Update in TNM Staging and Handling of Kidney Cancer

Kiril Trpkov, MD FRCPC

Department of Pathology and Laboratory Medicine

kiril.trpkov@cls.ab.ca

MOVING INFORMATION

106TH ANNUAL MEETING

USCAP
Creating a Better Pathologist

Disclosure of Relevant Financial Relationships

Dr. Kiril Trpkov declares no conflicts of interest to disclose.

Update in TNM Staging and Handling of Kidney Cancer - Objectives

Understand rationale for proper handling and staging of renal specimens

Identify differences in TNM staging compared to 7th AJCC edition

Understand prognostic rationale for changes of staging system for renal cancers

Prognostic factors in RCC

1. Pathologic stage
2. Tumor WHO/ISUP grade
3. Morphologic type
4. Sarcomatoid-rhabdoid differentiation
5. Tumor necrosis

(Microvascular invasion)

ISUP Consensus Meeting on Adult Renal Tumors Vancouver, March, 2012

The International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia

John R. Srigley, MD, Brett Delahunt, MD,† John N. Eble, MD,‡ Lars Egevad, MD, PhD,§ Jonathan I. Epstein, MD,‖ David Grignon, MD,‡ Ondrej Hes, MD, PhD,¶ Holger Moch, MD,# Rodolfo Montironi, MD,** Satish K. Tickoo, MD,†† Ming Zhou, MD, PhD,‡‡ Pedram Argani, MD,§§ and The ISUP Renal Tumor Panel*

Handling and Staging of Renal Cell Carcinoma

The International Society of Urological Pathology Consensus (ISUP) Conference Recommendations

Kiril Trpkov, MD, FRCPC, David J. Grignon, MD, FRCPC,† Stephen M. Bonsib, MD,‡ Mahul B. Amin, MD,§ Athanase Billis, MD,‖ Antonio Lopez-Beltran, MD,¶ Hemamali Samaratunga, MD, FRCPA,# Pheroze Tamboli, MD,** Brett Delahunt, MD, FRCPA,†† Lars Egevad, MD, PhD,††‡‡ Rodolfo Montironi, MD, FRCPath,§§ John R. Srigley, MD, FRCPC,‖‖¶¶ and the members of the ISUP Renal Tumor Panel*

The International Society of Urological Pathology (ISUP) Grading System for Renal Cell Carcinoma and Other Prognostic Parameters

Brett Delahunt, MD, John C. Cheville, MD,† Guido Martignoni, MD,‡ Peter A. Humphrey, MD,§ Cristina Magi-Galluzzi, MD,‖ Jesse McKenney, MD,‖ Lars Egevad, MD,¶ Ferran Algaba, MD,# Holger Moch, MD,** David J. Grignon, MD,†† Rodolfo Montironi, MD,‡‡ John R. Srigley, MD,§§‖‖ and The Members of the ISUP Renal Tumor Panel*

Renal Tumors

Diagnostic and Prognostic Biomarkers

Puay Hoon Tan, MD, FRCPA, Liang Cheng, MD,† Nathalie Rioux-Leclercq, MD,‡ Maria J. Merino, MD,§ George Netto, MD,‖ Victor E. Reuter, MD,¶ Steven S. Shen, MD,# David J. Grignon, MD,† Rodolfo Montironi, MD, FRCPath,** Lars Egevad, MD,†† John R. Srigley, MD, FRCPC,‡‡ Brett Delahunt, MD, FRCPA,§§ Holger Moch, MD,‖‖ and The ISUP Renal Tumor Panel*

ISUP Consensus Meeting on Adult Renal Tumors

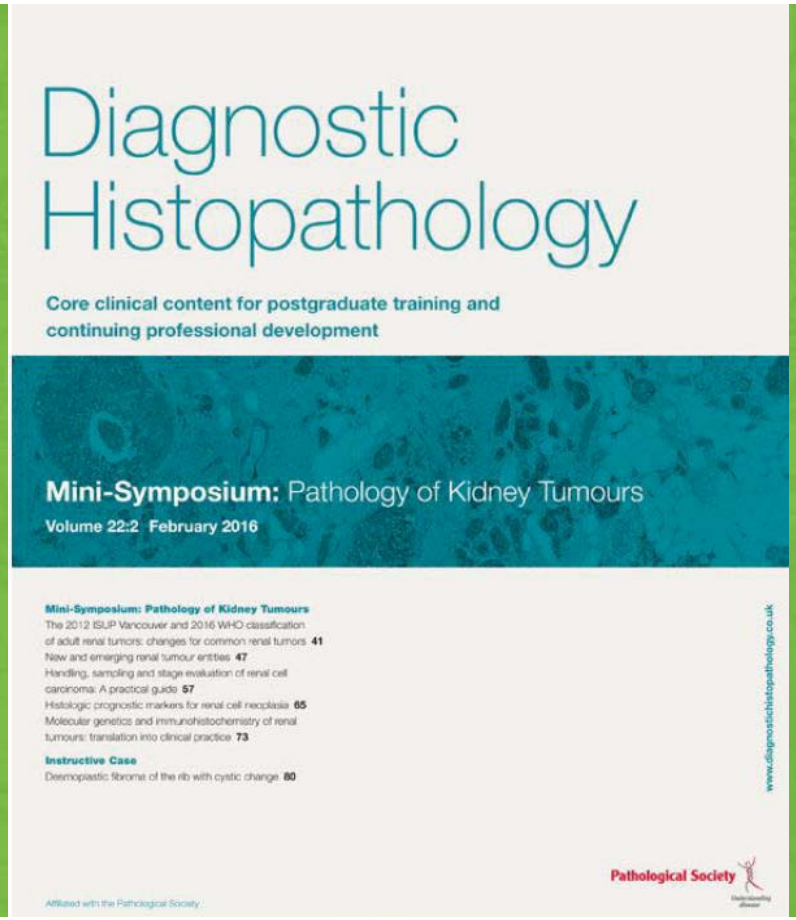
Vancouver, March, 2012

Handling and Staging of Renal Cell Carcinoma

The International Society of Urological Pathology Consensus (ISUP) Conference Recommendations

Kiril Trpkov, MD, FRCPC, David J. Grignon, MD, FRCPC,† Stephen M. Bonsib, MD,‡ Mahul B. Amin, MD,§ Athanase Billis, MD,‖ Antonio Lopez-Beltran, MD,¶ Hemamali Samaratunga, MD, FRCPA,# Pheroze Tamboli, MD,** Brett Delahunt, MD, FRCPA,†† Lars Egevad, MD, PhD,†††‡‡ Rodolfo Montironi, MD, FRCPath,§§ John R. Srigley, MD, FRCPC,‖‖¶¶ and the members of the ISUP Renal Tumor Panel*

Trpkov K et al. *Am J Surg Pathol* 2013; 37:1505-17



Bonert M, Kuo-Cheng H, Trpkov K.
Diagnostic Histopathology 2016;22(2):57-67

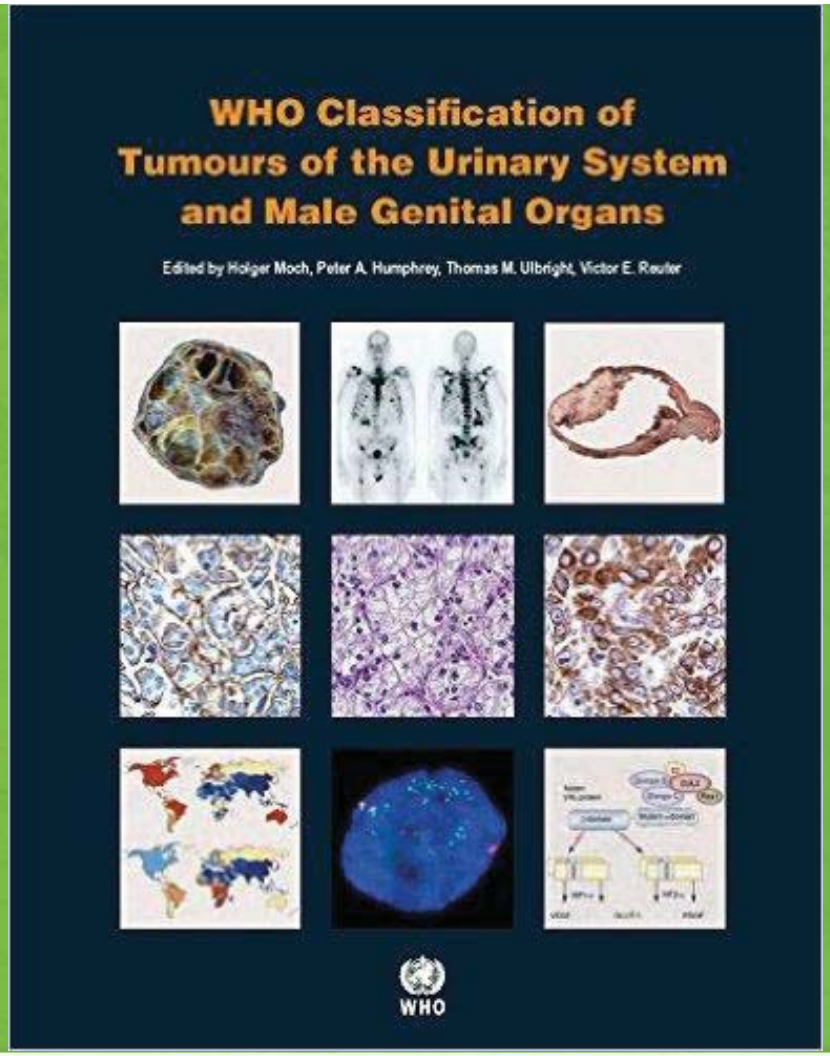
Handling, sampling and stage evaluation of renal cell carcinoma: A practical guide

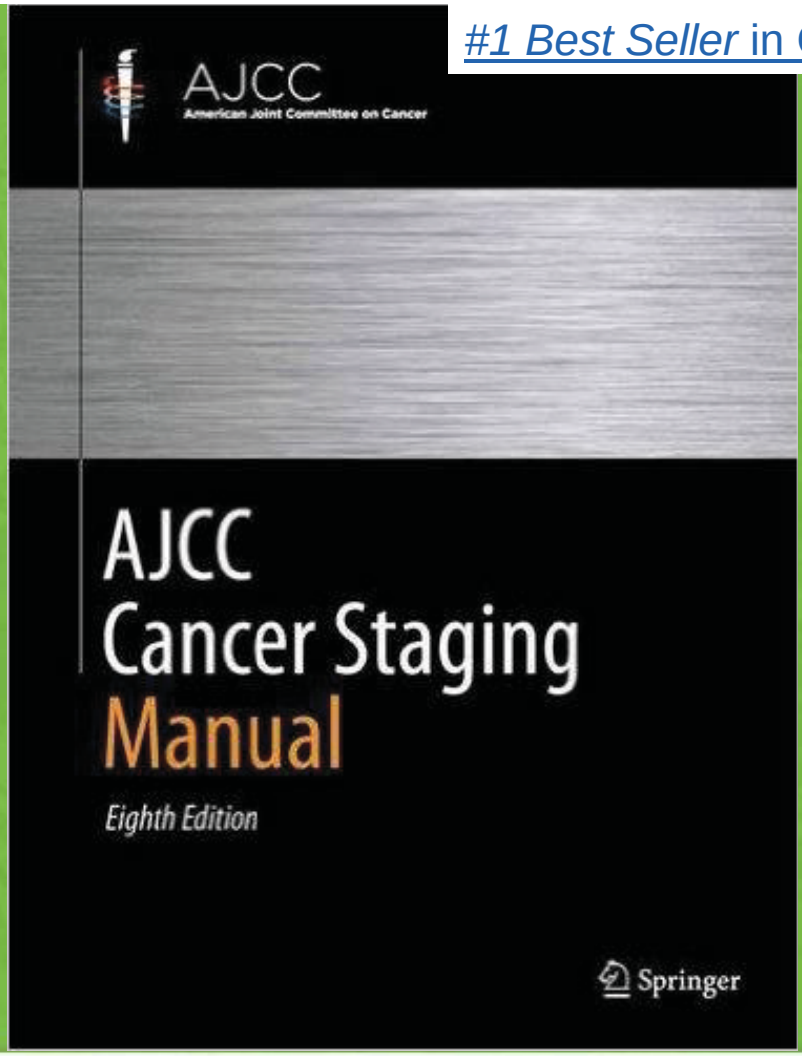
Michael Bonert
Kuo-Cheng Huang
Kiril Trpkov

Abstract

Tumor stage is considered the single most important prognostic factor in renal cell carcinoma. The most critical issue when determining the pathologic stage is whether the tumor is organ-confined or has spread outside of the organ and invaded the perinephric tissues and the adjacent structures. Proper handling and sampling of nephrectomy specimens is essential for accurate determination of pathologic stage and other relevant tumor parameters. Tumor staging requires careful assessment of various tumor characteristics, including tumor size, extent of tumor invasion in relation to specific kidney structures (sinus fat, renal vein and its segmental branches) and perinephric tissues (perinephric fat, Gerota fascia, adrenal gland and vena cava). Therefore, it is imperative that pathologists are familiar with the normal renal anatomy and histology, able to properly dissect surgically resected renal tumors, and able to assess specimens grossly and microscopically, to accurately determine and report pathologic stage and other relevant tumor parameters.

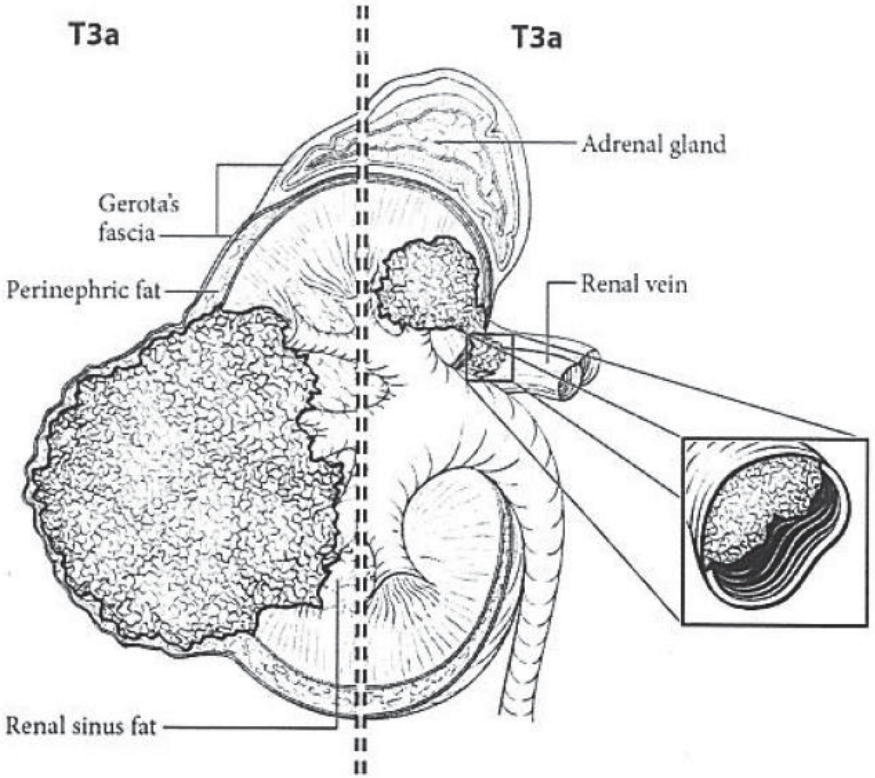
Keywords fat invasion; International Society of Urological Pathology; ISUP; kidney; renal cell carcinoma; renal sinus; renal vein invasion; specimen handling; stage





#1 Best Seller in Oncology

Stage pT3a



pT3

Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia

pT3a

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

Renal tumor stage summary of changes AJCC/TNM 8th edition

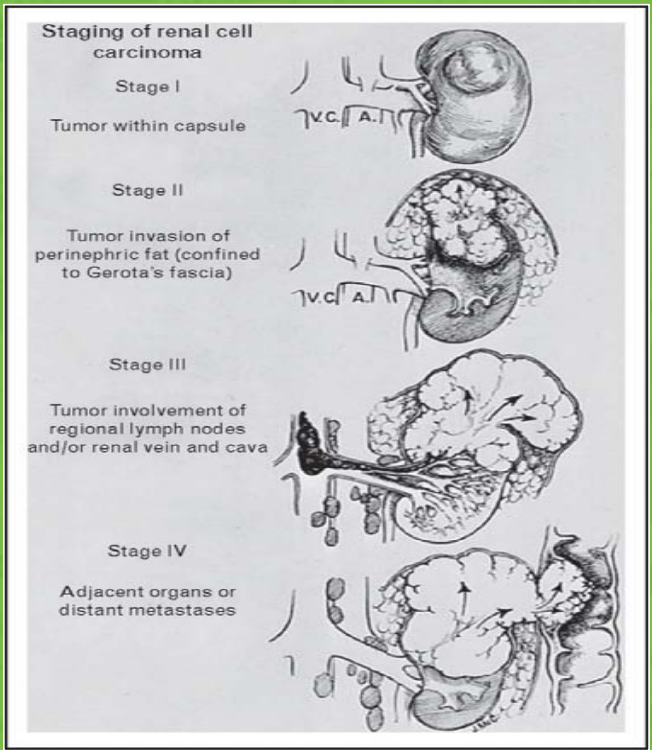
Definition of Primary Tumor (pT): T3a disease

