MATER HOSPITAL
A FACILITY OF
ST VINCENT'S
HEALTH AUSTRALIA

Mater Hospital
GP Education Seminar
Prostate cancer

November 17th 2021

MATER HOSPITAL
A FACILITY OF
ST VINCENT'S
HEALTH AUSTRALIA

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Royal North Shore Hospital
Mater Hospital – Sydney Medical Oncology
NHMRC Clinical Trials Centre

Learning Objectives

1. Describe the investigation and management of benign prostatic hypertrophy (BPH)
2. Describe the optimal use of PSA testing and its pitfalls
3. Explain the role for surgery and/or radiotherapy in the treatment of localised prostate cancer
4. Understand the role of systemic treatment in advanced disease

Case 1

- 52 year old male “Bill”
- Married, two teenage children
- Comes to you for a routine check-up
- His wife prompts him to tell you about nocturia over the past six months
- With prompting, Bill volunteers that he has also noticed some urinary frequency and urgency at times
- Bill’s mother had breast cancer at age 41 and his father had prostate cancer at age of 78

What next?

(A) Reassure him it's normal for his age, see as needed

(B) Refer him for consideration of TURP

(C) Prescribe Tamsulosin or Duodart

(D) Initiate investigations for UTI

LUTS – Lower urinary tract symptoms

- Storage
  - Frequency
  - Urgency
- Nocturia
- Voiding
  - Intermittent stream
  - Incomplete stream
  - Strain to urinate
  - Stream – poor
  - Hesitancy
  - Post micturition dribble

How to assess severity of LUTS

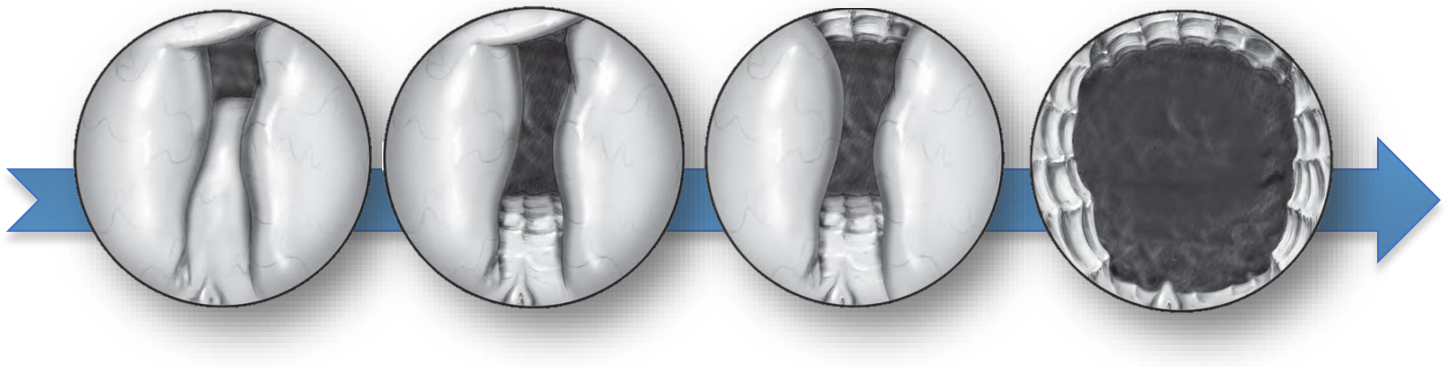
- IPSS questionnaire
- Ask about degree of bother and Quality of life
- Investigations:
- Renal function
- MSU
- Urine cytology if irritative symptoms (urgency, pain, haeamturia)
- Renal tract US:
  - High post-void residual volume
  - Upper tract dilatation
  - Prostate size
  - Bladder trabeculations, saccules, diverticula
  - Bladder stones

Management of LUTS

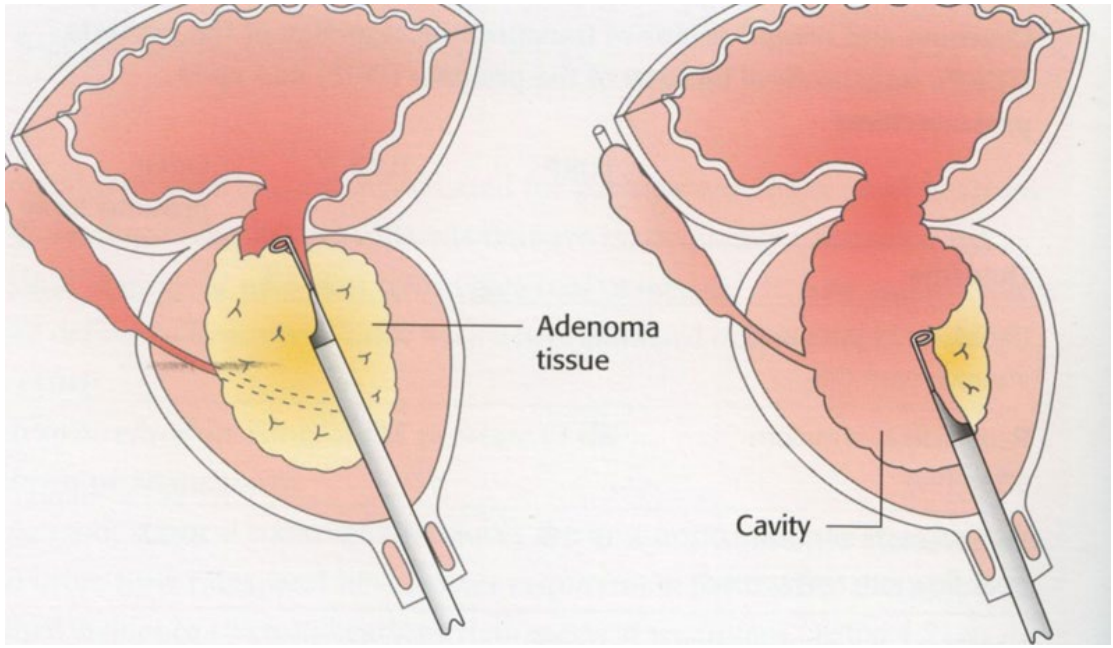
- Mild symptoms:
  - Watchful waiting/surveillance vs Medical therapy
- Moderate symptoms:
  - Medical therapy vs surgical therapy
- Severe symptoms:
  - Consider surgical therapy
- Special cases requiring complex management:
  - Neurological conditions: Parkinson's, MS, spinal cord injury, CVA, prior major pelvic surgery, others

Consider referral to a urologist

TURP



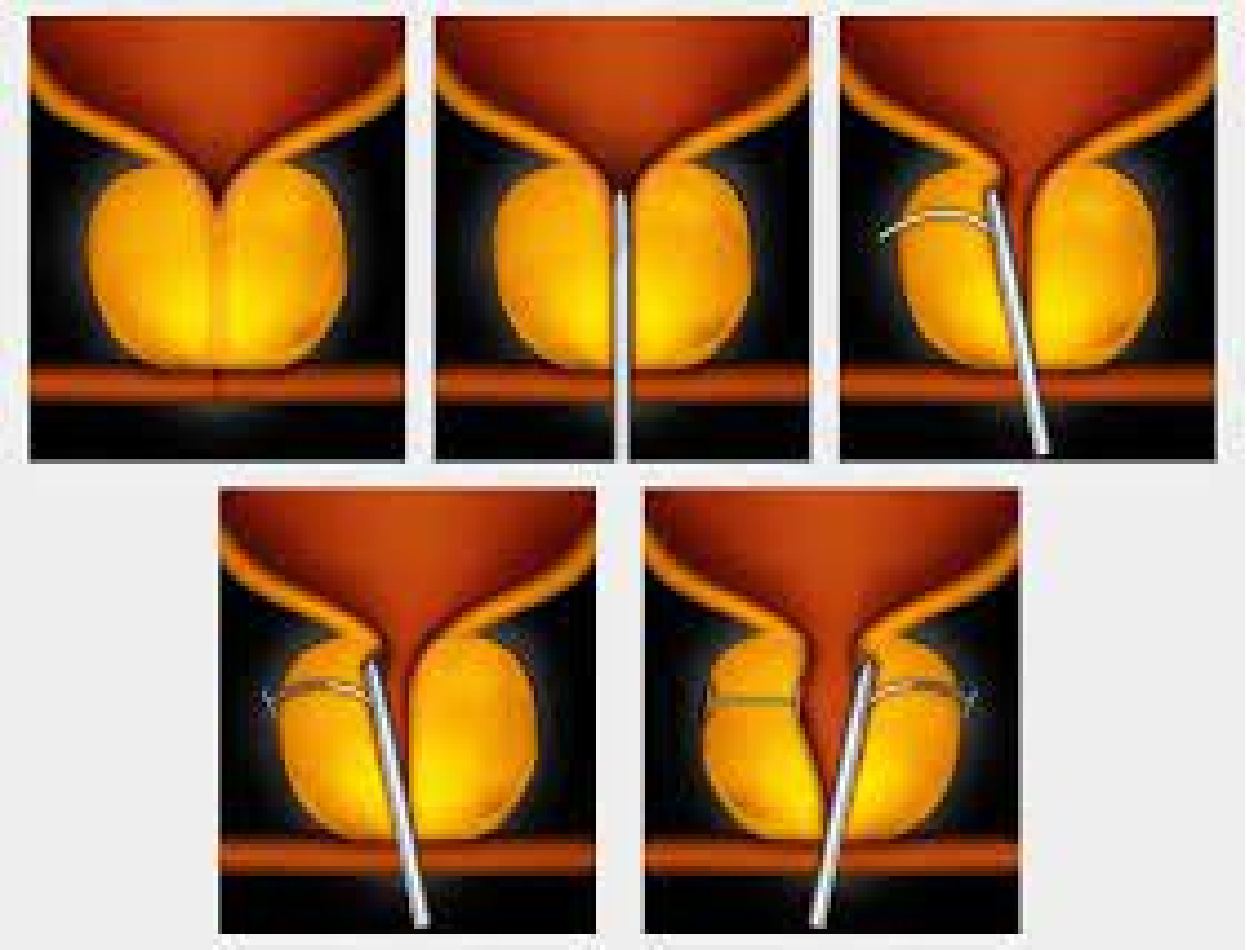
- Side effects
  - Bleeding, TURP syndrome, infection, retrograde ejaculation
- Ward problems
  - Irrigation
  - Block catheter
  - Failed trial of void



Urolift

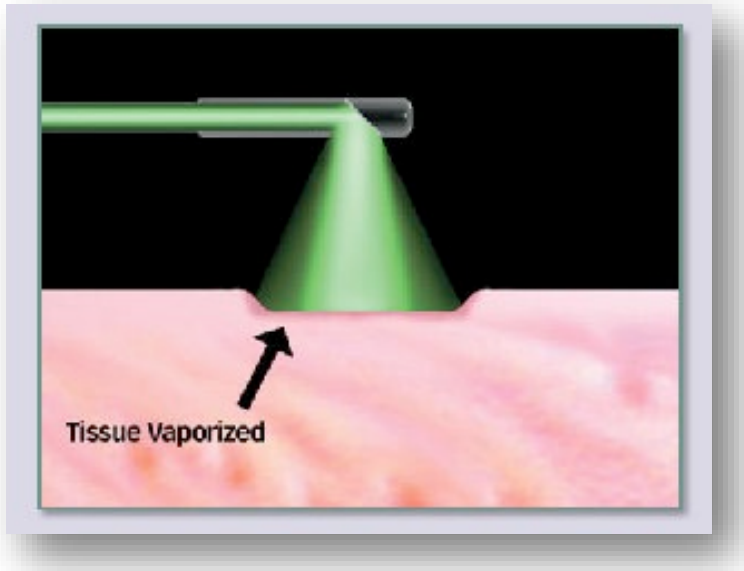
- Advantages:
  - Fast recovery
  - Shorter hospital stay and catheterisation
  - Minimal blood loss
  - No retrograde ejaculation

- Disadvantages:
  - Distortion of MRI images
  - Less durable or effective as TURP



OTHER SURGICAL TREATMENTS

- Laser
  - Holmium (HoLEP, HoLAP)
  - Green-light
- Microwave
- HIFU
- Rezum
- others



Case 2

- Bill decided to proceed with medical therapy
- Poor response to Tamsulosin
- Upgraded to Duodart with good clinical response

- Bill returns to your practice 2 years later for review
- He has been feeling great because he is no longer suffers from nocturia and is sleeping right through the night.
- He asks about having PSA test as his friend was recently diagnosed with prostate cancer and he “thinks he should get checked out”….

What next?

(A) Reassure him that PSA is not very specific and that prostate cancer usually grows slowly

(B) Send him off for a PSA test and Urology referral concurrently

(C) Discuss the pros and cons of PSA testing and arrange to see him next week

(D) Phone a friend

For men at average risk of prostate cancer who have been informed of the benefits and harms of testing and who decide to undergo regular testing for prostate cancer, offer PSA testing every 2 years from age 50 to age 69, and offer further investigation if total PSA is greater than 3.0 ng/mL.

If the necessary data become available and the required processes put in place to ensure effective implementation, consider replacing > 3.0 ng/mL with > 95th percentile for age as the criterion for further investigation.

Do not offer PSA testing at age 40 years to predict risk of prostate cancer death.

For men younger than 50 years who are concerned about their risk for prostate cancer, have been informed of the benefits and harms of testing, and who wish to undergo regular testing for prostate cancer, offer testing every 2 years from age 45 to age 69 years.

If initial PSA is at or below the 75th percentile for age, advise no further testing until age 50.

If initial PSA is above the 75th percentile for age, but at or below the 95th percentile for age, reconfirm the offer of testing every 2 years.

If a PSA test result before age 50 years is greater than the 95th percentile for age, offer further investigation.

Offer testing from age 50 years according to the protocol for all other men who are at average risk of prostate cancer.

Advise men 70 years or older who have been informed of the benefits and harms of testing and who wish to start or continue regular testing that the harms of PSA testing may be greater than the benefits of testing in men of their age.[i]

[NHMRC Fact Sheet on PSA testing]

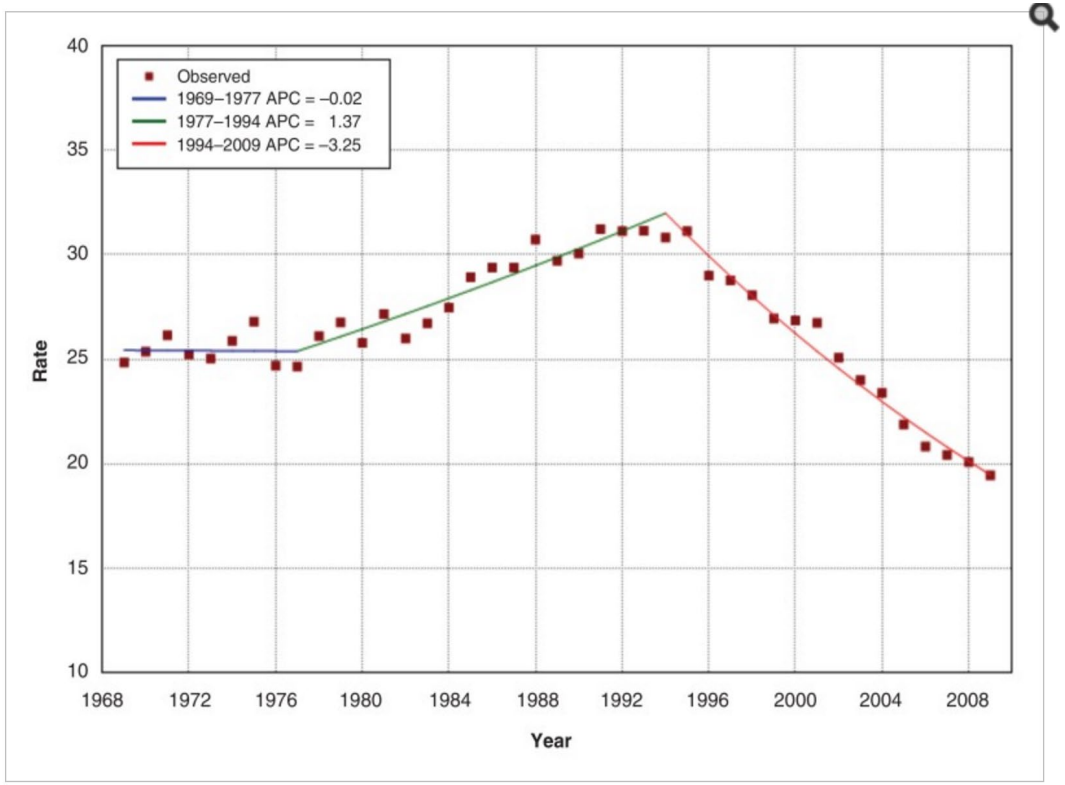
[Cancer Council Clinical Practice Guidelines on PSA testing]

Clinical Guidelines

DO	DO NOT
Provide guidelines on deciding when to start/stop testing, frequency of testing	Recommend population-based screening
When to refer to biopsy	
Family history	
Role of DRE	

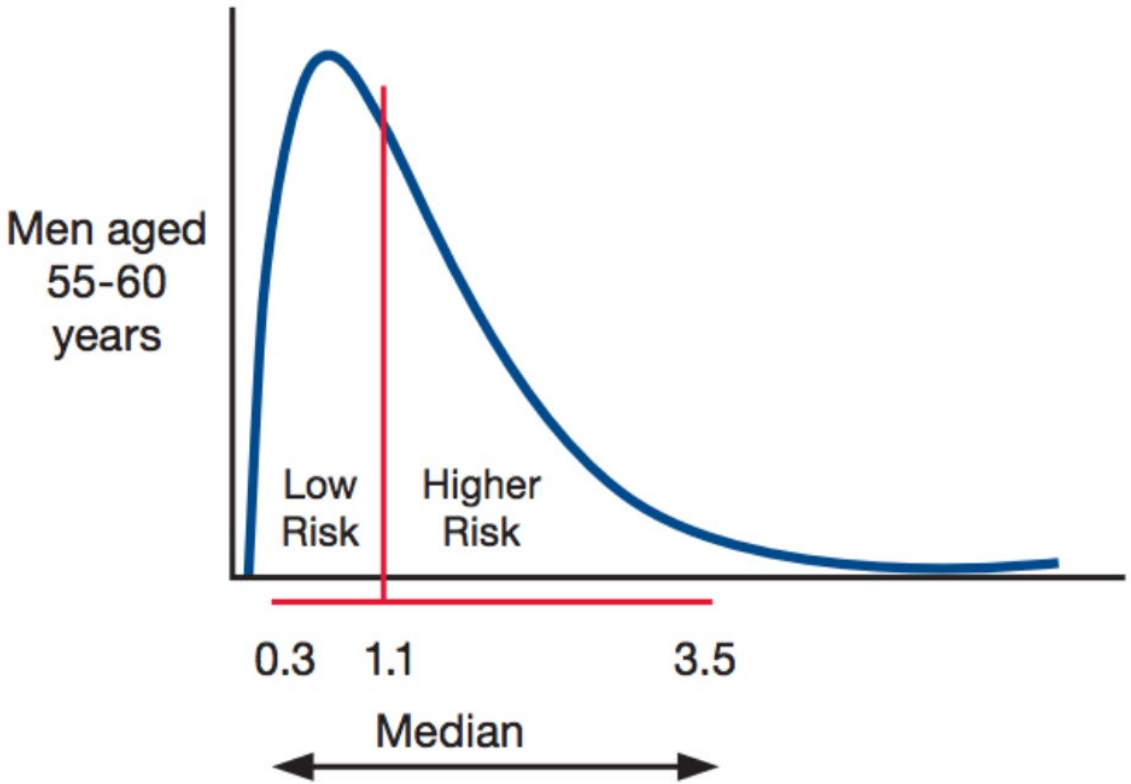
Facts About PSA

- NOT a very sensitive or specific test
- Before PSA era, 75% of men diagnosed with prostate cancer already had clinically metastatic disease.
- Post PSA era, the number of men diagnosed with prostatic cancer metastatic disease is less than 5%.
- Since PSA testing there has been significant reduction in prostate cancer specific mortality
- Despite Higher life expectancy
- Improvements in all definitive treatment modalities



Age-standardized mortality (per 100 000) and annual percent change (APC) of prostate cancer mortality, 1969-2009, Canada.

