Rad Path: Liver Masses

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RADIOLOGY

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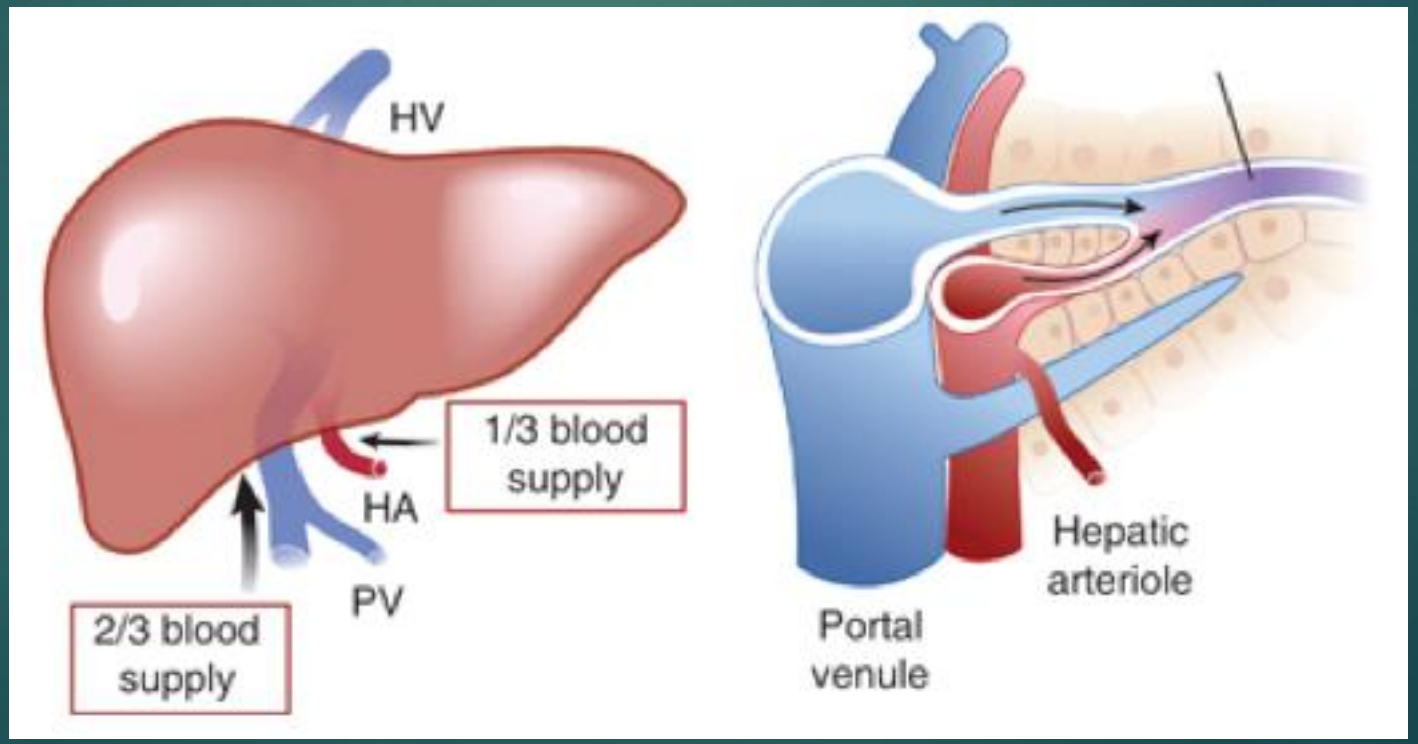
PATHOLOGY

Role of Contrast on CT

- IV contrast distinguishes parenchyma from mass
  - Parenchyma enhances on portal venous phase (PVP)
  - Tumors enhance on arterial phase



Oliver et al. Kidney International 77 (8): 669-80 Feb 2010

Role of Contrast on CT

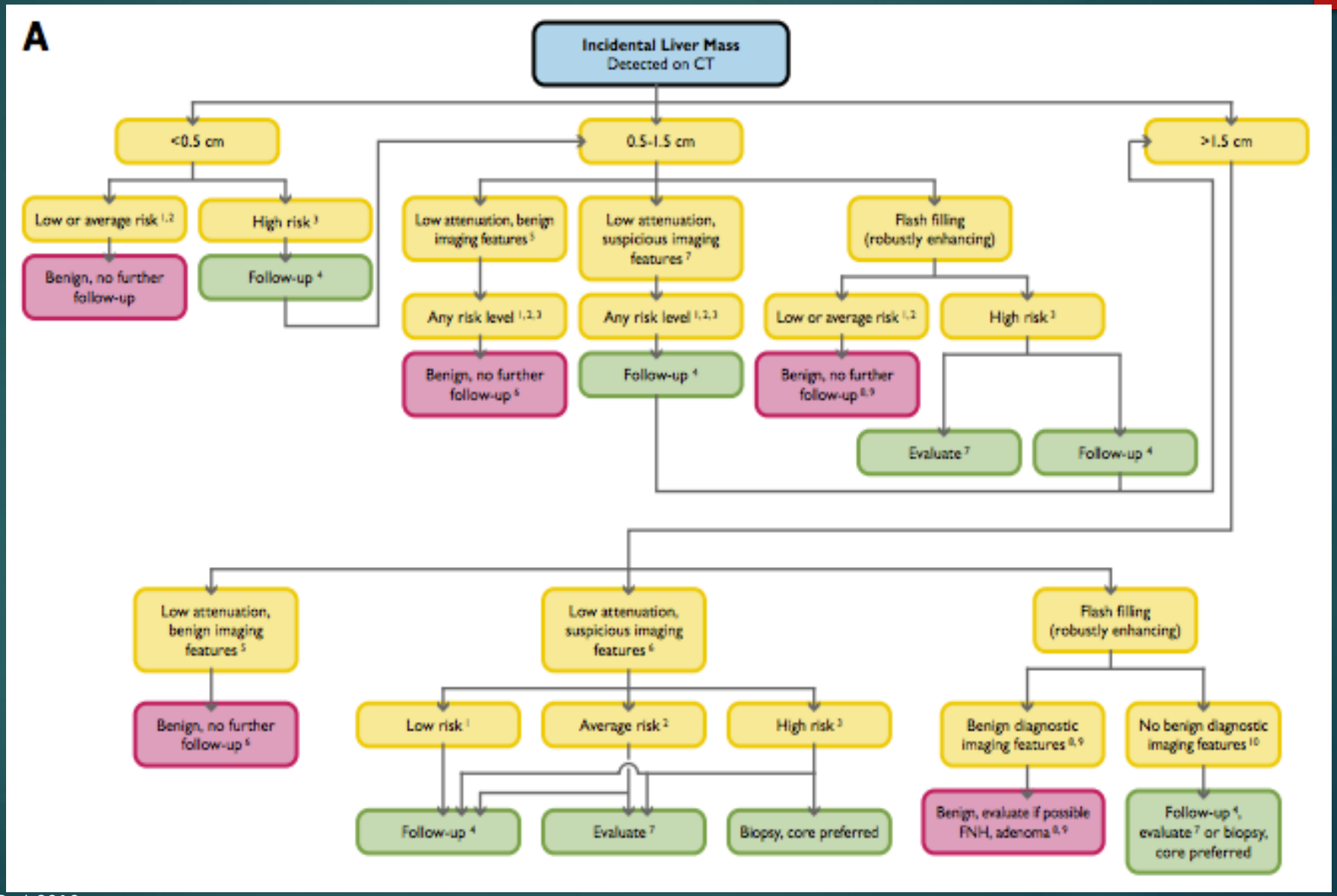
- Hypervascular tumors are best seen on late arterial phase (35 sec)
- Hypovascular tumors are best seen on PVP (75 sec)
- Delayed/equilibrium phase imaging (3-5 min):
  - Tumor washout (HCC)
  - Retention in capsules (fibrous tissue) or scarring (FNH, cholangiocarcinoma)

Oliver et al. Kidney International 77 (8): 669-80 Feb 2010

ACR: Indeterminate lesion on CT

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen without and with IV contrast	8	Consider this procedure if CT characterization is incomplete.	O
MRI abdomen without IV contrast	7	Consider this procedure if MRI with gadolinium is contraindicated. A noncontrast-enhanced MRI is superior to a noncontrast-enhanced CT.	O
US abdomen	5	Consider this procedure to diagnose a cyst versus solid lesion and to guide a percutaneous biopsy.	O
Percutaneous image-guided biopsy liver	5	Consider this procedure if imaging findings are atypical, inconclusive, or suspicious for malignancy after doing contrast-enhanced CT or MRI.	Varies
Tc-99m sulfur colloid scan liver	3	Consider this procedure to evaluate for FNH if GFR precludes CT or MRI contrast agents.	☢☢☢
Tc-99m RBC scan liver	3	Consider this procedure if a hemangioma is suspected and if GFR precludes CT or MRI contrast agents.	☢☢☢
In-111 somatostatin receptor scintigraphy	3	This procedure is not appropriate unless there is a known or suspected neuroendocrine tumor.	☢☢☢☢
FDG-PET/CT whole body	3	This procedure is not appropriate unless there is a known malignancy.	☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

ACR White Paper 2010



Berland, et al. ACR 7(10):754-773. Oct 2010

ACR Liver Metastases: Initial Imaging

Variant 1: **Suspected liver metastases. Initial imaging test following detection of primary tumor.**

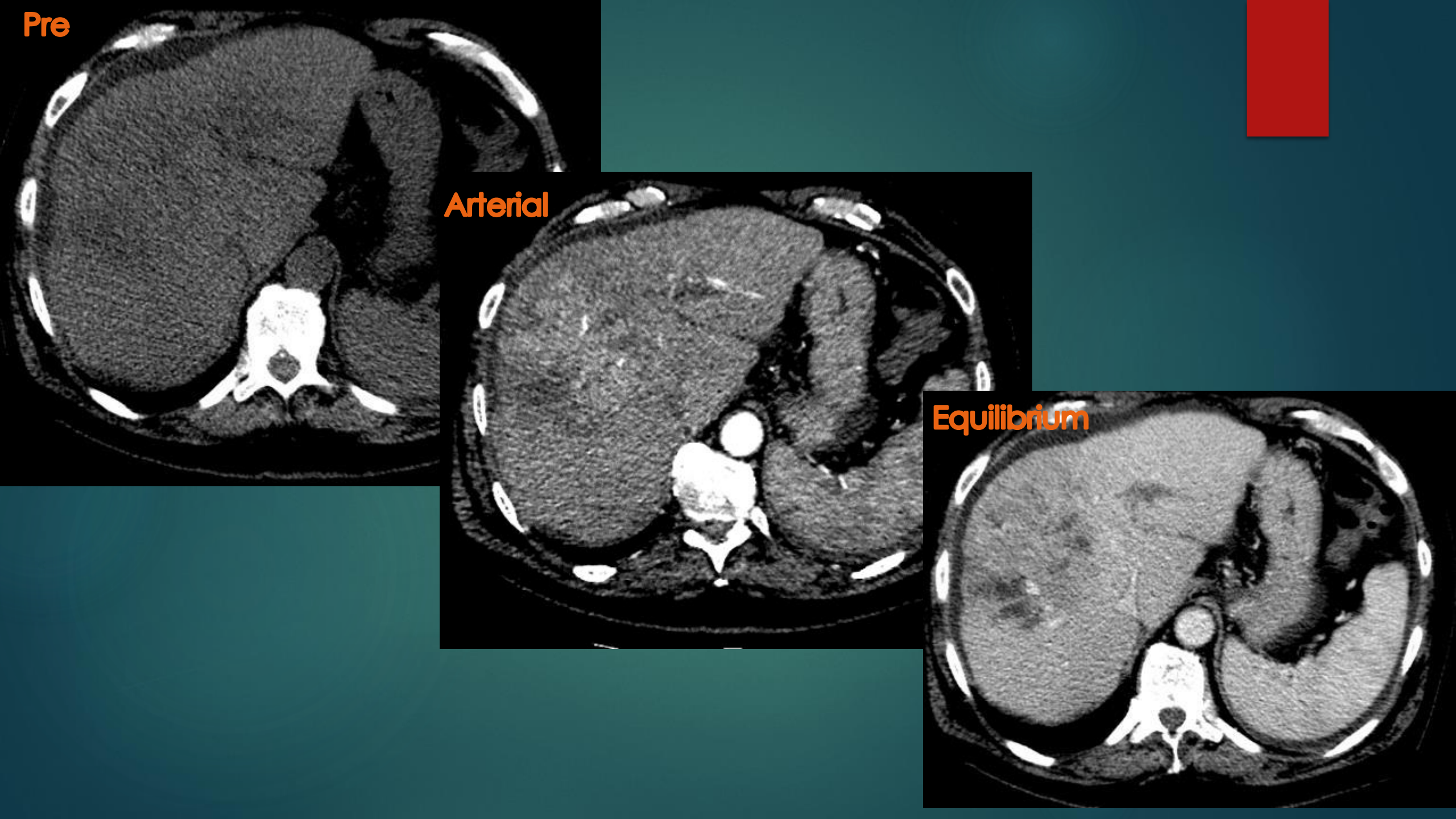
Radiologic Procedure	Rating	Comments	RRL*
CT abdomen with IV contrast	9		☢☢☢
MRI abdomen without and with IV contrast	8		O
CT abdomen without and with IV contrast	5		☢☢☢☢
MRI abdomen without IV contrast	5		O
FDG-PET/CT skull base to mid-thigh	5		☢☢☢☢
In-111 somatostatin receptor scintigraphy	5		☢☢☢☢
US abdomen	4		O
CT abdomen without IV contrast	4		☢☢☢

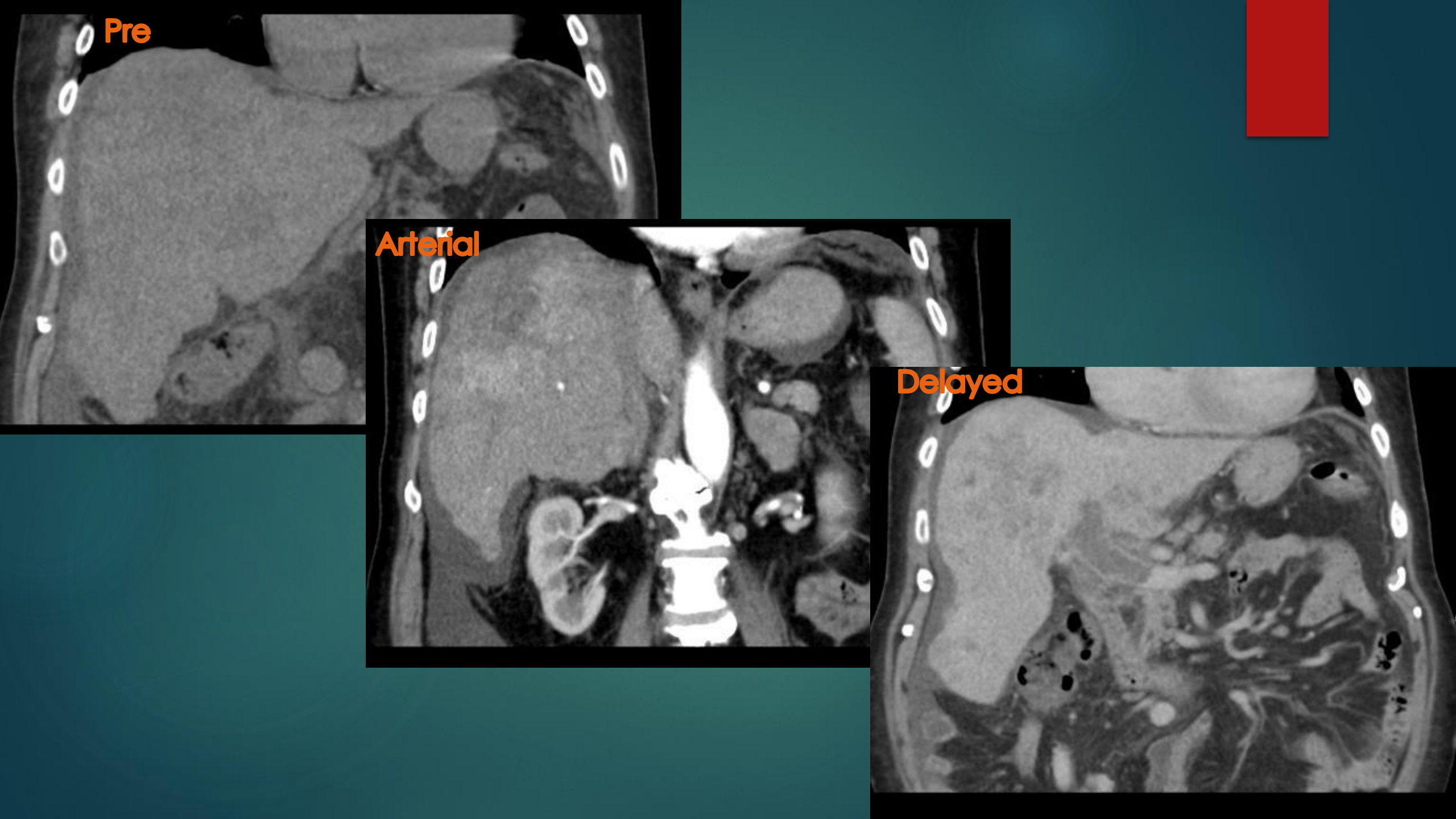
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level

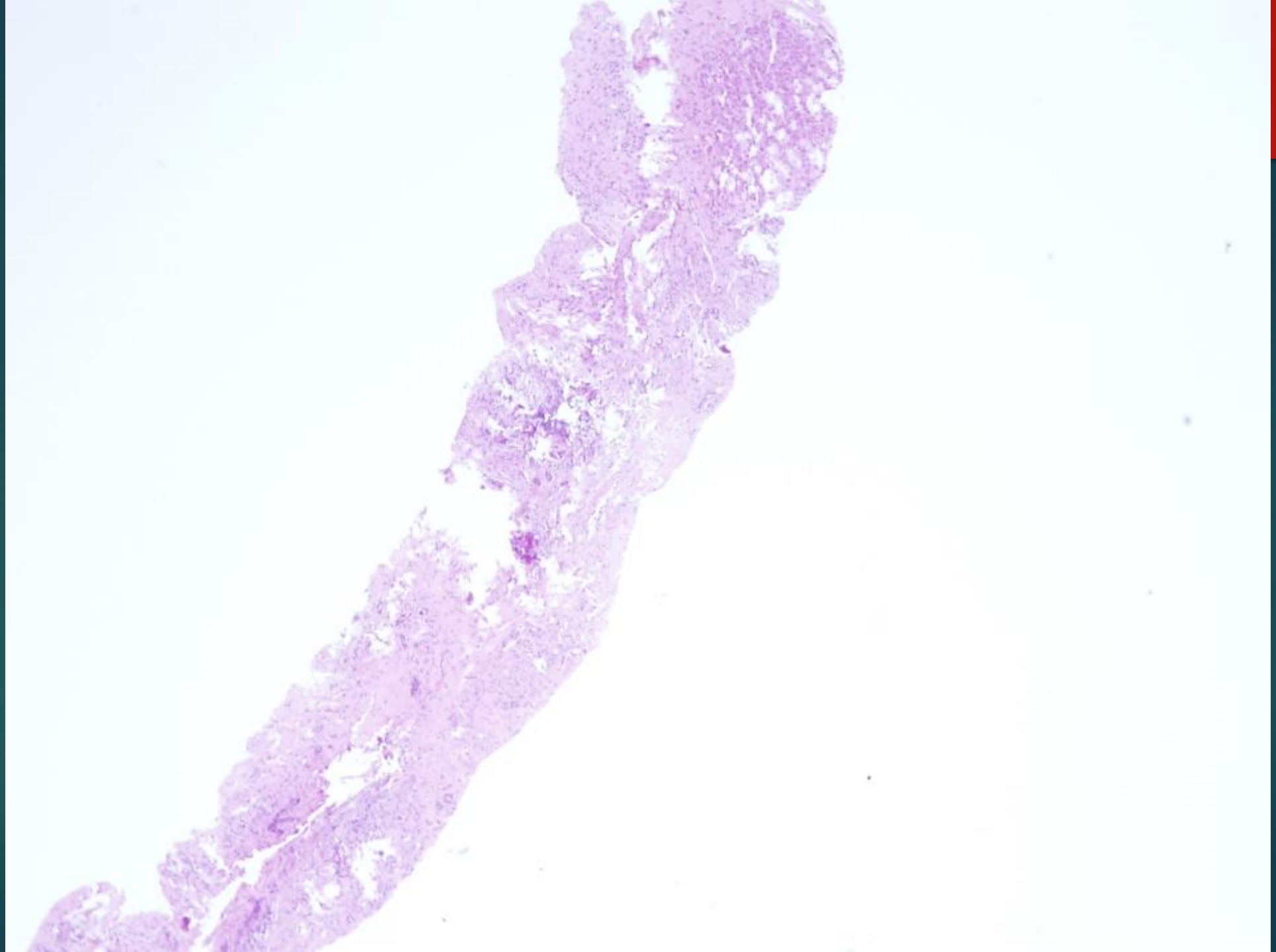
Case 1

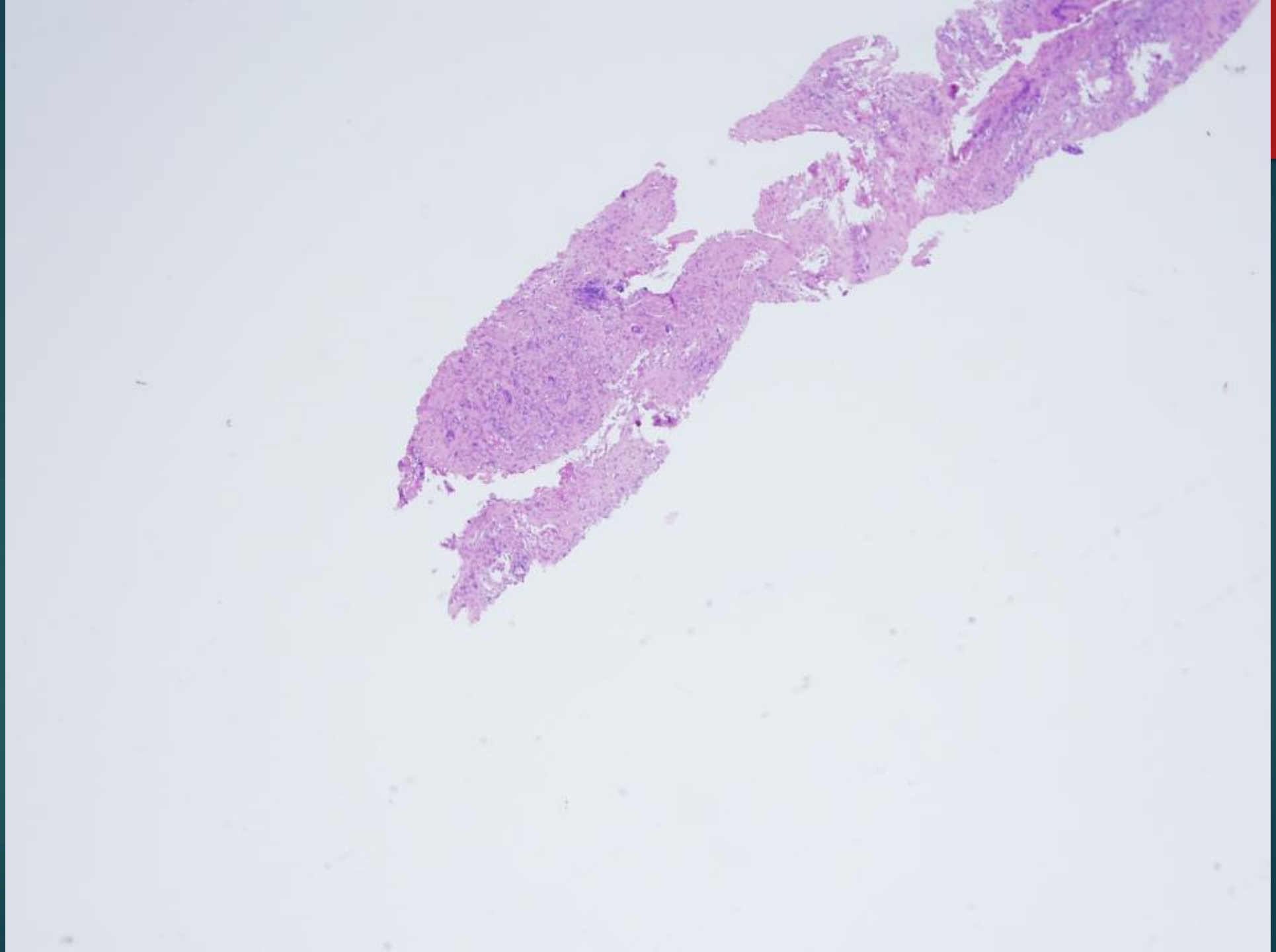
- 77 YOM with fatigue and iron deficiency anemia for 1 year
- Completely normal CT abdomen/pelvis 3 years prior
- AFP 2.2 (ref <7.9)

