

*Carcinoma renale:  
aspetti multidisciplinari*

NOVARA,  
12 Aprile 2013

**RCC e biopsia renale: quali indicazioni  
e difficoltà tecnico-interpretative?**

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SOC Urologia Dott. G. Fasolis  
Ospedale "San Lazzaro" ASL CN2 - Alba



# 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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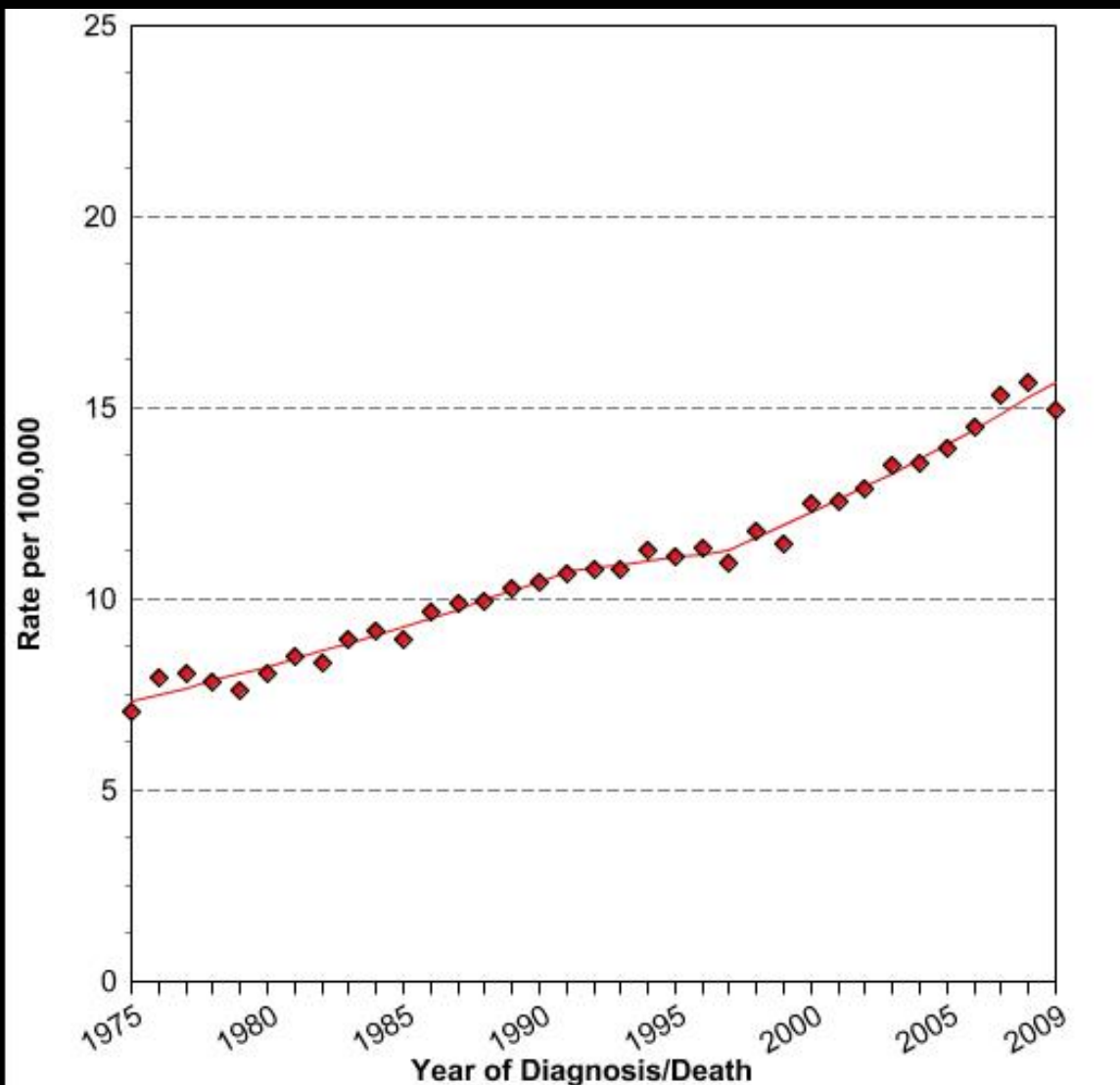
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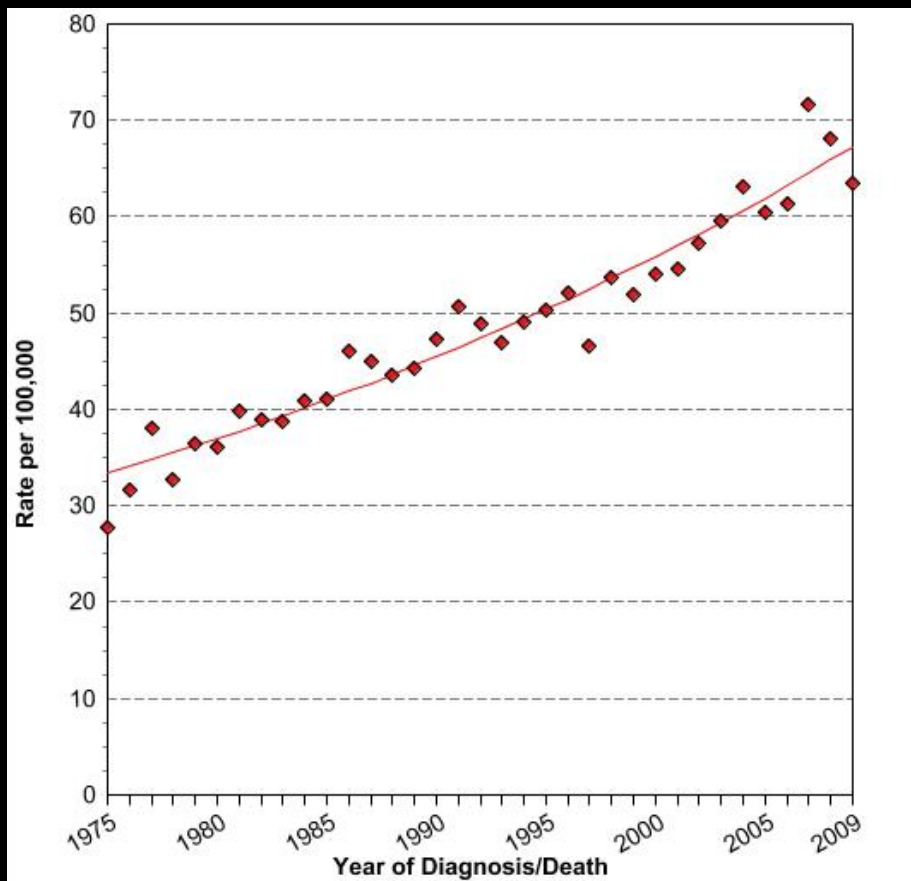
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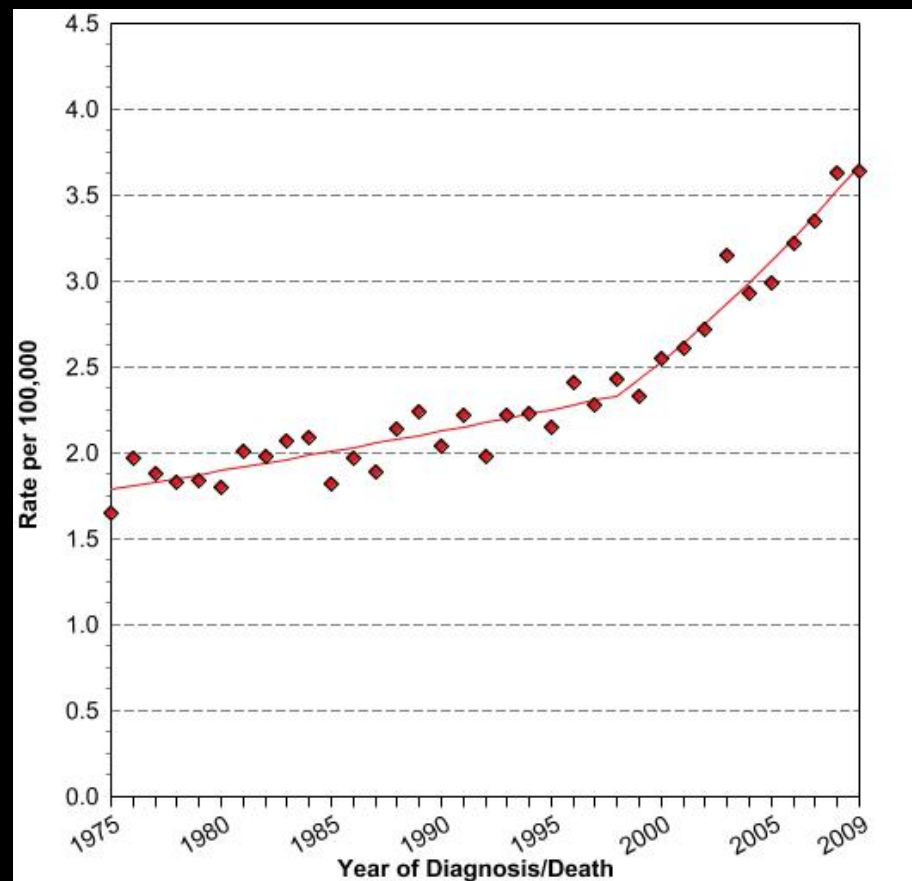
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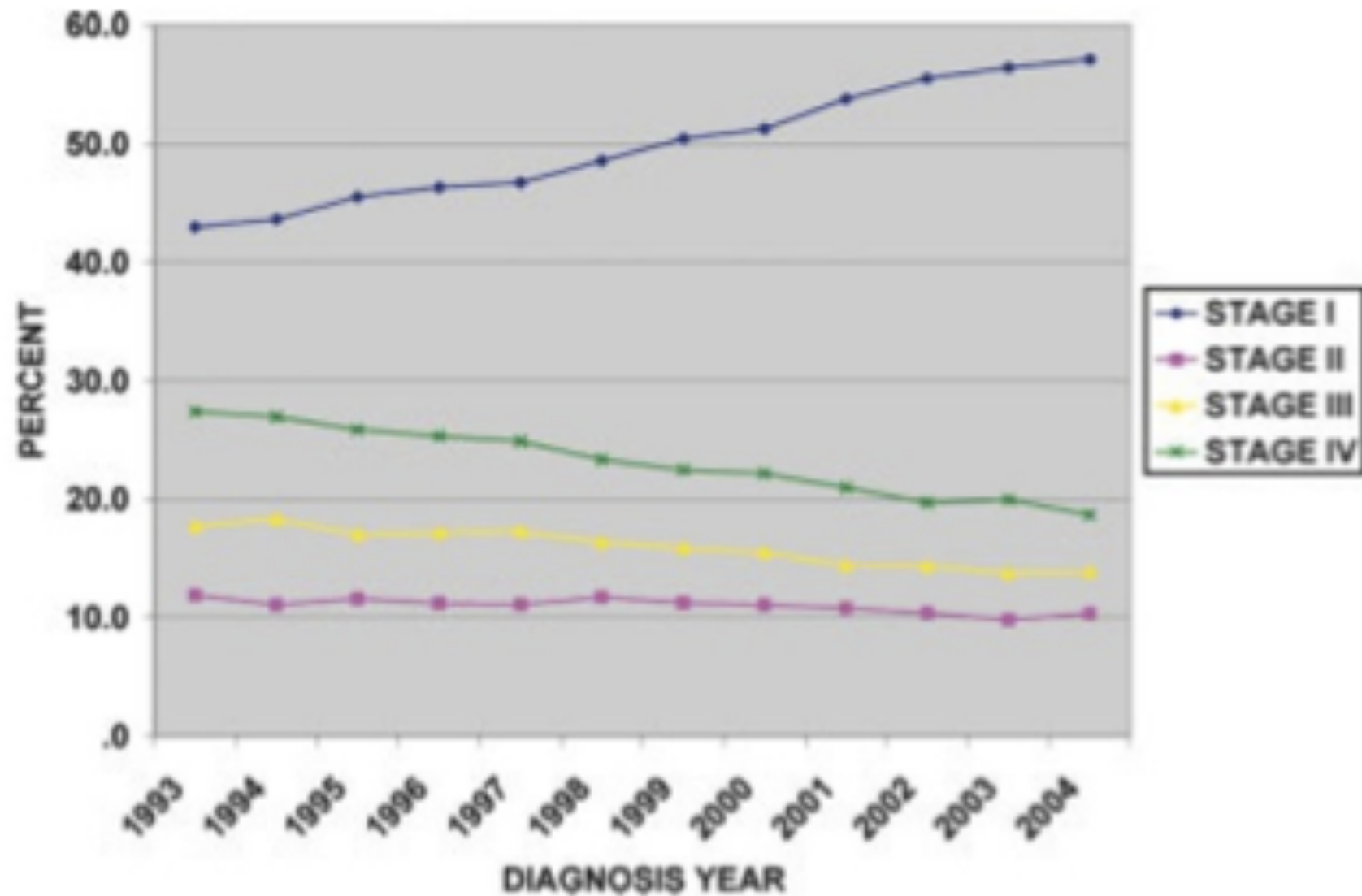


