Histologic Diagnosis of Renal Mass Biopsy (RMB)

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Histologic Diagnosis of RMB
Outline

• Indications
• Adequate material
• Types of renal tumors
• Renal tumor categorization & diagnosis
• Use of immunohistochemistry
• Case examples
Renal Tumor: Introduction

- **Increased** incidence of renal neoplasm and incidental mass
- **Increased** use of partial nephrectomy
- **Increased** treatment modalities (active surveillance, ablative and targeted therapies)
- **Increasing** Renal Mass Biopsy (RMB)
RMB: Indications

- Has other primary (r/o mets)
- Has prior renal tumor (r/o recurrence)
- Multiple synchronous tumors
- Suspecting abscess or lymphoma
- Candidates for active surveillance
- Candidates for ablative therapy
- Diagnosis in pts. with disseminated mets or unresectable tumor
RMB: Getting Adequate Material

Insufficient material is common

- **Rate variable:** 0-47% (Volpe A et al. Eur Urol 2012; 62: 491)
- **Factors:** radiologist, mass, and pathologist
- **More frequent in small, cystic or hemorrhagic, and necrotic lesion**

Ways to getting adequate material

- Communicate with radiologist!
- Correlate with cytology
- Histology protocols, deeper cut, IHC
RMB: Technical Recommendation

- Image guidance (CT/MRI/US)
- Use 18G or larger needle
- Take at least 2 cores
- Sample from peripheral & central
- Challenging: small size; cystic, hemorrhagic or necrotic; anatomical location
- Complications: rare, tumor seeding exceedingly rare, minimal morbidity

Tsivian M et al. BJUI. 2014
On-Site Cytology Evaluation

Clear cell RCC

Papillary RCC

Renal oncocytoma

Chromophobe RCC
RMB: Diagnostic Accuracy

86-100% Differentiating malignant from benign

~100% Specificity

86-98% Accuracy histol. subtyping

46-76% Accuracy in grading
RMB: Objectives

To establish the following:

- Neoplasm or not
- Histologic type
- Tumor grade
- Other features
Histologic Types of Renal Cell Neoplasm

- **Common types:** clear cell, papillary, chromophobe, clear cell papillary, unclassified

- **Less common types:** collecting duct/medullary, multilocular cystic neoplasm of LMP, MTSC-RCC, ACD-RCC, tubulocystic

- **Pediatric/young adult:** MiT family translocation RCC

- **Familiar types:** HLRCC, SDH-deficient RCC

- **Benign:** oncocytoma, papillary adenoma, metanephric adenoma
Most Frequent Adult Renal Cortical Neoplasms

- Clear cell RCC ~65%
- Papillary RCC ~15%
- Oncocytoma ~10%
- Chromophobe RCC ~5%
- Clear cell papillary RCC ~3%
- Others ...


Renal Tumor Morphologic Categories

- Clear cell
- Papillary
- Oncocytic
- Mixed
- Cystic
- Spindle cell
- High grade
“CLEAR CELL” TUMORS

- Clear cell RCC
- Chromophobe RCC
- Clear cell papillary RCC
- Papillary RCC
- MiT family translocation RCC
- Renal urothelial carcinoma
Clear Cell RCC often heterogeneous
Clear Cell RCC
Morphologic Spectrum

Growth Patterns
- Solid/acinar (classic)
- Tubular/Cystic
- Pseudopapillary
- Hemorrhagic
- Hyalinized

Cytomorphology
- Clear cell
- Granular
- Epithelioid
- Rhabdoid
- Spindly/sarcomatoid
Clear Cell RCC: Growth Patterns

- Solid/acinar
- Sinusoid
- Tubular
- Vascular
- Hyalinized
- Hemorrhagic
- Pseudopapillary
- Sclerotic
Clear Cell RCC: Cytologic and Nuclear Features
Clear cell RCC: Heterogeneous
Clear cell RCC: Heterogeneous
Non-clear cell RCC with clear cells

- Papillary RCC
- Chromophobe RCC
- Clear cell papillary RCC
- Renal urothelial carcinoma
“PAPILLARY” TUMORS

- Papillary RCC, type 1 and type 2
- Clear cell papillary RCC
- Clear cell RCC
- Chromophobe RCC (rarely)
- Mucinous tubular spindle cell RCC
- Metanephric adenoma
- Collecting duct carcinoma
- Metastatic
Non-papillary RCC with Papillary Growth

- Clear cell papillary
- Clear cell RCC
- Chromphobe RCC
- Collecting duct ca
Papillary tumor
“ONCOCYTIC” TUMORS

