21ST ANNUAL

PACIFIC NORTHWEST PROSTATE CANCER CONFERENCE

SATURDAY, OCTOBER 2ND 2021

Department of UROLOGIC SCIENCES UBC

UNIVERSITY OF WASHINGTON

OHSU KNIGHT CANCER Institute

21st Annual Pacific Northwest Prostate Cancer Conference

Saturday, October 2nd 2021

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Silver Sponsorship

21st Annual Pacific Northwest Prostate Cancer Conference

Saturday, October 2nd 2021

Conference Chairs

Larry Goldenberg, MD
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Celestia S. Higano, MD
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Tomasz M. Beer, MD
Division of Hematology & Medical Oncology
OHSU Knight Cancer Institute
Portland, OR, USA

Guest Faculty & Speakers

Alan So, MD
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Robert Meier, MD
Radiation Oncology
Swedish Radiosurgery Center
Seattle, WA, USA

Julie N. Graff, MD
VA Portland Health Care System, Hem/Onc
OHSU Knight Cancer Institute
Portland, OR, USA

Dan Lin, MD
Department of Urology
University of Washington
Seattle, WA, USA

Alex Wyatt, DPhil
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Michael Schweizer, MD
Fred Hutchinson Cancer Research Center
University of Washington
Seattle, WA, USA

Alexandra Sokolova, MD
Hematology & Medical Oncology
OHSU Knight Cancer Institute
Portland, OR, USA

Ryan Flannigan, MD
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Nicholas Pratap, CEP
Prostate Cancer Supportive Care Program
Vancouver, BC, Canada

Monica Hu, RCC
Prostate Cancer Supportive Care Program
Vancouver, BC, Canada

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21st Annual Pacific NW Prostate Cancer Conference

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AGENDA

8:35 - 8:40	a.m.	Program Introduction by Dr. Larry Goldenberg
8:40 - 9:04	a.m.	Introduction to Radical Prostatectomy: Surgical Treatments for Prostate Cancer Alan So, M.D.
9:04 - 9:23	a.m.	Advances in Radiation Therapy for Prostate Cancer Robert Meier, M.D.
9:23 - 9:44	a.m.	How to Manage PSA Recurrence and Active Surveillance Julie N. Graff, M.D.
9:44 - 10:03	a.m.	Contemporary Treatment for High Risk Localized Prostate Cancer Dan Lin, M.D.
10:03 - 10:13	**a.m.**	**MORNING BREAK**
10:13 - 10:33	a.m.	*Open panel - Speakers Q & A*
10:33 - 10:56	a.m.	What Blood Tests Can Tell Us About Metastatic Prostate Cancer Alex Wyatt, PhD
10:56 - 11:20	a.m.	Changing Landscape of Metastatic Prostate Cancer Michael Schweizer, M.D.
11:20 - 11:39	a.m.	Prostate Cancer: Breaking News 2021 Alexandra Sokolova, M.D.
11:39 - 12:05	p.m.	Challenges to Sexual Health Ryan Flannigan, M.D.
12:05 - 12:25	**p.m.**	**LUNCH BREAK**
12:25 - 12:45	p.m.	*Open panel - Speakers Q & A*
12:45 - 1:14	p.m.	Benefits of Exercise for Prostate Cancer Patients Nicholas Pratap, CEP
1:14 - 1:44	p.m.	Integrated Self-Care: Some Keys to Optimizing Our Well-Being Monica Hu, MA, RCC
1:44 – 2:04	p.m.	*Open panel - Speakers Q & A*
2:04 - 2:09	p.m.	Closing Remarks by Dr. Celestia Higano

*Agenda subject to change

8:40am – 9:04am

Introduction to Radical Prostatectomy:

Surgical Treatments for Prostate Cancer

Alan So, MD

INTRODUCTION TO RADICAL PROSTATECTOMY: Surgical Treatment for Prostate Cancer

Dr. Alan So
Associate Professor
Dept of Urologic Science
Vancouver Prostate Centre
University of British Columbia
Chair, GU Tumour Group at BC Cancer

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OVERVIEW

This presentation will cover the following:

- Anatomy of the prostate
- Description of Radical Prostatectomy
  - Open Radical Prostatectomy
  - Laparoscopic Robotic Assisted Radical Prostatectomy
- Discussion of the Possible Side Effects of Radical Prostatectomy
- Follow-up after surgery

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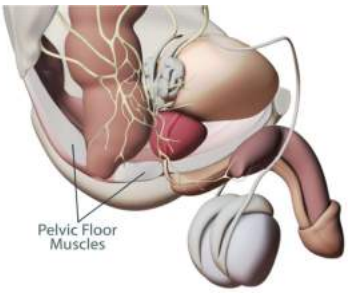
What is a Radical Prostatectomy

- "Radical" refers to surgery performed to remove cancer
- Radical prostatectomy is the removal of the prostate to treat prostate cancer and involves removal of:
  - Prostate
  - Seminal Vesicles
  - Small segment of Vas deferens
  - Sometimes lymph nodes in the pelvis



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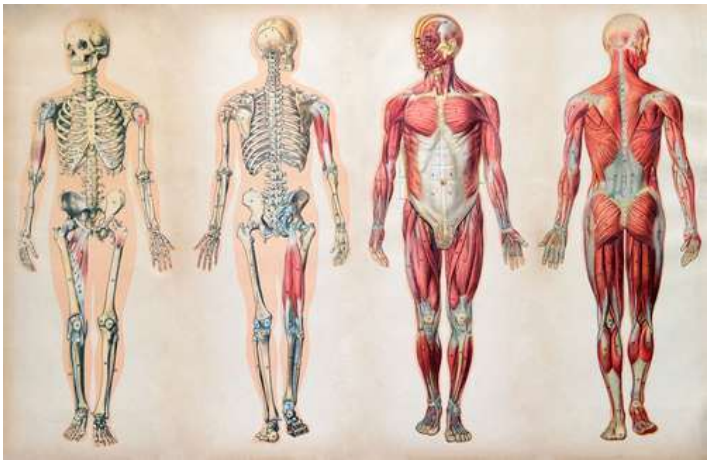
ANATOMY OF THE PROSTATE



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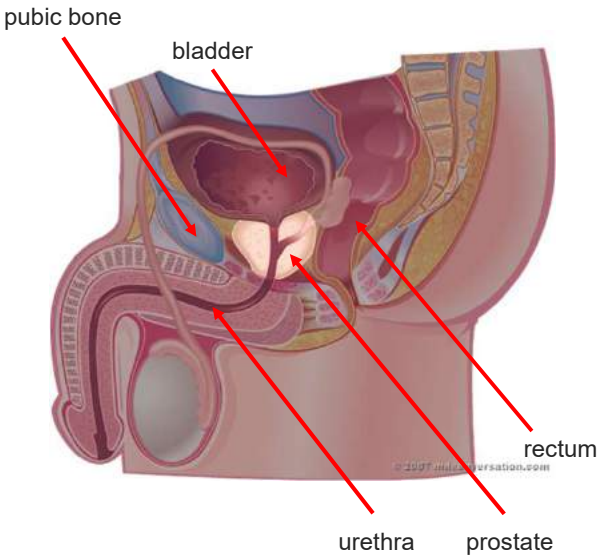
WHERE IS THE PROSTATE LOCATED?



The prostate gland is located deep in the pelvis

- Below the bladder
- In front of the rectum
- Behind the pubic bone
- Surrounds the urethra

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Who is best suited for a radical prostatectomy

•Men with disease that is confined to the prostate

•Medically fit for surgery

•> 10 year life expectancy

•Final decision: Informed Patient's Choice

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"LOCALIZED" PROSTATE CANCER

- When there is no evidence that the cancer has spread beyond the prostate gland, it is considered "**localized**". Localized disease is:
  - Treatable
  - Slow growing in most men, which allows for time to choose a treatment strategy
  - We do not perform "radical prostatectomy" when prostate cancer has spread, as this does not treat the cancer that has already spread

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Tests Performed Prior to Surgery

- Sometimes, when there is suspected metastases (symptoms, high PSA or high Gleason Score) tests are performed before surgery:
  - **Bone Scan** (to assess if cancer has spread to the bone)
  - **CT Scan** (to assess if cancer has spread to the lymph nodes or other organs)
- MRI may also be ordered to help with surgical planning

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SURGICAL OPTIONS FOR PROSTATECTOMY

- Open surgery (radical retropubic prostatectomy)
- Laparoscopic Robotic assisted surgery ("robotic", "RALP", "DVP")
- Laparoscopic RP
- Perineal

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Advantages of surgery

•Overall well tolerated

•Excellent long term results

•Lymph nodes can be sampled

•Assessment of the prostate by the pathologist

•Avoidance of "aging" urinary problems

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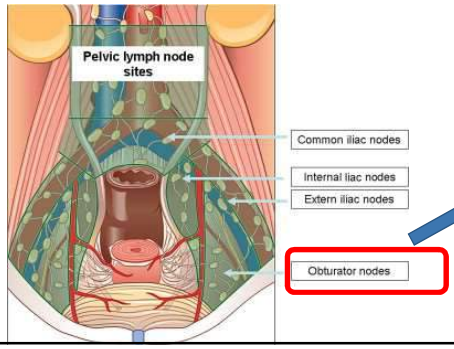
Other terminology:

- Nerve-sparing: the blood vessels and nerves that promote penile erections are left behind in the body and not taken out with the prostate

- Pelvic lymph node dissection: the lymph nodes surrounding and close to the prostate are taken out



The "Obturator" nodes are the ones usually taken out in those at risk of having cancer spread to them

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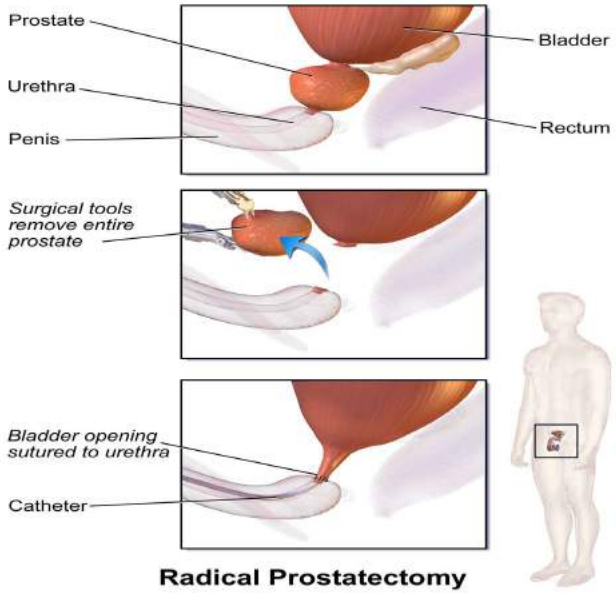
Steps of surgery:



Radical Prostatectomy

-Step 1: Removal of Prostate Gland, seminal vesicles, lymph nodes

-Step 2: Reconnection of the bladder to the urethra

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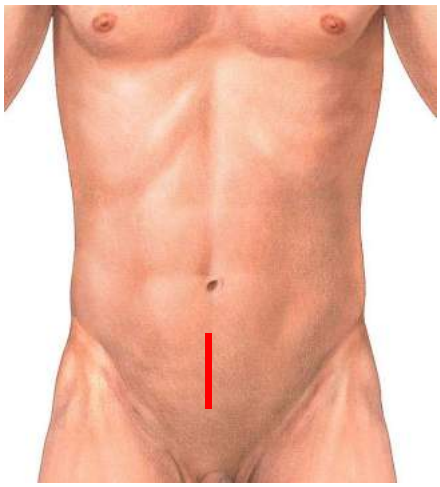
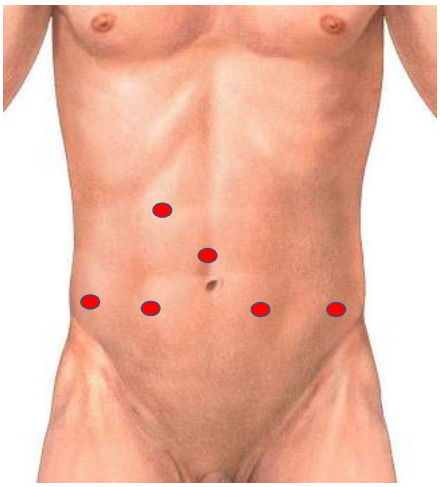
OPEN RP VS ROBOTIC RP



Incision for open prostatectomy

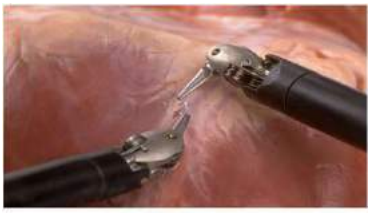


Incisions for Laparoscopic Prostatectomy

ROBOTIC PROSTATECTOMY

da Vinci® Surgical System

- 3-D visualization
- Surgeon direct instruments' movements using console controls



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Robotic Prostatectomy: Advantages

-Compared to open surgery:

- -Less bleeding
- -Potential for less pain / discomfort
- -Potential for earlier recovery of urinary control
- -Reduced “scarring” of bladder / urethra connection (called bladder neck contracture)
- -But…..doesnot appear to have better “cancer” control

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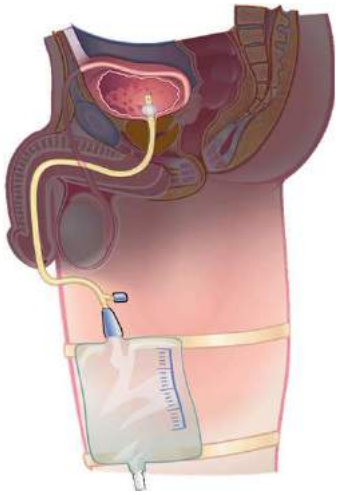
WHAT TO EXPECT AFTER SURGERY

- Hospital stay is usually 1 night
- Minimal to moderate discomfort
- Catheter in the penis to drain urine: 1-2 weeks
- 3-6 weeks off work (depending on type of work, more for manual or physically active jobs)



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ADVANTAGES of SURGERY as a Treatment for Prostate Cancer

- Generally well tolerated, recovery within 4-8 weeks in most
- Lymph nodes can be sampled to check for spread of cancer
- Assessment by a pathologist of the entire prostate
- Removal of cancer in the prostate may have long term benefit as well as short term psychological advantages
- Sometimes other additional treatments, such as radiation with or without hormone therapy, are also required
- Removal of the prostate prevents benign prostatic hypertrophy (BPH) related urinary problems

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SIDE EFFECTS RELATED TO SURGERY

- Erectile dysfunction (ED):
  - Depends on age and functional level before surgery
  - Younger men with full function have the best chance at recovery
  - May also experience penile shortening

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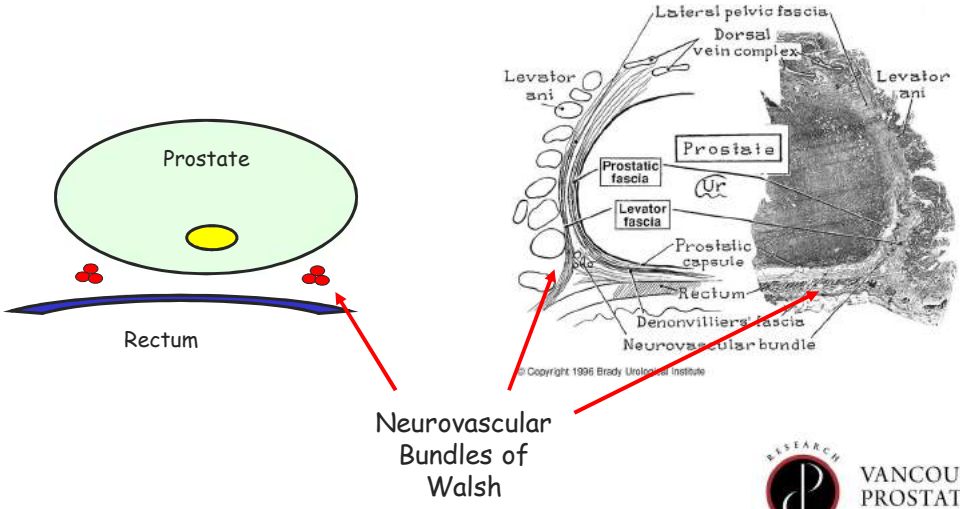
Erectile Dysfunction is due to damage to the erectile nerves

Cross-Section of Prostate



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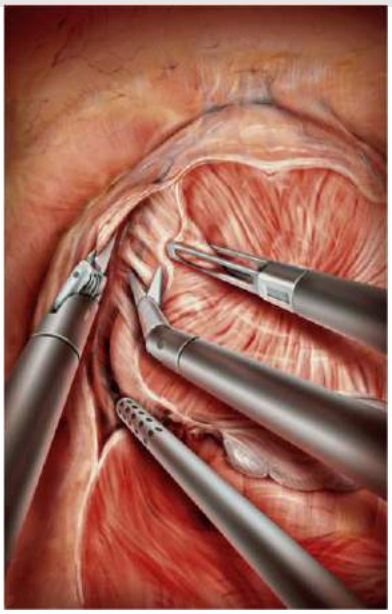
Surgical Approach



- Sparing of nerves maximizes return of normal erections
- This approach may not be possible is there is :
  - Significant volume of tumor in the area of the nerves
  - High grade tumor (aggressive disease) in the area of the nerves
- Climax and penile sensation not affected- just penile rigidity

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MANAGING ERECTILE DYSFUNCTION

- Sometimes called sexual or penile rehabilitation
- Treatments may include:
  - Medications
  - Intraurethral suppositories
  - Penile injections
  - Vacuum devices
  - Penile implants

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SIDE EFFECTS RELATED TO SURGERY

- Incontinence:
  - most experience incontinence during the first 3 months
  - 1 in 10 men continue to have some level of stress incontinence past a year but total loss of control is rare

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MANAGING URINARY INCONTINENCE

- Although long-term incontinence may be rare, a majority of men post-operatively will have some leakage of urine with straining / coughing etc. (Stress incontinence)
- Management is initially conservative with Kegel Exercises to strengthen the pelvic floor muscles
- Pelvic floor physiotherapy and biofeedback can be helpful to maximize recovery
- If incontinence persists, surgical option may be helpful

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Other potential rare side effects

- Blood transfusion: < 5 %
- Bladder neck scarring: rare
- Rectal injury: rare

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HOW DO WE KNOW WHETHER TREATMENT IS WORKING?

