Clinical Implications for Renal Mass Biopsy and Integration With Molecular Markers for Clinical Decision-Making

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Assistant Professor
2/6/2023

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Disclosure

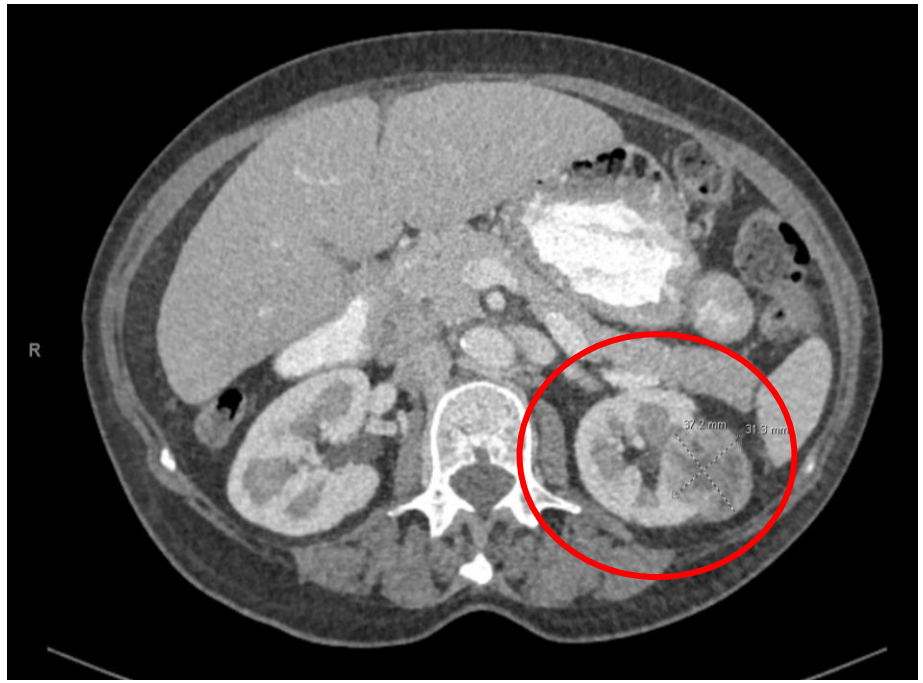
- I have no relevant financial relationships to disclose.

Objectives

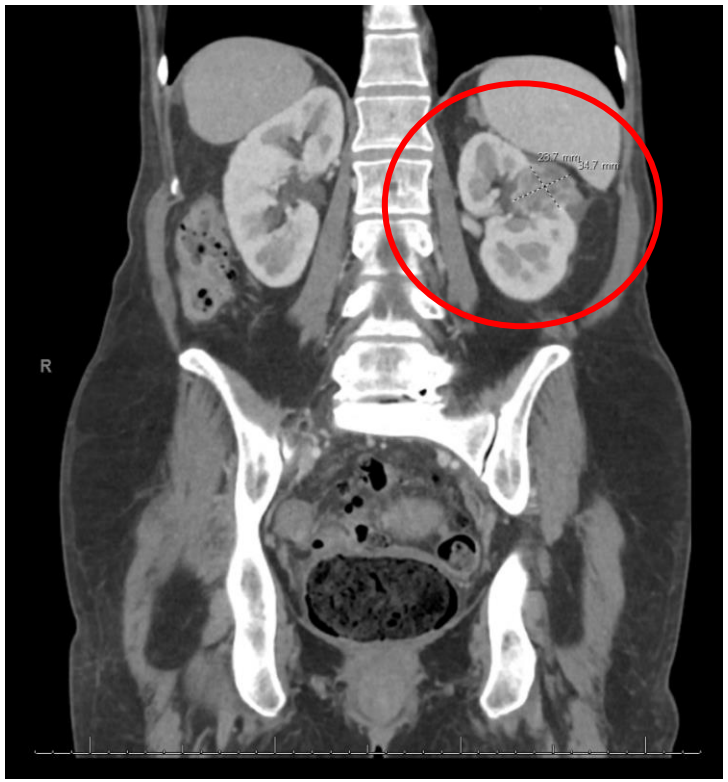
- At the conclusion of this activity, participants should be able to successfully:
  1. Understand surgical decision making around renal mass biopsy (RMB)
  2. Understand the utilization of RMB-based molecular biomarkers in renal cancer
  3. Identify clinical and research gaps for RMB and molecular biomarkers in renal cancer

Clinical Case for Discussion

HPI: 58yF incidentally detected LEFT renal mass
PMH: anxiety, cirrhosis, non-insulin dependent DM, HTN
Renal function: Cr 0.7/eGFR 95 mL/min, elevated alb/cr ratio in urine



3.1cm x 3.1 cm



2.4 cm x 3.5 cm

Small Renal Mass Clinical Decision Making

- Incidentally detected small renal mass (SRMs) (< or = 4 cm)

Q: surveillance vs treatment?

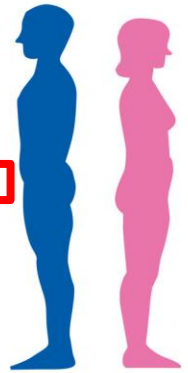
Important components of initial evaluation:

- History & Physical, assessment of overall patient health
- Hereditary renal cancer syndromes
- Baseline renal function and risk factors for chronic kidney disease
- Radiographic characteristics
- Possible renal mass biopsy

Epidemiology of Renal Cancer

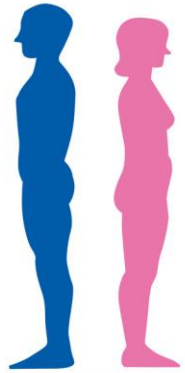
Estimated New Cases

Males			Females		
Prostate	268,490	27%	Breast	287,850	31%
Lung & bronchus	117,910	12%	Lung & bronchus	118,830	13%
Colon & rectum	80,690	8%	Colon & rectum	70,340	8%
Urinary bladder	61,700	6%	Uterine corpus	65,950	7%
Melanoma of the skin	57,180	6%	Melanoma of the skin	42,600	5%
Kidney & renal pelvis	50,290	5%	Non-Hodgkin lymphoma	36,350	4%
Non-Hodgkin lymphoma	44,120	4%	Thyroid	31,940	3%
Oral cavity & pharynx	38,700	4%	Pancreas	29,240	3%
Leukemia	35,810	4%	Kidney & renal pelvis	28,710	3%
Pancreas	32,970	3%	Leukemia	24,840	3%
All Sites	**983,160**	**100%**	**All Sites**	**934,870**	**100%**



