

MEDICAL UPDATE April 2019: Urological cancer

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Professor Robert Pickard (1961-2018)



Outline

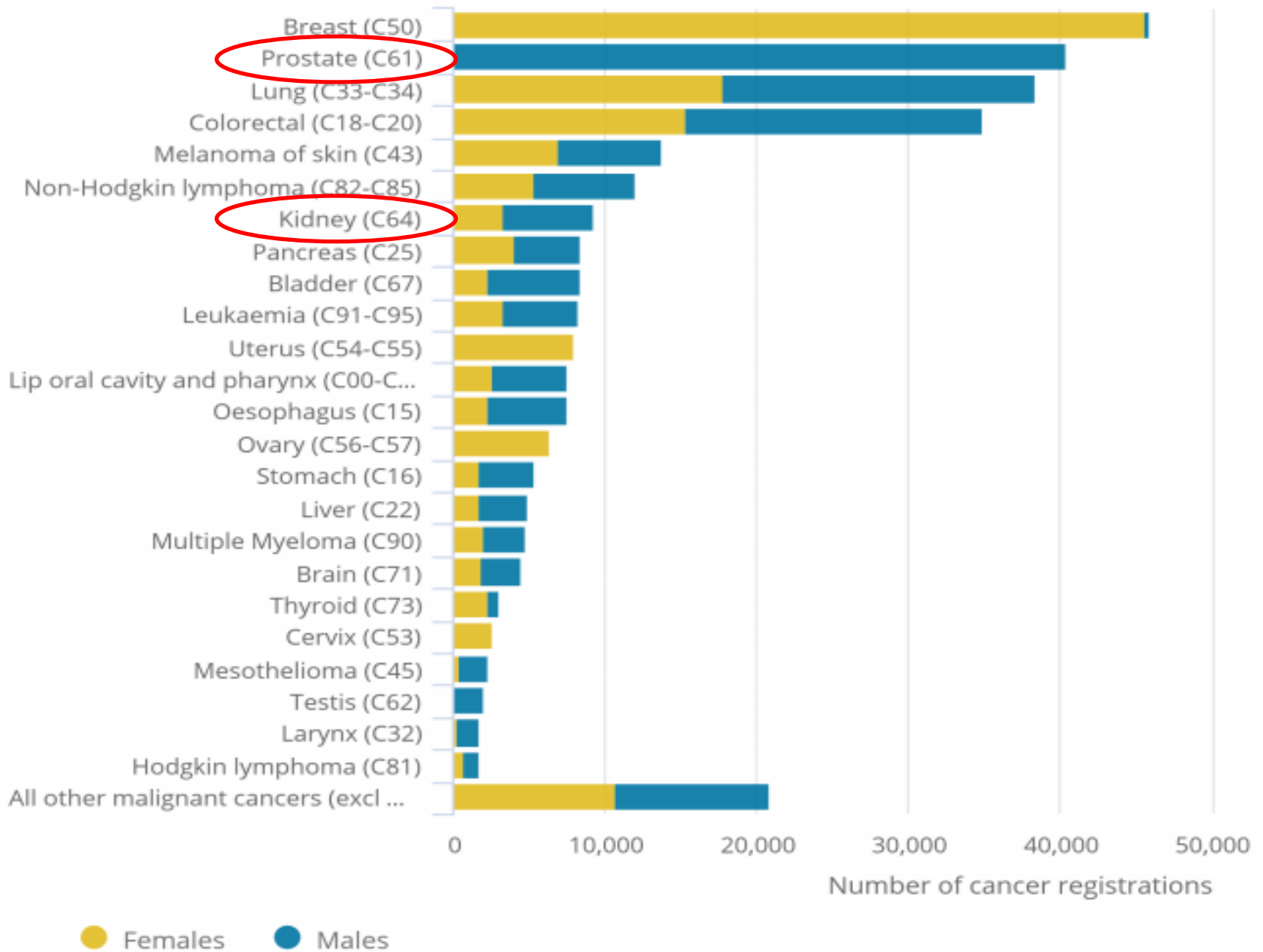
- Prostate cancer diagnostics

- PSA / Biopsy
- MRI

- Kidney cancer

- Presentation
- Diagnosis
- Surgical management





Urological cancer in Mauritius

ISLAND OF MAURITIUS DEATHS DUE TO NEOPLASMS BY TYPE AND SEX 2017			
TYPE OF NEOPLASM (ICD-10)	MALE	FEMALE	TOTAL
Malignant neoplasm of prostate	73		73
Other malignant neoplasm of urinary tract	18	14	32
TOTAL	655	716	1,371

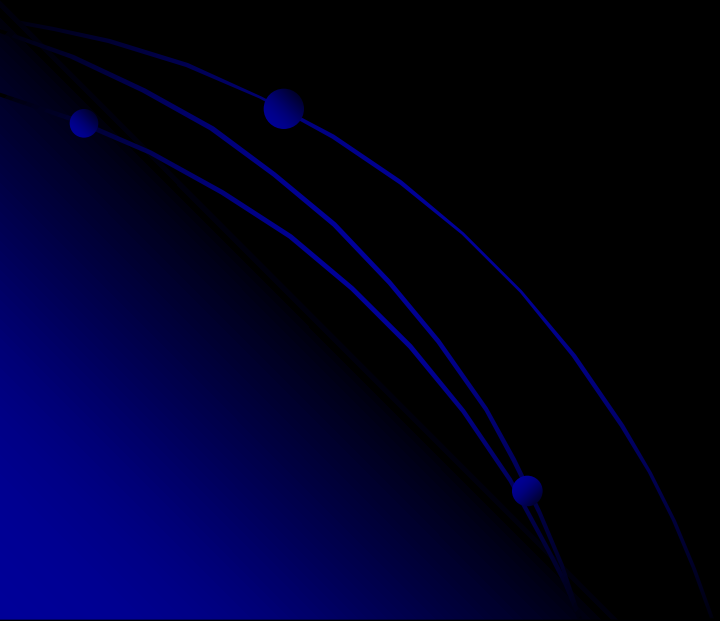
Prostate cancer

- *Incidence* ~50-80 new cases/yr (2013-15)
~150 new cases/yr (2017)
- *Mortality* 11% of male cancer deaths

Kidney cancer

- *Incidence* ~15-20 new cases/yr (2013-15)
~35 new cases/yr (2017)
- *Mortality* 3% of all cancer deaths

Prostate cancer diagnostics



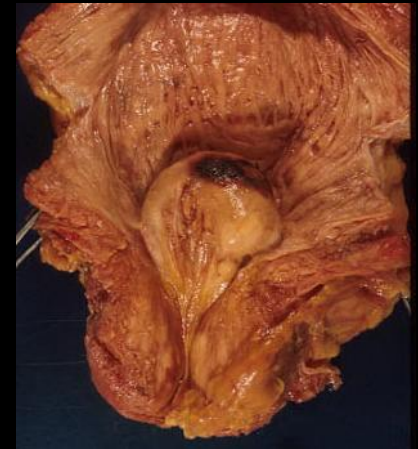
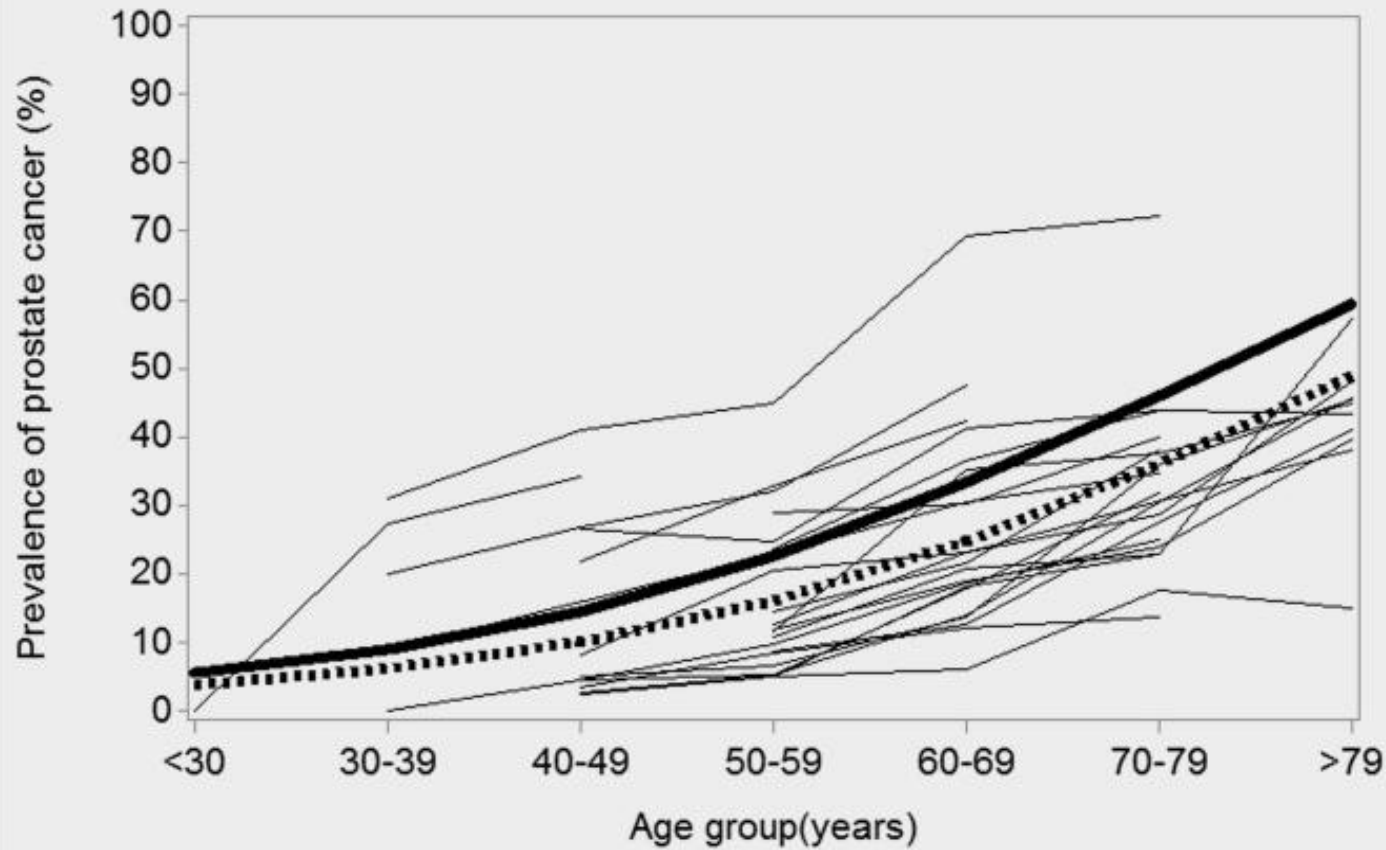
The disease

Adenocarcinoma arising from prostatic glands

Prostate cancer is a heterogenous disease ranging from indolent slow growing tumours to highly aggressive tumours with metastasis



Prostate cancer autopsy studies



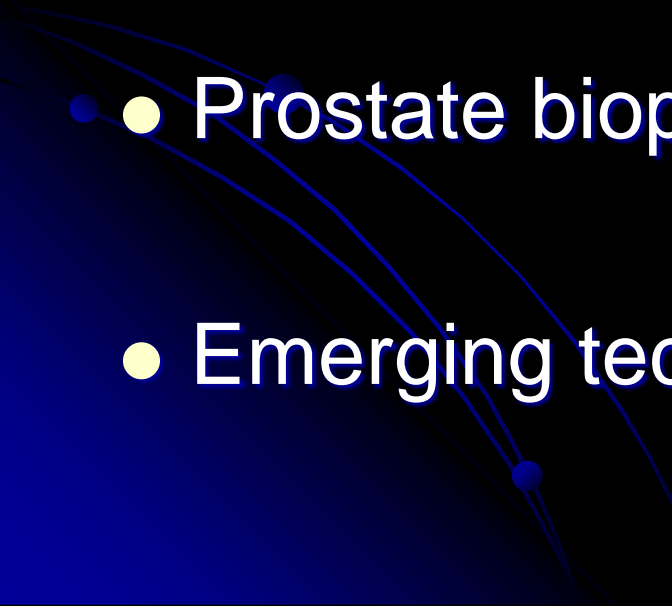
- ~50% in 70-80yrs
- ~60% in men above 80yrs
- Not clinically significant

Prostate cancer burden

- Worldwide burden
 - 2nd most common male cancer
 - estimated 1.1 million diagnoses 2013
 - ~15% of all cancers diagnosed worldwide
- Geographical variation
 - Highest incidence
 - Australia, Northern America, Europe
 - Low incidence
 - Eastern and South-Central Asia



