



The Gross Handling of Radical Nephrectomy Specimens: Pitfalls and How to Avoid Them

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LEARNING OBJECTIVES

- Review current CAP protocols for staging/reporting of kidney cancer
- Recognize common challenges in the gross examination of kidneys
- Interpret common problematic grossing scenarios and how to handle them
- Illustrate common and rare entities, focusing on gross/microscopic correlation



Protocol for the Examination of Resection Specimens from Patients with Renal Cell Carcinoma

Version: 4.3.0.0

Protocol Postina Date: June 2026

Tumor Focality

- ☐ Unifocal
☐ Multifocal (specify numbers of tumors): _____

+Tumor Site (select all that apply)

- ☐ Upper pole
☐ Middle
☐ Lower pole
☐ Other (specify): _____
☐ Not specified

Tumor Size

If multiple tumors are present, document the size of the largest tumor.

- ☐ Greatest dimension in Centimeters (cm): _____ cm
+Greatest Dimension of Other Tumor(s) in Centimeters (cm) (repeat as needed):
_____ cm
☐ Cannot be determined (explain): _____

Tumor Extent (Note D) (select all that apply)

- ☐ Limited to kidney
☐ Extends into perinephric tissue (beyond renal capsule)
☐ Extends into renal sinus
☐ Extends into pelvicalyceal system
☐ Extends into renal vein or its segmental branches
☐ Extends into inferior vena cava
☐ Extends beyond renal Gerota's fascia (renal fascia)
☐ Directly invades adrenal gland (T4)
☐ Involves adrenal gland non-contiguously (M1)
☐ Extends into other organ(s) / structure(s) (specify): _____
☐ Cannot be determined (explain): _____

Rhabdoid Features (Note E)

- ☐ Not identified
☐ Present
+Specify Percentage of Rhabdoid Component: _____ %
☐ Cannot be determined (explain): _____

Sarcomatoid Features (Note E)

- ☐ Not identified
☐ Present
+Specify Percentage of Sarcomatoid Component: _____ %
☐ Cannot be determined (explain): _____

Tumor Necrosis (Note E)

- ☐ Not identified
☐ Present
+Specify Percentage of Tumor Necrosis: _____ %
☐ Cannot be determined (explain): _____

Margin Status

- ☐ All margins negative for invasive carcinoma
☐ Invasive carcinoma present at margin

Margin(s) Involved by Invasive Carcinoma (select all that apply)

For partial nephrectomy only

- ☐ Renal parenchymal#: _____
☐ Renal capsular#: _____
☐ Renal sinus soft tissue#: _____
☐ Renal hilar soft tissue: _____
☐ Renal vein (tumor invades or is adherent to vein wall at margin): _____
☐ Ureteral: _____
☐ Perinephric fat: _____
☐ Gerota's fascia: _____
☐ Other (specify): _____



PROGNOSTIC FACTORS IN RCC

- Morphologic subtype
 - WHO/ISUP grade
 - Pathologic stage
- Sarcomatoid features
 - Rhabdoid features
 - Tumor necrosis

AJCC Cancer Staging Manual

Sixth Edition

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7 cm or less in greatest dimension, limited to the kidney
T1a	Tumor 4 cm or less in greatest dimension, limited to the kidney
T1b	Tumor more than 4 cm but not more than 7 cm in greatest dimension, limited to the kidney
T2	Tumor more than 7 cm in greatest dimension, limited to the kidney
T3	Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota's fascia
T3a	Tumor directly invades adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or vena cava below the diaphragm
T3c	Tumor grossly extends into vena cava above diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia

7th EDITION

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7 cm or less in greatest dimension, limited to the kidney
T1a	Tumor 4 cm or less in greatest dimension, limited to the kidney (Figure 43.4A)
T1b	Tumor more than 4 cm but not more than 7 cm in greatest dimension limited to the kidney (Figure 43.4B)
T2	Tumor more than 7 cm in greatest dimension, limited to the kidney (Figure 43.5)
T2a	Tumor more than 7 cm but less than or equal to 10 cm in greatest dimension, limited to the kidney
T2b	Tumor more than 10 cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota's fascia (Figure 43.6A)
T3b	Tumor grossly extends into the vena cava below the diaphragm (Figure 43.6B)
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava (Figure 43.6C)
T4	Tumor invades beyond Gerota's fascia (Figure 43.7A) (including contiguous extension into the ipsilateral adrenal gland) (Figure 43.7B)

8th Edition

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 7 cm in greatest dimension, limited to the kidney
T1a	Tumor ≤ 4 cm in greatest dimension, limited to the kidney
T1b	Tumor > 4 cm but ≤ 7 cm in greatest dimension limited to the kidney
T2	Tumor > 7 cm in greatest dimension, limited to the kidney
T2a	Tumor > 7 cm but ≤ 10 cm in greatest dimension, limited to the kidney
T2b	Tumor > 10 cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor extends into the renal vein or its segmental branches, or invades the pelvicalyceal system, or invades perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor extends into the vena cava below the diaphragm
T3c	Tumor extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

TUMOR SIZE IN RCC STAGING

- Size for low-stage, organ-confined (pT1a, pT1b, pT2)

T1	Tumor ≤ 7 cm in greatest dimension, limited to the kidney
T1a	Tumor ≤ 4 cm in greatest dimension, limited to the kidney
T1b	Tumor > 4 cm but ≤ 7 cm in greatest dimension limited to the kidney
T2	Tumor > 7 cm in greatest dimension, limited to the kidney
T2a	Tumor > 7 cm but ≤ 10 cm in greatest dimension, limited to the kidney
T2b	Tumor > 10 cm, limited to the kidney

- Renal sinus invasion $\rightarrow$ pT3a
- Renal vein invasion $\rightarrow$ pT3a
- Perinephric fat invasion $\rightarrow$ pT3a
- Tumor thrombus into IVC $\rightarrow$ pT3b/pT3c

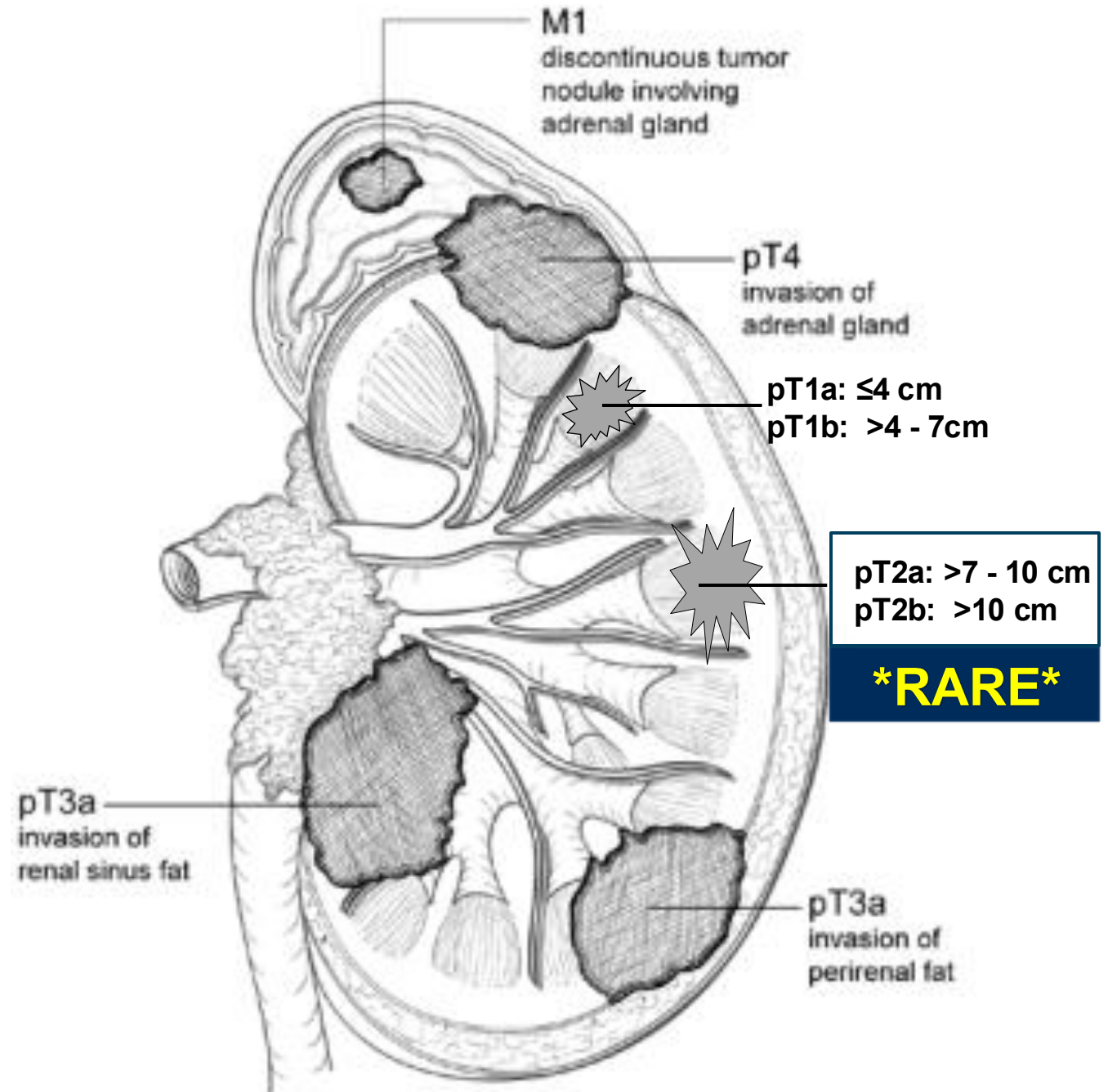
Upstages tumor that would have been low-stage by size alone

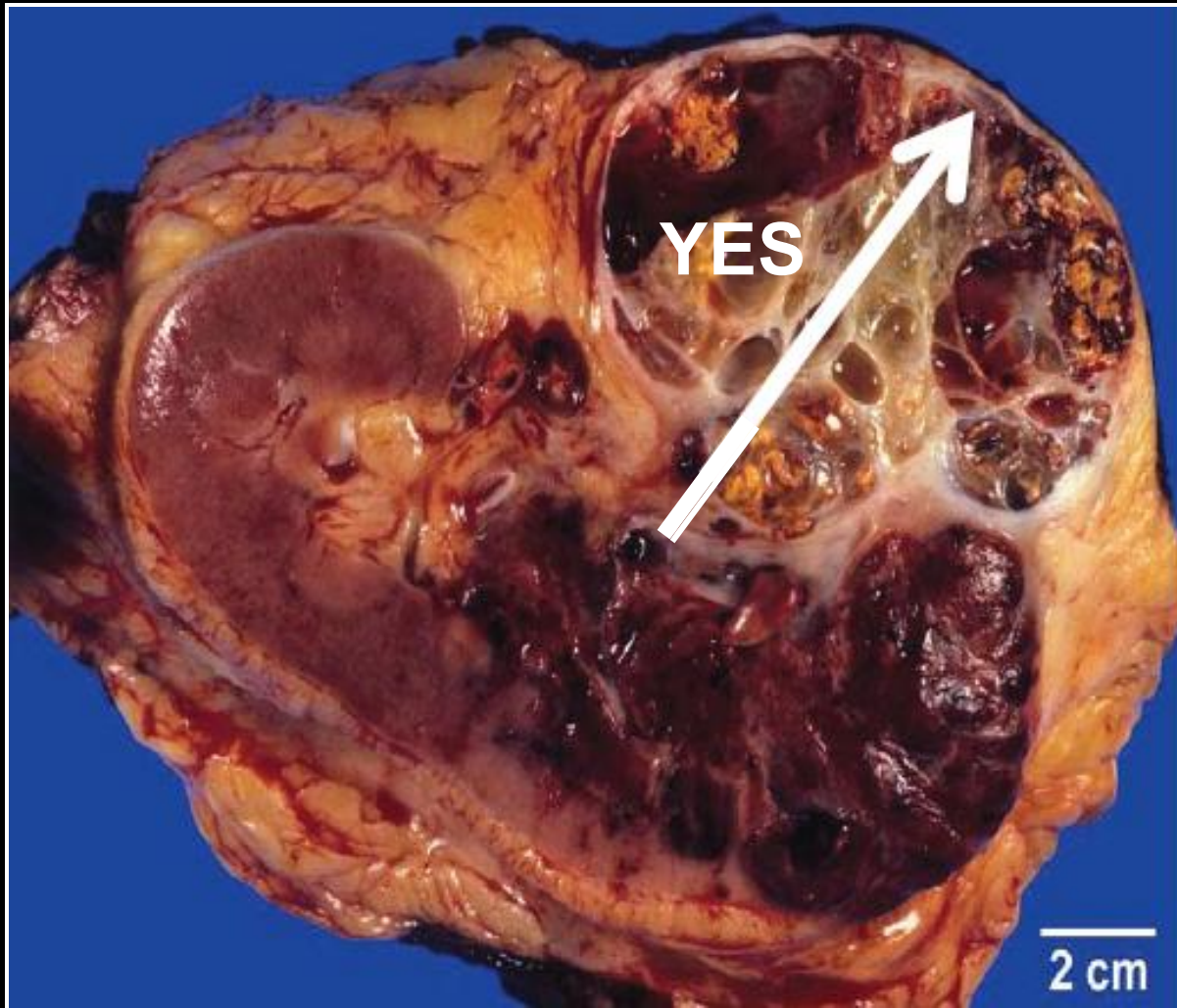
TUMOR SIZE: TIPS AND TRICKS

- Fresh vs fixed: best measured fresh
- Measure in 3 dimensions: largest dimension may be perpendicular to plane of section
- Compare with imaging
 - Radiologic measurements tend to overestimate
 - Double check for small tumors near cutoff

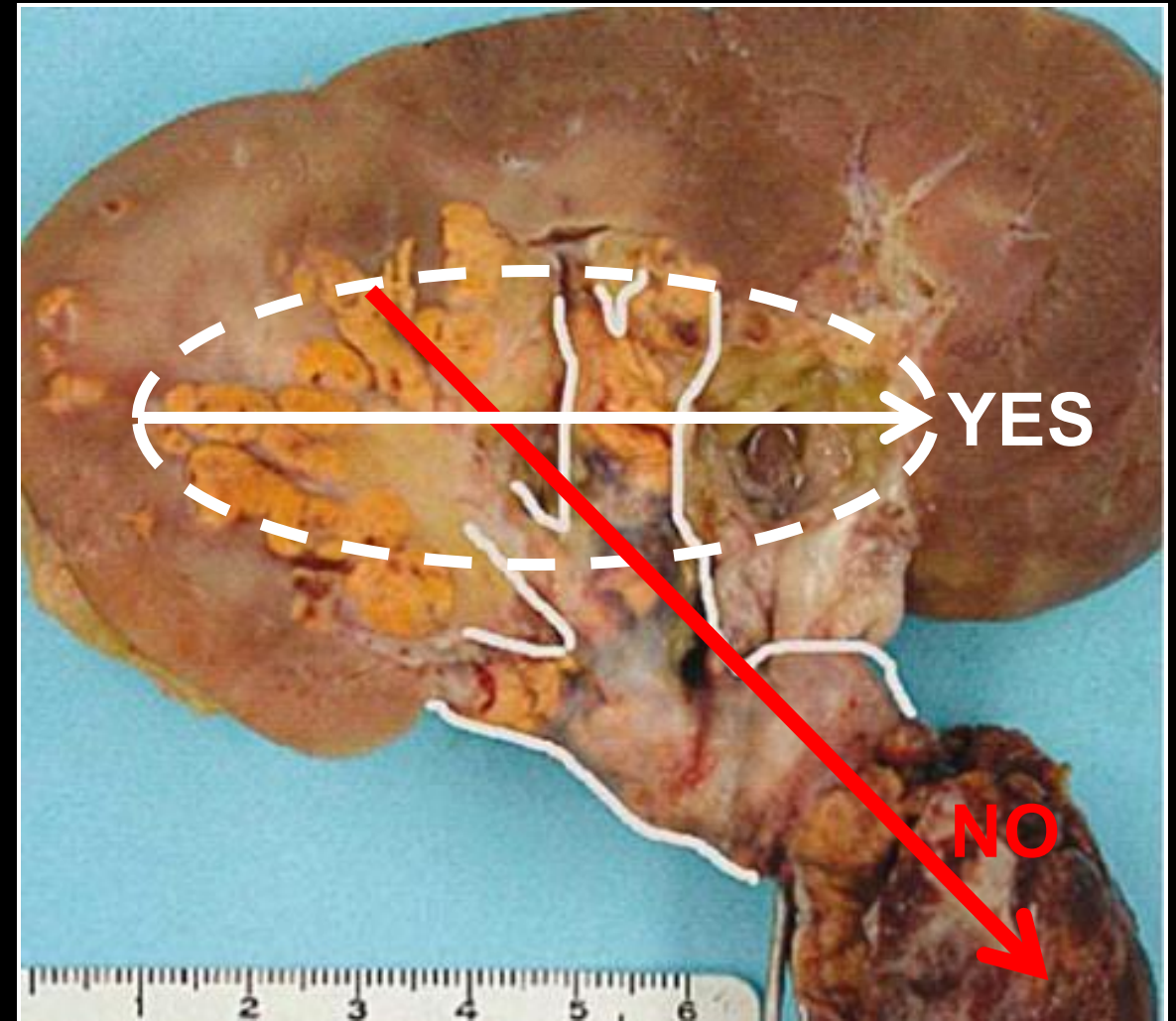
The most important
prognostic parameter in
RCC:

TUMOR STAGE





DO include portion of tumor invading into perinephric soft tissue and/or sinus

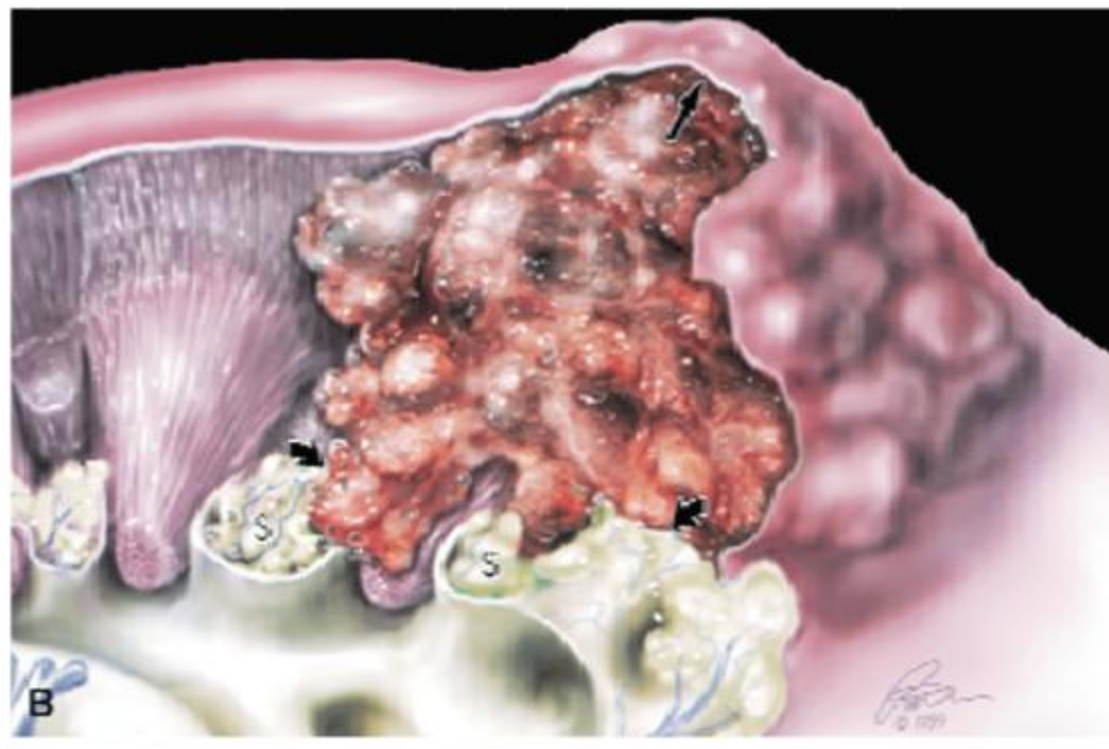
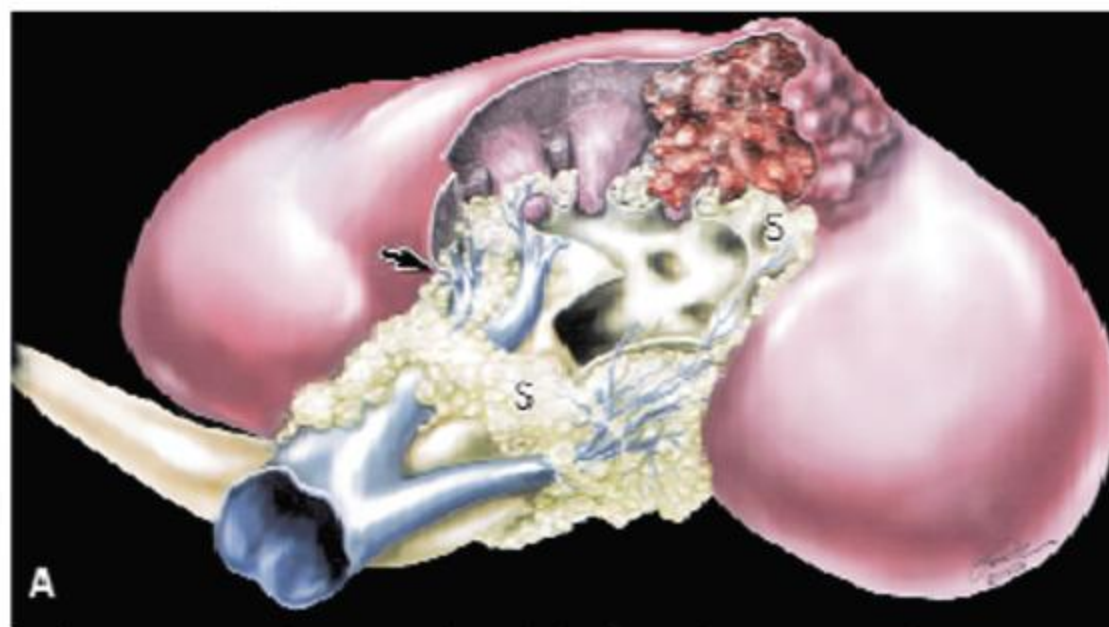


DO NOT measure tumor invading into renal vein/cava



RENAL SINUS

- Anatomical compartment separating the parenchyma from the collecting system
- Contains fat, lymphatics and thin-walled veins
- Main lymphovascular supply for the kidney



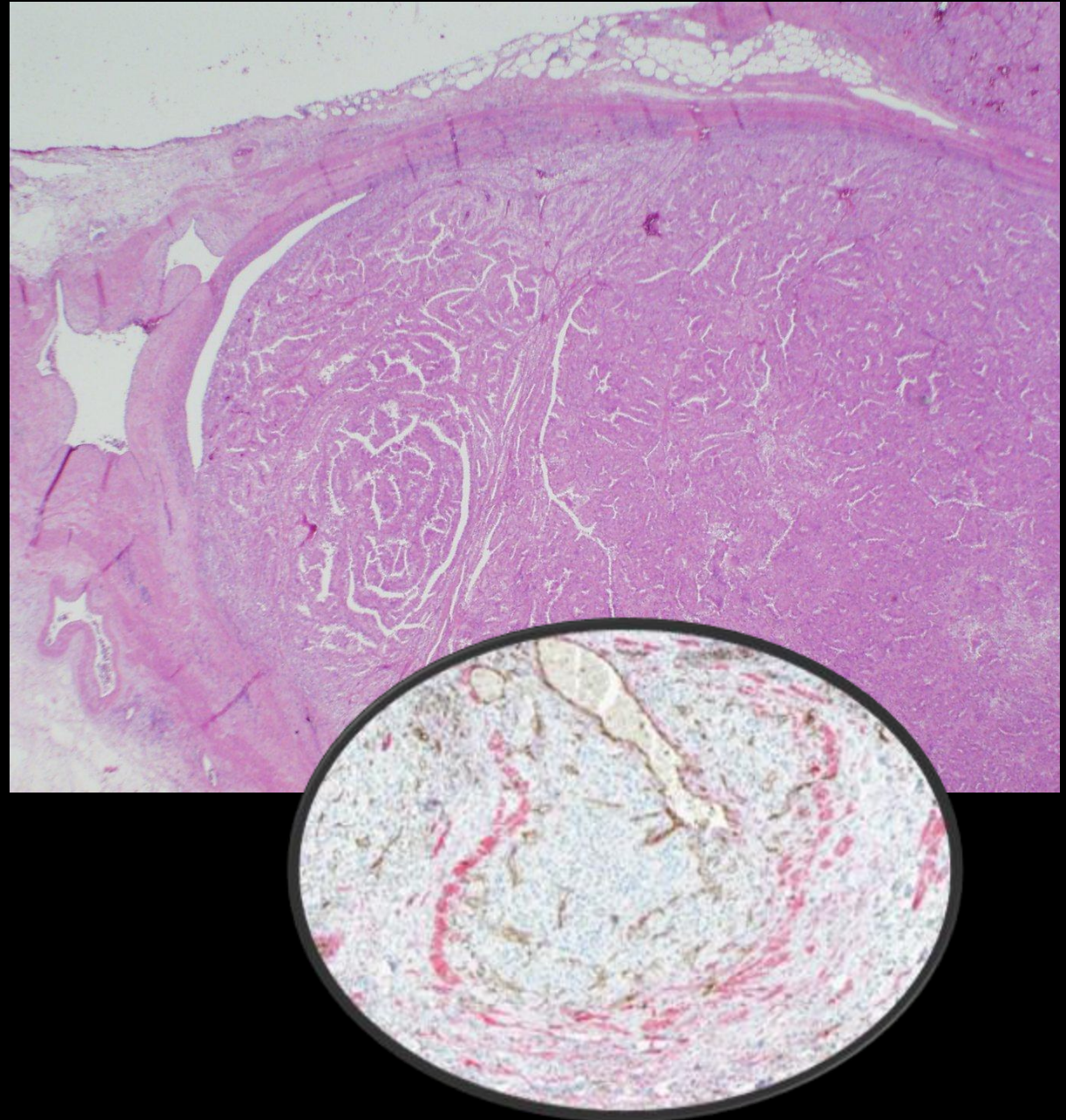
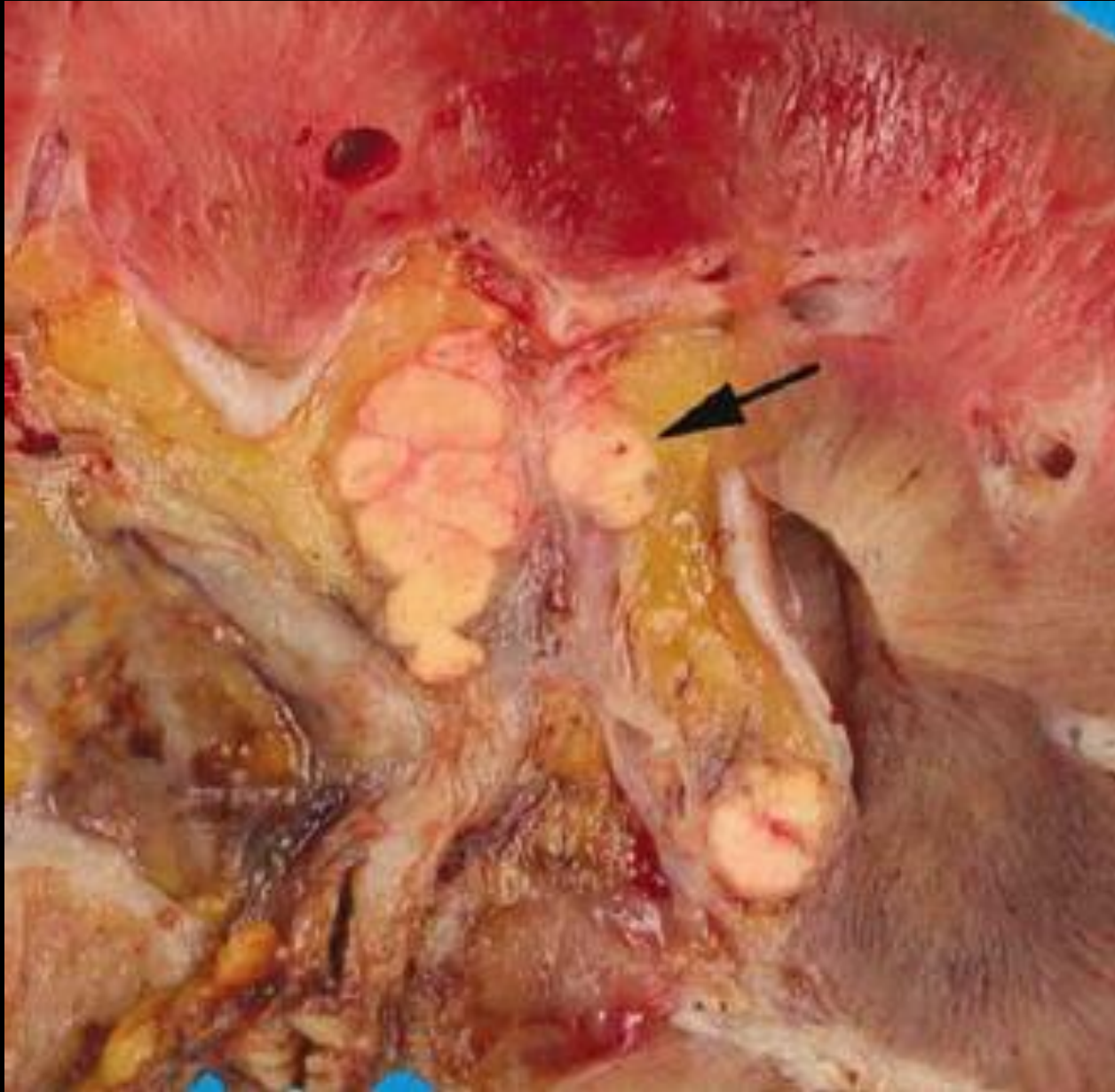
RENAL SINUS: WHY IMPORTANT?