>75 anni



<50 anni

# Migrazione di stadio



Il **30%** delle masse renali <4 cm rimosse chirurgicamente alla Mayo Clinic sono **benigne**

Frank, J Urol 2003

Circa il **30%** delle masse renali <4 cm rimosse con nefrectomia parziale laparoscopica sono **benigne**

Link , J Urol 2005

Moinzadeh, J Urol 2006

# La probabilità di istologia benigna aumenta al diminuire delle dimensioni

**TABLE 3.** *Proportion of benign versus RCC tumors according to tumor size*

Tumor Size (cm)	No. Benign (%)	No. RCC (%)
0.0–Less than 1.0	37 (46.3)	43 (53.8)
1.0–Less than 2.0	38 (22.4)	132 (77.7)
2.0–Less than 3.0	75 (22.0)	266 (78.0)
3.0–Less than 4.0	71 (19.9)	285 (80.1)
4.0–Less than 5.0	37 (9.9)	336 (90.1)
5.0–Less than 6.0	40 (13.0)	267 (87.0)
6.0–Less than 7.0	11 (4.5)	232 (95.5)
7.0 or Greater	67 (6.3)	998 (93.7)

Percentages indicate the proportion of tumors in each size category that are benign or RCC, respectively.

Frank, J Urol 2003

**Table 2.** *Benign tumors vs RCC according to size in patients treated surgically for renal mass*

Size (cm)	No. Benign (%)	No. RCC (%)
Less than 1	6 (37.5)	10 (62.5)
1–Less than 2	56 (19.2)	236 (80.8)
2–Less than 3	77 (16.5)	391 (83.5)
3–Less than 4	58 (13.0)	390 (87.0)
4–Less than 5	30 (8.7)	315 (91.3)
5–Less than 6	23 (10.0)	206 (90.0)
6–Less than 7	13 (6.6)	183 (93.4)
7 or Greater	48 (7.1)	633 (92.9)

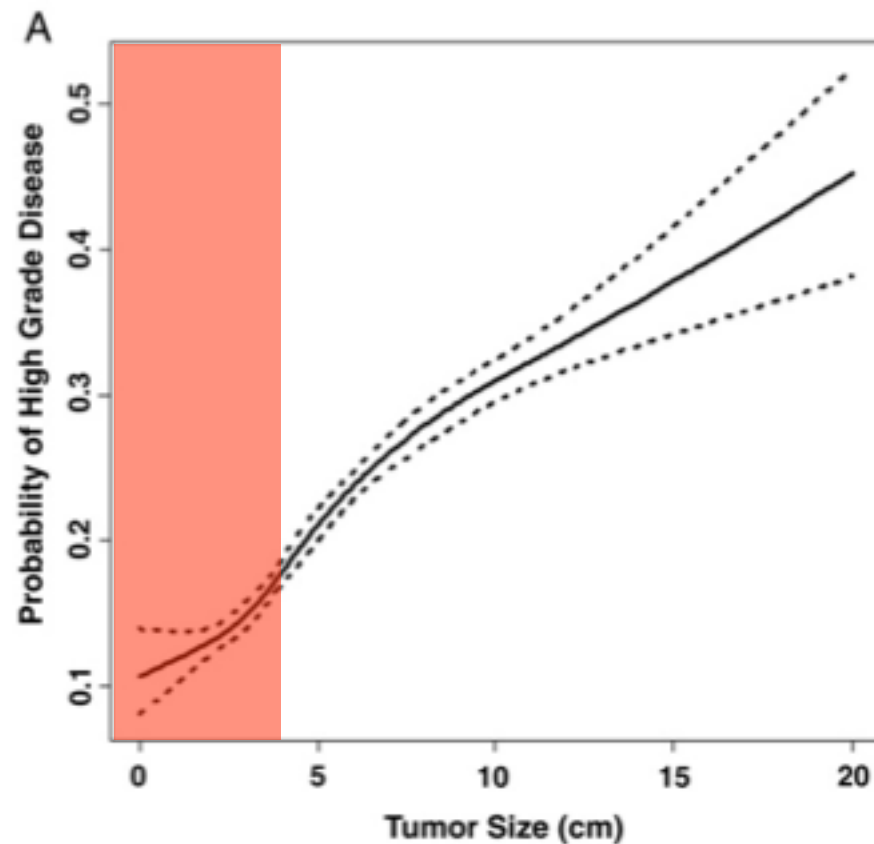
Thompson, J Urol 2009

## Adult Urology

### Oncology: Adrenal/Renal/Upper Tract/Bladder

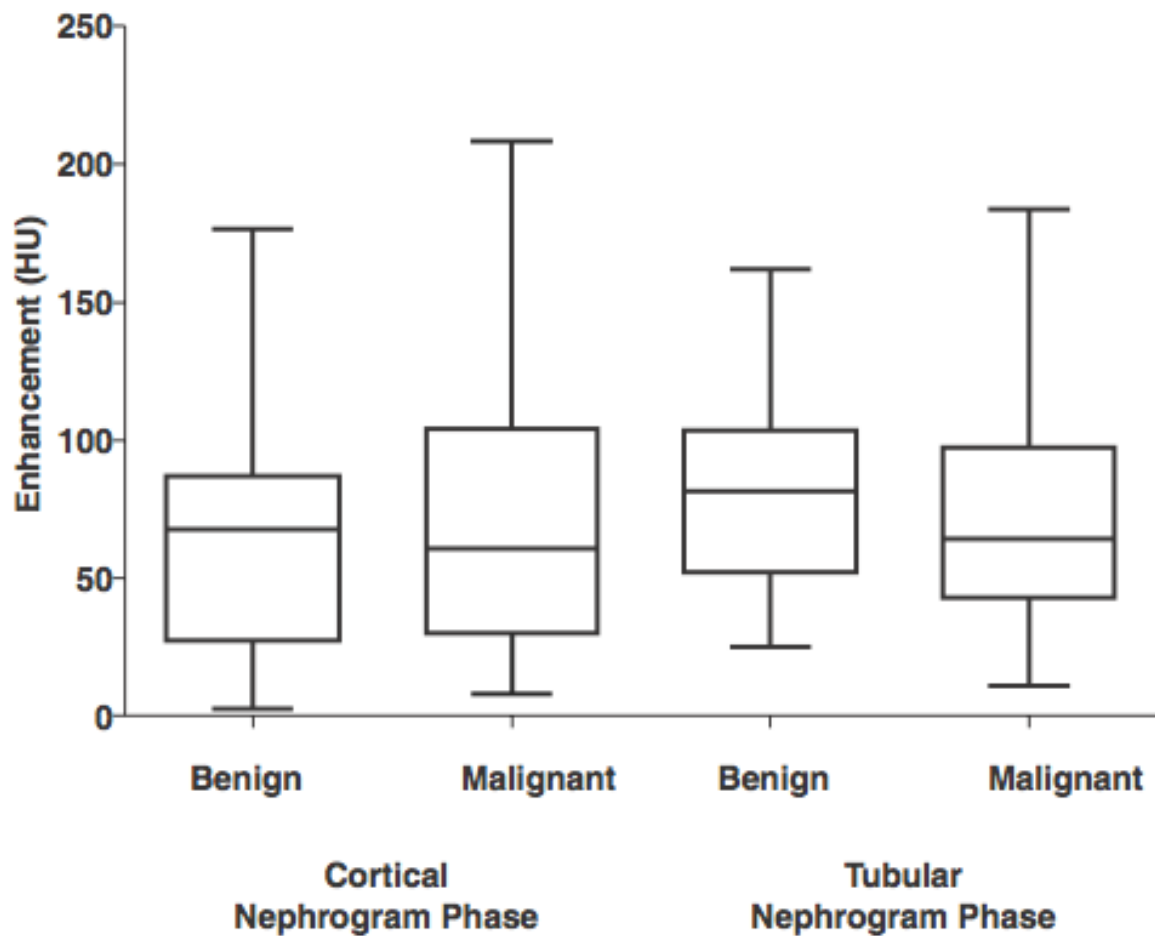
#### Histopathological Characteristics of Localized Renal Cell Carcinoma Correlate With Tumor Size: A SEER Analysis

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



Ingrid Millet<sup>1</sup>  
Fernanda Curros Doyon<sup>1</sup>  
Denis Hoa<sup>1</sup>  
Rodolphe Thuret<sup>2</sup>  
Samuel Merigeaud<sup>1</sup>  
Isabelle Serre<sup>3</sup>  
Patrice Taourel<sup>1</sup>

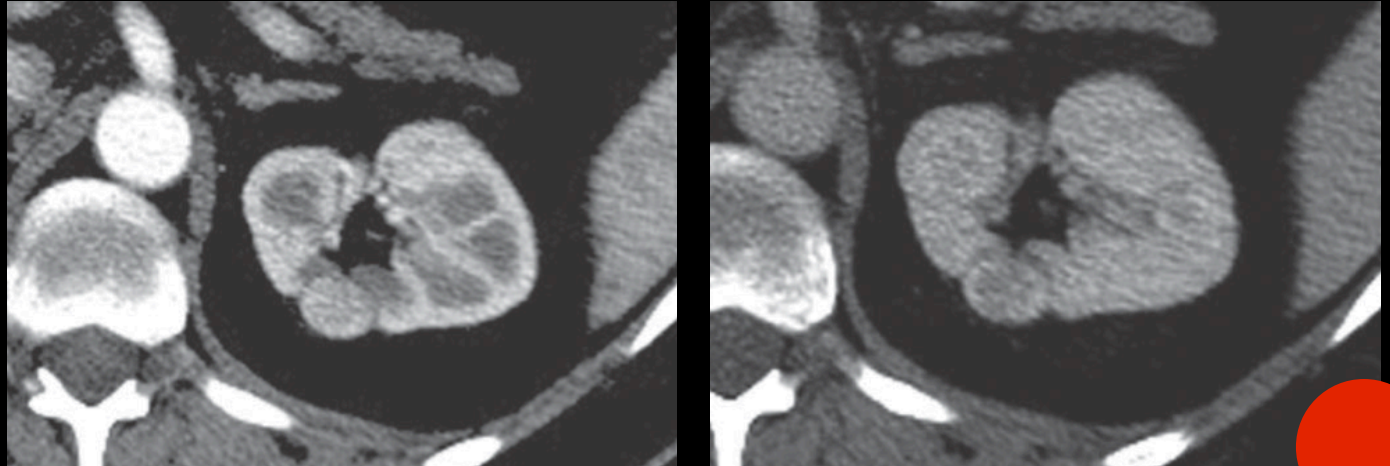
# Characterization of Small Solid Renal Lesions: Can Benign and Malignant Tumors Be Differentiated With CT?