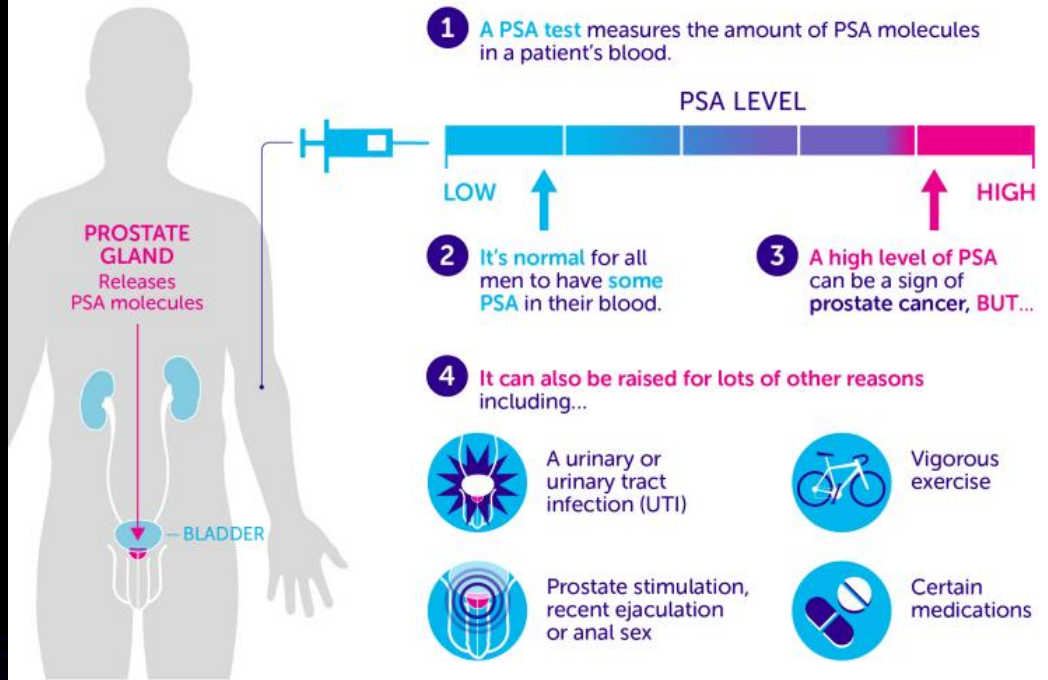
Diagnosis

- PSA and other markers
 - MRI
 - Prostate biopsy
 - Emerging technologies (fusion)
- 

PSA



THE PSA TEST AND WHY ITS RESULTS CAN BE CONFUSING



Prostate cancer risk at low PSA levels

PSA (ng/mL)	Prevalence of prostate cancer
0.5 or less	6.6%
0.6-1.0	10.1%
1.1-2.0	17%
2.1-3.0	23.9%
3.1-4.0	26.9%

Limitations of PSA test

- Not specific for cancer
- Benign conditions cause elevation (BPH, UTI, prostatitis)
- Morbidity with current diagnostic methods
- No PSA level guarantees the absence of cancer

PSA – Do's and Don'ts

- Adequate patient counselling before requesting
- Perform together with DRE
- Avoid testing
 - Active UTI / instrumentation / prostatitis / catheterisation
- Specific groups
 - Asymptomatic >75yrs
 - Multiple comorbidities



Is PSA the best test for prostate cancer?

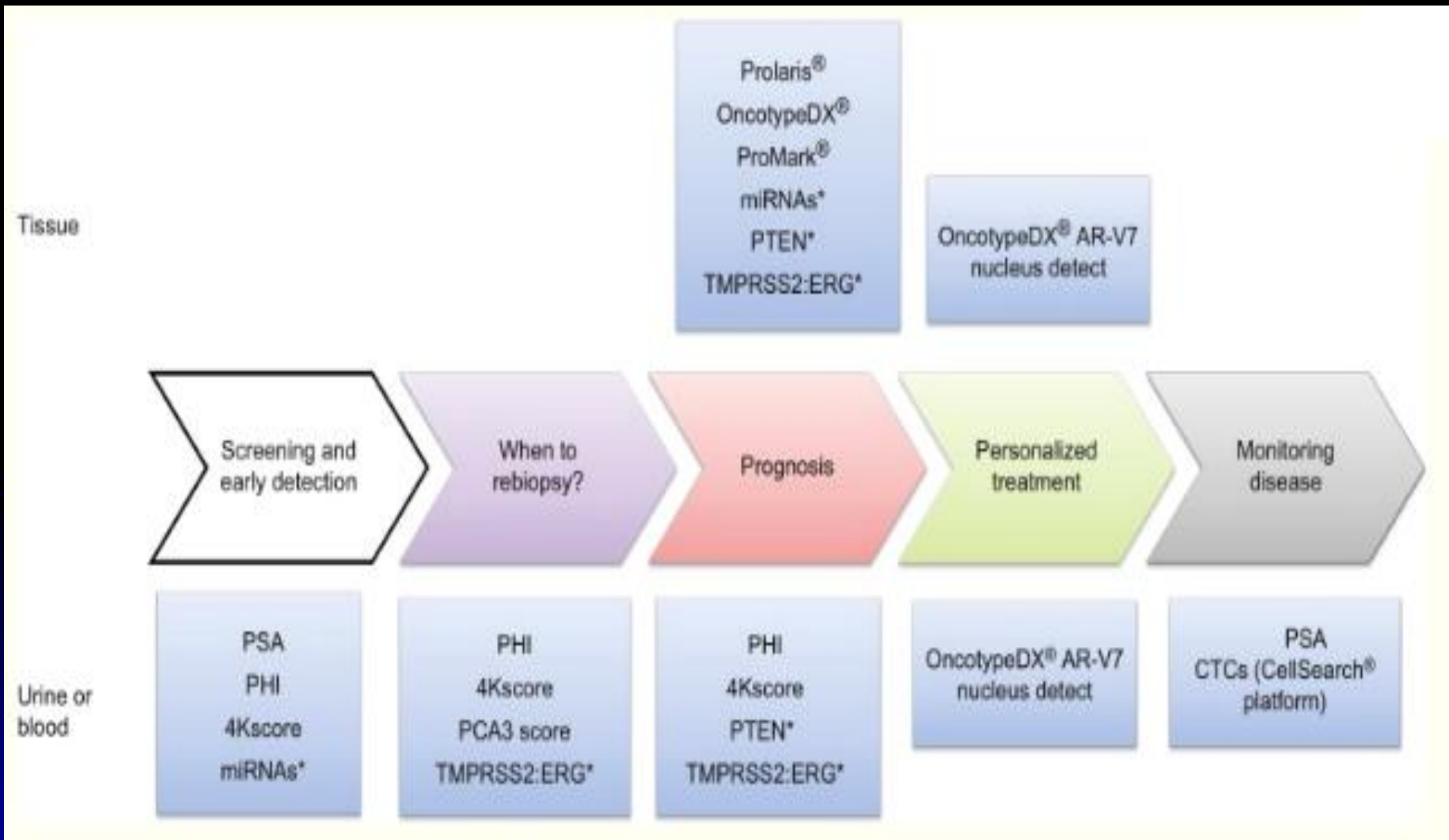
- No...
- Other markers
 - Free to total PSA
 - Prostate health index
 - 4K score
 - Urine PCA3

$$PHI = \frac{[-2] \text{ pro-PSA}}{fPSA} * \sqrt{tPSA}$$

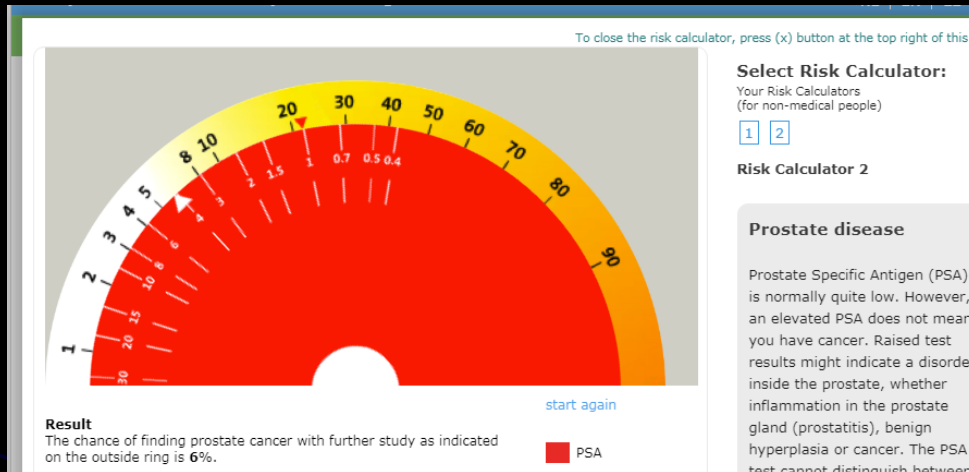
What is the 4Kscore Test?



Is PSA the best test for prostate cancer?



Prostate Cancer risk calculators



PCPT Risk Calculator Home Map

Characteristics

Race

Age

PSA [ng/ml]

Family History of Prostate Cancer

Digital rectal examination

Prior biopsy

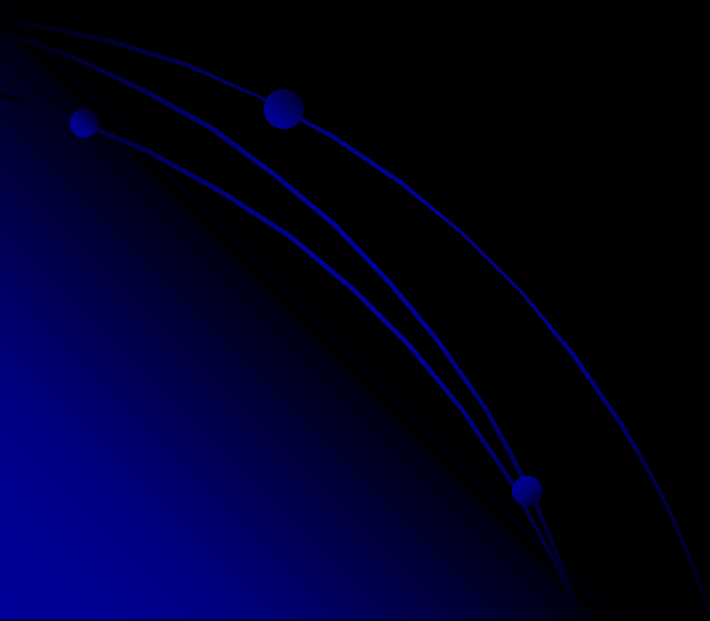
Percent free PSA available?

PCA3 available?