Follow up visits

- PSA
  - Expect it to be very low, if not undetectable, 3 months after surgical treatment
  - After surgery, PSA should be undetectable

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WHAT IF MY CANCER REOCCURS?

- Some of these treatment options can be explored, depending upon the initial treatment and the nature of the recurrence, e.g.:
  - Radiation to the pelvis
  - Androgen deprivation
  - May consider PSMA-PET Scan

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Conclusion

- Prostate cancer surgery for cure is called radical prostatectomy
- Surgery can be performed in those with localized disease
- There are different ways to perform radical prostatectomy
- There are some side effects that may be associated with surgery which can be treated with by your Urologist

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9:04am – 9:23am

Advances in Radiation Therapy for Prostate Cancer

Robert Meier, MD

Advances in Radiation Therapy for Prostate Cancer

21st Annual Pacific NW Prostate Cancer Conference

Robert Meier MD
Swedish Radiosurgery Center

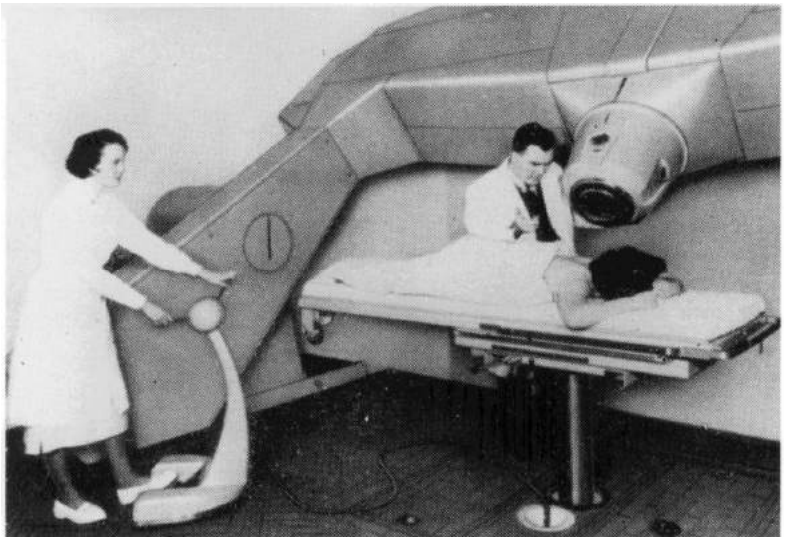
Advances in Radiotherapy for Prostate Cancer

- Evolution of Radiation Therapy
  - External Beam Radiotherapy
  - Brachytherapy
  - IMRT & Proton Beam
  - Hypofractionation
  - Stereotactic Radiotherapy
- Outcomes of SBRT for Organ-confined Prostate Cancer
- SBRT for Metastatic Prostate Cancer
  - Oligometastases
  - SABR-COMET and ORIOLE randomized trials

1953: 1st Medical Linear Accelerator

Newcastle General Hospital, England

Isocentric 4 MeV linac

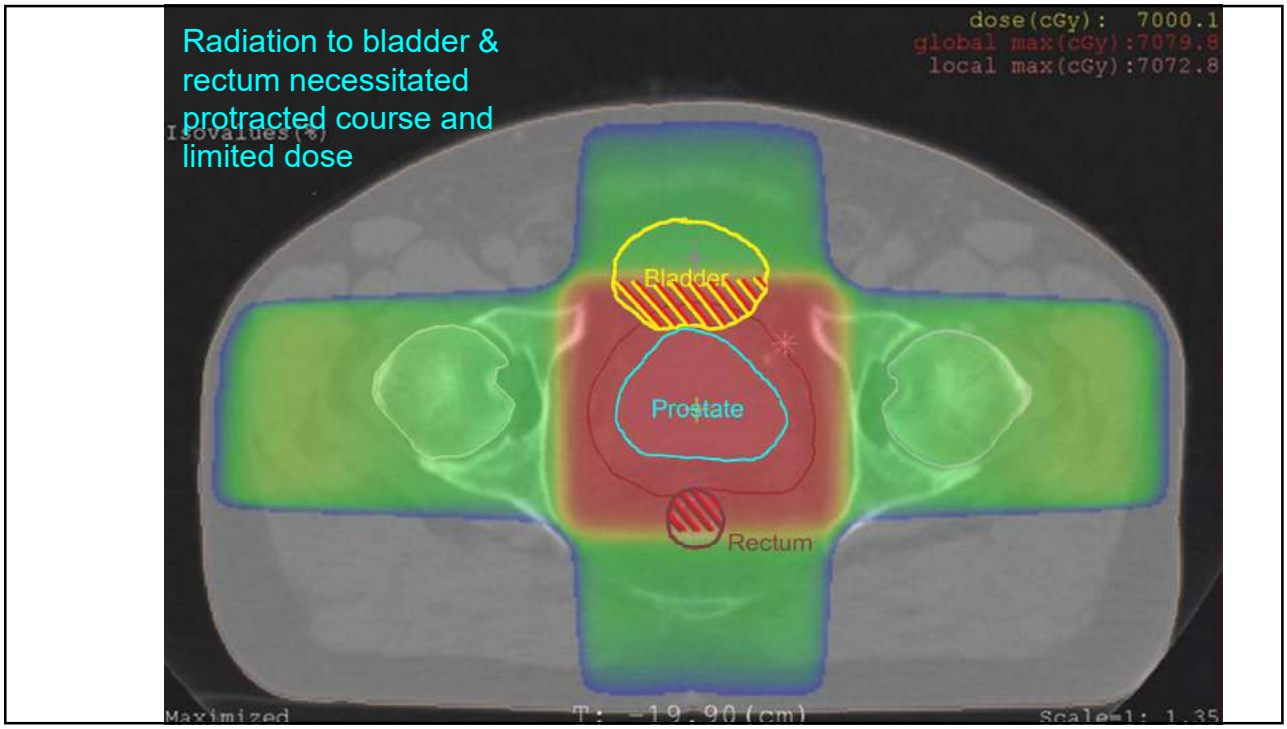


Modern Radiotherapy for Prostate CA

George FW, et al. Cobalt-60 telecurietherapy in the definitive treatment of carcinoma of the prostate: a preliminary report. J Urol. 1965;93:102–109.

Bagshaw MA, Kaplan HS, Sagerman RH. Linear accelerator supervoltage radiotherapy. VII. Carcinoma of the prostate. Radiology. 1965;85:121–129.

Del Regato JA. Radiotherapy in the conservative treatment of operable and locally inoperable carcinoma of the prostate. Radiology. 1967;88:761–766.



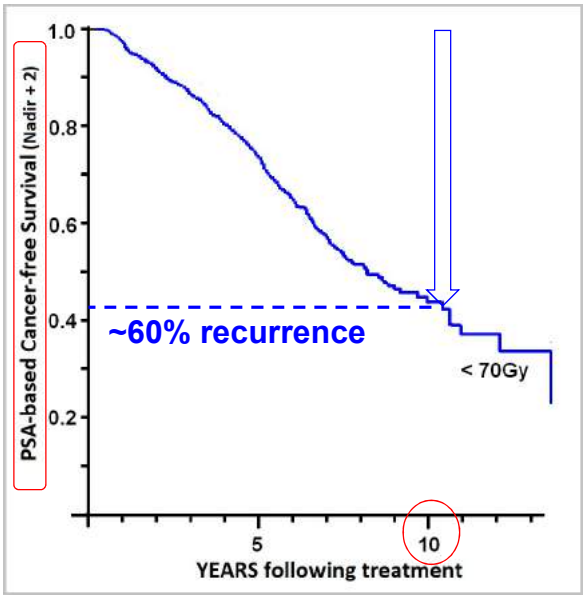
External Beam RT: Effect of Increasing Dose

*From 1960's – 1980's Prostate cancer treated with **65-70Gy***

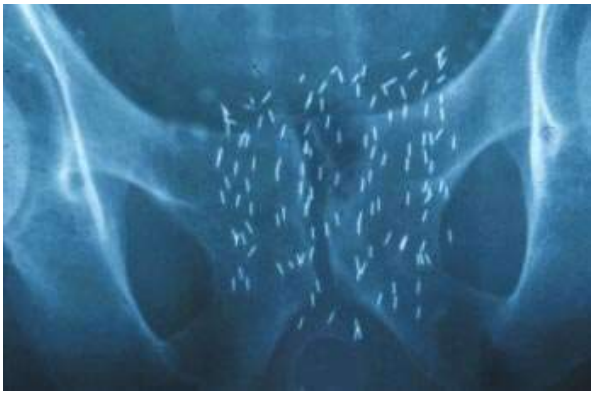
PSA allowed us to detect cancer recurrences

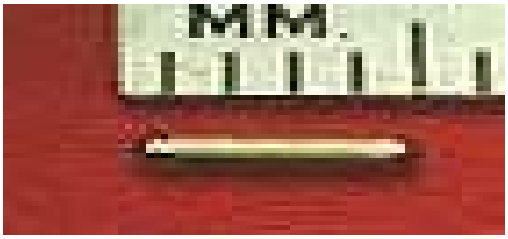
1530 pts from Fox-Chase Cancer Center

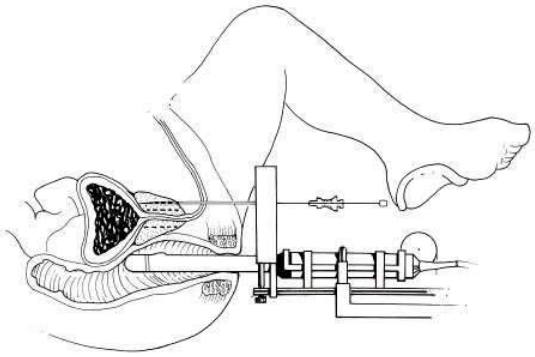
Eade IJROBP 68(3),682 (2007)

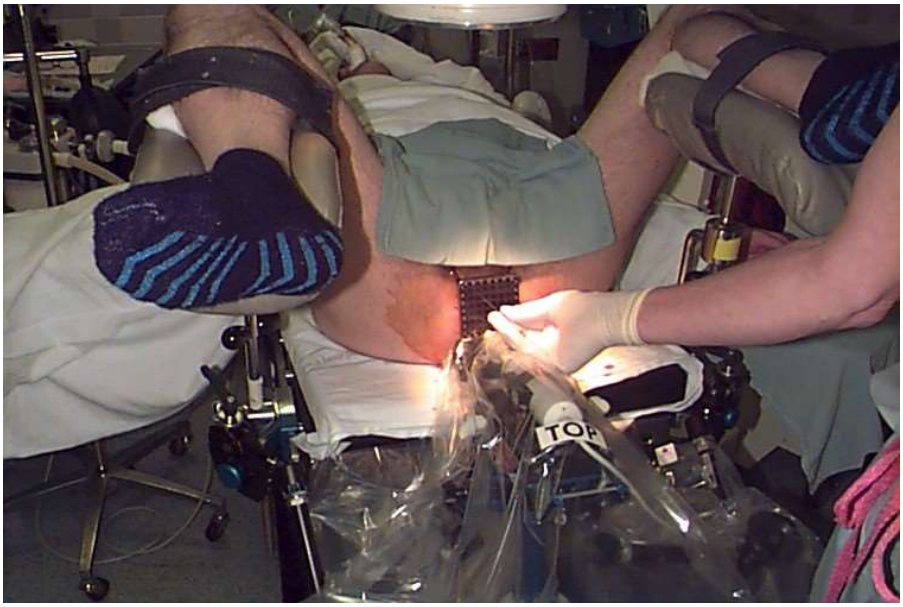


Brachytherapy

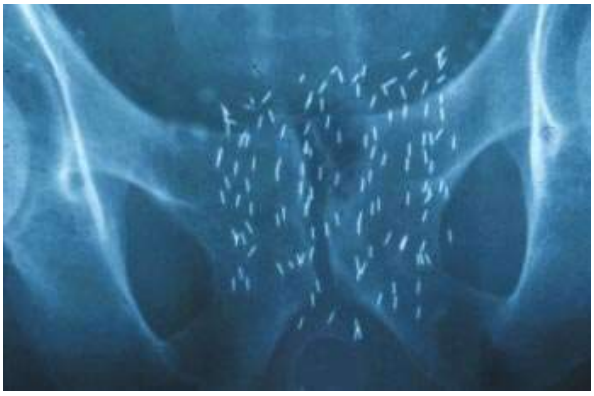








Brachytherapy

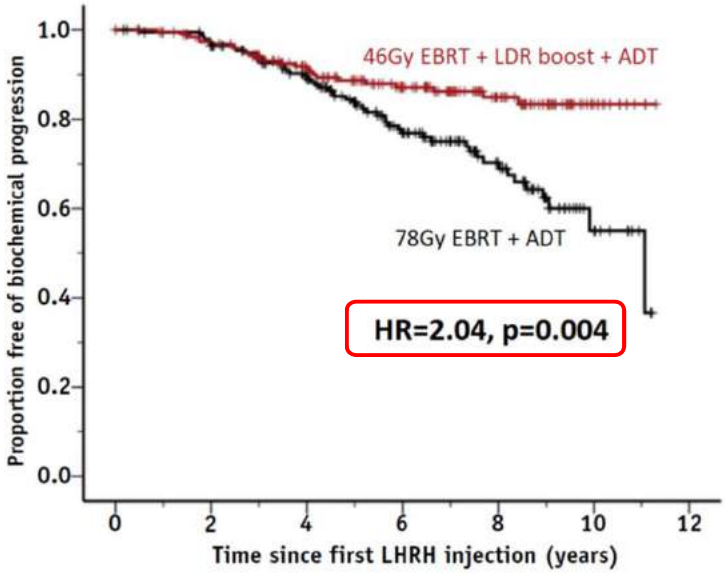


- Low-risk & favorable intermediate-risk pts treated with seed implant alone
- Higher risk patients also require 5 week course of daily external beam RT

ASCENDE-RT: Randomized Brachytherapy *vs* EBRT

398 Interm & high-risk 6.5 yrs f/u

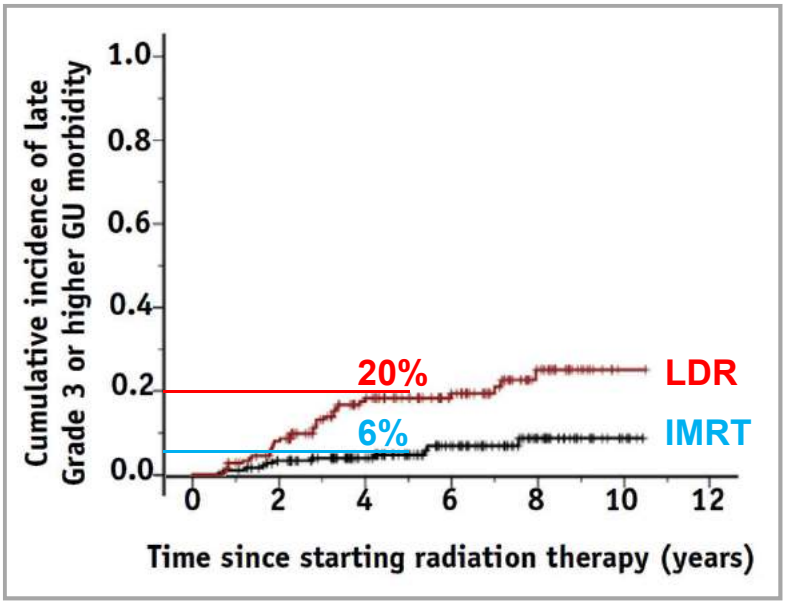
Morris et al, ASCENDE-RT trial, IJROBP:98(2),275-285