Word “grossly” was eliminated from the description of renal vein involvement

“Muscle containing” was changed into “segmental veins”

Invasion of the pelvicalyceal system was added

Renal tumor stage



Robson CJ et al. *J Urol* 1969; 101:297–301

Key prognostic parameter

Used in prognostic nomograms

7th edition (2009)

8th edition (2017)

Handling of renal tumors

Pathologist

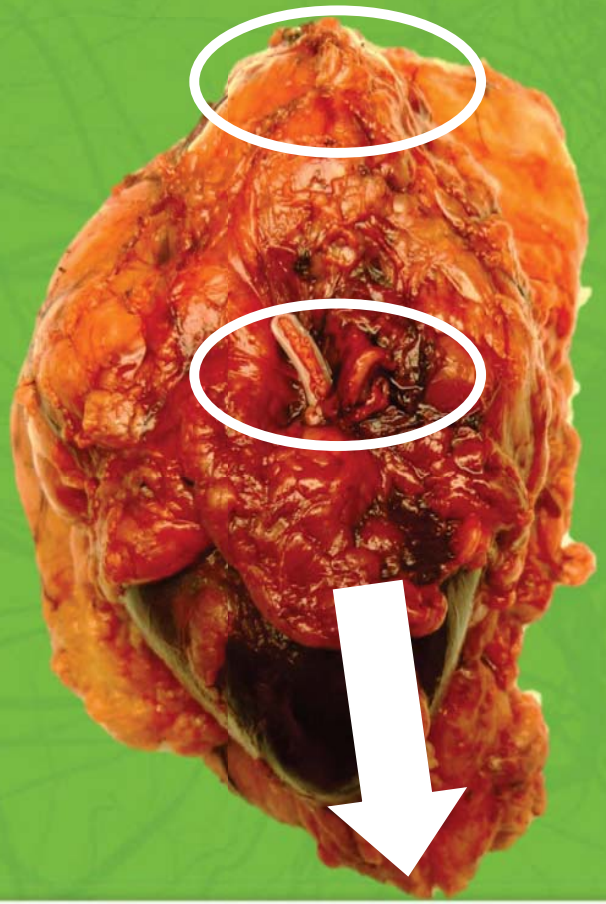
Goals:

Thorough gross examination

Adequate sampling

Reporting of stage and other important prognostic parameters

Specimen received in the lab



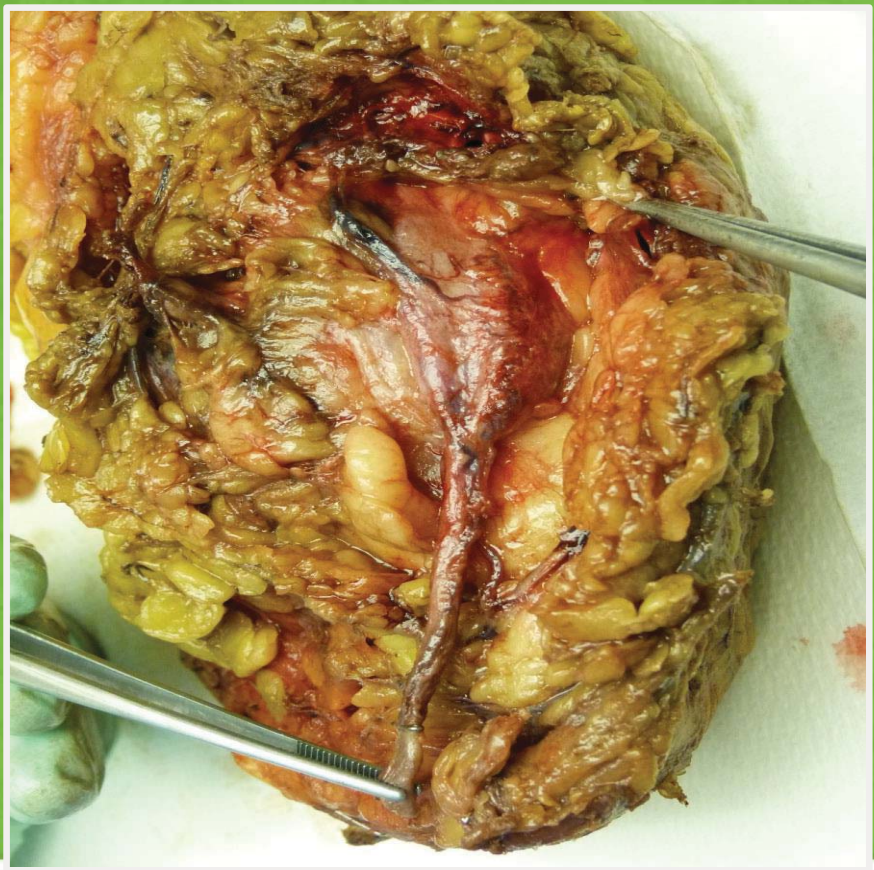
Identify and sample:

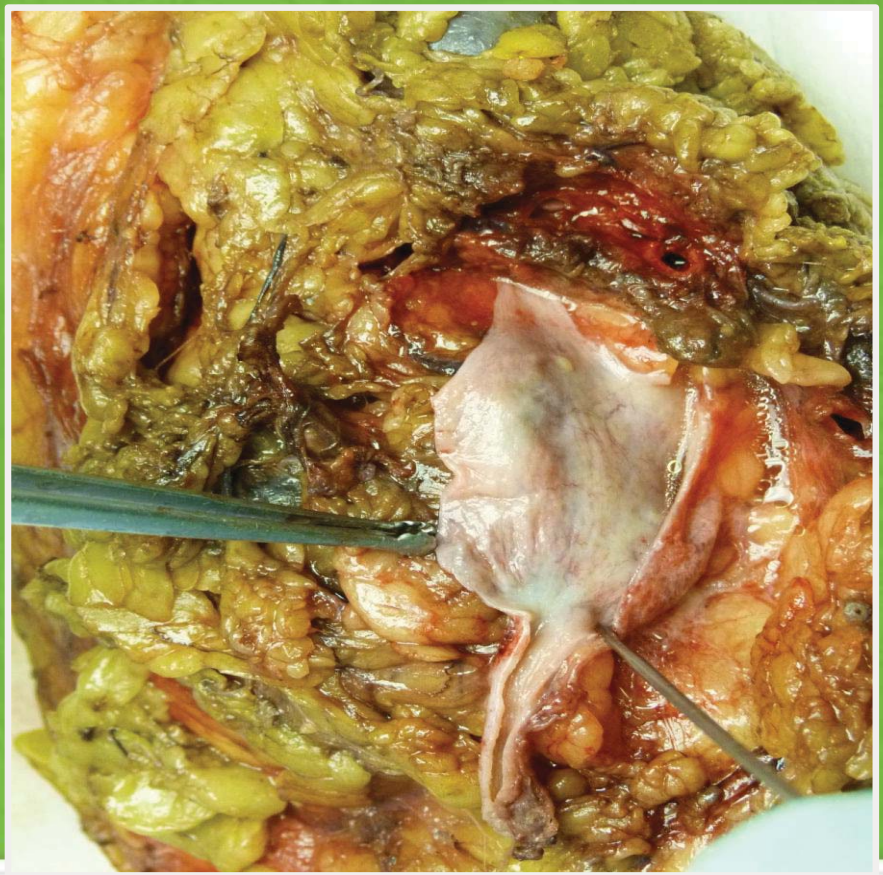
Adrenal gland

Vascular margins

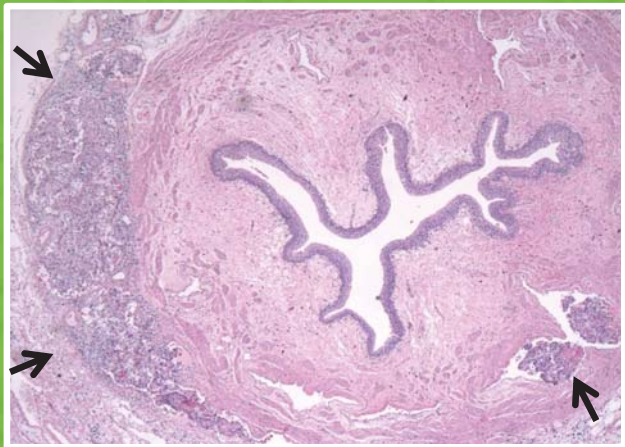
Ureter

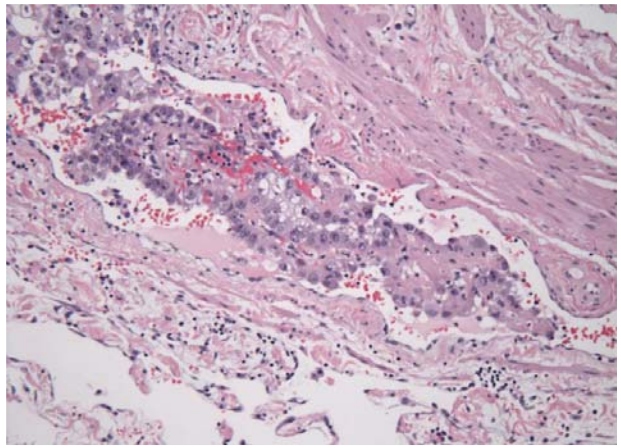
Ureteral stump opened and examined

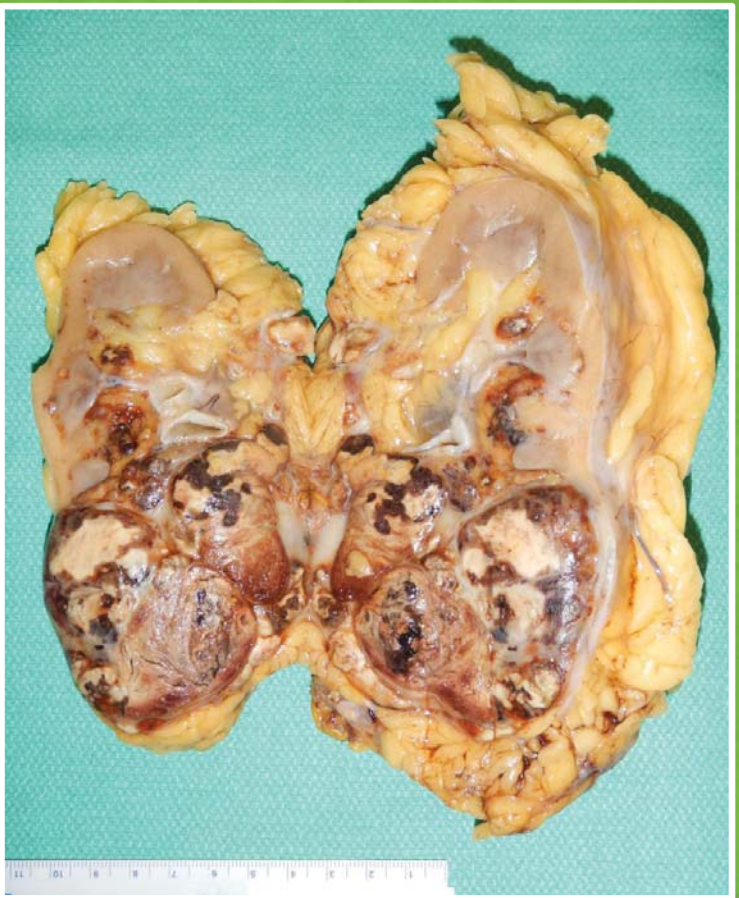




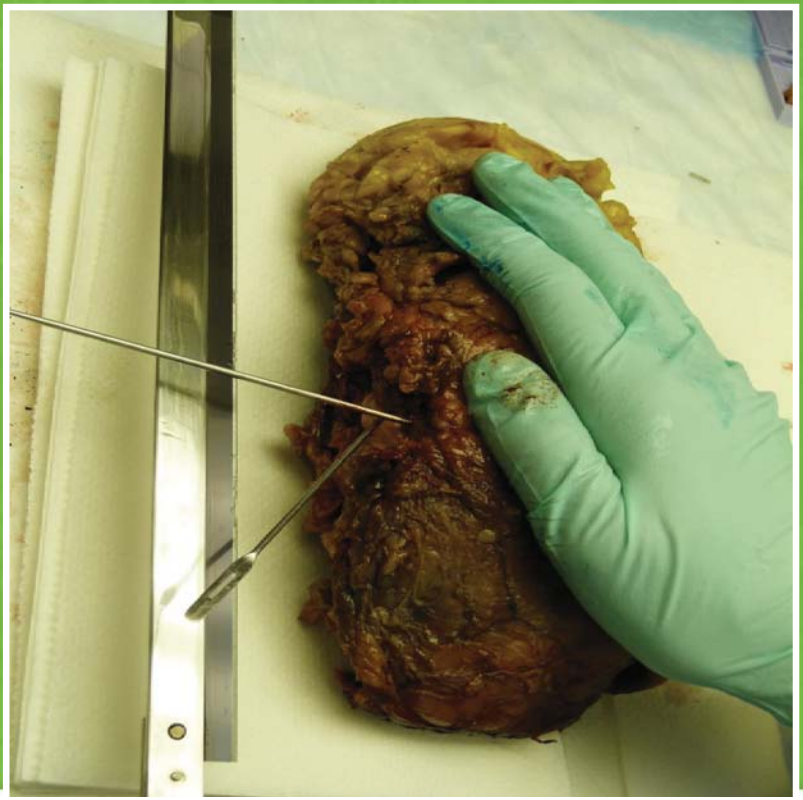
Ureteral invasion







Initial section of specimen along long axis (lateral or medial)

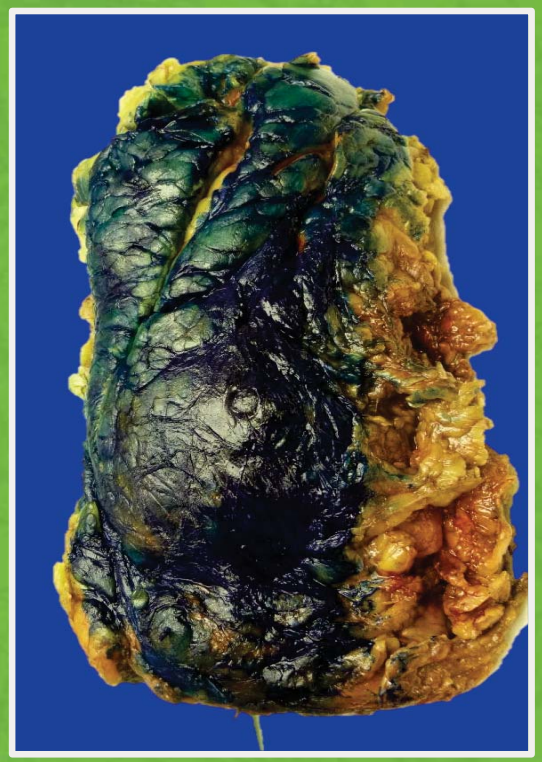


Probes in collecting system or in largest hilar veins

Initial section of specimen along long axis (lateral or medial)

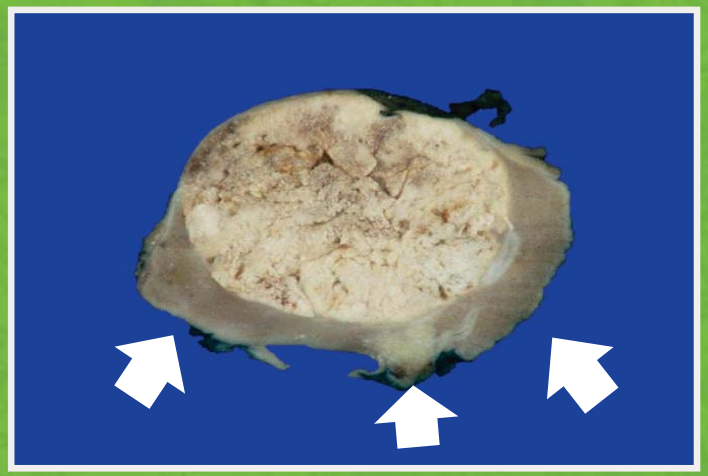
Consider additional parallel sections through venous system