Diagram 1. PSA Distribution for 55-60 years



PSA reference interval for 55-60 year age group

Age (yrs)	Reference (ug/L)	Median (ug/L)
20 - 29	0.20 - 2.0	0.70
30 - 39	0.20 - 2.1	0.75
40 - 44	0.25 - 2.2	0.80
45 - 49	0.25 - 2.5	0.85
50 - 54	0.25 - 3.0	0.95
55 - 59	0.30 - 3.5	1.1
60 - 64	0.30 - 4.5	1.2
65 - 69	0.30 - 5.5	1.3
70 - 74	0.30 - 6.5	1.4
75 - 79	0.30 - 7.5	1.5
80+	0.25 - 9.0	1.6

PSA Density

- Total serum PSA (ug/L) / Prostate volume (cc)
- TRUS gives most accurate prostate volume, DRE and renal tract US fair at estimating size
- Increased risk of cancer if PSA density > 0.1

PSA Velocity

- At least 3 PSA measurements are needed over a period of at least 12-18 months apart to obtain maximal benefit from the results.
- A PSA-V of 0.75 ug/L or greater per year was suggestive of cancer (72% sensitivity, 95% specificity).

Free to total PSA ratio (F/T%)

- Useful if PSA between 4-10ug/L
- If < 10%.... >90-95% chance is cancer related elevation in PSA
- If > 25%..... < 5% chance is cancer related elevation in PSA

2012 - The Year Of PSA Controversies

PLCO Trial (NEJM 2012)

- American RCT study
- 76,600 patients
- Issues:
  - 44% contamination of the control arm
  - 85% compliance in treatment arm
  - 7 year follow up

ERSPC Trial (NEJM 2012)

- European multicentre RCT study
- 162,000 patients
- Issues:
  - Variability in protocols and management and PSA cut offs
  - Contamination rate not reported
  - NNT 1 in 42 -> 33 -> 27

Mortality results from the Göteborg randomised population-based prostate-cancer screening trial

Jonas Hugosson, Sigrid Carlsson, Gunnar Aus, Svante Bergdahl, Ali Khatami, Pär Lodding, Carl-Gustaf Pihl, Johan Stranne, Erik Holmberg, Hans Lilja

www.thelancet.com/oncology **Vol 11 August 2010**

Swedish arm of ERSPC

- 20,000 men, RCT 1:1 ratio
- 50-69 years age
- Median follow up 14 years
- NNT = 12

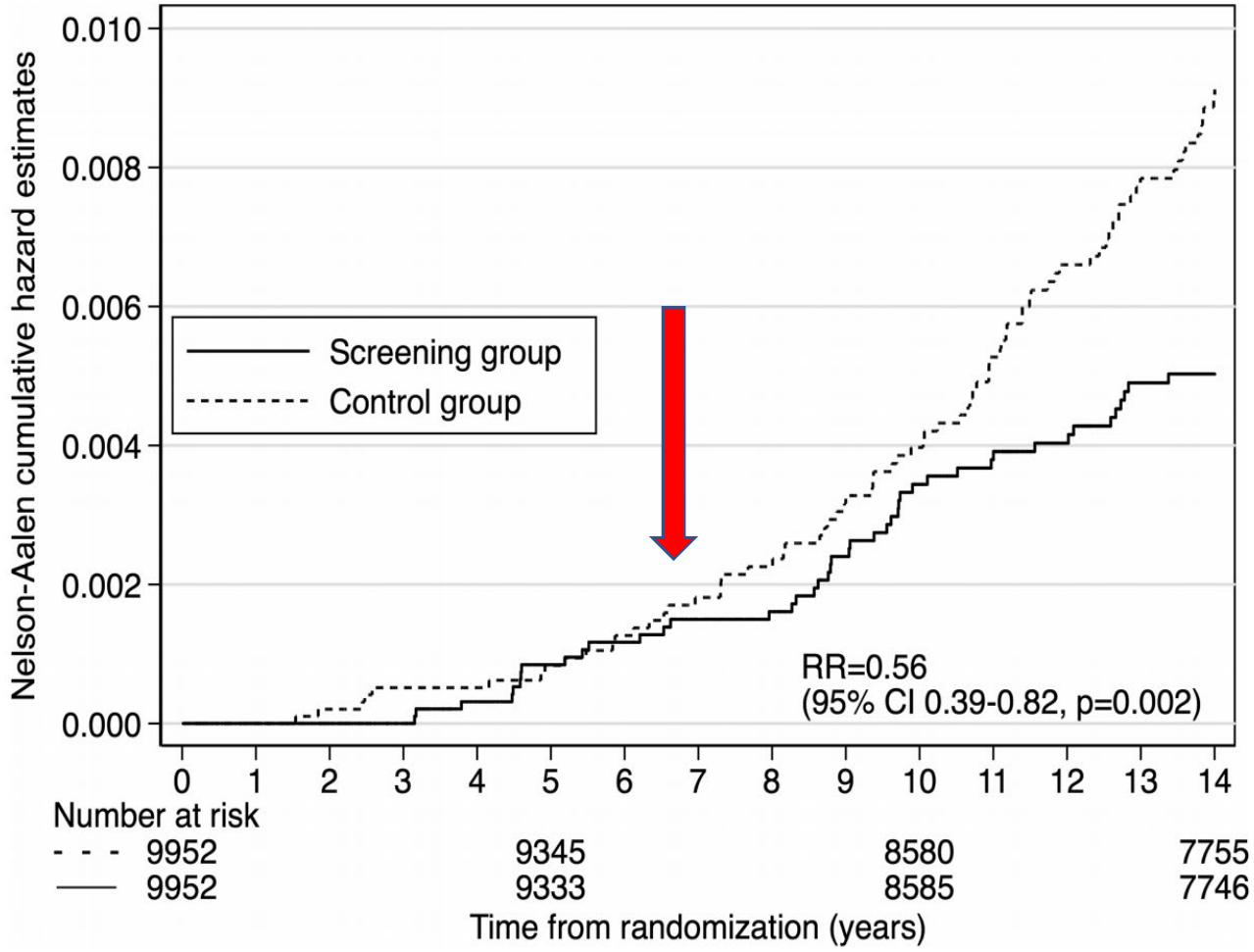


Figure 3.
Cumulative risk of death from prostate cancer using Nelson-Aalen cumulative hazard estimates

Impact of the United States Preventive Services Task Force 'D' recommendation on prostate cancer screening and staging

Eapen, Renu S.; Herlemann, Annika; Washington, Samuel L. III; Cooperberg, Matthew R.

- Substantial decline in PSA screening in USA
- Significant decline in rates of prostate biopsy and prostate cancer incidence
- Higher incidence of high grade or high stage cancer diagnosis
- Significant increase in rates of metastatic prostate cancer

Current Opinion in Urology: Post Author Corrections:
February 17, 2017, doi: 10.1097/MOU.0000000000000383

Specialist Pathologists
Dr. Lawrie Bott
Dr. Grant McBride
Dr. John Milross
Dr. Jane Nankervis
Dr. Raj Ramakrishna
Dr. Kimberley Hart
Dr. Bryan Knight
Dr. Chee Vun
Dr. Mohammad Al-Shididi
Dr. Vanita Bhargava
Dr. Christine Loo
Dr. Manal El Samman
Dr. Anita Iyer
Dr. Asma Naveed
Dr. Syed Abbas
Dr. Chandra Bura
Dr. Sabar Napaki
Dr. Moammar Alshimirti

PSA	23/02/09 08:55	12/08/11 10:33	08/02/13 08:25	14/11/14 08:00	**04/04/18 10:04**	Units	Reference
Lab number	12549378	480173928	481047208	482189157	**484787507**		
PSA	2.2	3.8	3.3	3.5	235 H	ug/L	(0.25-9.0)
Free PSA	0.5	0.8	0.8			ug/L	
Free PSA %	22.7	21	24			%	(10-60)

Comments on Collection 04/04/18 1004:

PSA
Total PSA levels over 150 ug/L are most commonly associated with prostatic neoplasia.

2017 USPSTF Screening Update

- **Reversal of the USPTF decision. New recommendation:**
  - **Recommendation Grade C** (Offer or provide this service for selected patients depending on individual circumstances)
  - **Men ages 55–69**

https://screeningforprostatecancer.org/#utm_source=google&utm_medium=cpc&utm_campaign=recommendation&utm_term=branded&utm_content=draft_uspstf

Case 3

- Bill’s PSA trend

2010	2016	2018	2019	2020	2021
1.5	1.79	1.92	1.96	2.42	2.79

What next?

(A) Reassure him about the steady PSA velocity

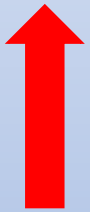
(B) Refer him to a urologist

(C) Advise him to stop having PSA tests

Case 3

- Bill’s PSA trend

2010	2016	2018	2019	2020	2021
1.5	1.79	1.92	1.96	2.42	2.79



Duodart started

Adjusted PSA Trend

2010	2016	2018	2019	2020	2021
1.5	1.79	1.92	1.96	4.84	5.58

Learning points:

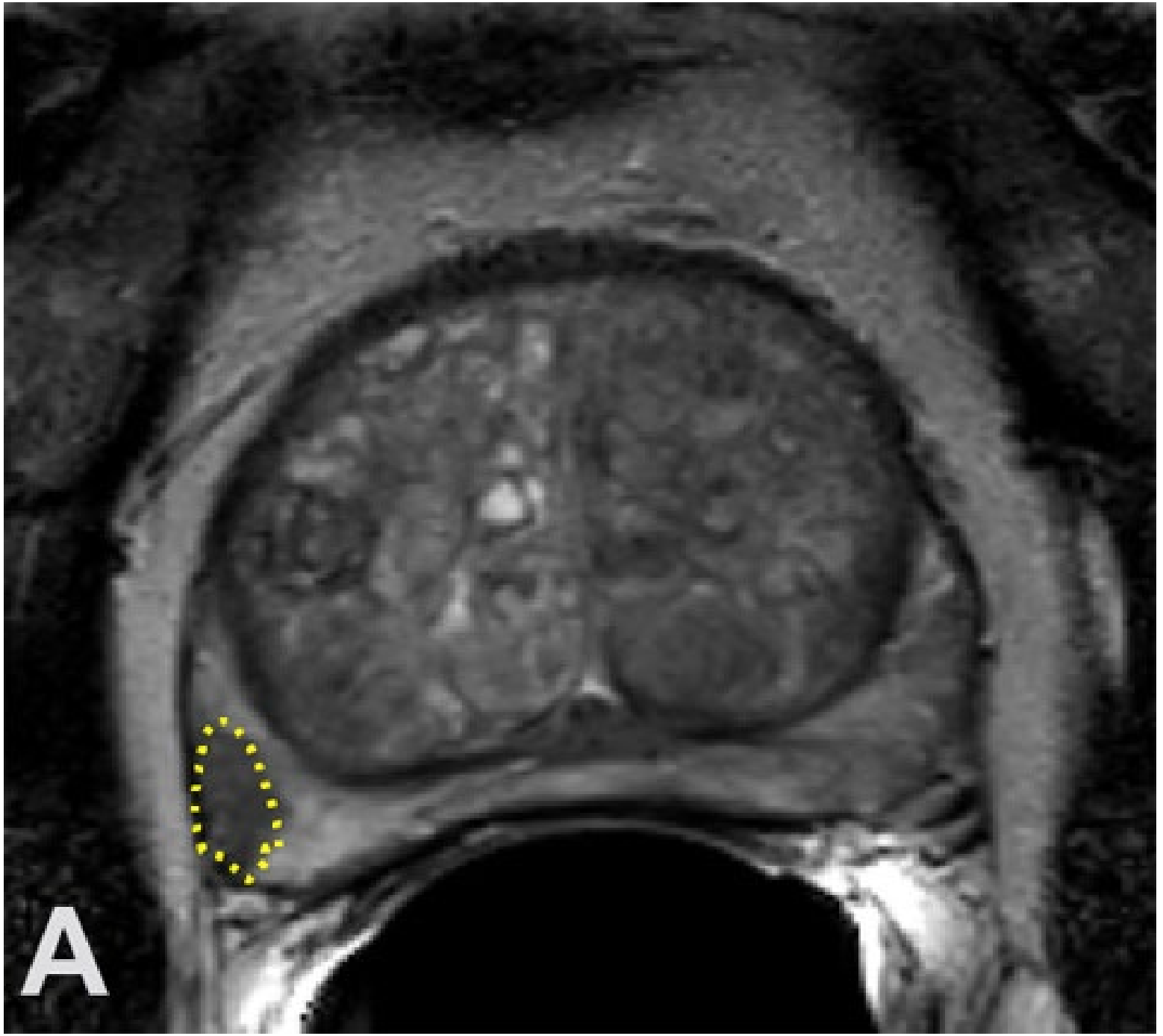
- PSA dynamics can change with 5-alpha reductase inhibitors (dutasteride, finasteride)
- Adjust the PSA while on these medications (multiply by 2)
- PSA not dropping by 50% or any rise of PSA while on these meds raises suspicion of prostate cancer
- PSA after TURP or other surgeries, would be the new baseline for comparison

When to Refer a Patient to a Urologist

- Abnormal Digital Rectal Examination
- PSA above than age specific **median** value
  - MSU clear and Repeat PSA still elevated
- Rising PSA trend
- Low Free/Total PSA ratio or high PSA density
- Red flags:
  - Family history of Prostate and Breast Cancer
  - Back pain and new onset incontinence or muscle weakness

Case 4

- Bill was referred to his local friendly urologist
- He was referred to have a prostate MRI and underwent prostate biopsy


