

BAUS section of Oncology Annual Meeting
London - Sep 15-16, 2014

THE CASE FOR SELECTIVE BIOPSY OF SMALL RENAL MASSES

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The British Association
of Urological Surgeons



HISTORICAL ROLE OF RENAL TUMOR BIOPSY

Very selective...

- Diagnosis of metastatic disease in patients with known extrarenal primary tumors
- Diagnosis of renal abscess or lymphoma
- Histologic confirmation of a renal primary tumor in presence of disseminated metastatic disease or unresectable retroperitoneal masses

WHAT WERE THE HISTORICAL REASONS FOR SELECTIVE INDICATIONS OF RENAL TUMOR BIOPSY?

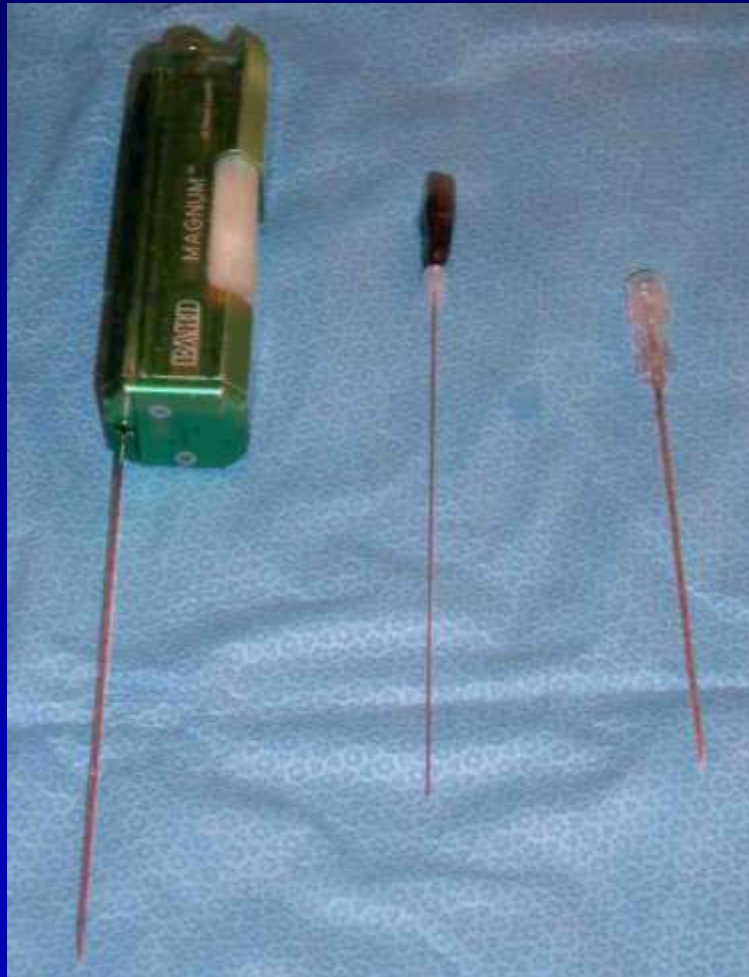
Uncertainties regarding...

- **SAFETY**
 - Bleeding
 - Needle track seeding
- **TECHNIQUE**
 - Non diagnostic biopsy
 - Sampling errors (intratumoral heterogeneity)
- **EFFICACY**
 - Diagnostic accuracy
 - Impact on clinical decision making

US/CT GUIDANCE



ADEQUATE INSTRUMENTS



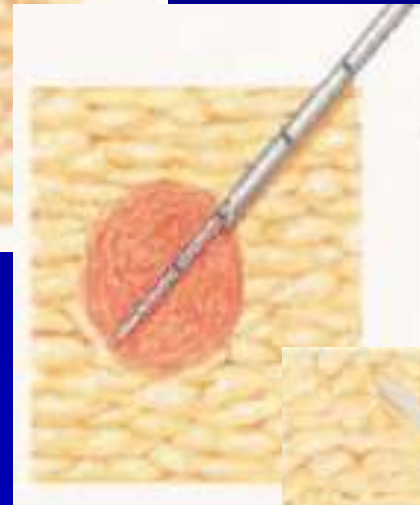
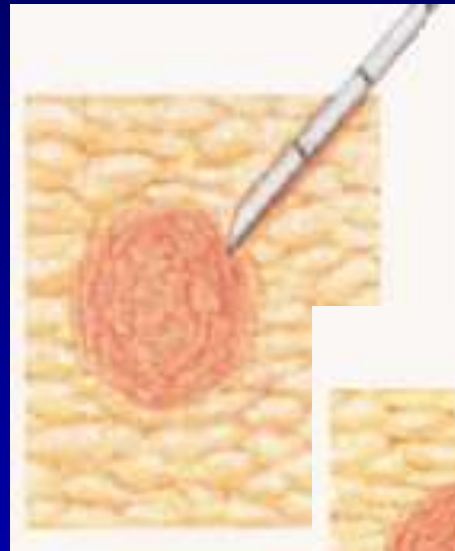
Right to left:

17 gauge guiding
cannula

22 gauge fine
needle for cytology

18 gauge needle on
automatic gun for
core biopsy

COAXIAL TECHNIQUE



Percutaneous renal tumour biopsy should be obtained with a coaxial technique.

Rationale for Percutaneous Biopsy and Histologic Characterisation of Renal Tumours

Alessandro Volpe^{a,}, Antonio Finelli^b, Inderbir S. Gill^c, Michael A.S. Jewett^b, Guido Martignoni^d, Thomas J. Polascik^e, Mesut Remzi^f, Robert G. Uzzo^g*



| | No. of tumours biopsied | No. of significant complications* (%) | No. of seeding (%) | No. of significant bleeding** (%) |
|-------------------------|-------------------------|---------------------------------------|--------------------|-----------------------------------|
| Neuzillet et al. [8] | 88 | 0 | 0 | 0 |
| Shannon et al. [9] | 235 | 2 (0.9) | 0 | 2 (0.9) |
| Schmidbauer et al. [10] | 78 | 1 (1.3) | 0 | 0 |
| Lebret et al. [11] | 119 | 0 | 0 | 0 |
| Maturen et al. [12] | 152 | 2 (1.3) | 0 | 2 (1.3) |
| Volpe et al. [13] | 100 | 1 (1) | 0 | 0 |
| Wang et al. [14] | 110 | 2 (1.8) | 0 | 1 (0.9) |
| Veltri et al. [15] | 150 | 0 | 0 | 0 |
| Leveridge et al. [16] | 345 | 1 (0.3) | 0 | 1 (0.3) |

BIOPSY QUALITY CHECK



Rationale for Percutaneous Biopsy and Histologic Characterisation of Renal Tumours

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| | No. of tumours biopsied | Diagnostic biopsies, % | Accuracy for malignancy, % | Accuracy for RCC subtyping, % | Accuracy for grading, % |
|-------------------------|-------------------------|------------------------|-------------------------------------|-------------------------------|-------------------------|
| Neuzillet et al. [8] | 88 | 91 | 92 | 92 | 69.8 |
| Shannon et al. [9] | 235 | 78 | 100 | 98 | NR |
| Schmidbauer et al. [10] | 78 | 97 | Sensitivity 93.5 Specificity 100 | 91 | 76 |
| Lebret et al. [11] | 119 | 79 | 86 | 86 | 46/74** |
| Maturen et al. [12] | 152 | 96 | Sensitivity 97.7 Specificity 100 | NR | NR |
| Volpe et al. [13] | 100 | 84 | 100 | 100 | 66.7/75** |
| Wang et al. [14] | 110 | 90.9 | 100 | 96.6 | NR |
| Veltri et al. [15] | 103 | 100 | NR | 93.2 | NR |
| Leveridge et al. [16] | 345 | 80.6 | 99.7 | 88 | 63.5 |

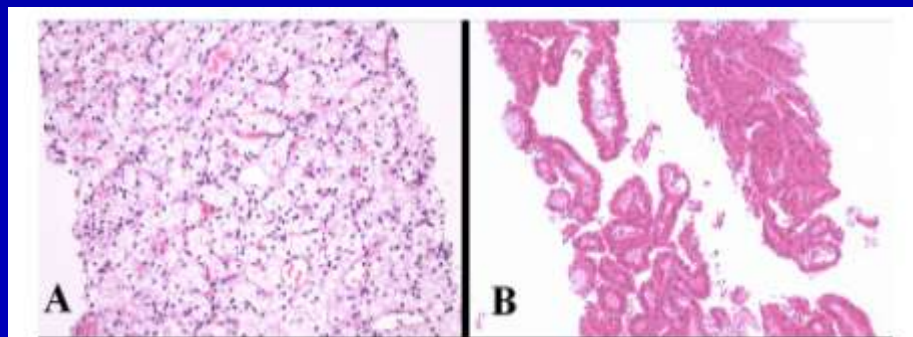
DIAGNOSTIC ACCURACY

TABLE 2. Accuracy of renal mass needle core biopsies in recent series

| References | No. Tumors Biopsied | Imaging Guidance | Needle Size (gauge) | % Nondiagnostic Biopsies | No. Malignant Biopsies/No. Pathologically Confirmed | % Outcomes |
|----------------------------------|---------------------|------------------|-------------------------|--------------------------|---|---|
| Wood et al ⁸ | 79* | CT/US | 22 (FNA), 17–20 (cores) | 6.3 | 49/41 | Sensitivity 93, accuracy 95 Concordance biopsy + surgical diagnosis 89 |
| Lechevallier et al ¹⁵ | 73 | CT | 18 | 21 | 48/26 | |
| Hara et al ¹³ | 33 | CT/US | 18 | 0 | 21/15 | Concordance biopsy + surgical diagnosis 86.7 |
| Caoili et al ²⁴ | 26 | US | 18 | 0 | 19/4 | Sensitivity + specificity 100 |
| Harisinghani et al ³⁹ | 28*, † | CT | 22 (FNA), 18 (cores) | 0 | 17/16 | Concordance biopsy + surgical diagnosis 100 |
| Neuzillet et al ⁹ | 88 | CT | 18 | 9.1 | 66/62 | Accuracy 92 |
| Eshed et al ¹⁴ | 22 | CT | 18 | 4.5 | 15/14 | Sensitivity 93, specificity 100 |
| Shah et al ²⁹ | 66 | CT/US | 18 | 21 | 37/15 | Accuracy 98 |

* Combined FNA and needle core biopsies were obtained in most patients.