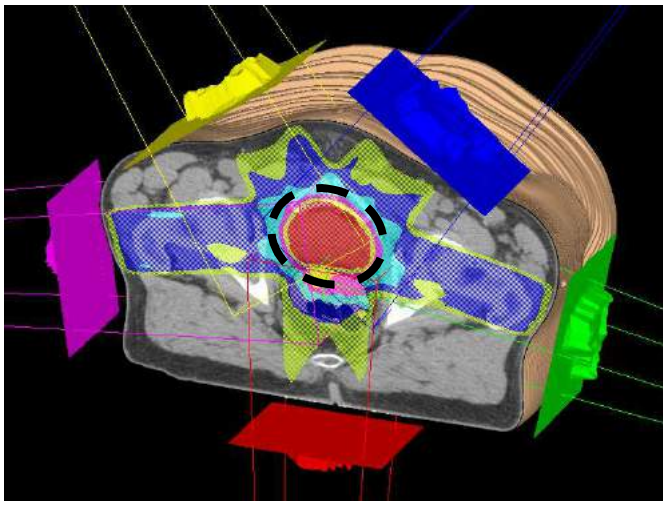
Urinary Toxicity: EBRT *vs* LDR+EBRT

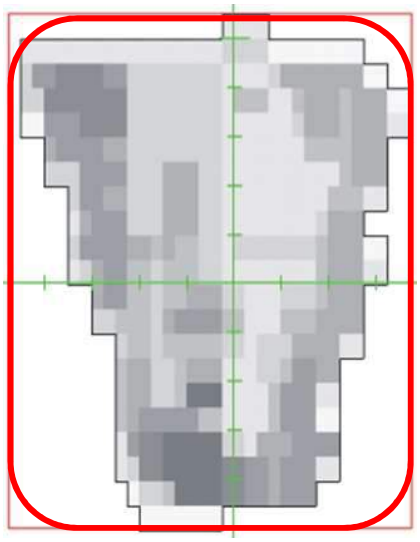
ASCENDE-RT

Morris. Int J Rad Onc Biol Phys, 98(2) 286, 2017

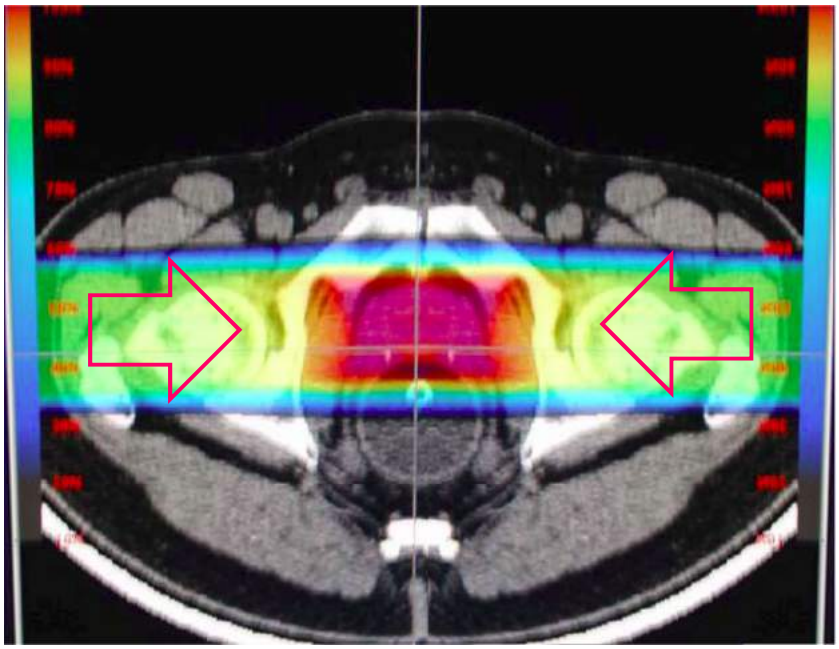


Intensity Modulated Radiotherapy (IMRT)

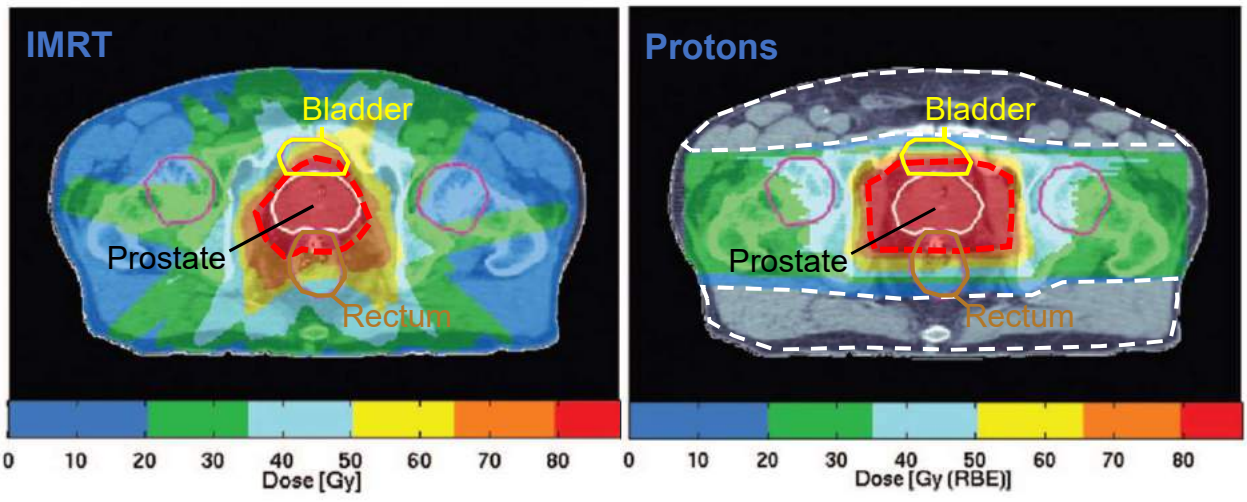




Proton Beam Therapy



IMRT and Proton Beam

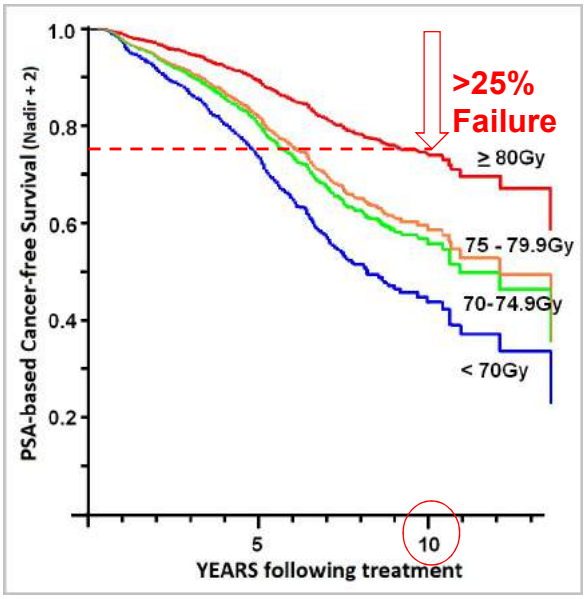


External Beam RT: Effect of Increasing Dose

Improvements in technology over the past 20 years have allowed dose escalation

1530 pts from Fox-Chase Cancer Center

Eade IJROBP 68(3),682 (2007)

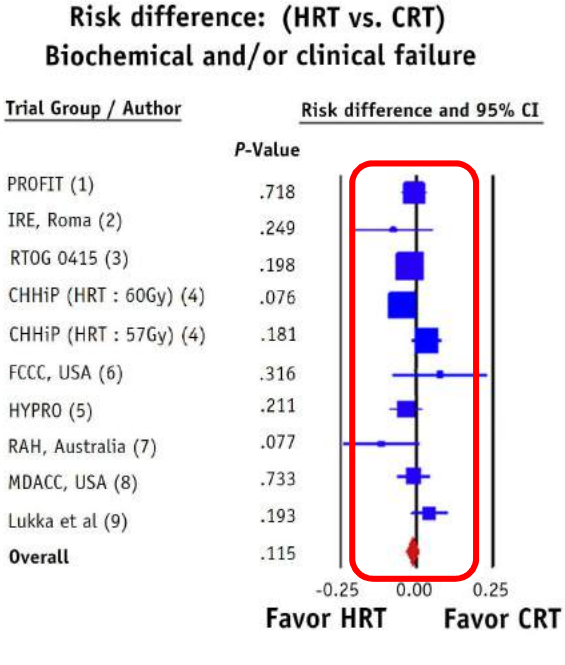


Conventional (7-8 weeks) *vs* Hypofractionation (4-5 weeks): Randomized Trials

No differences in cancer control

Short course had slightly more acute side effects, but no greater long-term side effects

Int J Radiation Oncol Biol Phys, Vol. 99, No. 3, pp. 573-589, 2017



Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial

Anders Widmark, Adalsteinn Gunnlaugsson, Lars Beckman, Camilla Thellenberg-Karlsson, Morten Hoyer, Magnus Lagerlund, Jon Kindblom, Claes Ginman, Bengt Johansson, Kirsten Björnlinger, Mihajl Seke, Måns Agrup, Per Fransson, Björn Tavelin, David Norman, Björn Zackrisson, Harald Anderson, Elisabeth Kjellén, Lars Franzén, Per Nilsson

1180 men randomized to
- conventional fractionation (78Gy, 2Gy/fx) vs
- ultra-hypofractionation (42.7Gy, 6.1Gy/fx)

89% intermediate-risk
11% high-risk

No ADT

Median follow-up = 5.0 years

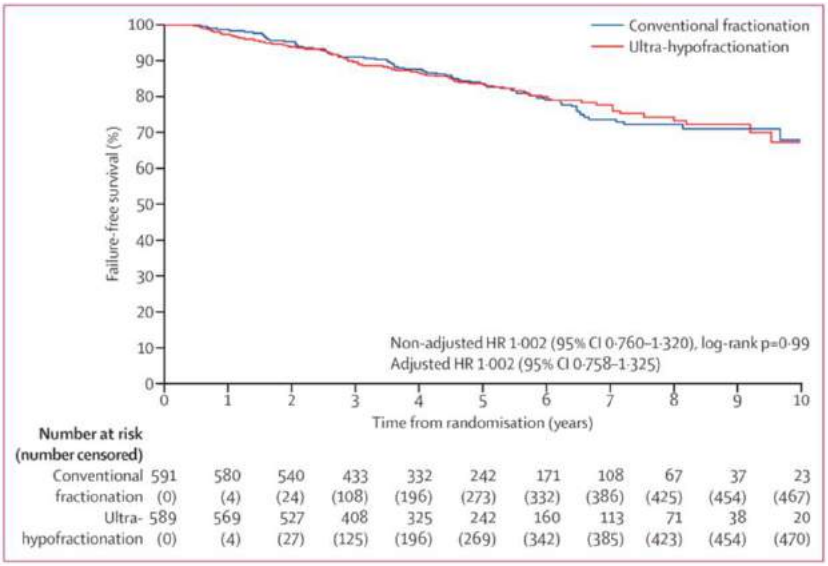
Lancet 2019; 394: 385–95

HYPO-RT-PC Randomized Trial: Conventional vs Ultra-hypofractionation

No difference in failure-free survival

Acute toxicity/QOL slightly worse acutely & at 1 year

No differences in later toxicity/QOL

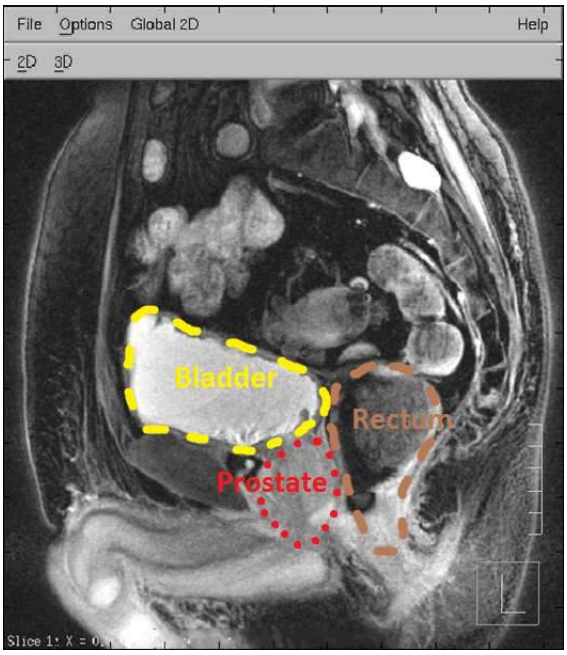


Widmark et al, Lancet 2019; 394: 385–95

Intra-fractional prostate movement

MRI cine

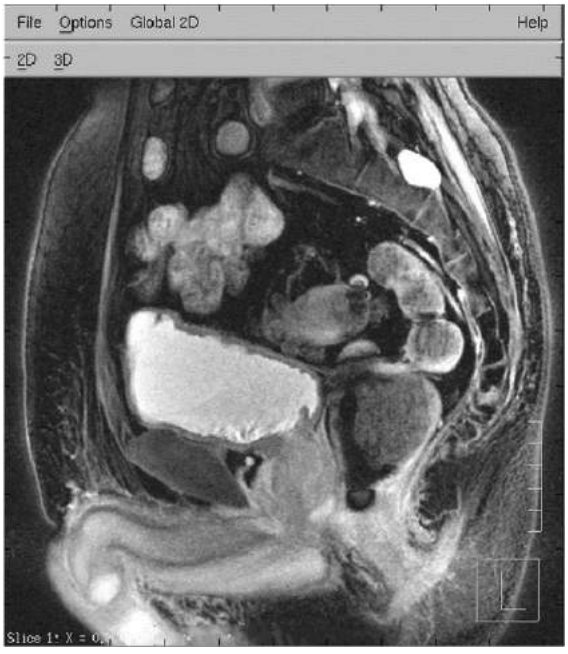
(courtesy
Alvaro Martinez, MD, William Beaumont Hospital Radiation Oncology)