- Important route of extrarenal spread of RCC
- A critical step in RCC staging
- All pT3a = sinus invasion, perinephric fat invasion, renal vein invasion

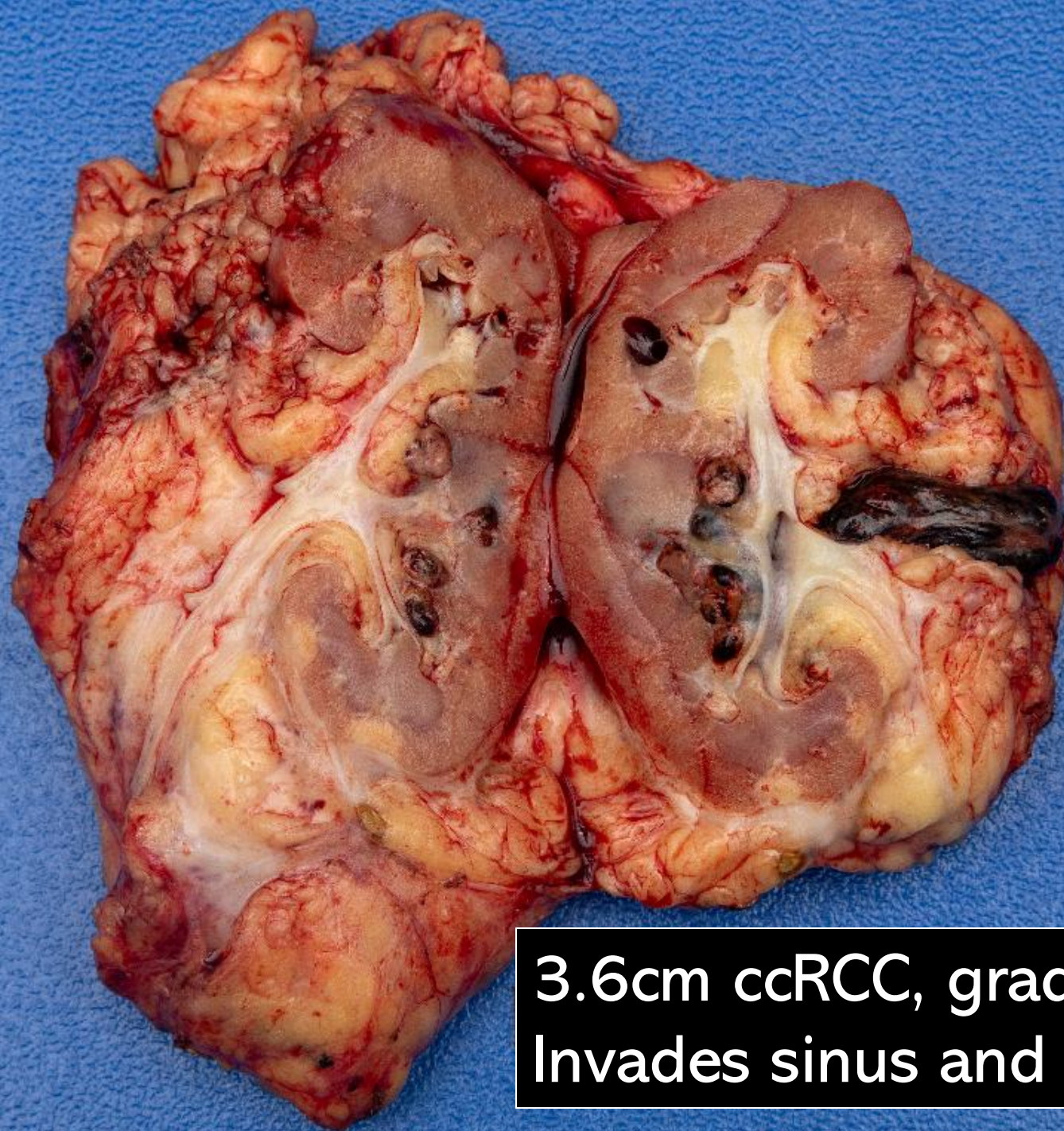
RENAL SINUS: WHAT IS THE ISSUE?

- Includes renal sinus veins and fat
 - Misconception that it only refers to tumor in sinus fat
- Renal sinus invasion can be subtle
- Renal sinus invasion is under-recognized
- Tumors >4-5cm: sinus should be sampled generously

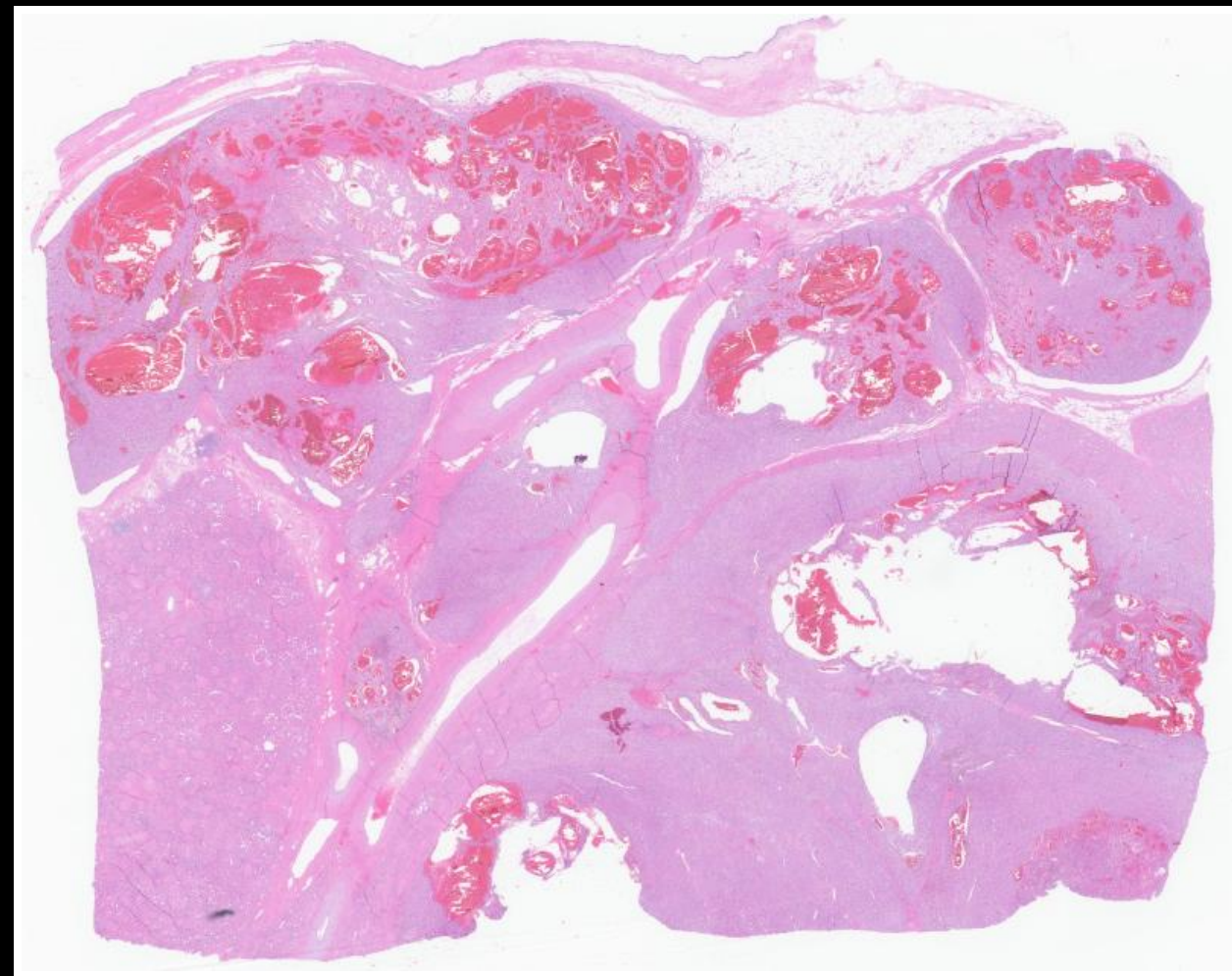
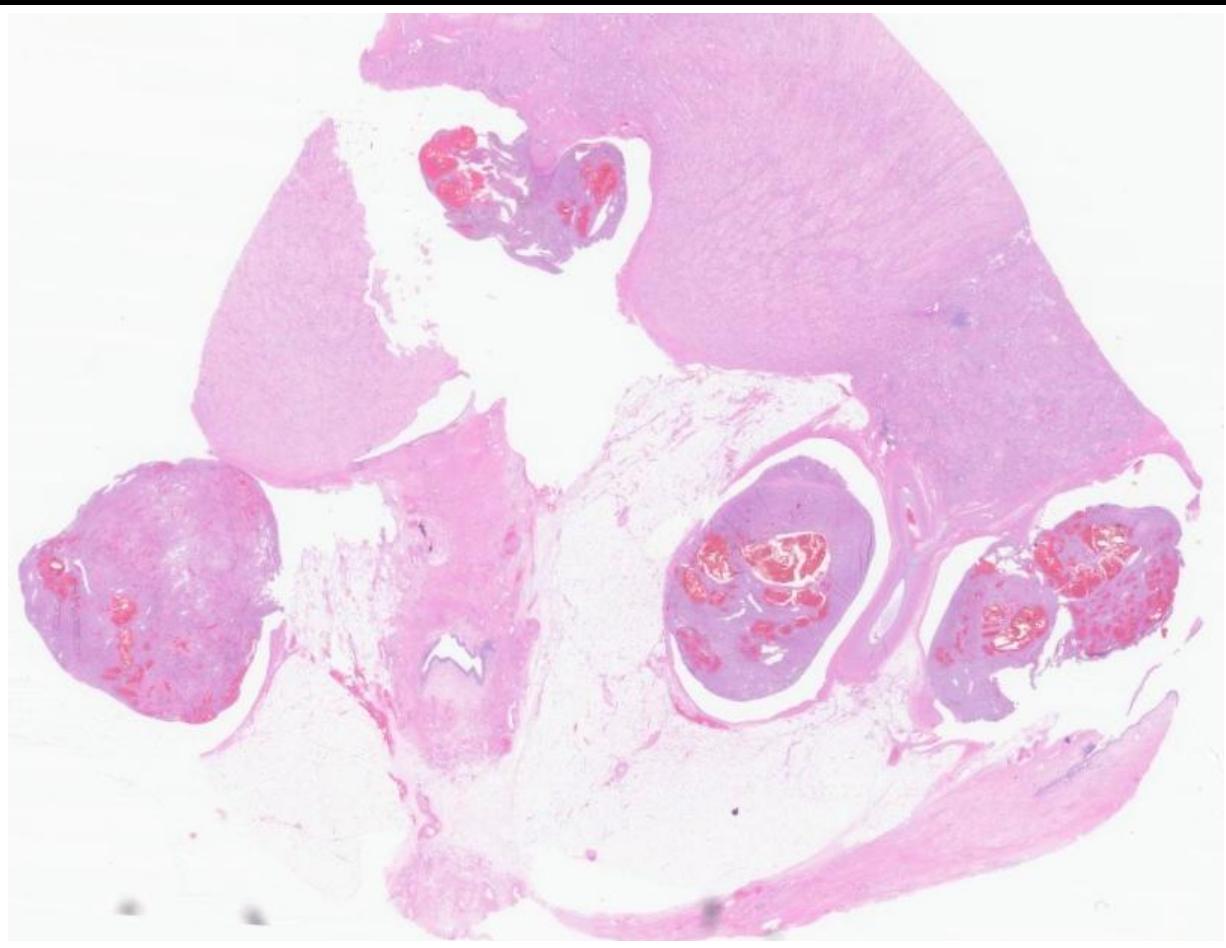








3.6cm ccRCC, grade 3
Invades sinus and RV, pT3a



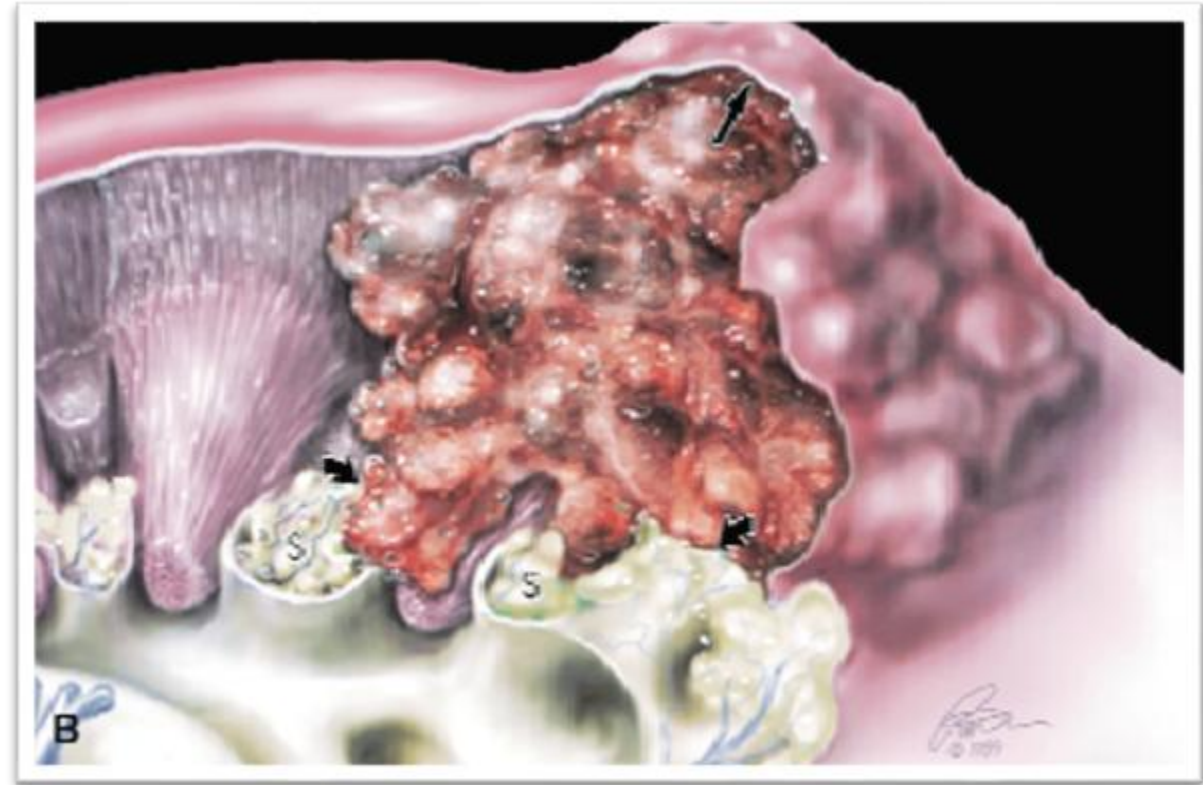
PERINEPHRIC FAT INVASION

PERINEPHRIC FAT INVASION

- Tumor in contact with fat
- Irregular tongues of tumor into perinephric tissue
- With or without desmoplasia

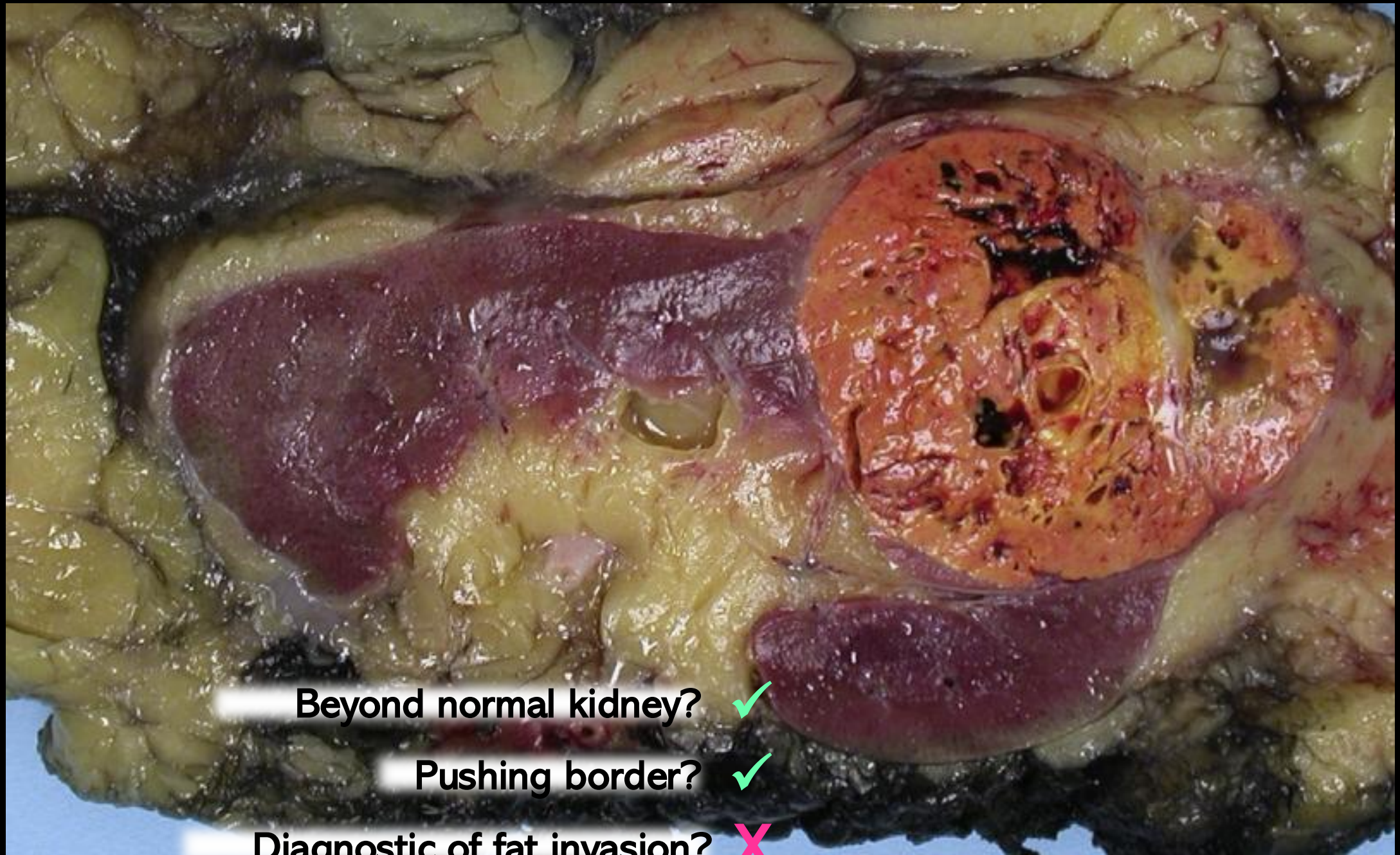
PERINEPHRIC FAT INVASION: WHY IMPORTANT?

- Criterion for pT3a tumors
- Renal capsule may be more of a barrier than the renal sinus
- Uncommon in the absence of renal sinus involvement
- Multiple patterns of extrarenal extension is associated with poor prognosis



PERINEPHRIC FAT INVASION: WHAT'S THE ISSUE?

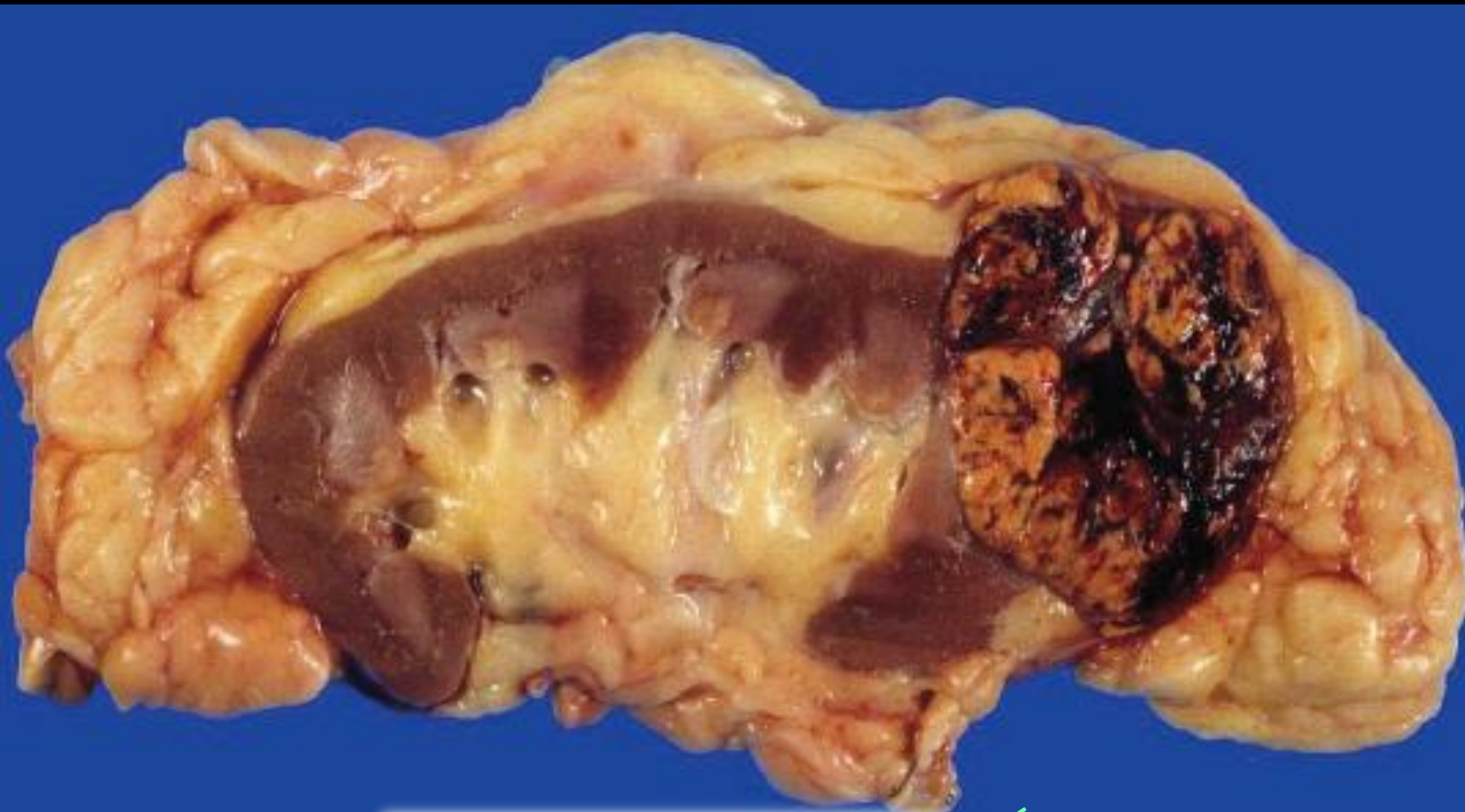
- Bulging into fat $\neq$ invasive into fat