Estimated Deaths

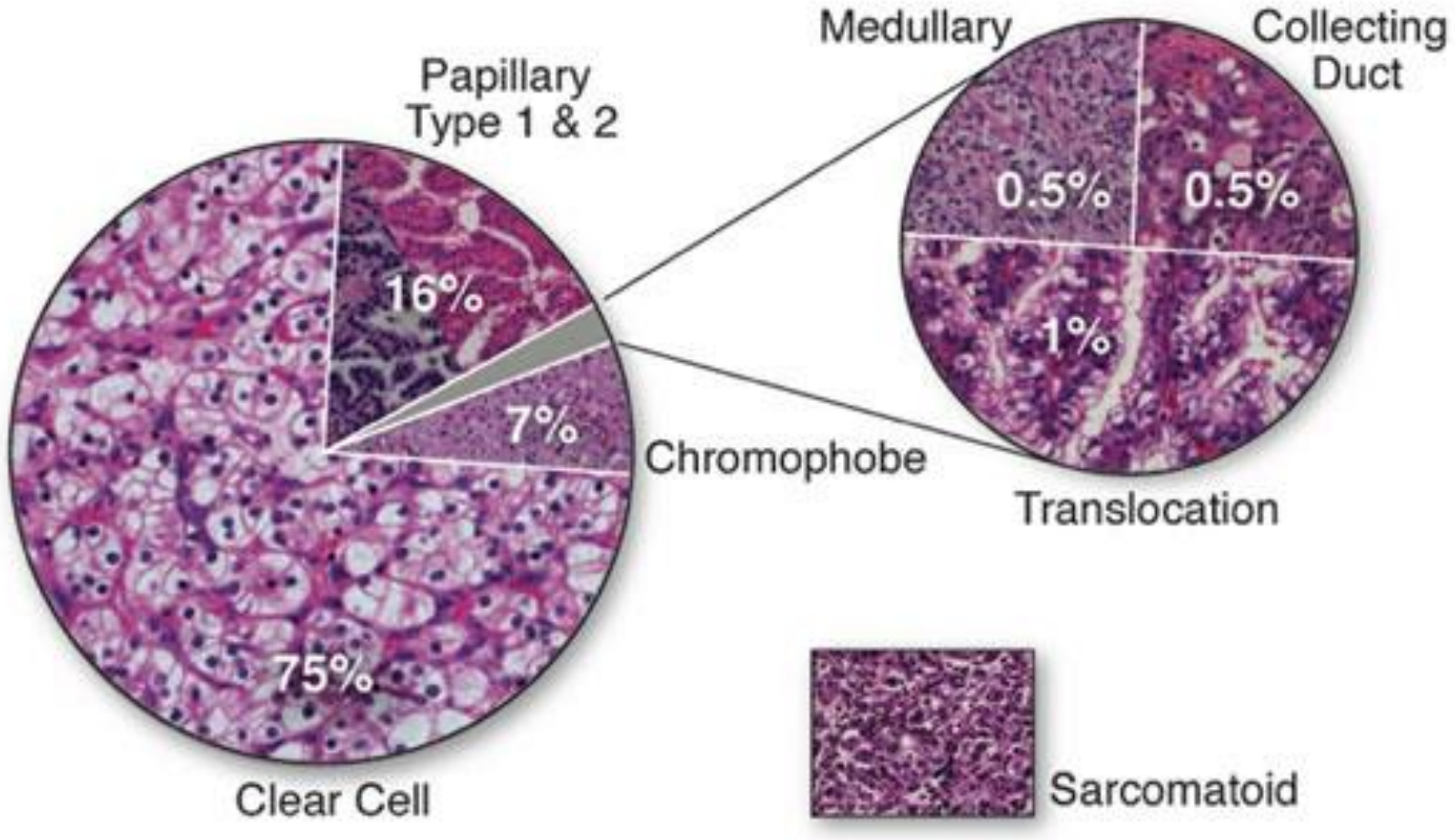
Males			Females		
Lung & bronchus	68,820	21%	Lung & bronchus	61,360	21%
Prostate	34,500	11%	Breast	43,250	15%
Colon & rectum	28,400	9%	Colon & rectum	24,180	8%
Pancreas	25,970	8%	Pancreas	23,860	8%
Liver & intrahepatic bile duct	20,420	6%	Ovary	12,810	4%
Leukemia	14,020	4%	Uterine corpus	12,550	4%
Esophagus	13,250	4%	Liver & intrahepatic bile duct	10,100	4%
Urinary bladder	12,120	4%	Leukemia	9,980	3%
Non-Hodgkin lymphoma	11,700	4%	Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,710	3%	Brain & other nervous system	7,570	3%
All Sites	**322,090**	**100%**	**All Sites**	**287,270**	**100%**



- 30% stage IV at diagnosis (synchronous)
- 30% develop metastases after treatment of localized disease (metachronous)

Siegel RL, *CA Cancer J*, 20022

Renal Cell Carcinoma is Not One Disease



5% of RCC are associated with hereditary syndromes

Shuch B, et al. *Eur Urol*, 2014

The Incidence of SRMs is Increasing

- Increased detection of asymptomatic SRMs
- 20-30% of biopsied or excised SRMs are benign (mainly oncocytoma and angiomyolipoma)
- 70% are malignant
- Benign tumors can grow
- Small number of SRM have metastatic potential (~2%)

Sanchez A, et al. *J Clin Oncol*, 2018

Radiographic Evaluation of SRMs

- Tumor size correlates with malignant pathology
- Presence of necrosis is a sign of aggressive disease
- Cystic masses are less aggressive
  - Less likely to biopsy a cystic mass as yield is lower
  - Bosniak III/IV resected lesions that have clear cell RCC have low malignant potential and very few metastatic events
- MRI to look at fat (AML)

Sanchez A, et al. *J Clin Oncol*, 2018
Silagi A, Sanchez A, et al. *Eur Urol Focus*, 2019

Radiographic Evaluation of SRMs

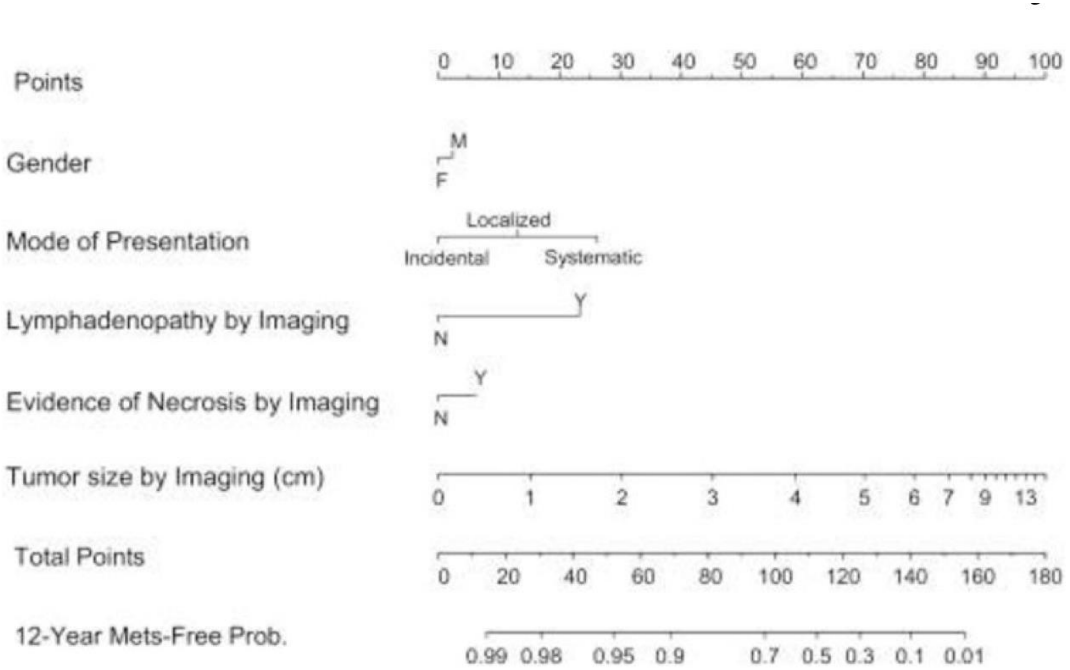


Figure 1 –.
Preoperative nomogram predicting freedom from metastatic recurrence at 12 years following definitive surgical management. Obtained with permission from: Raj GV, Thompson RH, Leibovich BC, Blute ML, Russo P, Kattan MW. Preoperative nomogram predicting 12-year probability of metastatic renal cancer. The Journal of Urology. 2008; 179:2146-51; https://www.auajournals.org/doi/10.1016/j.juro.2008.01.101