Radical and partial nephrectomies should be inked



Complete

Localized



Selective
(resection margin)

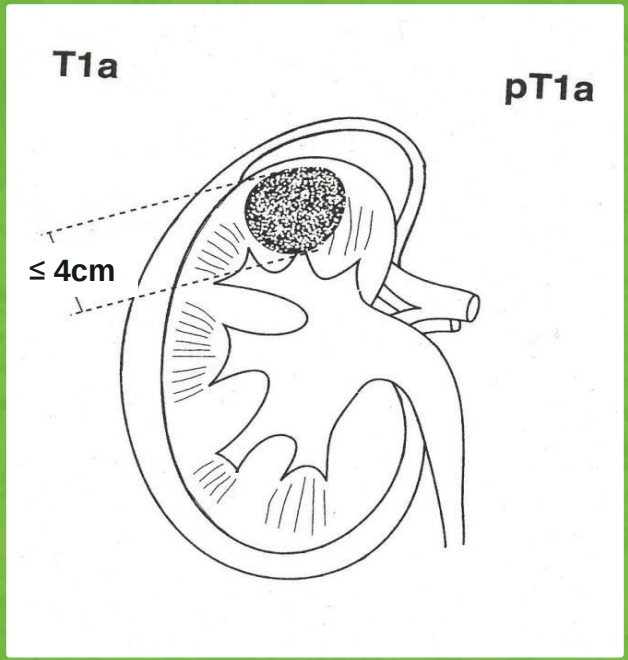
Renal tumor measurement (greatest dimension)

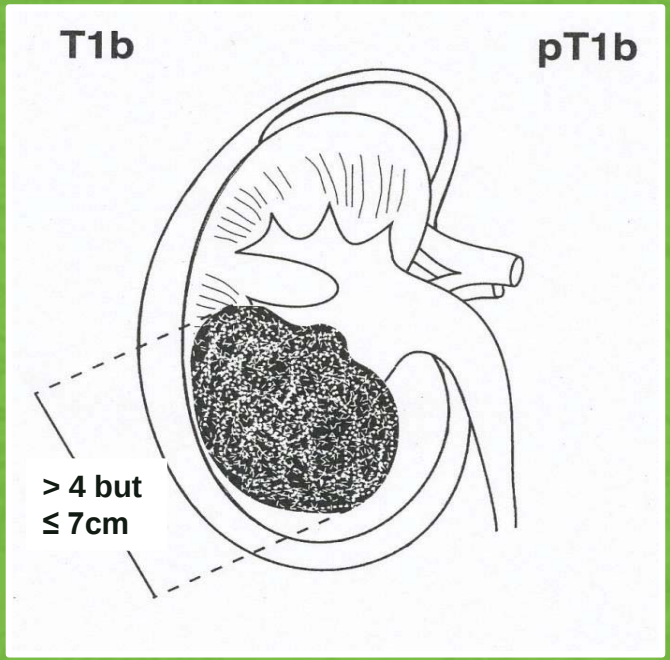
Measure any tumor invading into extracapsular tissue

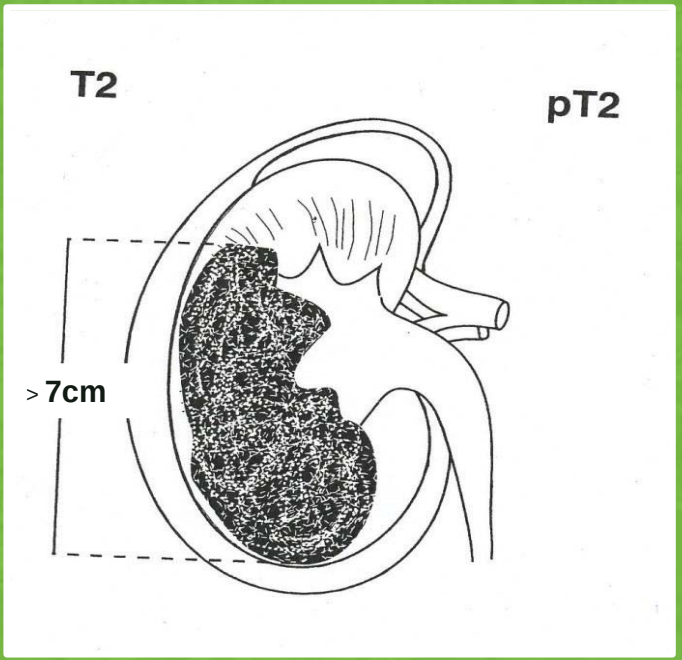
Do not measure tumor invading into renal/caval vein

Stage T1 and T2
Tumor limited to kidney!

TNM 2009 (7th edition) same in AJCC/TNM 2017 (8th edition)







T2a (>7 cm but ≤10 cm)
T2b (>10 cm)

How many blocks should you submit for examination?

Important to assess tumor relationship with:

Renal capsule (perirenal fat)

Renal sinus

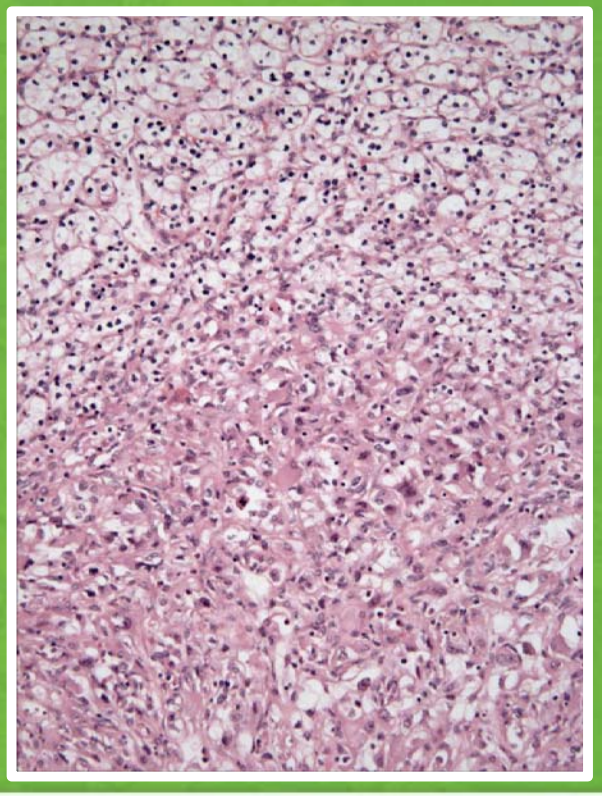
Adrenal gland

Renal pelvis

Areas of different appearance or consistency!

Sarcomatoid differentiation, necrosis etc.

Sarcomatoid carcinoma (dedifferentiation)



In any histologic type – poor prognosis! (report %)

Sampling of renal tumor for examination

One block per cm,

minimum of 3 blocks

(subject to modification)

Multiple renal tumors

Hereditary:

Von Hippel Lindau disease

Birt-Hogg Dubbé Sy

Hereditary papillary carcinoma

Tuberous sclerosis

Oncocytosis

Sporadic:

Table 1 | Frequency of multifocality in renal cell carcinoma

Study	Patients (*n*)	Multifocal disease (*n*)	Prevalence of multifocal disease (%)
Dimarco *et al.* (2004)[18]	2,373	101	4.3
Richstone *et al.* (2004)[22]	1,071	57	5.3
Crispen *et al.* (2008)[17]	1,113	60	5.4
Oya *et al.* (1995)[36]	108	7	6.5
Cheng *et al.* (1991)[29]	100	7	7.0
Saiki *et al.* (1995)[37]	43	3	7.0
Nissenkorn *et al.* (1995)[35]	27	3	11.1
Wunderlich *et al.* (1999)[26]	260	36	13.9
Lang *et al.* (2004)[19]	255	37	14.5
Gohji *et al.* (1997)[30]	64	10	15.6
Kletscher *et al.* (1995)[33]	100	16	16.0
Junker *et al.* (2002)[31]	372	61	16.4
Schlichter *et al.* (2000)[38]	281	48	17.1
Karayiannis *et al.* (2002)[32]	56	10	17.8
Mukamel *et al.* (1988)[34]	66	13	19.7
Baltaci *et al.* (2000)[28]	103	22	21.4
Whang *et al.* (1995)[39]	44	11	25.0

Bratslavsky, G. & Linehan, W. M. *Nat. Rev. Urol. 2010; 7: 267–275*

Multiple renal tumors

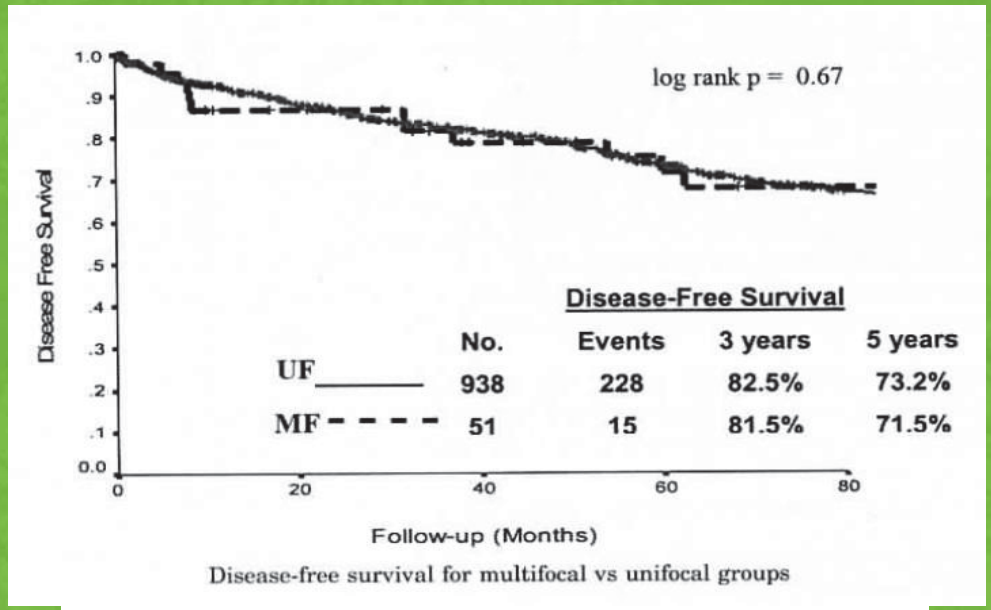
Papillary RCC and bilateral more common

Index and satellite tumors mostly identical

Discordant TU 17-26% (clear cell + papillary)

Likely local recurrence if nephron-sparing surgery

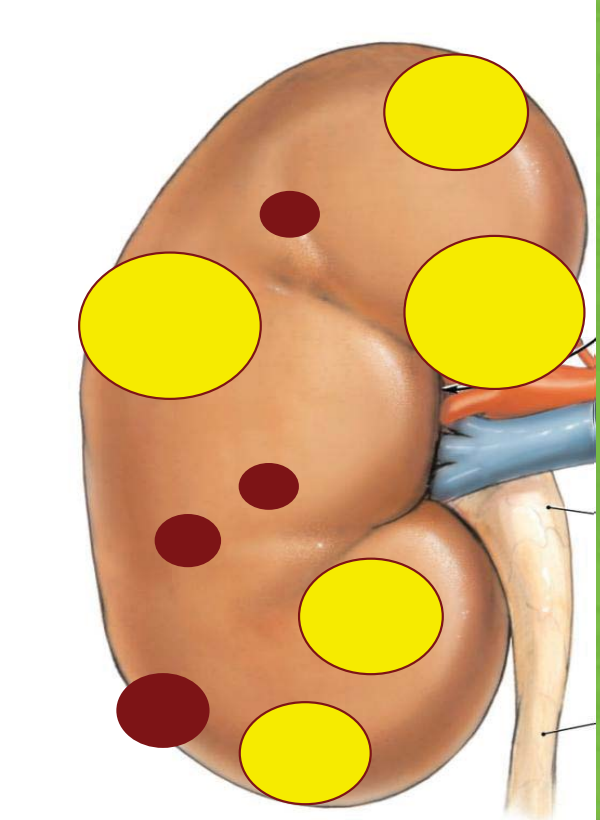
Prognosis (with radical surgery)



Disease-free survival for multifocal vs unifocal groups

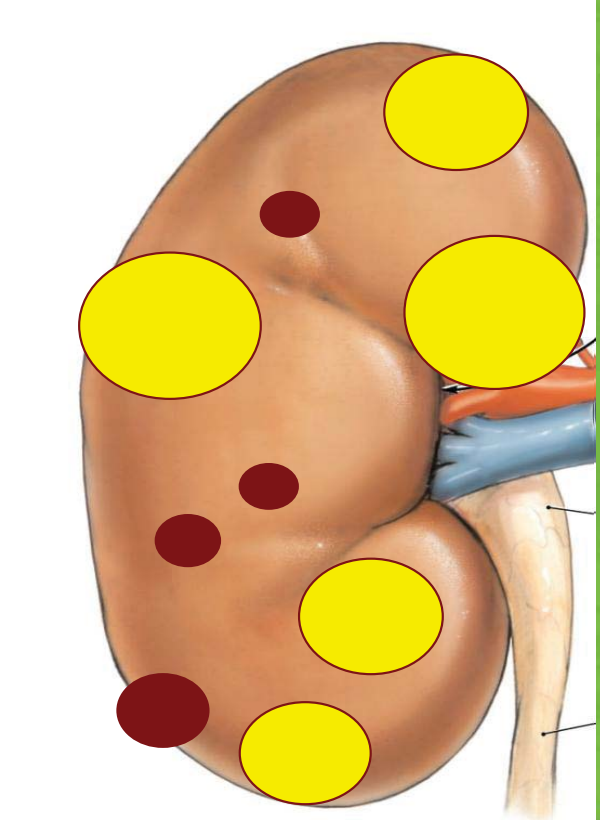
Richstone L et al *J Urol 2004; 171, 615–620*

Measurement of multiple tumors



Measure and report tumor dimensions for all tumors, up to a maximum of 5

Sampling and staging of multiple tumors



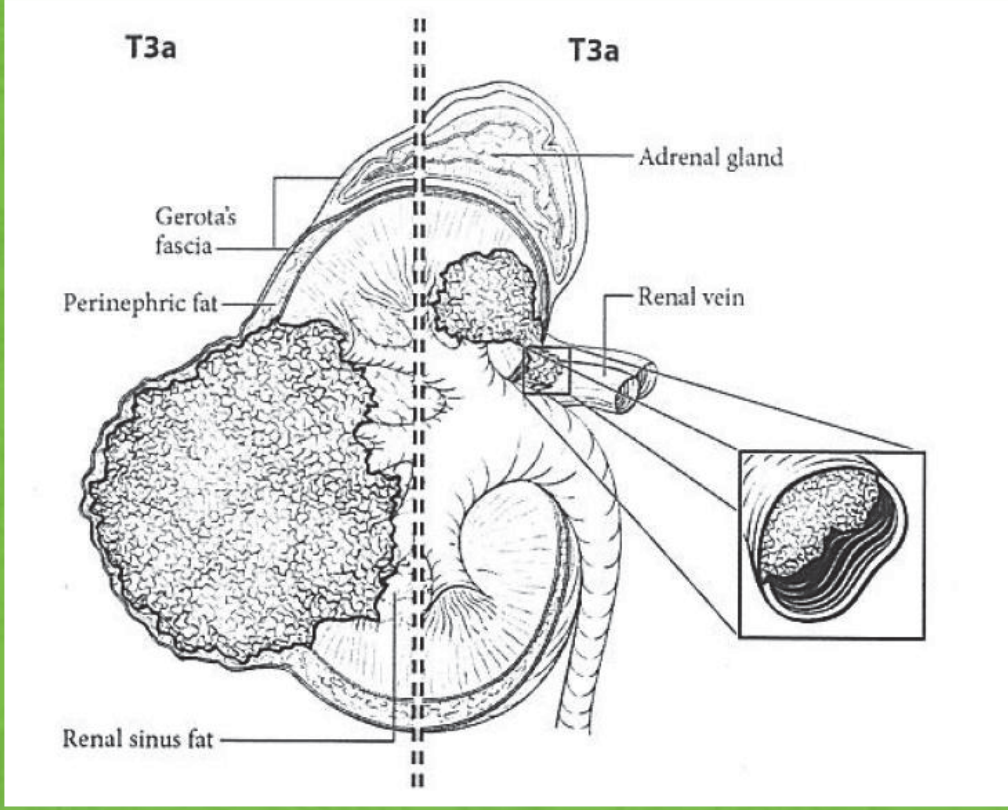
Minimum of 5 largest tumors (if smaller look similar)

