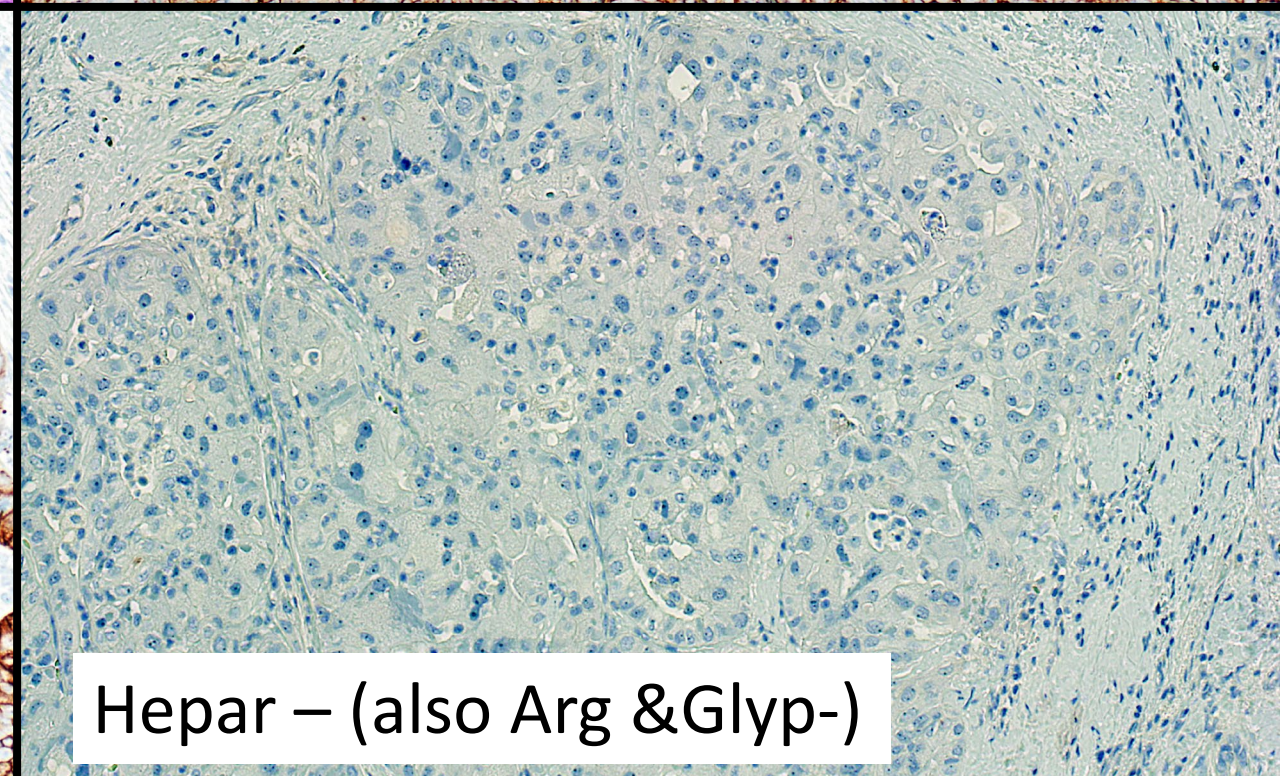
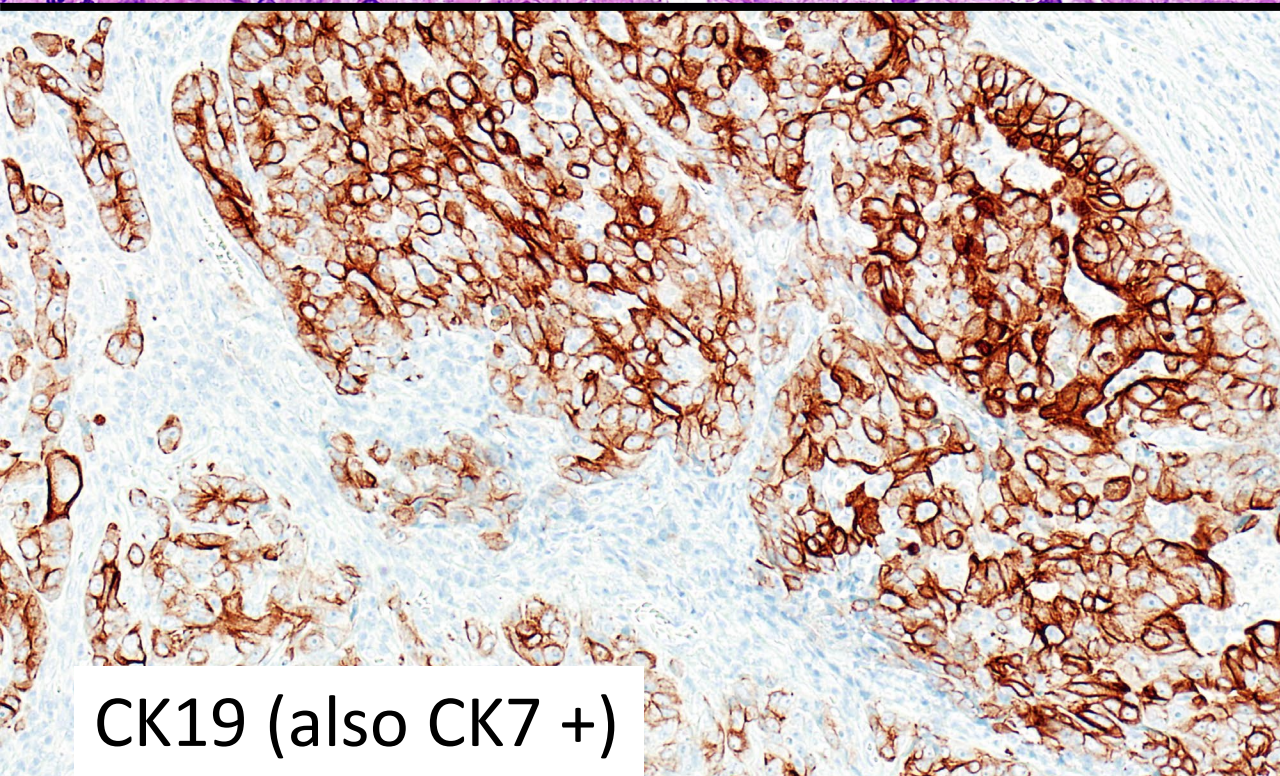
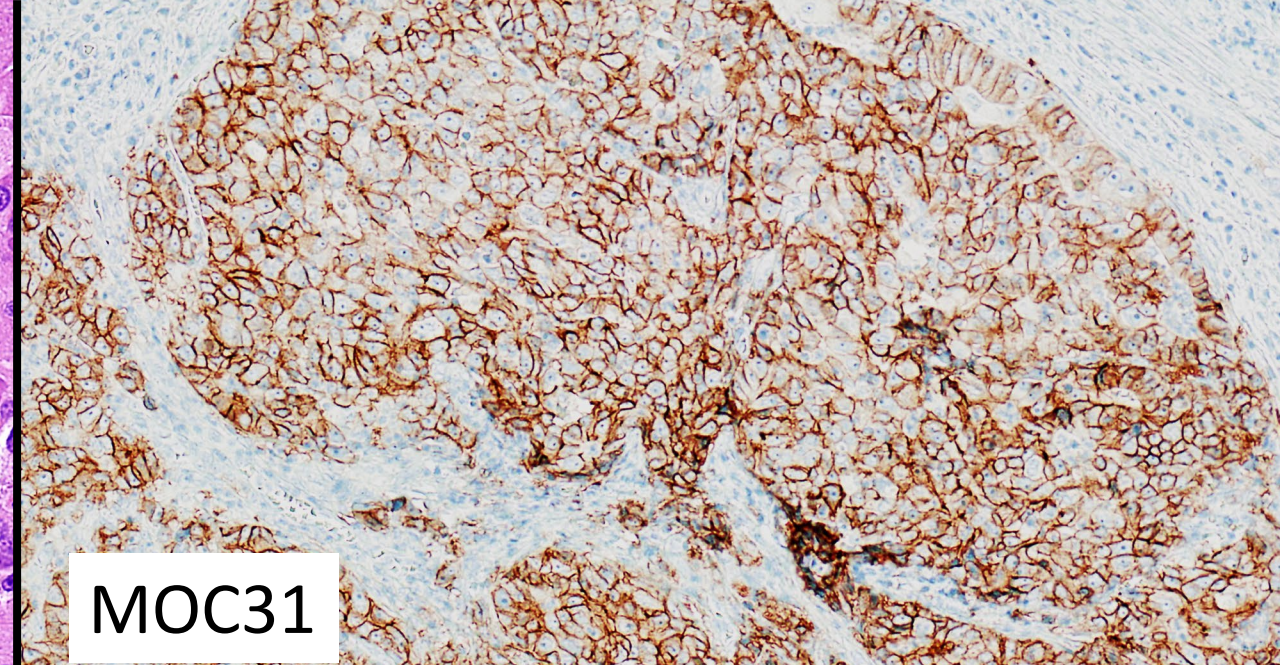
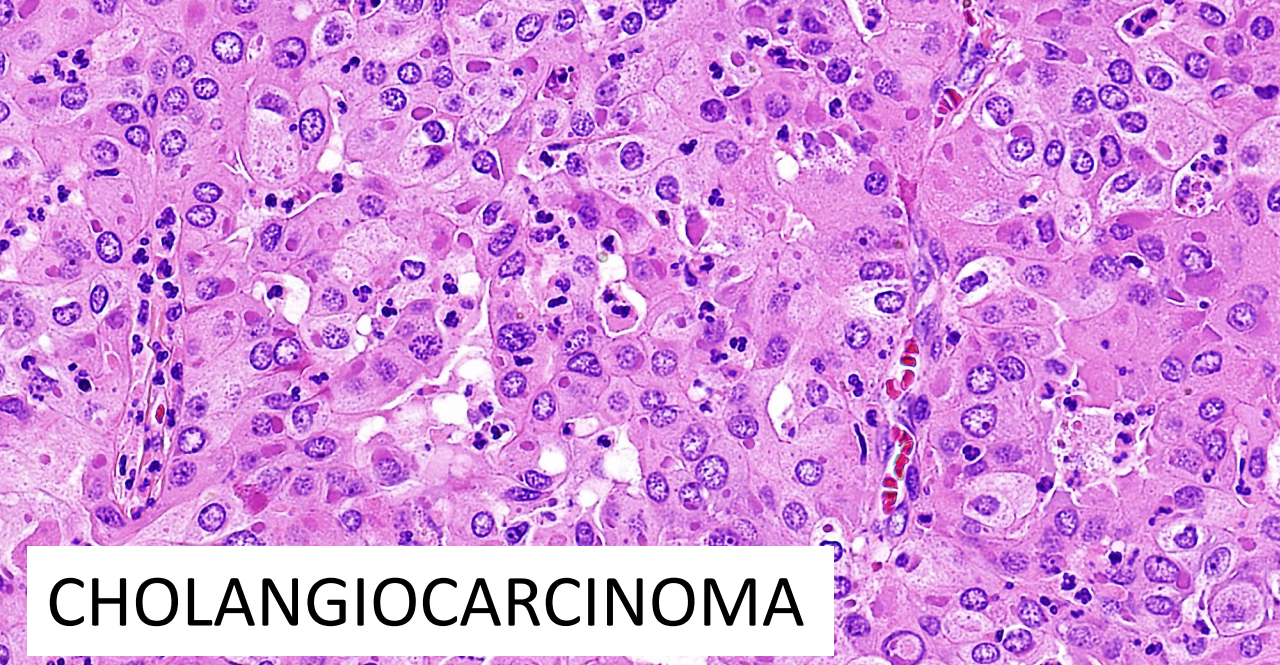
- 61 year old male with pancreas mass, also with liver mass

WELL DIFFERENTIATED
NEUROENDOCRINE TUMOR





Another liver mass case: Mallory Denk bodies?

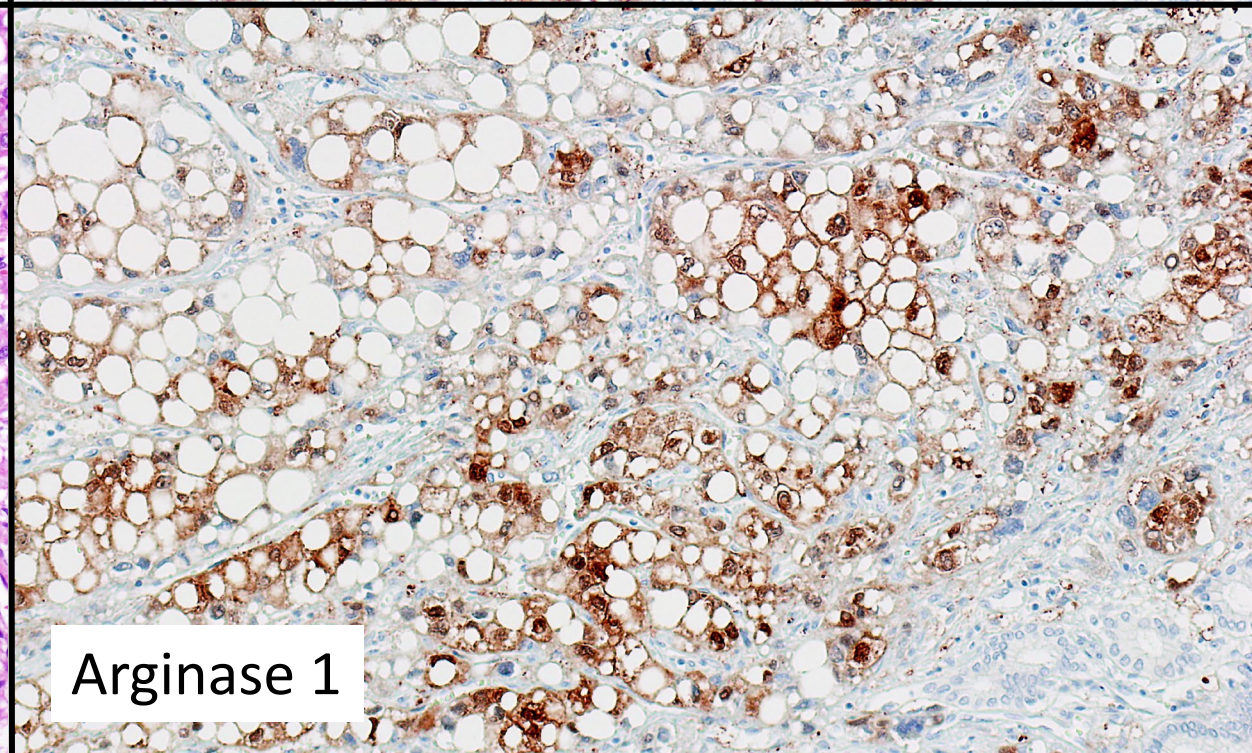
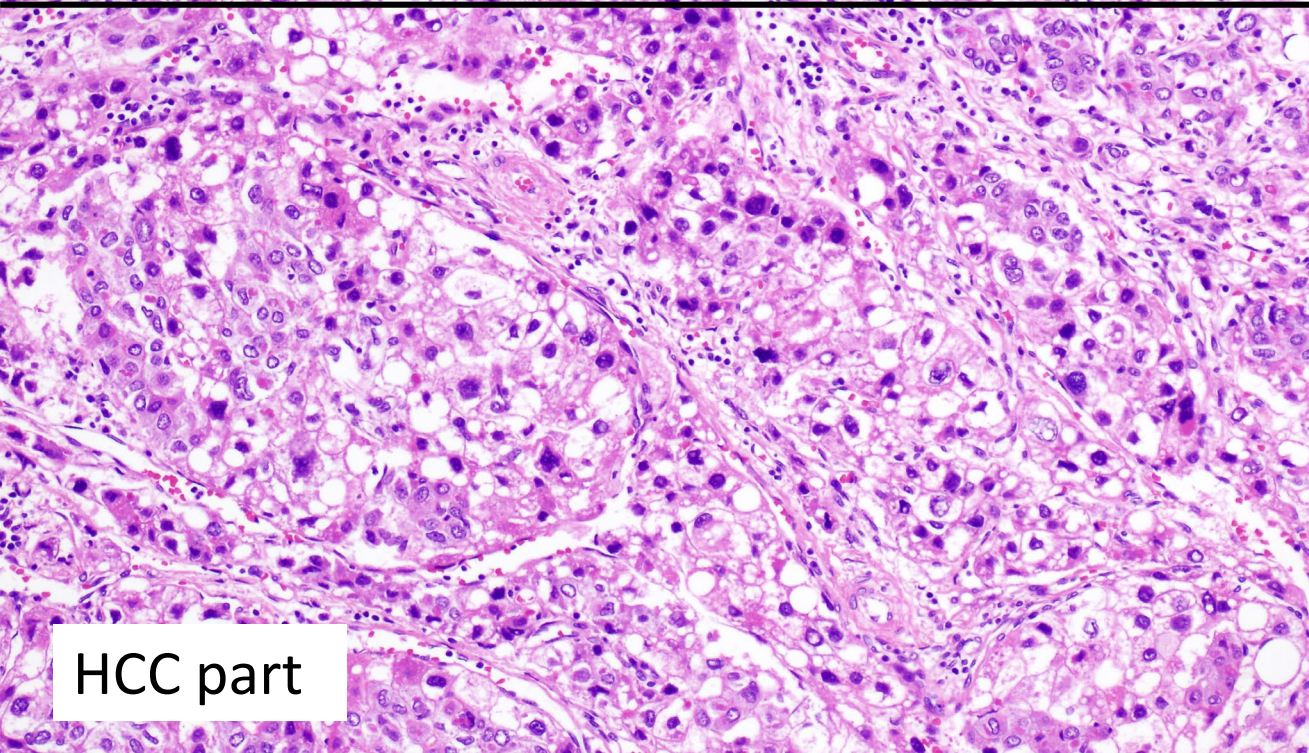
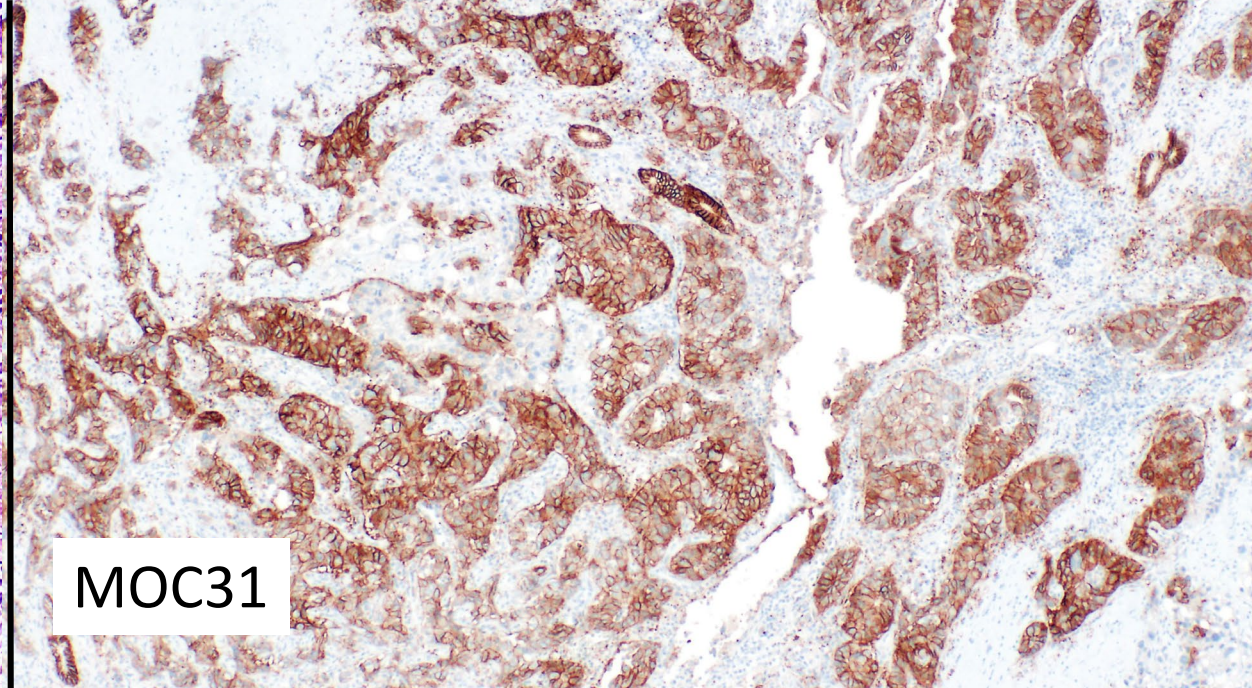
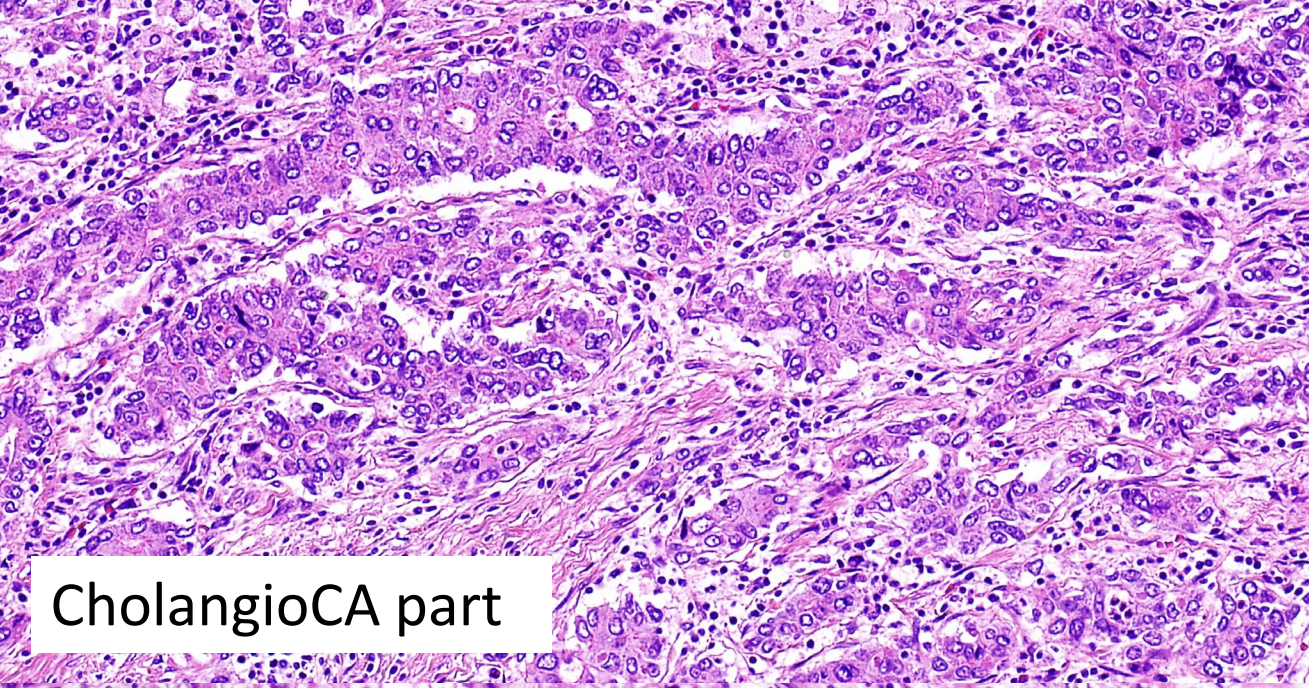