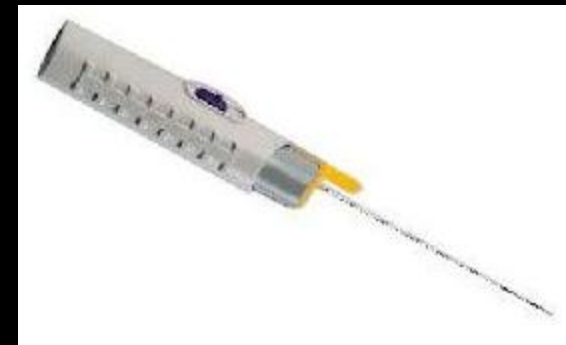
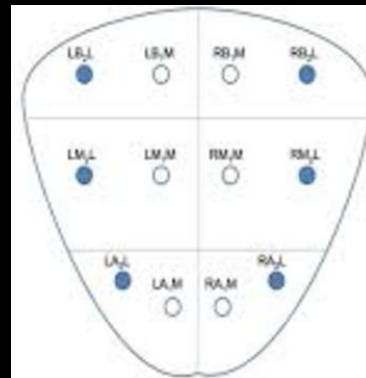
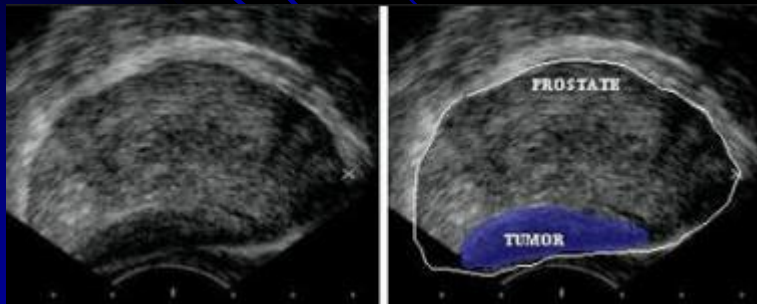
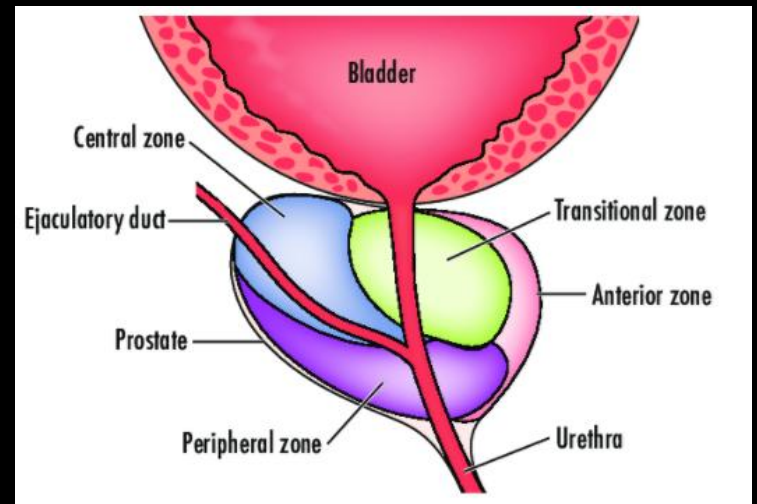
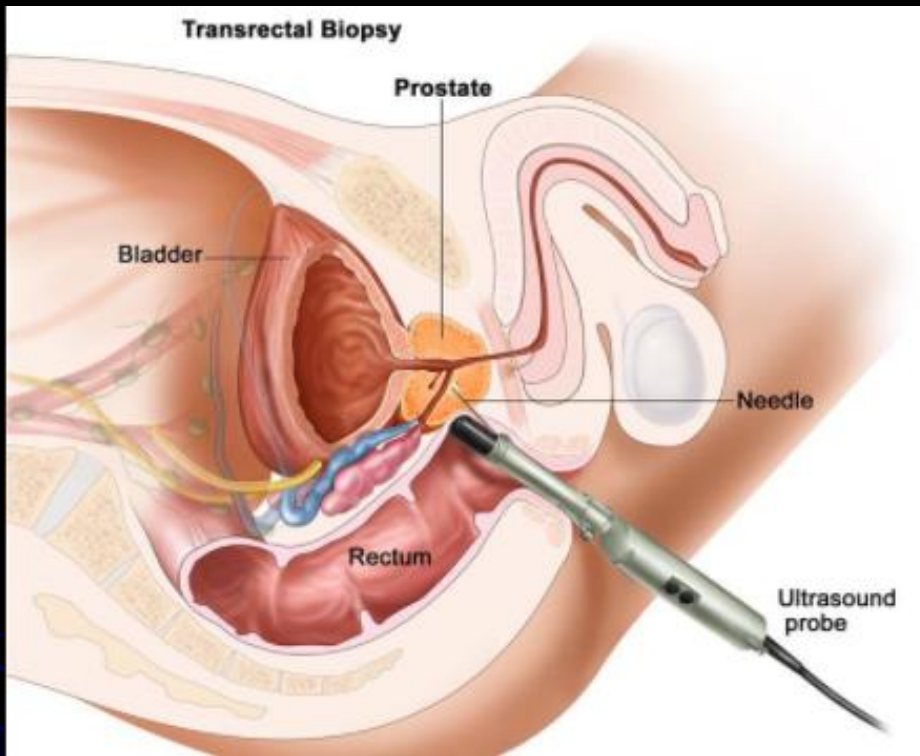
T2:ERG available?

[Calculate Risk](#)

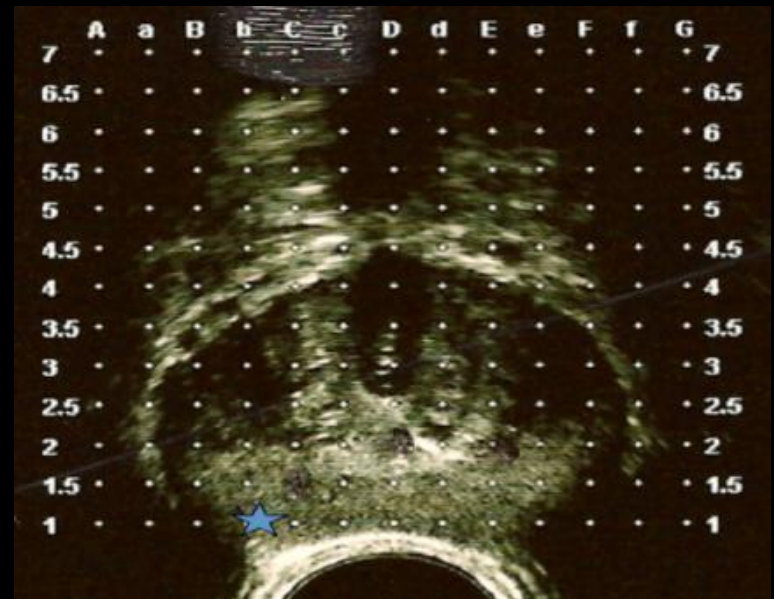
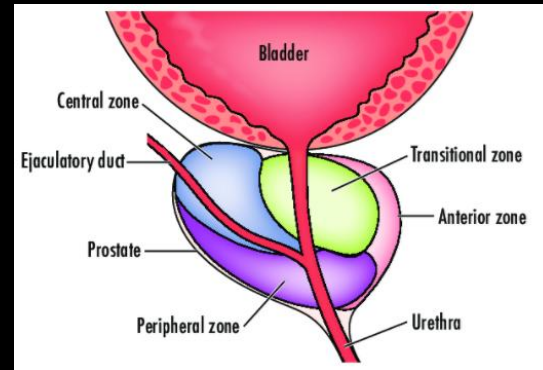
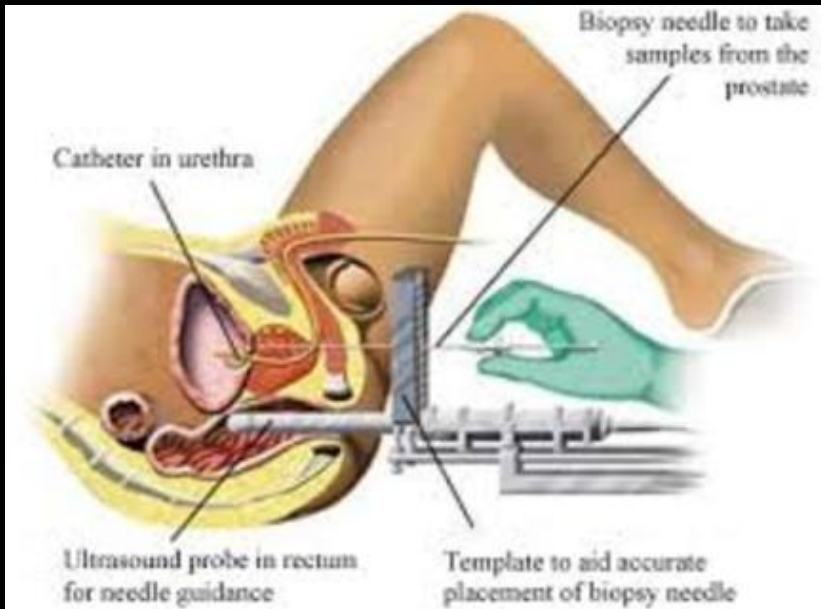
Biopsy



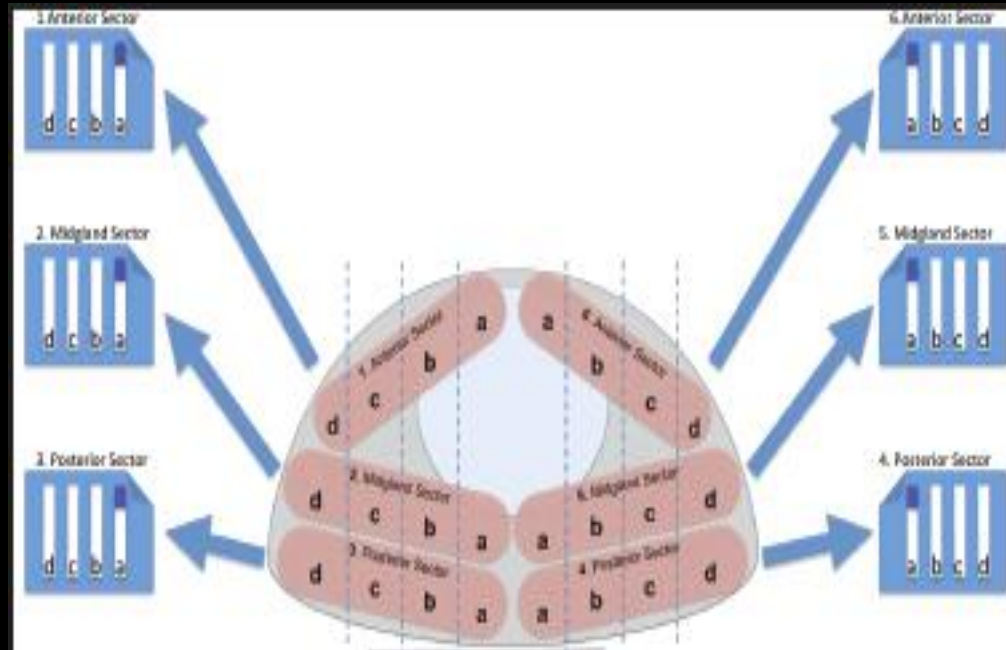
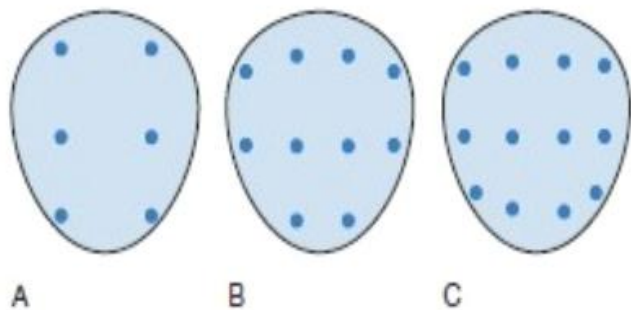
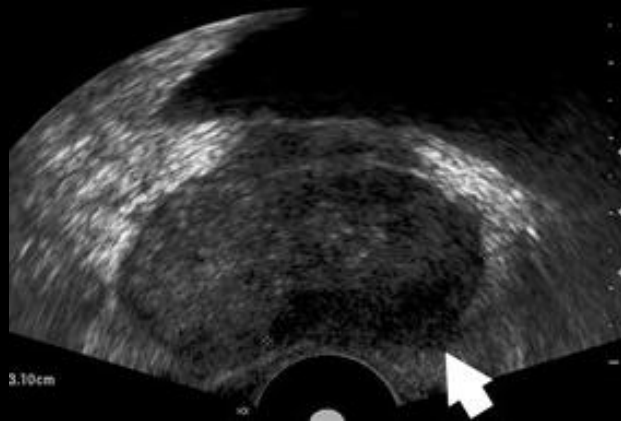
Transrectal USS and biopsy



Transperineal biopsy



Where to biopsy from?



Various reported systematic biopsy schemes.

A, **Sextant biopsy scheme** originally proposed by Hodge associates (Hodge et al, 1989b)

B, The **10-core biopsy** of Presti and coworkers (2000).

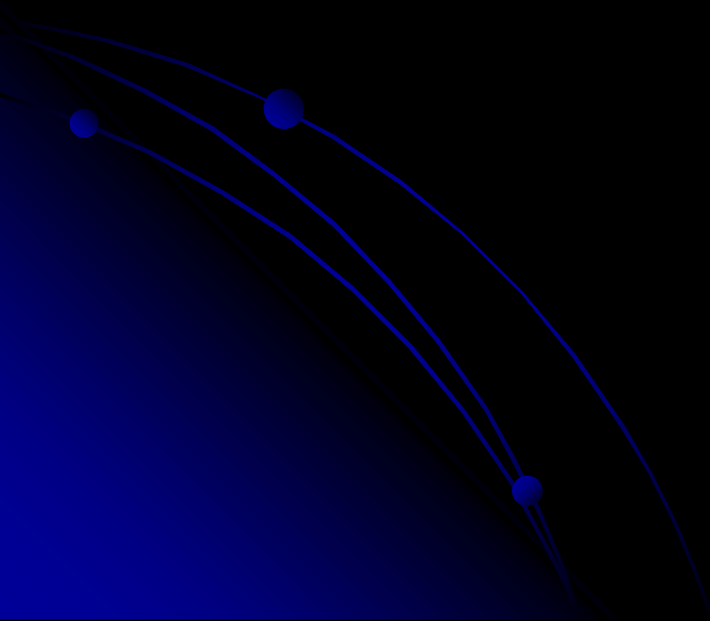
C, The **12-core, or double sextant, biopsy**.