A

Trans-Rectal Ultrasound Guided Prostate Biopsy - TRUS biopsy

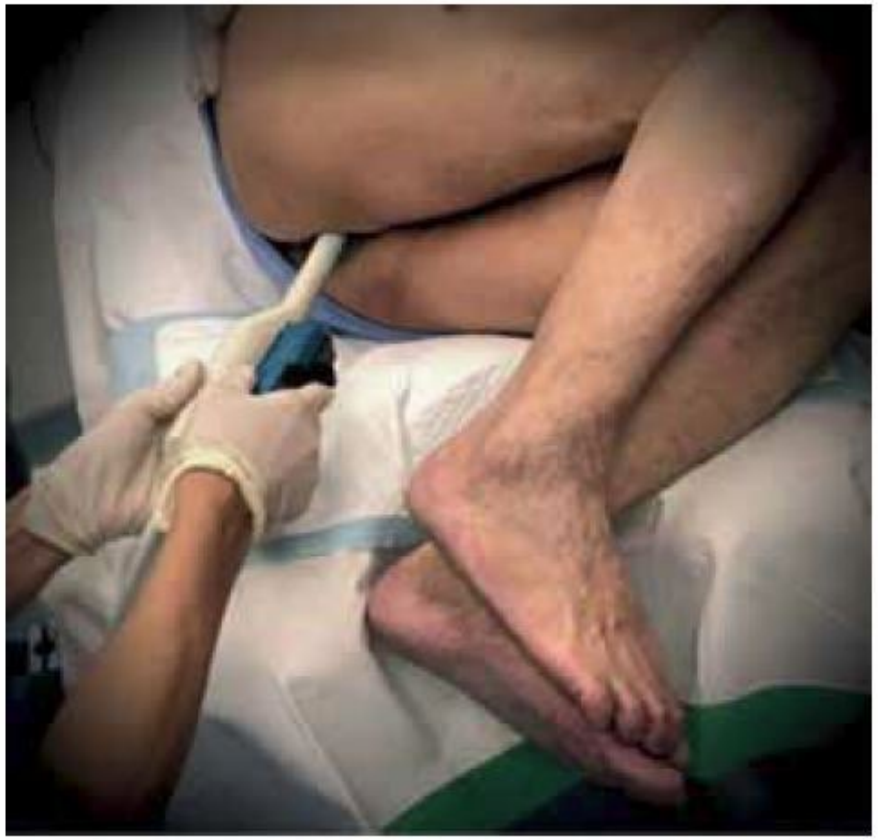
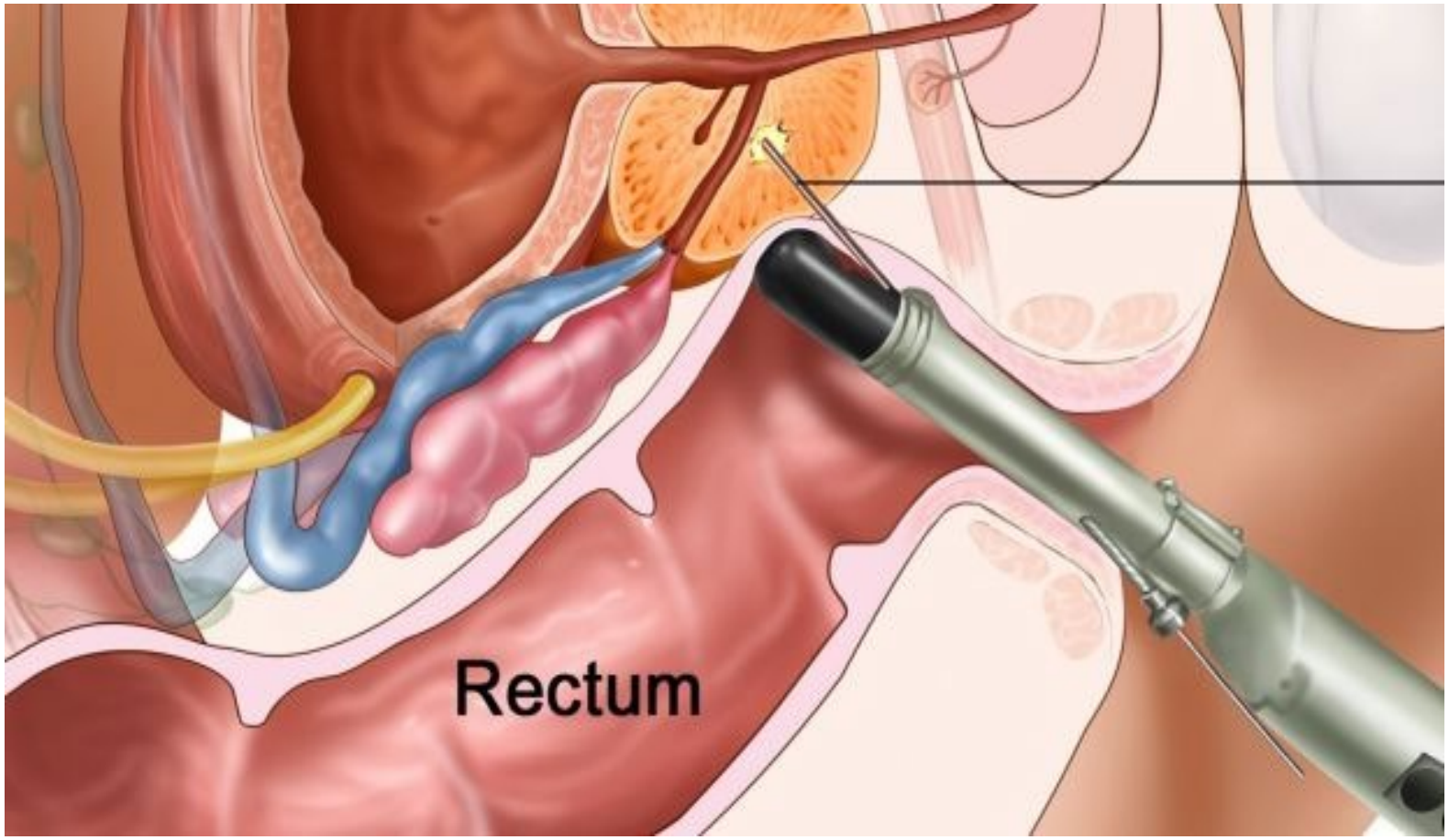
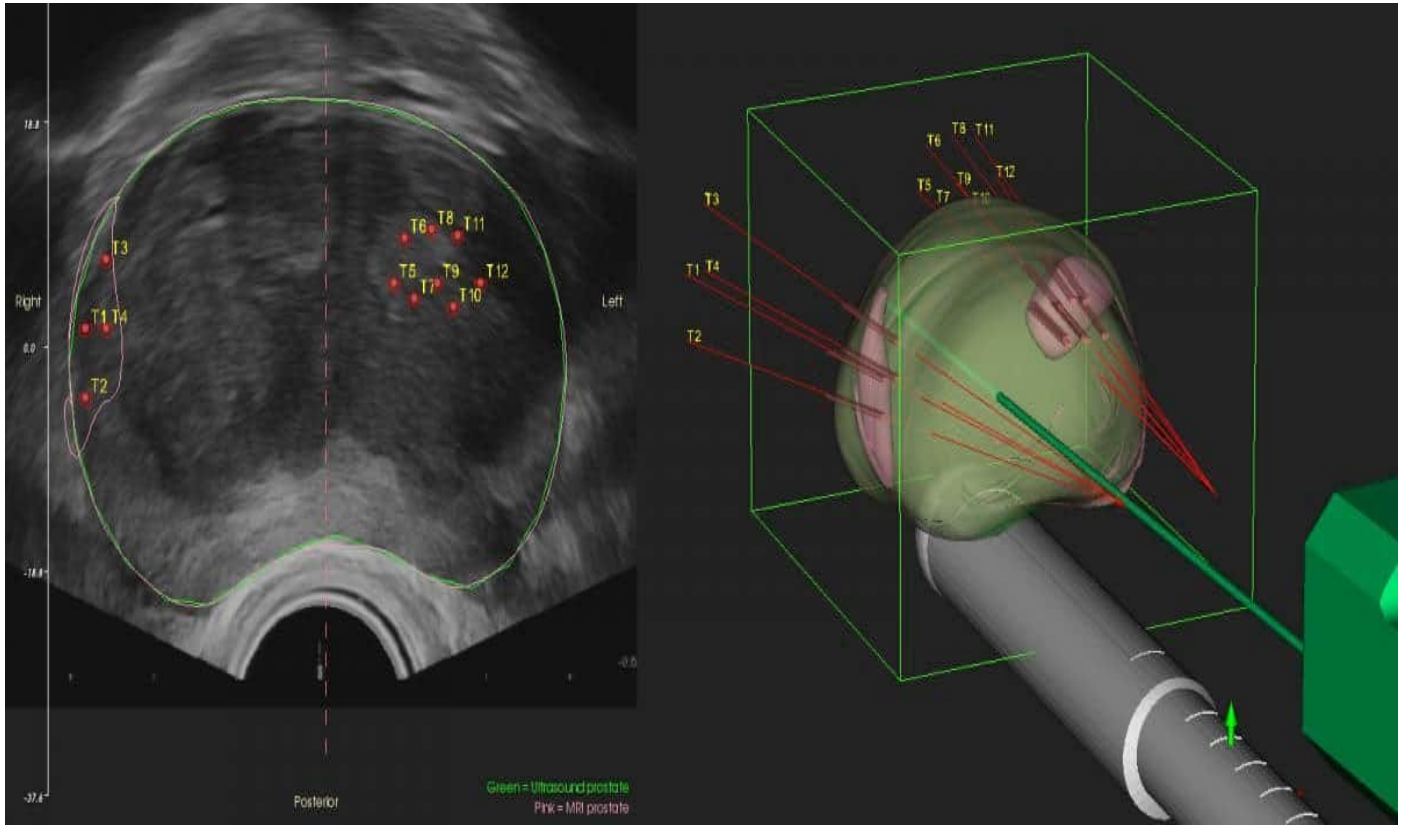
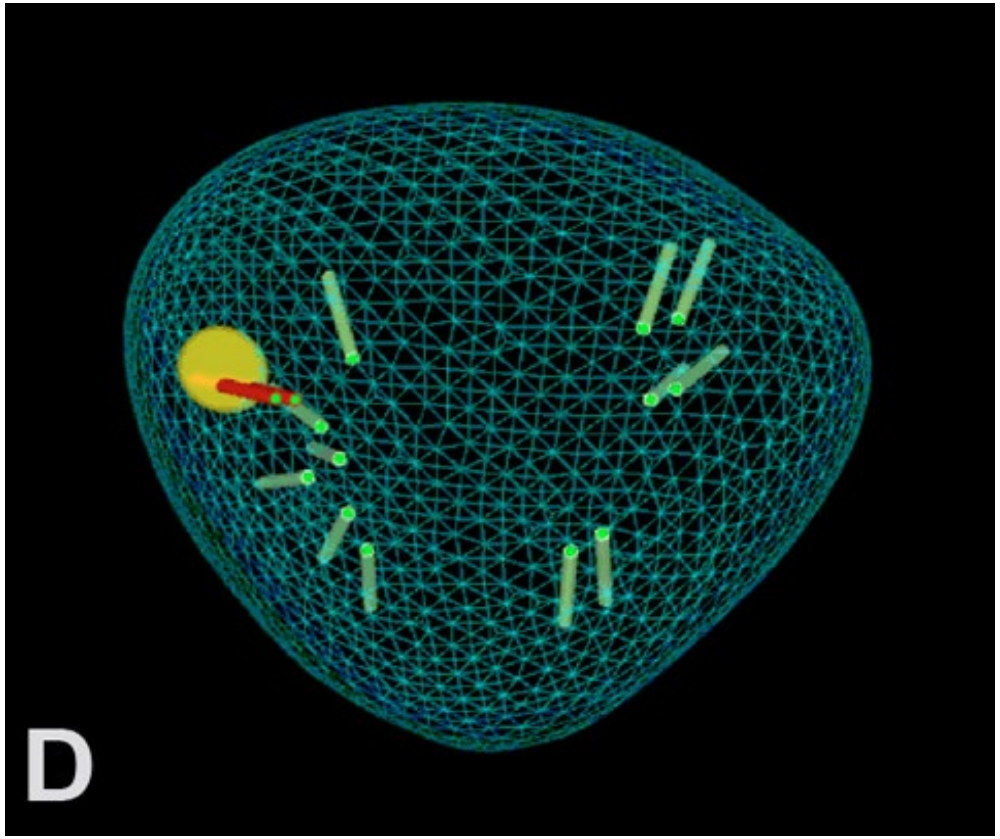


FIG 1. Positioning and route for transrectal ultrasound-guided biopsy



Trans-Perineal MRI/US fusion Targeted Prostate Biopsy





Imaging update – MRI and PI-RADS score

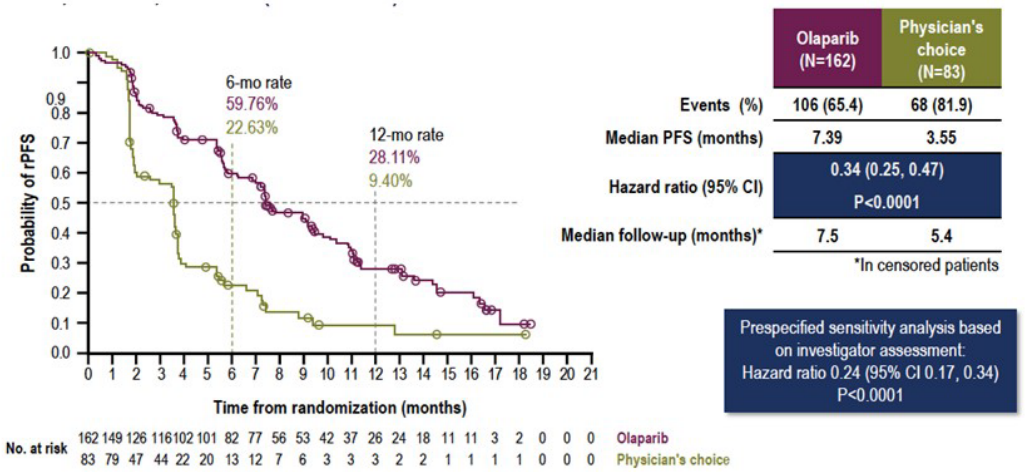
- The risk of clinically significant cancer (defined as Gleason 7 or above) based on MRI findings (alone)

- 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)

BRAC1/BRAC2 mutations

PROFOUND
(phase III trial Olaparib)

rPFS in patients with alterations in *ATM*, *BRCA1* and *BRCA2* (Cohort A)



	Olaparib (N=162)	Physician's choice (N=83)
Events (%)	106 (65.4)	68 (81.9)
Median PFS (months)	7.39	3.55
Hazard ratio (95% CI)	0.34 (0.25, 0.47) P<0.0001	
Median follow-up (months)*	7.5	5.4

*In censored patients

Prespecified sensitivity analysis based on investigator assessment: Hazard ratio 0.24 (95% CI 0.17, 0.34) P<0.0001

Less than half of patients with mutation have a positive family history. However a strong family history of prostate/breast & ovarian cancer warrants referral

- If have this mutation:
  - Don't do well on surveillance
  - Have worse prognosis
  - Respond to different treatments (PARPI)
- Geneticists are now important part of prostate cancer team

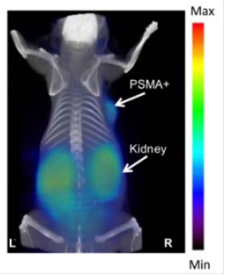
Presented By Elena Castro at 2020 Genitourinary Cancers Symposium

Case 5

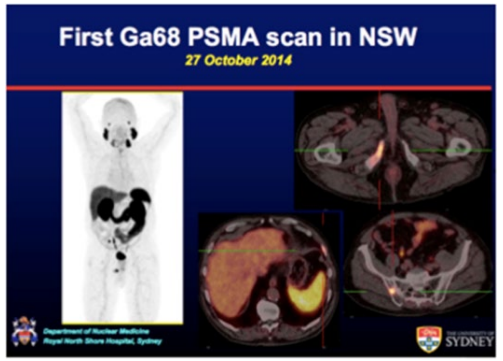
- Bill diagnosed with prostate cancer
  - Gleason 3+4 = 7 – ISUP grade group 2
  - 4/18 biopsy cores, Lesion (right posterolateral peripheral zones)
  - Lymphovascular invasion and perineural invasion

PSMA scanning a game changer in GU oncology

First animal studies published in 2012



Can detect a 4mm deposit of prostate cancer



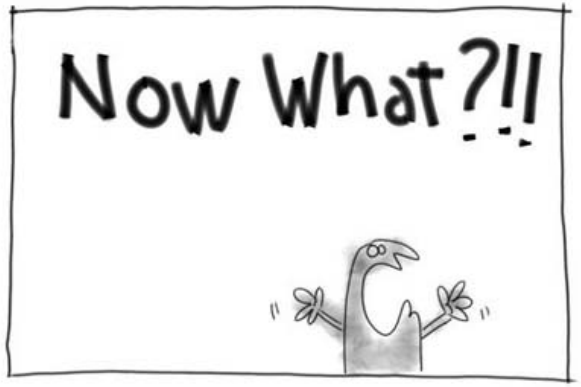
J Nucl Med. 2017 Jun 23. pii: jnumed.117.197160. doi: 10.2967/jnumed.117.197160. [Epub ahead of print]

The impact of 68Ga-PSMA PET/CT on management intent in prostate cancer: results of an Australian prospective multicenter study.

Roach PJ[1], Francis R[2], Emmett L[3], Hsiao E[1], Kneebone A[1], Hruby G[1], Eade T[1], Nguyen Q[4], Thompson B[4], Cusick T[4], McCarthy M[5], Tang C[2], Ho B[6], Stricker P[3], Scott A[7].

- By 2017 Australia has published a multicentre series of 431 patients showing that 68 Ga-PSMA Pet/CT led to a change in planned management in 51% of patients.
- Now used for better staging, identifying disease in prostate and in nodes, assessing response to treatment, SBRT protocols, identifying distant disease etc
- Still unfunded (costs $700-$1000) but perhaps will be in 2022

What next?



(A) Start androgen deprivation therapy immediately

(B) Reassure him that he has a low grade cancer and doesn't need anything further.

(C) Refer him to a Urologist

(D) Refer him to Radiation Oncologist

Offer active surveillance to men with prostate cancer if all the following criteria are met:

— PSA ≤ 20 ng/mL

— clinical stage T1–2

— Gleason score 6.

Consider offering active surveillance to men with prostate cancer if all the following criteria are met:

— PSA ≤ 10.0 ng/mL

— clinical stage T1–2a

— Gleason score ≤ (3 + 4 = 7) and pattern 4 component < 10% after pathological review.

For men aged less than 60 years, consider offering active surveillance based on the above criteria, provided that the man understands that treatment in these circumstances may be delayed rather than avoided.

Consider offering definitive treatment for:

— men with clinical stage T2b-c prostate cancer

— men with biopsy-diagnosed prostate cancer with PSA 10.0–20.0 ng/mL who do not meet the other criteria for active surveillance.

If the man strongly prefers active surveillance, offer repeat biopsy to ensure that disease classification is accurate.

Consider offering definitive treatment to men aged less than 60 years with either of the following:

— clinical stage T2b-c prostate cancer

— PSA 10.0–20.0 ng/mL and biopsy-diagnosed prostate cancer which does not meet the other criteria for active surveillance.

If the man strongly prefers active surveillance, offer repeat biopsy.

For men with prostate cancer managed by an active surveillance protocol, offer monitoring with PSA measurements every 3 months, and a physical examination, including digital rectal examination, every 6 months.

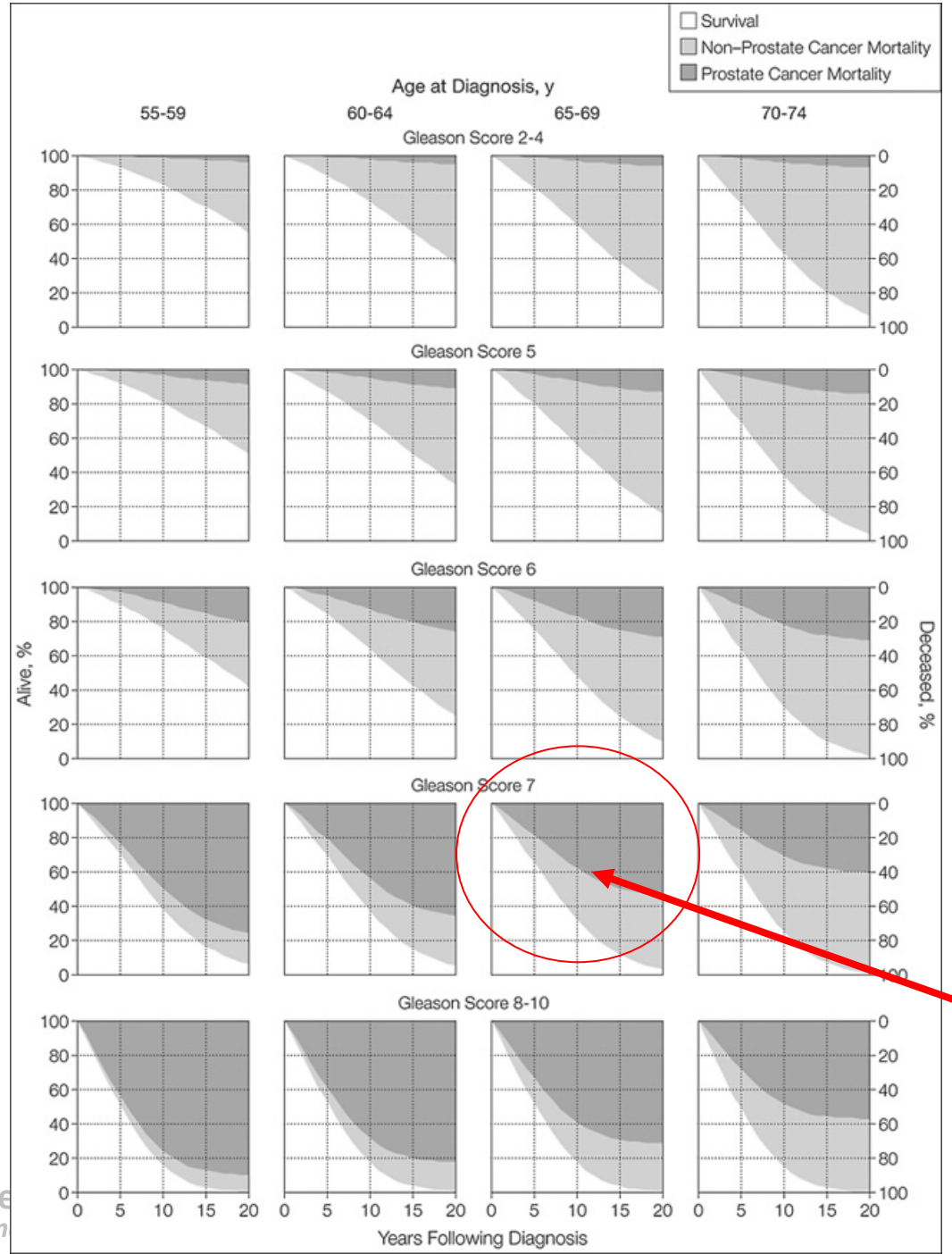
Offer a reclassification repeat prostate biopsy within 6–12 months of starting an active surveillance protocol.

Offer repeat biopsies every 2–3 years, or earlier as needed to investigate suspected disease progression: offer repeat biopsy and/or multiparametric MRI (in specialised centres) if PSA doubling time is less than 2–3 years or clinical progression is detected on digital rectal examination.