- Oncocytoma
- Chromophobe RCC
- Hybrid oncocytic tumor
- Clear cell RCC
- Type 2 and oncocytic papillary RCC
- Acquired cystic renal disease associated RCC
- SDH-deficient RCC
- Epithelioid angiomyolipoma
- Renal carcinoid
- Adrenal cortical tumor
“Oncocytic” Tumors

Chromophobe RCC

Oncocytoma

Angiomyolipoma

Clear cell RCC
“CYSTIC” TUMORS

- Clear cell RCC
- Papillary RCC
- Clear cell papillary RCC
- Oncocytoma/chromophobe RCC
- Tubulocystic RCC
- Cystic nephroma/mixed epithelial and stromal tumor of kidney
- Benign cystic renal disease
“SPINDLE CELL” TUMORS

- RCC (all) with sarcomatoid
- Mucinous tubular spindle cell RCC
- Leiomyoma/leiomyosarcoma
- Other renal sarcoma
- Myoid-rich angiomyolipoma
“HIGH GRADE” TUMORS

- RCC
  - Clear cell
  - Papillary
  - Collecting duct/medullary
  - Unclassified
- Urothelial carcinoma
- Metastatic carcinoma
What type of RCC does this image look like?

Chromophobe RCC
Role of Immunohistochemistry in Diagnosing Renal Neoplasms
When Is It Really Useful?

Steven S. Shen, MD, PhD; Luan D. Truong, MD; Marina Scarpelli, MD; Antonio Lopez-Beltran, MD, PhD

- RCC vs. non-RCC
- Histologic subtyping
- Rare primary renal neoplasms
- Small mass biopsy
- Metastasis RCC

Arch Pathol Lab Med. 2012;136:410-17
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>
<thead>
<tr>
<th>Diagnosis</th>
<th>Positive Markers</th>
<th>Negative Markers</th>
</tr>
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<tbody>
<tr>
<td>Clear cell RCC</td>
<td>Vim, <strong>CAIX</strong>, CK, EMA, CD10, RCCm, PAX8, PAX2</td>
<td><strong>CK7</strong>, Ksp-cadherin, Parvalbumin</td>
</tr>
<tr>
<td>Papillary RCC</td>
<td>CK, <strong>CK7</strong>, AMACR, RCCm</td>
<td>CD117, Ksp-cadherin, WT1</td>
</tr>
<tr>
<td>Chromophobe RCC</td>
<td>E-cad, <strong>Ksp-cad</strong>, CD117, CK, CK7</td>
<td>Vim, <strong>CAIX</strong>, AMACR</td>
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<tr>
<td>Collecting duct RCC</td>
<td>p63, HMCK, <strong>PAX8</strong>, IN1</td>
<td>CD10, RCCm, CK20, <strong>GATA3</strong></td>
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<tr>
<td>Medullary carcinoma</td>
<td>P63, HMCK, OCT4, PAX8</td>
<td><strong>IN1</strong>, RCCm, <strong>GATA3</strong></td>
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<tr>
<td>Clear cell papillary RCC</td>
<td><strong>CK7</strong>, CAIX, PAX8</td>
<td><strong>AMACR</strong>, RCCm</td>
</tr>
<tr>
<td>MiTF-TFE Translocation</td>
<td>Cathepsin-K, <strong>TFE3</strong>, TFEB, RCCm</td>
<td><strong>CK</strong> (or weak)</td>
</tr>
<tr>
<td>RCC with sarcomatoid</td>
<td><strong>PAX8</strong>, CD10, vim, AMACR</td>
<td></td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>HMB45, Melan-A, SMA</td>
<td><strong>CK</strong>, CD10, RCCm, <strong>PAX8</strong></td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>Ksp-cad, CD117, Parvalbumin, S100A1</td>
<td><strong>CK7</strong>, MOC31, CD82</td>
</tr>
<tr>
<td>Metanephric adenoma</td>
<td><strong>WT1</strong>, CD57, S100</td>
<td>AMACR, RCCm</td>
</tr>
</tbody>
</table>

Reuter V et al. AJSP **2014**; 38:e35-e49
Use of IHC for Histologic Subtyping?