CholangioCA
part

HCC part

CK7

Combined HCC-cholangiocarcinoma



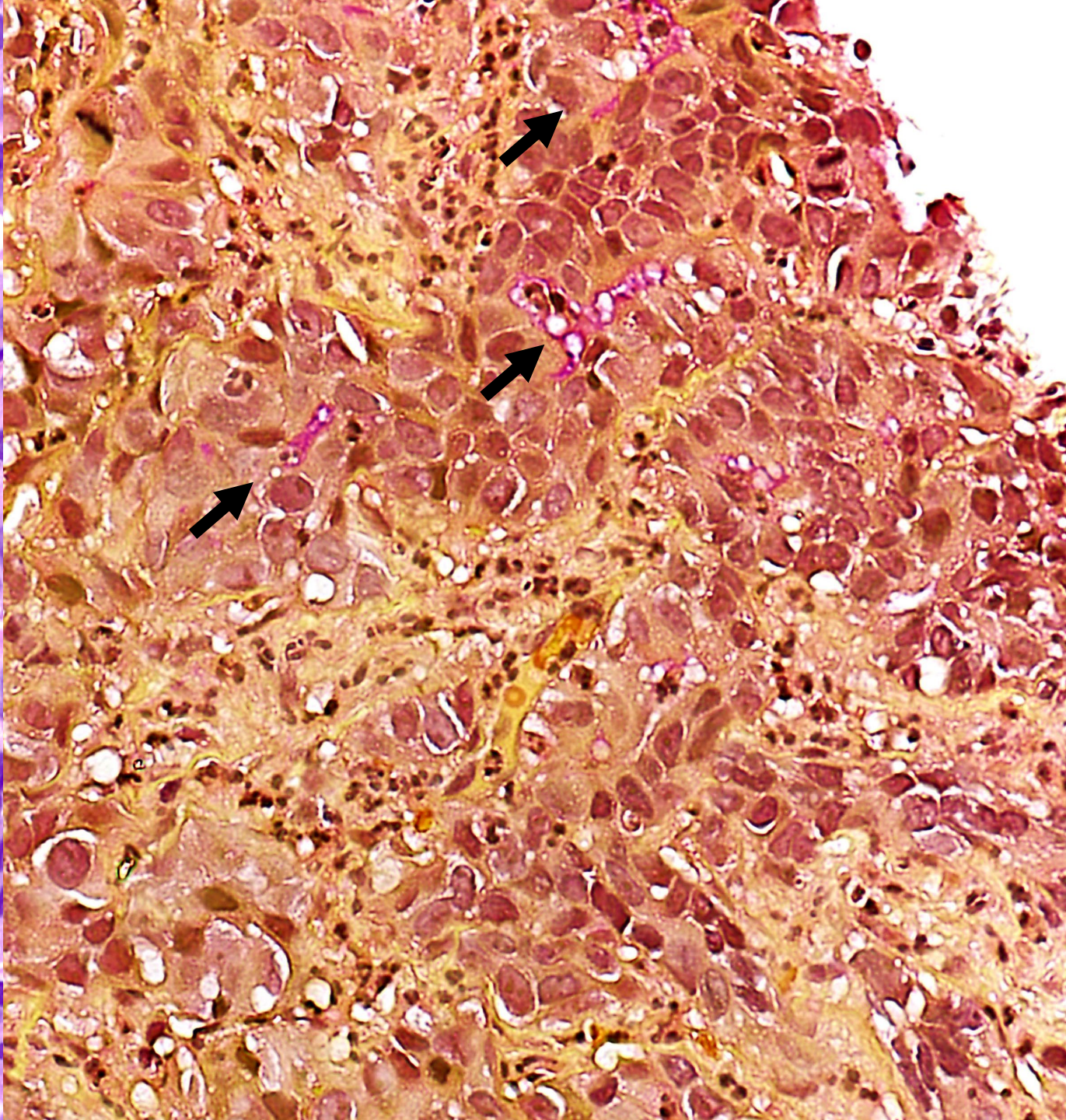
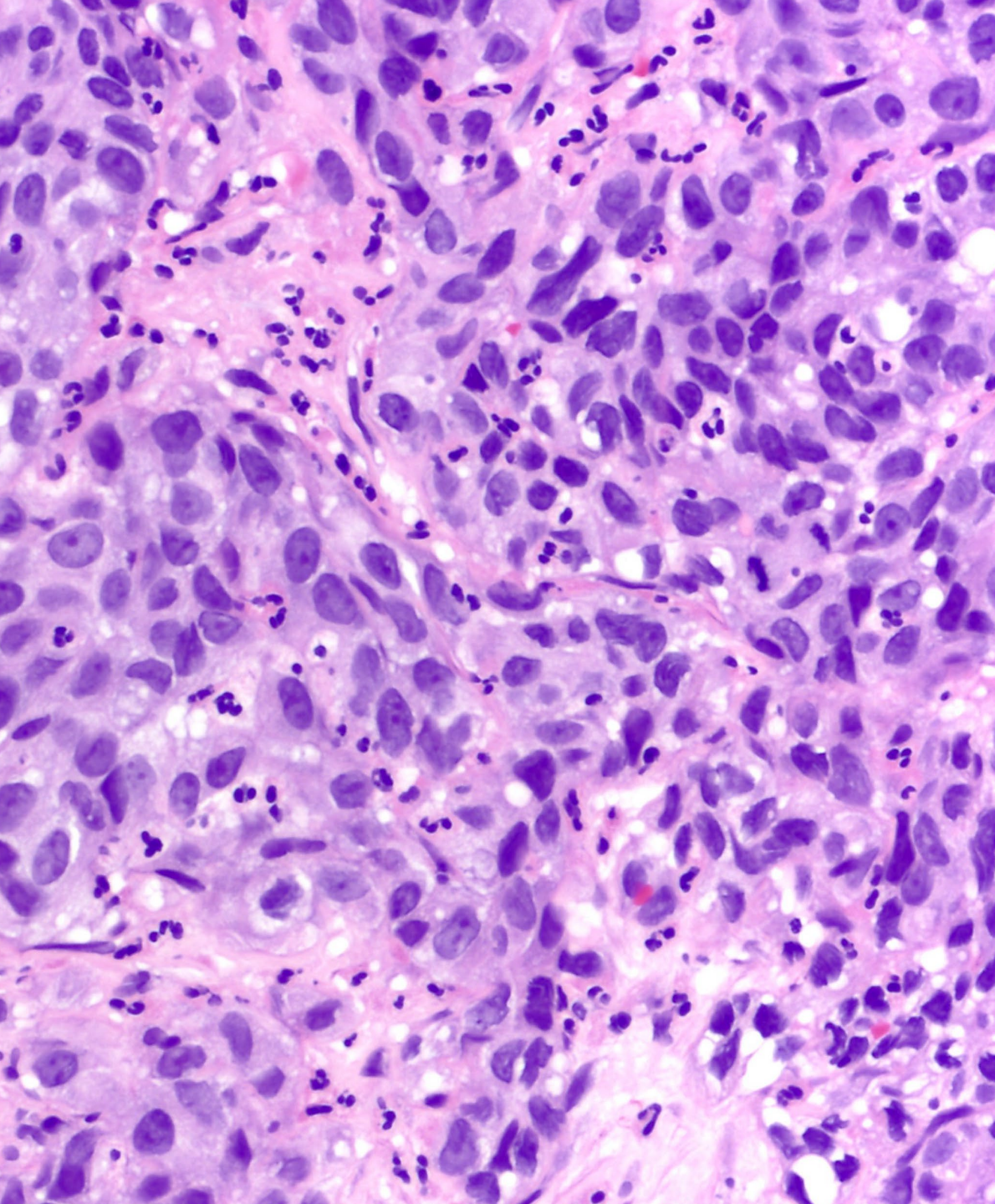
Combined HCC-CholangioCA

HCC part

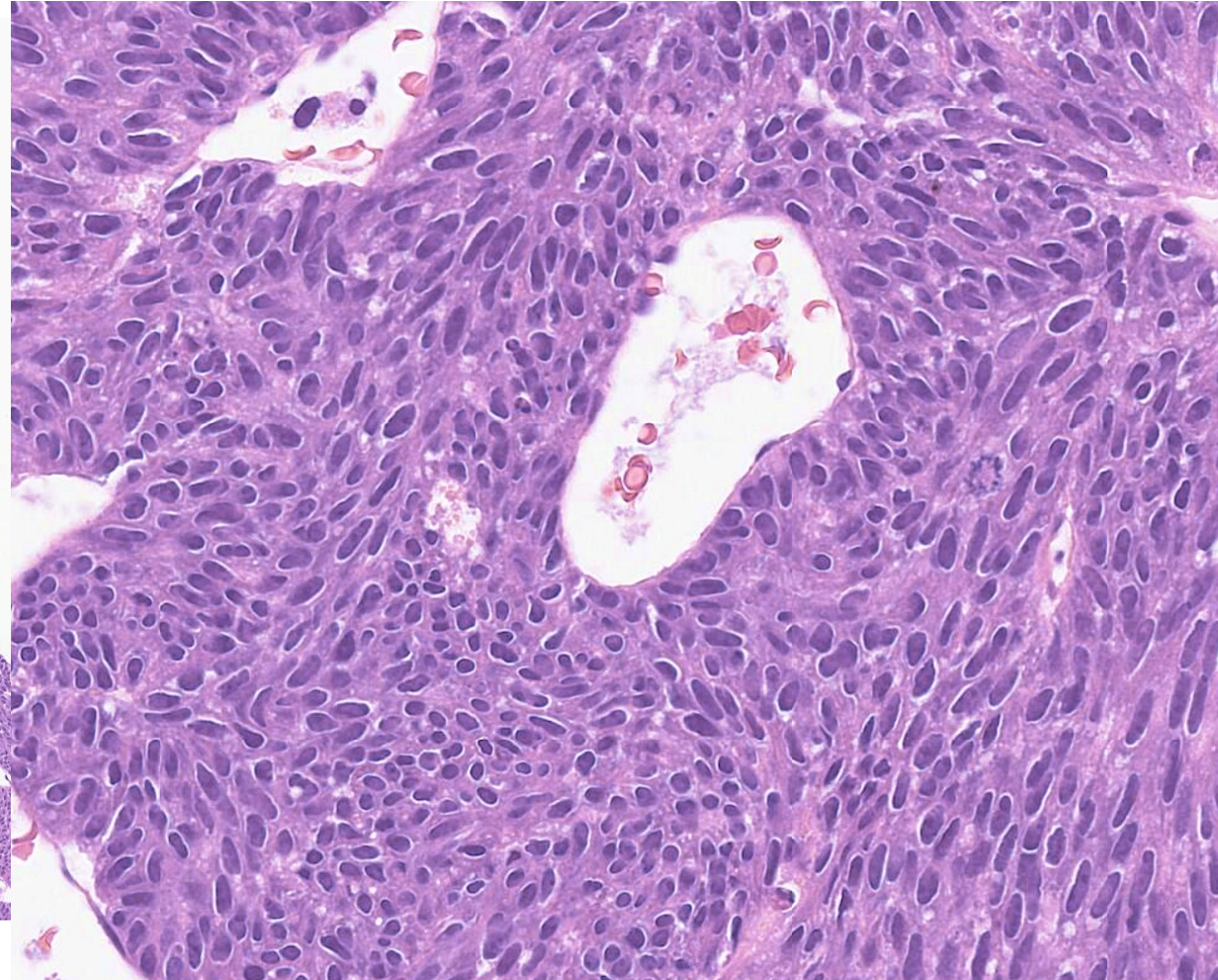
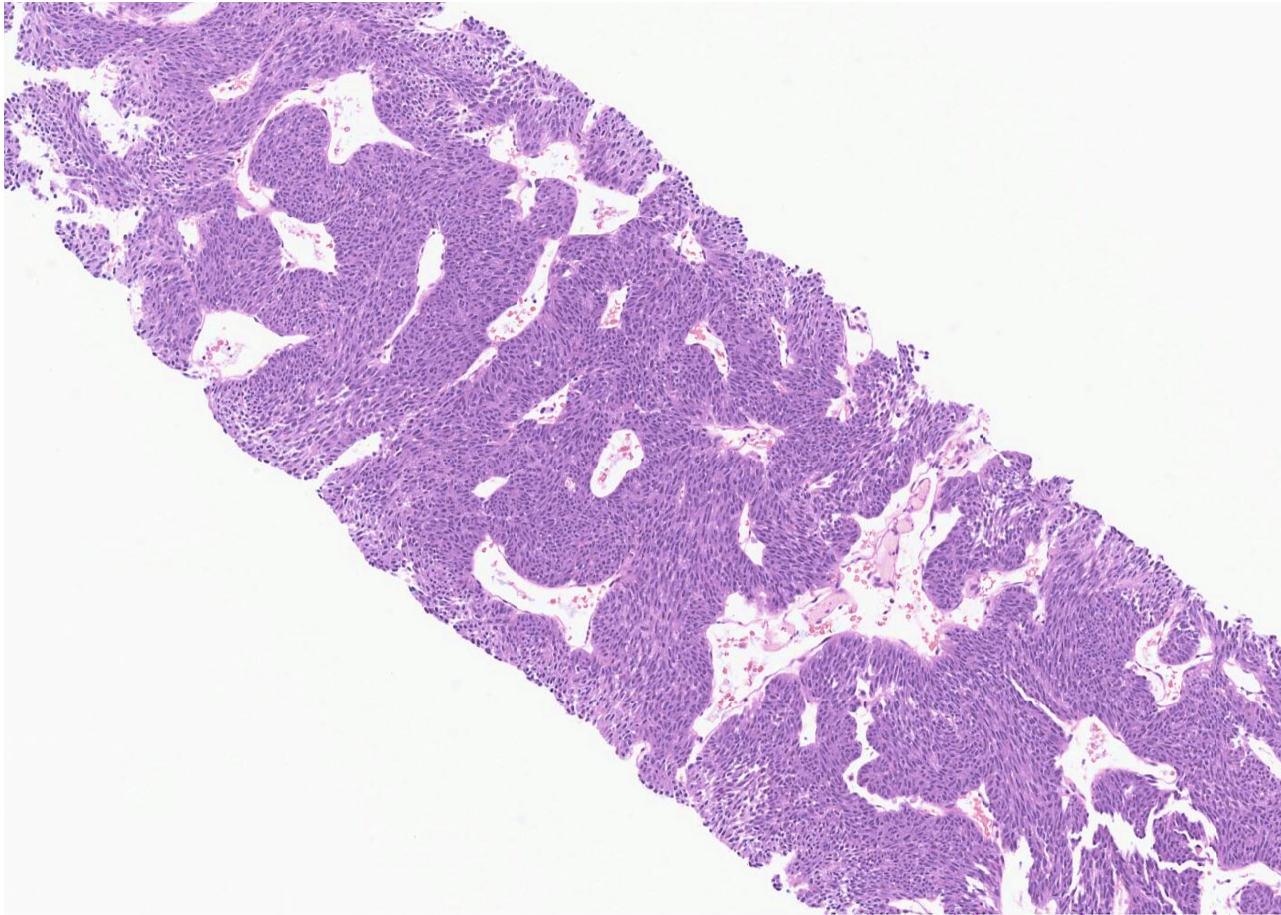
- Polygonal cells, trabecular architecture, bile production, steatotic
- I like to see 2 of these positive:
 - Arginase1++
 - Hep Par 1
 - Glypican 3 (use with caution → 5% cholangioCA can be +)

Cholangiocarcinoma part

- Gland forming
- Use with caution:
 - MOC31 (positive in ~5-10% HCC)
 - CK19 (also ~10% of HCC)
 - Mucicarmin useful when +

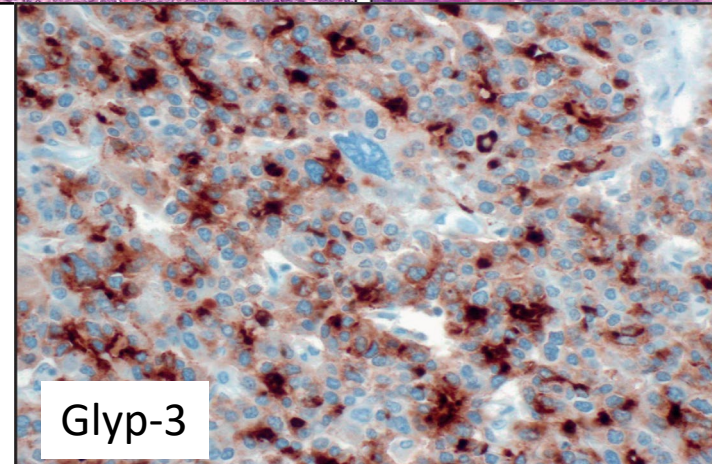
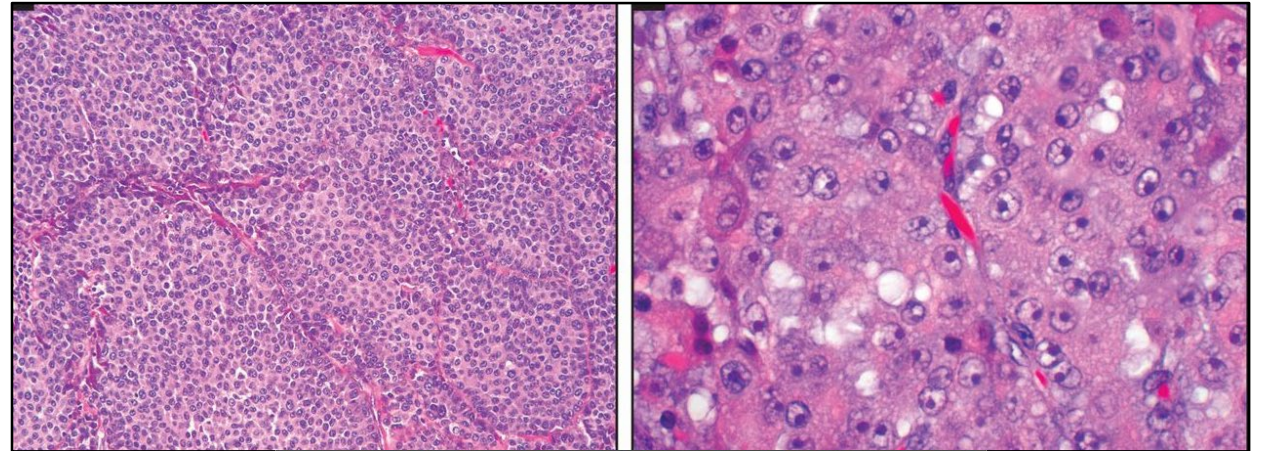


Case: 67-year-old female with firm subcutaneous nodules and lipase >1000



Hepatocellular Markers Positive in Acinar Cell Carcinoma

- Can be positive for:
 - **Glypican 3 – 25%**
 - **Albumin ISH – 25%**
 - Hep Par 1 – 4%
- Negative for Arginase-1



Non-Hepatocytic Tumors that can be Positive for HCC Markers

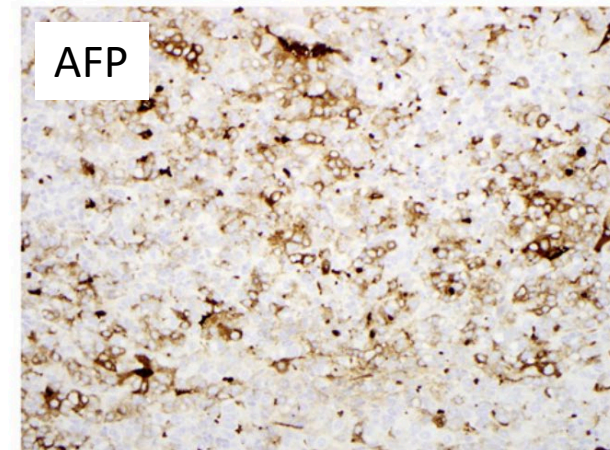
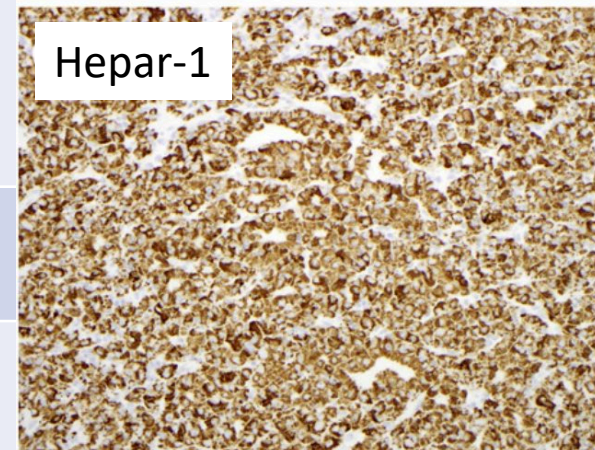
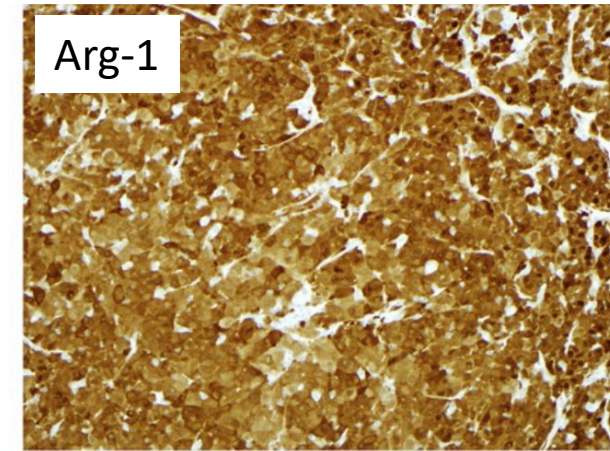
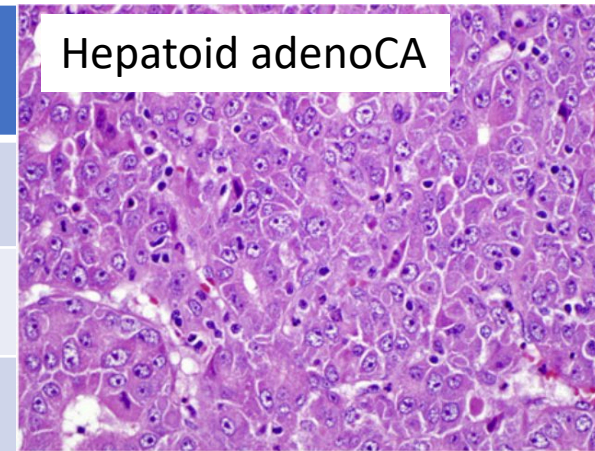
| | Hep Par-1 | Arg-1 | Glypican-3 |
|---|-----------|---------------|------------|
| Gastric, esophageal | x | x rare focal | |
| Lung | x | | |
| Acinar cell (1 marker + separately) | x rare | | x |
| Prostate | x | x rare focal | |
| Germ cell | | | x |
| NET/NEC | x | | x rare |
| Ovarian | x | | x |
| Colon | | x rare focal | |
| Breast | | x rare focal | |
| Pancreas | x | x rare, focal | |
| Gallbladder | x | | |
| Melanoma | x | | x rare |
| Hepatoid adenoCA (can also form bile and have elevated AFP) | x | x | x |

- Scrutinize the **MORPHOLOGY**
- Use additional **IHC**

Hum Pathol. 2016 Sep;55:101-7.
 Am J Surg Pathol. 2002 Aug;26(8):978-88.
 Am J Clin Pathol. 2004 Nov;122(5):721-7.
 Surg Pathol Clin. 2018 Jun;11(2):367-375.

Hepatoid Adenocarcinoma (usually Gastric)

| | HCC | Hepatoid adenoCA |
|---|-----------------------|---------------------|
| Bile | + | + |
| Positive HCC markers, AFP levels | + | + |
| Advanced fibrosis in background liver | Favors HCC | - |
| Areas of tumor with NON-hepatoid morphology (mucin, gland formation) | - | + |
| Strong CDX2 or other stain of other organ positivity | Focal/patchy in 5-10% | + |
| History of gastric mass (or other sites GB, colon, gyn, lung, kidney) | - | + |
| SALL4 | Rare in West | + |



Hum Pathol. 2016 Sep;55:11-6.
 Mayo Clin Proc 1997;72:1154-1160
 Am J Surg Pathol. 2010 Apr;34(4):533-40.

How HCC can Mimic Non-hepatocytic Tumors

Immunohistochemical Stains that can Spuriously be Positive in HCC

SATB2 (up to 60%)

CDX2 (5-8%; usually focal/patchy, higher grade HCC)

CK20 (5-10%, higher grade HCC)

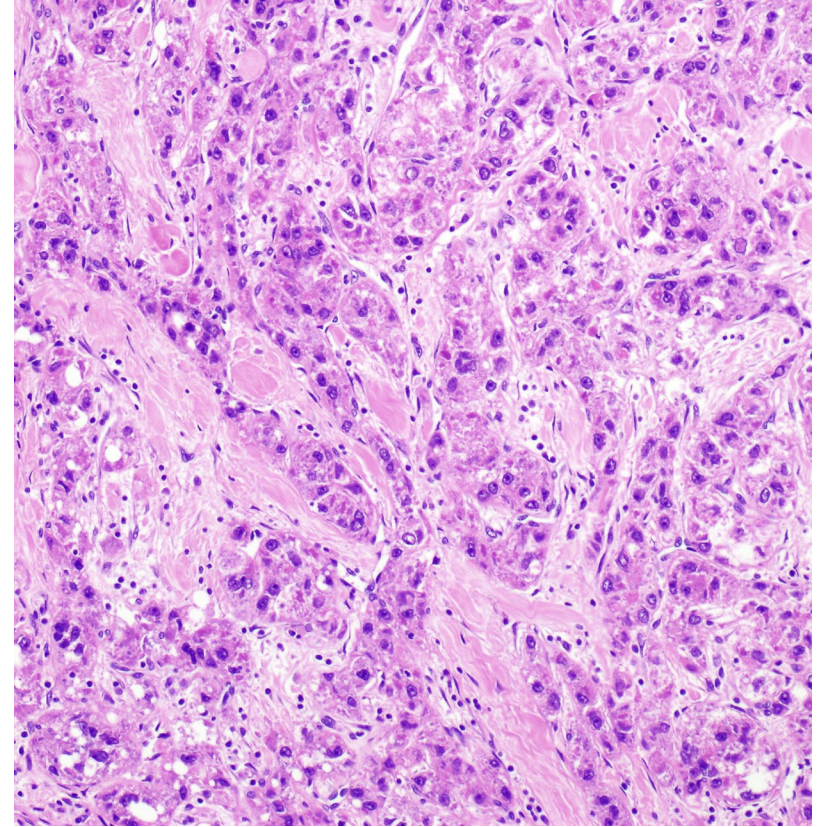
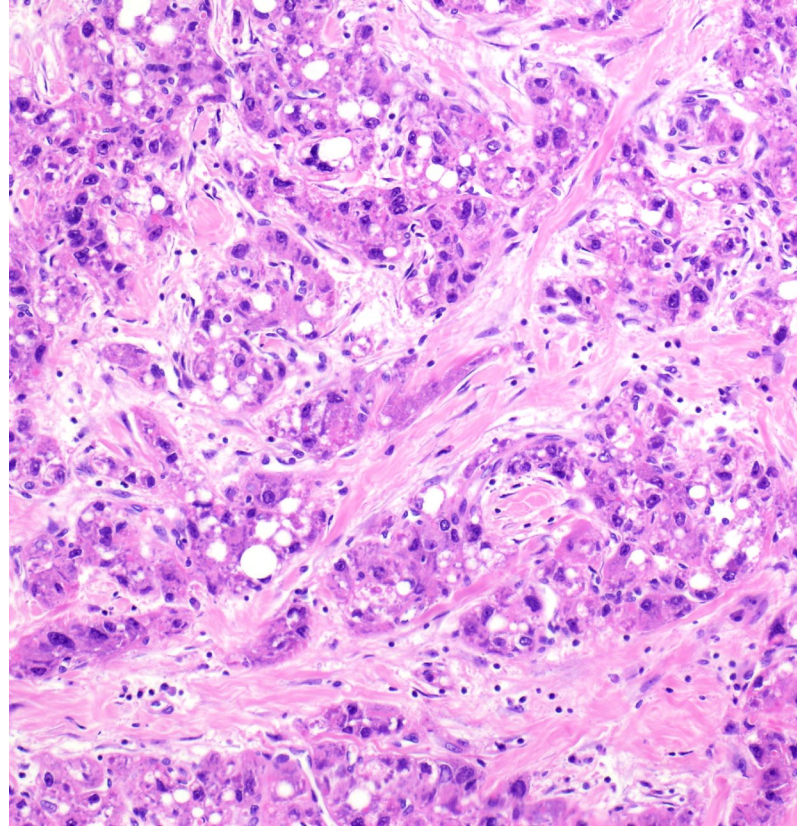
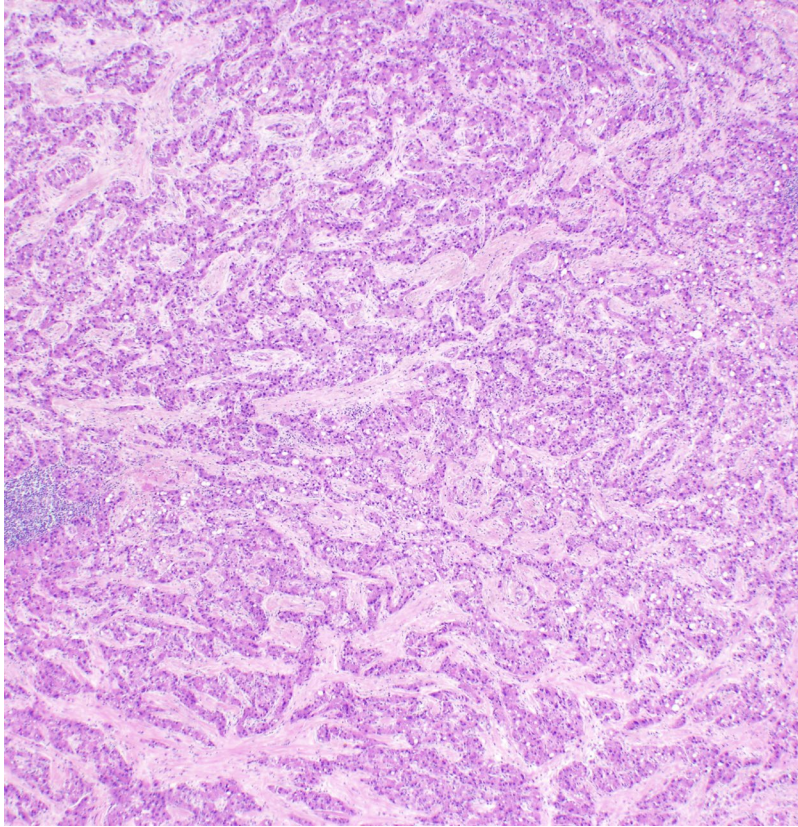
CK7 (30%)