HPI: 58yF incidentally detected LEFT renal mass
PMH: anxiety, cirrhosis, non-insulin dependent DM, HTN
Renal function: Cr 0.7/eGFR 95 mL/min, elevated alb/cr ratio in urine

3.5 cm = 55 points
12-yr MFS ~ 95%

Radiographic Evaluation of SRMs: MRI ccRCC-LS

ORIGINAL RESEARCH · GENITOURINARY IMAGING

Radiology

Multicenter Evaluation of Multiparametric MRI Clear Cell Likelihood Scores in Solid Indeterminate Small Renal Masses

Nicola Schieda, MD • Matthew S. Davenport, MD • Stuart G. Silverman, MD • Barun Bagga, MD • Daniel Barkmeier, MD • Zane Blank, MD • Nicole E. Curci, MD • Ankur M. Doshi, MD • Ryan T. Downey, MD • Elizabeth Edney, MD • Elon Granader, MD • Isha Gujrathi, MD • Rebecca M. Hibbert, MD • Nicole Hindman, MD • Cynthia Walsh, MD • Tim Ramsay, PhD • Atul B. Shinagare, MD • Ivan Pedrosa, MD, PhD

From the Department of Medical Imaging, The Ottawa Hospital, University of Ottawa, Ottawa, Canada (N.S., R.M.H., C.W.); Departments of Radiology (M.S.D., D.B., N.E.C.) and Urology (M.S.D.), University of Michigan Medical Center, Ann Arbor, Mich; Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Mass (S.G.S., I.G., A.B.S.); Department of Radiology, NYU Langone Medical Center, New York, NY (B.B., A.M.D., N.H.); Department of Radiology, University of Nebraska Medical Center, Omaha, Neb (Z.B., R.T.D., E.E., E.G.); Department of Epidemiology, Ottawa Hospital Research Institute, Ottawa, Canada (T.R.); and Departments of Radiology and Urology, Advanced Imaging Research Center, University of Texas Southwestern Medical Center, 2201 Inwood Rd, 2nd Floor, Suite 202, Dallas, TX 75390-9085 (I.P.). Received July 3, 2021; revision requested August 16; revision received November 23; accepted December 30. **Address correspondence to** I.P. (e-mail: *ivan.pedrosa@UTSouthwestern.edu*).

Conflicts of interest are listed at the end of this article.

See also the editorial by Mileto and Potretzke in this issue.

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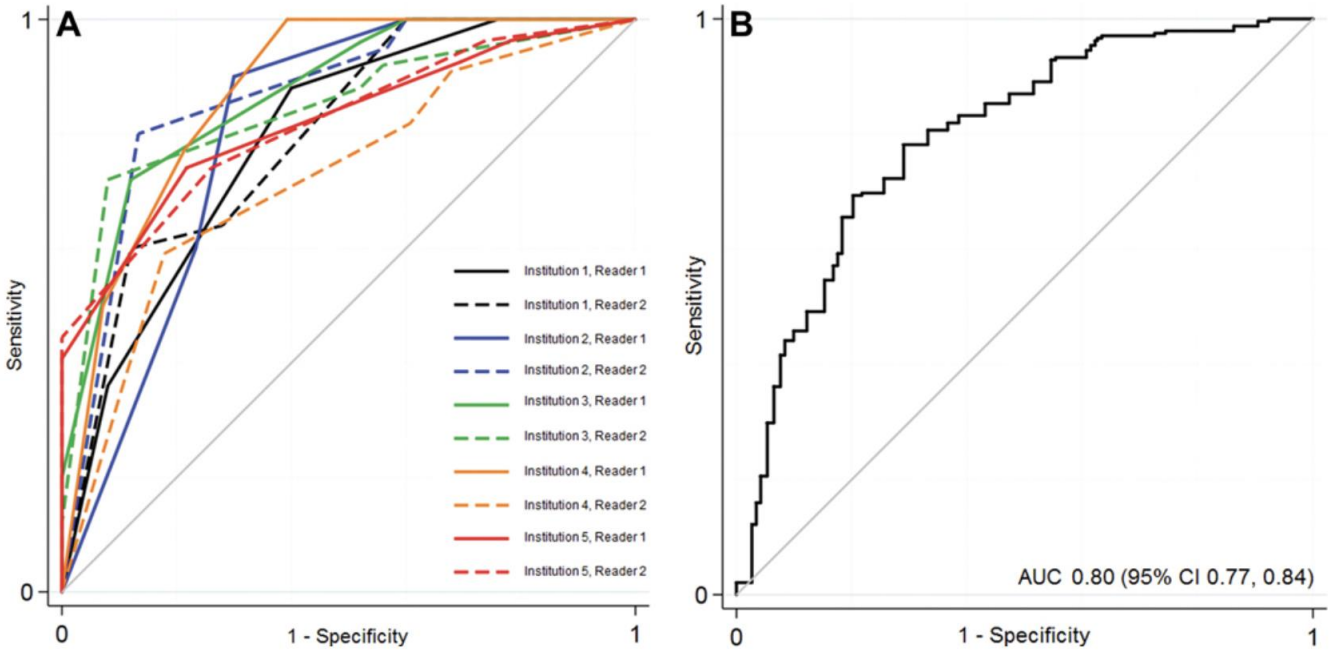
Radiographic Evaluation of SRMs: MRI ccRCC-LS

Figure 2.



Receiver operating characteristic (ROC) curve depicting the diagnostic performance of the multiparametric MRI clear cell likelihood score system across ten radiologists at five academic institutions (a) and overall (b), with the results pooled using a random-effects logistic regression model. AUC, area under the ROC curve.

Predictors of SRM behavior

- What other features are correlated with tumor growth or need for intervention?

- Growth trajectory (> or = 0.5 cm / year)
- Radiographic progression
- New local/systemic symptoms
- Biopsy-obtained histology and grade

Sanchez A, et al. *J Clin Oncol*, 2018

Campi R, et al. *Minerva Urol Nefrol*, 2020

Predictors of SRM behavior: Tumor Size

EUROPEAN UROLOGY 74 (2018) 489–497

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journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Kidney Cancer

Editorial by Uzoma A. Anele, Lance J. Hampton, Mayer B. Grob and Riccardo Autorino on pp. 498–500 of this issue

The Probability of Aggressive Versus Indolent Histology Based on Renal Tumor Size: Implications for Surveillance and Treatment

Bimal Bhindi [a], R. Houston Thompson [a], Christine M. Lohse [b], Ross J. Mason [a], Igor Frank [a], Brian A. Costello [c], Aaron M. Potretzke [a], Robert P. Hartman [d], Theodora A. Potretzke [d], Stephen A. Boorjian [a], John C. Cheville [e], Bradley C. Leibovich [a,]*

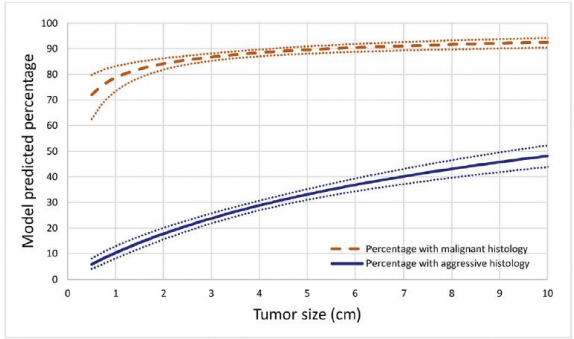
[a] *Department of Urology, Mayo Clinic, Rochester, MN, USA;* [b] *Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA;* [c] *Department of Medical Oncology, Mayo Clinic, Rochester, MN, USA;* [d] *Department of Radiology, Mayo Clinic, Rochester, MN, USA;* [e] *Department of Pathology, Mayo Clinic, Rochester, MN, USA*

