Renal Cell Carcinoma

- More common N Europe and N America
- Lowest Asian Countries & S America
- M:F 2:1
- Risk Factors: Cigarette smoking 20% cases
  Obesity 30% cases
  Hypertension
  Renal dialysis (acquired cystic kidney disease)

Clinical Features

Classically: Flank pain, renal mass and haematuria

Mostly not however!

Around 1/3 present with paraneoplastic features:

- Fever, malaise, night sweats, anorexia
- Neuropathy, non-metastatic hypercalcaemia (PTH-like peptide)
- Erythrocytosis (increased erythropoietin)
- Non-metastatic hepatic dysfunction

Familial Renal Tumours

Von Hippel –Lindau Disease
- Aut Dominant
- Mutation of VHL gene 3p25-26
- Cap haemangioblastomas of CNS and retina
- Clear cell RCC / Phaeo / Pancreatic tumours

Hereditary papillary renal carcinoma (HPRC)
- Aut Dom
- Late onset of multiple Papillary tumours
- Mutation of MET oncogene on 7q31

Hereditary leiomyomatosis and RCC (HLRCC)
- Aut Dominant
- Cutaneous and uterine leiomyomas
- Uterine leiomyosarcoma
- Renal papillary Ca

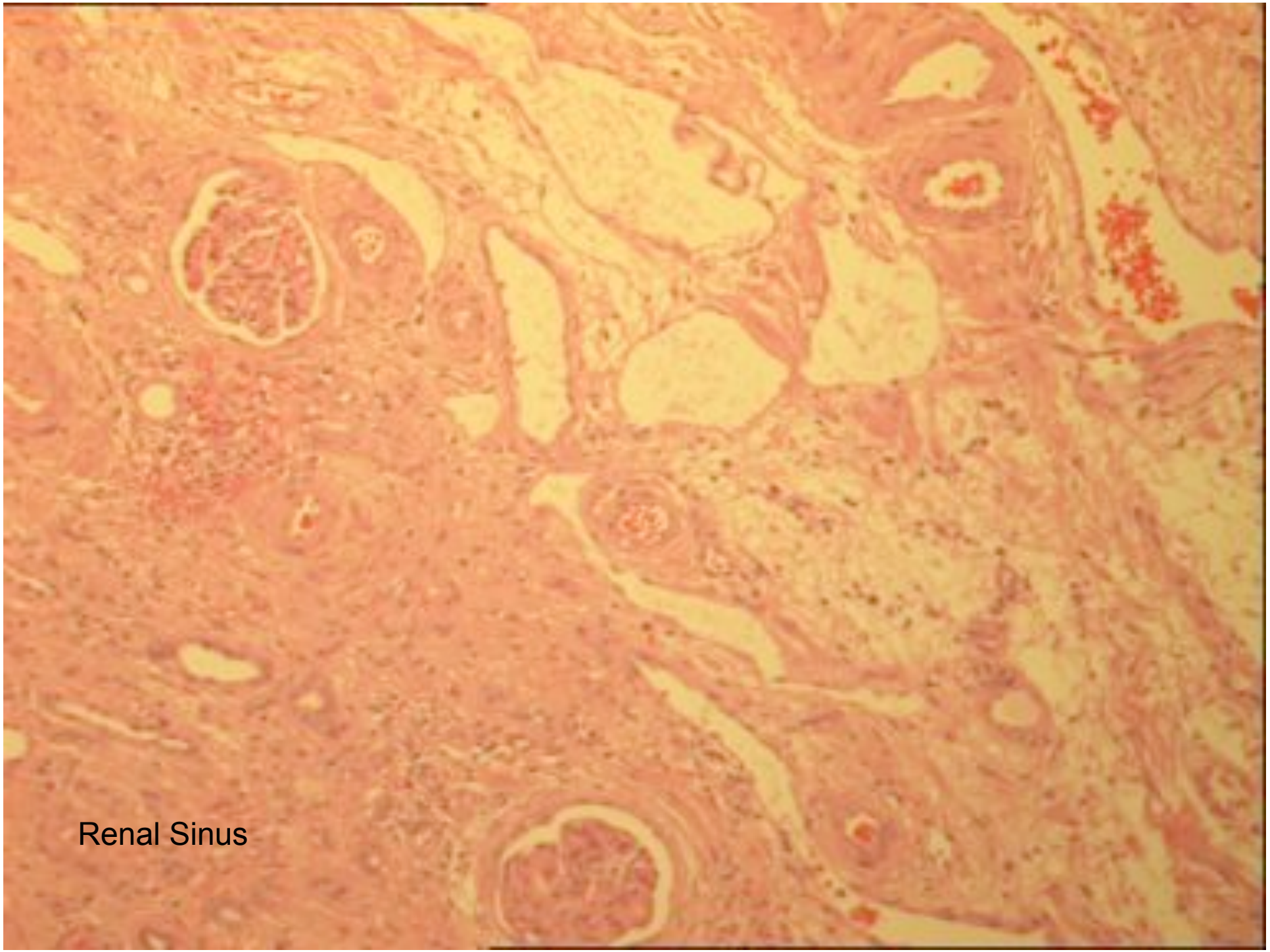
Tuberous sclerosis
- Bilateral angiomyolipomas
- skin angiofibromas / cardiac rhabdomyomas

Genetic Alterations

Clear cell Ca	Deletions of 3p / mutations in VHL gene
Papillary Ca	Trisomy 7, 17 and loss of Y (others)
Chromophobe Ca	Extensive chromosomal loss
Collecting duct Ca	Multiple genetic events
Oncocytoma	Mix of cells with normal and abnormal karyotypes Some show t(5;11) CCND1 is at 11q13 Some show loss of 1 and 14

Grading

- Always causes problems! Why?
- Fuhrman Nuclear Grading
  - Start at x100. If irregular nuclei and prominent nucleoli then it's grade 3. If also bizarre nuclei then it's grade 4
  - If neither, go to higher powers to decide between grades 1 and 2.
- Liebovitch (Mayo)
  - Almost same as Fuhrman but requires 1HPF's worth for highest grading


Renal Sinus

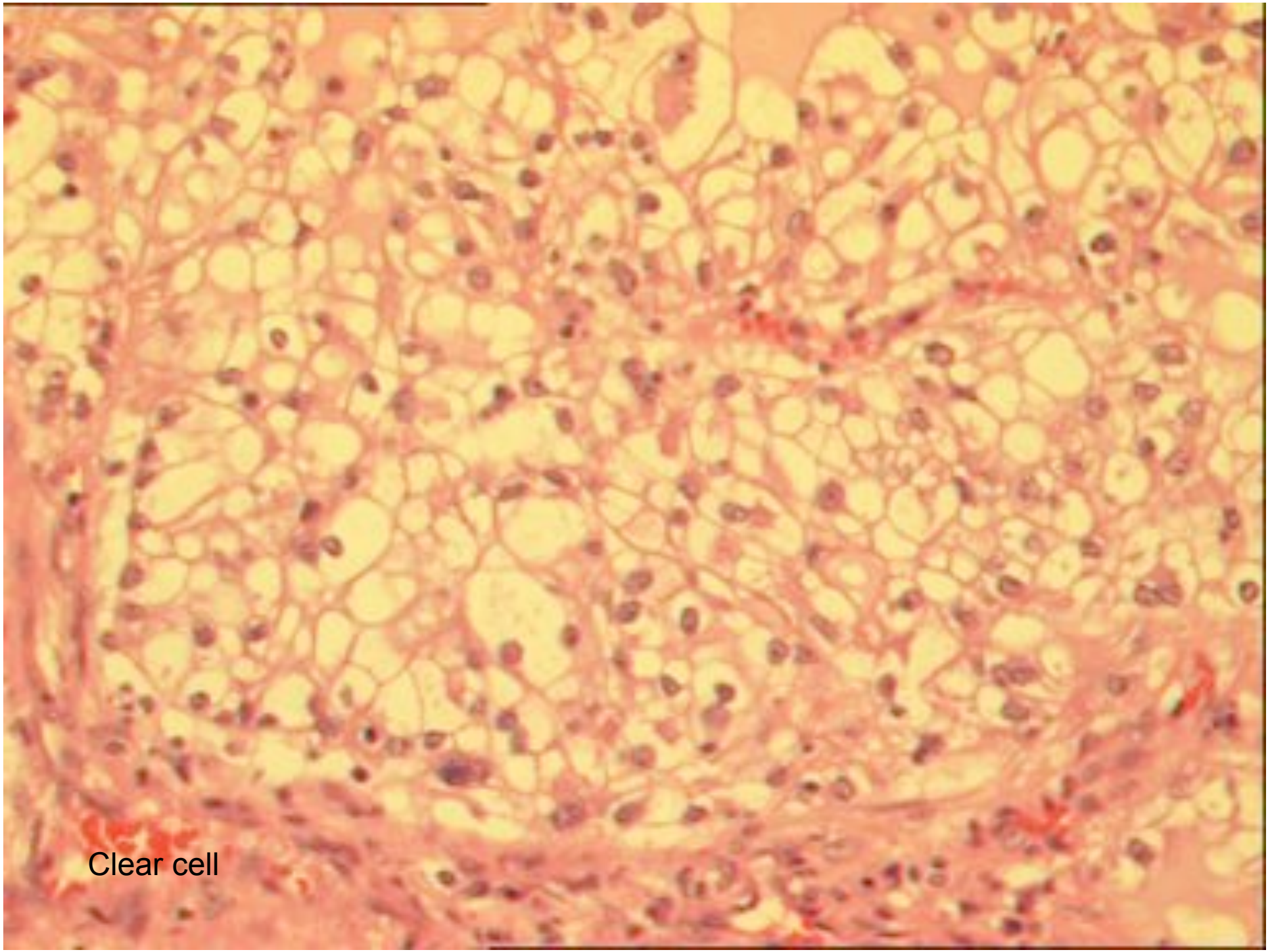
Sinus invasion correlates with:

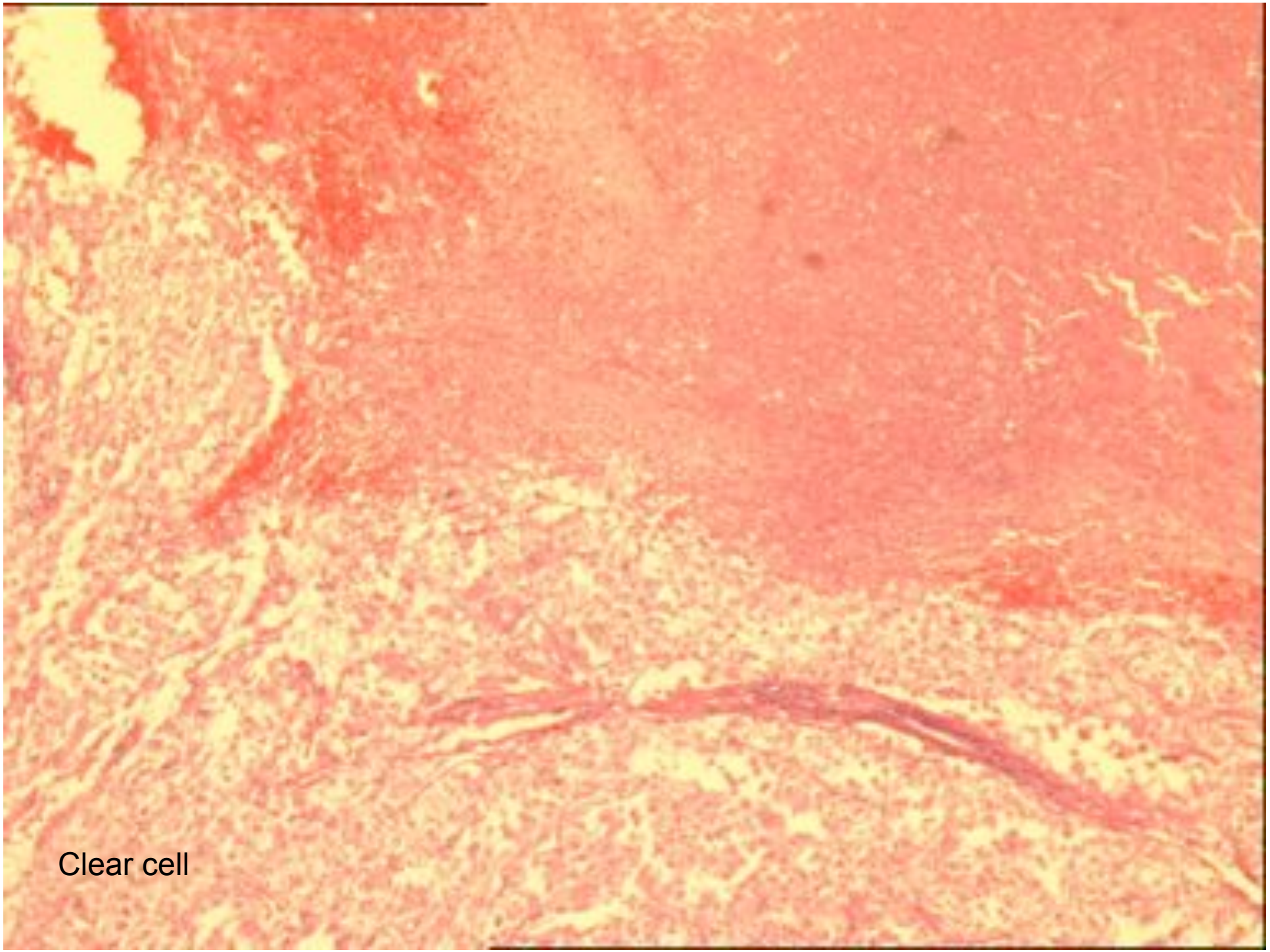
Tumour > 4cm (NB pT1 and pT2 may be pT3)

Fuhrman grade 3 and 4

Veins first then fat
Fat first is less common

Sinus invasion is more common than capsular invasion


Clear cell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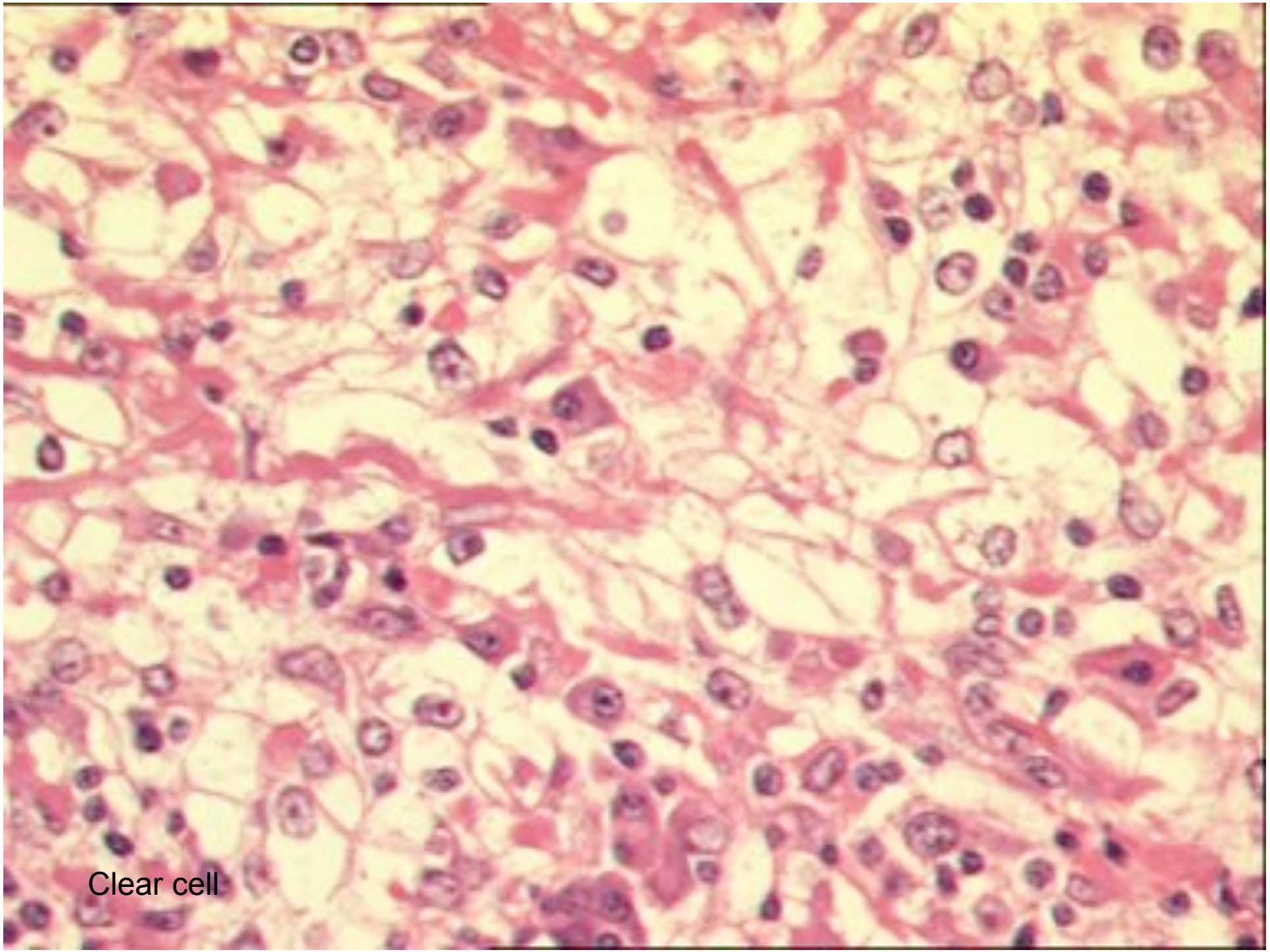
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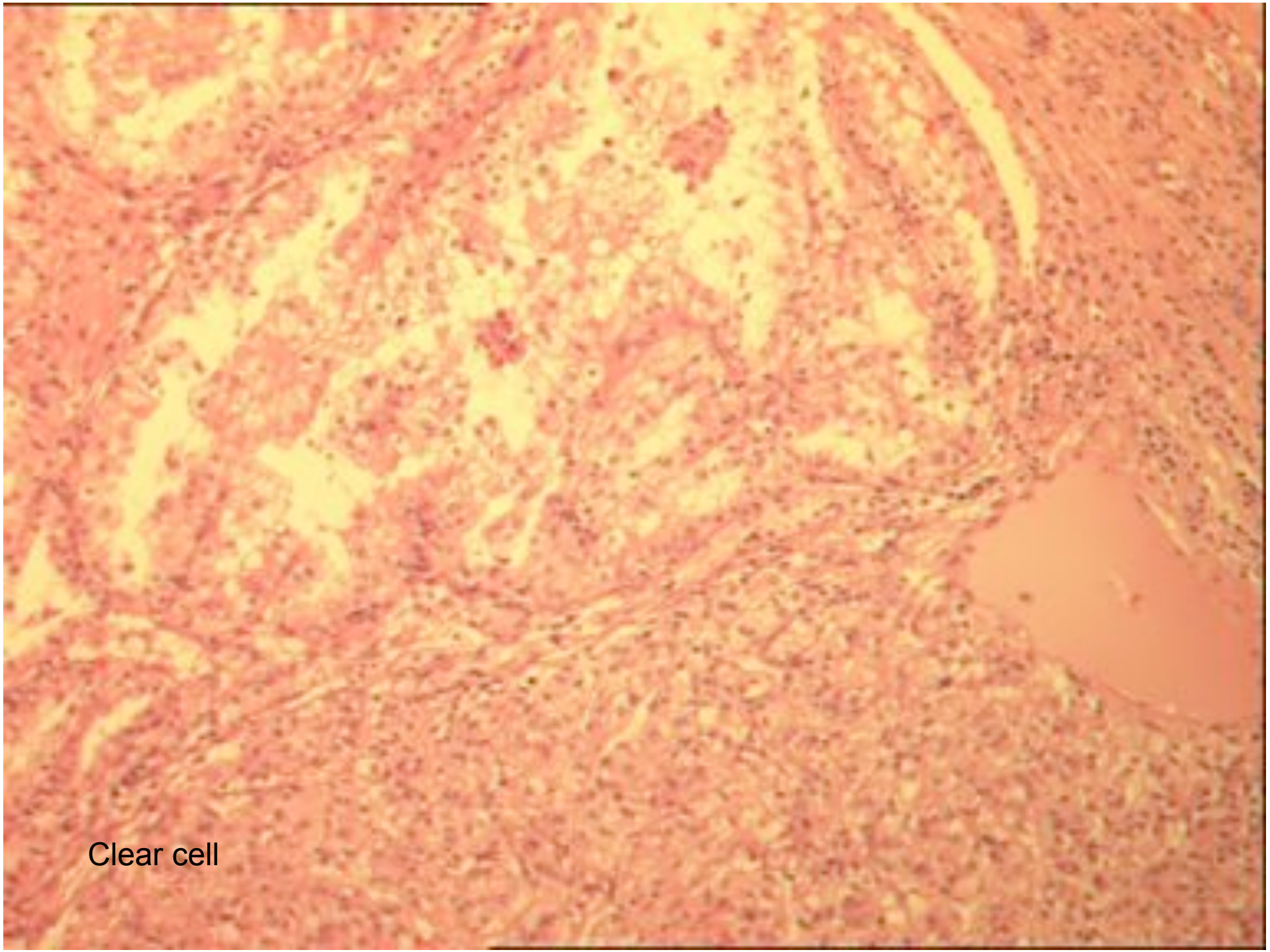
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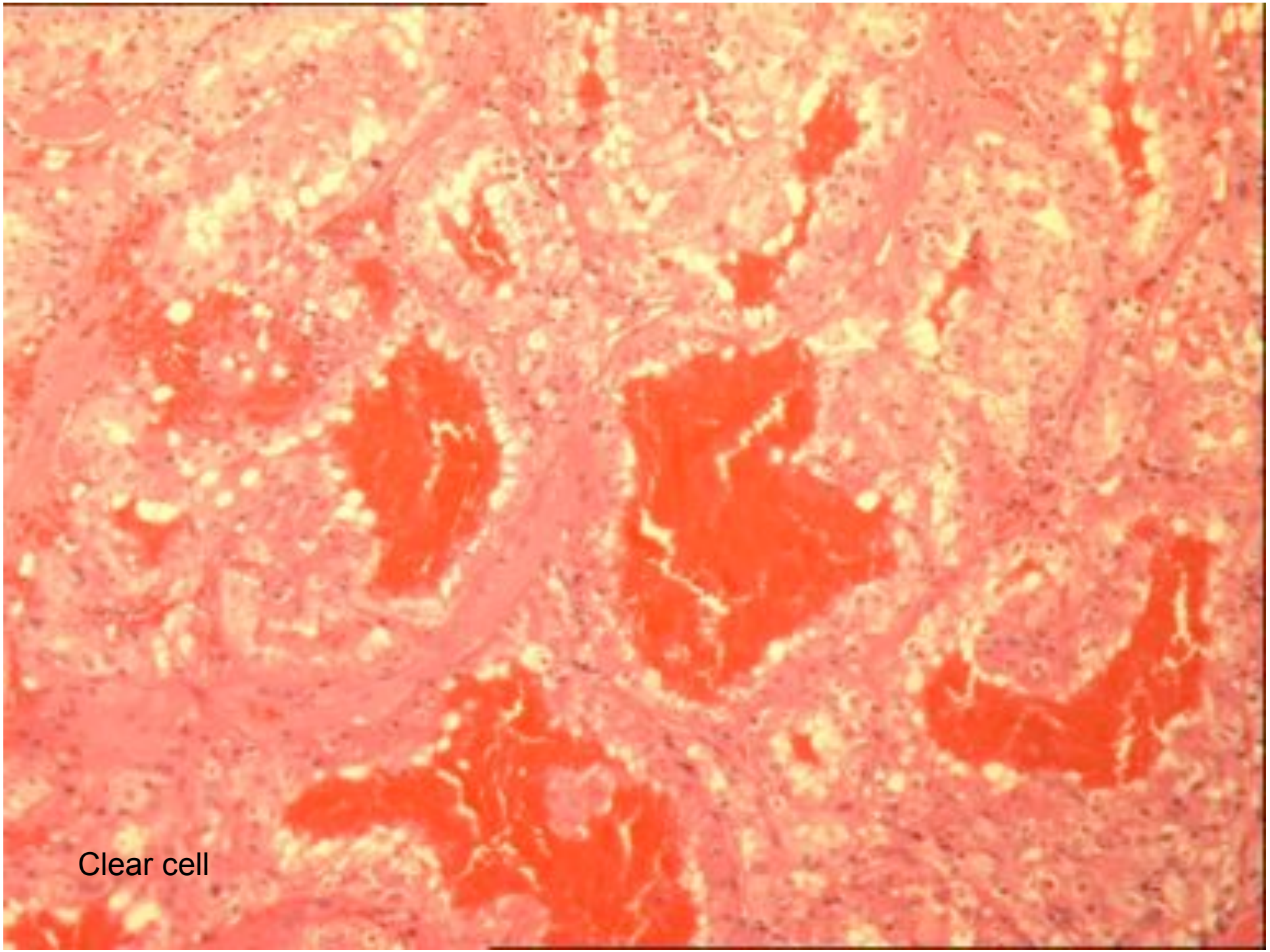
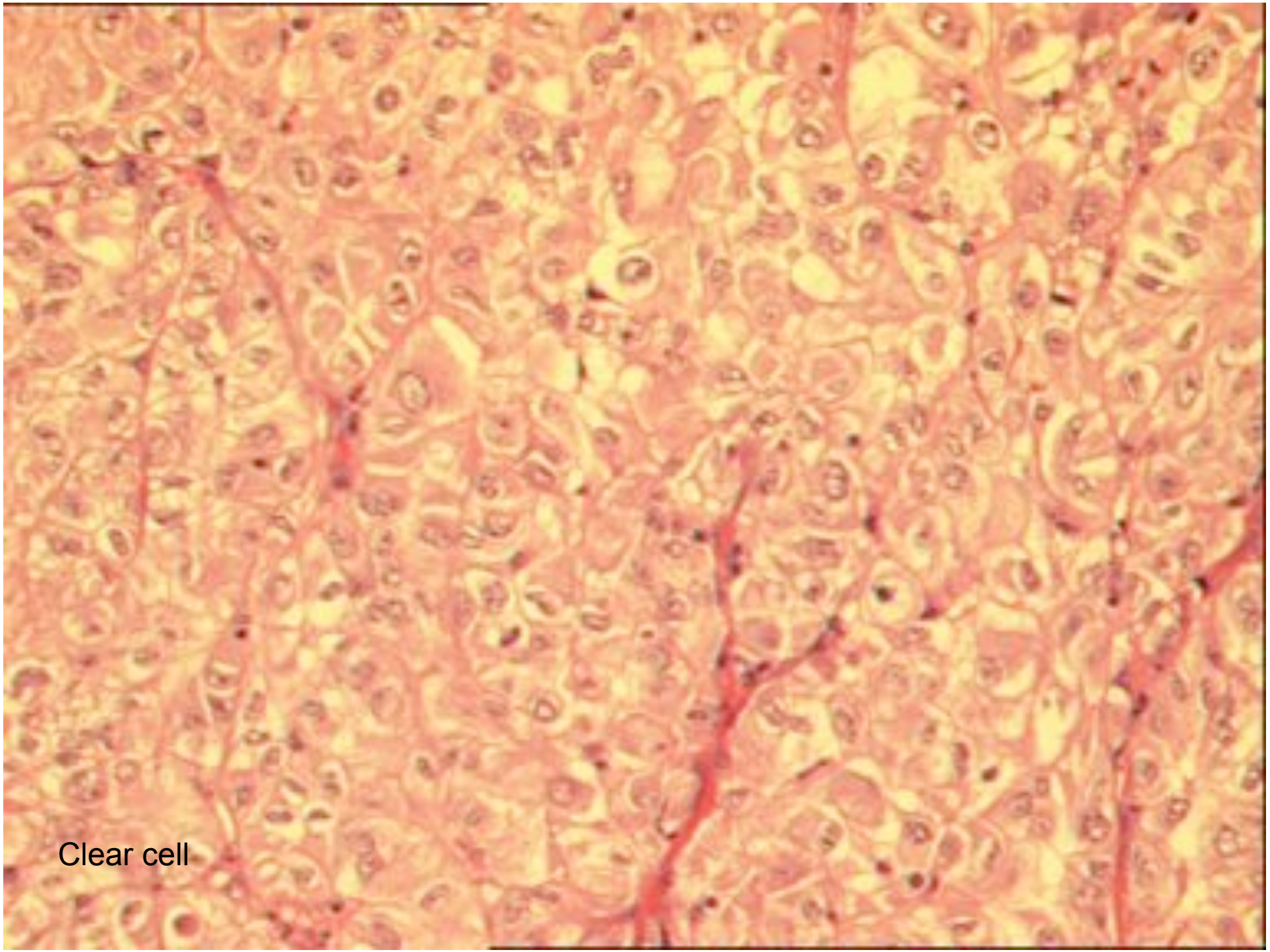