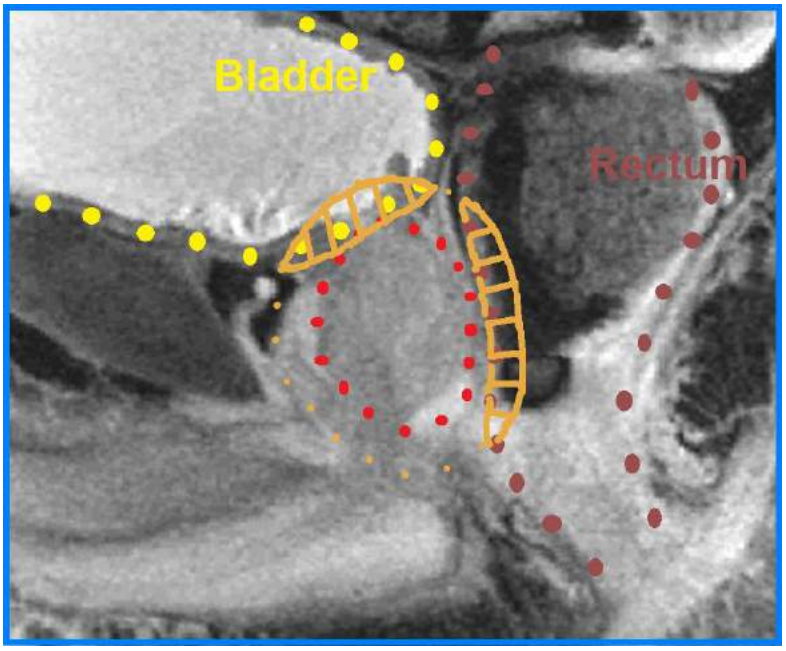


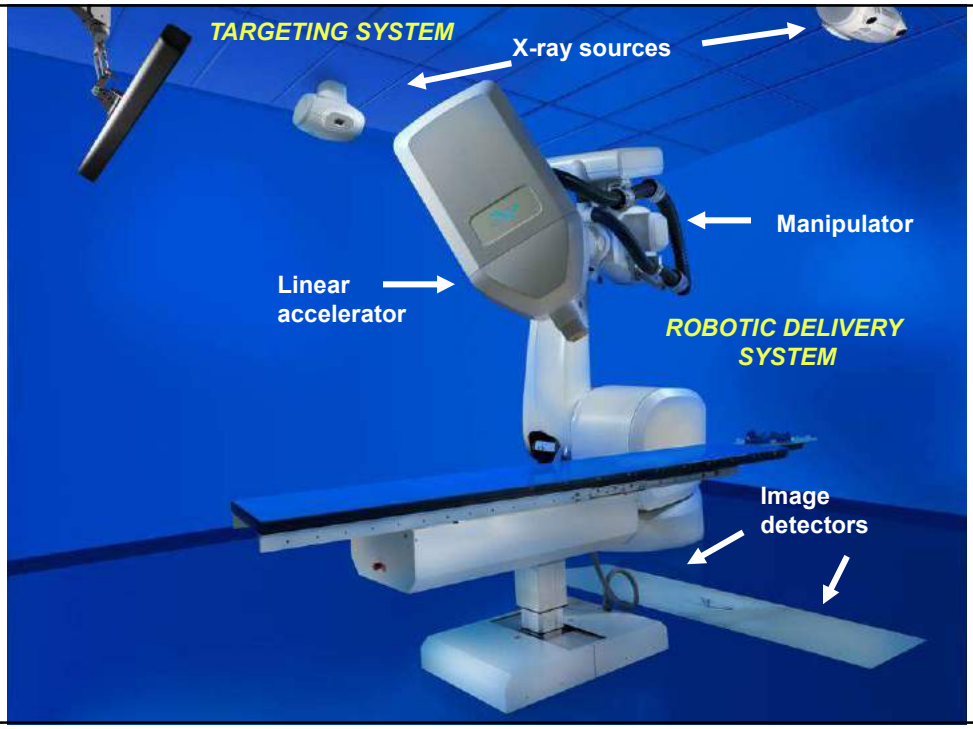
Intra-fractional prostate movement

MRI cine

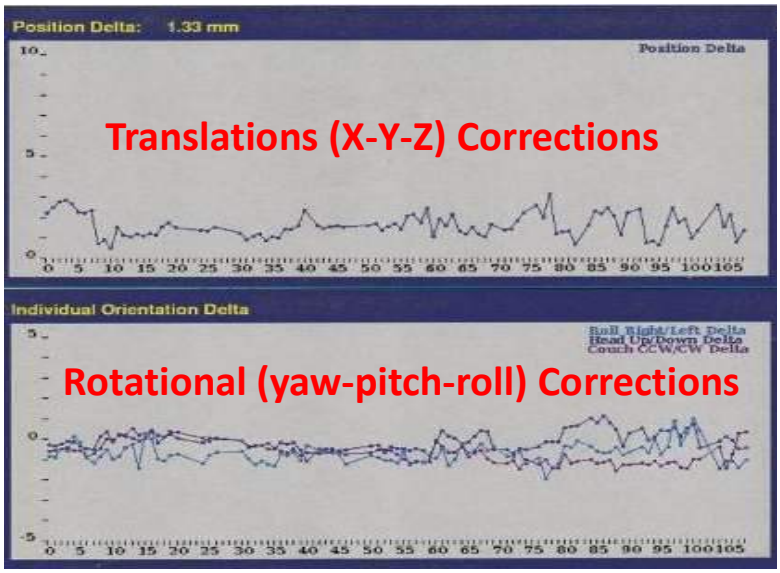
(courtesy
Alvaro Martinez, MD, William Beaumont Hospital Radiation Oncology)




Bladder
Rectum

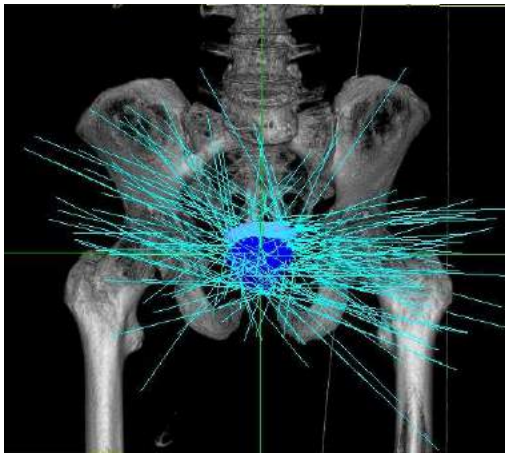

TARGETING SYSTEM
X-ray sources
Manipulator
Linear accelerator
ROBOTIC DELIVERY SYSTEM
Image detectors

Fiducials Tracked with Real-Time Corrections



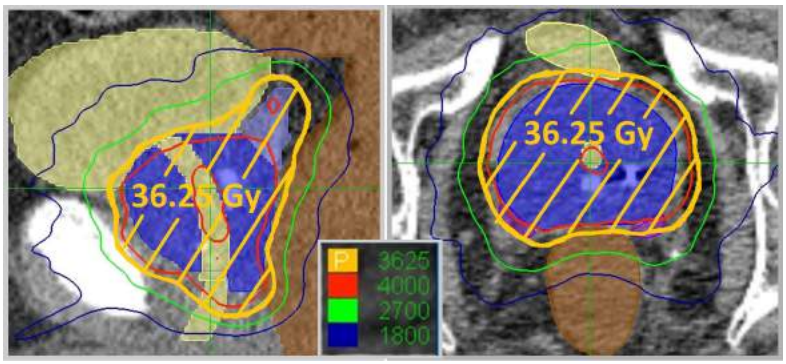
CyberKnife

- 6-joint articulated robotic arm allows non-coplanar delivery of >100 intersecting beams



Stereotactic Body Radiotherapy (SBRT)
The precise delivery of high-dose RT in 1-5 doses

- Prostate prescribed **8** Gy x **5** = **40** Gy: $EQD_{2,\ \alpha/\beta=2}$ = **100** Gy
- Seminal vesicles + 3-5mm outside prostate: **7.25** x **5** = **36.25**G



International Journal of Radiation Oncology biology • physics
www.redjournal.org

Multicenter Trial of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer: Survival and Toxicity Endpoints

Robert M. Meier, MD,* Daniel A. Bloch, PhD,† Cristian Cotrutz, PhD,* Alan C. Beckman, MD,‡ George T. Henning, MD,‖ Shermian A. Woodhouse, MD,‖ Shirnett K. Williamson, MD,¶ Najeeb Mohideen, MD,# John J. Dombrowski, MD,** Robert L. Hong, MD,†† David G. Brachman, MD,‡‡ Patrick W. Linson, MD,§§ and Irving D. Kaplan, MD‖‖

*Swedish Cancer Institute, Seattle, Washington; †Stanford University Biostatistics, Stanford, California; ‡Central Baptist Hospital, Lexington, Kentucky; §St Joseph Mercy, Ypsilanti, Michigan; ‖Community Cancer Center, Normal, Illinois; ¶Capital Health Medical Center, Pennington, New Jersey; #Northwest Community Hospital, Arlington Heights, Illinois; **St Louis University Hospital, St Louis, Missouri; ††Virginia Hospital, Arlington, Virginia; ‡‡St Joseph's Hospital and Medical Center, Phoenix, Arizona; §§Scripps Health, La Jolla, California; and ‖‖Beth Israel Deaconess Medical Center, Boston, Massachusetts

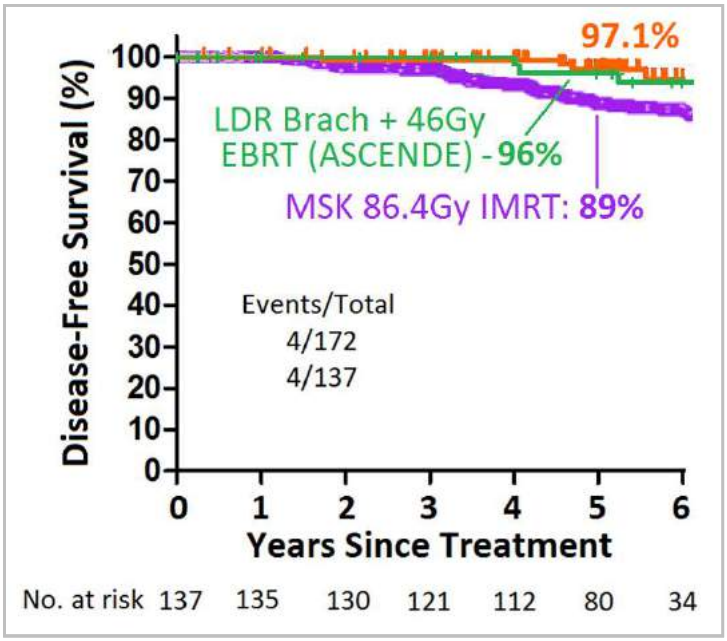
ESTRO 2021

Robert Meier, MD
Swedish Cancer Institute, Seattle WA USA

10-year outcome of ultrahypofractionated stereotactic RT from two multicenter prostate cancer trials

Intermediate-risk Patients

5-yr Nadir+2 Disease-Free Survival



RFS by Risk Group

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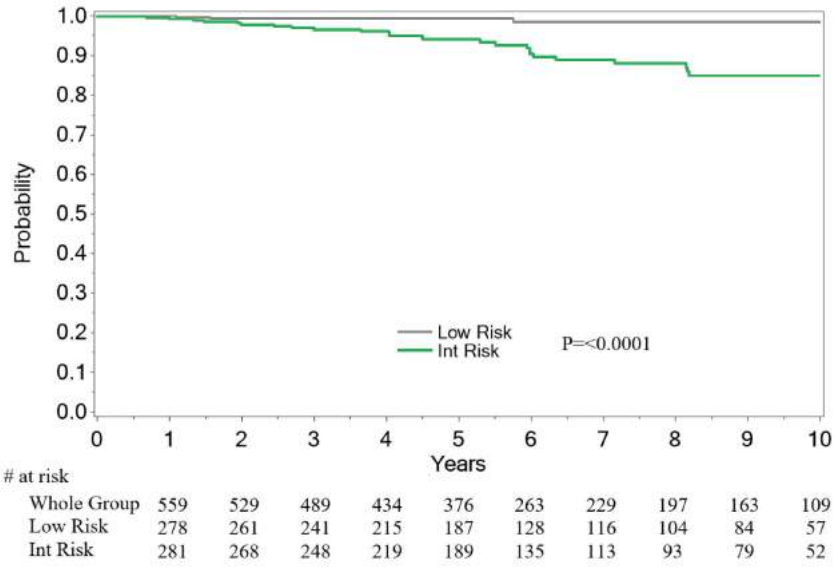
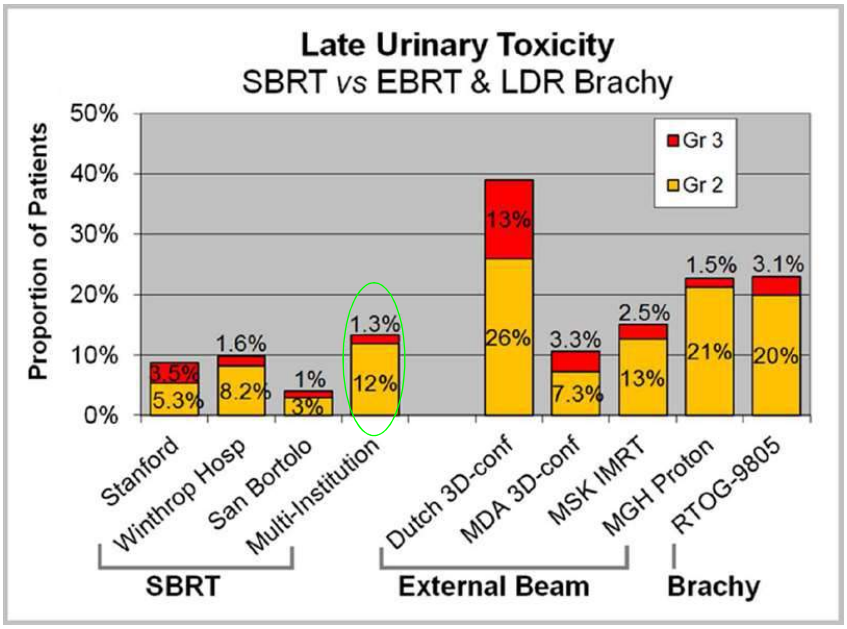
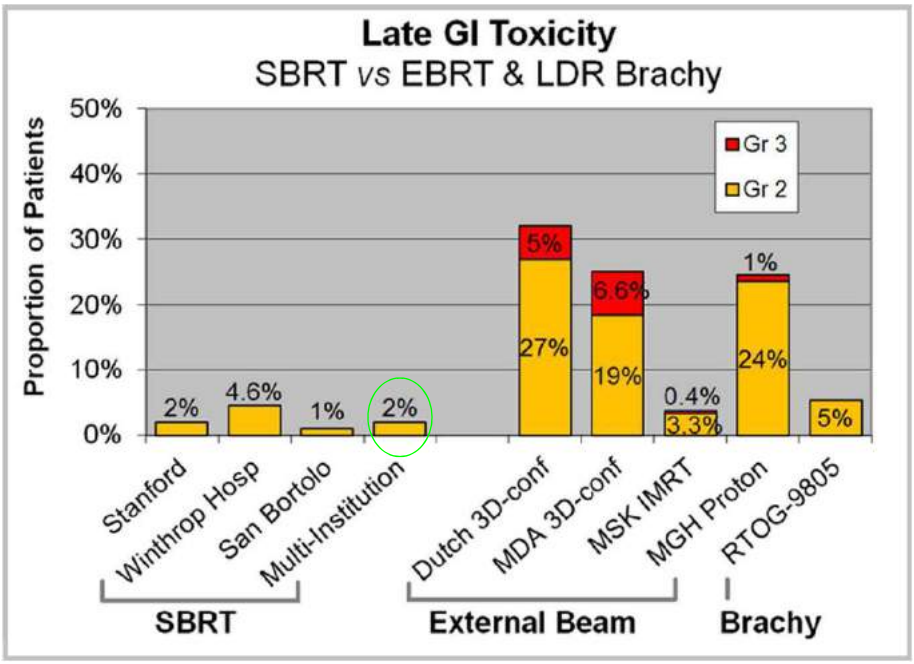


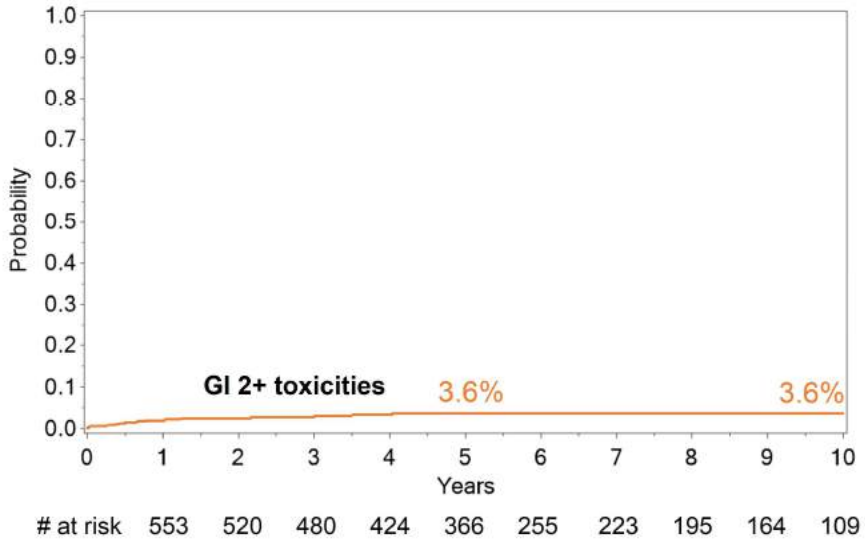
-98.5% Low-Risk

-85% Interm-Risk

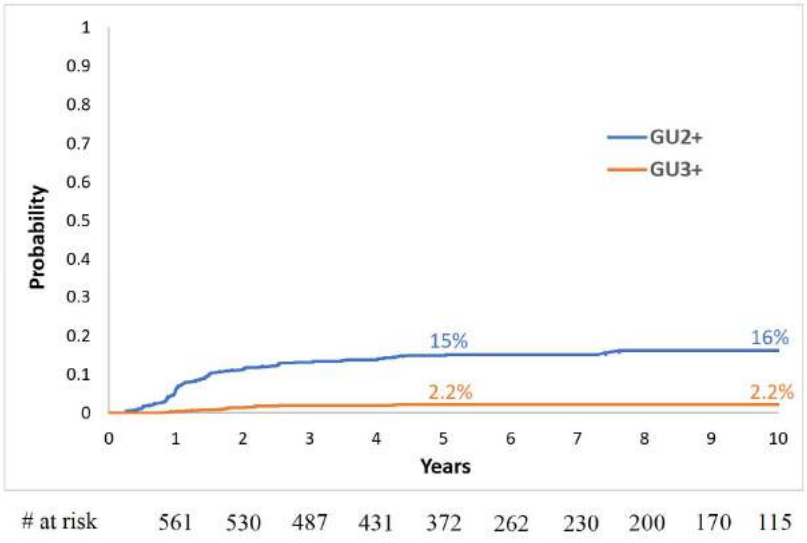

Late Urinary Toxicity
SBRT vs EBRT & LDR Brachy
Proportion of Patients
50%
40%
30%
20%
10%
0%
Gr 3
Gr 2
3.5%
5.3%
1.6%
8.2%
1%
3%
1.3%
12%
13%
26%
3.3%
7.3%
2.5%
13%
1.5%
21%
3.1%
20%
Stanford
Winthrop Hosp
San Bortolo
Multi-Institution
Dutch 3D-conf
MDA 3D-conf
MSK IMRT
MGH Proton
RTOG-9805
SBRT
External Beam
Brachy