CK19 (12% bad prognosis)

MOC31 (10-30%; patchy, weak)

CD117 (2.5%)

SALL4 (bad prognosis; 1% in West; 20% in Asia)



Scirrhou HCC

- Radiologically mimics Cholangiocarcinoma
- Rare
- >50% of cancer shows dense intratumoral fibrosis
- But lacks mucin and you can sometimes spot bile

Scirrhous HCC

- No difference in prognosis from HCC
- May be difficult to identify as an HCC and distinguish from cholangiocarcinoma – tend to be more **Hepar-, MOC31 & CK7 +** than other HCC

Table 2 Immunohistochemical staining of scirrhous hepatocellular carcinoma, classical hepatocellular carcinoma, and intrahepatic cholangiocarcinoma

| | <i>CEA^a</i> | <i>HepPar-1</i> | <i>GPC3</i> | <i>ARG1</i> | <i>CK7</i> | <i>CK19</i> | <i>EPCAM</i> |
|--|------------------------|-----------------|-------------|-------------|------------|-------------|--------------|
| Scirrhous hepatocellular carcinoma (<i>n</i> = 20) ^b | 37 | 26 | 79 | 85 | 53 | 26 | 63 |
| Classical hepatocellular carcinoma (<i>n</i> = 169) ^b | 54 | 74 | 69 | 95 | 2 | 2 | 11 |
| Cholangiocarcinoma (<i>n</i> = 16) ^b | 0 | 7 | 6 | 0 | 100 | 94 | 100 |
| <i>P</i> -value (scirrhous vs classical hepatocellular carcinoma) | 0.223 | <0.001 | 0.440 | 0.189 | <0.001 | <0.001 | <0.001 |
| <i>P</i> -value (scirrhous hepatocellular carcinoma vs cholangiocarcinoma) | 0.026 | 0.209 | <0.001 | <0.001 | 0.001 | 0.001 | 0.011 |

Scirrhous HCC

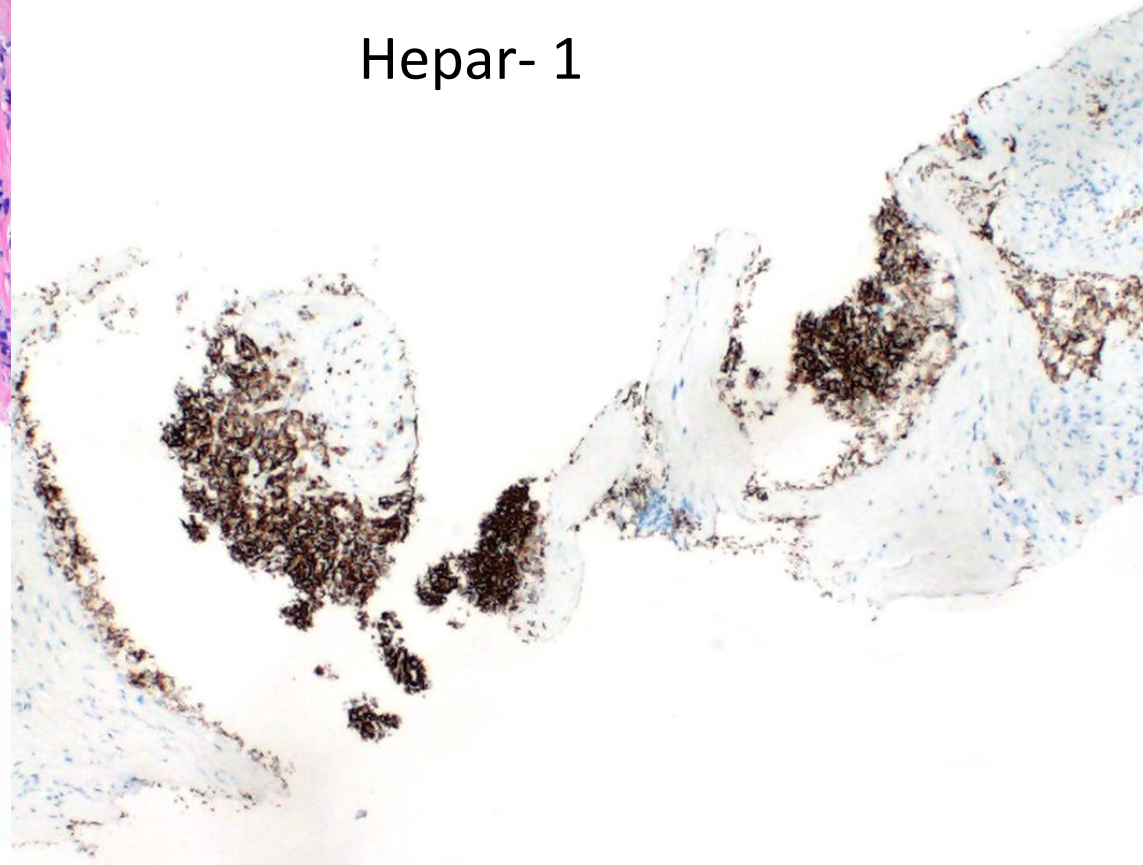
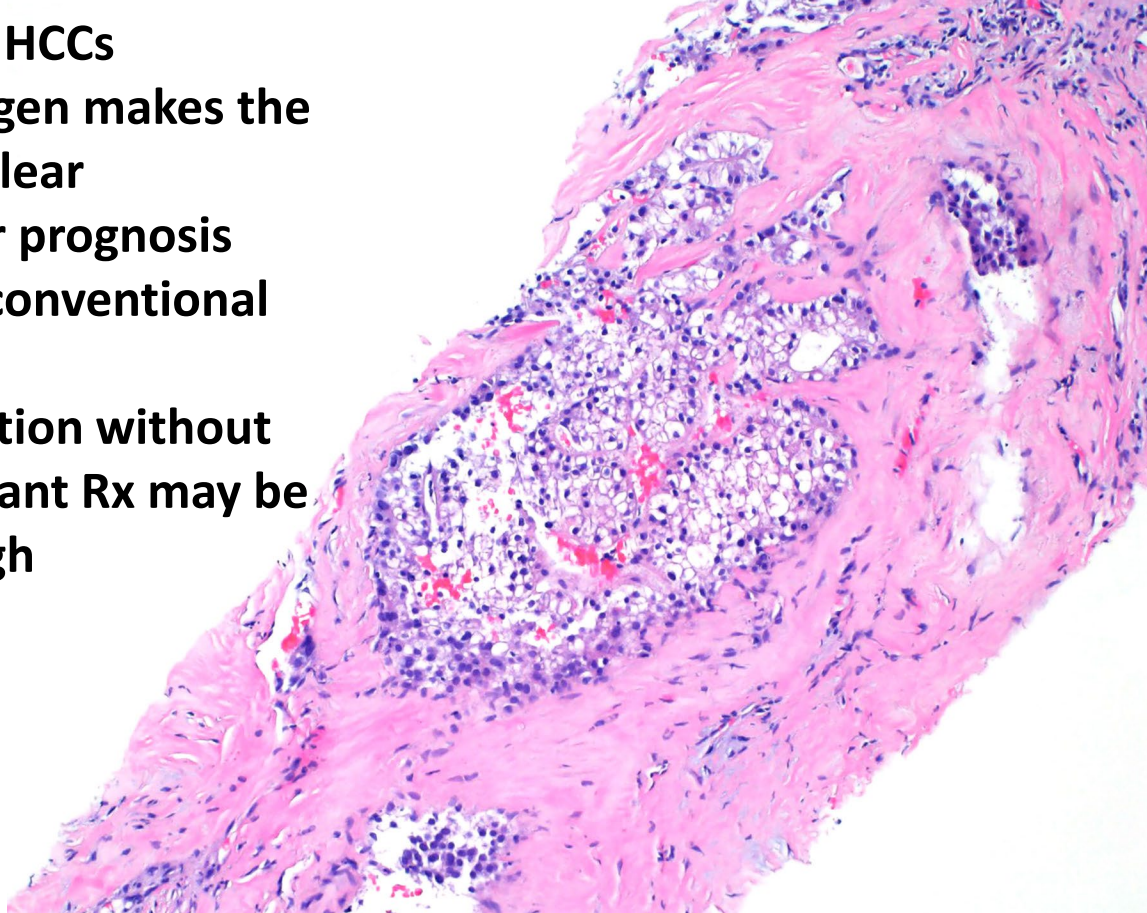
- No difference in prognosis from HCC
- May be difficult to identify as an HCC and distinguish from cholangiocarcinoma – tend to be more Hepar-, MOC31 & CK7 + than other HCC, **use Arg & Glypican3 + to distinguish from CholangioCA**

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Clear cell HCC

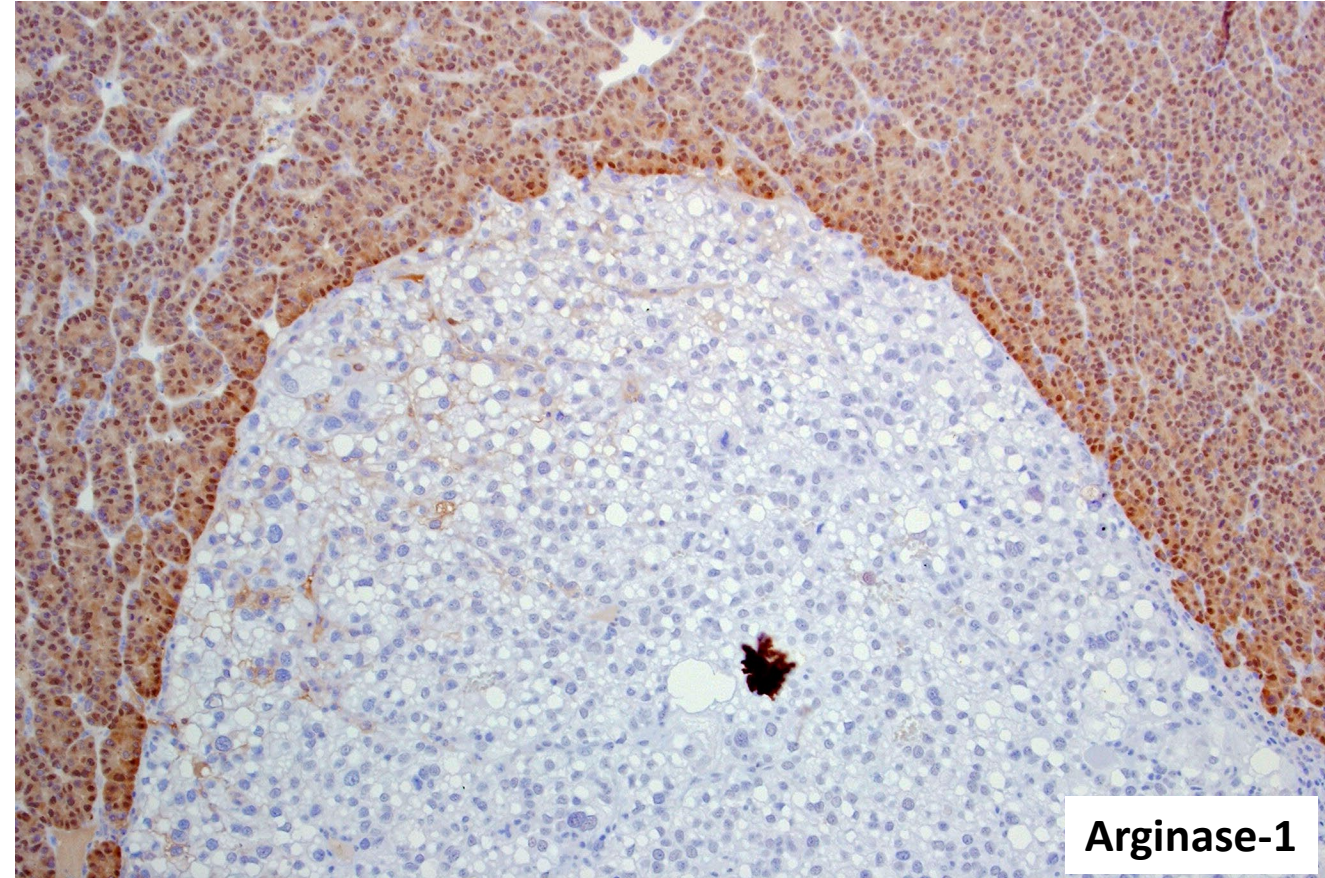
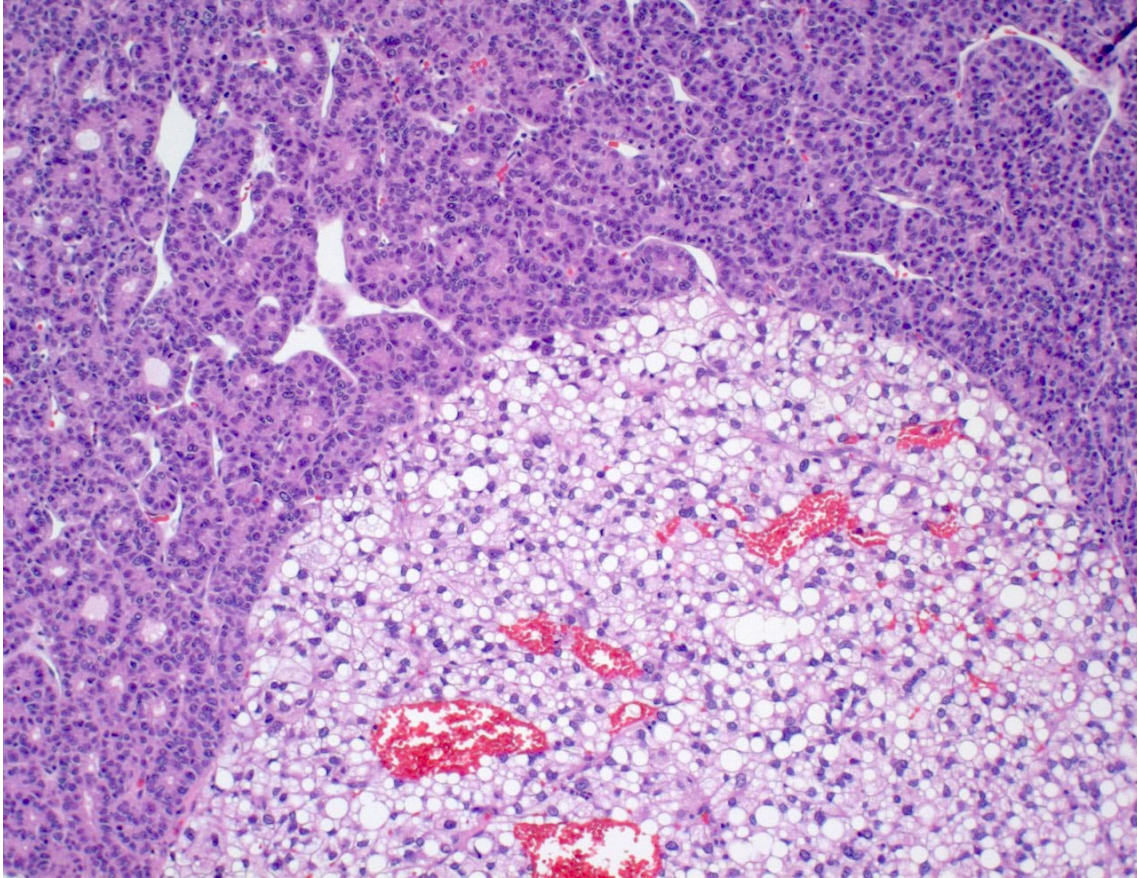
- ✓ 3% of HCCs
- ✓ Glycogen makes the cells clear
- ✓ Better prognosis than conventional HCC
- ✓ Resection without Adjuvant Rx may be enough



Hepar- 1

Courtesy of Dr. Laura Lamps

Clear cell HCC may be Tough to Diagnose on Biopsies



Courtesy of Dr. John Hart

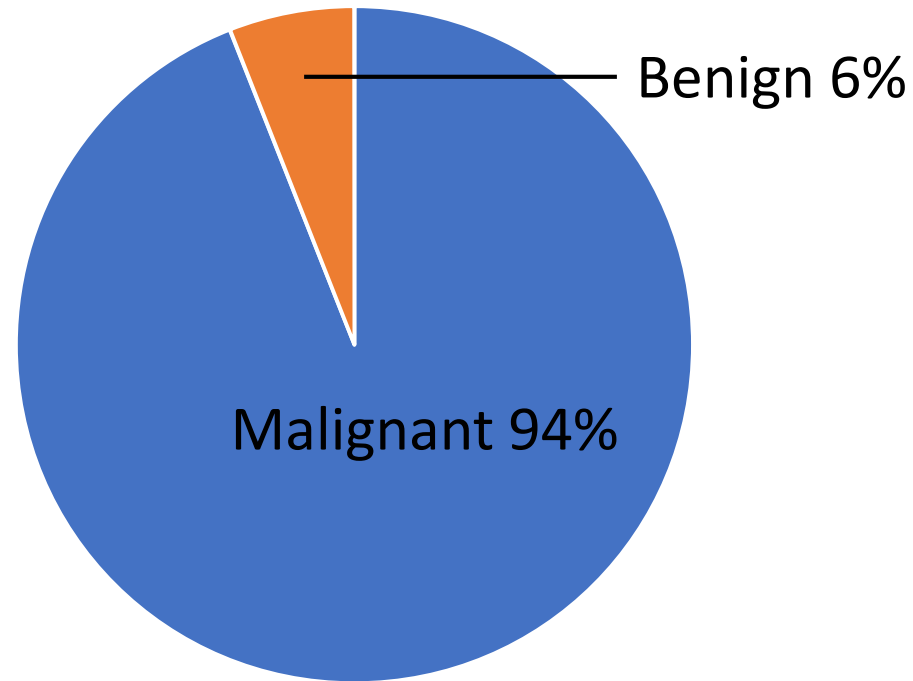
Summary of Part I: Establishing that a malignant tumor is HCC

- Use all that you have to help you to diagnose HCC:
 - Clinical information of background liver disease, AFP levels, imaging
 - Microscopic: Look for bile formation, findings typical of hepatocytes (such as steatosis, Mallory-Denk bodies, pale bodies)
 - IHC: a combination of markers: Arginase1, Glypican-3, albumin-ISH
- Beware of metastases that can mimic HCC
- Beware of HCC that can mimic non-hepatocytic tumors

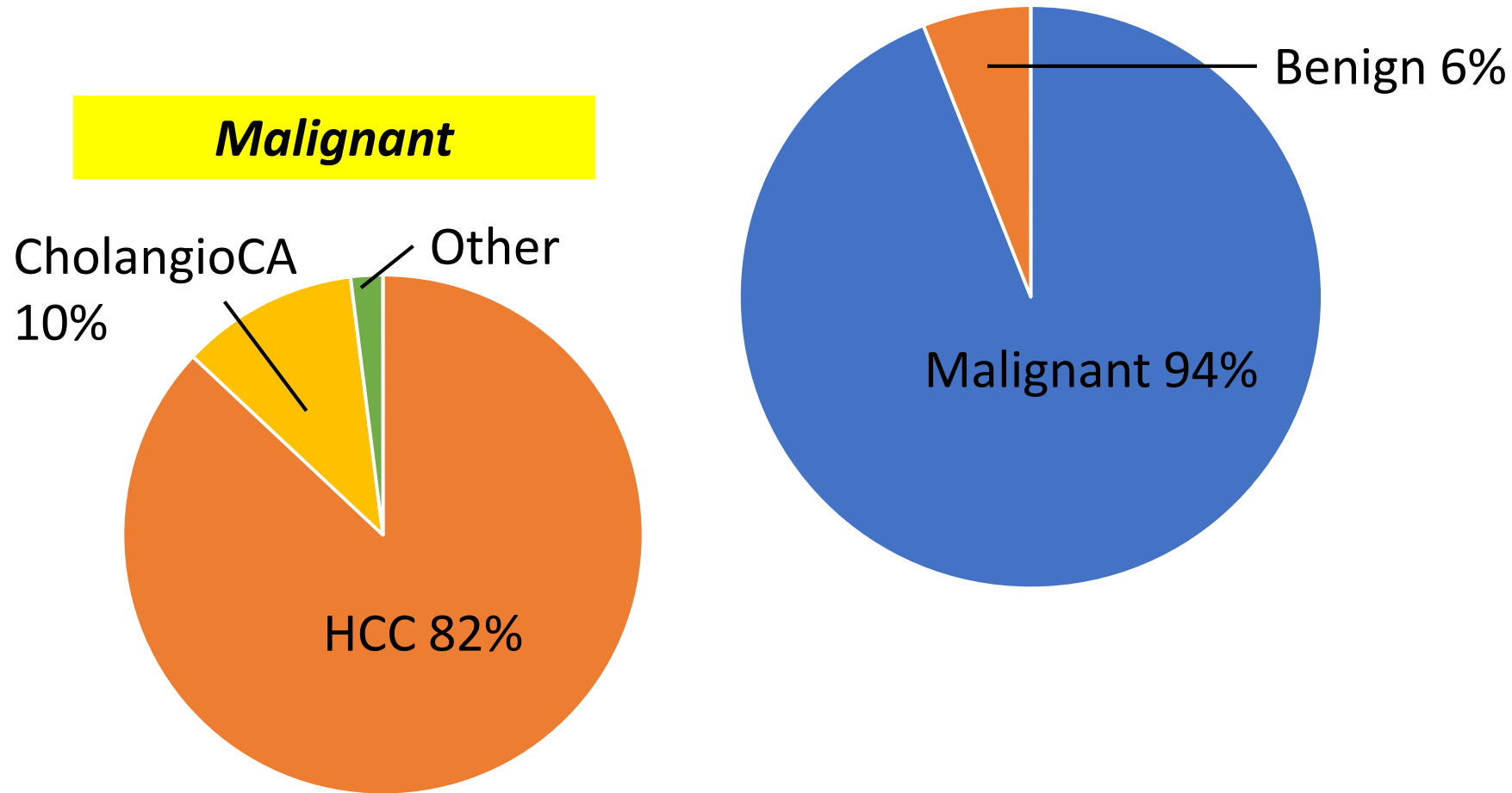
Outline

- ~~I. Distinguishing HCC from metastases or iCCA~~
- II. Distinguishing HCC from benign hepatocellular conditions (You know it is hepatocytic but can't tell for sure if it is malignant or not)

Primary Hepatic Tumors in the USA (excluding Hemangioma and Bile duct hamartoma)

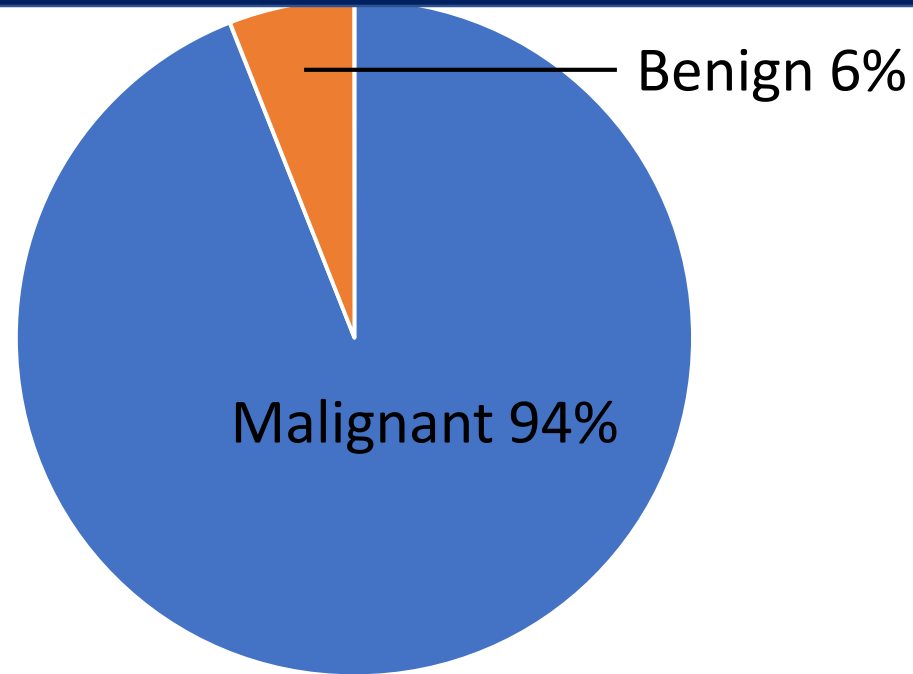
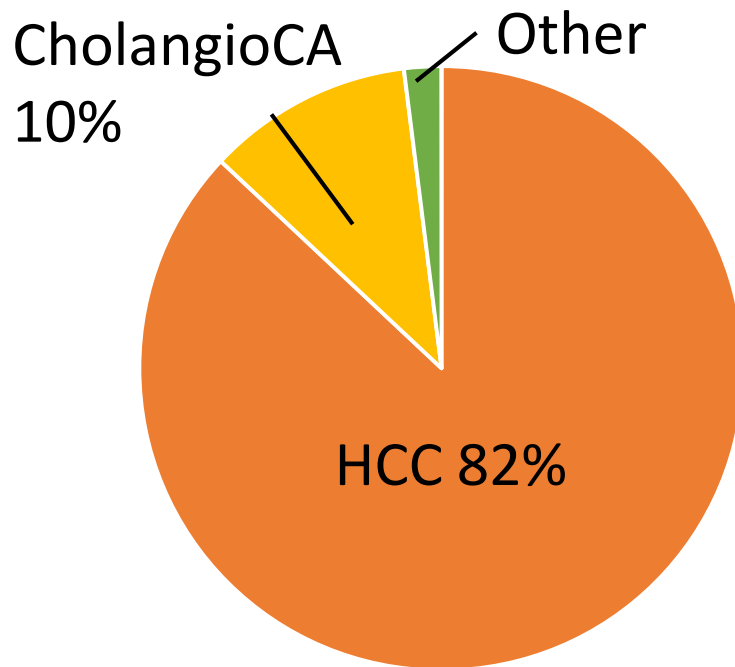


Primary Hepatic Tumors in the USA (excluding Hemangioma and Bile duct hamartoma)

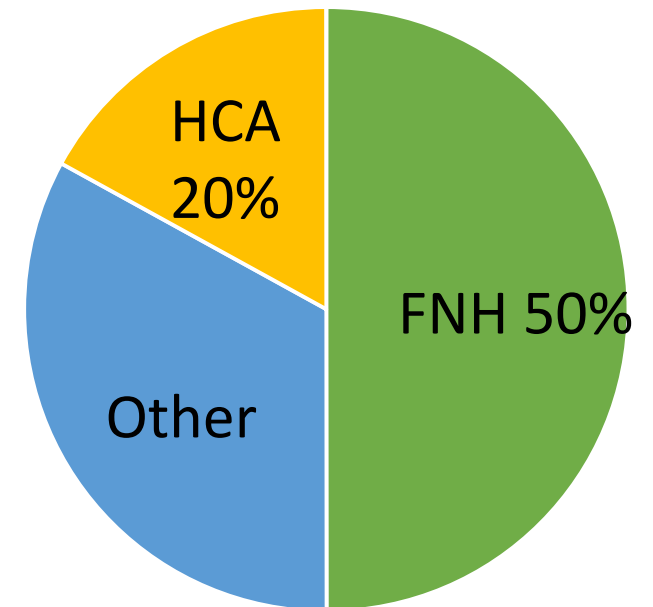


In Sum, Expect most biopsy samples of hepatocellular lesions to be HCC

Malignant



Benign



Organize Liver Masses based on Background Liver Disease



Cirrhotic liver

• IS IT HEPATOCYTIC?