Clear cell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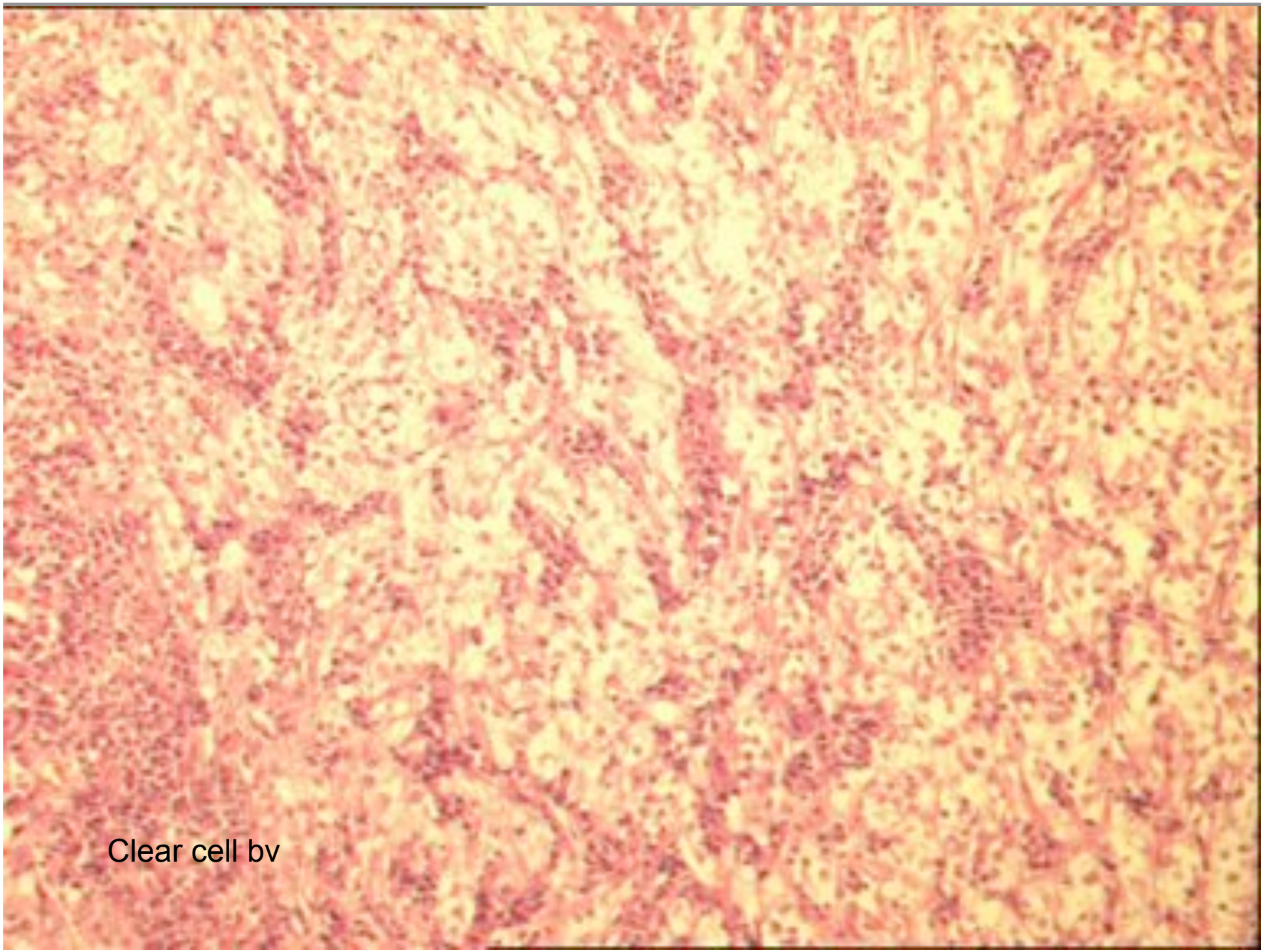

Clear cell bv

Papillary Carcinoma

Approx 10% of renal carcinomas

Papillae and tubules
Foamy histiocytes in cores
Solid variants + /- necrosis

Sarcomatoid dedifferentiation in 5% cases

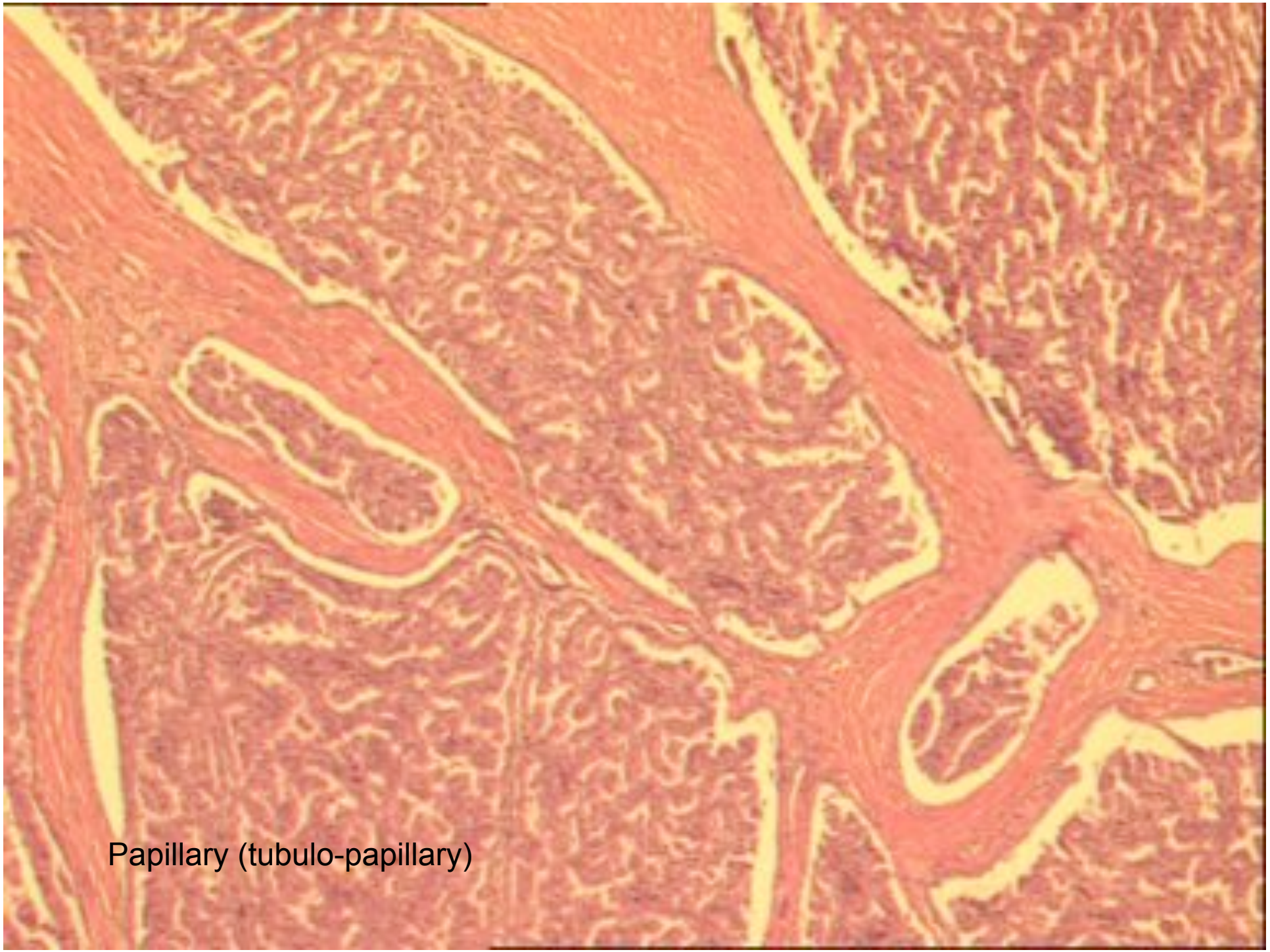
Papillary Carcinoma

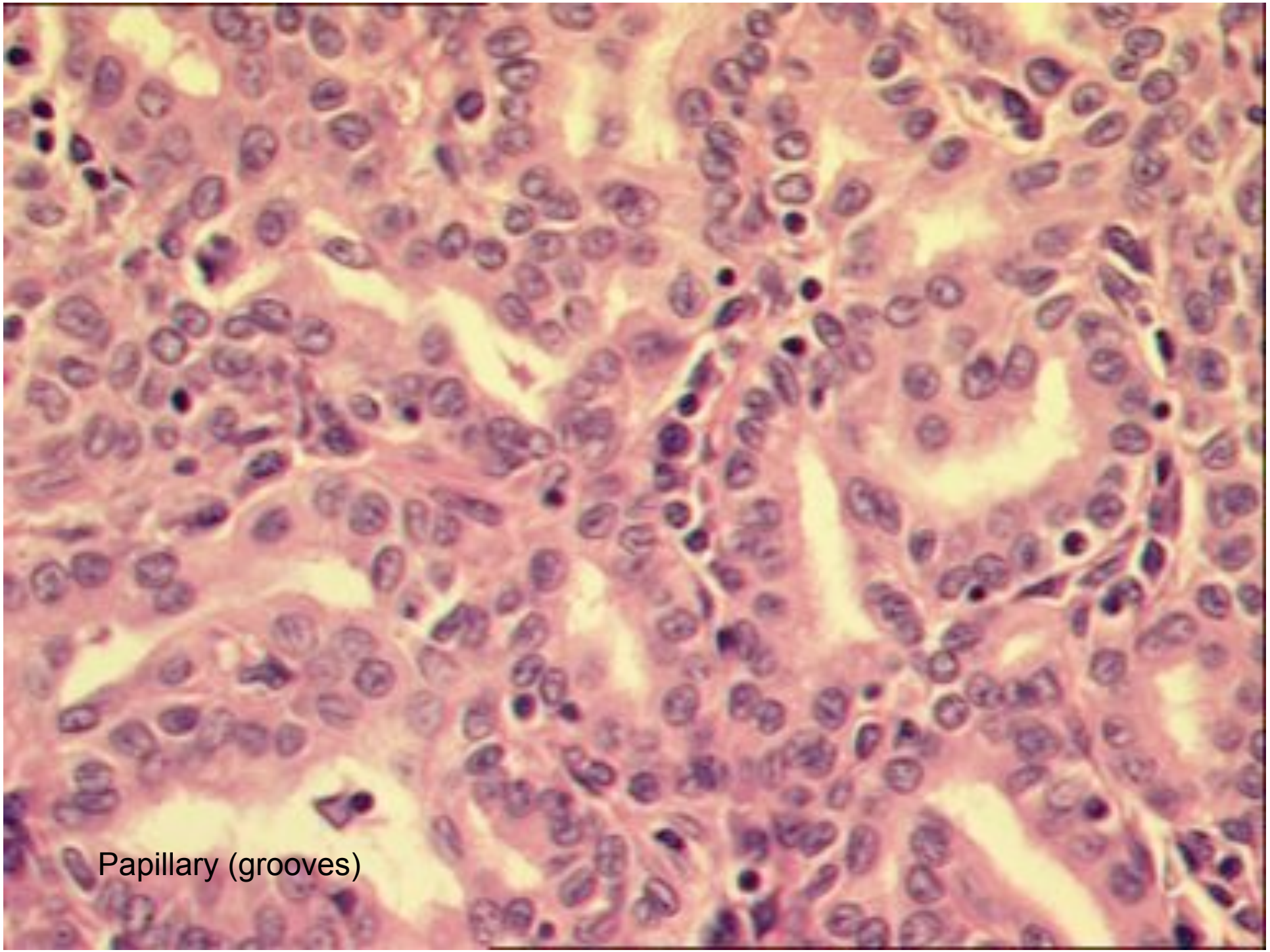
Type 1: small cells, scanty cytoplasm. More frequently multifocal

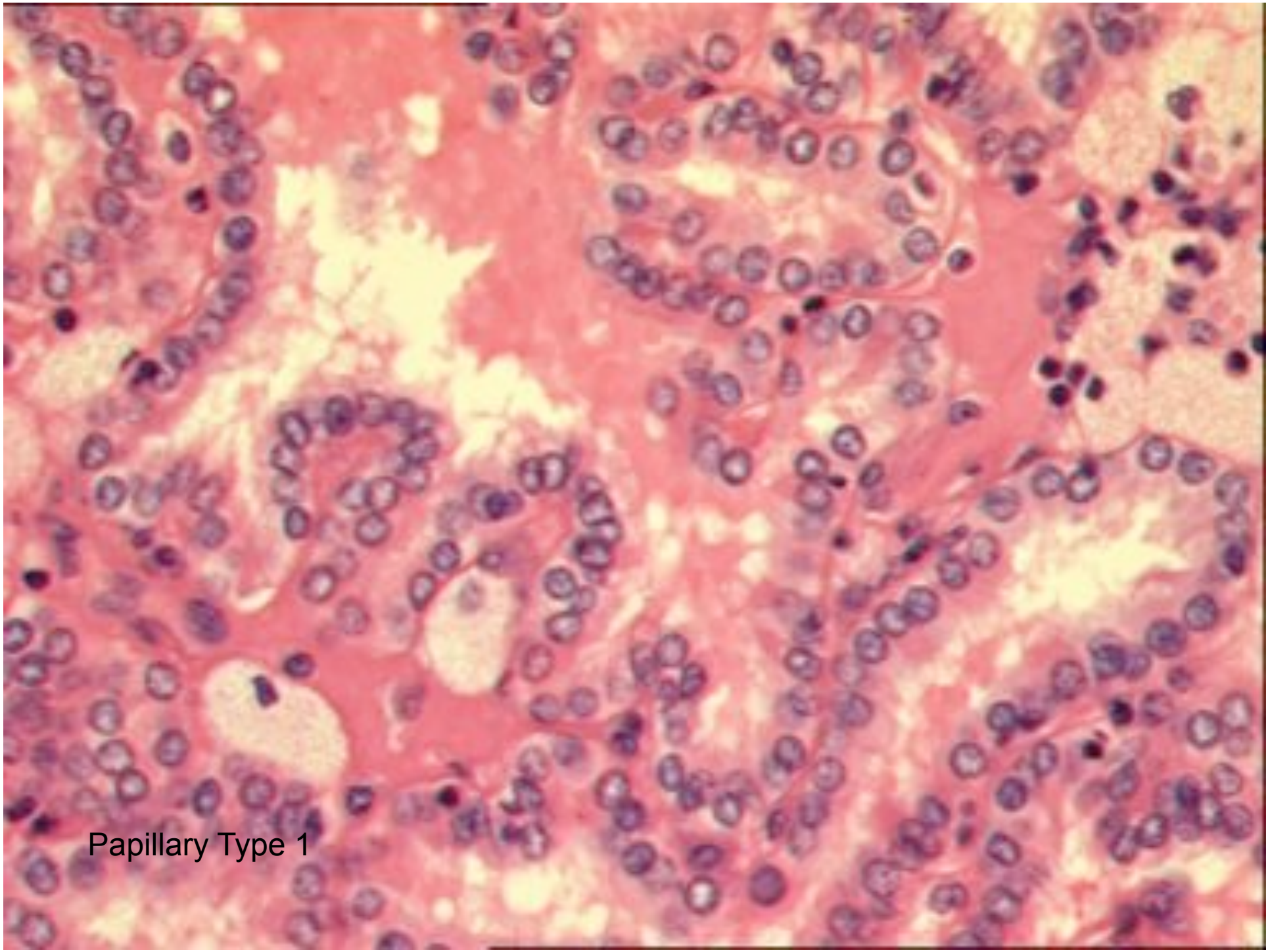
Type 2: bigger tumours larger cells, higher nuclear grade eosinophilic cytoplasm

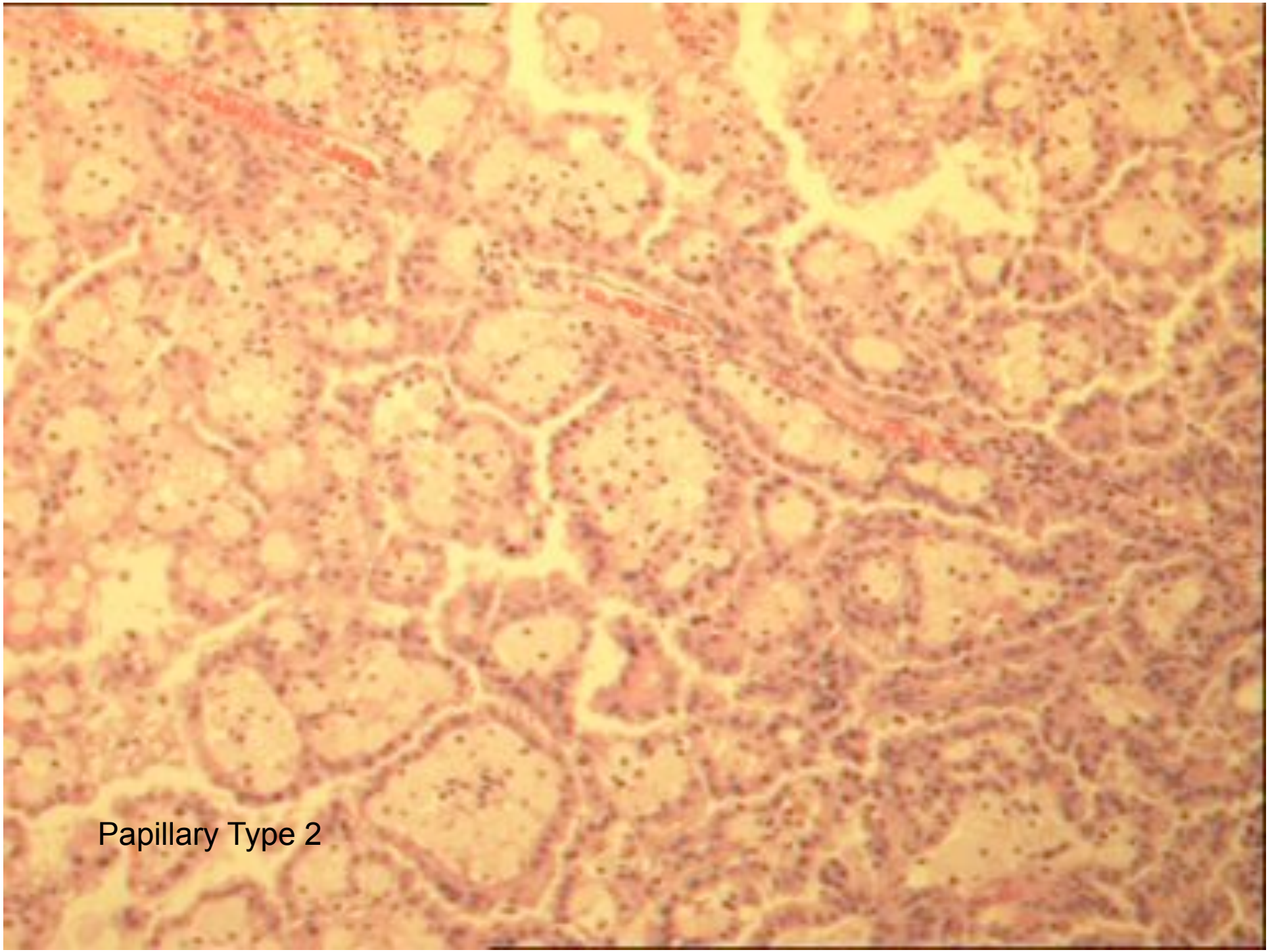
Type is correlated with survival

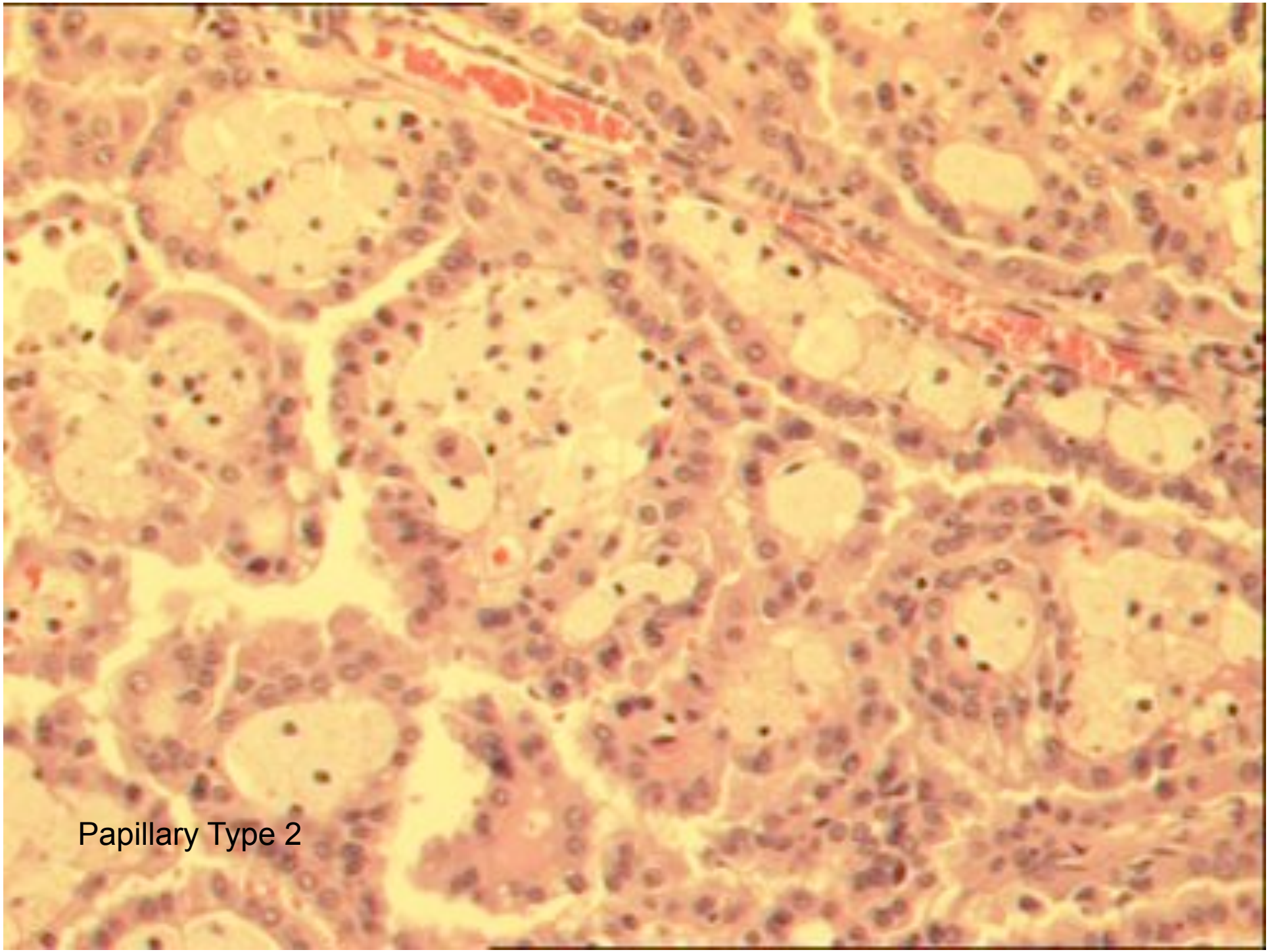
Fuhrman grading used

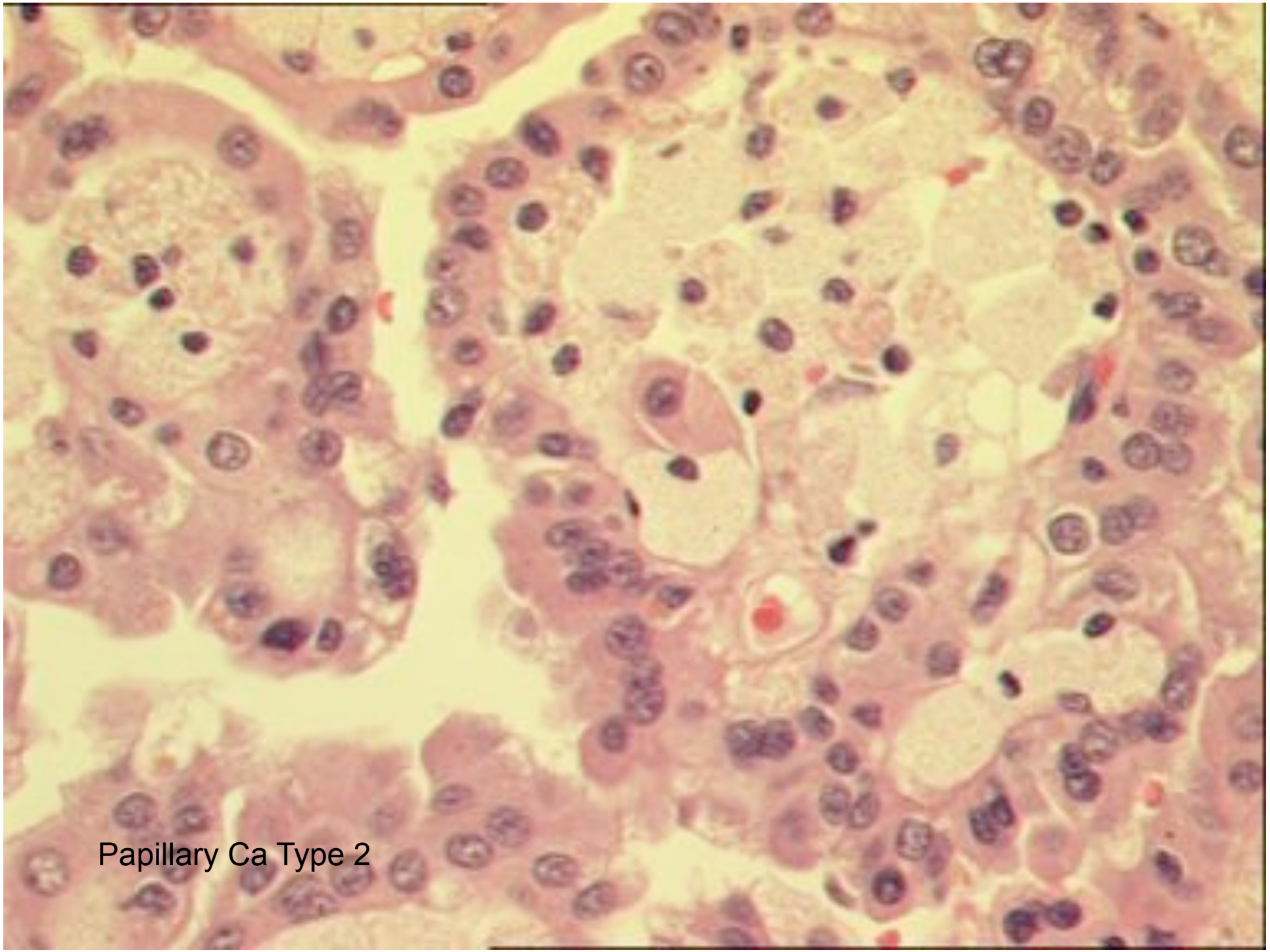

Papillary (tubulo-papillary)