† Includes only biopsies of Bosniak III complex cystic renal masses.



Volpe et al., J Urol 2007

RENAL TUMOR BIOPSY

CURRENT UNCERTAINTIES

- **Factors related to biopsy technique**
 - Non standardized pattern of biopsy
- **Factors related to renal tumor histology**
 - difficult differential diagnosis among tumor histotypes
 - difficult assessment of Fuhrman grade on biopsy
 - intratumoral heterogeneity
- **Factors related to histological assessment of biopsy**
 - intraobserver and interobserver variability in the assessment of biopsy

RENAL TUMOR BIOPSY

HISTORICAL UNCERTAINTIES

- **SAFETY**

- Bleeding~~X~~
- Needle track seeding~~X~~

- **TECHNIQUE**

- Non diagnostic biopsy
- Sampling errors (intratumoral heterogeneity)

- **EFFICACY**

- Diagnostic accuracy
- Impact on clinical~~X~~ decision making

WHAT ARE THE CURRENT REASONS FOR SELECTIVE INDICATIONS OF RENAL TUMOR BIOPSY?

- **Presence of tumor features leading to lower diagnostic yield/higher risk of complications**
 - Cystic renal tumors
 - Renal tumors <15 mm in size
 - Tumors in difficult locations (anterior, perihilar)
- **Presence of patient features limiting the impact of RTB on clinical decision making**
 - Patient age
 - Patient comorbidities

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Contemporary Results of Percutaneous Biopsy of 100 Small Renal Masses: A Single Center Experience

Alessandro Volpe, Kamal Mattar, Antonio Finelli, John R. Kachura, Andrew J. Evans,
William R. Geddie and Michael A. S. Jewett*

From the Departments of Surgical Oncology (Division of Urology) (AV, KM, AF, MASJ), Medical Imaging (JRK) and Pathology (AJE), Princess Margaret Hospital and University Health Network, University of Toronto, Toronto, Ontario, Canada

At multivariate analysis smaller tumor size
and cystic pattern correlate significantly
with a lower diagnostic yield of biopsies

| | Odd Ratio | 95% CI | p-value |
|-----------------------------------|-----------|-------------|-------------|
| Tumor size ¹ | 6.0 | 1.1 - 32.1 | 0.04 |
| Biopsy core length | 3.7 | 0.9 - 14.9 | 0.07 |
| <u>Tumor type²</u> | 5.9 | 1.04 - 34.0 | 0.05 |
| <u>Image guidance³</u> | 2.6 | 0.7 - 9.6 | <u>0.17</u> |

Outcomes of Small Renal Mass Needle Core Biopsy, Nondiagnostic Percutaneous Biopsy, and the Role of Repeat Biopsy

Michael J. Leveridge^a, Antonio Finelli^b, John R. Kachura^c, Andrew Evans^d, Hannah Chung^b, Daniel A. Shiff^c, Kimberly Fernandes^e, Michael A.S. Jewett^{b,*}

Table 3 – Univariate analysis of predictors of a diagnostic small renal mass biopsy

| Predictor | Odds ratio | 95% CI | p value |
|---|------------|-----------|---------|
| Size, cm (per 1-cm increase) | 2.30 | 1.54–3.43 | <0.0001 |
| Tumor type: solid vs cystic | 5.73 | 2.49–13.2 | <0.0001 |
| Image guidance: US vs CT or US plus CT | 1.74 | 1.01–2.99 | 0.047 |
| Location Mid vs lower pole | 1.13 | 0.47–2.68 | 0.009 |
| Upper vs lower pole | 0.34 | 0.15–0.80 | |

CI = confidence interval; US = ultrasound; CT = computed tomography



Table 4 – Multivariate analysis of predictors of a diagnostic small renal mass biopsy

| Predictor | Odds ratio | 95% CI | p value |
|---|------------|-----------|---------|
| Size, cm (per 1-cm increase) | 3.11 | 1.54–6.28 | 0.002 |
| Tumor type: solid vs cystic | 13.9 | 3.78–50.7 | <0.0001 |
| Image guidance: US vs CT or US plus CT | 1.48 | 0.54–4.09 | 0.45 |
| Location Mid vs lower pole | 0.78 | 0.24–2.47 | 0.91 |
| Upper vs lower pole | 0.91 | 0.25–3.32 | |

CI = confidence interval; US = ultrasound; CT = computed tomography.

Biopsies, n = 345

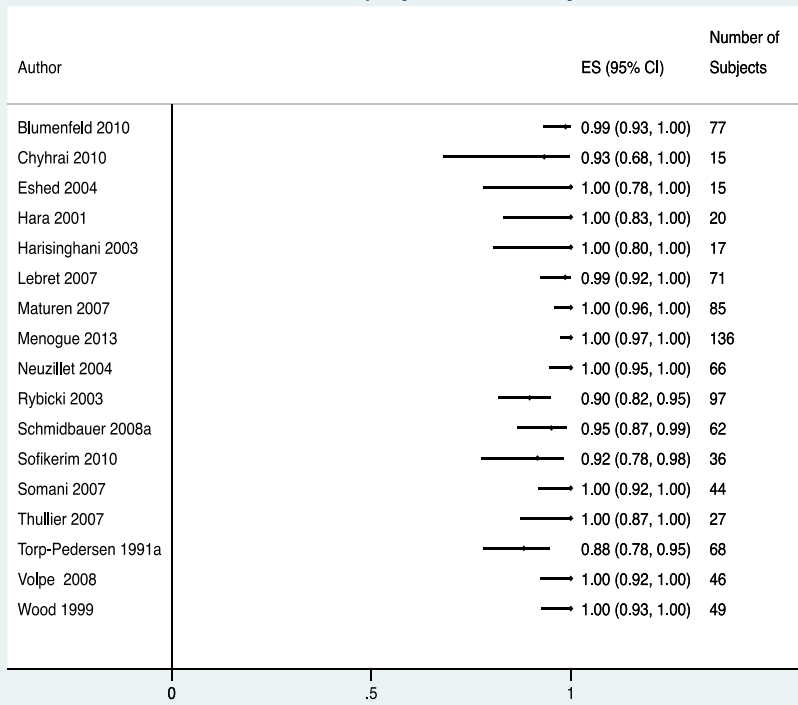
Patients, n = 294 (mean age: 63 yr)

Lesions, n = 314 (mean diameter:
2.5 cm)

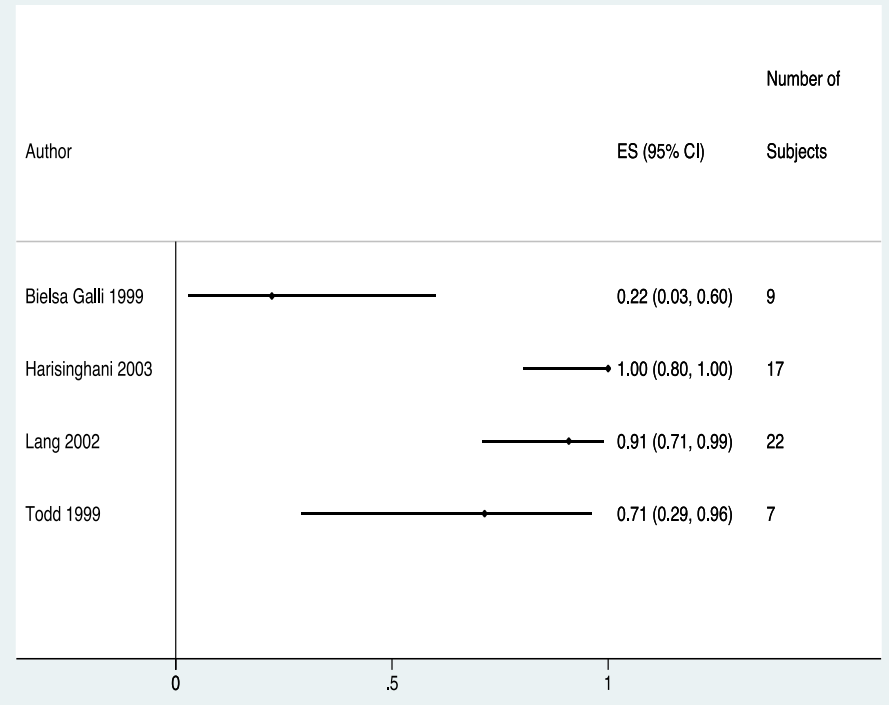
META-ANALYSIS

DIAGNOSTIC ACCURACY OF RTBs

Core Biopsy Sensitivity



Cystic Sensitivity



Guidelines on Renal Cell Carcinoma

B. Ljungberg (chair), K. Bensalah, A. Bex (vice-chair),
S. Canfield, S. Dabestani, F. Hofmann, M. Hora, M.A. Kuczyk,
T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders,
T. Powles, M. Staehler, A. Volpe

Core biopsies have a low diagnostic yield for cystic renal masses and should not be recommended alone in these cases, unless areas with a solid pattern are present (Bosniak IV cysts) (47,50) (LE: 2b).