TO TREAT OR NOT TO TREAT

THAT IS THE QUESTION

- Patients need a good understanding of the the severity of their prostate cancer
- Many prostate cancers are harmless and many over-estimate the threat of their cancer to their life…
- Need to discuss active surveillance with many men



The Gleason Score remains our best guide…

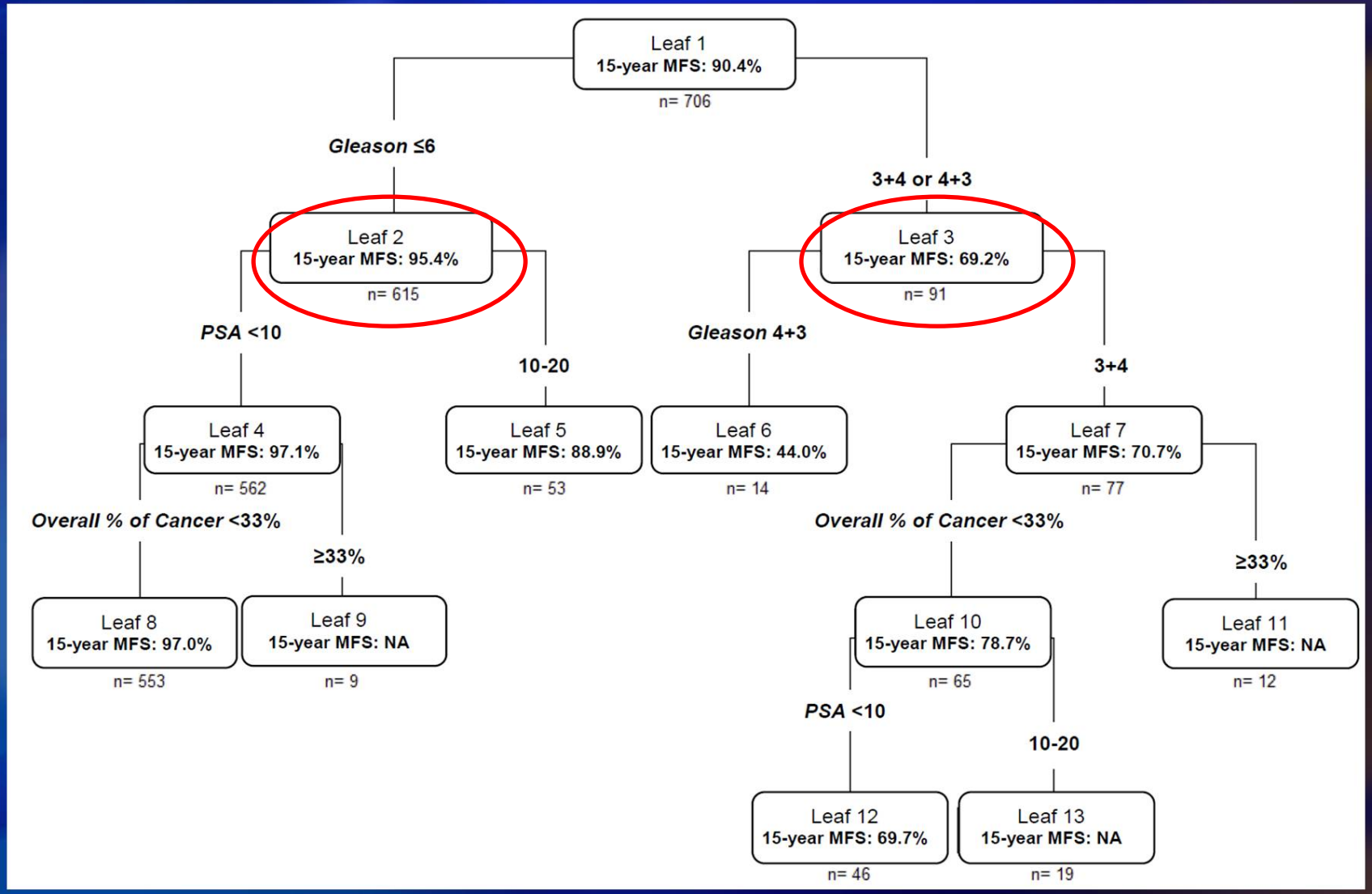
The Albertson graphs of "no treatment" were published in 2009 and are a useful guide but don't reflect current outcomes

A Gleason 7 cancer has a 40% chance of killing a 65-69 year old man at 10 years if initially observed

Toronto Surveillance Cohort

- 993 patients, median f/u of 8.9 years (0.5 – 19.8 years)
- Serial PSA, biopsy (no MRI until 2012)
  - 78% low risk
  - 22% patients intermediate risk (G7 or PSA > 10)
    - 38% of these < 70 years
- 30 patients have developed metastases
  - 15 died of prostate cancer
  - 4 died other causes, 11 alive with mets

Recursive partitioning analysis: Metastasis free survival by risk group



Presented By Laurence Klotz at 2017 Genitourinary Cancers Symposium

Early Stage Prostate Cancer

ORIGINAL ARTICLE

10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

Freddie C. Hamdy, F.R.C.S.(Urol.), F.Med.Sci., Jenny L. Donovan, Ph.D., F.Med.Sci., J. Athene Lane, Ph.D., Malcolm Mason, M.D., F.R.C.R., Chris Metcalfe, Ph.D., Peter Holding, R.G.N., M.Sc., Michael Davis, M.Sc., Tim J. Peters, Ph.D., F.Med.Sci., Emma L. Turner, Ph.D., Richard M. Martin, Ph.D., Jon Oxley, M.D., F.R.C.Path., Mary Robinson, M.B., B.S., F.R.C.Path., et al., for the ProtecT Study Group*

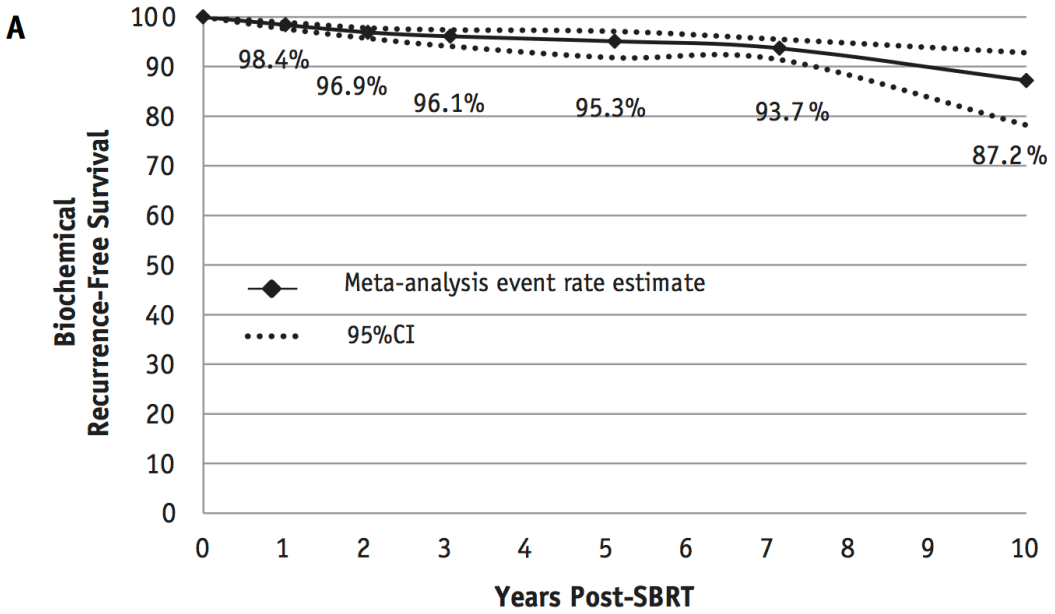
Published in NEJM October 2016, this randomised trial of 1643 patients was designed to give us the answer of whether surveillance, surgery or radiation was the best treatment for low and intermediate risk prostate cancer

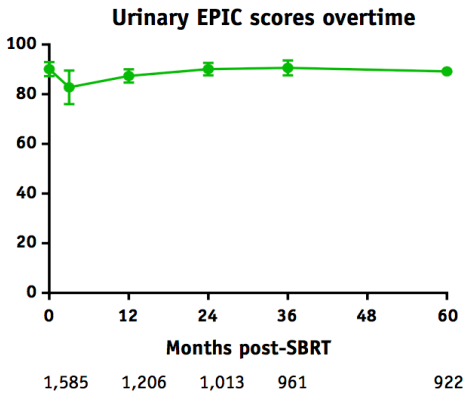
Interpretation

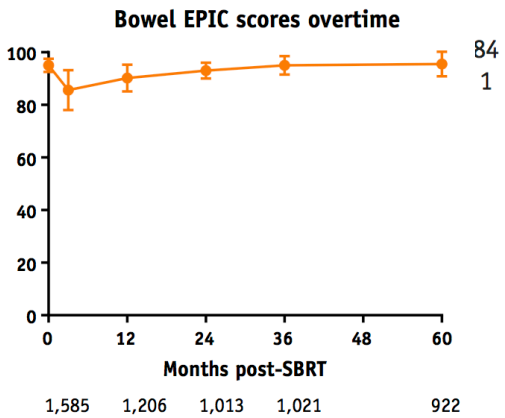
- Reassure men that survival and 10 years is excellent with low-intermediate risk prostate cancer
- Even though 77% in this study had “harmless” Gleason 6 disease, 20% had metastatic disease at 10 years on active surveillance despite half of this group having intervention. Most of these patients had Gleason 7 disease which suggests treating this subgroup beneficial if long life expectancy
- Surgery and Radiation had equivalent cancer control
- Although toxicity seemed less with RT, many surgeons argue better outcomes with good quality surgery.
- Not all questions answered!!

Clinical Investigation William Jackson et al. IJROBP. April 2019

Stereotactic Body Radiation Therapy for Localized Prostate Cancer: A Systematic Review and Meta-Analysis of Over 6,000 Patients Treated On Prospective Studies





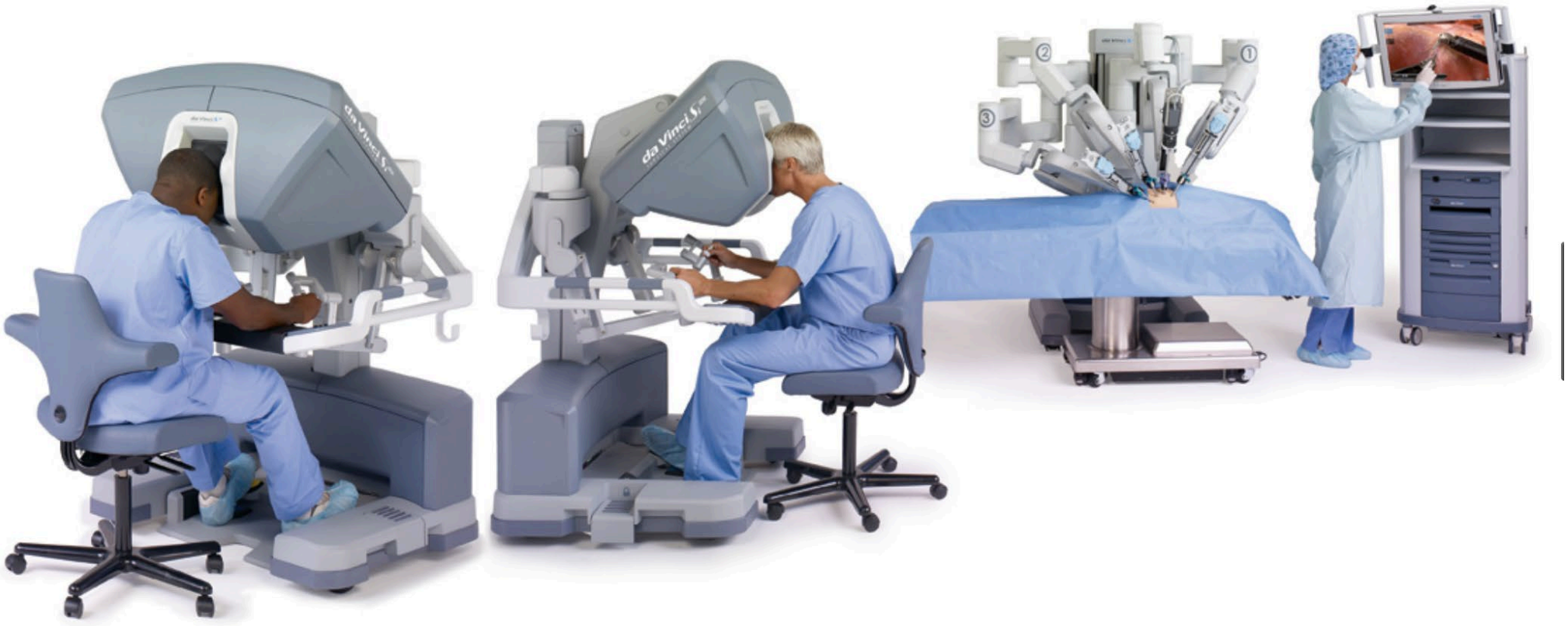


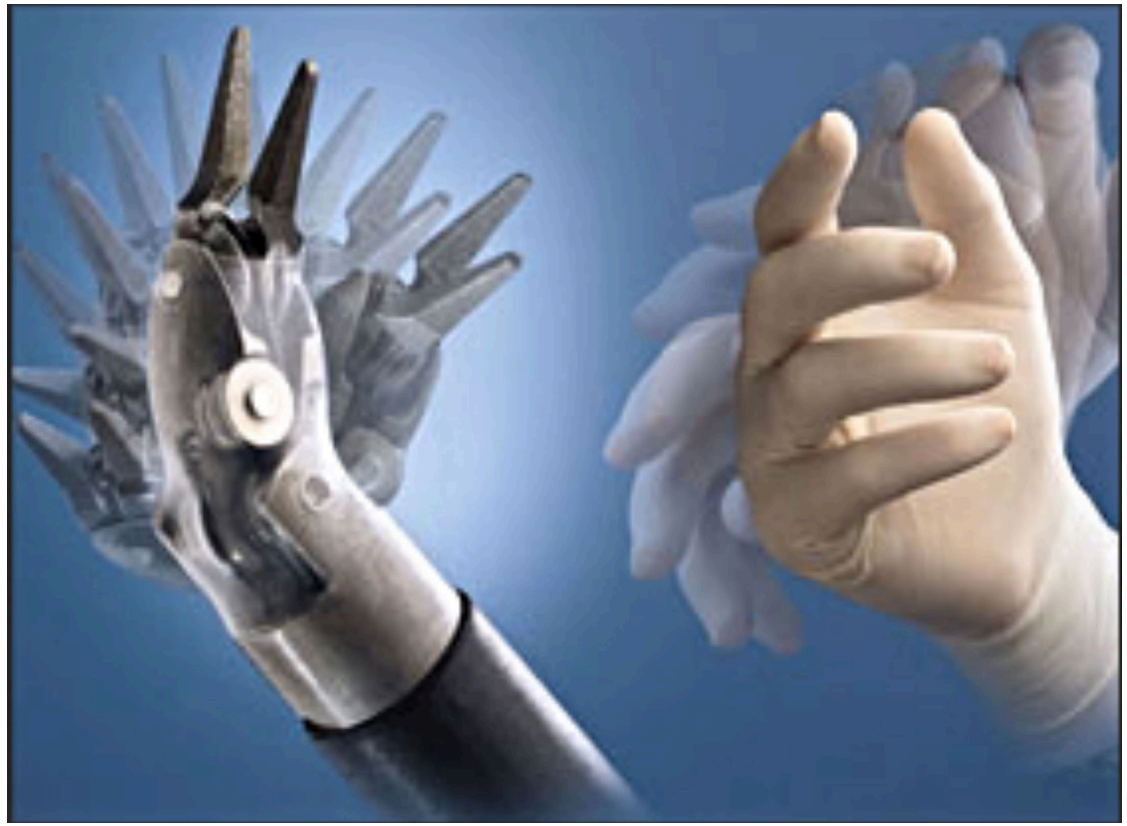
- All available data suggests that radiation and surgery offer very equivalent cure rates for localised prostate cancer
- All men should see a radiation oncologists to be informed of this option

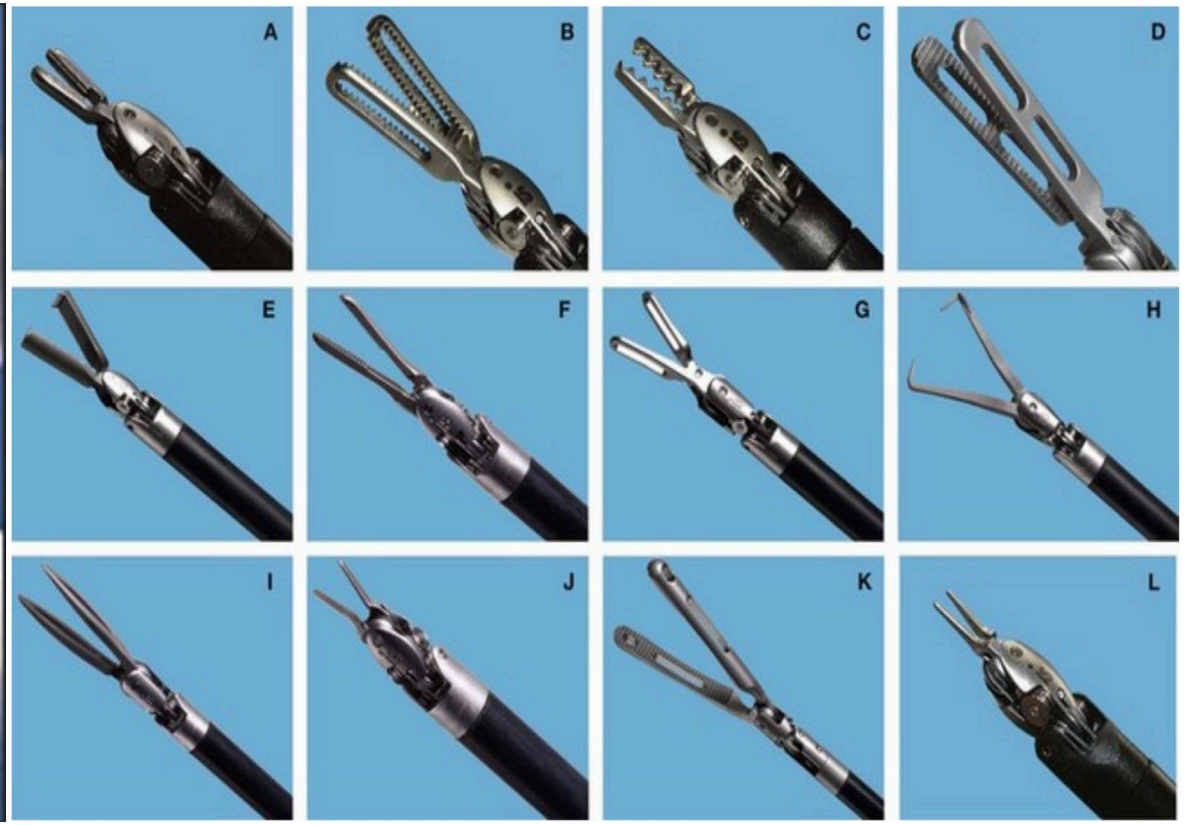
- Advantages:
  - Non invasive (apart from fiducial/hydrogel insertion)
  - Can now give in 5 treatments over 2 weeks (conventional standard is 20 treatments)
  - High rates of loco-regional control
  - Majority with good QOL in long term
  - Overall 25% of people having surgery will have their cancer return

- Disadvantages:
  - Doesn't improve urinary function
  - Don't have pathologic specimen
  - Side effects can manifest themselves many years after radiation and later pelvic surgery if required can be challenging