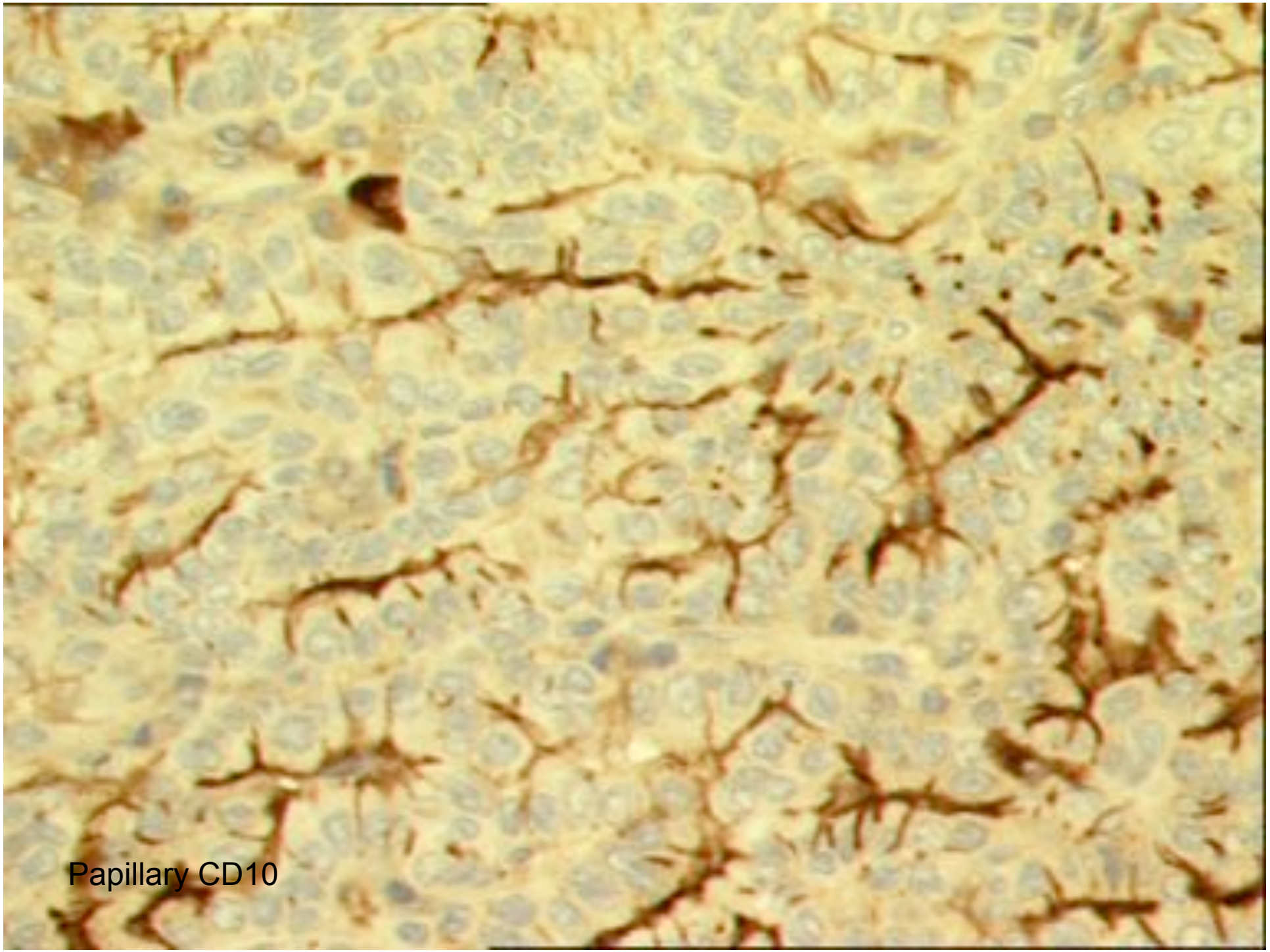

Papillary (grooves)

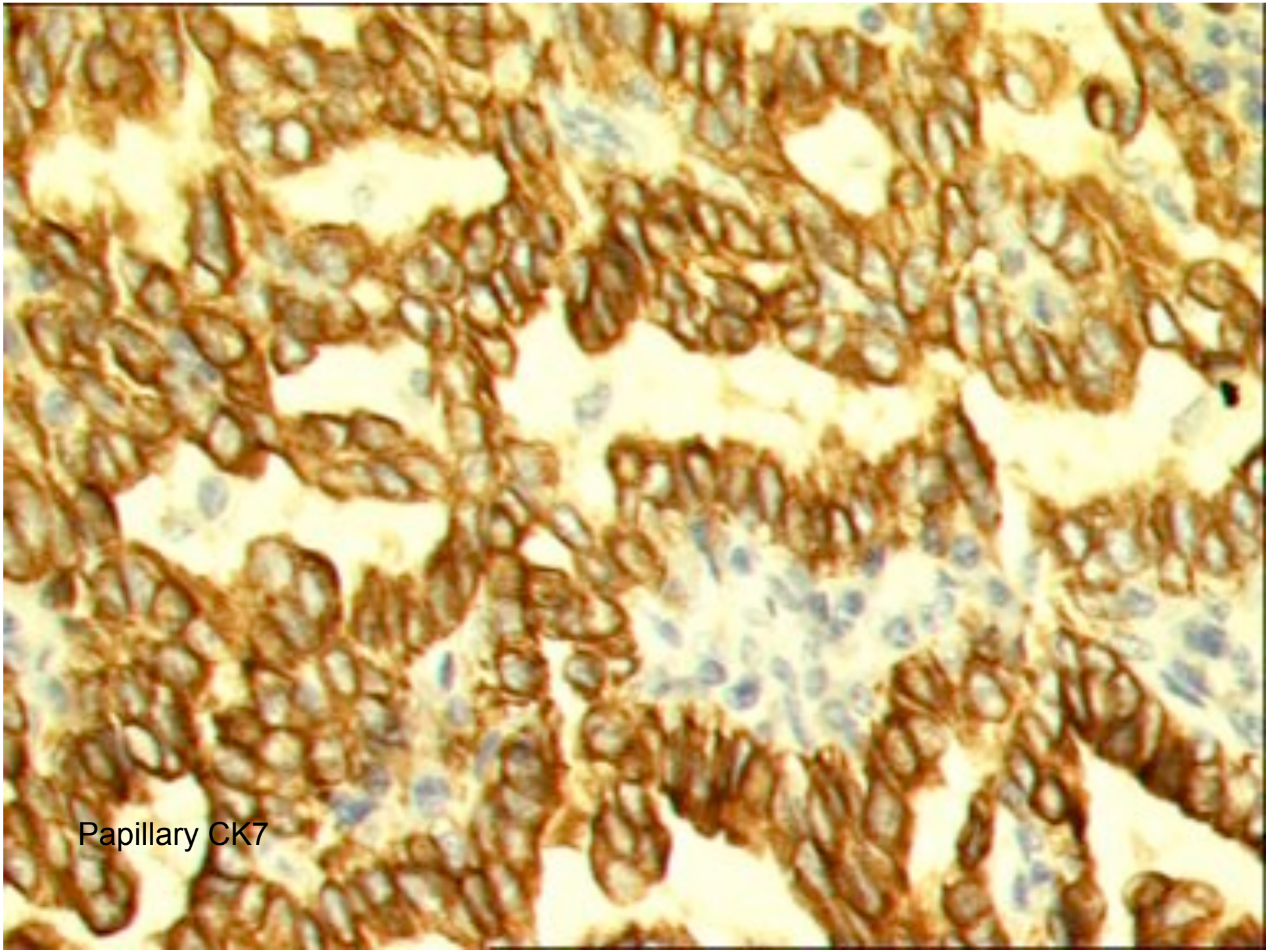

Papillary Type 1


Papillary Type 2


Papillary Type 2


Papillary Ca Type 2

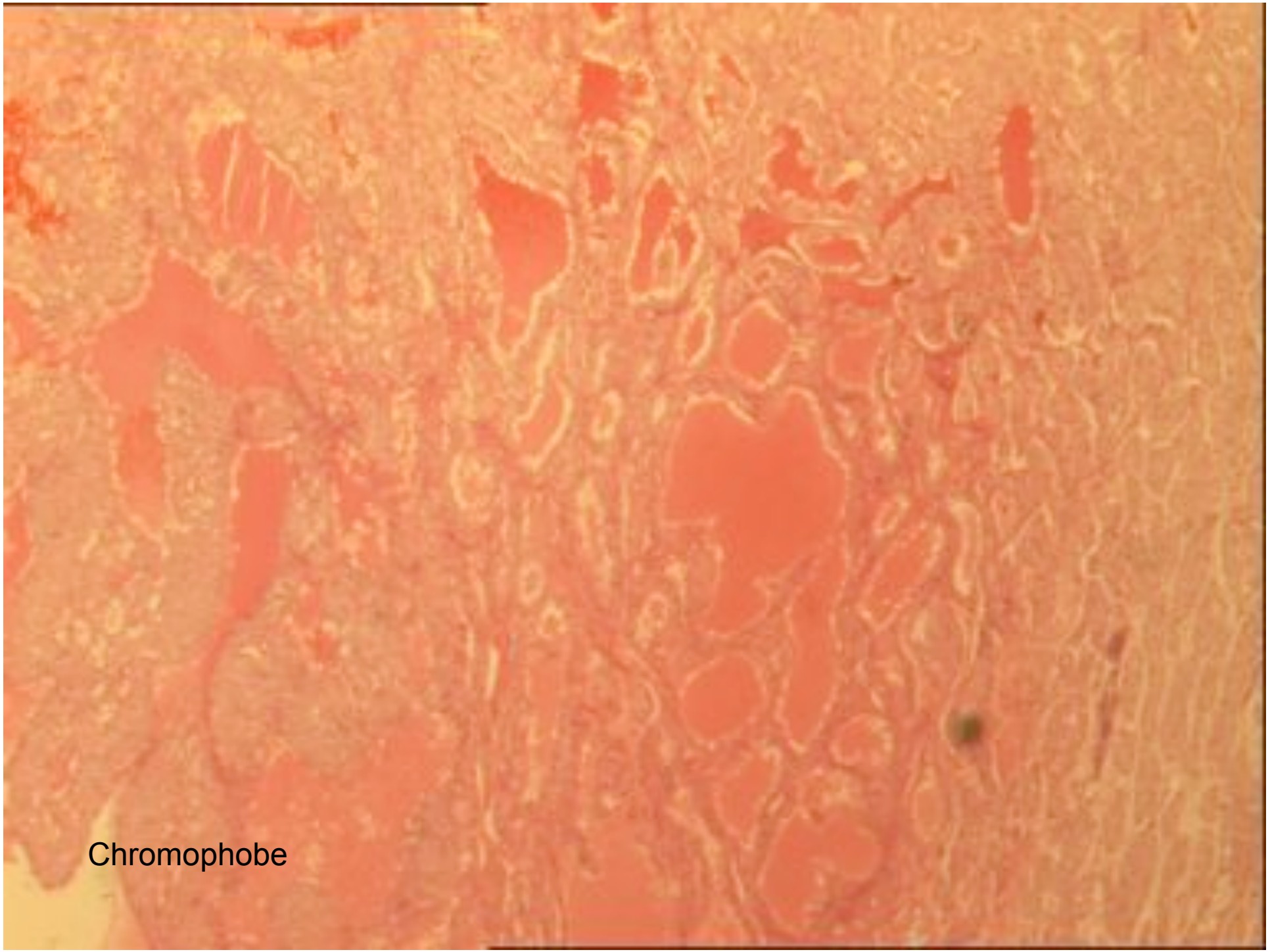

Papillary CD10

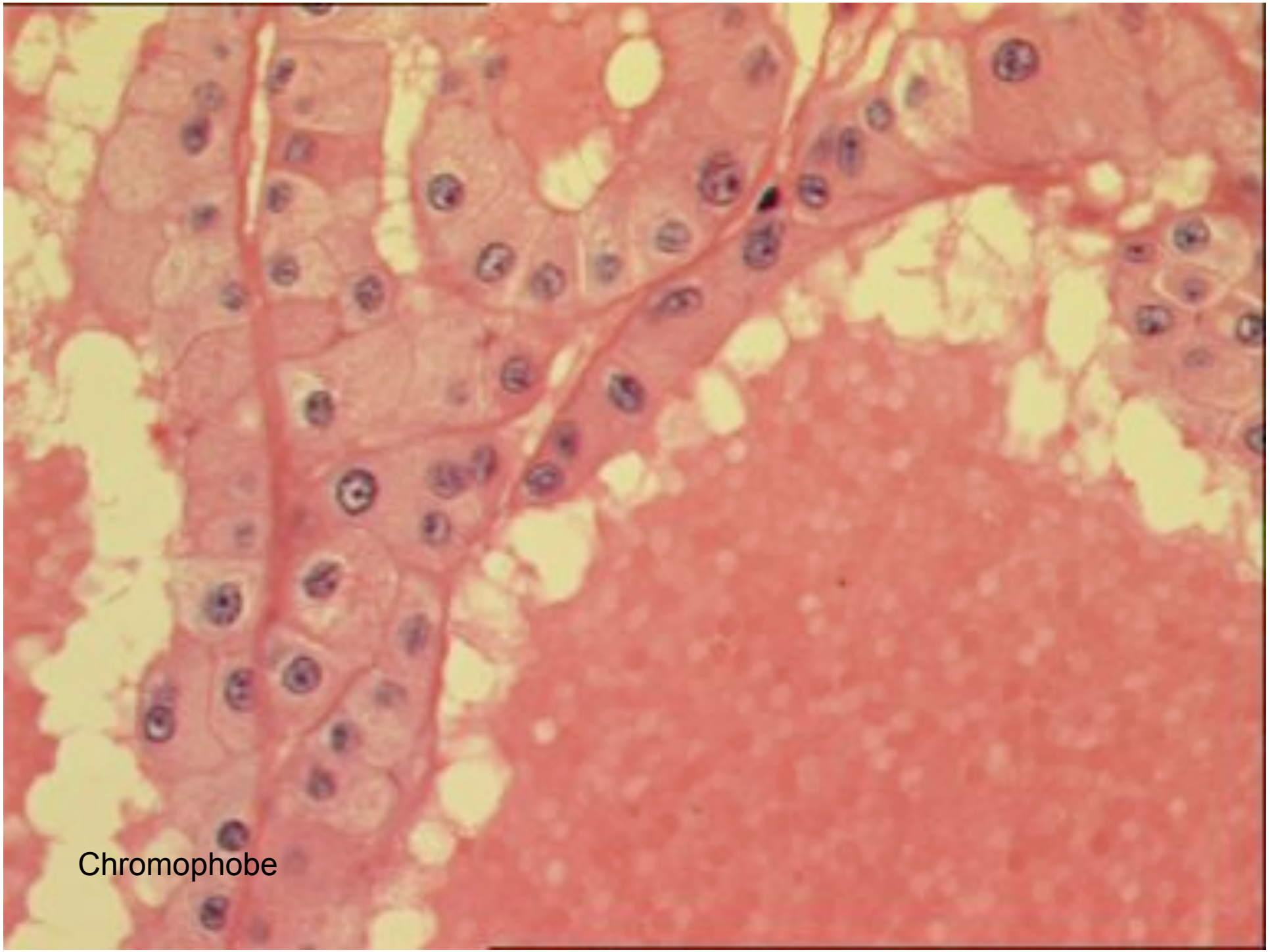

Papillary CK7

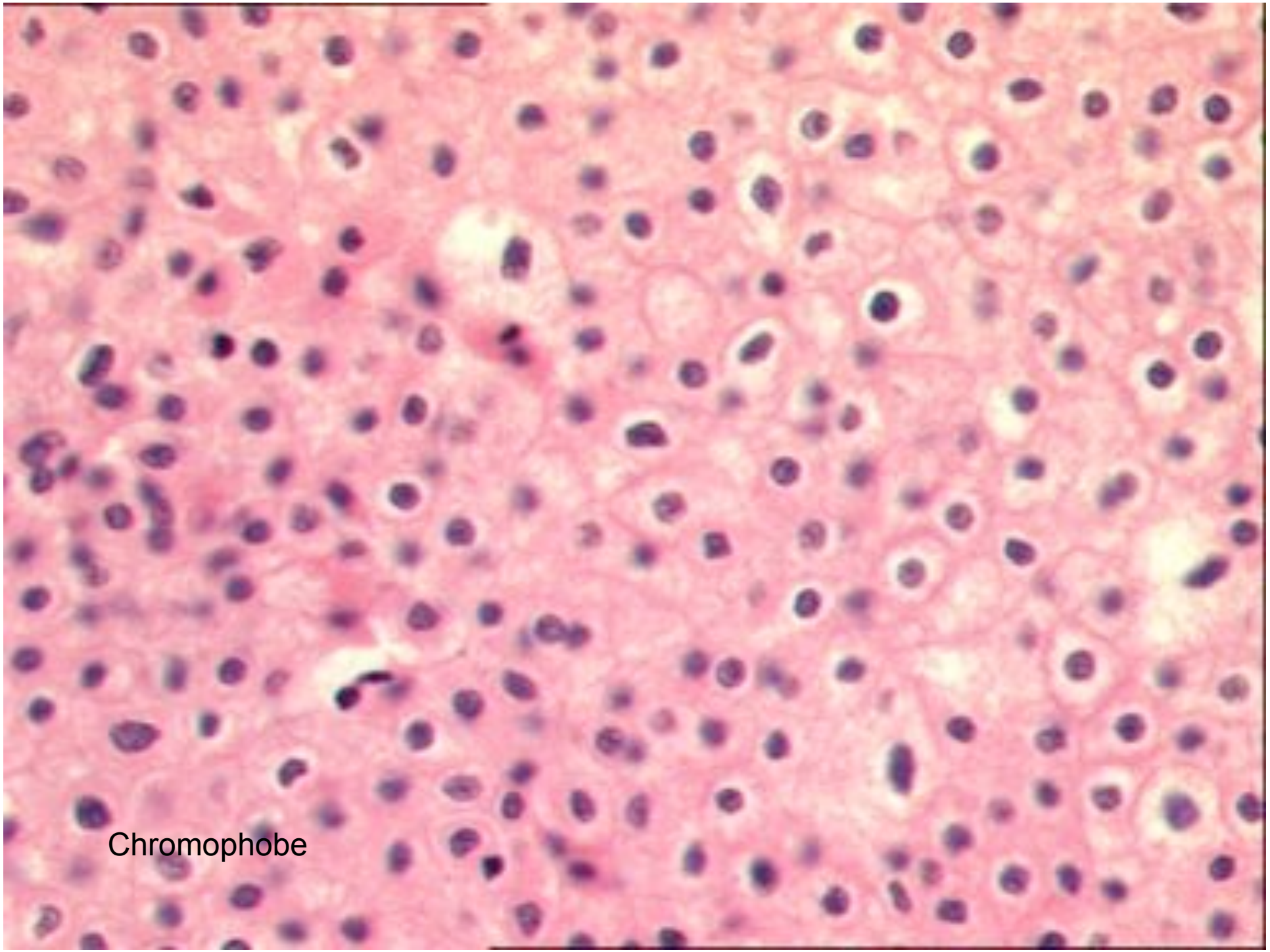
Chromophobe Carcinoma

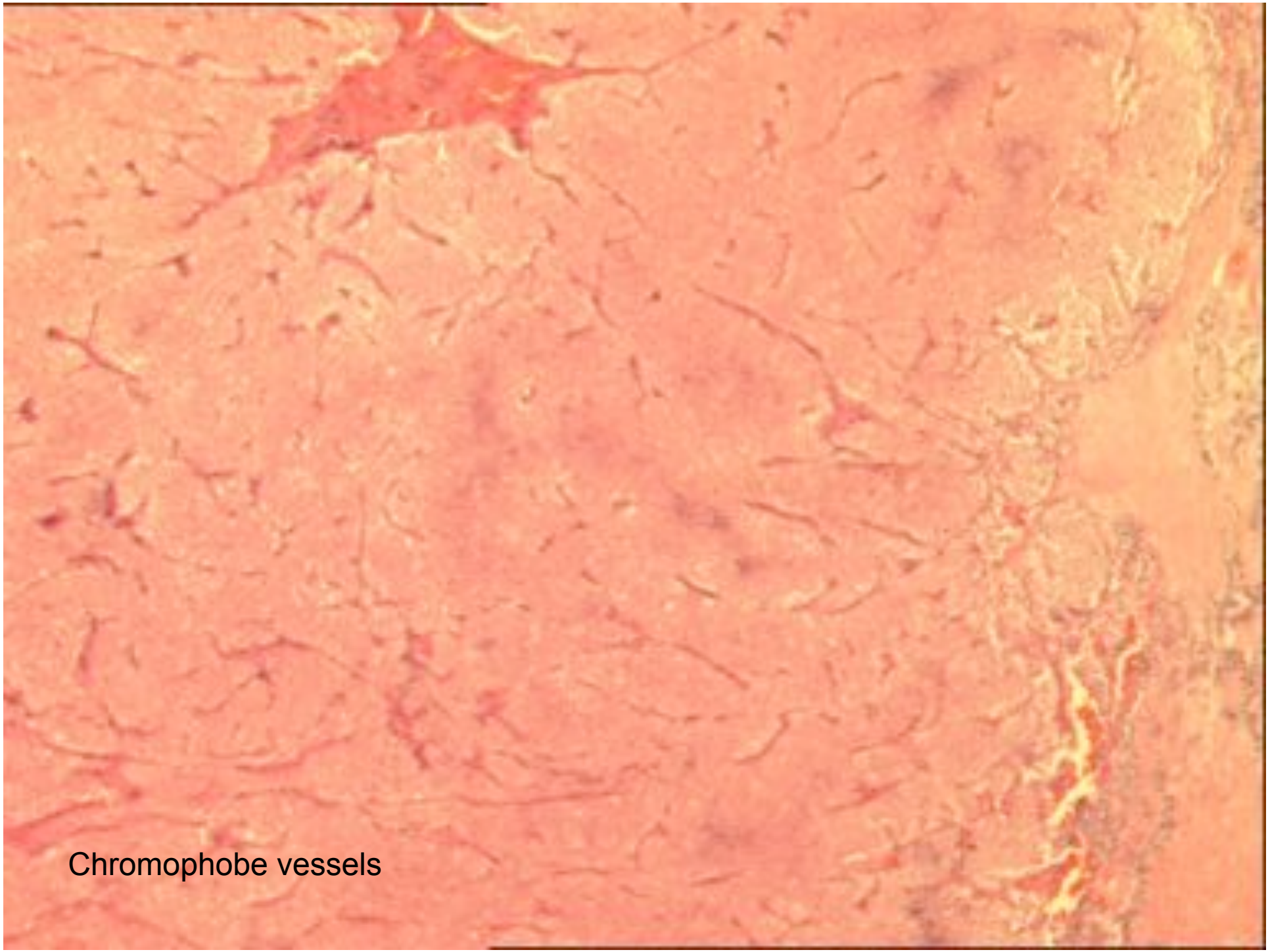
- 5% of renal carcinomas
- Mainly solid growth pattern
- Many blood vessels are thick walled
- Perivascular cells are enlarged

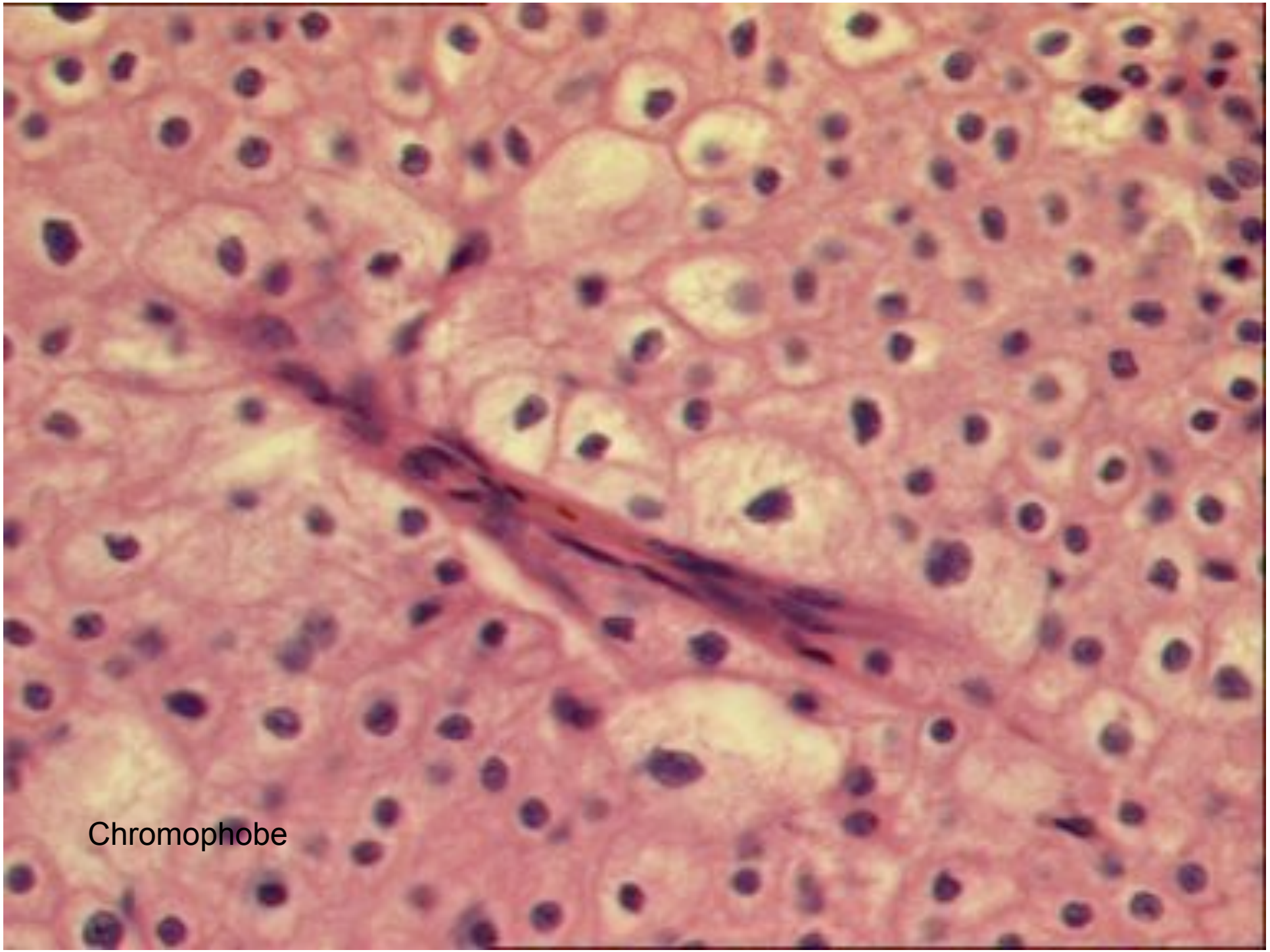
- Raisinoid nuclei and well defined cell
- Membranes
- Flocculent cytoplasm
- Eosinophilic variant
- Perinuclear halos

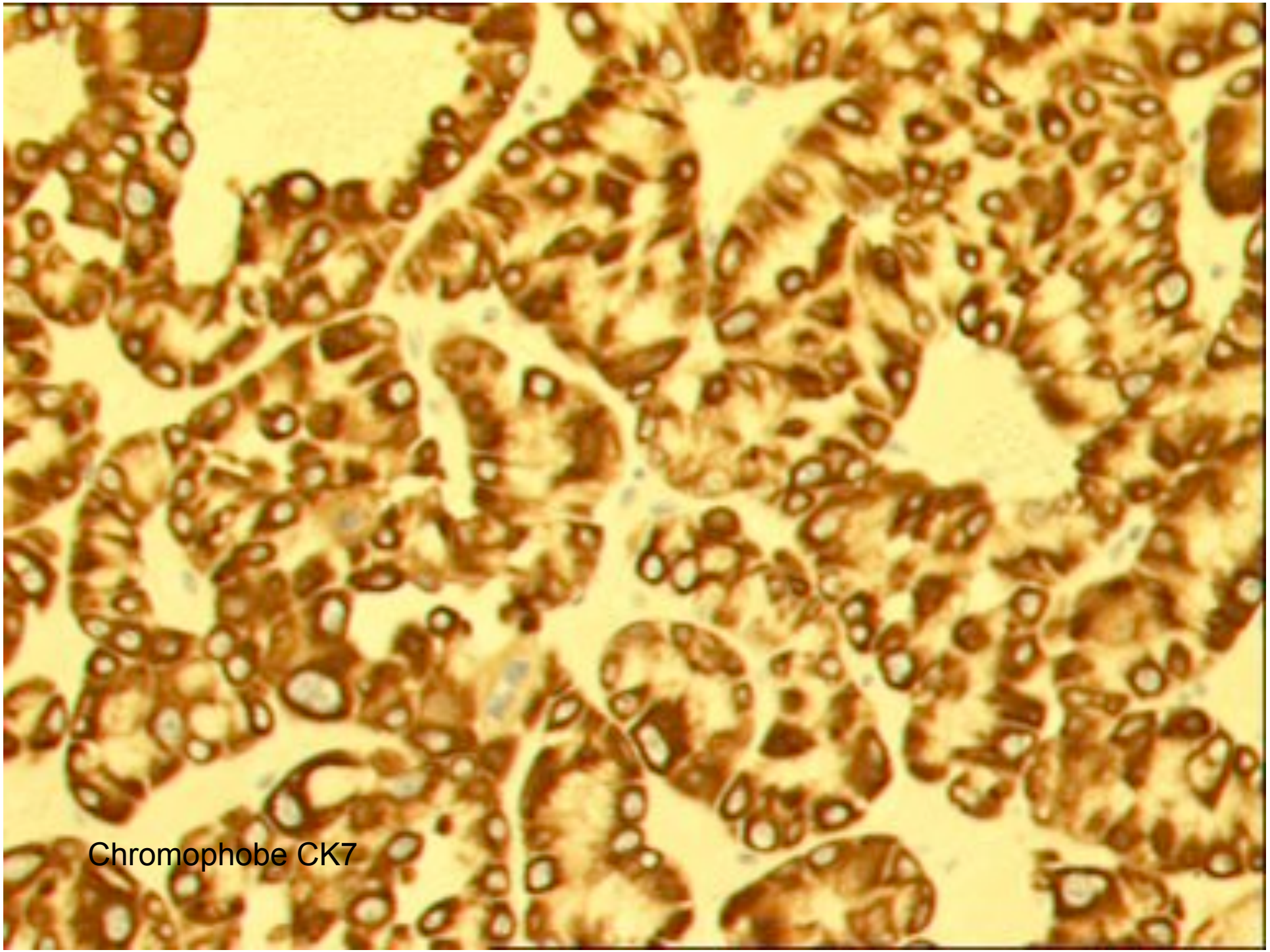

Chromophobe


Chromophobe


Chromophobe


Chromophobe vessels


Chromophobe


Chromophobe CK7

Grading of Chromophobe Carcinoma

Grade 1: Usual range of nuclear appearances

Grade 2: Nuclear crowding AND pleomorphism

Grade 3: Ananplasia or sarcomatoid change

Chromophobe Tumour Grade correlates better with stage and adverse outcome than Fuhrman Grade (for non-sarcomatoid tumours)