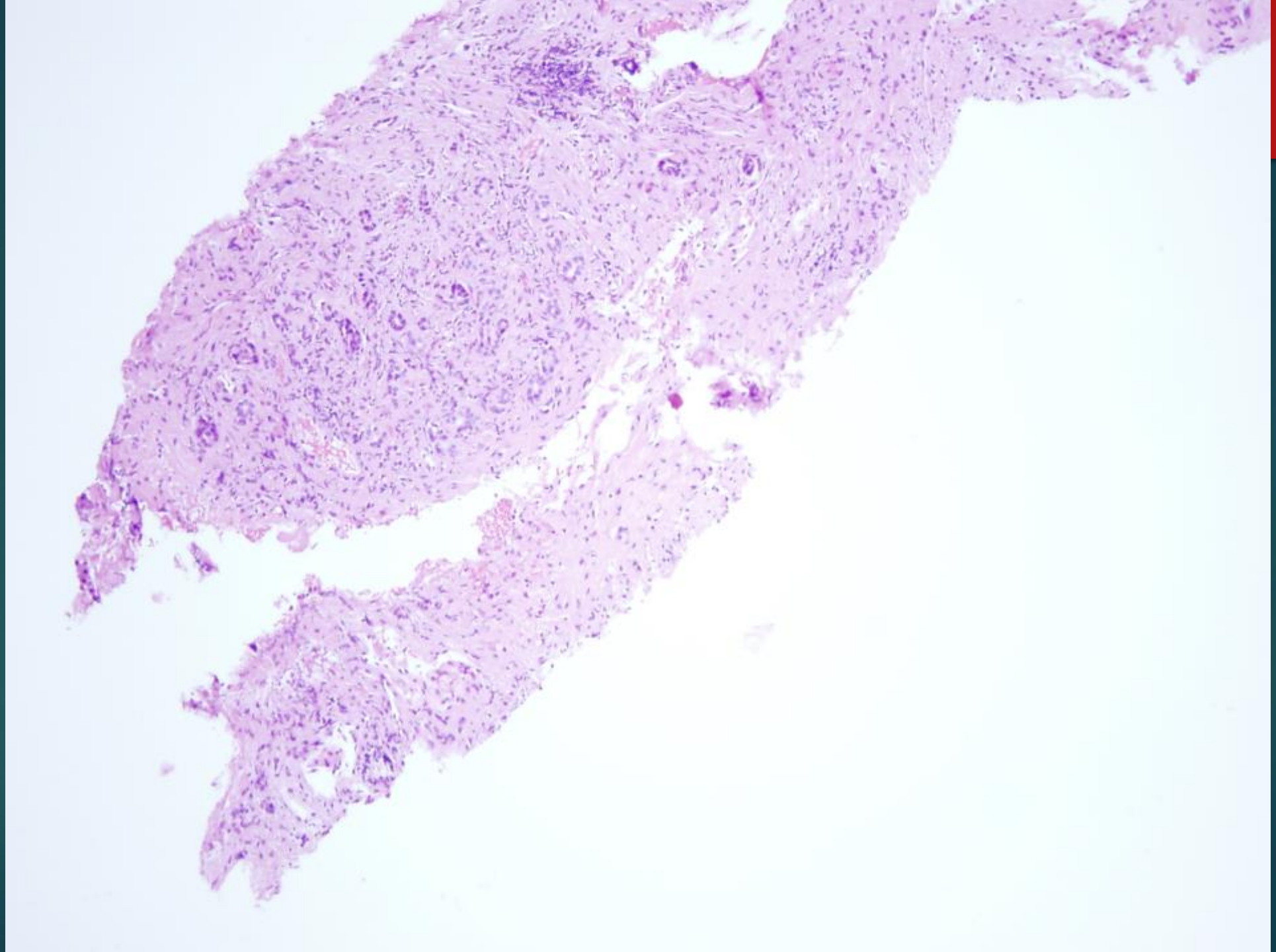

Pre
Arterial
Equilibrium

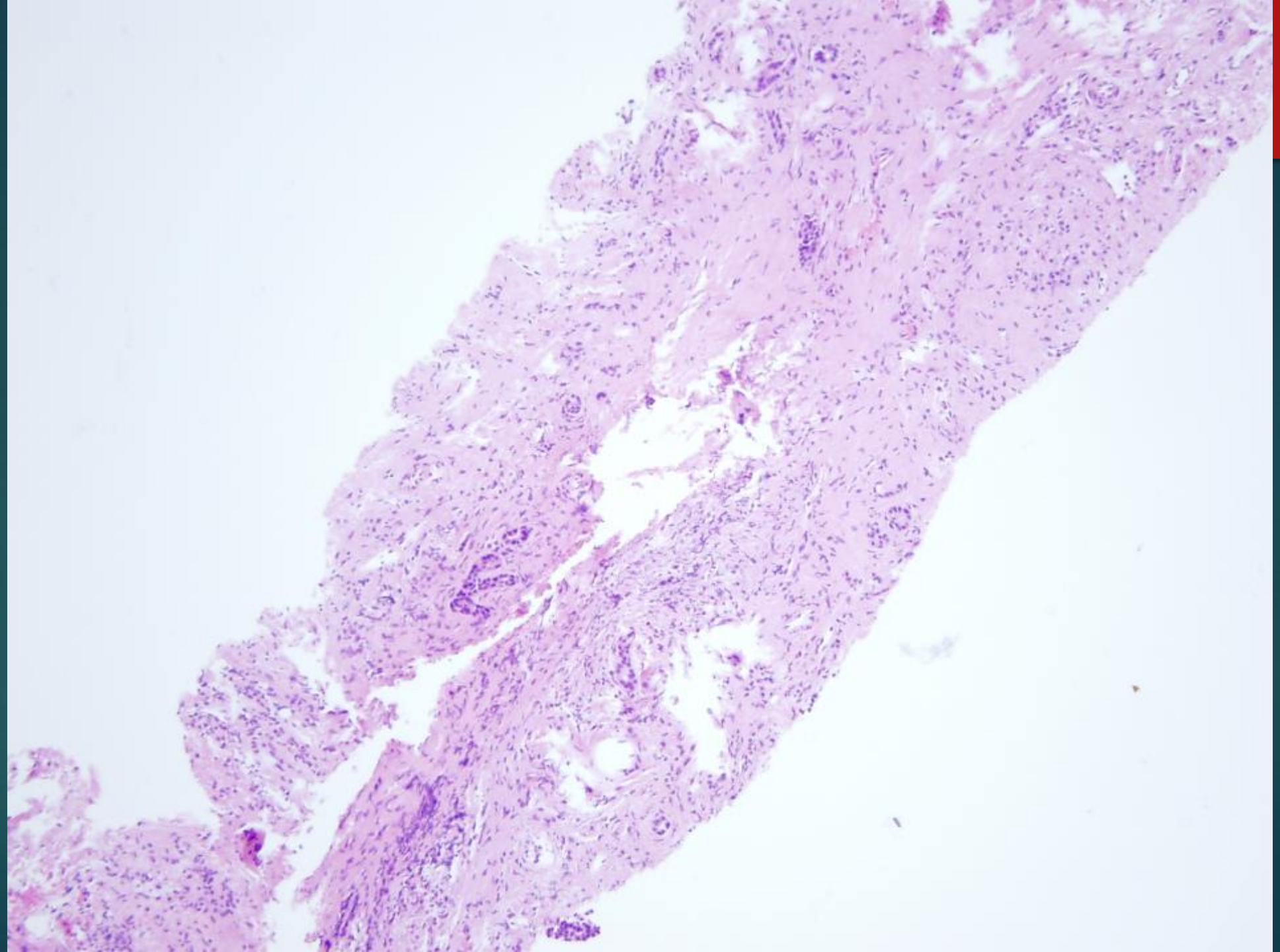

Pre
Arterial
Delayed

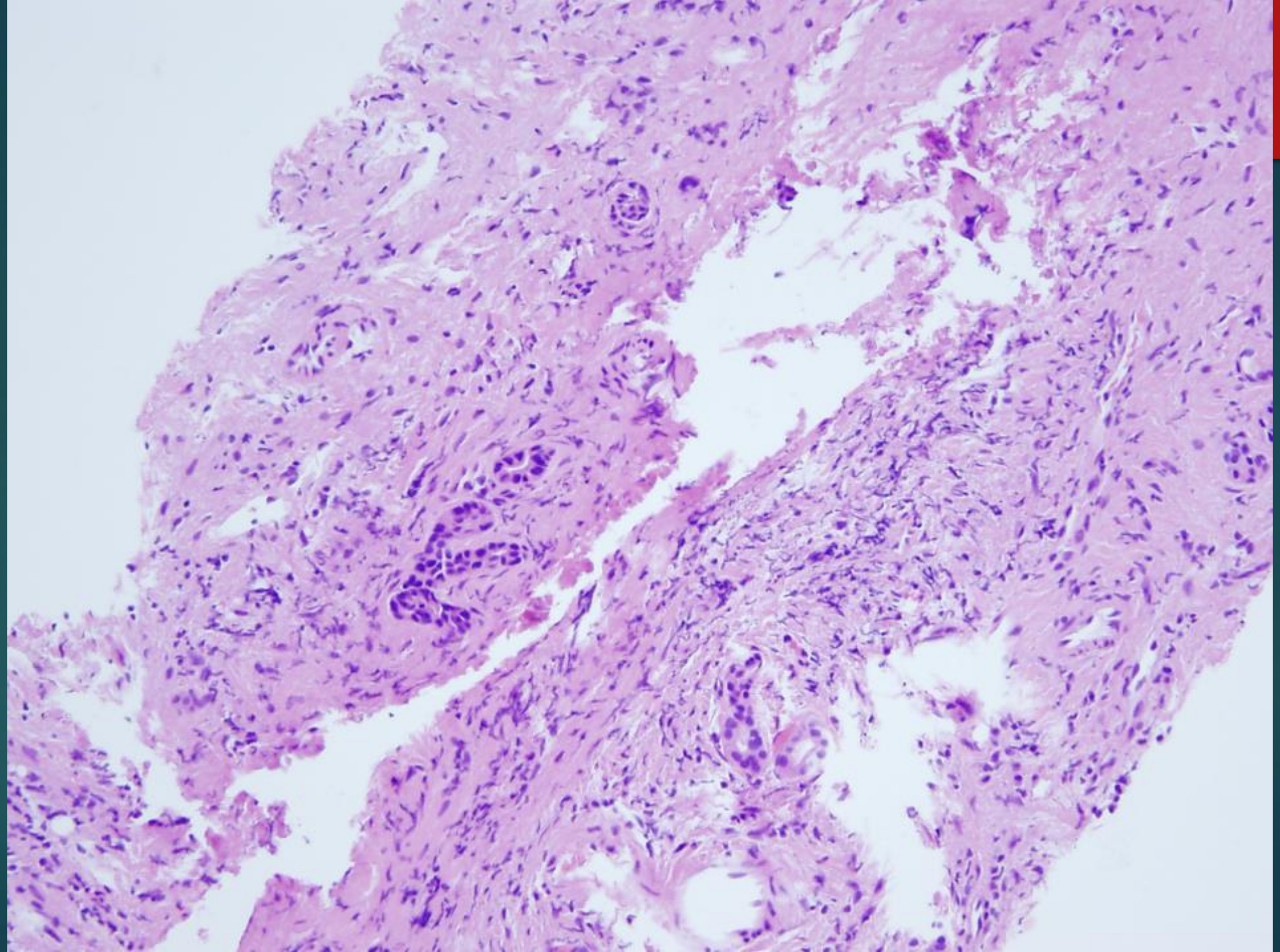
MRN: 34234336
BS-16-65482
(liver biopsy)











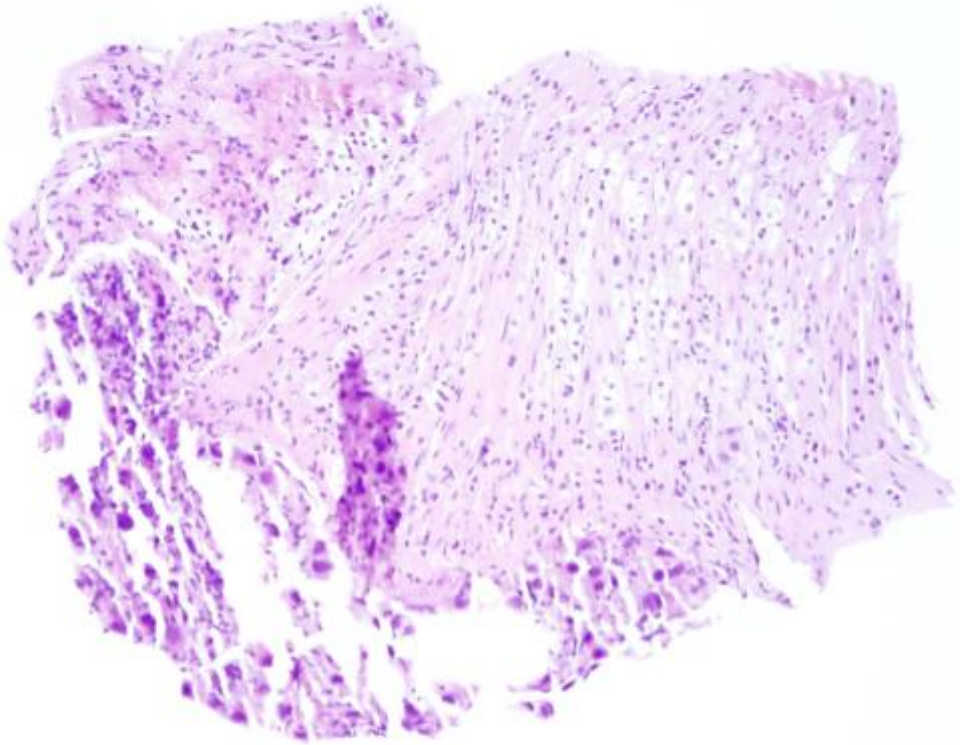
A. LIVER MASS BIOPSY:

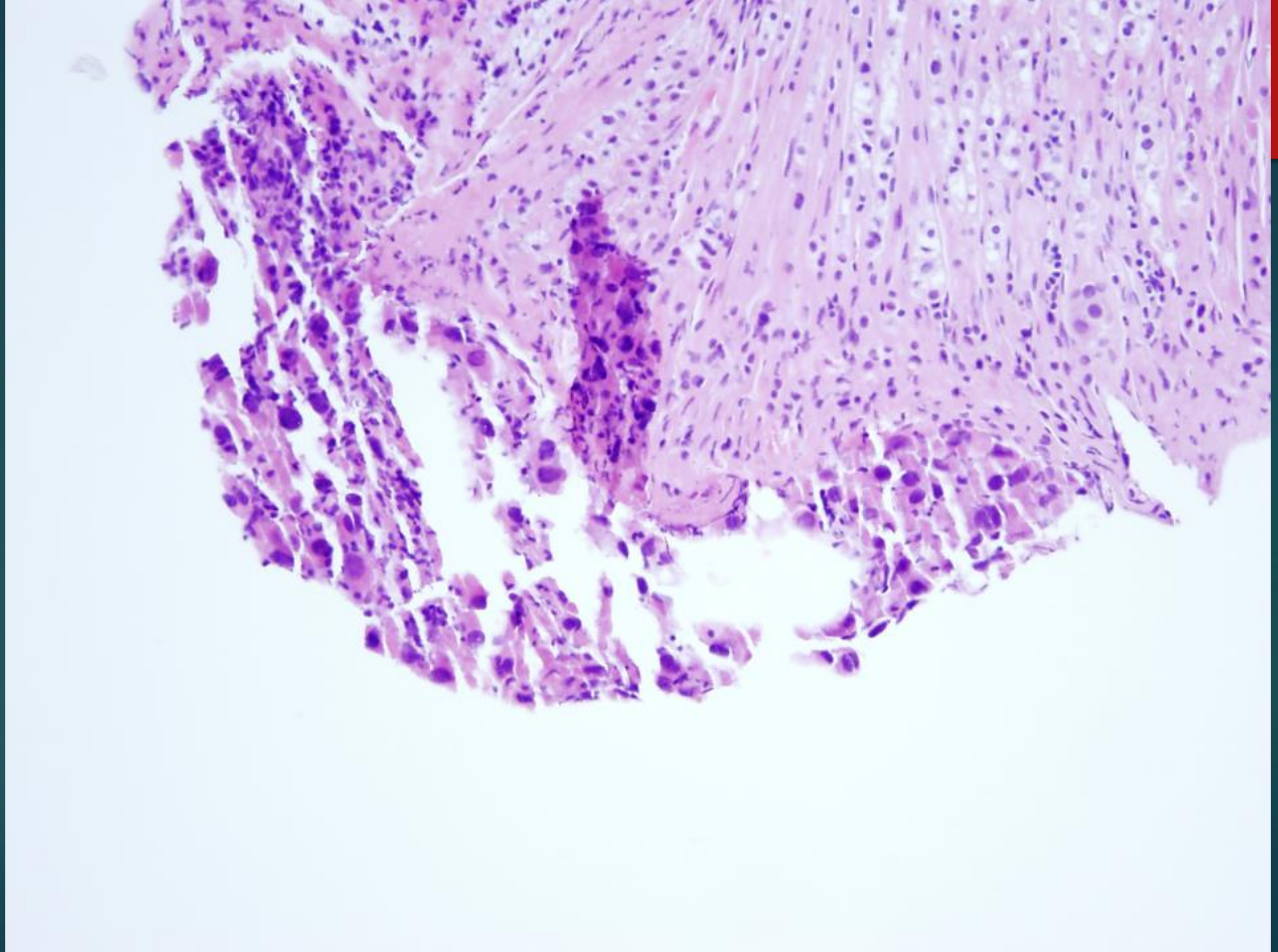
Cirrhotic liver parenchyma with extensive multi-acinar collapse and florid ductular proliferation with focal atypia, SEE NOTE

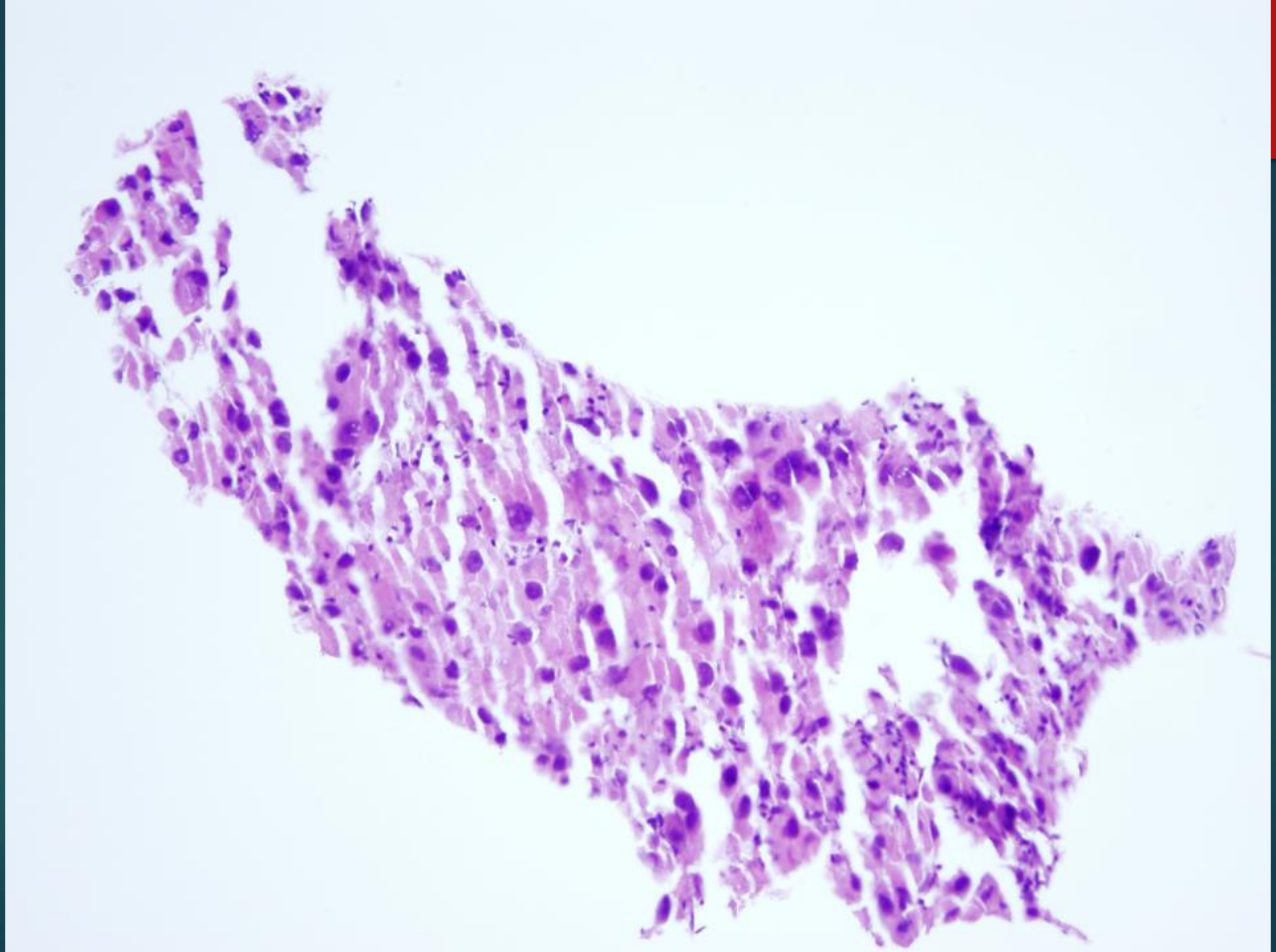
NOTE: Although some morphological atypia is seen within foci of ductular proliferation, diagnostic features for hepatocellular carcinoma or cholangiocarcinoma are not present in these biopsies.

A reticulin stain and immunostains for SMAD4 (intact), p53, MIB-1, Glypican-3, glutamine synthetase, CD34, CK7 and beta-catenin were also performed for final diagnosis.

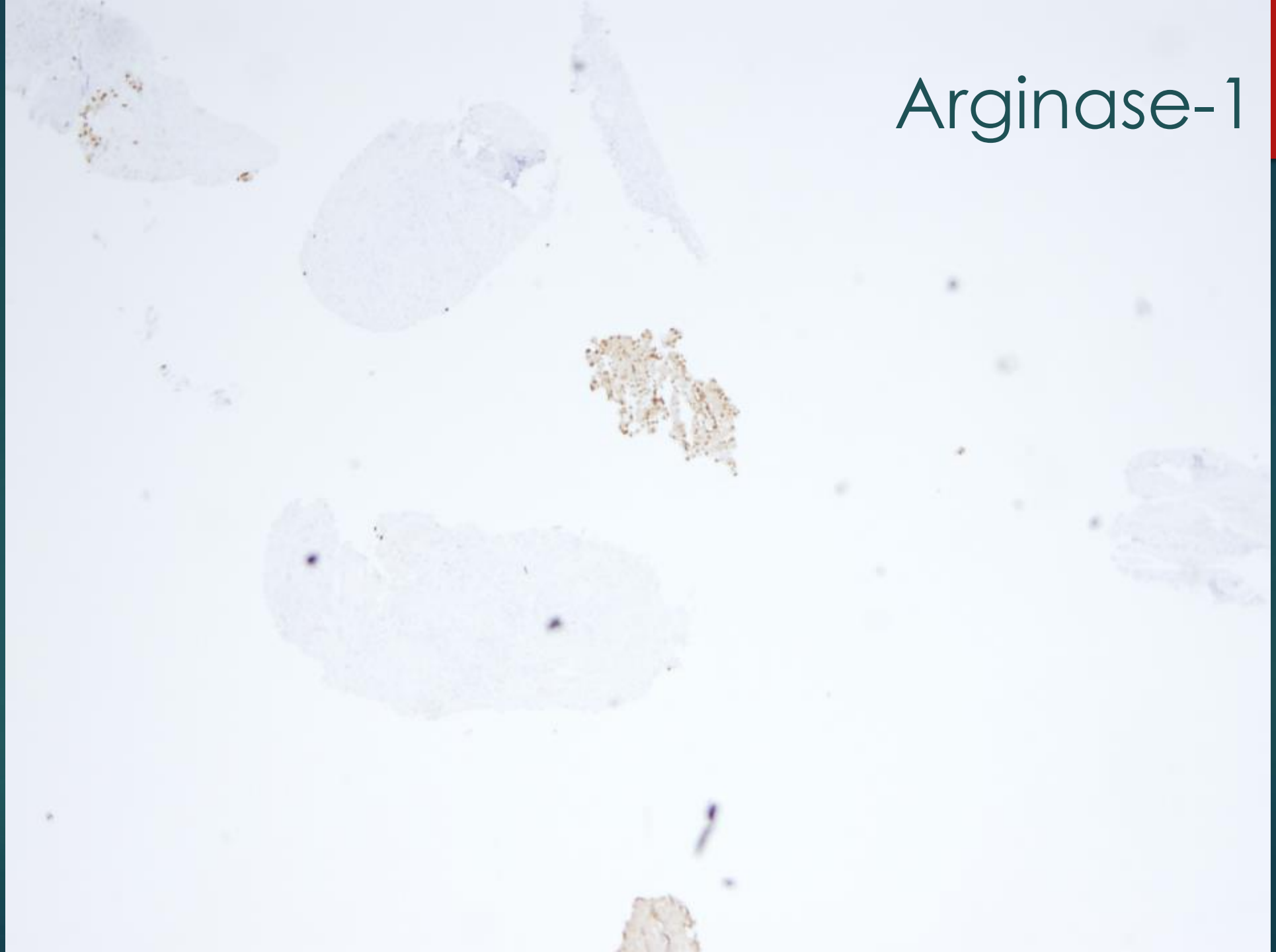
MRN: 34234336
BS-16-65482
(adrenal biopsy)







Arginase-1



SPECIMEN DESIGNATED "LEFT ADRENAL MASS, CORE BIOPSY":

Morphologically and immunohistochemically consistent with HEPATOCELLULAR CARCINOMA, moderately differentiated by WHO grading system (Edmonson/Steiner grade 3), with necrosis, present as detached fragments together with background adrenal parenchyma and inflamed fibrous tissue. See note.

