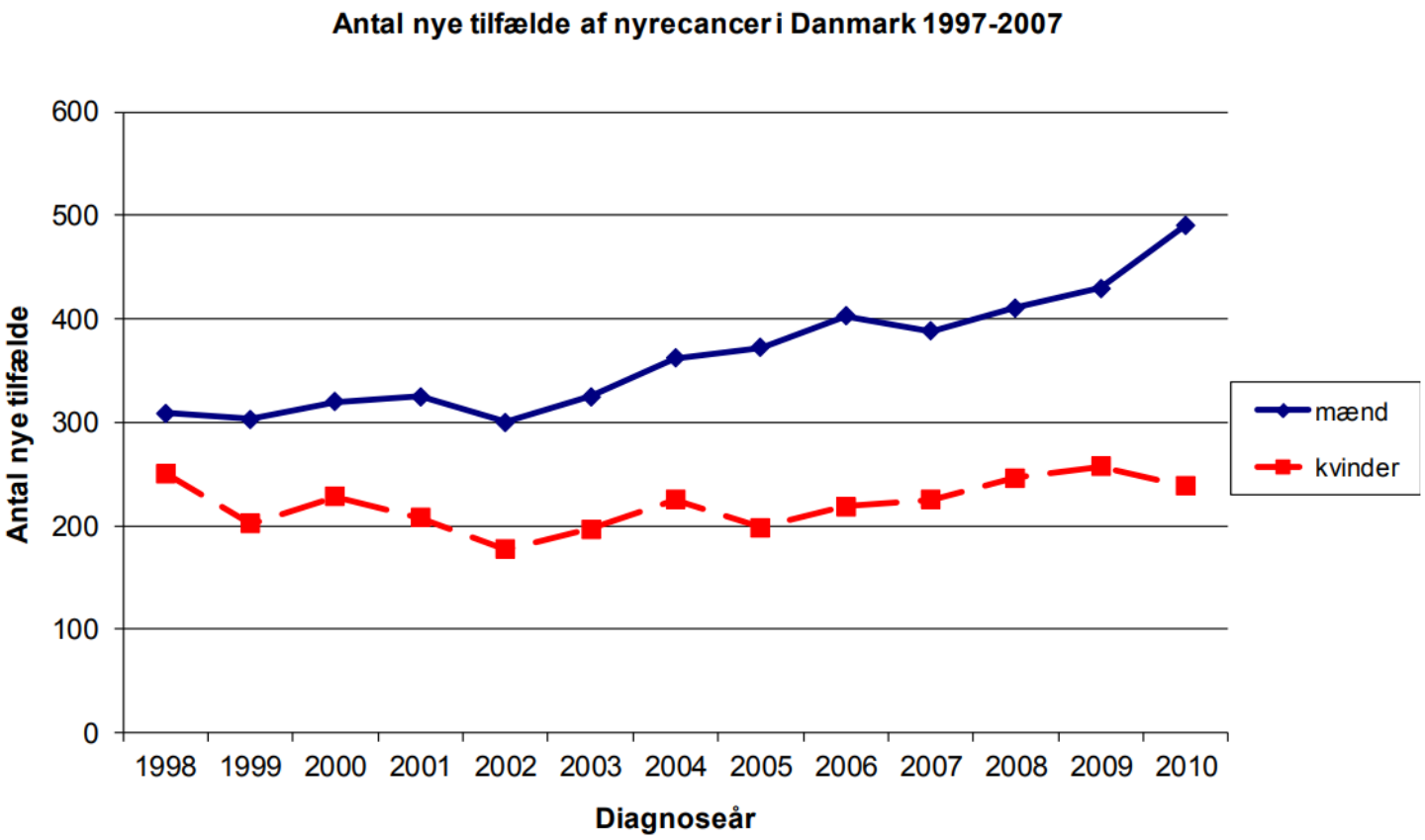
Histopathologic aspects of renal masses

Niels Marcussen

DRUS May 4, 2018


Antal nye tilfælde af nyrecancer i Danmark 1997-2007
Antal nye tilfælde
600
500
400
300
200
100
0
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Diagnoseår
mænd
kvinder

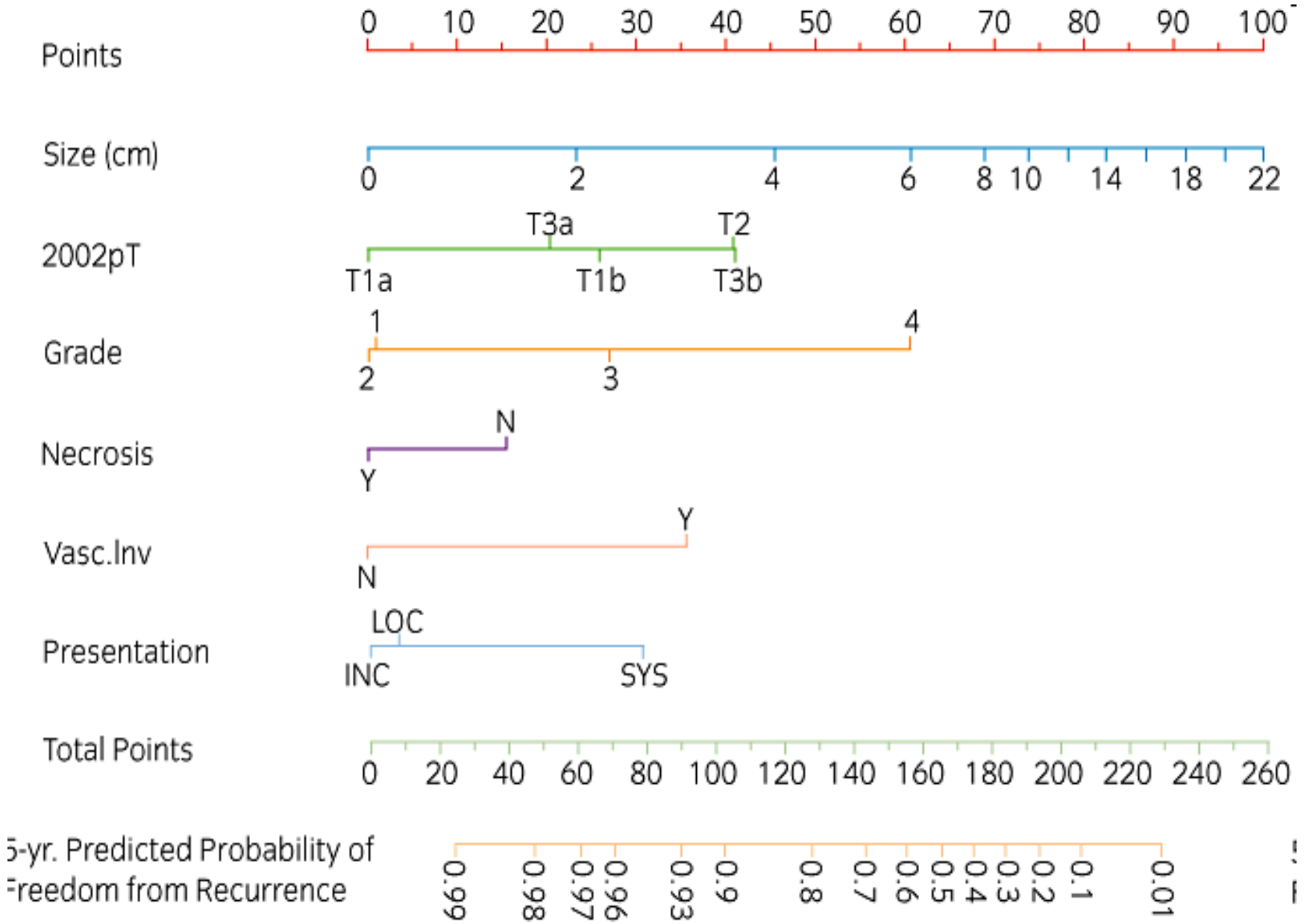
REFERENCEPROGRAM

NYRECANCER

Betænkning fra
Dansk Renal Cancer Gruppe (DaRenCa)
under
Uro Onkologisk Forum (UoF)

When does the patient see the physician?

- OUH: 52% has the tumor detected by random
- Internationally, the randomly detected tumors are smaller

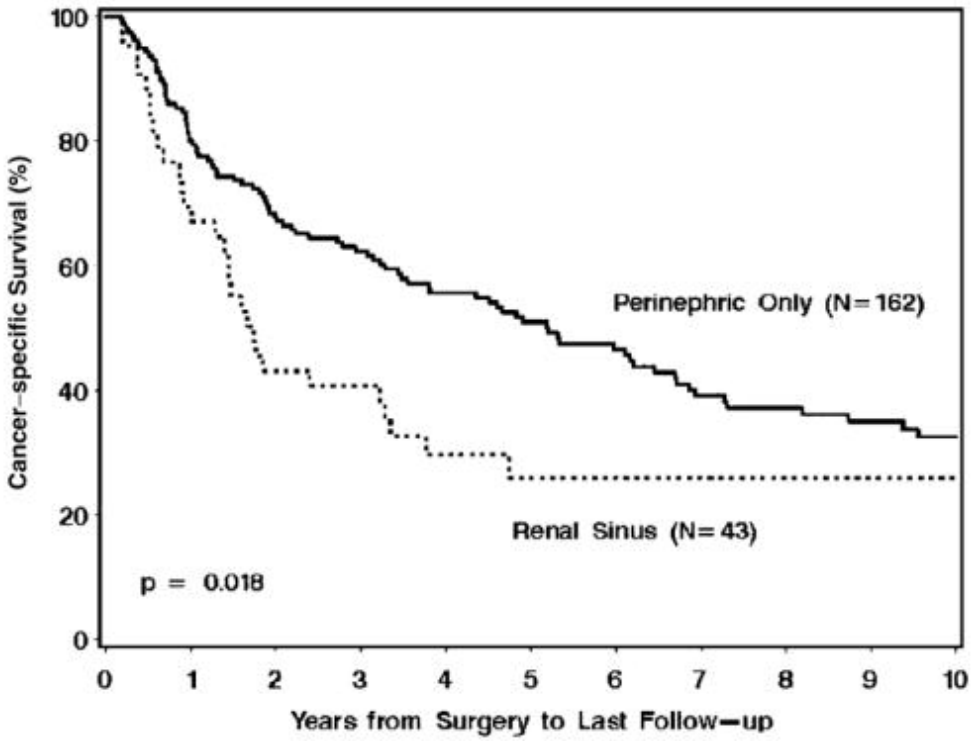


Nomogram predicting the probability of freedom from recurrence after nephrectomy for clear cell renal cell carcinoma. Sorbellini *et al. J. Urol.* 2005; **731**: 5

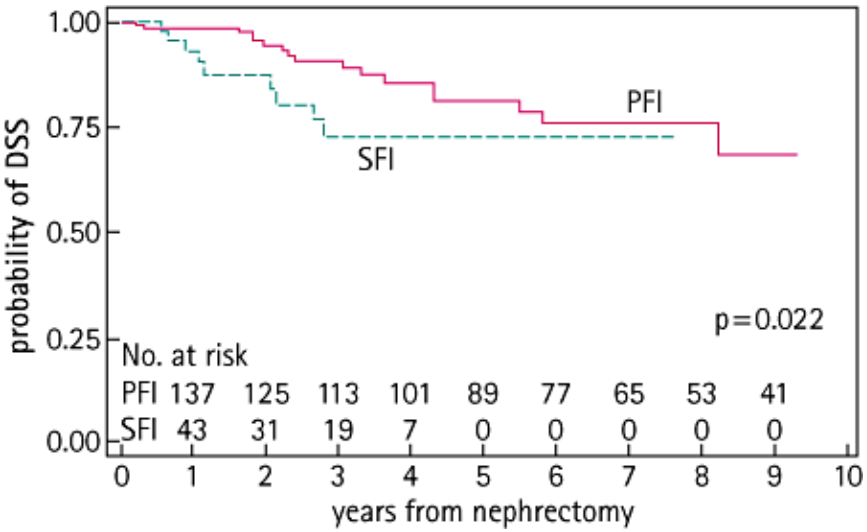
Hilar lymph nodes

- 50 consecutive RNS (37 cc, 6 papillary, pelvic uroth carc)
- Either
  - Standard gross examination protocol
  - Total submission protocol
- 10/50 had LN identified
- 4/50 had nodal metastases (2 CC, 2 urothelial)
- All identified by standard protocol

Phan et al. Path Res Pract 206:310, 2010



J.Urol. 2005; 174:1218



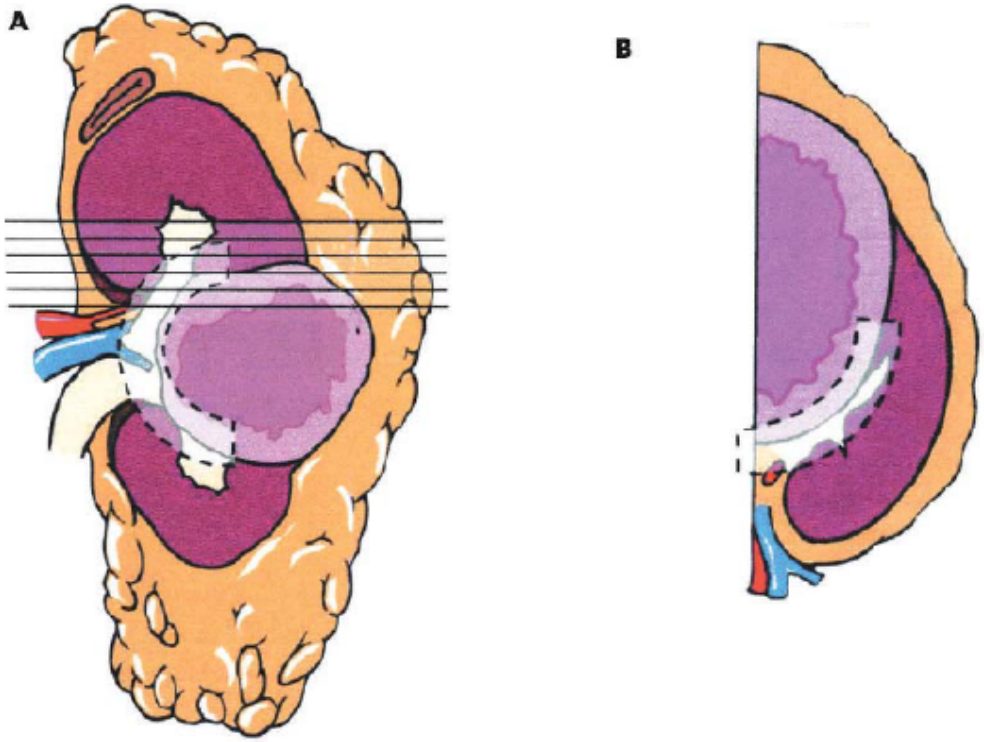
SFI: sinus fat invasion
PFI: perirenal fat invasion

Poon-SA et al. BJUI 103:1622, 2008

Size, cm	Number sinus positive, %
< 1	0
3.1-4	25
5.1-6	71
> 7	97

N=120 clear cell RCC

J Urol 174:1199, 2005


A
B

VOLUME 27 · NUMBER 28 · OCTOBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Presence of Intratumoral Neutrophils Is an Independent Prognostic Factor in Localized Renal Cell Carcinoma

Hanne Krogh Jensen, Frede Donskov, Niels Marcussen, Marianne Nordsmark, Finn Lundbeck, and Hans von der Maase

Other histological prognostic factors

Necrosis – at least 10% by macroscopy

Sarkomatoid growth is a negative prognostic parameter.