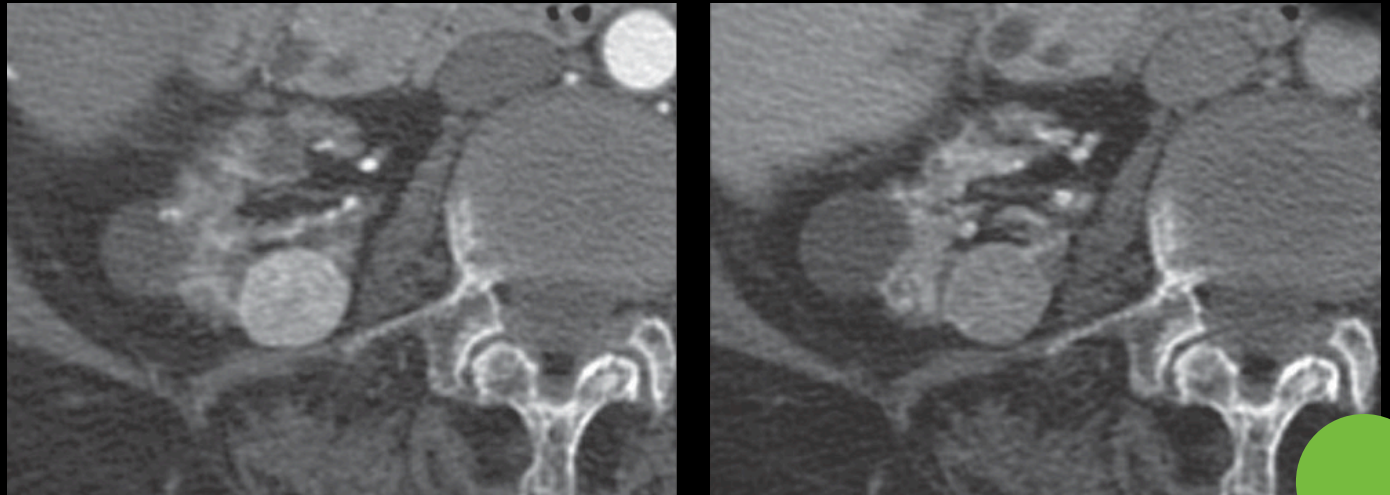


# Enhancement

Carcinoma renale

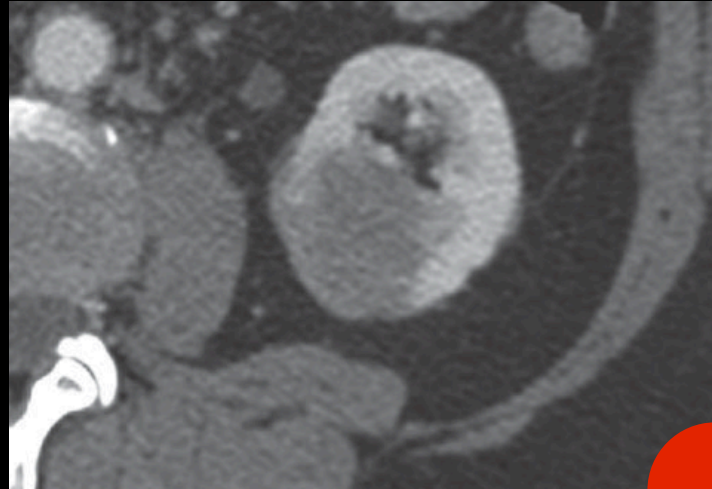


Oncocytoma

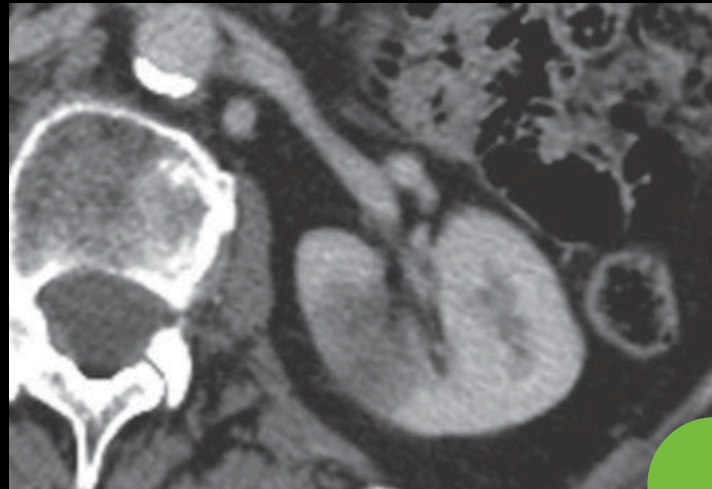


# Margini

Linfoma

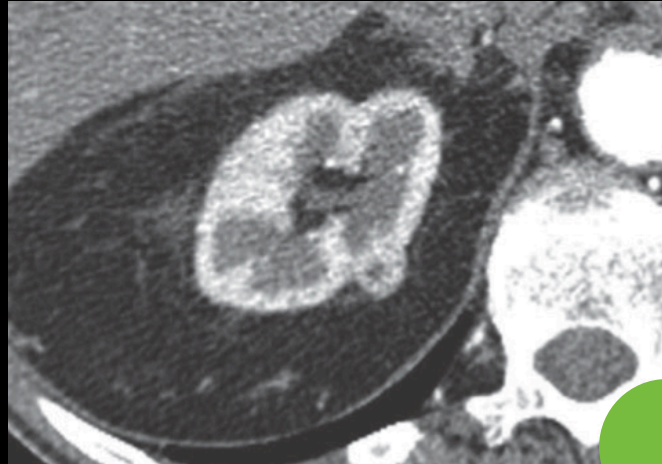


Wegener

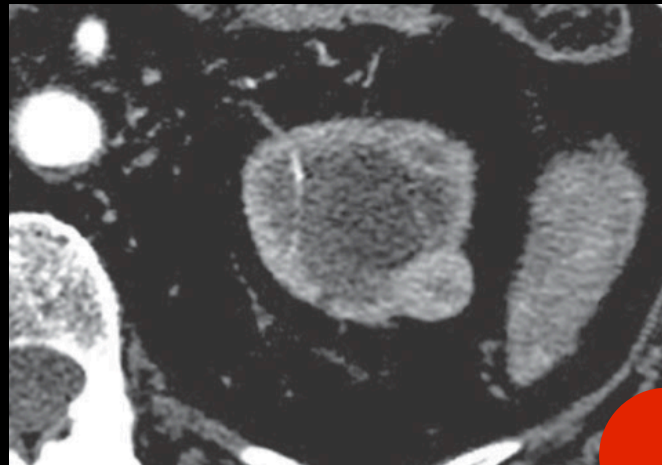


# Cicatrice centrale

Oncocitoma

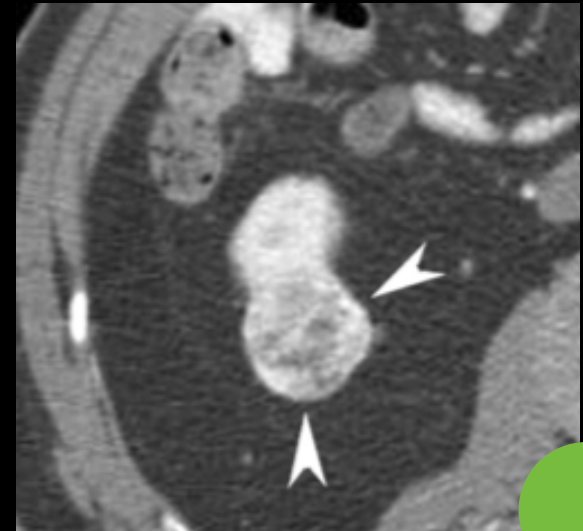
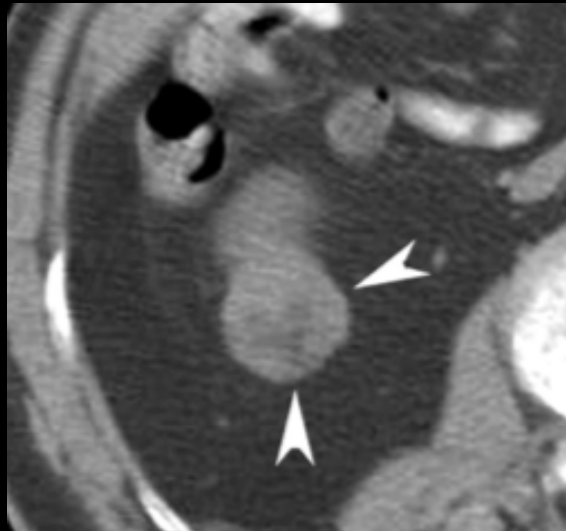


Carcinoma renale

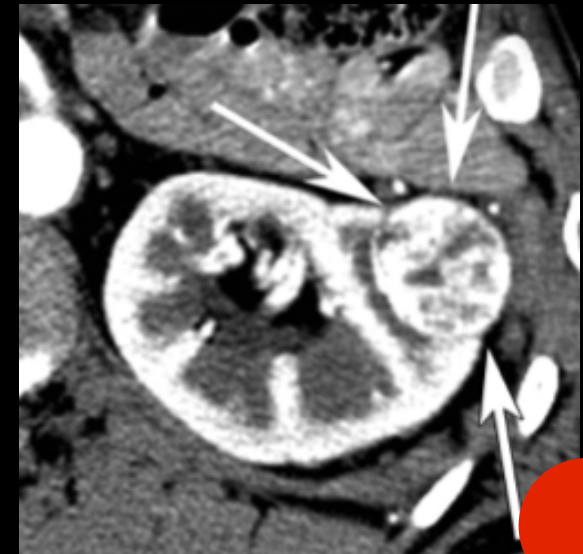


# AML vs RCC

Angiomiolipoma con  
ridotta componente  
adiposa

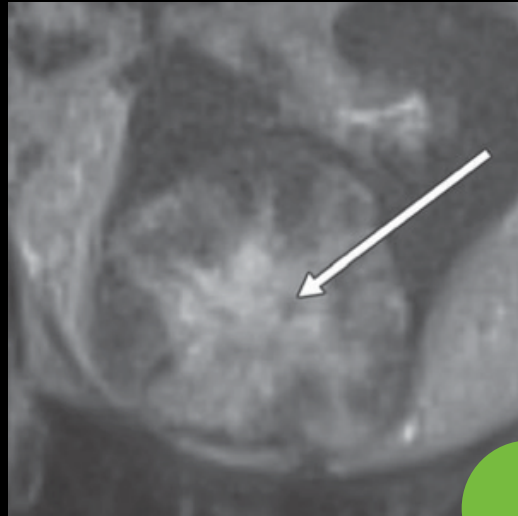


Carcinoma renale

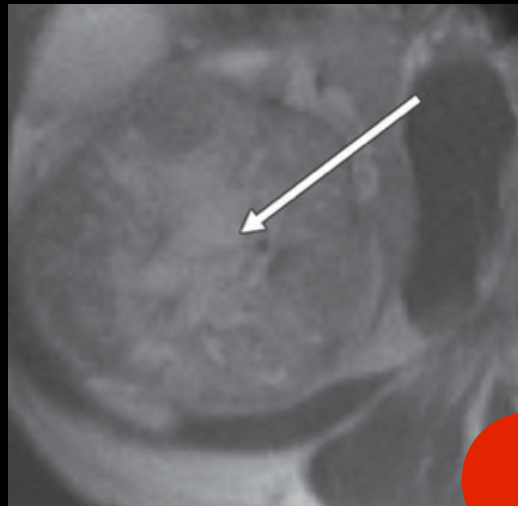


# RMN

Oncocytoma



RCC Cromofobo



Feature
Peripheral location
Microscopic fat
Subacute hemorrhage
Hemosiderin
T2 hyperintensity
T2 homogeneity
Cysts
Enhancement homogeneity
Corticomedullary phase hyperintensity
Nephrographic phase hyperintensity
Excretory phase hyperintensity
Central scar
Segmental enhancement inversion
Infiltrative margins
Perinephric fat invasion
Renal vein invasion

# Ruolo tradizionale della biopsia

Diagnosi di malattia metastatica in pazienti con nota neoplasia primitiva extrarenale

Diagnosi di ascesso renale o linfoma

Conferma istologica di un tumore primitivo renale in presenza di metastasi disseminate o di massa retroperitoneale non resecabile

# Le incertezze

SICUREZZA

Rischio di sanguinamento  
Rischio di seeding