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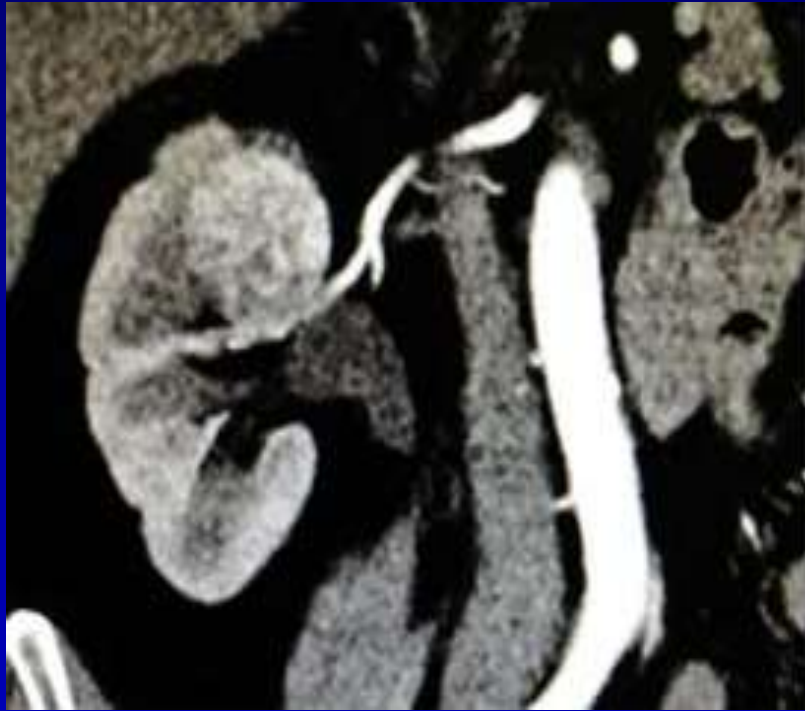
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 - Patient age
 - Patient comorbidities



WHAT ARE THE CURRENT REASONS FOR SELECTIVE INDICATIONS OF RENAL TUMOR BIOPSY?

- Presence of tumor features leading to lower diagnostic yield/higher risk of complications
 - Cystic renal tumors
 - Tumors with significant necrosis or in difficult locations
- **Presence of patient features limiting the impact of RTB on clinical decision making**
 - Patient age
 - Patient comorbidities



Surveillance Epidemiology and End Results

providing information on cancer statistics to help reduce the burden of these diseases on the U.S. population

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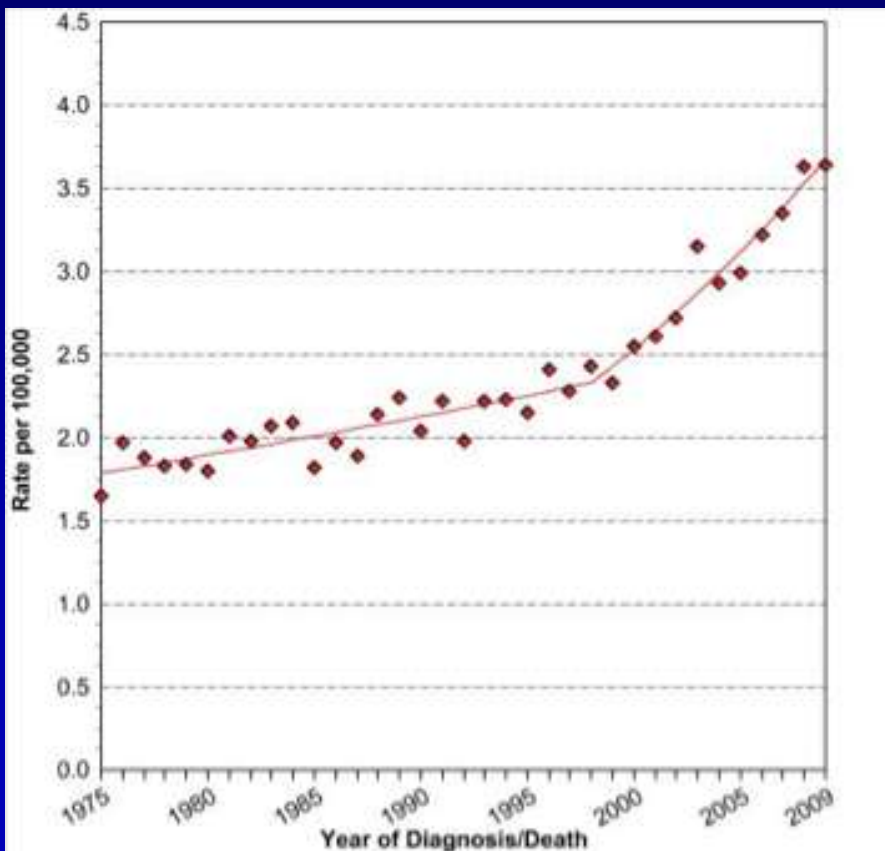
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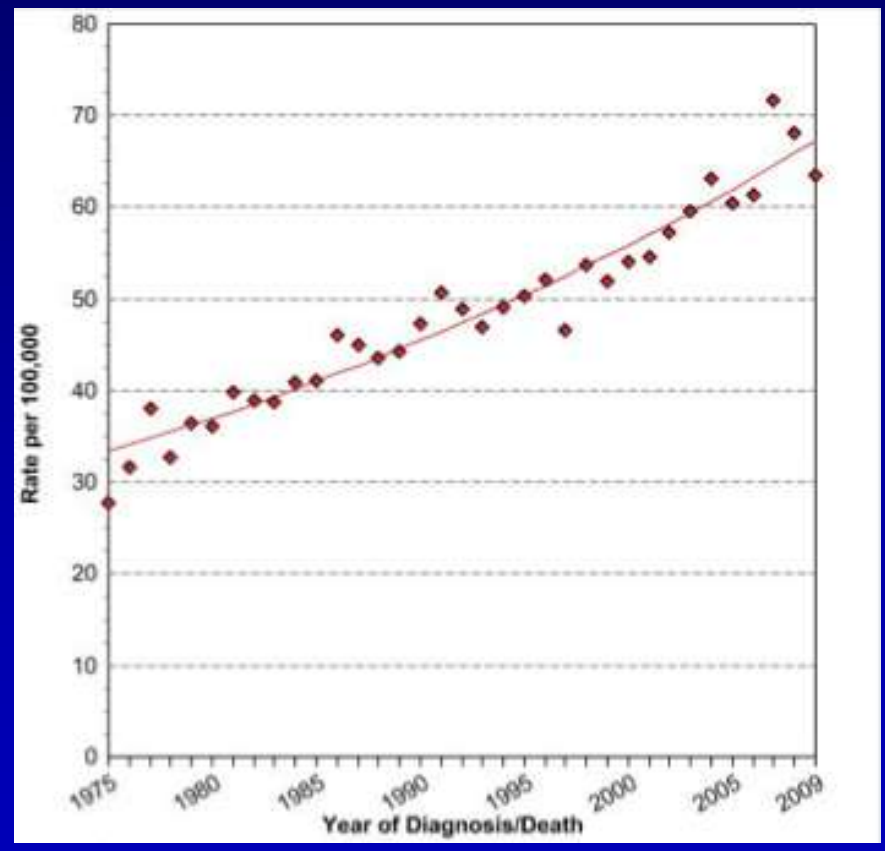
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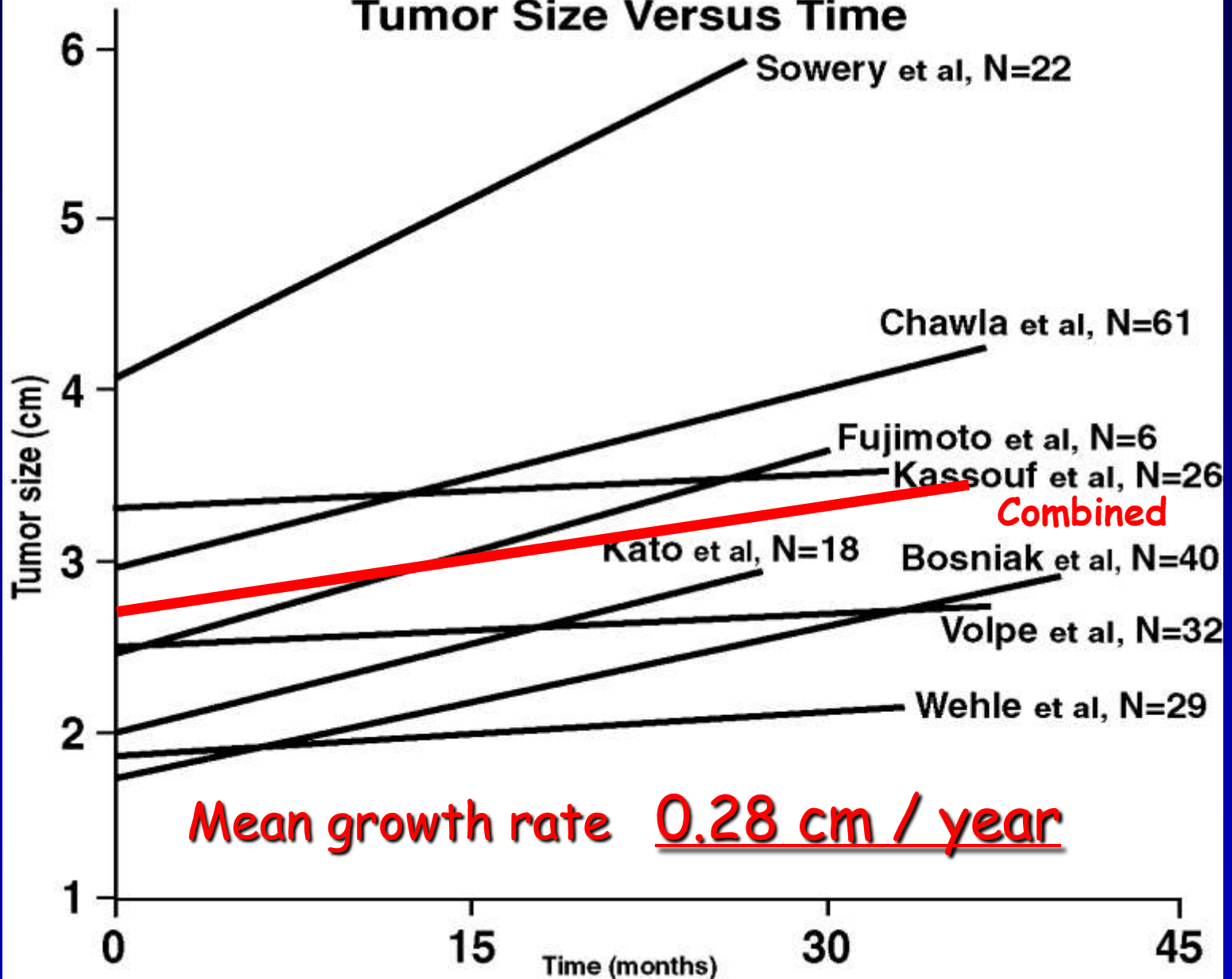