Late GI Toxicity
SBRT vs EBRT & LDR Brachy
Proportion of Patients
50%
40%
30%
20%
10%
0%
Gr 3
Gr 2
2%
4.6%
1%
2%
5%
27%
6.6%
19%
0.4%
3.3%
1%
24%
5%
Stanford
Winthrop Hosp
San Bortolo
Multi-Institution
Dutch 3D-conf
MDA 3D-conf
MSK IMRT
MGH Proton
RTOG-9805
SBRT
External Beam
Brachy

Late GI Toxicity



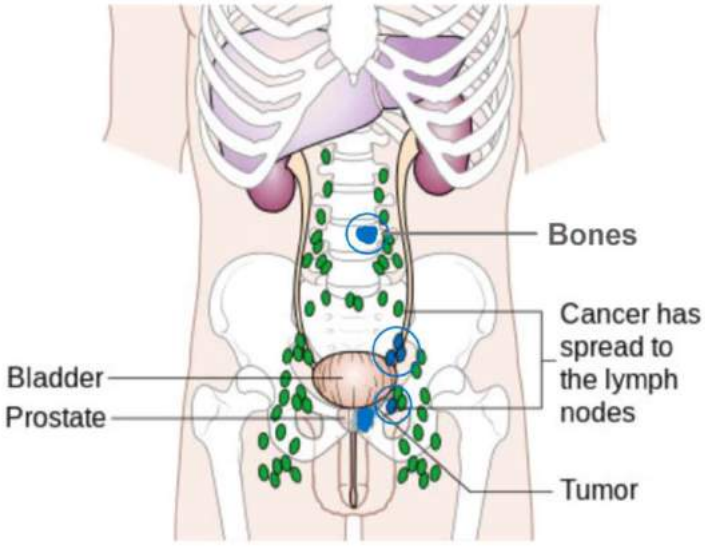
Late GU Toxicity



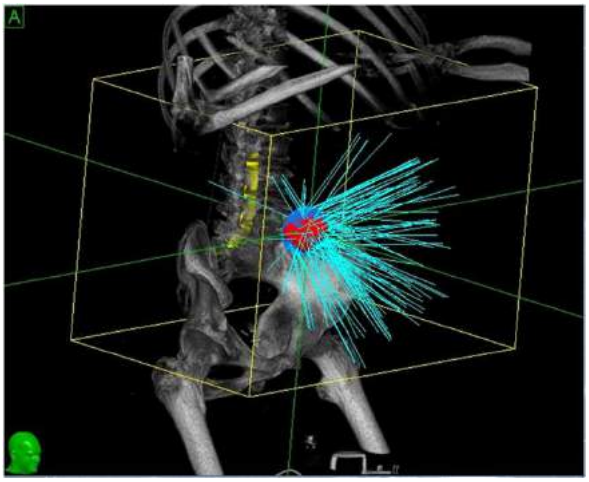
In Organ-confined Prostate Cancer, SBRT

- Allows completion of treatment in just 5 fractions
- Has less rectal complications than other radiation treatment
- Has less urinary complications than brachytherapy
- Yields cancer control rates similar to brachytherapy, and superior to external beam radiotherapy

Prostate Cancer Metastases



SBRT for Metastases



- Older radiation technologies could palliate symptoms from metastases, but were too inaccurate to reliably *ablate* metastatic deposits
- Modern radiation devices can safely focus ablative doses of radiotherapy on metastatic tumors
- Cross-firing beams that precisely target the cancer is called:
  - **SBRT** (stereotactic body radiotherapy), or
  - **SAbR** (stereotactic ablative radiotherapy)

Oligometastases

- A distinct condition where cancer has metastasized, but disease elsewhere is probably limited
- Definition: up to 5 metastases
- Detected on conventional or PET imaging
- Primary site is controlled
- In prostate cancer, patients may be hormone-naïve, or hormone-resistant

CyberKnife for Oligometastases

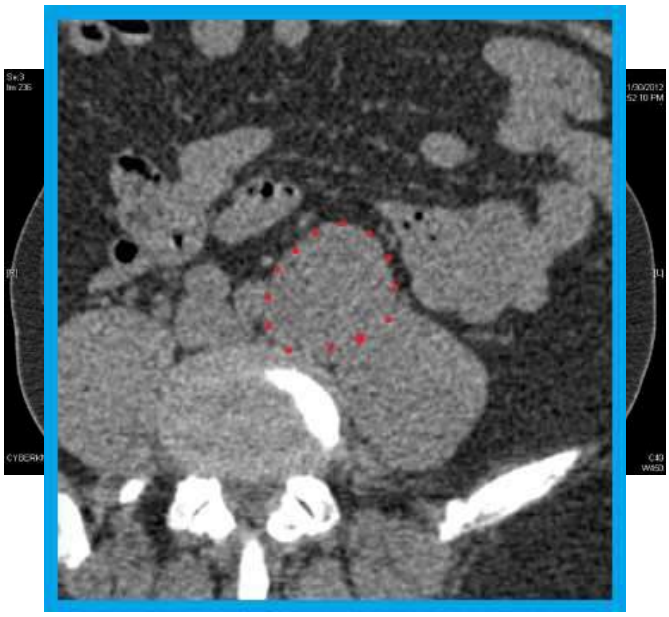
60 yr old, prostatectomy

PSA rise: Lupron x 3 yrs

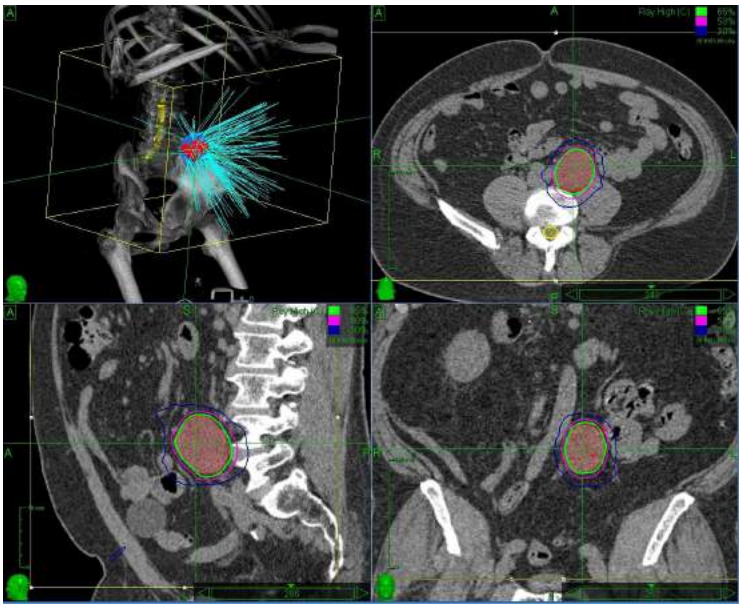
PSA ↑, lymph node on CT scan

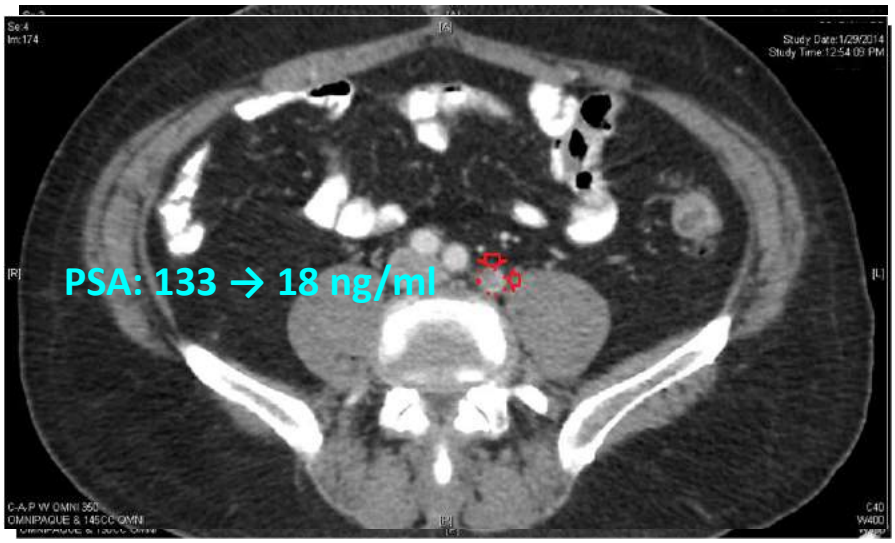
Provenge

6 mos later PSA=133 & Node larger (see CT)

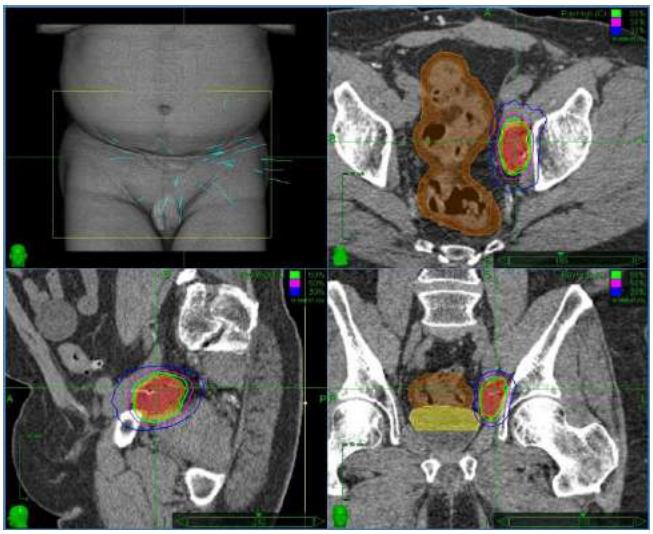


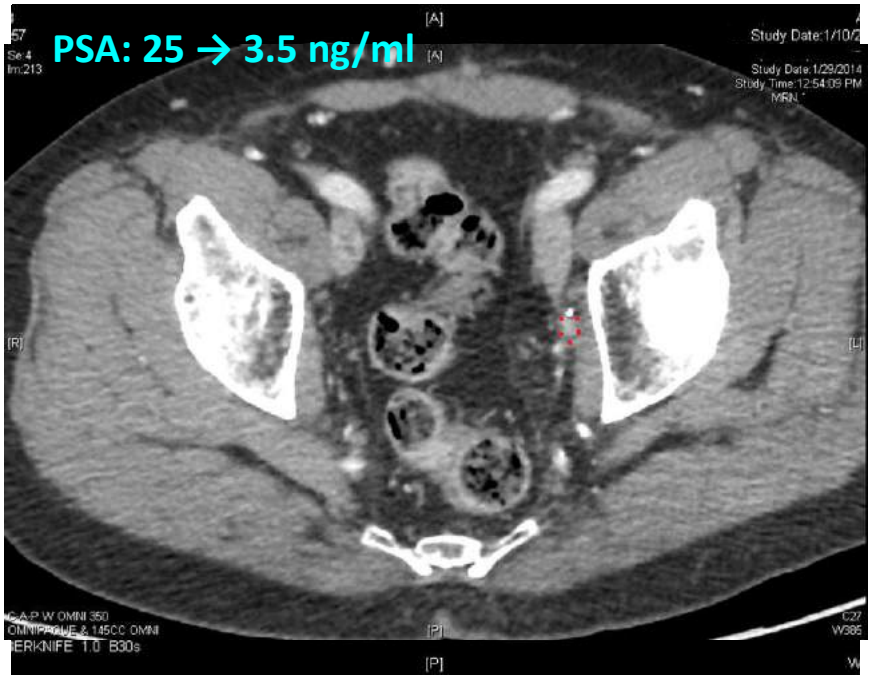
CyberKnife: 5 Fractions Given





- PSA: 18 → 25
- 2nd nodal metastasis discovered
- CyberKnife: 5 fractions

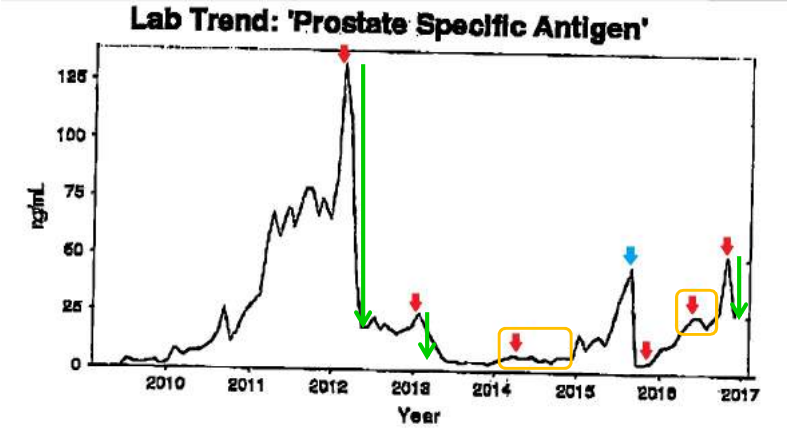




Ongoing Treatment of Oligometastases

6 Cyberknife Txs (red arrow), 1 surgery (blue arrow) for nodal mets

Disease progression controlled for 5 years with local treatment only



THE LANCET

Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial

David A Palma, Robert Olson, Stephen Harrow, Stewart Gaede, Alexander V Louie, Cornelis Haasbeek, Liam Mulroy, Michael Lock, George B Rodrigues, Brian P Yaremko, Devin Schellenberg, Belal Ahmad, Gwendolyn Griffioen, Sashendra Senthi, Anand Swaminath, Neil Kopek, Mitchell Liu, Karen Moore, Suzanne Currie, Glenn S Bauman, Andrew Warner, Suresh Senan

Journal of Clinical Oncology® ascopubs.org/journal/jco
https://doi.org/10.1200/JCO.20.00818

Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial

David A. Palma, MD, PhD[1]; Robert Olson, MD, MSc[2]; Stephen Harrow, MBChB, PhD[3]; Stewart Gaede, PhD[1]; Alexander V. Louie, MD, PhD[4]; Cornelis Haasbeek, MD, PhD[5]; Liam Mulroy, MD[6]; Michael Lock, MD[1]; George B. Rodrigues, MD, PhD[1]; Brian P. Yaremko, MD, PEng[1]; Devin Schellenberg, MD[7]; Belal Ahmad, MD[1]; Sashendra Senthi, MD, PhD[8]; Anand Swaminath, MD[9]; Neil Kopek, MD[10]; Mitchell Liu, MD[11]; Karen Moore, MSc[3]; Suzanne Currie, MSc[3]; Roel Schlijper, MD[2]; Glenn S. Bauman, MD[1]; Joanna Laba, MD[1]; X. Melody Qu, MD, MPH[1]; Andrew Warner, MSc[1]; and Suresh Senan, MBBS, PhD[5]

SABR-COMET

100 patients with 1-5 metastases

- Primary: breast, colorectal, lung, prostate, other
- Primary controlled
- ECOG 0-1
- Life expectancy 6+ months

Randomized: Standard of Care +/- SAbR

Characteristic	Arm, No. (%) Control (n = 33)	SABR (n = 66)
Site of original primary tumor		
Breast	5 (15)	13 (20)
Colorectal	9 (27)	9 (14)
Lung	6 (18)	12 (18)
Prostate	2 (6)	14 (21)
Other	11 (33)	18 (27)

Progression-Free Survival

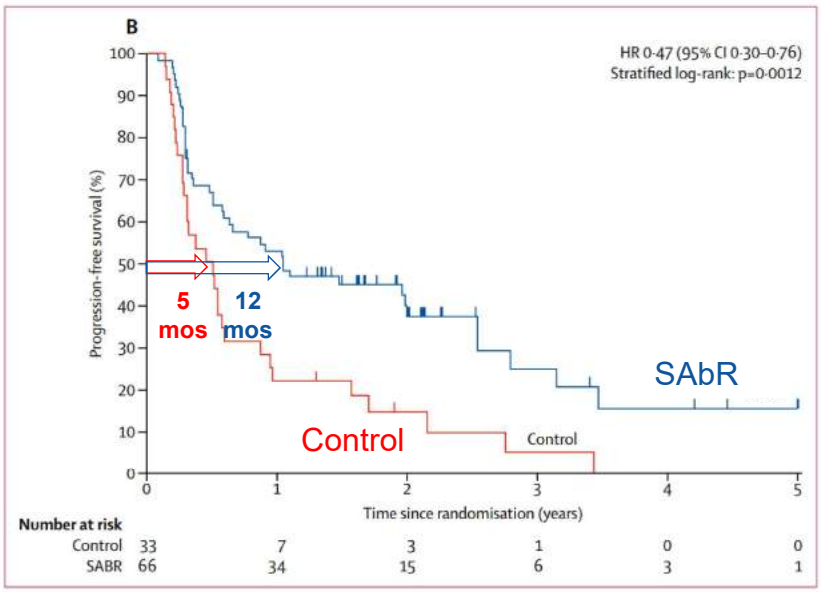
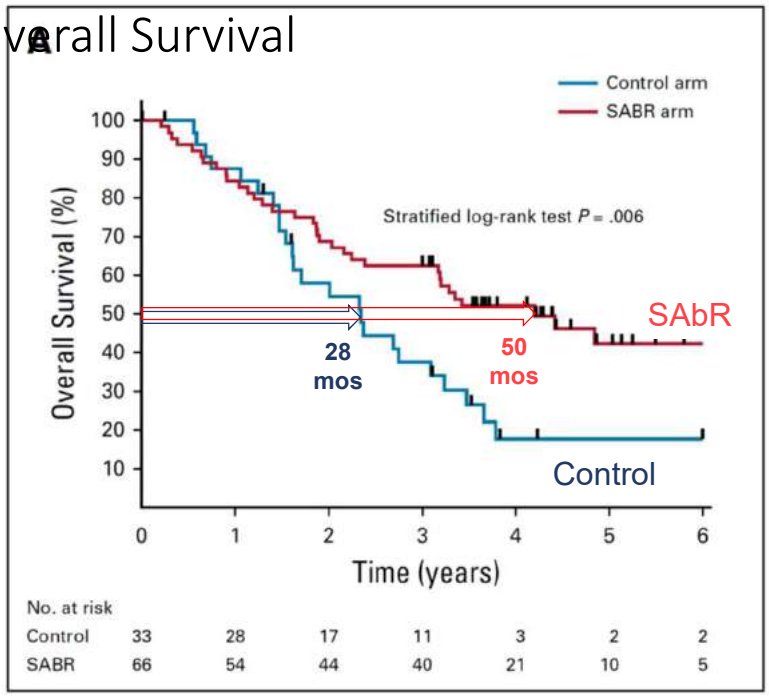


Figure 2: **progression-free survival (B)** SABR=stereotactic ablative radiotherapy. HR=hazard ratio.