Note: Focal green/brown pigment is noted in association with tumor cells (nonspecific, but in context possibly bile pigment). Hyaline cytoplasmic globules are also noted. The architecture of the microfragments is focally suggestive of a thick trabecular growth pattern (best seen on H&E; reticulin stain also examined). Immunostains show that the tumor cells are positive for ARG-1 (cytoplasmic and nuclear) and TTF1 (multifocal, cytoplasmic) and negative for SOX10. Immunostains for SF1 and Melan-A/A103 highlight the adrenal parenchyma, but the tumor cells are negative for these markers.

Which is NOT a macroscopic growth pattern of HCC?

- A) Nodular
- B) Follicular
- C) Massive
- D) Infiltrative

Hepatocellular Carcinoma

- HCC is the 2nd leading cause of cancer death in men, and 6th in women worldwide
- Typically large with mosaic pattern
- Capsule, hemorrhage, necrosis and fat evolution
- Most are hypervascular; only 10% are hypovascular

Reynolds et al. Radiographics. 35(2) Mar-Apr 2015

Infiltrative HCC

- Infiltrative (cirrhotomimetic-type) HCC accounts for 7-20%, commonly in HBV patients, and has substantially worse prognosis
- Least likely to correlate with AFP levels
- Imaging features of infiltrative HCC are different:
  - Minimal, patchy or miliary arterial enhancement
  - Hypointense or reticular on venous phase
  - Washout is less frequent, and irregular or heterogeneous

Reynolds et al. Radiographics. 35(2) Mar-Apr 2015

Metastases

TABLE 8. Sites and Frequencies of Metastases (225 Cases)

Organ and tissue	No. of cases	Relative frequency
Mainly hematogenous	126 (56.0%)	87.5%
Lung	116 (51.6%)	80.6%
Adrenal	19 (8.4%)	
Bone	12 (5.8%)	
Pancreas	7 (3.1%)	
Kidney	5 (2.2%)	
Thyroid	2 (0.8%)	
Meninx	2 (5.4%)*	
Heart	2 (0.8%)	
Brain	1 (2.7%)*	
Mainly lymphogenous (lymph nodes)	60 (26.7%)	41.7%
Hilar	33 (14.7%)	22.9%
Head of pancreas	24 (10.7%)	16.7%
Around aorta	18 (8.0%)	
Retroperitonum	13 (5.8%)	
Around stomach	12 (5.3%)	
Mediastinum	11 (4.9%)	
Around trachea	11 (4.9%)	
Around carina	9 (4.0%)	
Neck	7 (3.1%)	
Virchow	5 (2.2%)	
Inguinal	1 (0.4%)	
Mainly infiltrating and disseminating	49 (21.8%)	34.0%
Diaphragm	23 (10.2%)	16.0%
Douglas' pouch	14 (6.2%)	
Gallbladder	13 (5.8%)	
Stomach, intestine	9 (5.8%)	
Peritoneum	9 (5.8%)	
Pancreas surface	8 (3.6%)	
Heart	3 (1.3%)	
Esophagus	1 (0.4%)	
Ovary	1 (0.4%)	
Total	225 (100%)	144 (100%)

Nakashima et al. Cancer 1983. 51(863-877)

LI-RADS is used for:

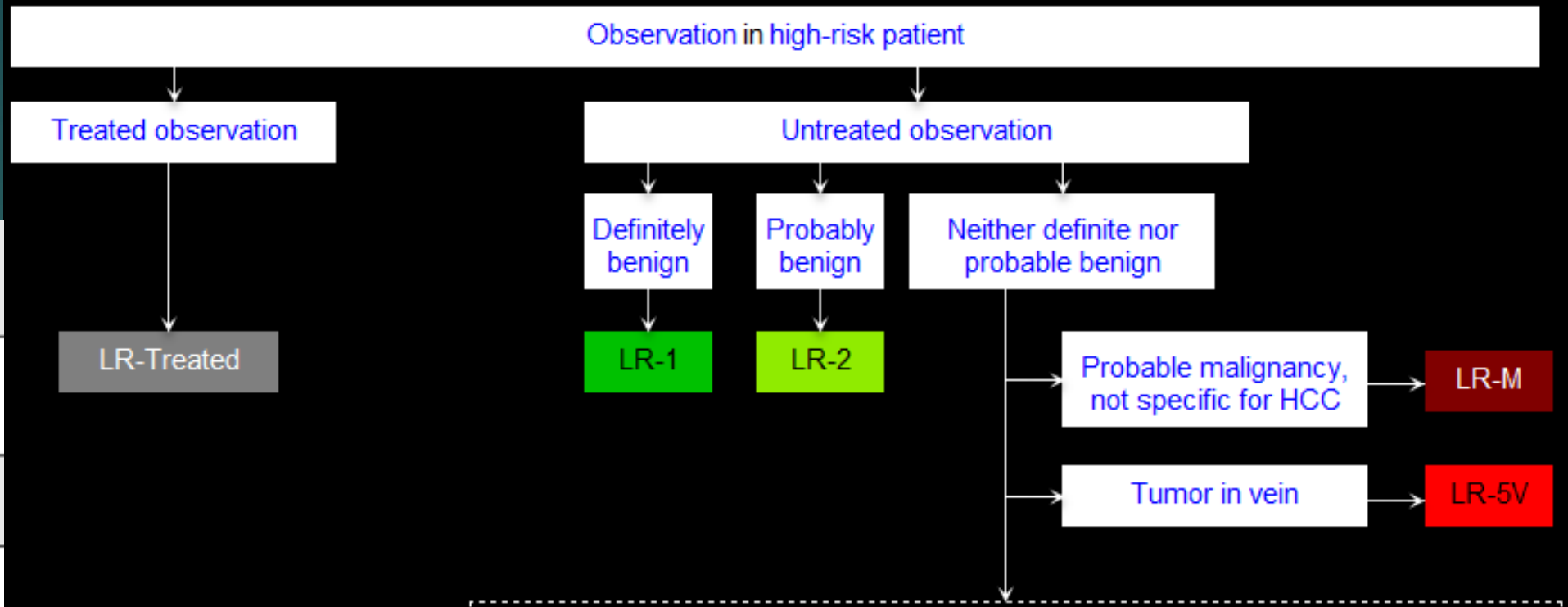
- A) Any focal liver mass
- B) Known extra-hepatic primary
- C) Only cirrhotic/Hepatitis patients
- D) Treated HCC

LI-RADS

Liver Imaging Reporting and Data System (LI-RADS)

LR-1	Definitely Benign
LR-2	Probably Benign
LR-3	Intermediate probability for HCC
LR-4	Probably HCC
LR-5	Definitely HCC
LR-5V	Definitely HCC with Tumor in Vein
LR-M	Probable malignancy, not specific for HCC
LR-Treated	Treated Observation

v2014



		Arterial phase hypo- or iso-enhancement		Arterial phase hyper-enhancement		
Diameter(mm):		< 20	≥ 20	< 10	10-19	≥ 20
•"Washout" •"Capsule" •Threshold growth	None:	LR-3	LR-3	LR-3	LR-3	LR-4
	One:	LR-3	LR-4	LR-4	LR-4 / LR-5	LR-5
	≥ Two:	LR-4	LR-4	LR-4	LR-5	LR-5

Apply ancillary features and then tie-breaking rules to adjust category

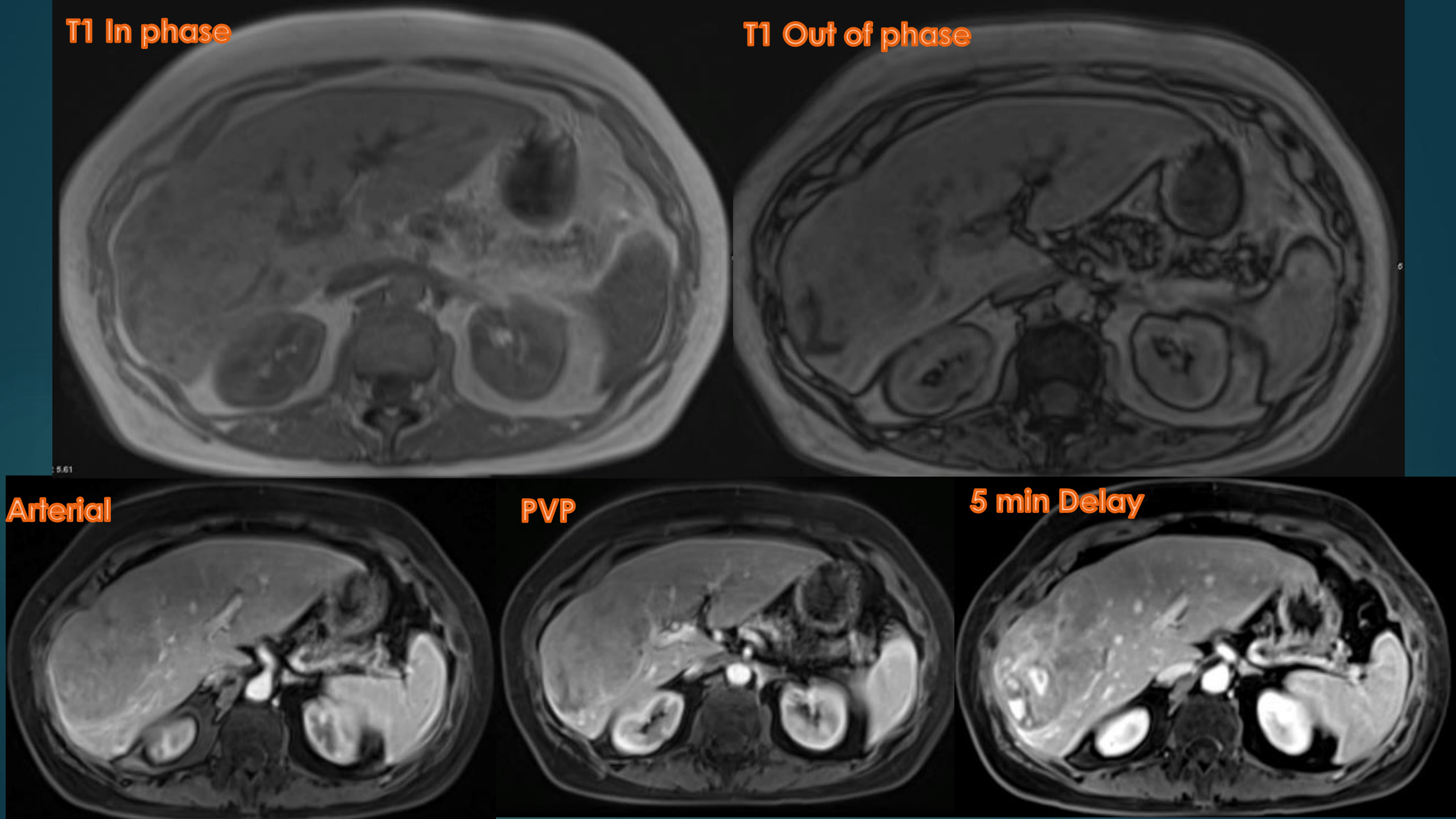
LI-RADS v 2014. American College of Radiology. https://nrdr.acr.org/lirads/

Case 2

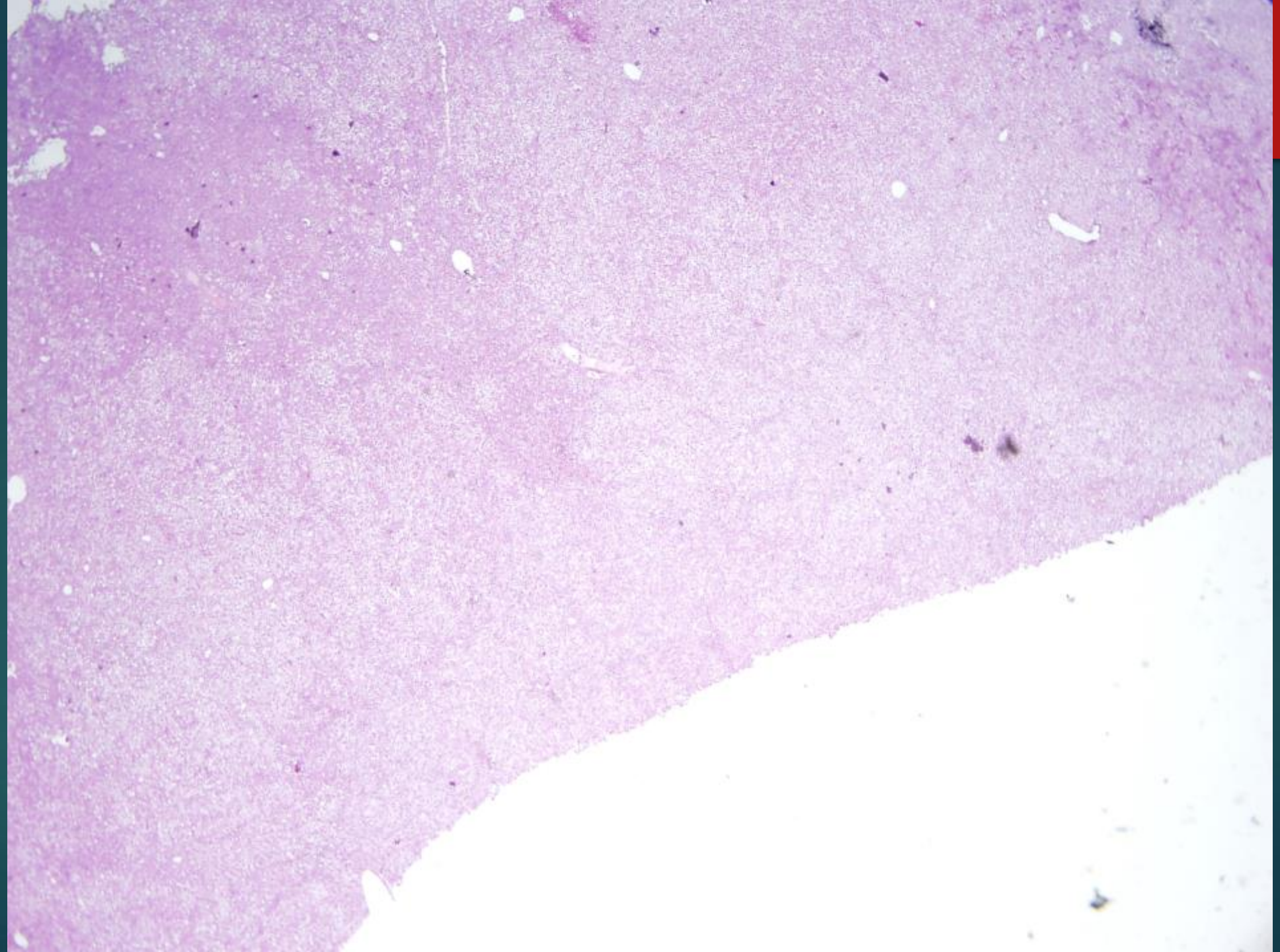
- 55 YOF with 3-4 years of pruritus and elevated LFTs
- AFP = 1.7
- Normal mammogram and colonoscopy

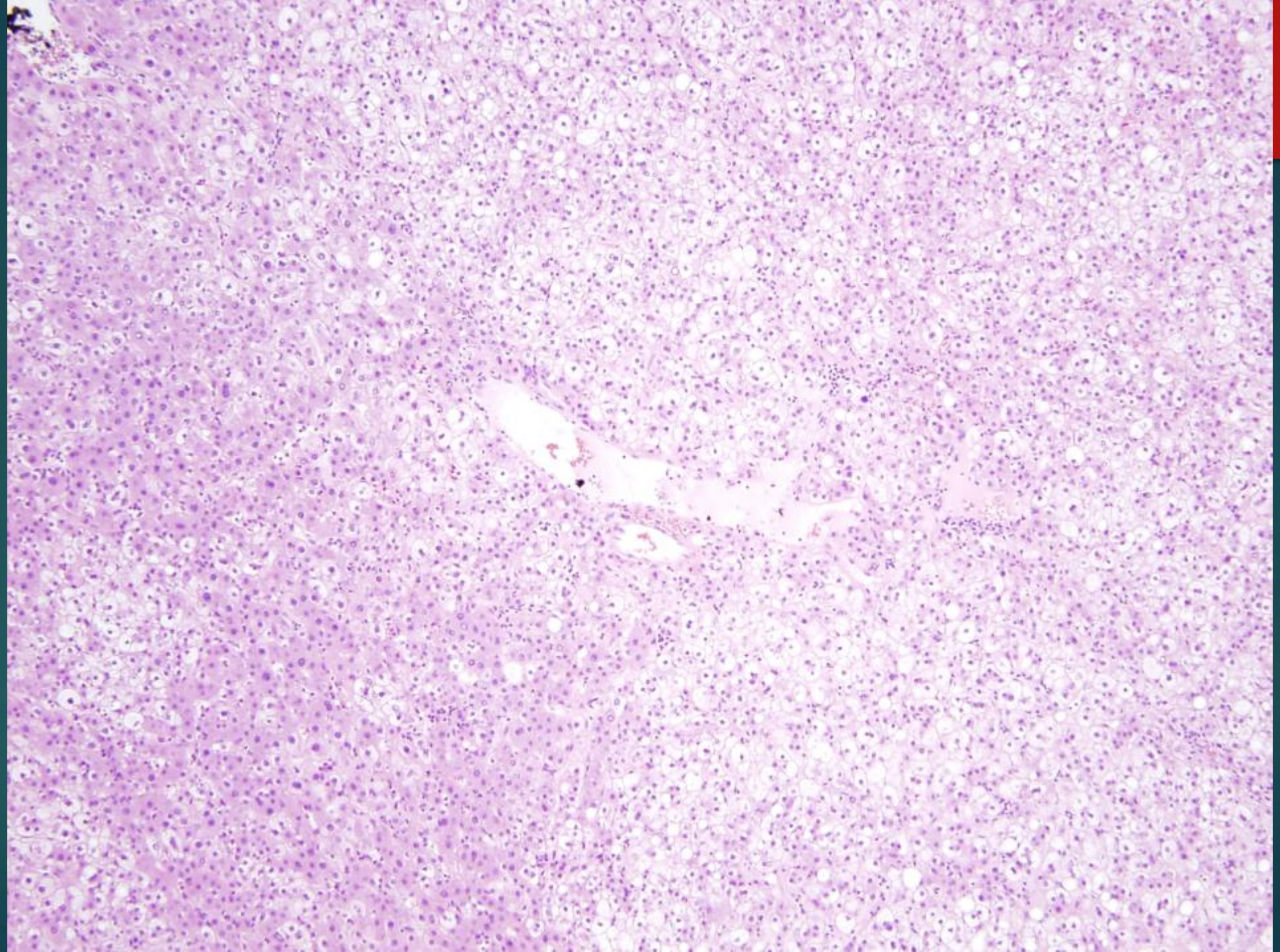

Arterial

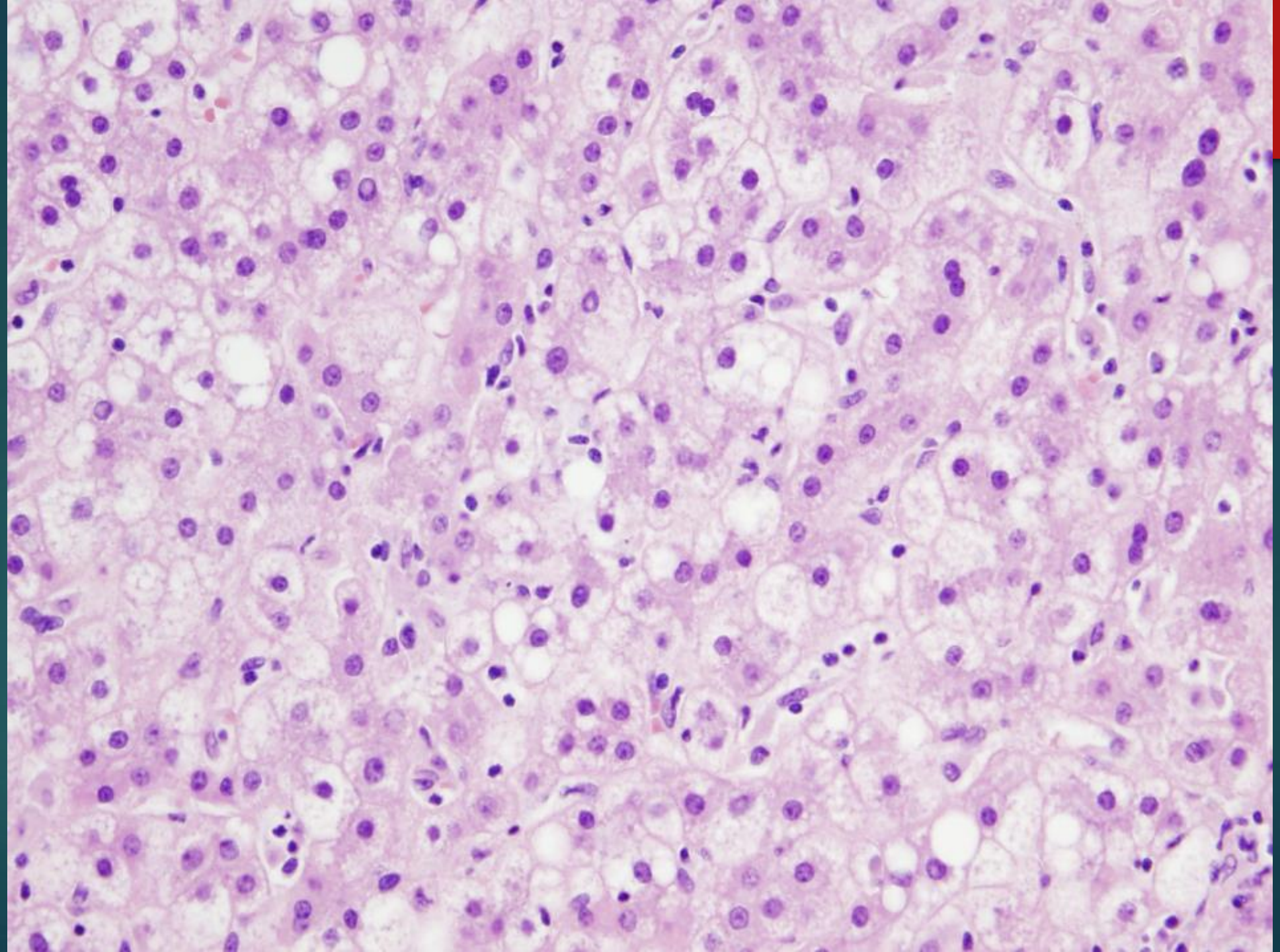

8 min Delay


T1 In phase
T1 Out of phase
Arterial
PVP
5 min Delay

MRN: 05844824
BS-14-44976
(resection only, biopsy unavailable)

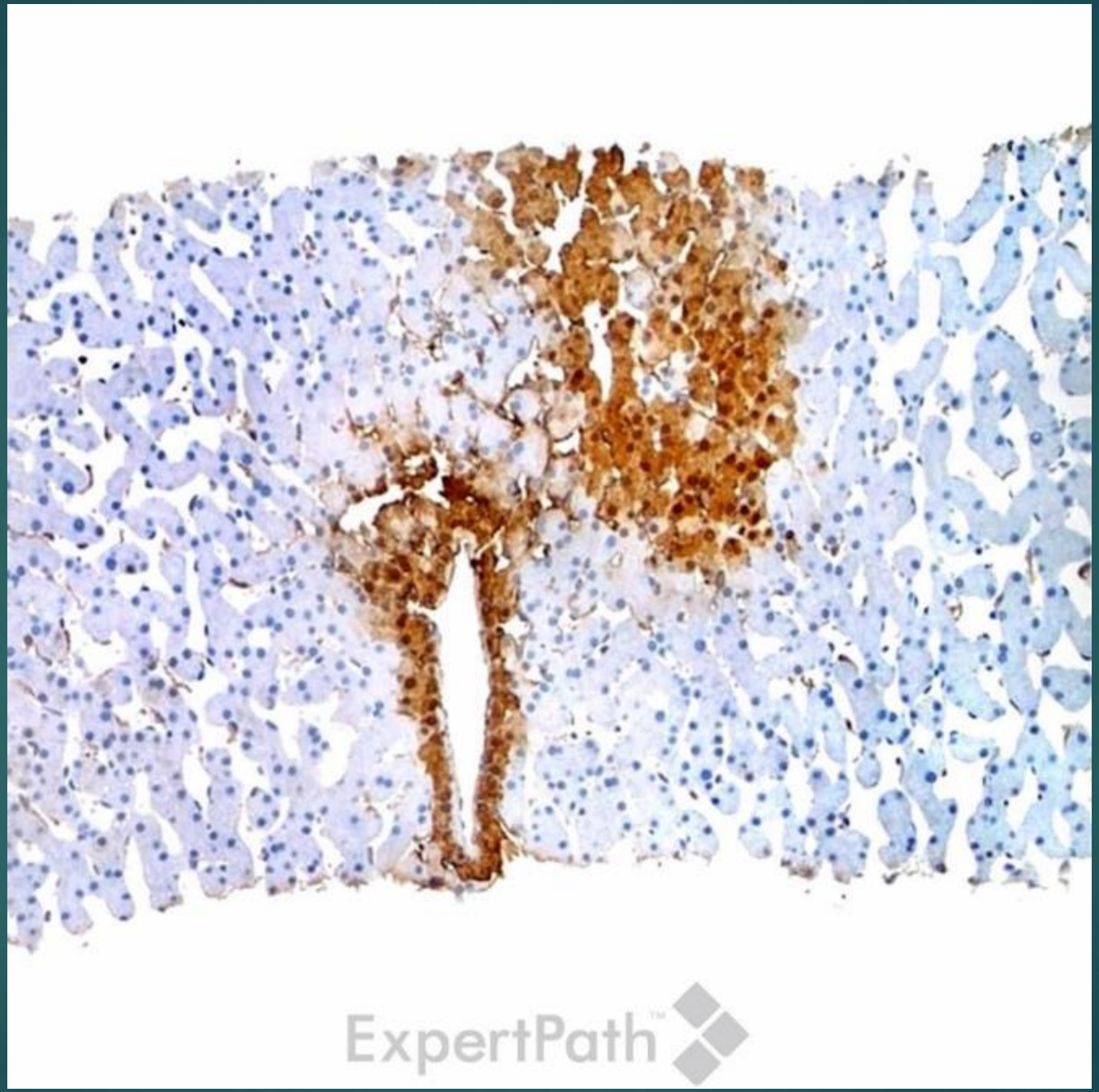






IHC

- Beta-catenin: negative (HCC positive)
- Glutamine synthetase: perivascular (HCC diffusely positive)
- Glypican-3 negative (HCC positive)


ExpertPath™

A. LIVER MASS, CORE BIOPSIES:
BENIGN HEPATOCELLULAR PROLIFERATION, see NOTE.

B. LIVER PARENCHYMA, CORE BIOPSIES:
Fragments of BENIGN HEPATOCELLULAR PROLIFERATION, see NOTE.
Non-neoplastic liver parenchyma with focal mild steatosis.
No fibrosis.
No iron.