Intratumoral neutrophil granulocyttes in areas without necrosis is also a negative prognostic factor

Types of specimen

- Biopsies
- Resection (partiel nephrectomy)
- Nephrectomy

Classification

- Renal tumors in childhood
- Benign renal cell tumors
- Mixed epithelial and stromal tumors
- Tumors of low malignancy
- Malign tumors
- - in endstage kidneys

Table 2 Modified classification of renal cell tumors in adults

Familial renal cancer

Malignant renal cell tumors

- Clear cell RCC
- Papillary RCC
- Chromophobe RCC
- Carcinoma of the collecting ducts of Bellini
- Tubulocystic carcinoma
- Renal medulary carcinoma
- Renal carcinoma associated with Xp11.2 translocations/TFE3 gene fusions (MiTF/TFE family translocation carcinomas)
- RCC in long-term survivors after neuroblastoma
- Mucinous tubular and spindle cell carcinoma
- Thyroid follicular carcinoma-like tumor of kidney
- RCC unclassified

Renal cell neoplasms in end-stage renal disease

- RCC associated to acquiered cystic disease
- Clear cell papillary RCC

Renal cell neoplasms of low malignant potential

- Multilocular cystic renal cell neoplasm of low malignant potential (multilocular clear cell RCC)

Benign renal cell tumors

- Papillary adenoma
- Oncocytoma
- Metanephric adenoma and adenofibroma

Mixed stromal and epithelial tumors (renal epithelial and stromal tumor)

- Cystic nephroma
- Mixed epithelial and stromal tumor

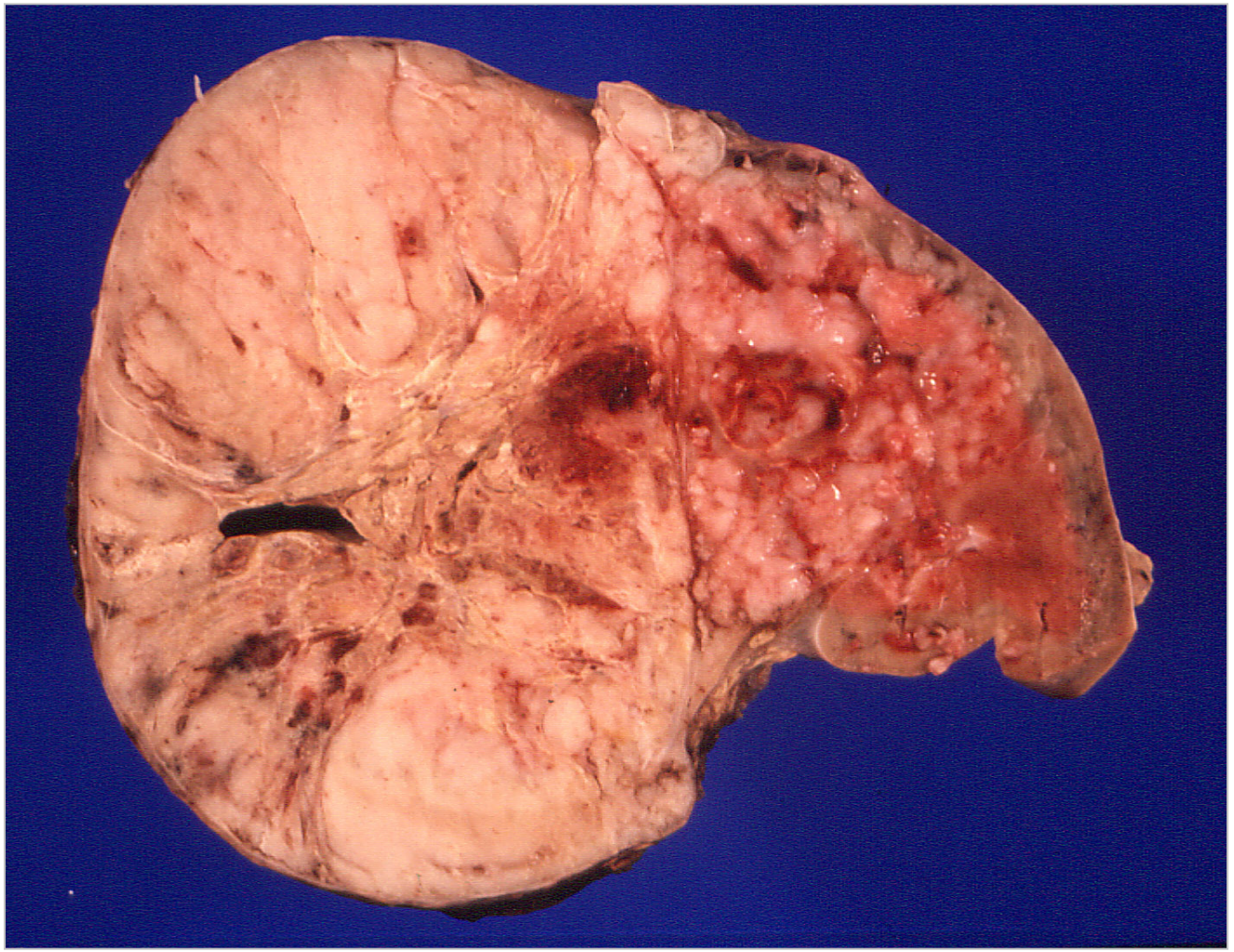
RCC, renal cell carcinoma.

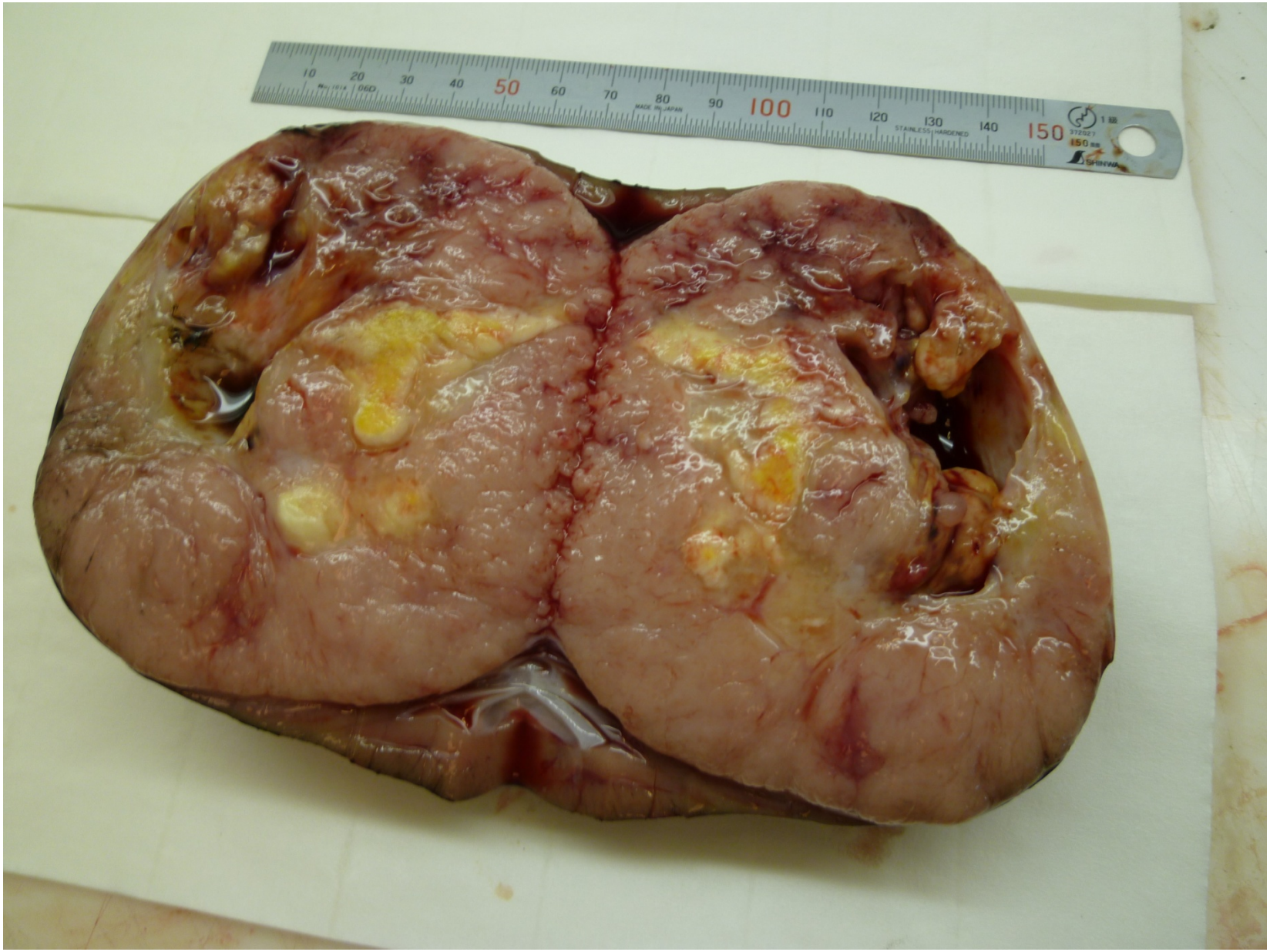
Lopez-Beltran et al.
Int. J Urol. 2009

Tumors in childhood

- Wilms tumor (nephroblastoma)
- Others (rare)

Nefroblastom (Wilms tumor)