TECNICA

Rischio di prelievo non diagnostico  
Errori di campionamento

EFFICACIA

Accuratezza diagnostica  
Impatto sulle decisioni cliniche



...alcune incertezze  
sono state superate

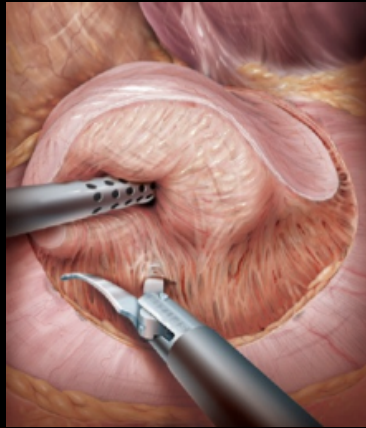
Moderne tecniche di biopsia

Miglioramento tecniche di imaging

Maggiore esperienza di urologi e radiologi interventisti

Maggiore esperienza dei patologi





# Chirurgia conservativa

## Recommendations

Surgical therapy remains the mainstay of therapy to achieve a cure in the management of RCC.

Patients with low-stage RCC (T1) should undergo nephron-sparing surgery rather than radical nephrectomy whenever possible.

Adrenalectomy is not recommended, provided a pre-operative CT scan shows the adrenal gland is normal and the intra-operative findings do not suggest intra-adrenal metastatic spread or a direct invasion of the adrenal gland.

Extended lymphadenectomy is not recommended since it does not appear to improve survival. It should be restricted to staging purposes with dissection of palpable and/or enlarged lymph nodes.

In patients unfit for surgery and suffering from massive haematuria or flank pain, embolisation can be a beneficial palliative approach.

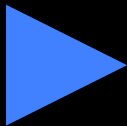
For solitary renal tumours up to a diameter of 7 cm, nephron-sparing surgery is the standard procedure, whenever technically feasible.