If uncertain about histologic type or adverse findings in remaining tumors, do additional sampling

Largest T used – label with (m)
mpT

Different subtype – separate stage

Stage pT3a



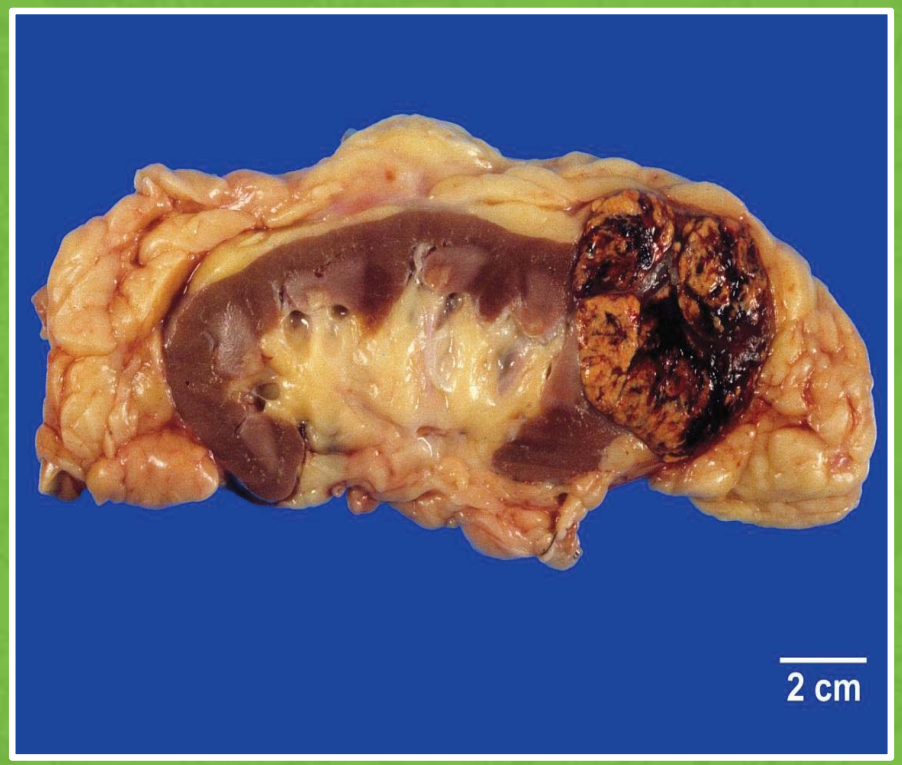
pT3

Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia

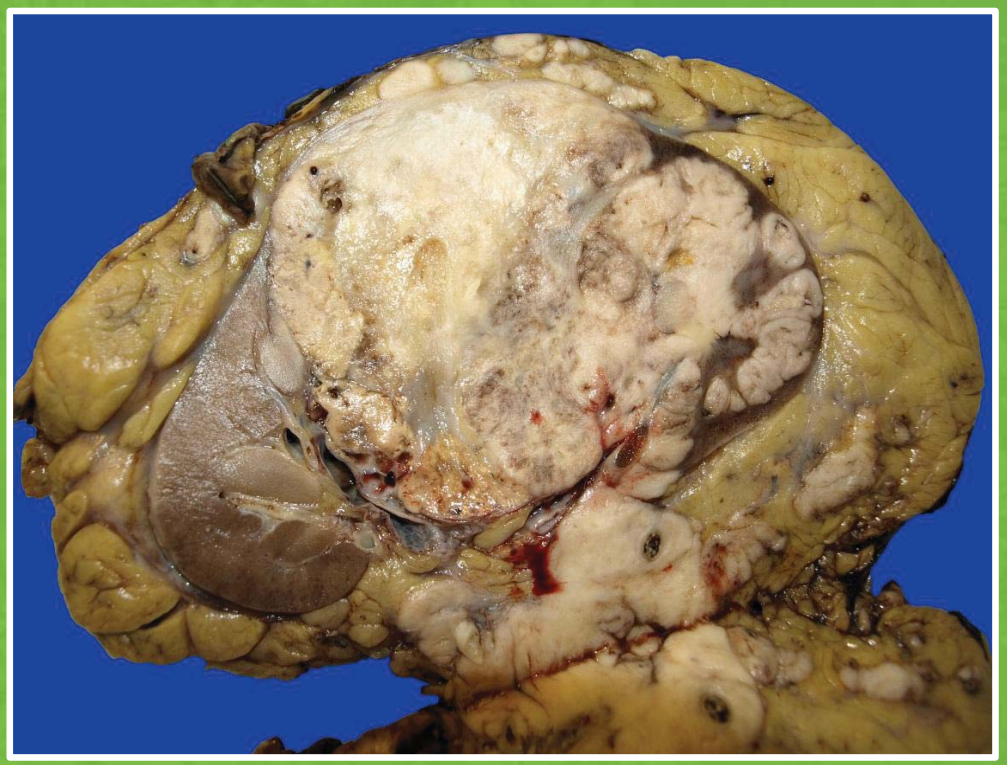
pT3a

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

Assesment of perinephric fat invasion (pT3a)

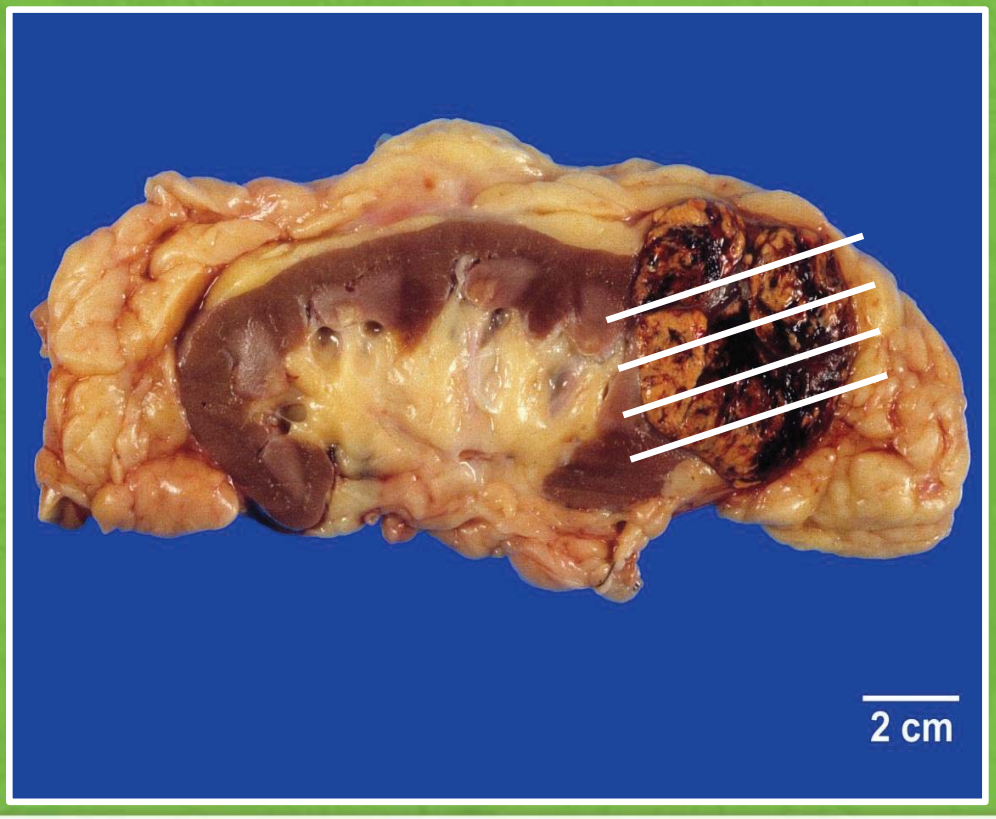


Pushing border, even if beyond normal kidney, NOT diagnostic of fat invasion



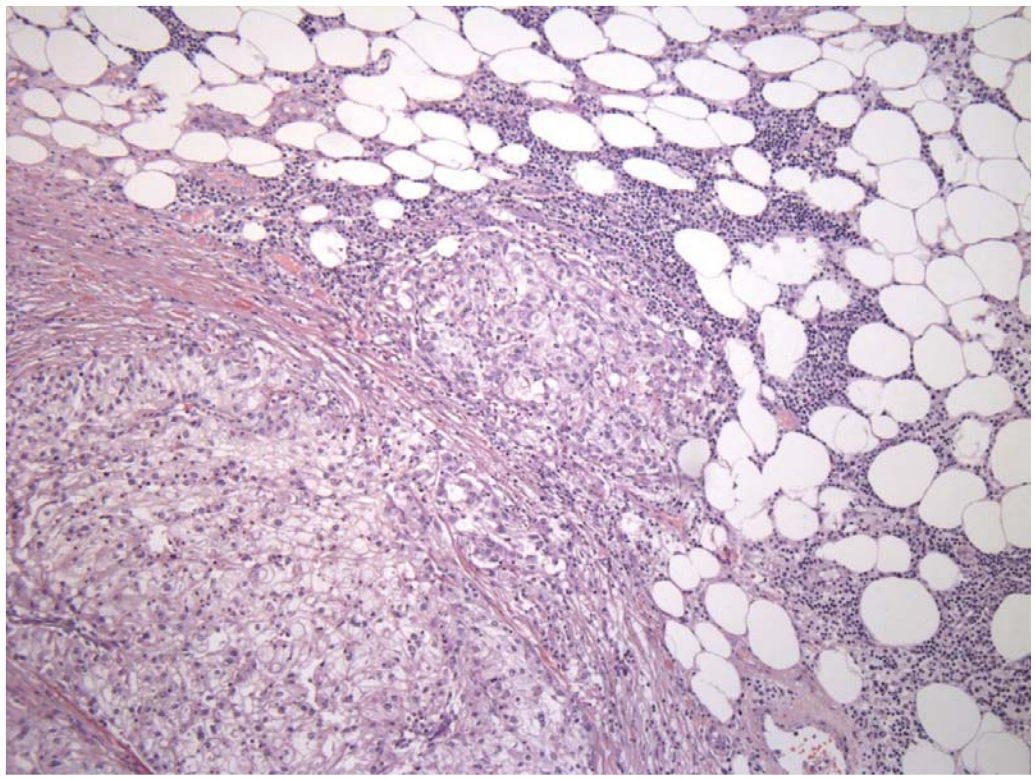
Invasion: lost smooth interface, or irregular nodules protruding into fat

Assesment of perinephric fat invasion (pT3a)