< 50 years



> 75 years

Tumor Size Versus Time

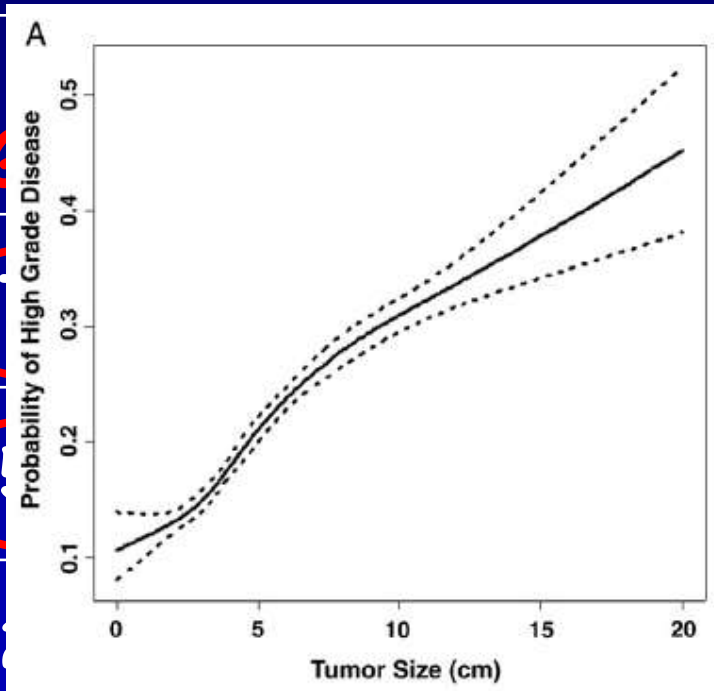


Histopathological Characteristics of Localized Renal Cell Carcinoma Correlate With Tumor Size: A SEER Analysis

Jason Rothman, Brian Egleston, Yu-Ning Wong, Kevan Iffrig, Steve Lebovitch and Robert G. Uzzo*

From the Departments of Urologic Oncology (JR, SL, KI, RGU), Medical Oncology (YW) and Biostatistics (BE) of Fox Chase Cancer Center, Philadelphia, Pennsylvania

| Tumor Size | | Totals |
|------------|--------|--------|
| < 4 cm | | 8979 |
| 4-7 cm | | 6376 |
| > 7 cm | | 3463 |
| | 15 102 | |



Guidelines on Renal Cell Carcinoma

B. Ljungberg (chair), K. Bensalah, A. Bex (vice-chair), S. Canfield, S. Dabestani, F. Hofmann, M. Hora, M.A. Kuczyk, T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders, T. Powles, M. Staehler, A. Volpe

| Recommendations | GR |
|---|----|
| <u>Surgery is recommended to achieve cure in localized RCC.</u> | B |
| <u>Nephron-sparing surgery is recommended in patients with T1a tumours.</u> | A |
| Nephron-sparing surgery should be favoured over radical nephrectomy in patients with T1b tumour, whenever technically feasible. | B |

Guideline for Management of the Clinical T1 Renal Mass

Steven C. Campbell,* ,† Andrew C. Novick,‡ Arie Belldegrun,§ Michael L. Blute, George K. Chow, Ithaar H. Derwees, Raymond J. Leveillee,|| Surena F. M

From the American Urological Association Education and R

● RN, particularly laparoscopic RN, is very appealing to patients and physicians but it is greatly overutilized.⁹ Nephron-sparing approaches should be considered in all patients with a clinical T1 renal mass as an overriding principle, presuming adequate oncologic control can be achieved, based on

NCCN Clinical Practice Guidelines in Oncology

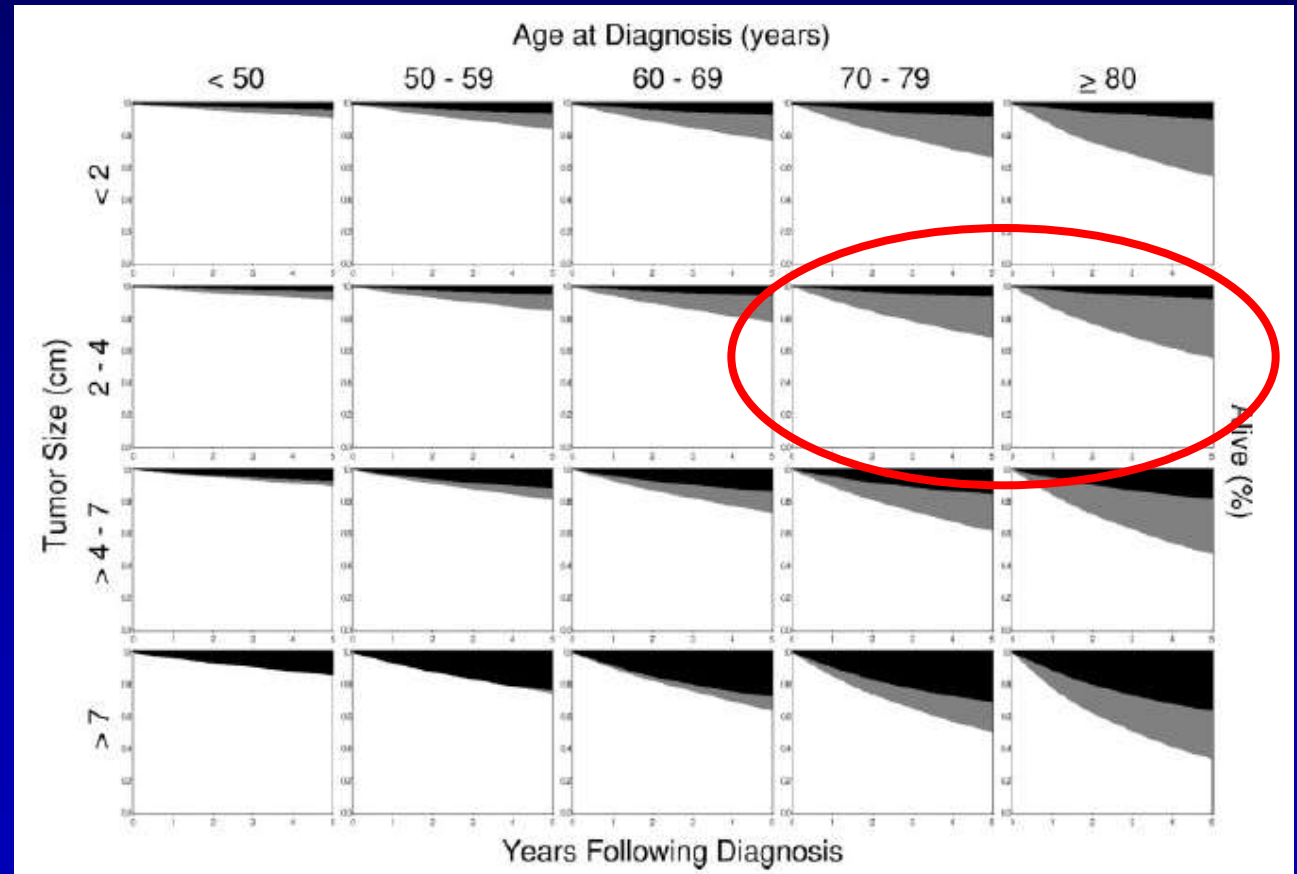
Kidney Cancer

- Nephron-sparing surgery (partial nephrectomy) is appropriate in selected patients, for example:
 - ▶ Small unilateral tumors (T1a and selected patients T1b)
 - ▶ Uninephric state, renal insufficiency, bilateral renal masses, familial renal cell cancer

Five-Year Survival After Surgical Treatment for Kidney Cancer

A Population-Based Competing Risk Analysis

John M. Hollingsworth, MD¹
David C. Miller, MD, MPH²
Stephanie Daignault, MS¹
Brent K. Hollenbeck, MD, MS¹



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DOI 10.1002/cncr.22600

Published online 9 March 2007 in Wiley InterScience (www.interscience.wiley.com).