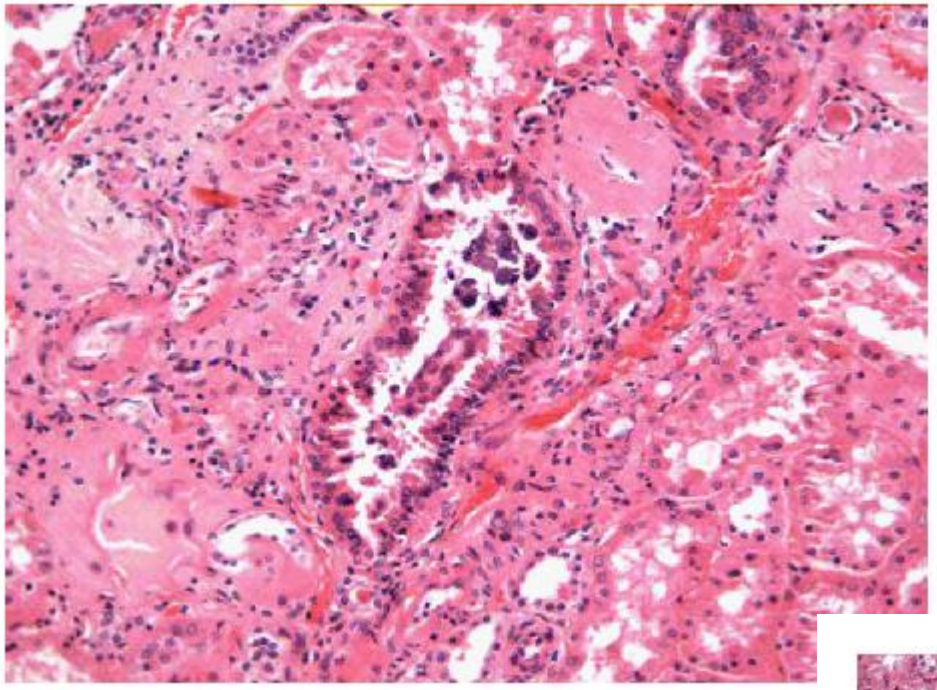




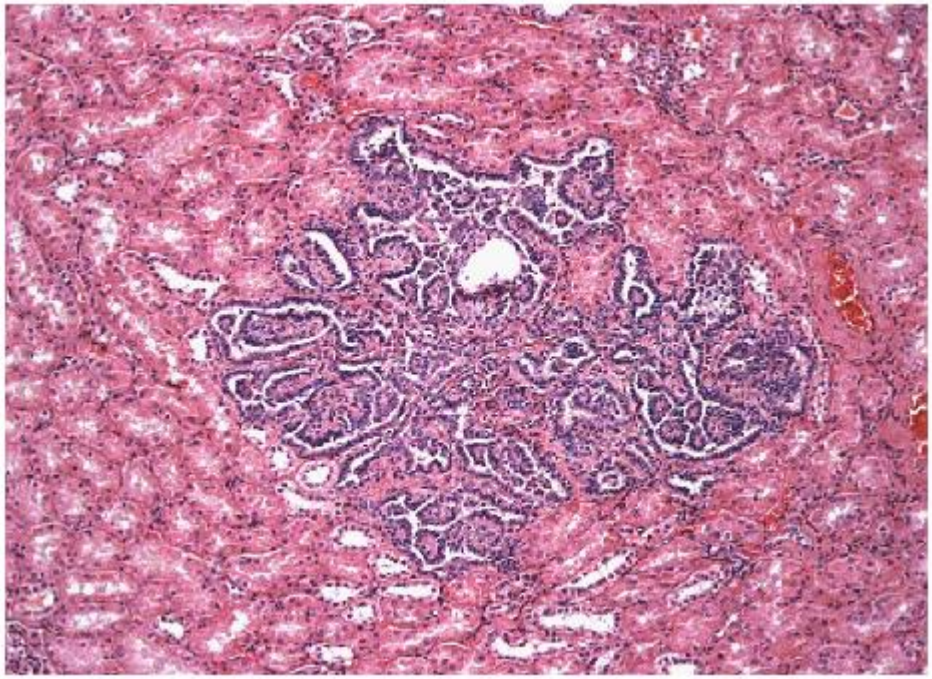
Wilms

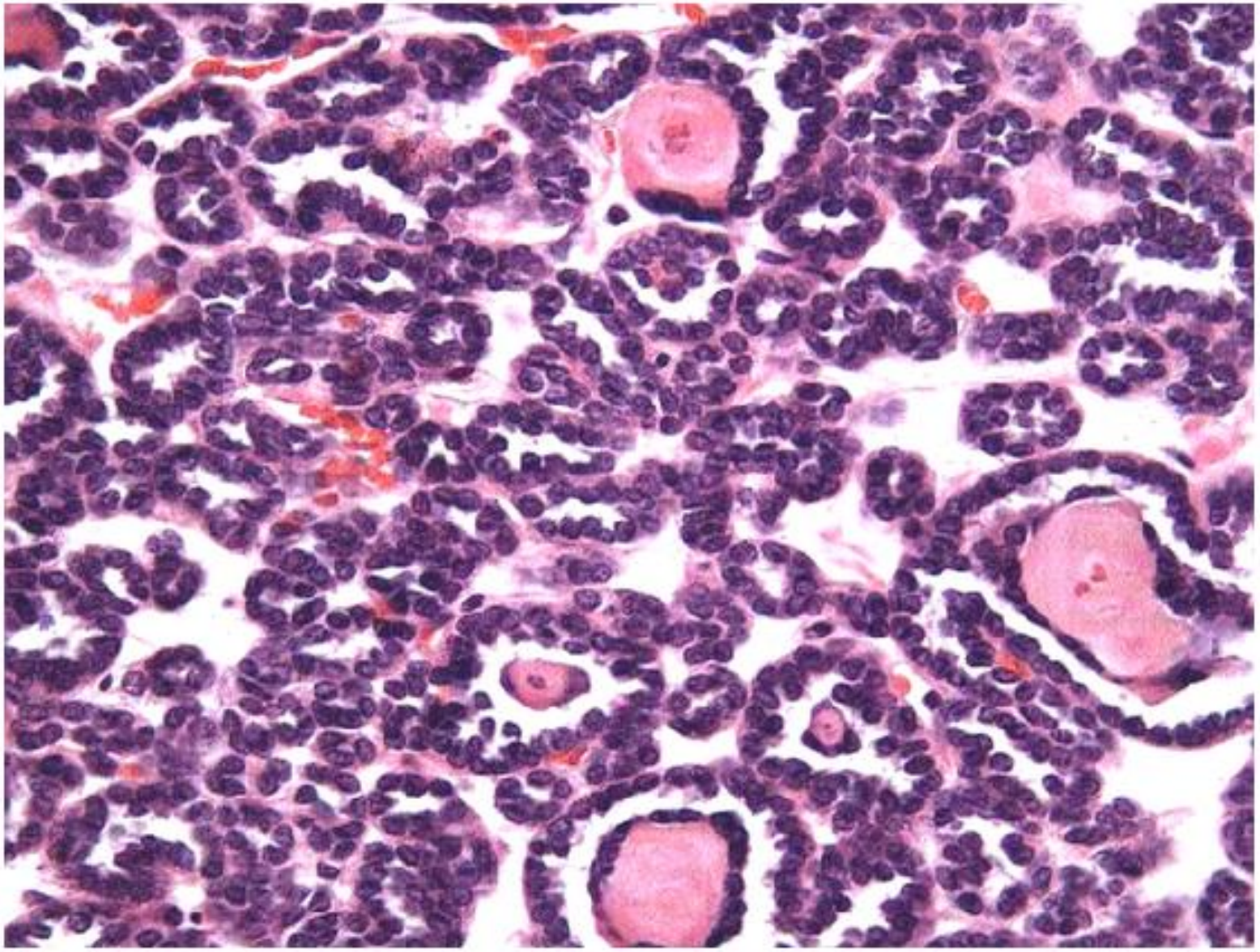
Benigne renal cell tumors

- Papillary adenoma
- Oncocytoma
- Angiomyolipoma
- Renal interstitiel cell tumor (fibroma)
- Cystic nephroma
- Metanefric adenoma