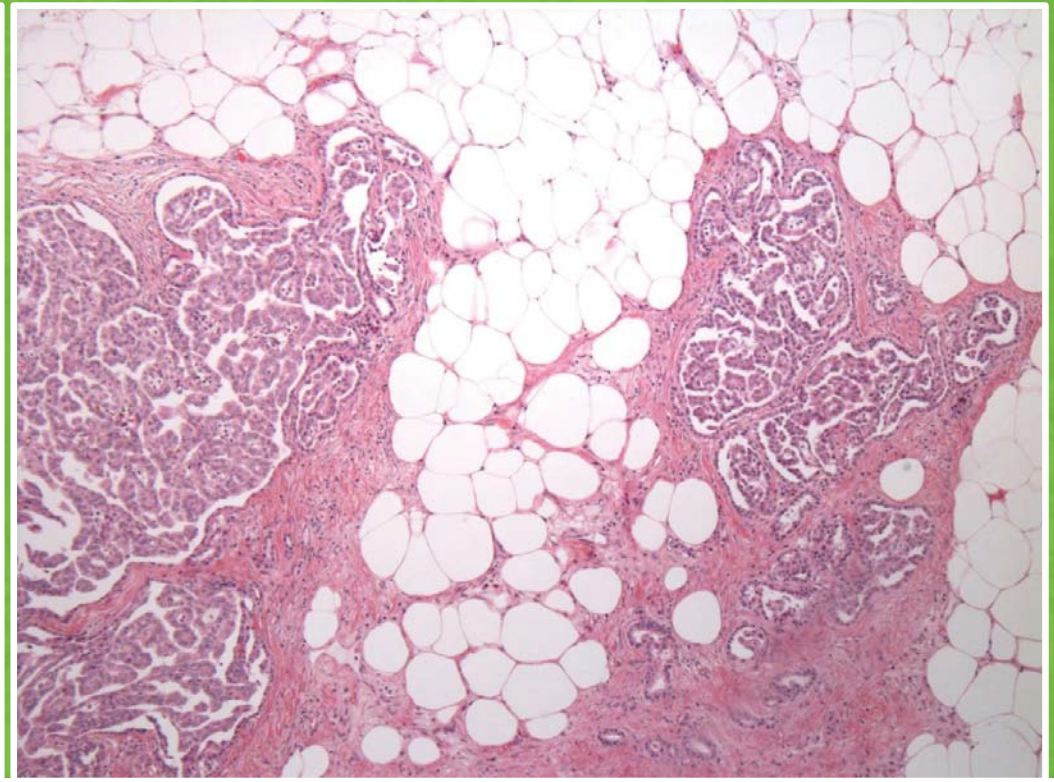


Multiple perpendicular sections of tumor fat interface

Assesment of perinephric fat invasion (pT3a) - micro

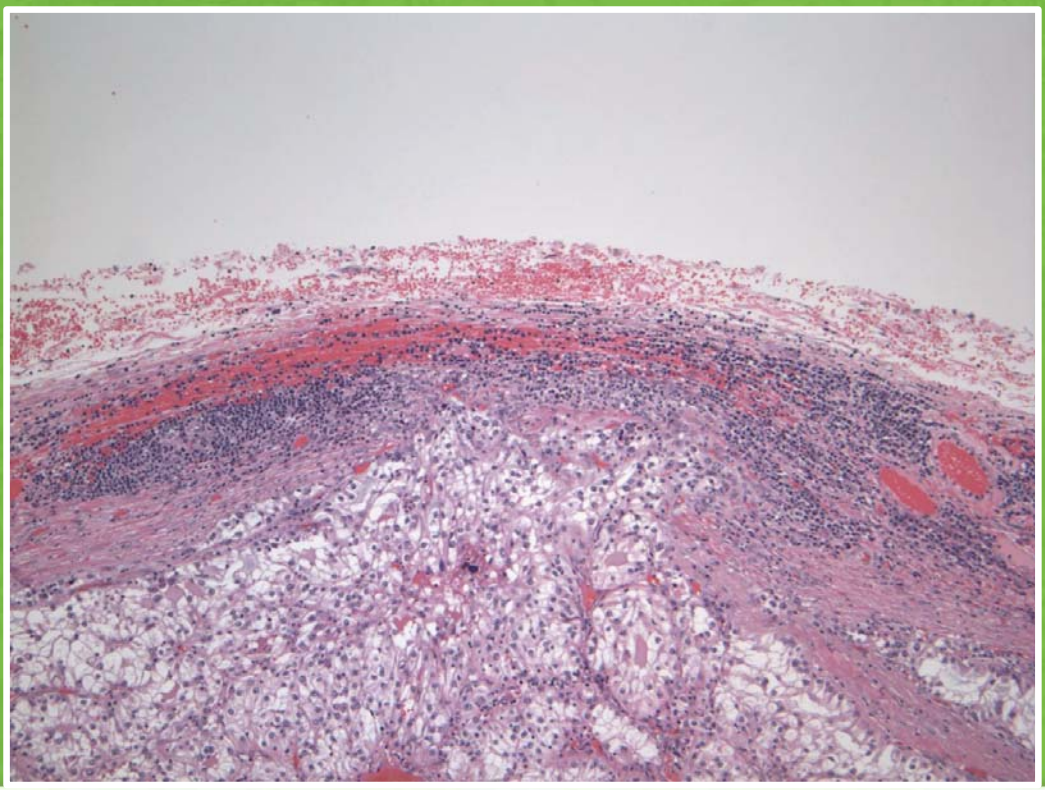


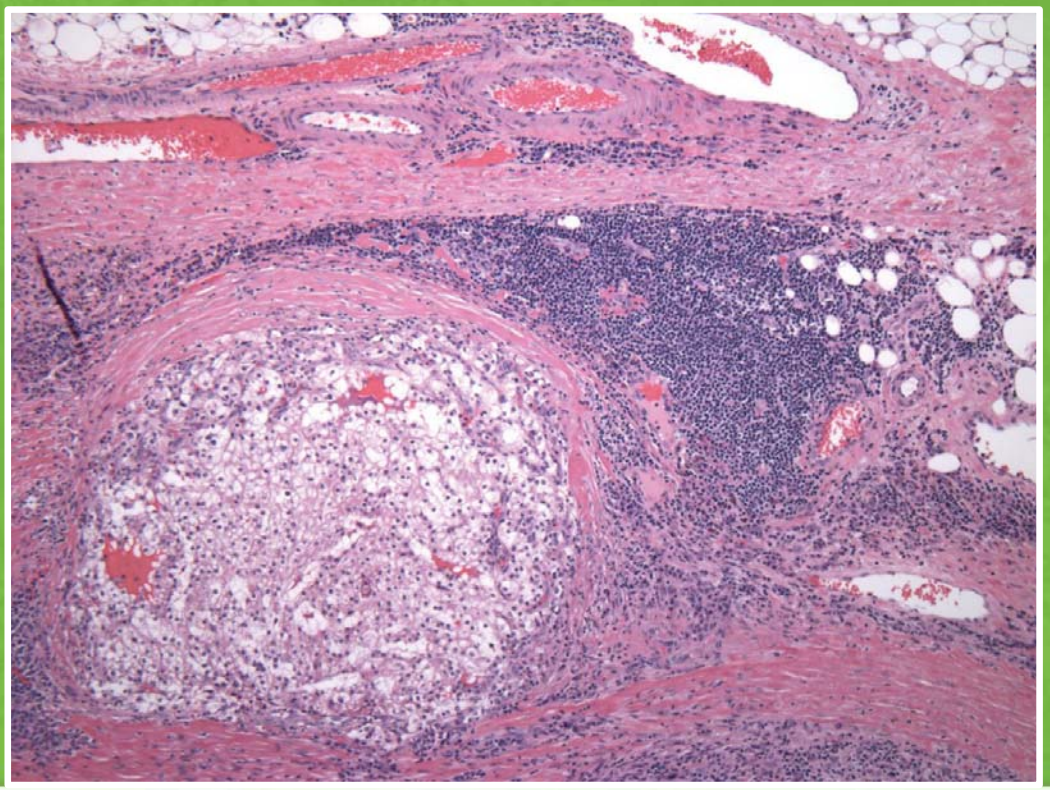
Tumor touching fat



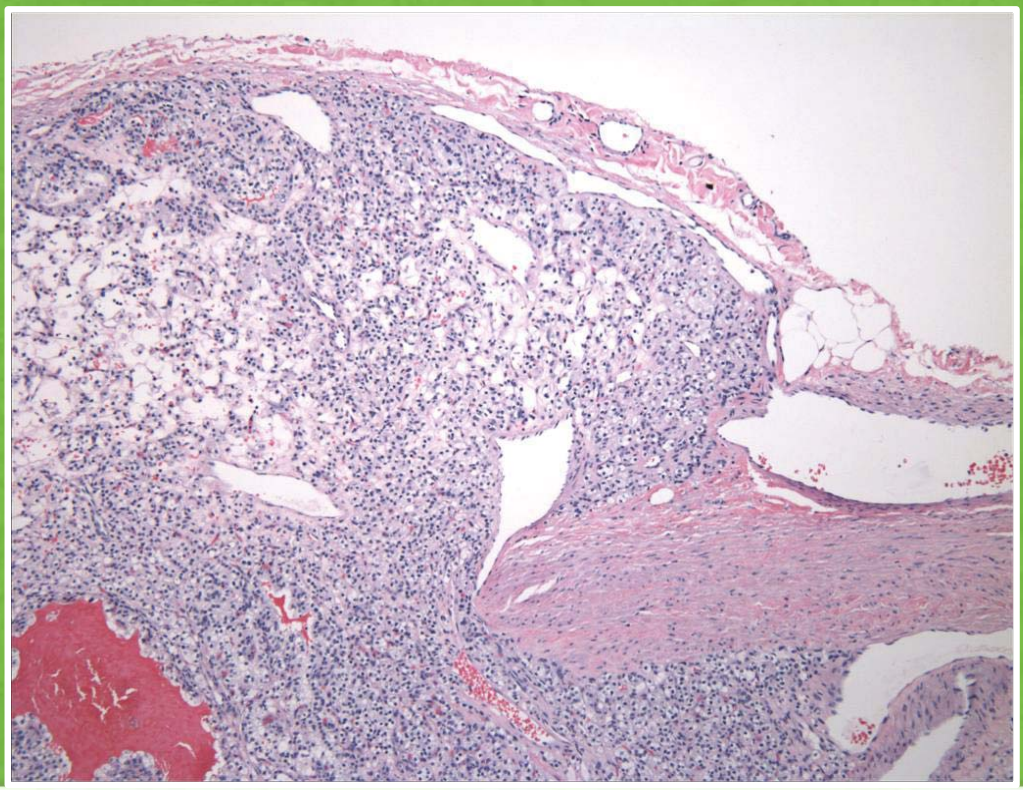
Tumor extending as irregular tongues into fat (with or without desmoplasia)

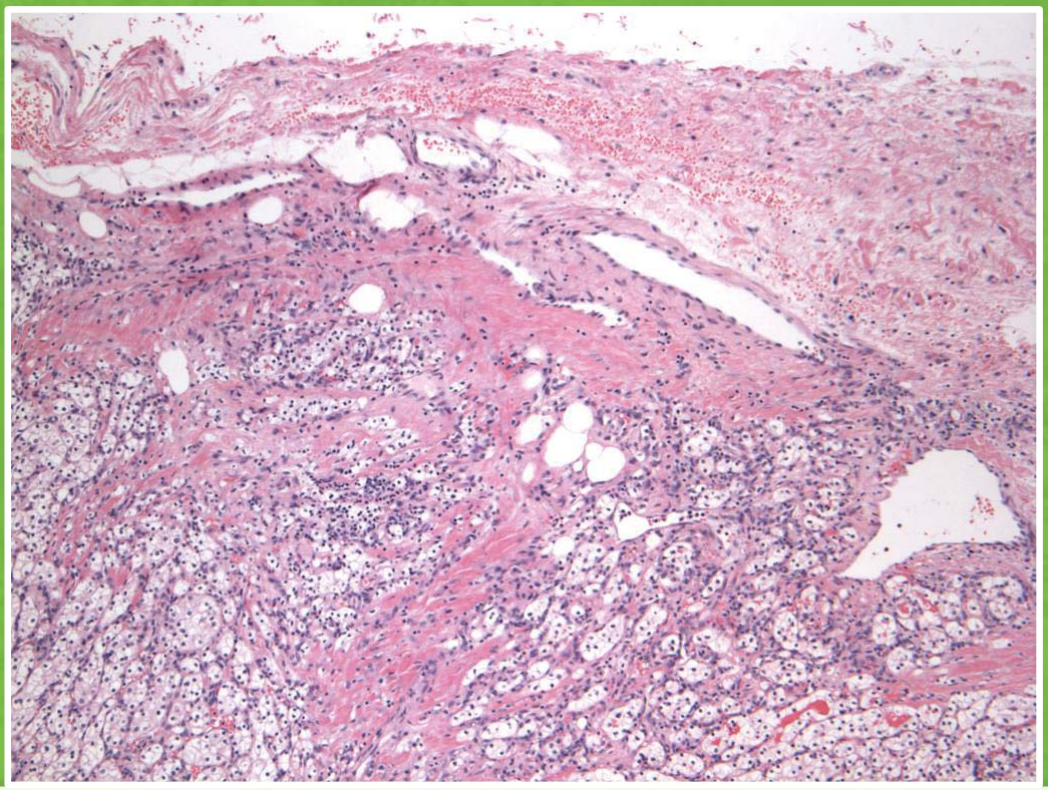
Problematic perinephric fat invasion (pT3a)



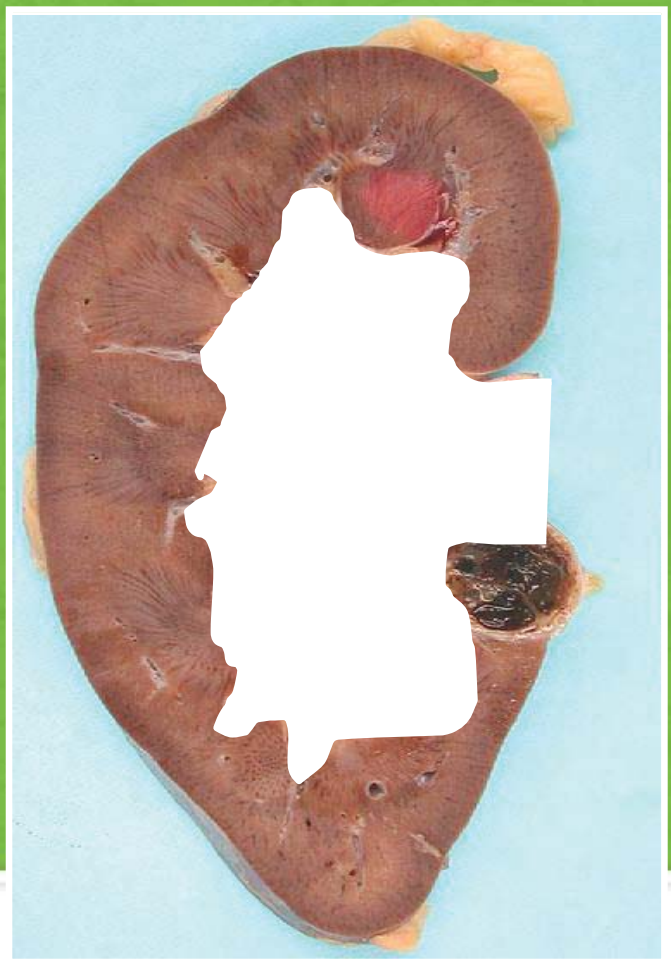


Problematic perinephric fat invasion (pT3a)





Renal sinus

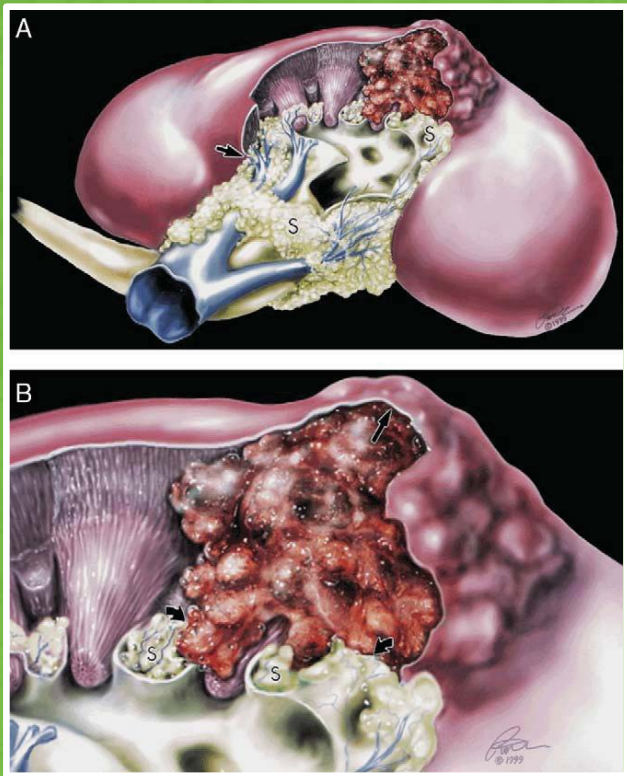


Central perinephric fat compartment

Between pelvicalyceal system and renal parenchyma

Main lymphovascular supply of kidney

Renal sinus invasion (pT3a)



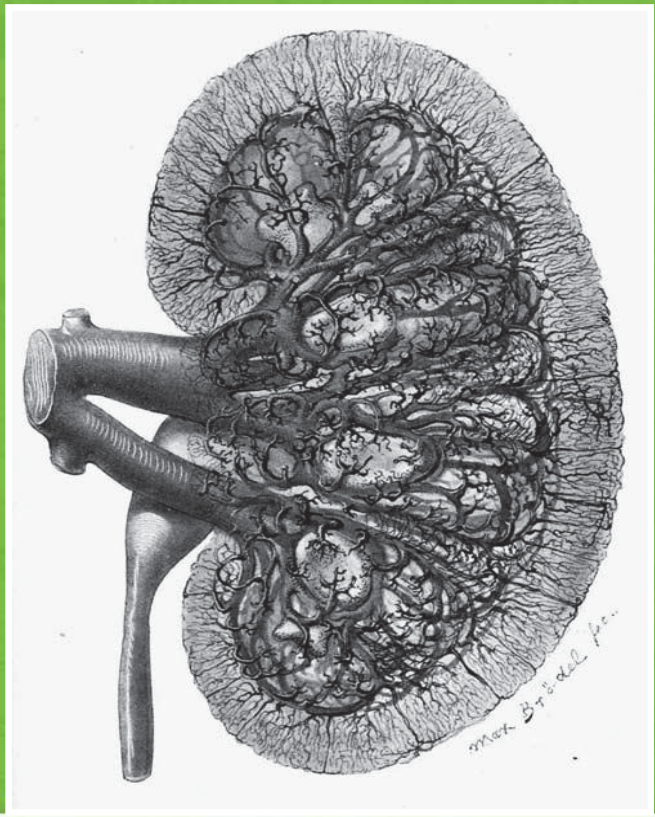
Principal route for extrarenal extension:

Clear cell RCC, but also other types

>90% of clear cell RCCs ≥7 cm invaded renal sinus

Bonsib SM. *J Urol.* 2005;174:1199-1202.

Renal sinus invasion (pT3a)



Invasion into sinus - worse prognosis than perinephric fat invasion

Recognition of renal sinus invasion in the last 10-15 years prompted practice changes

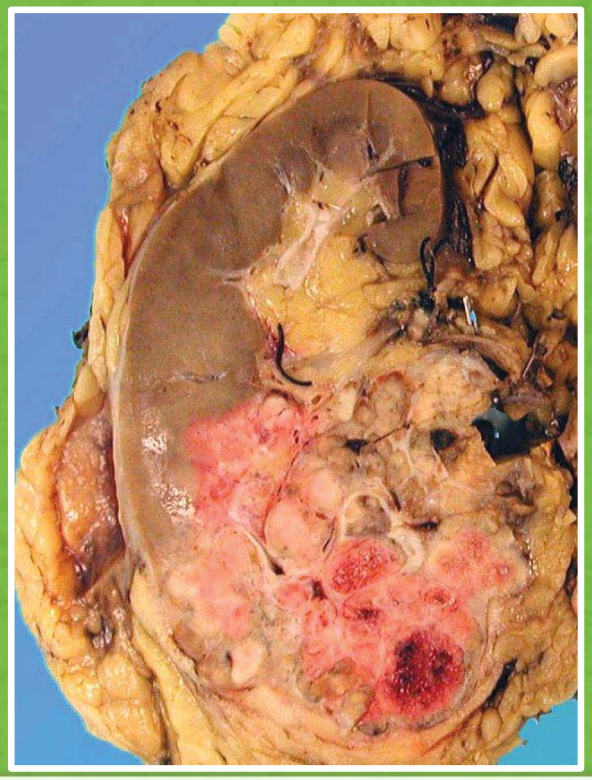
Targeted sampling of renal sinus in nephrectomies – routine practice!

Brödel M. Johns Hopkins Hospital Bulletin 1901;118:10–13.