What is Robotic surgery



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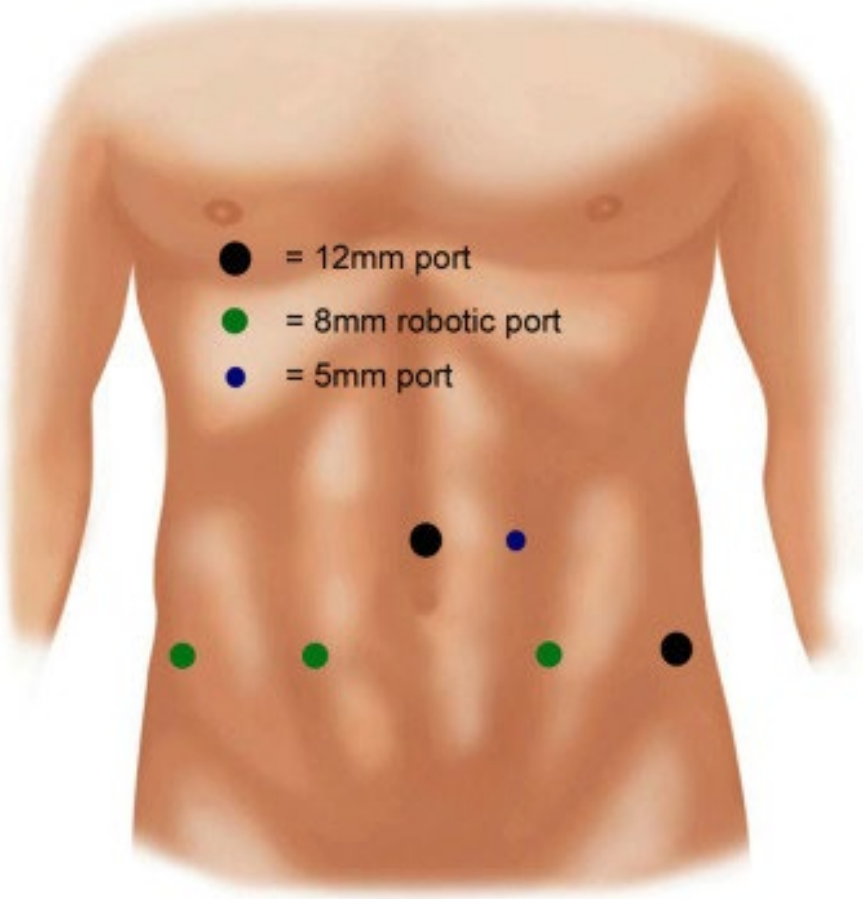
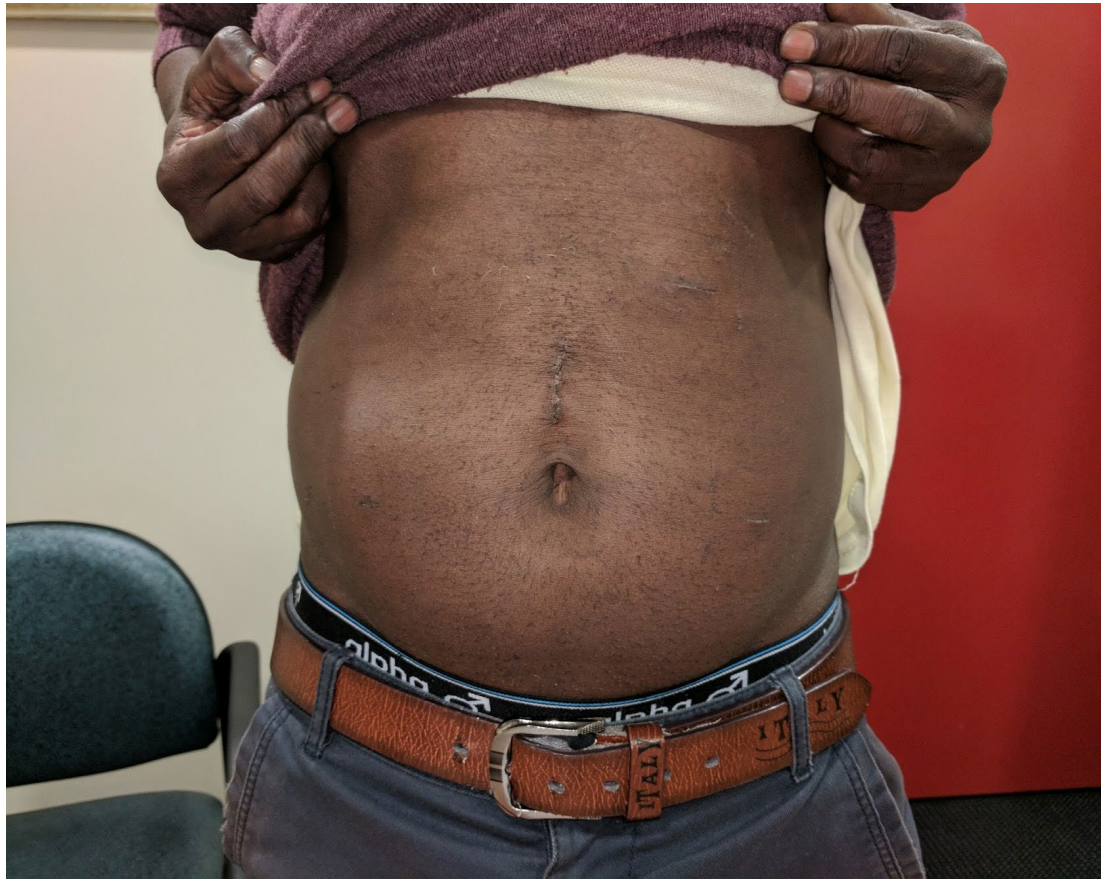
Advantages

- **Vision:**
  - 3D, High Definition, magnification
- **Dexterity and movement**
  - 6 degrees of movement, intuitive motion
  - Precision of movements
  - Motion scaling and Tremor reduction
- **Access and manoeuvrability in deep cavities and limited spaces**
- **Comfort of the surgeon**

Disadvantages

- **Cost**
  - Monopoly and lack of competition
- **Learning curve**
  - Lack of haptic feed back
  - Complications

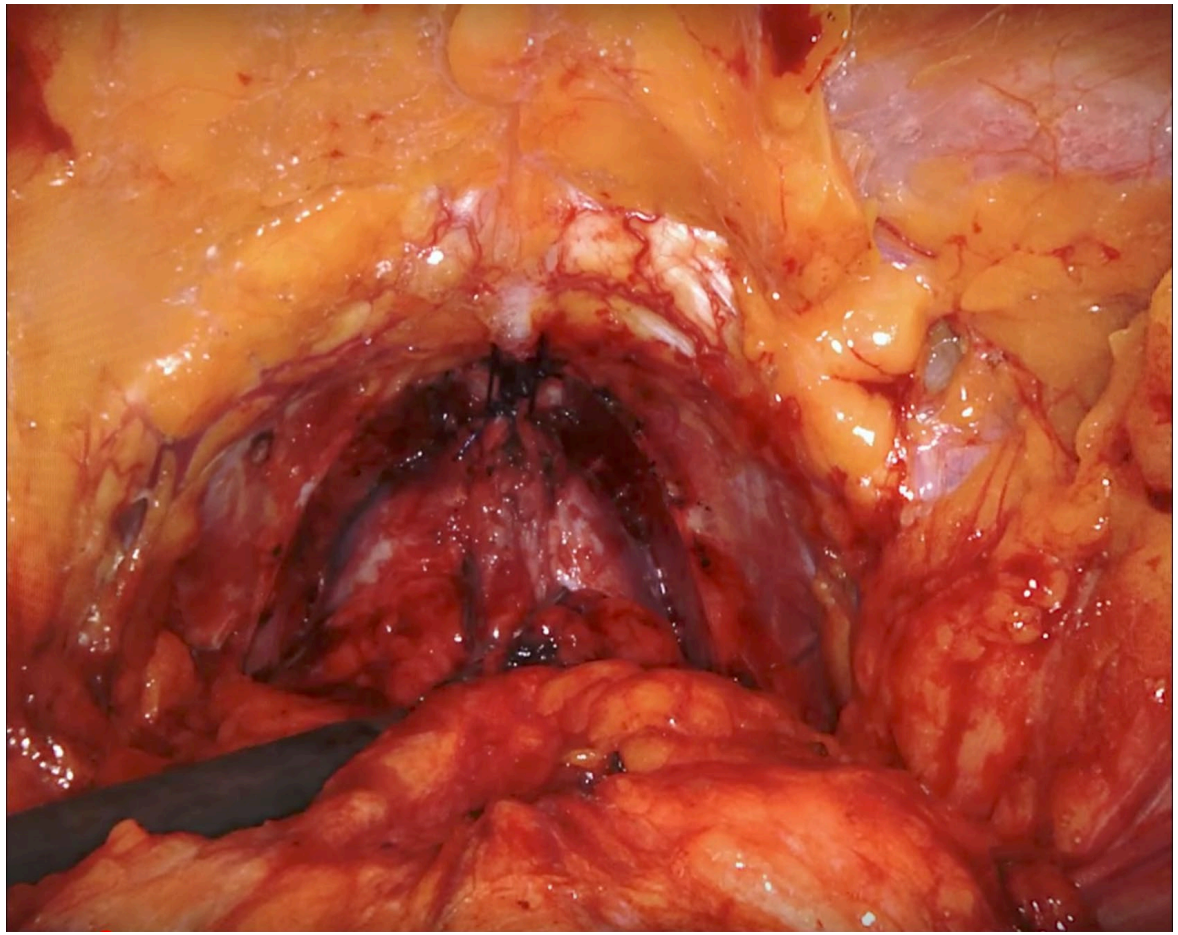

= 12mm port
= 8mm robotic port
= 5mm port

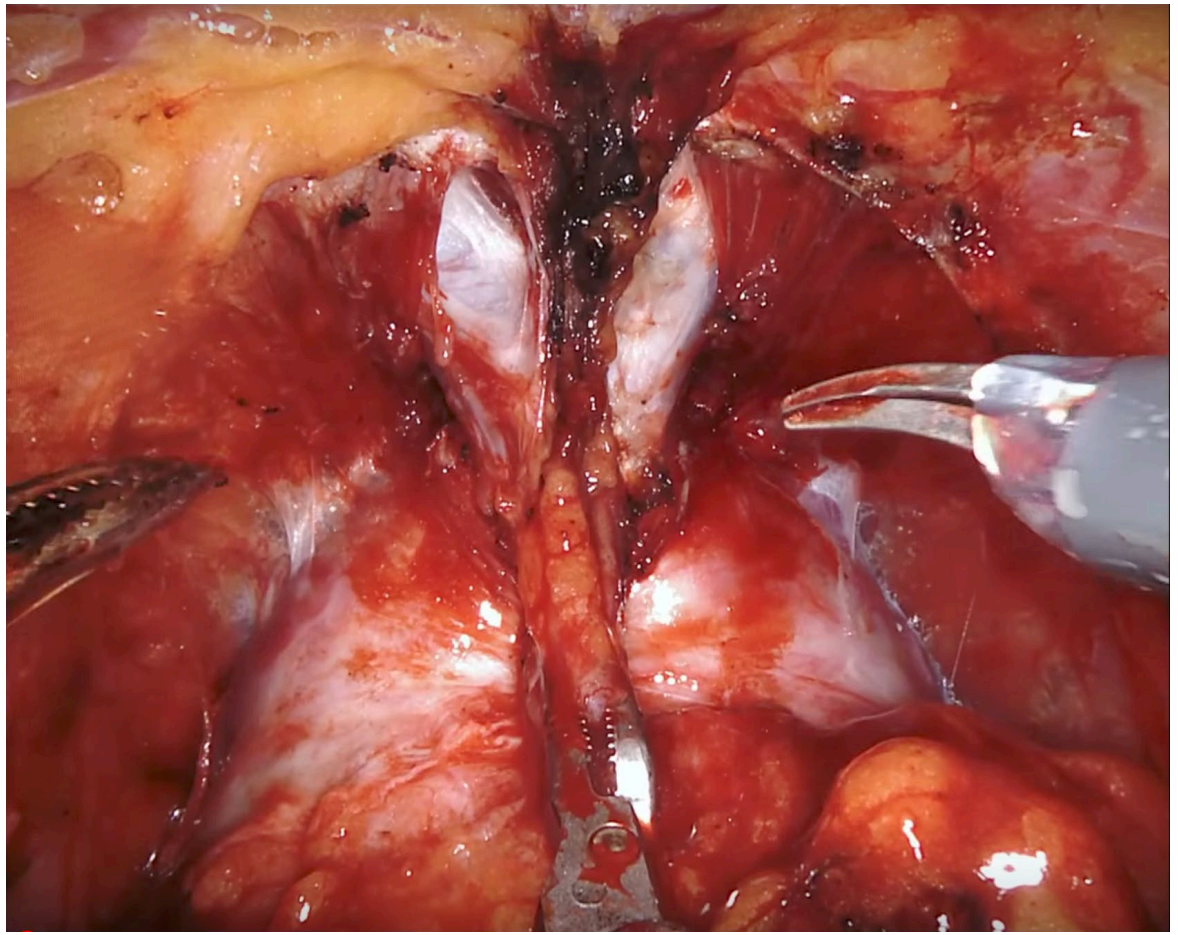

ITALY

Early return of continence

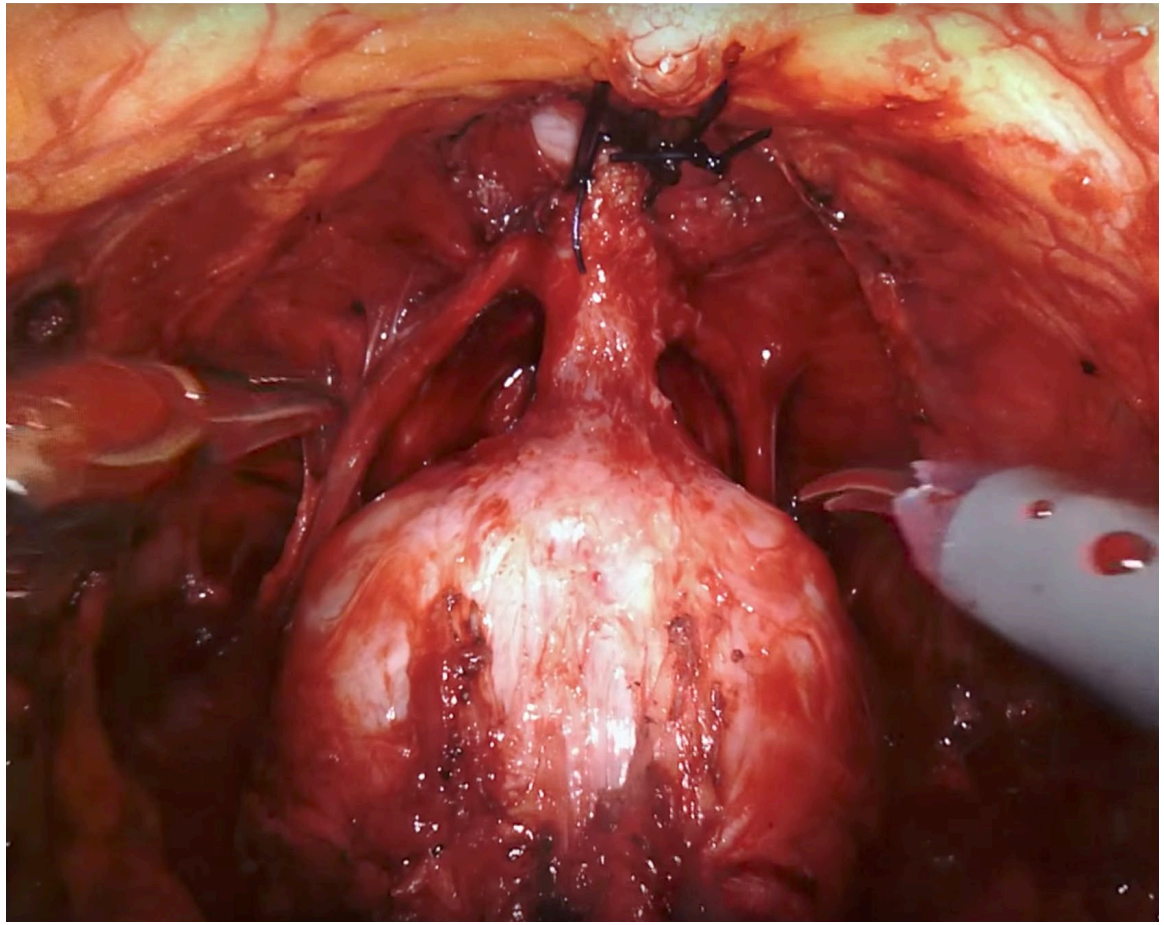
- Strategies:
  - Preservation of rhabdosphincter and pelvic floor
  - Posterior reconstruction (Rocco suture)
  - Plication and anterior reconstruction
  - Preservation of urethral length
  - Fascial sling techniques