Beyond normal kidney? ✓

Pushing border? ✓

Diagnostic of fat invasion? ✗



Beyond normal kidney? ✓

Pushing border? ✓

Diagnostic of fat invasion? X

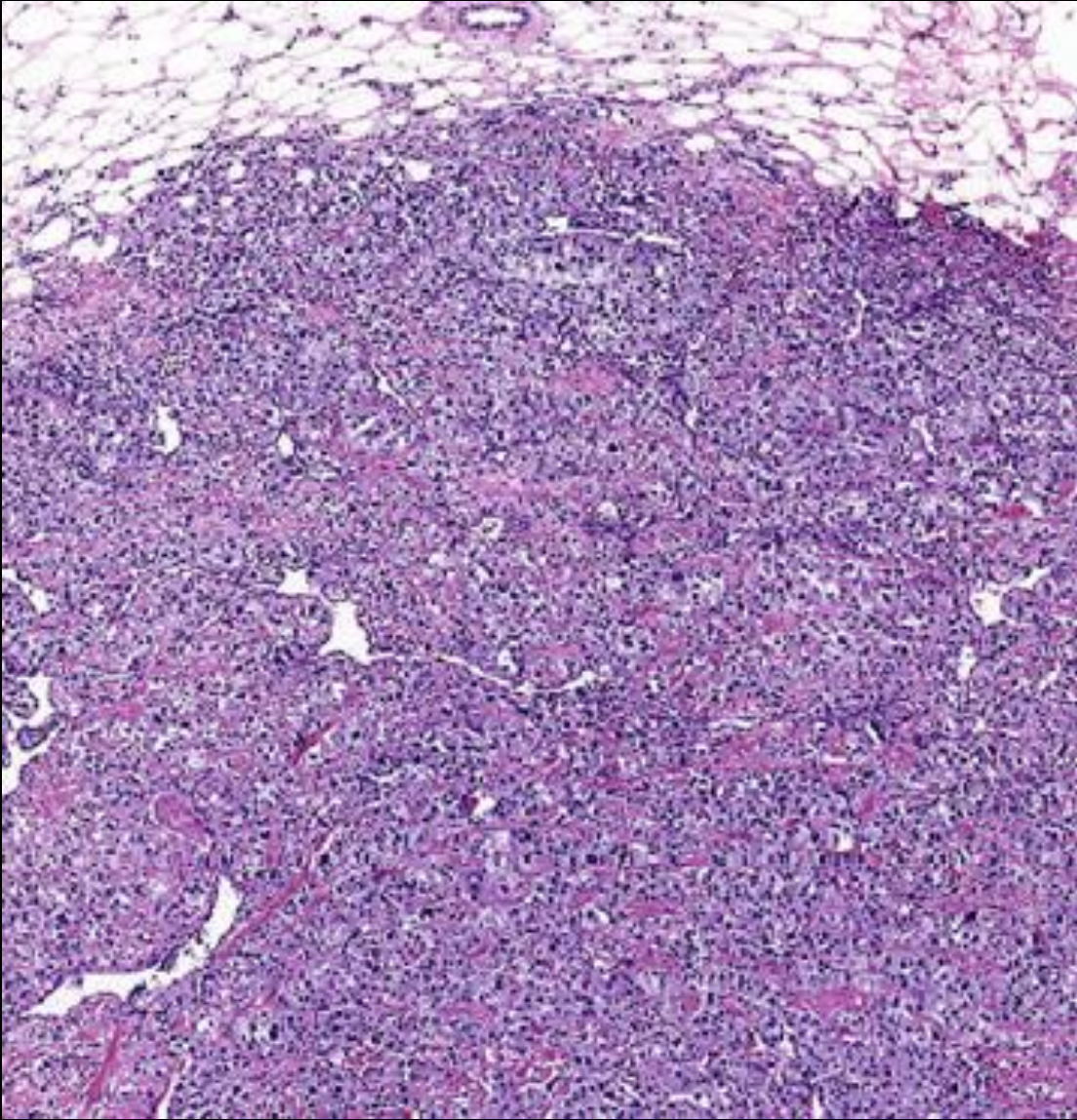


Beyond normal kidney? ✓

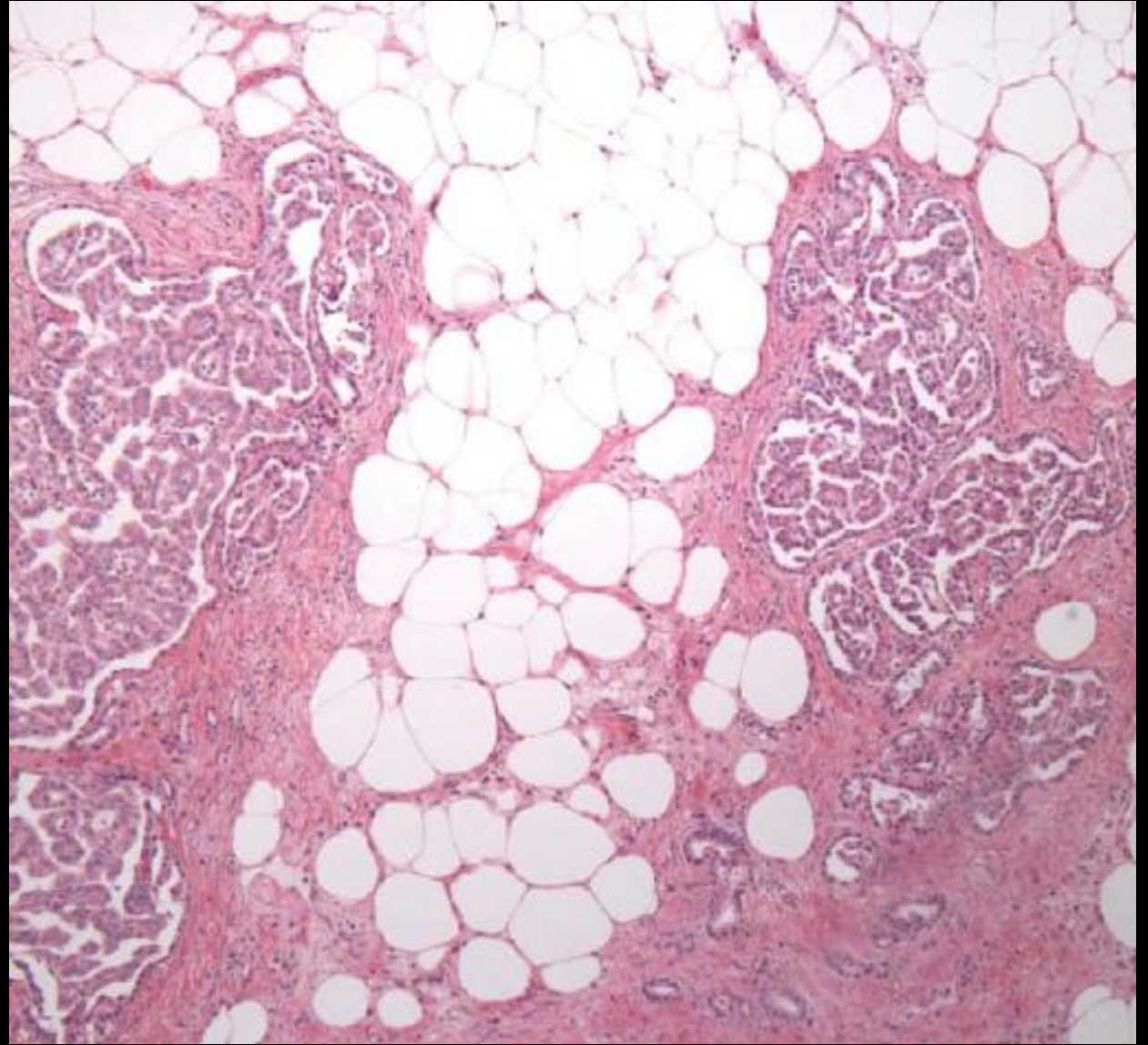
Pushing border? X (infiltrative)

Diagnostic of fat invasion? ✓

Microscopic evaluation of perinephric fat invasion (pT3a)



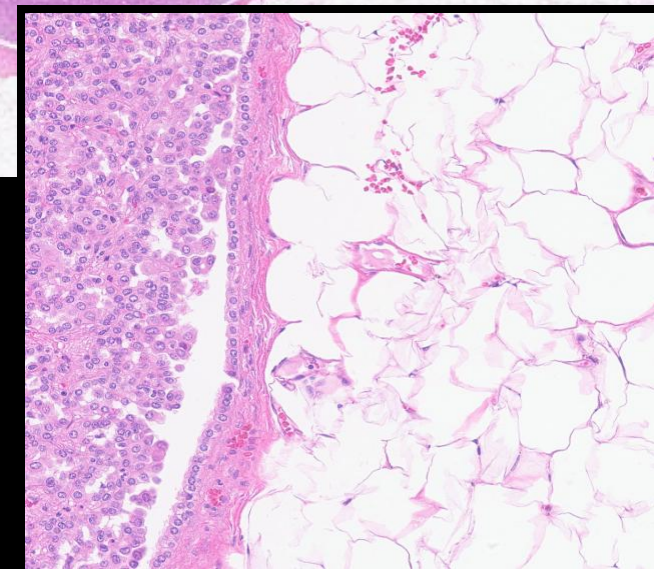
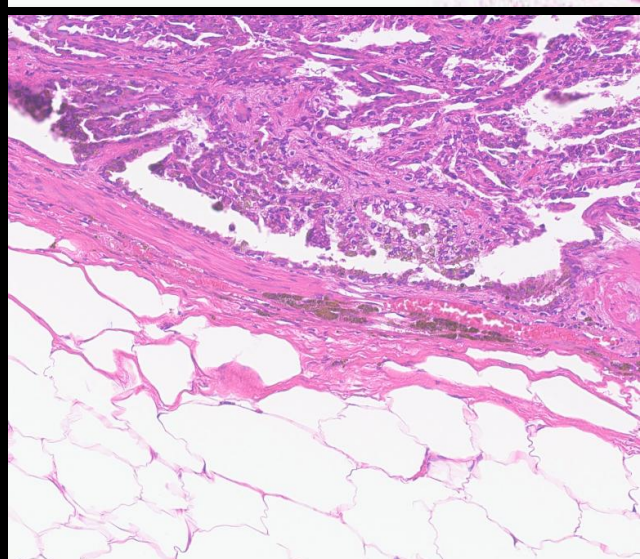
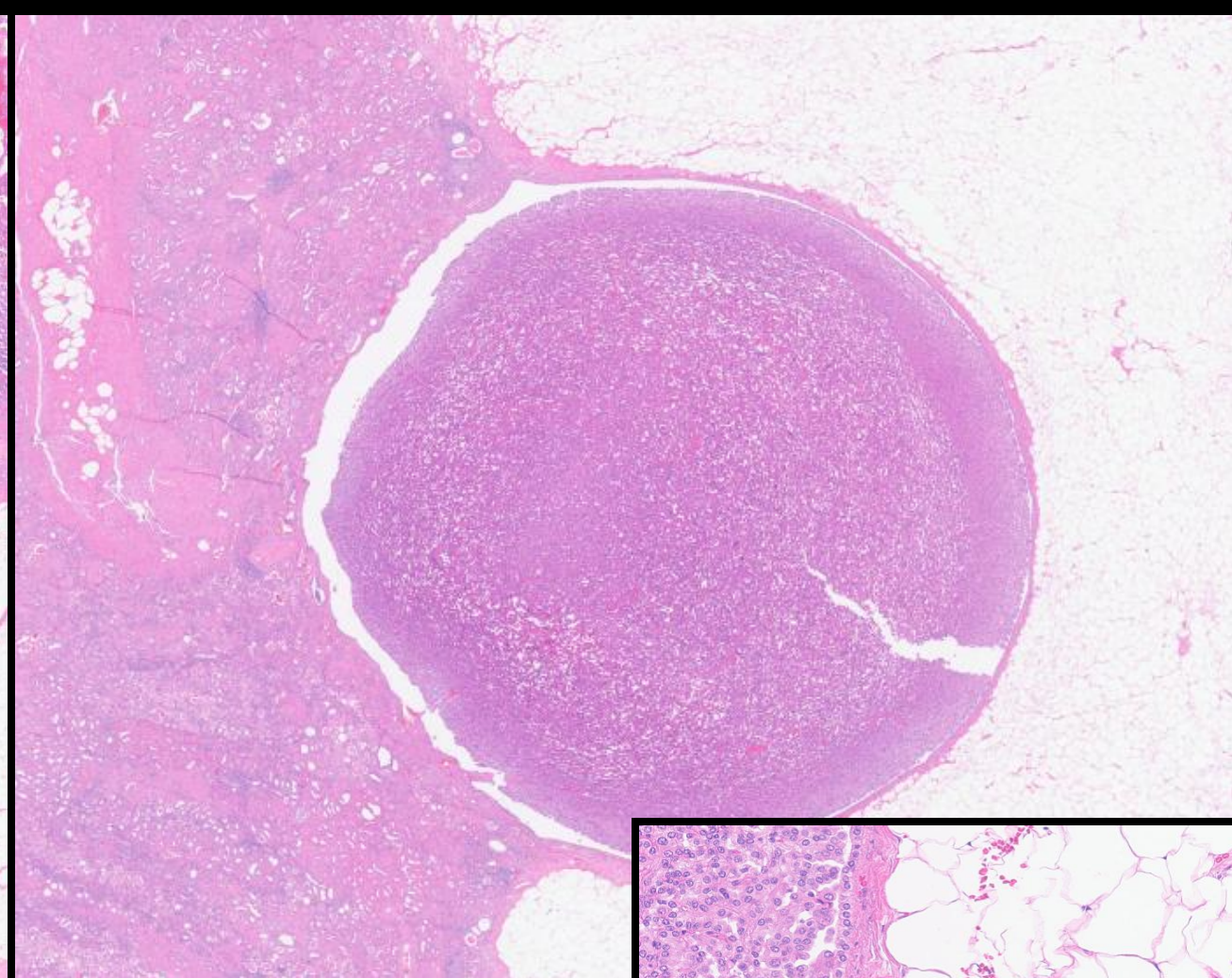
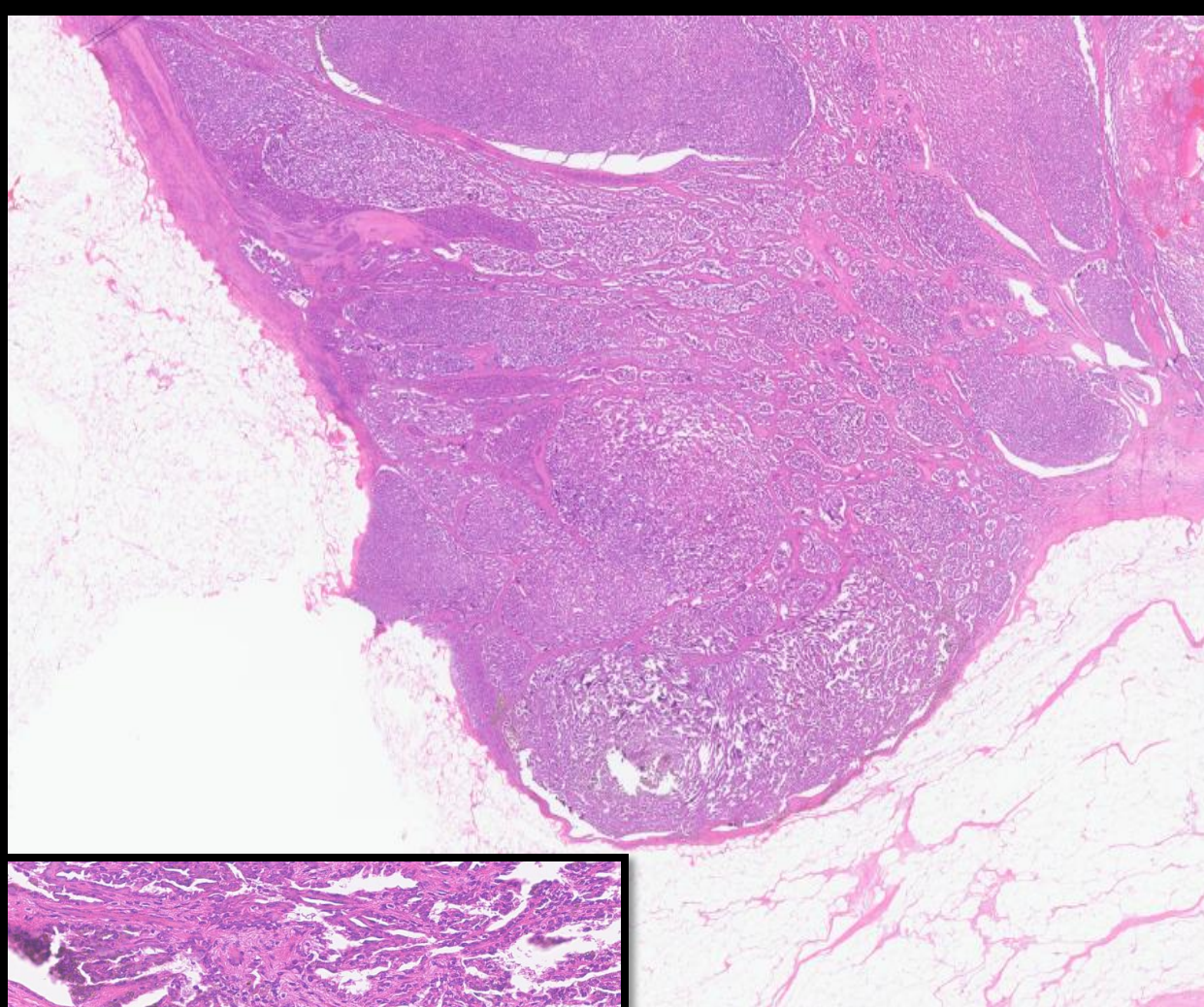
Tumor touching fat



Irregular tongues of tumor in fat



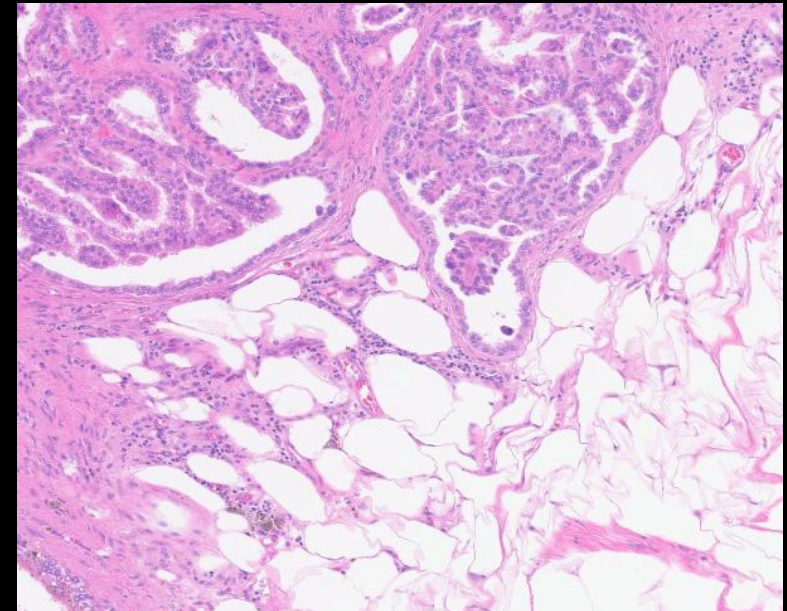
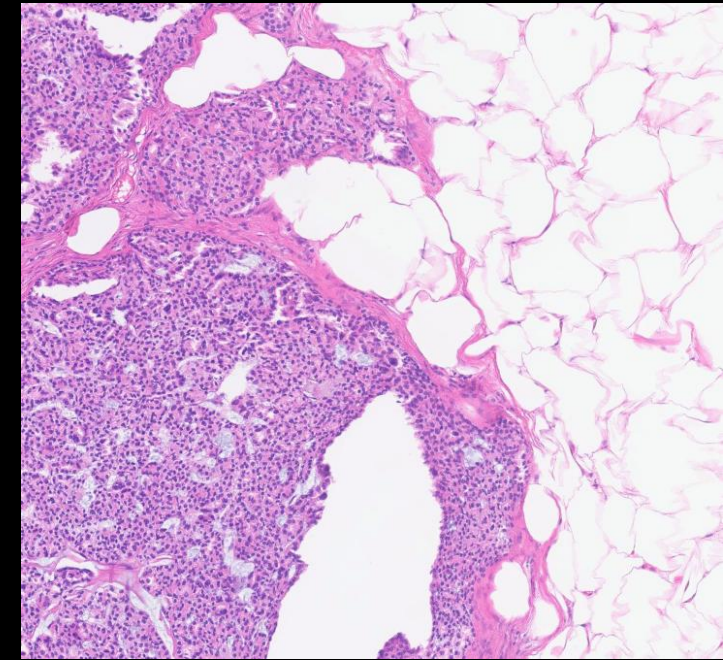
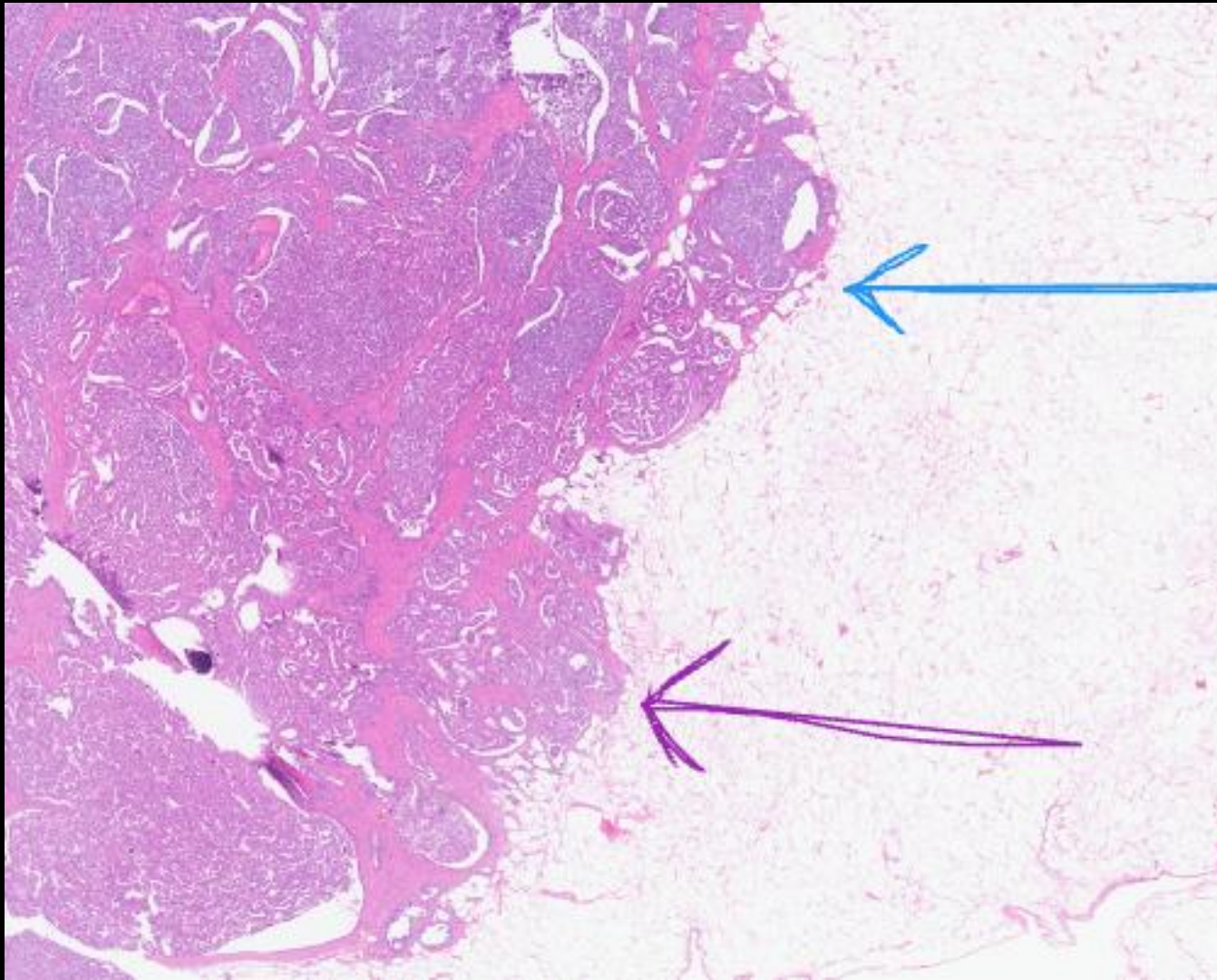




Beyond normal kidney? ✓

Pushing border? ✓

Diagnostic of fat invasion? ✗



Beyond normal kidney? ✓

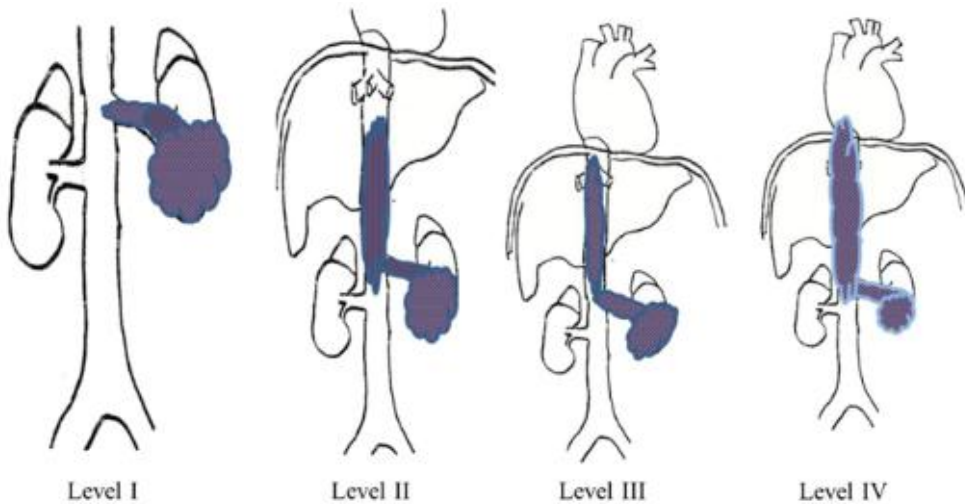
Pushing border? ✗

Diagnostic of fat invasion? ✓

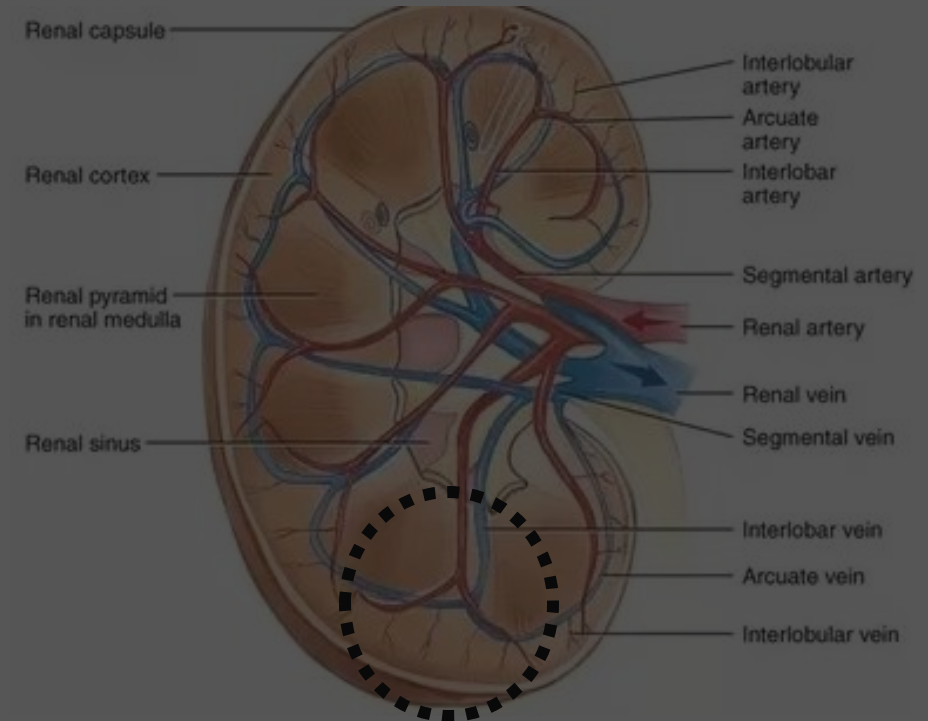
RENAL VEIN MARGIN

VENOUS SPREAD IN RCC

Antegrade = tumor thrombus into major veins



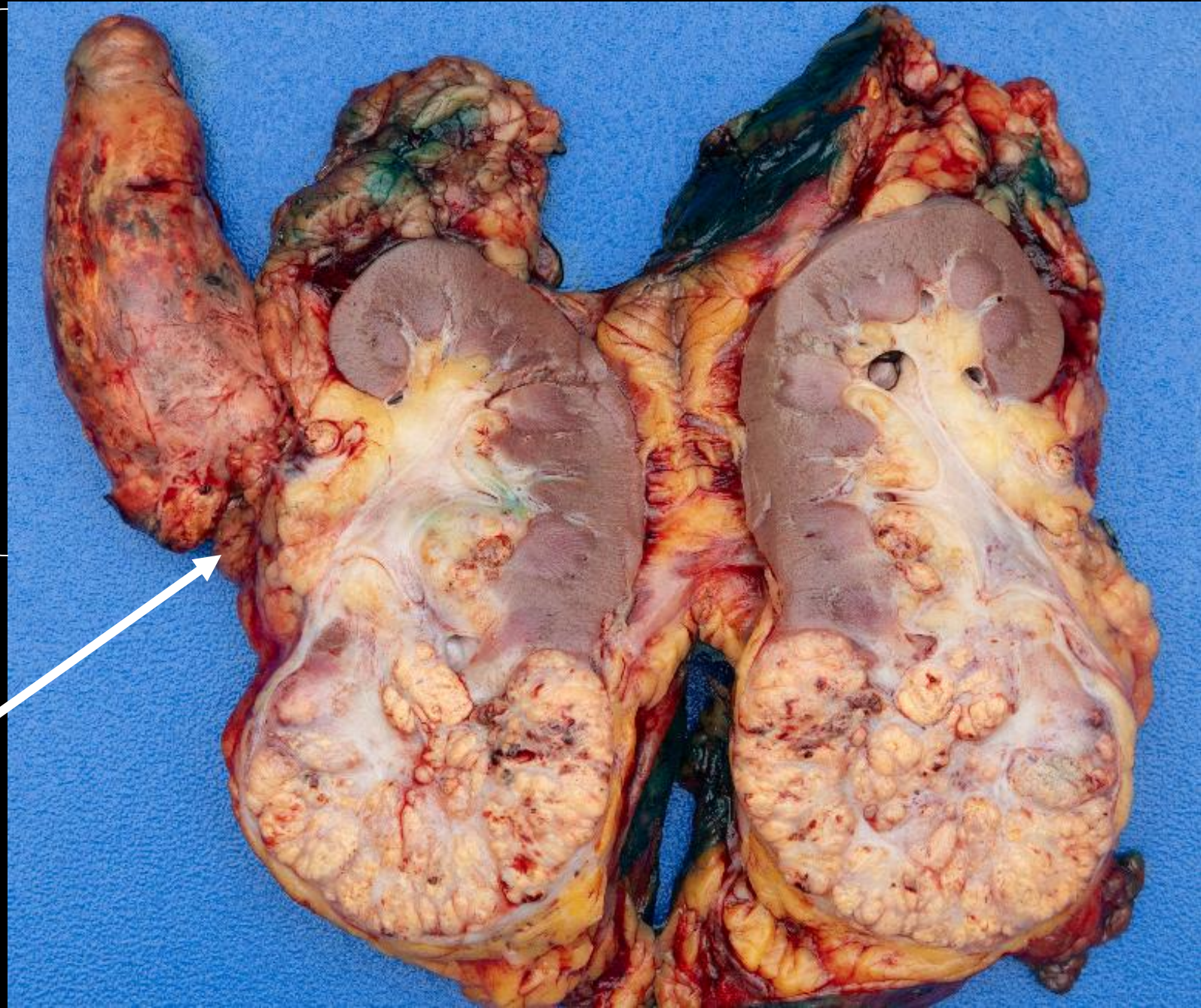
Retrograde = into proximal tributaries of the renal vein