Overall Survival



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ASTRO'S 61ST ANNUAL MEETING
September 15-18, 2019
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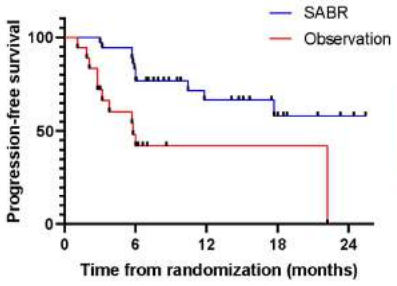
JOHNS HOPKINS MEDICINE
RADIATION ONCOLOGY & MOLECULAR RADIATION SCIENCES

JAMA Oncology | Original Investigation

Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer
The ORIOLE Phase 2 Randomized Clinical Trial

Ryan Phillips, MD, PhD; William Yue Shi, BS; Matthew Deek, MD; Noura Radwan, MD; Su Jin Lim, ScM; Emmanuel S. Antonarakis, MD; Steven P. Rowe, MD, PhD; Ashley E. Ross, MD, PhD; Michael A. Gorin, MD; Curtiland Deville, MD; Stephen C. Greco, MD; Hailun Wang, PhD; Samuel R. Denmeade, MD; Channing J. Paller, MD; Shirl Dipasquale, MS, RN; Theodore L. DeWeese, MD; Daniel Y. Song, MD; Hao Wang, PhD; Michael A. Carducci, MD; Kenneth J. Pienta, MD; Martin G. Pomper, MD, PhD; Adam P. Dicker, MD, PhD; Mario A. Eisenberger, MD; Ash A. Alizadeh, MD, PhD; Maximilian Diehn, MD, PhD; Phuoc T. Tran, MD, PhD

SABR significantly improved progression-free survival (PFS)



Hazard Ratio: 0.30
95% CI: 0.11 - 0.81
p-value: 0.0023

Number at risk					
SABR	36	26	13	7	2
Observation	18	8	1	1	0

JOHNS HOPKINS MEDICINE
RADIATION ONCOLOGY & MOLECULAR RADIATION SCIENCES
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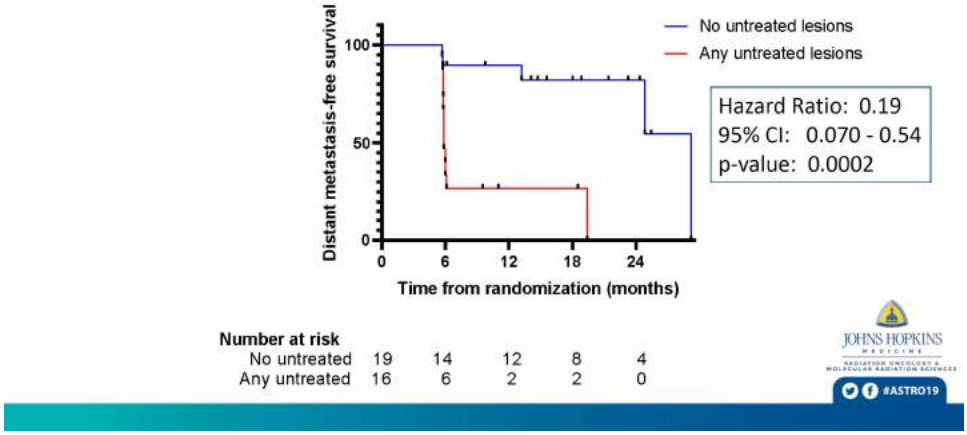
Total consolidation improved distant metastasis-free survival



CONCLUSIONS

- Improvements in technology allow the precise delivery of ablative radiotherapy in prostate cancer, requiring just a few doses
- Modern stereotactic platforms deliver **SBRT** with sub-mm precision, achieving better cancer control and less side effects
- In organ-confined prostate cancer, SBRT yields excellent cancer control and few side effects 10 years after treatment
- Stereotactic RT (aka **SAbR** = **S**tereotactic **Ab**lative **R**adiotherapy) can also safely ablate metastatic deposits
- In patients with 1-5 metastases (oligometastases), SAbR (SBRT):
  - Yields prolonged cancer remission
  - May delay new metastases, and improve survival

9:23am – 9:44am

How to Manage PSA Recurrence and Active Surveillance

Julie N. Graff, MD

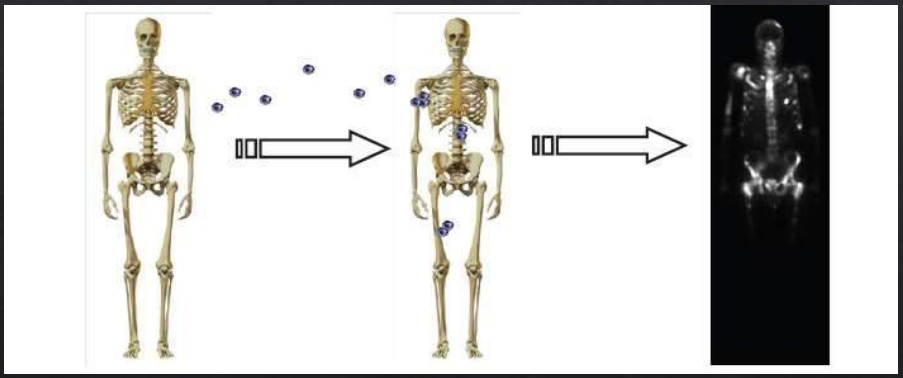
How to Manage PSA Recurrence + Active Surveillance

Julie N. Graff, MD
Section Chief of Hematology/Oncology
VA Portland Health Care System
Associate Professor of Medicine
Knight Cancer Institute, Oregon Health & Science University

Scope of this discussion

- Definition of "PSA Recurrence" and other commonly used terms
- Natural History of PSA Recurrence (without intervention)
- Using the PSA to predict prostate-specific mortality
- Androgen Deprivation Therapy (ADT) in patients with PSA Recurrence
- Toxicities of ADT
- Predicting life span by response to ADT
- Active Surveillance

What is a PSA recurrence?



No evidence of disease:
Nothing on imaging
PSA undetectable

PSA Recurrence:
Nothing on imaging
PSA detectable

Metastatic Cancer:
Spread on imaging
PSA detectable

Adapted from Saylor. Journal of Clinical Oncology 2011; 29(27): 3705.

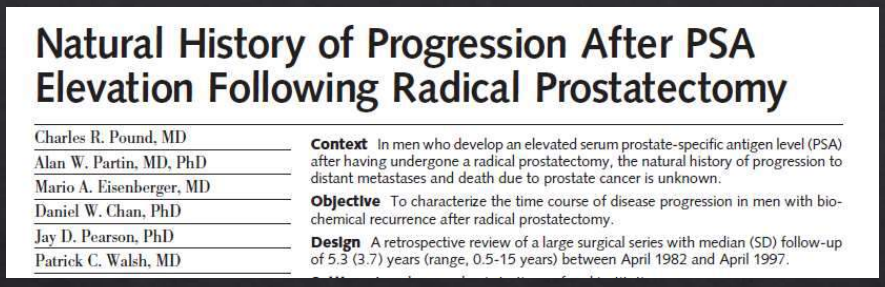
What is the definition of PSA recurrence?*

- After radical prostatectomy, 0.2 ng/ml
  - Freedland. Urology 2003; 61(2): 365.
- After radiation, three consecutive rises with the time of failure being the midpoint between the PSA nadir and the first rise.
  - Int J Radiat Oncol Biol Phys 1997; 37(5): 1035.

*Some disagreement

Example

- 71 yo man diagnosed with prostate cancer in 2013. He underwent a radical prostatectomy that revealed Gleason 4+4 disease and no lymph nodes involved. After the surgery, his PSA was undetectable.
- In January 2016, his PSA became 0.1 ng/ml.
- Repeat in March 2016 was 0.5 ng/ml.
- What does this mean?



Natural History of Progression After PSA Elevation Following Radical Prostatectomy

Charles R. Pound, MD
Alan W. Partin, MD, PhD
Mario A. Eisenberger, MD
Daniel W. Chan, PhD
Jay D. Pearson, PhD
Patrick C. Walsh, MD

Context In men who develop an elevated serum prostate-specific antigen level (PSA) after having undergone a radical prostatectomy, the natural history of progression to distant metastases and death due to prostate cancer is unknown.

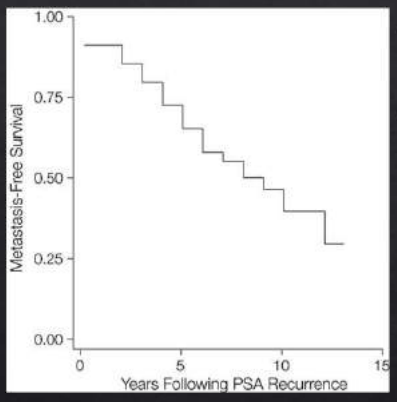
Objective To characterize the time course of disease progression in men with biochemical recurrence after radical prostatectomy.

Design A retrospective review of a large surgical series with median (SD) follow-up of 5.3 (3.7) years (range, 0.5-15 years) between April 1982 and April 1997.

Pound. JAMA 1999; 28 (17): 1591.

This study included **1997 men** who had a radical prostatectomy at Johns Hopkins between 1982 and 1997. They were followed for a mean of **5.3 years** (range of 0.5-15 years).

Of the 1997 men, **315 (15%) had a biochemical recurrence**, defined as a PSA ≥ 0.2 mg/ml. Eleven of them received early hormonal therapy and were not included in this analysis.

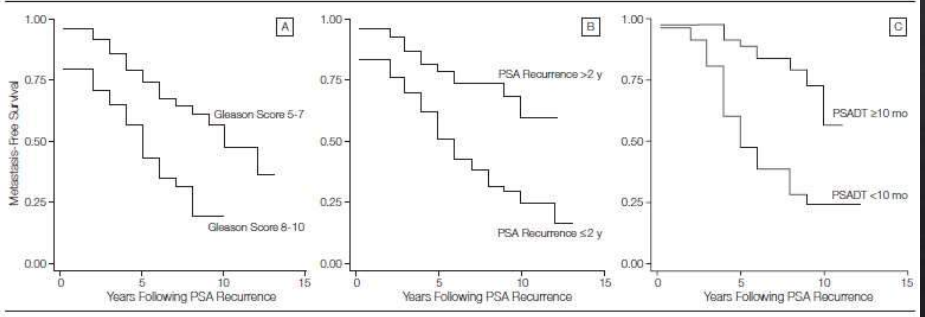


- The median time to developing metastases was **8 years.**
- In this analysis, 103 (34%) did develop metastases.

Pound. JAMA 1999; 281 (17): 1591.

Subgroup Analysis

Figure 3. Actuarial Likelihood of Metastasis-Free Survival in 304 Men With Prostate-Specific (PSA) Antigen Elevation After Radical Prostatectomy



A, Based on Gleason scores in the radical prostatectomy specimen ($P<.001$). B, Based on years until initial biochemical recurrence ($P<.001$). C, Based on prostate-specific antigen doubling time (PSADT) ($P<.001$).

Pound. JAMA 1999; 281 (17): 1591.

Treating the rising PSA

- Options:
  - Some may be candidates for salvage curative therapies (surgery or radiation)
  - Some may choose to watch the PSA
  - Others start androgen suppression therapy

There may not be an obvious choice. Personal preference is important.

Toxicities from Androgen Deprivation Therapy (ADT)

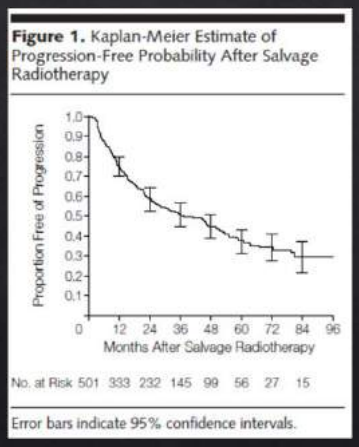
Those you can see	Those you can feel	Other
Weight gain	Hot flashes	Bone density loss
Muscle loss	Fatigue	Lipid changes
Hair pattern changes	Depression	Decreased insulin sensitivity
Fat redistribution	Mental slowing	Heart disease(?)
Testicle/penis size decrease	Anemia	

What can you do to stay healthy?

- Talk to your urologist or oncologist about all of your concerns.
- Exercise- weight bearing is best for the bones, but it is not always possible.
- Take supplemental calcium and vitamin D to protect your bones.
- Eat healthy foods- beware of weight gain.
- Continue to be seen by your primary care physician so that you can optimize your cardiovascular risk factors (blood pressure, cholesterol, smoking cessation, etc).

What About "Salvage" Radiation?

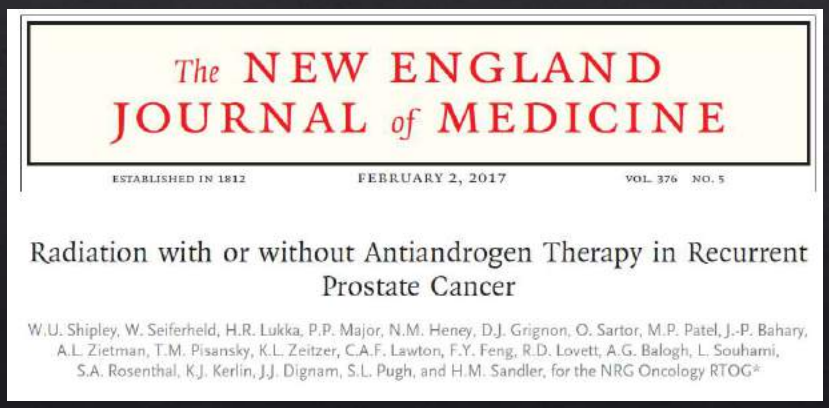
Salvage Radiation Therapy



JAMA. 2004;291:1325-1332

- Statistics
- Some may not do well
  - Gleason 8, 9, 10
  - Pre-treatment PSA > 2.0 ng/ml
  - Negative margins
  - PSA doubling time ≤ 10 months
  - Seminal vesicle invasion

Bicalutamide with Salvage RT



Patients and Treatment

- Men who had undergone **radical prostatectomy** (surgery) with lymph node dissection and then had biochemical recurrence.
- Stage T2 (confined to the prostate but also with a positive surgical margin) or T3 (with histologic extension of the tumor beyond the prostatic capsule) without nodal involvement.
- Detectable PSA at least 8 weeks after surgery that was 0.2 to 0.4 ng/ml.
- Received radiation plus either bicalutamide 150 mg daily or placebo for 2 years.

Outcomes

- 840 patients were randomized from 1998-2003
- 760 patients participated (384 in the bicalutamide group, 376 in the placebo group)
- There was more breast enlargement and tenderness in the bicalutamide group.

Bicalutamide plus radiation versus radiation alone

Table 2. Antitumor Efficacy with Respect to Key Secondary End Points at 12 Years.