NOTE: The findings are most consistent with adenoma, and the radiologic features of multiple smaller nodules with a similar enhancement pattern (as well as the presence of lesional tissue in both the mass and parenchymal biopsies) raises the possibility of adenomatosis. Histologic features of hepatocellular carcinoma are not seen. Clinical correlation is needed.

B-catenin, glypican-3 and glutamine synthetase immunostains examined for the final diagnosis (part A). Iron, trichrome, and reticulin stains were examined for the diagnosis (part B).

What is the average size of a hepatic adenoma?

- A) <1cm
- B) 1-8 cm
- C) 8-15 cm
- D) 15-25 cm

Chaib, et al. Hepato-gastroenterology. 2007; 54(1382-1387)

Hepatic Adenoma

- Sheets of hepatocytes without bile ducts or portal areas
- Prone to necrosis and hemorrhage, lacks of central vascular supply
- Hypervascular but without neoplastic neovascularity fast wash-out
- Well-defined contour with subcapsular feeding arteries
- Consider in patients on oral contraceptives, anabolic steroids, or history of glycogen storage disease
- Surgical resection is recommended for >5cm, given risk of malignant transformation
- Biopsy is not recommended due to misdiagnosis and hemorrhage

Gragioli et al. Radiographics 2001. 24(4)

Thin fibrous pseudocapsule - 30%

- Less arterial enhancement
- Even hypodense on portal venous phase because fibrous tissue enhances slowly
- Best seen on delayed phase as relatively hypodense
- DDx: Adenoma, HCC, cystadenoma or cystadenocarcinoma
- HCC is most common

10% of Adenomas Contain Fat

Table 1
Liver Lesions Containing Macroscopic Fat

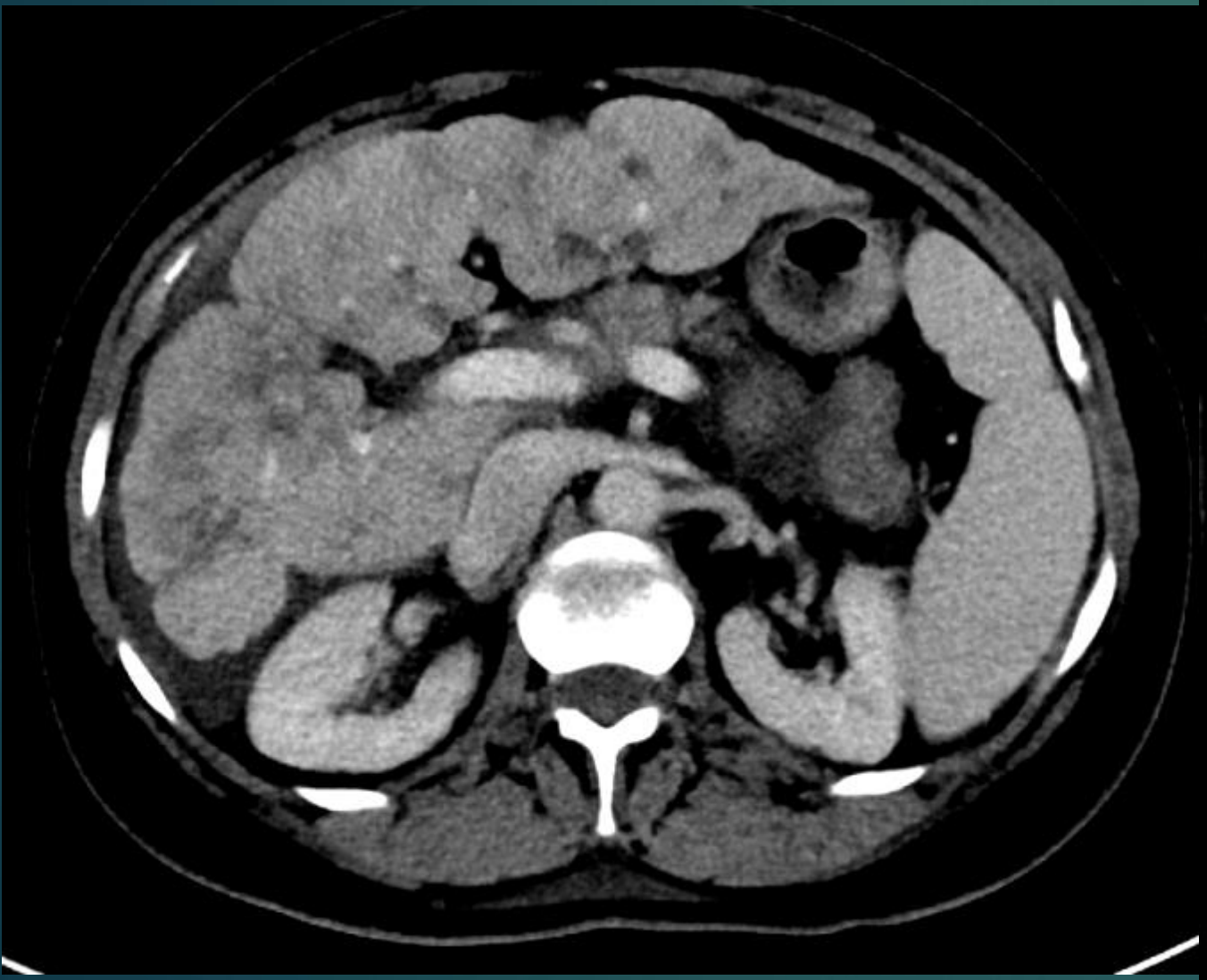
Type of Lesion	Lesions Containing Only Fat	Lesions Containing Fat and Soft Tissue
Benign	Lipoma	Adenoma
	Xanthoma (Langerhans cell histiocytosis)	Hepatic adrenal rest tumor
	Postoperative packing material (omentum)	Angiomyolipoma
		Teratoma
Malignant	Primary liposarcoma	Hepatocellular carcinoma
	Metastatic liposarcoma	Metastases
		Primary liposarcoma
		Metastatic liposarcoma

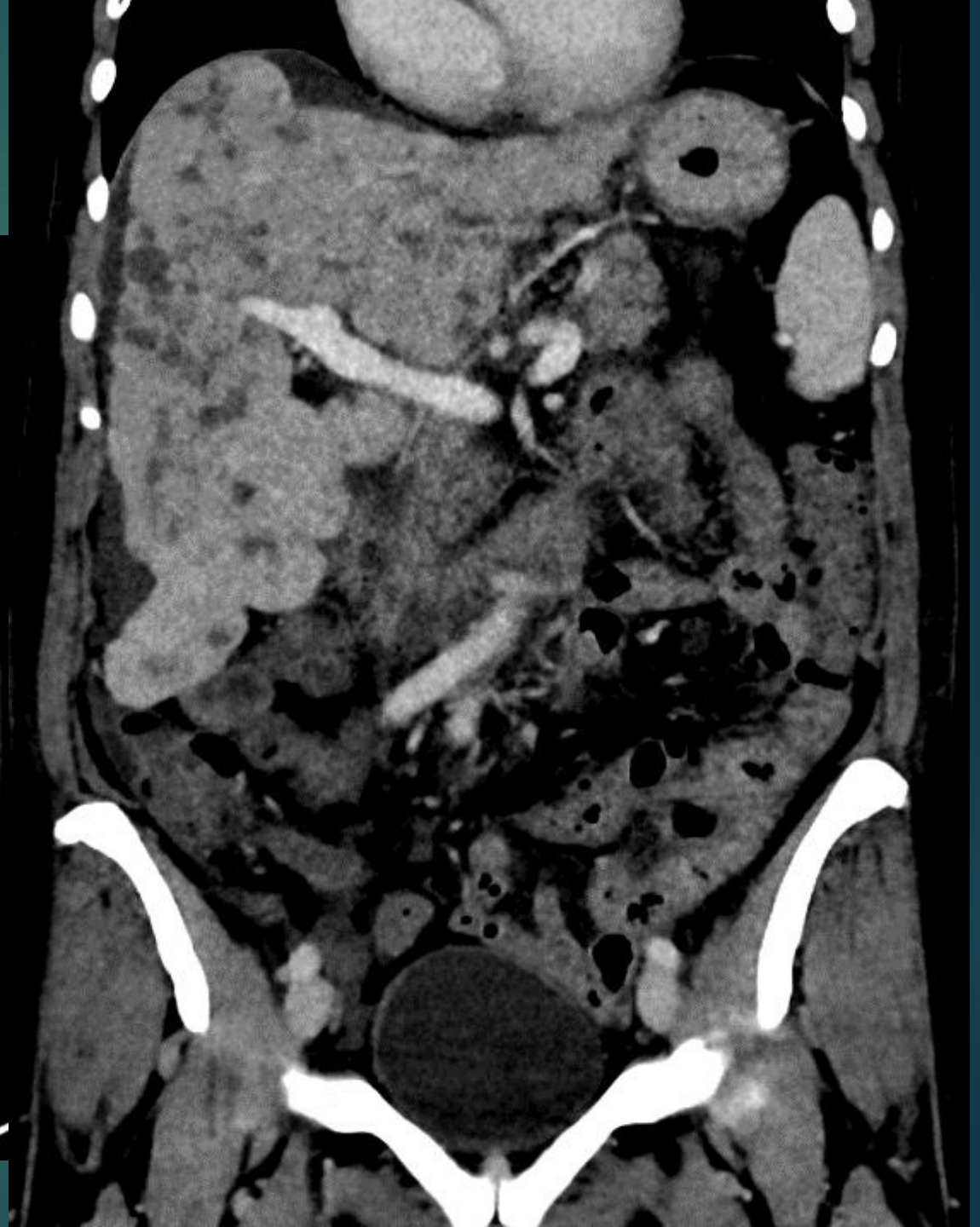
Prasad et al. RadioGraphics 2005; 25(321-331)

Case 3

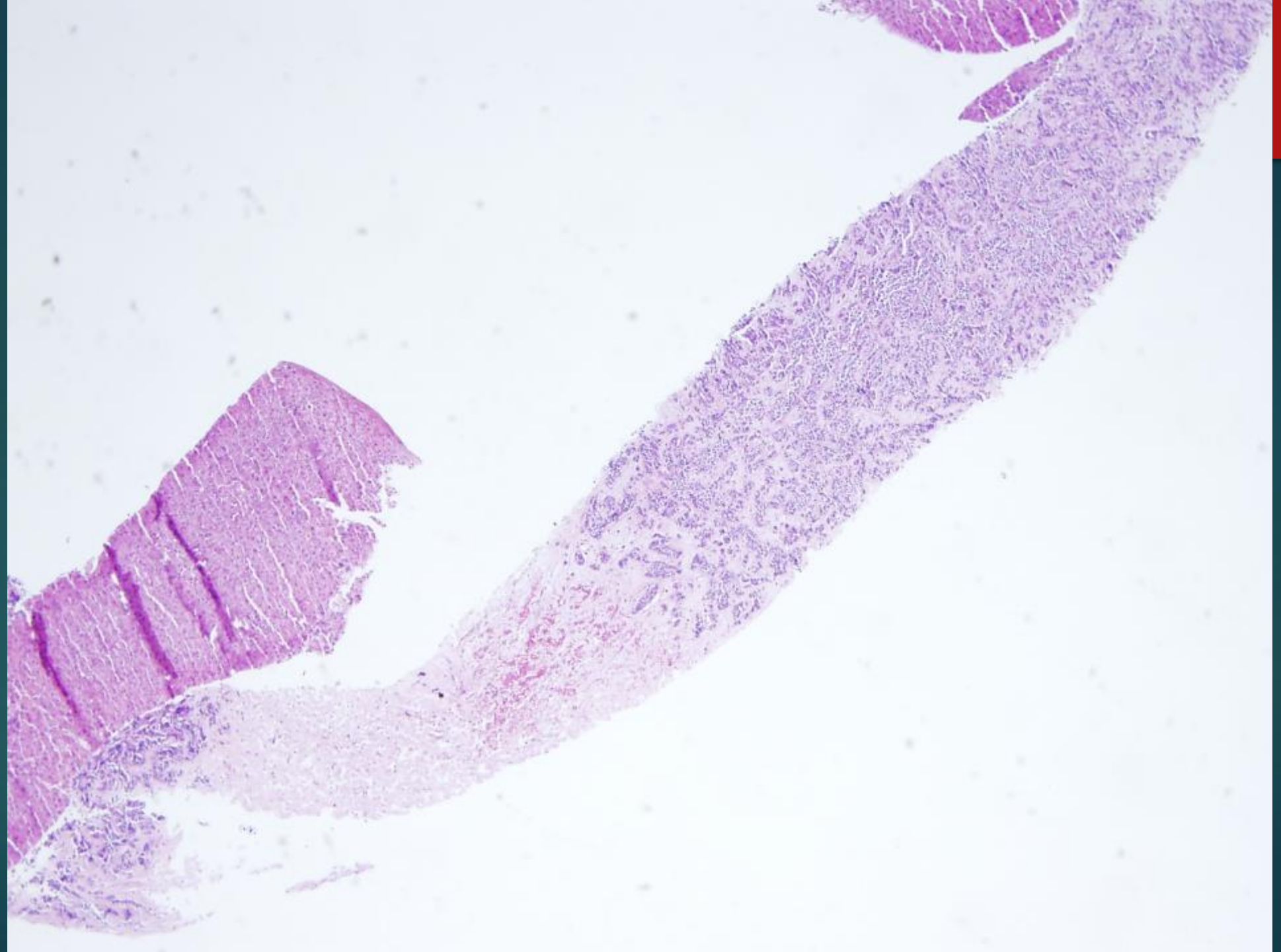
- 64 YOF presenting to the ED with epigastric discomfort
- History of brain meningioma, bilateral mastectomies and oophorectomy

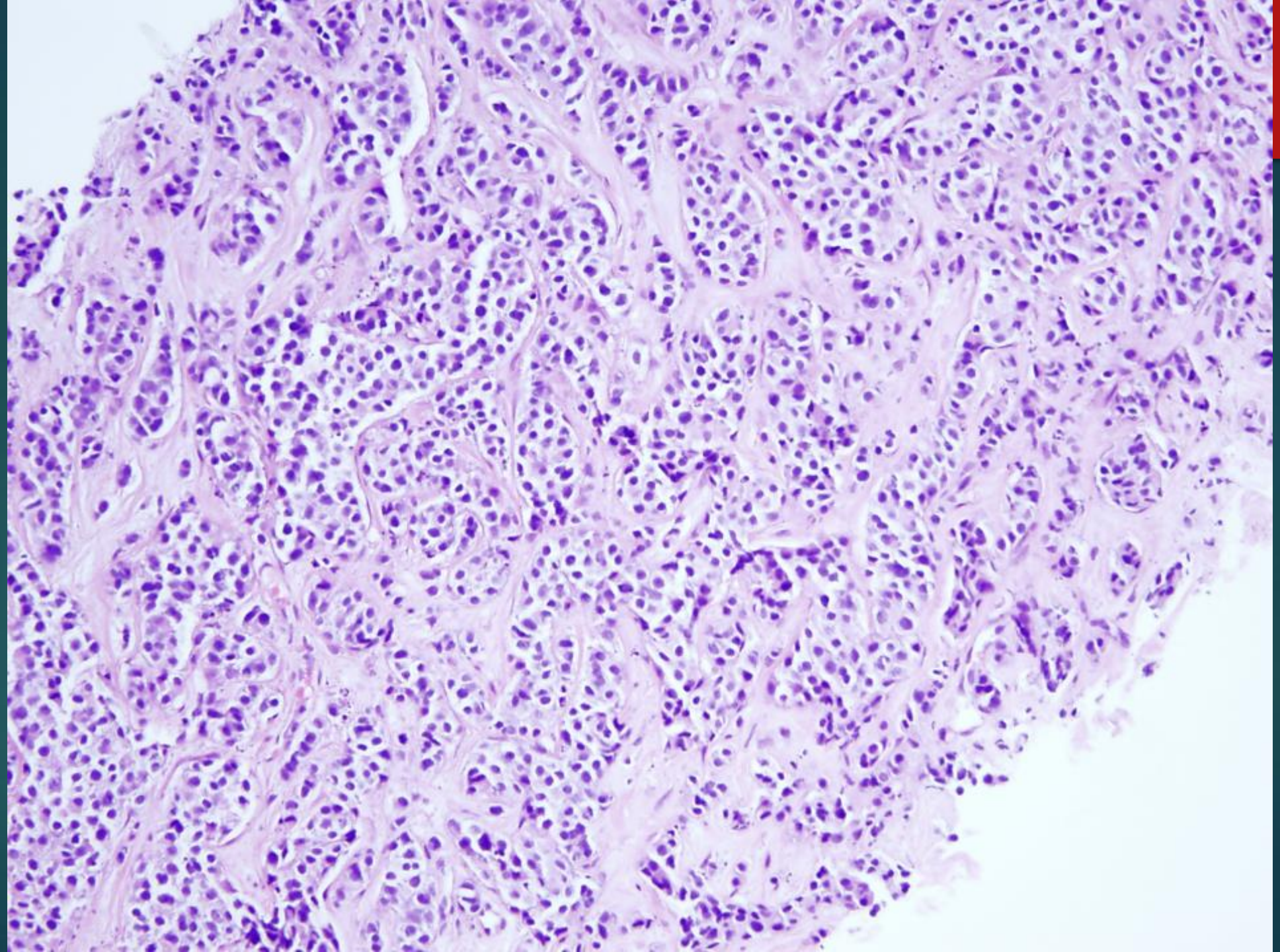
Case 3





MRN: 02526671
BS-16-01572
(liver biopsy)





LIVER, CORE NEEDLE BIOPSY FOR A MASS:

METASTATIC CARCINOMA to the liver, consistent with spread from a breast primary carcinoma (see note).

Immunoperoxidase studies were performed at BWH on formalin fixed tissue with the following results for metastatic carcinoma (block A1):

ESTROGEN RECEPTOR	POSITIVE (>95% moderate to strong)
PROGESTERONE RECEPTOR	NEGATIVE (0%)
HER2/NEU (C-ERB-B2)	NEGATIVE (0)

External controls are evaluated and show appropriate immunoreactivity.

NOTE: The patient has a history of left breast DCIS and LCIS in 1999, and is status post bilateral mastectomies. She was found to have neck metastasis in 2012, most consistent with a breast primary, which was estrogen receptor positive, progesterone receptor negative and HER2 negative.

Fibrous liver mets that can cause capsular retraction include all EXCEPT?

- A) Lung
- B) Breast
- C) Neuroendocrine
- D) RCC
- E) Colon

Tan et al. Imaging Insights. 2016. 7(831)

Retraction of liver capsule

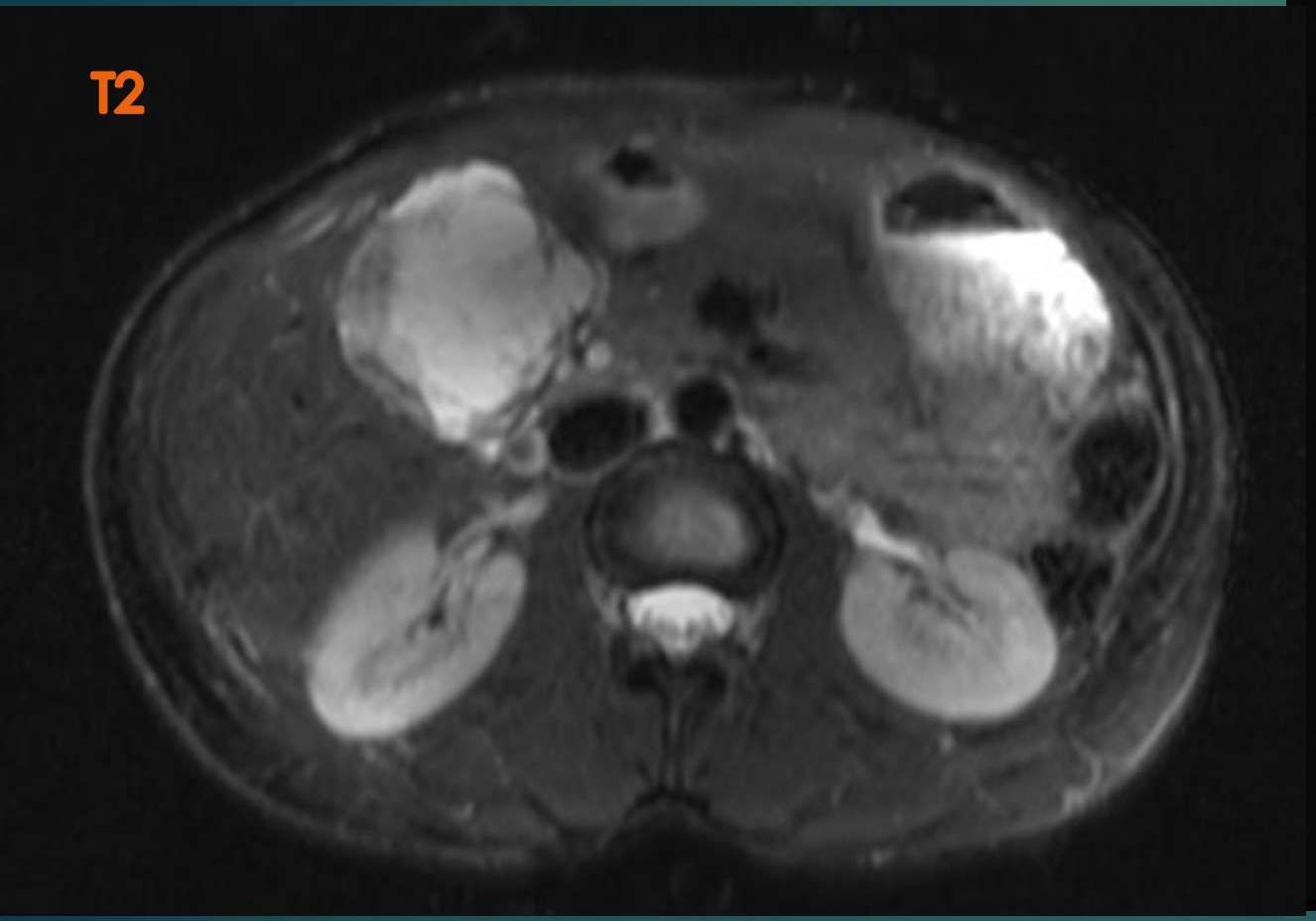
- Tumors with infiltrative growth and dense fibrous tissue that do not cause mass effect
- Treated breast mets can cause "pseudo-cirrhosis" appearance
- DDx: infiltrative cholangiocarcinoma, focal atrophy due to biliary or portal venous obstruction, sclerosed hemangioma, confluent hepatic fibrosis (cirrhosis)