A minimal tumour-free surgical margin following partial resection of RCC is sufficient to avoid local recurrence.

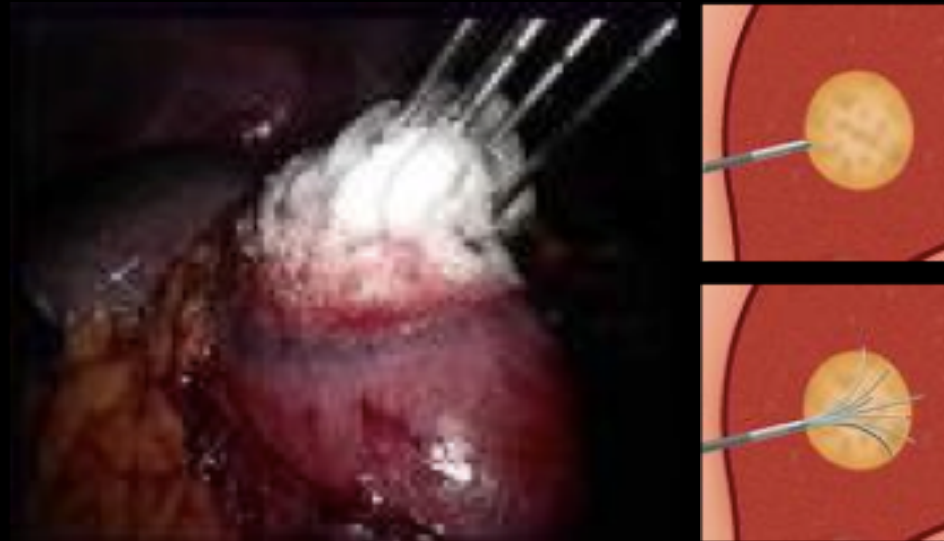
3	C
1b	A
	C
3	C
	B

## Guidelines on Renal Cell Carcinoma

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



# Terapie mini-invasive



Recommendations	GR
Active surveillance is a reasonable option for elderly and/or comorbid patients with small renal masses and limited life expectancy.	C
Patients with small renal tumours and/or significant co-morbidity who are unfit for surgery should be considered for an ablative approach, e.g. cryotherapy and radiofrequency ablation.	C
Pre-treatment biopsy has to be carried out as a standard before ablative therapy and is useful when active surveillance is considered and in order to stratify follow-up based on tumor histology.	C
Other image-guided percutaneous and minimally invasive techniques, such as microwave ablation, laser ablation, and high-intensity focused ultrasound ablation are experimental and are recommended only in studies.	
Outside controlled clinical trials, there is no indication for adjuvant therapy following surgical resection.	

## Guidelines on Renal Cell Carcinoma

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

# Five-Year Survival After Surgical Treatment for Kidney Cancer

*A Population-Based Competing Risk Analysis*

Nei pazienti >70 anni mortalità  
per cause competitive 28,2 %

*Hollingsworth, Cancer 2007*

Original Article

## Active Treatment of Localized Renal Tumors May Not Impact Overall Survival in Patients Aged 75 Years or Older

Brian R. Lane, MD, PhD<sup>1</sup>; Robert Abouassaly, MD<sup>1</sup>; Tianming Gao, MS<sup>2</sup>; Christopher J. Weight, MD<sup>1</sup>;  
Adrian V. Hernandez, MD, PhD<sup>2</sup>; Benjamin T. Larson, MD<sup>1</sup>; Jihad H. Kaouk, MD<sup>1</sup>; Inderbir S. Gill, MD<sup>1</sup>;  
and Steven C. Campbell, MD, PhD<sup>1</sup>

*Lane, Cancer 2010*

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



European Association of Urology

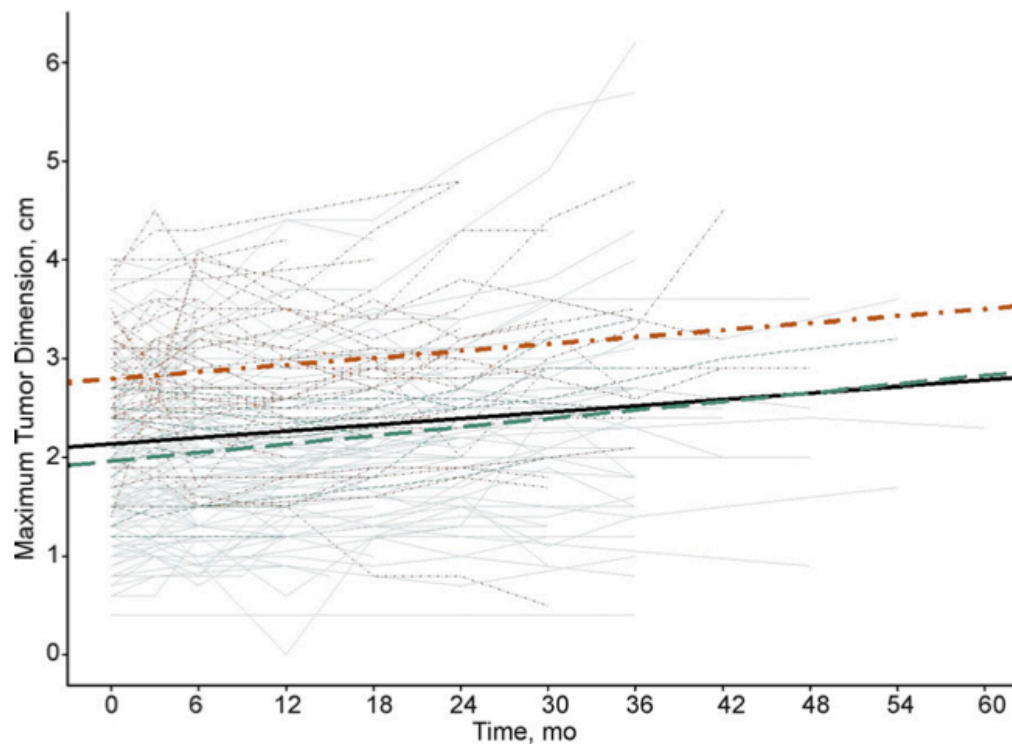


### Platinum Priority – Kidney Cancer

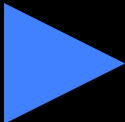
Editorial by David R. Yates and Morgan Rouprêt on pp. 45–47 of this issue

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

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



# Sorveglianza attiva



Recommendations	GR
Active surveillance is a reasonable option for elderly and/or comorbid patients with small renal masses and limited life expectancy.	C
Patients with small renal tumours and/or significant co-morbidity who are unfit for surgery should be considered for an ablative approach, e.g. cryotherapy and radiofrequency ablation.	C
Pre-treatment biopsy has to be carried out as a standard before ablative therapy and is useful when active surveillance is considered and in order to stratify follow-up based on tumor histology.	C
Other image-guided percutaneous and minimally invasive techniques, such as microwave ablation, laser ablation, and high-intensity focused ultrasound ablation are experimental and are only in studies.	
Outside controlled clinical trials, there is no indication for adjuvant therapy following surgery.	

**Guidelines on  
Renal Cell  
Carcinoma**

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

# Target therapies



# Tasso diagnostico

<b>Autore</b>	<b>N biopsie</b>	<b>Diametro medio tumore</b>	<b>Biopsie diagnostiche</b>
Leveridge	345	2,5	80,6%
Blumenfeld	81	5,3	98%
Wang	110	-	90%
Sofikerim	42	6,3	93%
Kingler	118	4,1	97,5%
Shannon	235	2,9	78%
Neuzillet	88	2,8	91%
Lebret	119	3,3	79%
Volpe	100	2,4	84%
Schmidbauer	78	4,0	97%
Veltri	103	3,4	100%
Maturen	152	4,1	96%

# Tru-Cut



a.



b.



c.



