ISUP 2013 VANCOUVER MODIFICATION OF HISTOLOGICAL TYPES

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*

TABLE 2. ISUP Vancouver Modification of WHO (2004) Histologic Classification of Kidney Tumors

- Renal cell tumors
  - Papillary adenoma
  - Oncocytoma
  - Clear cell renal cell carcinoma
    - Multilocular cystic clear cell renal cell neoplasm of low malignant potential*
  - Papillary renal cell carcinoma†
  - Chromophobe renal cell carcinoma
    - Hybrid oncocytic chromophobe tumor*
  - Carcinoma of the collecting ducts of Bellini
  - Renal medullary carcinoma
  - MiT family translocation renal cell carcinoma*
    - Xp11 translocation renal cell carcinoma
    - t(6;11) renal cell carcinoma*
  - Carcinoma associated with neuroblastoma
  - Mucinous tubular and spindle cell carcinoma
  - Tubulocystic renal cell carcinoma*
  - Acquired cystic disease associated renal cell carcinoma*
  - Clear cell (tubulo) papillary renal cell carcinoma*
  - Hereditary leiomyomatosis renal cell carcinoma syndrome-associated renal cell carcinoma*
  - Renal cell carcinoma, unclassified

- Metanephric tumors
  - Metanephric adenoma
  - Metanephric adenofibroma
  - Metanephric stromal tumor
- Nephroblastic tumors
  - Nephrogenic rests
  - Nephroblastoma
    - Cystic partially differentiated nephroblastoma
- Mesenchymal tumors
  - Occurring mainly in children
    - Clear cell sarcoma
    - Rhabdoid tumor
    - Congenital mesoblastic nephroma
    - Ossifying renal tumor of infants
  - Occurring mainly in adults
    - Leiomyosarcoma (including renal vein)
    - Angiosarcoma
    - Rhabdomyosarcoma
    - Malignant fibrous histiocytoma
    - Hemangiopericytoma
    - Osteosarcoma
    - Synovial sarcoma*
    - Angiomyolipoma
      - Epithelioid angiomyolipoma*
    - Leiomyoma
    - Hemangioma
    - Lymphangioma
    - Juxtaglomerular cell tumor
    - Renomedullary interstitial cell tumor
    - Schwannoma
    - Solitary fibrous tumor
- Mixed mesenchymal and epithelial tumors
  - Cystic nephroma/mixed epithelial stromal tumor
- Neuroendocrine tumors
  - Carcinoid (low-grade neuroendocrine tumor)
  - Neuroendocrine carcinoma (high-grade neuroendocrine tumor)
  - Primitive neuroectodermal tumor
  - Neuroblastoma
  - Pheochromocytoma
- Hematopoietic and lymphoid tumors
  - Lymphoma
  - Leukemia
  - Plasmacytoma
- Germ cell tumors
  - Teratoma
  - Choriocarcinoma

TABLE 1. Proposed New Renal Epithelial Tumors and Emerging/Provisional Tumor Entities

New epithelial tumors
Tubulocystic renal cell carcinoma
Acquired cystic disease associated renal cell carcinoma
Clear cell (tubulo) papillary renal cell carcinoma
MiT family translocation renal cell carcinoma (including t(6;11) renal cell carcinoma)
Hereditary leiomyomatosis renal cell carcinoma syndrome associated renal cell carcinoma
Emerging/provisional entities
Thyroid-like follicular renal cell carcinoma
Succinic dehydrogenase B deficiency associated renal cell carcinoma
ALK-translocation renal cell carcinoma

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*

Best Practices Recommendations in the Application of Immunohistochemistry in the Kidney Tumors

Report From the International Society of Urologic Pathology Consensus Conference

Victor E. Reuter, MD, Pedram Argani, MD,† Ming Zhou, MD, PhD,‡ Brett Delahunt, MD, FRCPA,§ and Members of the ISUP Immunohistochemistry in Diagnostic Urologic Pathology Group*

TABLE 2. Tumors Composed Predominantly of "Clear" Cells

Tumor Type	CA IX	CK7	CD117	Cathepsin-K	HMB-45
Clear cell RCC	Positive, diffuse membranous	Negative	Negative	Negative	Negative
Clear cell PRCC	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	Variable	Positive (50%), cytoplasmic	Negative
t(6;11)	Variable but focal	Negative	Negative	Positive, cytoplasmic	Positive (always focal)

TABLE 3. Tumors With a Significant Papillary Component

	CAIX	CK7	AMACR	Cathepsin-K	34βE12	TFE3/TFEB
ccRCC with papillary growth	Positive, membranous	Negative	Negative	Negative	Negative	Negative
PRCC "type I"	Negative	Positive	Positive	Negative	Negative	Negative
PRCC "type II"	Negative	± Positive	Positive	Negative	Negative	Negative
Clear cell PRCC	Positive, cup-like	Positive, diffuse	Negative	Negative	Negative	Negative
MiTF-TFE trans-assoc	Variable but focal	Negative	Positive	Positive (50%)	Negative	Positive*

*Antibodies are difficult to standardize on automated platforms. FISH assays are more reliable.