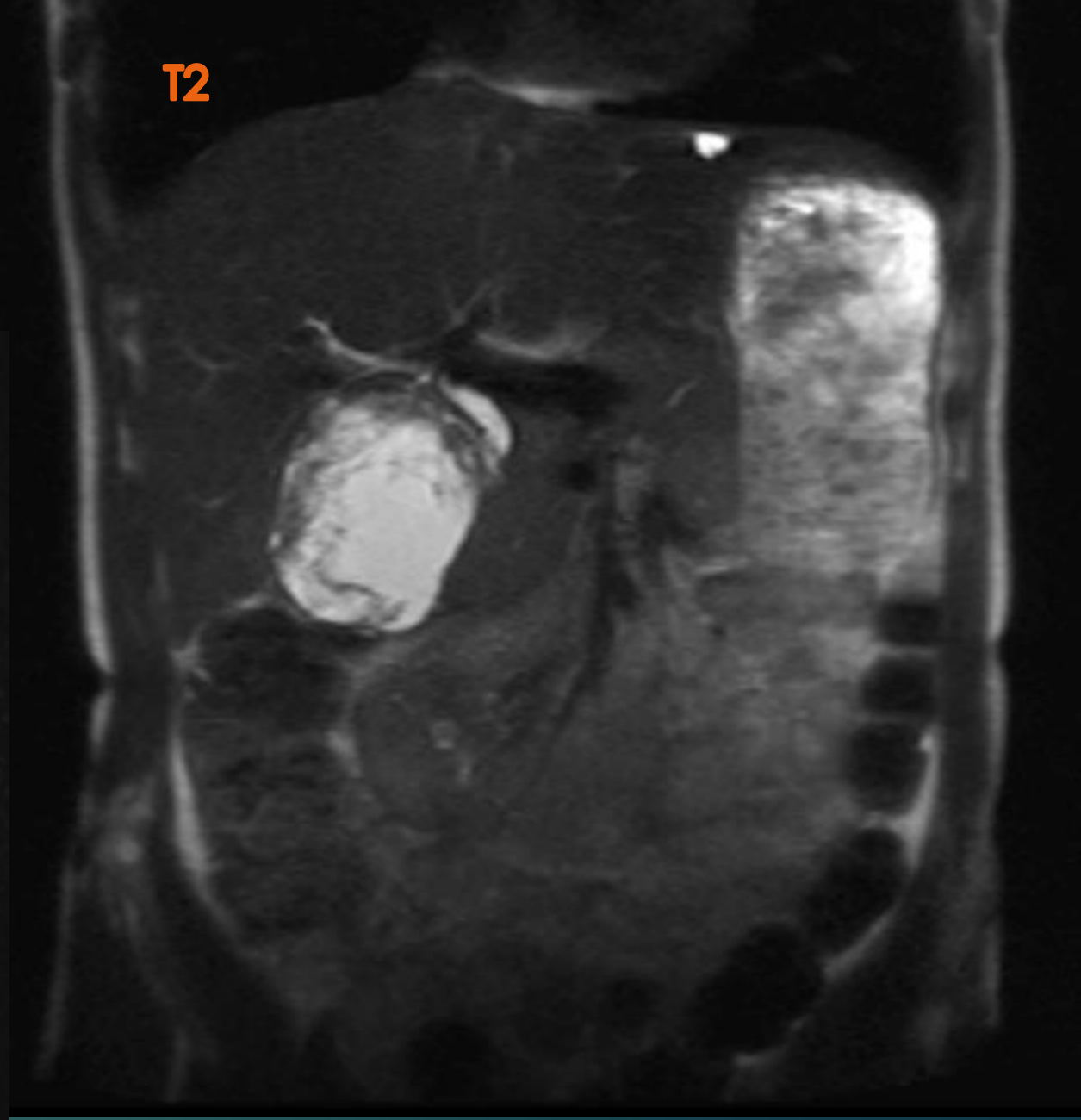
Tan et al. Imaging Insights. 2016. 7(831)

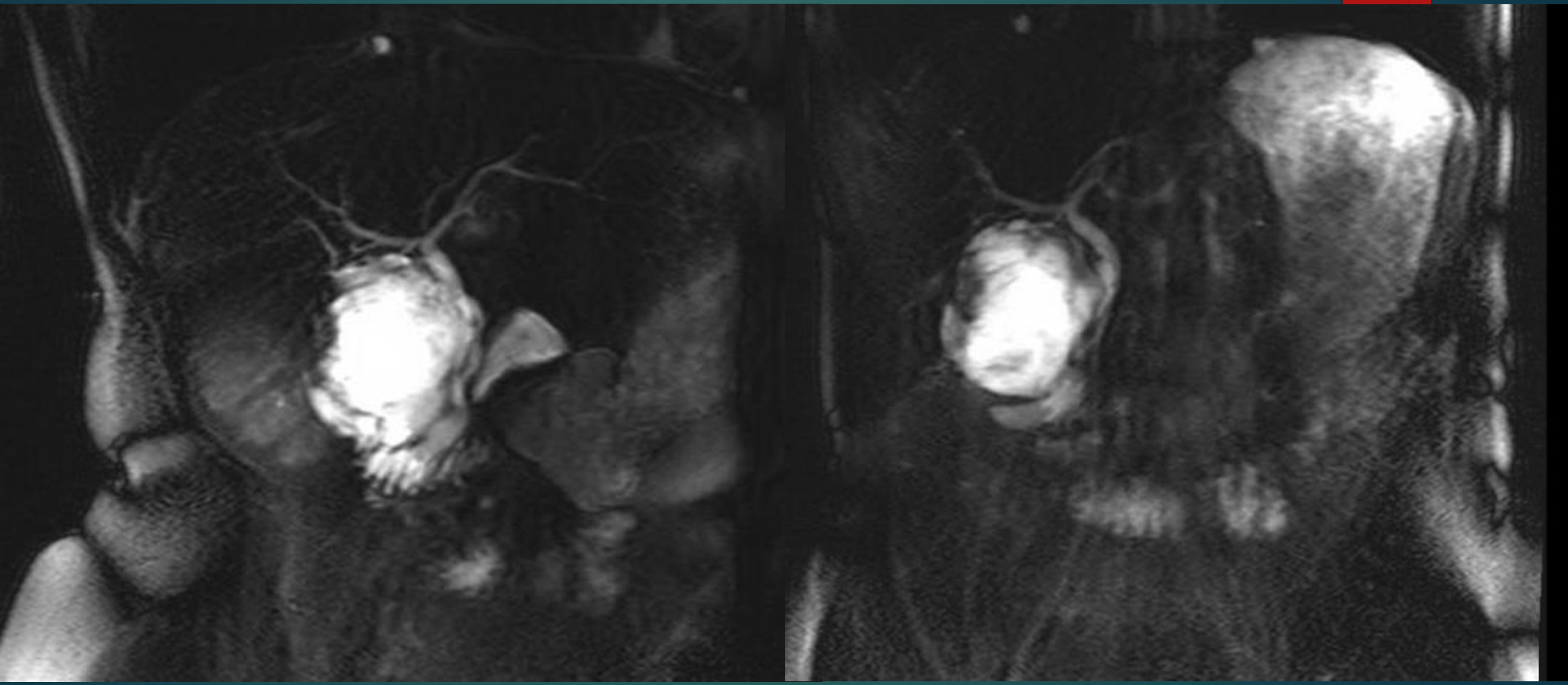
Case 4

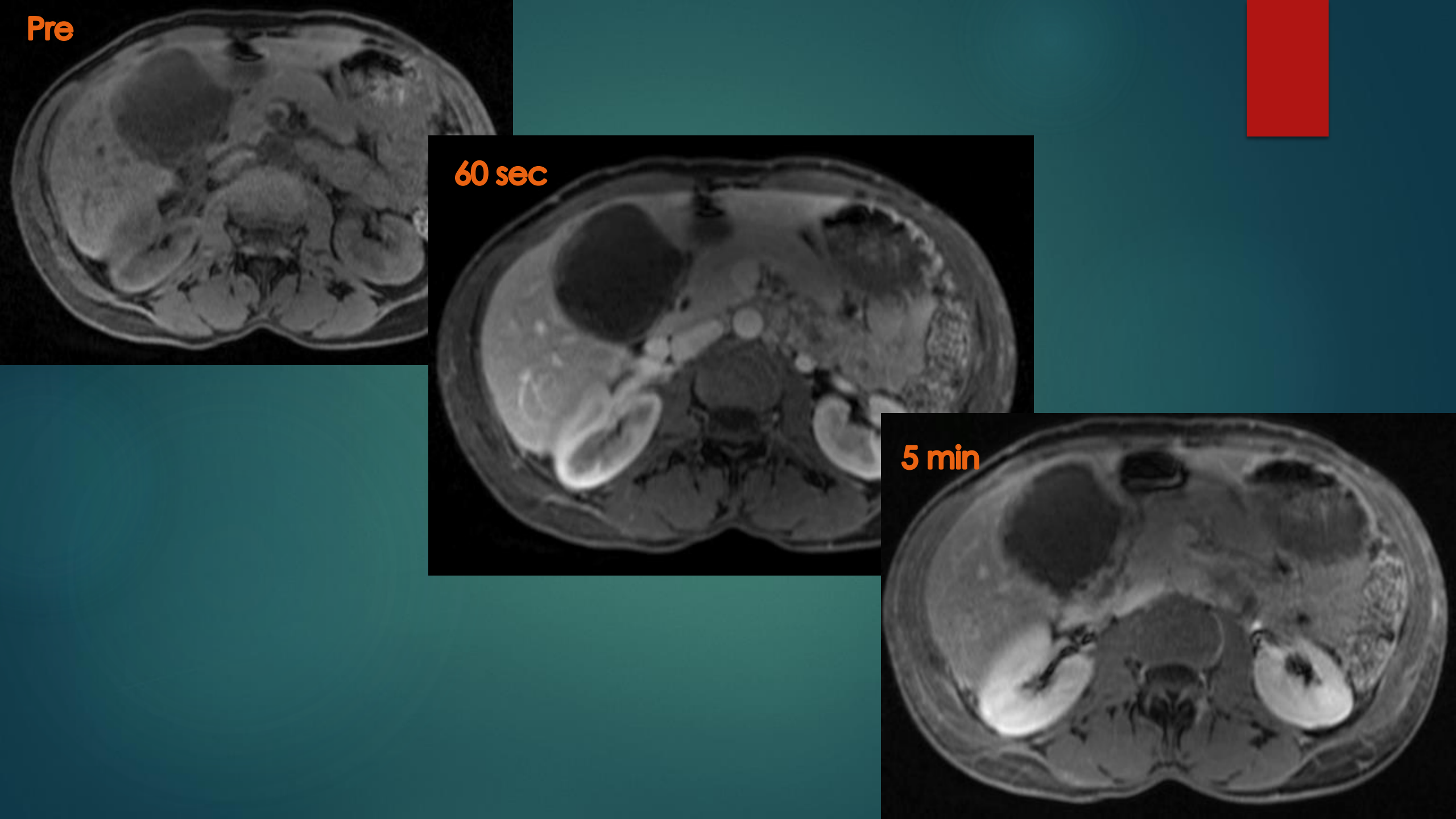
- 52 YOF underwent colonoscopy that found an unusual indentation felt to represent extrinsic compression from the liver

Case 4

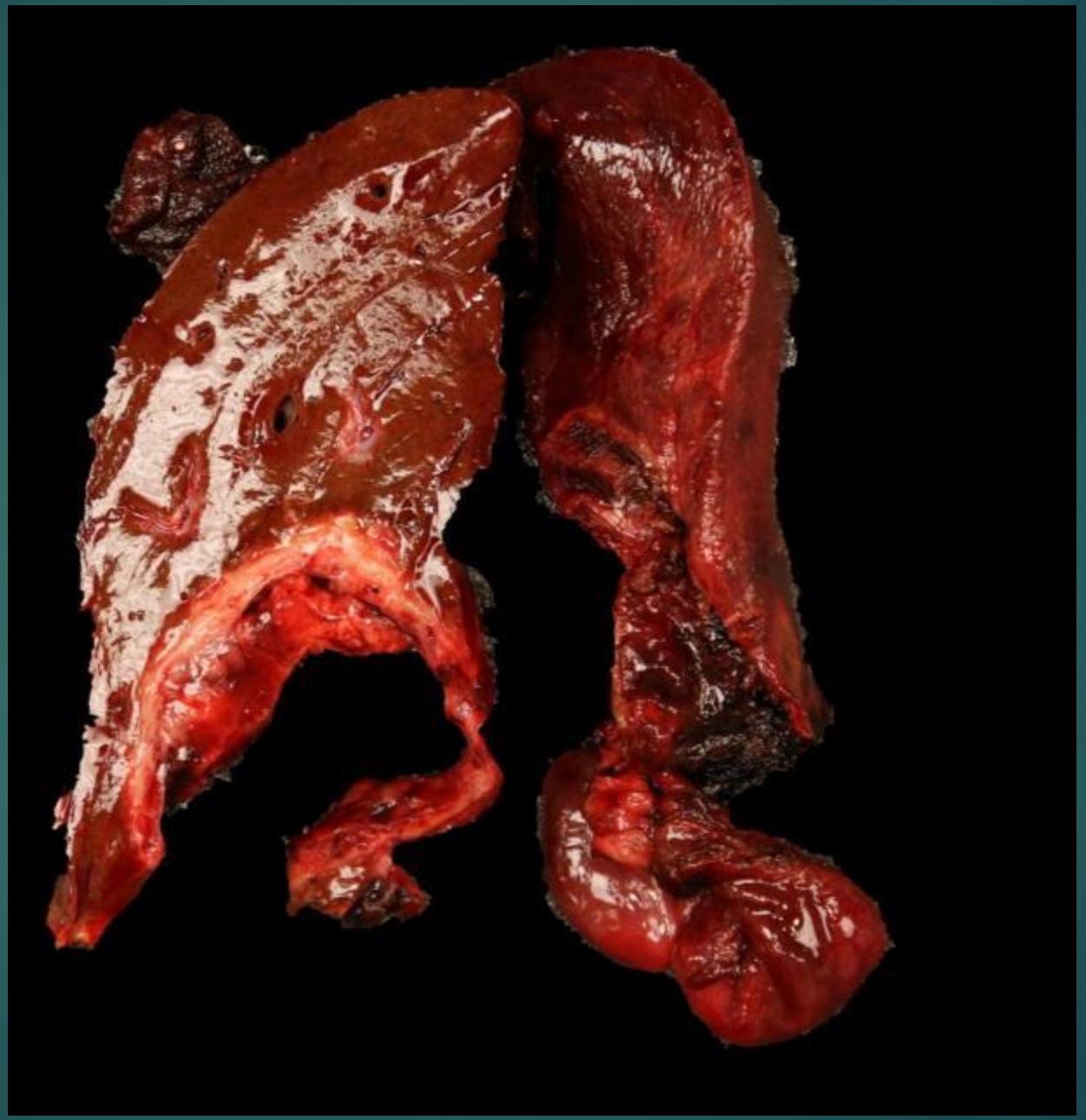


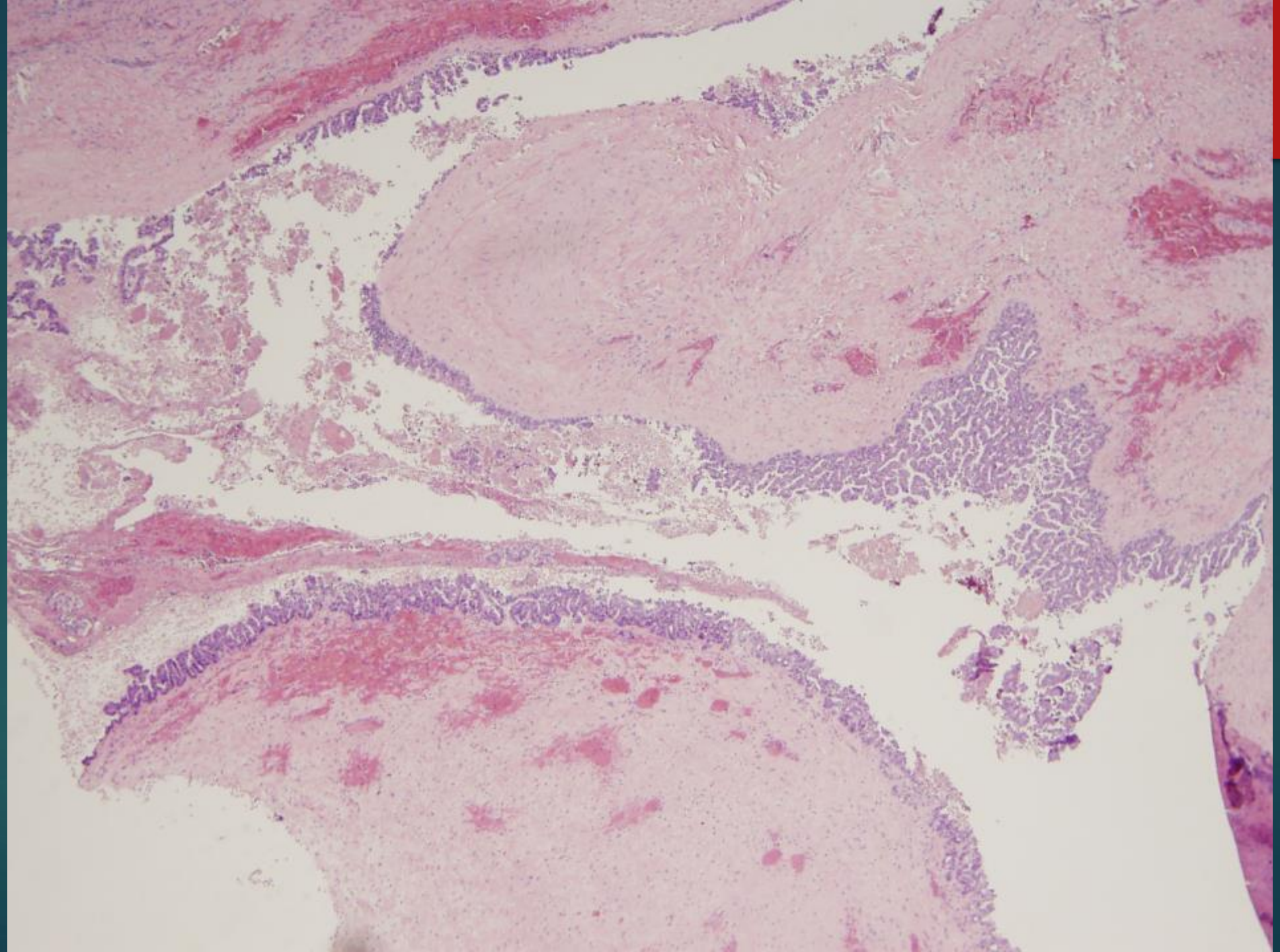


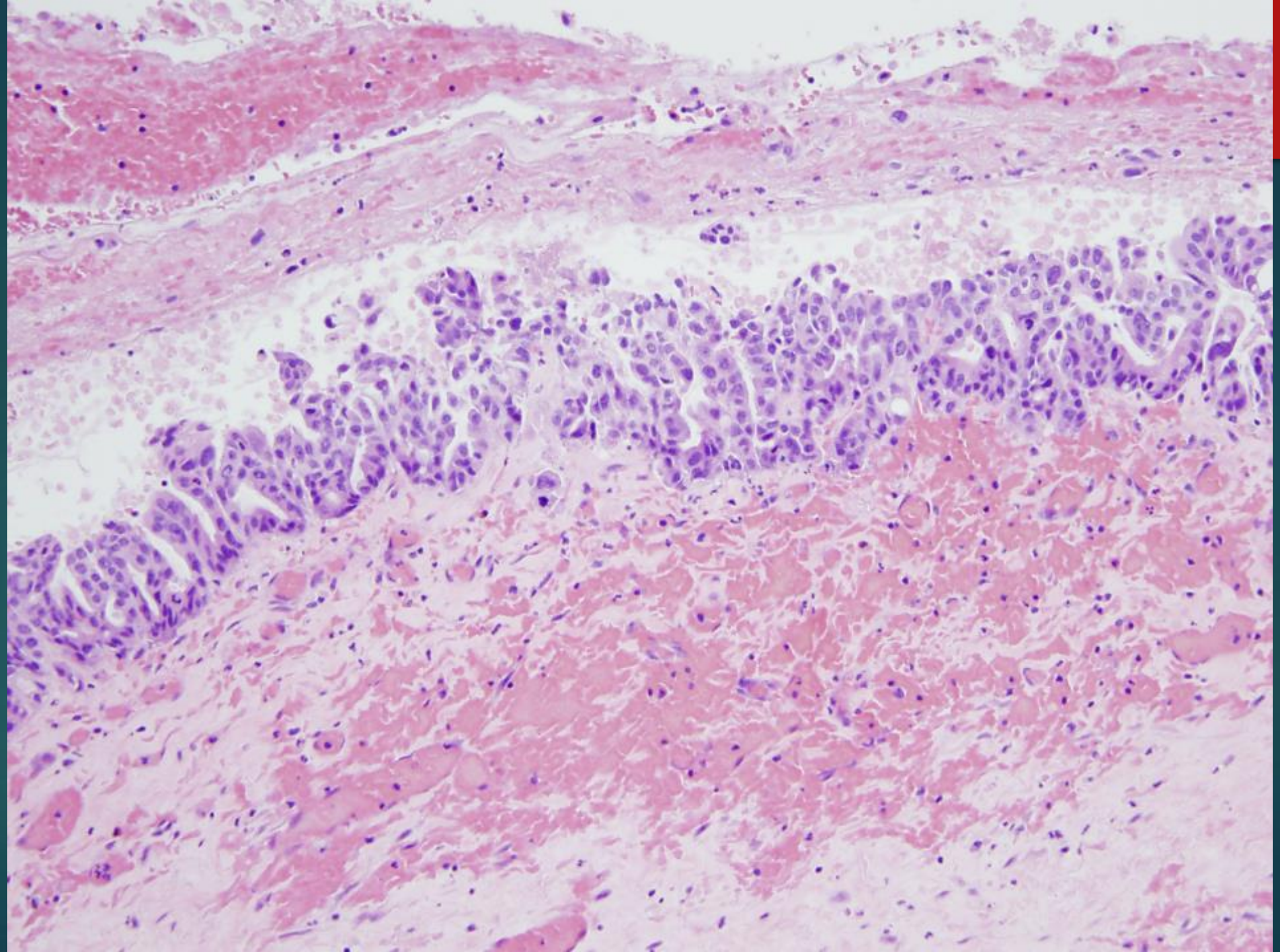


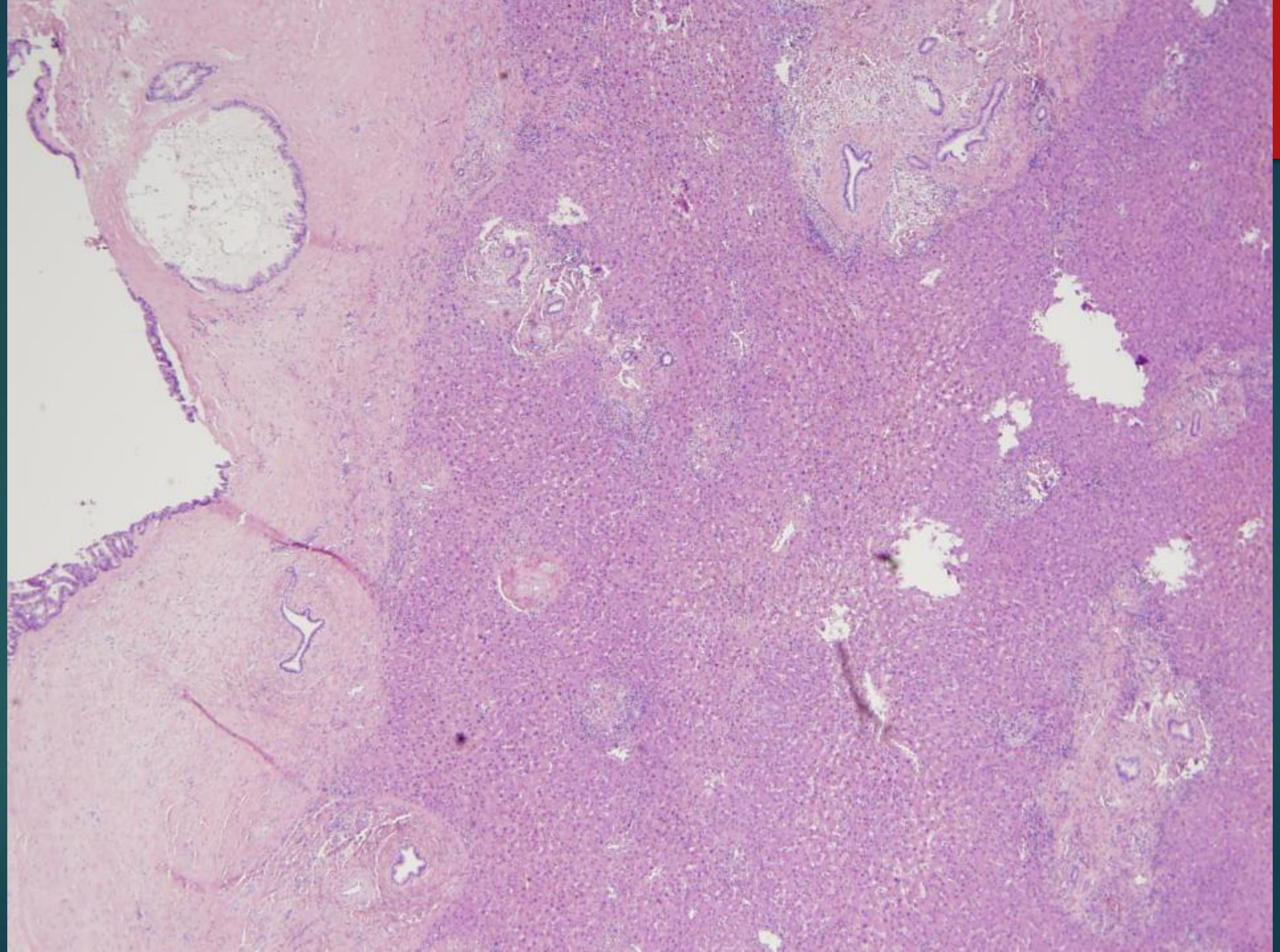

Pre
60 sec
5 min

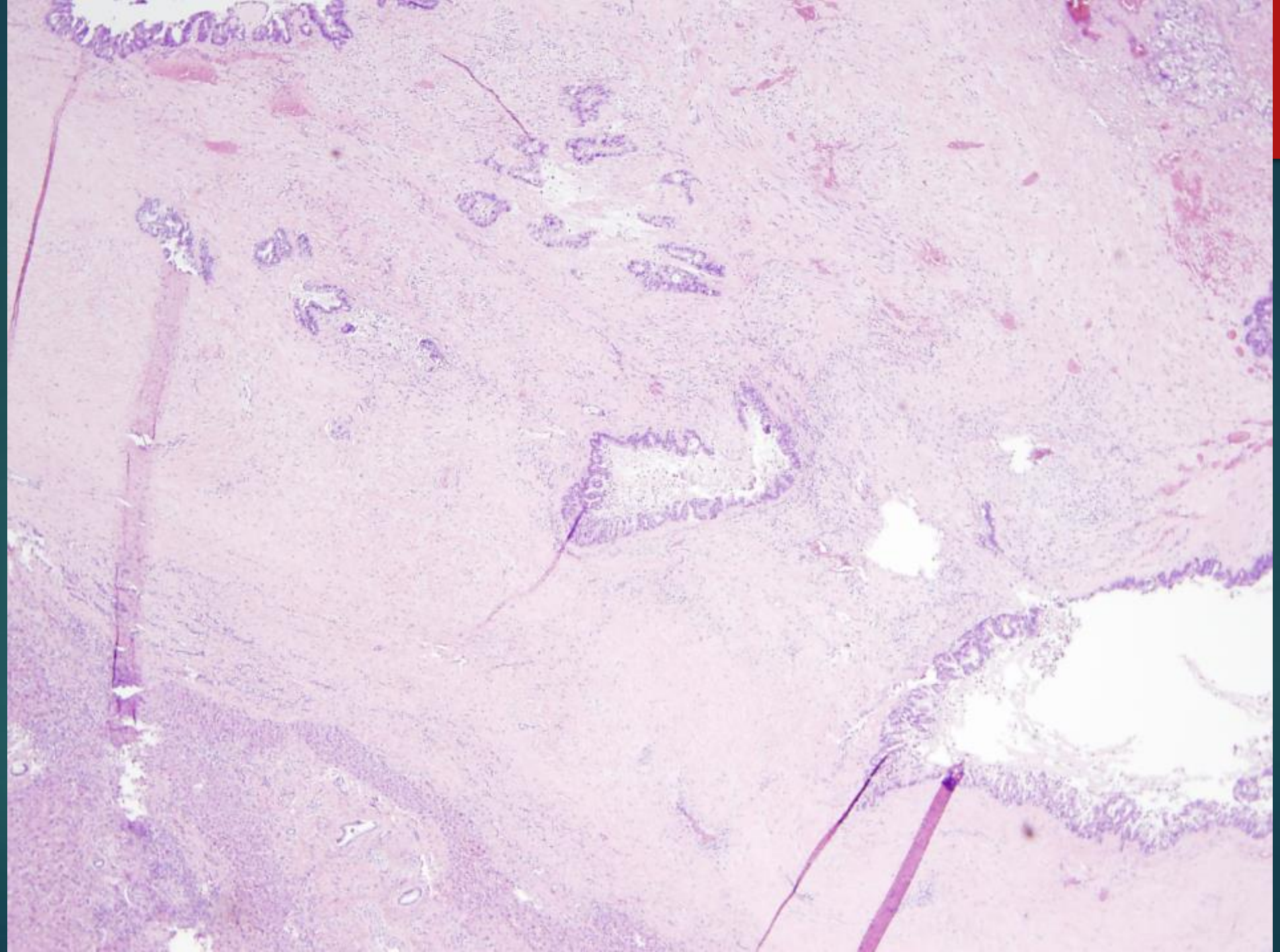
MRN: 31615537
BS-15-60008
(liver resection)

