Histologic Heterogeneity of Extirpated Renal Cell Carcinoma Specimens: Implications for Renal Mass Biopsy

Lauren M. Nahouraii\(^1\); Jordan L. Allen, M.D.\(^2\); Suzanne B. Merrill, M.D.\(^2\); Erik Lehman\(^3\); Matthew G. Kaag,\(^2\) M.D.; Jay D. Raman,\(^2\) M.D., F.A.C.S.

\(^1\)Pennsylvania State University, College of Medicine, Hershey, PA, United States
\(^2\)Division of Urology, Department of Surgery, Penn State College of Medicine, Hershey, PA, United States
\(^3\)Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA, United States

Authors have no financial disclosures
Renal Mass Biopsy

**AUA**
- Should be *considered* when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious
- *Not recommended* for young or healthy patients who are unwilling to accept uncertainties, or for patients who will be managed conservatively

**EUA**
- Recommended in candidates for active surveillance of small masses, to obtain histology before ablative treatments, or to select the most suitable medical and surgical treatment strategy in the setting of metastatic disease
Objective

• Evaluate the incidence of:
  • Histologic heterogeneity
  • Necrosis
  • Lymphovascular invasion (LVI)
  • Sarcomatoid features

• Optimize RMB interpretation and accuracy
Patients and Methods

Inclusion
• Surgical resection of cT1/T3 renal masses < 7cm between January 2000 and August 2017

Exclusion
• Incomplete data
• Benign mass
• Masses >7cm
Methods
## Results

|                  | Total n=659 | pT1a (n=404) | pT1b (n=169) | pT3a (n=86) | p value |
|------------------|-------------|--------------|--------------|-------------|---------|
| Clear Cell       |             | 299          | 127          | 63          | 0.938   |
| Papillary        |             | 81           | 33           | 14          | 0.724   |
| Chromophobe      |             | 26           | 6            | 6           | 0.351   |
| Sarcomatoid      |             | 0            | 4 (2%)       | 10 (12%)    | <0.001  |
| Low-grade        | 336 (83%)   | 120 (71%)    | 46 (53%)     | <0.001      |
| High-grade       | 68 (17%)    | 49 (29%)     | 40 (45%)     | <0.001      |
| LVI              | 9 (2%)      | 10 (6%)      | 19 (22%)     | <0.001      |
| Necrosis         | 66 (16%)    | 72 (43%)     | 33 (38%)     | <0.001      |
|                  | Total n=573 | pT1a (n=404) | pT1b (n=169) | p value |
|------------------|-------------|--------------|--------------|---------|
| Clear Cell       | 299 (74%)   | 127 (75%)    | 1            |         |
| Papillary        | 81 (20%)    | 33 (20%)     | 1            |         |
| Chromophobe      | 26 (6%)     | 6 (4%)       | 1            |         |
| Sarcomatoid      | 0 (0%)      | 4 (2%)       | 0.006        |         |
| Low-grade        | 326 (81%)   | 114 (68%)    | <0.001       |         |
| High-grade       | 68 (17%)    | 49 (29%)     | <0.001       |         |
| LVI              | 9 (2%)      | 10 (6%)      | 0.024        |         |
| Necrosis         | 66 (16%)    | 72 (43%)     | <0.001       |         |
RCC

0-4 cm

T1a

Nuclear Grade

Low

High

LVI

Necrosis

T3a

Nuclear grade

Low

High

LVI

Necrosis

>4-7 cm

T1b

LVI

Sarcomatoid

T3a

Nuclear grade

Low

High

LVI

Sarcomatoid
|                | Total n=659 | T1 (n=573) | T3a (n=86) | p value |
|----------------|-------------|------------|------------|---------|
| Clear Cell     | 426 (74%)   | 63 (73%)   | 1          |         |
| Papillary      | 114 (20%)   | 14 (16%)   | 1          |         |
| Chromophobe    | 32 (6%)     | 6 (7%)     | 1          |         |
| Sarcomatoid    | 4 (1%)      | 10 (12%)   | <0.001     |         |
| Low-grade      | 440 (77%)   | 46 (53%)   | <0.001     |         |
| High-grade     | 117 (20%)   | 39 (45%)   | <0.001     |         |
| LVI            | 19 (3%)     | 19 (22%)   | <0.001     |         |
| Necrosis       | 138 (24%)   | 33 (38%)   | 0.005      |         |
|               | Total n=433 | T1a (n=404) | T3a ≤ 4 cm (n=29) | p value |
|---------------|-------------|-------------|-------------------|---------|
| Clear Cell    | 299 (69%)   | 19 (4%)     |                   | 1       |
| Papillary     | 81 (19%)    | 8 (2%)      |                   | 1       |
| Chromophobe   | 26 (6%)     | 1 (<1%)     |                   | 1       |
| Sarcomatoid   | 0           | 1 (<1%)     |                   | 0.065   |
| Low-grade     | 326 (75%)   | 20 (5%)     |                   | 0.128   |
| High-grade    | 68 (16%)    | 9 (2%)      |                   | 0.053   |
| LVI           | 9 (2%)      | 3 (<1%)     |                   | 0.037   |
| Necrosis      | 66 (15%)    | 11 (3%)     |                   | 0.003   |
|                  | Total n=226 | T1b (n=169) | T3a 4-7cm (n=57) | p value |
|------------------|-------------|-------------|------------------|---------|
| Clear Cell       |             |             |                  | 1       |
|                  | 127 (56%)   | 44 (19%)    |                  |         |
| Papillary        |             |             |                  | 0.120   |
|                  | 33 (15%)    | 6 (3%)      |                  |         |
| Chromophobe      |             |             |                  | 0.143   |
|                  | 6 (3%)      | 5 (2%)      |                  |         |
| Sarcomatoid      |             |             |                  | <0.001  |
|                  | 4 (2%)      | 9 (4%)      |                  |         |
| Low-grade        |             |             |                  | 0.003   |
|                  | 114 (50%)   | 26 (12%)    |                  |         |
| High-grade       |             |             |                  | 0.001   |
|                  | 49 (22%)    | 30 (13%)    |                  |         |
| LVI              |             |             |                  | <0.001  |
|                  | 10 (4%)     | 16 (7%)     |                  |         |
| Necrosis         |             |             |                  | 1       |
|                  | 72 (32%)    | 22 (10%)    |                  |         |
Discussion

• Limited qualitative data comparing histologic heterogeneity based on size and stage in literature
• Correlation between tumor size with grade, and stage of lesions
Discussion

Abel et al. 2015: Use of at least four biopsies from separate, solid enhancing areas of tumor decreased nondiagnostic rate (11% to 0%) and improved sensitivity for detecting sarcomatoid features (25% to 87%) without increasing the rate of complications.
Conclusion

RCC masses >4 cm and pT3a tumors (irrespective of size) exhibit considerable histologic heterogeneity and may harbor elements not easily appreciated with limited renal sampling
Conclusion

Multi-quadrant biopsy is requisite for these tumors to ensure accurate capture of histologic elements that may better reflect the differing underlying biology of these tumors.