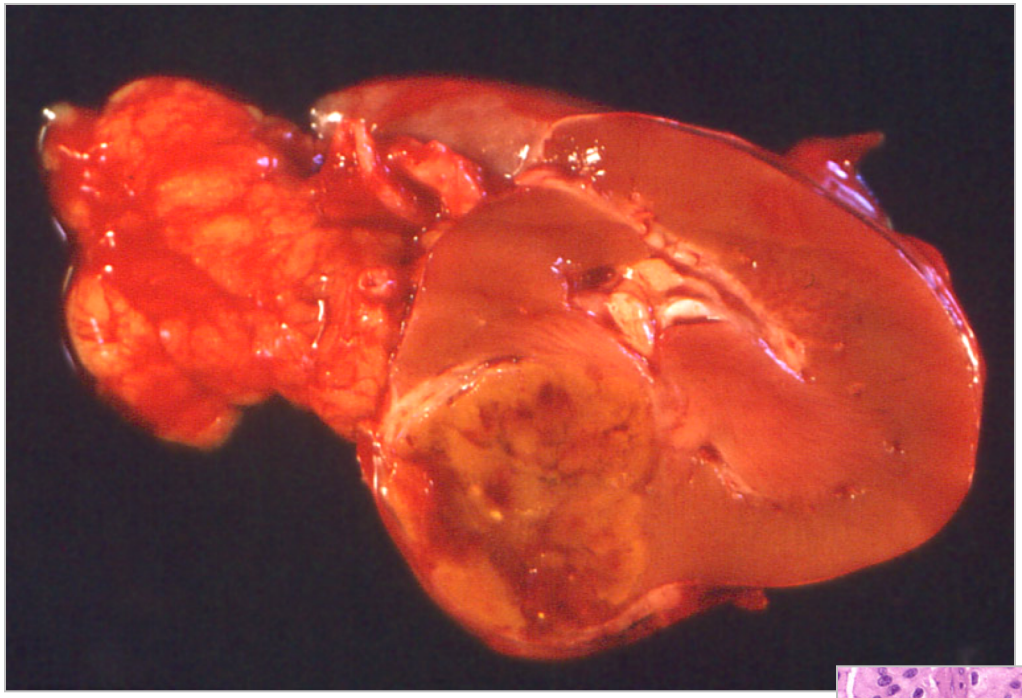
Papillary adenoma of the kidney

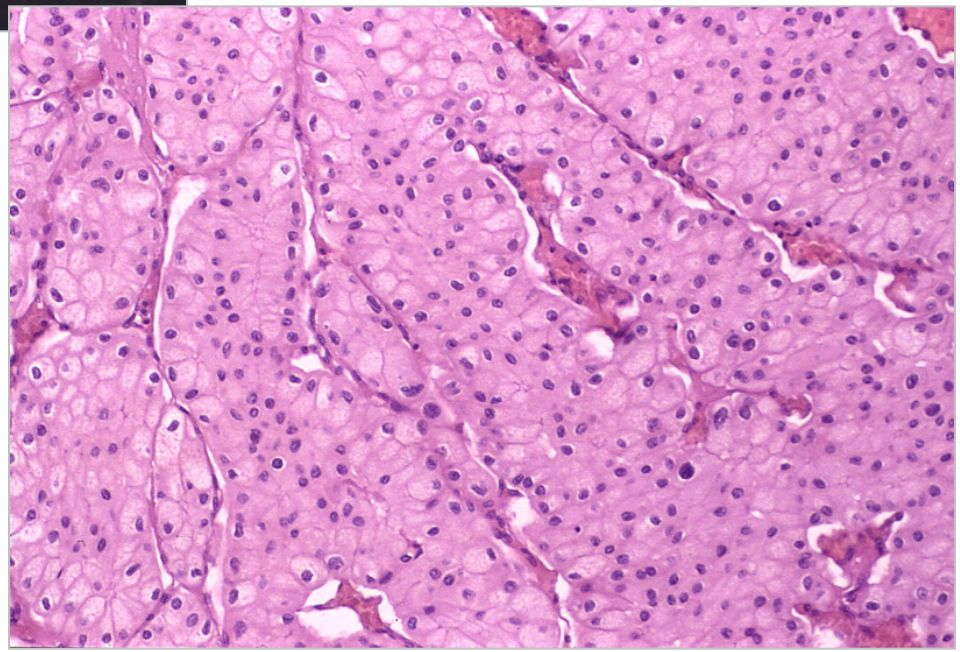




Metanephric adenoma

Oncocytoma

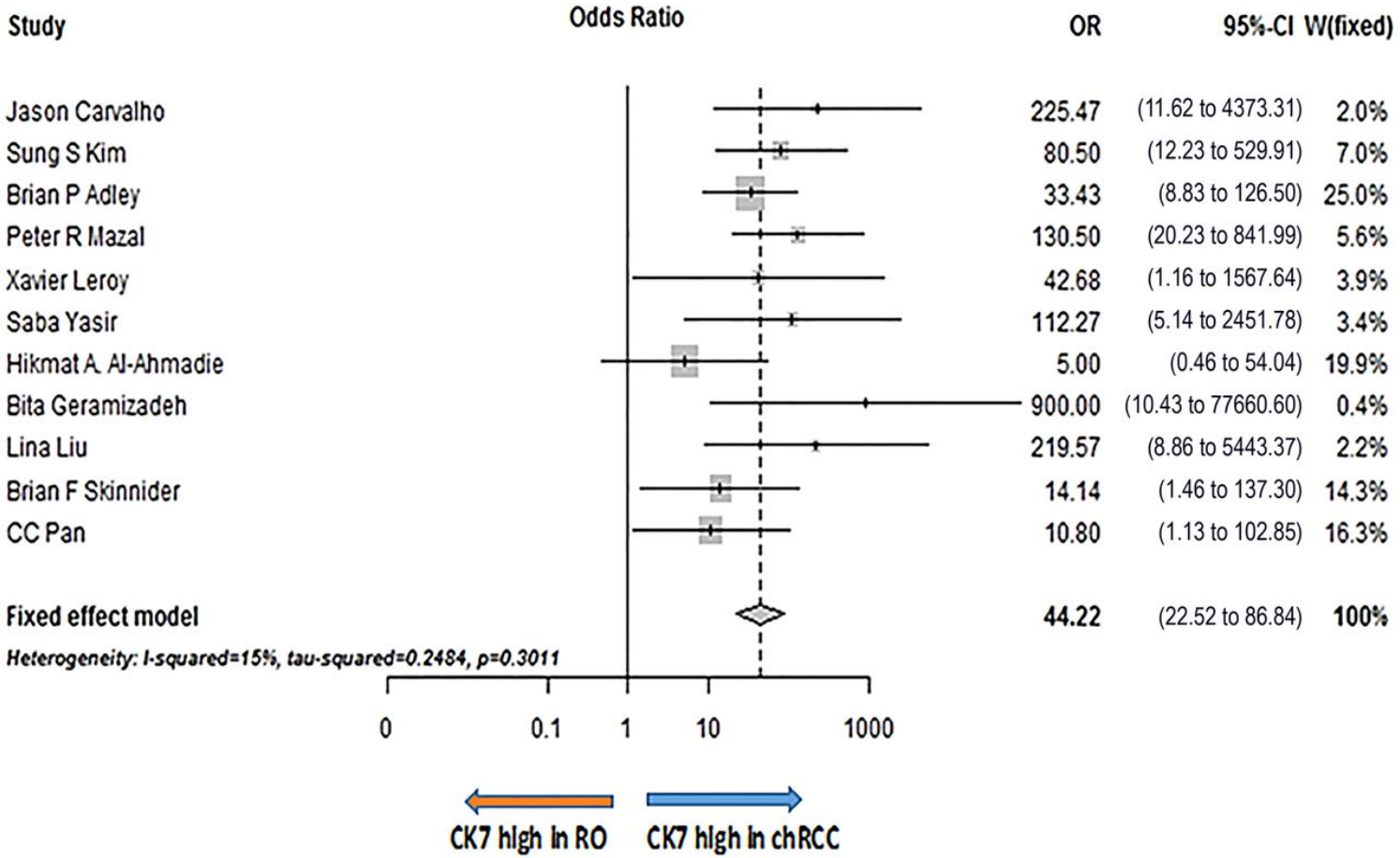




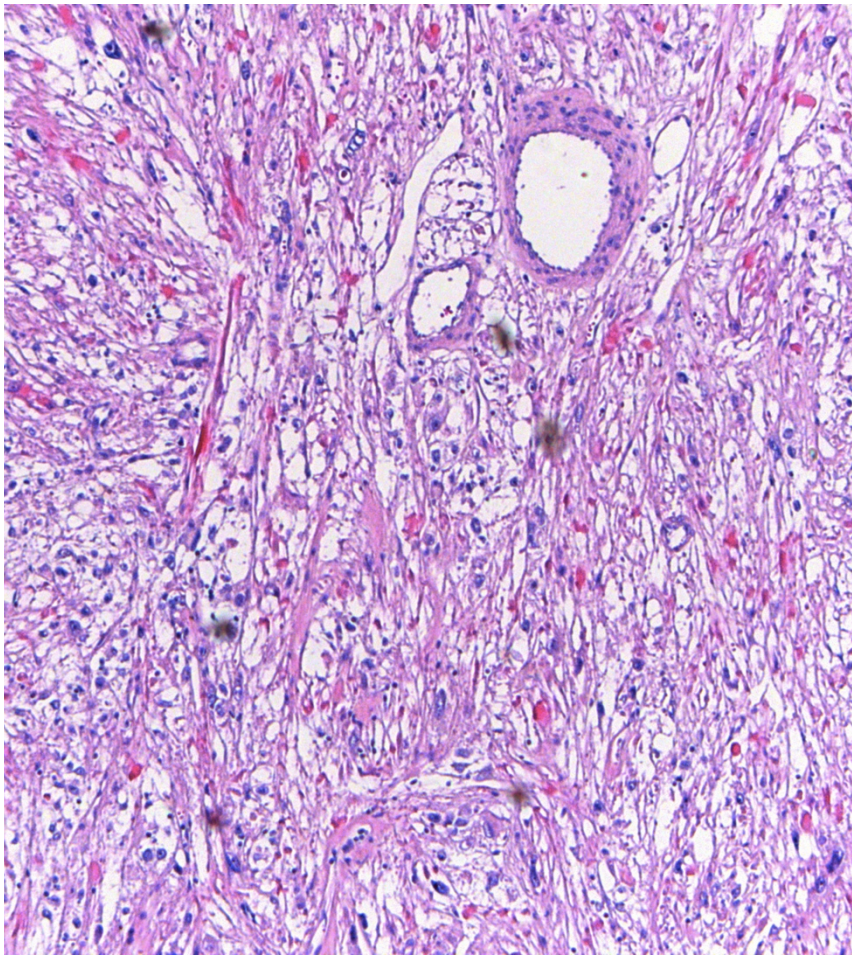
Oncocytoma

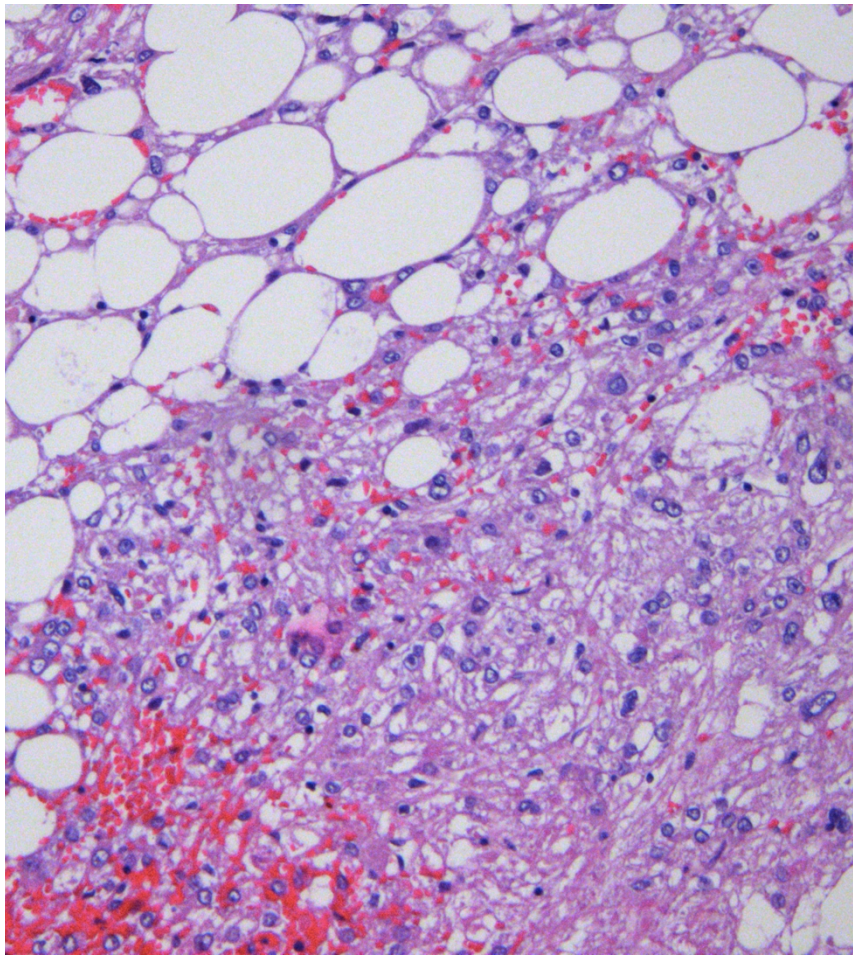
- Important clinical and radiological differential diagnosis to RCC, spec. chromophobe RCC.
- Benigne tumor.
- Multiple form: oncocytosis.
- Immune histochemistry: CK7 (negativ, focal positive), e-cadherin (pos.), c-kit (pos.), S-100A1 (pos),vimentin (neg.).

Oncocytoma vs RCC (chRCC)