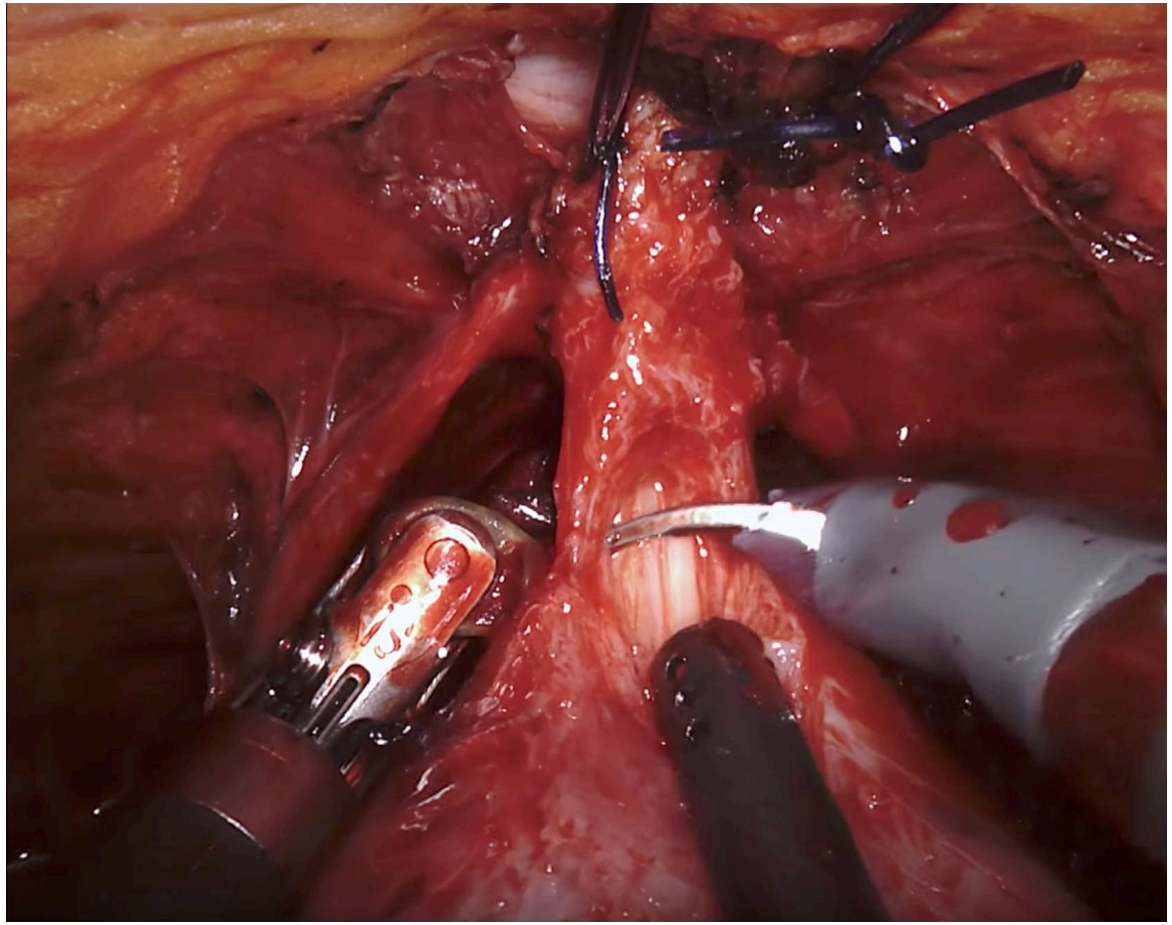
Preservation of rhabdosphincter





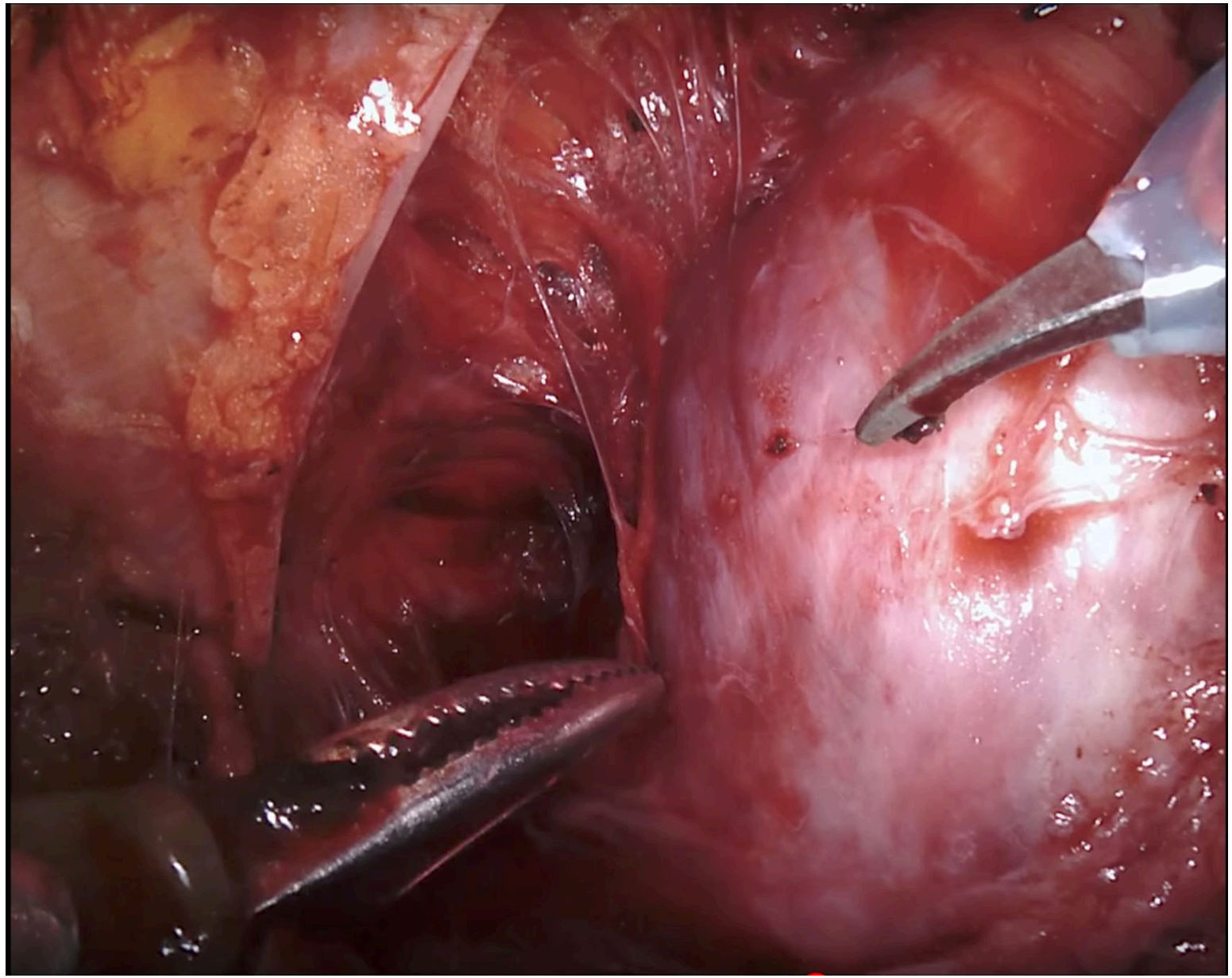
Preservation of urethra

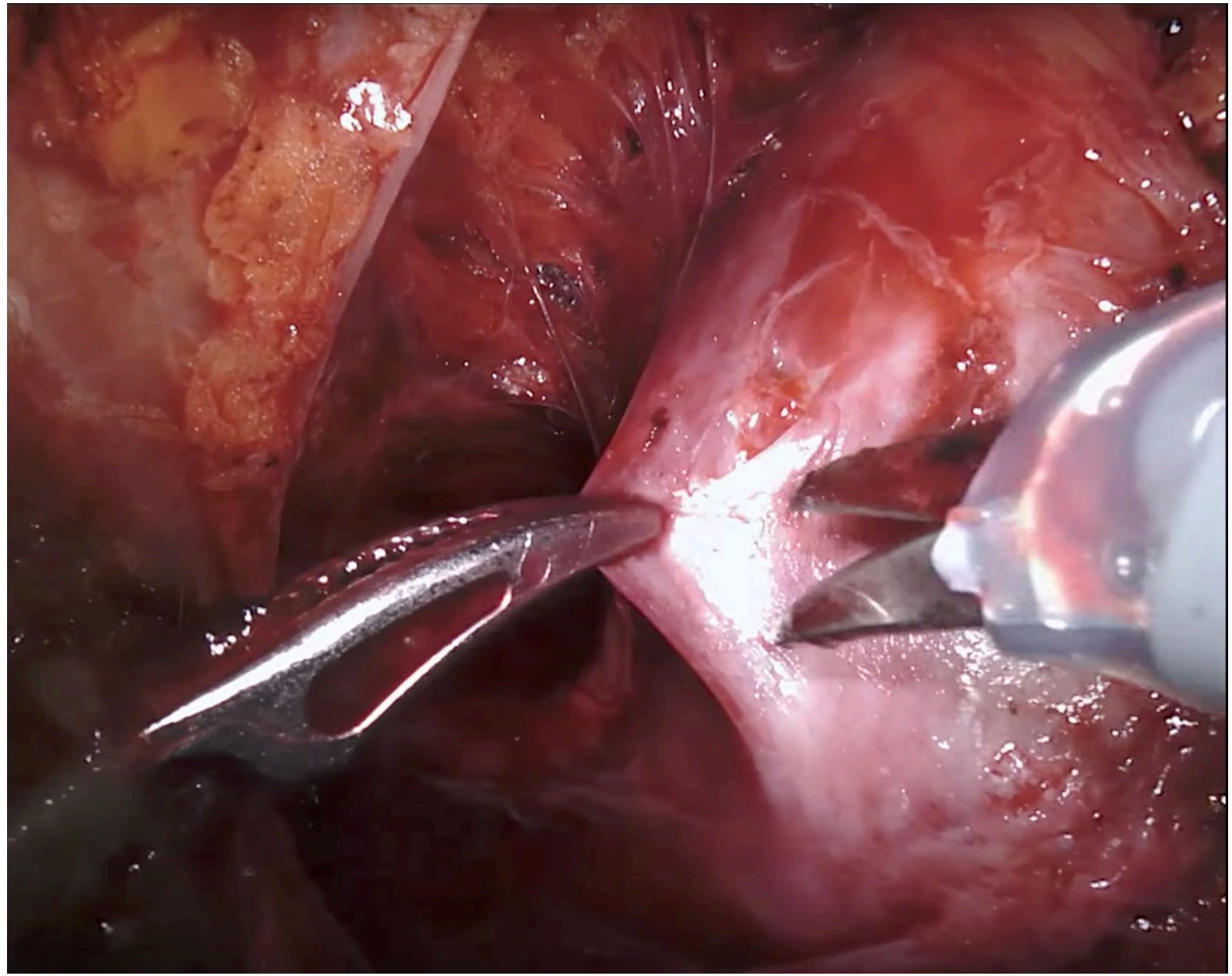


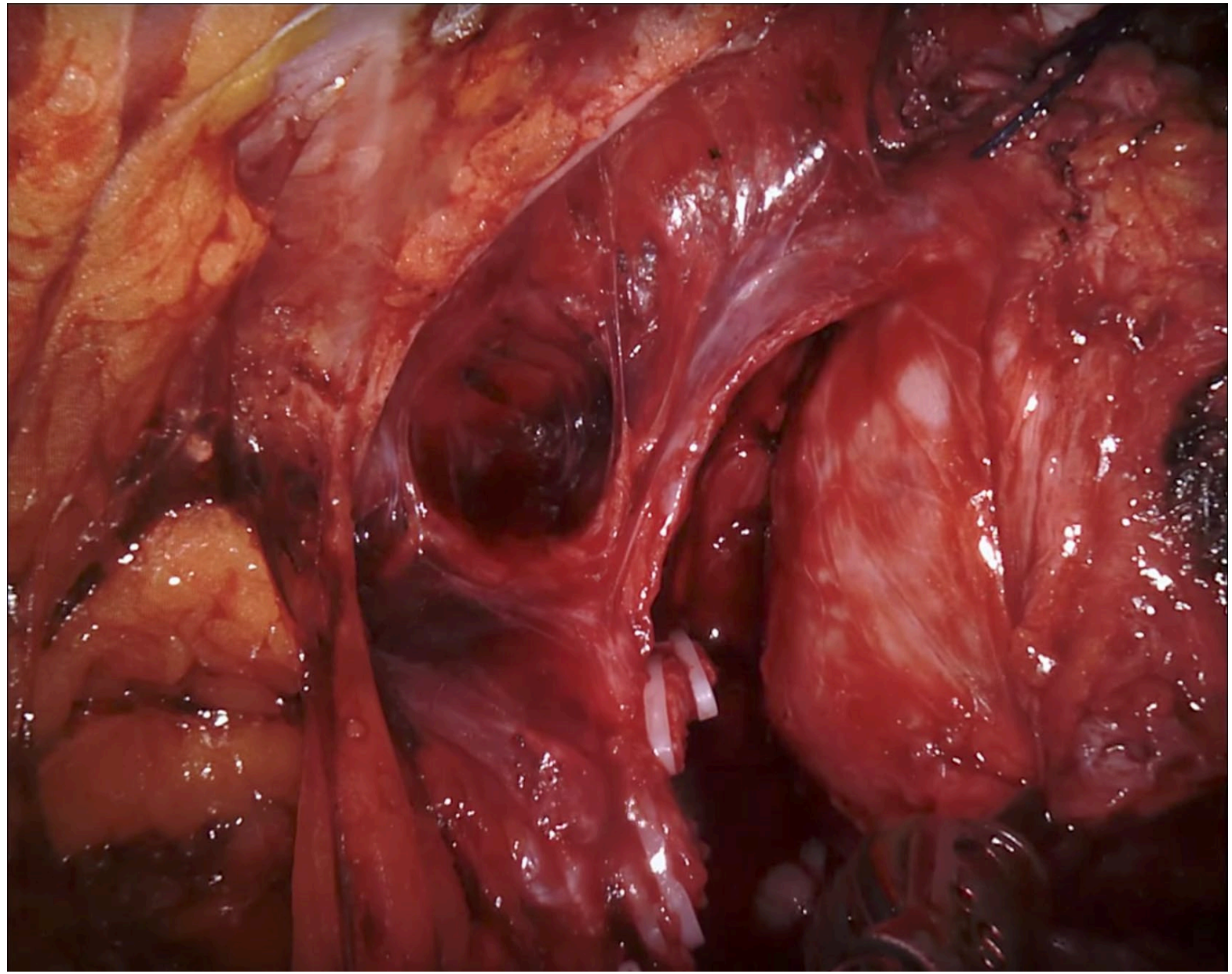


Nerve sparing robotic prostatectomy

- Degree of nerve-sparing (depending on the MRI and biopsy)
  - Inter-fascial
  - Intra-fascial
- Pre-operative and post-operative penile rehabilitation







Surgery vs radiation therapy

Radical prostatectomy

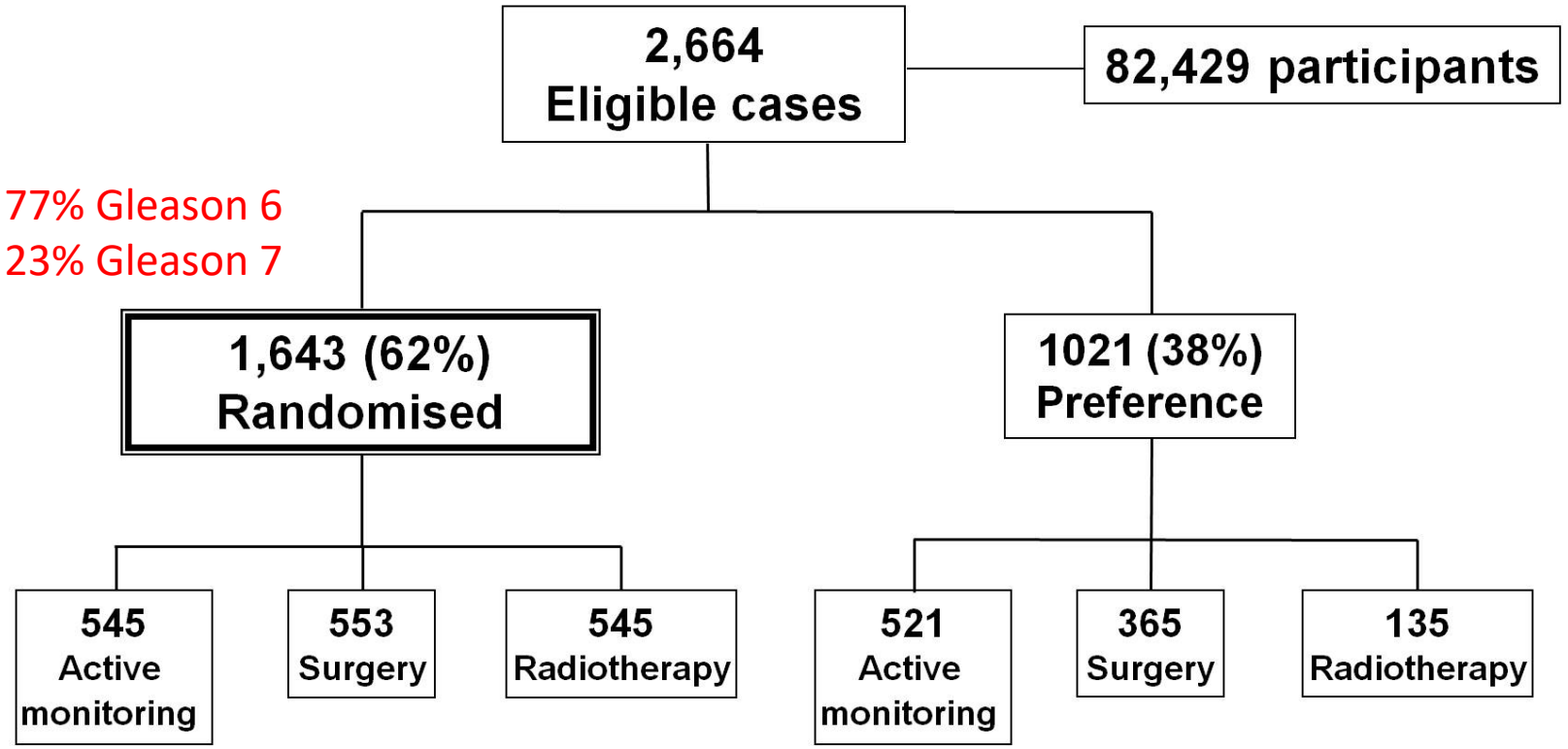
- Benefits:
  - PSA surveillance easier
  - Salvage options available
- Downside:
  - Hospitalisation 1-3 days
  - Catheter for 7-10 days
  - Stress urinary Incontinence
  - Erectile dysfunction
  - Penile shortening
  - Other surgery risks
    - Bleeding, infection, DVT, hernia etc

Radiation therapy

- Benefits:
  - Avoiding surgery and anaesthetics
- Downside:
  - 5-6 weeks duration, ~30 visits
  - Need for hormone therapy
  - Radiation cystitis and proctitis
  - Urethral or bladder neck stricture
  - Secondary malignancy
  - Failed therapy options are difficult – salvage surgery

ProtecT study flow chart

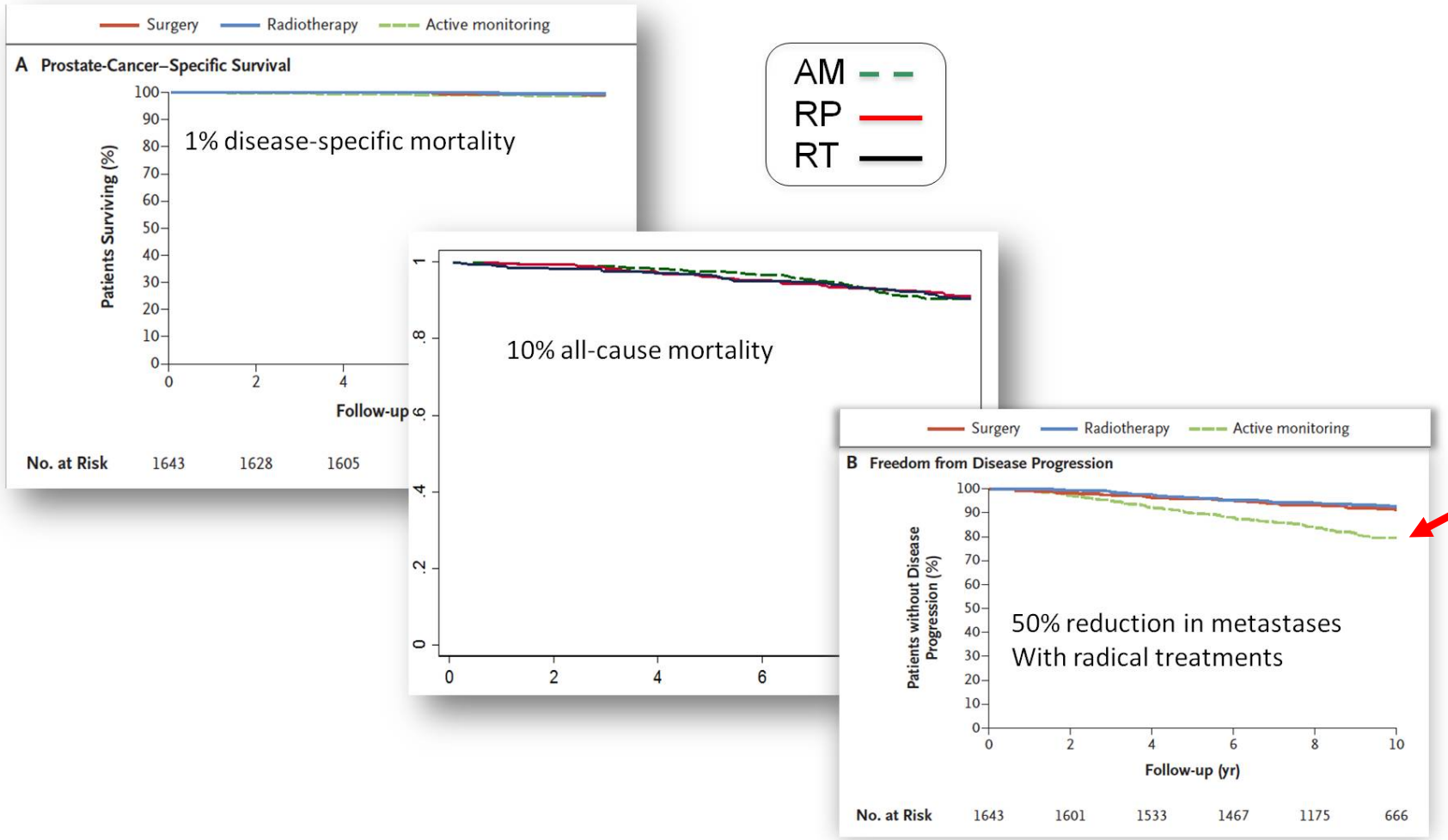
NHS
National Institute for Health Research