-NO

- Cholangiocarcinoma

-YES

- HCC
- Dysplastic Nodule
- Macroregenerative Nodule

Non-cirrhotic liver

IS IT HEPATOCYTIC?

- NO

- Metastatic tumor

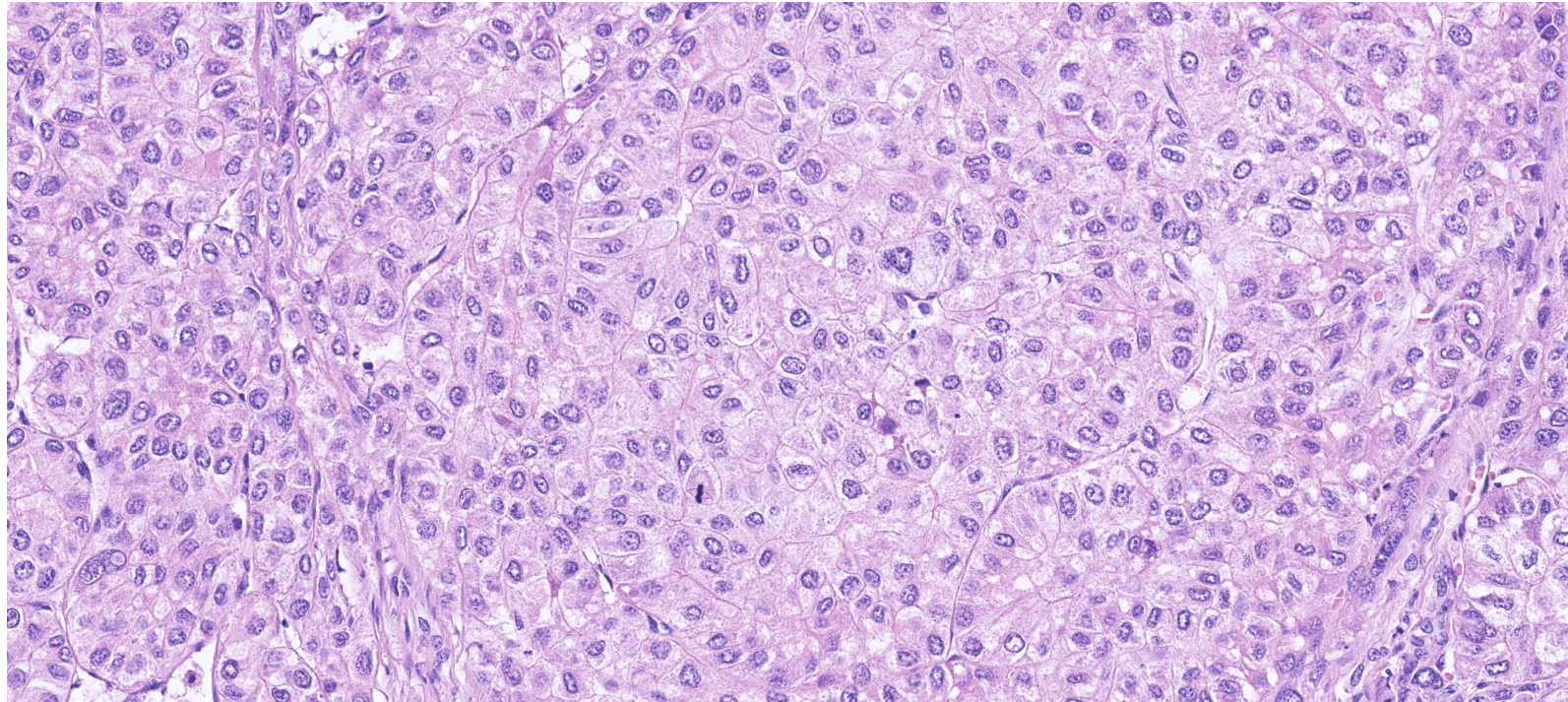
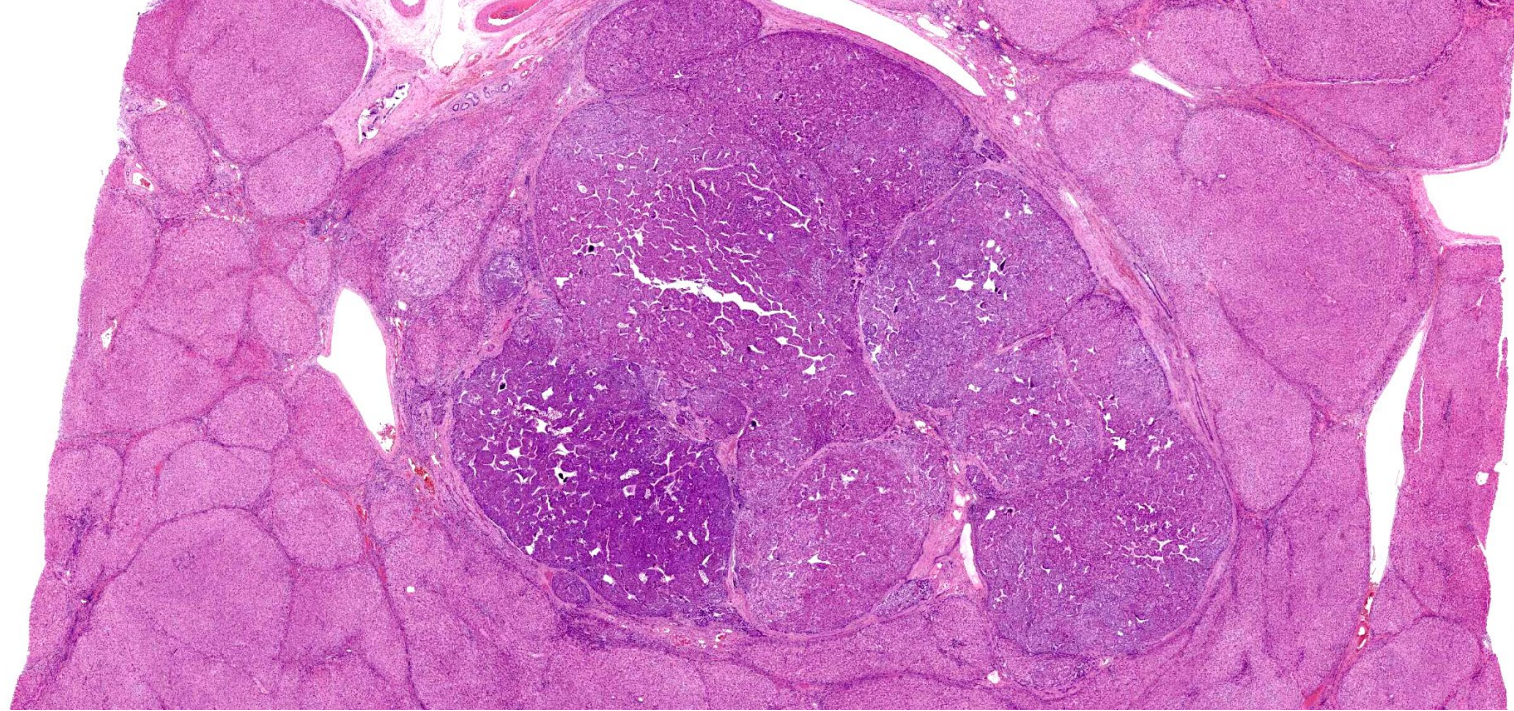
- Cholangiocarcinoma, benign biliary
- Epithelioid Hemangioendothelioma
- Angiomyolipoma

- YES

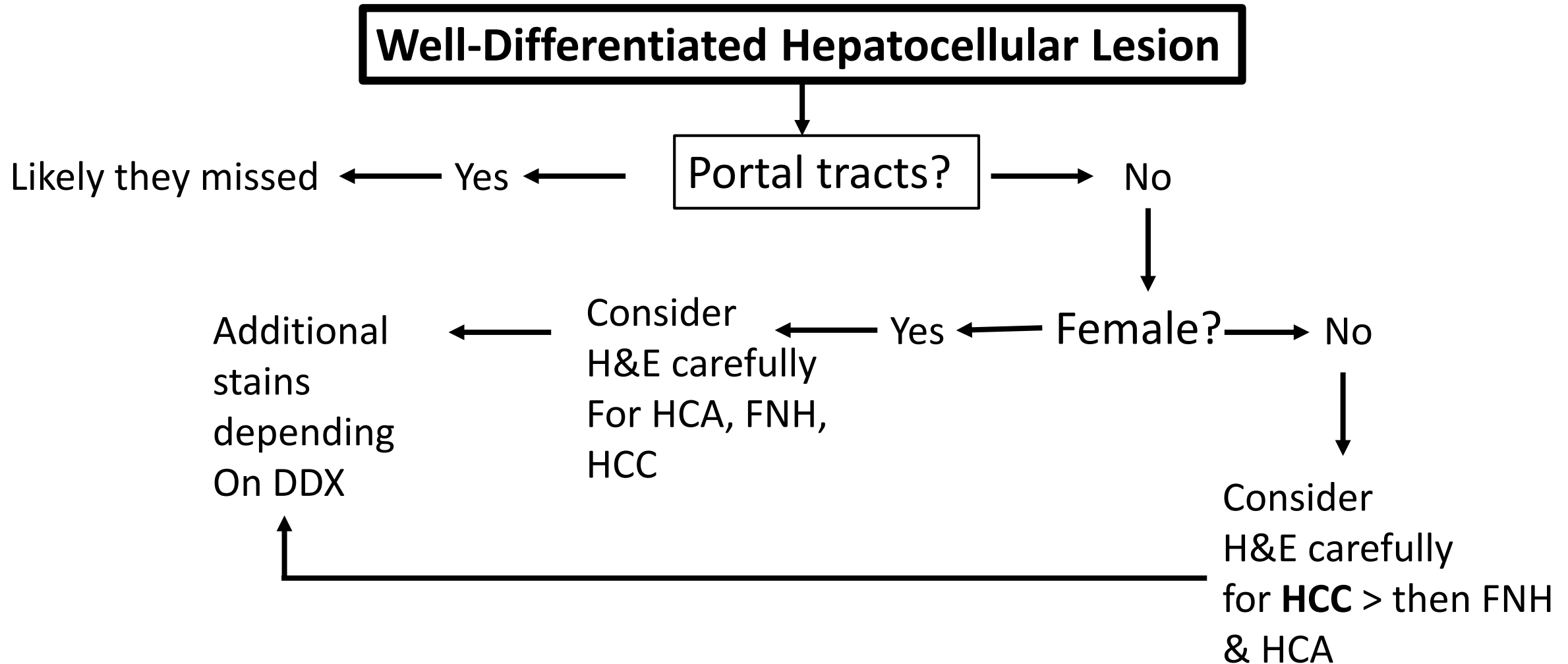
- HCC
- FNH
- HCA

55 Male with Hepatitis C and Liver Mass

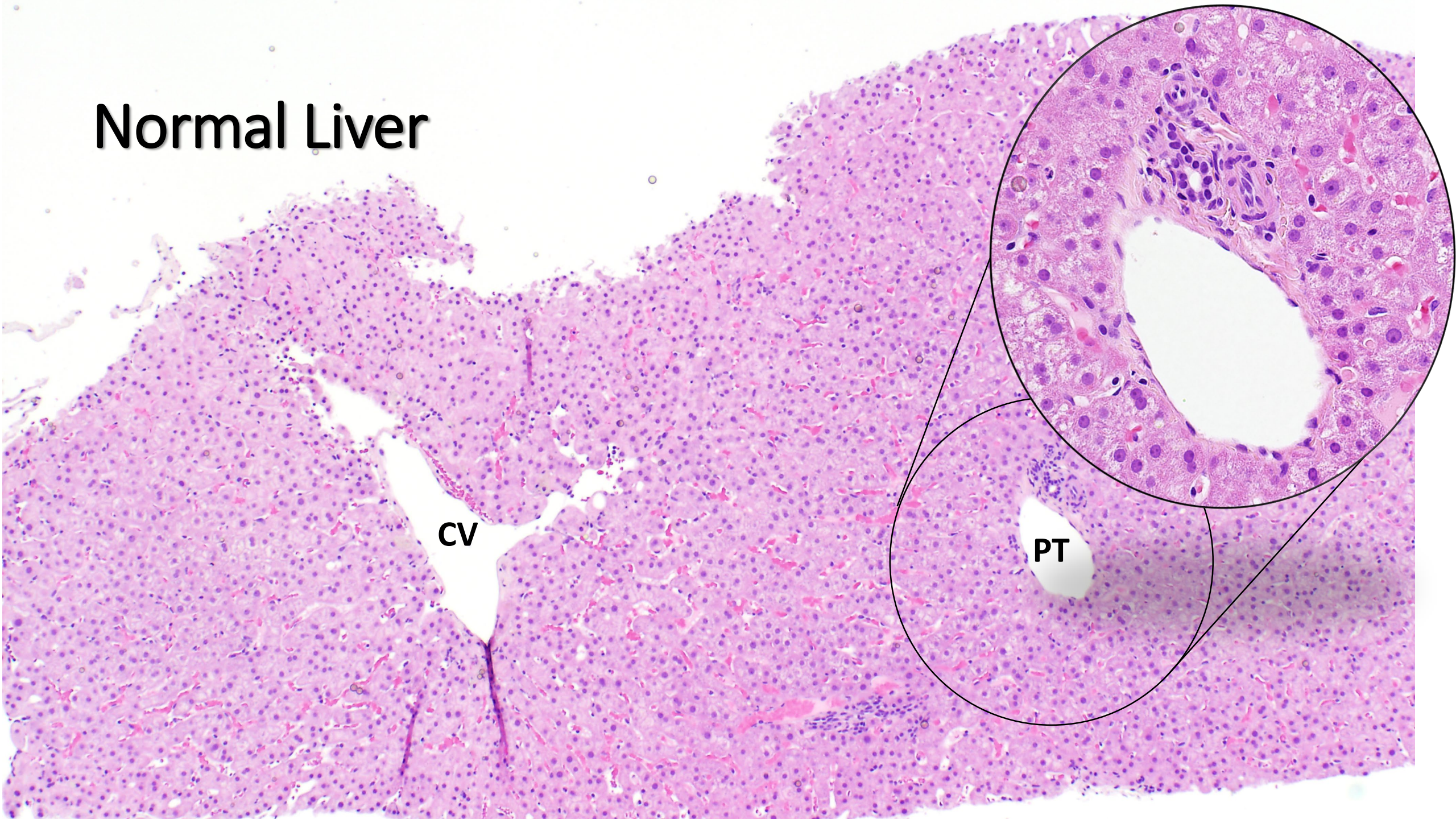
- Helpful features that favor carcinoma
 - ✓ Cirrhotic background
 - ✓ Heterogeneous, nodule within nodule
 - ✓ Cytologic atypia
 - ✓ Mitoses



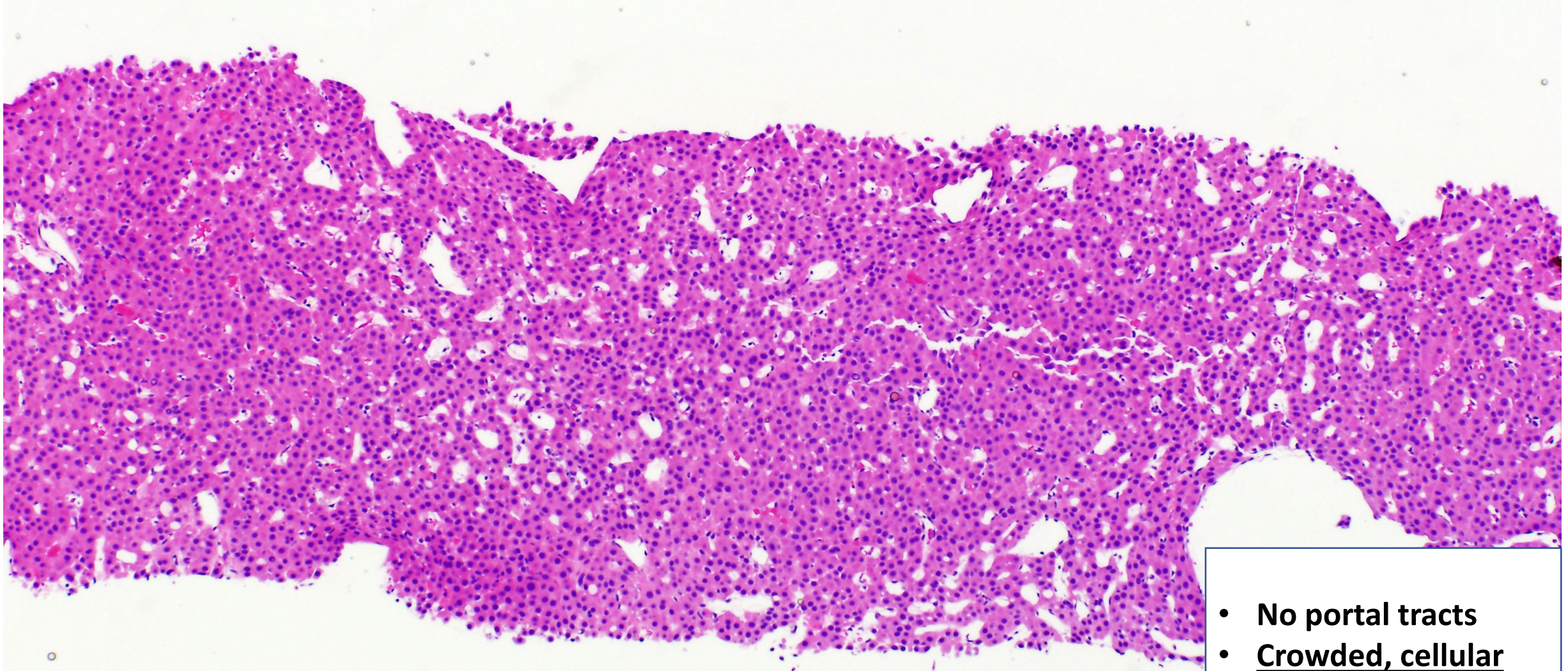
Real Life Practice “Liver Mass Biopsy” no background liver sampled, no clinical info



Normal Liver



Well differentiated Hepatocellular Carcinoma



- No portal tracts
- Crowded, cellular
- Atypia

| HCC | HCA | FNH |
|--|---|---|
| Atypia | Minimal atypia | No atypia |
| Pseudoglands/pseudoacinar frequent | Pseudoglands infrequent | Can have pseudoglands – cholestatic phenomenon |
| Mitoses | Mitoses unusual | Mitoses unusual |
| Can be steatotic | Can be steatotic | Steatosis unusual (but reported) |
| Unpaired arteries | Unpaired arteries | Dystrophic large vessels with thick walls |
| No central scar unless fibrolamellar | No central scar | Central scar |
| No fibrotic bands, but can have stromal invasion | No prominent fibrotic bands | Fibrotic bands containing arteries & flanked by ductules (think cirrhotic looking) |
| Glypican 3+ | Glypican 3- | Glypican 3- |
| Reticulin lost or expanded trabeculae | Reticulin intact (only look in non-steatotic areas) | Reticulin intact (rarely shows focal expansion, near periphery of lesion, like cirrhosis) |
| CD34 diffuse sinusoidal | CD34 not diffuse | CD34 patchy |
| GS diffuse if beta catenin activated | GS focal, only diffuse if beta catenin activated | GS maplike – sometimes confusing on biopsy |

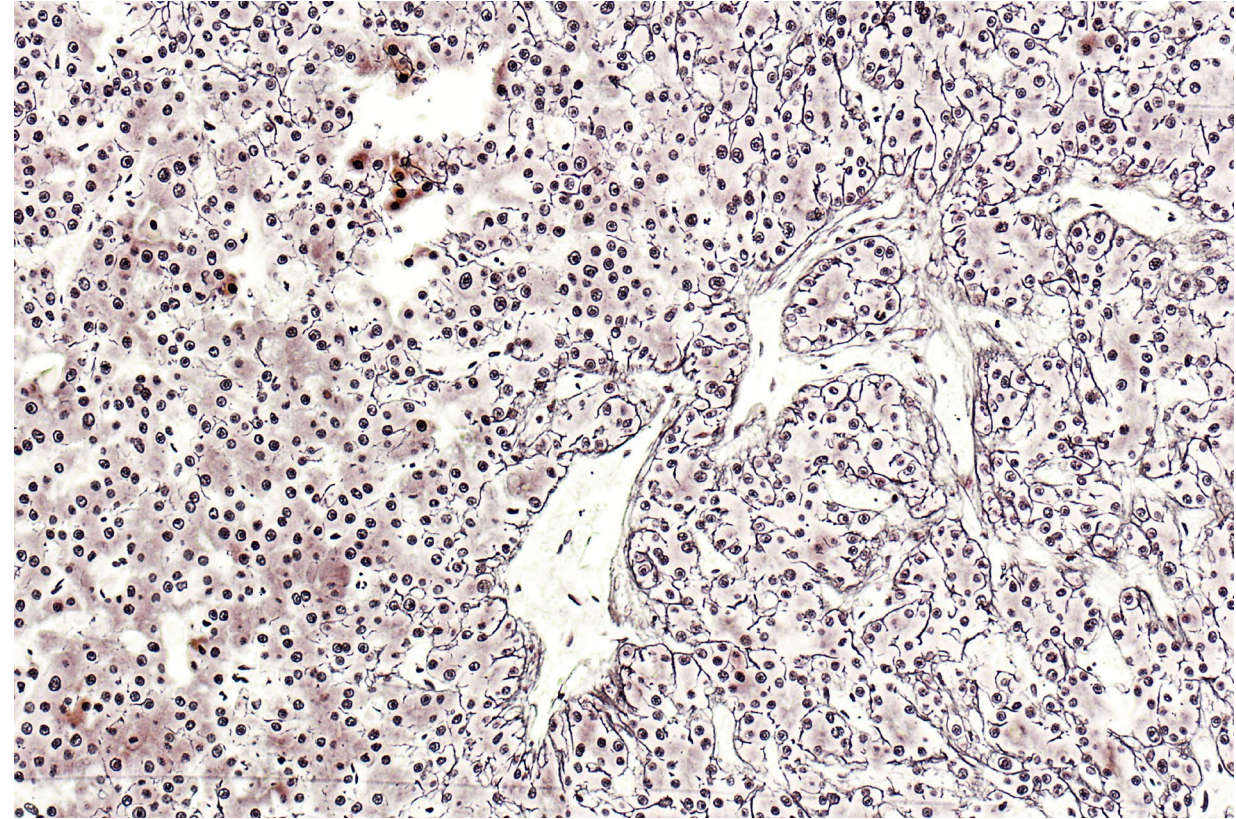
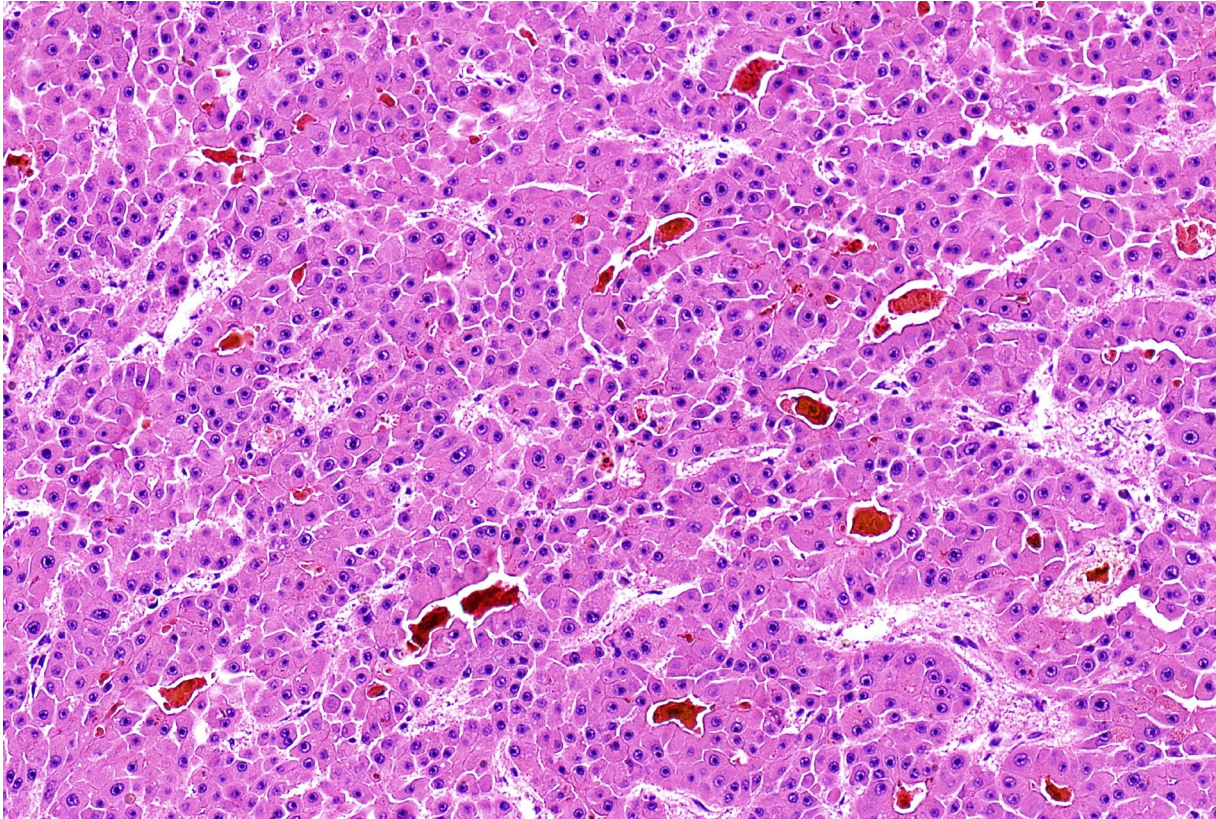
HCC vs. Benign Liver Lesions