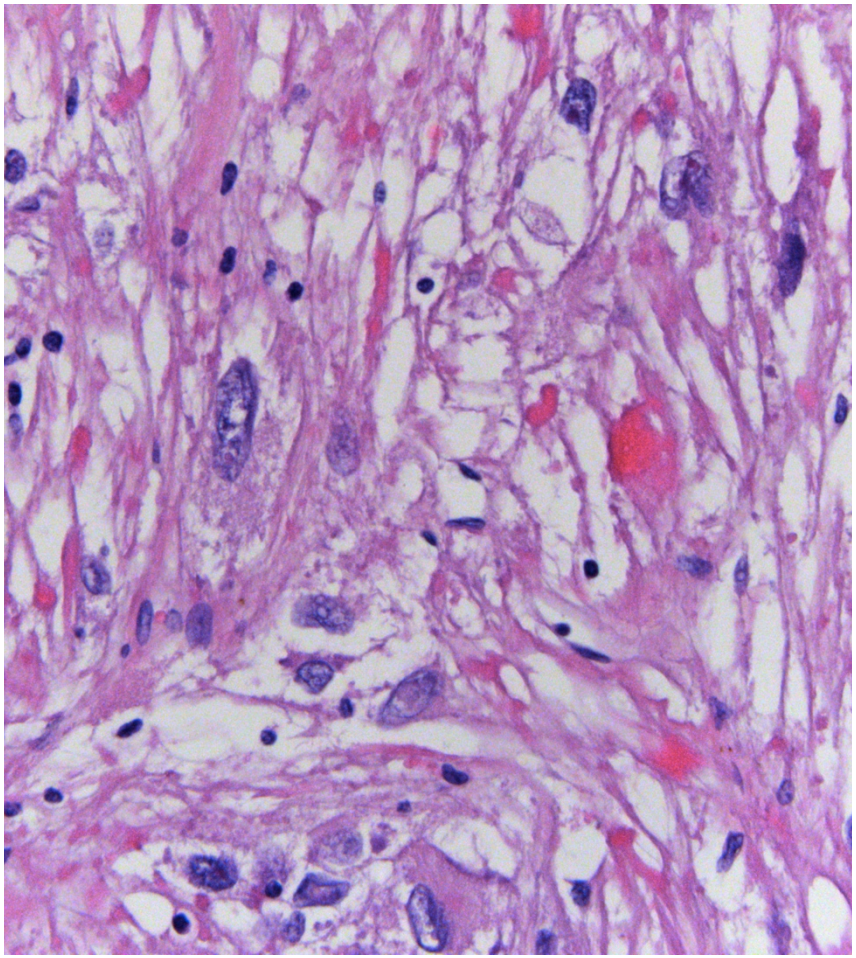


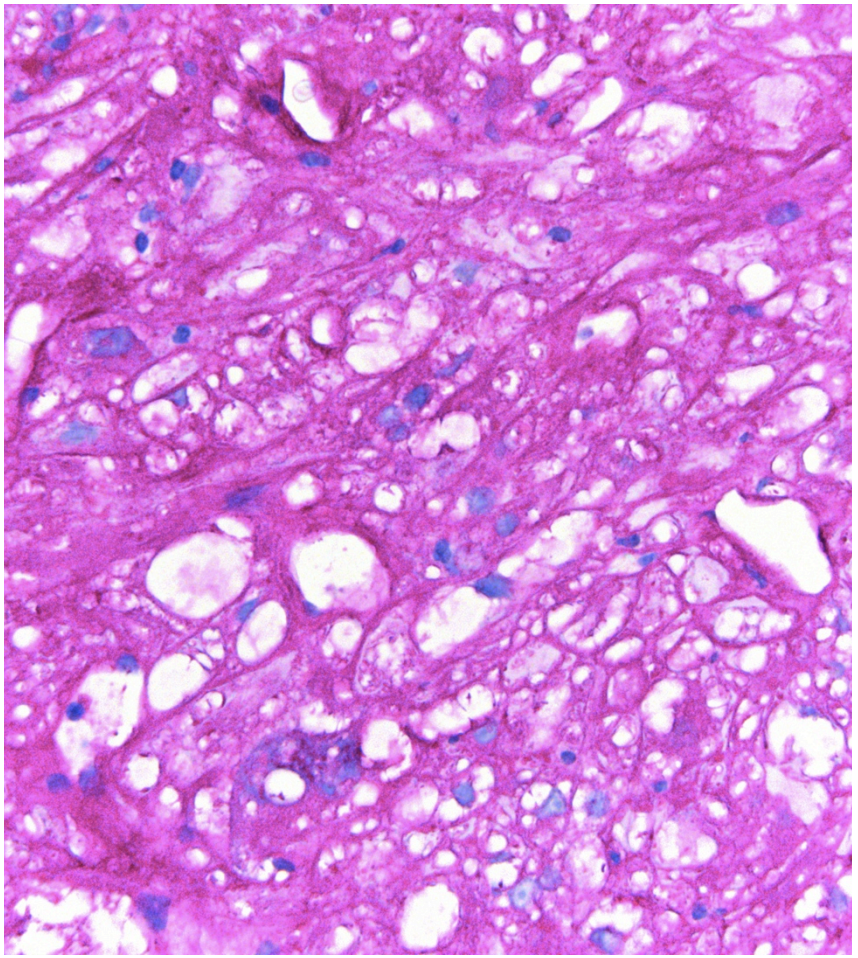
Angiomyolipoma



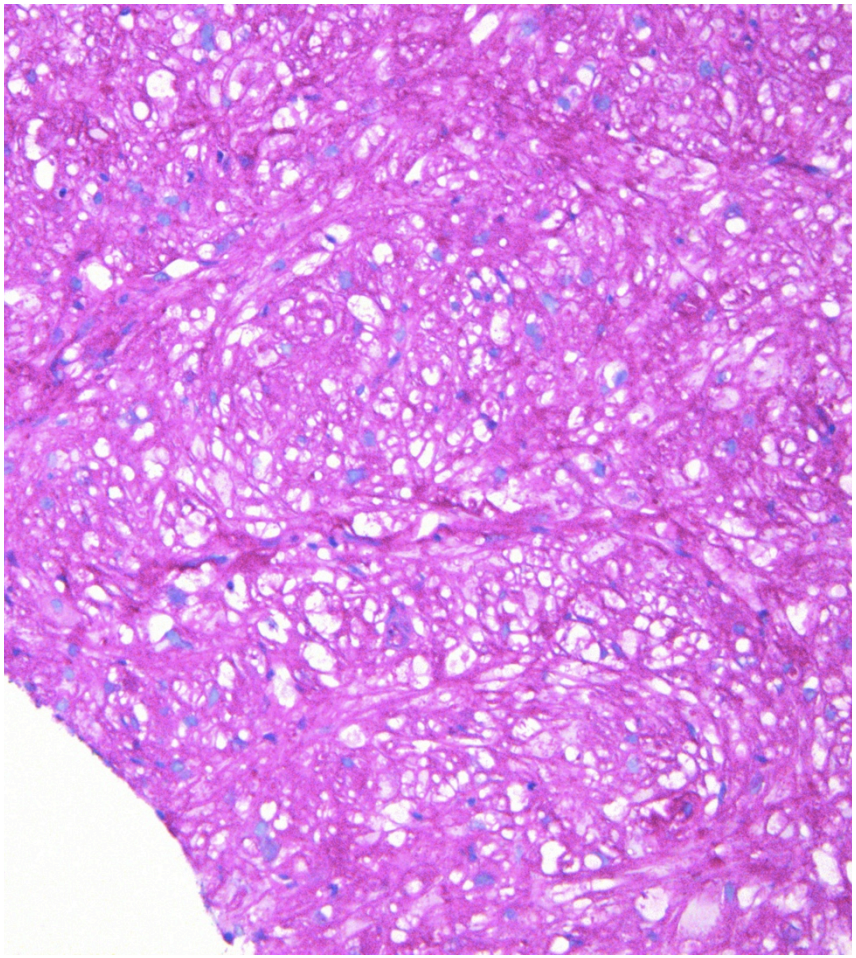


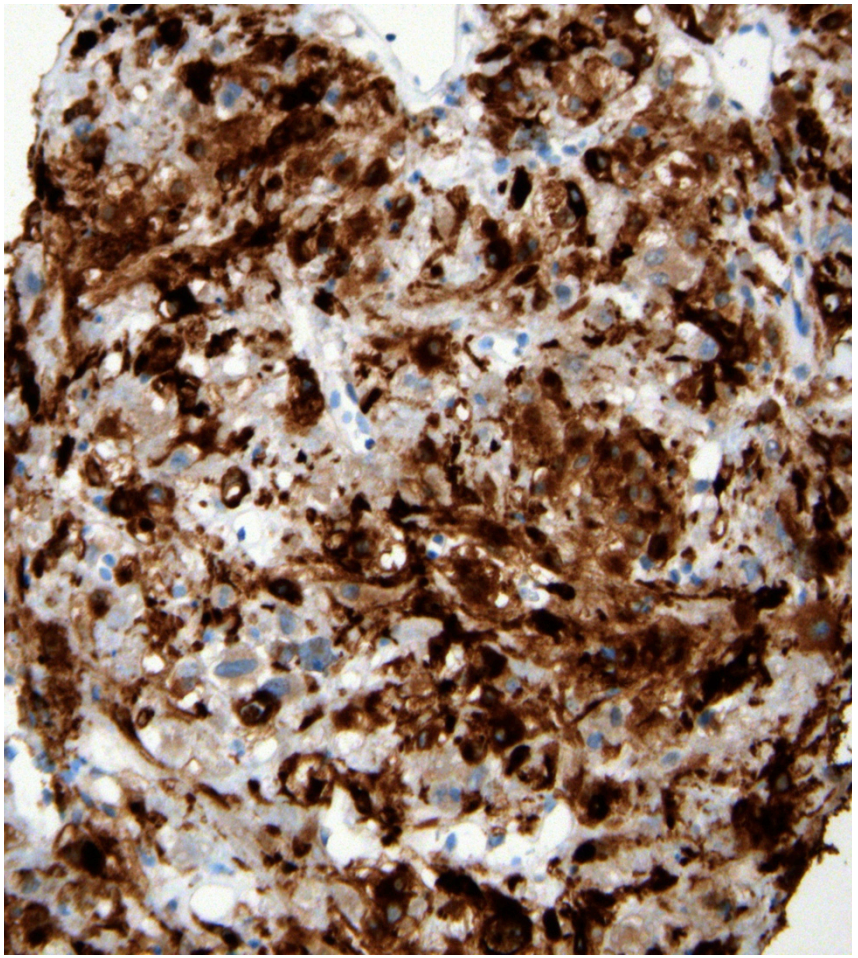
Angiomyolipoma





Angiomyolipoma





HMB-45

Low malignant renal tumors

- Multilocular cystic RCC
  - Multiple cysts with clear cells
  - Clear cells in the stroma between the cysts

Malignant tumors in the kidney

- Clear cell RCC
- Papillary RCC
- Chromophobe RCC
- Collecting duct carcinoma
- Unclassified RCC
  - Sarcomatoid RCC

Molecular markers in RCC

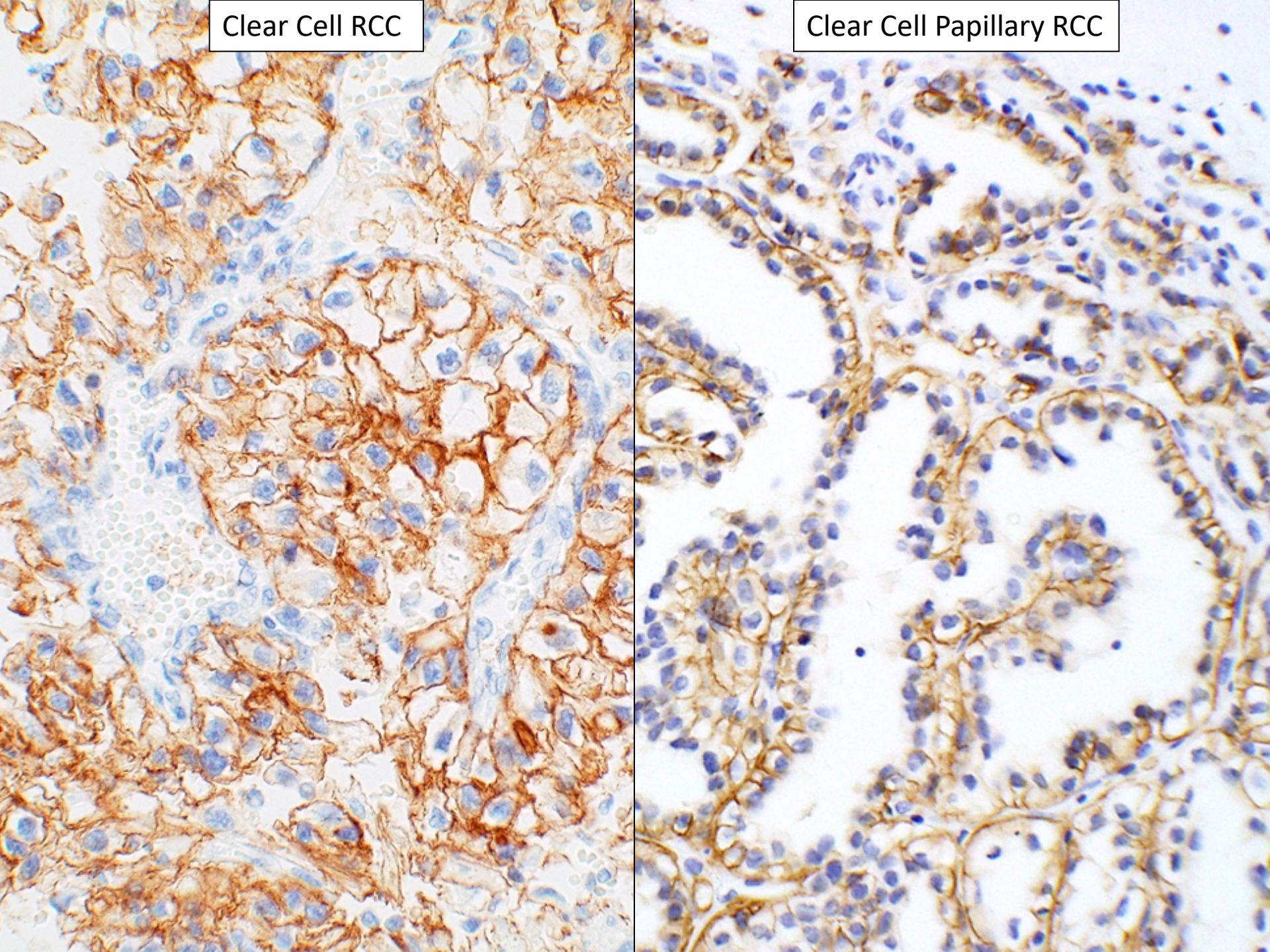
The most important are:

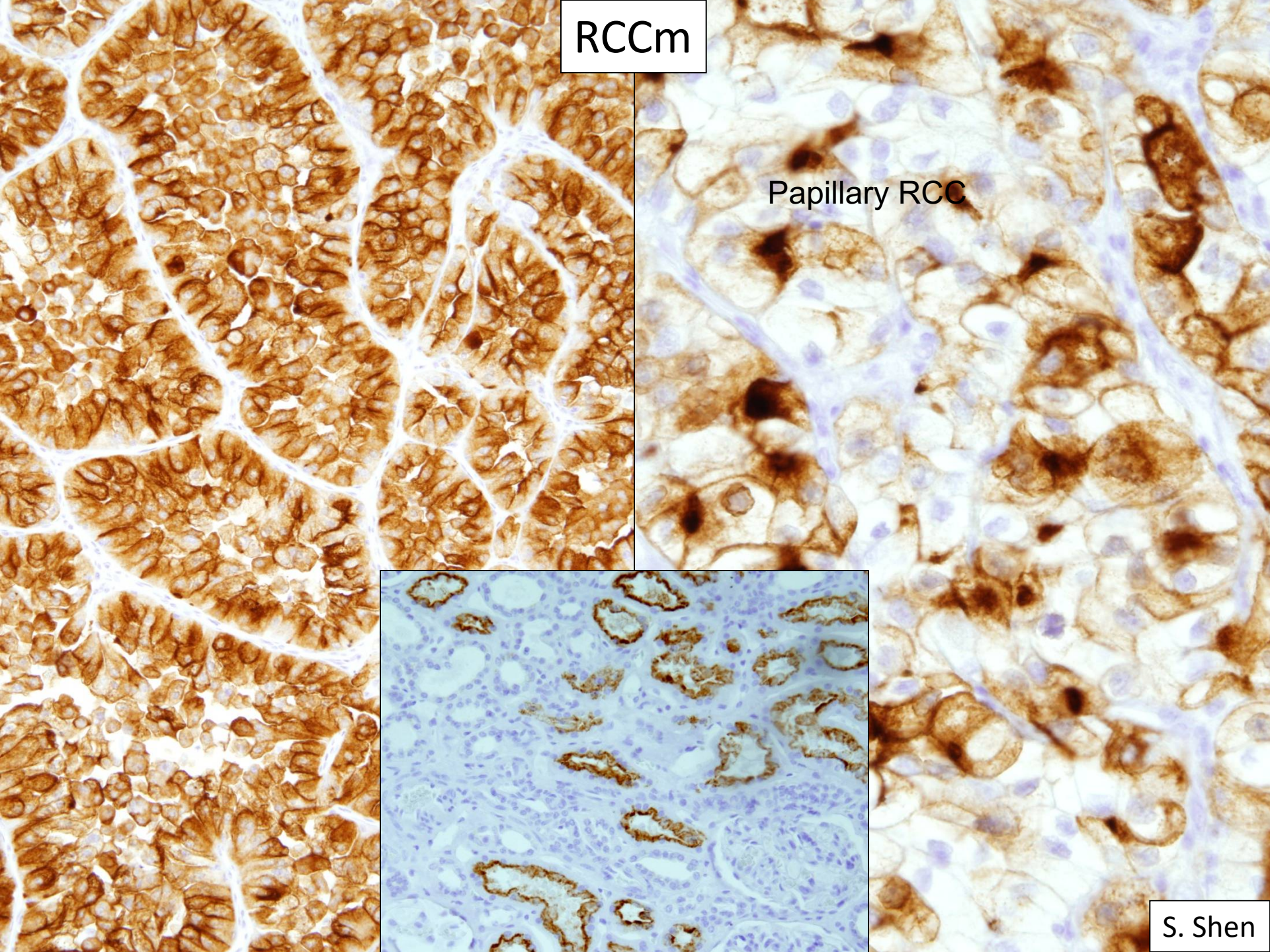
VHL-genet

CA9/CAIX	VEGF
PDGF	HIF1a
mTOR	P53
Ki67	CXR3
CXR4	MMP-2
MMP-9	IGF2
EpCAM	vimentin
Fascin	livin
survivin	CK2

DIFFERENTIAL DIAGNOSIS OF RENAL TUMORS
potentially useful markers

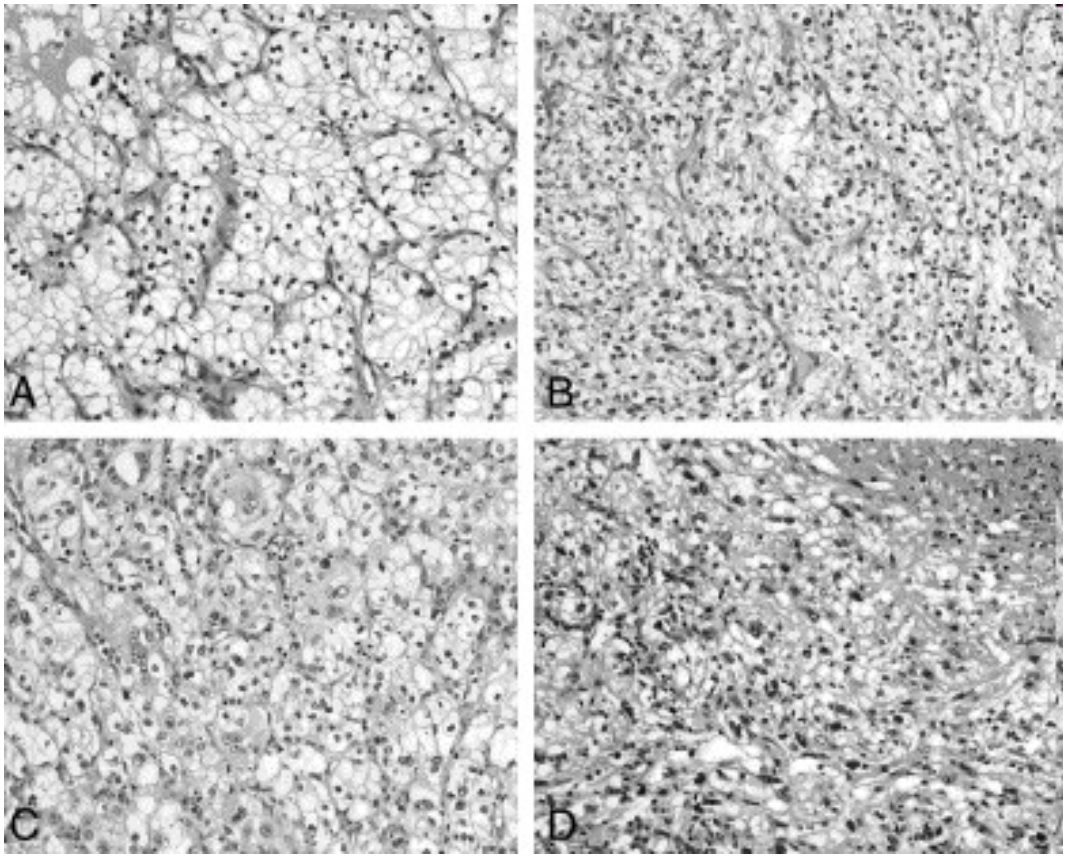
	Positive markers	Negative markers
Clear cell RCC	Vim, CK, EMA, CD10, CAIX	CK7, Ksp-cadherin, 34ßE12,RCCm
Clear cell papillary RCC	CAIX, CK7, 34ßE12	CD10, AMACR, RCCm
Papillary RCC (“type I”)	CK7, AMACR, RCCm	CAIX, CD117, Ksp-cadherin
Papillary RCC (“type II”)	AMACR, +/- CK7	+/- CK7, Ksp-cadherin
Chromophobe RCC, classic	CK7, CD-117, Ksp-cadherin	CAIX, AMACR, Vim
Chromophobe RCC, eosinophilic	+/- CK7, CD-117, Ksp-cadherin	CAIX, AMACR, +/- CK7, Vim
Oncocytoma	CD-117, Ksp-cadherin	CK7, AMACR
MiTF-TFE (Xp11)	CD10, TFE3*, Cath-K	CK/EMA **
MiTF-TFE (6;11)	TFEB*, HMB-45, Mart-1, Cath-K	CK/EMA**
Epithelioid AML	HMB-45, Mart-1, Cath-K	CK/EMA
Collecting duct carcinoma	EMA, 4A4, CK7, 34ßE12, Pax 2/8	CD10, CK20, RCCm