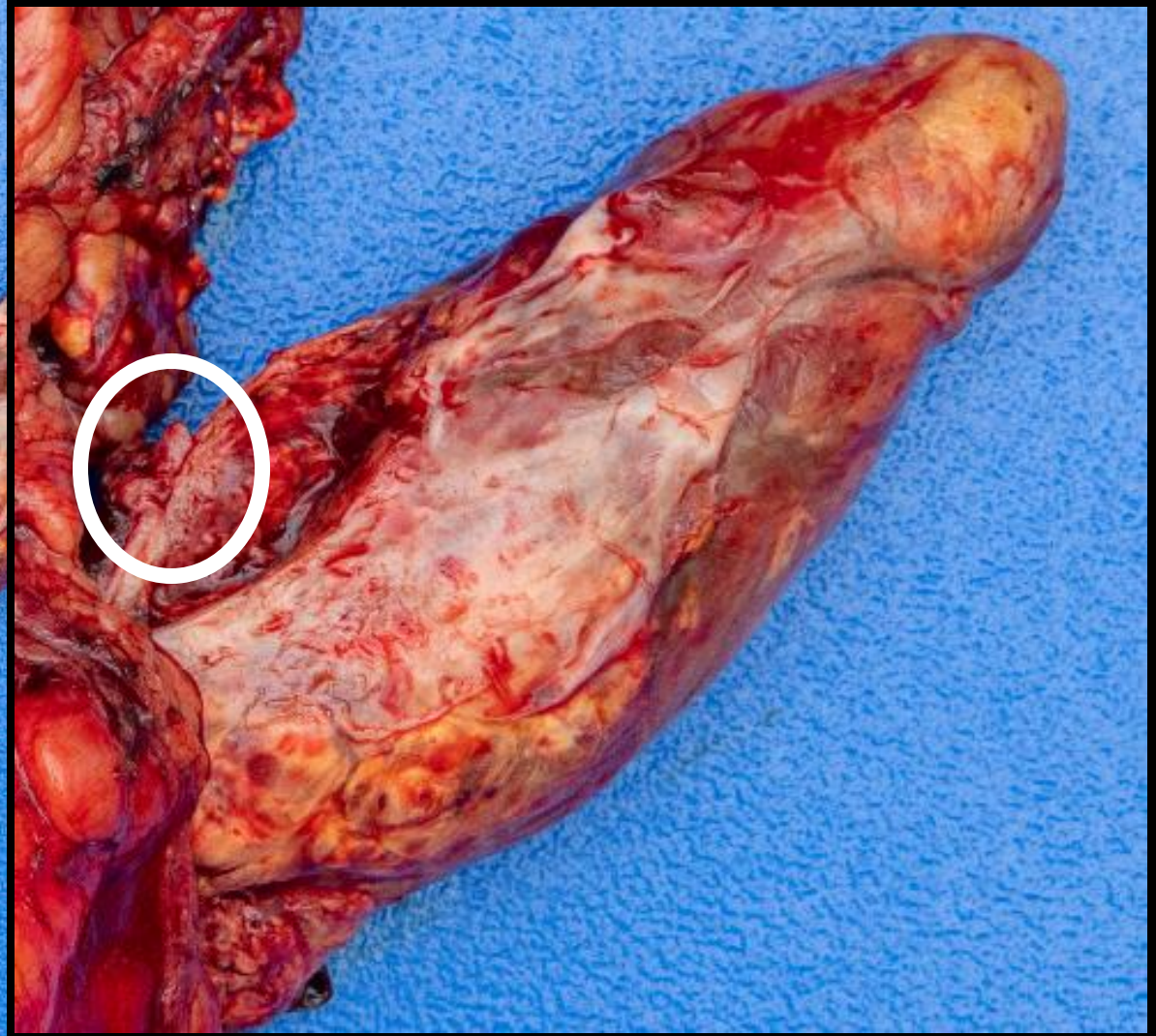
ccRCC with 5% sarcomatoid. pT3c: tumor thrombus → right atrium

Tumor thrombus
removed en bloc
with kidney

Margin can be difficult to find

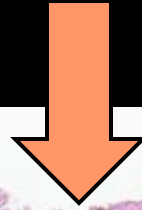


8cm ccRCC. pT3c: tumor thrombus → right atrium

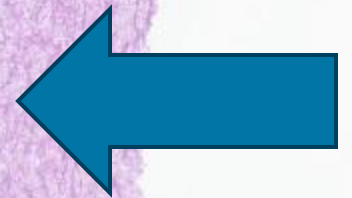


Renal vein margin
(inked, perpendicular section)

NEGATIVE

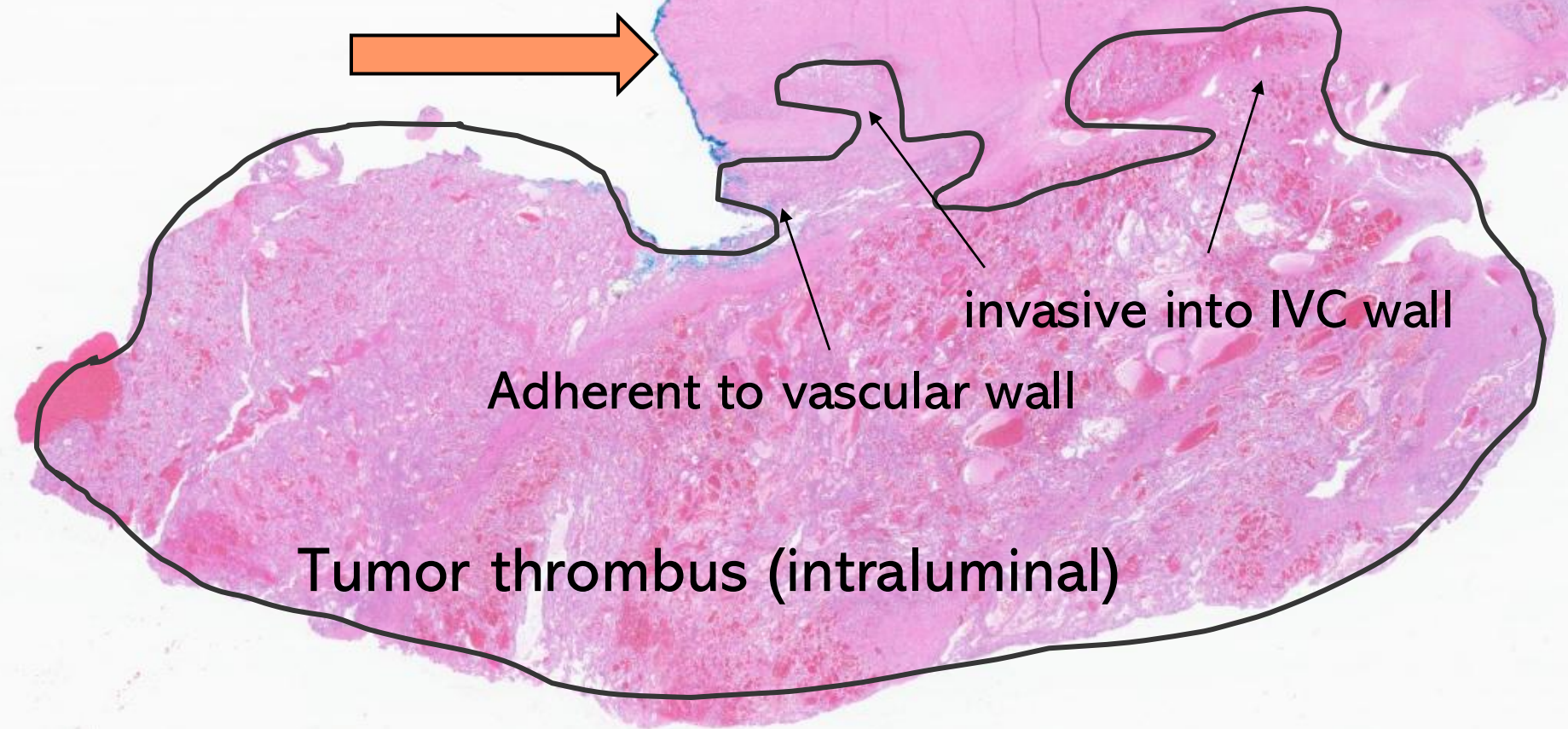


free



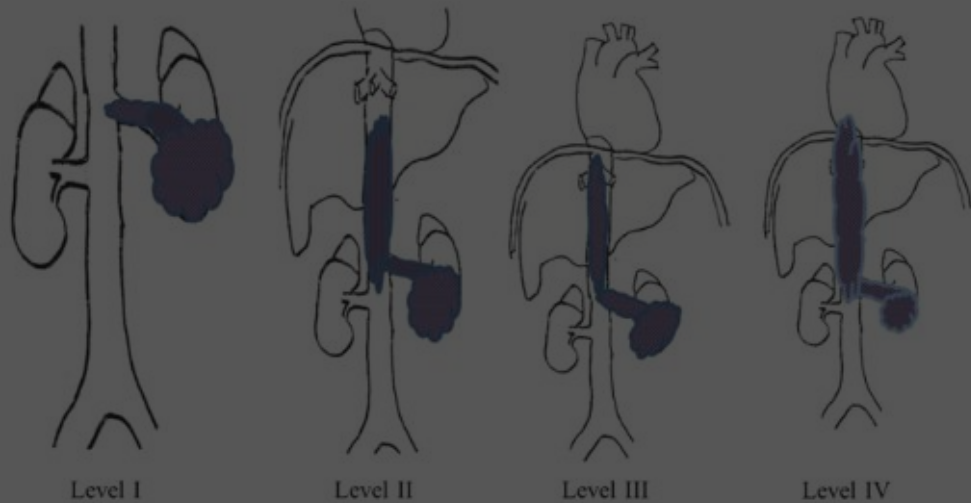
Tumor thrombus (intraluminal)

Margin = POSITIVE
(inked, perpendicular section)

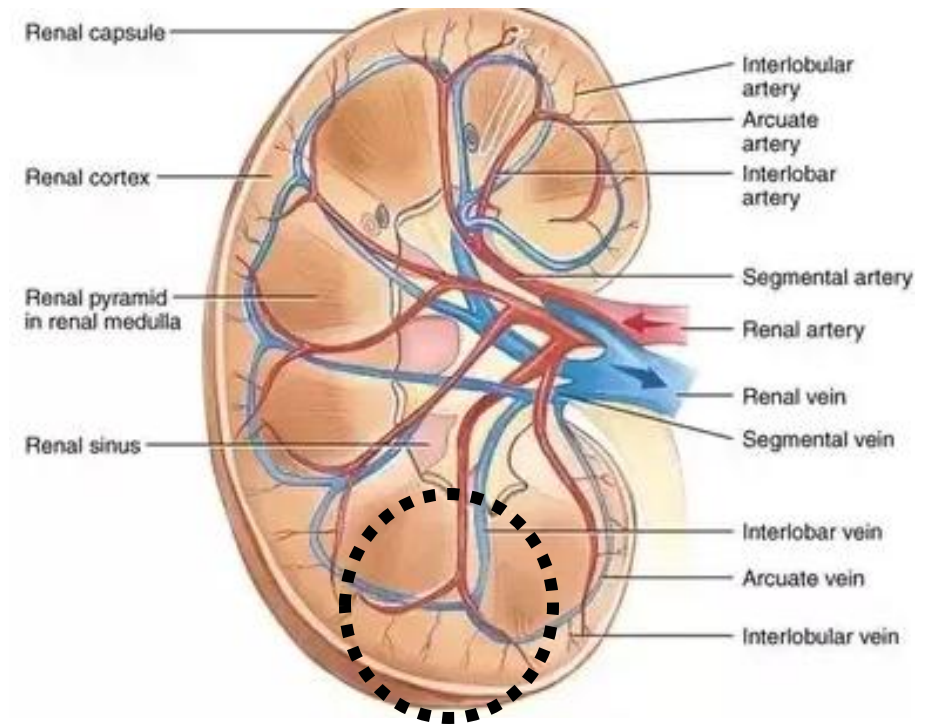


VENOUS SPREAD IN RCC

Antegrade = tumor thrombus into major veins



Retrograde = into proximal tributaries of the renal vein



RETROGRADE VENOUS INVASION

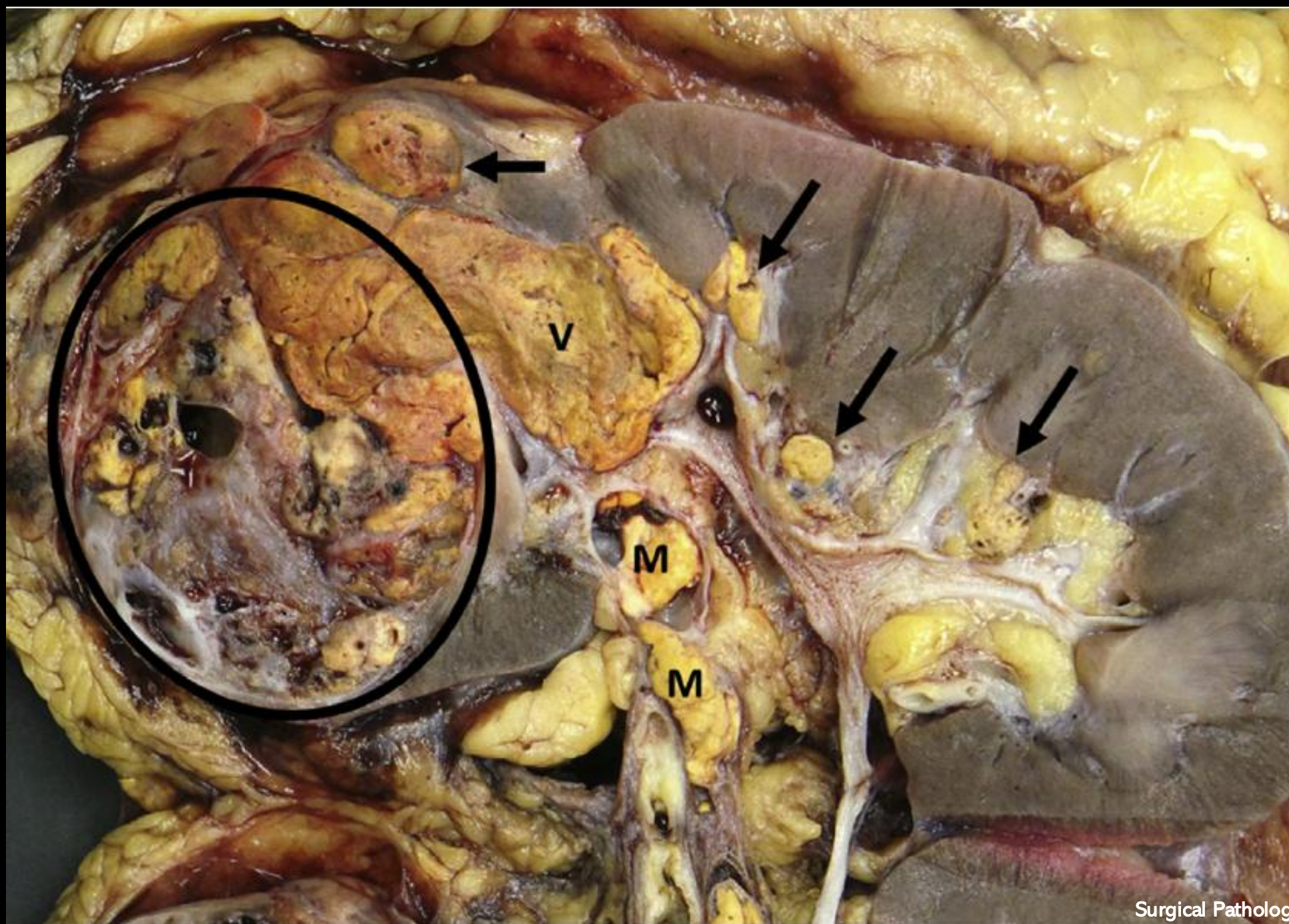
- Definition: Intravenous growth of tumor in noncontiguous areas, separated from original tumor by normal parenchyma
- Difficult to tell where primary tumor ends and venous spread begins



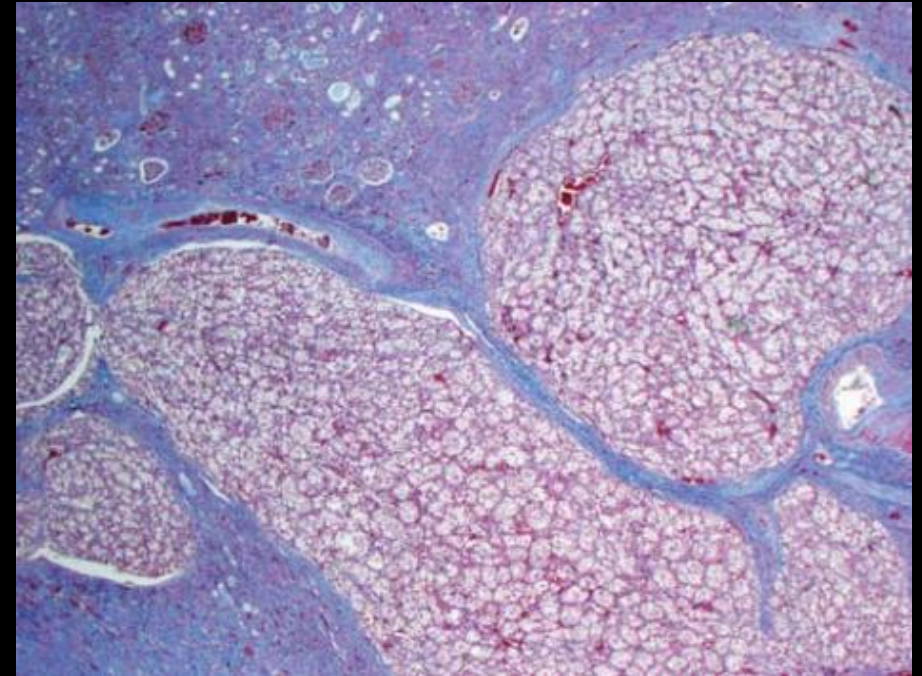
X Do not include in tumor size

X Not multifocal





- Seen in ~5% of cases, almost always ccRCC
- Be cautious: if ccRCC and “satellites”
- Keep in mind: Other subtypes can be multifocal (papillary)

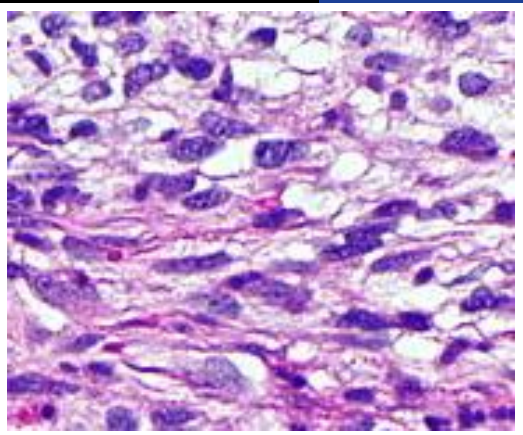


Ensure the “satellites” conform to the normal venous outflow: b/w pyramids, at corticomedullary junction

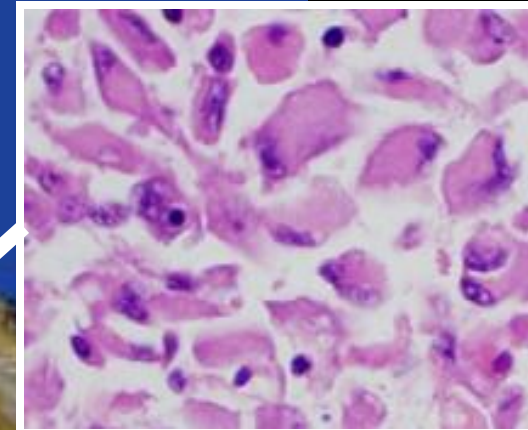
SARCOMATOID/RHABDOID FEATURES

SARCOMATOID/RHABDOID FEATURES

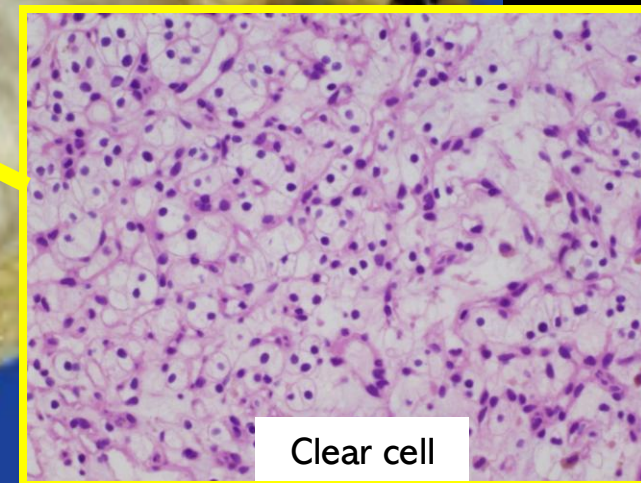
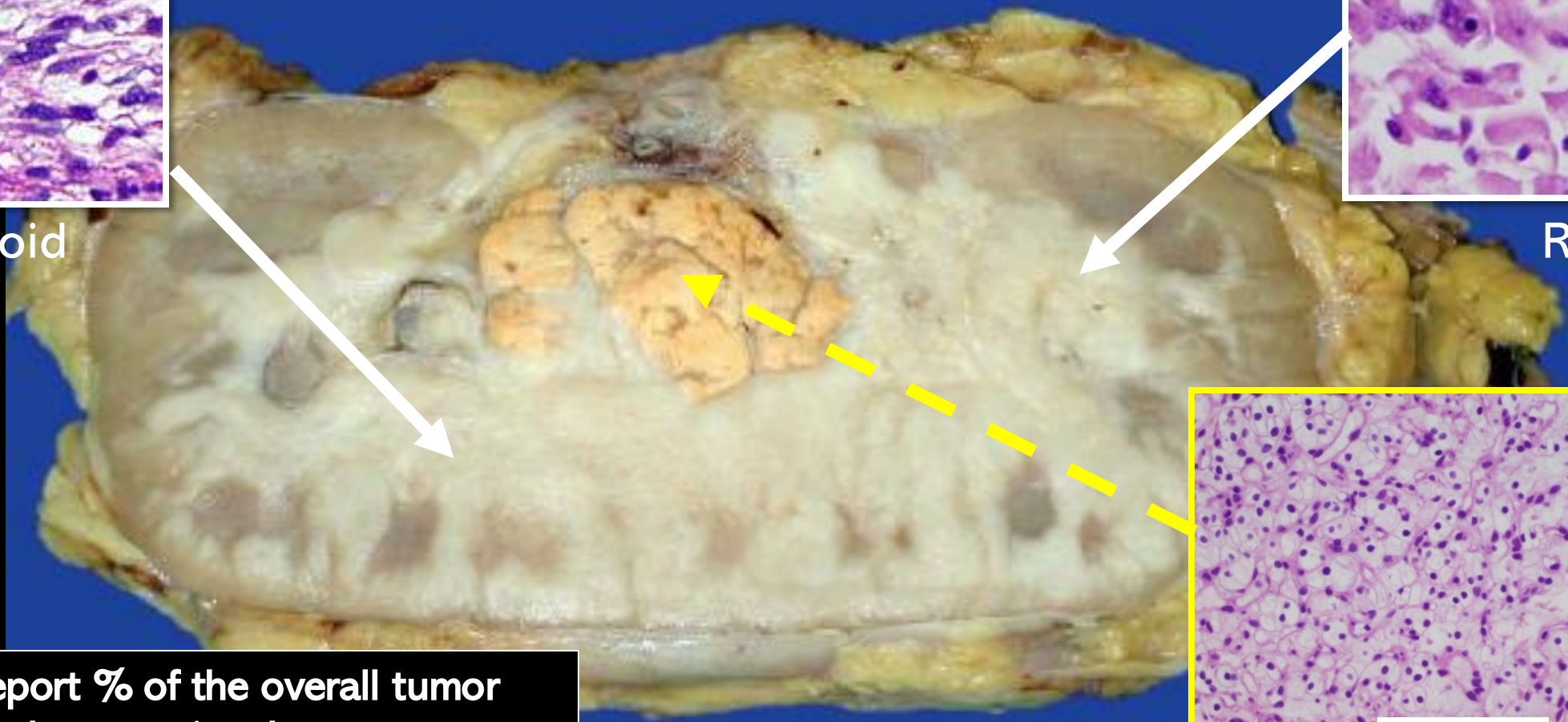
- Both are markers of tumor dedifferentiation
- Adverse histologic feature = poor prognosis (automatic WHO/ISUP grade 4)
- Can be seen with any histologic subtype
- Recognized grossly