Renal sinus invasion - sampling

If sinus invasion **grossly evident, or obviously absent,** *(e.g. small peripheral tumor):*

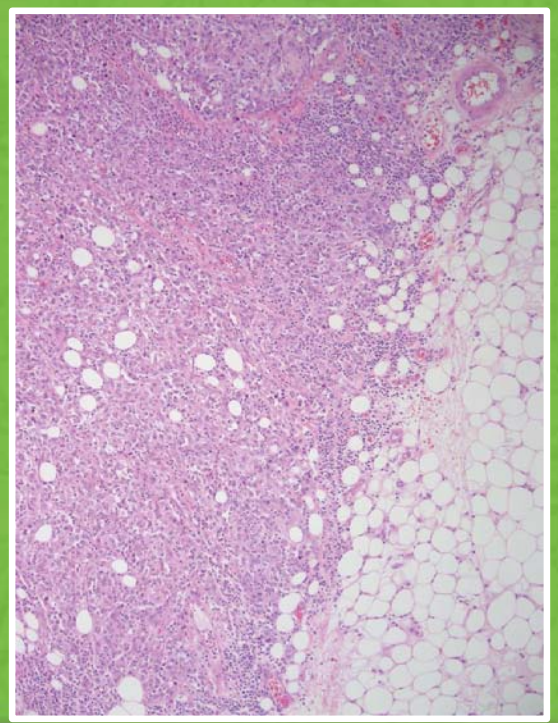
Sample only 1 block to confirm sinus invasion present or absent



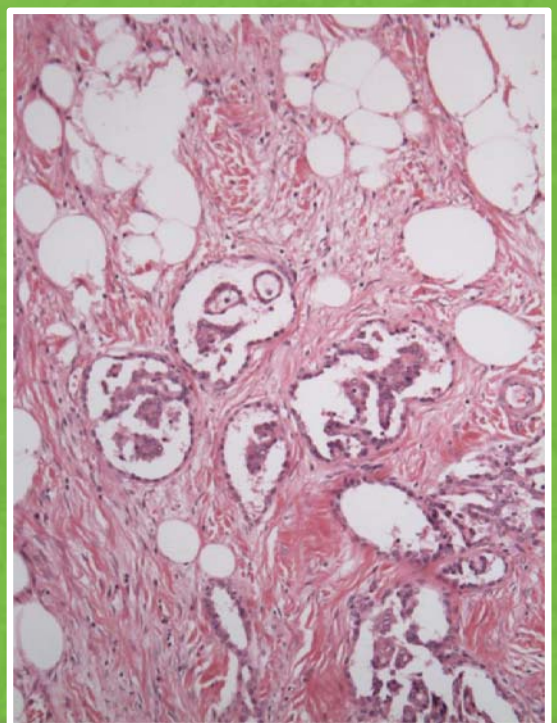
When uncertain if sinus invasion present:

Sample at least 3 blocks of tumor – sinus interface

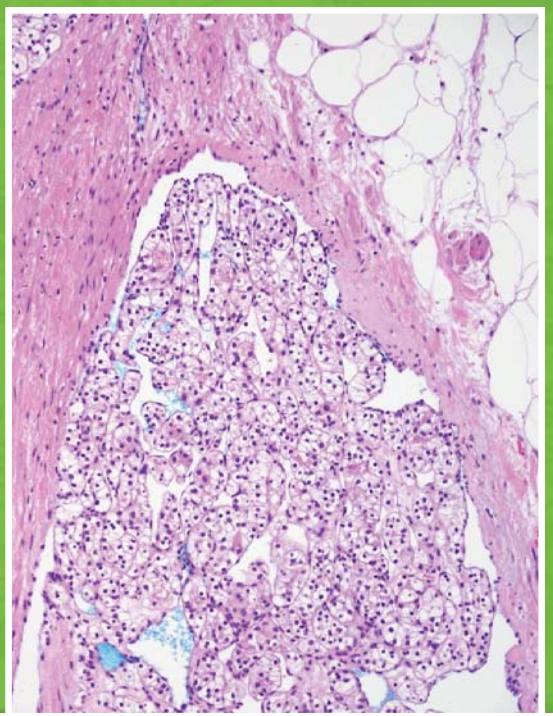
Renal sinus invasion present on micro if tumor seen in:



Direct contact with sinus fat

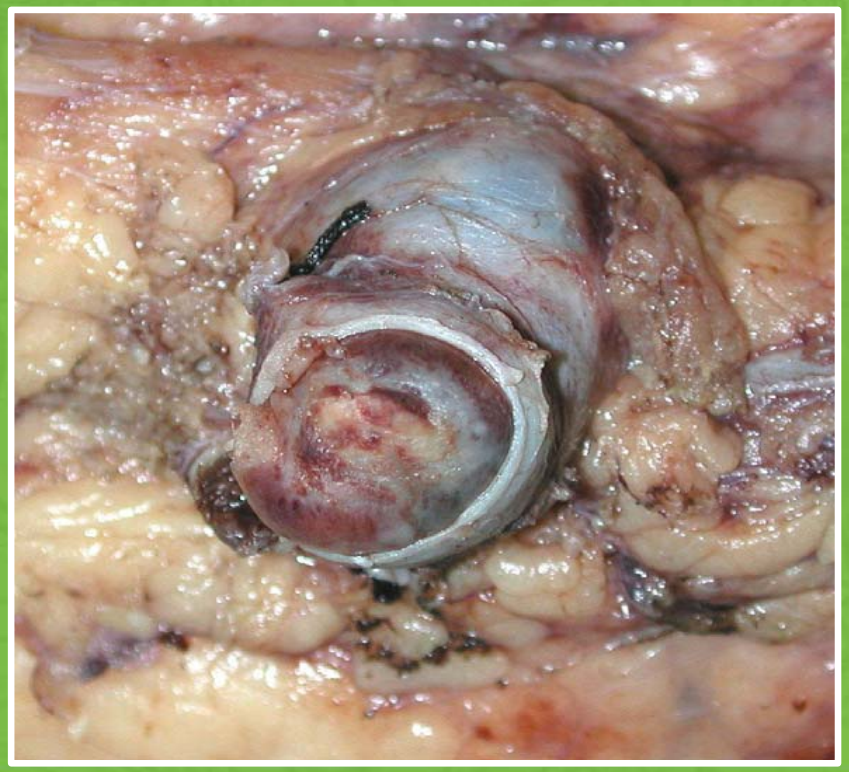


In loose connective tissue beyond renal parenchyma



Any endothelial lined space within sinus, regardless of size

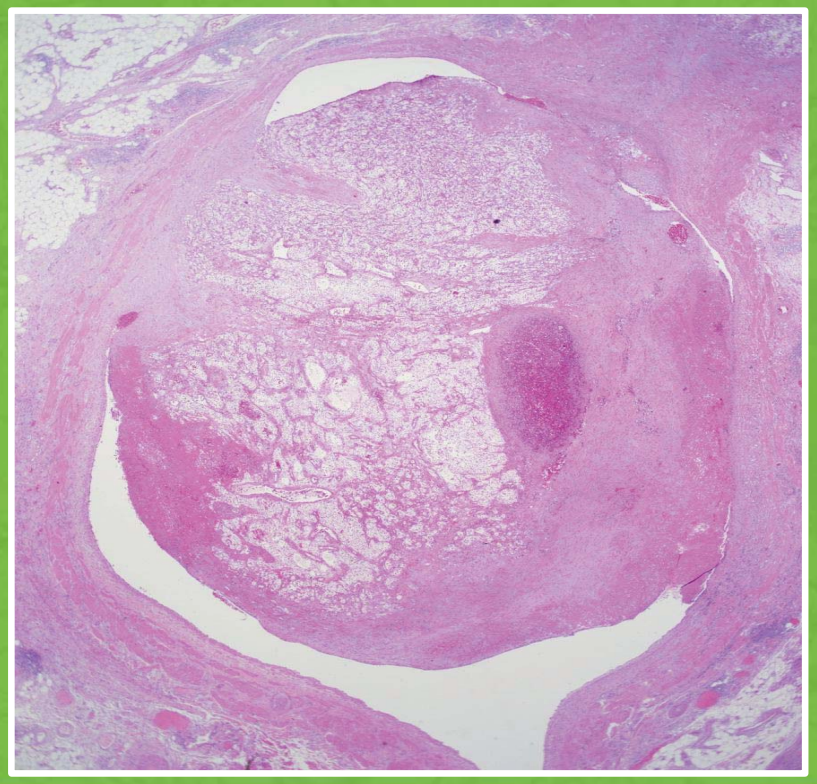
Renal vein invasion – AJCC 8th edition



Renal vein invasion (pT3a):

"tumor (grossly) extends into renal vein or segmental branches"

Renal vein invasion

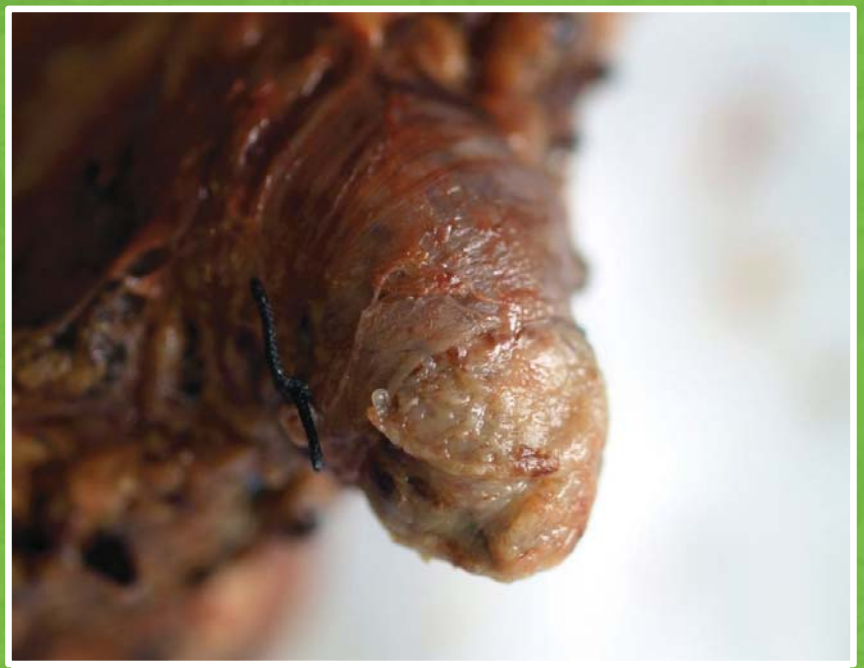


Tumor attached to the vessel wall or

Tumor fills and distends vessel lumen

Vein invasion in the renal sinus (segmental)

Renal vein and margin sampling



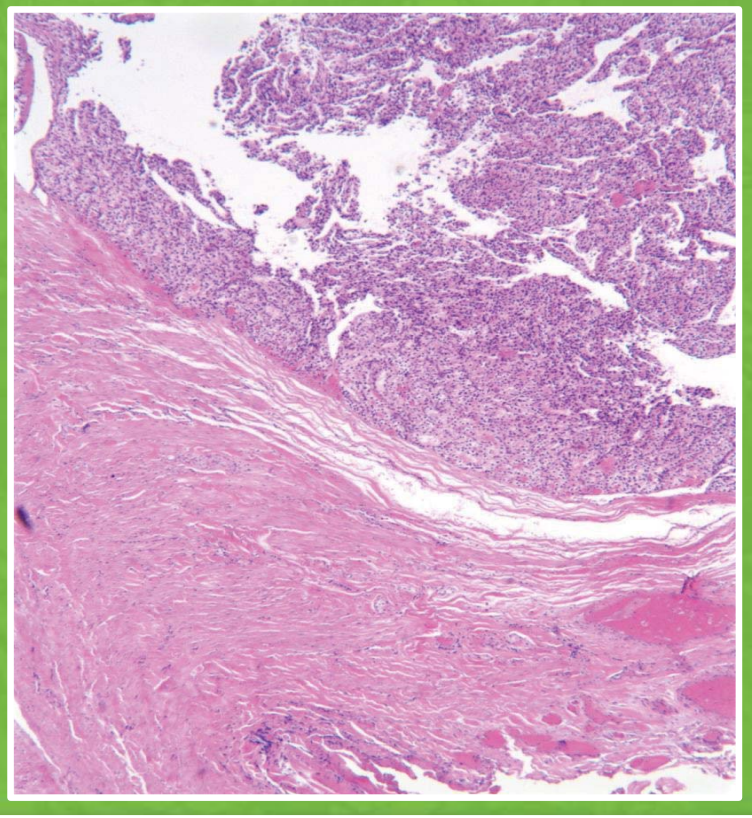
Renal margin negative – retraction of vein after fixation

Submit actual margin

+

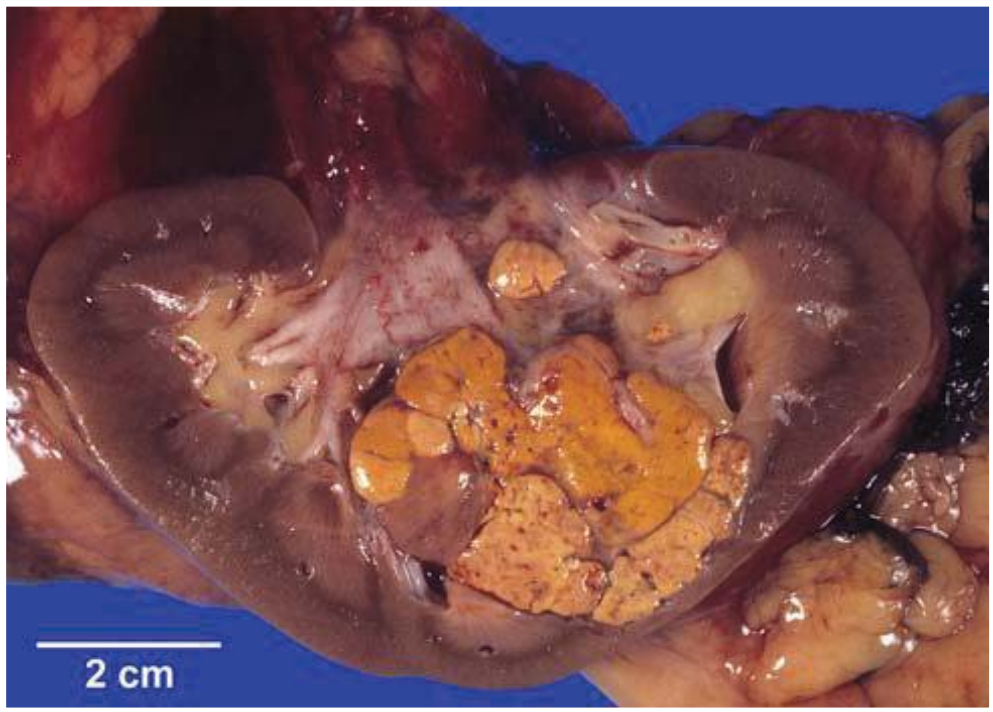
Additional sections of tumor thrombus, if grossly suspected to be adherent to vein wall

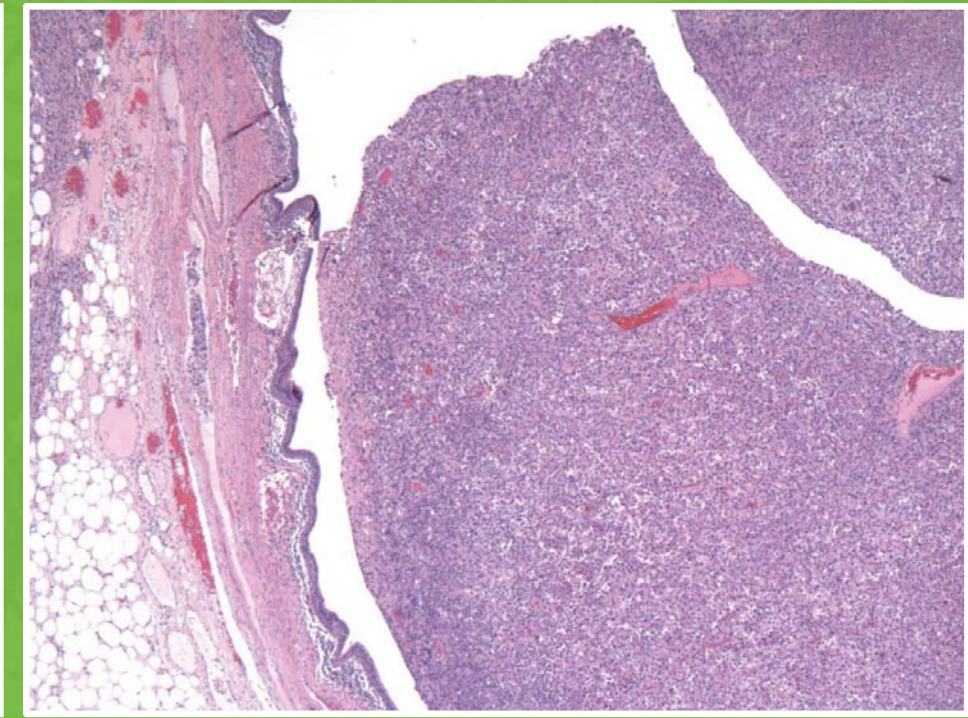
Renal vein margin positivity



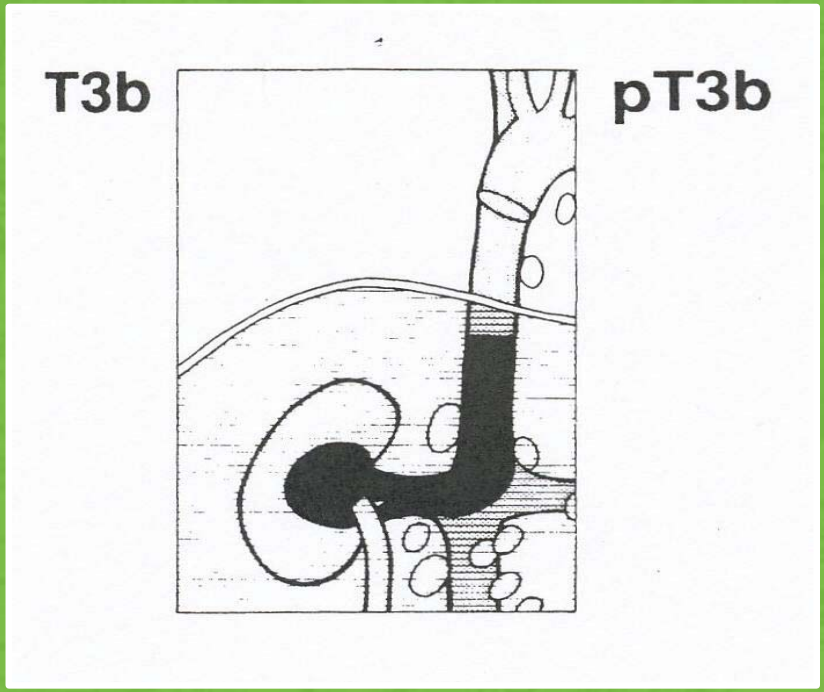
Renal margin positive only if tumor adherent at actual margin, confirmed microscopically