Table 1 – Histologic classification

Indolent [a]	Aggressive [a]
Benign and indolent	Aggressive clear-cell RCC [c]
Oncocytoma	Aggressive papillary RCC [c]
Non-epithelioid angiomyolipoma [b]	Collecting duct RCC
Papillary adenoma	Unclassified RCC
Metanephric adenoma	Translocation-associated RCC [27]
Other benign tumors	Hereditary leiomyomatosis RCC [28]
	Other malignant non-RCC tumors
Malignant and indolent	
Epithelioid angiomyolipoma [b]	
Indolent clear-cell RCC [c]	
Indolent papillary RCC [c]	
Chromophobe RCC [d]	
Clear-cell papillary RCC [28,30]	
Tubulocystic RCC [32]	
Mucinous tubular and spindle cell RCC [31]	
Succinyl dehydrogenase deficient RCC [28]	

RCC = renal cell carcinoma.
[a] The presence of any sarcomatoid differentiation led to the classification of malignancies as aggressive. The presence of coagulative necrosis also led to the classification of malignancies as aggressive, except for low-grade (1–2) papillary RCC, where it does not appear to portend a poor prognosis [26].
[b] Epithelioid angiomyolipoma was considered malignant given its ability to metastasize, but indolent in behavior [33,34].
[c] In addition to sarcomatoid differentiation (both clear-cell and papillary RCC) and necrosis (clear-cell RCC), any high-grade (3–4) component led to aggressive classification for clear-cell and papillary RCC.
[d] Chromophobe RCC was not graded as per International Society of Urological Pathology 2012 Consensus Recommendations [29] and was considered indolent if sarcomatoid differentiation and coagulative necrosis were absent.

Tumor Size Correlates with Malignant and Aggressive Histology



Radiographic tumor size (cm)	1	2	3	4	5	6	7	8	9	10
Percentage with malignant histology (95% CI)	79 (74–83)	84 (82–86)	87 (85–88)	88 (87–90)	90 (88–91)	90 (89–92)	91 (89–93)	92 (90–93)	92 (90–94)	93 (90–94)
Percentage with aggressive histology (95% CI)	10 (8–13)	18 (16–20)	24 (22–26)	29 (27–31)	33 (31–35)	37 (34–39)	40 (37–43)	43 (40–47)	46 (42–50)	48 (44–52)

Fig. 1 – Predicted percentage with malignant and aggressive histology based on tumor size. Model-derived plots showing the percentage of malignant histology and aggressive histology based on radiographic tumor size in centimeters.
CI = confidence interval.

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Bhindi B, et al. *Eur Urol*, 2018

Some SRMs Have Metastatic Potential

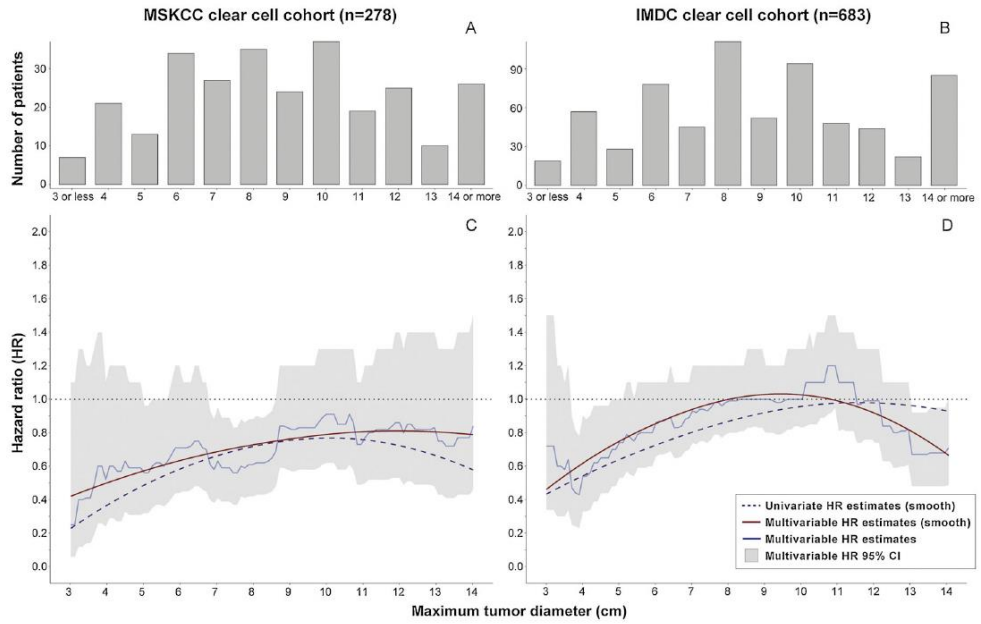

Fig. 5 –.
Relative effect of primary tumor size on survival across the size spectrum accounting for other prognostic factors. Results of the univariate and multivariable Cox regression analyses using sequential size cutoffs (0.1 cm increments). The top panels represent the distribution of tumor size in the (A) MSK and (B) IMDC cohorts. (C and D) The bottom panels show the hazard ratios and 95% confidence intervals for a small tumor compared with a large one at each size cutoff. Smaller tumor size seems to be associated with better survival in both cohorts. CI = confidence interval; HR = hazard ratio; IMDC = International Metastatic Database Consortium; MSK = Memorial Sloan Kettering; MSKCC = Memorial Sloan Kettering Cancer Center.

DiNatale R, et al. Eur *Urol Oncol*, 2020

Current Utilization of Renal Mass Biopsy for SRMs

2021 American Urological Association Guidelines

Renal Mass Biopsy (RMB)

10. When considering the utility of RMB, patients should be counseled regarding rationale, positive and negative predictive values, potential risks and non-diagnostic rates of RMB. (Moderate Recommendation; Evidence Level: Grade C)

11. Clinicians should consider RMB when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious. (Clinical Principle)

12. In the setting of a solid renal mass, RMB should be obtained on a utility-based approach whenever it may influence management. RMB is not required for 1) young or healthy patients who are unwilling to accept the uncertainties associated with RMB; or 2) older or frail patients who will be managed conservatively independent of RMB findings. (Expert Opinion)

13. For patients with a solid renal mass who elect RMB, multiple core biopsies should be performed and are preferred over fine needle aspiration (FNA). (Moderate Recommendation; Evidence Level: Grade C)

Campbell SC, et al. *J Urol*, 2021

Current Utilization of Renal Mass Biopsy for SRMs

- How are they performed?
  - 2-3 cores with 16-18G core needle under US or CT guidance
- Why is RMB underutilized in the urology community?
  - Complications related to RMB (2% Clavien 2 or > complications)
  - Potential to make renal surgery more difficult
  - Information not useful (particular oncocytic tumors)
- Who performs these biopsies?
  - IR, urologists (some clinic based)

Kapur P, et al. Eur Urol Oncol, 2022

Sanchez A, et al. *J Clin Oncol*, 2018

Current Utilization of Renal Mass Biopsy for SRMs

ELSEVIER

Urologic Oncology: Seminars and Original Investigations 39 (2021) 79.e1–79.e8

UROLOGIC ONCOLOGY

Clinical-Kidney cancer

Utilization of renal mass biopsy in patients with localized renal cell carcinoma: A population-based study utilizing the National Cancer Database