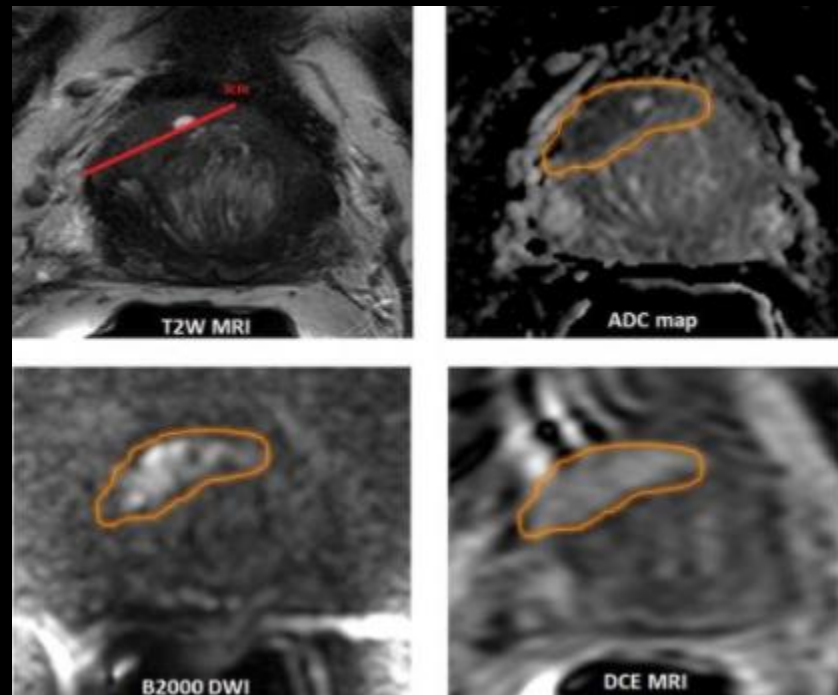
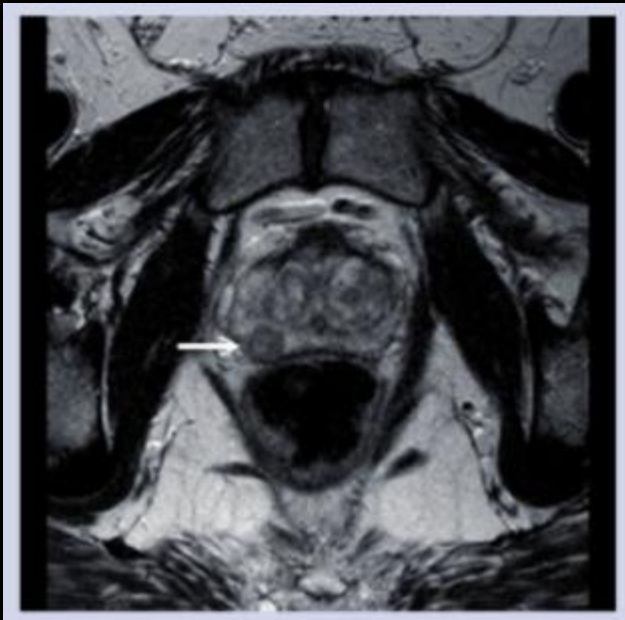
Biopsy complications

Severe haematuria	2%
Urinary tract infection	10%
Urosepsis	2%
Urinary retention	1-5%
Missing cancer	2-10%
Mortality	0.095%



MRI





PI-RADS

- PI-RADS 1 = Very low (clinically significant cancer highly unlikely)
- PI-RADS 2 = Low (clinically significant cancer unlikely)
- PI-RADS 3 = Intermediate (clinically significant cancer equivocal)
- PI-RADS 4 = High (clinically significant cancer likely)
- PI-RADS 5 = Very high (clinically significant cancer highly likely)

Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study



Hashim U Ahmed*, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes,

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MRI has 93% sensitivity (vs. 48% TRUS)

Using MRI first, biopsy can be avoided in 27%

followed by both TRUS-biopsy and TPM-biopsy. On TPM-biopsy, 408 (71%) of 576 men had cancer with 230 (40%) of 576 patients clinically significant. For clinically significant cancer, MP-MRI was more sensitive (93%, 95% CI 88–96%) than TRUS-biopsy (48%, 42–55%; $p < 0.0001$) and less specific (41%, 36–46% for MP-MRI vs 96%, 94–98% for TRUS-biopsy; $p < 0.0001$). 44 (5.9%) of 740 patients reported serious adverse events, including 8 cases of sepsis.

H Ahmed FRCS,
A El-Shater Bosaily MBBCh,
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NHS Foundation Trust, London

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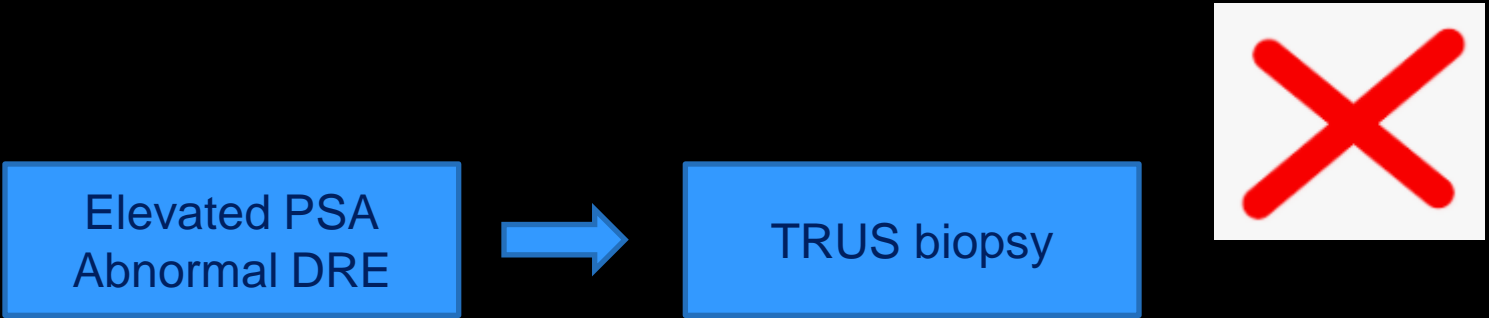
MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

V. Kasiyanathan, A.S. Denzil, M. Parhi, V. Parthasarathy, L.A. Muddana, M.H. Venk, A. Prasad, L. Prady

Biopsy of MRI target lesion
38% Cancer diagnosis
Vs.
26% for TRUS

In a multicenter, randomized, noninferiority trial, we assigned men with a clinical

London W1W 7FS, United Kingdom, or at
veeru.kasi@ucl.ac.uk.



MRI – current controversies

How accurate is MRI in diagnosis?

Are the results replicable to my local practice?

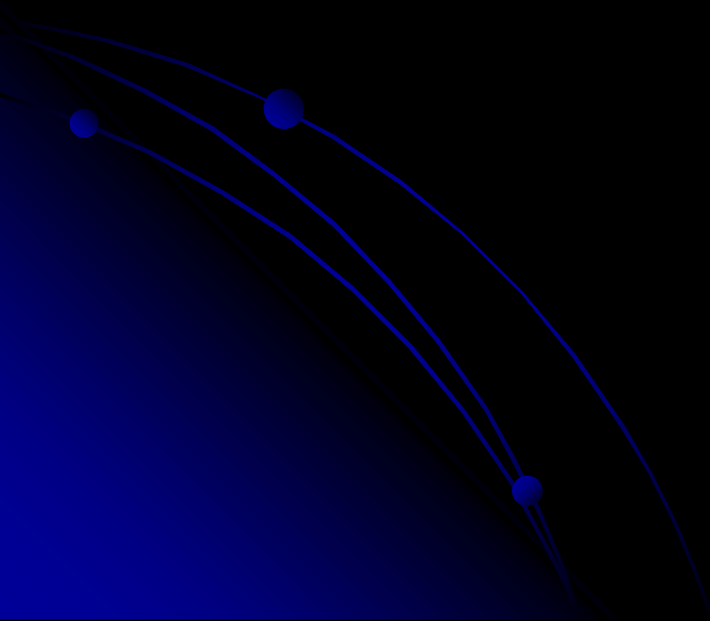
What is optimum biopsy strategy?

1. Biopsy of MRI target only
2. Biopsy of MRI target + systematic

What to do with negative biopsy and positive MRI lesion?

1. Repeat biopsy
2. PSA observation

In practice...



Case 1

63yr old male Caucasian

Fit and well, nil medications

PSA test following counselling 12.0ng/ml

DRE – abnormal feeling prostate

MRI – PIRAD 4 lesion right Pz (T2a)

TRUS and biopsy – Gleason 8 CaP

Staging (bone scan NAD)

Risk group – Intermediate

Management – surgery or radiotherapy

Case 2

59yr old male

Fit and well, nil medications

Had PSA testing due to media advert 5.0ng/ml

DRE – normal feeling prostate

• MRI – PIRAD 3 lesion right Pz

• TRUS and biopsy – benign

• Uro-sepsis with 7 days hospital stay

• *'Wished I had never had it done'*

Case 3

72yr old male

T2DM, IHD, severe COPD

Routine PSA done by medical team

PSA 8.5ng/ml ; DRE – normal

- No further Ix following urology consultation

Annual PSA – stable between 7-9 over 4 years

Avoided morbidity of testing in patient with potential life expectancy on <10yrs

Case 4

62yr old male

LUTs with frequency, poor flow and urgency

PSA 2.0

DRE – malignant prostate

• MRI – PIRAD 5 peripheral zone ?T3b

Biopsy – Gleason 9 adenocarcinoma prostate

Staging – no metastatic disease

• Management – radical radiotherapy therapy

Case 4

62yr old male

LUTs with frequency, poor flow and urgency

PSA 2.0

DRE – malignant prostate

- MRI – PIRAD 5 peripheral zone ?T3b

Biopsy – Gleason 9 adenocarcinoma prostate

Staging – no metastatic disease

Management – radical radiotherapy therapy

Case 5

83yr old male

Cachexia, weight loss, anorexia

Haematuria and urinary frequency and urgency

DRE – malignant prostate (T3)

PSA done – 850 ng/ml

Bone scan – metastatic disease

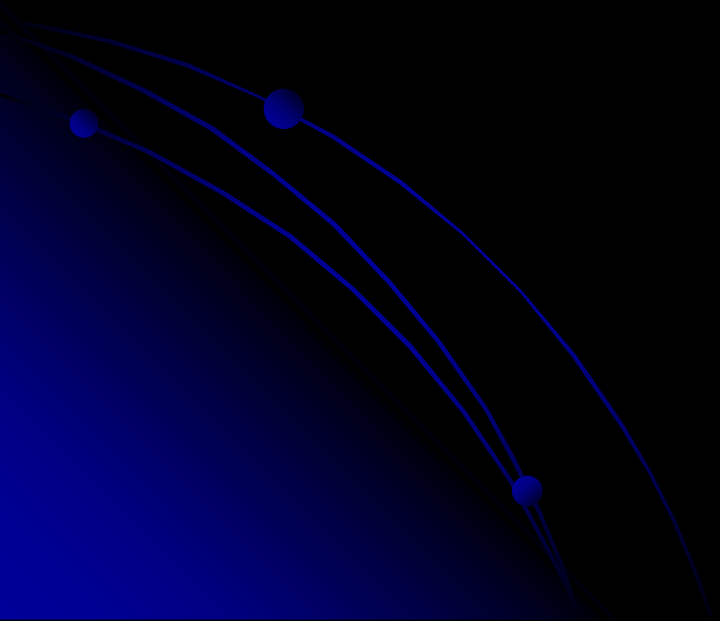
Management – androgen deprivation therapy