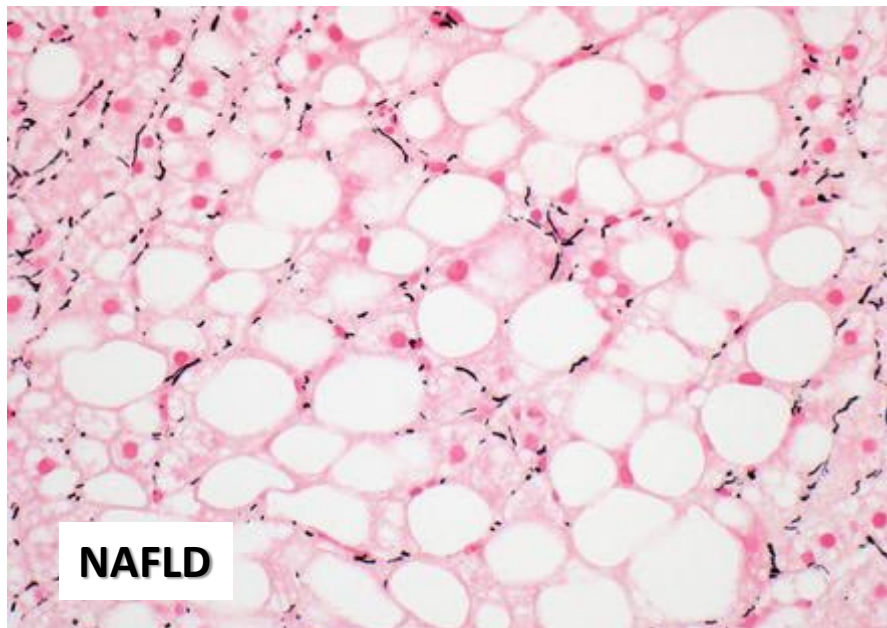
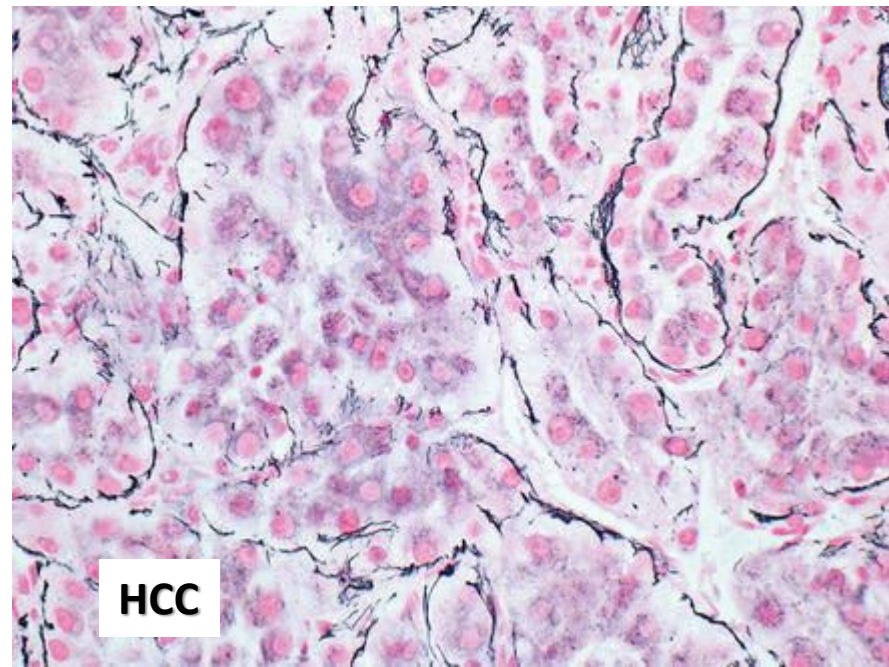
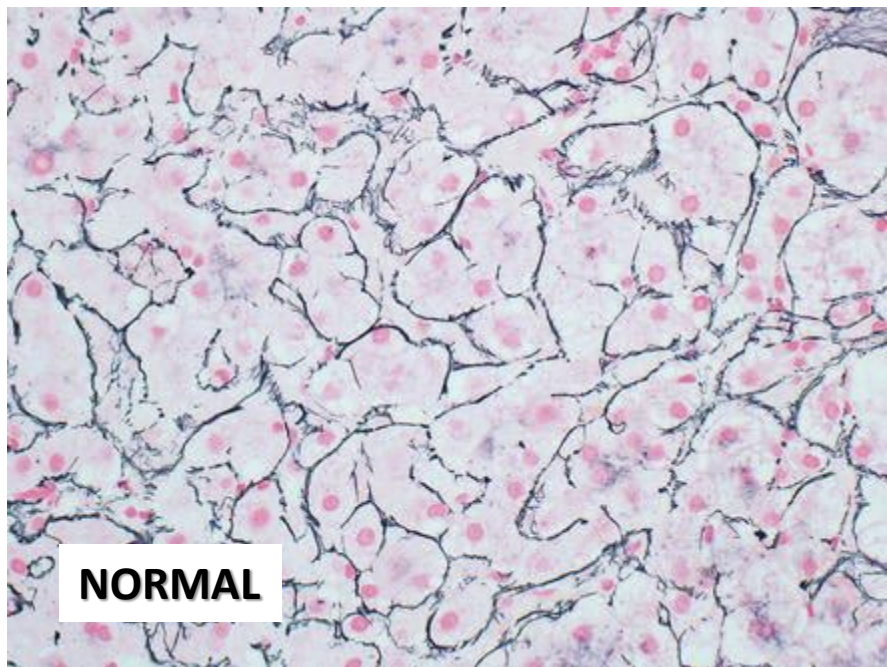
Useful Immunomarkers for Distinguishing Well-Differentiated Hepatocellular Carcinoma (WDHCC) From Hepatocellular Adenoma (HCA) and High-Grade Dysplastic Nodule (HGDN)

| Marker | WDHCC, % | HCA, % | HGDN, % |
|---|--|----------|--|
| Glypican-3 | 50–69 | 0 | <10 |
| Glutamine synthetase (strong and diffuse) | 35–60 | 10-15 | <15 |
| Heat shock protein 70 | 40–78 | 0 | <10 |
| Positive in at least 2 of the above 3 markers | 50–72 | 0 | 0 |
| CD34 (diffuse sinusoidal pattern) | 95 ^a | 20 | +/- |
| Clusterin (enhanced canalicular pattern) | 75 | 0 | No data |
| CK7 | Absence of ductules at border (invasive growth) | No value | Presence of ductules at border (noninvasive growth) |

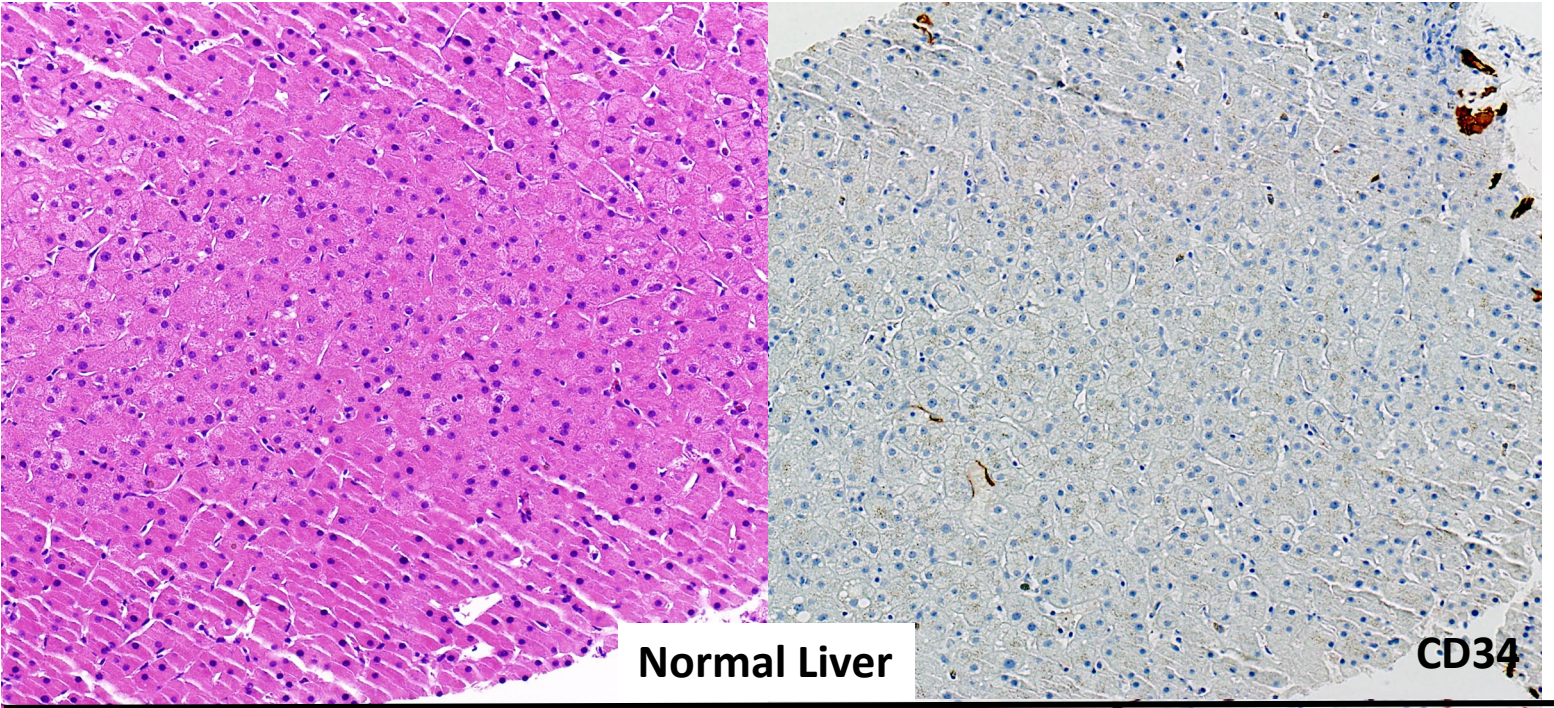
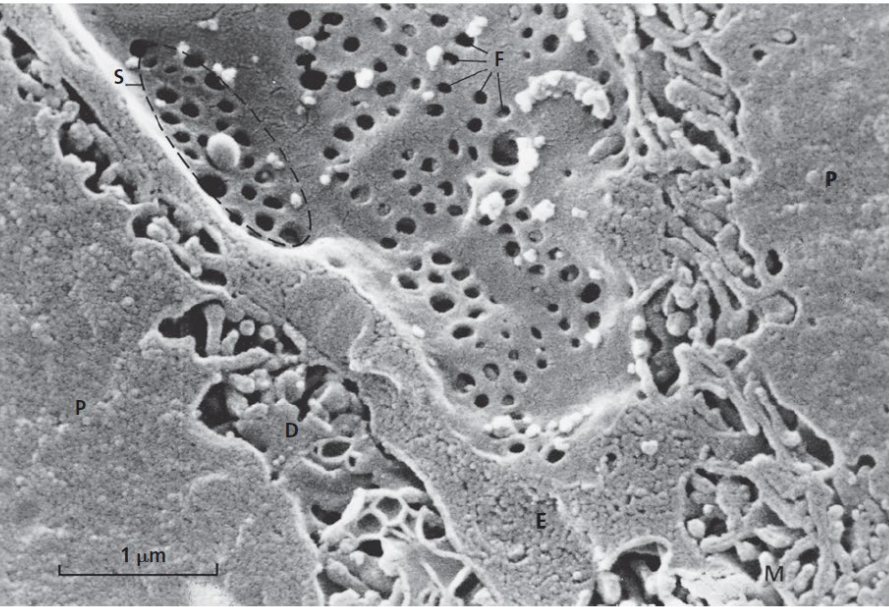
- I use these most: reticulin, CD34 (glypican-3, glutamine synthetase if I am still not sure)

HCC – Loss of reticulin



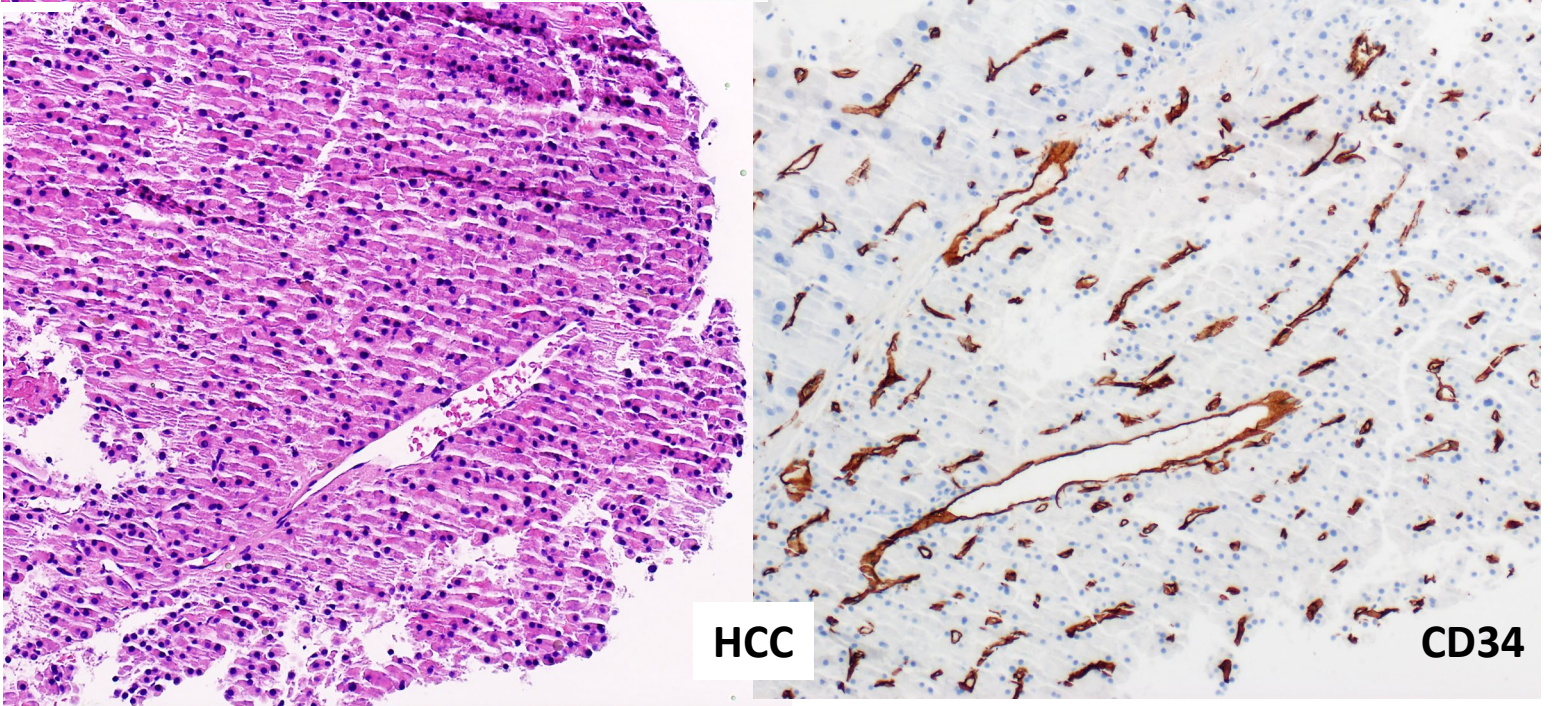


**Watch out for Fatty liver disease:
Non-neoplastic cause for Spurious reticulin loss**

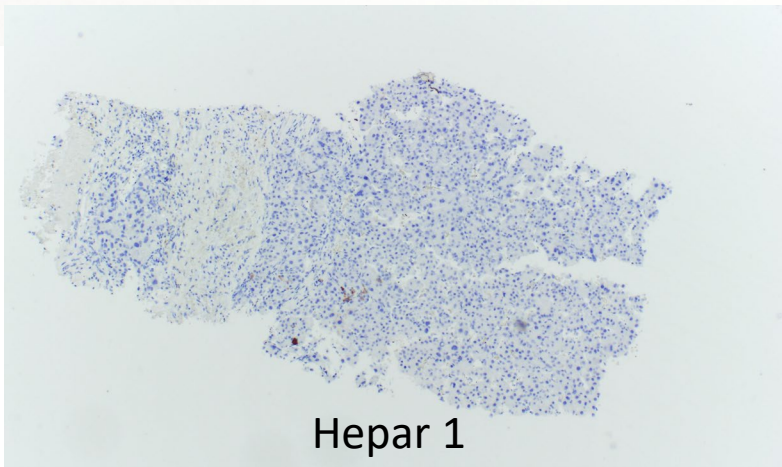
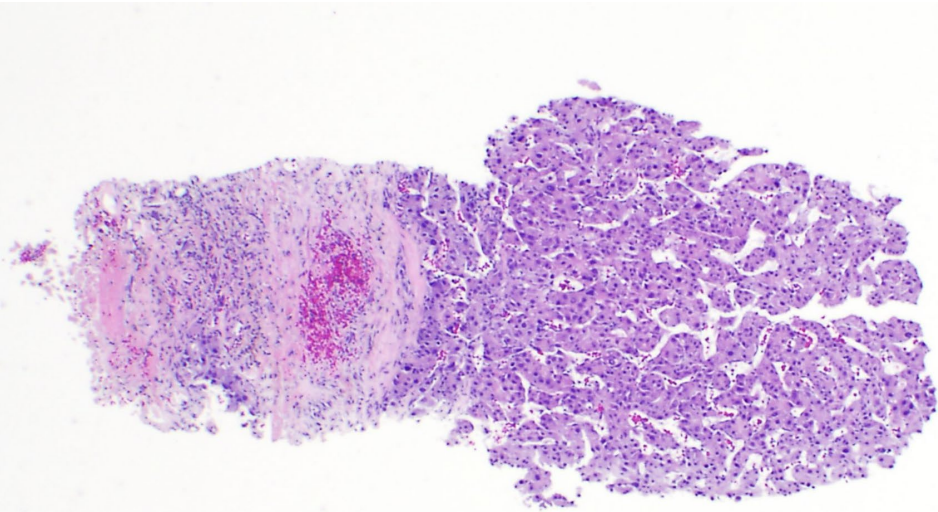
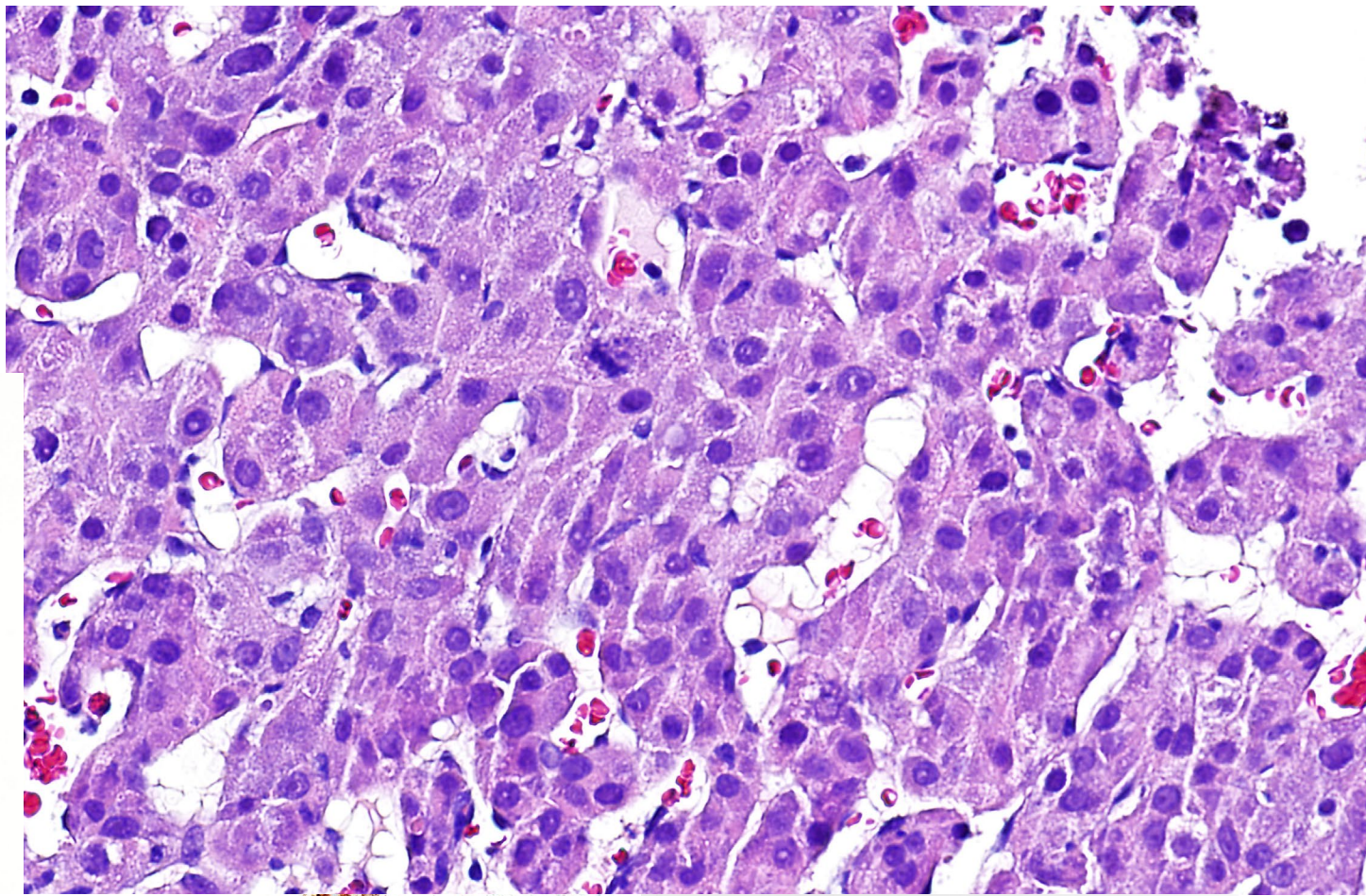


CD34

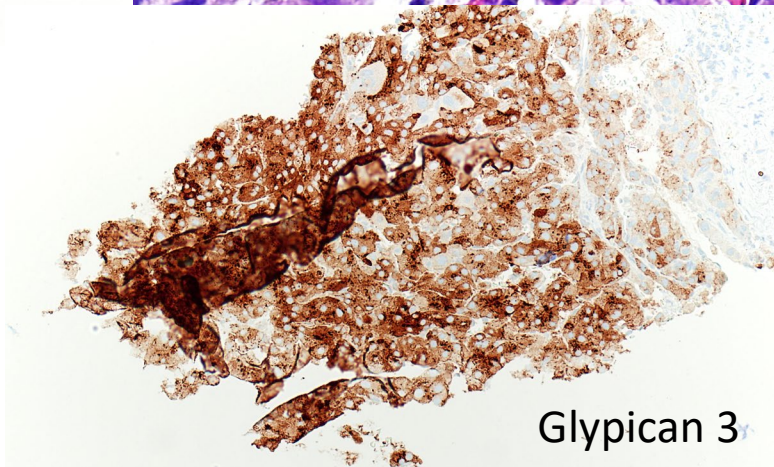
- Normal Liver sinusoids are fenestrated; act as filtration barrier
- CD31,34 negative, unlike regular endothelial cells
- HCC has diffuse CD34 positivity in sinusoids