Devin N. Patel, M.D.[a], Fady Ghali, M.D.[a], Margaret F. Meagher, B.A.[a], Juan Javier-Desloges, M.D.[a], Sunil H. Patel, M.D.[a], Shady Soliman, M.S.[a], Kevin Hakimi, B.S.[a], Julia Yuan, B.S.[a], James Murphy, M.D.[b], Ithaar H. Derweesh, M.D.[a,*]

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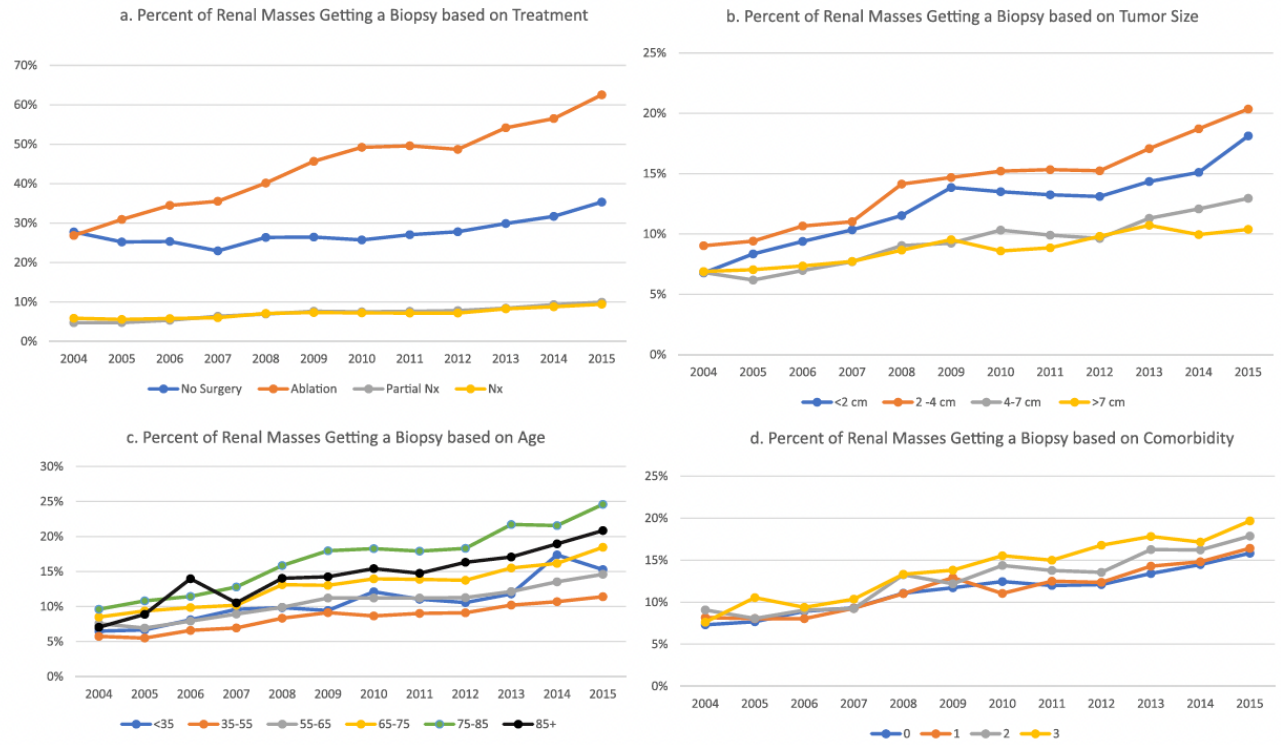

Fig. 2. (A–D) Unadjusted temporal trends of renal mass biopsy stratified by type of (A) treatment, (B) tumor size, (C) age subgroup, and (D) comorbidity.

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Patel DN, et al. Urol Oncol, 2021

What Information Can We Get From RMB?

- Accuracy for malignancy/histologic subtype: 100% PPV, 60% NPV, 15% non-diagnostic
  - Oncocytoma is a challenge, 25% have RCC on pathology
- Accuracy for histologic grade: good for high- vs low-grade tiered system
  - 20% with low-grade have high-grade on surgical pathology
- Results depend on size of lesion, cystic vs non-cystic, body habitus, etc
- Need good markers of 1) cancer vs no cancer and 2) disease aggressiveness associated with metastatic potential/development

- RMB wish list:
  - Sarcomatoid features
  - Clinically relevant molecular markers

Sanchez A, et al. *J Clin Oncol*, 2018

Challenges of RMB

- False negative and non-diagnostic biopsy (NPV 60%, non-diagnostic 15%)
- Oncocytic neoplasms
- Tumor heterogeneity

Addition of targeted WES results to RMB

Table 2.

Univariable and multivariable Cox models for predictors of metastasis-free probability (N=254)

		Univariable				Multivariable			
		N(E)	HR	[95% CI]	p-value	N(E)	HR	[95% CI]	p-value
VHL	Yes	152 (48)	1.41	[0.86 2.32] -	0.18		---		
	No	102 (23)	REF				---		
PBRM1	Yes	91 (34)	1.78	[1.112.83] -	**0.016**		1.41	[0.85 2.35] -	0.18
	No	163 (37)	REF				---		
SETD2	Yes	32 (19)	3.30	[1.94 5.59] -	**<.001**		2.09	[1.19 3.67] -	**0.011**
	No	222 (52)	REF				---		
BAP1	Yes	19 (9)	2.44	[1.21 4.93] -	**0.013**		0.83	[0.37 1.87] -	0.65
	No	235 (62)	REF				---		
KDM5C	Yes	19 (8)	1.58	[0.76 3.31] -	0.22		---		
	No	235 (63)	REF				---		
Nomogram Linear Predictor *		254 (71)	2.62	[2.10 3.27] -	**<.001**		2.58	[2.01 3.30] -	**<.001**

* The nomogram linear predictor includes the following factors: age, gender, mode of presentation, evidence of lymphadenopathy, evidence of necrosis and tumor size based on preoperative imaging.

The following equation from Raj et al, was used to calculate the value of the nomogram linear predictor: −3.1830084 – 0.00065242845*age + 0.10166342*gender + 0.56585476*presentation + 1.0072686*lymphadenopathy + 0.26592168*necrosis + 0.65408506*size - 0.0086883408*max(size-2, 0)**3 + 0.013366678*max(size-4.8, 0)**3-0.0046783373*max(size-10, 0)**3. Size was treated as a cubic spline.

N = Total # patients for level; E = # events for level; HR = hazard ratio; 95%CI = 95% confidence interval

Mano R, et al. *Urol Oncol*, 2021

Prognostic Molecular Markers Available in Localized RCC

Table 1 –

Identified prognostic genomic patterns that included SRMs

Study	Assay	Nomogram integration	Categorization	Source	Material	Histology	SRM analysis	Prognostic utility
Brooks et al [47]	Clear Code34	Leibovich [69]	ccA/ccB	Radical tumor	RNA	ccRCC	No	RFS, CSS, OS
Rini et al [48]	16 genes	Leibovich [69]	0–100 recurrence score	Radical tumor	RNA[a]	ccRCC	T1 tumors	RFS
Morgan et al [49]	CCP	Karakiewicz [70]	High/low risk	Radical tumor	RNA	Chromophobe RCC, papillary RCC, & ccRCC	No	RFS, CSS
Manley et al [50,52]	Targeted somatic gene mutations	None	*KDM5C* mutation	Radical tumor	DNA	ccRCC	Yes	Worse OS

ccA = clear cell type A; ccB = clear cell type B; CCP = cell cycle progression; ccRCC = clear cell RCC; CSS = cancer-specific survival; OS = overall survival; PCR = polymerase chain reaction; RCC = renal cell carcinoma; RFS = recurrence-free survival; SRM = small renal mass.