TABLE 5. Tumors With Oncocytic Features*

	CD117	CK7	Ksp-cadherin	HMB-45	Cathepsin-K
Oncocytoma	Positive, membranous	Negative	Positive	Negative	Negative
Chromophobe RCC, eosinophilic	Positive, membranous	Positive but variable	+/−Positive	Negative	Negative
Oncocytic PRCC	Negative	Positive but focal	Not known	Negative	Unknown
Oncocytic AML	Negative	Negative	Negative	Positive, focal	Negative

Other Abs said to be differentially expressed on oncocytomas and chromophobe RCC.

Positive in oncocytoma, negative in chromophobe: S100A1.

*Hale colloidal iron: Although a histochemical rather than an IHC stain, it can be useful in differentiating chromophobe carcinoma (cytoplasmic granular staining) from oncocytoma (negative or luminal staining). However, this is a technically demanding stain and reliability is laboratory-dependent.

TABLE 6. Tumors With a Predominant Sarcomatoid Pattern of Growth*

	Vimentin†	CAIX‡	PAX 8	CK7	34βE12	GATA3	P63
ccRCC	Positive	Positive, membranous	Positive	Negative	Negative	Negative	Negative
PRCC	Positive	Negative	Positive	Focal or negative	Negative	Negative	Negative
Chromophobe RCC	Positive	Negative	Positive	Positive	Negative	Negative	Negative
MTSC	Positive	Negative	Positive	Positive	Variable	Negative	Negative
Urothelial CA	Positive	+/−Negative	Negative§	Positive	Positive	Positive	Positive
Sarcoma	Positive	Negative	Negative	Negative	Negative	Negative	Negative

*Stains should be performed in the better differentiated or most epithelioid areas.
†In sarcomatoid component.
‡Positive adjacent to necrosis or focal cytoplasmic in high-grade areas of various tumors.
§Positive in up to 20% of upper tract UC.

TABLE 4. Solid PRCC Versus Metanephric Adenoma Versus Wilms Tumor

	CK7	AMACR	WT-1	CD57
Solid papillary	Positive	Positive	Negative	Negative
Metanephric adenoma	Negative or isolated cells	Negative	Positive, nuclear	Positive
Wilms	Negative or isolated cells	Negative	Positive, nuclear	Negative