At least 2 areas to concur on the grade

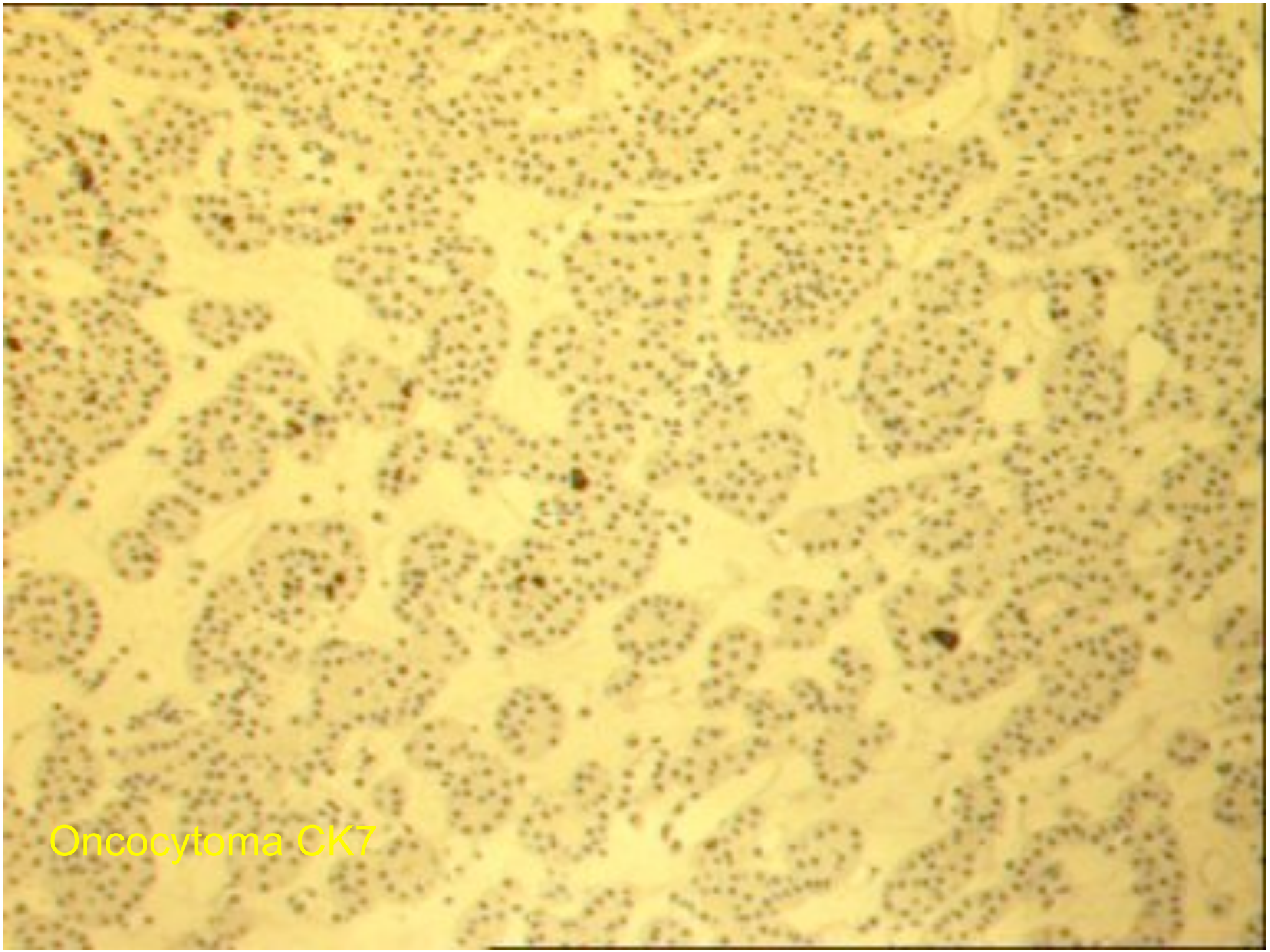
Oncocytoma (benign)

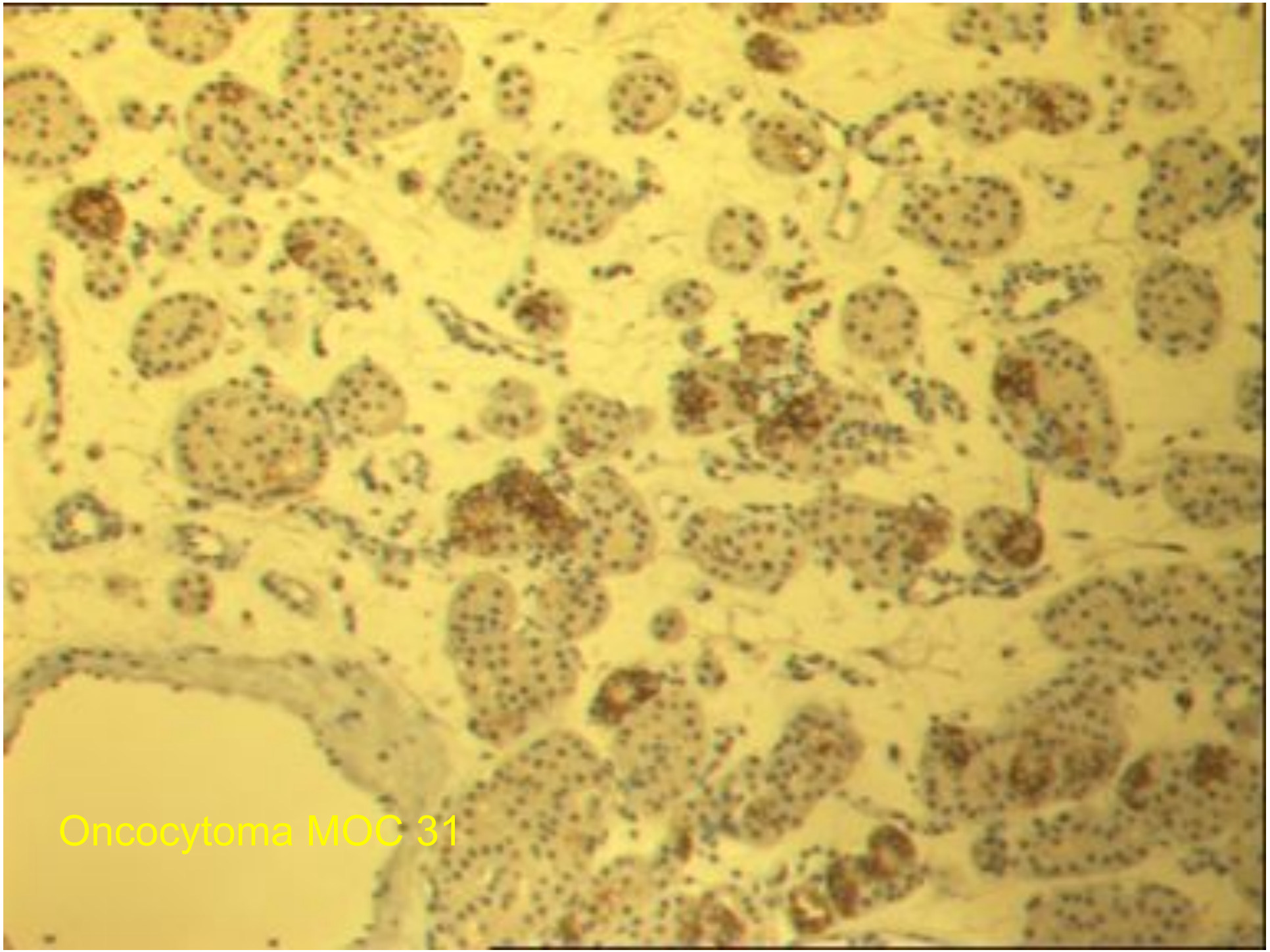
Well circumscribed
Tan brown
Central scar

Nests, tubules, cysts in hypocellular stroma

Round nuclei, plentiful eosinophilic cytoplasm
A few clusters of pleomorphic nuclei

Tiny clear cell or papillary areas OK
Can get capsular & vascular invasion


Oncocytoma CK7


Oncocytoma MOC 31

	Clear Cell	Pap	Chromophobe	CDC	Oncocytoma
Pan CK	+	+	+	+	+
HMWCK	-	-	-	-	-
LMWCK	+	+	+	+	+
MOC 31	-	-	+	-	-
RCC	+/-	+/-	-	-/+	-
Ber EP4	-	+/-	+	-	-
CD 10	+/-	+	-/+	-/+	-
Vimentin	+	+	-	-/+	-
CK 7	-	+	+(diff)	+/-	+(foc)
AMACR	-	+	-	-	-
CD15	-	+	-	-	+

Immunoprofiles

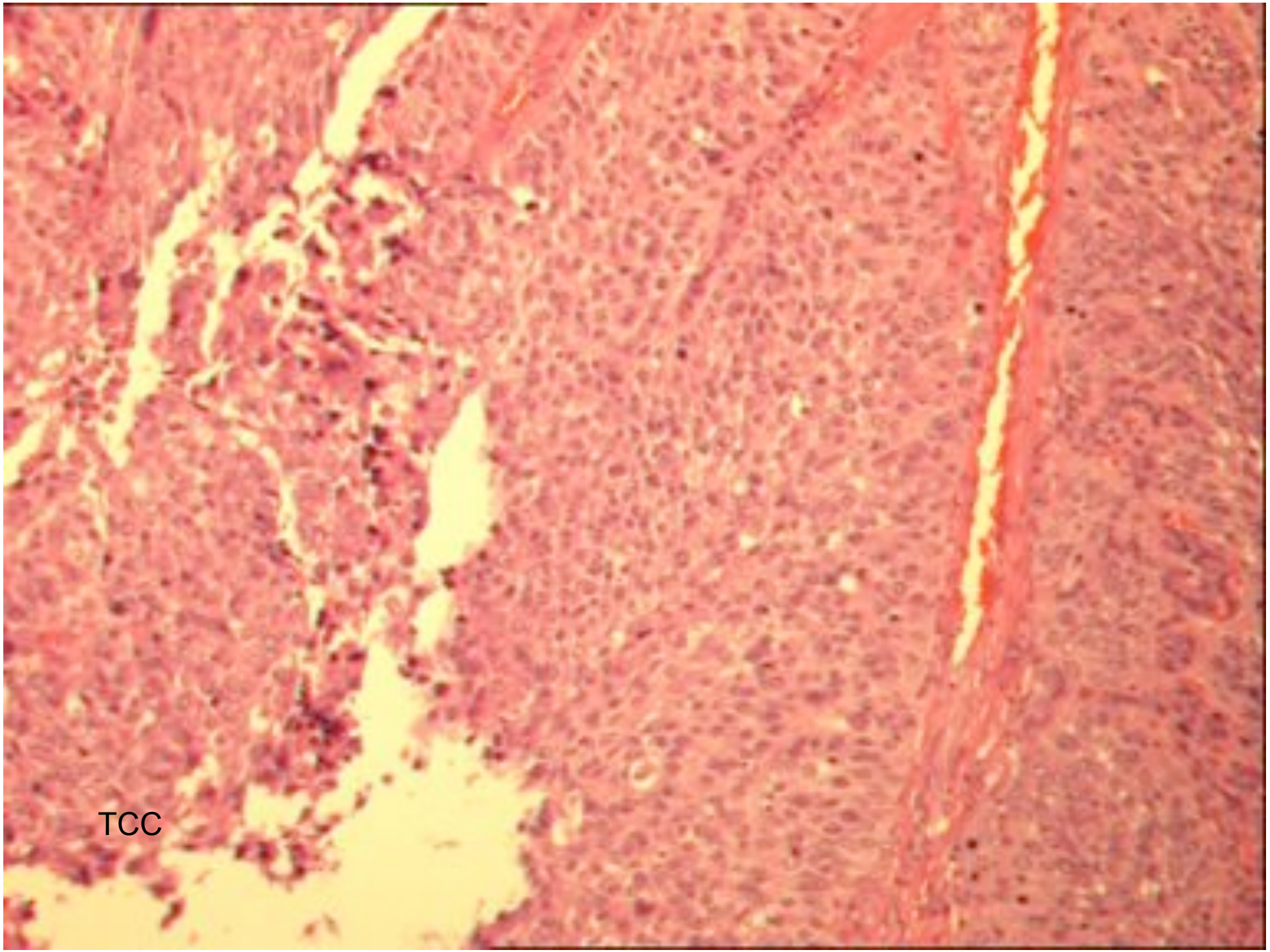
Chromophobe Vs Oncocytoma	MOC31 Ber EP4 CK 7 CK 20 CD10
Chromophobe Vs Clear cell	MOC 31 CD10 RCC Ber EP4
Papillary Ca Vs CDC	Immuno not much use
Papillary Ca Vs Met adenoma	CK 7 AMACR CD57 WT-1
Papillary Ca Vs Mucinous tubular and spindle cell Ca	Immuno not much use
Sarcomatoid RCC Vs MTS Cell Ca	CK7 + in MTS

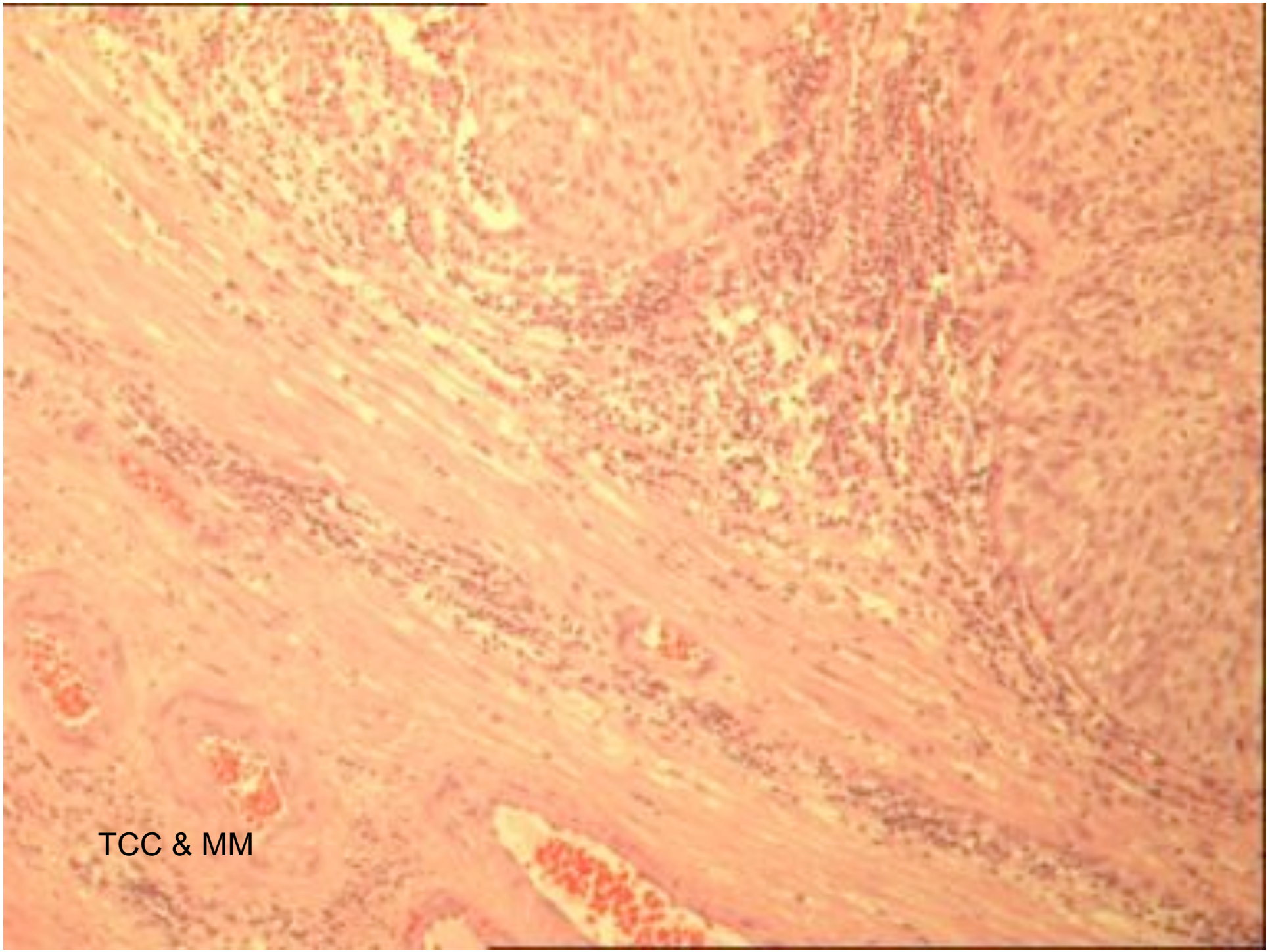
Transitional cell carcinoma

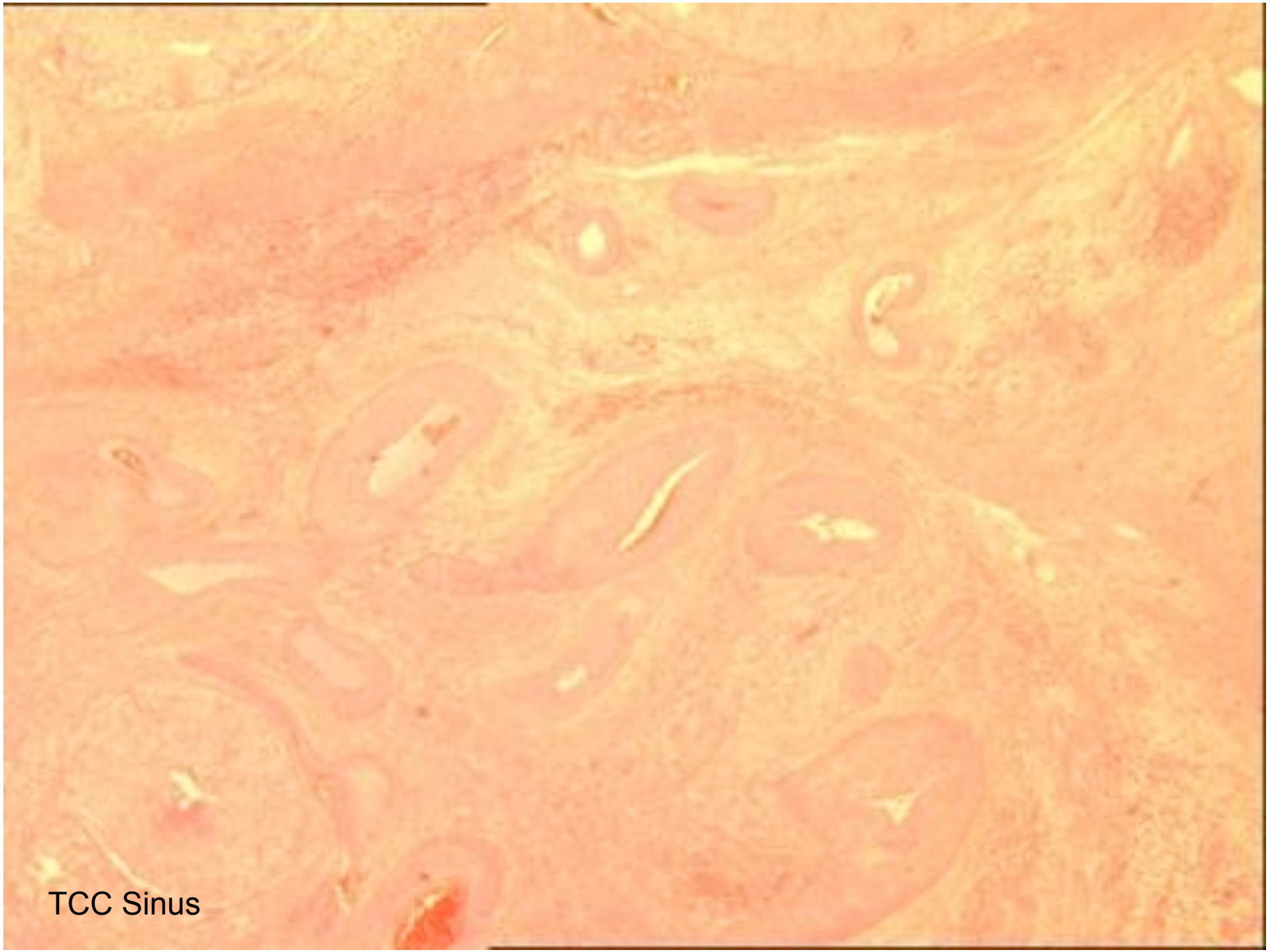
Renal pelvis
7% of all renal tumours
5% of all urothelial tumours

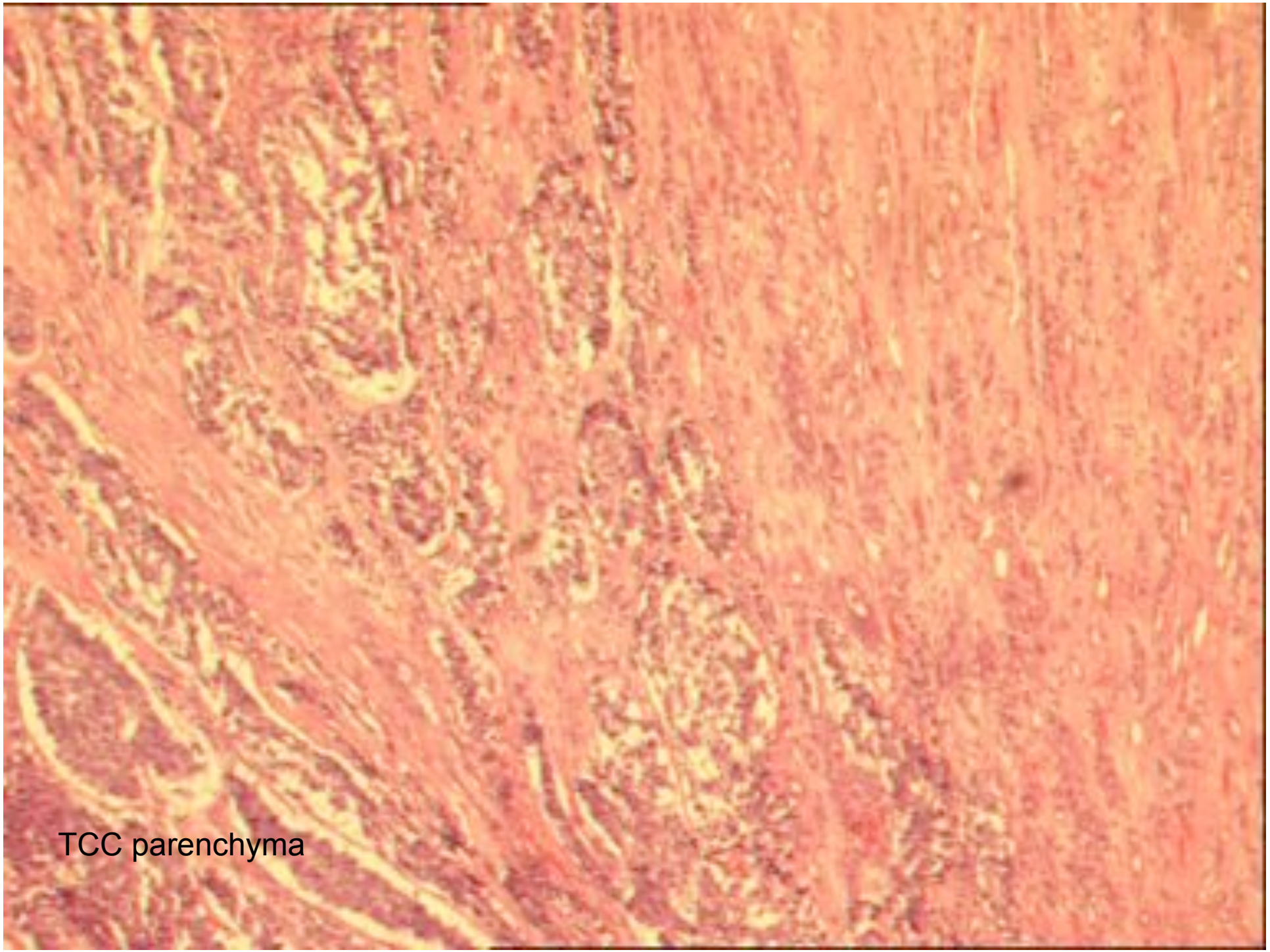
Prognostic indicators:

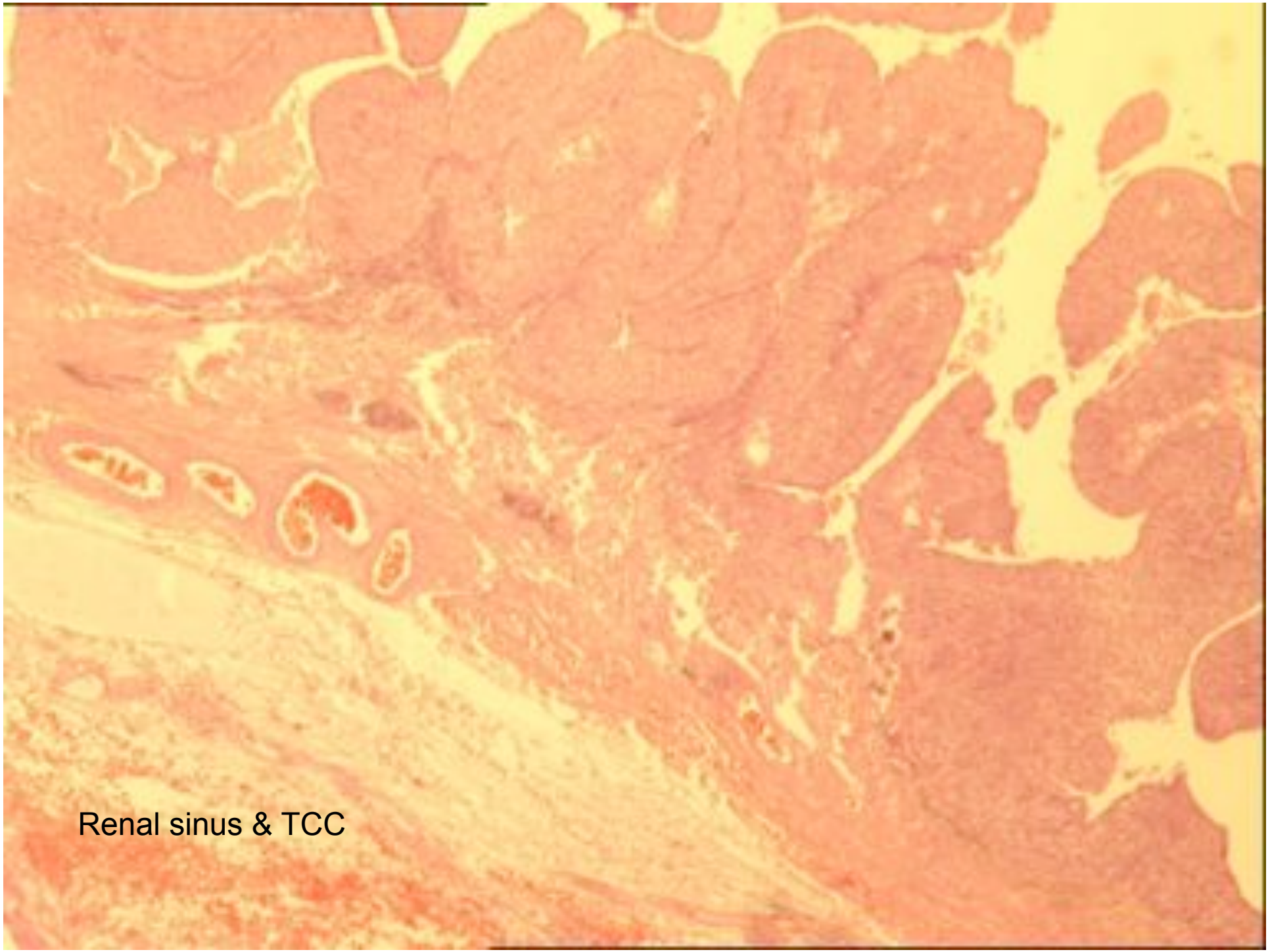
- grade
- ureteric margin status
- vascular invasion
- stage (most important)