[a]RNA underwent reverse transcription PCR to determine gene expression.

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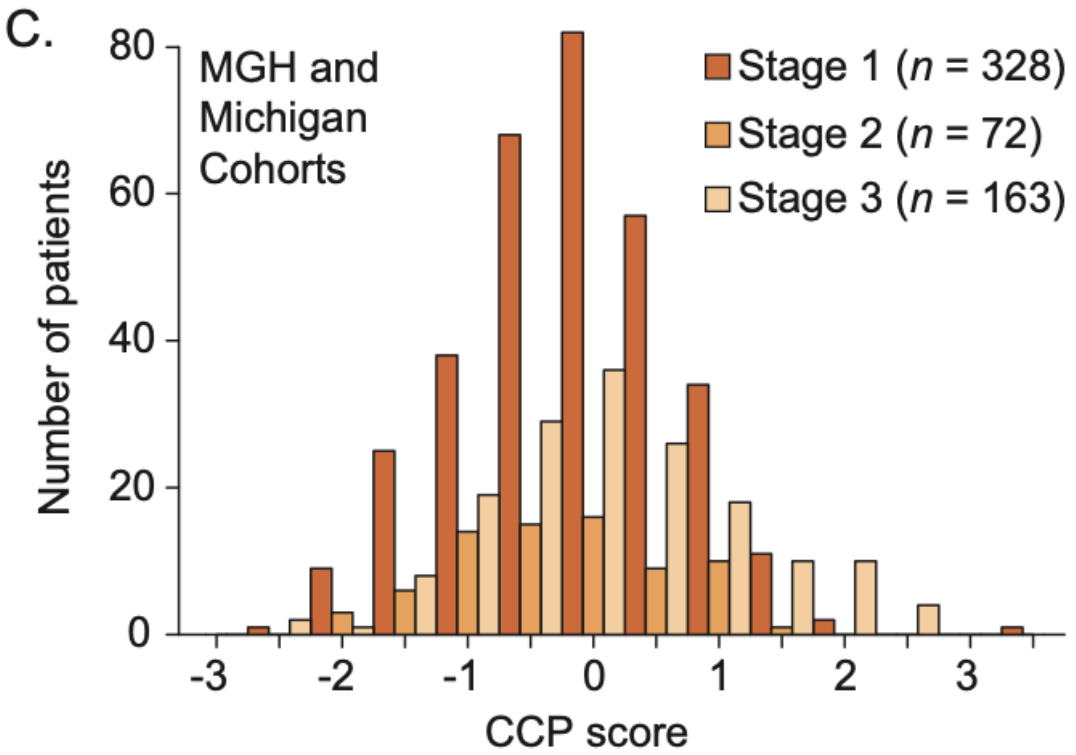
Silagy AW, et al. *European Urol Focus*, 2019

Existing biomarkers in localized ccRCC: CCP

- Cell-cycle progression (CCP) score by Myriad genetics (SLC, UT) improves prediction of 5-year DSM and adverse pathology (G3-4, pT stage >= 3, mets at surgery or papillary type 2) on biopsy

- CCP = 31 cell cycle genes normalized to the expression of 15 housekeeping genes

PROGNOSTIC

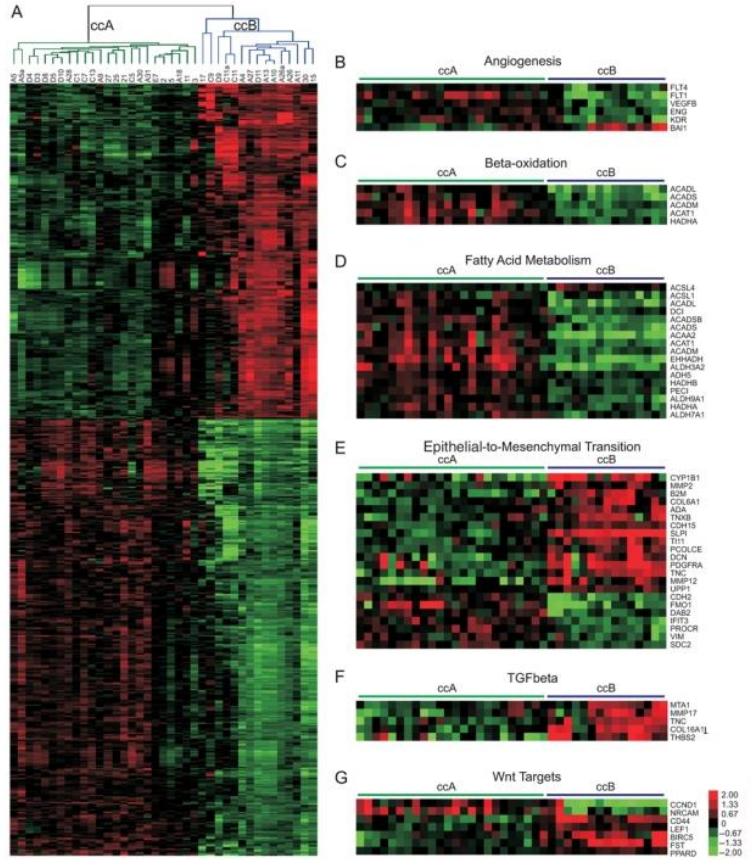


Morgan T, et al. *Eur Urology*, 2017
Tosoian JJ, et al. Eur Urol, 2020

Existing biomarkers in localized ccRCC: ccA/ccB

- ClearCode34 (initially 110 genes -> 34 genes)
- Developed in 72 patients -> validated in TCGA
- C-index 0.65-0.70

PROGNOSTIC

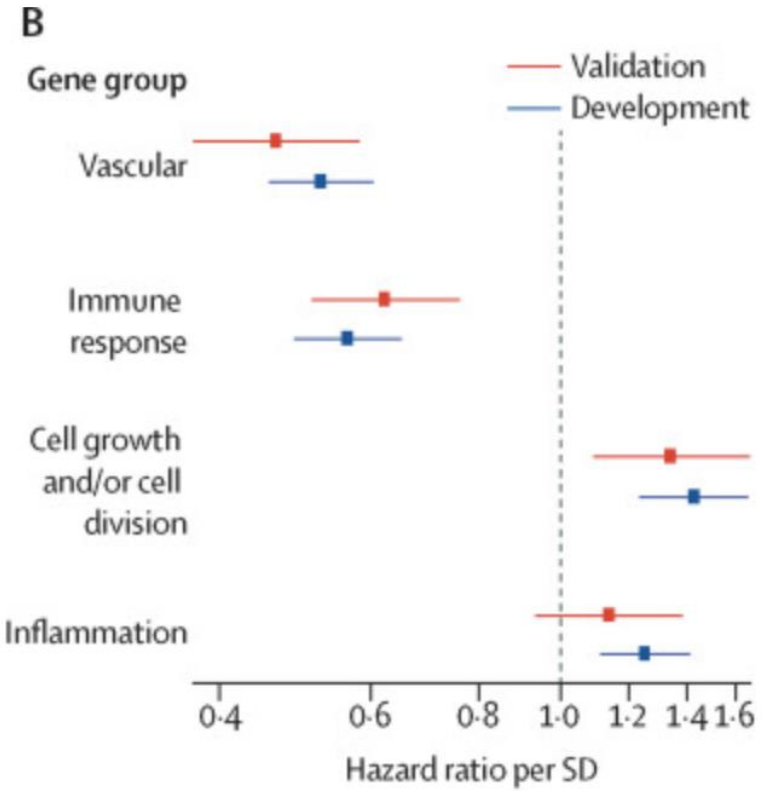


Brannon, et al. *Eur Urology*, 2012
Brannon, et al. *Genes Cancer*, 2010

Existing biomarkers in localized ccRCC

- 16 cancer-related genes
- Independently associated with cancer recurrence
- C-index of 0.81