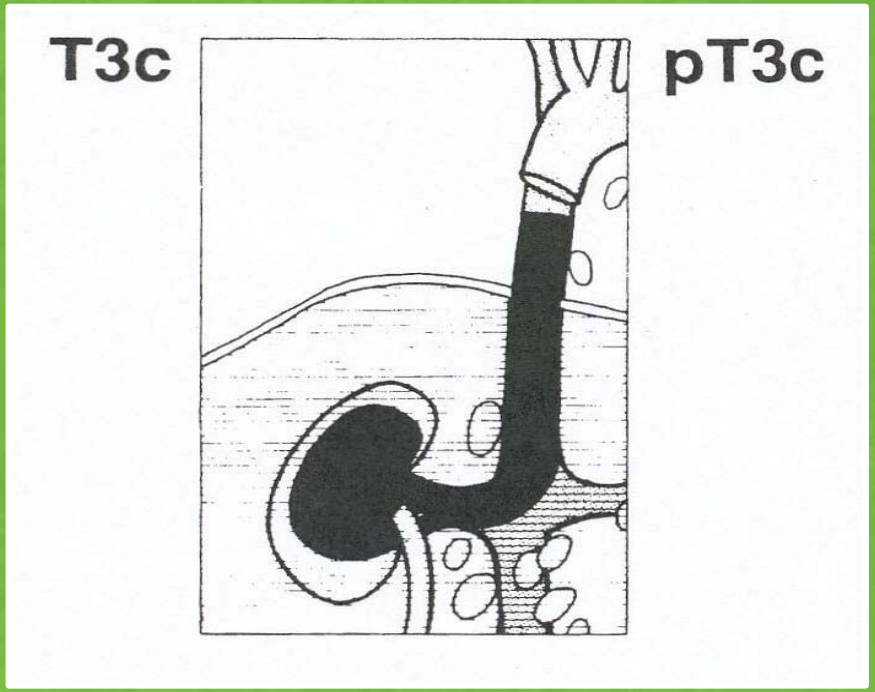
Invasion into pelvicalyceal system = pT3a (new in AJCC 8th edition)





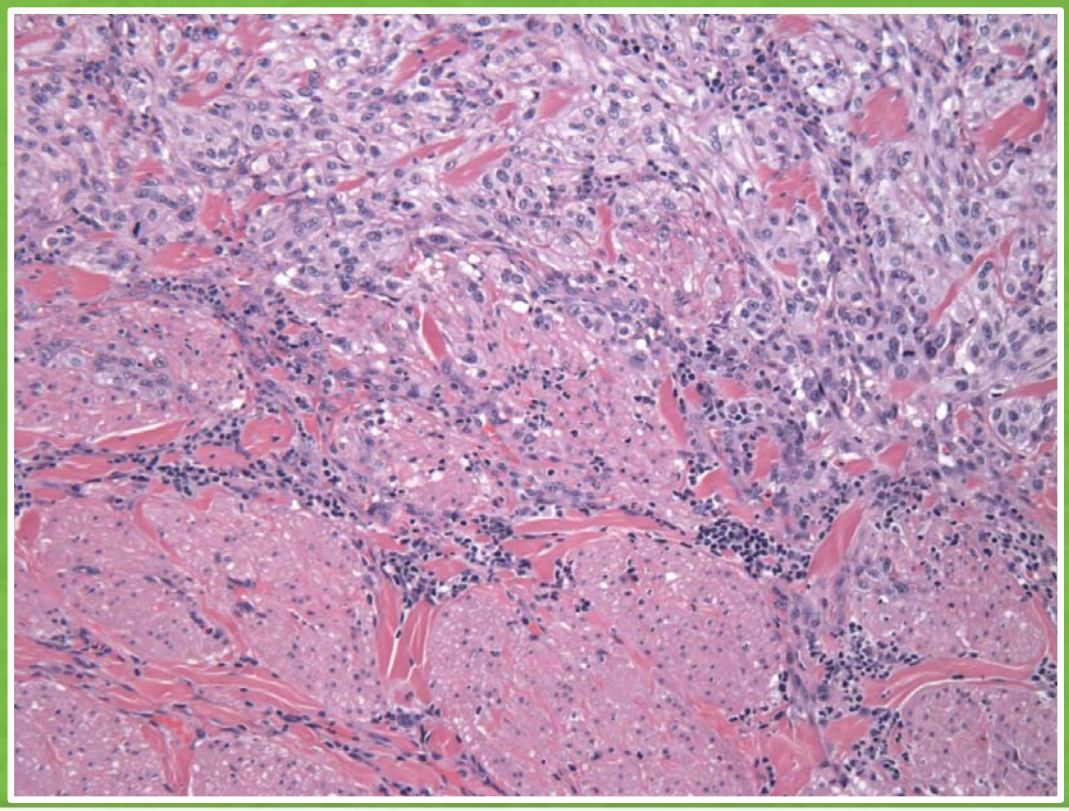
Vena cava invasion





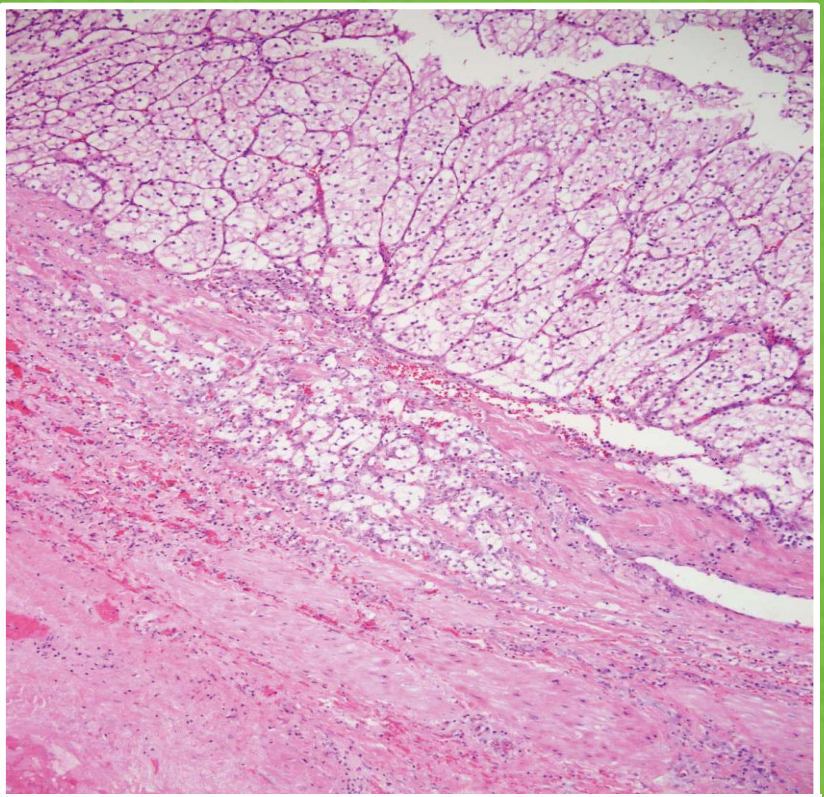
Tumor into vena cava below or above diaphragm

Vena cava invasion – pT3c



Tumor grossly extends into vena cava above diaphragm or invades wall of vena cava

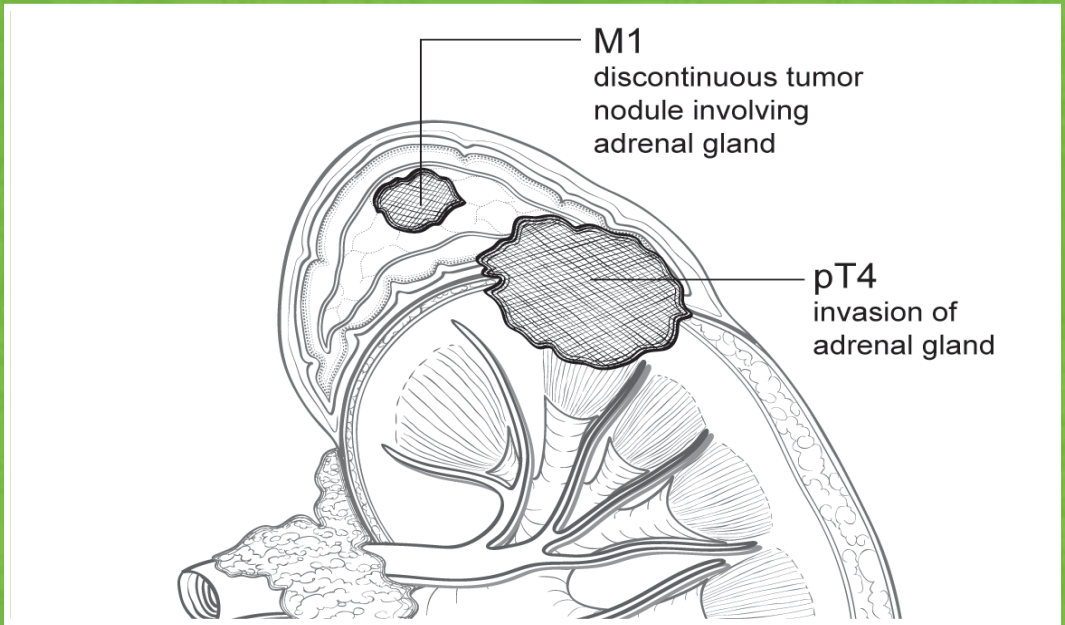
Specimen submitted as “caval thrombus”



Tumor invades the wall of vena cava (pT3c)

Include 2 or more sections to search for adherent caval wall tissue and possible invasion

Adrenal gland involvement

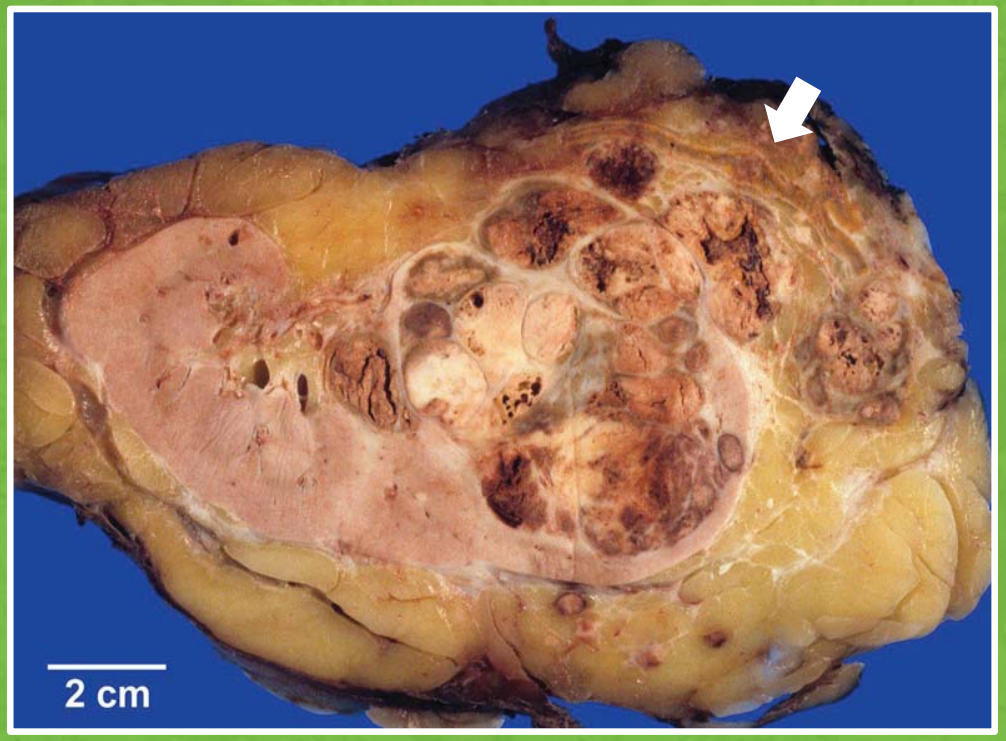


Contiguous spread (pT4)

Metastasis (pM1)

Prognostic significance!

Direct adrenal gland involvement - pT4

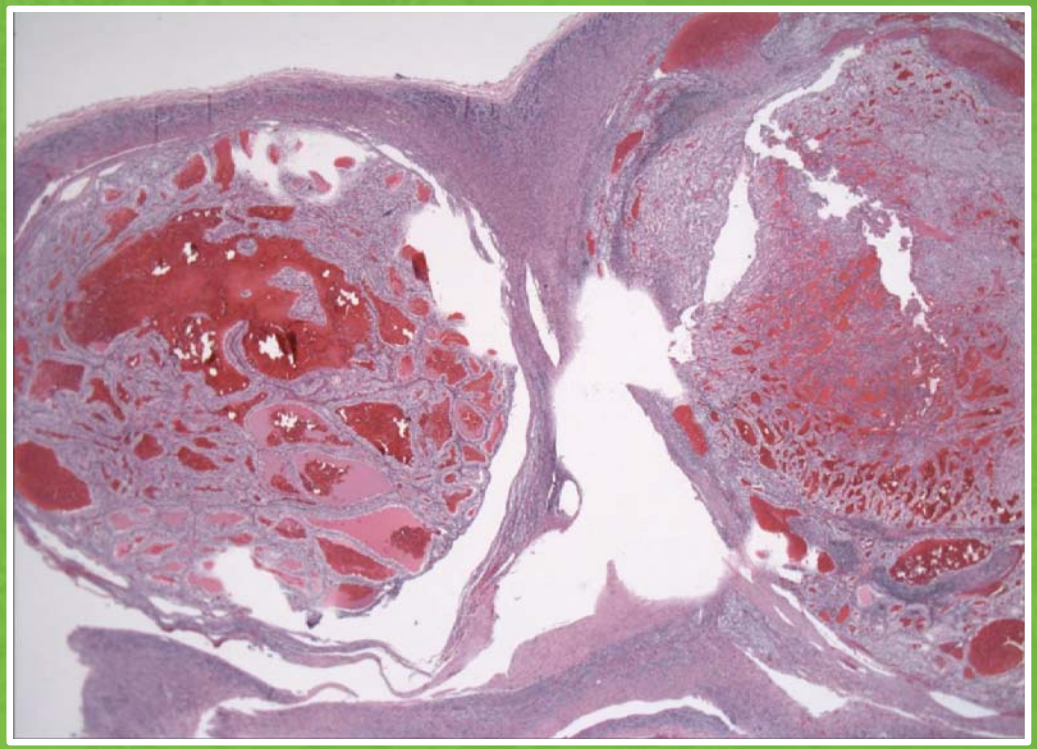


Direct invasion into adrenal – **pT4 disease**

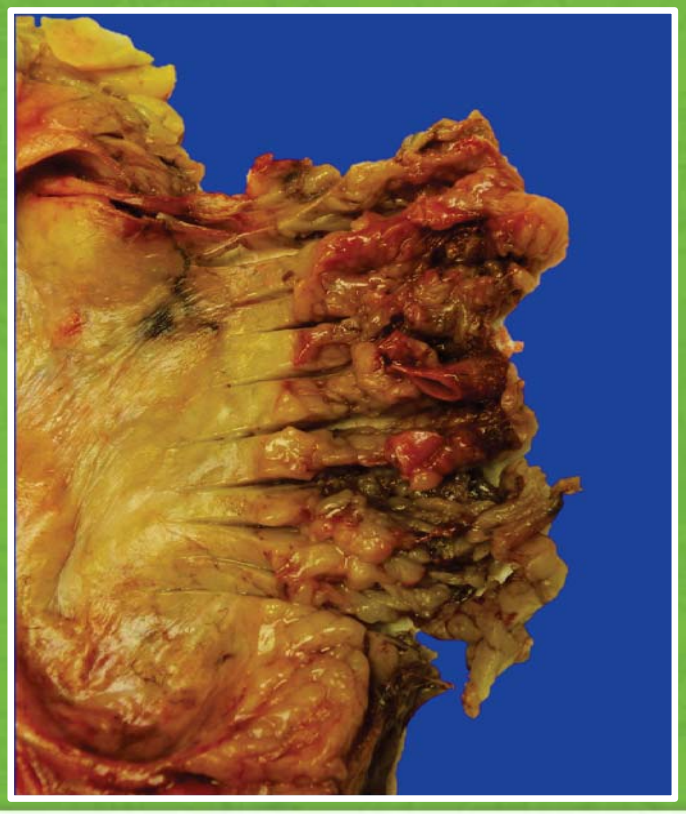
Associated with significantly worse prognosis than perinephric fat invasion!