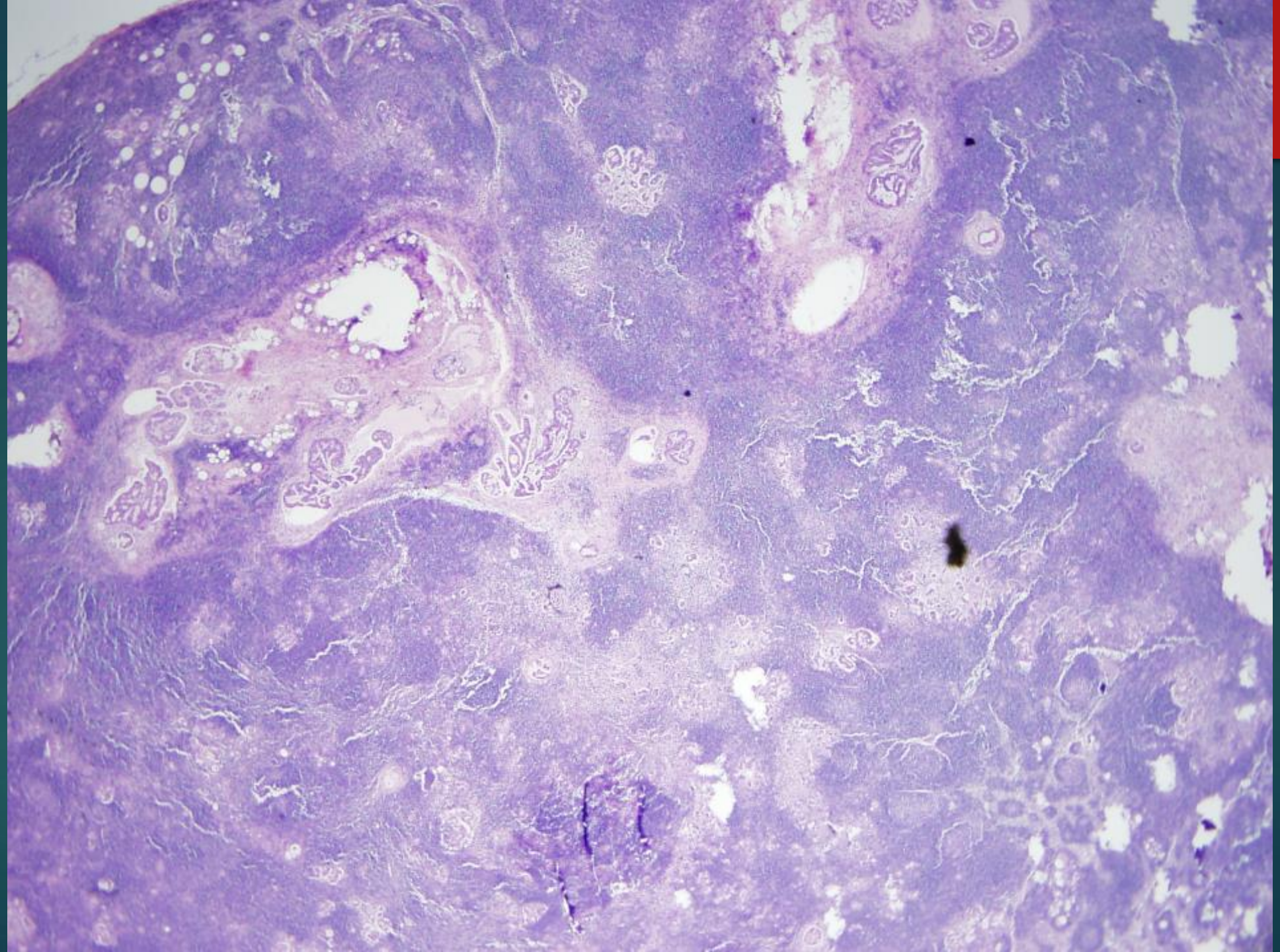










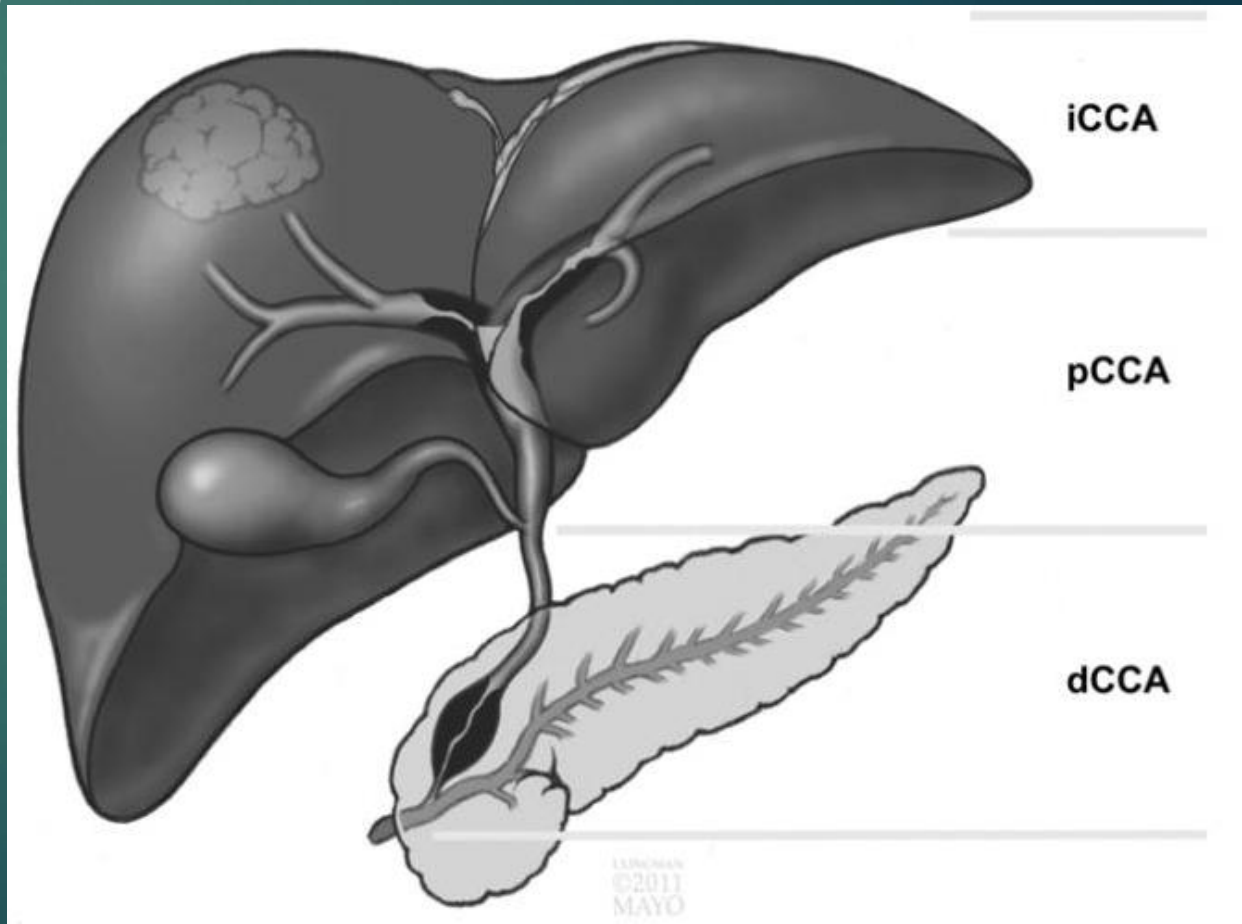


C. COMMON DUCT LYMPH NODE (INCLUDING FSC):
METASTATIC ADENOCARCINOMA involving lymph node.

D. RIGHT LIVER SEGMENT 5, 6, 7, 8 WITH GALLBLADDER (INCLUDING FSD):
INTRAHEPATIC CHOLANGIOCARCINOMA, MODERATELY DIFFERENTIATED (5.6 cm).
Carcinoma is present as a unifocal cystic mass.
The right hepatic duct margin is negative for carcinoma.
The venous resection margins are negative for carcinoma.
Invasive carcinoma is 0.4 cm from the hepatic parenchymal resection margin and 1.5 cm from the right hepatic duct resection margin.
Carcinoma does not perforate the hepatic capsule.
Extensive lymphovascular invasion is present in adjacent liver parenchyma.
Macroscopic/microscopic venous invasion is not identified.
Perineural invasion is not identified.
Non-neoplastic hepatic parenchyma within normal limits.
1+ stainable iron.
Iron, trichrome, and reticulin stains were examined for the diagnosis.
Gallbladder with no significant pathologic change.
AJCC Classification (7th edition): pT1 N1.

What is the most common location for cholangiocarcinoma (CCA)?

- A) Intrahepatic (iCCA)
- B) Perihilar (pCCA)
- C) Distal (dCCA)
- D) All are equal



Razumilava et al. Clinical Gasteroenterology and Hepatology. 2013;11(1)

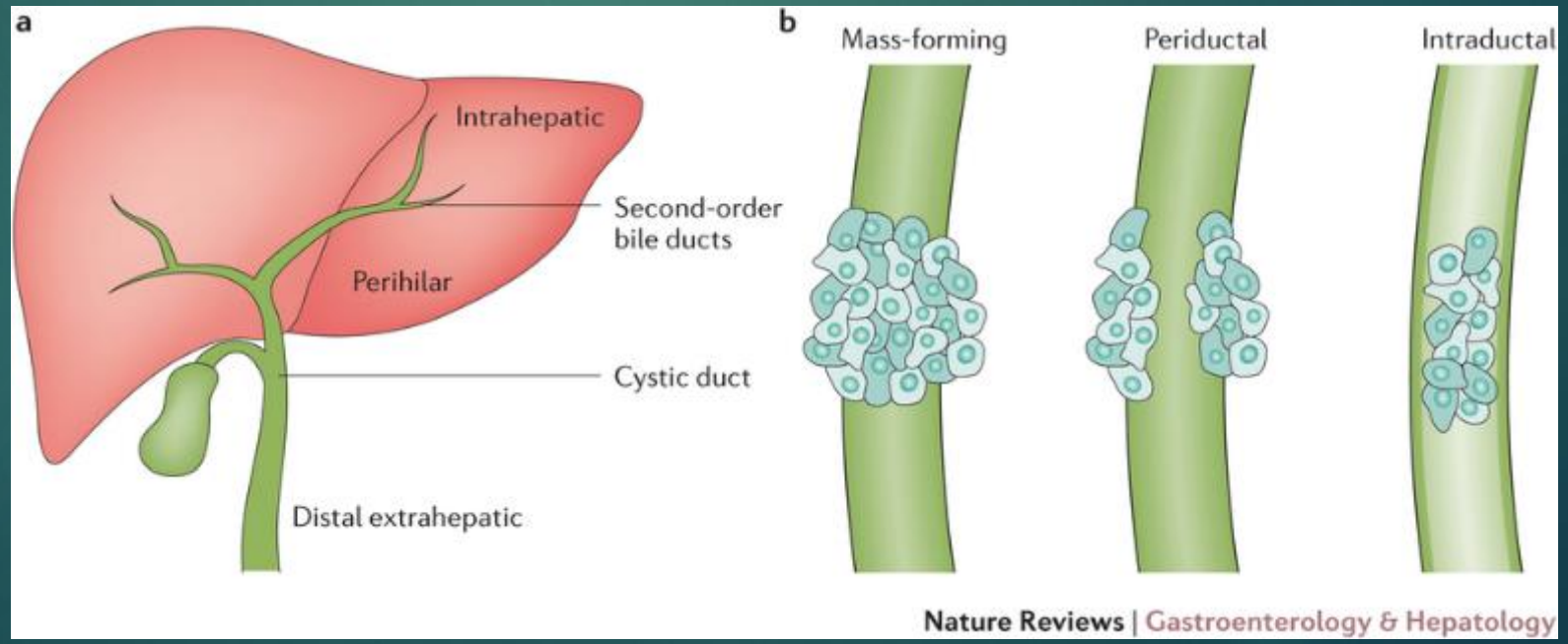
Cholangiocarcinoma

- Arise from cholangiocytes anywhere from the terminal ductules to the ampulla of Vader
- 90% adenocarcinoma, 10% squamous cell carcinoma
- Produces variable amounts of mucin, that mostly remains within the tumor
- Papillary, mucin-producing, or cystic type
- Lifetime risk with primary sclerosing cholangitis (PSC) is 5-10%
- Bile duct disorders and hepatitis C infection increase risk

Razumilava et al. Clinical Gasteroenterology and Hepatology. 2013;11(1)

Intraductal Papillary Biliary Neoplasm (IPNB)

- Similar to IPMN of the pancreas
- Variant of bile duct carcinoma and characterized by intraductal growth
- Precursor for invasive carcinoma
- Difficult to distinguish from mucinous cystic neoplasms on imaging

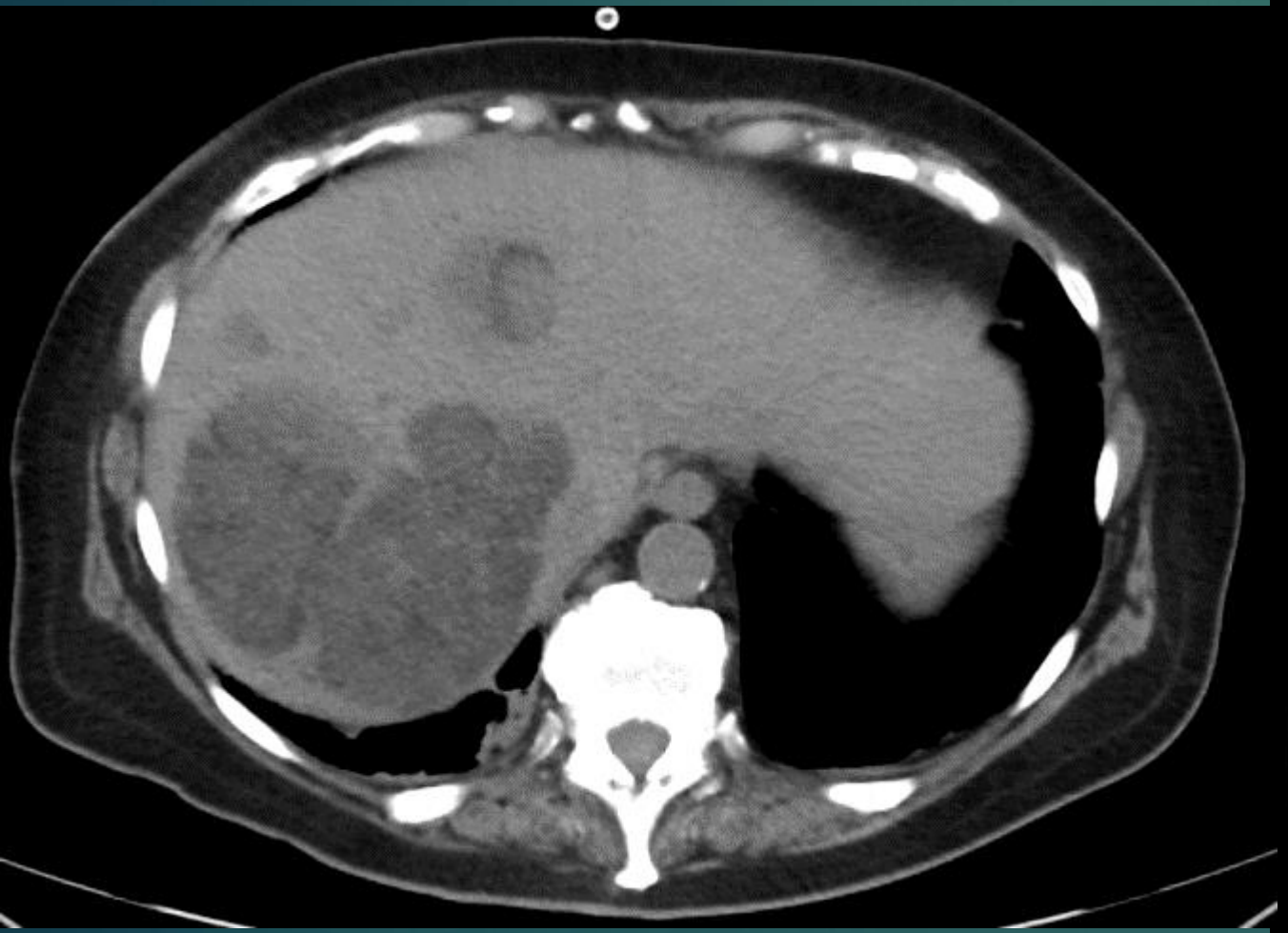


Banales, et al. Nature Reviews Gastroenterology and Hepatology. 2013; 16 (261-281)

Case 5

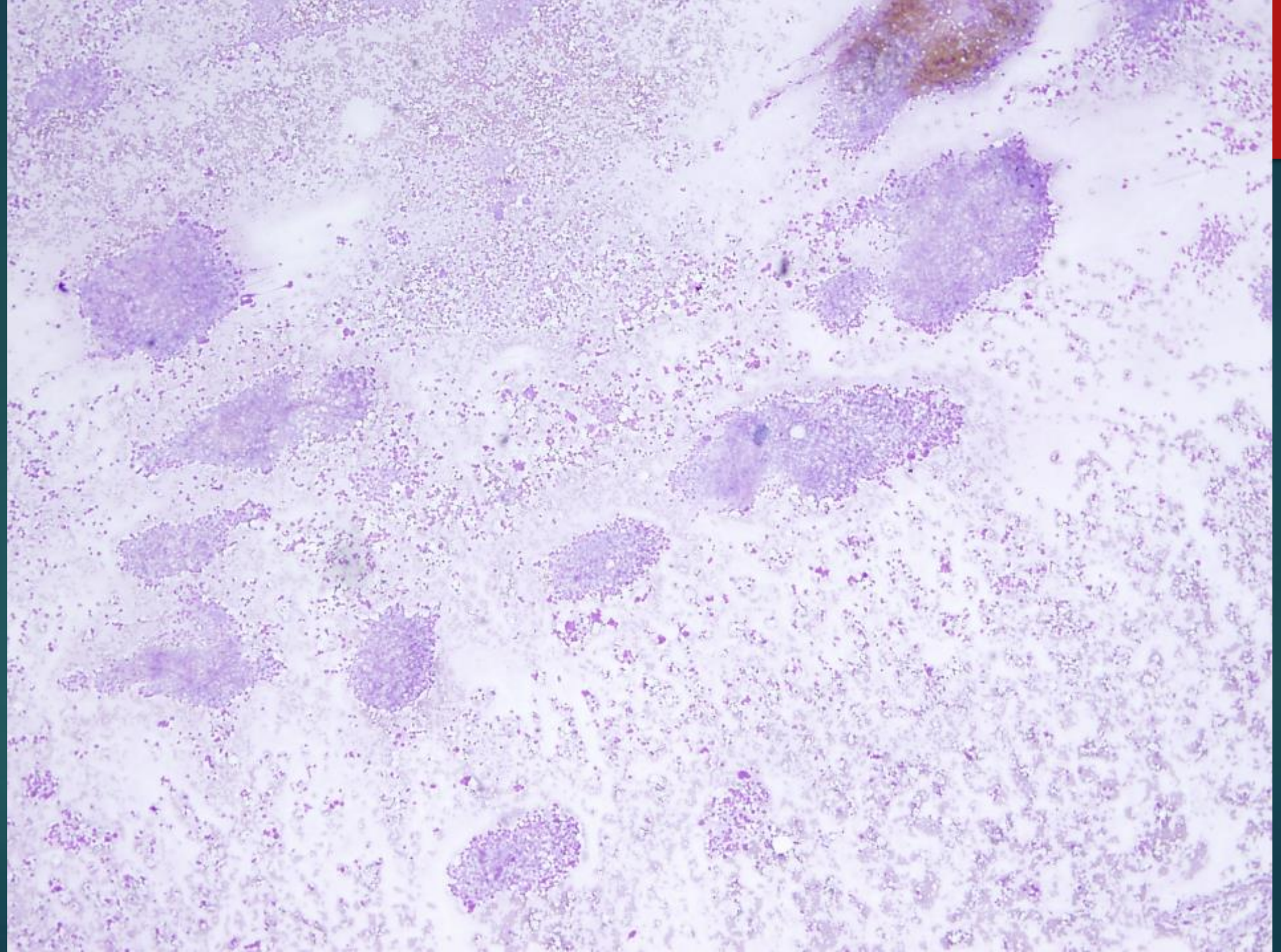
- 66 YOF with nausea, vomiting and dull achy right flank pain after striking herself against a picture frame while working as a cashier
- Denies fever, vomiting, nausea
- History of HTN, HL, and “Hepatitis-D”
- Elevated creatinine and LFTs