Clear Cell RCC
Clear Cell Papillary RCC


RCCm
Papillary RCC
S. Shen

Gradering

- Fuhrmann



- Fuhrman nuclear grading:

1 Tumor cells with small (approximately 10 m) round uniform nuclei without nucleoli
2 Tumor cells with larger nuclei (approximately 15 m) with irregularities in outline nucleoli when examinated under high power (400)
3 Tumor cells with even larger nuclei (approximately 20 m) with obviously irregular outline prominent larger nucleoli even at low power (100)
4 Tumor cells with bizarre, multilobed nuclei heavy clumps of chromatin

Stadieinddeling

- TNM

pT1 Tumor ≤ 7 cm og begrænset til nyren

pT1a Tumor ≤ 4 cm og begrænset til nyren

pT1b Tumor > 4 cm og begrænset til nyren

pT2 Tumor > 7 cm og begrænset til nyren

pT2a Tumor ≤ 10 cm og begrænset til nyren

pT2b Tumor > 10 cm og begrænset til nyren

pT3 Tumor udenfor nyren, men ikke i samsidig binyre eller gennem fascia renalis (Gerotas fascie)

pT3a Invasion i perirenalt fedt inkl. fedt i sinus renalis eller makroskopisk i vena renalis inkl. dennes muskelholdige grene

pT3b Makroskopisk invasion i vena cava inferior (eller dennes væg) under diafragma

pT3c Makroskopisk invasion i vena cava inferior (eller dennes væg) over diafragma

pT4 Invasion gennem fascia renalis (Gerotas fascie) eller invasion i samsidig binyre

pTx Stadium ikke fastlagt/kan ikke fastlægges

pN0 Ingen lymfeknuder metastaser påvist histologisk

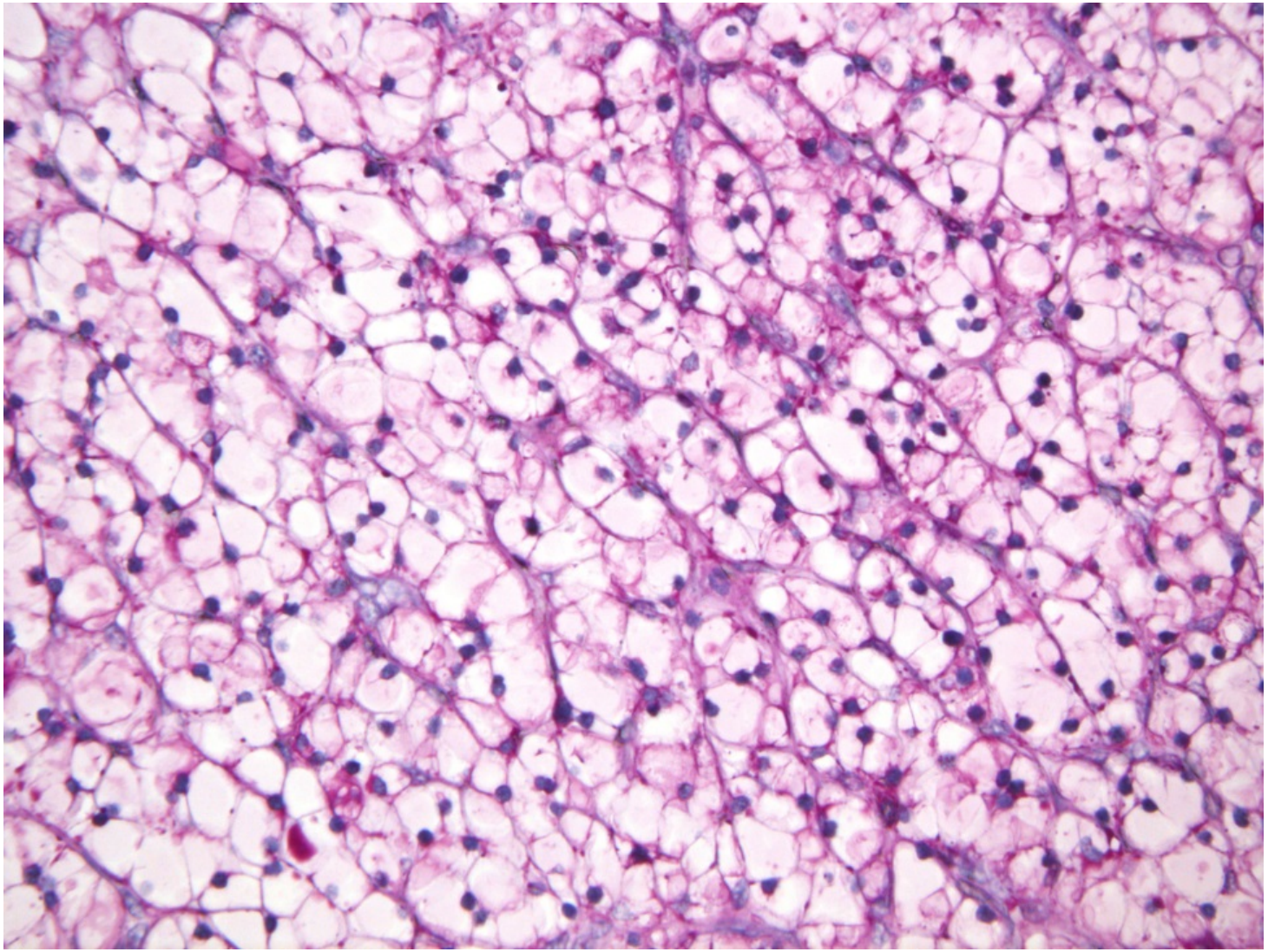
pN1 1 regional lymfeknudemetastase påvist histologisk

pN2 >1 regional lymfeknudemetastase påvist histologisk

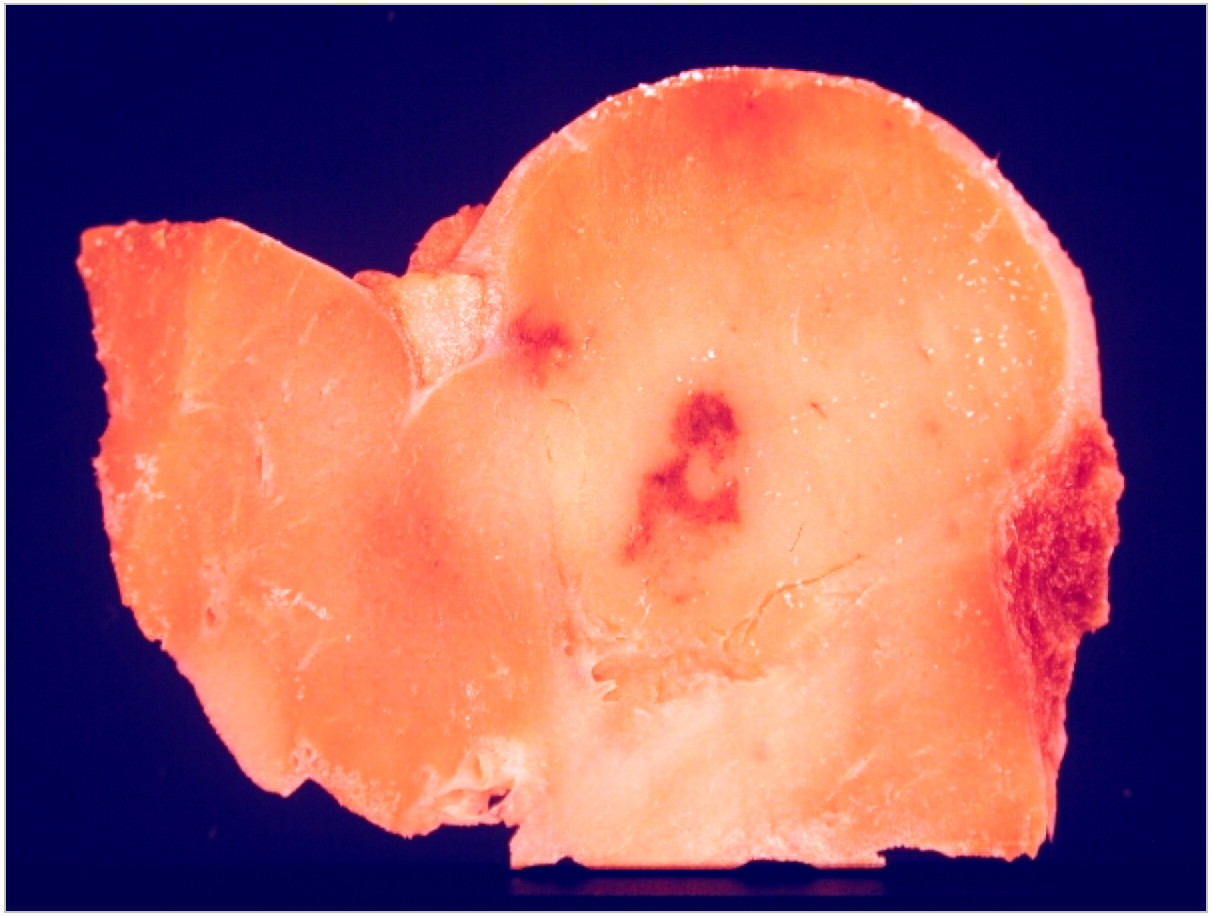
pNx Lymfeknuder ikke undersøgt/lymfeknudestatus ukendt

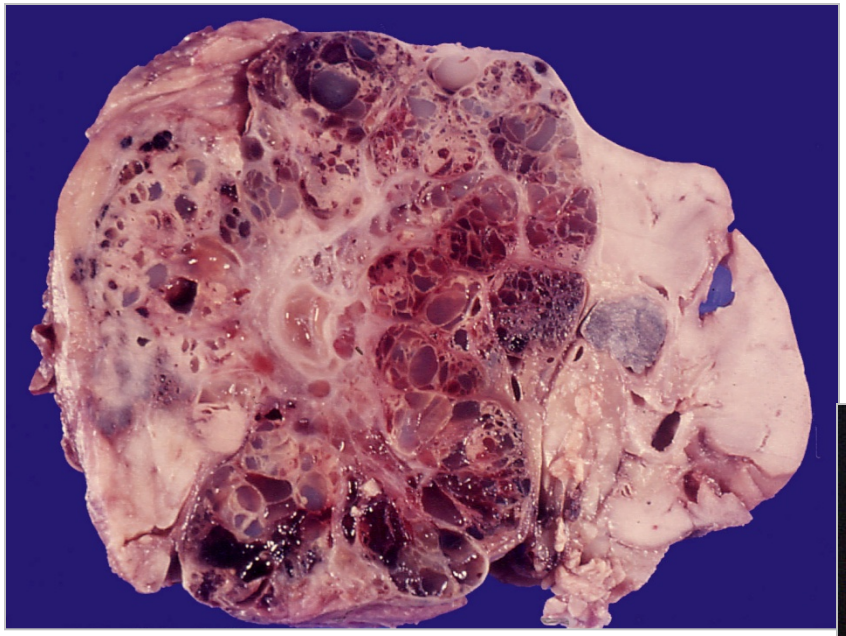
bruges, når der ikke er fjernet eller fundet lymfeknuder