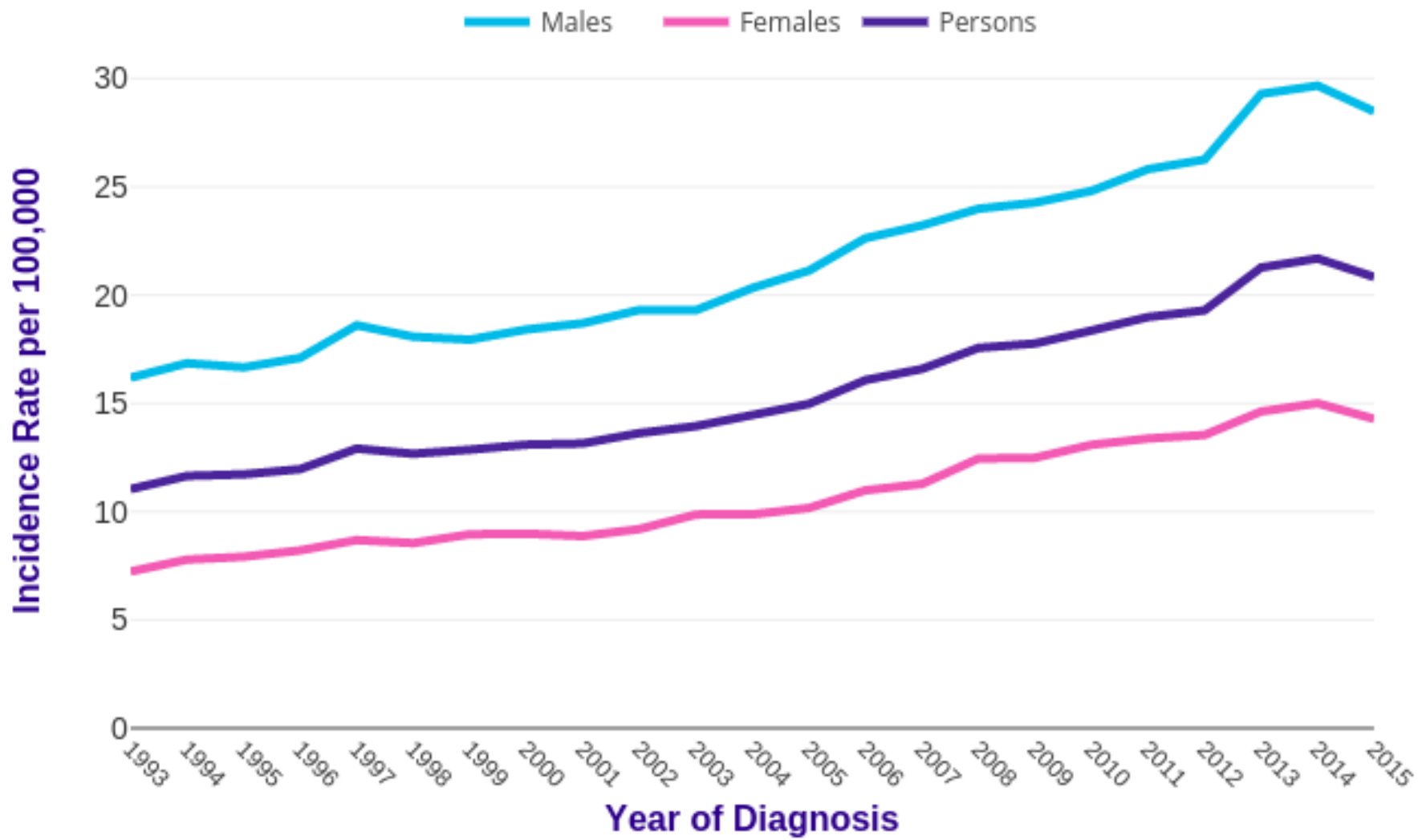
Take home messages

- Prostate cancer likely to become an increasingly detected disease
- PSA measurement in asymptomatic men should be done after careful thought
- Diagnosis moving toward MRI followed by biopsy

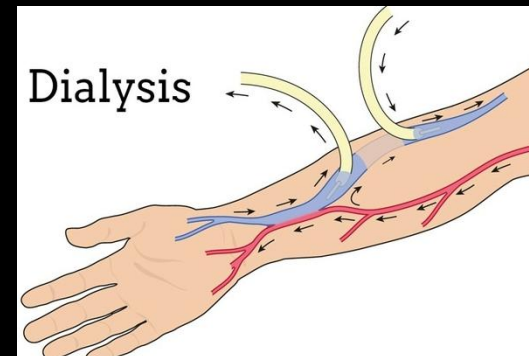
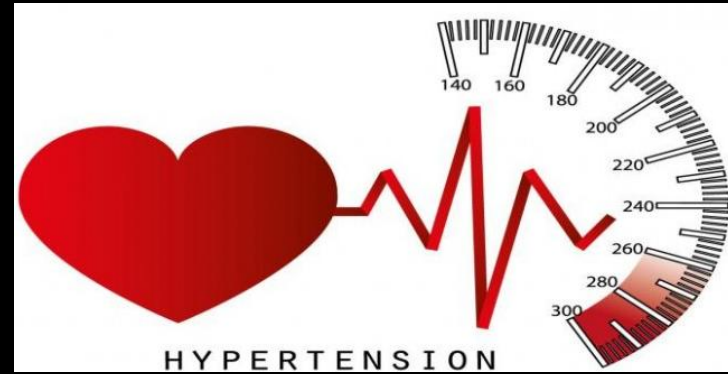


Kidney cancer





Risk factors

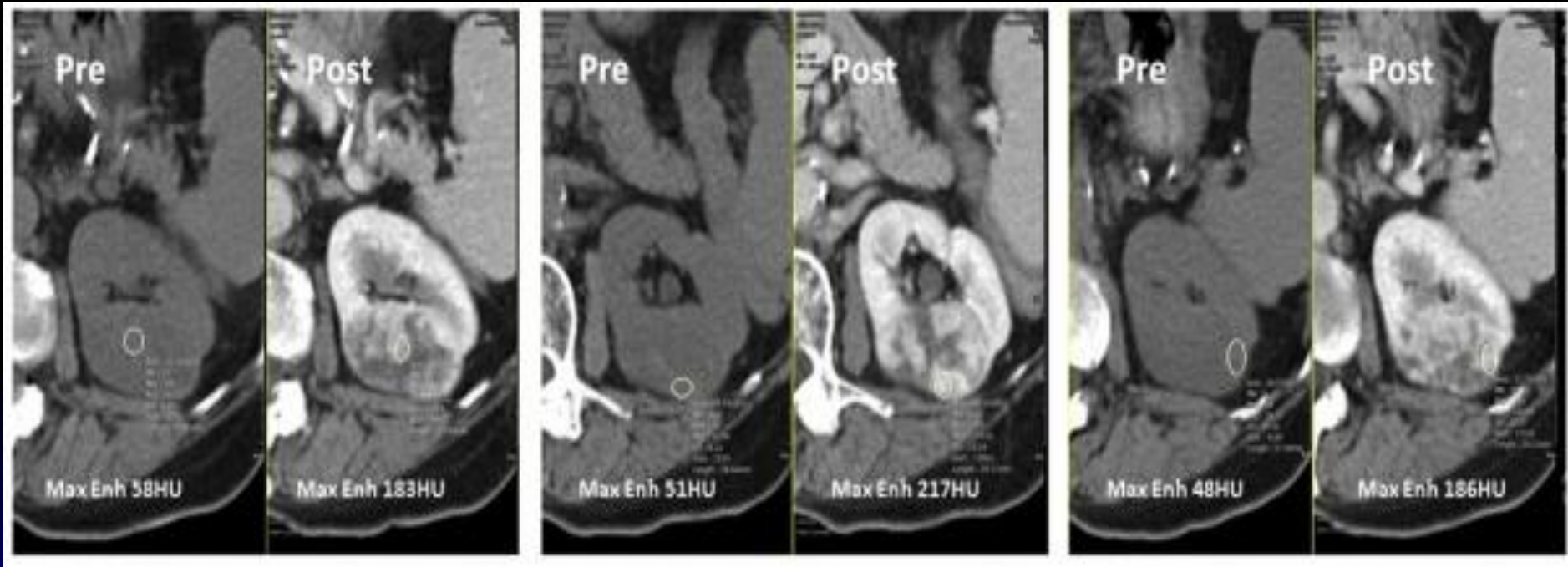


Presentation

- Asymptomatic – Imaging
- Loin pain
- Haematuria
- Mass
- Abnormal bloods
 - Hypercalcaemia, Polycythaemia, Altered LFTS
- Advanced disease

Diagnosis - Imaging

RCC exhibits contrast enhancement of at least 15HU on CT



Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net



Contrast-enhanced CT in 100 clear cell renal cell cancers — an analysis of enhancement, tumour size, and survival

R. Veeratterapillay^{a,*}, R. Ijabla^a, D. Conaway^a, P. Haslam^b, N. Soomro^a, R. Heer^a



Diagnosis - Biopsy

- Traditionally not performed due to risks and concerns about pathology accuracy
- Expanding role in contemporary practice



Perform a renal tumour biopsy before ablative therapy and systemic therapy without previous pathology.

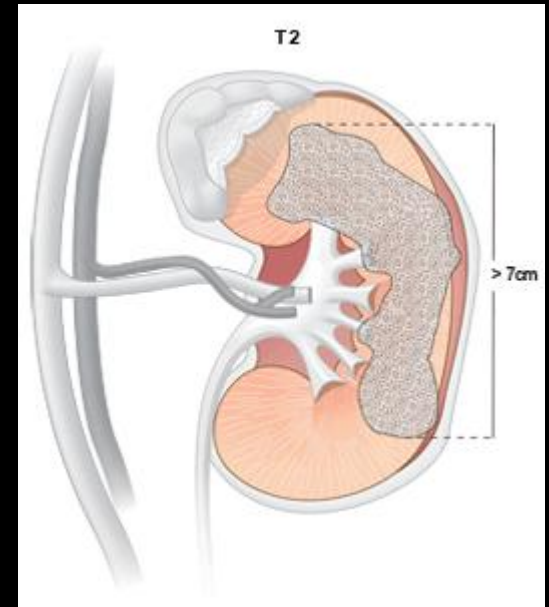
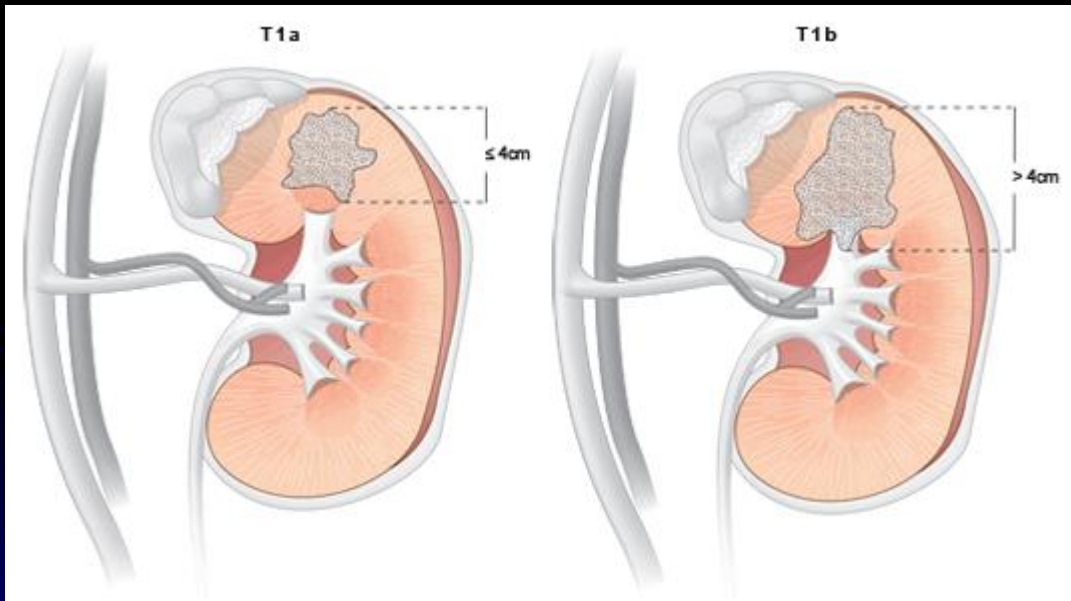
Perform a percutaneous biopsy in select patients who are considered for active surveillance.

Use a coaxial technique when performing a renal tumour biopsy.

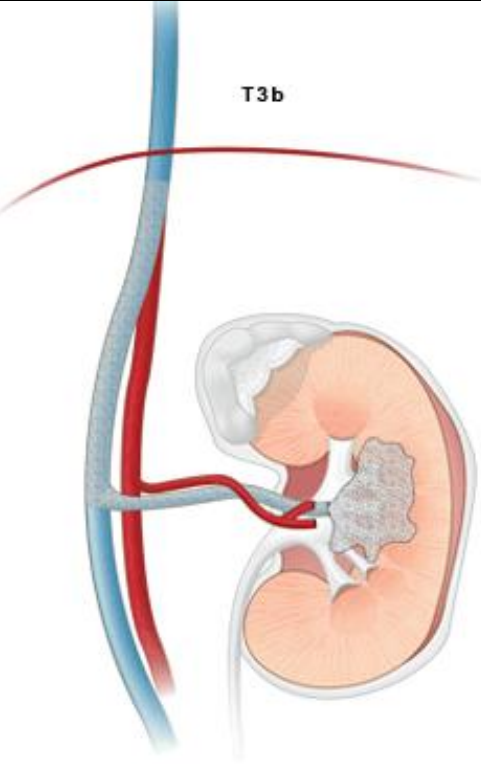
Do not perform a renal tumour biopsy of cystic renal masses.