# Full Core



a.



b.



c.





# Accuratezza nella diagnosi di malattia maligna

	No. of tumours biopsied	Mean tumour size, cm	No. of pathologically confirmed tumours	Accuracy for malignancy, %
Neuzillet et al. [8]	88	2.8	62	92
Shannon et al. [9]	235	2.9	108	100
Schmidbauer et al. [10]	78	4.0	78	Sensitivity 93.5 Specificity 100
Lebret et al. [11]	119	3.3	64	86
Maturen et al. [12]	152	4.1	106	Sensitivity 97.7 Specificity 100
Volpe et al. [13]	100	2.4	20	100
Wang et al. [14]	110	2.7	36	100
Veltri et al. [15]	103	3.4	40	NR
Leveridge et al. [16]	345	2.5	74	99.7

# Accuratezza nella diagnosi di istotipo e grading

	No. of tumours biopsied	Mean tumour size, cm	No. of pathologically confirmed tumours	Accuracy for RCC subtyping, %	Accuracy for grading, %
Neuzillet et al. [8]	88	2.8	62	92	69.8
Shannon et al. [9]	235	2.9	108	98	NR
Schmidbauer et al. [10]	78	4.0	78	91	76
Lebret et al. [11]	119	3.3	64	86	46/74**
Maturen et al. [12]	152	4.1	106	NR	NR
Volpe et al. [13]	100	2.4	20	100	66.7/75**
Wang et al. [14]	110	2.7	36	96.6	NR
Veltri et al. [15]	103	3.4	40	93.2	NR
Leveridge et al. [16]	345	2.5	74	88	63.5

## Review Articles

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### Renal Mass Biopsy—A Renaissance?

**Brian R. Lane, Mary K. Samplaski, Brian R. Herts, Ming Zhou, Andrew C. Novick  
and Steven C. Campbell\***

*From the Glickman Urological Institute (BRL, MKS, ACN, SCC) and Departments of Radiology (BRH) and Anatomic Pathology (MZ),  
Cleveland Clinic, Cleveland, Ohio*

# 2474 biopsie di tumori renali

Valore predittivo positivo 97,5%

Valore predittivo negativo 82%

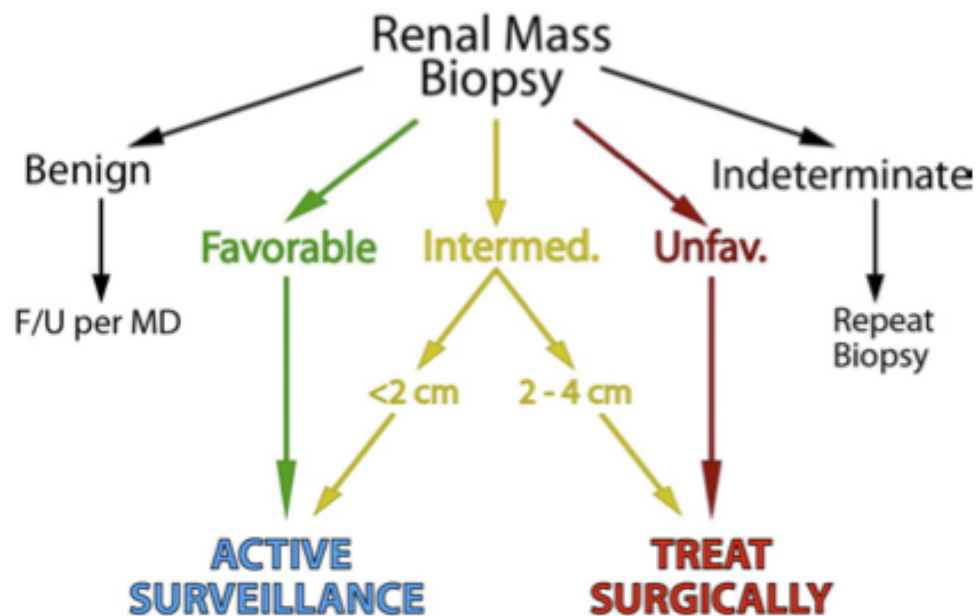
Sensibilità 92,1%

Specificità 89,7%

# Accuracy of Determining Small Renal Mass Management with Risk Stratified Biopsies: Confirmation by Final Pathology

Schuyler J. Halverson,\* Lakshmi P. Kunju,\* Ritu Bhalla,\* Adam J. Gadzinski,\* Megan Alderman,\* David C. Miller,† Jeffrey S. Montgomery,\* Alon Z. Weizer,\* Angela Wu,\* Khaled S. Hafez\* and J. Stuart Wolf, Jr.\*,‡

*From the Departments of Urology (DCM, JSM, AZW, KSH, JSW), Pathology (LPK, RB, MA, AW) and Medical School (SJH, AJG), University of Michigan Health System, Ann Arbor, Michigan*



VPP 100%

VPN 86%

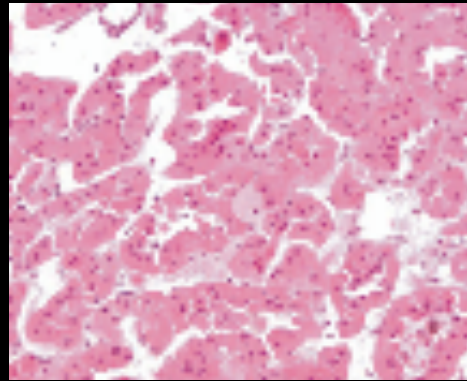
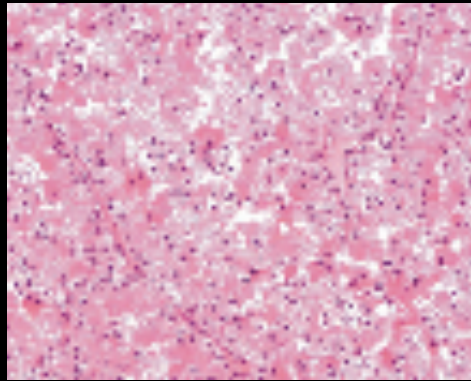
# Sicurezza

	No. of tumours biopsied	Image guidance	Needle size, gauge	No. of biopsies taken	No. of significant complications* (%)	No. of seeding (%)	No. of significant bleeding** (%)
Neuzillet et al. [8]	88	CT	18	≥2	0	0	0
Shannon et al. [9]	235	CT/US	18	1-4	2 (0.9)	0	2 (0.9)
Schmidbauer et al. [10]	78	CT	18	2-3	1 (1.3)	0	0
Lebret et al. [11]	119	CT/US	18	1-4	0	0	0
Maturen et al. [12]	152	CT/US	18	2-4	2 (1.3)	0	2 (1.3)
Volpe et al. [13]	100	CT/US	18	≥2	1 (1)	0	0
Wang et al. [14]	110	CT/US	18	≥2	2 (1.8)	0	1 (0.9)
Veltri et al. [15]	150	US	18	1-2	0	0	0
Leveridge et al. [16]	345	CT/US	18	≥2	1 (0.3)	0	1 (0.3)

CT = computed tomography; US = ultrasound.  
 \* Complications requiring active treatment or hospital admission.  
 \*\* Bleeding requiring active treatment, including transfusions or hospital admission.