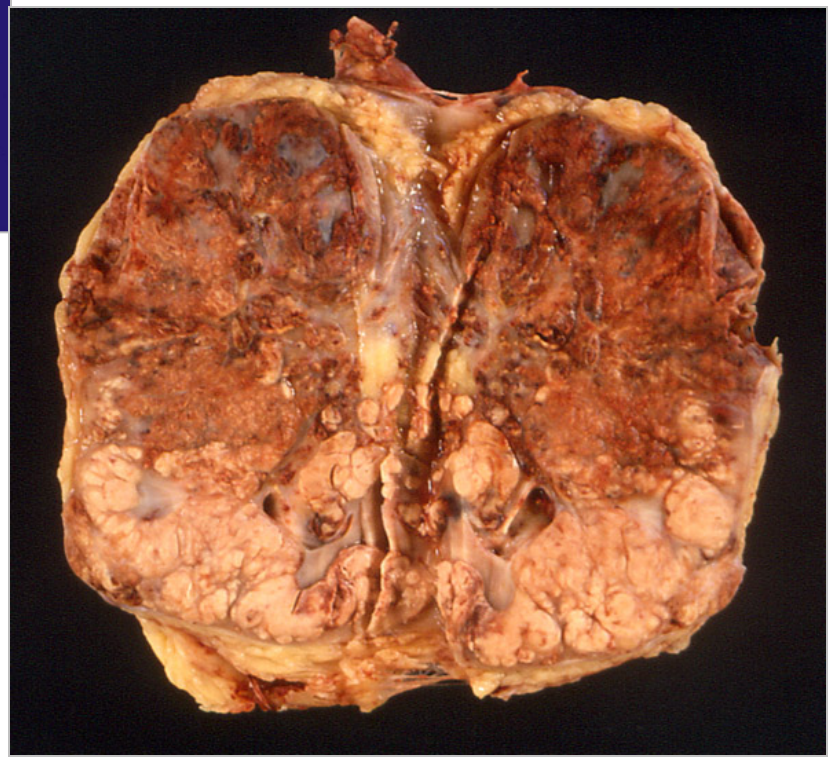
ccRCC



Renal cell carcinoma

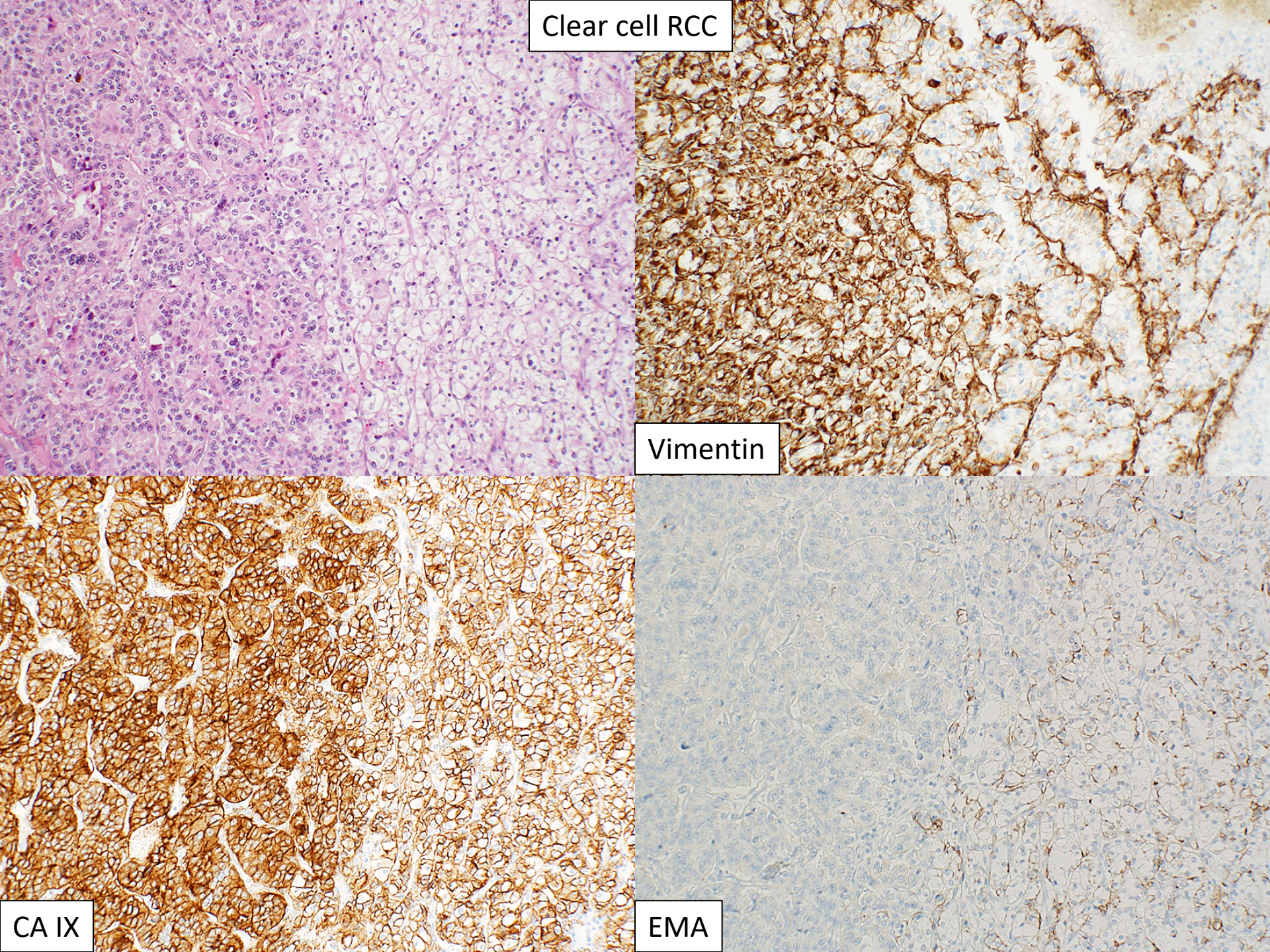




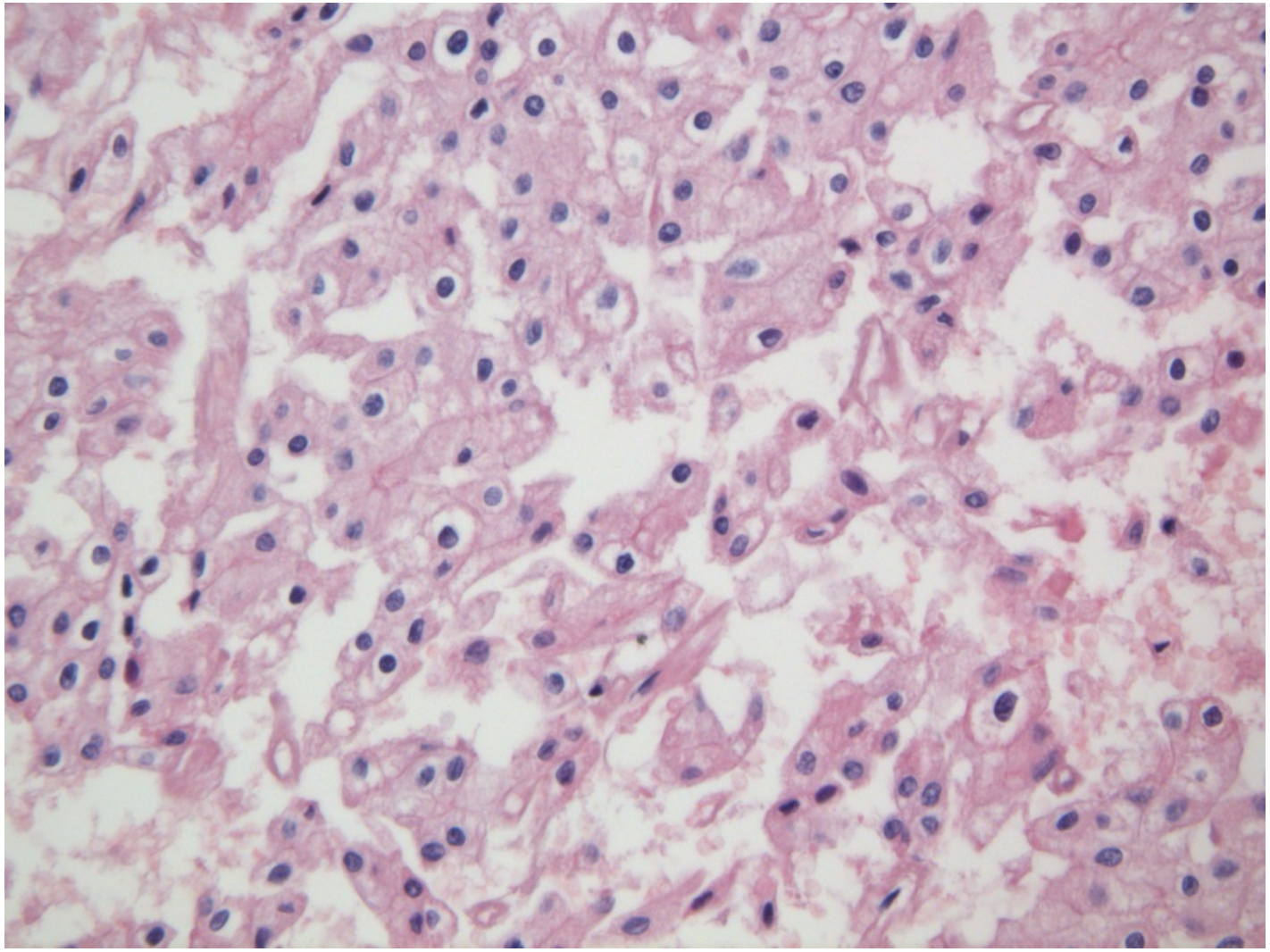


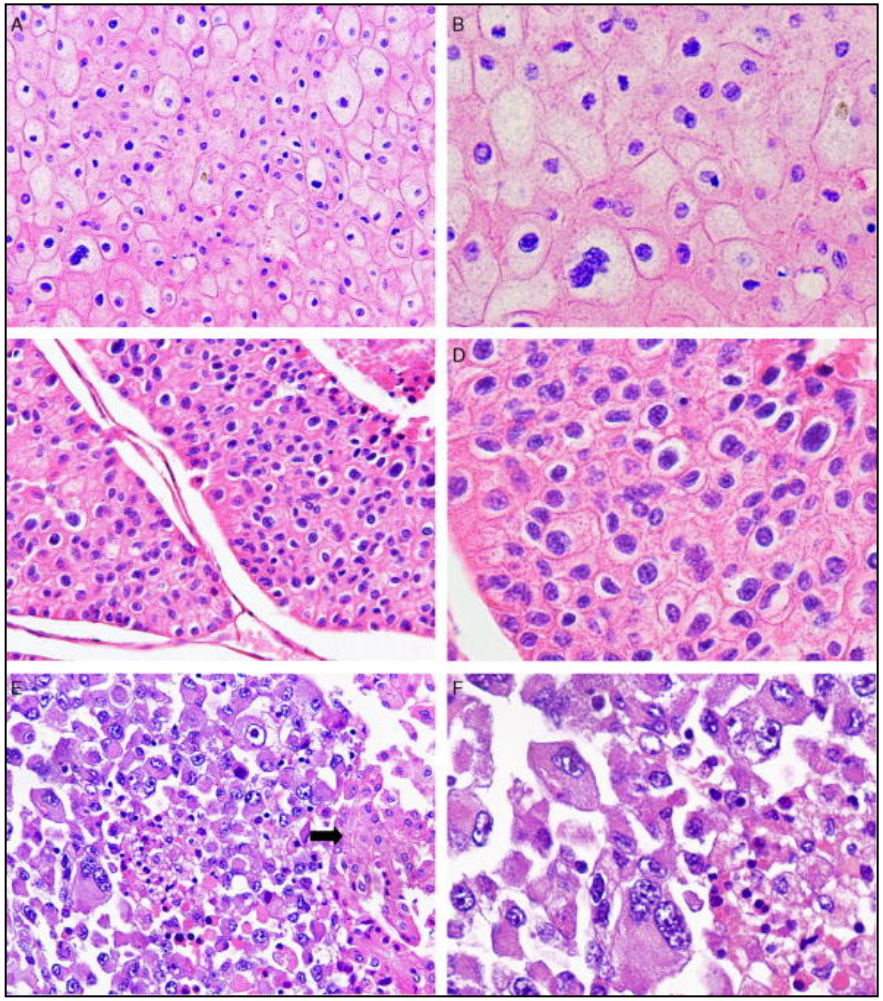
TUMORS COMPOSED PREDOMINANTLY OF "CLEAR" CELLS

Tumor type	CA IX	CK7	CD 117	Cathepsin-K	HMB45
Clear cell RCC	Positive, diffuse membranous	Negative	Negative	Negative	Negative
Clear cell papillary RCC	Positive, cup-like	Positive	Negative	Negative	Negative
Chromophobe RCC, classic	Negative	Positive, cytoplasmic	Positive, membranous	Negative	Negative
Epithelioid AML	Negative	Negative	Negative	Positive, cytoplasmic	Positive, cytoplasmic
MiTF-TFE tumors					
Xp11 family	Variable but focal	Negative	Negative	Positive (50%), cytoplasmic	Negative *


Clear cell RCC
Vimentin
CA IX
EMA

Chromophobe RCC





A Novel Tumor Grading Scheme for Chromophobe Renal Cell Carcinoma: Prognostic Utility and Comparison With Fuhrman Nuclear Grade.