TCC


TCC & MM


TCC Sinus


TCC parenchyma


Renal sinus & TCC

Collecting duct carcinoma

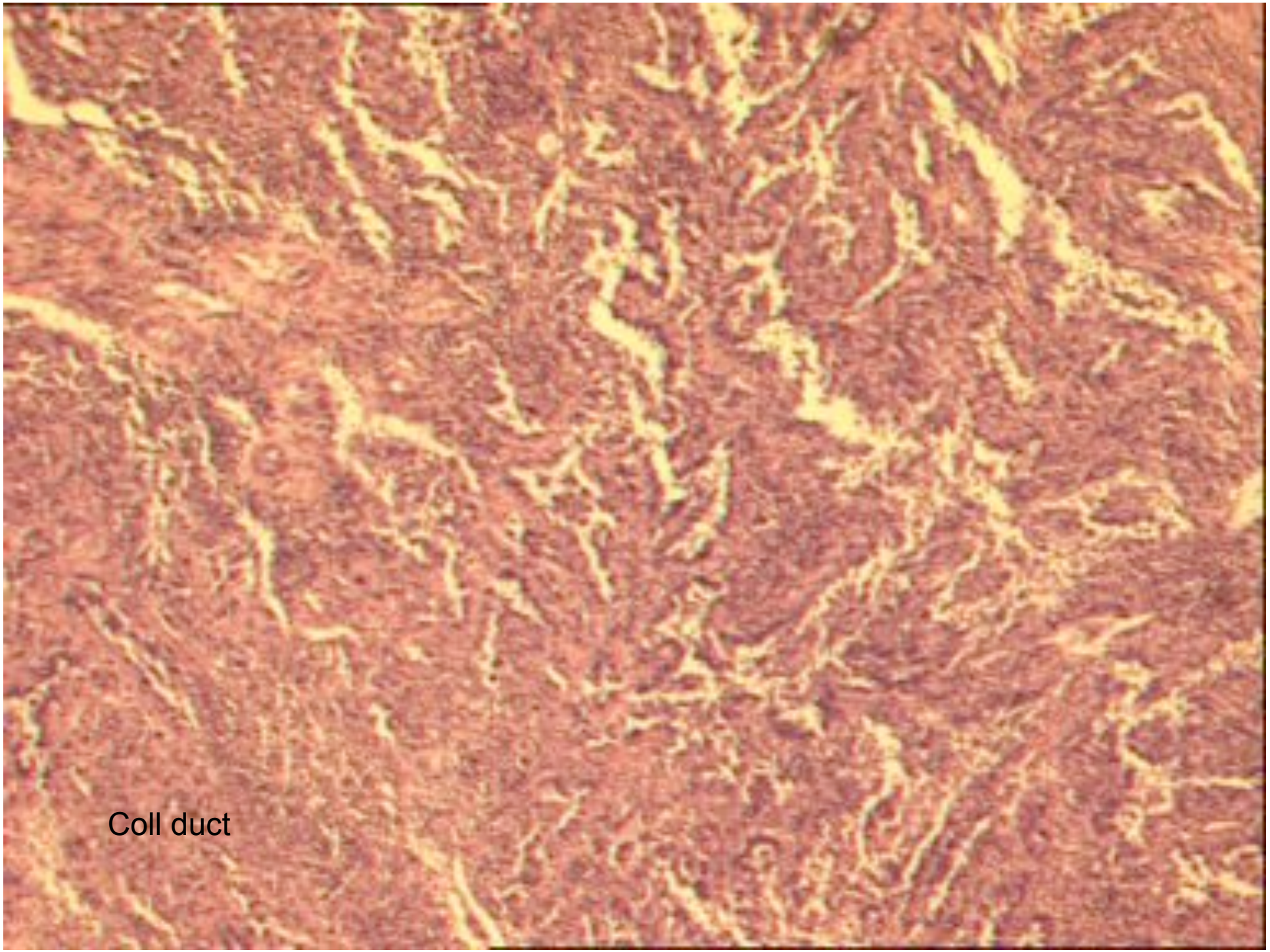
Rare – less than 1% renal tumours
Can be metastatic at presentation

Centrally located
Tubular / tubulo-papillary
Angulated glands infiltrating renal parenchyma
Desmoplastic stroma

Tubular epithelial dysplasia may be seen

High nuclear grade

Poor prognosis: Two thirds dead within 2 years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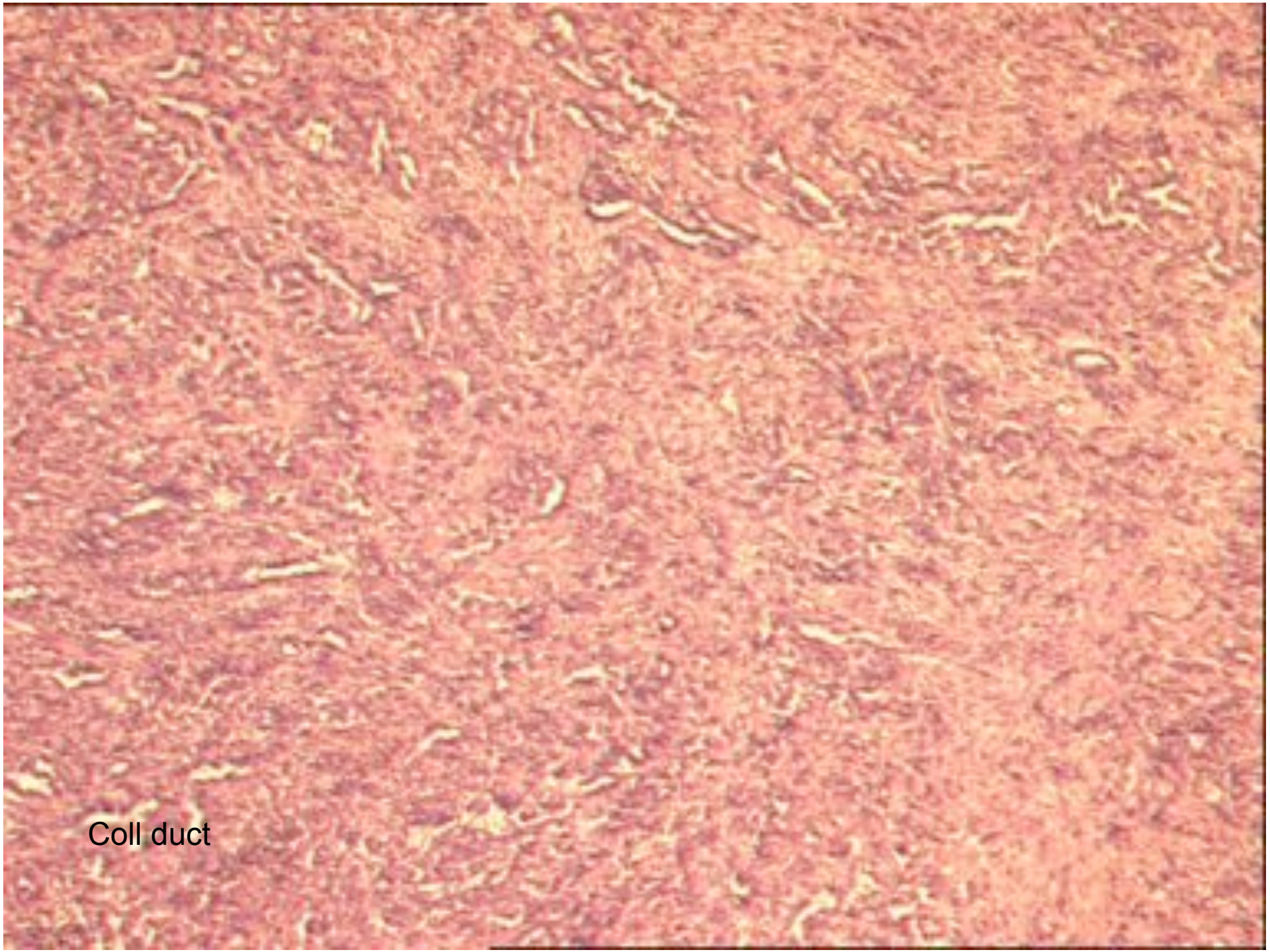
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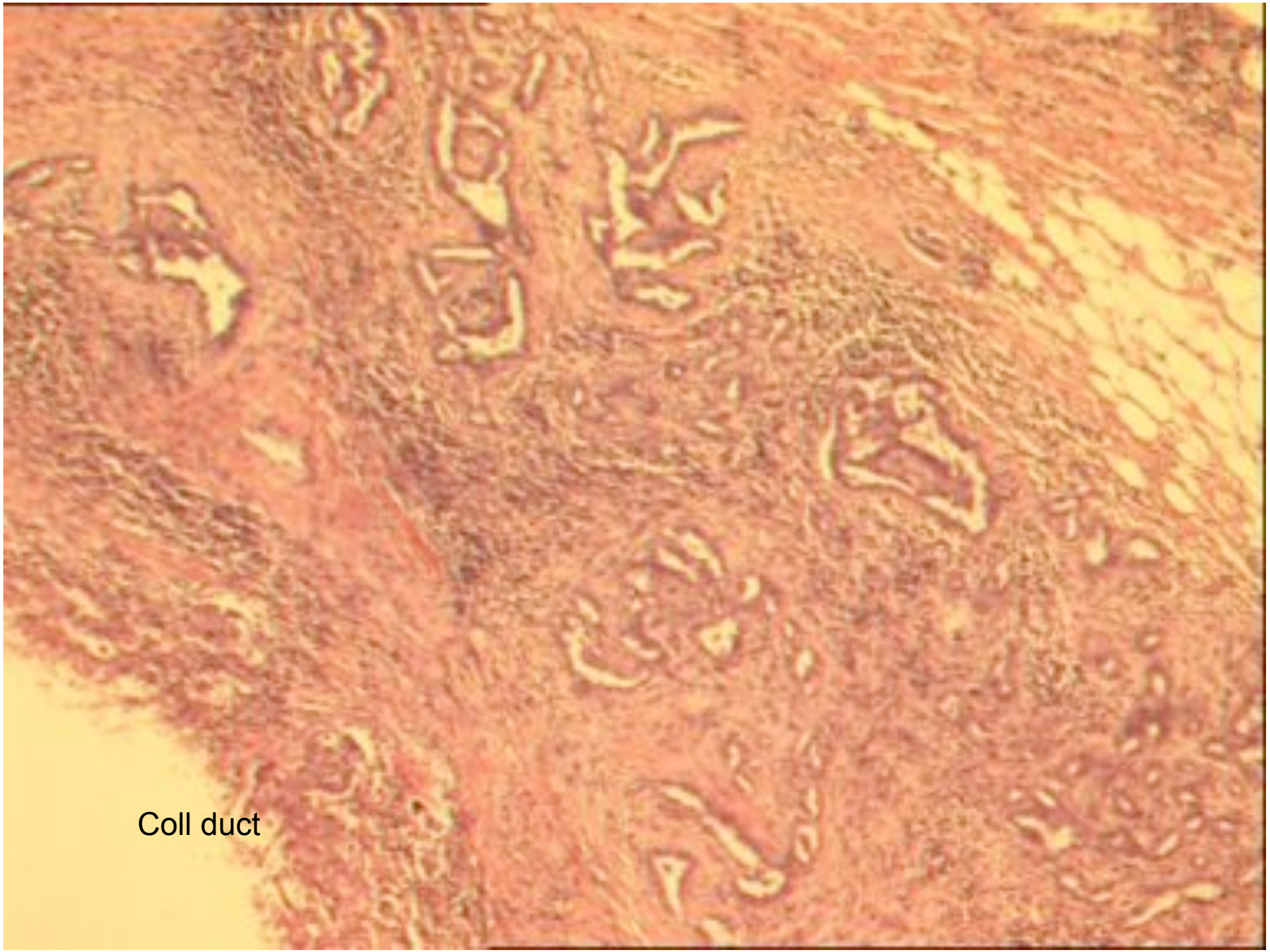
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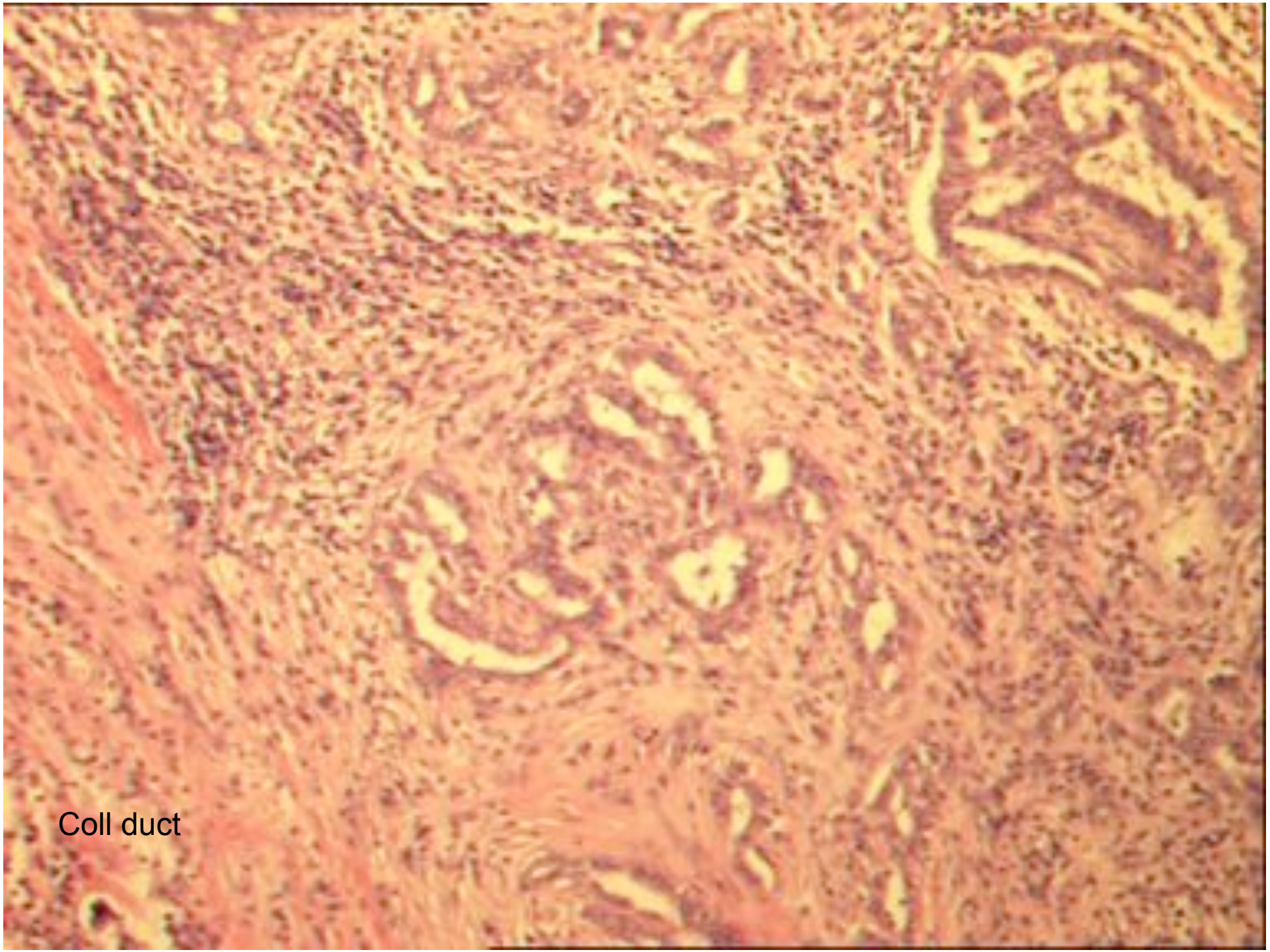
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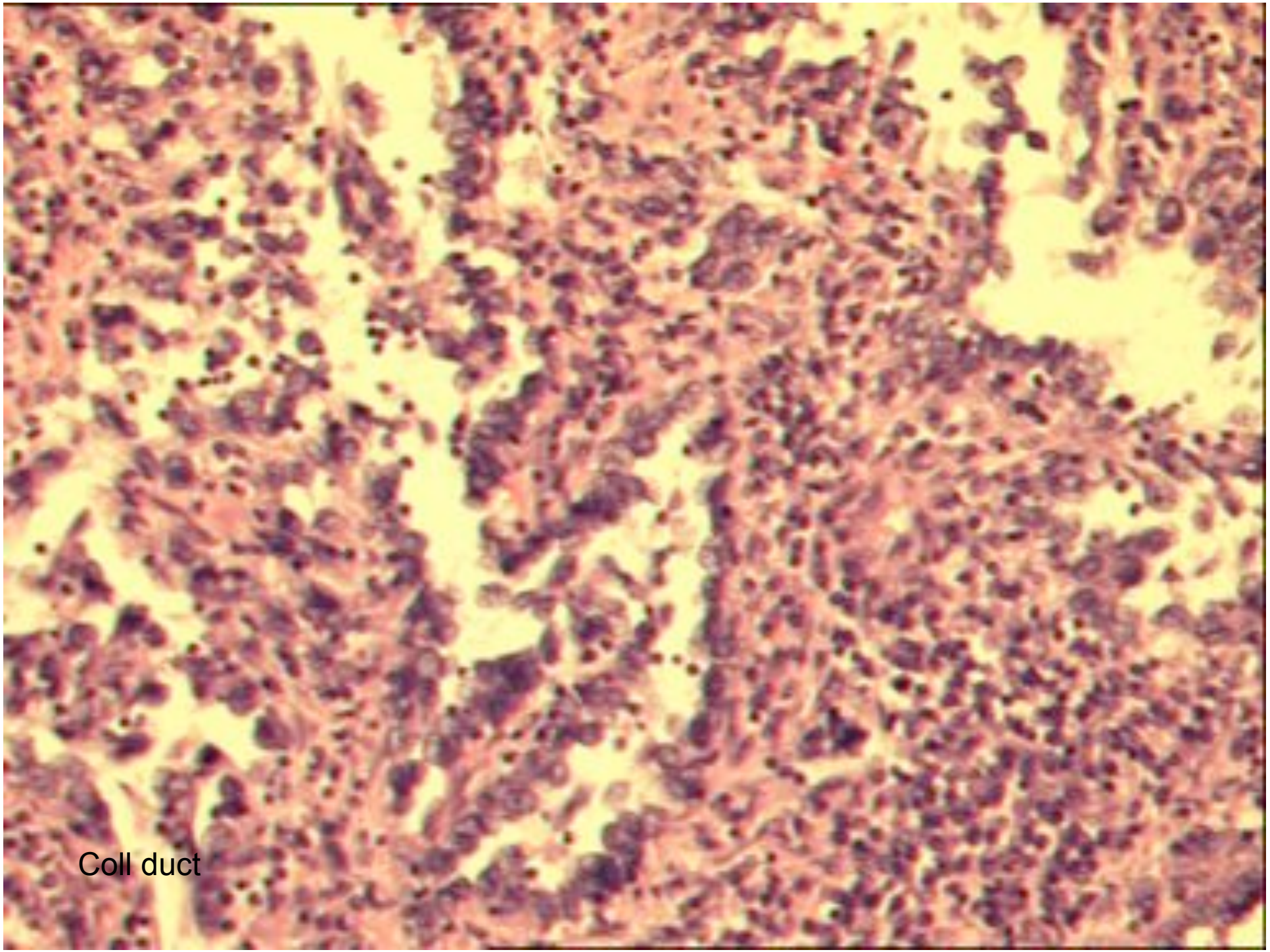
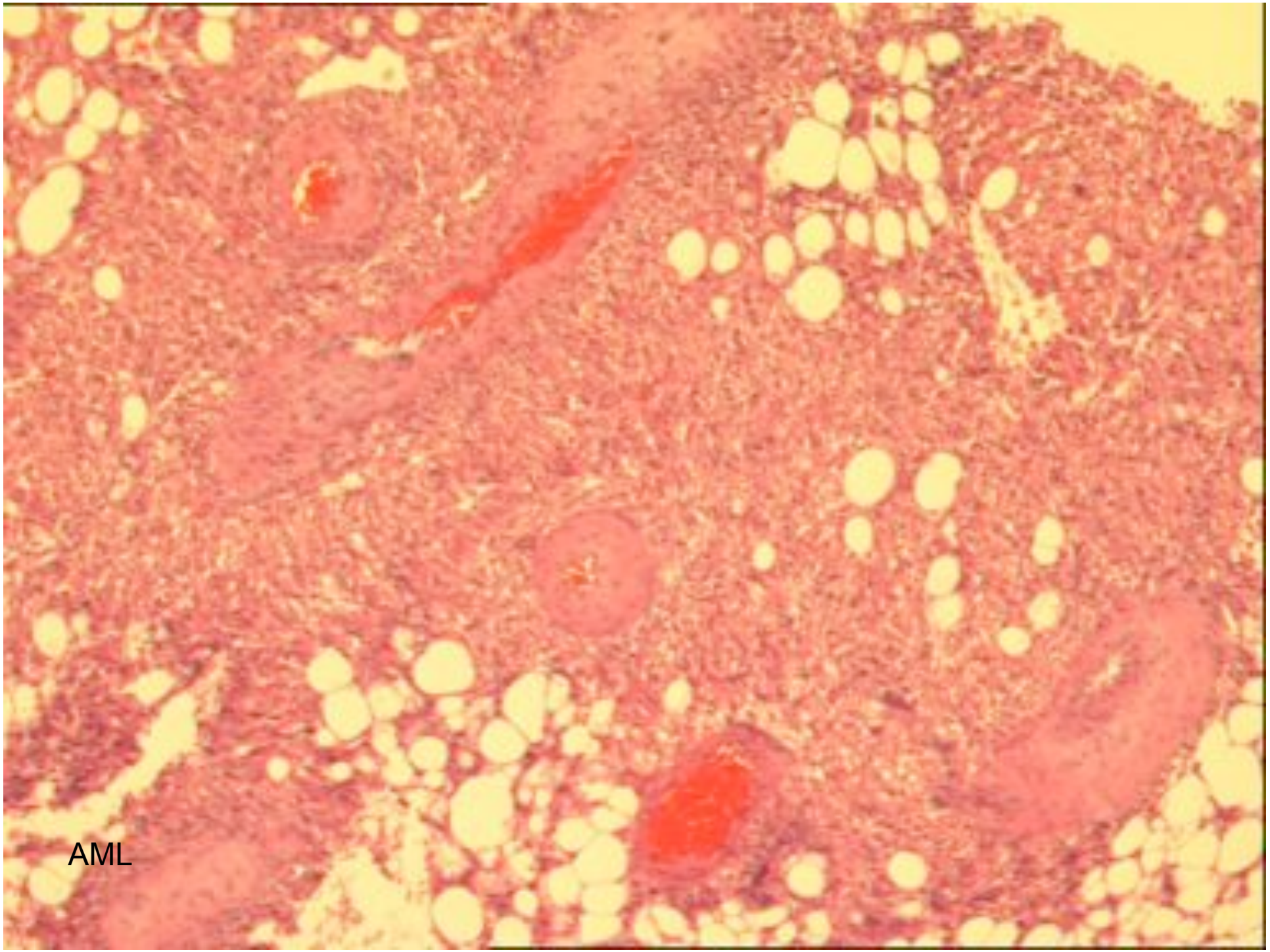

Coll duct

Angiomyolipoma

1% renal tumours
Thought to arise from perivascular epithelioid cells
Can lose attachment to kidney and grow in retroperitoneum
Associated with tuberous sclerosis