PROGNOSTIC



Rini, et al. *Lancet Oncol*, 2015

Summary of clinical, radiographic, and molecular features of SRMs

Table 2 –

Distinguishing features between aggressive and nonaggressive SRM profiles

	Higher-risk SRM profile	**Lower-risk SRM profile**
Clinical characteristics		
Sex [15]	Male	Female
Presentation [15]	Symptomatic	Asymptomatic
Smoking history [71]	Active smoker	Nonsmoker
Pathological characteristics		
Clinical stage	≥T3a	T1a
Histology	ccRCC, papillary type 2, unclassified	Papillary type 1, chromophobe
Grade	3 or 4	1 or 2
Sarcomatoid features	Present	Absent
Imaging characteristics		
Size (cm) [15]	3–4	1–2
Tumor growth rate (cm/yr) [24]	≥0.5	<0.5
Necrosis [15]	Present	Absent
Molecular profiling		
Somatic mutations [50–52]	*KDM5C, BAP1, SETD2, TP53*	
Copy number alteration [64]	Increased no. of alterations	Decreased no. of alterations
Transcriptomic profiles [47,49]	ccB	ccA
	High CCP score	Low CCP score
Clonal drivers [56]	"VHL wild type," "multiple clonal drivers," "BAP1 driven"	"VHL monodriver"

ccA = clear cell type A; ccB = clear cell type B; CCP = cell cycle progression; ccRCC = clear cell RCC; SRM = small renal mass.

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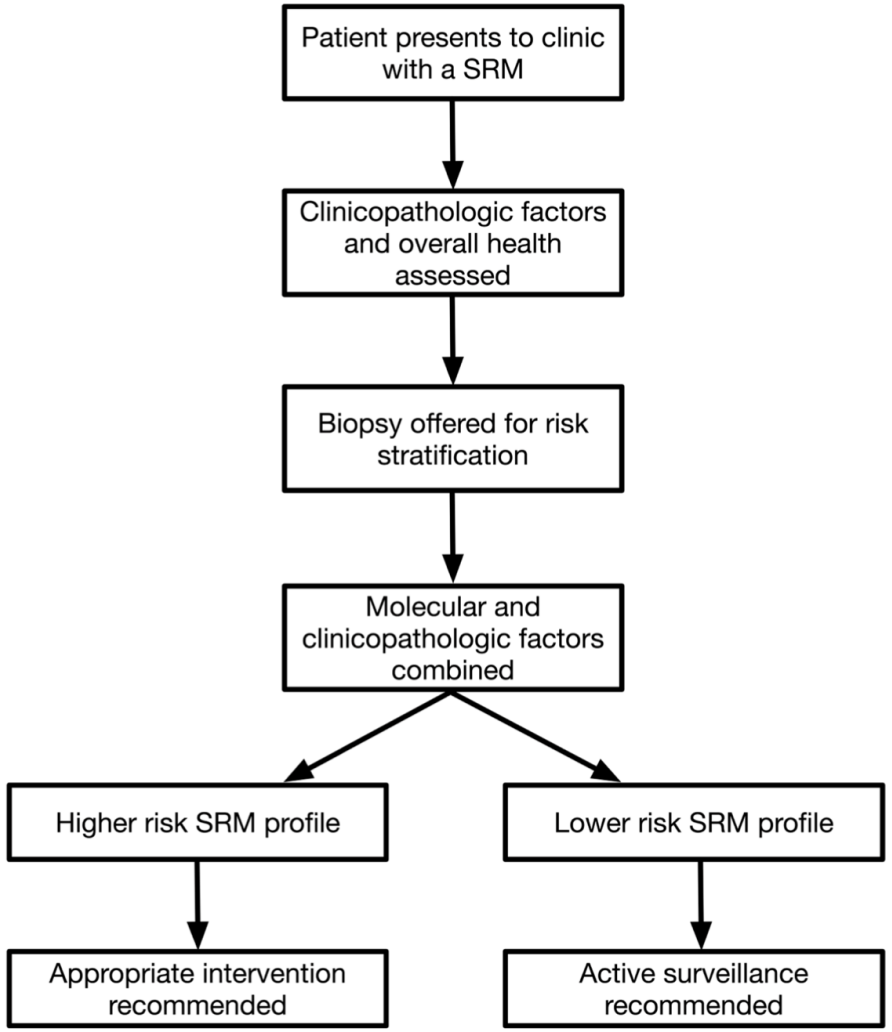
Proposed Integration of Molecular Markers



Additional information that could be obtained from RMB: BAP1 IHC

Table 4 – Multivariable Cox proportional hazards model for time to metastasis in SRM[RCC], controlling for TNM stage at diagnosis

N = 1093*	Metastasis Events/ Total (%)	Hazard Ratio (95% CI)	Cox *p*
BAP1 IHC			**0.02**
ccRCC BAP1+	21/660 (3.2)	Reference	
ccRCC BAP1−	8/55 (15)	3.05 (1.30, 7.15)	
Non-ccRCC	8/378 (2.1)	0.85 (0.37, 1.98)	

* SRM[RCC] with available BAP1 status and TNM stage.

Table 5 – Hazard ratios for time to metastasis and p-values for BAP1 expression after adjusting for SSIGN score in SRM[RCC]

N = 791*	Metastasis Events/ Total (%)	Hazard Ratio (95% CI)	Cox *p*
BAP1 IHC			**0.003**
ccRCC BAP1+	19/525 (3.6)	Reference	
ccRCC BAP1−	8/47 (17)	3.58 (1.53, 8.35)	
Non-ccRCC	7/219 (3.2)	0.72 (0.30, 1.74)	
SSIGN score		1.94 (1.71, 2.19)	**<0.001**

* SRM[RCC] with available BAP1 status and SSIGN score.

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Kapur P, et al. Eur Urol Oncol, 2022

Biomarker Limitations to Consider

- Gene expression biomarkers
  - Heterogeneity
  - Platform used
  - Overlap between signatures
- Patient population being studied
- Statistical power
- Dichotomizing biomarkers, arbitrary cut-points

Validation of existing ccRCC biomarkers

- 17 of 28 published genetic and transcriptomic *prognostic* ccRCC markers were validated in an independent cohort
- Of those, only ccB gene expression was significant in MVA

Table 4

Multivariate survival analysis

Variable	Including *BAP1* mutations and chromosome 19 deletion		Excluding *BAP1* mutations and chromosome 19 deletion	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
Tumour stage				
Stage I	1.00 (Ref)		1.00 (Ref)	
Stage II	3.48 (1.20–10.06)	0.022	3.40 (1.18–9.82)	0.024
Stage III	4.61 (1.93–11.00)	<0.001	4.86 (2.05–11.55)	<0.001
Stage IV	18.01 (7.89–41.12)	<0.001	17.77 (7.79–40.53)	<0.001
Chromosome 19 deletion	4.18 (1.27–13.69)	0.018	–	–
ccA status	1.00 (Ref)		1.00 (Ref)	
ccB status	2.99 (1.87–4.80)	<0.001	2.95 (1.84–4.72)	<0.001

CI = confidence interval.

Gulati S, Eur Urol, 2014

Biomarker Driven Neoadjuvant Therapy Clinical Trial in ccRCC

Beuselinck et al.