# Tumori renali con citoplasma eosinofilo

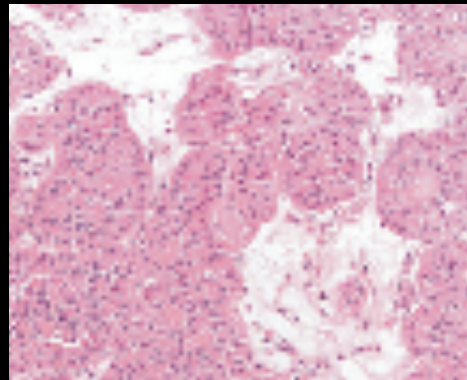
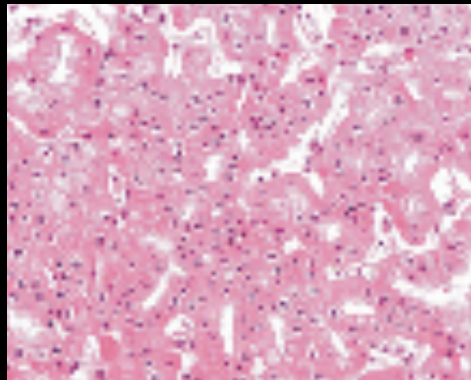
cellule  
chiare



papillare



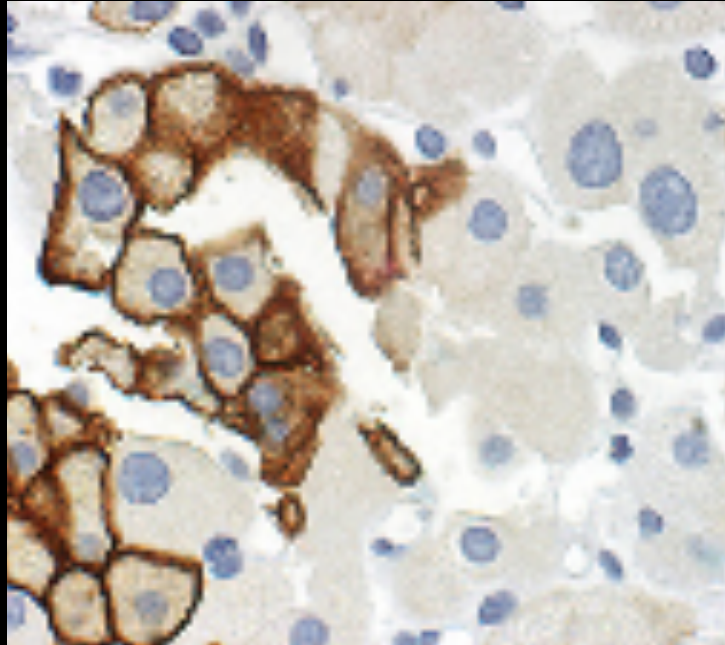
cromofobo



oncocitoma



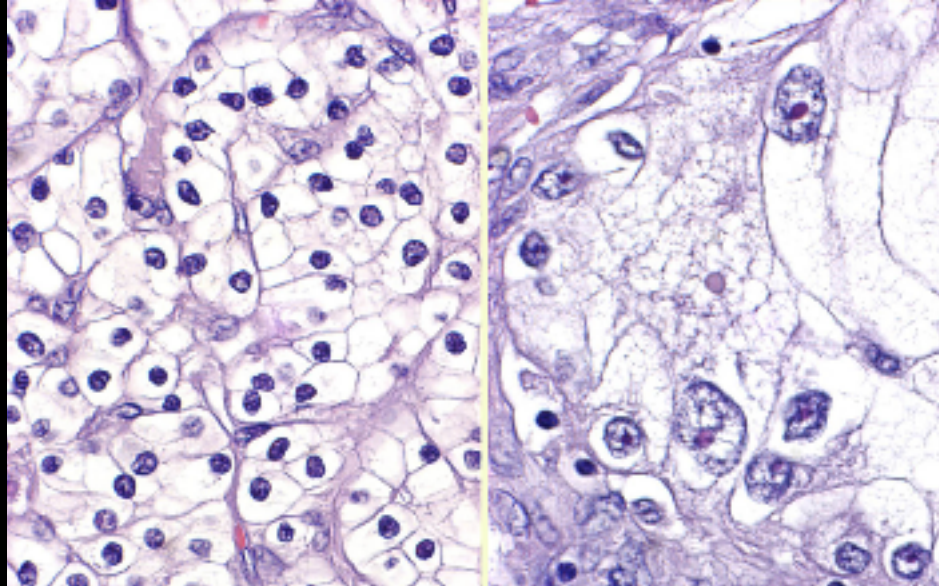
# Eterogeneità intratumorale di istotipo



Forma ibrida di oncocitoma contenente foci di carcinoma cromofobo (CK7 positive)

# Eterogeneità intratumorale di grado

Biopsia



Pezzo operatorio

carcinoma renale  
cellule chiare  
Fuhrman II

carcinoma renale  
cellule chiare  
Fuhrman II con foci III



2010

# Guidelines on Renal Cell Carcinoma

B. Ljungberg, N. Cowan, D.C. Hanbury, M. Hora, M.A. Kuczyk, A.S. Merseburger, P.F.A. Mulders, J.-J. Patard, I.C. Sinescu

2013

# Guidelines on Renal Cell Carcinoma

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

### 3.3 Renal biopsy

Renal tumour biopsies are increasingly being used in diagnosis, in follow-up surveillance, and in ablative therapies (40-45) (LE: 3). In most series, a core biopsy demonstrates high specificity and high sensitivity for the presence of malignancy (40-44), though it should be noted that 10-20% of biopsies are non-conclusive.

Biopsy aims to determine eventual malignancy, type, and grade of the evaluated renal mass.

A percutaneous mass biopsy is rarely required for large renal masses scheduled for nephrectomy.

The positive predictive value of imaging findings is so high that a negative biopsy result does not alter management (45) (LE: 3).

7 references

### 3.3 Renal tumour biopsy (42-111)

Percutaneous renal tumour biopsies are increasingly being used: 1, for histological diagnosis of radiologically indeterminate renal masses; 2, to select patients with small renal masses for surveillance approaches; 3, to obtain histology before ablative treatments; 4, to select the most suitable form of targeted pharmacologic therapy in the setting of metastatic disease (42-51) (LE: 3).

Percutaneous sampling of a renal mass can be carried out using needle core biopsy and/or fine-needle aspiration (FNA). The aim is to determine malignancy, histological type, and grade of the renal tumour evaluated.

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biopsies is p

42-50,54,55,57-75) (LE: 2b).

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).

Combined FNA and core biopsies can provide complementary results, especially for complex cystic lesions

(49,55,57,58,73,76,77) (LE: 3).

70 references

# Indicazioni

Sospetta lesione renale metastatica in presenza di nota neoplasia extrarenale

SRM in paziente potenzialmente candidato a sorveglianza attiva o terapie ablative

Follow up di SRM sottoposte a terapie ablative

Neoplasia primitiva renale con mts a distanza per la selezione della terapia biologica quando la nefrectomia citoreducente non è indicata o se si prevede una terapia neoadiuvante

Utile in tumori T1-2 non metastatici per rinforzare indicazione a chirurgia parziale se istologia favorevole

# Limiti degli studi

Limitata numerosità di pazienti

Non multicentrici

Tecnica e schema bioptico non standardizzato

Differenti definizioni di successo delle biopsie

Mancanza di conferma istologica in gran parte dei casi

Differenti protocolli di follow up

# Punti deboli

Falsi negativi

Prelievi non diagnostici

Tumori oncocitici

Accuratezza del grading

Lesioni cistiche

Variabilità interosservatore

Curva di apprendimento (urologo/radiologo e patologo)

# Nuovi sviluppi

## Immunohistochimica

*CD10, parvalbumina, AMACR, CK7, S100A1, catepsina K, CA IX*

## Citogenetica

*FISH: gains 7,17; losses 1,2,3p,6,10,17,Y*

## Analisi molecolare

*Estrazione ed amplificazione DNA e RNA per analisi genomiche*