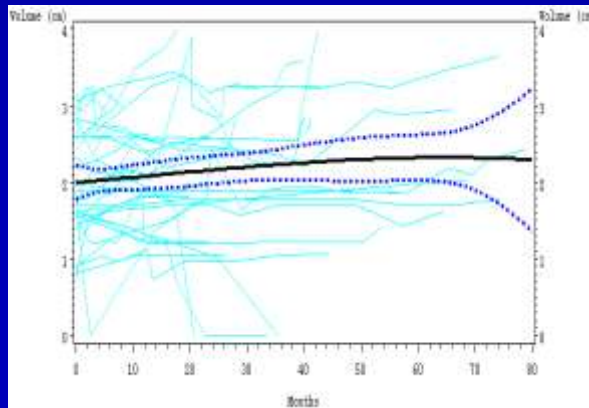
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T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders,
T. Powles, M. Staehler, A. Volpe

Recommendations

In the elderly and/or comorbid patients with small renal masses and limited life expectancy, active surveillance, radiofrequency ablation and cryoablation can be offered.

C



CAN IMAGING SUPPORT CLINICAL CHOICES IN PATIENTS WITH LIMITED LIFE EXPECTANCY?

- Providing accurate diagnosis of renal lesions
 - Benign/malignant
 - Tumor histotype
- Predicting tumor aggressiveness

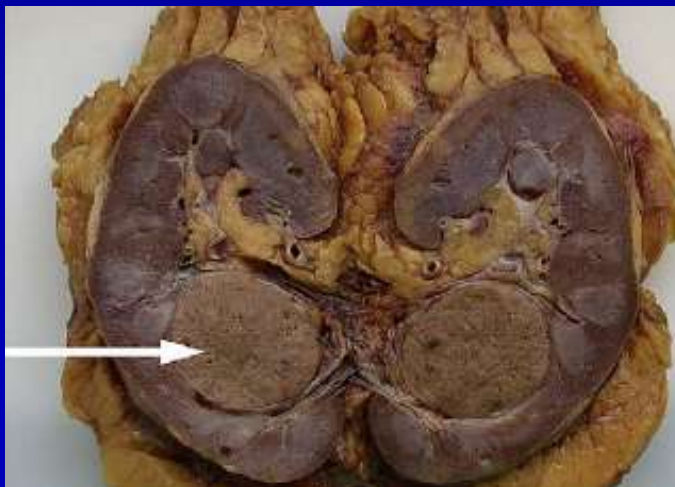
Renal oncocytoma: CT features cannot reliably distinguish oncocytoma from other renal neoplasms

Clinical Radiology (2009) 64, 517–522

S. Choudhary^a, A. Rajesh^{a,*}, N.J. Mayer^b, K.A. Mulcahy^a, A. Haroon^a

Departments of ^aRadiology, and ^bPathology, University Hospitals of Leicester NHS Trust, Leicester General Hospital, Leicester, UK

CONCLUSION: Renal oncocytoma is typically described as being hypervascular and homogeneous, with a characteristic central stellate scar on CT. The present study demonstrates that these imaging features are found in only a small proportion of these tumours. Therefore, imaging characteristics alone are unreliable when differentiating between oncocytoma and renal cell carcinoma, and histopathological diagnosis remains the reference standard.



CONTRAST ENHANCED MRI

Renal Cortical Tumors: Use of Multiphasic Contrast-enhanced MR Imaging to Differentiate Benign and Malignant Histologic Subtypes¹

Hebert Alberto Vargas, MD
Joshua Chaim, DO
Robert A. Lefkowitz, MD
Yulia Lakhman, MD
Junting Zheng, MS
Chaya S. Moskowitz, PhD
Michael J. Sohn, BS
Lawrence H. Schwartz, MD
Paul Russo, MD
Oguz Akin, MD

Purpose:

To investigate the use of quantitative multiphasic contrast material-enhanced magnetic resonance (MR) imaging in differentiating between common benign and malignant histologic subtypes of renal cortical tumors.

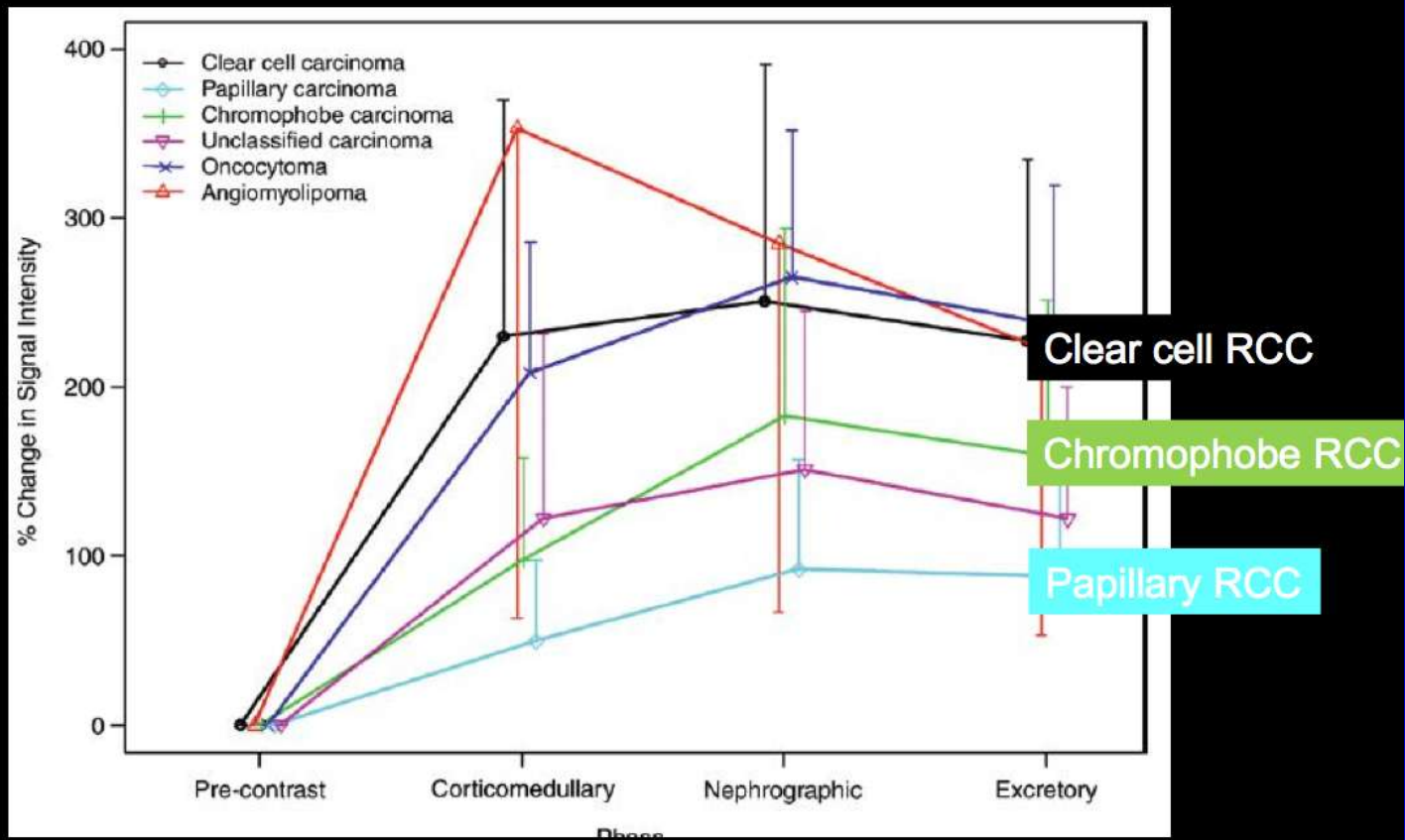
Materials and Methods:

The institutional review board waived informed consent and approved this retrospective HIPAA-compliant study of 138 patients who underwent preoperative contrast-enhanced MR imaging during the period of January 2004–December 2008. At surgery, 152 renal tumors were