Sarcomatoid



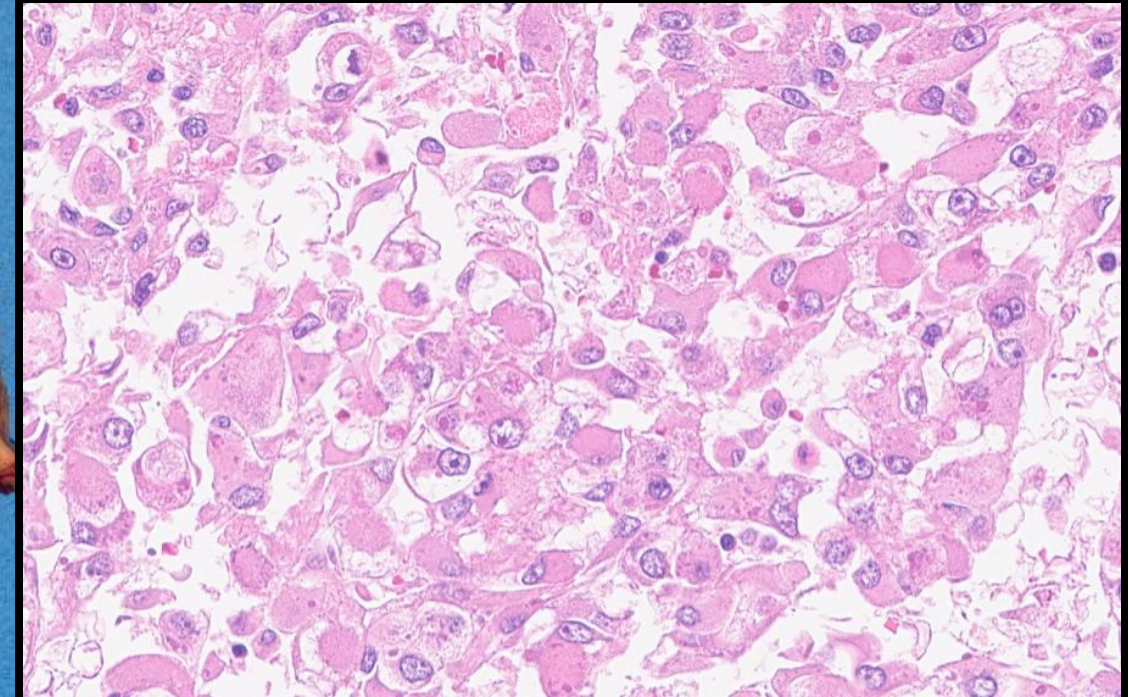
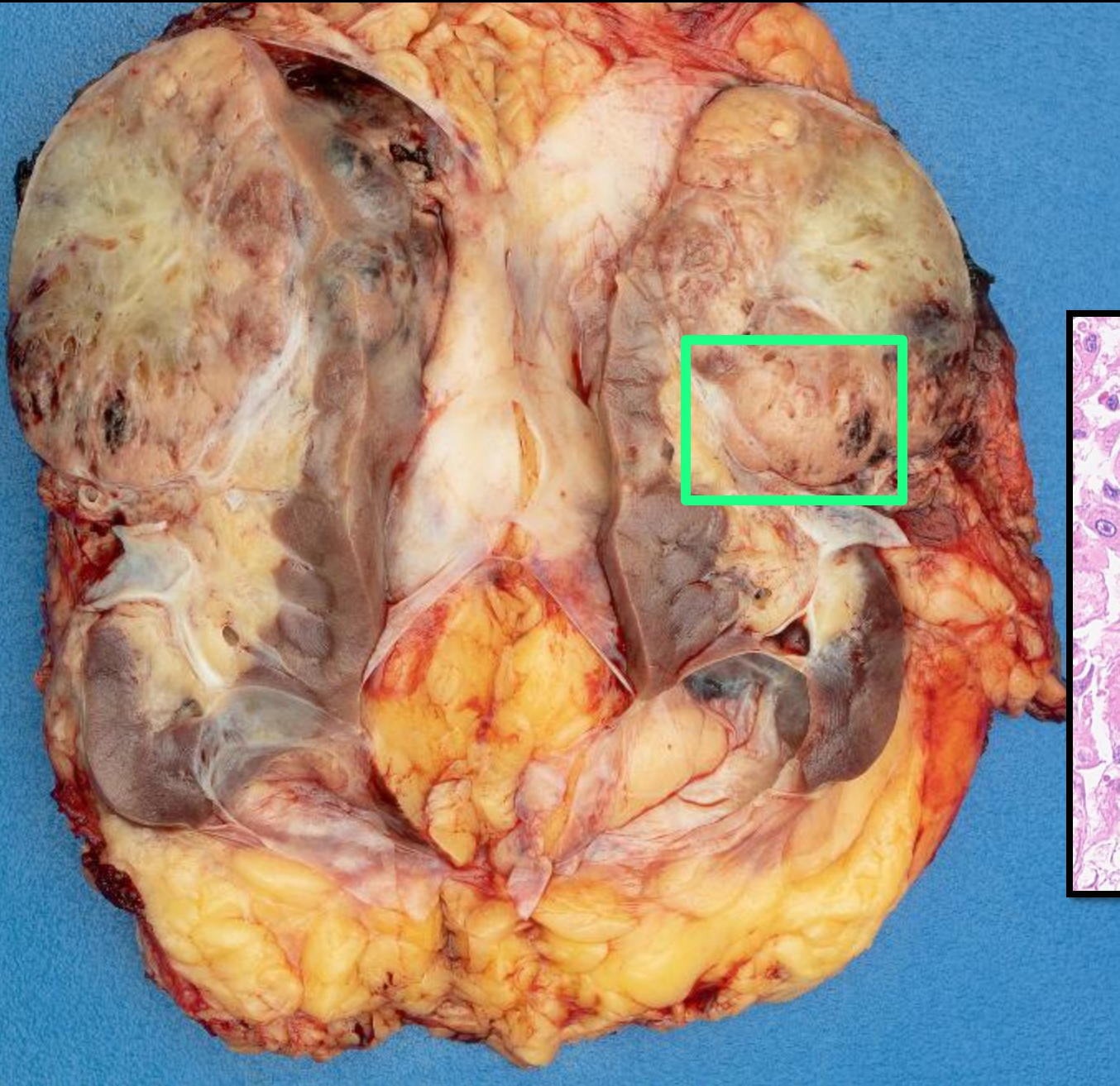
Rhabdoid



Clear cell

- Try to report % of the overall tumor
- Try to find conventional areas

ccRCC, WHO/ISUP grade 4 with rhabdoid features. pT3b

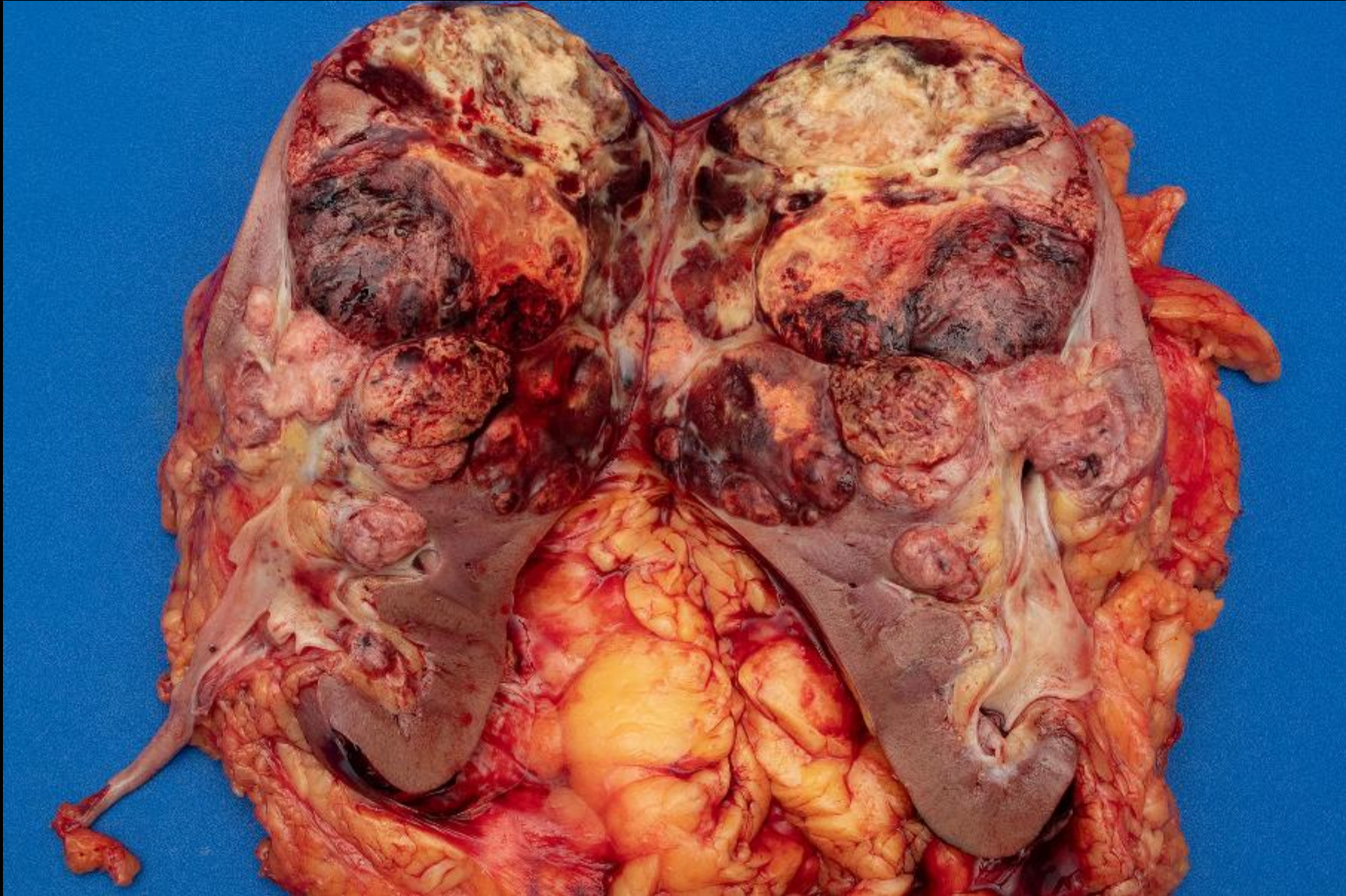


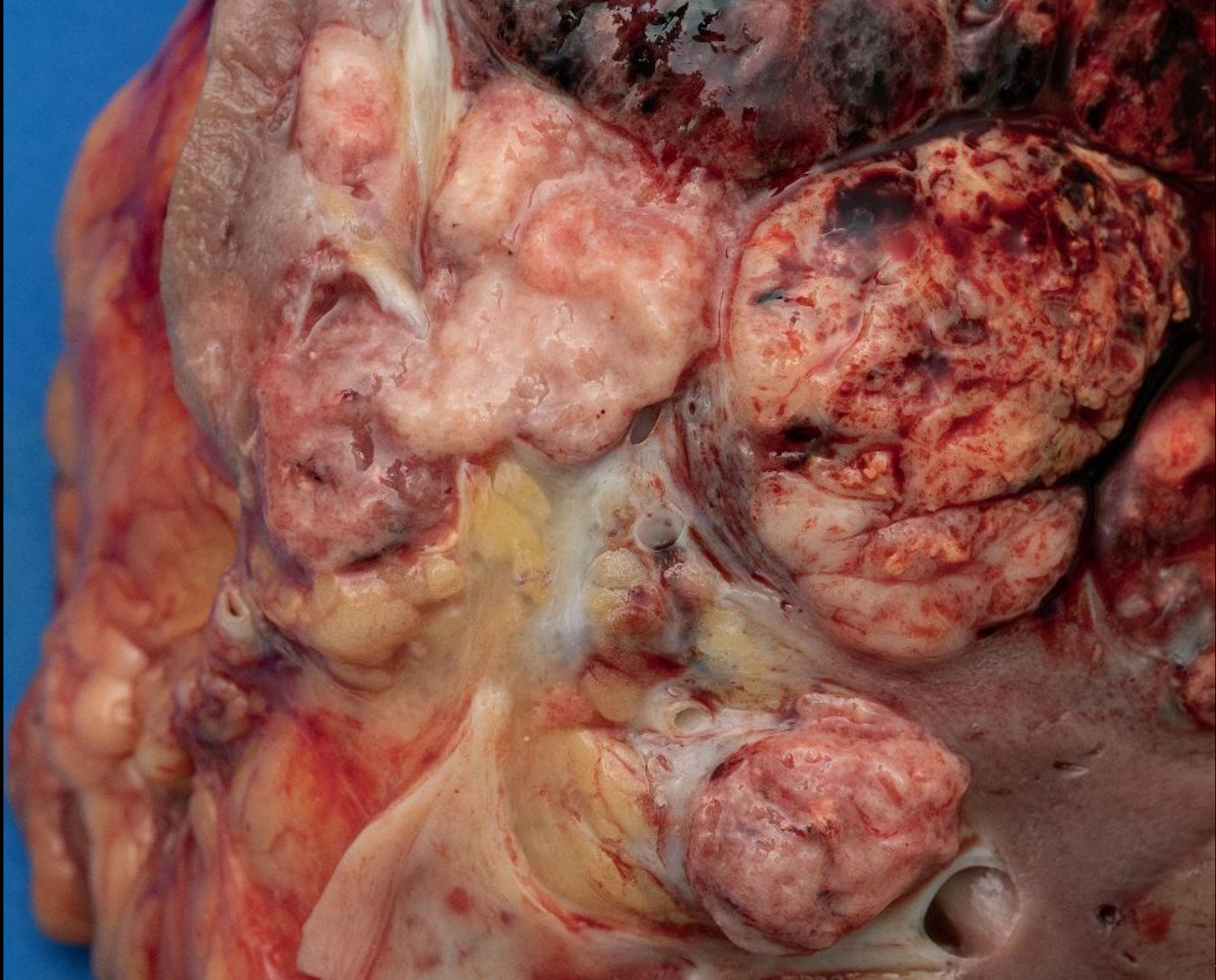
TUMOR NECROSIS

TUMOR NECROSIS

- Another prognostic factor (esp in ccRCC)
- Can be seen with any histologic subtype
 - Though significance may vary
- Can be recognized grossly

15cm ccRCC with 30% necrosis, WHO/ISUP grade 4 with rhabdoid features
pT3c (level 4 thrombus)

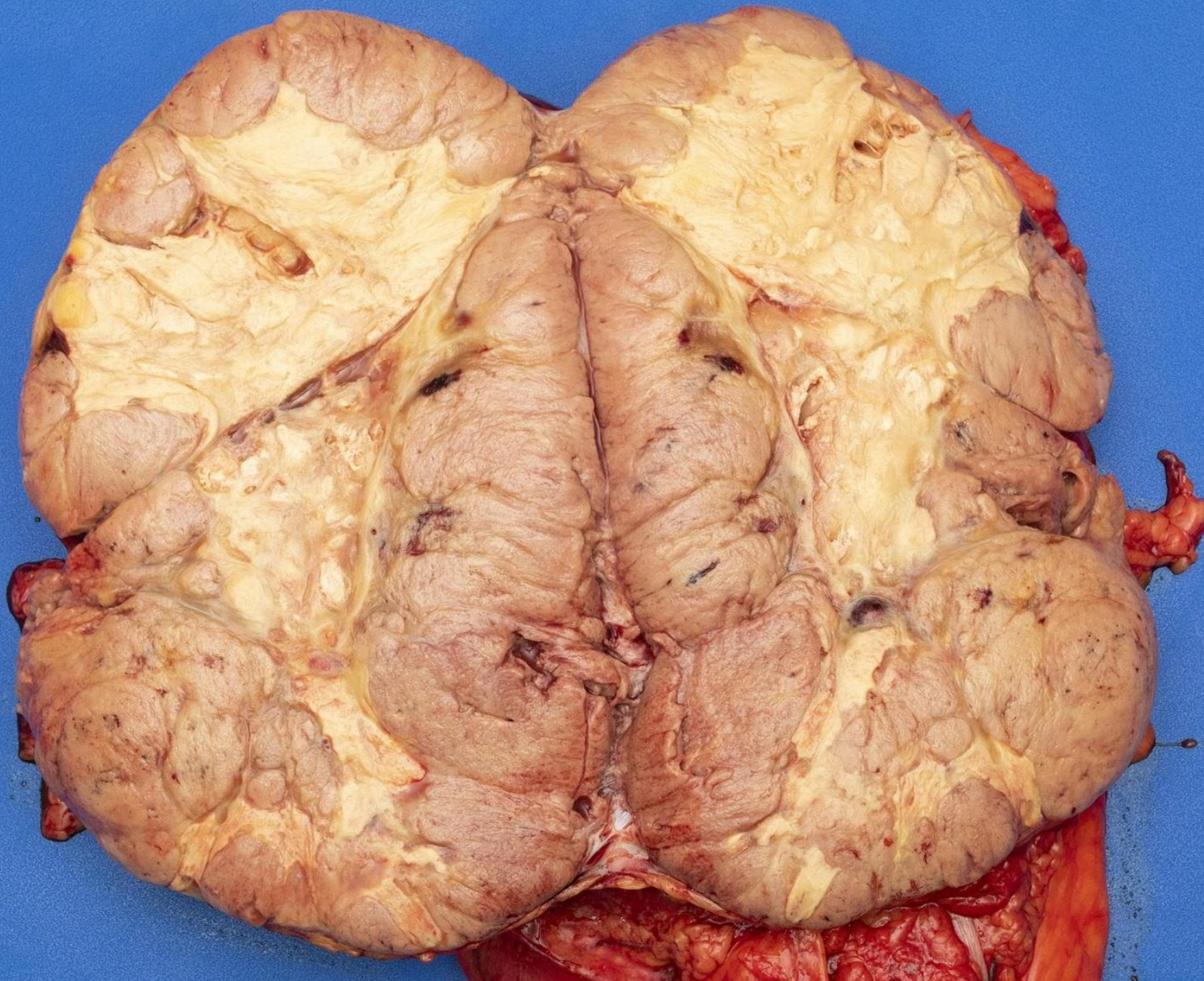




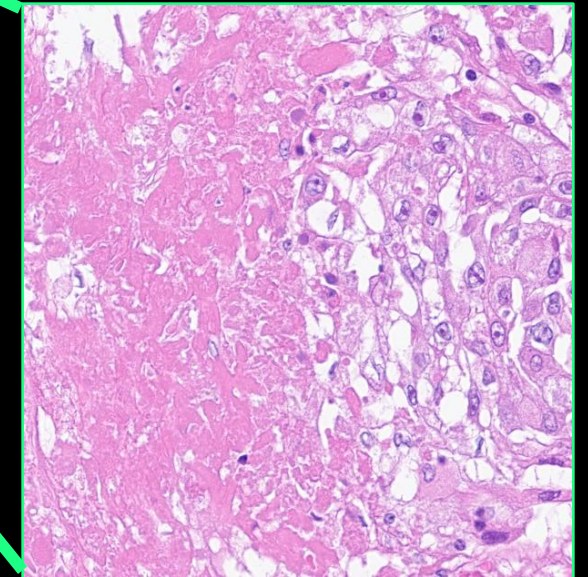
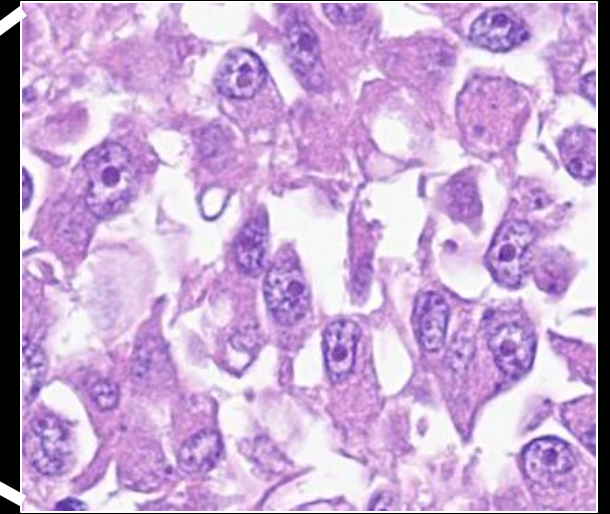
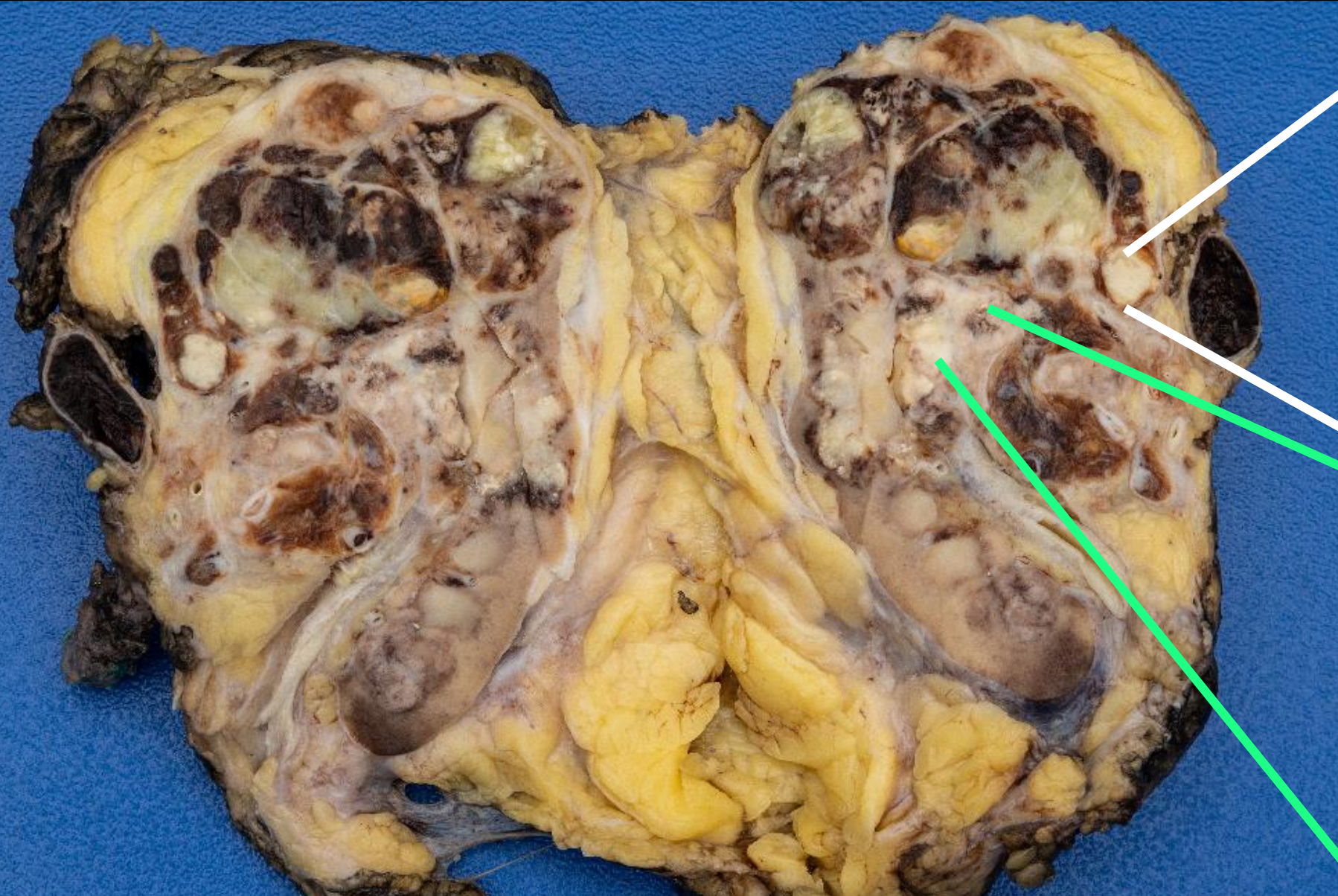
19cm ccRCC with 95% necrosis and rhabdoid features, pT3a



20cm chromophobe RCC with 50% necrosis

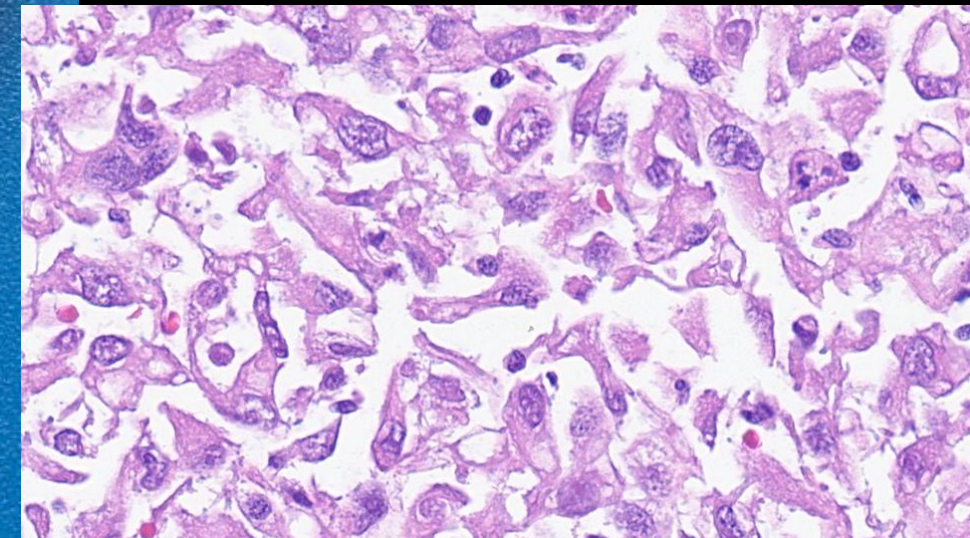
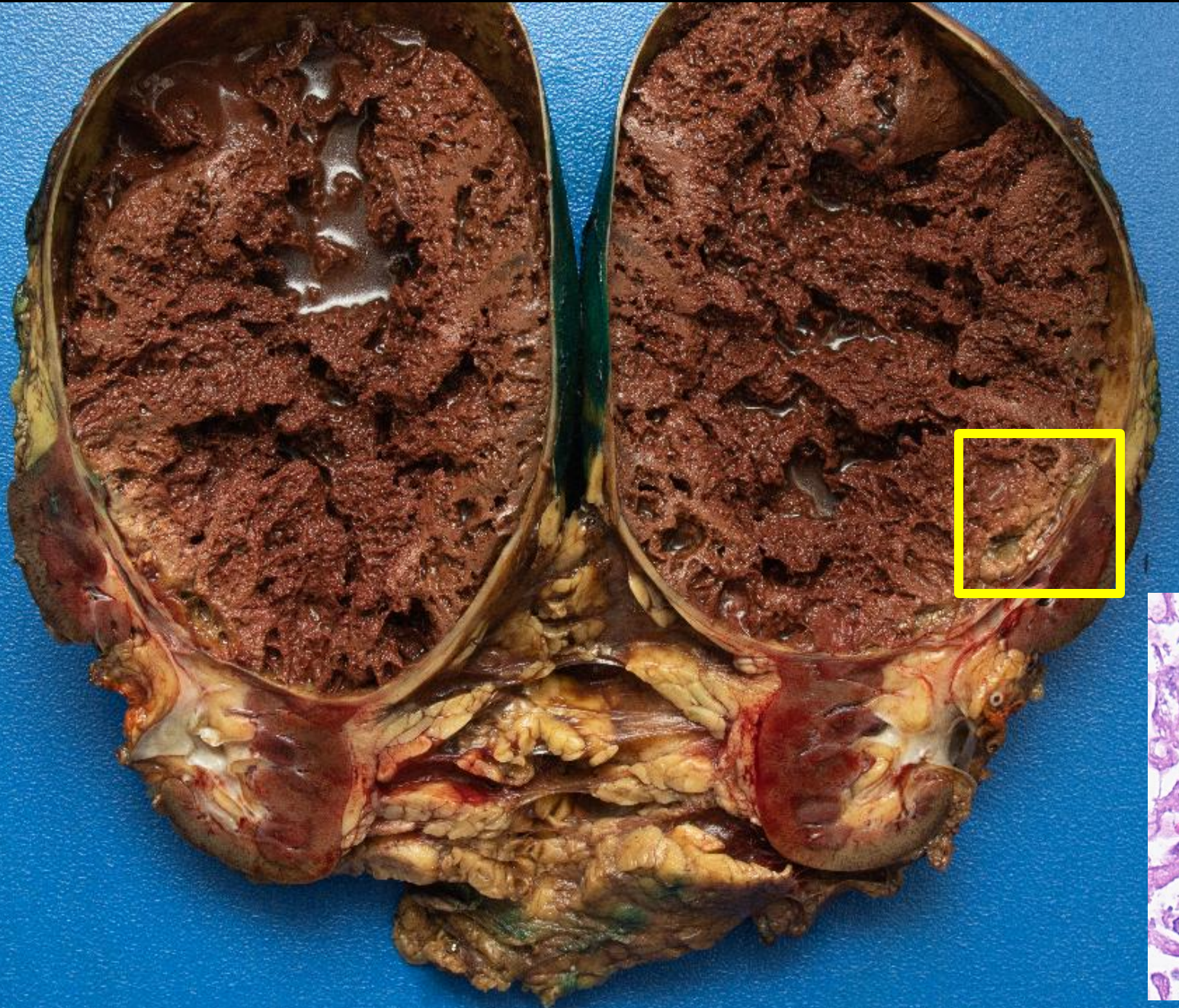