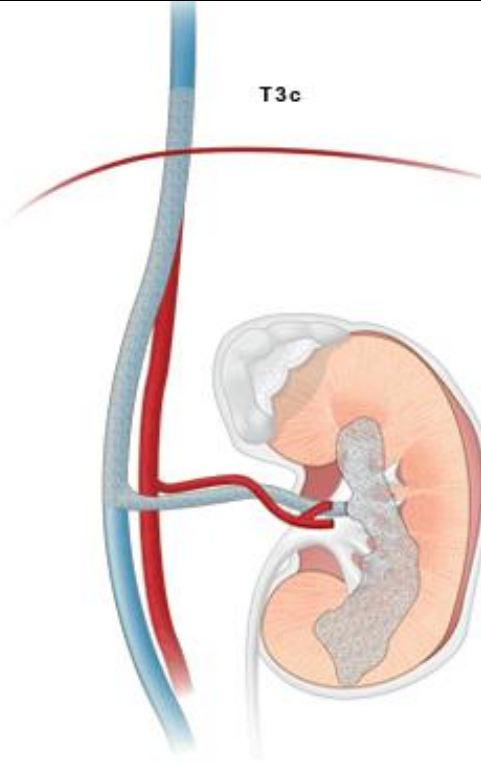
Staging



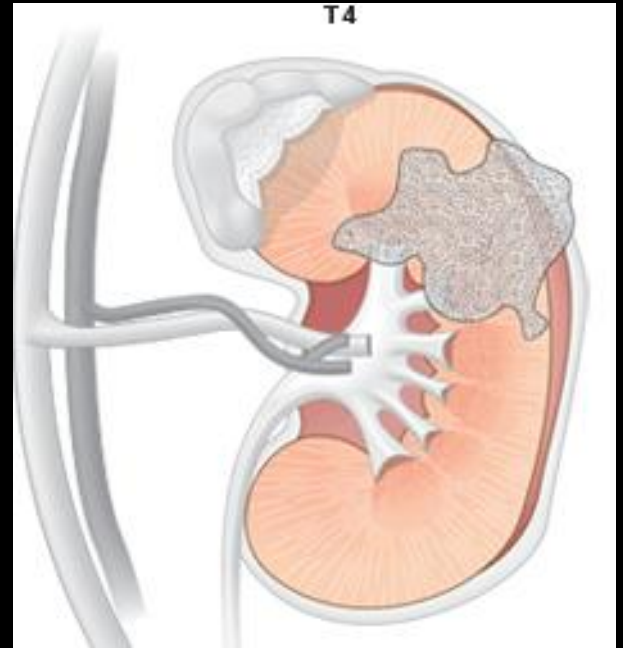
T3b



T3c



T4



Accuracy of the revised 2010 TNM classification in predicting the prognosis of patients treated for renal cell cancer in the north east of England

R Veeratterapillay,¹ R Simren,² A El-Sherif,² M I Johnson,¹ N Soomro,¹ R Heer^{1,3}

¹Department of Urology, Freeman Hospital, Newcastle upon Tyne, UK

²Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne, UK

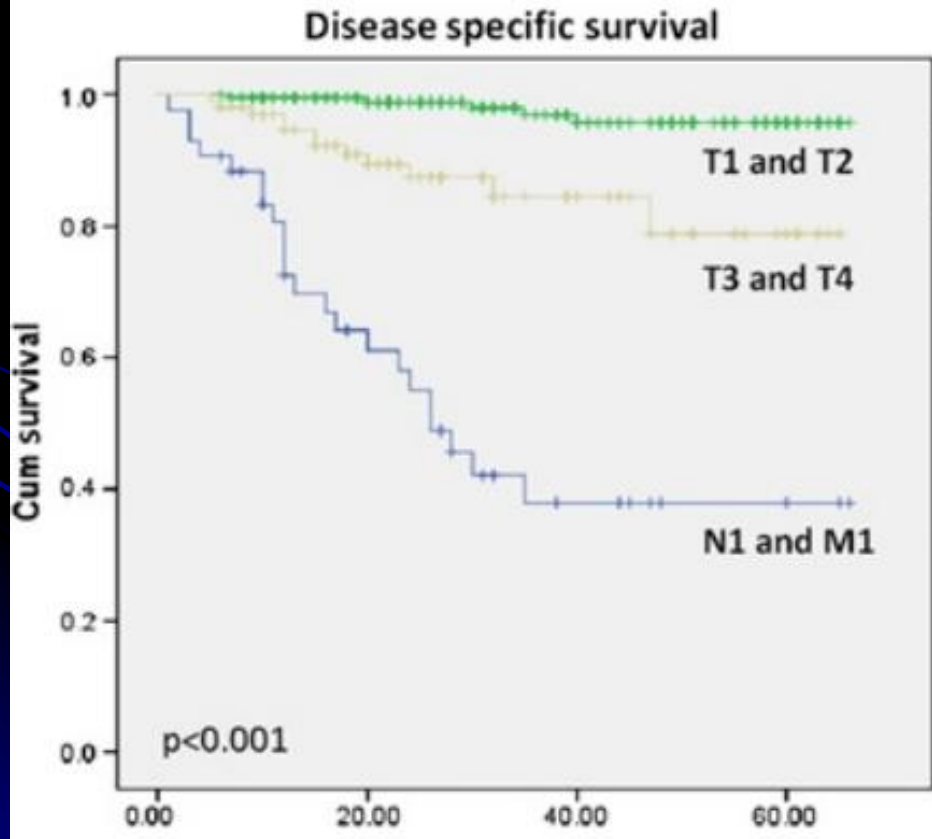
³Northern Institute for Cancer Research, Newcastle University, Newcastle upon Tyne, UK

ABSTRACT

Background The TNM classification for renal cell cancer (RCC) should accurately predict and assign prognostic information for patients. In this study the recent 2010 revision to the TNM classification was compared with the previous 2002 classification with regard to survival outcomes.

Methods All patients having radical nephrectomy for RCC in the 5-year period 2004–8 at a tertiary referral

subgroups based on tumour size (T2a \leq 10 cm and T2b $>$ 10 cm). Furthermore, the AJCC also reclassified contiguous adrenal invasion from T3a to T4 and invasion of the renal vein by tumour from T3b to T3a, which also includes renal fat invasion (peripheral and sinus). These changes were based on growing evidence that reassignment of pathological features to specific stages would more accurately predict the cancer-specific survival



Management

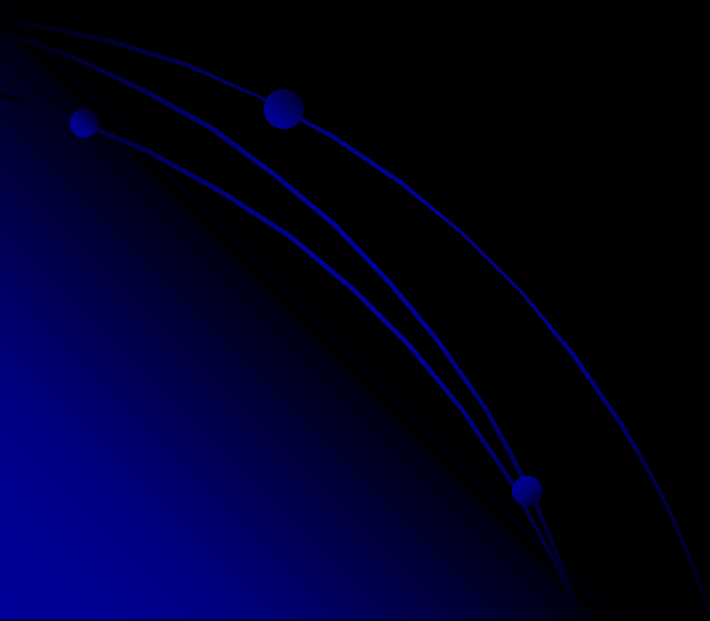
- **Localised disease**

- Surveillance
- Ablation
- Surgery
 - Radical nephrectomy (open/lap/robotic)
 - Partial nephrectomy (open/lap/robotic)

- **Metastatic**

- Cytoreductive nephrectomy / Metastatectomy
- Tyrosine kinase inhibitors
- Immunotherapy

Surveillance



Surveillance

- Small renal mass
 - <4cm
 - 20% benign
 - Slow growth rate
 - Risk of metastasis <1%
 - Significant comorbidities
- ?biopsy

The Natural History of Observed Enhancing Renal Masses: Meta-Analysis and Review of the World Literature

Sam N. Chawla, Paul L. Crispin, Alexandra L. Hanlon, Richard E. Greenberg, David Y. T. Chen and Robert G. Uzzo*

From the Departments of Urologic Oncology and Biostatistics (ALH), Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania



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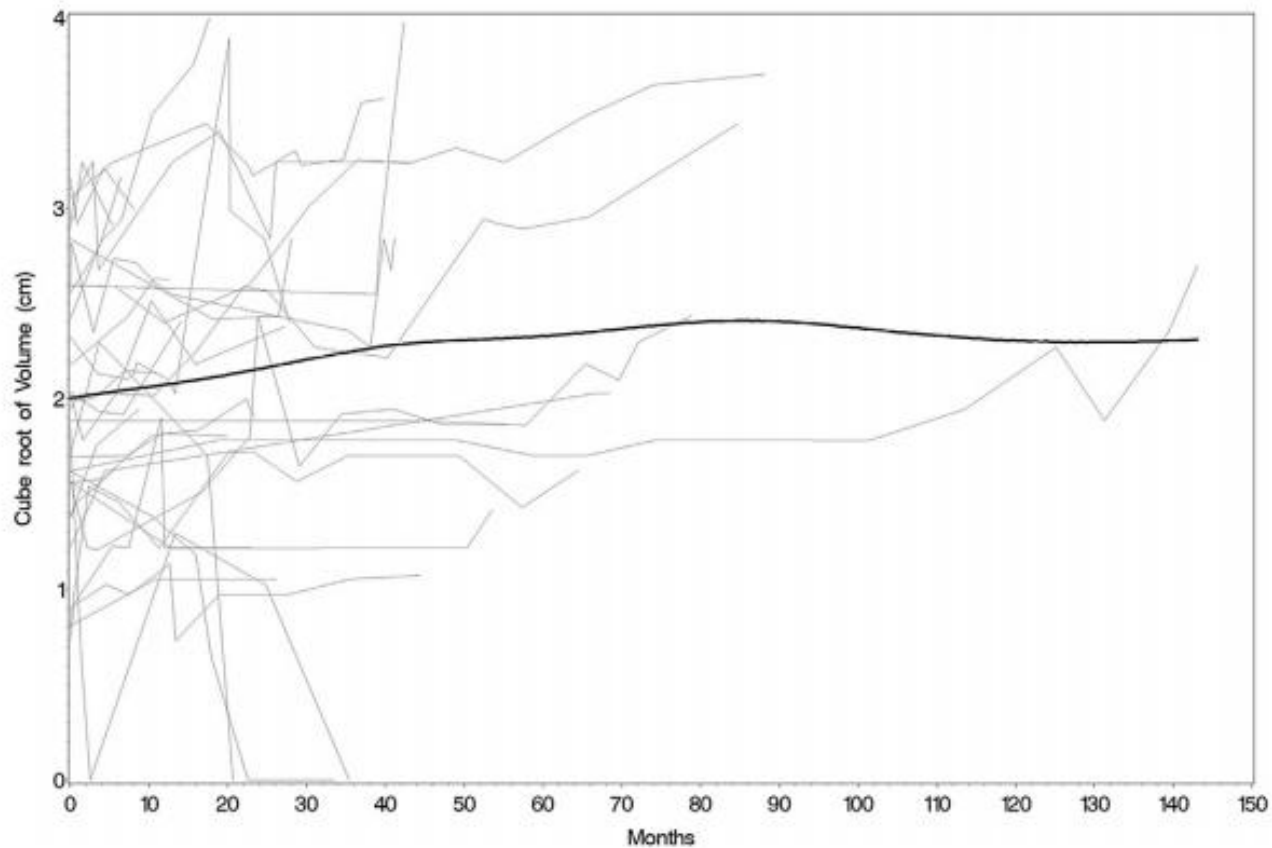


Review

The role of active surveillance of small renal masses

Alessandro Volpe

Division of Urology, Department of Translational Medicine, University of Eastern Piedmont, Maggiore della Carità Hospital, Corso Mazzini, 18, 28100, Novara, Italy



Ablation



Ablation

- Radiofrequency ablation
- Cryotherapy
- Microwave
- HIFU




Ablation outcomes?