Lane et al, Lancet Oncol 2014

10-y median clinical outcomes

Hamdy et al, N Eng J Med 2016

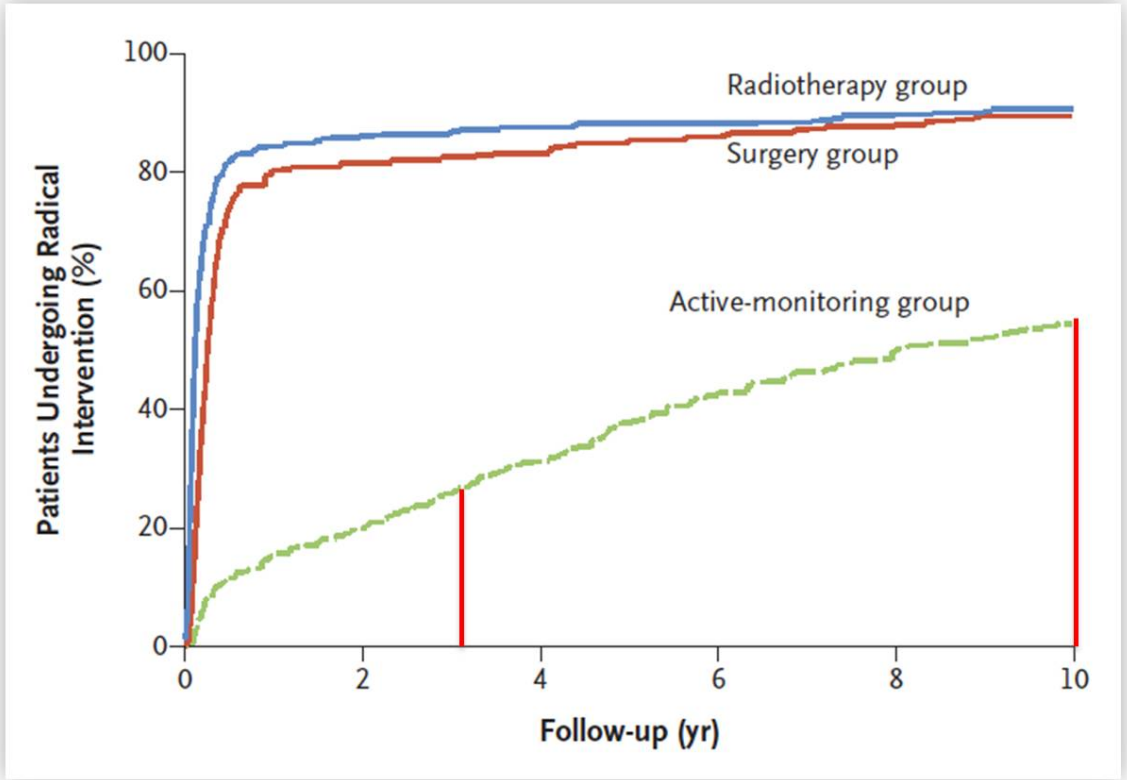


20% Metastases in AS arm

Presented By Freddie Hamdy at 2017 Genitourinary Cancers Symposium

Patients receiving treatments

Hamdy et al, N Eng J Med 2016



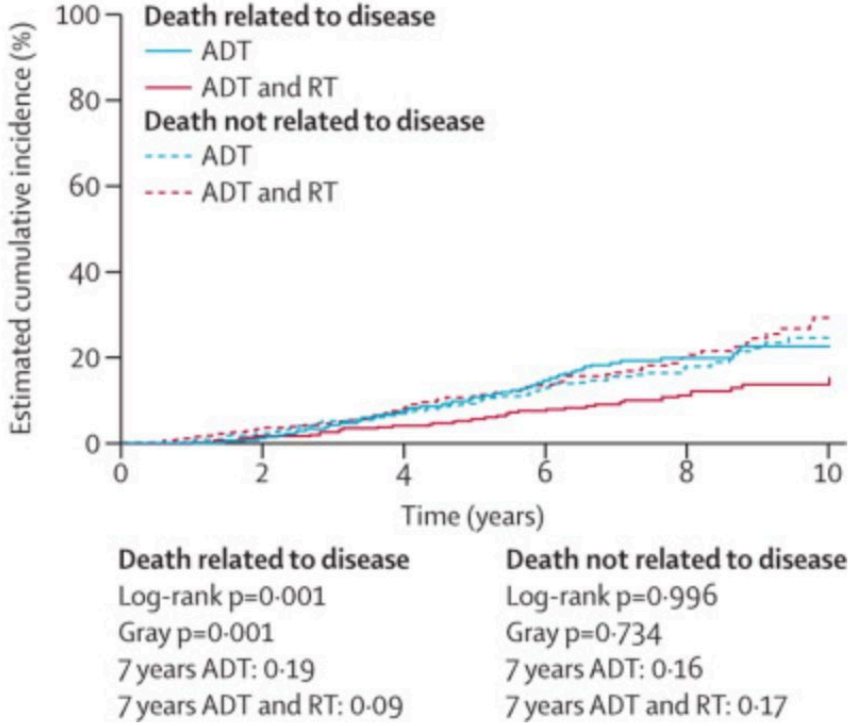
- Approximately 80% of men on active monitoring had no sign of progression
- More than half had received treatment by 10 years
- 44% of men on active monitoring avoided treatment

This is to be contrasted with high risk disease (T3/Gl8-10/PSA >20 /node +ve)

Combined androgen deprivation therapy and radiation therapy for locally advanced prostate cancer: a randomised, phase 3 trial

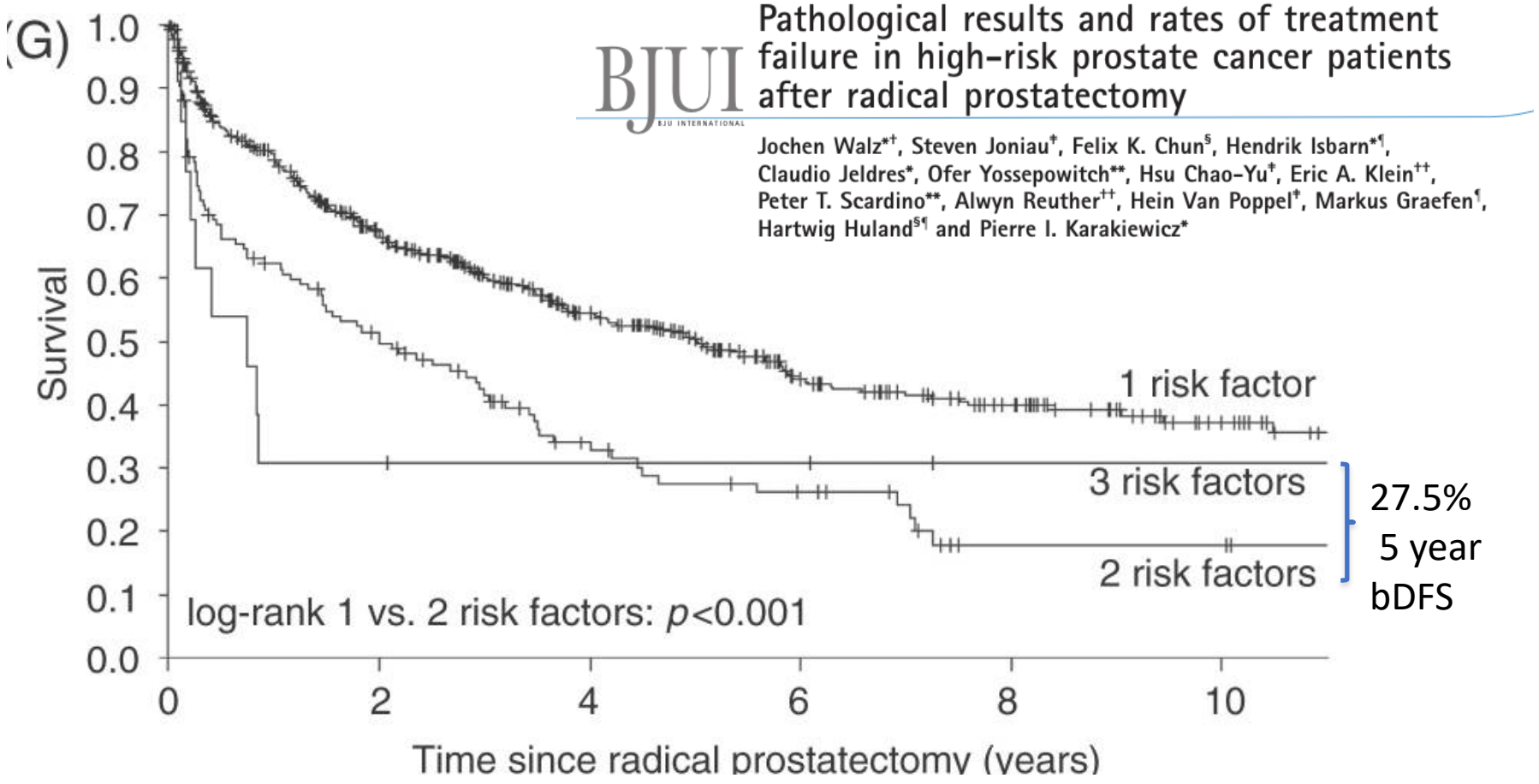
Padraig Warde*, Malcolm Mason*, Keyue Ding, Peter Kirkbride, Michael Brundage, Richard Cowan, Mary Gospoda

- 1205 patients with high risk prostate cancer were randomised to indefinite ADT vs ADT + RT



- **95 patients in ADT+RT group had progressive disease vs 251 with ADT alone**
- **Radiation halved the death rate from cancer at 7 years (9 vs 19%)**

Surgery can be an option for selected high risk prostate cancer but patients need to be aware that relapse rates can be high…



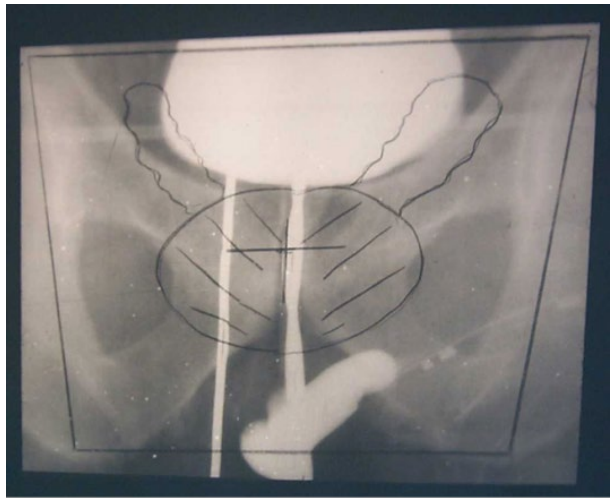
BJUI

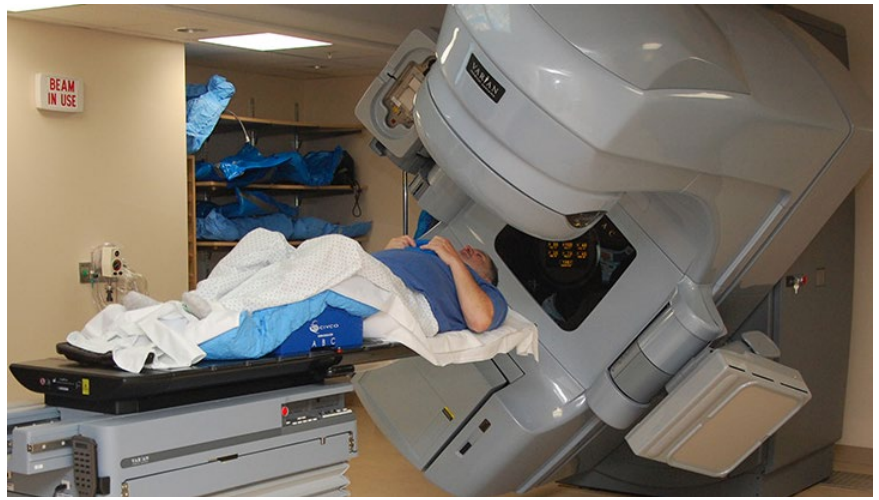
Pathological results and rates of treatment failure in high-risk prostate cancer patients after radical prostatectomy

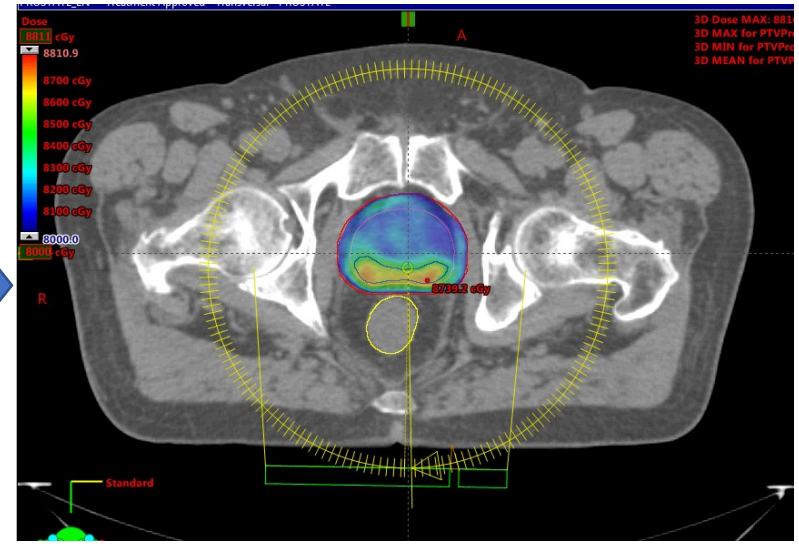
Jochen Walz*†, Steven Joniau‡, Felix K. Chun§, Hendrik Isbarn*¶, Claudio Jeldres*, Ofer Yossepowitch**, Hsu Chao-Yu‡, Eric A. Klein††, Peter T. Scardino**, Alwyn Reuther††, Hein Van Poppel‡, Markus Graefen¶, Hartwig Huland§¶ and Pierre I. Karakiewicz*

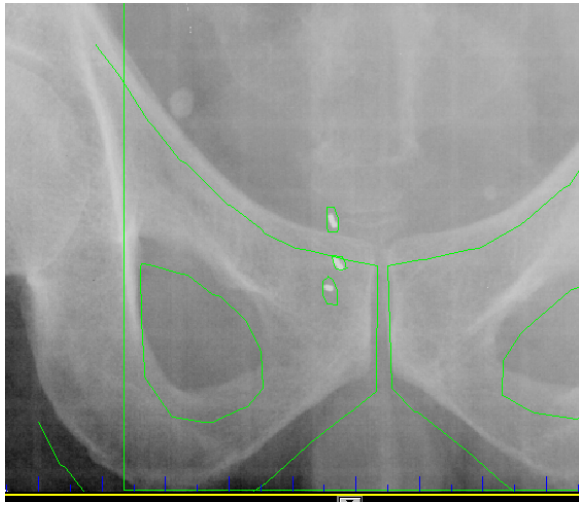
Overall, nearly a quarter of patients having a radical prostatectomy will have a rising PSA, meaning they are not cured with surgery. <half of high risk patients are cured.

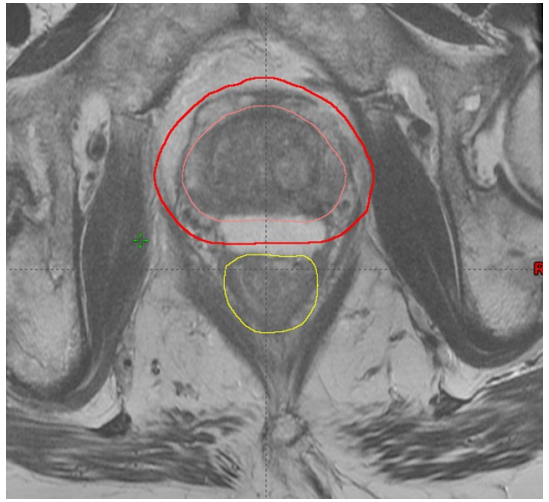
Radiation Treatment has improved dramatically over the last 2 decades

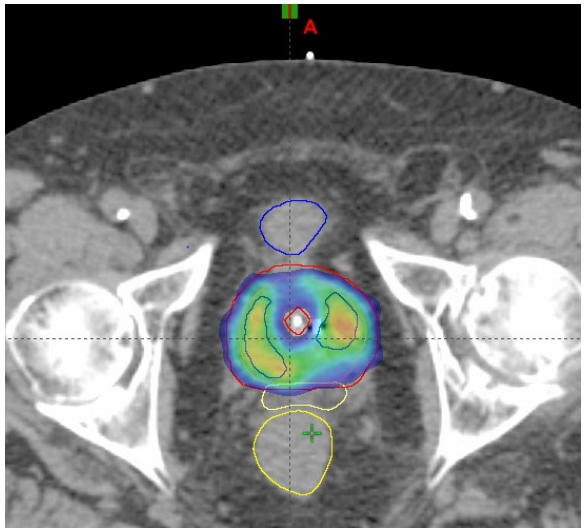












Rising PSA post prostatectomy

EUF-754; No. of Pages 4
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EUROPEAN UROLOGY FOCUS XXX (2019) XXX–XXX
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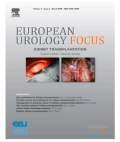
journal homepage: www.europeanurology.com/eufocus



Guidelines – Prostate Cancer

Biochemical Recurrence in Prostate Cancer: The European Association of Urology Prostate Cancer Guidelines Panel Recommendations

Thomas Van den Broeck [a,], Roderick C.N. van den Bergh [b], Erik Briers [c], Philip Cornford [d], Marcus Cumberbatch [e], Derya Tilki [f,g], Maria De Santis [h,i], Stefano Fanti [j], Nicola Fossati [k,l], Silke Gillessen [m,n,o], Jeremy P. Grummet [p], Ann M. Henry [q], Michael Lardas [r], Matthew Liew [s], Malcolm Mason [t], Lisa Moris [a,u], Ivo G. Schoots [v], Theodorus van der Kwast [w], Henk van der Poel [x], Thomas Wiegel [y], Peter-Paul M. Willemse [z], Olivier Rouvière [A], Thomas B. Lam [B,C], Nicolas Mottet [D]*

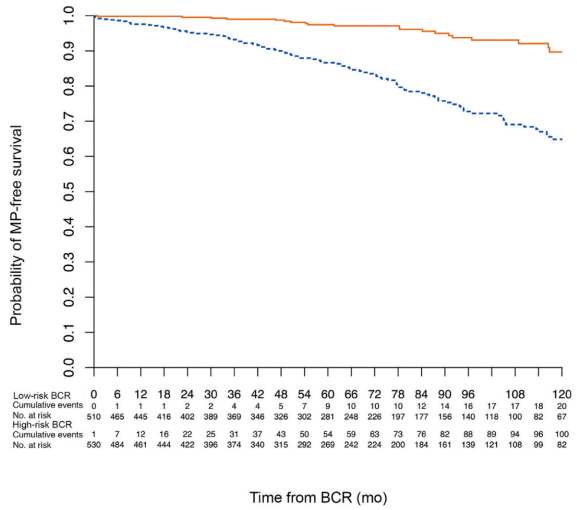


Fig. 1 – Kaplan-Meier plot of metastatic progression (MP)-free survival stratified according to the European Association of Urology biochemical recurrence (BCR) risk groups. The red line denotes low-risk and the blue line high-risk patients.