Fat, blood vessels and smooth muscle – variable

Can be malignant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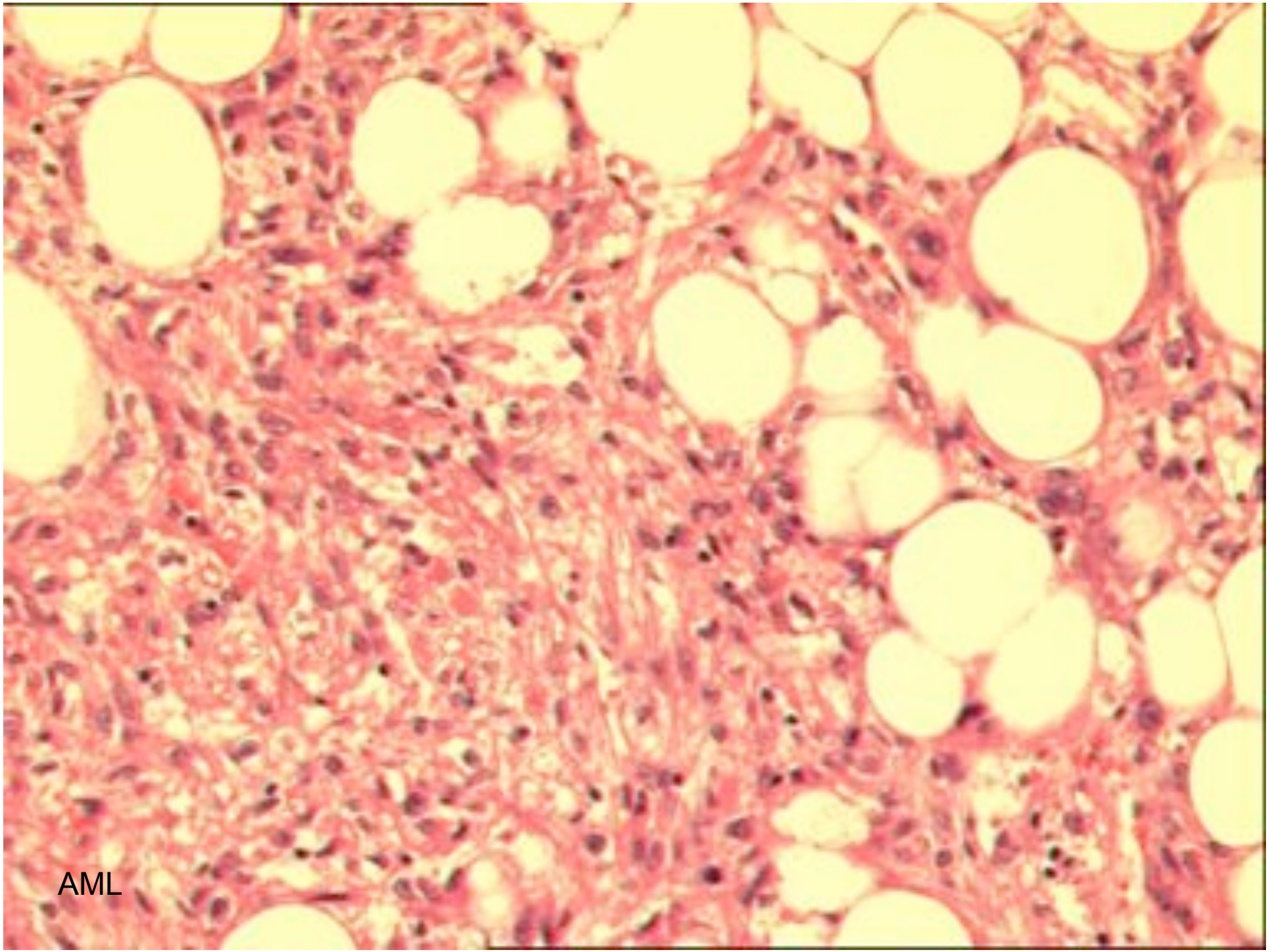
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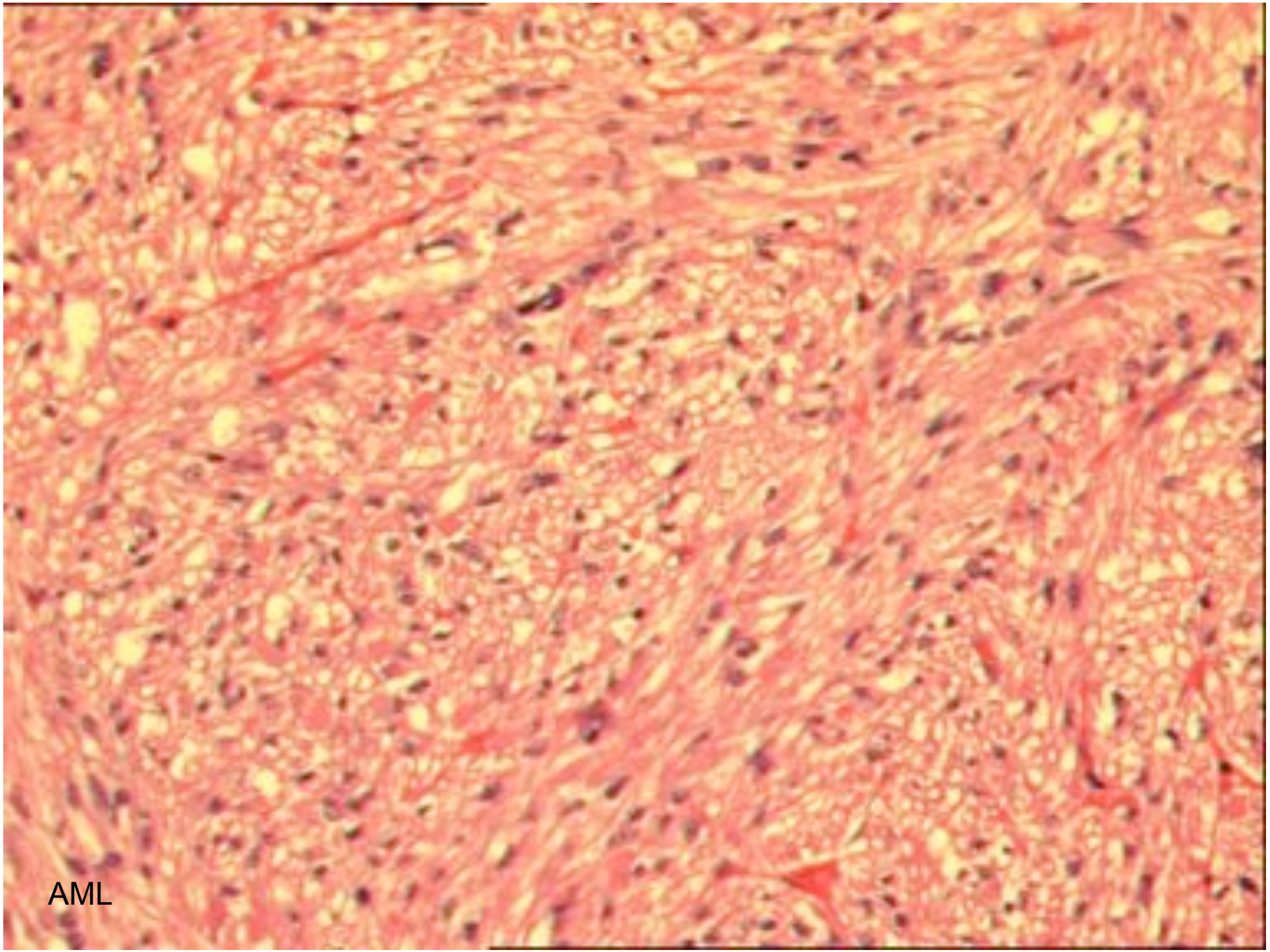
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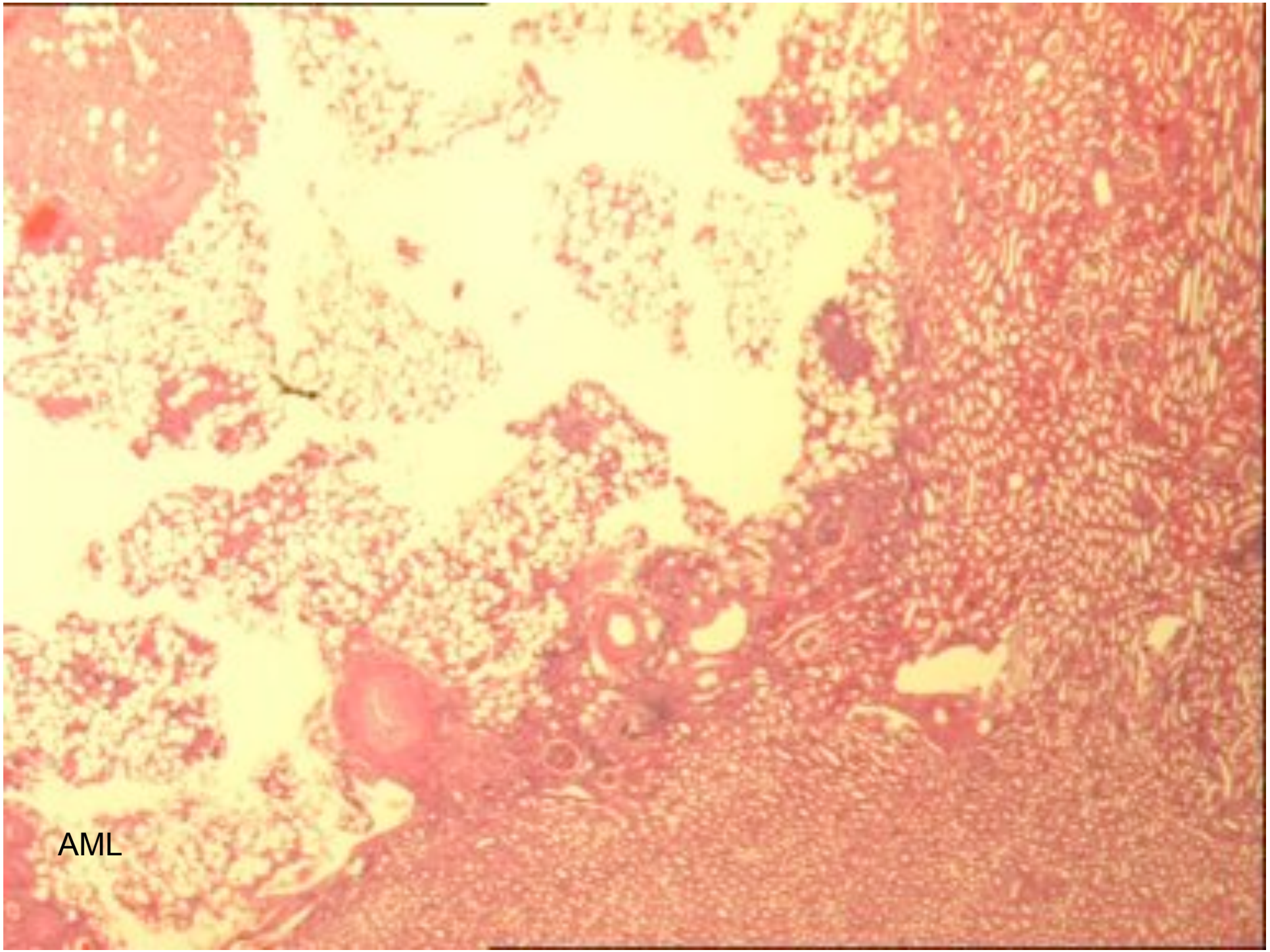
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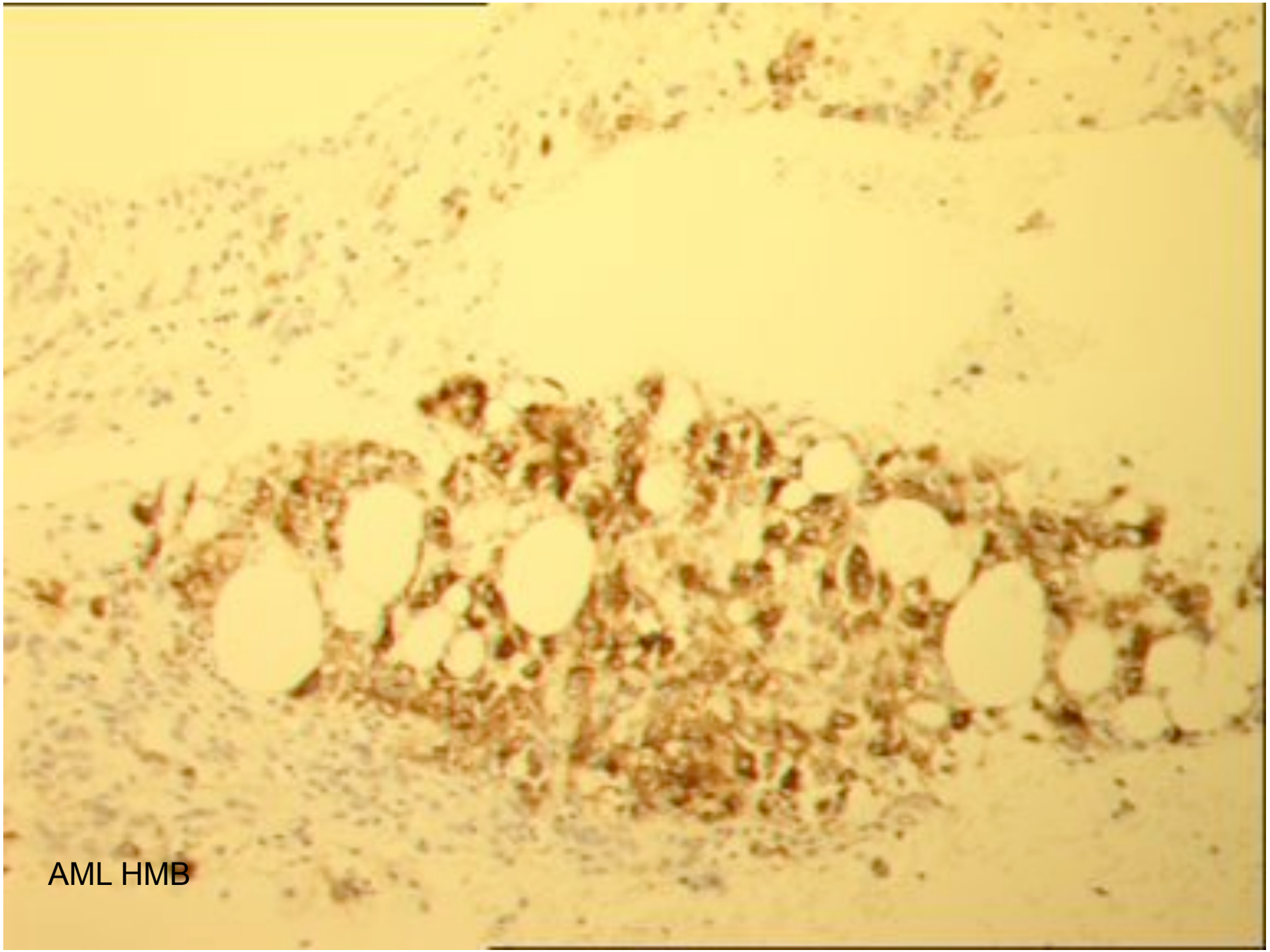
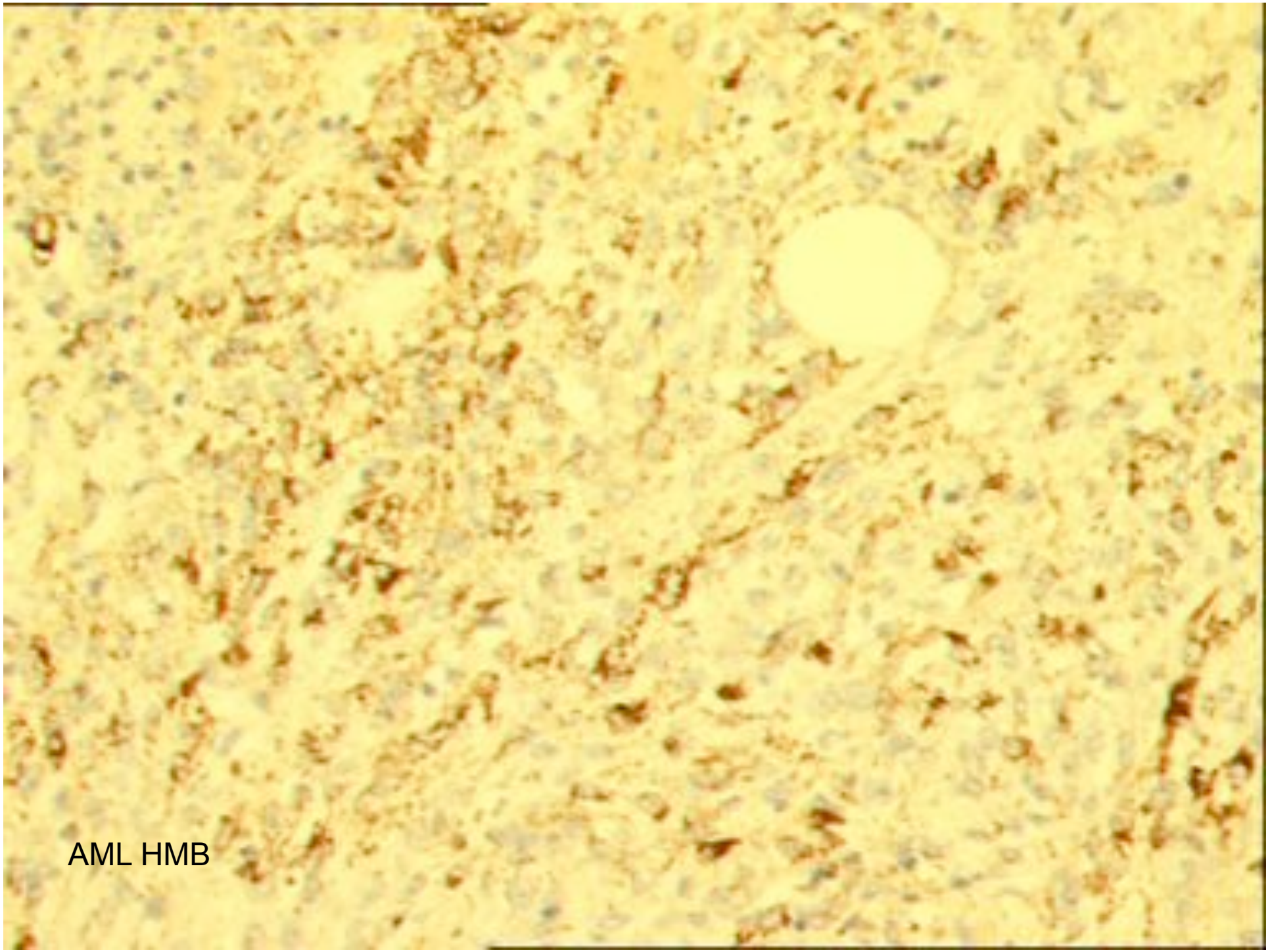

AML HMB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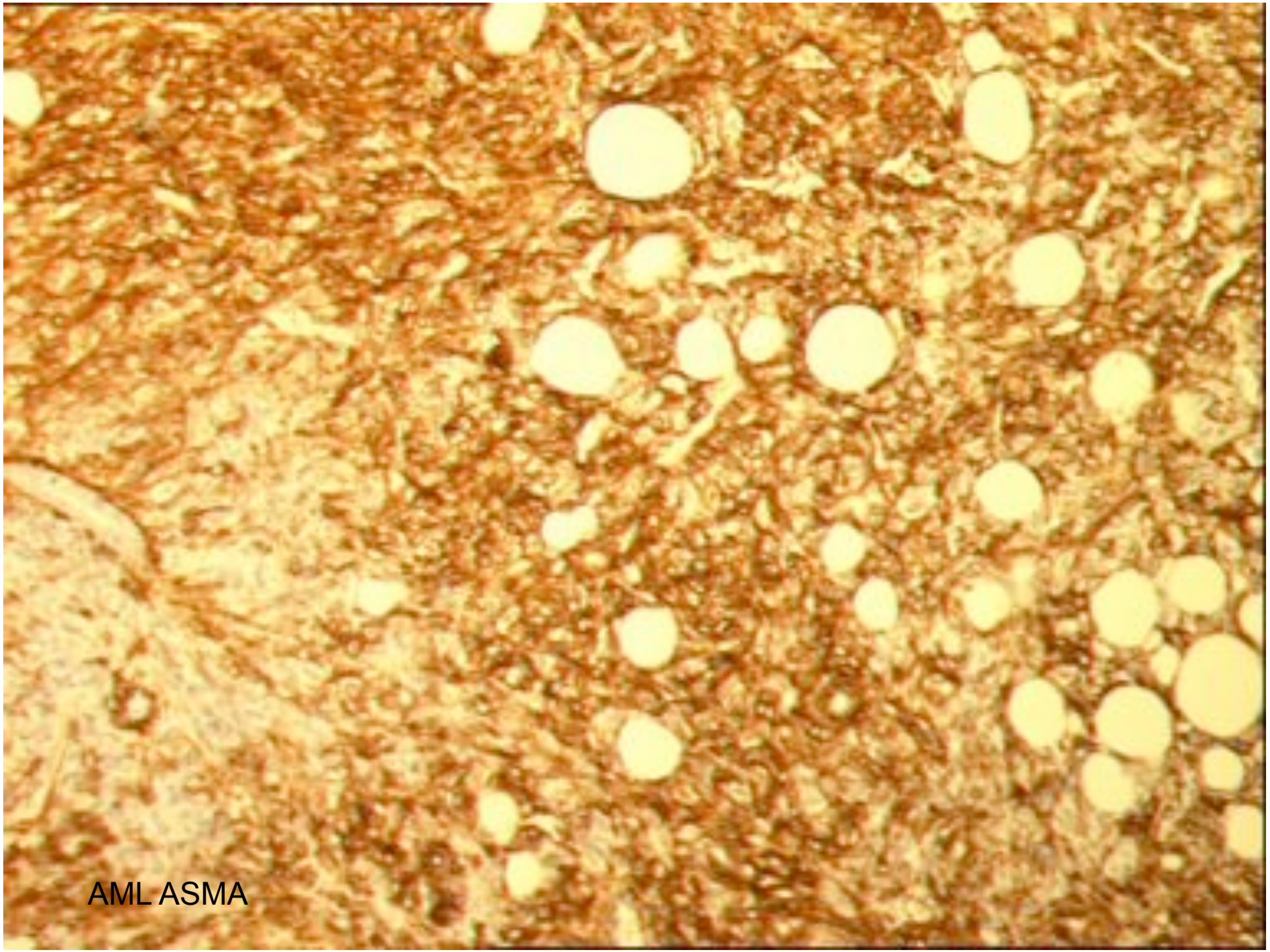
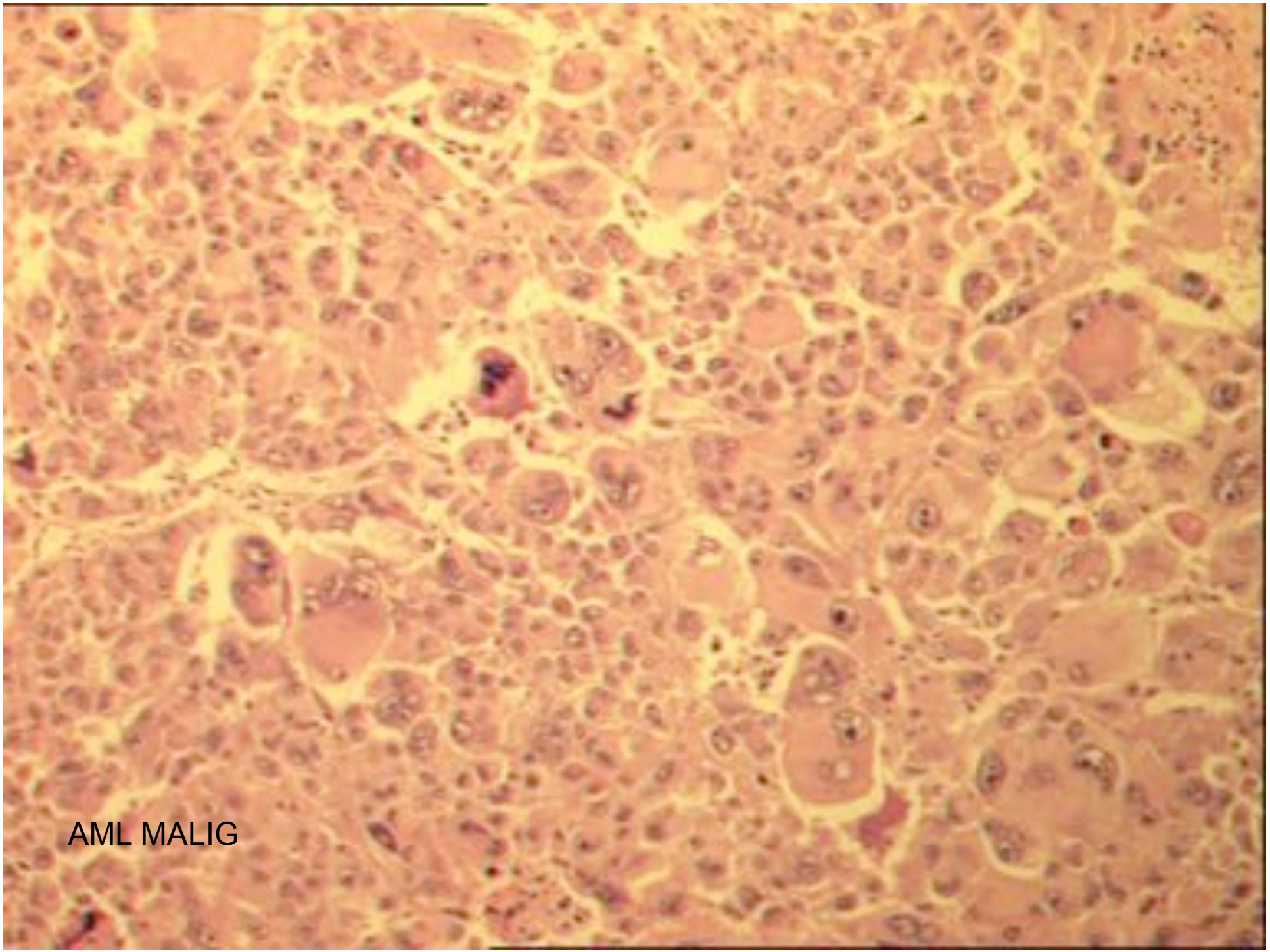
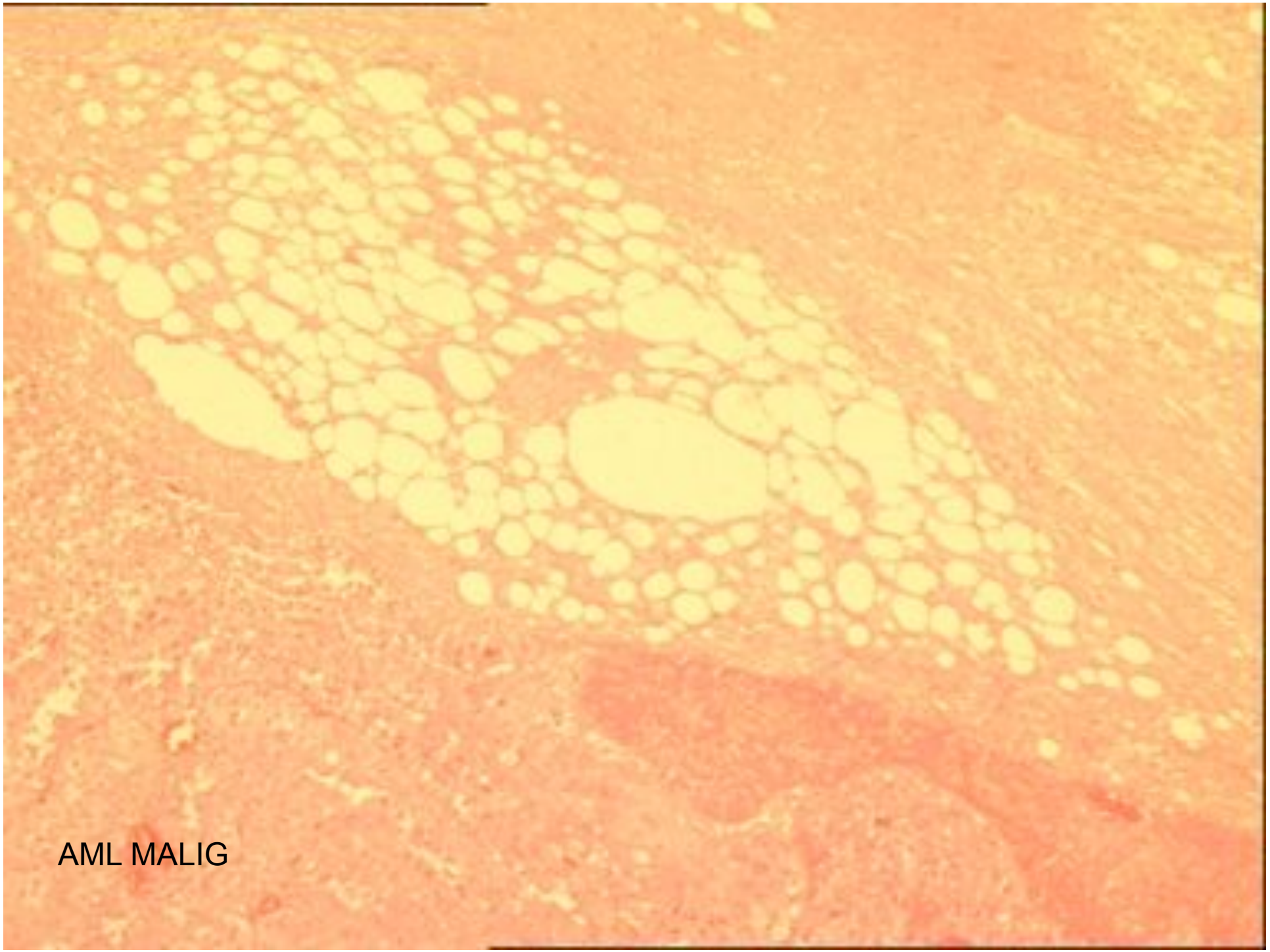

AML ASMA

Epithelioid Angiomyolipoma

The presence of 3 or more of the following are predictive of malignant behaviour:

- > 70% atypical epithelioid cells
- > 2 mitoses per 10hpf
- Atypical mitoses
- Necrosis