9cm ccRCC with 30% necrosis*, WHO/ISUP grade 4. pT3b, pN1



*cytoreductive nephrectomy after neoadjuvant therapy

12cm papillary RCC with rhabdoid features



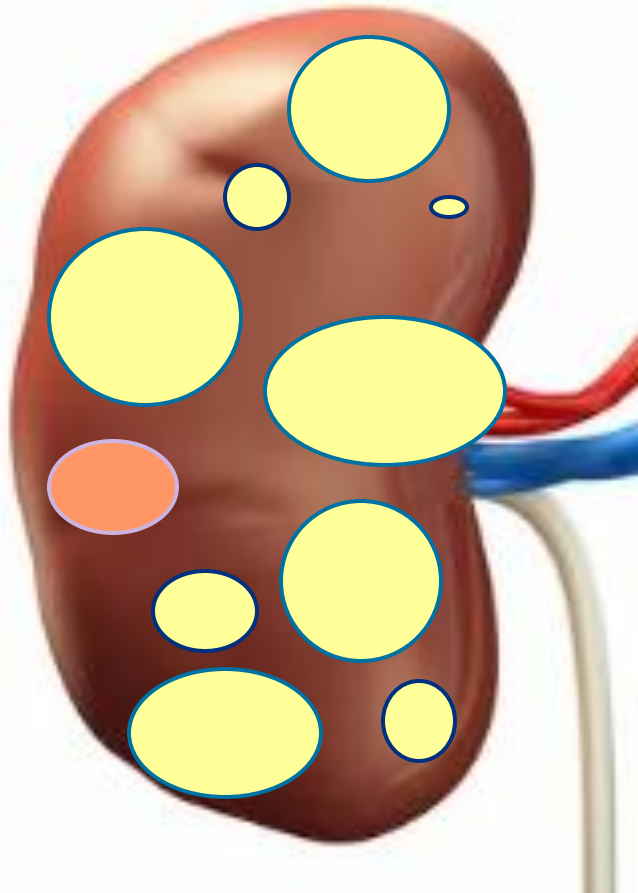
MULTIFOCALITY

MULTIFOCAL TUMORS

- Before describing multifocal tumors, consider:
 - Antegrade extension into sinus veins
 - Retrograde extension into cortical veins
- Common with papillary, oncocytoma, clear cell tubulopapillary tumors
- Most have the same histology
- About 5% of cases are truly multifocal

Richstone L et al *J Urol* 2004; 171, 615–620

MULTIFOCALITY

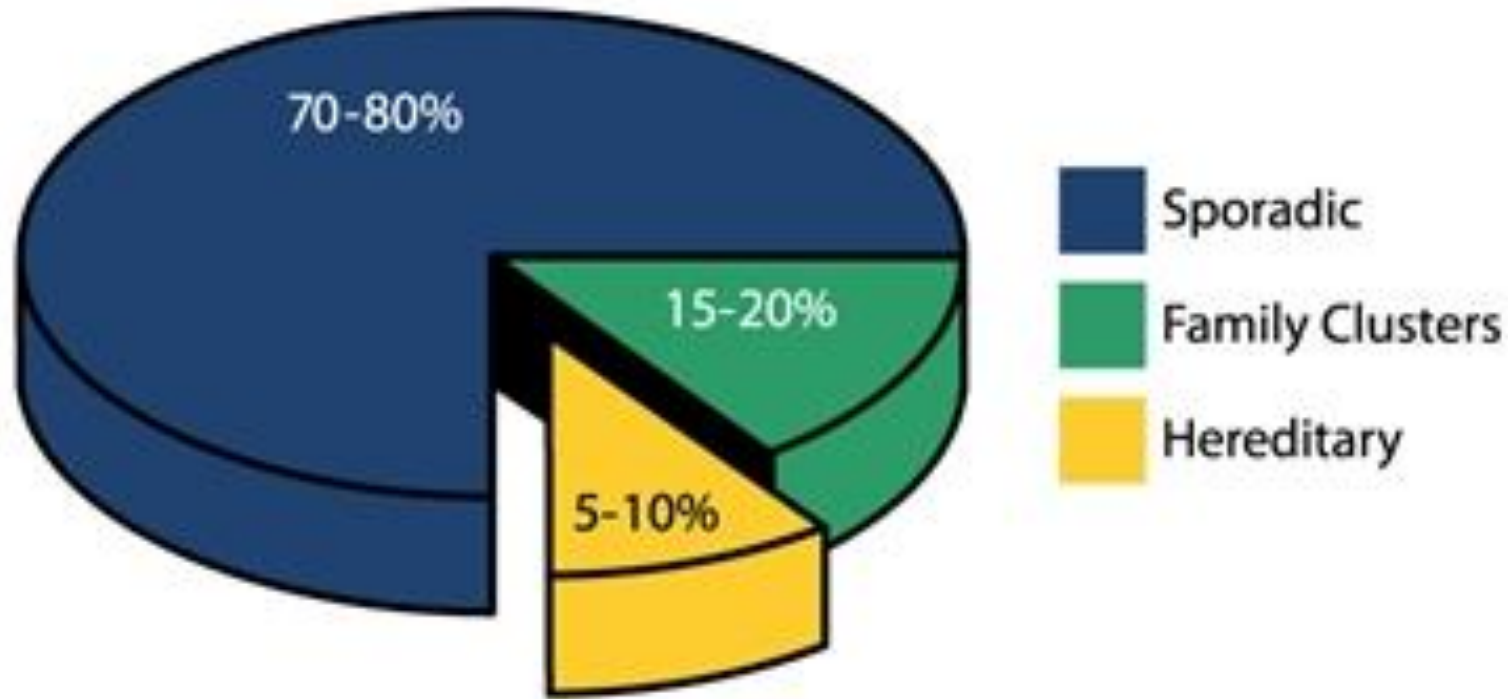


If tumors appear similar

- Measure and report up to 5 largest tumors
- Largest used to assign mpT

If tumors appear dissimilar

- Report and sample separately
- Will have separate staging



Sporadic Cancer:

Most cancers develop due to genetic damage we sustain over a lifetime. When genes acquire defects that impact the cells ability to grow and divide properly tumors form.

Familial Cancer:

Occurs in families more often than what would be expected by chance. Familial clusters have been reported for many types of cancer and are believed to be due to a combination of risk factors which include inherited susceptibility, environmental factors and chance. Probably more common than we realize.

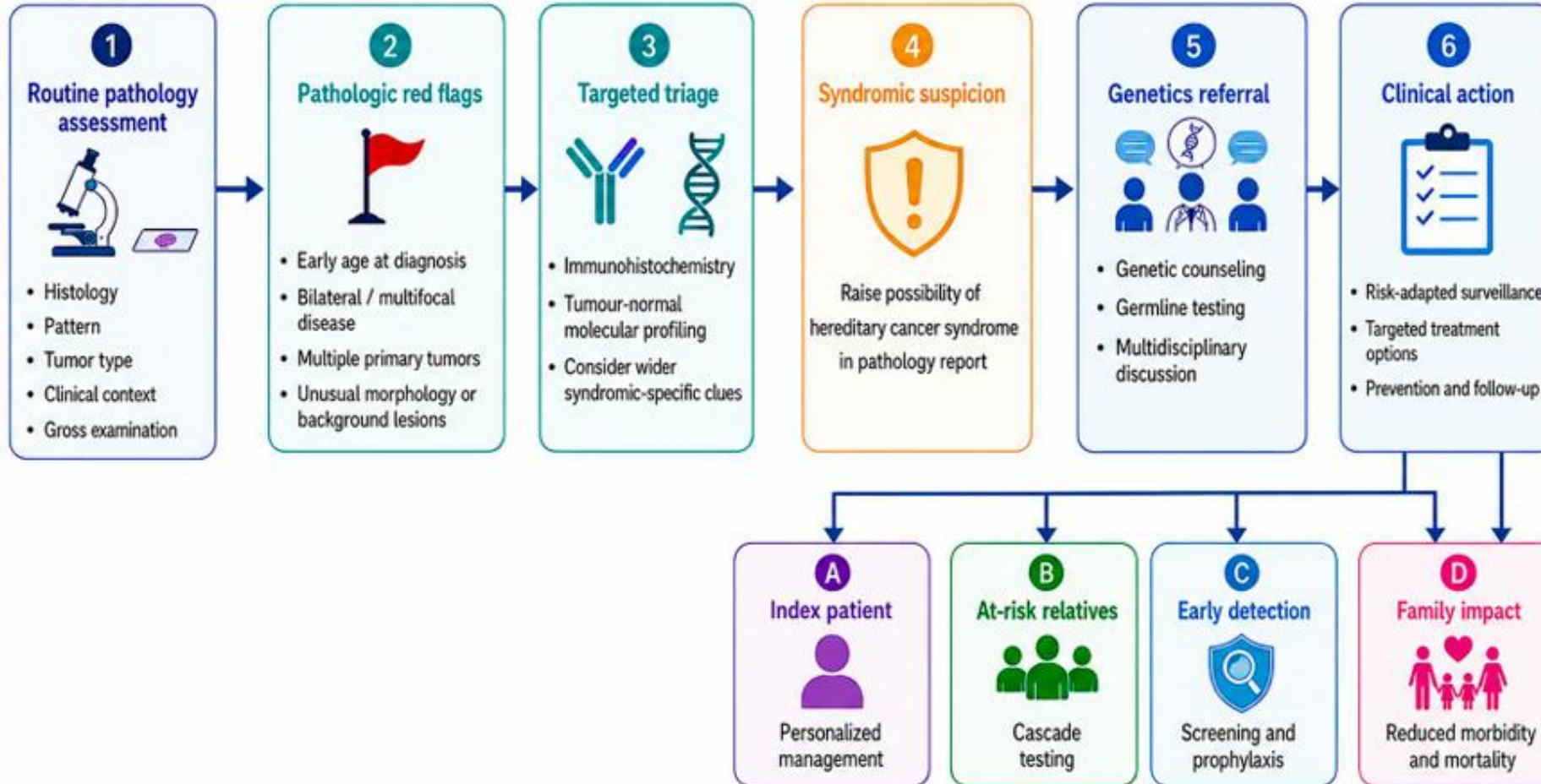
Hereditary Cancer:

Cancer that results from genetic changes that are passed on from one generation to the next is considered hereditary. 5-10% of all cancers.

Syndrome	Gene Locus, Type (Protein)	Pathway	Renal Tumor Histology	Other Clinical Features
von Hippel-Lindau (VHL)	VHL 3p25, tumor suppressor	HIF-1	ccRCC (multifocal)	CNS hemangioblastoma, retinal angioma, pheo, pan NET, cystadenoma of epididymis
Hereditary leiomyomatosis renal cell carcinoma (HLRCC)	Fumarate hydratase 1q42.1, tumor suppressor (fumarase)	Krebs cycle/HIF-1	“Papillary”/HLRCC-type RCC	Cutaneous/uterine leiomyomata
Birt-Hogg-Dube (BHD)	FLCN 17p11.2, tumor suppressor (folliculin)	mTOR	-Chromophobe -Oncocytoma -Hybrid RCC	Fibrofolliculoma, trichodiscoma; lung cyst, spontaneous pneumo
Hereditary papillary renal cancer (HPRC)	MET 7q31 proto-oncogene (hepatocyte growth factor receptor)		Papillary type 1 (multifocal)	None known
Hereditary paraganglioma and pheochromocytoma	SDH subunits 5p15	Krebs cycle	-SDH-deficient -Clear cell Chromophobe RCC	Pheochromocytoma, paraganglioma
Tuberous sclerosis complex (TSC)	TSC1, TSC2 9p34, 16p13	HIF-1	-Angiomyolipoma -RCC variants	CNS Tubers
BAP1 tumor syndrome	BAP1	A variety of chromatin-associated processes	-Clear cell RCC	Uveal melanoma, mesothelioma (w/out asbestos exposure), atypical Spitz

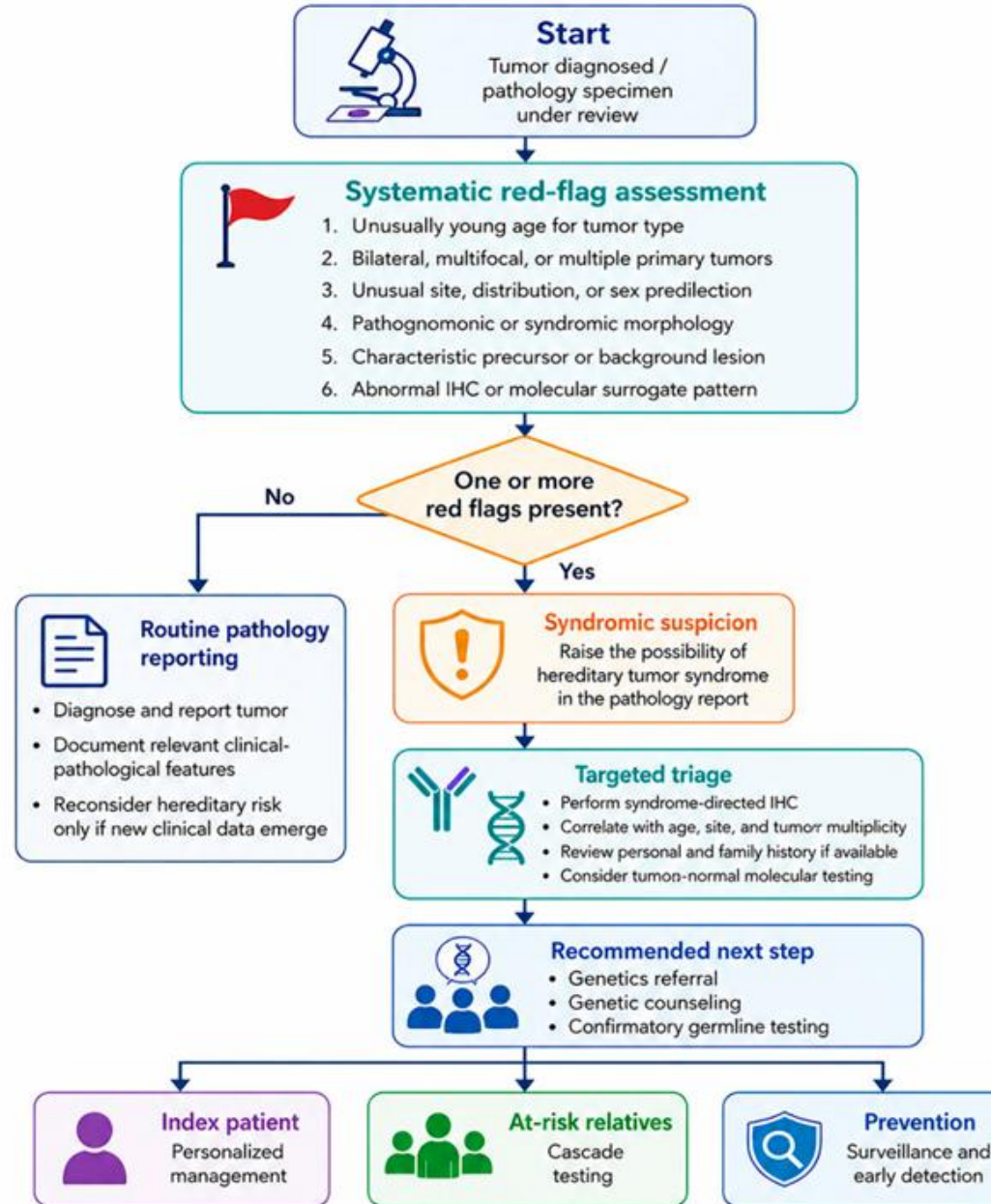
Pathology as a Sentinel of Hereditary Cancer Predisposition

From routine tissue diagnosis to germline evaluation, surveillance, and family impact



Red-Flag Diagnostic Algorithm

When should a pathologist suspect a hereditary tumor syndrome?



Structured recognition of red flags allows the pathologist to trigger timely hereditary cancer evaluation.

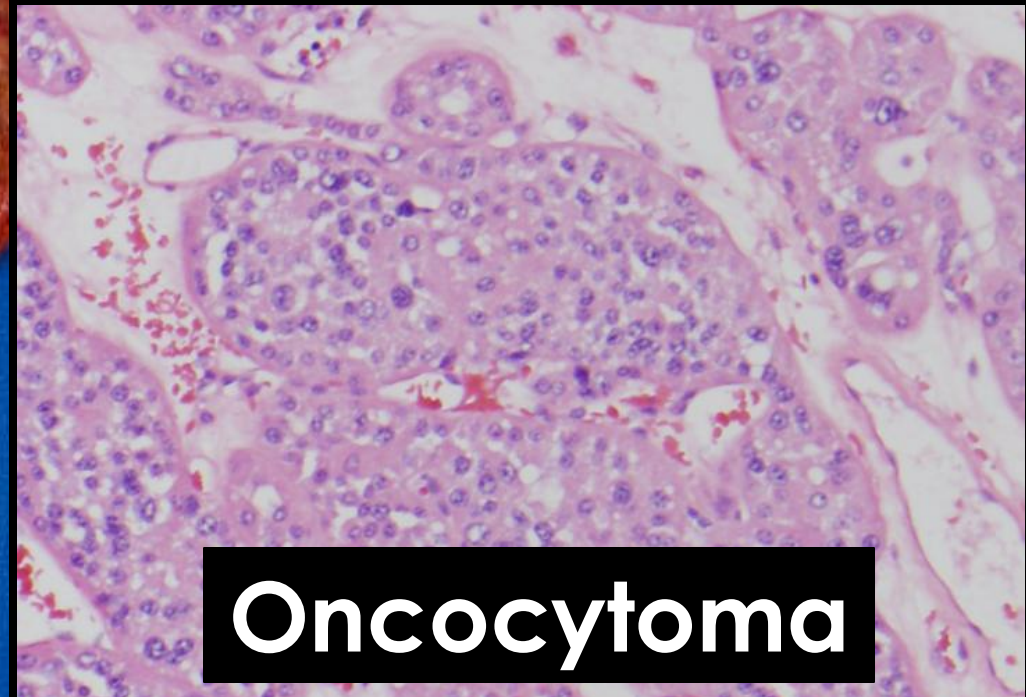
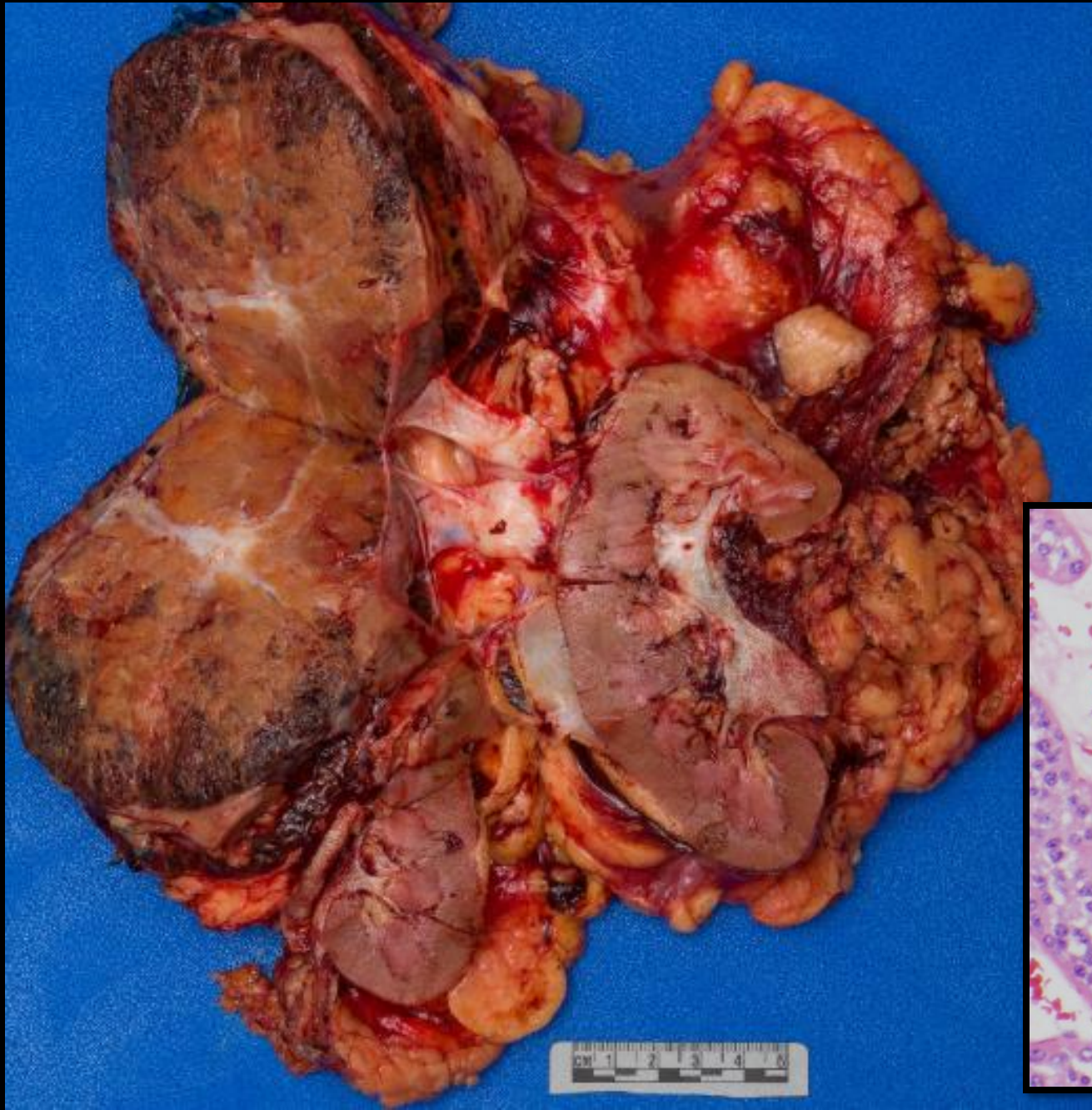
HEREDITARY RCC SYNDROMES

- Suspect if:
 - Patient is <50 years old
 - Bilateral, multifocal renal tumors
 - Has a history of a syndrome-defining lesion
 - Has a family history of renal tumors

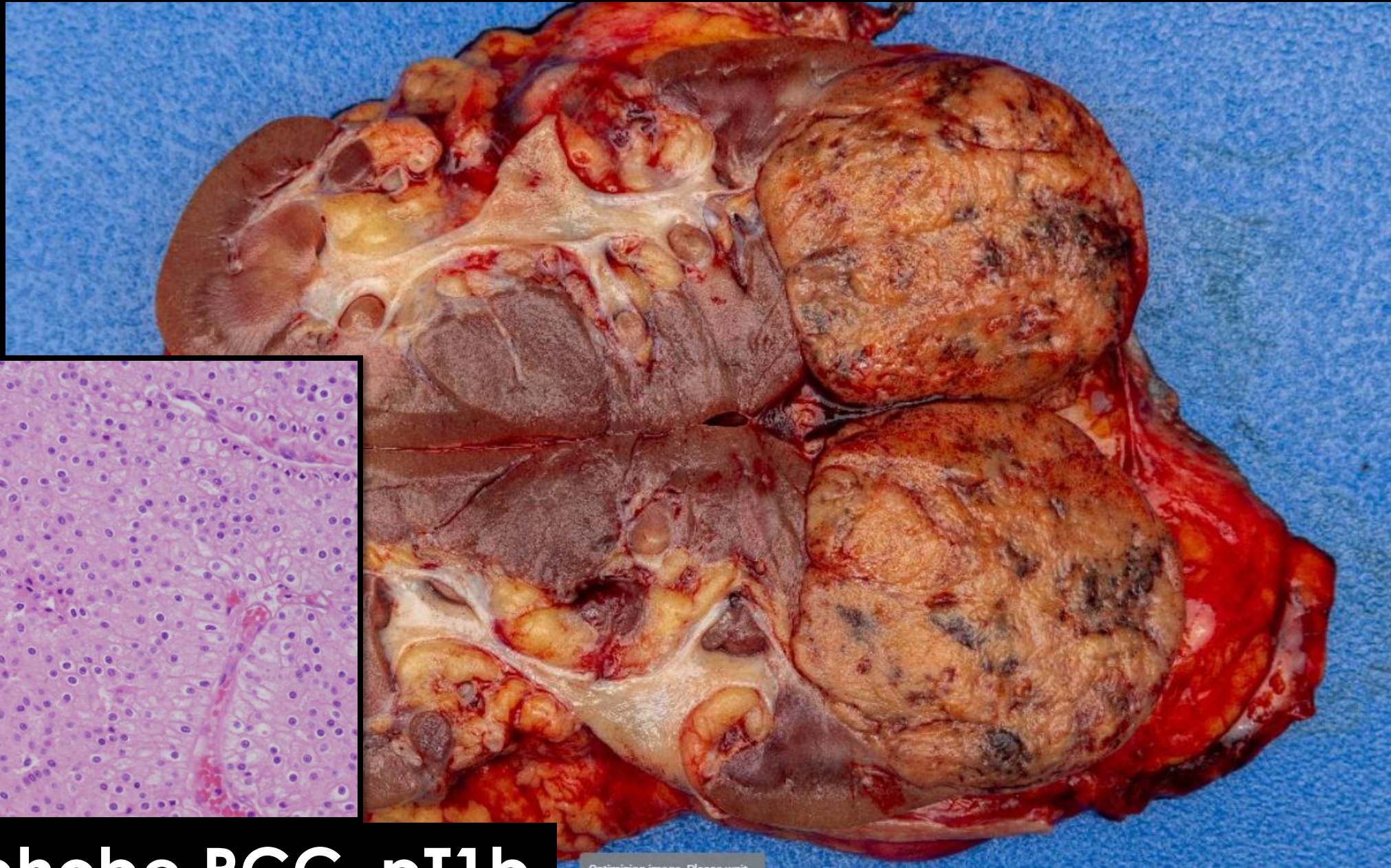
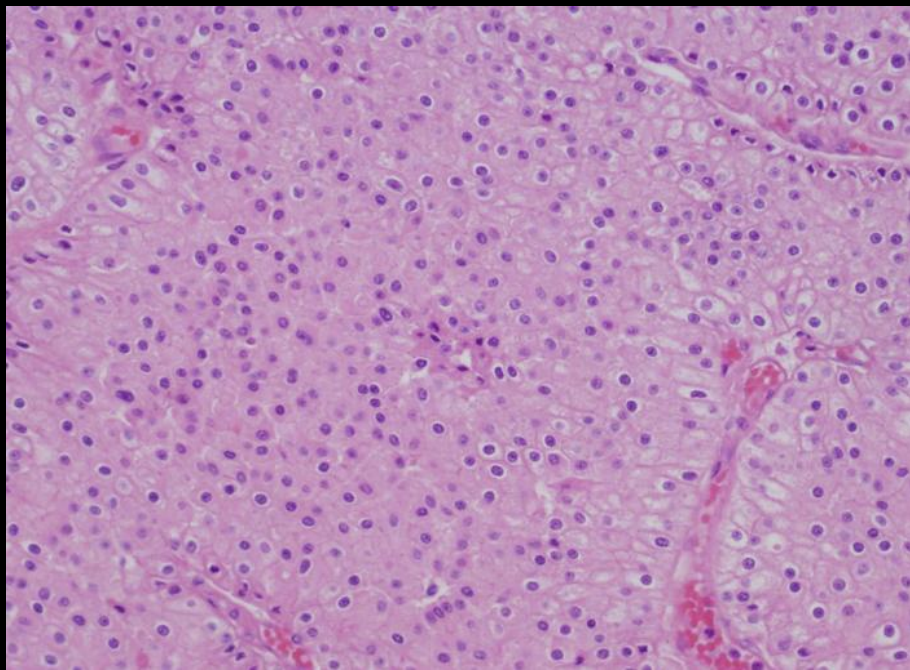
Sometimes we are the first to suggest a syndromic relationship.