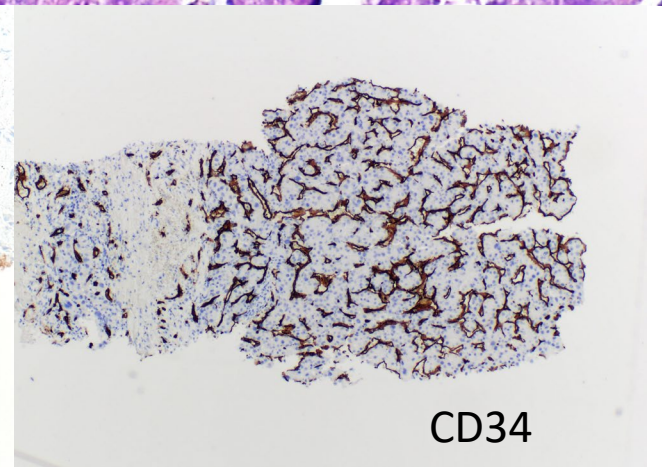
HCC on a Small Biopsy



Hepar 1

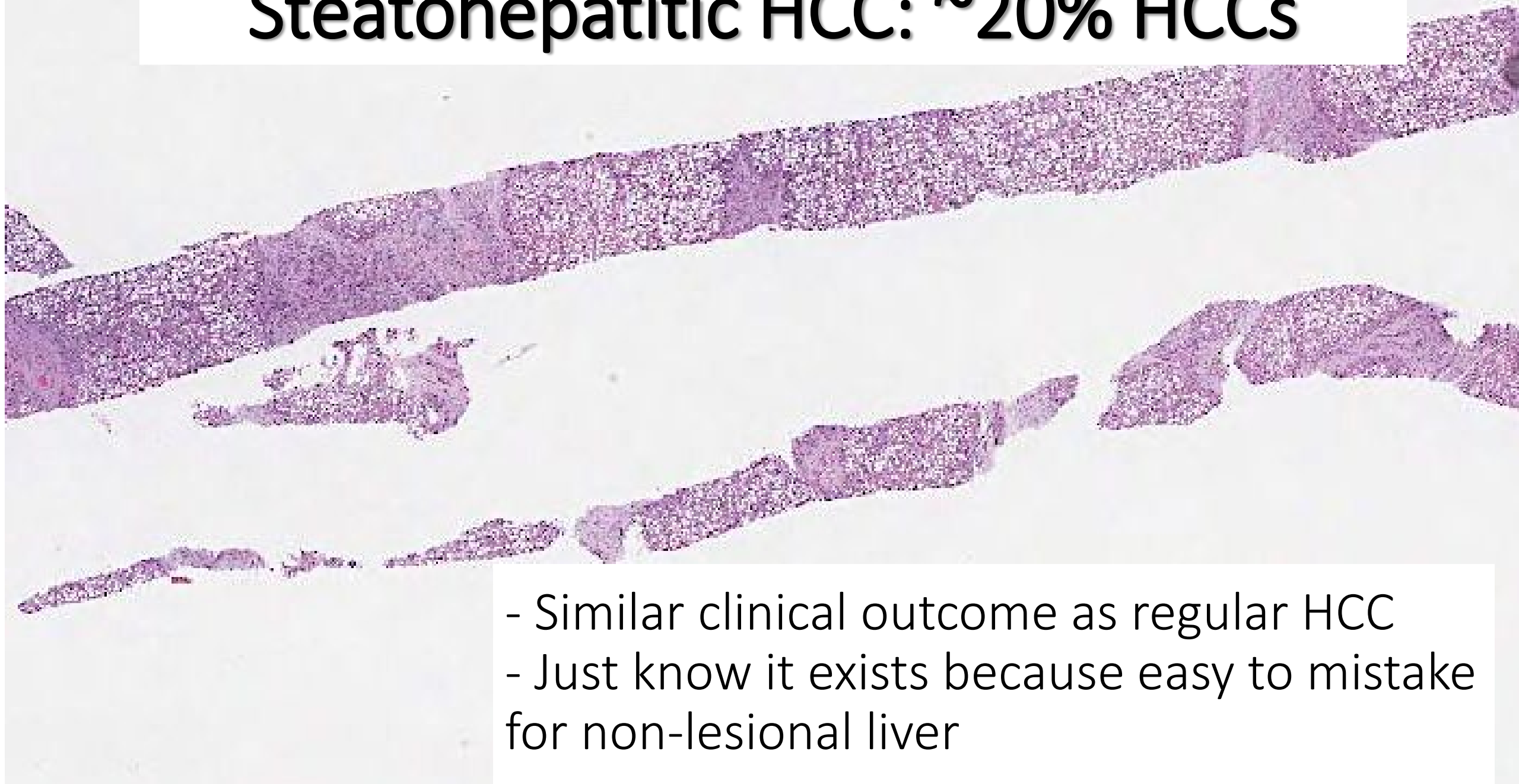


Glypican 3

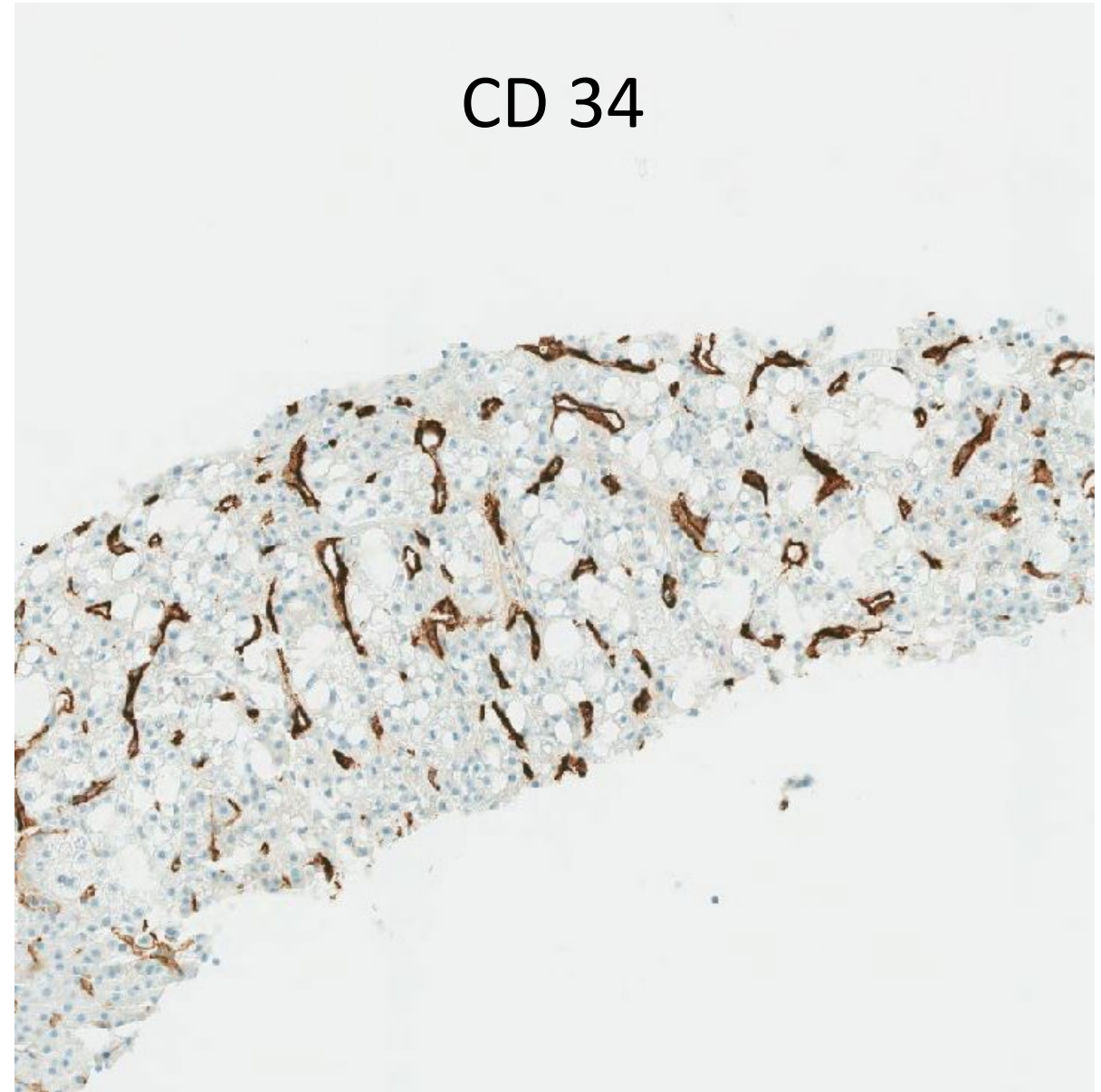
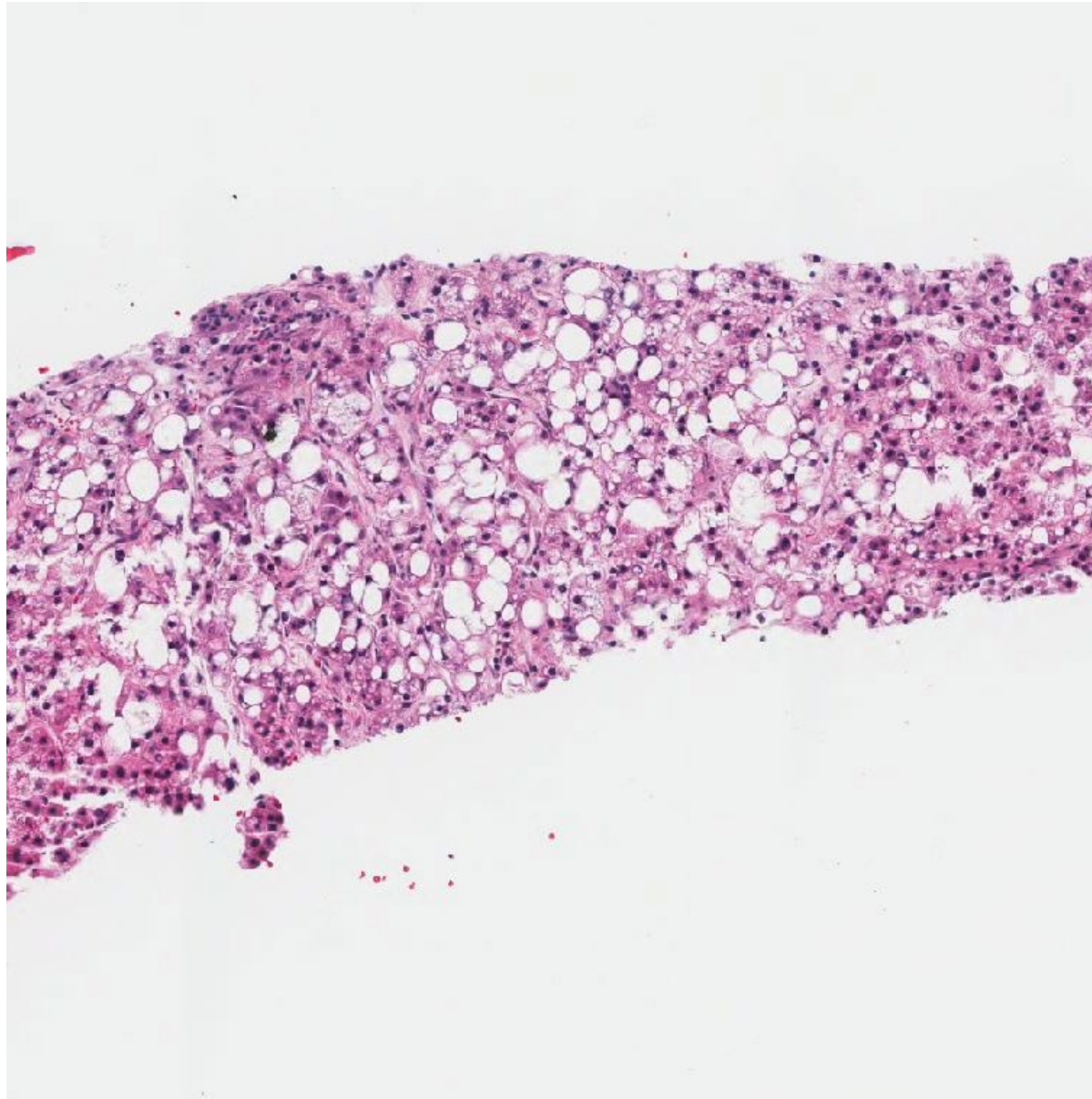


CD34

Steatohepatitic HCC: ~20% HCCs



- Similar clinical outcome as regular HCC
- Just know it exists because easy to mistake for non-lesional liver



Hepatocellular Adenoma

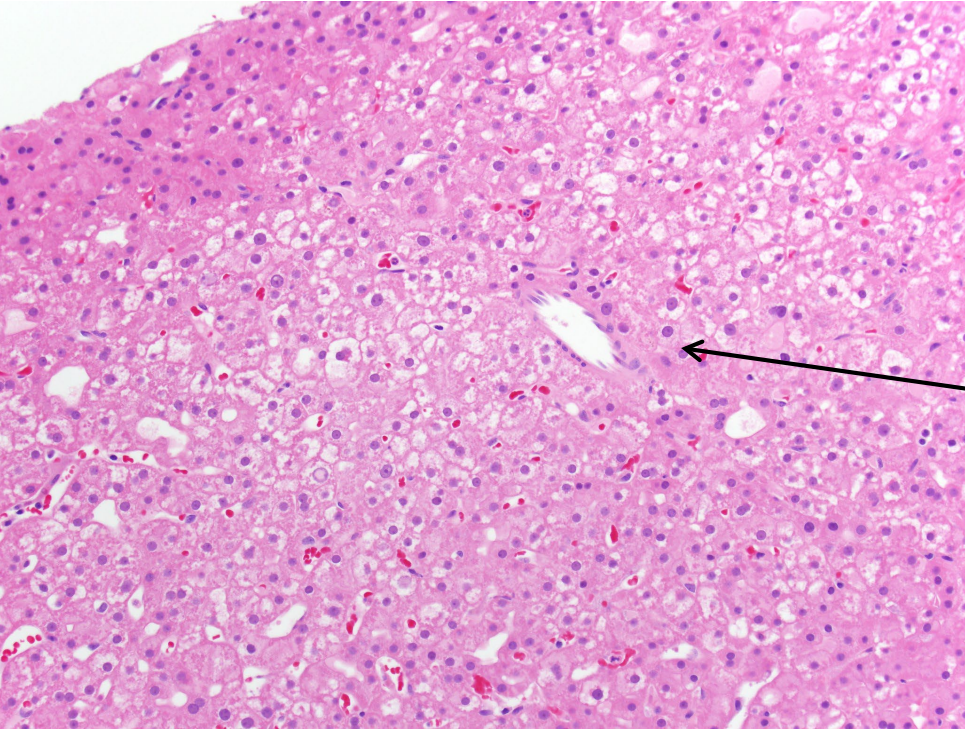
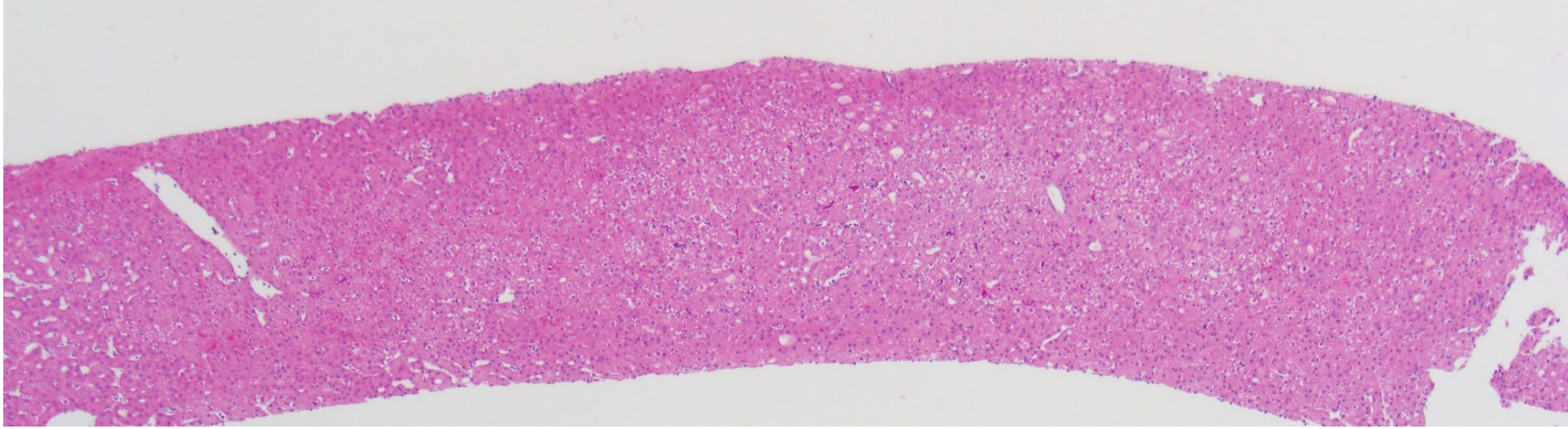
♀ - OCPs major risk factor

Can bleed (25%) or turn into HCC (4-8%)

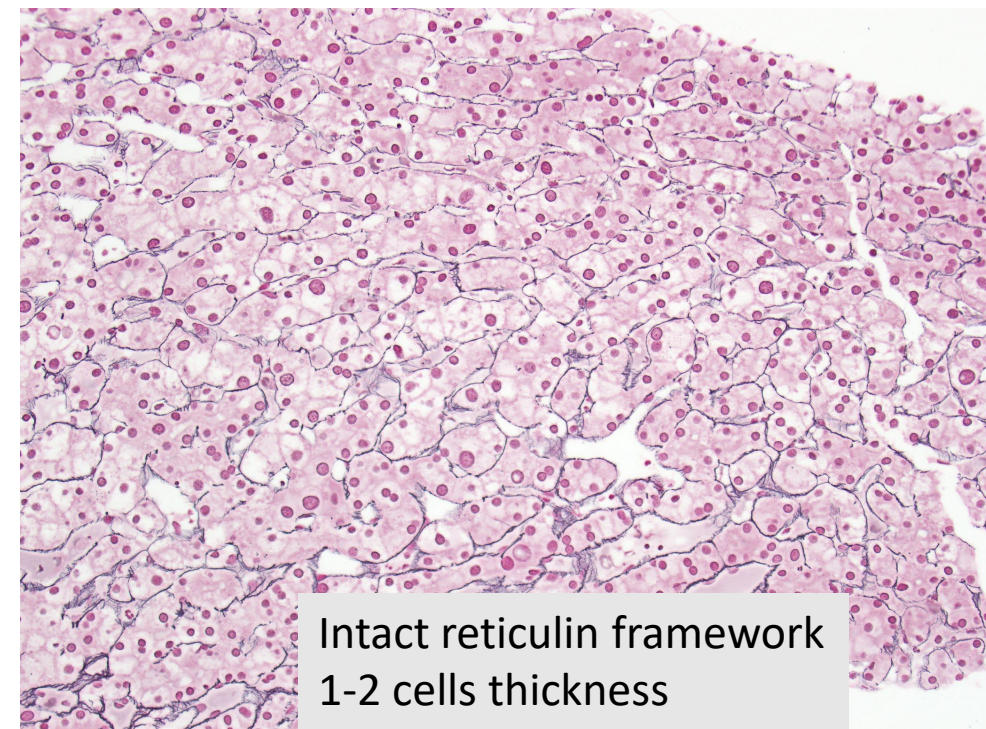
35% incidental

33%-45% >1 HCA

No portal tracts in a long stretch of benign-appearing hepatic parenchyma

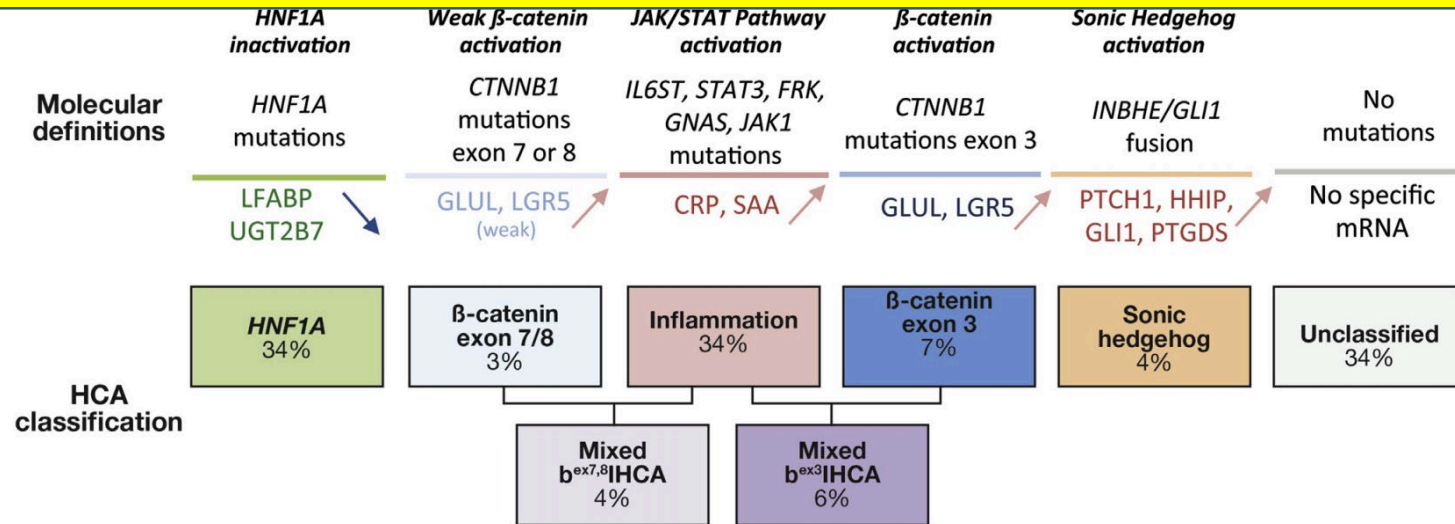


- ✓ Arises in non-cirrhotic liver
- ✓ Benign neoplastic hepatocytes devoid of portal tracts; unpaired arteries present
- ✓ Minimal atypia
- ✓ Mitoses unusual



Intact reticulin framework
1-2 cells thickness

DO I NEED TO SUBTYPE?



Risk of hemorrhage:

- Beta catenin exon 7/8
- Sonic hedgehog

Highest risk of cancer:

- Beta catenin exon 3

Gastroenterology 2017;152:880–894

Molecular Classification of Hepatocellular Adenoma Associates With Risk Factors, Bleeding, and Malignant Transformation



Jean-Charles Nault,^{1,2,3} Gabrielle Couchy,¹ Charles Balabaud,⁴ Guillaume Morcrette,¹ Stefano Caruso,¹ Jean-Frederic Blanc,^{4,5} Yannick Bacq,⁶ Julien Calderaro,^{1,7} Valérie Paradis,⁸ Jeanne Ramos,⁹ Jean-Yves Scoazec,¹⁰ Viviane Gnemmi,¹¹ Nathalie Sturm,¹²

EASL Guideline: HCA Management

- HCA resection recommended irrespective of size in 1) males and in any instance of proven 2) β -catenin mutation
 - Males have 60% risk of progression to HCC; risk of HCC with beta catenin mutation is 40%
- Female with HCA (irrespective of size) will be advised to lose weight and stop OCP → repeat MRI in 6 months → resection if >5 cm or significant increase in size, otherwise, annual imaging

- In one study, 27% of HCA were biopsied prior to resection and biopsy was definitive in 61%
- The remaining 39% were either insufficient tissue (33%) or could not be distinguished from HCC (56%) or FNH (11%)

HCA Subtypes Summary

HNF1 alpha
mutated
30%

- Marked steatosis
- IHC: Loss of LFABP
- **Having mutation excludes B-catenin**

Inflamm-
atory
40%

- Assoc. w obesity
- Sinusoidal dilat + inflammation
- IHC: CRP & SAA +

Beta
catenin
Activated
10%

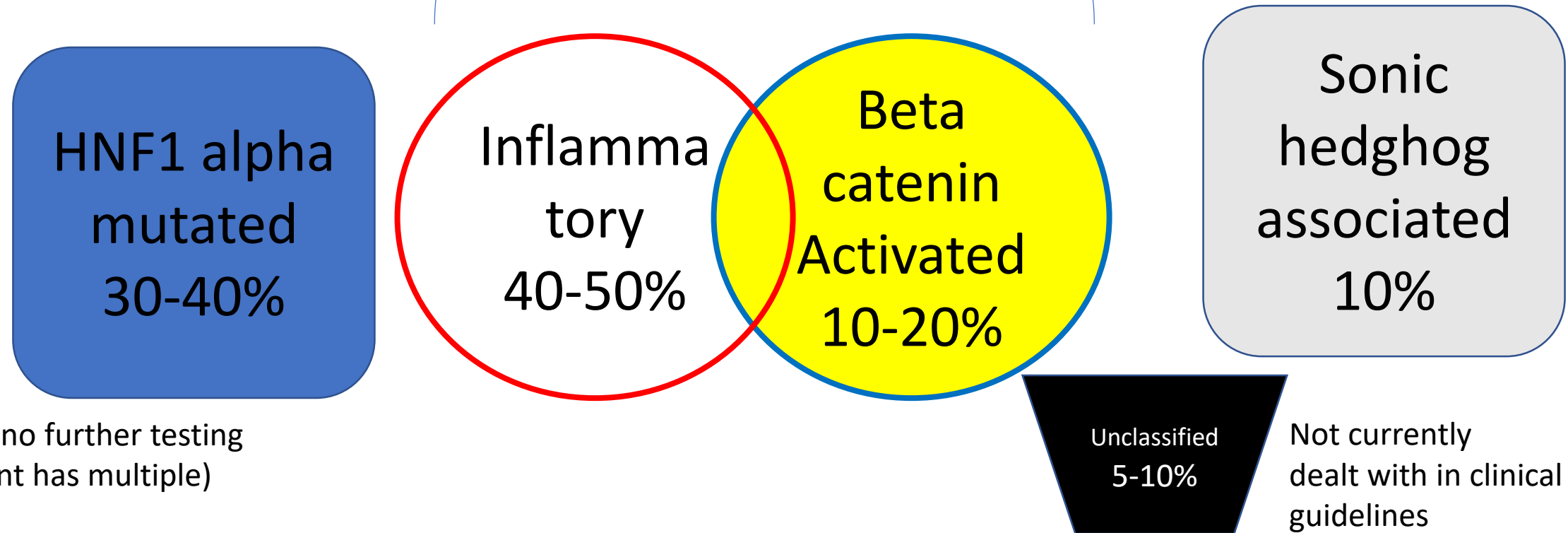
- ↑Risk of Cancer; ♂
- IHC: GS diff +, b-cat +
- **Resection regardless of size**

