Update in TNM Staging and Handling of Kidney Cancer

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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

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Handling and Staging of Renal Cell Carcinoma
The International Society of Urological Pathology
Consensus (ISUP) Conference Recommendations

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

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Renal Tumors
Diagnostic and Prognostic Biomarkers

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Bonert M, Kuo-Cheng H, Trpkov K.
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**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
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

Key prognostic parameter

Used in prognostic nomograms

7th edition (2009)

8th edition (2017)

Robson CJ et al. *J Urol* 1969; 101:297–301
Handling of renal tumors

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)

- **T1a**: ≤ 4 cm
- **T1b**: > 4 but ≤ 7 cm
- **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:

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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)

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
Assessment 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
Assessment of perinephric fat invasion (pT3a)

Multiple perpendicular sections of tumor fat interface
Assessment 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

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!

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

Submit actual margin

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

Renal margin negative – retraction of vein after fixation
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
Assessment 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!
Assessment 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!

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, tubulointerstitial 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\textsuperscript{a}, Vincenzo Ficarra\textsuperscript{a,*}, Alessandro Antonelli\textsuperscript{b}, Walter Artibani\textsuperscript{a}, Roberto Bertini\textsuperscript{c}, Marco Carini\textsuperscript{d}, Sergio Cosci\textsuperscript{a}, Ciro Imbimbo\textsuperscript{a}, Nicola Longo\textsuperscript{e}, Guido Martignoni\textsuperscript{f}, Giuseppe Martorana\textsuperscript{g}, Andrea Minervini\textsuperscript{d}, Vincenzo Mirone\textsuperscript{e}, Francesco Montorsi\textsuperscript{e}, Roberto Schiavina\textsuperscript{g}, Claudio Simeone\textsuperscript{h}, Sergio Serni\textsuperscript{d}, Alchide Simonato\textsuperscript{h}, Salvatore Siracusano\textsuperscript{1}, Alessandro Volpe\textsuperscript{1}, Giorgio Carmignani\textsuperscript{h}

members of the SATURN Project–LUNA Foundation\textsuperscript{1}

It is expected that AJCC 8\textsuperscript{th} edition staging for renal cancer will perform (at least) as well as the 7\textsuperscript{th} 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