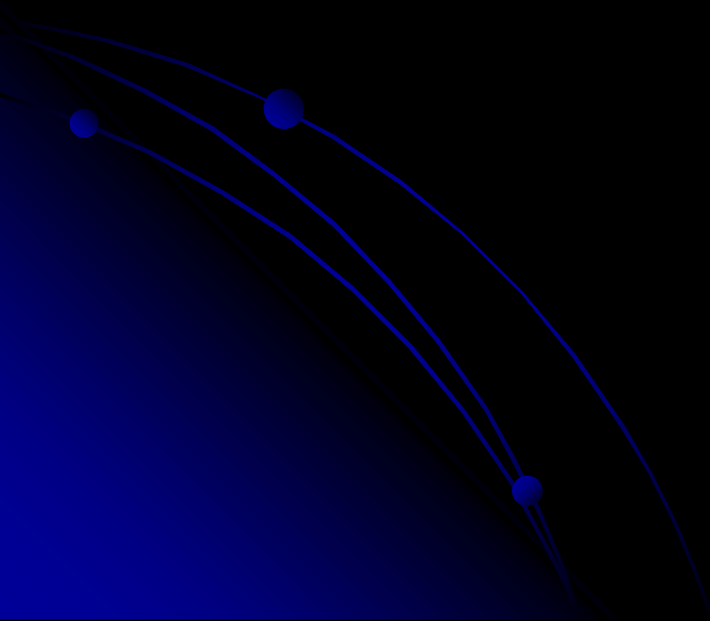
Evidence-Based Review

Partial Nephrectomy versus Thermal Ablation for Clinical Stage T1 Renal Masses: Systematic Review and Meta-Analysis of More than 3,900 Patients

J. Ricardo Rivero MD ^a, Jose De La Cerda III MD, MPH ^a, Hanzhang Wang MD, MPH ^a, Michael A. Liss MD ^{a, b}, Ann M. Farrell MLS ^d, Ronald Rodriguez MD, PhD ^{a, b}, Rajeev Suri MD ^c, Dharam Kaushik MD ^{a, b} 

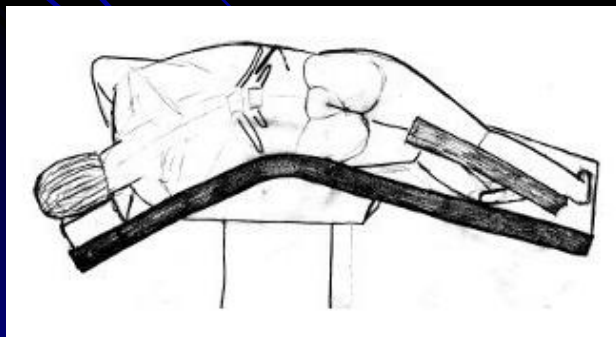
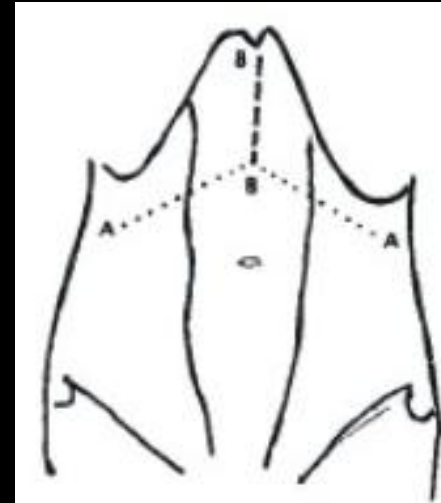
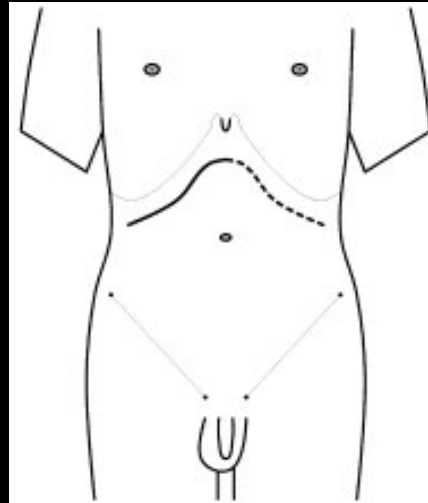
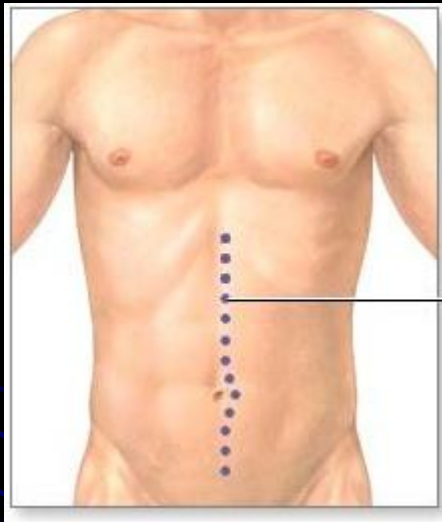
- No difference in metastasis
- No difference in local recurrence (?)
- Better side effect profile
- Worse cancer specific survival

Radical nephrectomy



Radical nephrectomy – T1/T2

T1 consider partial nephrectomy first



Radical nephrectomy – T3a/b



ELSEVIER

Urologic Oncology: Seminars and Original Investigations 31 (2013) 1298–1304

UROLOGIC
ONCOLOGY

Original article

The surgical management and prognosis of renal cell cancer with IVC tumor thrombus: 15-Years of experience using a multi-specialty approach at a single UK referral center

Ased S. M. Ali, M.R.C.S.^{a,b}, Nikhil Vasdev, F.R.C.S.(Urol)^{a,*},
Selvaraj Shanmuganathan, F.R.C.S.(C/Th)^c, Edgar Paez, F.R.C.S.(Urol)^a,
John H. Dark, F.R.C.S.(C/Th)^{b,c}, Derek Manas, F.R.C.S.^d, David J. Thomas, F.R.C.S.(Urol)^a

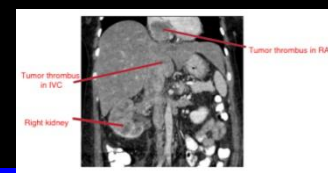
^a Department of Urology, Newcastle upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK

^b Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK

^c Department of Cardiothoracic Surgery, Newcastle upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK

^d Department of Hepatobiliary and Transplant Surgery, Newcastle upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK

Radical nephrectomy – T3c



#P77 Oncological outcomes following Radical Nephrectomy with Deep Hypothermic Circulatory Arrest (DHCA) in patients with supra-diaphragmatic thrombus extension.

The Newcastle upon Tyne Hospitals NHS Foundation Trust

The British Association of Urological Surgeons

Mr J. Barclay¹, Mr R. Veeratterapillay², Mr E. Paez³, Mr J. Hamilton², Prof D. Manas², Mr D. Thomas³

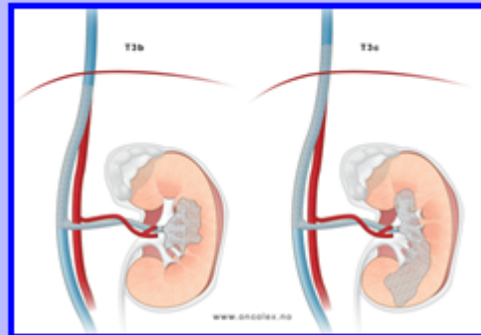
1 - Department of Urology, Freeman Hospital, Newcastle-upon-Tyne, UK, 2 - Department of Cardiothoracic surgery, Freeman Hospital, Newcastle-upon-Tyne, UK, 3 - Department of Hepato-biliary and Transplantsurgery, Freeman Hospital, Newcastle-upon-Tyne, UK

Introduction:

Radical nephrectomy with DHCA for T3c RCC involves complex, multi-disciplinary surgery with significant associated morbidity and mortality. We report oncological outcomes for a patient cohort undergoing this procedure at a single centre UK teaching Hospital.

Methods:

17 patients undergoing radical nephrectomy with DHCA during 2004-2014 were identified from a prospectively-acquired departmental database. A review of medical, radiology and pathology records was performed and relevant data extracted. Kaplan Meier (KM) plots were used for survival analyses. A standard 'Mercedes-Benz' incision was used in all cases. Hepatopancreatobiliary surgery assisted with 4 cases requiring a caval patch.



Picture of a T3c (www.oncolink.org)

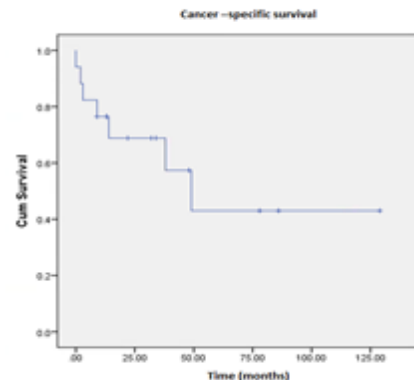
Results:

- The mean patient age was 59yrs (48-79yrs).
- Pre-operative ECOG statuses were: 1 (35%), 2 (41%) and 3 (24%).
- 5 patients (29%) had radiologically-confirmed lung metastases at presentation.
- Mean DHCA time was 23mins (14-39mins), with all-but-one patient cooled to 18°C.
- Mean tumour size was 13.8cm (range 11.0-26.0cm)
- Fuhrmangrades reported: 2 (n=1), 3 (n=13) and 4 (n=3)
- Histology showed clear cell (n=16) and papillary (n=1) carcinoma.
- There was one perioperative death within 30 days – from multi-organ failure related to intra-abdominal candida sepsis.
- 35% of patients suffered major (>Grade III) complications according to Clavien-Dindo classification. (Table 1)
- Overall survival for our cohort was 59%, with 3-yr disease specific survival 68% and 5-yr disease specific survival 43%.
- The KM estimated median survival was 49±12 months.
- Eight patients (47%) developed new/ progressive post-operative metastases: Lung (n=5), Bone (n=3), Liver (n=2), Adrenal/ Bone/ Local recurrence (n=1 each).
- Additional therapy included Tyrosine Kinase Inhibitors (n=8) and palliative radiotherapy (n=5).

Table 1.

Clavien-Dindo classification: Grade of complication	Complication	Number of patients
I	Delirium	3
	Ileus	2
	AF	6
IIIb	Cardiac Tamponade	1
IVa	Dialysis	3
	Period of prolonged ventilation	4
V	Death	1

Kaplan Meier survival analysis plot



Conclusion: Disease-specific survival outcomes appear comparable with published literature. Although surgery is associated with considerable morbidity, our cohort demonstrates good medium term outcomes for selected patients in a specialist centre, even in a cytoreductive setting.

Why radical nephrectomy?