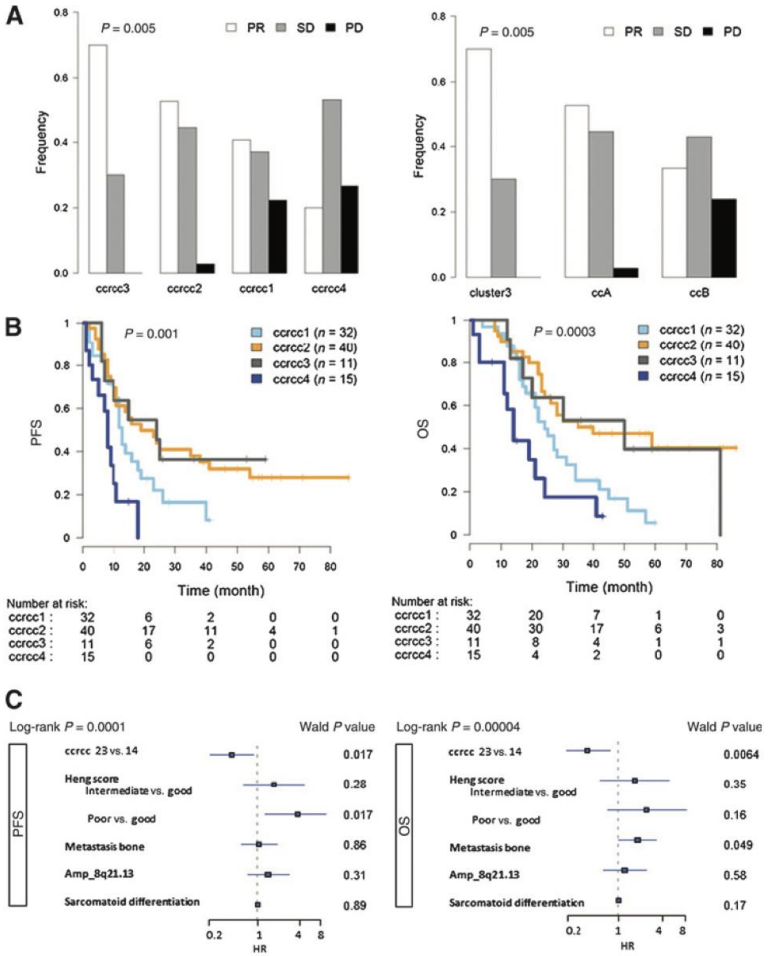


Figure 3.
Correlation of the four molecular subgroups and outcome on sunitinib in the metastatic setting. A, association of sunitinib response with the unsupervised subgroups ccrcc1 to ccrcc4 (left) and the Brannon subgroups (right). The *P* values result from Fisher exact tests. B, association of the four unsupervised subgroups with PFS (left) and OS (right). Log-rank *P* values are on the top right. C, forest plots of the multivariate Cox models for PFS and OS.

Epaillard N, et al. *Bulletin du Cancer*, 2020
Beuselinck et al., *Clin Cancer Research*, 2015

NCT02960906

Existing Biomarker Questions

- How can we evaluate/incorporate *prognostic* biomarkers derived from systemic therapy trials in patients with localized ccRCC to guide treatment selection for neoadjuvant and adjuvant clinical trials?
- Can we derive some of these biomarkers from biopsy samples of tumors?
- How should we critically evaluate these biomarkers before incorporating them into practice/trials?
- What can we learn about the pathology/biology of tumors with these different signatures?
  - E.g., angiogenesis gene expression signatures -> go back to path to look at differences in angiogenesis

Small Renal Mass Clinical Case for Discussion

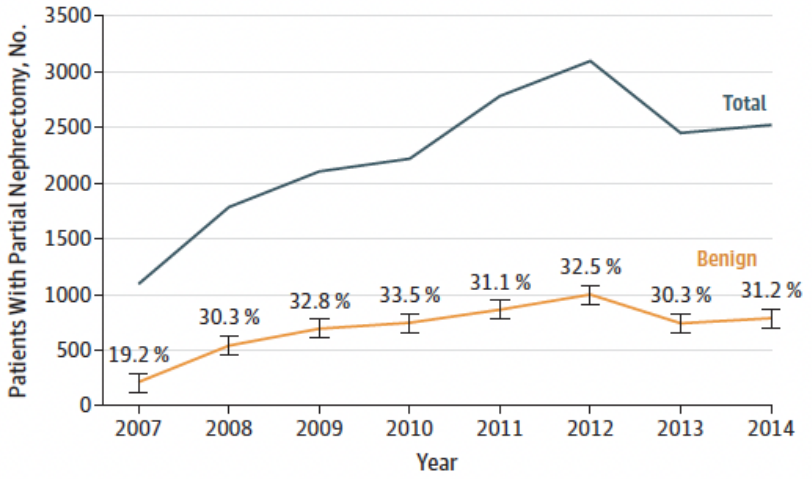
HPI: 58yF incidentally detected LEFT renal mass
PMH: anxiety, cirrhosis, non-insulin dependent DM, HTN
Renal function: Cr 0.7/eGFR 95 mL/min, elevated alb/cr ratio in urine

3.5 cm = 55 points
12-yr MFS ~ 95%

- Elected for LEFT robotic partial nephrectomy
- 30 minutes warm ischemic time
- **Pathology:** AML with expansile histiocytic inflammation
- 1 year Cr 0.82/eGFR 82 mL/min

Benign Pathology on Surgical Resection

Figure. Annual Prevalence of Benign and Malignant Findings From 2007 to 2014



Percentages represent the annual proportion of benign prevalence among total patients who underwent PNx.

Table 4. Multiple Logistic Analysis to Predict Benign Pathologic Findings After Partial Nephrectomy

Variable	OR (95% CI)[a]	*P* Value[a]	OR (95% CI)[b]	*P* Value[b]
Sex, female vs male	0.62 (0.58-0.66)	<.001	0.62 (0.58-0.66)	<.001
Age	0.989 (0.986-0.991)	<.001	0.989 (0.986-0.991)	<.001
Imaging pattern				
Any CT	NA		1.01 (0.90-1.14)	.87
Any MRI			1.07 (0.99-1.15)	.08
Any USG			0.94 (0.89-1.01)	.07
Any Biopsy			1.38 (1.21-1.57)	<.001
Imaging combination pattern				
All other combinations vs CT only	1.16 (1.05-1.28)	.004	NA	NA
CT + MRI vs CT only	1.07 (0.96-1.20)	.25		
CT + MRI + USG vs CT only	1.03 (0.93-1.15)	.54		
CT + USG vs CT only	0.93 (0.86-1.01)	.08		
Geographic region				
North Central vs West	0.88 (0.79-0.98)	.02	0.88 (0.79-0.97)	.01
Northeast vs West	1.05 (0.94-1.17)	.37	1.06 (0.95-1.18)	.30
South vs West	1.03 (0.93-1.14)	.57	1.03 (0.93-1.14)	.56
Unknown vs West	1.02 (0.83-1.25)	.85	1.02 (0.83-1.25)	.85

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; NA, not applicable; OR, odds ratio; USG, ultrasonography.

[a] Multiple logistic regression analysis was done without adjustment of imaging pattern.

[b] Multiple logistic regression analysis was done without adjustment of imaging combination pattern.

Female sex, older age > 65, and CT only pre-op imaging associated with benign pathology

Kim JH, et al., JAMA Surgery, 2019

Future Directions

- RMB will need to be used to guide neoadjuvant therapies once FDA approved
- Combine RMB with radiomic markers (e.g., MRI characteristics)
- Biopsy of patients with systemic treatment resistance for future treatment selection (e.g., biopsy of lung met)