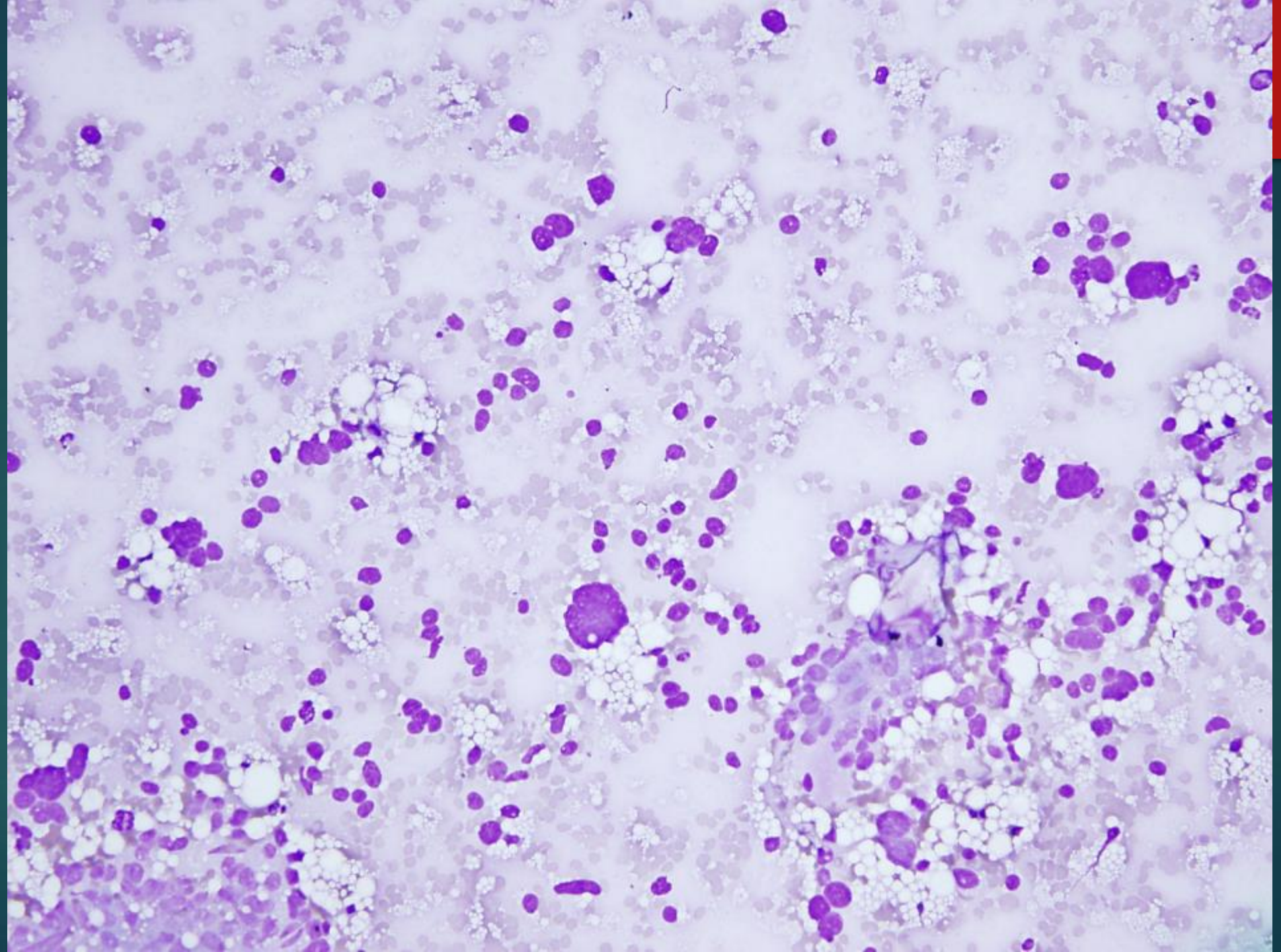
Case 5

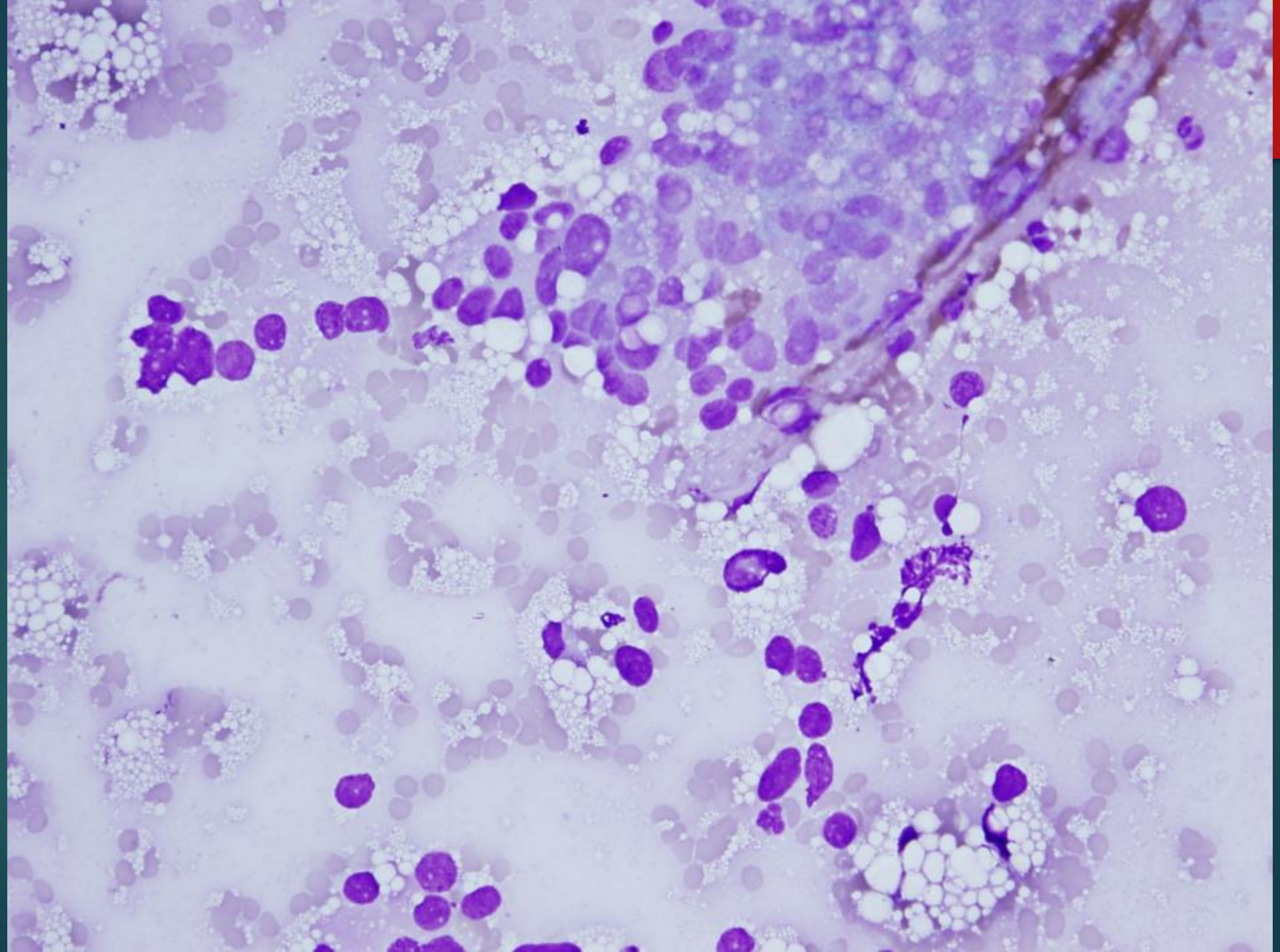


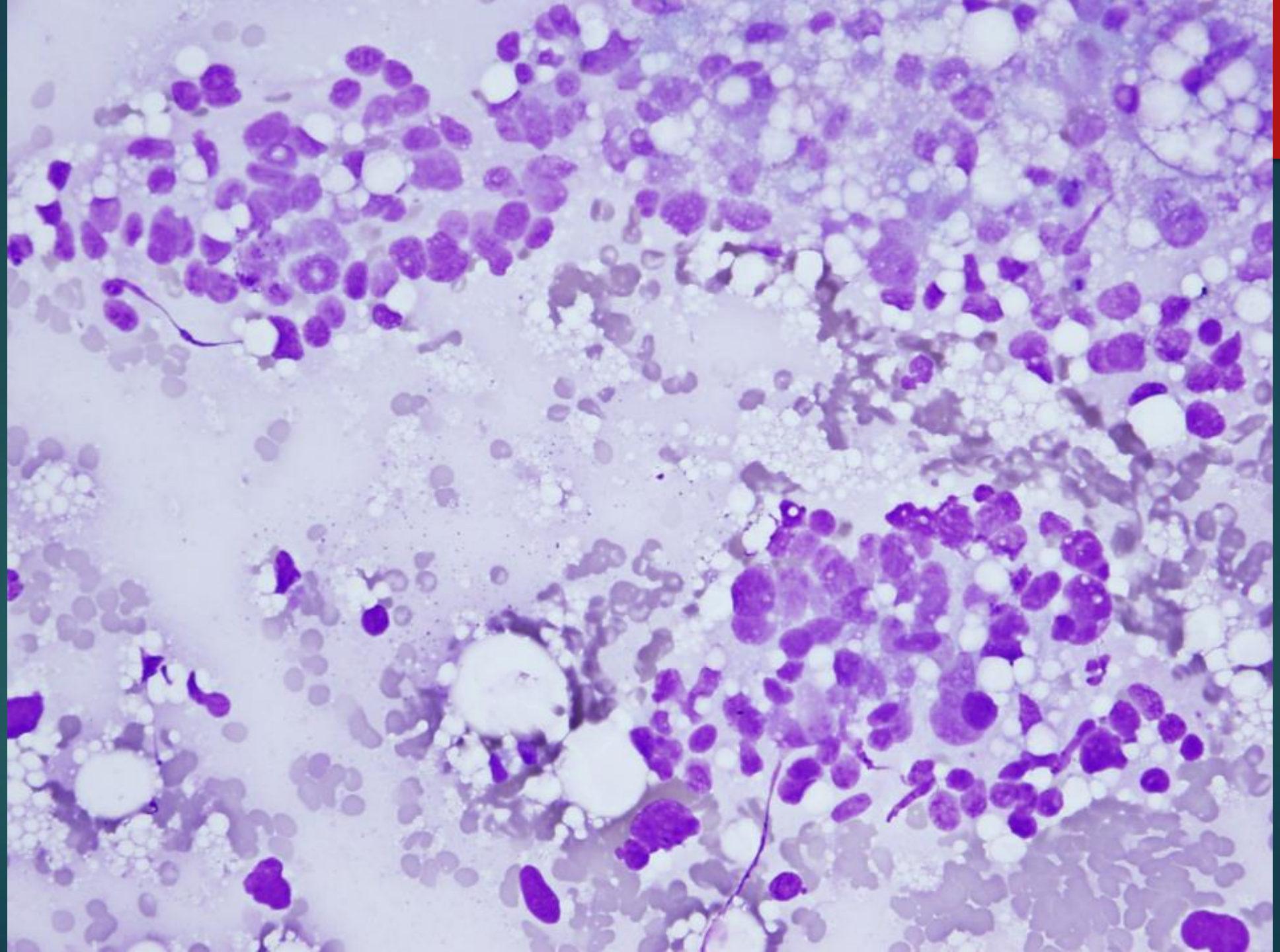
Case 5

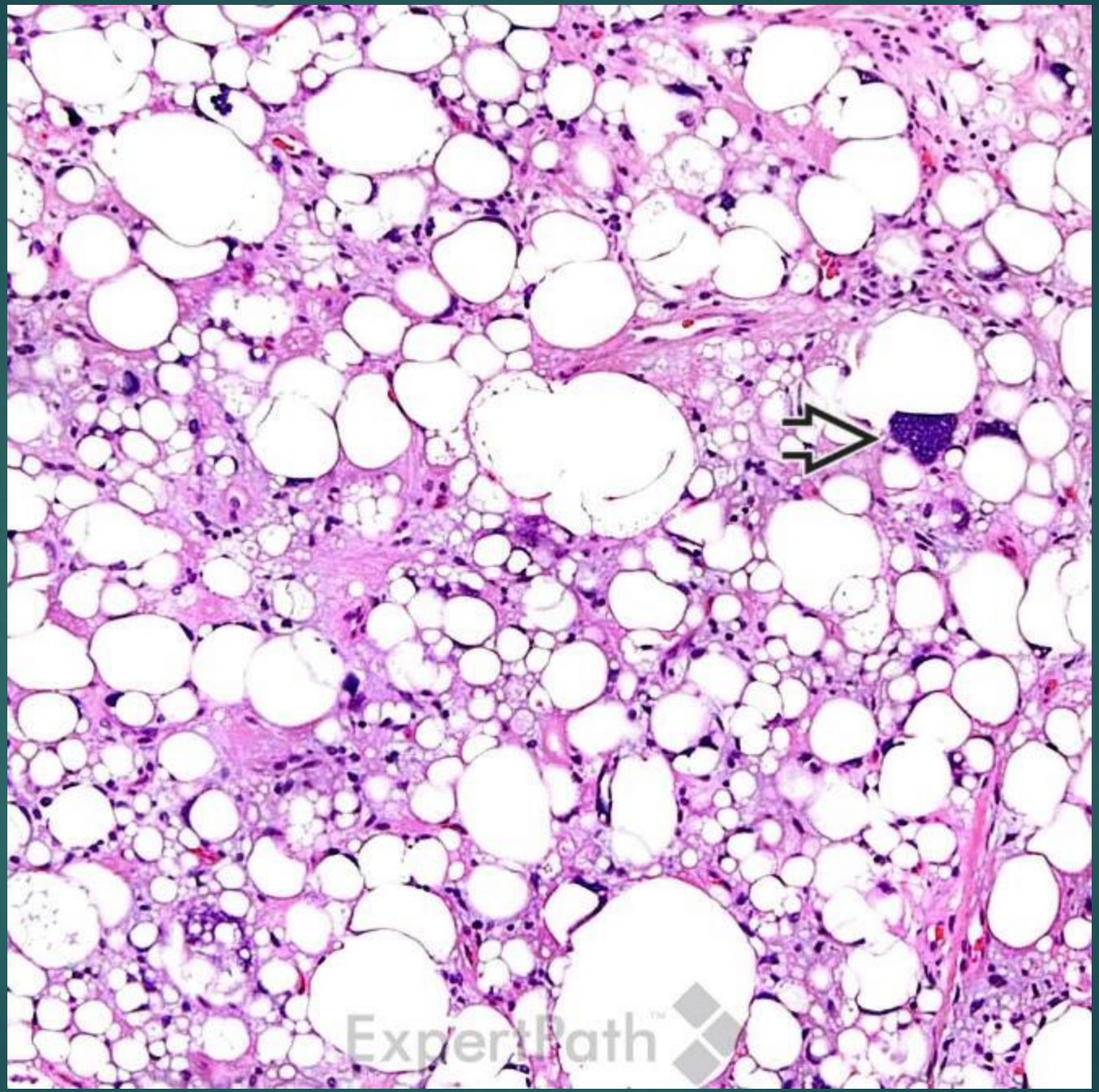
MRN: 28402014
BC-13-23535
(liver fine needle aspiration)










ExpertPath

FINAL CYTOLOGIC INTERPRETATION

INTERPRETATION:
POSITIVE FOR MALIGNANT CELLS.

DIAGNOSIS:
Morphologically consistent with pleomorphic liposarcoma. See note.

NOTES AND RECOMMENDATIONS:
NOTE: On smears and cell block sections, most cells in this pleomorphic neoplasm show intracytoplasmic lipid-filled vacuoles (lipid best seen on direct smears prior to coverslipping). Many morphologically classic lipoblasts are present. Necrosis is noted, and mitoses number up to 20 per 10 high power fields. No recognizable epithelial structures are present. Immunostains show that the tumor cells are positive for CD10 and negative for S100, HMB45, MART1, CD34, and SMA, and show only weak/focal staining for PAX8, MDM2, and CDK4. Attempted cytogenetic analysis is in progress and will be reported separately.

Pleomorphic liposarcoma in the liver usually represents metastasis. In the clinical context of a uterine mass with presumed fatty component, the liver tumor likely represents metastasis of a (pleomorphic) liposarcomatous component of a malignant mixed mullerian tumor. Clinical correlation is essential. Case reviewed at Cytology Staff Conference and with Dr. C. Fletcher.

Which is NOT one of the four types of liposarcoma?

- A) Moderately differentiated liposarcoma
- B) Well-differentiated liposarcoma
- C) Pleomorphic liposarcoma
- D) Myxoid/round cell liposarcoma
- E) Dedifferentiated liposarcoma

Pleomorphic liposarcoma

- Rarest type of liposarcoma (5-10%)
- High grade in nature
- Primary is often in the extremities (76%) or retroperitoneum (9%)
- Rarely see metastases to liver
- Patients over 50

Muzio et al. Radiopaedia. https://radiopaedia.org/articles/liposarcoma
Murphey et al. AFIP Archives. 2005;25(5) 1371-1395

Liver Lesions with Macroscopic Fat

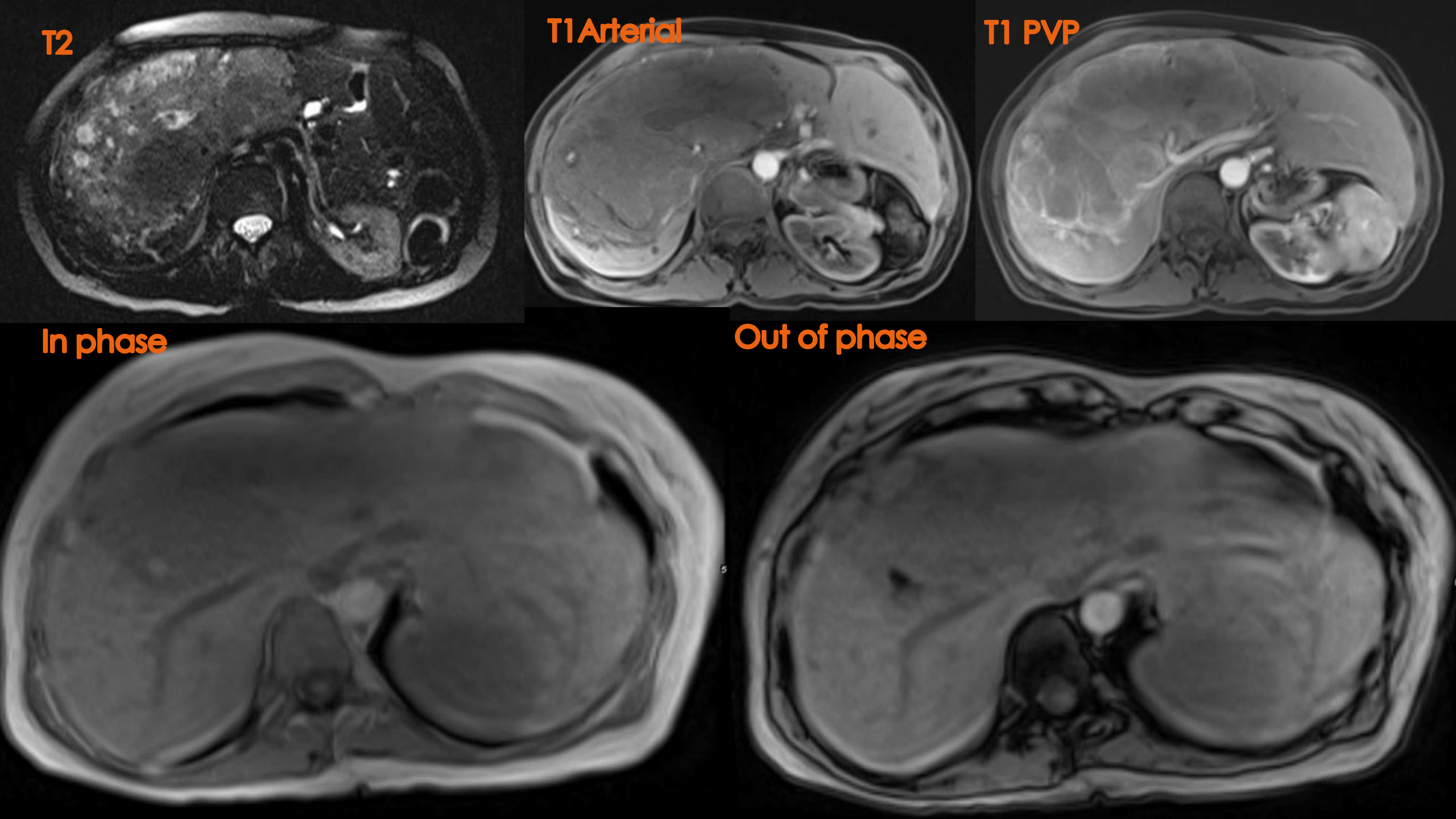
Table 1
Liver Lesions Containing Macroscopic Fat

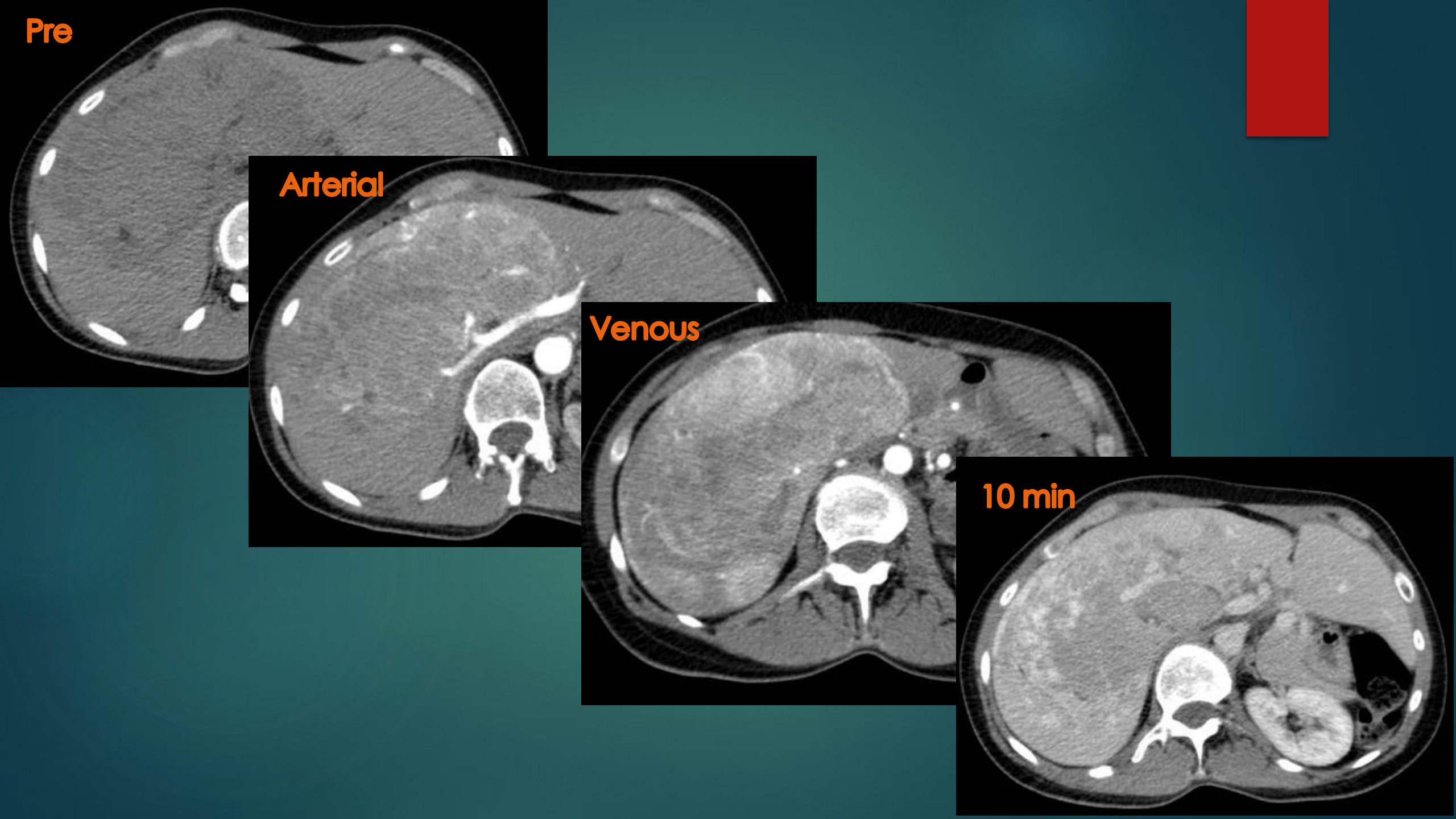
Type of Lesion	Lesions Containing Only Fat	Lesions Containing Fat and Soft Tissue
Benign	Lipoma	Adenoma
	Xanthoma (Langerhans cell histiocytosis)	Hepatic adrenal rest tumor
	Postoperative packing material (omentum)	Angiomyolipoma
		Teratoma
Malignant	Primary liposarcoma	Hepatocellular carcinoma
	Metastatic liposarcoma	Metastases
		Primary liposarcoma
		Metastatic liposarcoma

Prasad et al. RadioGraphics 2005; 25(321-331)

Case 6

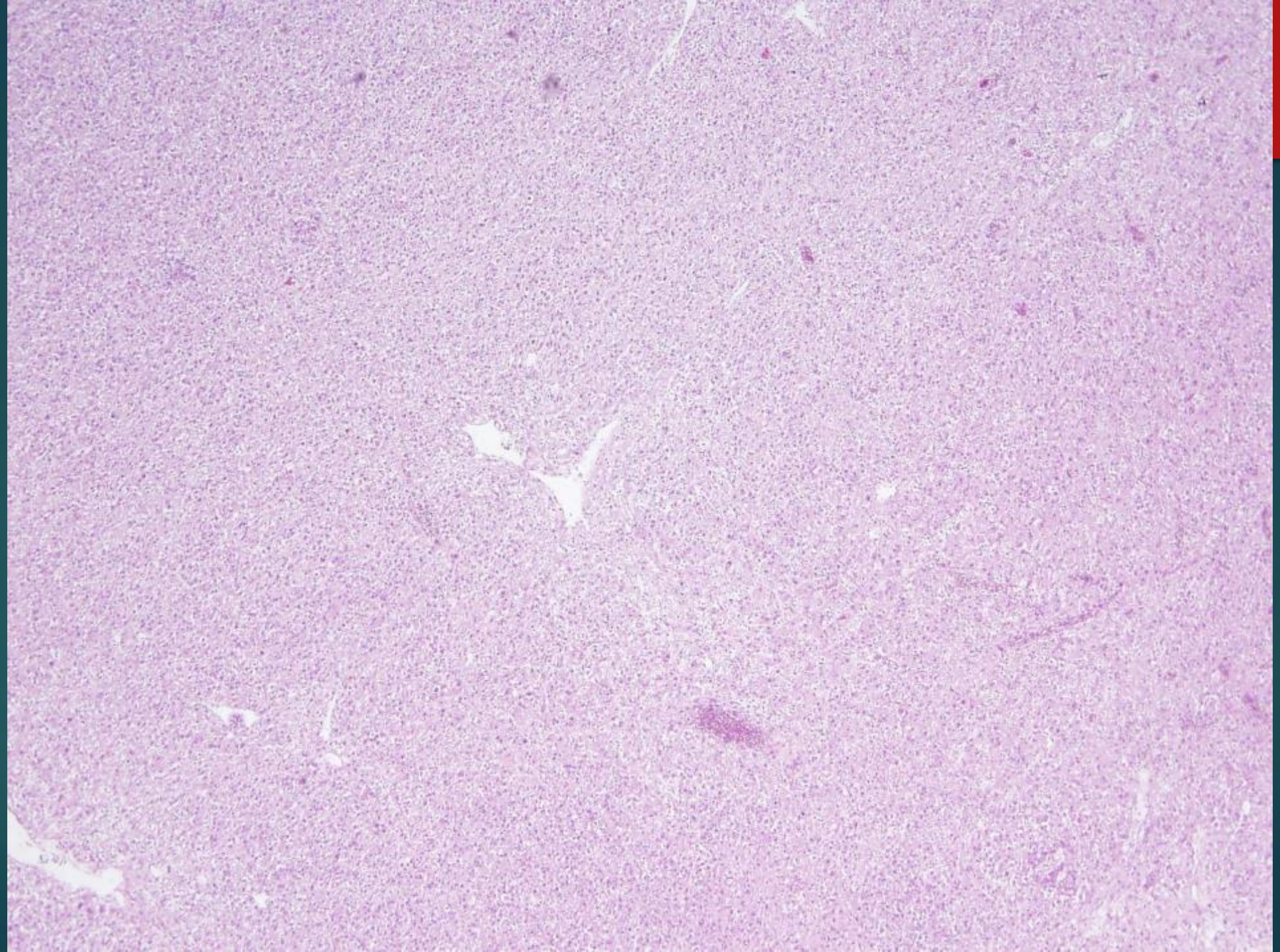
- 53 YOF with incidental liver mass
- LFTs normal