T1	95%
T2	85%
T3a	75%
T3b	50%
T3c	30%
T4+	<10%

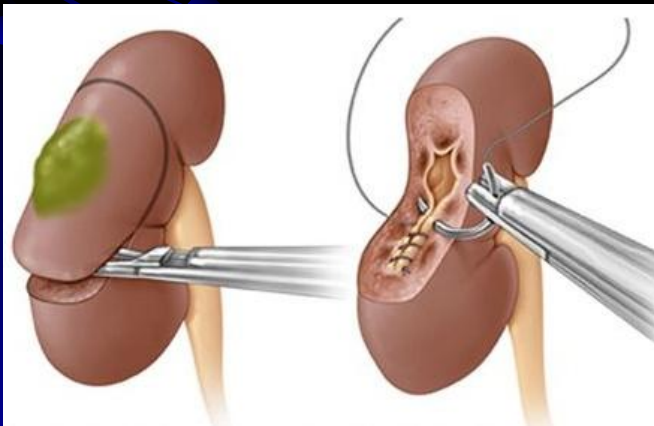


Partial nephrectomy

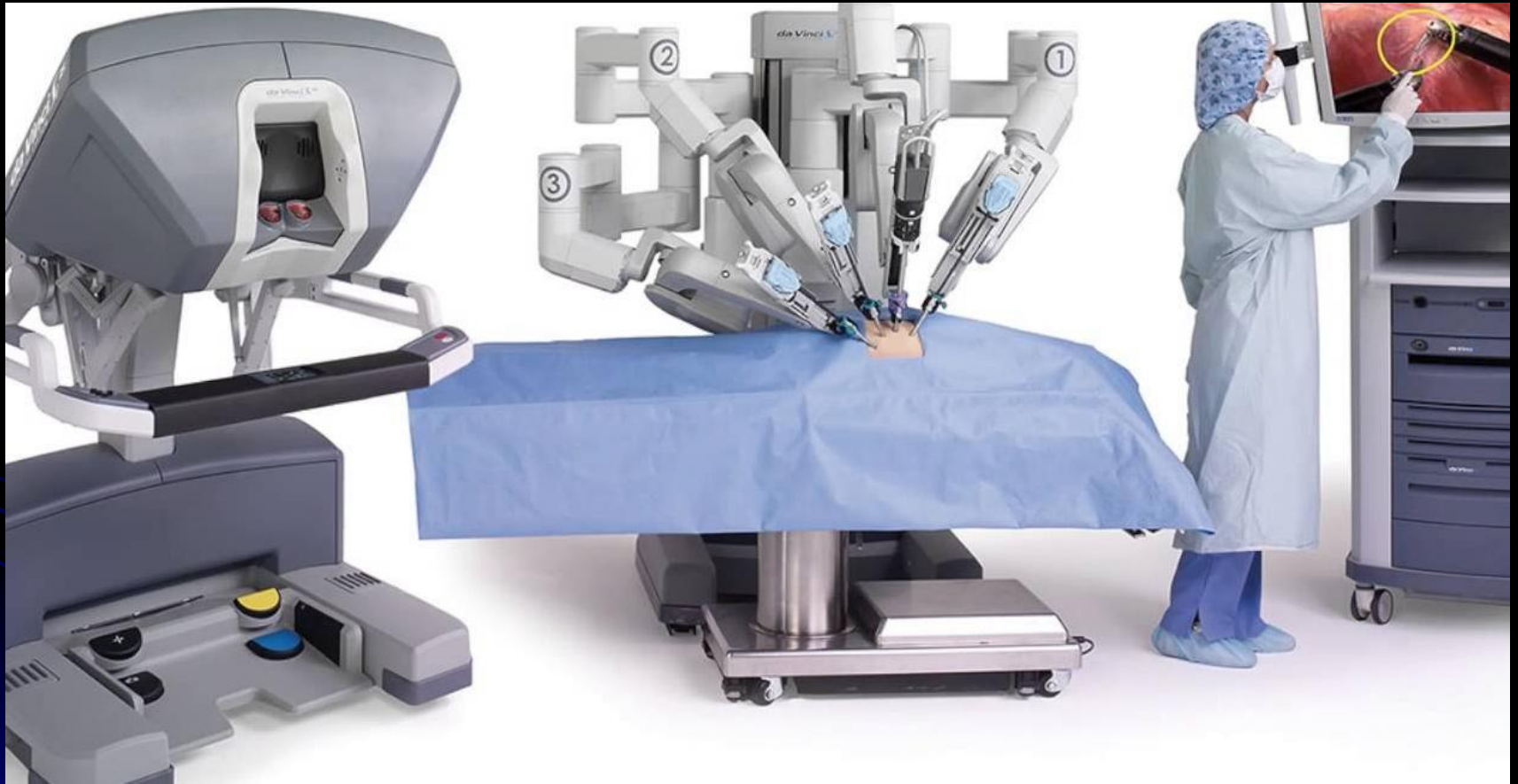


Partial nephrectomy

- T1 tumours
- Solitary kidney
- Conditions impairing renal function



DaVinci Robotic platform



Partial nephrectomy

Robotics and Laparoscopy

BJUI
BJU International

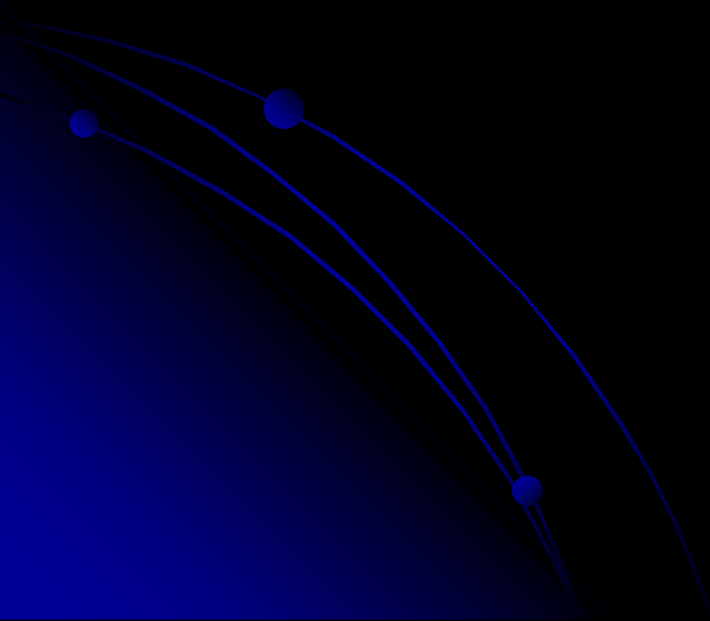
Early surgical outcomes and oncological results of robot-assisted partial nephrectomy: a multicentre study

Rajan Veeratterapillay*, Sanjai K. Addla†, Clare Jelley†, John Bailie*, David Rix*, Steve Bromage‡, Neil Oakley‡, Robin Weston§ and Naeem A. Soomro*

**Department of Urology, Freeman Hospital, Newcastle Upon Tyne, †Department of Urology, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, ‡Department of Urology, Stepping Hill Hospital, Stockport, and §Department of Urology, Royal Liverpool University Hospital, Liverpool, UK*

- Safe
- ‘Nephron sparing’
- Emergence of robotic technology
- Oncological outcomes comparable to RN

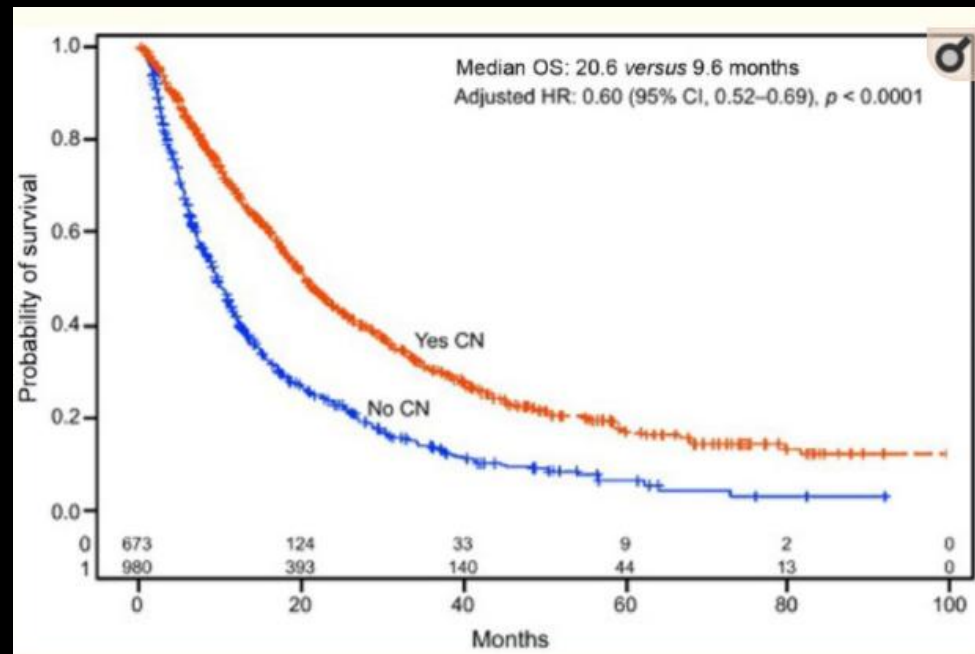
Surgery in metastatic disease



Cytoreductive nephrectomy

- Performing surgery in certain patients with metastatic RCC results in improved survival!

- Good PS
- Good prognostic group
- Low volume mets
- Resectable tumour

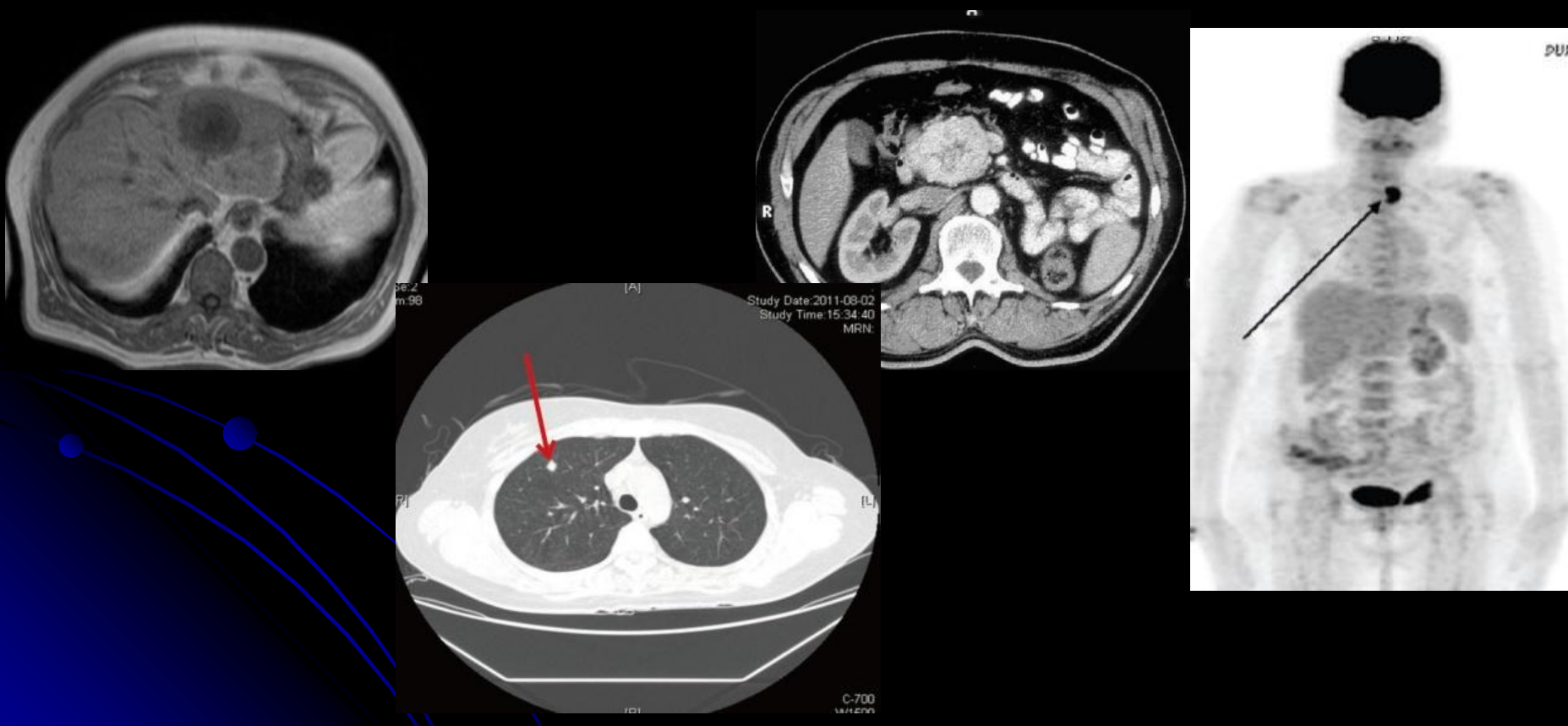


Metastatectomy



Role of metastasectomy in metastatic renal cell carcinoma

Arun Z. Thomas; Mehrad Adibi; Leonardo D. Borregales; Christopher G. Wood; Jose A. Karam



Summary

Patients with isolated surgically resectable metastatic disease, with long disease-free intervals, and with good performance status are likely to benefit the most from metastasectomy.

Figure 7.1: Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer.

	First-line therapy	Second-line therapy	Third-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab	cabozantinib or nivolumab
IMDC intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy	cabozantinib or an alternative targeted therapy
	cabozantinib, sunitinib or pazopanib*	VEGF targeted therapy or nivolumab	An alternative targeted therapy or nivolumab



Summary

- Increase detection of RCC due to imaging
- Increasing consideration of renal biopsy
- Localised disease
 - Surveillance
 - Ablation
 - Surgery (can be very radical)
- Metastatic disease
 - Cytoreductive nephrectomy / metastatectomy
 - Immune agents

Letter | Published: 13 February 2019

Large teams develop and small teams disrupt science and technology

Lingfei Wu, Dashun Wang & James A. Evans 

Nature **566**, 378–382 (2019)

... smaller teams have tended to disrupt science and technology with new ideas and opportunities, whereas larger teams have tended to develop existing ones



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