End Point and Subgroup	Bicalutamide Group		Placebo Group		Hazard Ratio (95% CI)	P Value
	Patients at Risk	Rate of End Point	Patients at Risk	Rate of End Point		
	no.	%	no.	%		
Metastatic prostate cancer						
All patients	384	14.5	376	23.0	0.63 (0.46–0.87)	0.005
Gleason score						
2–6	111	7.8	103	16.5	0.64 (0.30–1.36)	0.25
7	205	15.4	208	19.8	0.80 (0.52–1.22)	0.31
8–10	67	21.2	64	44.7	0.35 (0.18–0.67)	0.001
PSA level at trial entry						
<0.7 ng/ml	210	13.4	195	17.1	0.76 (0.47–1.22)	0.26
0.7–1.5 ng/ml	119	17.4	118	28.4	0.67 (0.40–1.12)	0.13
>1.5 ng/ml	55	13.1	63	31.1	0.36 (0.15–0.84)	0.01
Positive surgical margin						
No	96	22.9	95	31.1	0.79 (0.47–1.32)	0.38
Yes	288	11.8	281	20.3	0.56 (0.38–0.84)	0.005
Death from prostate cancer*	384	5.8	376	13.4	0.49 (0.32–0.74)	<0.001
Death from other causes	384	17.9	376	15.3	1.10 (0.79–1.53)	0.58

* Death from prostate cancer included all deaths from prostate cancer or treatment complications as well as death from an unknown process in patients with active prostate cancer on the basis of central review.

What Happens When The Shots Stop Working?

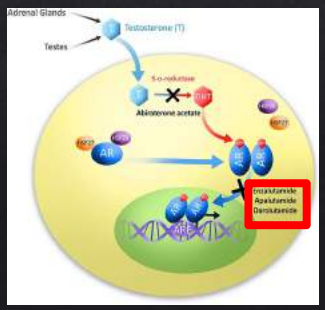
Return to the Case

71 yo man diagnosed with prostate cancer in 2013. He had a radical prostatectomy, but his PSA came up in 2016.

- He receives salvage radiation with bicalutamide in 2016, but his PSA recurs in 2018.
- At a PSA of 4 ng/ml, he starts androgen deprivation therapy with Lupron and his PSA decreases to undetectable.
- His PSA initially decreases to undetectable, but then it starts to climb even though he continues to receive Lupron.

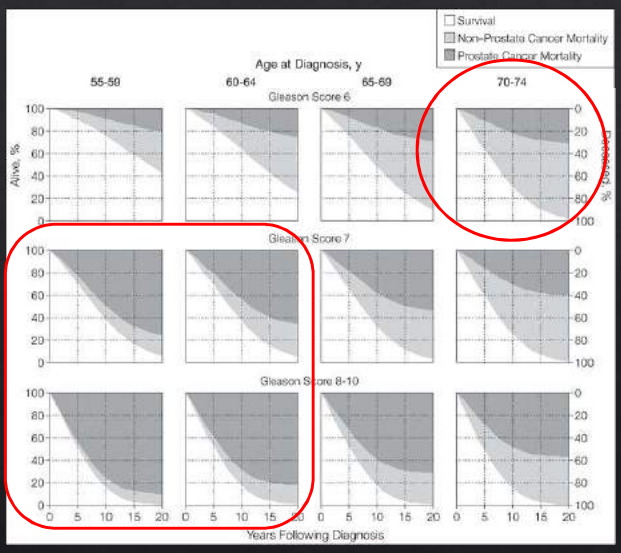
Three New Options

- **Enzalutamide** (=Xtandi), **darolutamide** (=Nubeqa) or **Apalutamide** (=Erleada)
- All block interactions with the Androgen Receptor
- All delay the time to metastatic disease, decrease the PSA, and help people live longer
- All add toxicity



Active Surveillance
(Watchful Waiting)

Active Surveillance



Albertsen, P. C. et al. JAMA 2005;293:2095-2101.

Active Surveillance

- Patient selection: low PSA, low Gleason, low stage T1c-T2a
- PSA, DRE q 3 months x 1 years, then q 6 months
- Repeat biopsy at years 1, 3, 6, 9, 12….
- Treatment if PSA increasing rapidly or biopsy shows more aggressive cancer.
  - Radical Prostatectomy
  - Radiation Therapy

Inclusion Criteria AS Protocols

AS protocol	Clinical stage	PSA	Gleason	Positive cores	Core positivity (%)
Tosoian et al. (Johns Hopkins)	<T2a	–	≤3 + 3	≤2	≤50
Klotz et al. (University of Toronto)		≤10*	≤3 + 3*	–	–
Bul et al. (PRIAS)	≤T2	≤10	≤3 + 3	≤2	
Dall'Era et al. (UCSF)	≤T2a	≤10	≤3 + 3	≤33%	≤50
Berglund et al. (MSKCC)	≤T2a	≤10	≤3 + 3	≤3	≤50
Van As et al. (Royal Marsden)	≤T2a	≤15	≤3 + 3	≤50%	–
Soloway et al. (Miami)	≤T2a	≤10	≤3 + 3	≤2	≤20

*Until 1999, PSA ≤15 and Gleason ≤3+4 were used.

Follow-up for AS Protocols

Protocol	DRE	PSA	Biopsy	Imaging techniques
Tosoian et al. (Johns Hopkins)	6 months	6 months	Annual	
Klotz et al. (University of Toronto)	3 months (2 years) 6 months if PSA stable	3 months (2 years) 6 months if stable	Confirmation: 6–12 months Repetition: 2 years (to age 80 years)	MRI optional
Bul et al. (PRIAS)	3 months (2 years) 6 months (after)		1, 4, and 7 years If PSADT = 3–10, repeat biopsy	
Dall'Era et al. (UCSF)	3 months	3 months	1–2 years (since 2003)	TRUS 6–12 months
Berglund et al. (MSKCC)			Confirmation: 3 months Repetition: annual	MRI prior to confirmation biopsy
Soloway et al. (Miami)	3 months (2 years) 6 months if PSA stable	3 months (2 years) 6 months if stable	Confirmation: 9–12 months Repetition: annual	
Carter et al. (Johns Hopkins)	6 months	6 months	Annual	

Romero-Otero J, et al. Int J Urol 2015; Epub Nov 2015

Criteria for Progression

Protocol	Gleason	Positive cores	Percentage of core affected	PSADT
Tosoian et al. (Johns Hopkins)	>6	>2	>50	–
Klotz et al. (University of Toronto)	4 + 3	–	–	<3 yrs
Dall'Era et al. (UCSF)	Increase	–	–	–
Soloway et al. (Miami)	>3 + 3	>2	–	–
Thomsen et al. (University of Copenhagen)	≥4 + 3	>3	–	<3/5 yrs

Romero-Otero J, et al. Int J Urol 2015; Epub Nov 2015

Long-term Follow-up of AS Cohort
University of Toronto (Sunnybrook)

- N=993 (220 followed ≥10 yrs, 50 more than 15 yrs)
- Median follow-up: 6.4 years
- Mets in 2.8% at median 7.3 yrs (from dx)
- 15 deaths (1.5%) from prostate cancer
- Cumulative hazard non-prostate to prostate cancer mortality: 9.2:1

Laurence Klotz et al. JCO 2015;33:272-277

Thank you!

9:44am – 10:03am

Contemporary Treatment for High-Risk Localized Prostate Cancer

Dan Lin, MD

Contemporary Treatment for High Risk Localized Prostate Cancer

Daniel W. Lin, MD
Professor and Chief of Urologic Oncology
Pritt Family Endowed Chair in Prostate Cancer Research
Director, Institute for Prostate Cancer Research
University of Washington

UNIVERSITY of WASHINGTON

Agenda

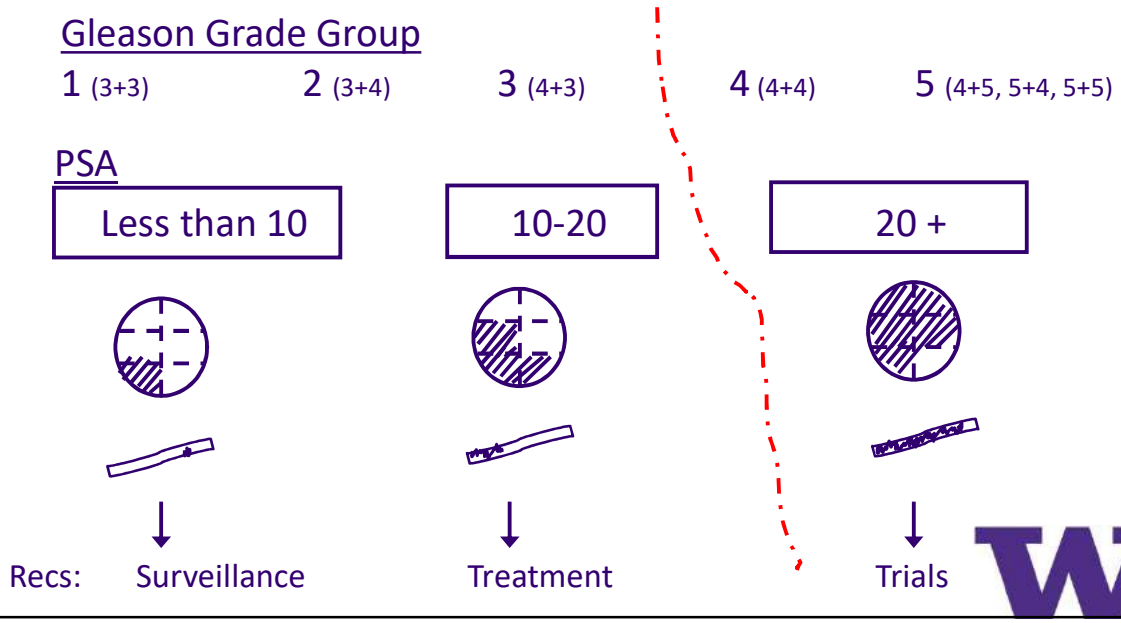
- Introduce how to determine if a cancer is “high risk”
- Describe current treatment options and outcomes
- Outline future directions in improving therapy and personalizing approach in high risk prostate cancer

UNIVERSITY of WASHINGTON

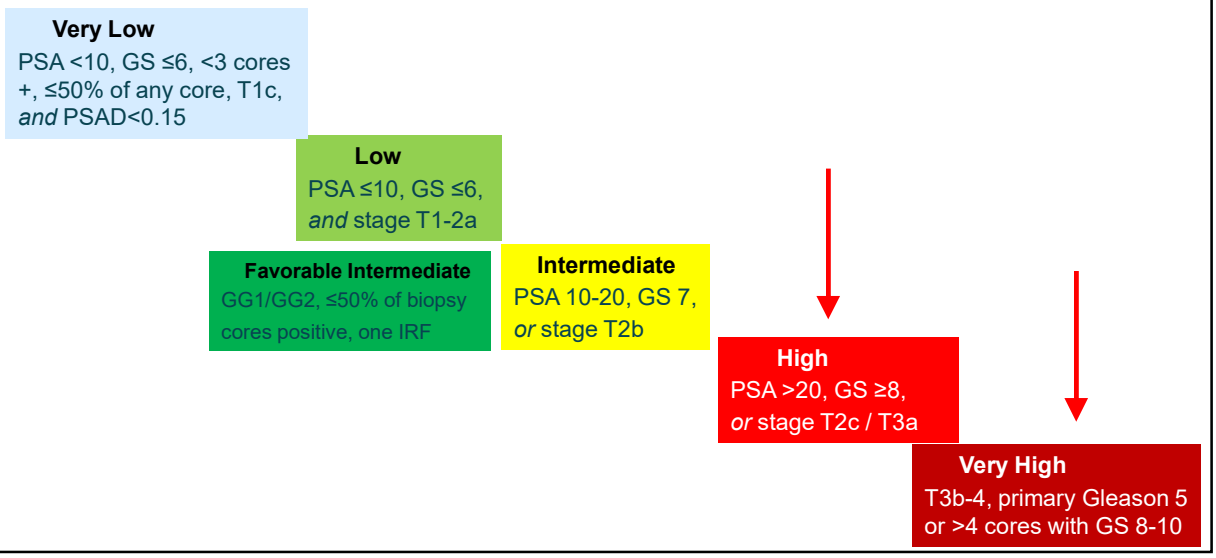
Factors that affect prostate cancer behavior

- Stage: what is felt on digital/manual examination
- Grade: what the cancer looks like under the microscope
- PSA: how high (or low) the blood test is
- Biopsy information: how many biopsies had cancer, how much of each biopsy

Putting it all together



Clinical Risk Assessment: AUA/NCCN/D'Amico



Agenda

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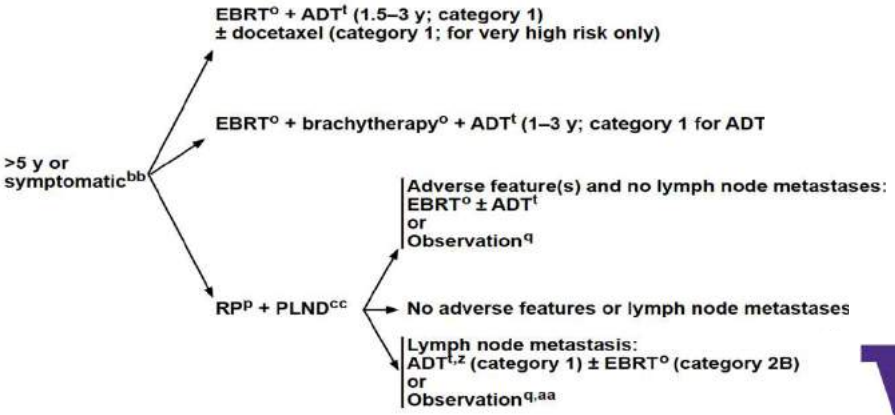
National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2020
Prostate Cancer

HIGH OR VERY HIGH RISK GROUP

EXPECTED PATIENT SURVIVAL[k]	INITIAL THERAPY	ADJUVANT THERAPY



The NEW ENGLAND JOURNAL of MEDICINE

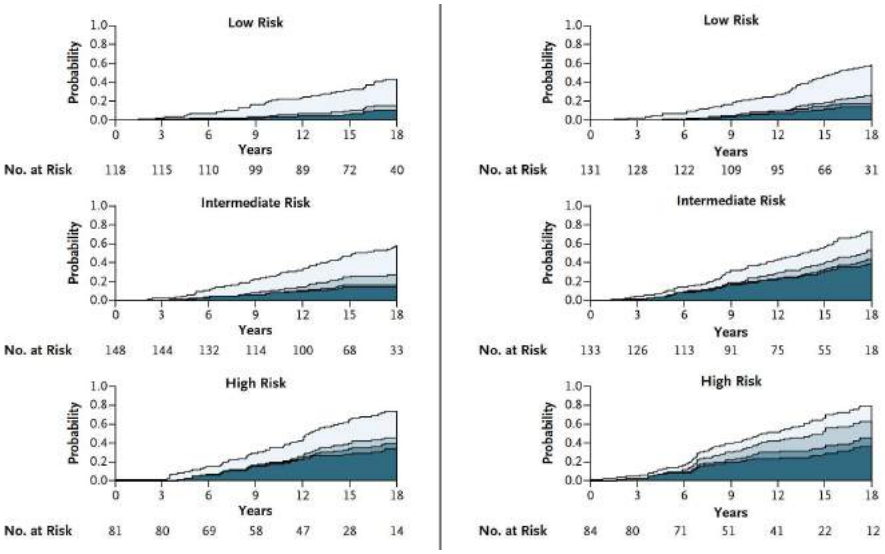
ORIGINAL ARTICLE

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Lars Holmberg, M.D., Ph.D., Mirja Ruutu, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Stefan Bratell, M.D., Ph.D., Anders Spångberg, M.D., Ph.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Hans Garmo, Ph.D., Juni Palmgren, Ph.D., Hans-Olov Adami, M.D., Ph.D., Bo Johan Norlén, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D., for the Scandinavian Prostate Cancer Group Study No. 4*

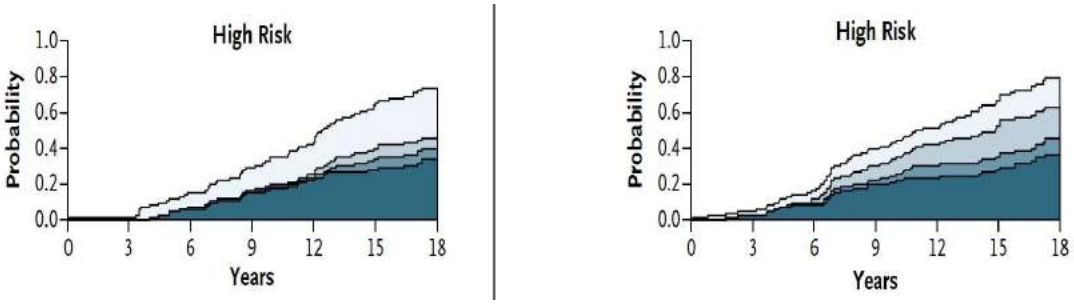
- 695 men randomized to surgery (347) or “watchful waiting” (348)
- Localized disease, all risk groups (low, intermediate, high)
- Outcomes assessed after approx 13 years