Radiology 2012

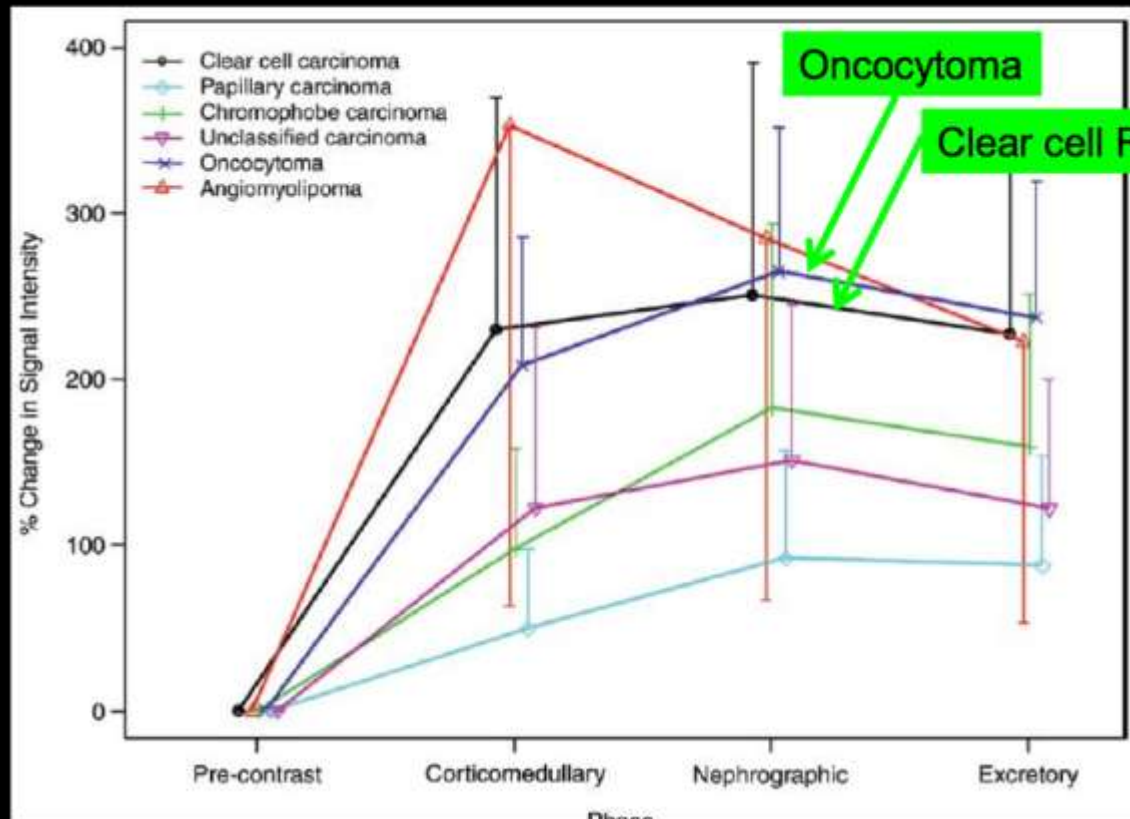
CONTRAST ENHANCED MRI

Percentage change in signal intensity between precontrast and each postcontrast phase



CONTRAST ENHANCED MRI

Percentage change in signal intensity (%SI change) between precontrast and each postcontrast phase



MRI Features of Renal Oncocytoma and Chromophobe Renal Cell Carcinoma

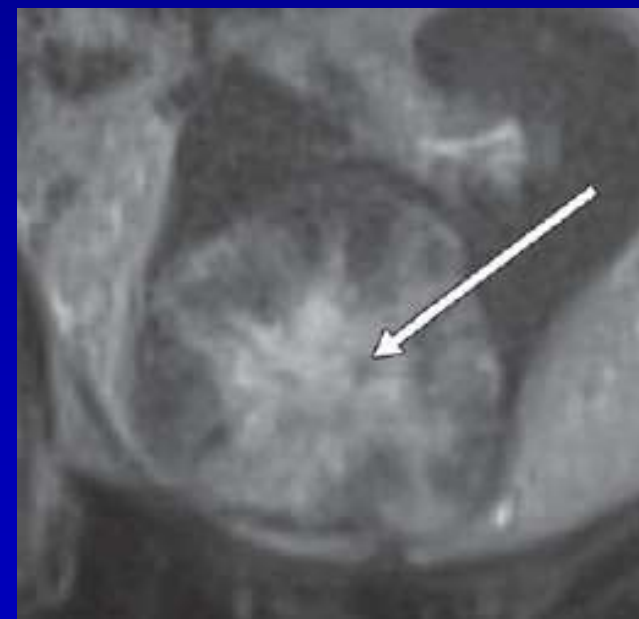
Andrew B. Rosenkrantz¹
 Nicole Hindman¹
 Erin F. Fitzgerald¹
 Benjamin E. Niver¹
 Jonathan Melamed²
 James S. Babb¹

OBJECTIVE. The purpose of this study was to retrospectively describe the MRI features of the pathologically related entities renal oncocytoma and chromophobe renal cell carcinoma (RCC).

MATERIALS AND METHODS. Twenty-eight cases of histologically proven renal oncocytoma and 15 of chromophobe RCC evaluated with preoperative MRI from January 2003 through June 2009 at our institution were independently reviewed for an array of MRI features by two radiologists blinded to the final histopathologic diagnosis. These features were tabulated and compared between chromophobe RCC and renal oncocytoma by use of the Mann-Whitney test and binary logistic regression.

| | | | | | | |
|--|--------------|-------------|--------|--------------|-------------|--------|
| <u>Central scar</u> | 50.0 (14/28) | 33.3 (5/15) | 0.2920 | 60.7 (17/28) | 40.0 (6/15) | 0.2092 |
| <u>Segmental enhancement inversion</u> | 28.6 (8/28) | 13.3 (2/15) | 0.2640 | 42.9 (12/28) | 26.7 (4/15) | 0.2960 |

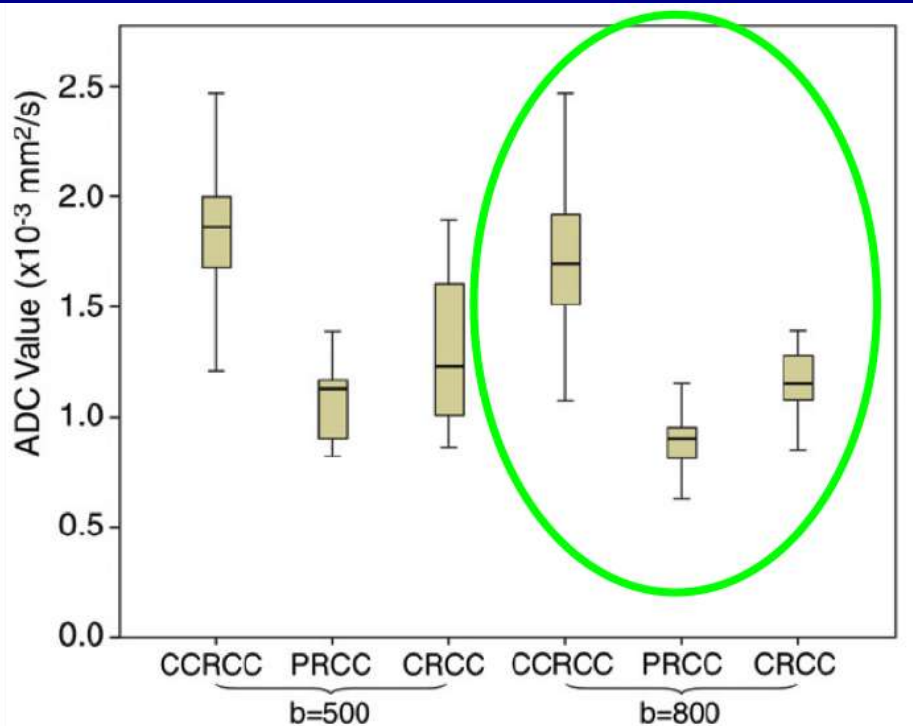
as suggestive of renal oncocytoma in limited contexts, were observed in a similar proportion of the two lesions. No MRI features were reliable for differentiating these two entities, and histologic examination remains necessary for establishing either diagnosis.



DIFFUSION WEIGHTED MRI

Renal Cell Carcinoma: Diffusion-weighted MR Imaging for Subtype Differentiation at 3.0 T¹

Wang et al
Radiology
2010



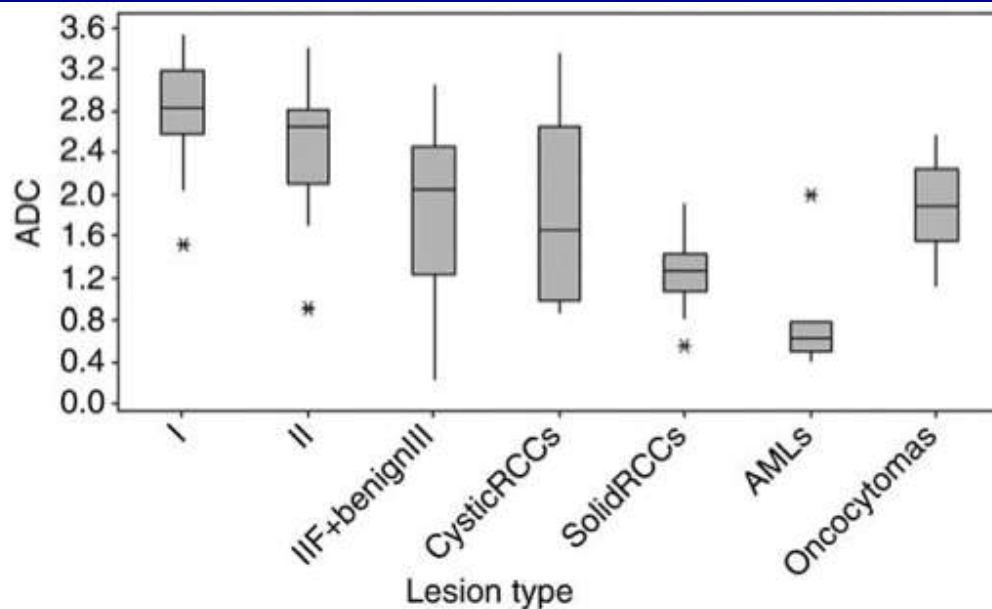
In conclusion, clear cell and non-clear cell RCCs possess different diffusion characteristics that can be distinguished with high sensitivity and specificity when *b* values of 0 and 800 sec/mm² are used to calculate the ADC, potentially improving the accuracy of pretreatment diagnosis and selection of clinical therapy.

DIFFUSION WEIGHTED MRI

Renal Lesions: Characterization with Diffusion-weighted Imaging versus Contrast-enhanced MR Imaging¹

Radiology

Taouli,
Radiology
2009



DW MRI can be used to characterize renal lesions; however, compared with CE-MRI, it is less accurate.