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

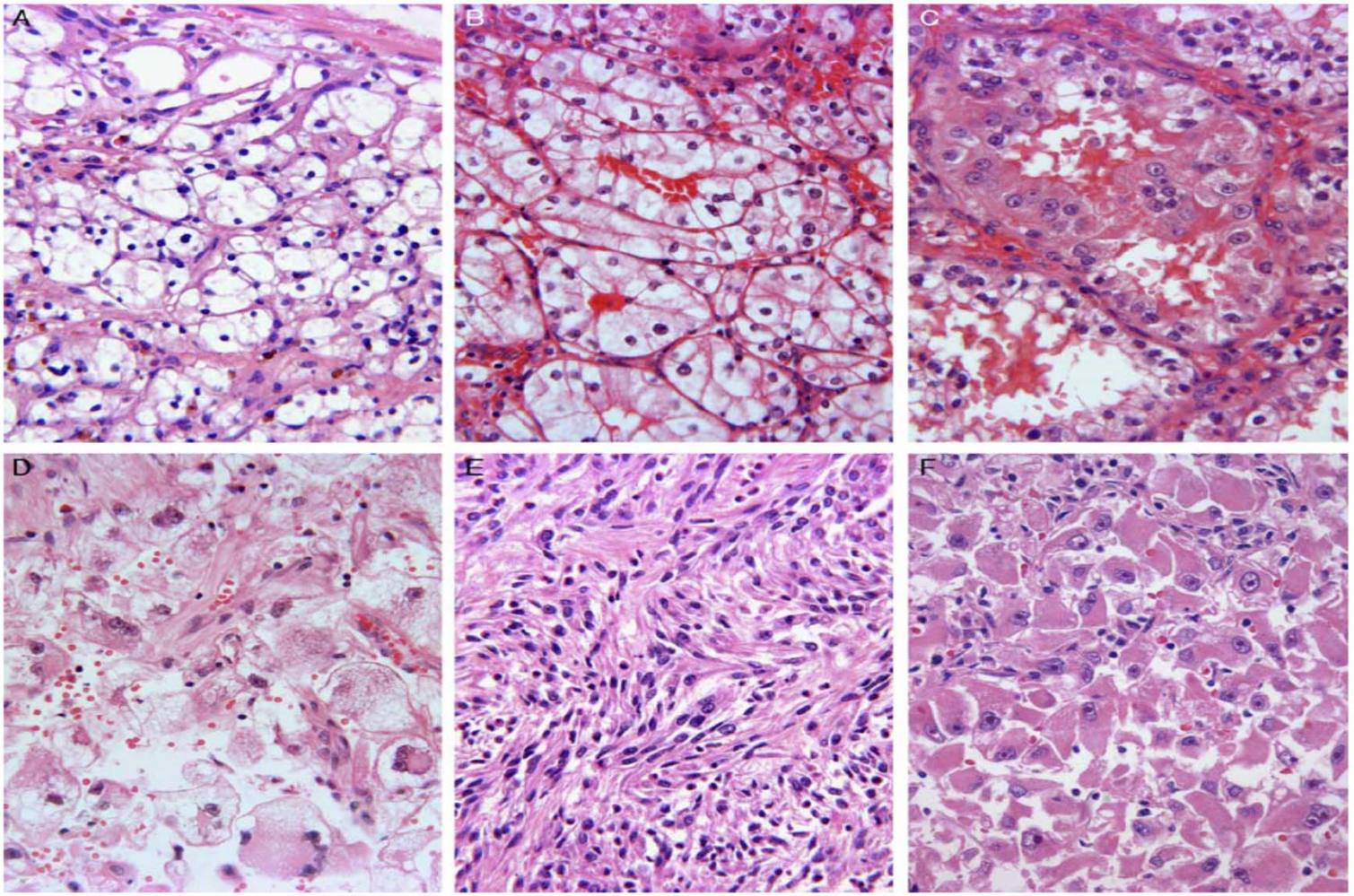
Brett Delahunt, MD, John C. Cheville, MD,† Guido Martignoni, MD,‡ Peter A. Humphrey, MD,§ Cristina Magi-Galluzzi, MD,‖ Jesse McKenney, MD,‖ Lars Egevad, MD,¶ Ferran Algaba, MD,# Holger Moch, MD,** David J. Grignon, MD,†† Rodolfo Montironi, MD,‡‡ John R. Srigley, MD,§§‖‖ and The Members of the ISUP Renal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

GRADING SYTEM (ISUP 2012)

TABLE 2. Survey Results Relating to Grading Practices

	Positive	Responses
What system do you use for grading RCC?		206*
Fuhrman	96	
WHO	7	
Broder	0.5	
Japanese	2	
Nucleolar	11	
Other	2	
Do you provide a grade for		204*
Clear cell RCC	100	
Multilocular cystic RCC	67	
Papillary adenoma	5	
Papillary RCC	85	
Chromophobe RCC	57	
Oncocytoma	1	
Collecting duct carcinoma	41	
Renal medullary carcinoma	31	
Translocation carcinoma	50	
Mucinous tubular spindle cell carcinoma	37	
Tubulocystic carcinoma	37	
End-stage renal disease–associated carcinoma	52	
Unclassified carcinoma	66	
How do you assess Fuhrman grade?		204
Most frequent (1°) pattern	2	
Highest grade	83	
Combined most frequent and highest grade	13	
Provide % of each grade present	2	
What is the minimum area of tumor assessed for grading purposes?		194
1 low-power field (×10 objective)	37	
1 high-power field (×40 objective)	41	
5 high-power fields	10	
Other	12	
For Fuhrman grading do you evaluate?		205*
Nucleolar prominence	99	
Nuclear shape	57	
Nuclear pleomorphism	79	
In case of discordance, which parameter do you put most emphasis on?		205
Nucleolar prominence	68	
Nuclear shape	2	
Nuclear pleomorphism	28	
None	2	

NUCLEOLAR GRADING SYTEM (ISUP 2012)



PROGNOSTIC FACTORS

1. Histological/Morphological types
    1. Clear Cell and Papillary Type 2 (-)
    2. Difference Papillary Type 1/2
    3. Clear Cell tubulo-papillary (+)
    4. Mit Translocation Familly ?? (TFB3 ou TFBB)
2. Grading (*ISUP Nucleolar)*
3. Sarcomatoid & Rhabdoid differentiation (%)
4. Necrosis
5. Vascular invasion L1 (and MicroVI Intrarenal)

TAKE HOME MESSAGE

1. RENAL TUMOR
    1. Primitif RCC
    2. Primitif Urothelial
    3. Metastasis

2. IF PRIMITIF RENAL
    1. Classic Morphologic type(new classification) HE +/- IHC+/- Genotype (prognosis)+ others prognostic factor
    2. If Unclassified+ **others prognostic factors** and sent to EXPERT