Sonic
hedghog
associated
10%

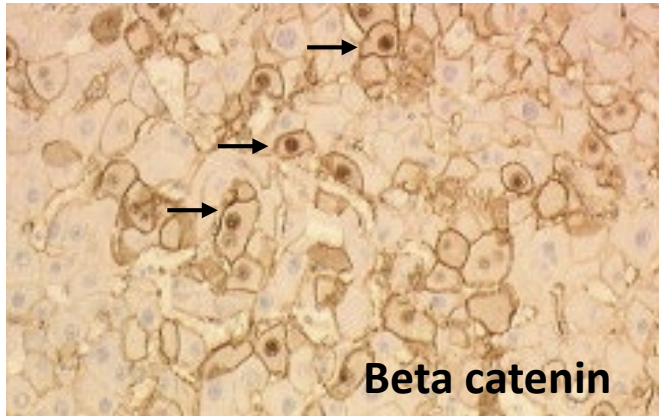
- Associated with hemorrhage, regardless of size
- IHC: ASS-1 +

Practical approach: HCA Subtypes

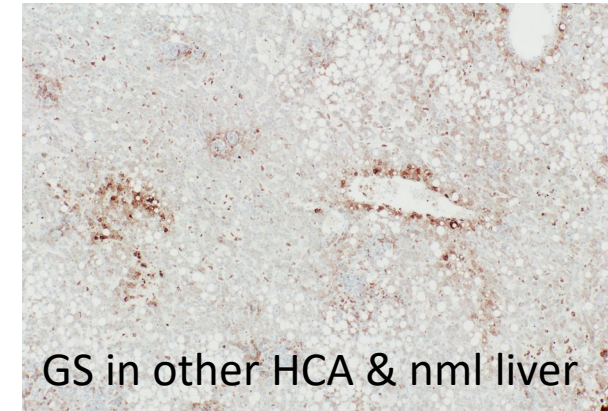
If positive for beta catenin, diffuse GS: no further testing; needs to be resected
If GS stain confusing, offer molecular testing for b-catenin & TERT (DDX is FNH)



HCA Subtype – Beta catenin Activated



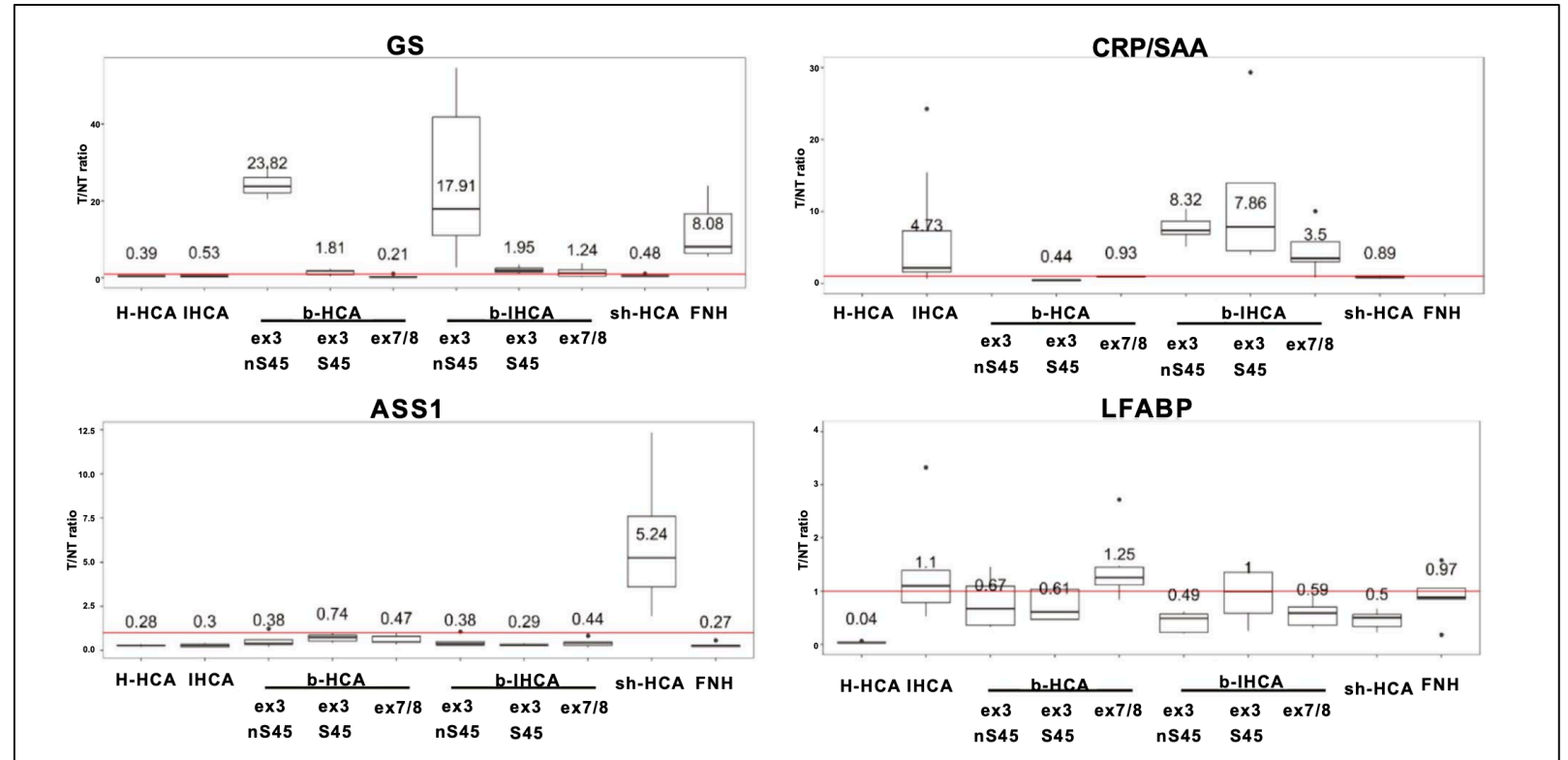
Vs



- IHC not great:
 - Focal beta catenin+
 - Diffuse GS + (target gene of b-cat)
 - Together 100% specificity, but low sensitivity ~75%

Proteomic Profiling

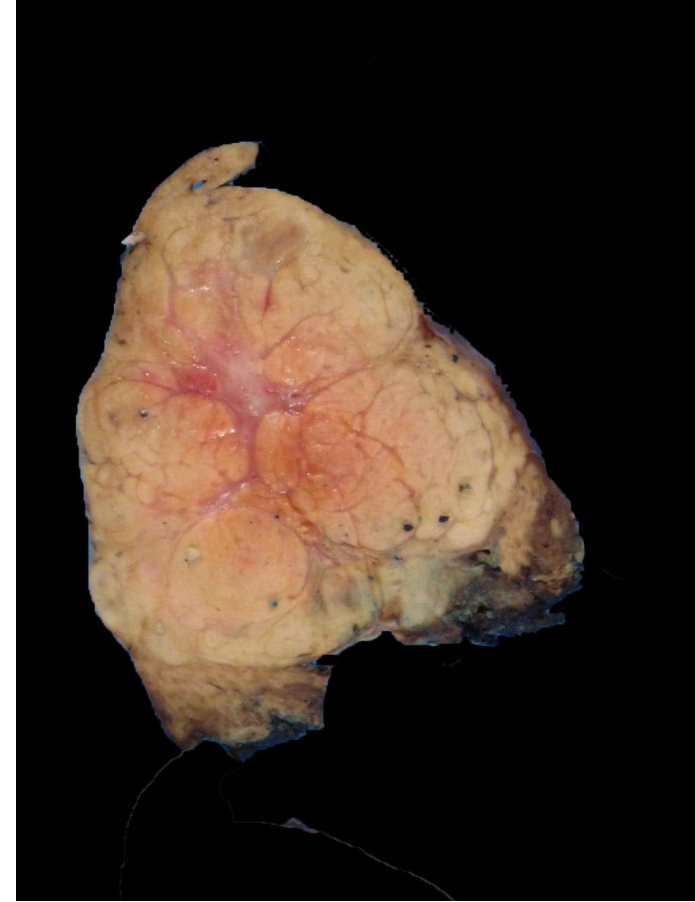
- FFPE tissue, 1 mm² on 3 × 5 µm section cuts
- Used mass-spectrometry–based proteomic analysis and defined a specific proteomic profile of each of the HCA subgroups based on abundance of proteins observed



- Not much noticeable utility (that I can tell) ID'ing **the HCA** subtypes of interest except for sonic Hedgehog HCA
- However, they claim to be able to tell the difference between **HCC and HCA** via observing how close the proteomic profile of a tumor is to HCA or HCC based on a reference database of proteomic profiles

Focal Nodular Hyperplasia

- FNH - 2nd most common benign liver lesion
- F:M 8:1, 30-50
- Most asymptomatic and incidentally found
- Biopsy if imaging is inconclusive



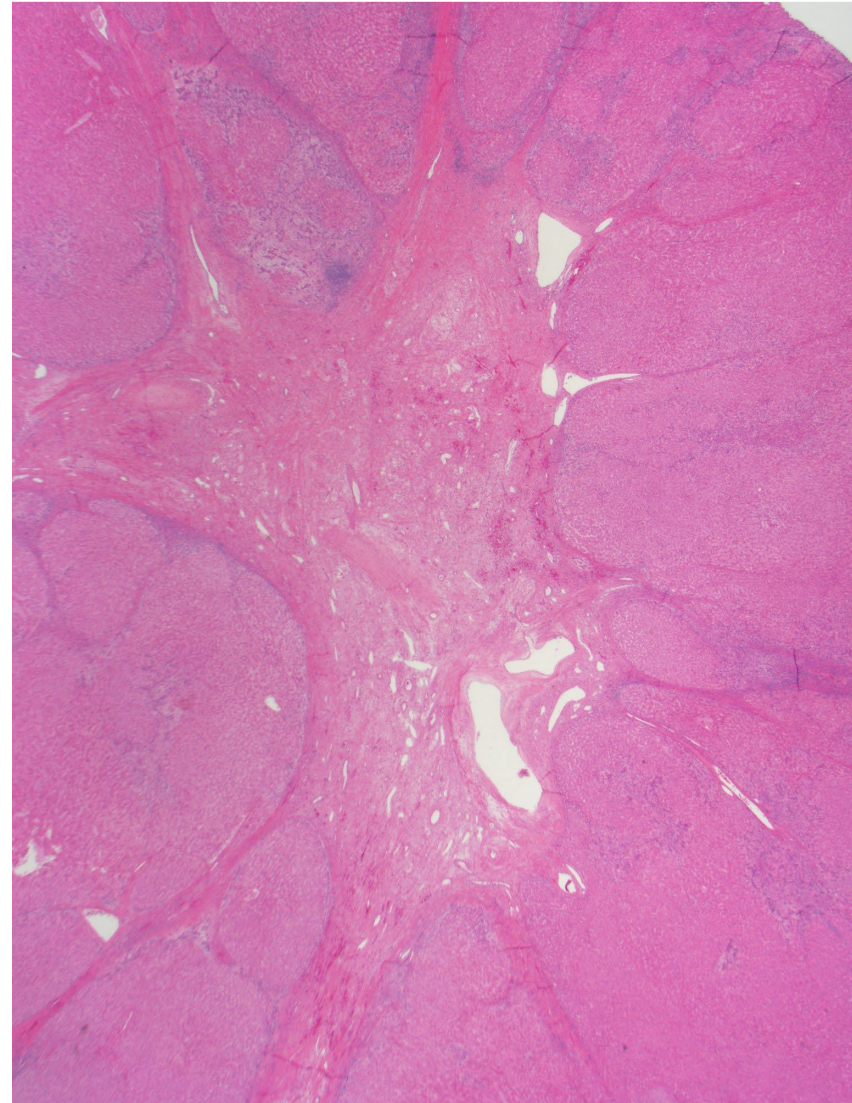
Gastroenterology. 2000 Mar;118(3):560-4.

Nat Rev Gastroenterol Hepatol. 2014 Dec;11(12):737-49.

EASL Clinical Practice Guidelines. J Hepatol (2016)

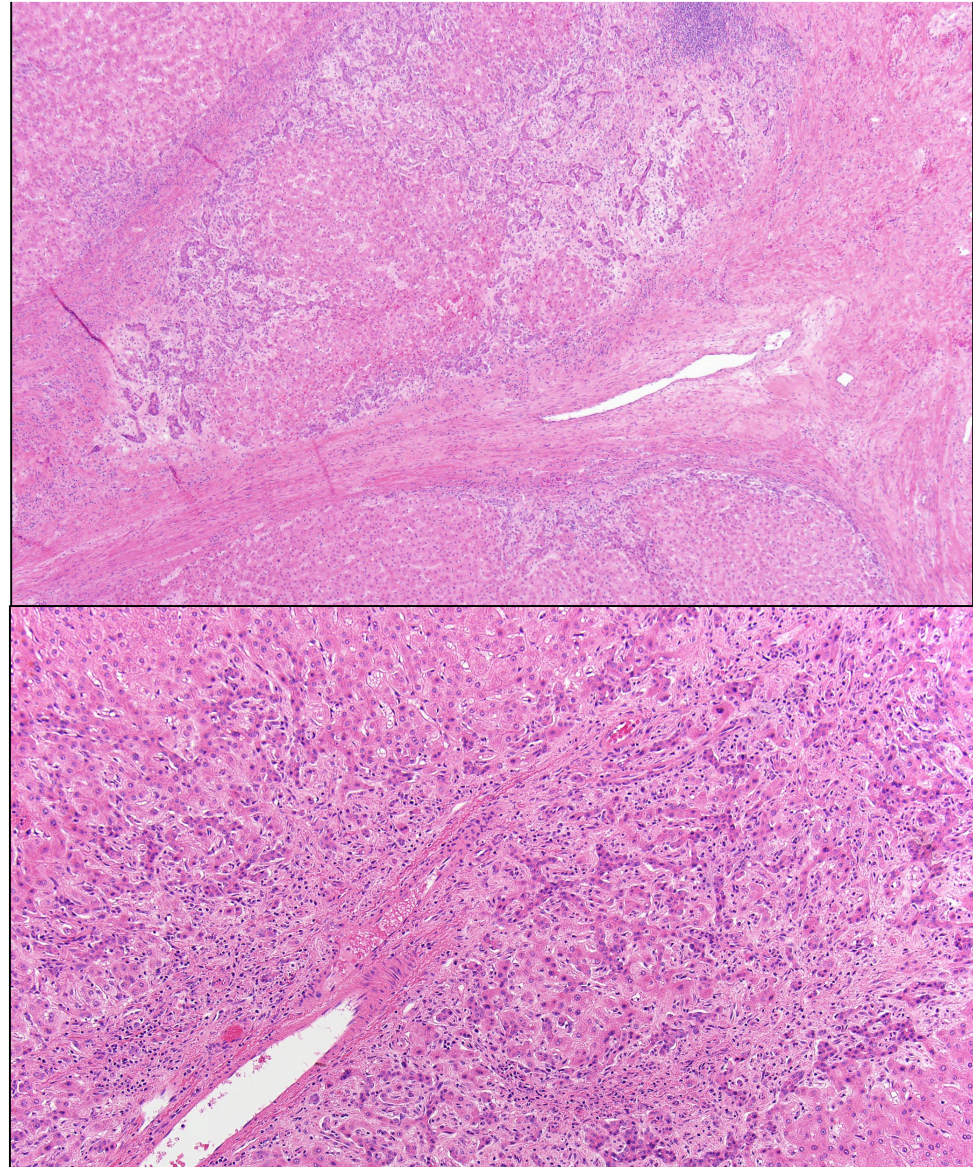
Focal Nodular Hyperplasia Histology

- Microscopic:
 - Nodular/ “pseudo-cirrhotic” architecture surrounding a central scar:
 - Nodules of benign hyperplastic hepatocytes separated by fibrous septa radiating from central scar

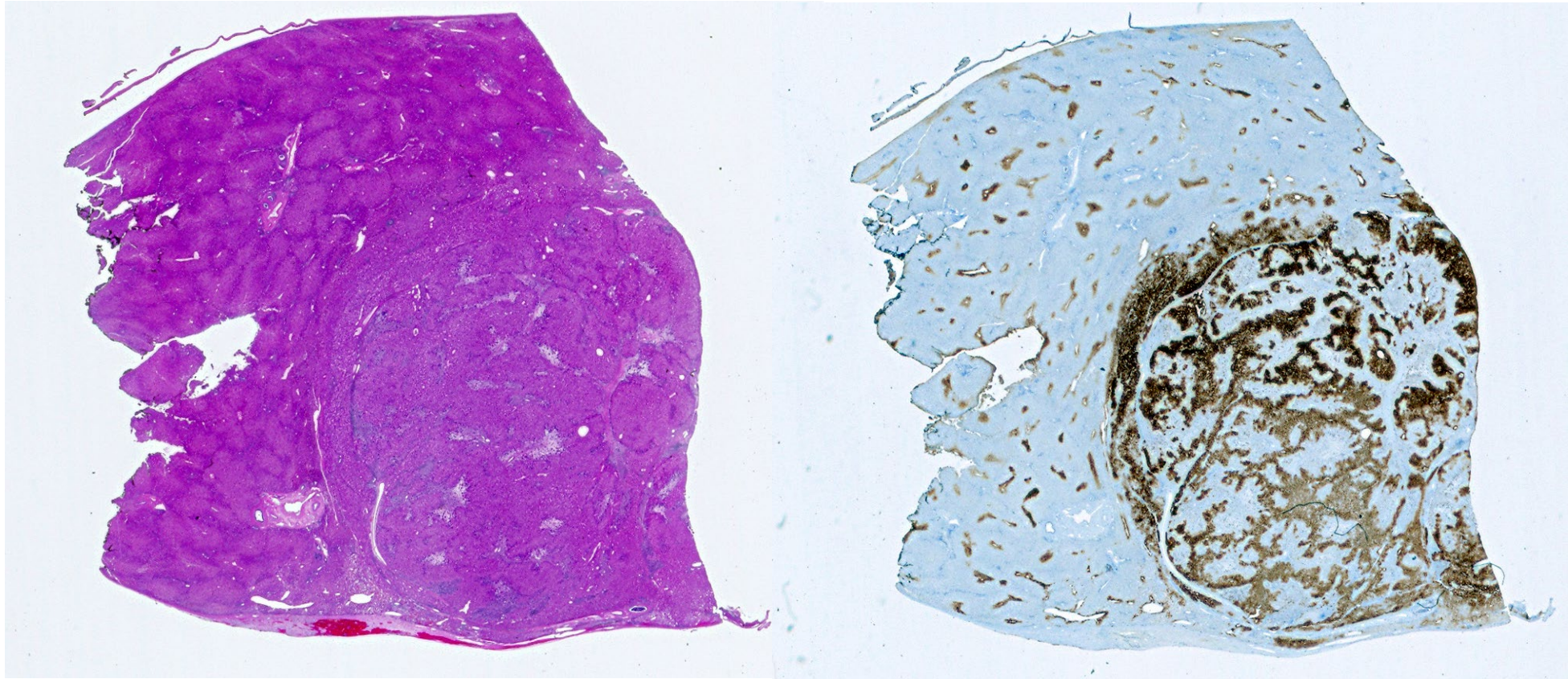


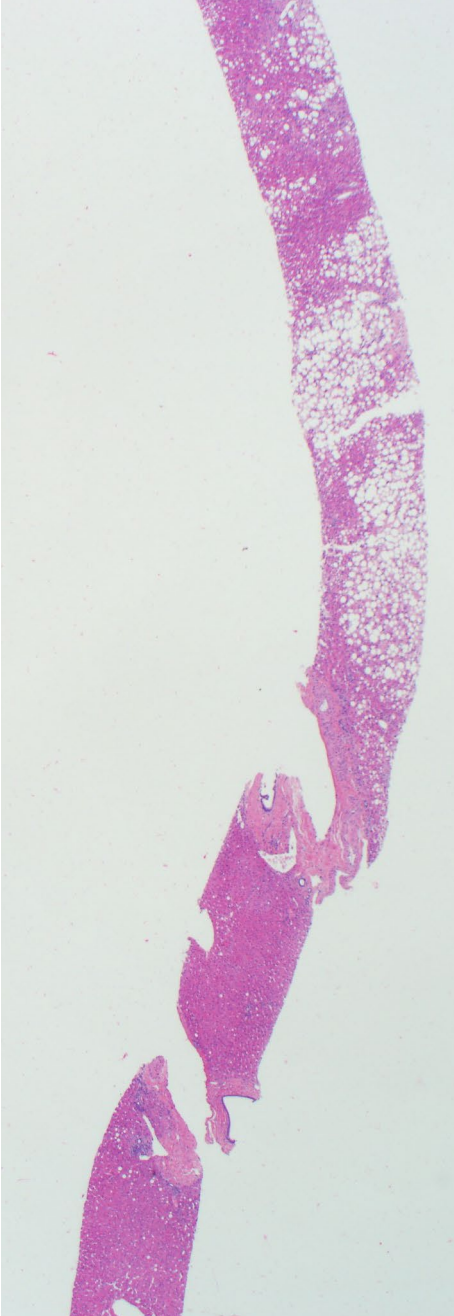
Focal Nodular Hyperplasia

- Microscopic:
- NO NORMAL PORTAL TRACTS
 - Fibrous bands contain:
 - **Dystrophic arteries**, abnormally large
 - Presence of **ductular reaction** at interface of fibrous bands and the parenchyma
 - No portal venule, no normal duct
 - Hepatocytes 2 cells in thickness



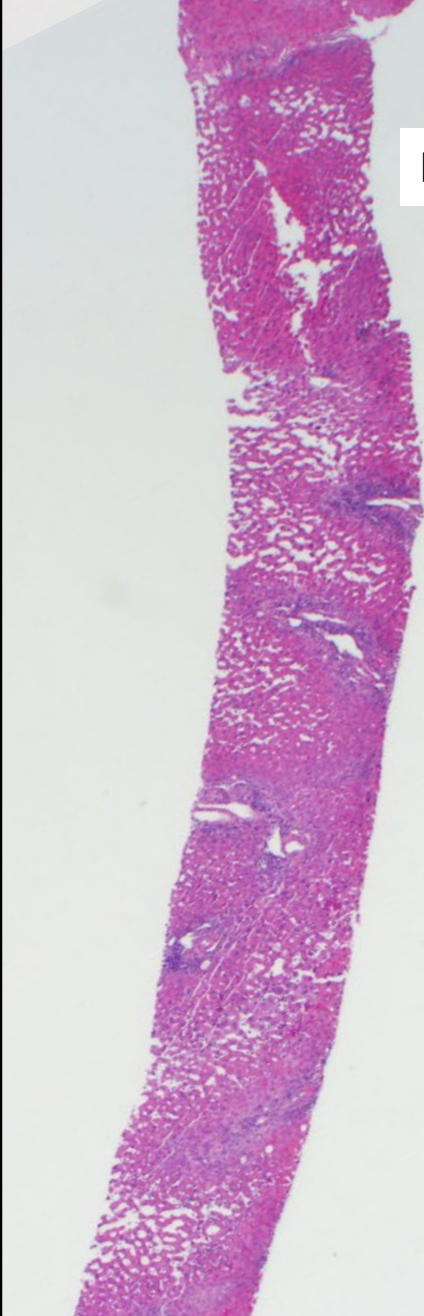
Glutamine Synthetase staining in FNH





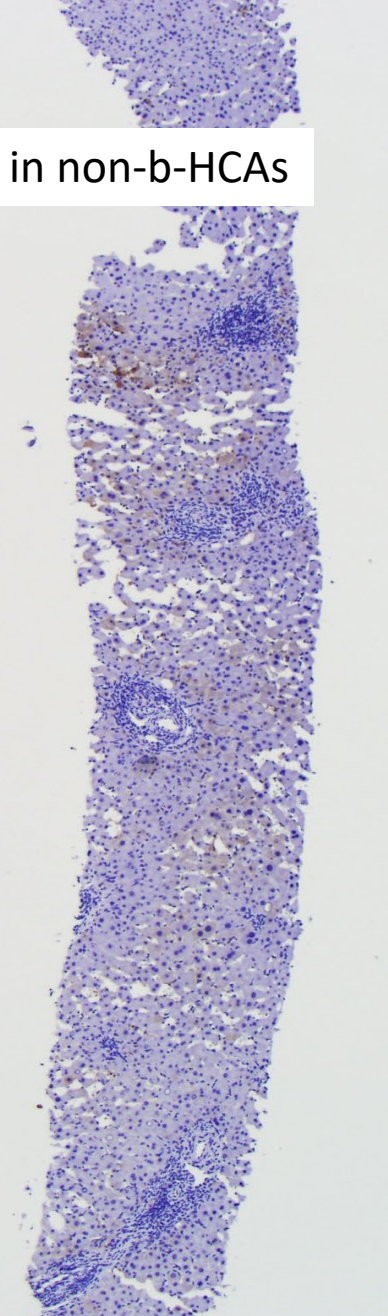
Maplike GS

FNH



Focal GS in non-b-HCAs

HCA



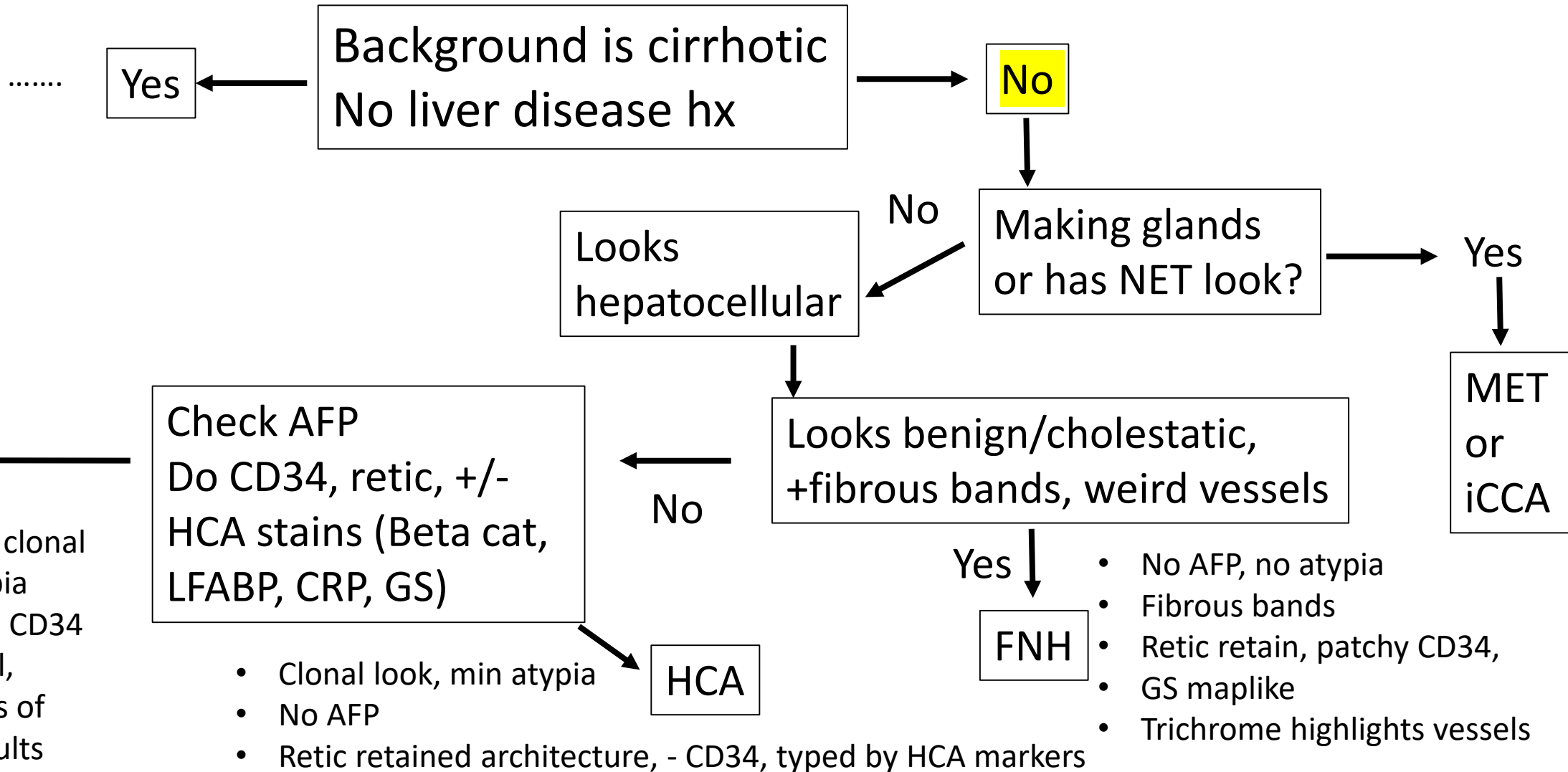
Management of FNH

- No complications, so no follow-up indicated
- No need to stop OCP, pregnancy OK
- **No resection** indicated, even with slow growth