Matches pT4 tumors (invasion into adjacent organs)

Metastatic adrenal gland involvement – M1



Assesment of hilar lymph nodes

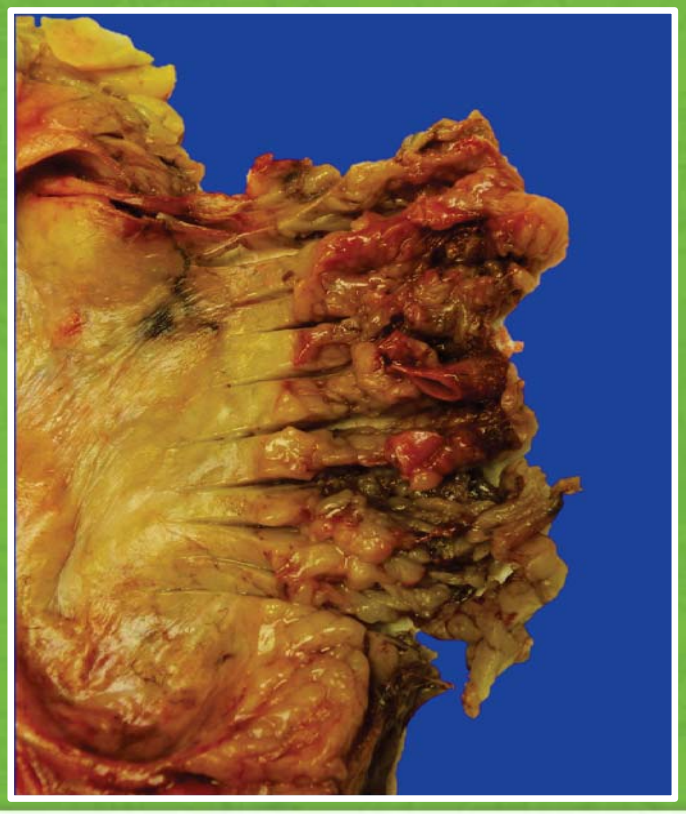


Restrict evaluation to palpation and dissection of hilar fat only

Nodes found in less than 10% of cases

Nodes rarely identifiable!

Assesment of hilar lymph nodes



Grossly visible hilar nodes positive in 80% of cases

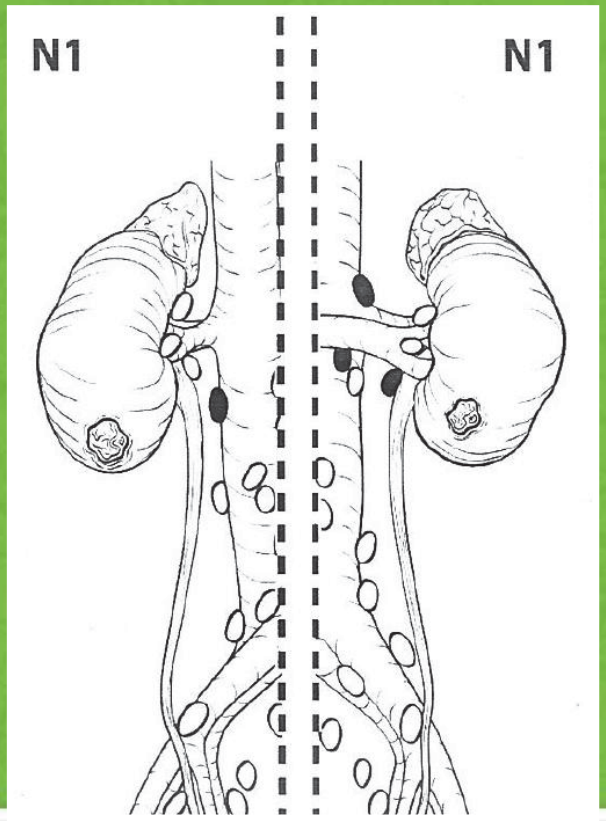
Microscopic nodes found in only 25% of cases

= all benign!

Searching for occult nodes not practical!

Mehta V et al. *Arch Pathol Lab Med* 2013; 137:1584-90.

Regional lymph nodes – N1

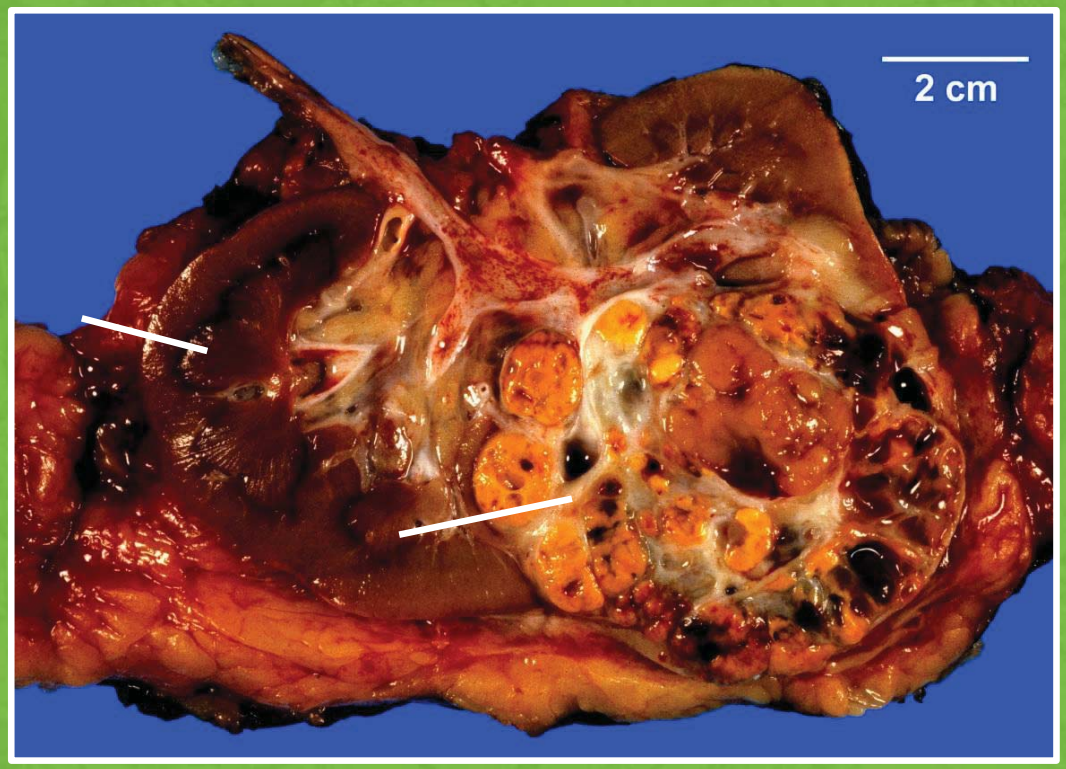


Single or multiple regional nodes involved

Examine all submitted separately

- Renal hilar
- Caval (pre-, para-, retro)
- Aortic (pre-, para-, retro-, interaortocaval)

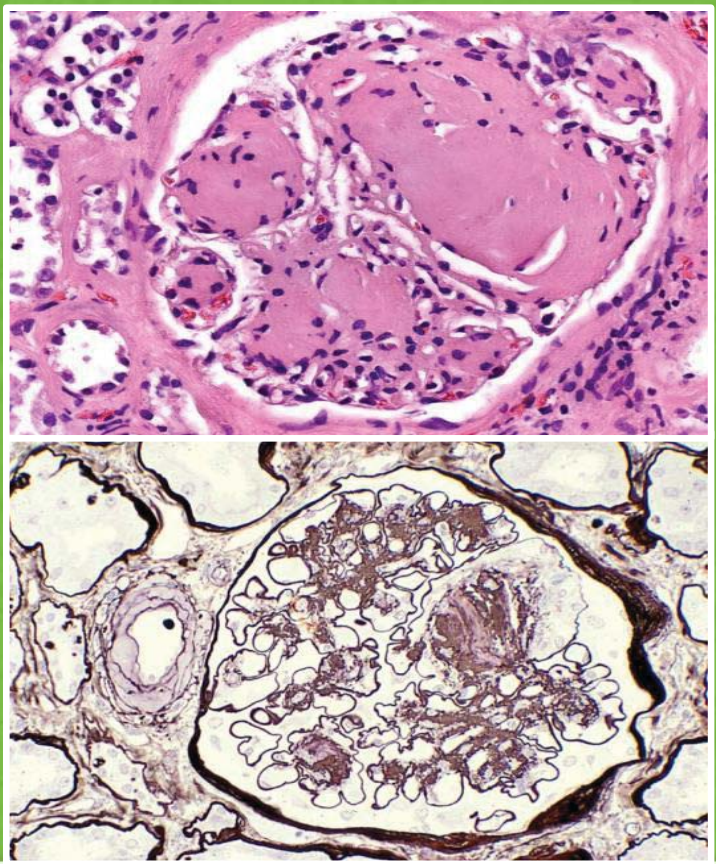
Sampling uninvolved renal parenchyma



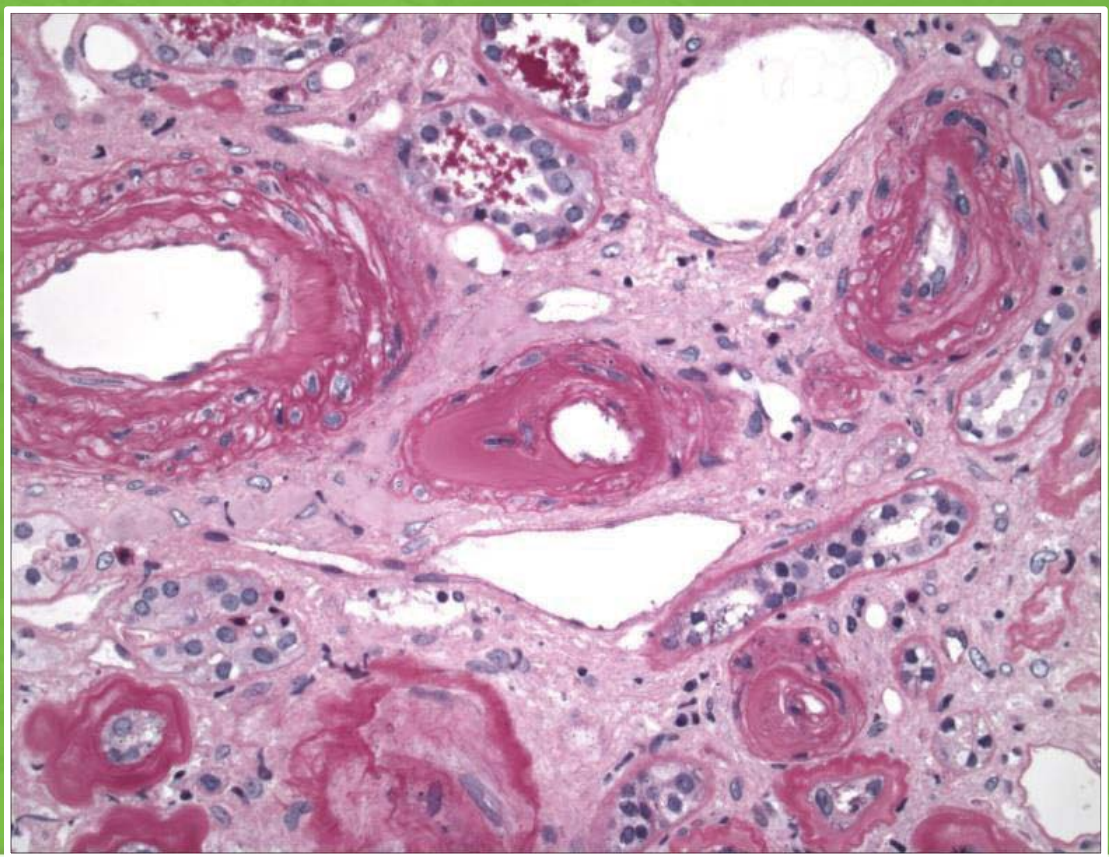
Adjacent to tumor, as well as distant from tumor

Routine assessment for concurrent glomerular, tubulointerstital and vascular kidney disease

Non-neoplastic kidney pathology



Diabetic nephropathy (KW nodules)



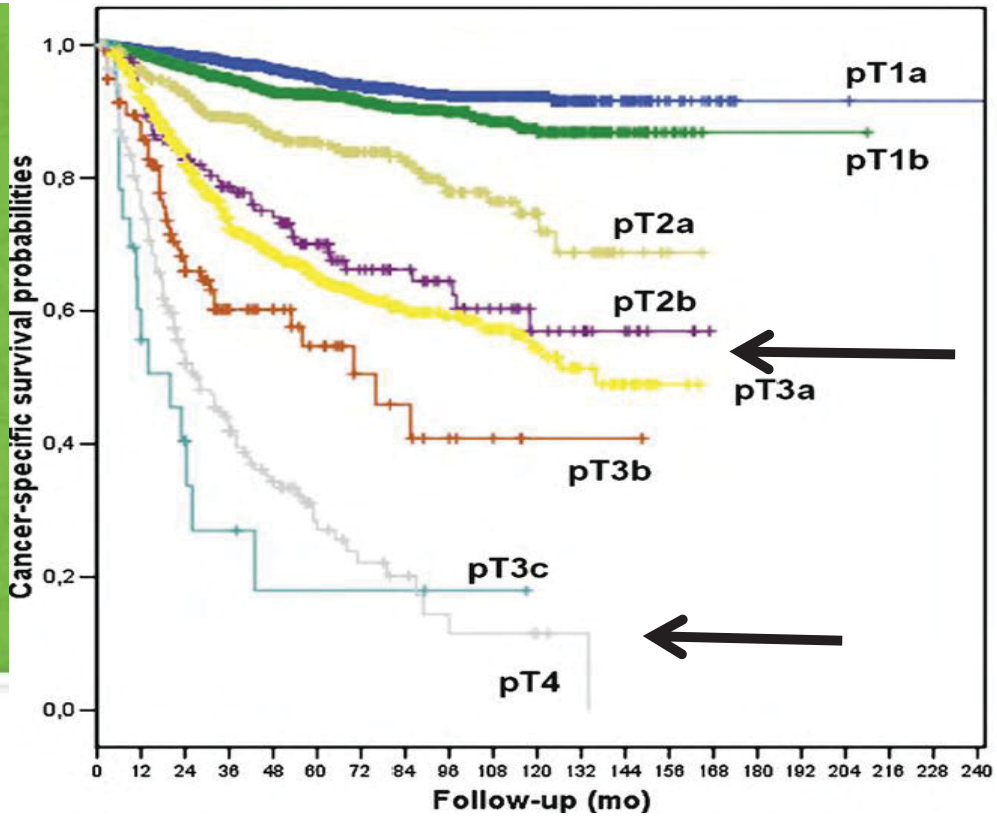
Hypertensive vascular disease

Validation of the 2009 TNM Version in a Large Multi-Institutional Cohort of Patients Treated for Renal Cell Carcinoma: Are Further Improvements Needed?

Giacomo Novara [a], Vincenzo Ficarra [a,], Alessandro Antonelli [b], Walter Artibani [a], Roberto Bertini [c], Marco Carini [d], Sergio Cosciani Cunico [b], Ciro Imbimbo [e], Nicola Longo [e], Guido Martignoni [f], Giuseppe Martorana [g], Andrea Minervini [d], Vincenzo Mirone [e], Francesco Montorsi [c], Roberto Schiavina [g], Claudio Simeone [b], Sergio Serni [d], Alchiede Simonato [h], Salvatore Siracusano [i], Alessandro Volpe [j], Giorgio Carmignani [h]*

members of the SATURN Project–LUNA Foundation [1]

Eur Urol 2010; 58: 588-95



It is expected that AJCC 8th edition staging for renal cancer will perform (at least) as well as the 7th AJCC/TNM edition

Take home messages

Proper staging depends on adequate sampling of renal specimens

Stage is key to prognostication of renal cancer patients

AJCC 8th edition introduces some (minor) staging changes and refines some definitions, but retains most of the 7th edition parameters

THANK YOU