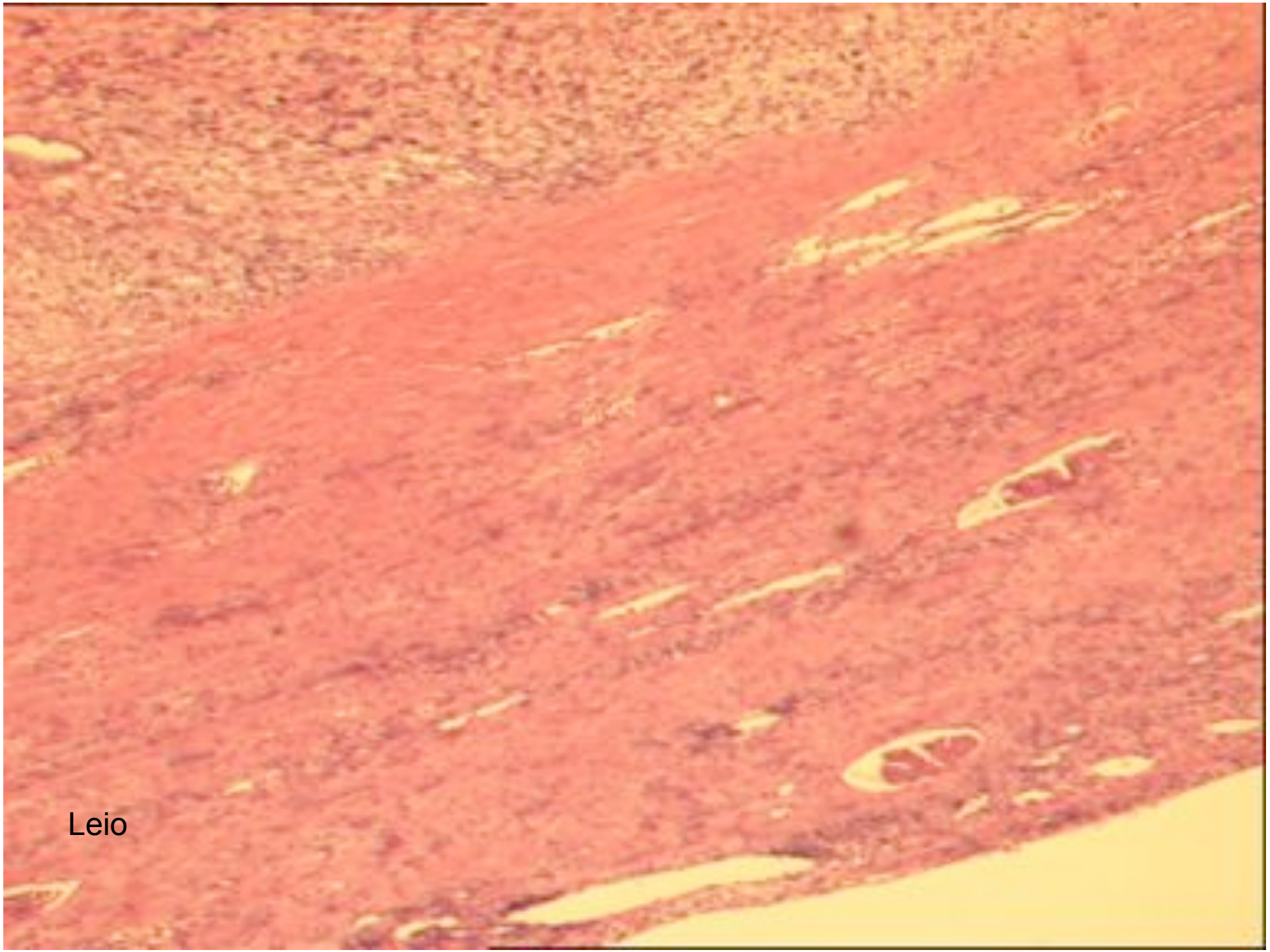

AML MALIG

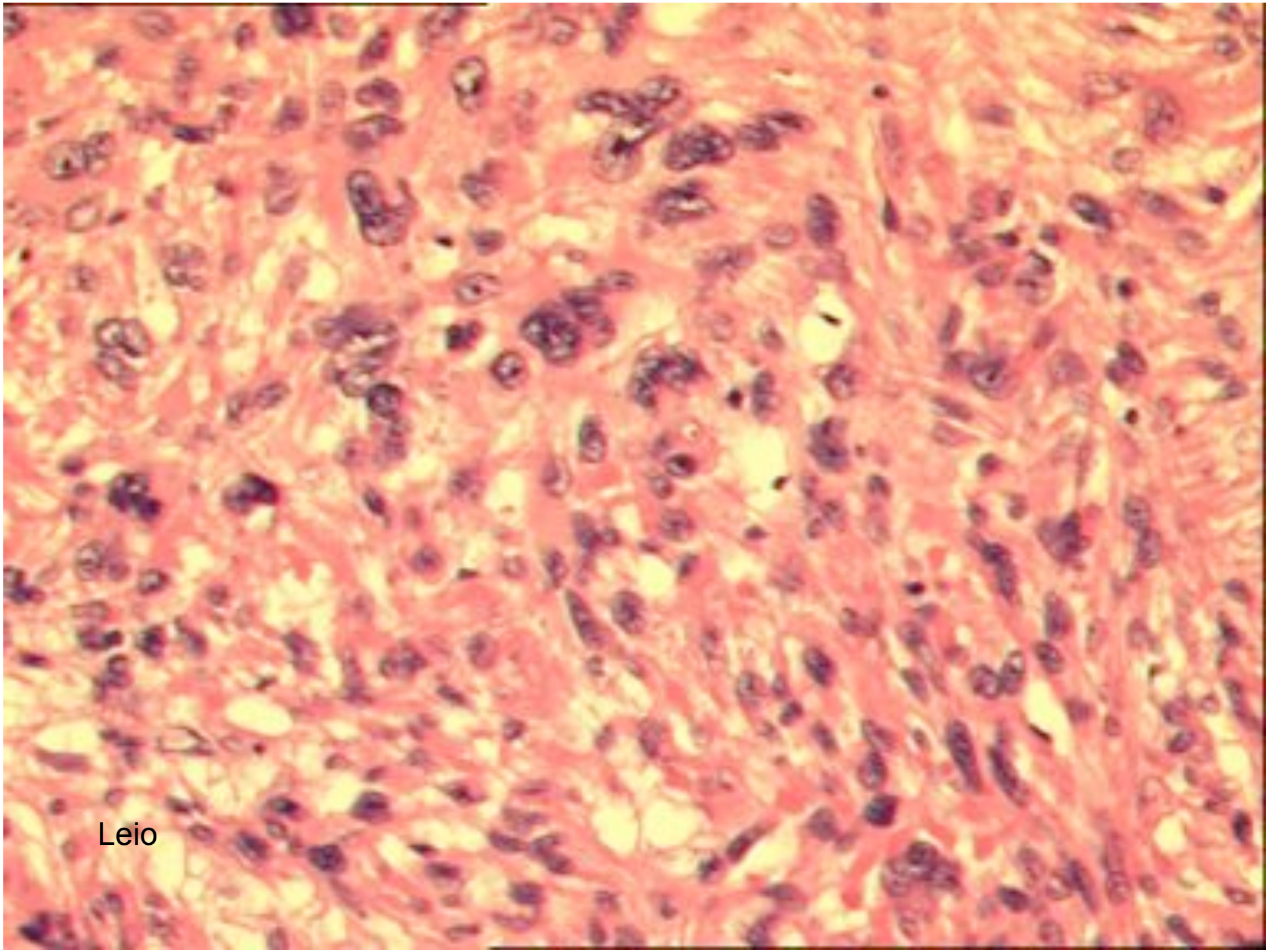

AML MALIG

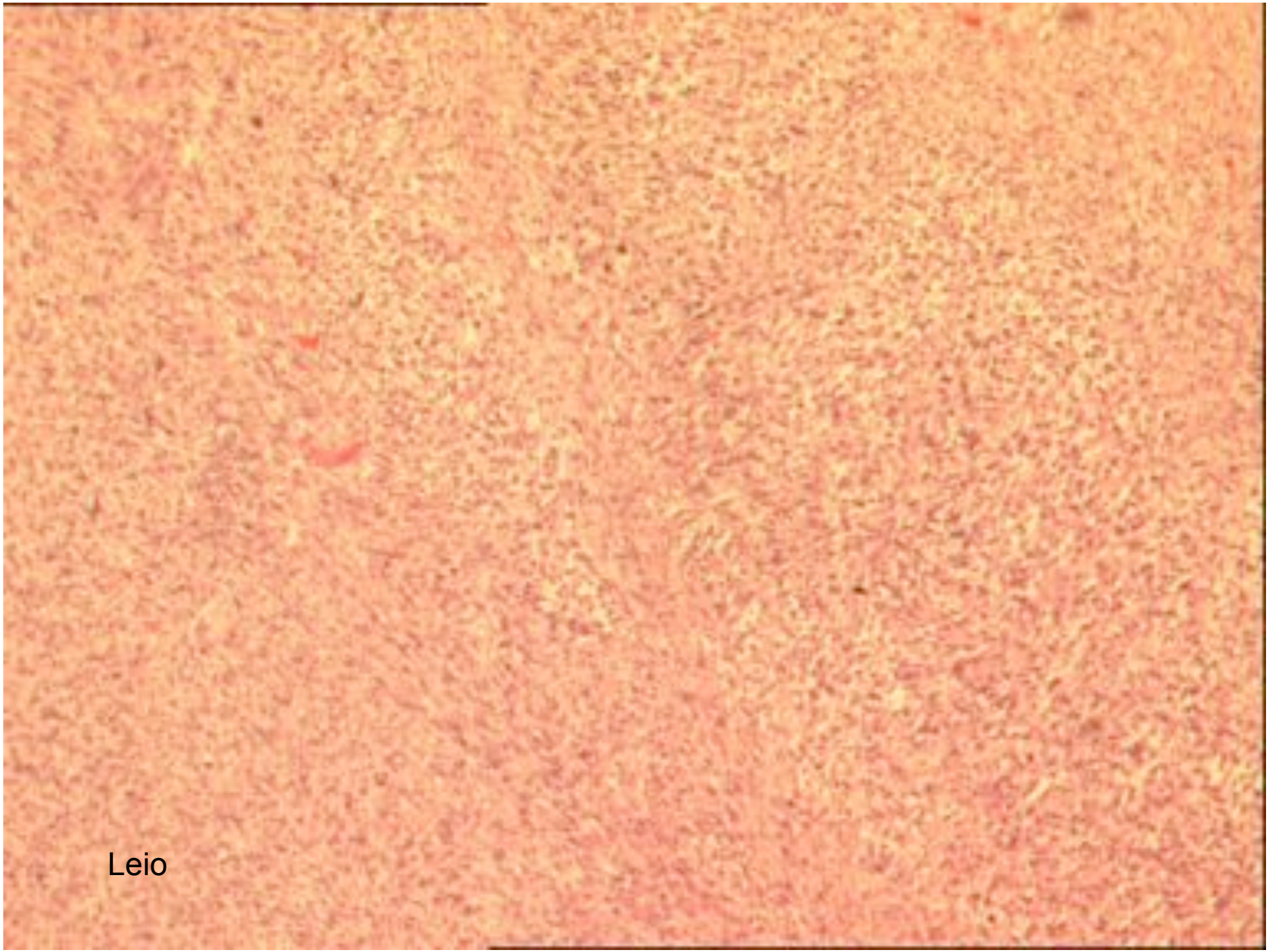
Renal Leiomyosarcoma

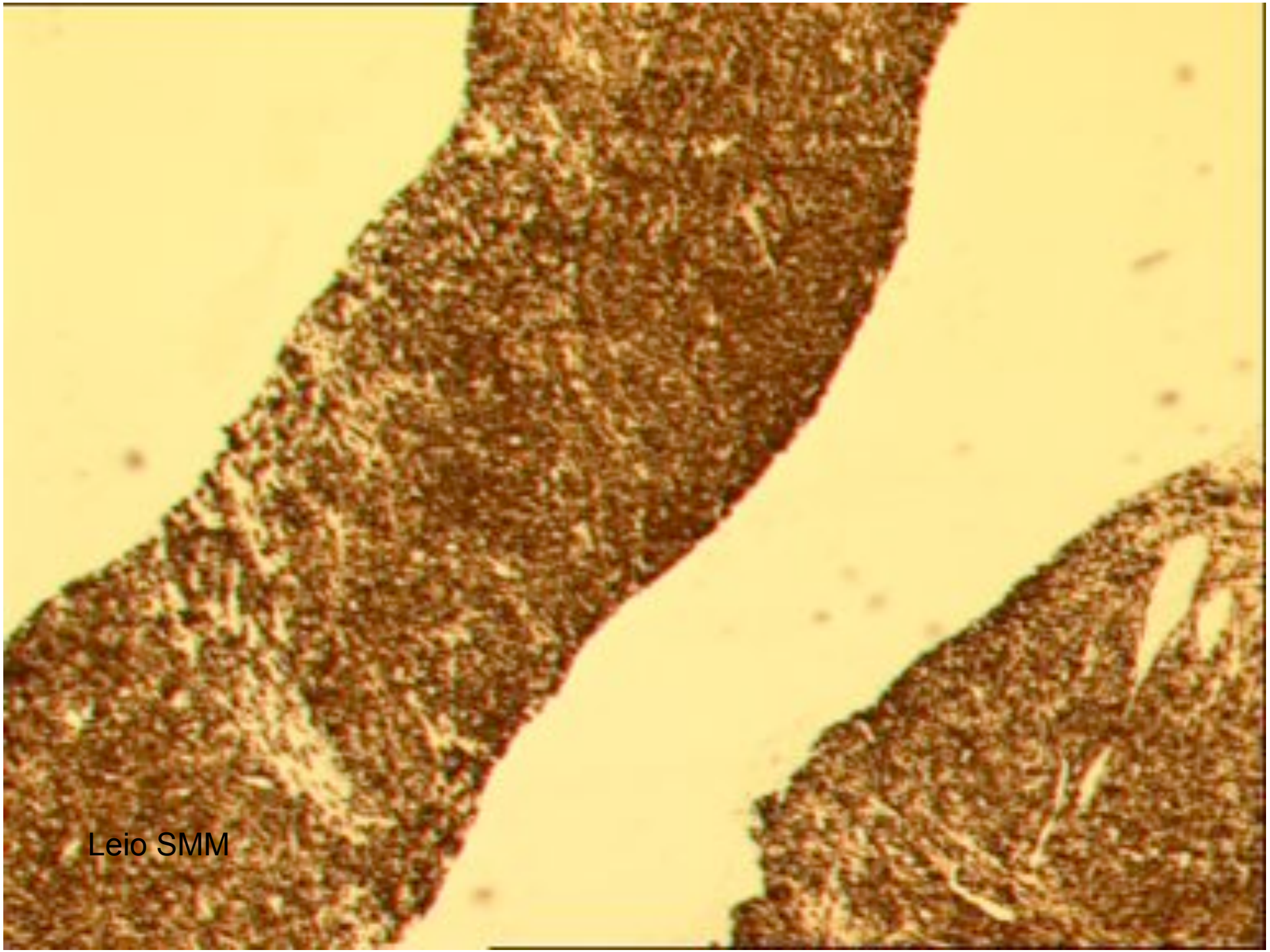
Rare but is the most common sarcoma

Most patients die within a year


Leio

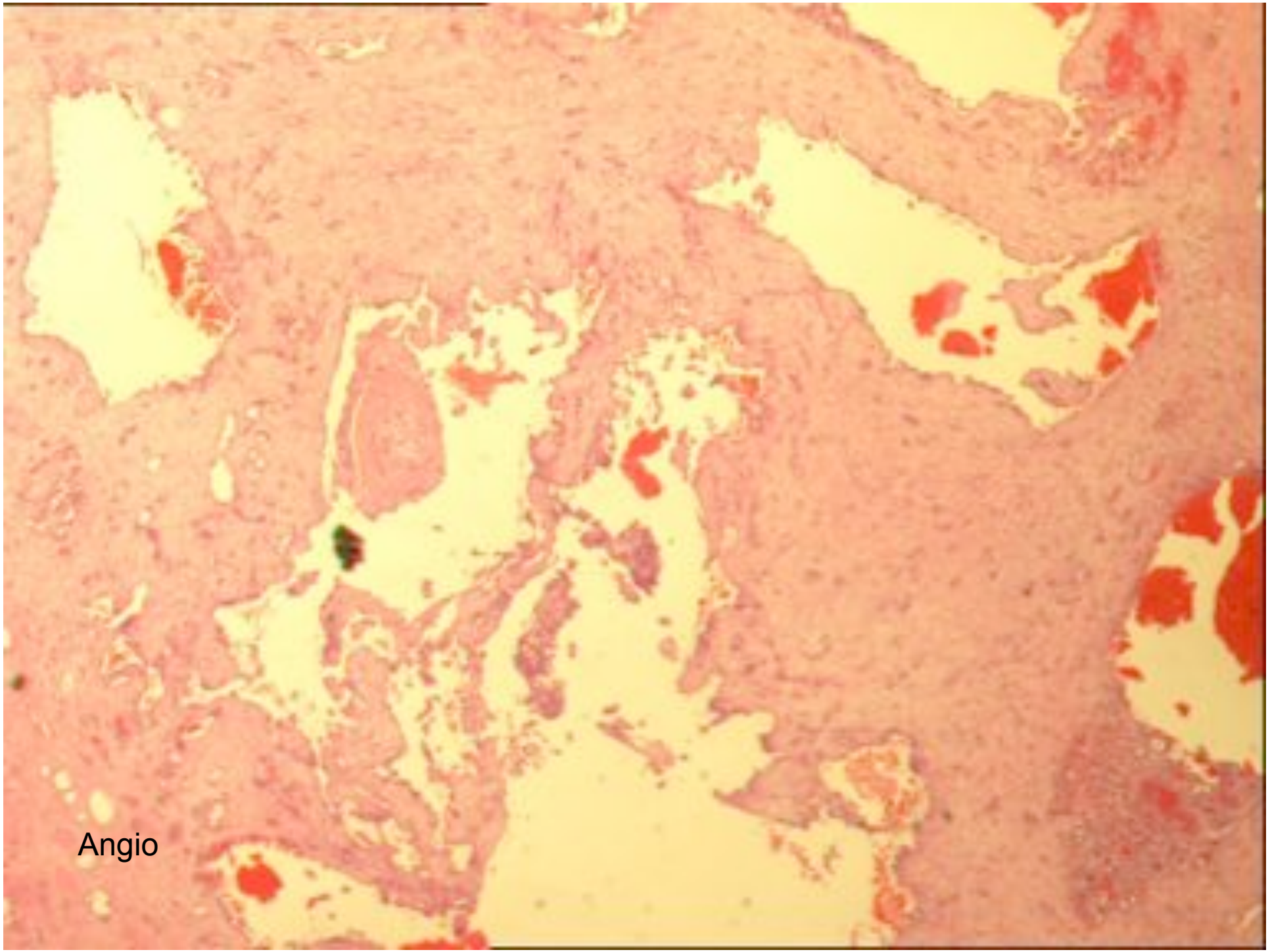

Leio

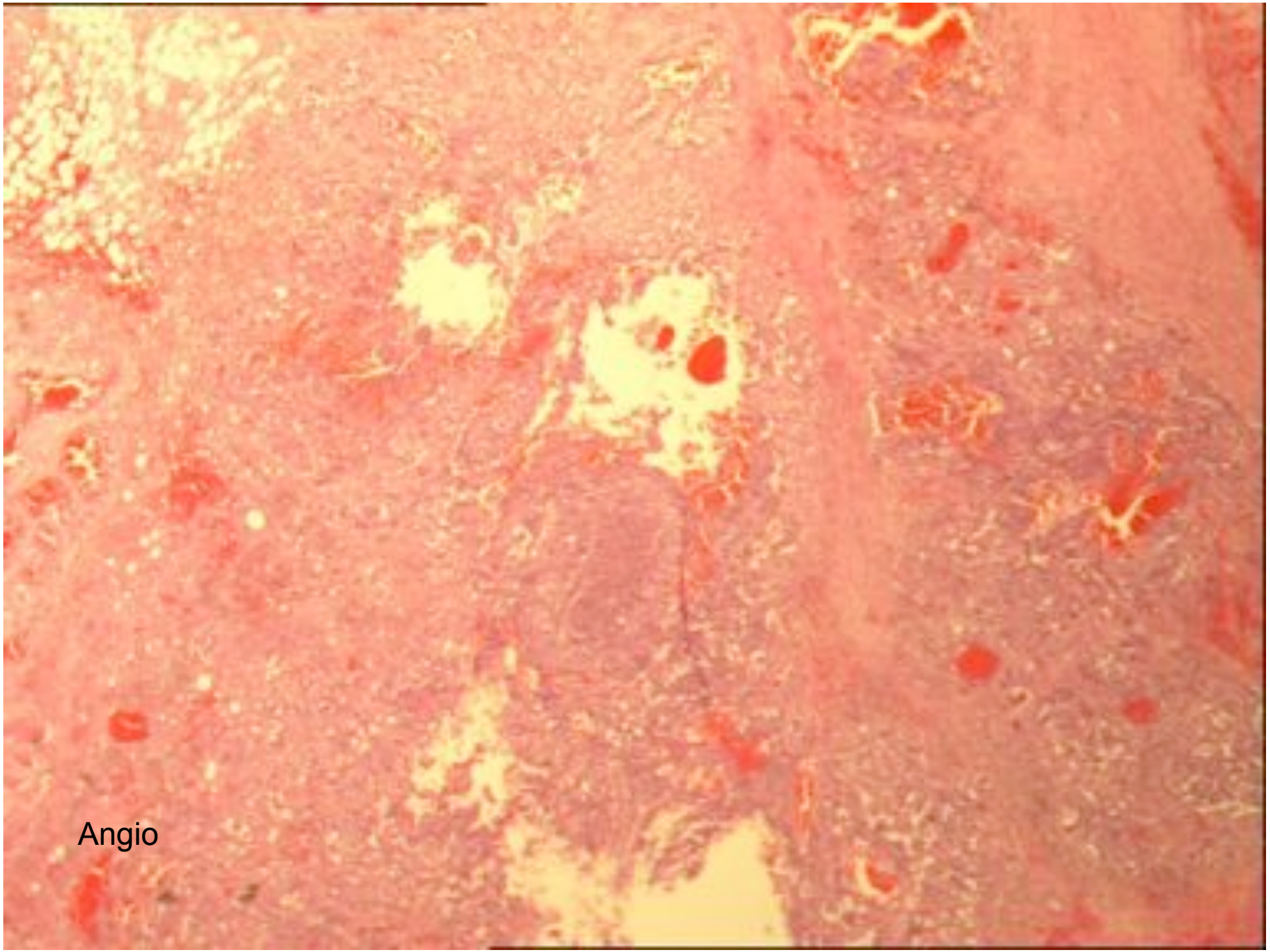

Leio


Leio SMM

Renal angiosarcoma

Very rare and very aggressive


Angio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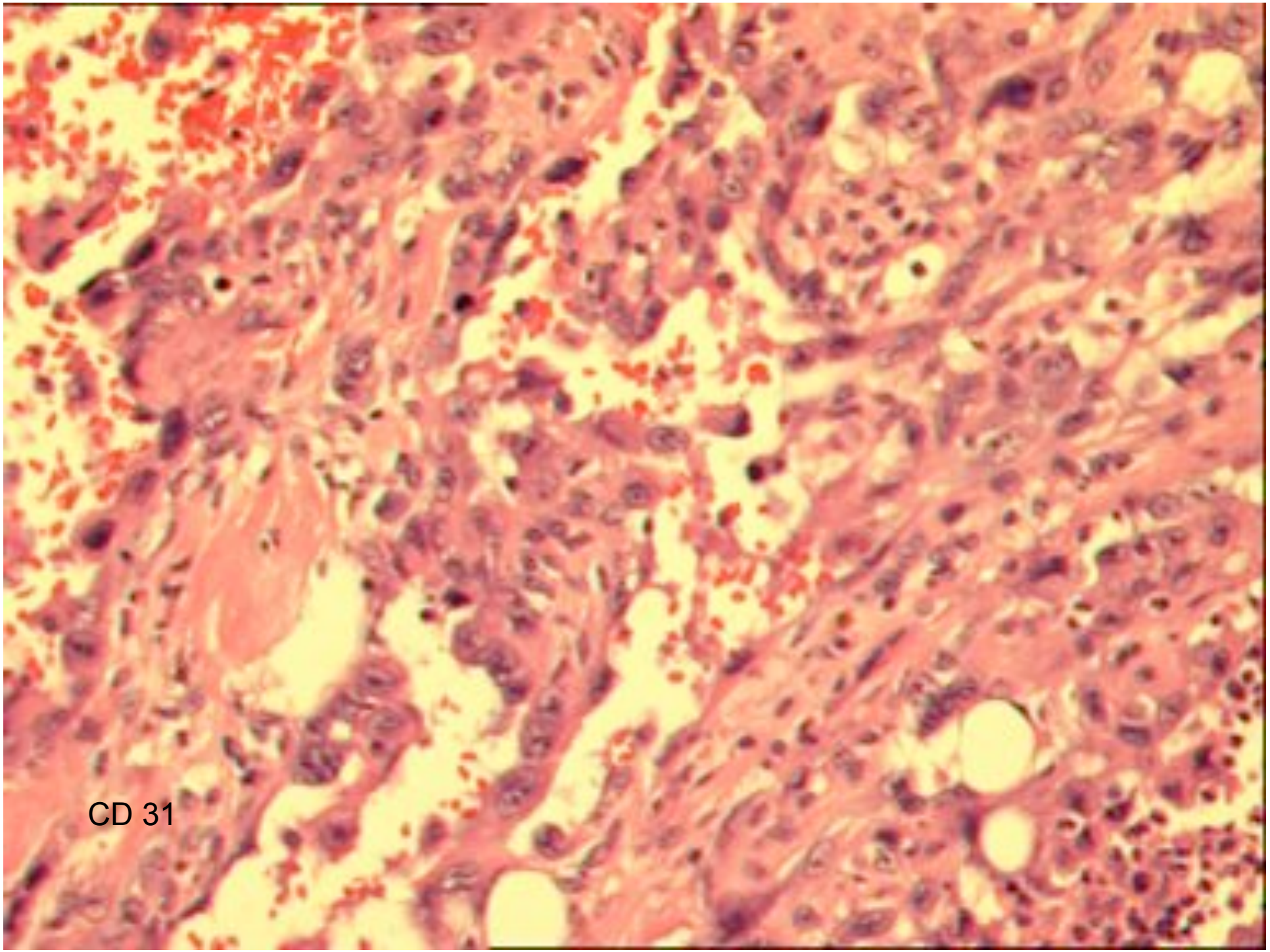
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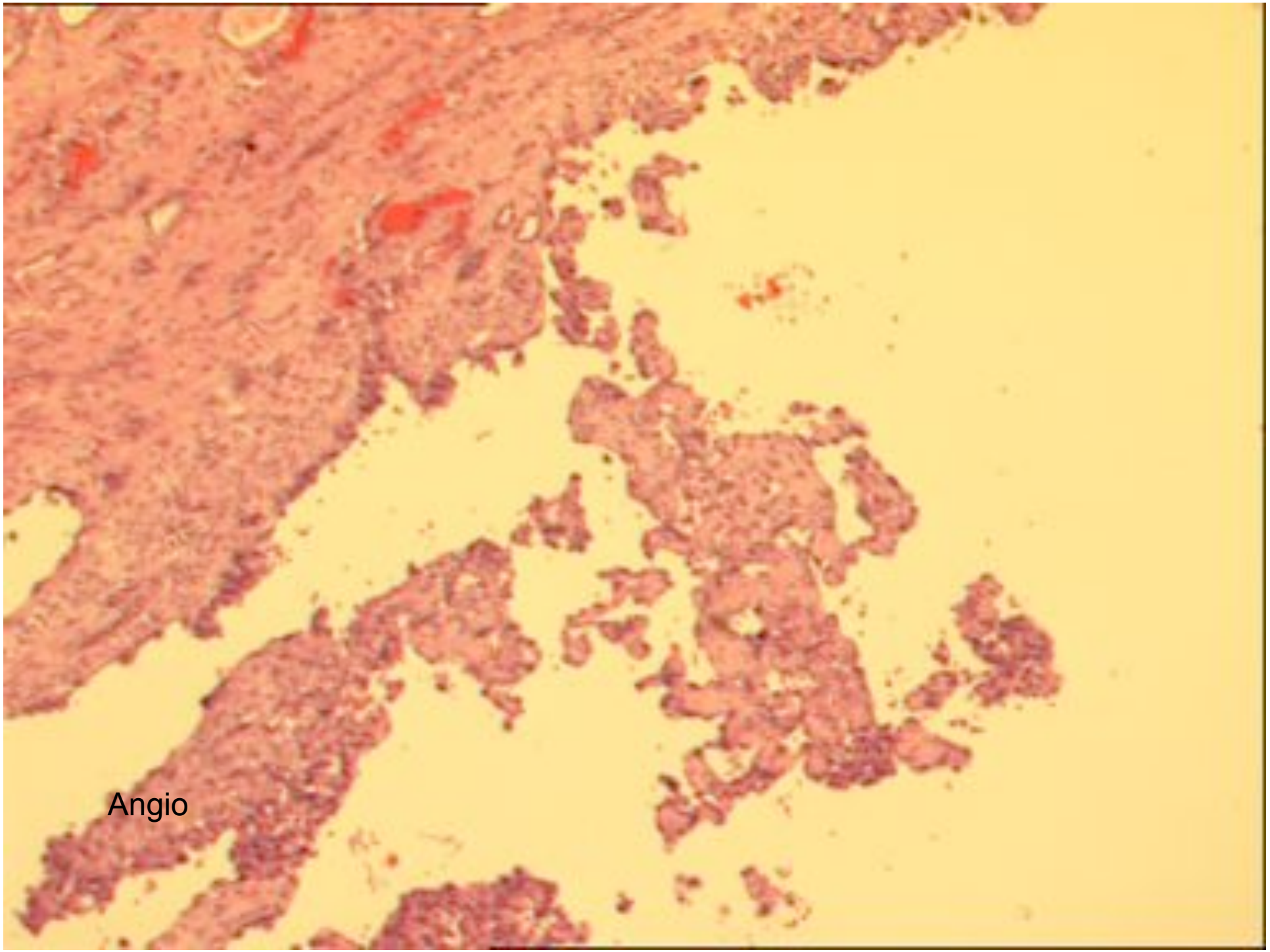
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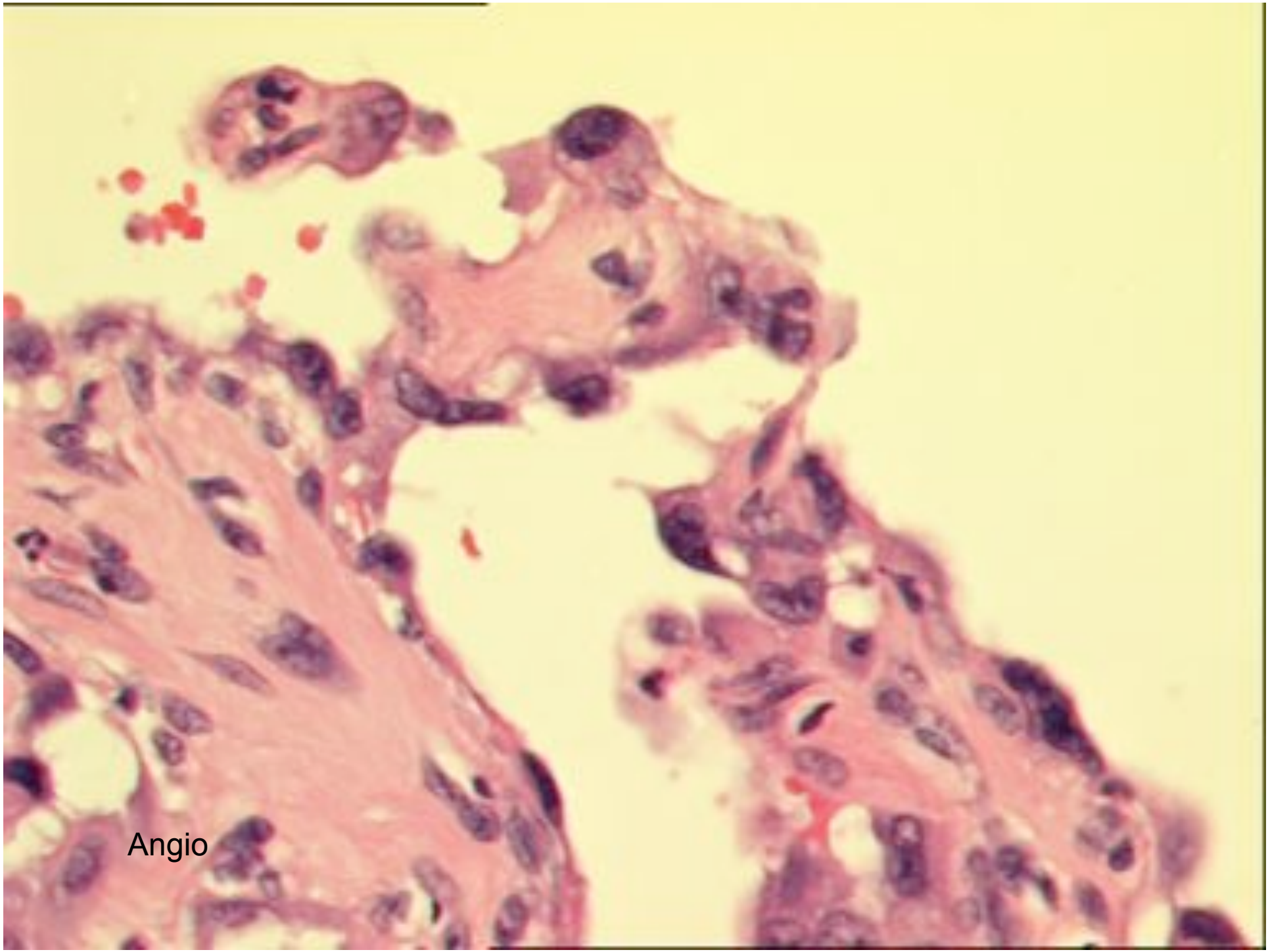
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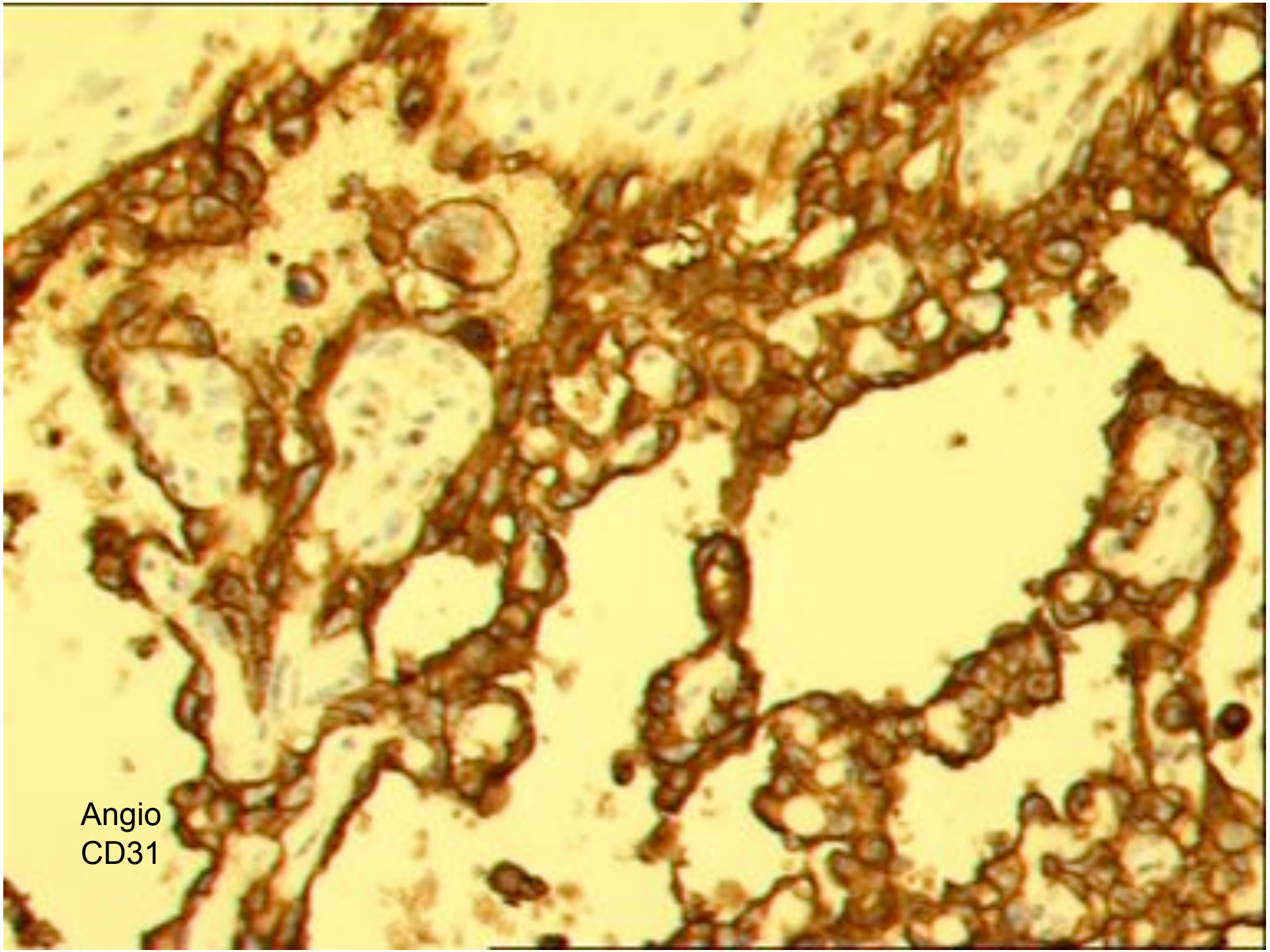