INTERESTING CASES

57 y/o man, 13cm right upper pole mass



Oncocytoma



Chromophobe RCC, pT1b



Chromophobe RCC, pT2

57 y/o man, 12.5cm right lower pole mass



Chromophobe RCC, pT3a

40 yo man, 17cm right upper pole mass

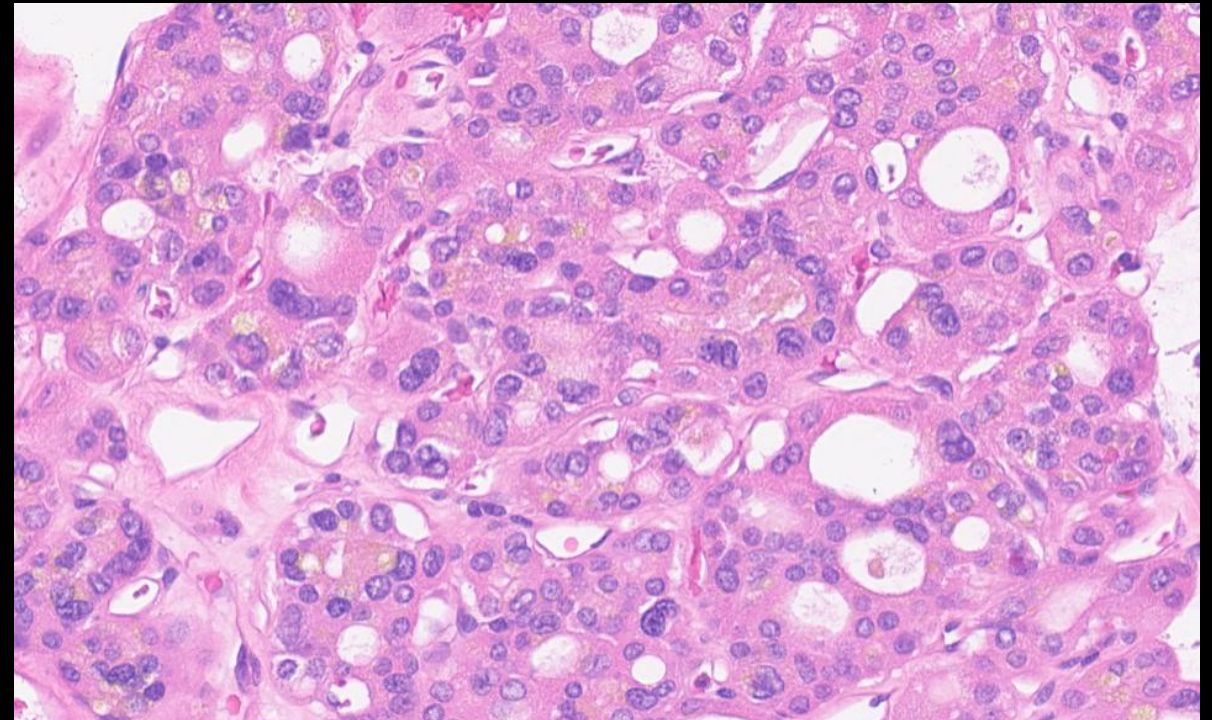


Chromophobe RCC, 80% necrosis, pT3a

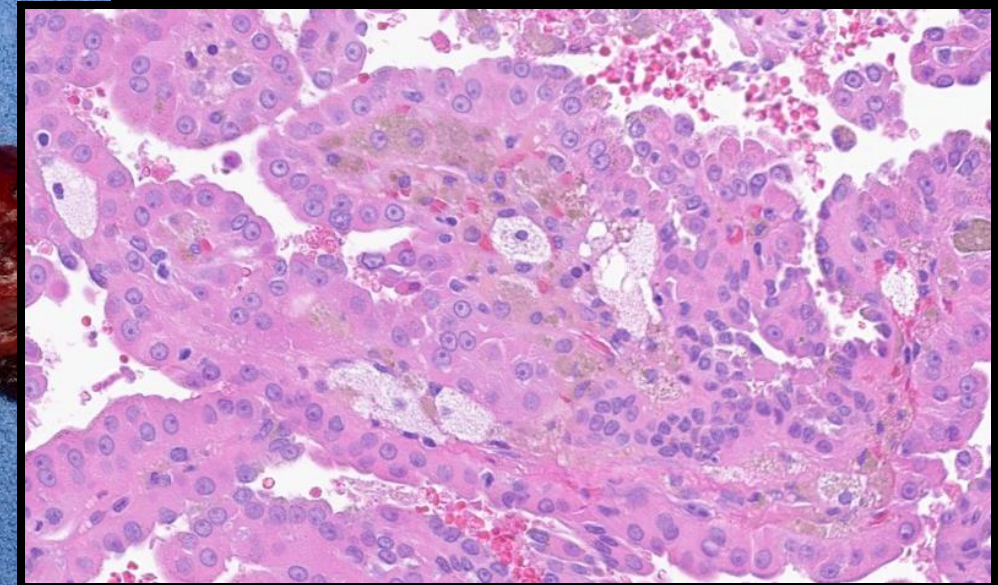
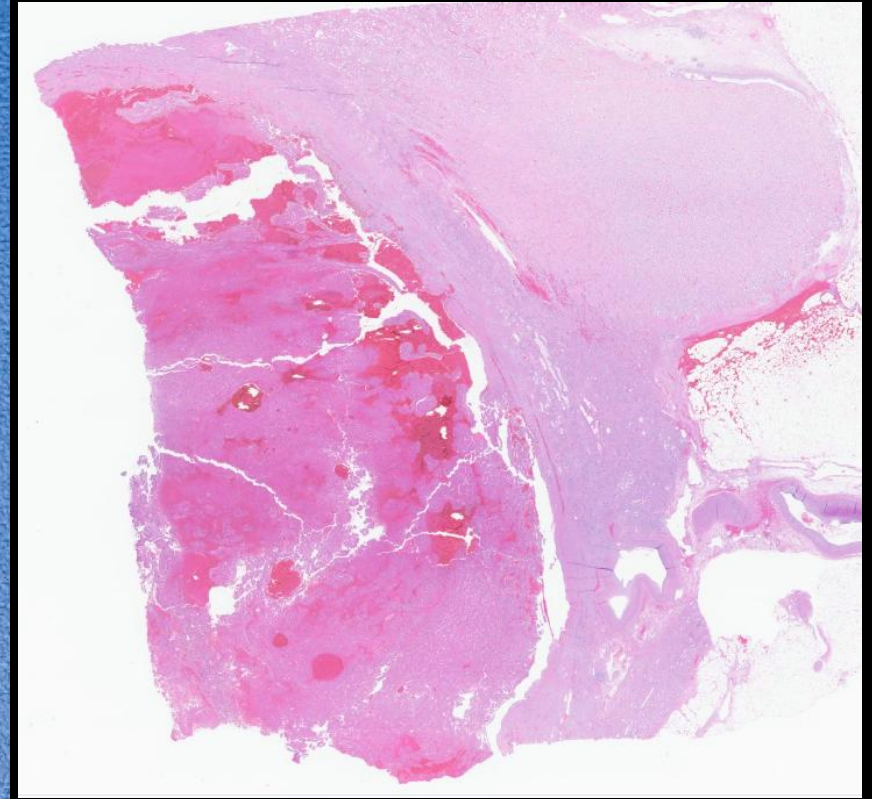
73yo man, retired coal miner, 12cm right renal mass

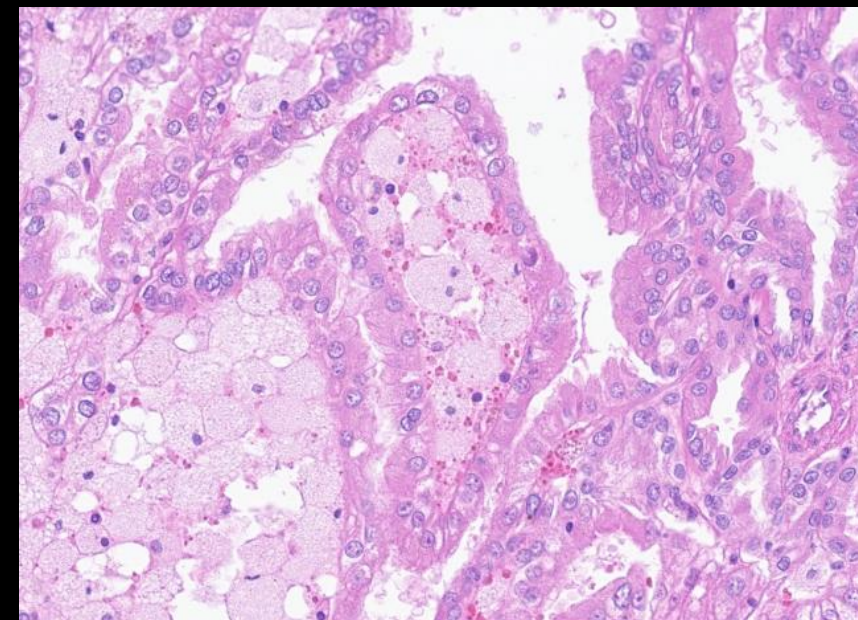
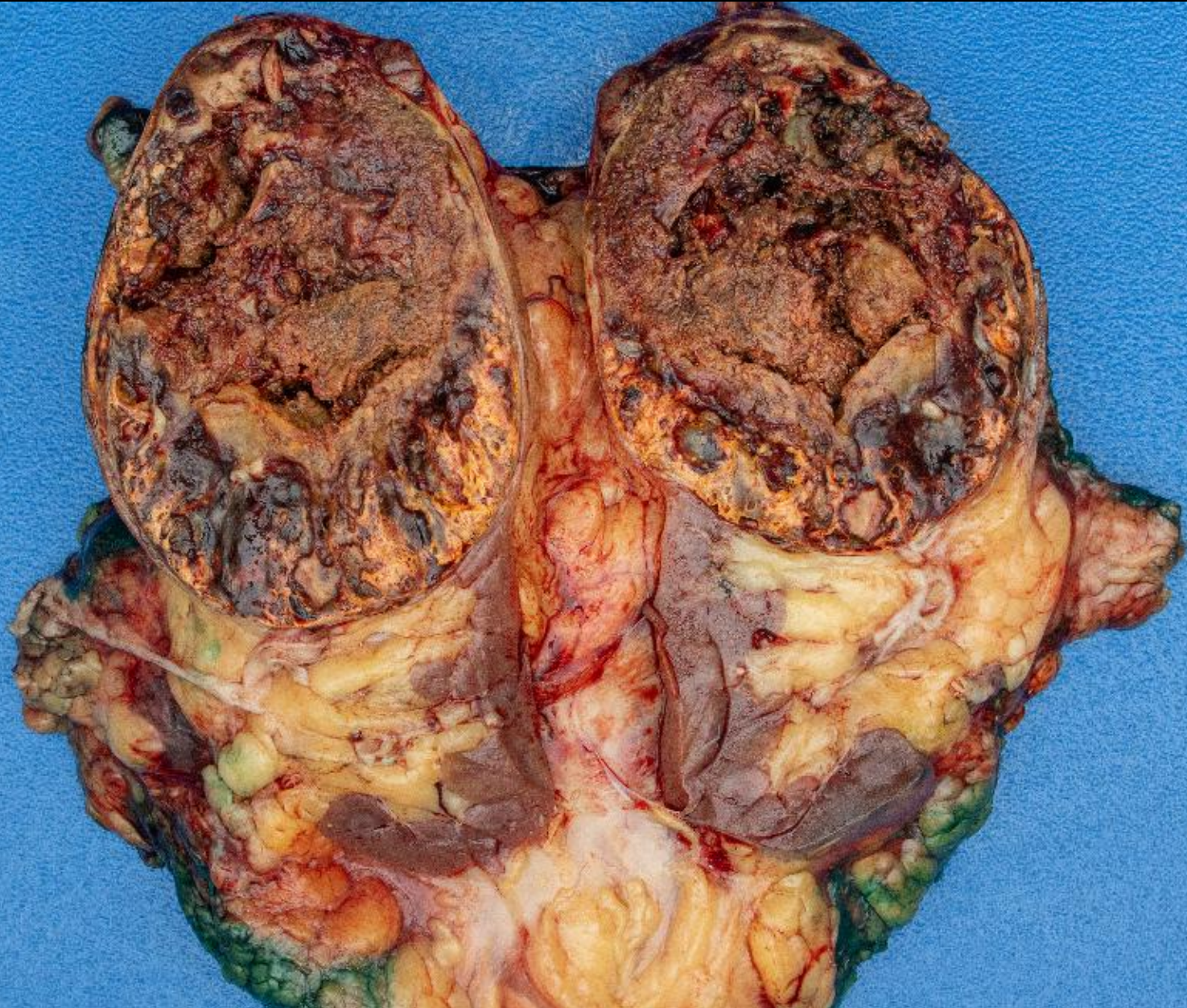


Differential Diagnosis?



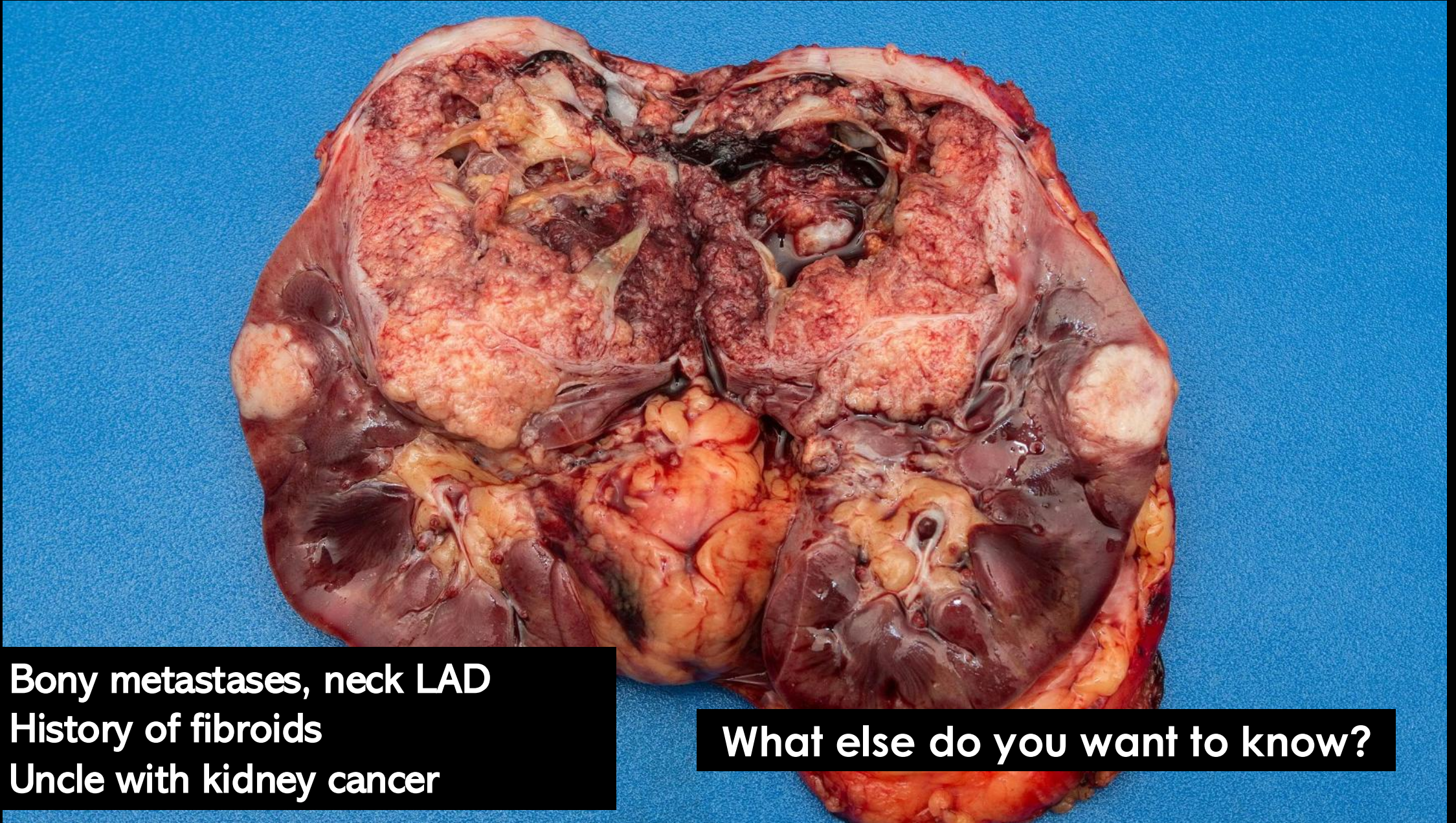
Chromophobe RCC, pT3a
Pigmented microcystic subtype





11cm Papillary RCC, pT2b

29 y/o woman, 9cm left upper pole mass

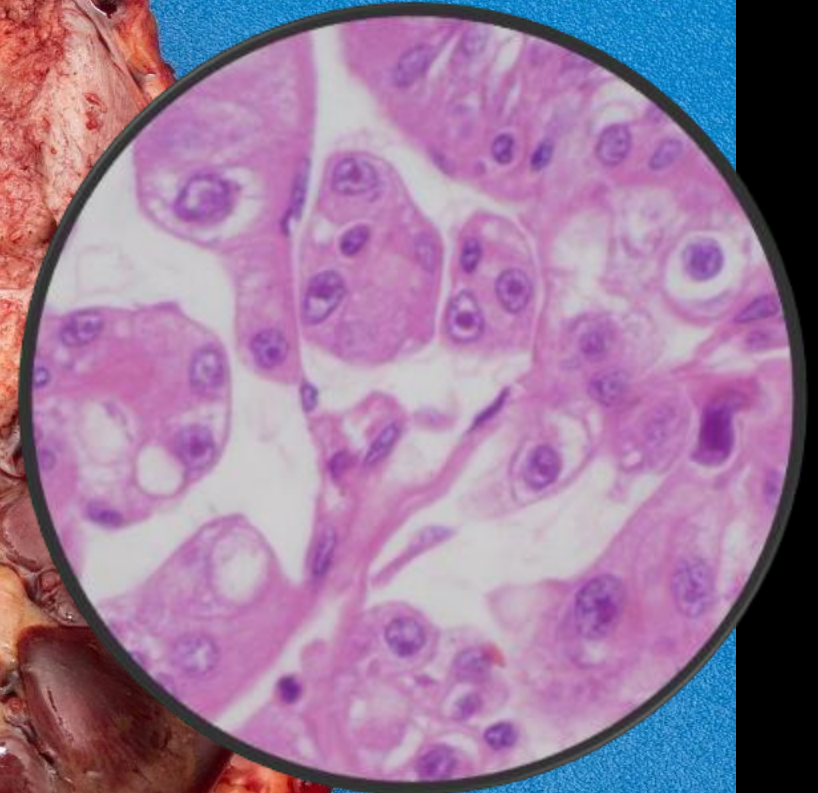


- Bony metastases, neck LAD
- History of fibroids
- Uncle with kidney cancer

What else do you want to know?