Should be based on morphologic patterns and differential diagnosis

Reuter V et al. AJSP 014; 38:e35-e49
# Renal tumors with clear cell

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>CA IX</th>
<th>CK7</th>
<th>CD117</th>
<th>Cathepsin K</th>
<th>HMB45</th>
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<tbody>
<tr>
<td>Clear cell</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clear cell pRCC</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(cup-like)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chromophobe</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>AML</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Xp11</td>
<td>-/+</td>
<td>-</td>
<td>-/+</td>
<td>+(50%)</td>
<td>-</td>
</tr>
<tr>
<td>T(6;11)</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+(focal)</td>
</tr>
</tbody>
</table>

Reuter V et al. AJSP 2014; 38:e35-e49
# Renal tumors with papillary

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>CA IX</th>
<th>CK7</th>
<th>AMACR</th>
<th>Cathepsin K</th>
<th>TFE3/TFEB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell RCC</td>
<td>++</td>
<td>-</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pRCC, type 1</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pRCC, type 2</td>
<td>-</td>
<td>-/+</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clear cell pRCC</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(cup-like)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MiTF-TFE RCC</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
<td>+(50%)</td>
<td>+</td>
</tr>
</tbody>
</table>

Reuter V et al. AJSP 2014; 38:e35-e49
# Oncocytic renal tumors

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>CD117</th>
<th>CK7</th>
<th>Ksp-cad</th>
<th>HMB45</th>
<th>Cath_K</th>
</tr>
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<tbody>
<tr>
<td>Oncocytoma</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chromophobe, eosinophilic</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pRCC, oncocytic</td>
<td>-</td>
<td>+ (focal)</td>
<td>N/A</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>AML, oncocytic</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+ (focal)</td>
<td>-</td>
</tr>
</tbody>
</table>

Reuter V et al. AJSP 2014; 38:e35-e49
## Renal tumor with spindle cells

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Vim</th>
<th>CAIX</th>
<th>Pax8</th>
<th>CK7</th>
<th>34βE12</th>
<th>GATA3</th>
<th>p63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell RCC</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Papillary RCC</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chromophobe</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MTSC RCC</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Urothelial Ca</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Reuter V et al. AJSP 2014; 38:e35-e49
Do we need IHC for all cases of renal mass biopsy?

No!

For many tumors that have classic morphology, a histologic diagnosis can be made on H&E section.
Share we see some case examples?

Do I have a good sample?

What’s overall category based on patterns/cells?

Do I see features that are classic for a histologic subtype?

Is it typical enough for a specific diagnosis?

If not, what are my differential?

What are the IHC markers that I may use?

Can I reach a definitive diagnosis?
Case #1: 82 yo man with large R renal mass and inferior vena cava extension
Case #1: Clear cell RCC
Case #2: 54M 5.5 cm R renal mass
Case #2: Papillary RCC
Case #3: 80 yo man 6 cm R renal mass
Case #3: Oncocytoma

Vimentin

CK7

RCCm

Vimentin
Case #4: 58 yo woman
Case #4: Chromophobe RCC

CK7
Case #5: 70 yo man 4.5 cm R renal mass
Case #5: Clear cell RCC

- CK7
- CD10
- Vimentin
Case #6: 48 yo woman with 6.5 cm left renal mass
Case #6: Angiomyolipoma
Case #7: 52M with 3.5 cm L renal mass
Case #7: Papillary RCC, type 1
Metanephric adenoma

Papillary RCC

AMACR-/CD57+/WT1+

AMACR+/CD57-/WT1-
Case #8: 78 yo woman with 2.7 cm R RMB
Case #8: Clear cell papillary RCC
Clear cell papillary renal cell carcinoma is the fourth most common histologic type of renal cell carcinoma in 290 consecutive nephrectomies for renal cell carcinoma

Haijun Zhou MD, PhD<sup>a,b</sup>, Shaojiang Zheng MD, PhD<sup>c</sup>, Luan D. Truong MD<sup>a,b</sup>, Jae Y. Ro MD, PhD<sup>a,b</sup>, Alberto G. Ayala MD<sup>a,b</sup>, Steven S. Shen MD, PhD<sup>a,b,*</sup>

Hum Pathol. 2014; 45:59-64

- A new RCC entity
- Unique IHC profile
- Indolent tumor
- Likely the 4<sup>th</sup> most common RCC
- DDx: clear cell RCC
Case #9: 69 yo woman with 6.5 cm right renal mass
Case #9: High grade unclassified RCC with spindle cells

Pan CK

CK7

Pax 8
Radical Nephrectomy

- Positive: CK7 (focal), Vim, CD10
- Negative: RCCm, AMACR
- Clear cell RCC with sarcomatoid changes
- T3aN1 (5/25)
Case #10: 57 yo man with a large renal tumor
Case #10: Invasive urothelial carcinoma
#11: 67 yo woman with history of bladder ca and thyroid cancer, now with 3.5 cm renal mass
Case #11: Metastatic papillary thyroid ca
Histologic Diagnosis of RMB

Summary

- Critical to obtain adequate material
- Get familiar with renal tumor entities
- Adopt a systematic, pattern-based approach (categorization)
- Use IHC in selective situations
- Acknowledge the limitations
Thank you