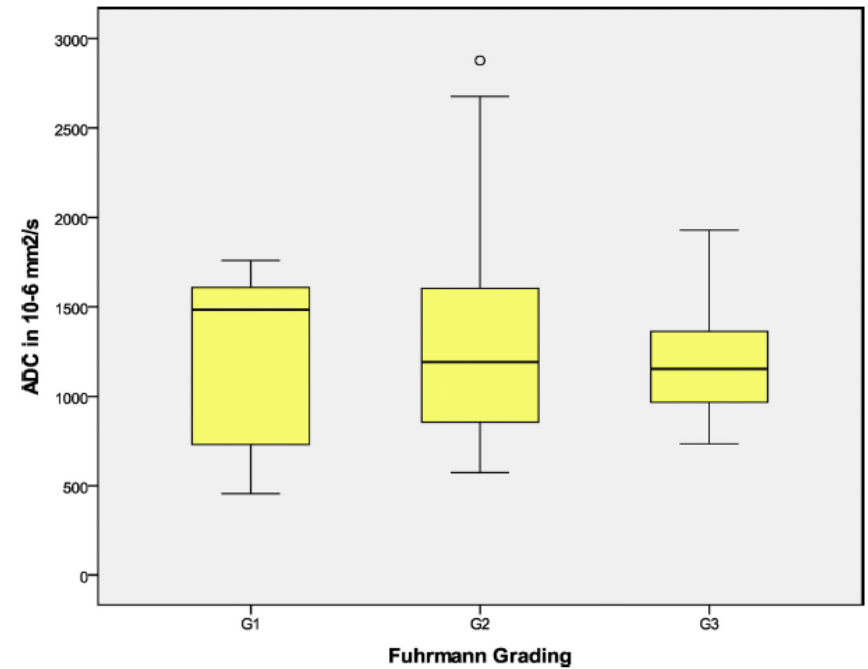
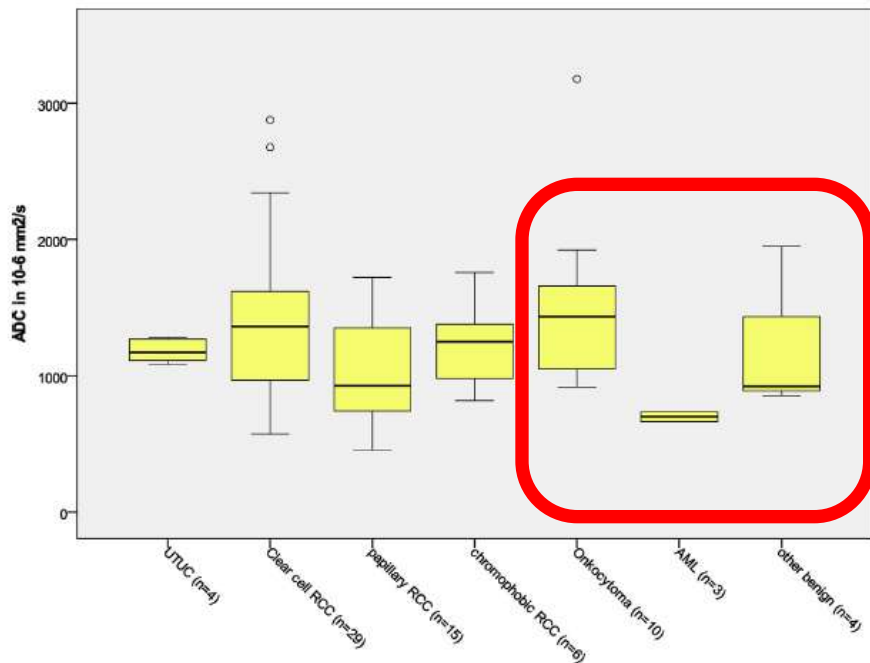
Utility and limitations of 3-Tesla diffusion-weighted magnetic resonance imaging for differentiation of renal tumors



S. Sevcenco^{a,1}, G. Heinz-Peer^{b,2}, L. Ponhold^{b,2}, D. Javor^{b,2}, F.E. Kuehhas^{a,1},
H.C. Klingler^{a,1}, M. Remzi^{a,3}, P. Weibl^{a,1}, S.F. Shariat^{a,1}, P.A. Baltzer^{b,4}

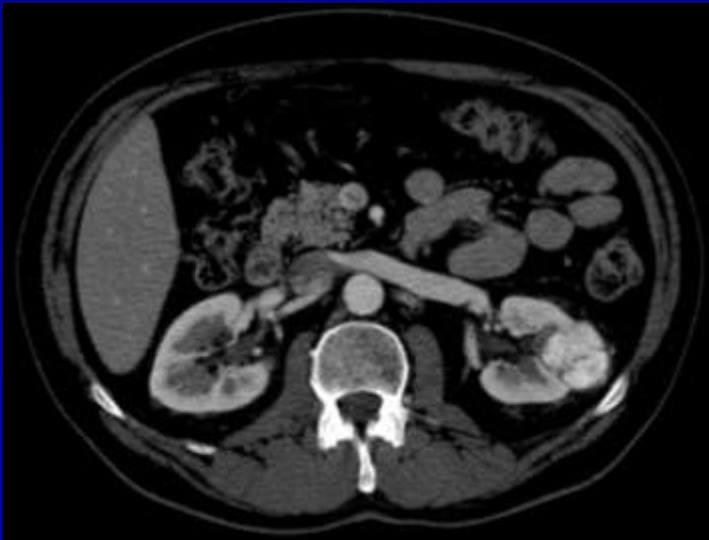
^a Medical University of Vienna, Dept. of Urology, Waehringer Gürtel 18-20, 1090 Vienna, Austria

^b Medical University of Vienna, Dept. of Biomedical Imaging and Image-guided Therapy, Waehringer Gürtel 18-20, 1090 Vienna, Austria



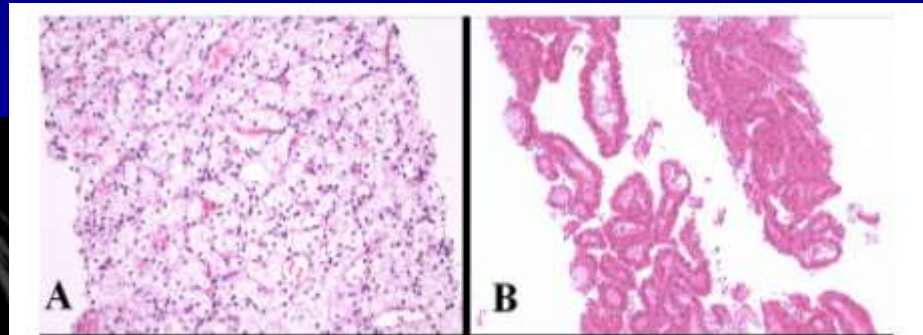
CT/MRI IMAGING

- High, but not excellent accuracy for the diagnosis of malignancy
- Poor ability to differentiate oncocytomas and "fat free" epithelioid angiomyolipomas



CT/IMAGING

Limited ability to differentiate tumor aggressiveness



**Small renal masses
Treatment options**

TUMOR CHARACTERISTICS

SIZE

LOCATION

GROWTH PATTERN

EXOPHYTIC RATE

INDICATIONS

ABSOLUTE

RELATIVE

ELECTIVE

PATIENT CHARACTERISTICS

AGE

COMORBIDITIES

OPEN NSS

**LAPAROSCOPIC
NSS**

**ROBOT-ASSISTED
NSS**

**ABLATIVE
THERAPIES**

*ACTIVE
SURVEILLANCE*

SMALL RENAL MASSES

We need better histological definition by percutaneous needle biopsy

- Malignancy
- Grade



Guidelines on Renal Cell Carcinoma

B. Ljungberg (chair), K. Bensalah, A. Bex (vice-chair),
S. Canfield, S. Dabestani, F. Hofmann, M. Hora, M.A. Kuczyk,
T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders,
T. Powles, M. Staehler, A. Volpe

| | |
|--|---|
| <u>Renal tumour biopsy is recommended before ablative therapy and systemic therapy without previous pathology.</u> | C |
| <u>Percutaneous biopsy is recommended in patients in whom active surveillance is pursued.</u> | C |
| Percutaneous renal tumour biopsy should be obtained with a coaxial technique. | C |