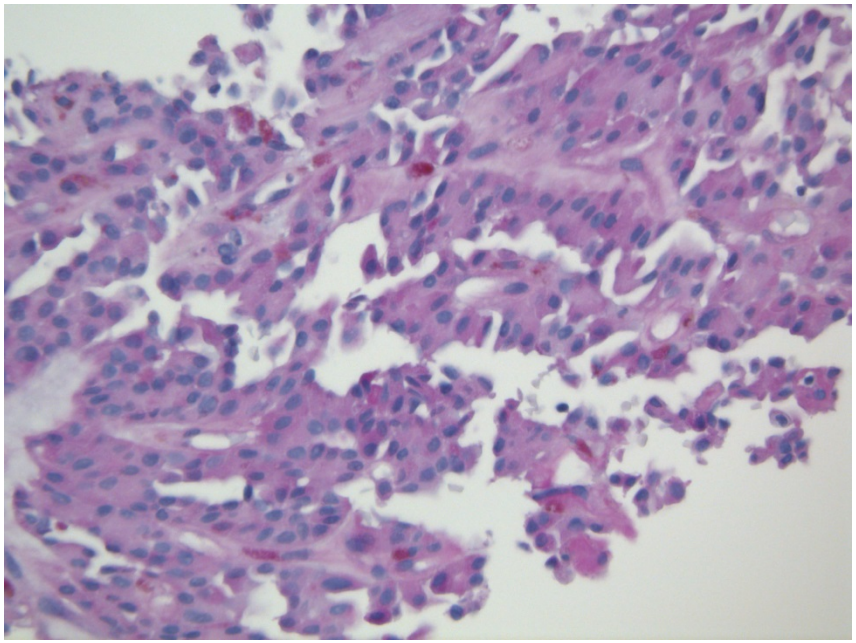
Paner, Gladell; Amin, Mahul; Alvarado-Cabrero, Isabel; Young, Andrew; MD, PhD; Stricker, Hans; Moch, Holger; Lyles, Robert

American Journal of Surgical Pathology. 34(9):1233-1240, September 2010.
DOI: 10.1097/PAS.0b013e3181e96f2a

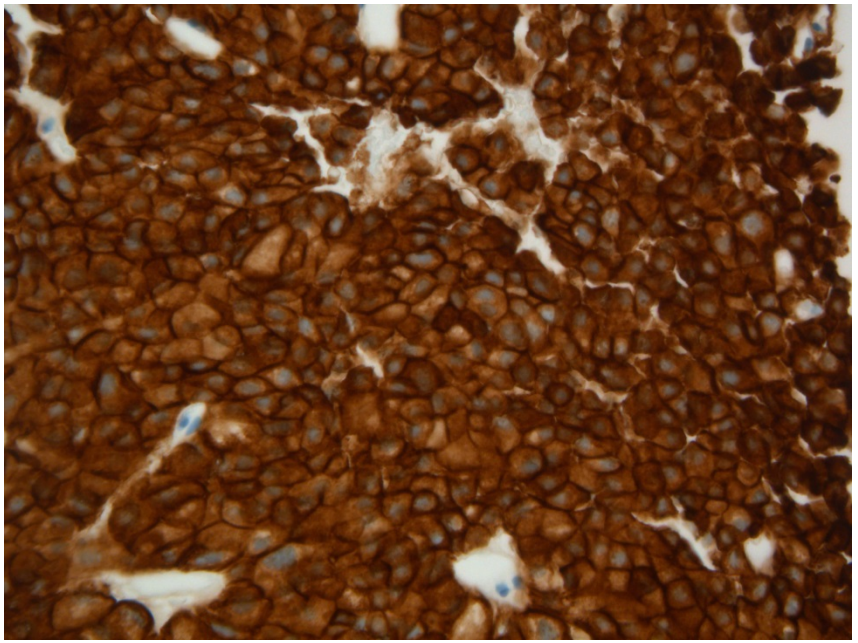
FIGURE 2. Degenerate or symplastic nuclear atypia. A, There is moderate to severe nuclear pleomorphism usually as distinct foci, and can have abrupt transition with chromophobe renal cell carcinoma cells with typical nuclei. B, These nuclei have hyperchromatic, smudged or degenerate appearing nuclear chromatin.

Eosinophilic variant of chRCC

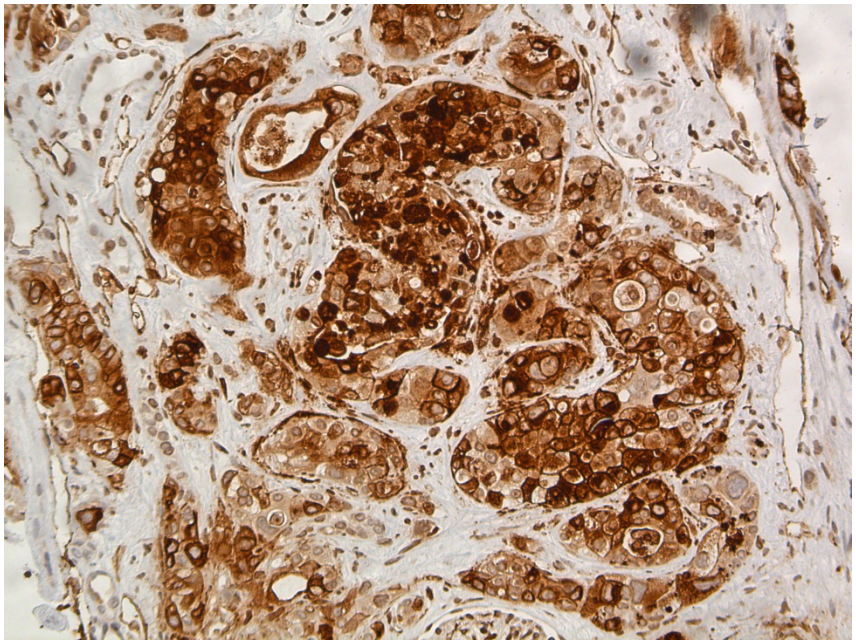
PAS



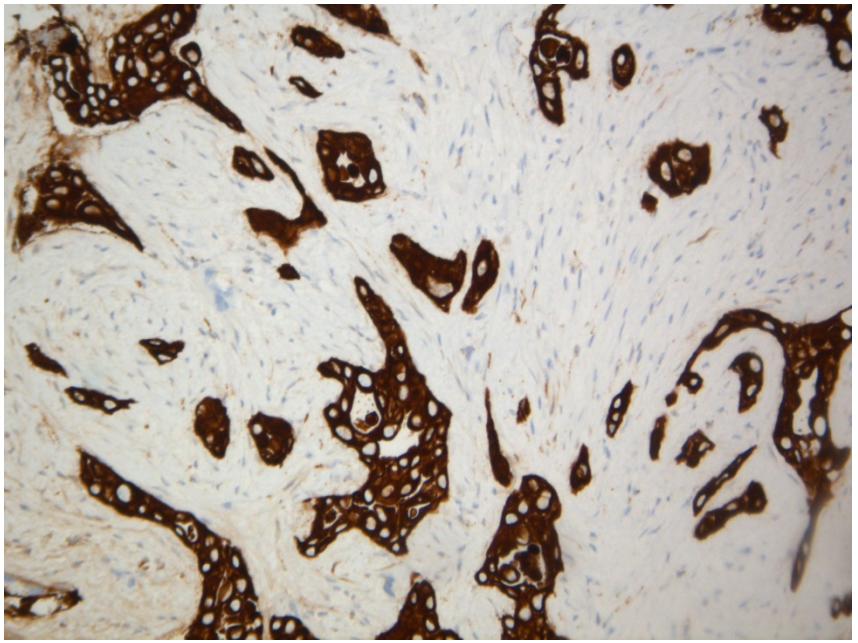
CD117



Collecting duct carcinoma



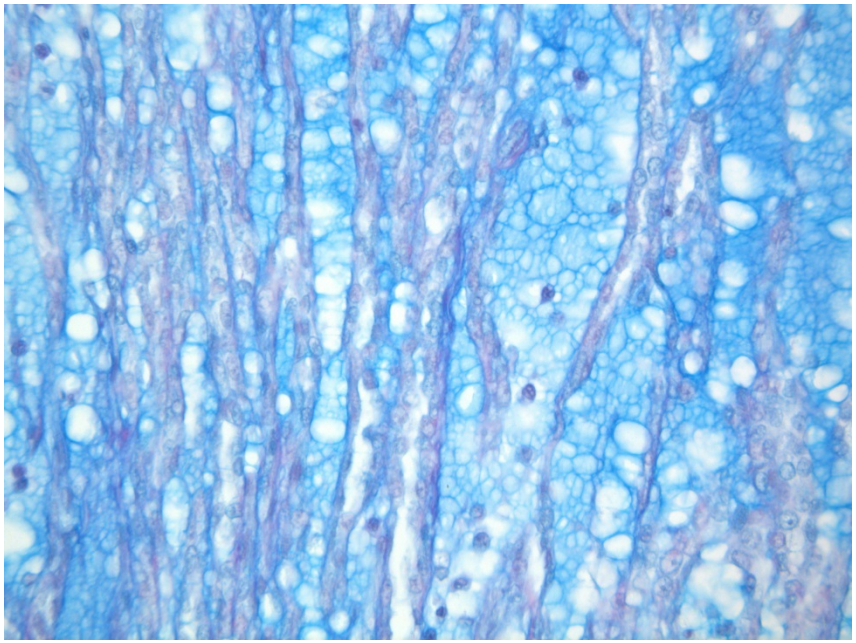
Ubiquitin



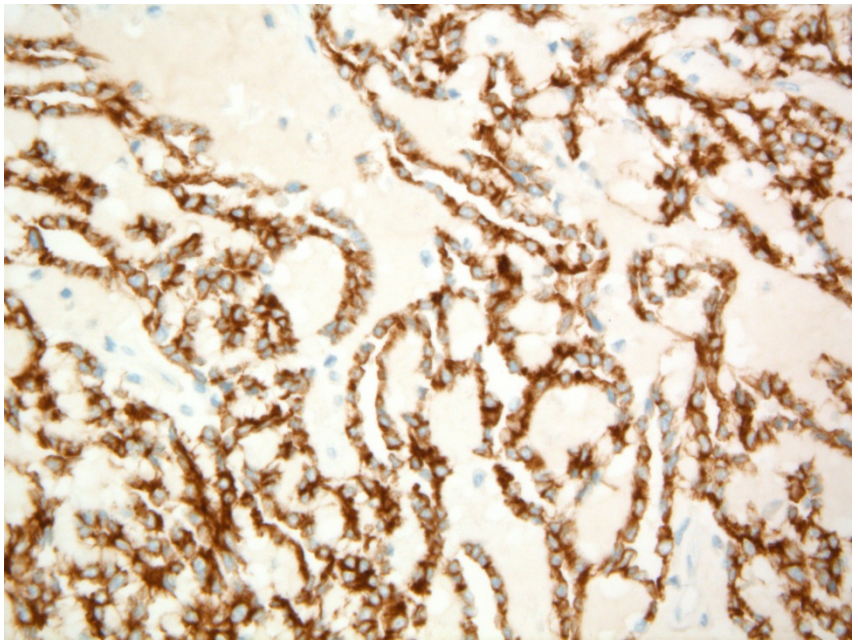
CK7

Tubular and spindle cell carcinoma

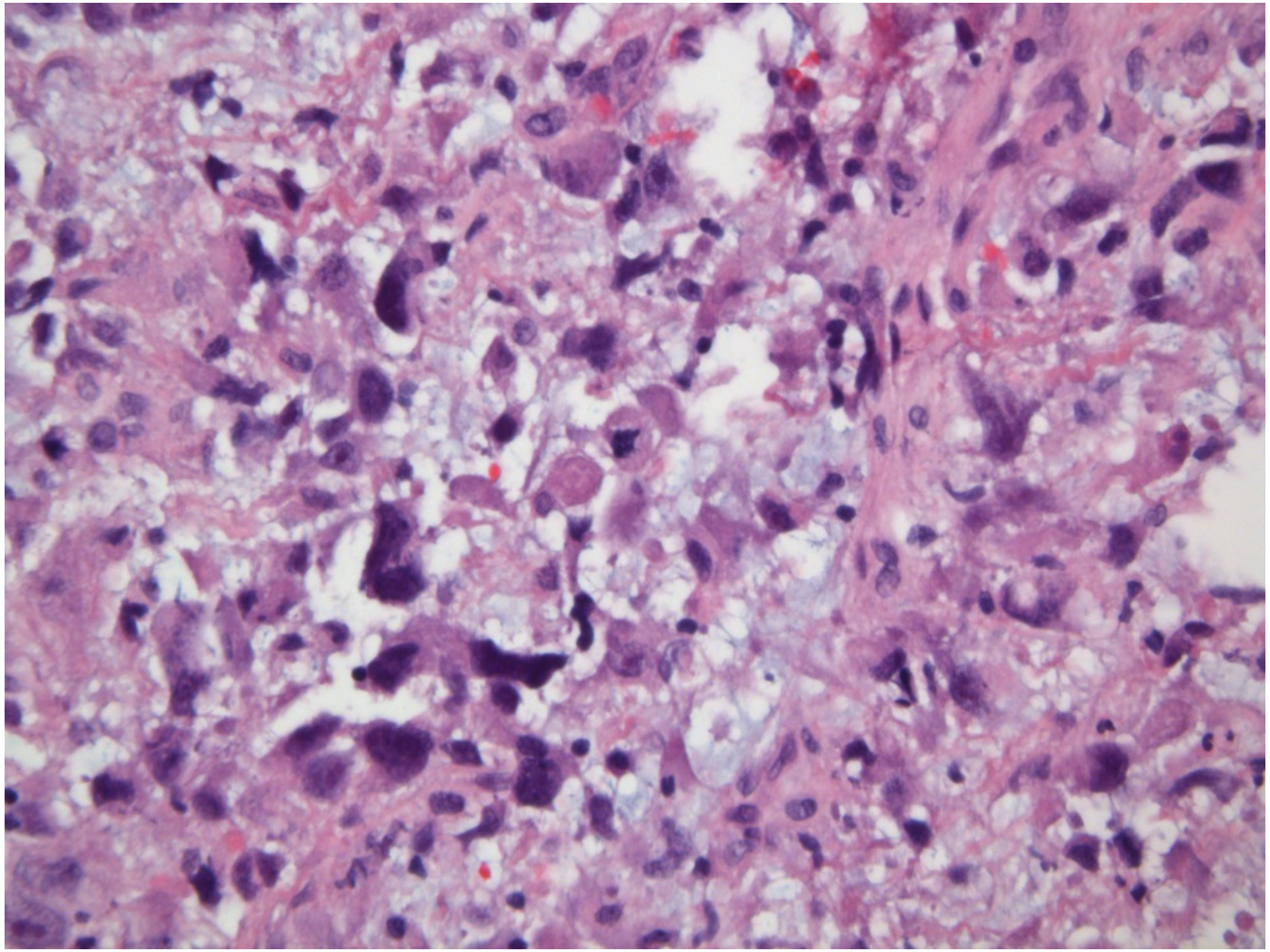
Pas/AB



CK19



Urothelial carcinoma



Pathology sign out

- Tumor type (WHO)
- Fuhrman grade
- Leibovich score
- Tumor diameter
- pT-, pN- og evt. pM-stage
- Vascular invasion ?
- Necrosis or eller sarkomatoid growth
- Radicality ?
- Type of specimen.

Leibovich (Mayo) Score

• Pathological T stage	0-4
• Nodal status	0-2
• Tumour size	
– <10cm	0
– >10cm	1
• Nuclear Grade	0-3
• Histological tumour necrosis	0-1

Scores from 0 – 11 Low=0-2, Intermediate=3-5 & High=6 or more

Leibovich et al; Cancer 2003