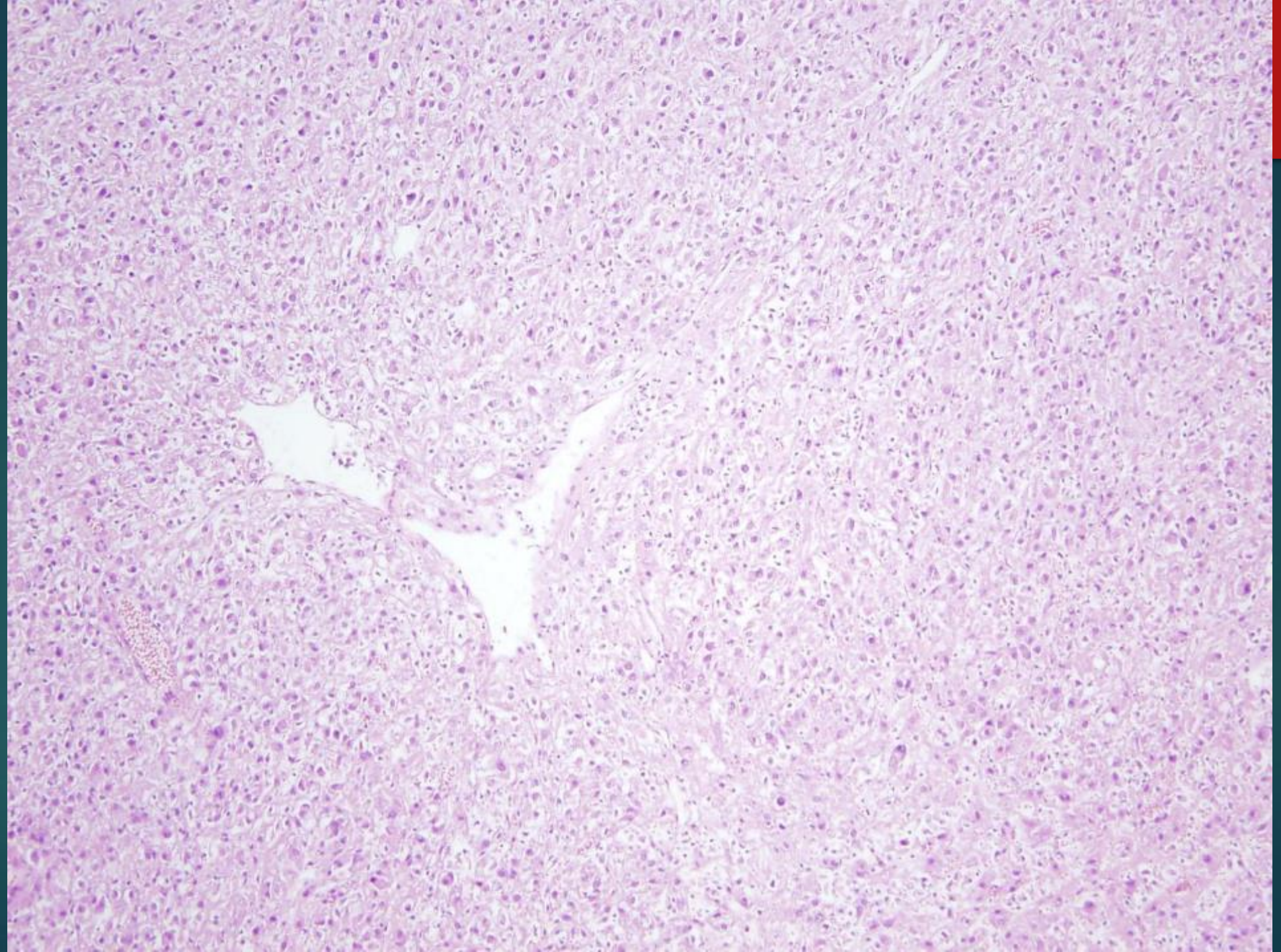

T2
T1 Arterial
T1 PVP
In phase
Out of phase

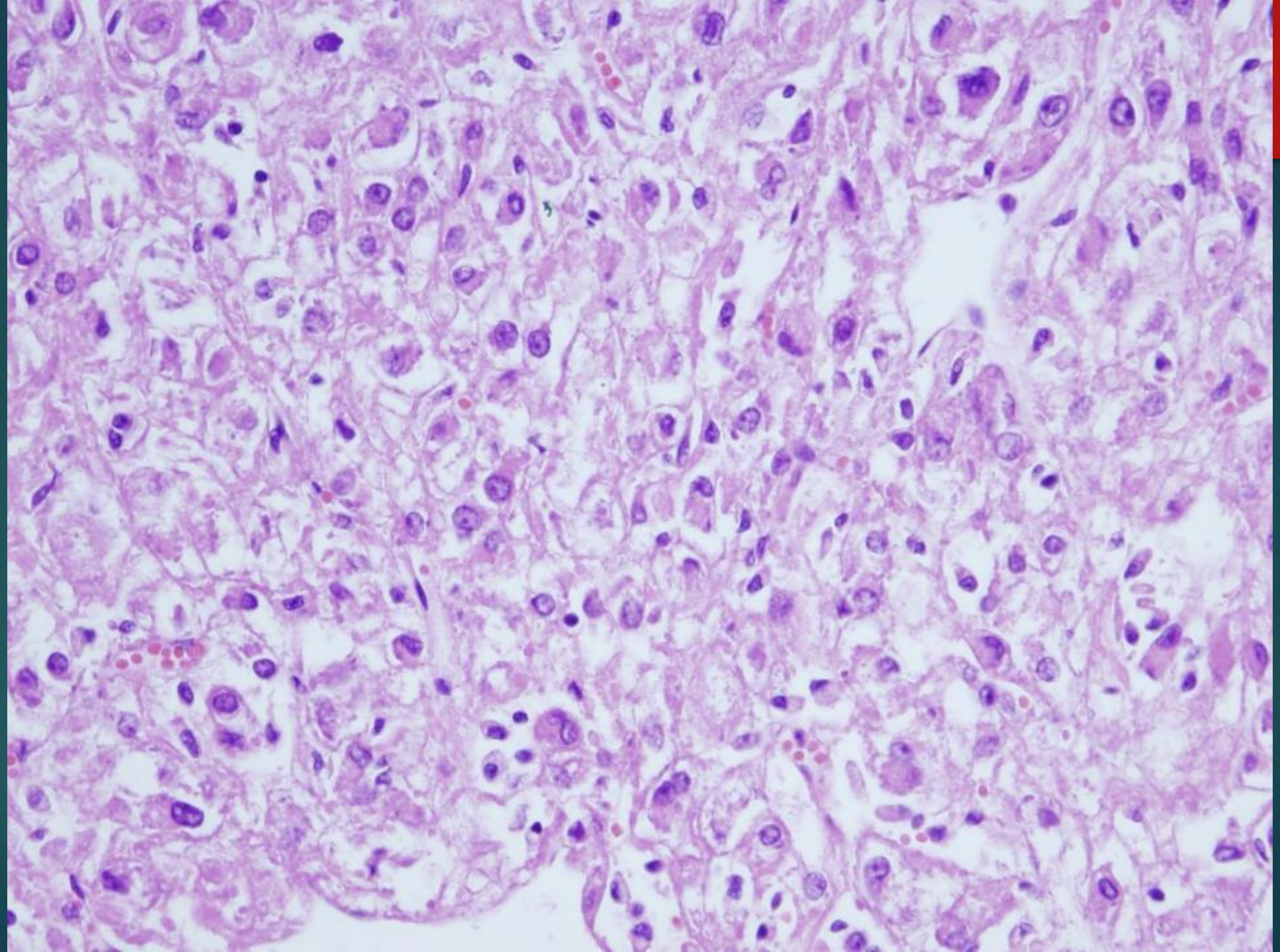

Pre
Arterial
Venous
10 min

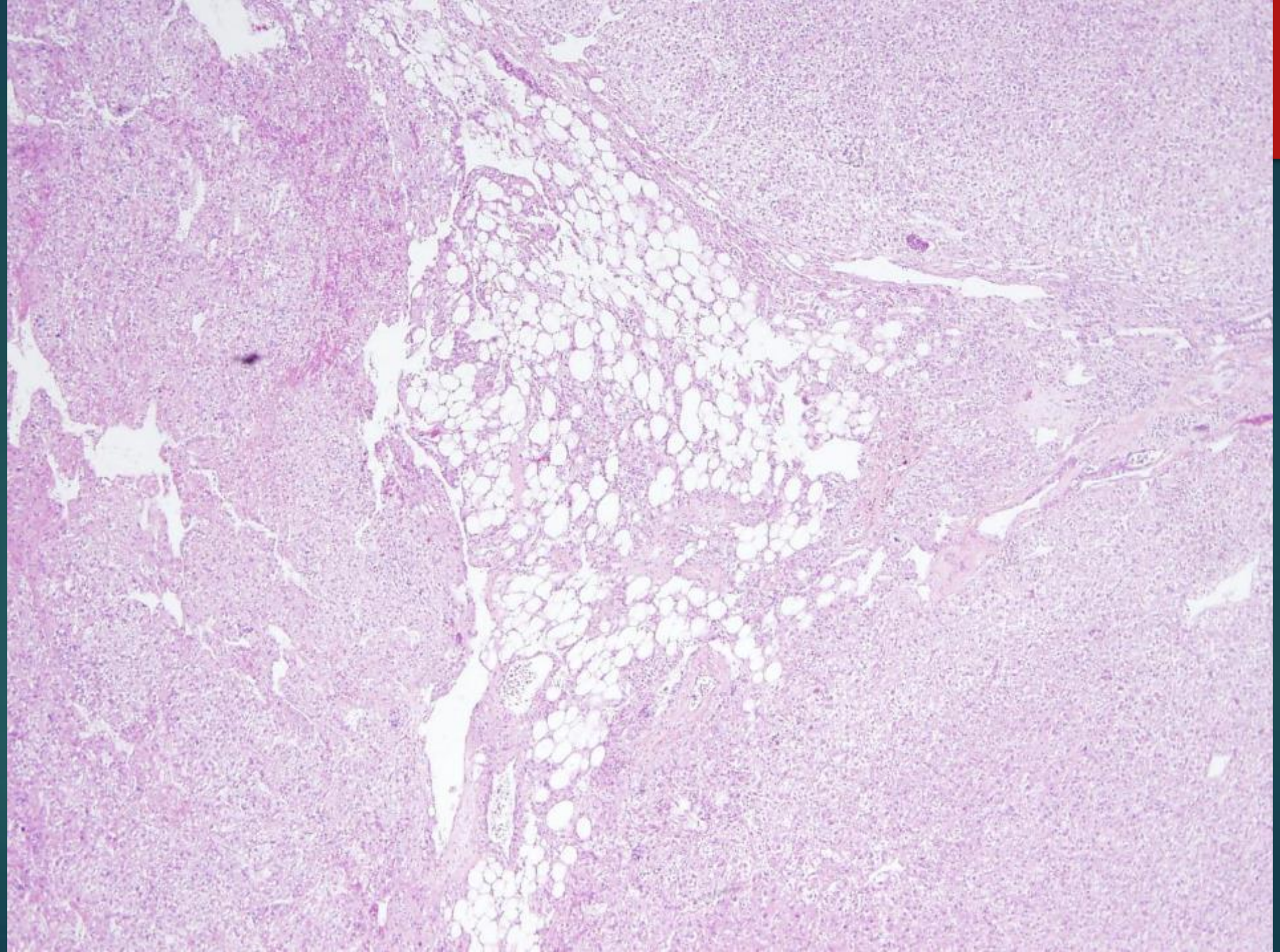
MRN: 29645264
BS-16-42026
(liver resection)

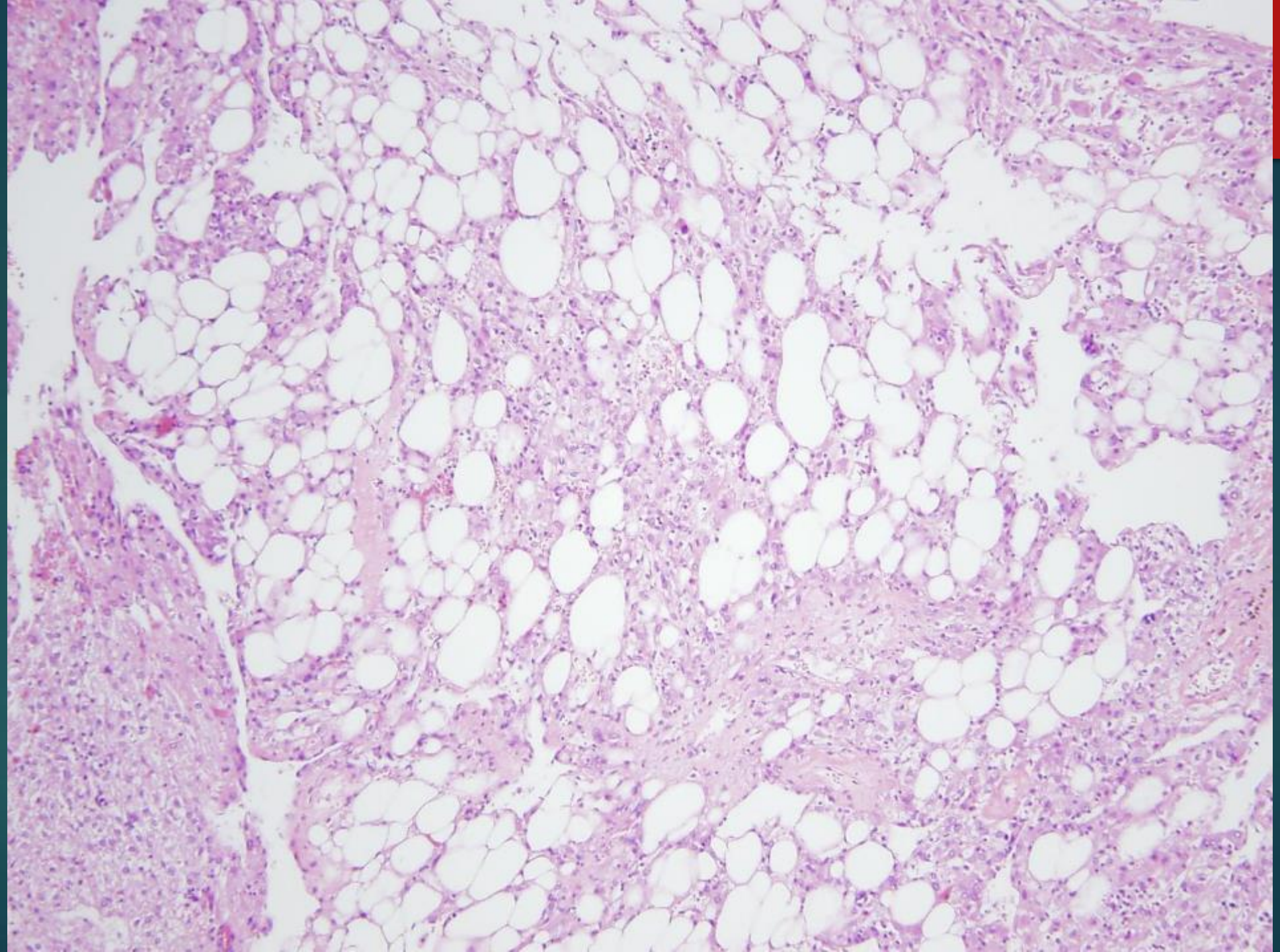

0 1 2 CM 3 4
BS-16-42026
BWH Pathology



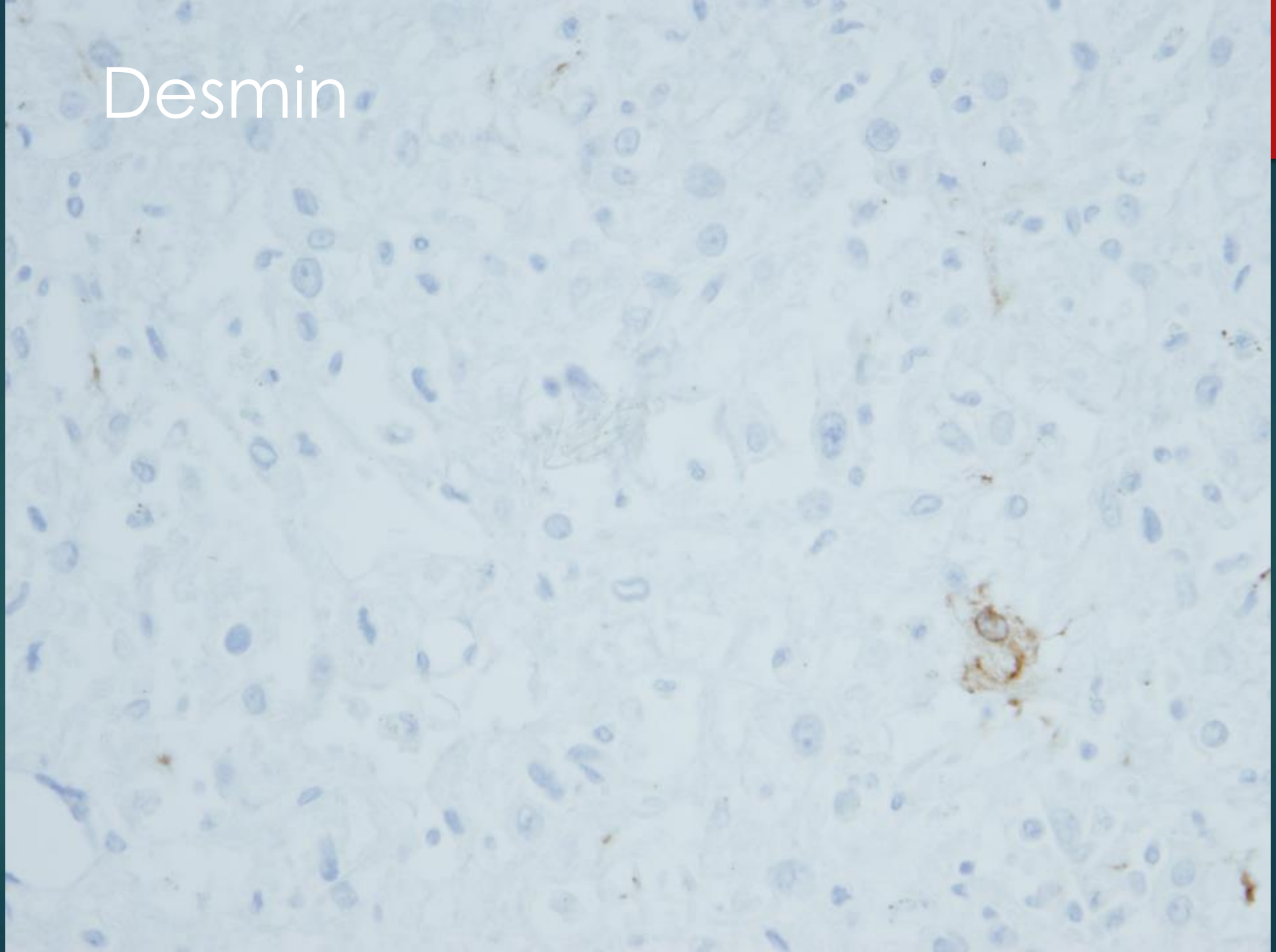


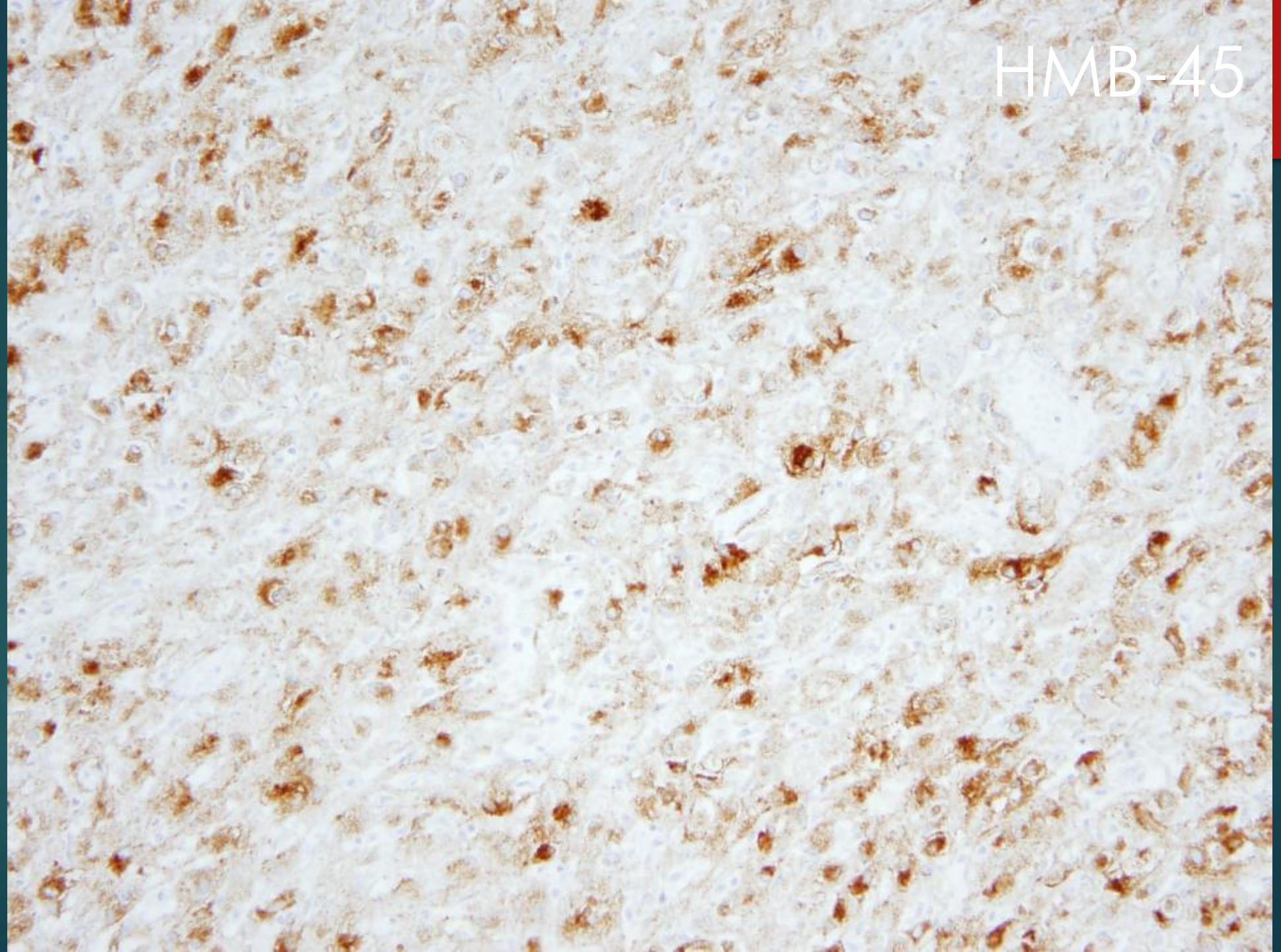






Desmin





HMB-45

C. RIGHT LIVER SEGMENTS 5,6,7,8 (INCLUDING FSC1, FSC2):
Epithelioid ANGIOMYOLIPOMA (16.0 cm) with scattered foci of extramedullary hematopoiesis.
Tumor present grossly at surgical resection margin
There are no overt features of malignancy.

Immunohistochemistry performed at BWH demonstrates the following staining profile in lesional cells:

Positive - SMA, Melan-A, MART-1, HMB45, Desmin (focal)
Negative - S-100

The immunohistochemical profile supports the above diagnosis.

NOTE: The gross specimen was reviewed intraoperatively and two separate sections were submitted from the main tumor mass and the grossly positive surgical resection margin. The tumor morphology was similar in both sections and no overt features of malignancy were identified.

Angiomyolipomas are most associated with?

- A) Female gender
- B) Serum tumor markers
- C) Hepatitis infection
- D) Cirrhosis
- E) Age over 50

Zhu et al. Br J Radiol. 2014;87(1034)

Angiomyolipoma

- AKA PEComa – Perivascular epithelioid cell tumor
- Blood vessels (angioid), smooth muscle (myoid) and mature fat (lipoid) components
- Large early draining vein
- No vessel compression
- 6% association with tuberous sclerosis, less strong than for renal AMLs (20%)
- Fat content can vary from 10-95%.

Knipe et al. Radiopaedia. Hepatic angiomyolipoma

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Prasad et al. RadioGraphics 2005; 25(321-331)

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