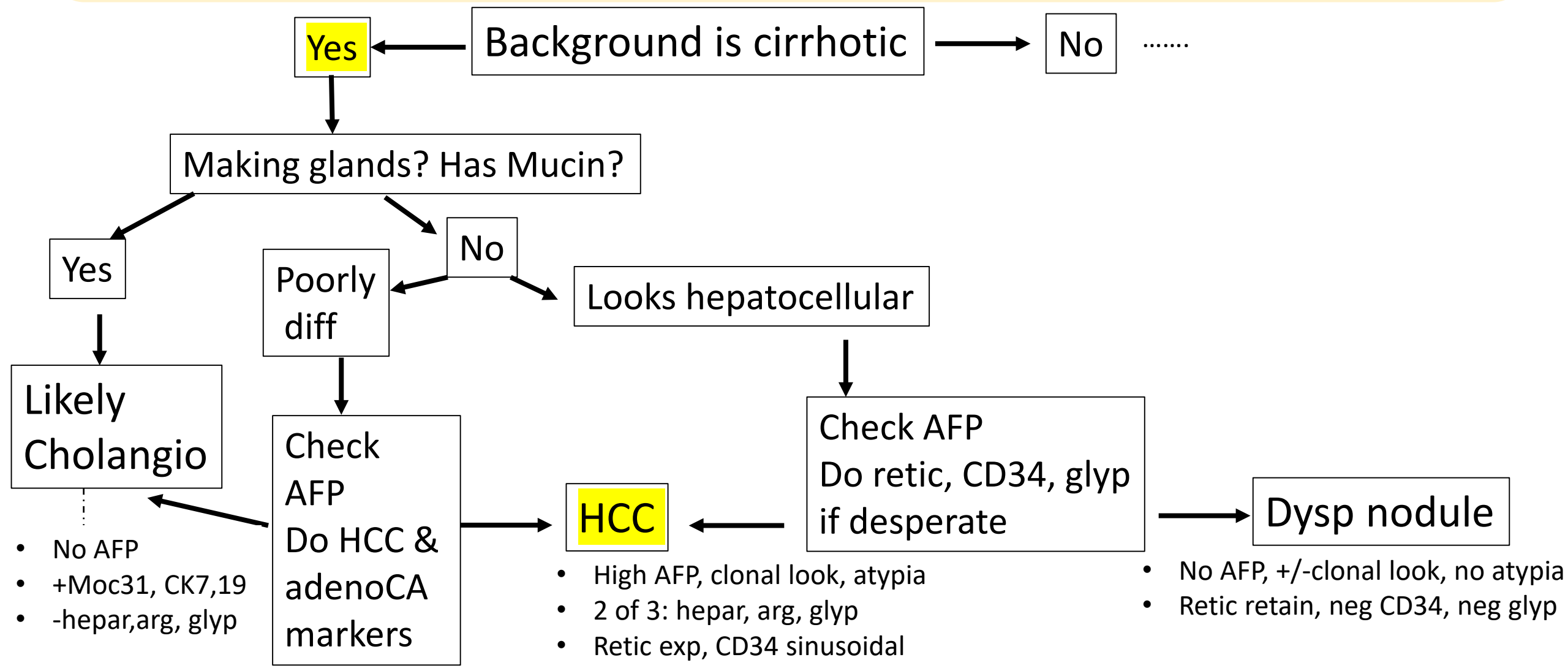
[Am J Gastroenterol.](#) 2014 Sep;109(9):1328-47

EASL Clinical Practice Guidelines. J Hepatol (2016)

Conclusion: Liver Mass Biopsy

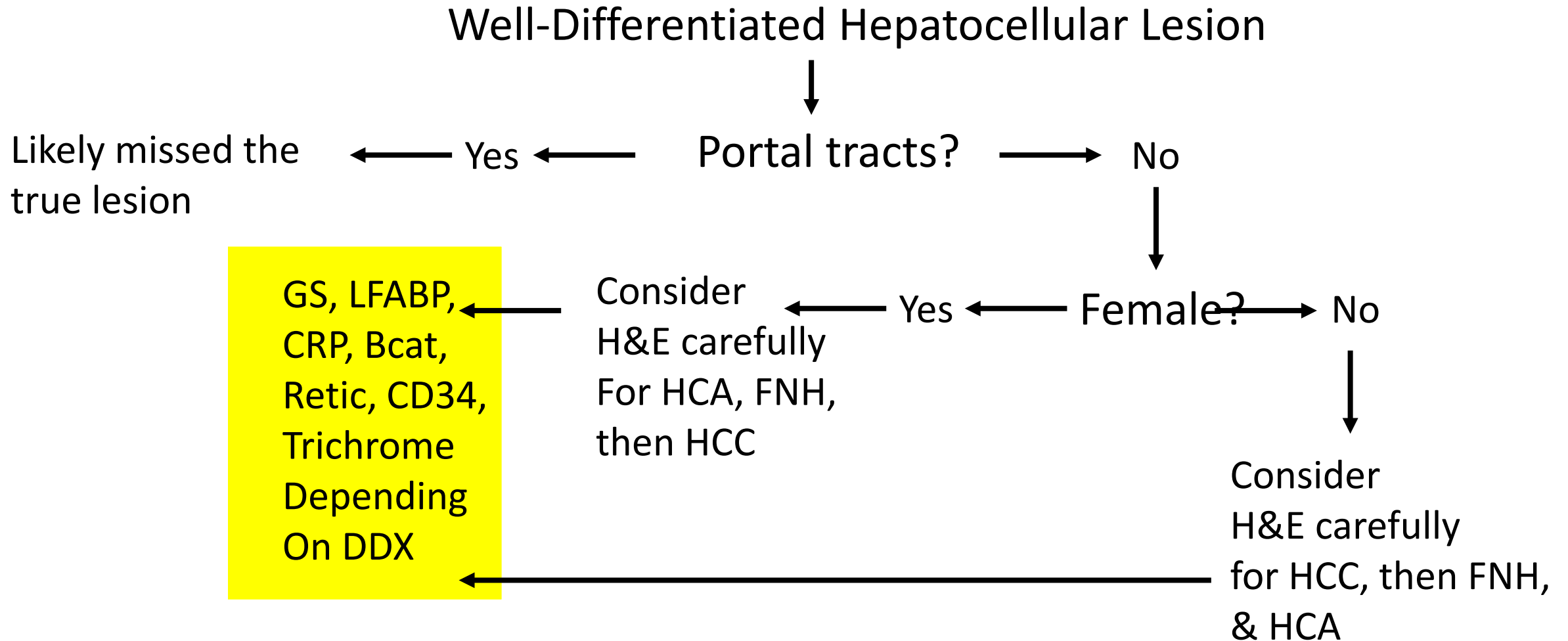


Conclusion: Liver Mass Biopsy



Real Life Practice “Liver Mass Biopsy”

No background liver sampled, no clinical info





LAMPS



APPELMAN



GREENSON



OWENS



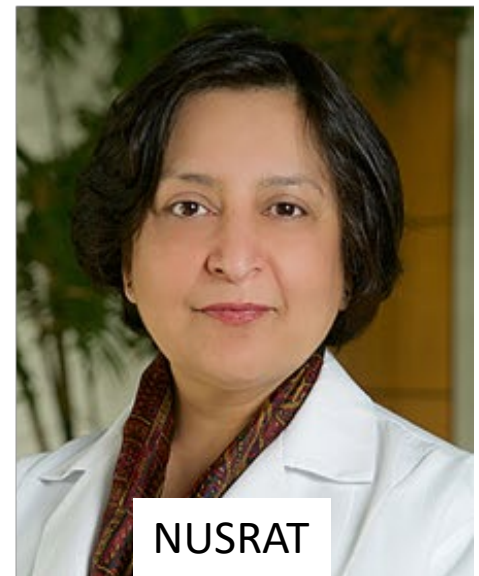
SHI



ASSARZADEGAN



CHOI



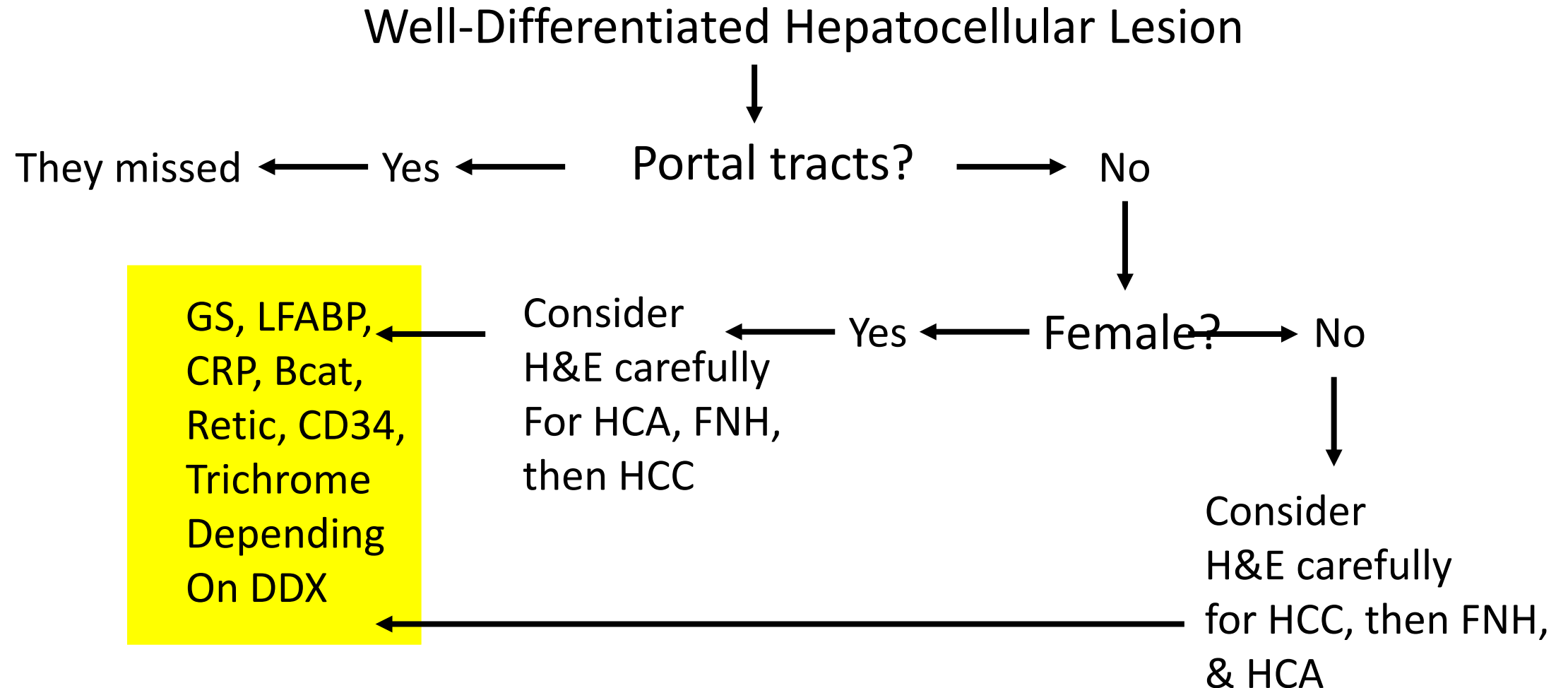
NUSRAT

Thank You

mwesterh@med.umich.edu

Real Life Practice “Liver Mass Biopsy”

No background liver sampled, no clinical info

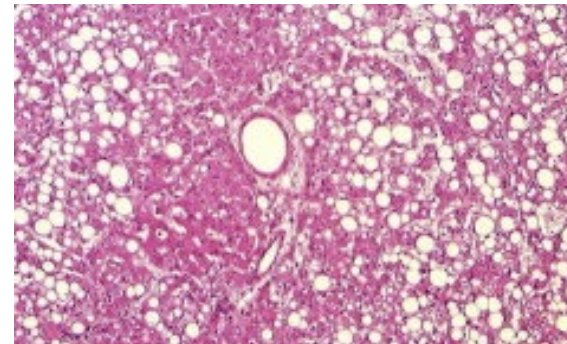
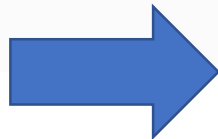


HCA Subtype – HNF1A

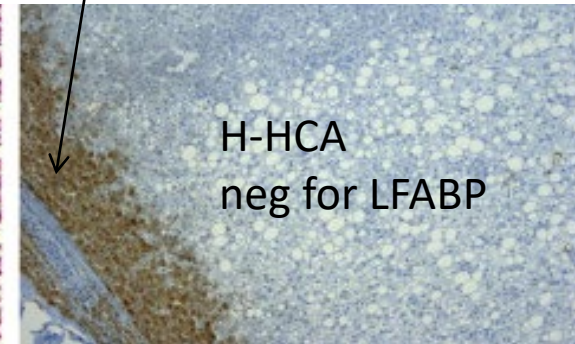
**HNF1 alpha
mutated
30-40%**

➤ ~~HNF1A~~

INACTIVATING MUTATION

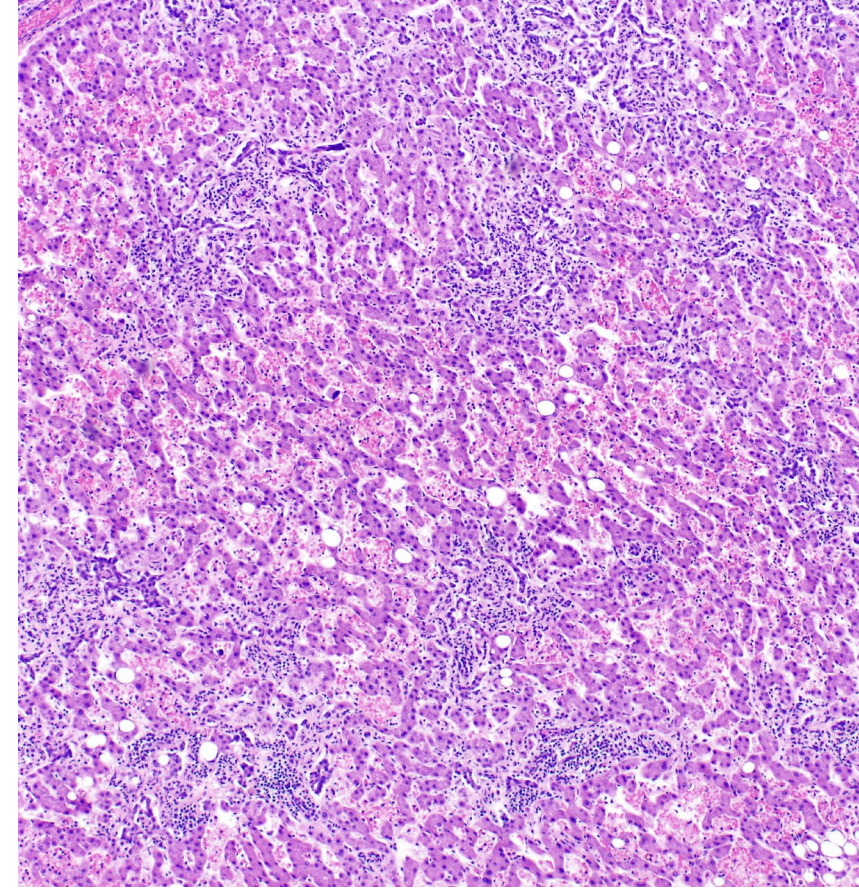
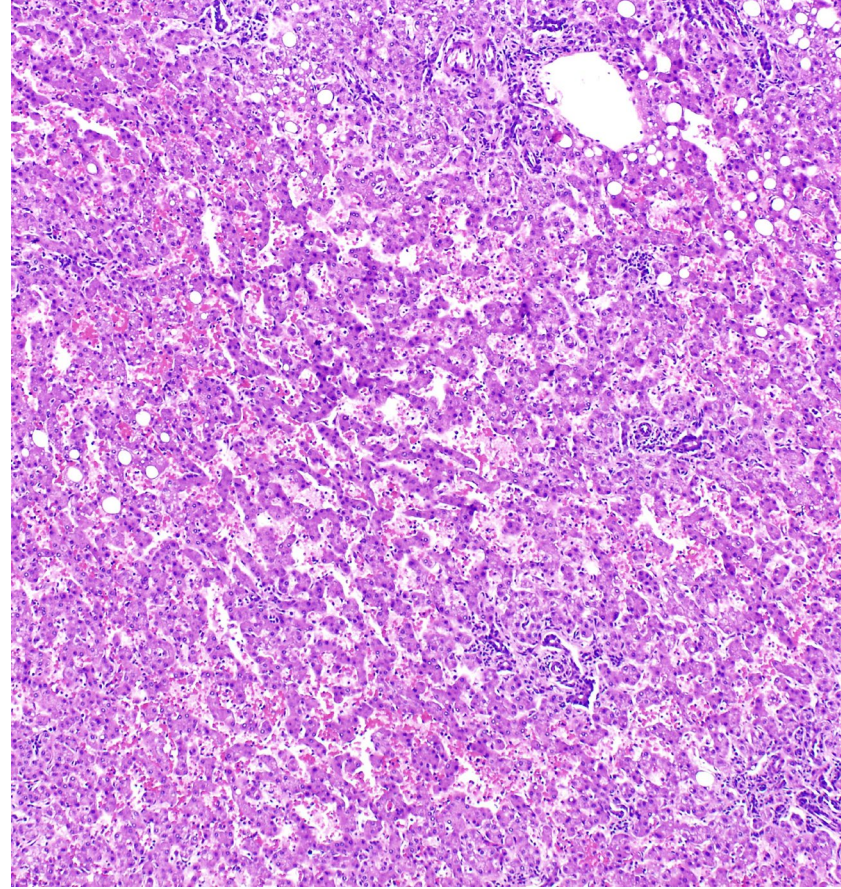
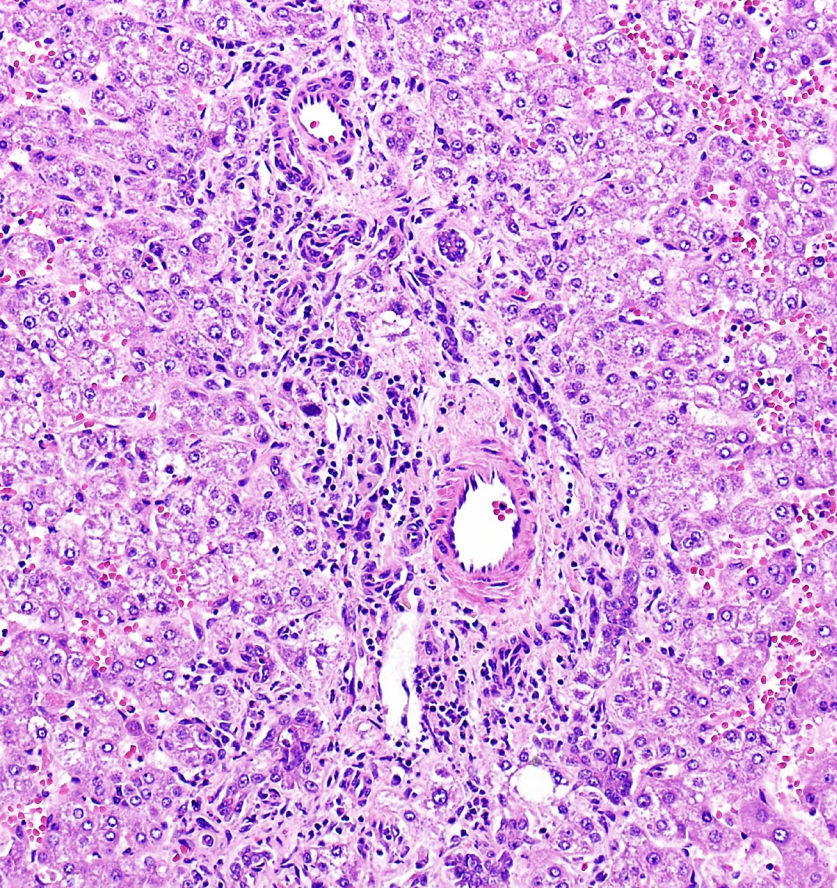


Background liver is +LFABP



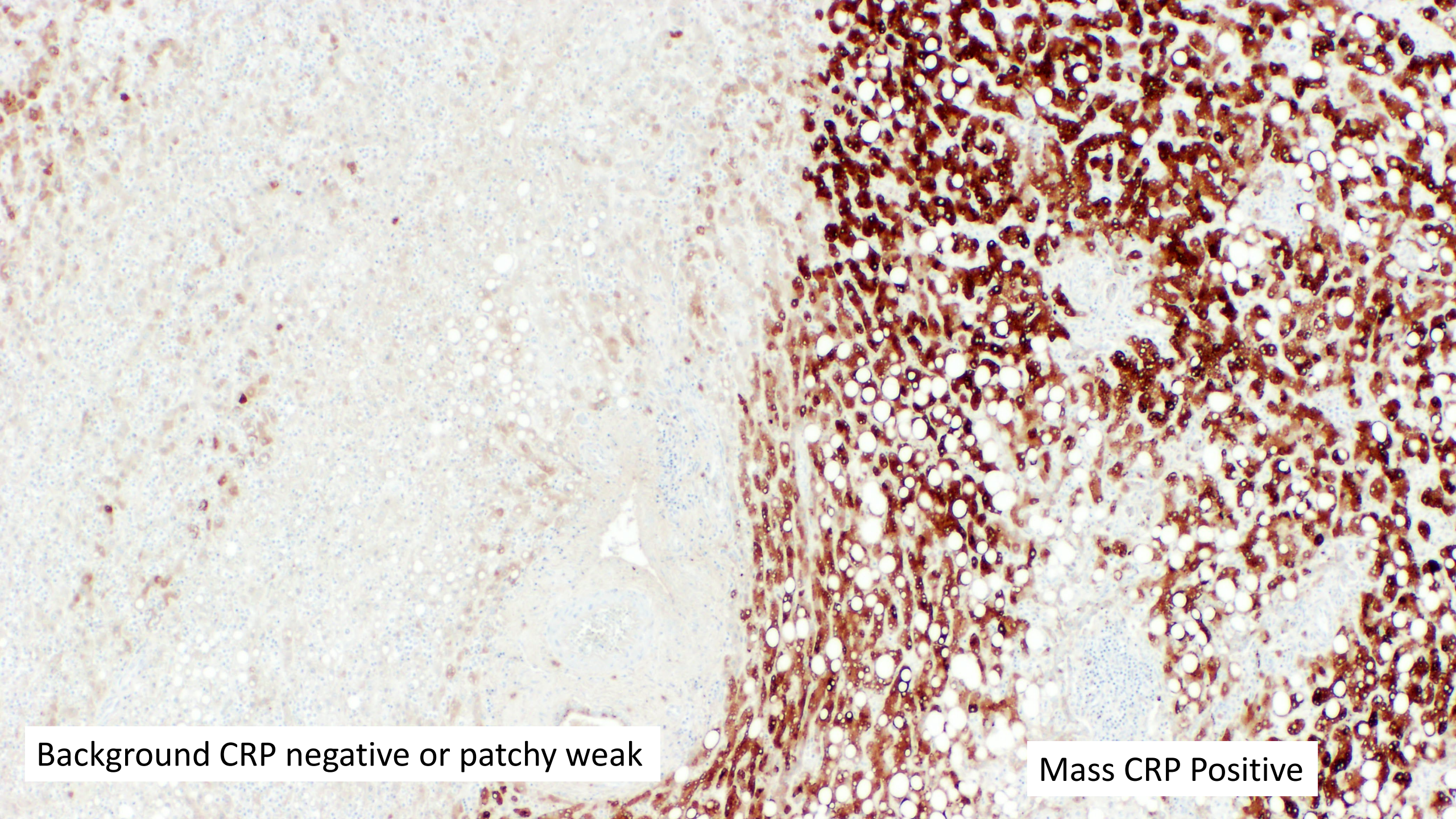
H-HCA
neg for LFABP

- Marked Steatosis in HCA
- Absence of expression of genes controlled by HNF1A
 - ❖ IHC Hallmark: LOSS of LFABP (100% sens, spec)



Inflammatory HCA

- Unpaired arteries with small bile ductules (“pseudo-portal tracts”)
- Sinusoidal Dilatation
- Inflammatory cells
- Diffuse + Serum amyloid A or C-reactive protein



Background CRP negative or patchy weak

Mass CRP Positive