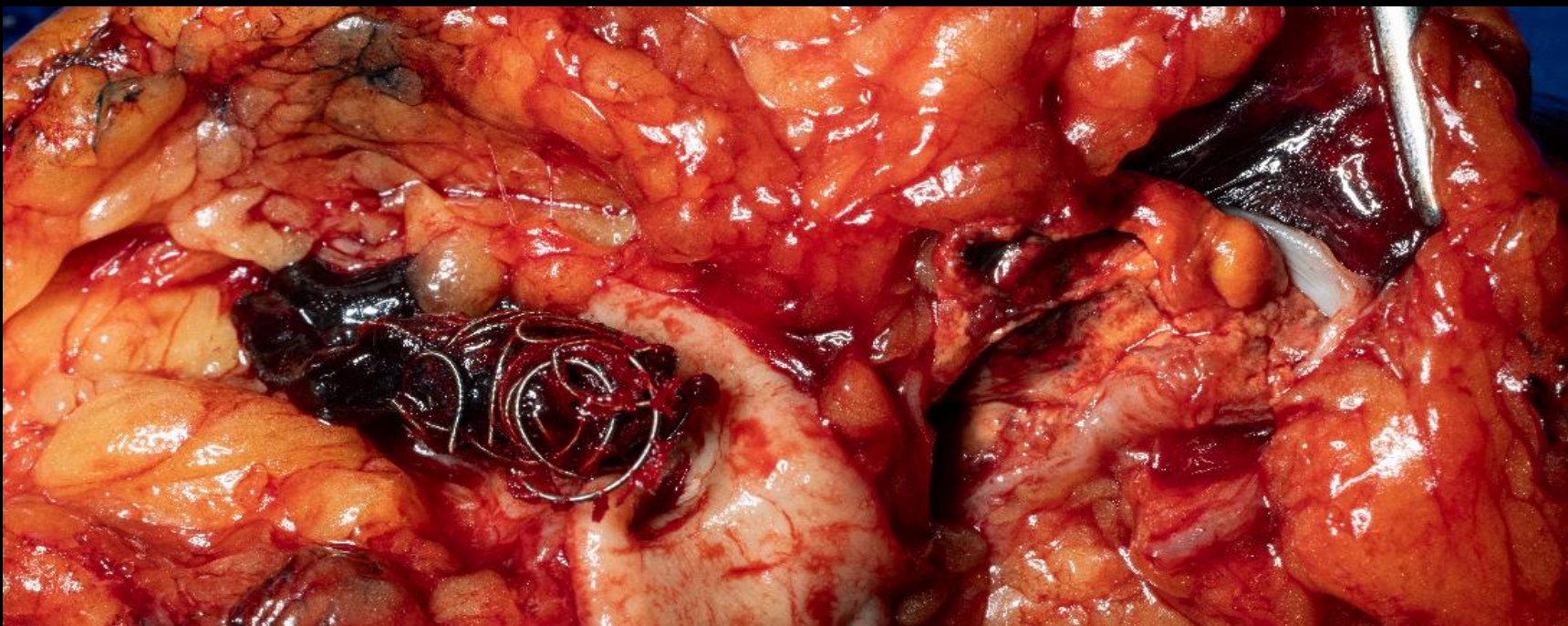
29 y/o woman, 9cm left upper pole mass

Sarcomatoid



Fumarate hydratase-deficient RCC

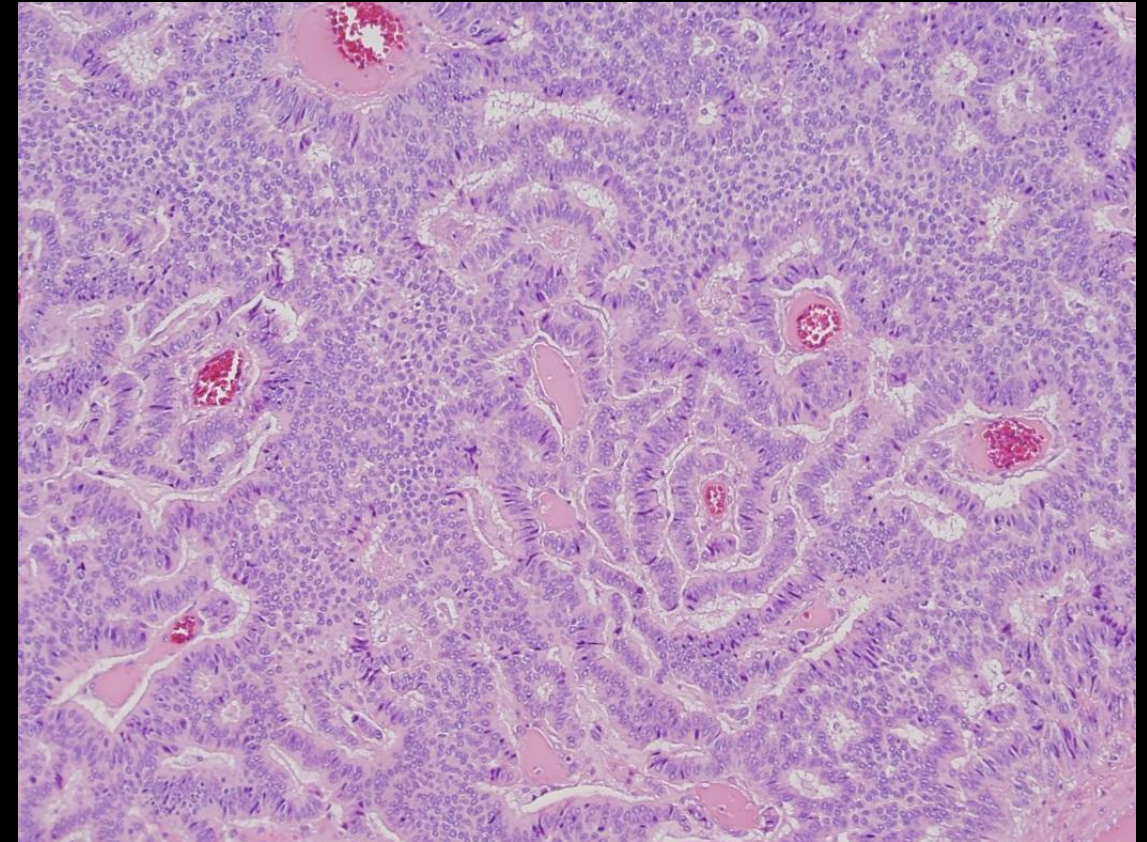
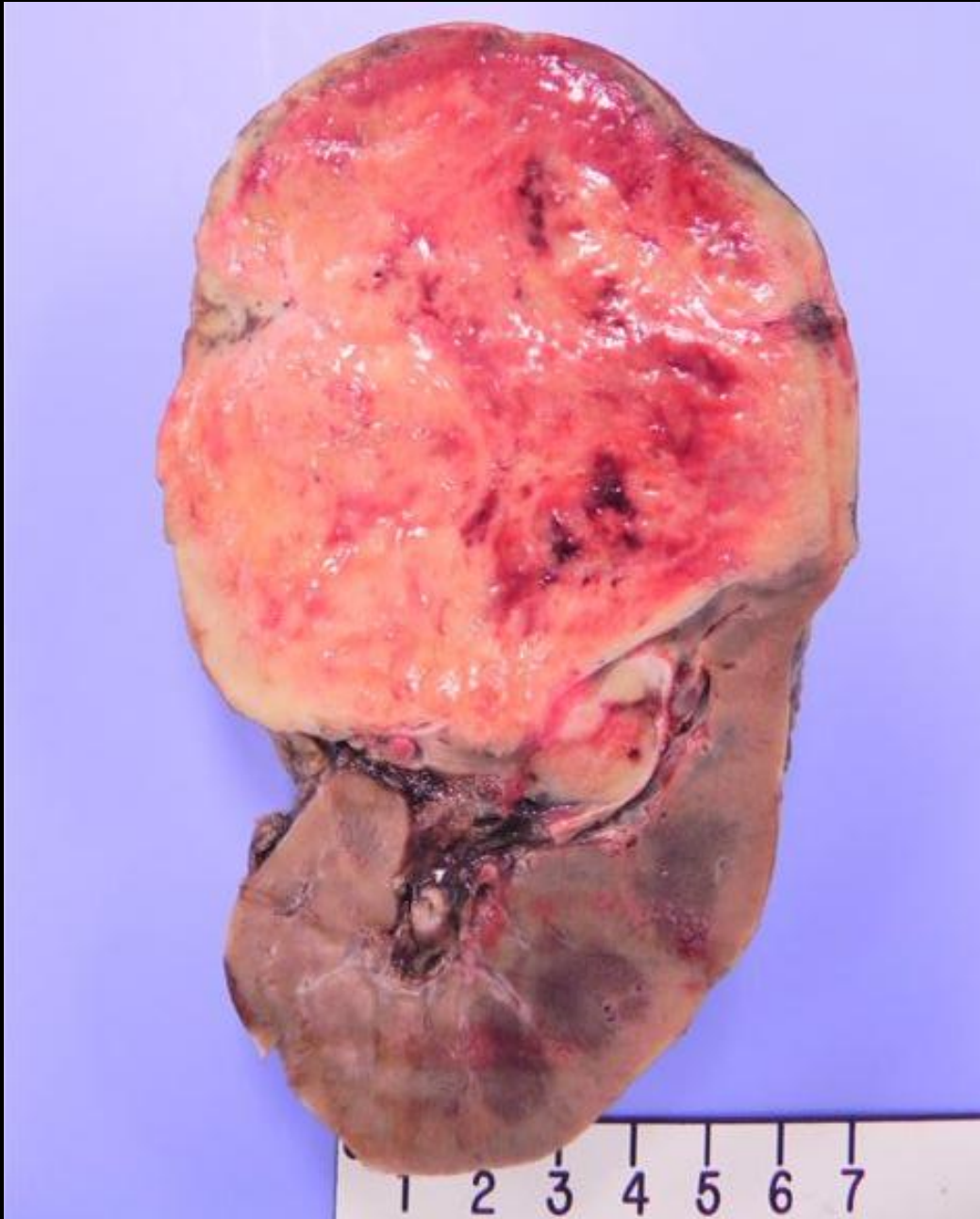
HLRCC syndrome



6cm ccRCC invading RV, surgery delayed d/t CAD.
XRT as a bridge and IR embolization of the RA (morning of surgery)

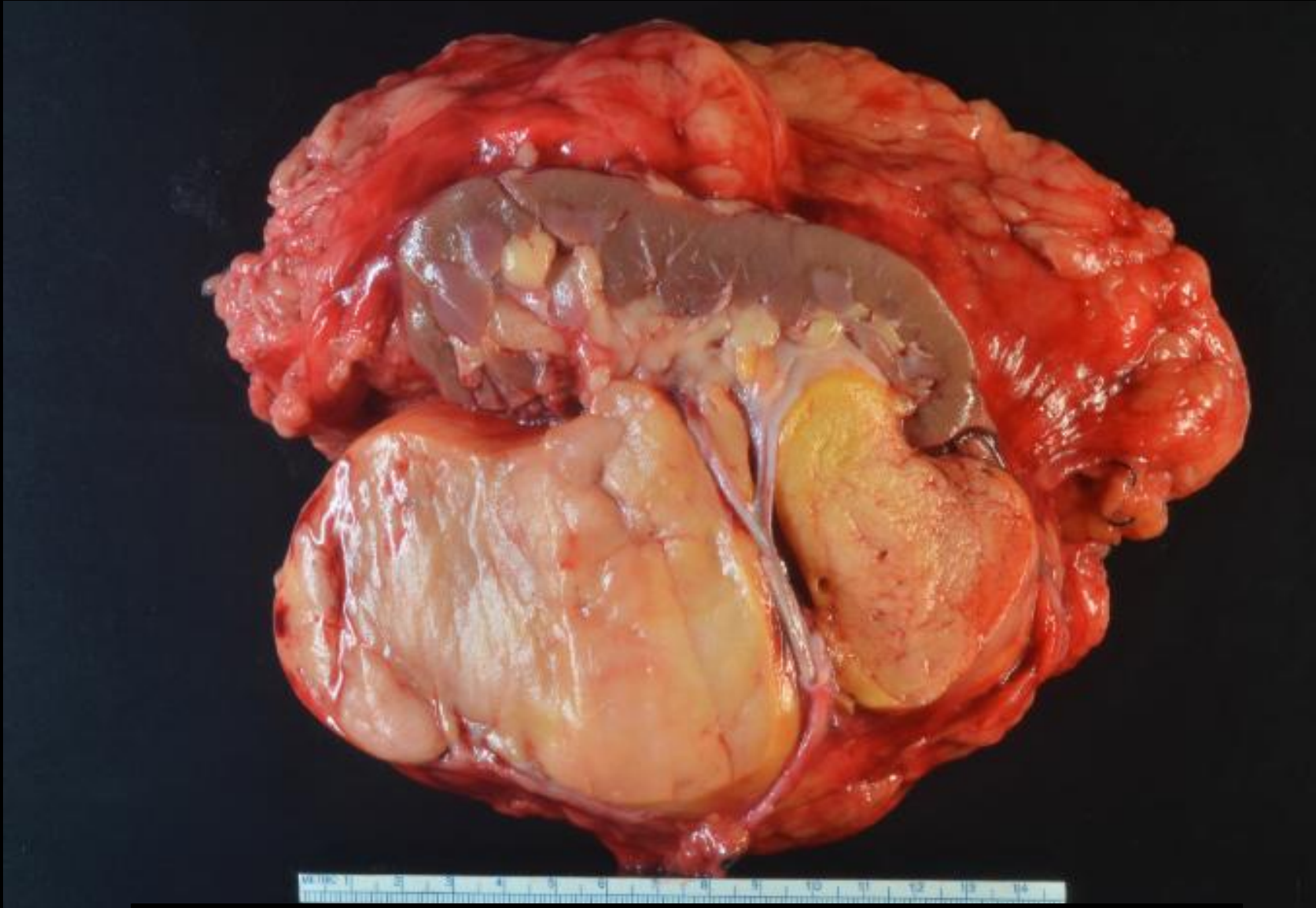


40 y/o woman, 9cm kidney mass



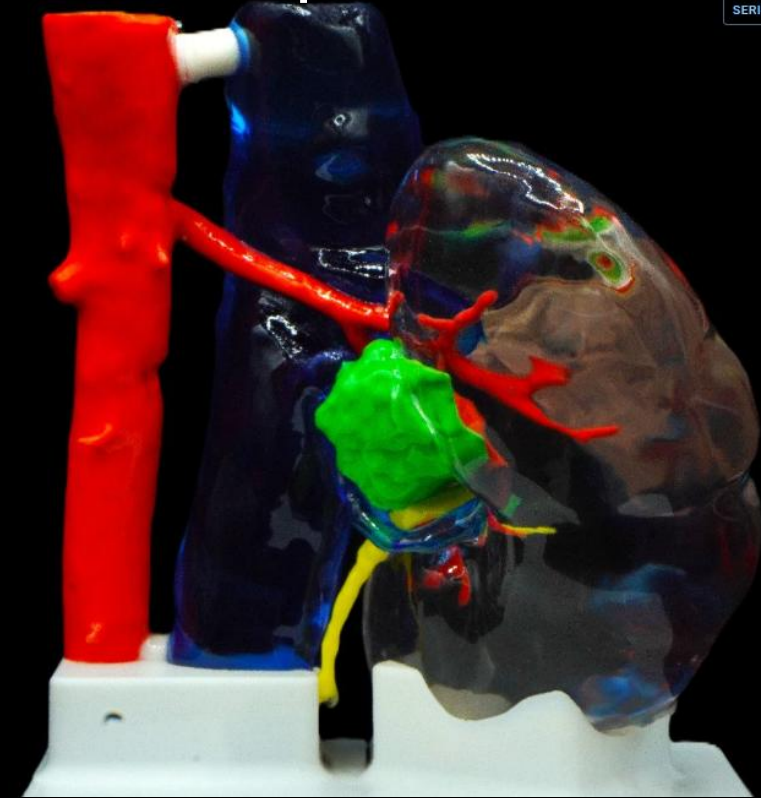
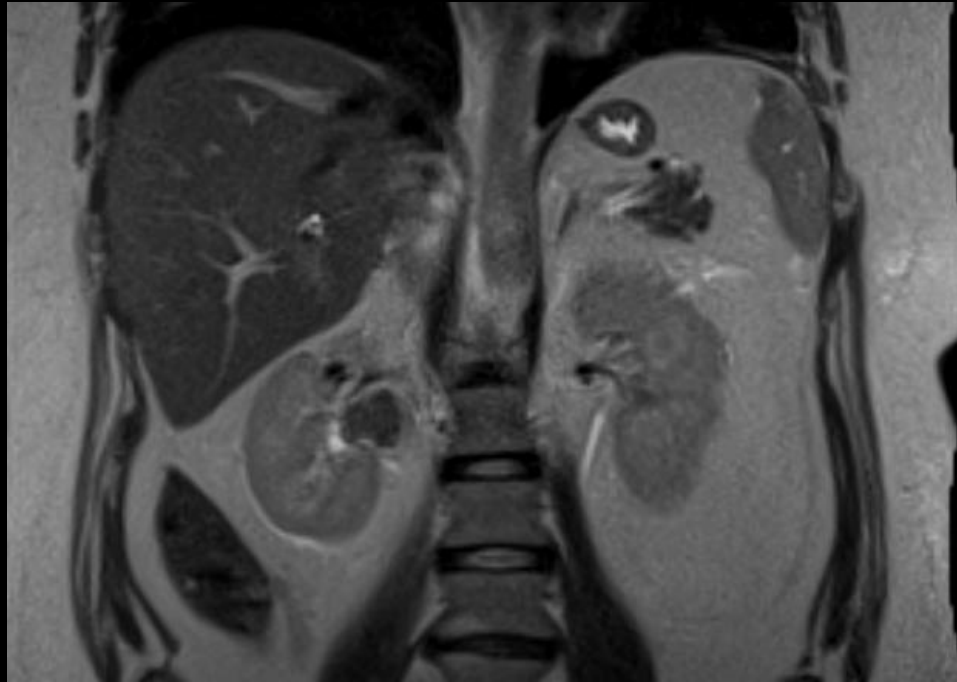
Well-differentiated neuroendocrine tumor
“renal carcinoid”

76 y/o woman, 15cm right hilar mass

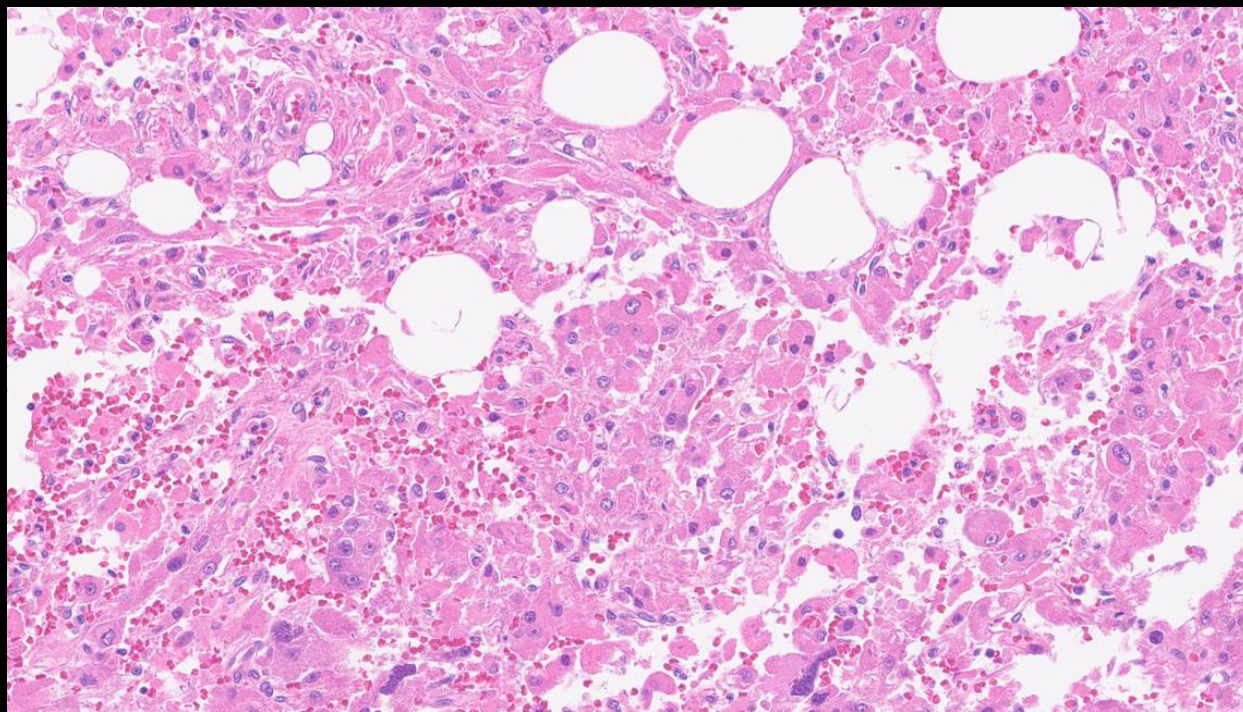
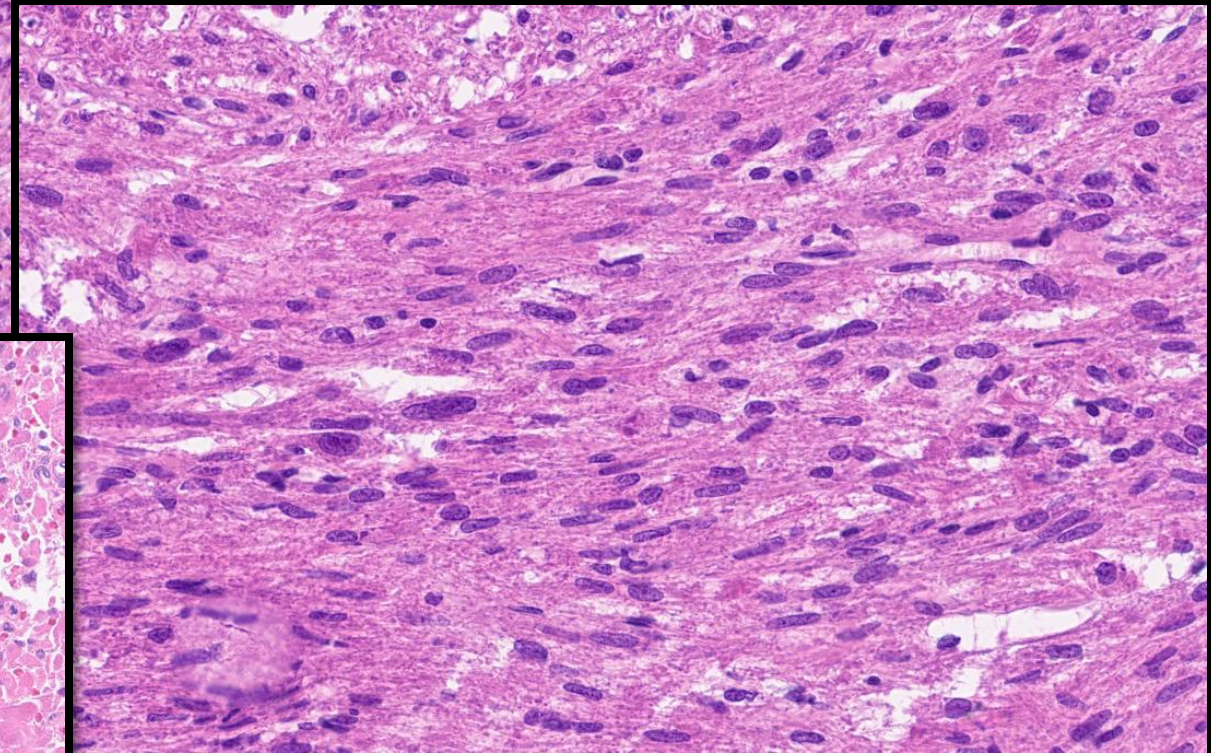
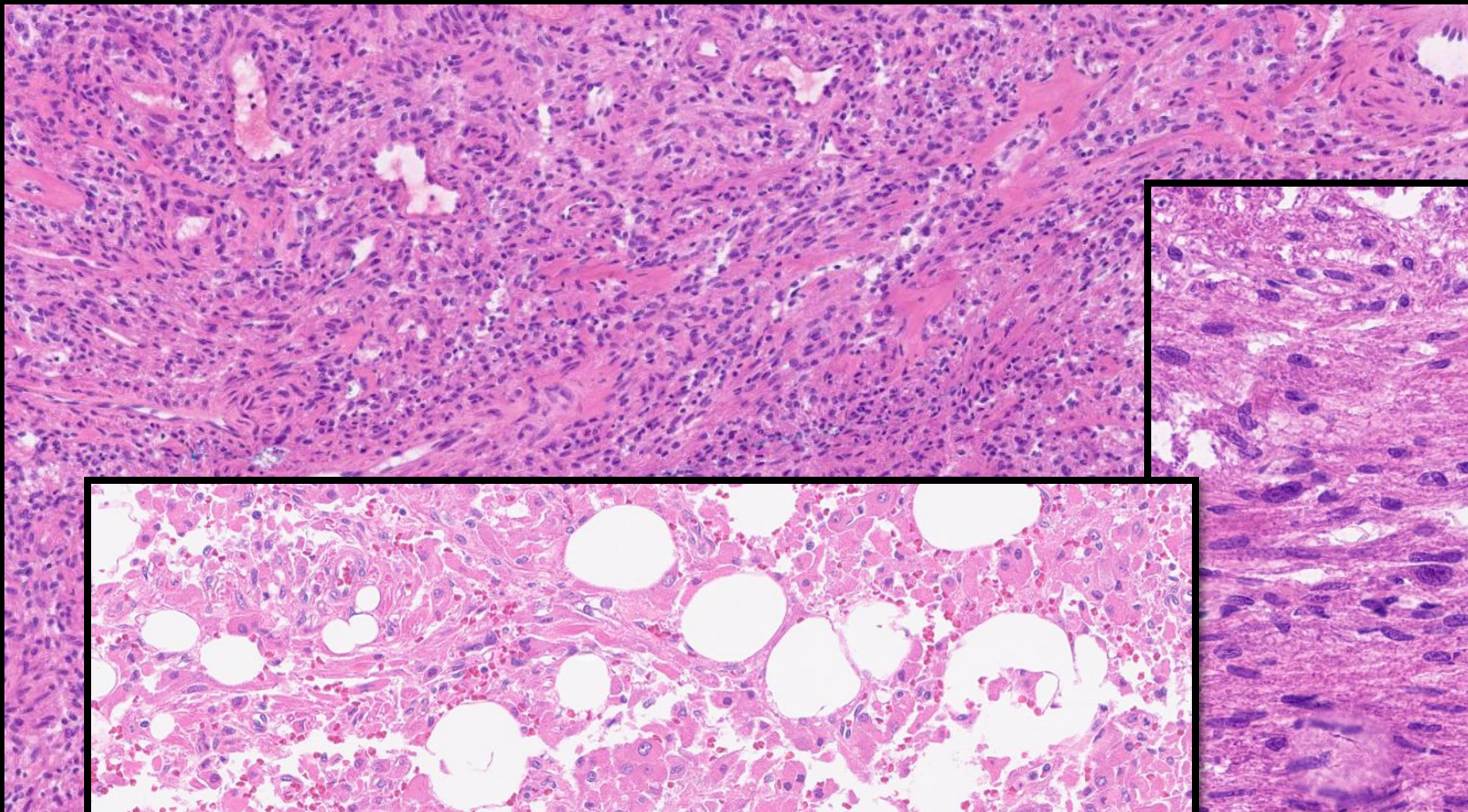


Angiomyolipoma (PEComa)

44yo woman, bilateral renal masses
2.7cm exophytic, right interpolar mass, posterior.

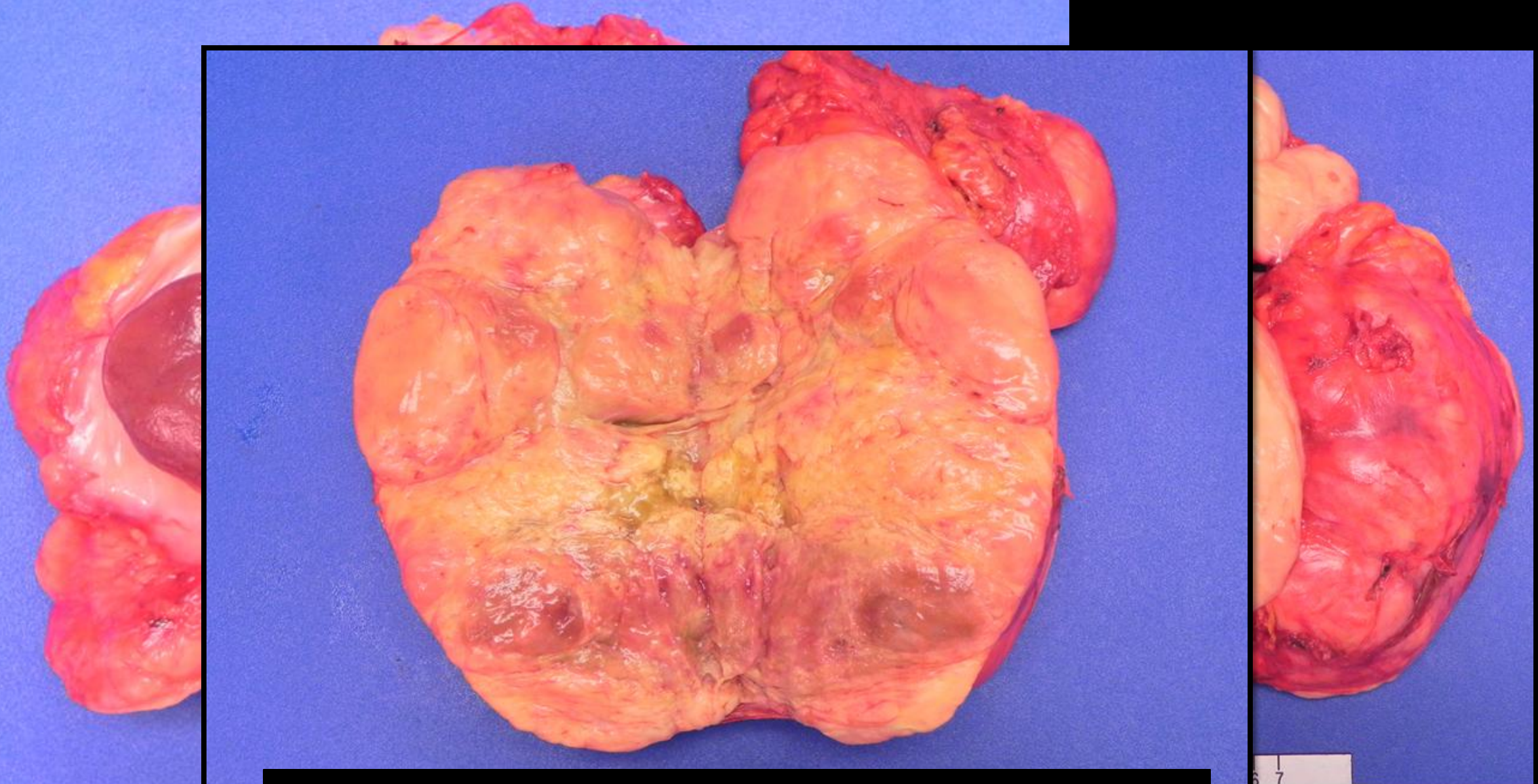


CT & MR: Suspicious for papillary RCC
OR: Surgeon notes a friable, vascular appearance.
Partial nephrectomy sent for frozen section.



Angiomyolipoma

81 y/o man, 25cm hemorrhagic kidney mass



Dedifferentiated liposarcoma

CHECKLIST FOR NEPHRECTOMY SPECIMENS

1) Clinical history

- Age, past medical history
- Imaging
- Prior biopsy?
- Prior therapy?

2) Tumor size

- Yes: perinephric tissue/sinus
- No: renal vein/thrombus
- If multifocal, measure/sample 5 largest

3) Evaluate renal sinus carefully

- If grossly involved, then confirm
- If not grossly involved, then a few sections
- If equivocal, then extensively sample

4) Document % necrosis

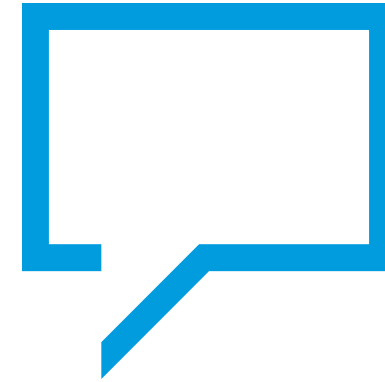
5) Assess for sarcomatoid/rhabdoid areas







QUESTIONS ?



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