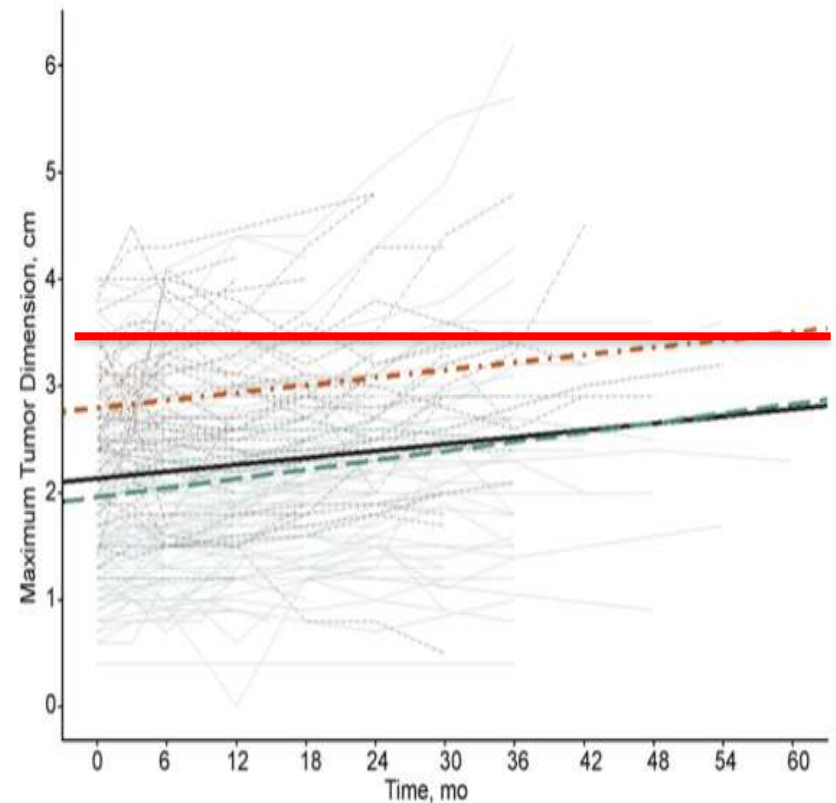
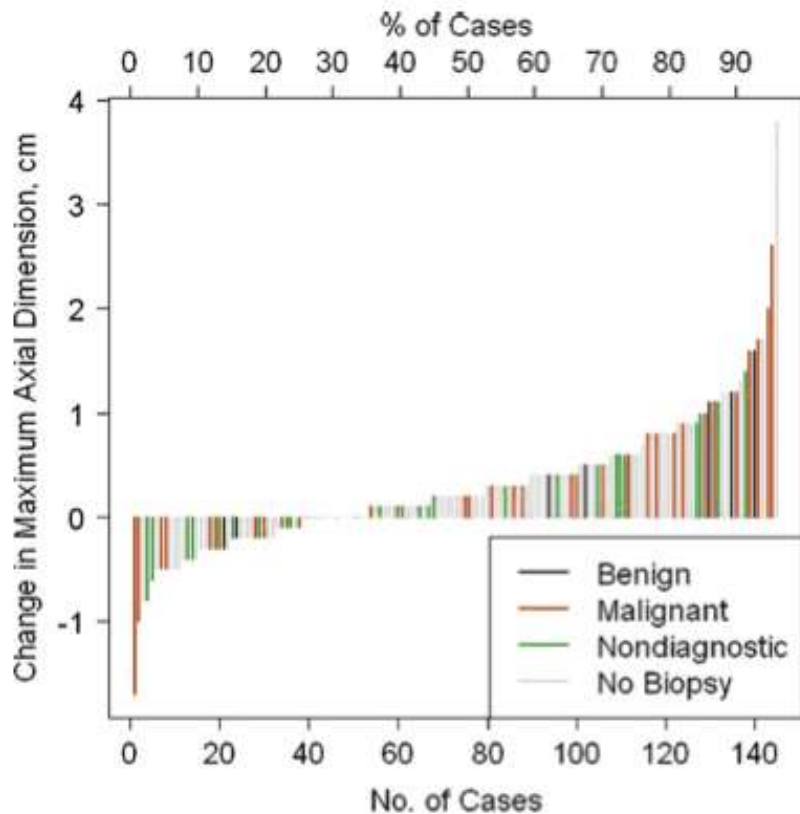
Follow-up for Clinically Localized Renal Neoplasms: AUA Guideline

Sherri M. Donat, Mireya Diaz, Jay Todd Bishoff, Jonathan A. Coleman,
Philipp Dahm, Ithaar H. Derweesh, S. Duke Herrell III, Susan Hilton, Eric Jonasch,
Daniel W. Lin, Victor E. Reuter and Sam S. Chang

16. Percutaneous biopsy may be considered in patients planning to undergo active surveillance. (Option; Evidence Strength: Grade C)

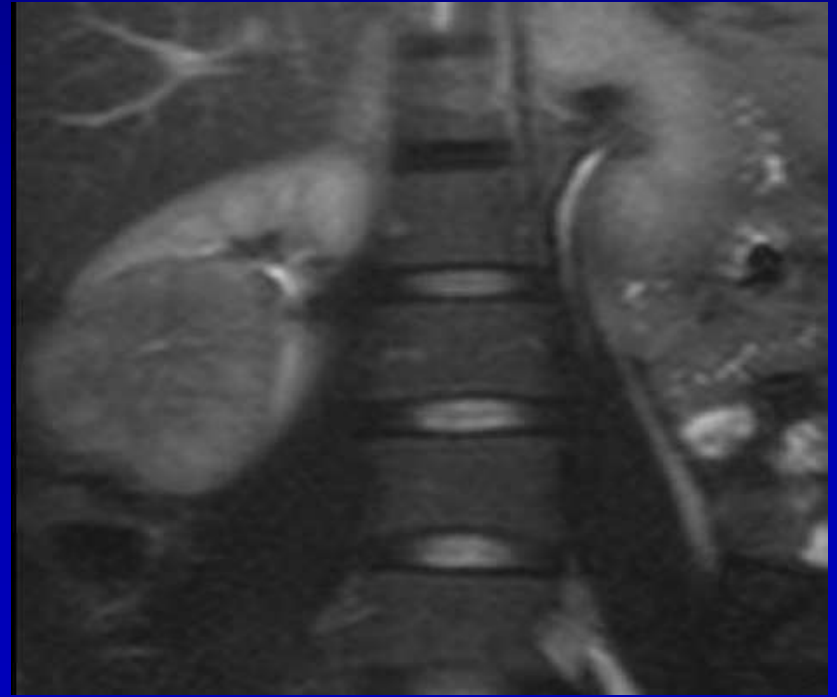
Active Surveillance of Small Renal Masses: Progression Patterns of Early Stage Kidney Cancer

Michael A.S. Jewett^{a,*}, Kamal Mattar^a, Joan Basiuk^a, Christopher G. Morash^b, Stephen E. Pautler^c, D. Robert Siemens^d, Simon Tanguay^e, Ricardo A. Rendon^f, Martin E. Gleave^g, Darrel E. Drachenberg^h, Raymond Chowⁱ, Hannah Chung^a, Joseph L. Chin^j, Neil E. Fleshner^a, Andrew J. Evans^k, Brenda L. Gallie^l, Masoom A. Haider^m, John R. Kachura^m, Ghada Kurban^a, Kimberly Fernandesⁿ, Antonio Finelli^a



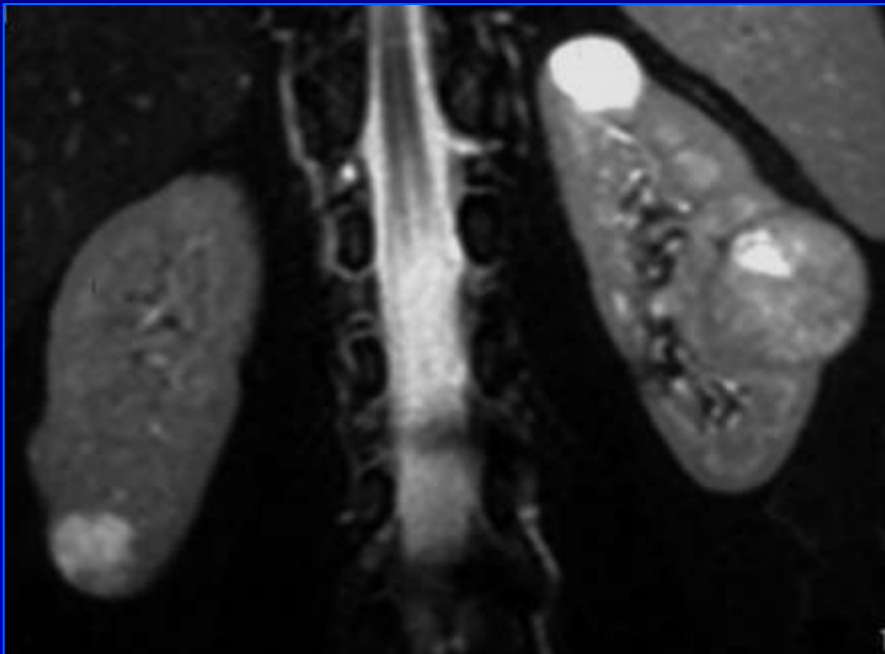
WHAT CAN RTB PROVIDE IN CLINICAL MANAGEMENT OF SRMs?

It may support "extreme" nephron-sparing treatment in young patients with large, anatomically complex tumors



WHAT CAN RTB PROVIDE IN CLINICAL MANAGEMENT OF SRMs?

It may support clinical decisions in patients with multiple and bilateral renal masses



WHAT CAN RTB PROVIDE IN CLICAL MANAGEMENT OF SRMs?

To avoid some unnecessary surgeries for benign pathology

To support decision making in pts with SRMs who are candidates for conservative treatment

To better define the oncologic outcomes of minimally-invasive ablative therapies

To support in the choice of the best treatment for patients with metastatic RCC

CONCLUSIONS

Percutaneous biopsy is safe and adequate biopsy cores yields an accurate histological diagnosis in the majority of cases

Current abdominal imaging does not have an optimal accuracy and provides poor information for the selection of patients for a non-surgical treatment

CONCLUSIONS

- Renal tumor biopsy is not necessary for most solid contrast-enhancing renal masses in young and fit patients with long life expectancy
- Renal tumor biopsy should not be performed for cystic lesions Bosniak ≤ 3 and has a lower diagnostic yield for smaller (<15mm) tumors

CONCLUSIONS

Renal tumor biopsy is important for treatment decision-making in selected patients

It should be recommended:

- ✓ for renal masses with indeterminate imaging
- ✓ in patients with SRMs who are candidates for non-surgical treatment
- ✓ in patients with metastatic RCC who are not candidates for cytoreductive nephrectomy

CONCLUSIONS

Further studies are needed to define standardized patterns of biopsy and to optimize the diagnostic yield and the accuracy of biopsies in defining tumor histotype and grade

The use of cytogenetics, molecular biology, microarrays may potentially lead to a further increase of the clinical utility of percutaneous biopsy of renal tumors