- A PSA rising to 0.2 is diagnostic of a “biochemical failure”
- European guidelines state that having Gleason 8-10 disease or a doubling time of PSA <12 months indicates high risk disease.
- These patients have >30% risk of metastases at 10 years
- This man needs treatment!

Short Term Androgen Deprivation Therapy Without or With Pelvic Lymph Node Treatment Added to Prostate Bed Only Salvage Radiotherapy: The NRG Oncology/RTOG 0534 SPPORT Trial

A. Pollack[1], T.G. Karrison[2], A.G. Balogh Jr.[3], D. Low[4], D.W. Bruner[5], J.S. Wefel[6], L.G. Gomella[7], E. Vigneault[8], J.M. Michalski[9], S. Angyalfi[10], H. Lukka[11], S.L. Faria[12], G. Rodrigues[13], M.C. Beauchemin[14], S.A. Seaward[15], A.M. Allen[16], D.C. Monitto[17], W. Seiferheld[2], H.M. Sandler[18]

1792 patients
Biochemical relapse post RP. PSA 0.1-2.0

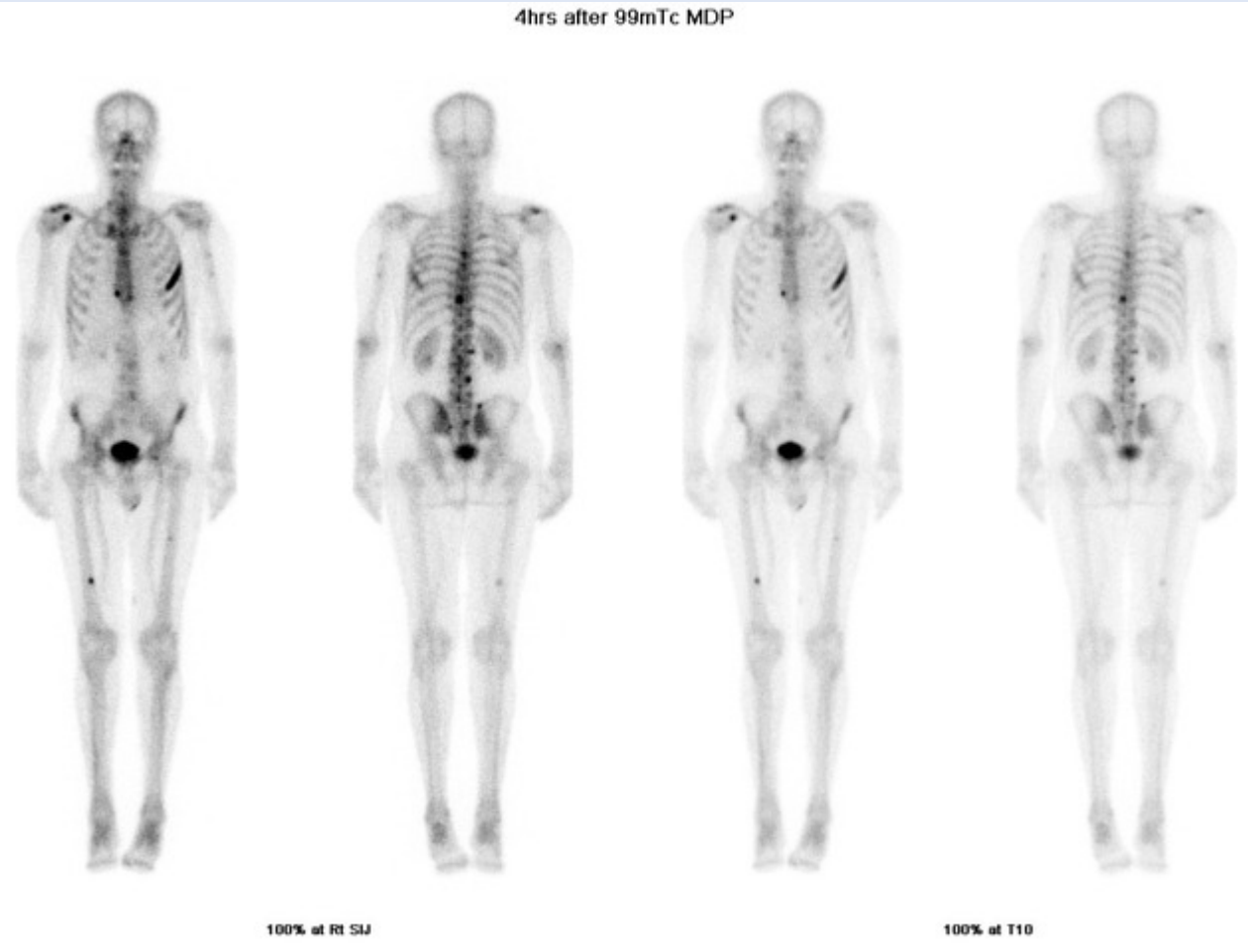
- Prostate Bed RT alone
- Prostate Bed RT + 4-6 months of ADT
- Prostate Bed + Nodal RT + 4-6months ADT

5 year FFP	Grade 3 GU tox	Grade 3 GI tox
71.1%	4.3%	0.7%
82.7%	4.9%	0.4%
89.1%	6.0%	1.1%

Freedom from Failure = PSA Nadir +2 or clinical failure

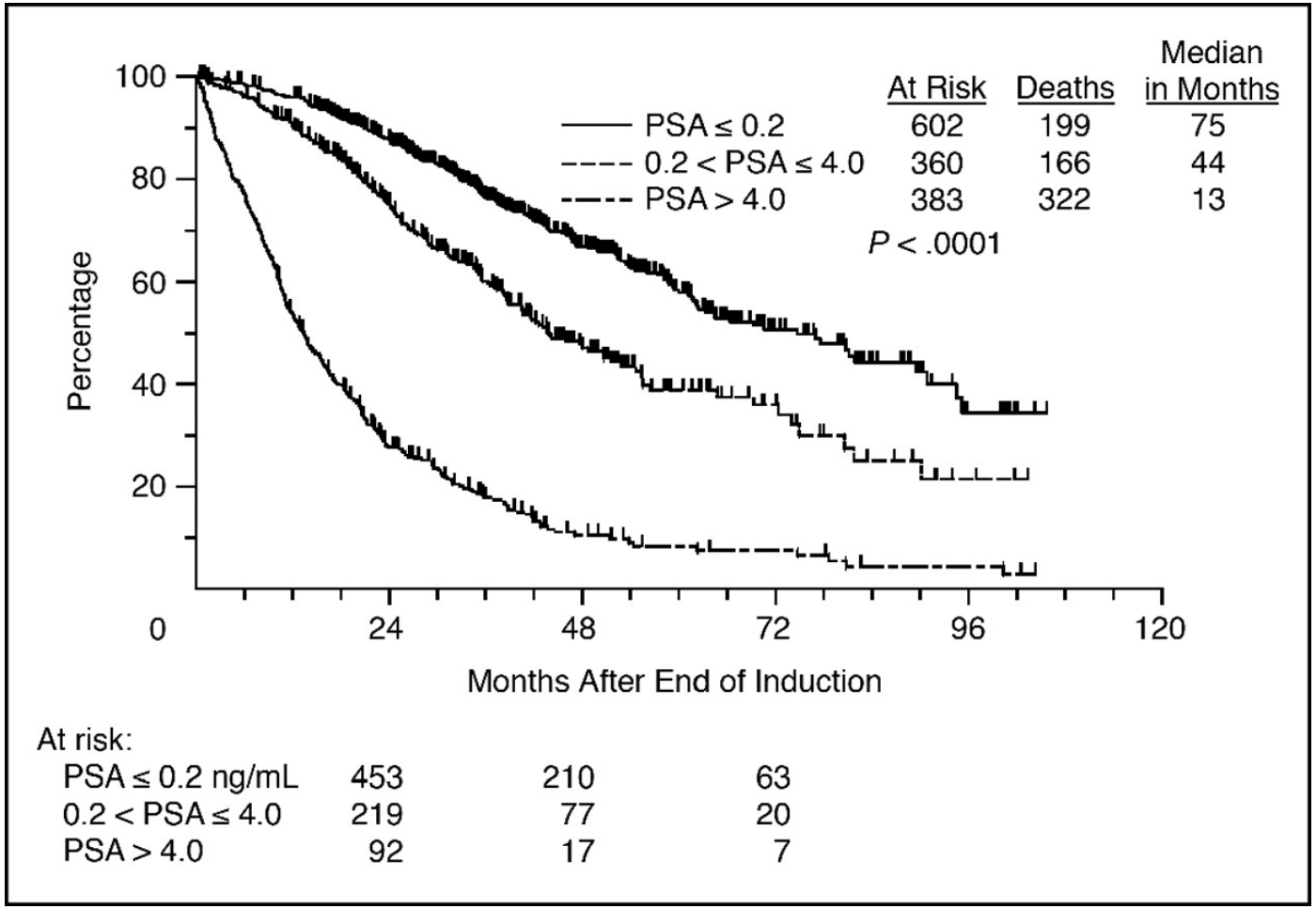
Case 6

- Bill is lost to follow up after getting fed up of seeing “too many specialists…they told me I was cured anyway”
- He complains of generalised aches and pains, particularly in his left chest.
- You organise a whole body bone scan to further investigate this



Source: Radiopaedia

Androgen Deprivation (ADT) is the cornerstone of managing advanced disease Response and survival varies but fall in PSA after 6 months very prognostic



Hussain, M. et al. J Clin Oncol; 24:3984-3990 2006

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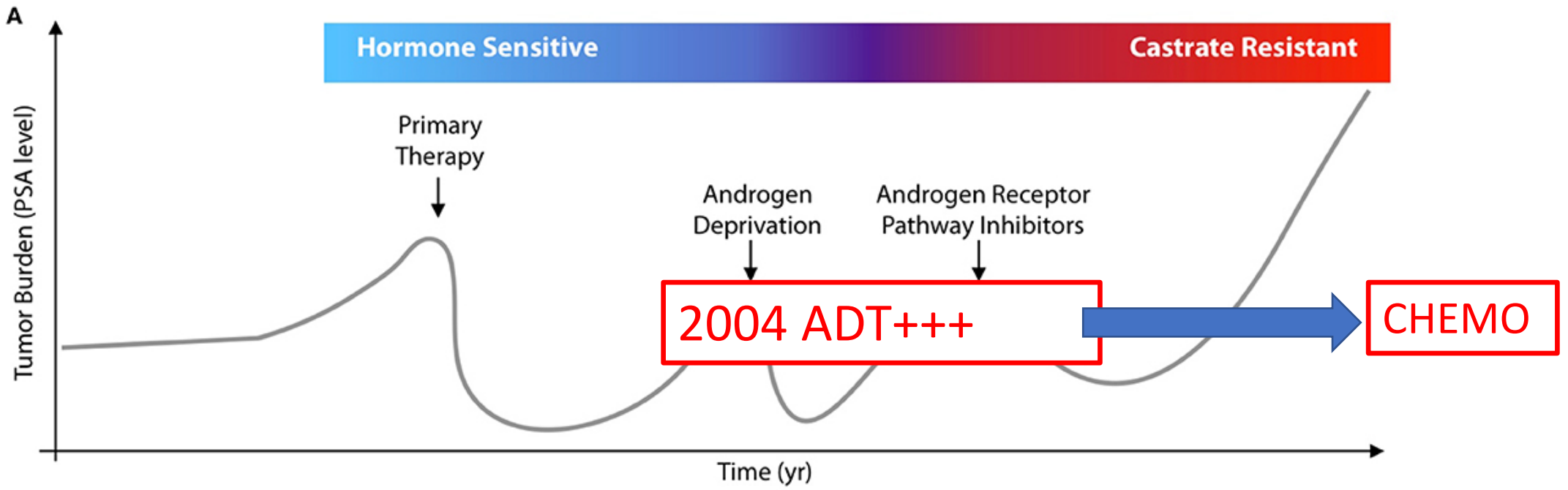
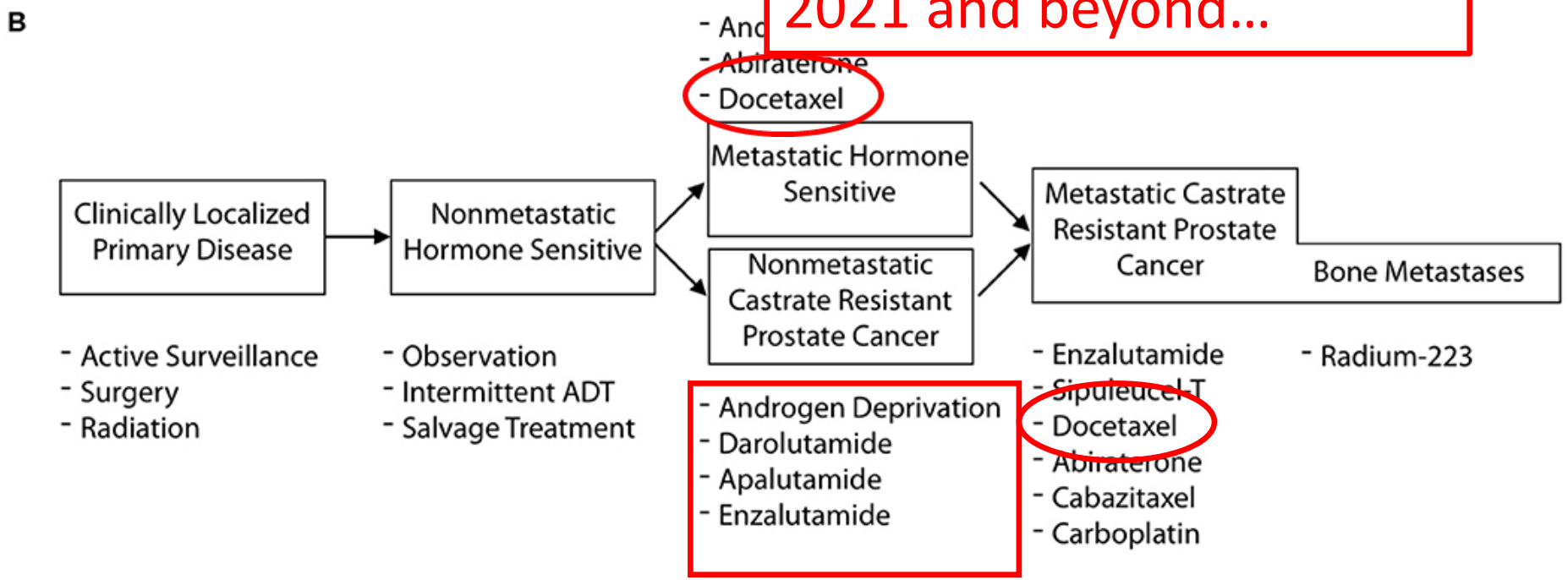


2021 and beyond…

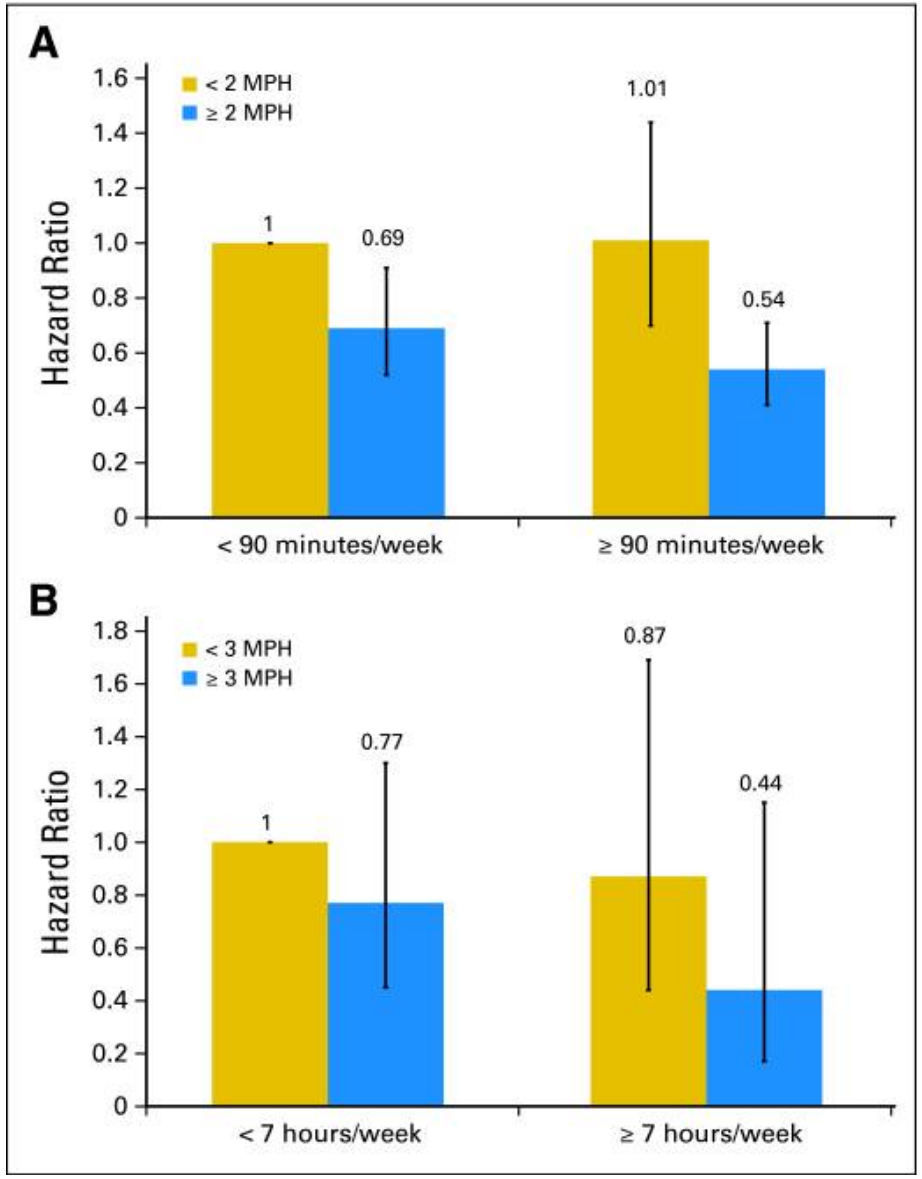


Side effects of drugs used in advanced disease

Side effect	Management
ADT	
GnRH agonists: Zoladex, Eligard, Lucrin, Dipherelin, Firmagon	
Anti-androgens: Cosudex, Androcur, Flutamin, Anandron,	
Hot flushes	SSRI, SNRI, megestrol acetate
Metabolic - loss of muscle mass, weight gain	Exercise
Reduced bone density	Lifetsyle (smoking), Vitamin D supplement, Bisphosphonates
Mood swings	CBT, Pharmacological
Gynaecomastia	Surgical
Reduced libido	
Androgen receptor inhibitors: Zytiga, Xtandi	
Hypertension	Antihypertensives, Dose interruption
Fluid retention	Dose interruption
Hypokalaemia	Dose interruption
LFT derangement	Dose interruption
Corticosteroid side effects	
Chemotherapy (Docetaxel)	
Myelosuppression, febrile neutropaenia	

Managing the whole patient

- Metabolic syndrome
- Cardiovascular risk factors
- Bone health
- Psycho-social (depression, erectile dysfunction)
- >3h/week vigorous exercise 49% lower all-cause mortality, 61% prostate ca mortality



Summary

- PSA testing a mainstay of screening asymptomatic men
- Gleason scores define risk, increasing role for multidisciplinary management using advanced imaging (MRI,PSMA-PET) in tertiary centres
- Managing long-term effects of ADT – exercise improves mortality!
- Systemic treatment is changing rapidly – be alert to side effects
- If in doubt…

Questions?