Angio
CD31

Mixed Epithelial Stromal Tumours of Kidney (MESTK)

- Age 41 – 75
- Almost always female
- Unilateral
- Do not recur
- Solitary
- Solid and cystic

Microscopy

Multicystic

Hobnail cells

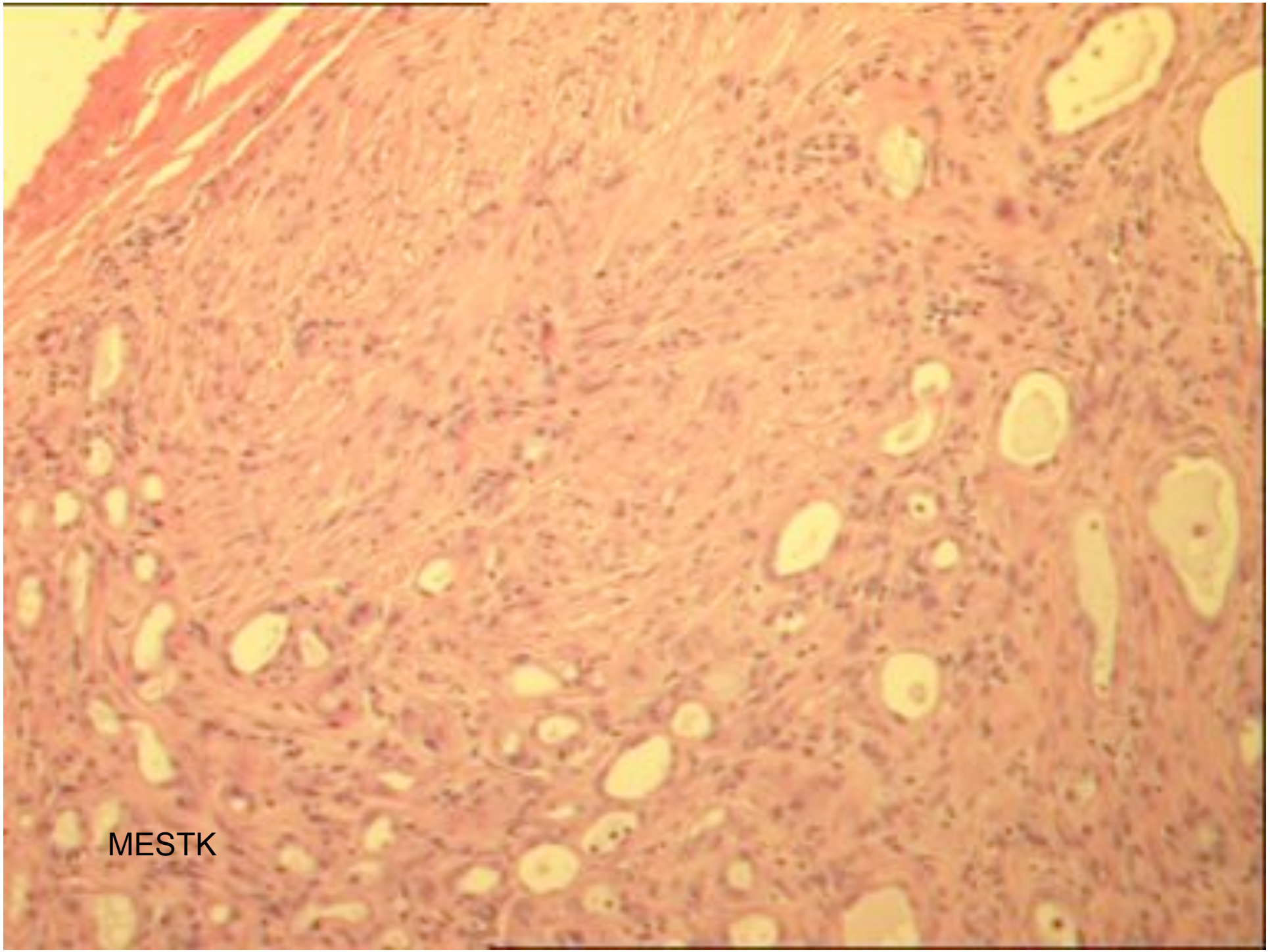
Haemorrhage

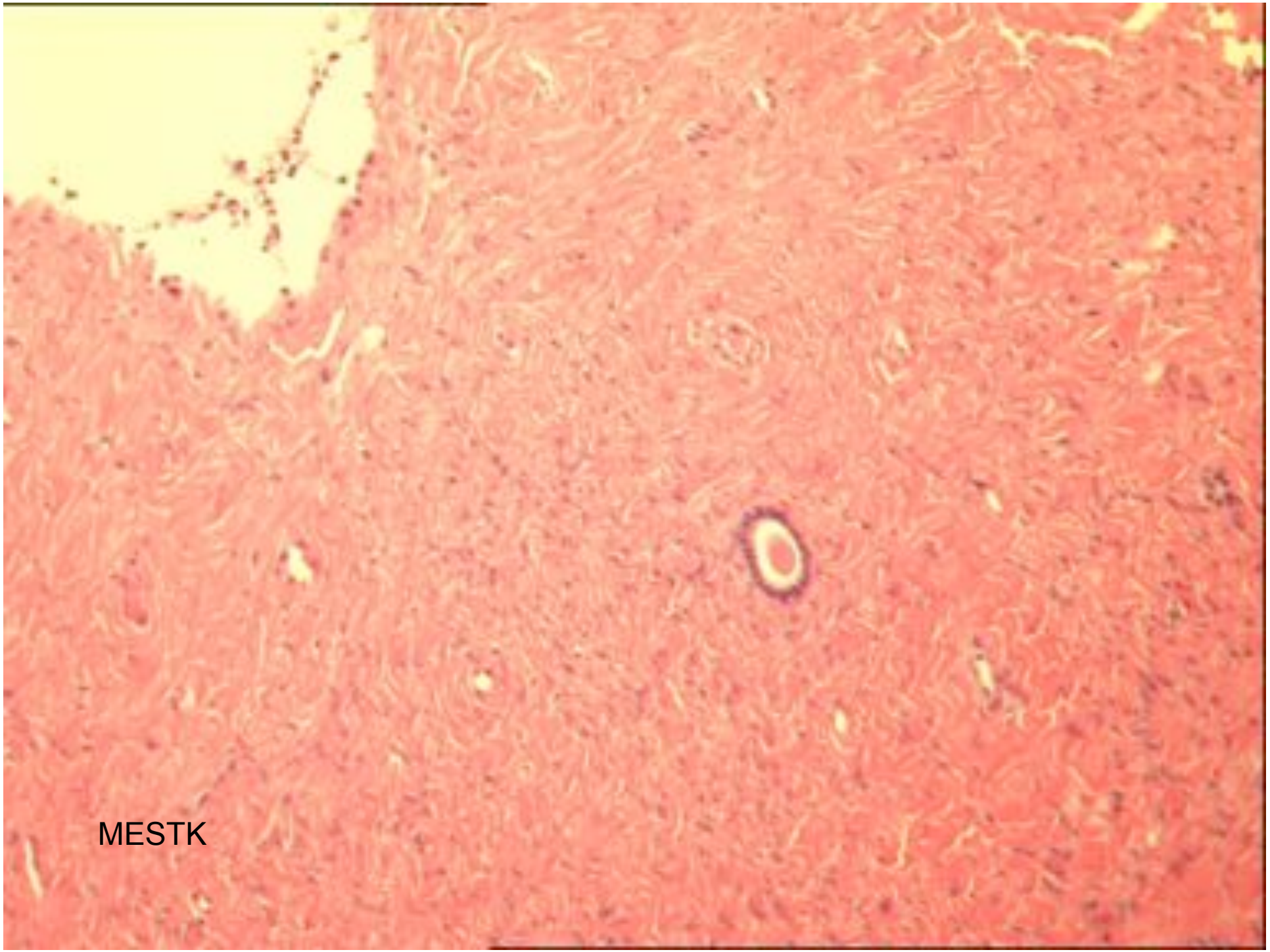
Glandular areas

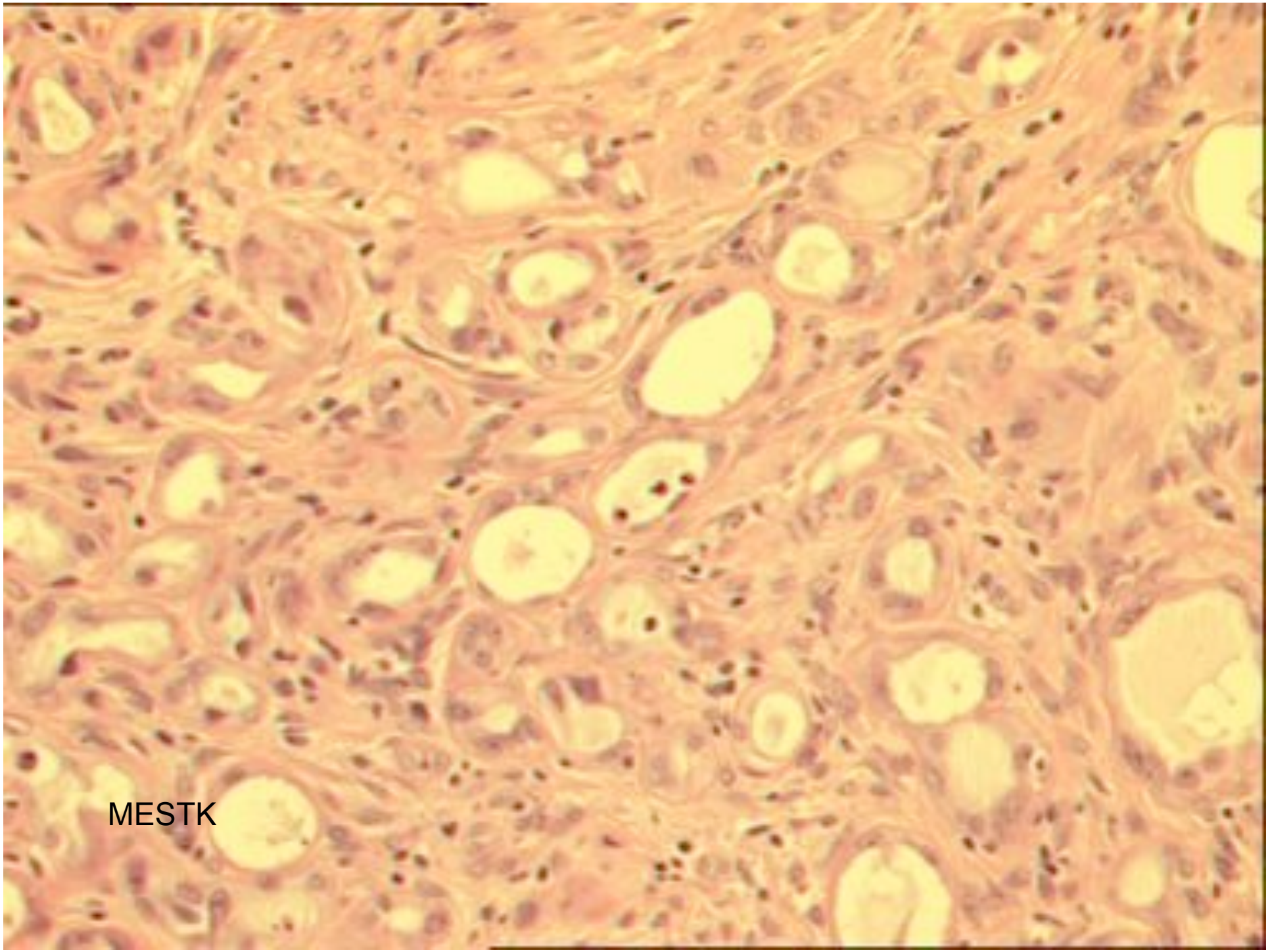
Stroma - Fibroleiomyomatous

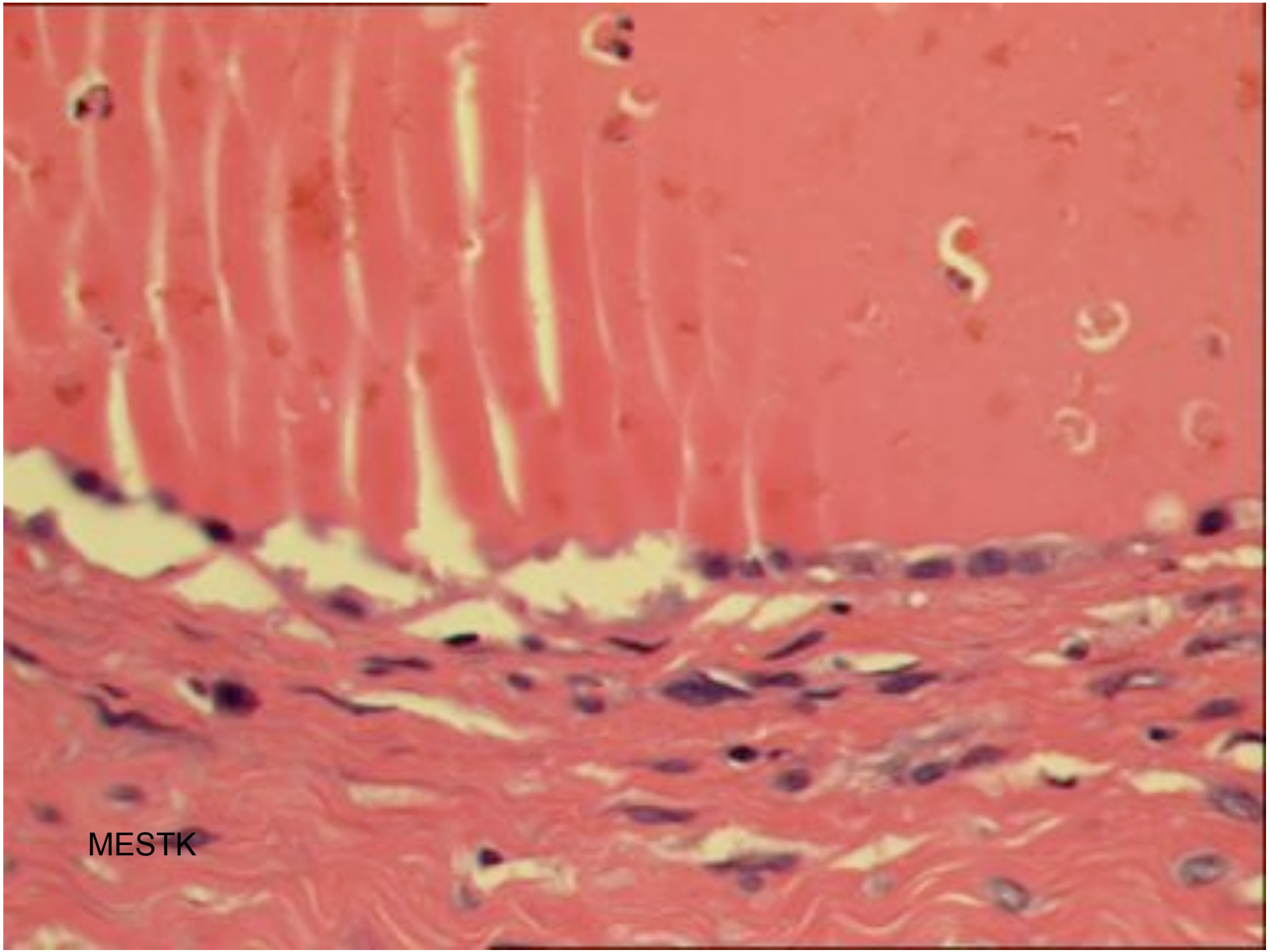
Ovarian like

ER / PgR positive


MESTK


MESTK


MESTK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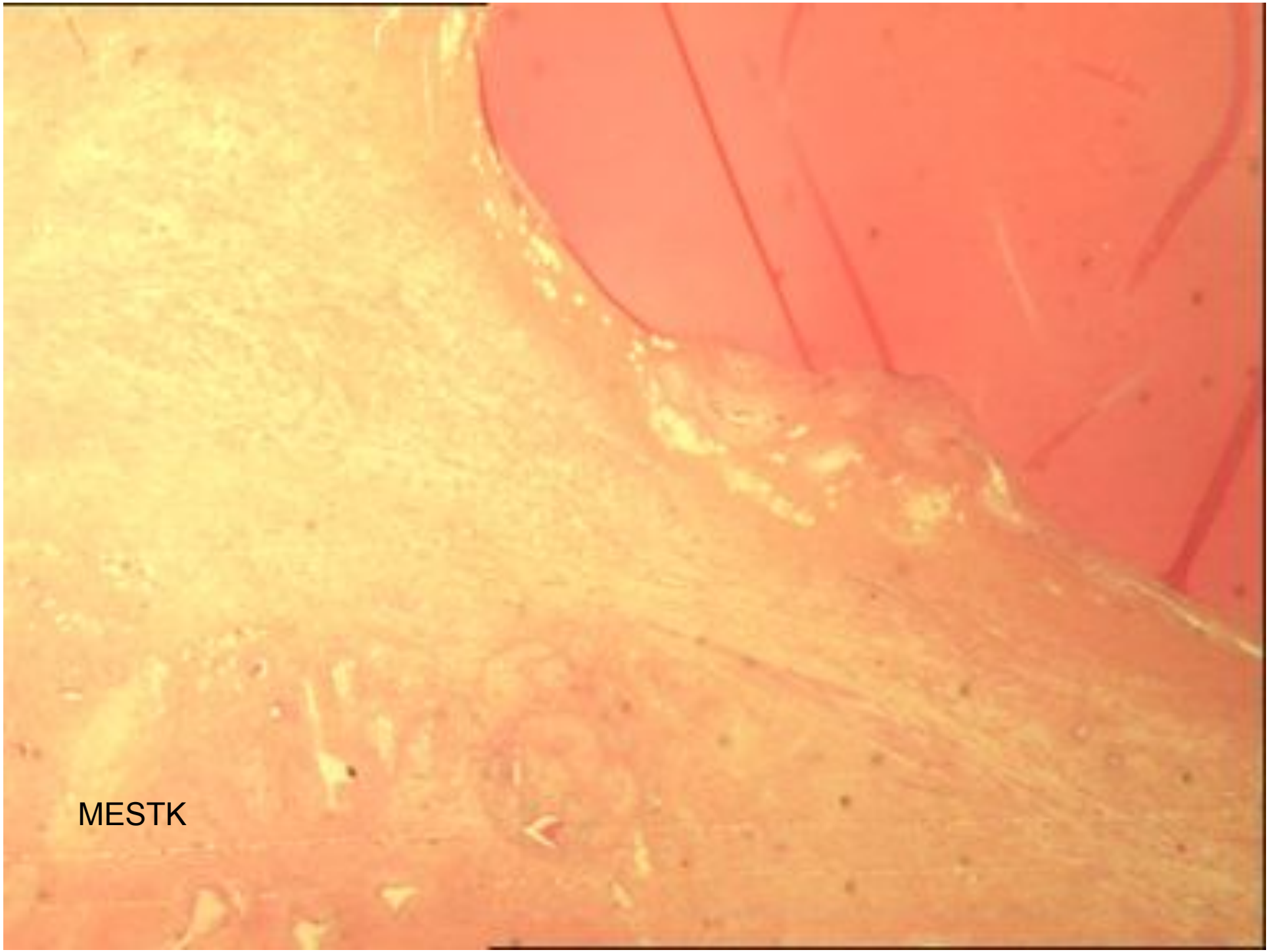
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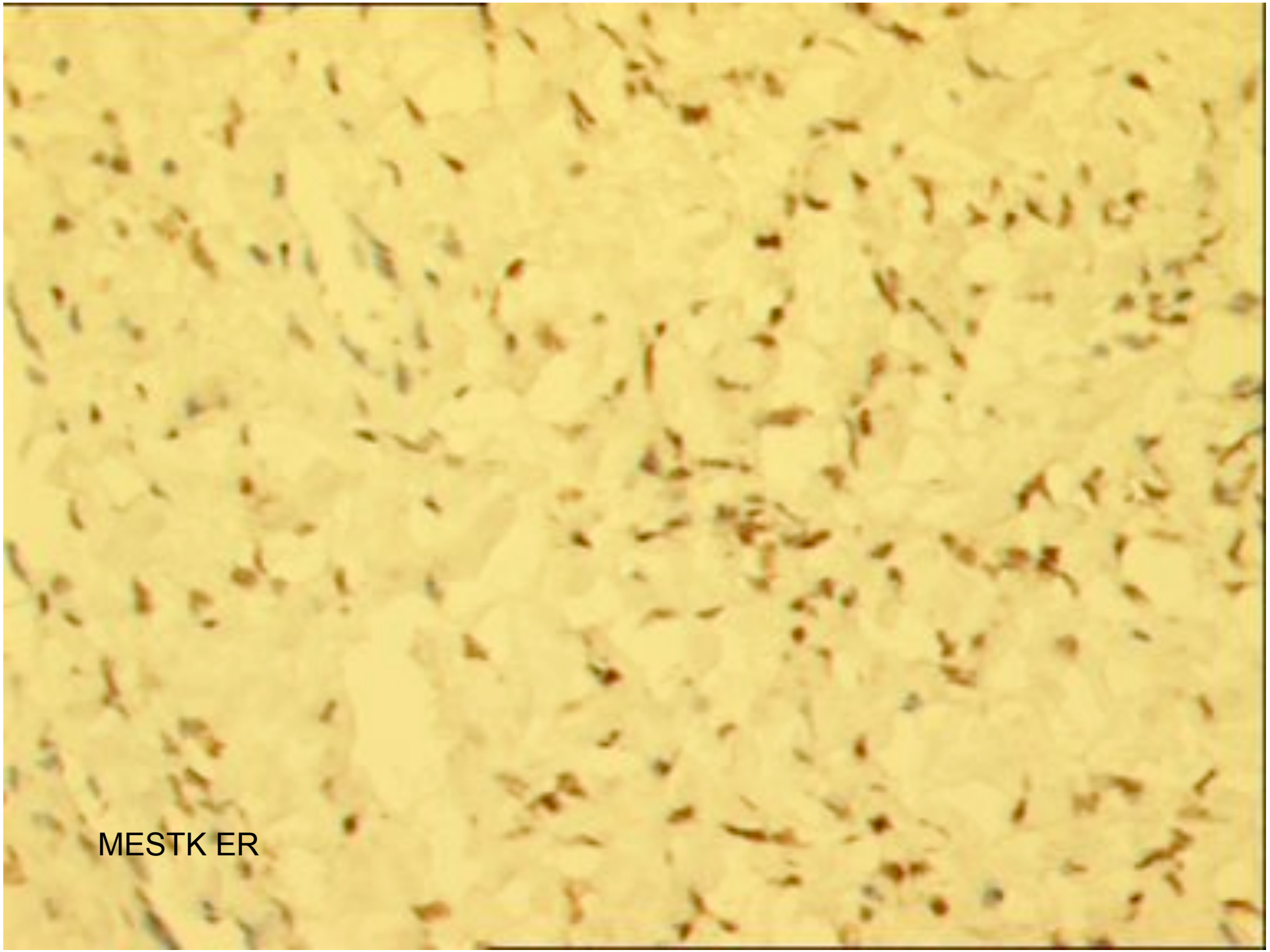
MESTK ER

Re: Cystic Nephroma

1. MESTK
2. Really Cystic nephroma (male)
3. Cystic partially differentiated nephroblastoma

Multilocular cystic renal cell carcinoma (benign)

- 3p deletion
- Grade 1 or 2
- Cystic spaces lined by clear cells
- No expansile nodules. Ovarian stroma

Mucinous tubular spindle cell carcinoma

- Polymorphic low grade Ca (CD 10 Neg)
- Favourable prognosis

Papillary adenoma

- 5mm or less
- Most common neoplasm of renal tubles
- More common in haemodialysis and acquired renal cystic disease