Prostate Cancer Mortality by Risk: Radical Prostatectomy vs. Watchful Waiting



Prostate Cancer Mortality in High Risk Cancer:

Radical Prostatectomy vs. Watchful Waiting



Outcomes of Surgery and Radiation in High Risk Prostate Cancer

- At least 50% recurrence after treatment with “monotherapy” (radiation or surgery alone)
- Testosterone suppression improves radiation outcomes
- Addition of radiation after surgery may improve outcomes
- Tumor dissemination likely early event

Theoretical Advantages of Surgery

- Influence of cancer in the prostate on (future) spread of cancer?
- Selection of virulent/resistant cells in prostate, in response to treatments, that may influence future metastatic disease?
- Availability of radiation after surgery (not vice versa)

Agenda

- Introduce how to determine if a cancer is “high risk”
- Describe current treatment options and outcomes
- Outline future directions in improving therapy and personalizing approach in high risk prostate cancer

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JAMA Oncology | Original Investigation

Diagnostic Accuracy of ^{68}Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection

A Multicenter Prospective Phase 3 Imaging Trial

Thomas A. Hope, MD; Matthias Eiber, MD; Wesley R. Armstrong; Roxanna Juarez, MD; Vishnu Murthy; Courtney Lawhn-Heath, MD; Spencer C. Behr, MD; Li Zhang, PhD; Francesco Barbato, MD; Francesco Ceci, MD; Andrea Farolfi, MD; Sarah M. Schwarzenböck, MD; Marcus Unterrainer, MD; Helle D. Zacho, MD, PhD; Hao G. Nguyen, MD; Matthew R. Cooperberg, MD; Peter R. Carroll, MD, MPH; Robert E. Reiter, MD; Stuart Holden, MD; Ken Herrmann, MD; Shaojun Zhu, MSc; Wolfgang P. Fendler, MD; Johannes Czernin, MD; Jeremie Calais, MD

- 785 intermediate and high-risk patients underwent PSMA PET
  - 277 (36%) underwent surgery
    - 49 (18%) with positive ^{68}Ga-PSMA PET
    - 75 (27%) pathologically positive nodes
  - Sensitivity 40%, Specificity 95%, PPV 75%, NPV 81%

Hope et al, JAMA Oncology, 2021

VA Cooperative Studies # 553: Adjuvant Chemotherapy in High Risk Disease

cT1-T2b

↓

RRP→

- pT3b or pT4
- pT3a and G7-10
- pT2R1, G8-10
- Preop PSA > 20
- Must be Node (-)

Post-RP:
PSA ≤ 0.1

RANDOMIZE

1:1

Observation
(Standard of Care)

Docetaxel Chemotherapy + Prednisone
(Duration of treatment = 6 cycles)

n=297

PI's: D. Lin, B.Montgomery

Scandanavian Prostate Cancer Group Trial #12 Docetaxel compared with Observation after Prostatectomy

RRP→

- pT3b or pT4
- pT3a, GI ≥ 4+3
- pT2R1, GI ≥ 4+3
- PLND if PSA > 10

Post-RP: PSA < 0.5

RANDOMIZE

Observation
(Standard of Care)

Docetaxel Chemotherapy
(Duration of treatment = 6 cycles)

n=459

PI: G. Ahlgren

RTOG 0521: Adjuvant Docetaxel

- Gleason ≥ 9, PSA ≤ 150, any T category
- Gleason 8, PSA < 20, ≥ T2
- Gleason 7-8, PSA 20-150, any T category

RANDOMIZE

→ RT + Hormonal therapy (2 yrs)

→ RT + Hormonal therapy (2 yrs) + 6 cycles docetaxel

Docetaxel 75mg/m2 q 3wks x 6 cycles

n = 563

CALGB 90203: Phase III Study of Radical Prostatectomy alone vs. ADT and Docetaxel in High Risk Localized Prostate Cancer

- **cT1-3a,NX,M0**
- **Kattan nomogram: ≤60% PFS at 5 yrs**

RANDOMIZE

→ Radical Prostatectomy

→ Neoadjuvant Docetaxel 70 mg/m2 x 8 cycles + ADT x 6 months → Prostatectomy

N =750

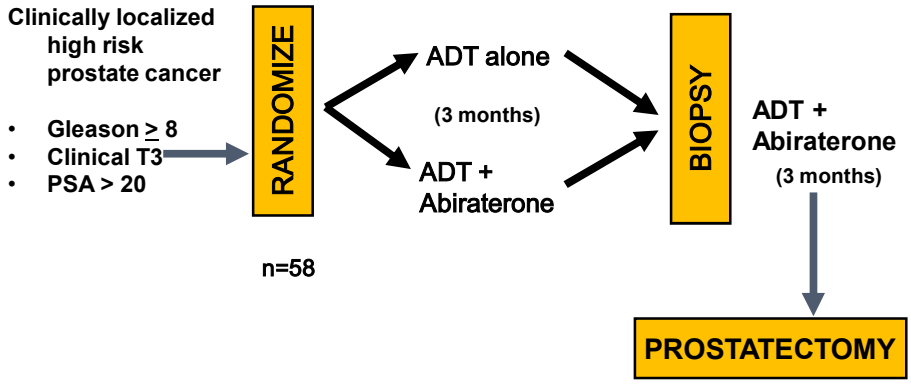
PI: J. Eastham

Summary of Chemotherapy Trials (before/after treatment)

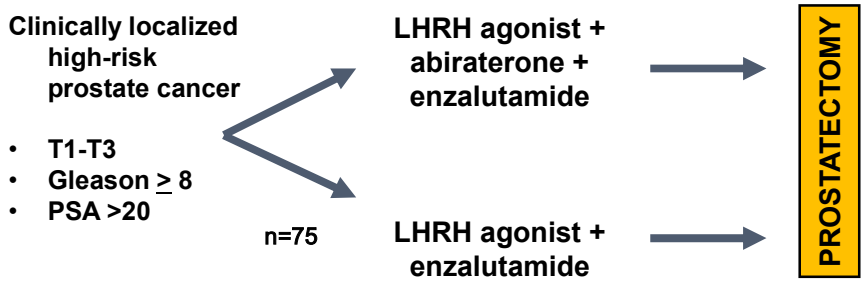
- Slight improvement in outcome if used after radiation
- Conflicting results in use after surgery
- ? Potential advantage in use before surgery ?
- Bottom line: chemotherapy not considered standard of care before or after surgery/radiation

Targeted Androgen Pathway Suppression (TAPS)

Maximal Androgen Blockade with Abiraterone before RP

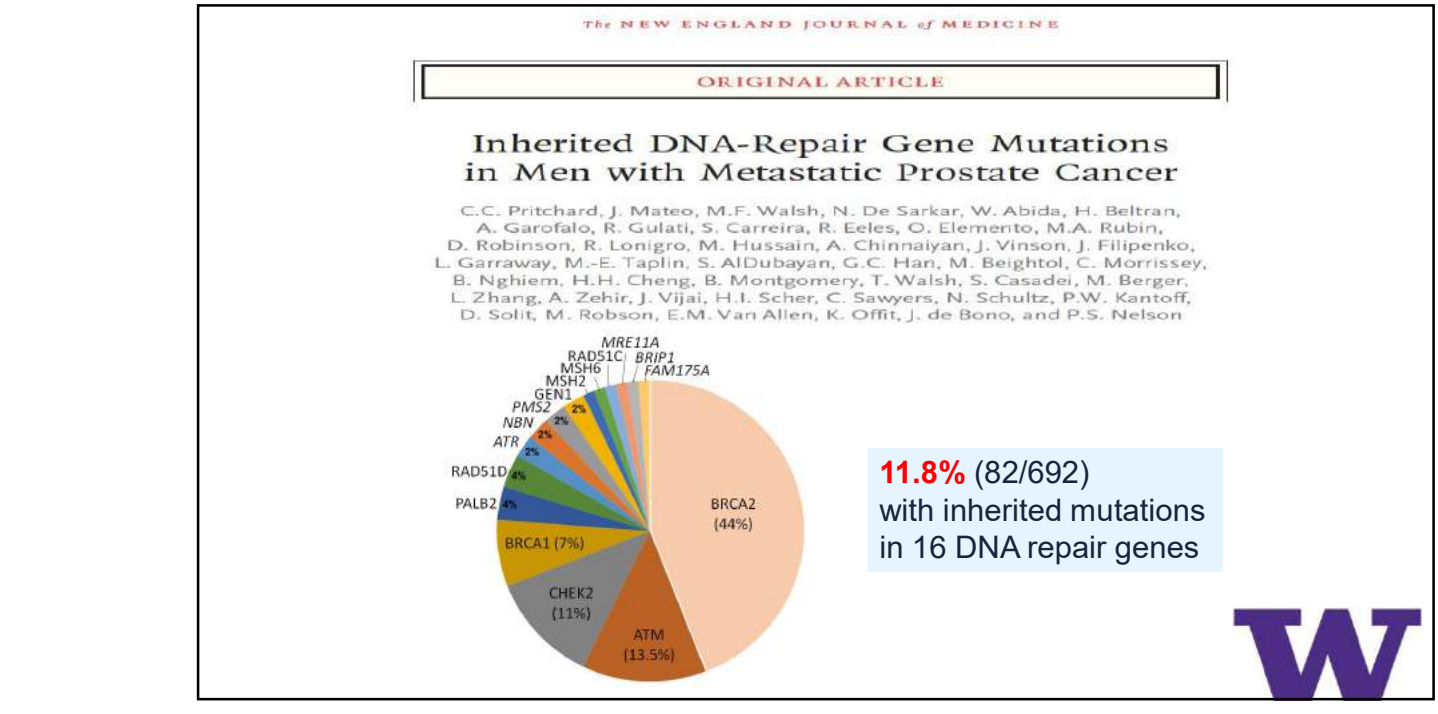


Neoadjuvant Complete Androgen Pathway Suppression



Summary of Hormone Therapy Trials

- Major response to hormonal treatment in <u>subset</u> of patients
  - Little to no cancer left in the prostate!
- More potent testosterone suppression = more response in prostate
- Suggestion of decreased recurrence with potent testosterone suppression



Biomarker-Driven Neoadjuvant Strategies in High-risk Prostate Cancer

- Genomic sequencing → match molecularly targeted agents to distinct genomic and molecular aberrations
  - Most defects arise in small proportion of pts (10-20%)
  - Clinical trials difficult with multiple single-agent, single-arm studies
- Opportunity to test ability of novel combinations, based on actionable genomic alterations, to increase response rates

Genomic Umbrella Neoadjuvant Study (GUNS) to Pathologically Define Conditional Lethality of Targeted Therapy

Multi-arm, multi-stage trial to evaluate targeted therapeutics in biomarker pre-selected patients with high risk localized PCA

Primary endpoint - complete (pCR) rate

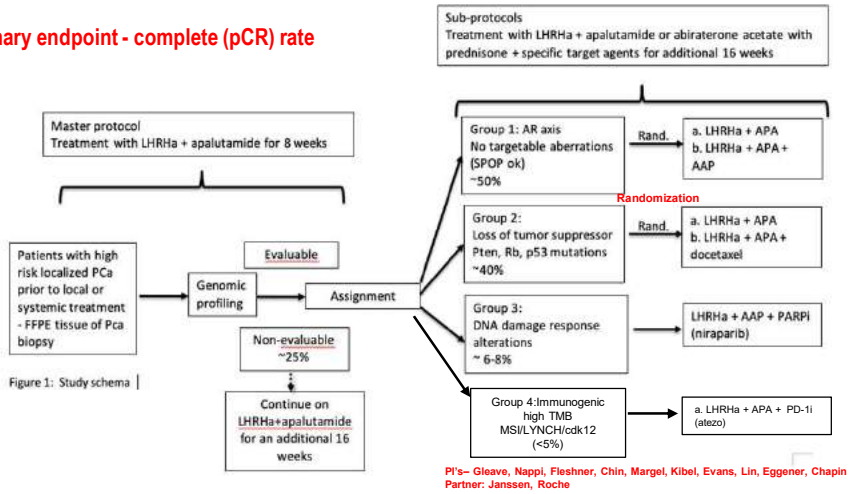


Figure 1: Study schema

PI's– Gleave, Nappi, Fleshner, Chin, Margel, Kibel, Evans, Lin, Eggener, Chapin
Partner: Janssen, Roche

Take Home Points

- High-risk disease issues
  - Inadequate primary therapy, early tumor dissemination
- All standard therapies associated with substantial recurrence
- Future:
  - Neoadjuvant or adjuvant therapy in high-risk disease
  - Personalized therapies (e.g. emerging biomarkers, BRCA and related genes)
  - Await clinical trial results

Thank You!

•Questions?

•dlin@uw.edu

10:33am – 10:56am

What Can Blood Tests Tell Us About Metastatic Prostate Cancer: What's New?

Alex Wyatt, PhD

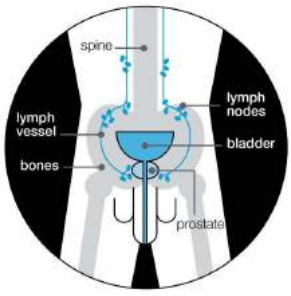
Pacific Northwest Prostate Cancer patient conference
2nd October 2021

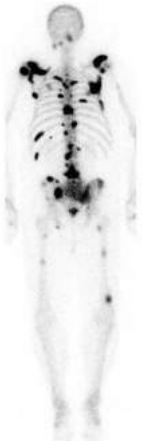
What is a biomarker?

Dr Alex Wyatt
Assistant Professor, University of British Columbia
Senior Research Scientist, Vancouver Prostate Centre
Scientist, Michael Smith Genome Sciences Centre, BC Cancer

Metastatic (advanced) prostate cancer

- Prostate cancer is very common but is typically localized at diagnosis
  - Non-lethal if appropriately managed / surveyed
- In 10% of cases the cancer spreads outside of the prostate
  - Can be lethal, given sufficient time





Several types of biomarkers in cancer

	Risk	Diagnostic	Prognostic	Predictive	Response	Safety
Goal	Identify cancer susceptibility	Indicate type of cancer	Estimate cancer aggression	Predict efficacy from treatment	Monitor therapy benefit	Indicate toxicity from treatment
Example	Inherited mutations in BRCA2	Tissue biopsy pathology	Extent of disease by Imaging (CT, MRI, PET)	HRR gene mutations	PSA decline	Patient reported side-effects

- Somatic alterations are not always simple to *identify* or *characterize*
- Cancer biology is complex and cannot always be reduced to biomarker 'positive' vs 'negative'

Increasingly complex therapeutic landscape

- Metastatic prostate cancer is driven by persistent AR signaling
- Potent AR inhibition extends overall survival, but resistance evolves
- Shifting consensus on timing of taxane chemotherapy and AR inhibitors

Not all patients derive benefit from all treatments

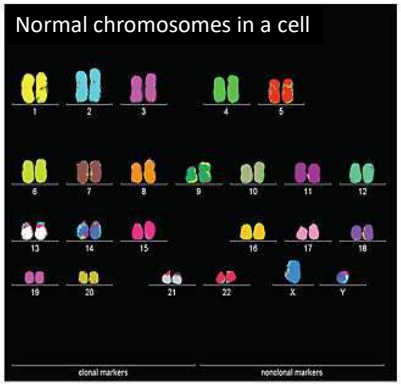
Need for 'biomarkers' to predict disease response to treatment

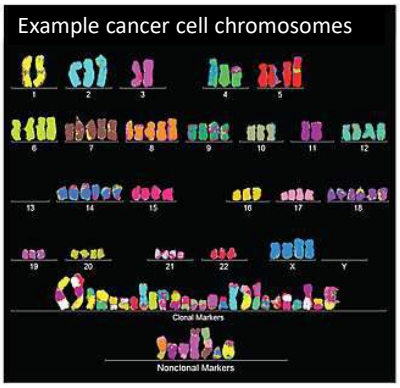
To help us practice precision medicine and individualize clinical management

Swami *et al.*, Trends in Cancer 2020

Cancer is a disease of the genome

- Mutations to the DNA can result in a proliferative cancer cell
- The whole genome is often remodelled in advanced disease





Sanders R. "Are cancers newly evolved species?" Berkley News. Available at: https://news.berkeley.edu/2011/07/26/are-cancers-newly-evolved-species/ [Accessed February 2021].

Tumour and patient 'heterogeneity' helps explain differential therapy response

- Each cancer and person is different at the genome level (and every other level)
- This can affect therapy response
- Particular relevance for new targeted therapies – the target or vulnerability must be present!

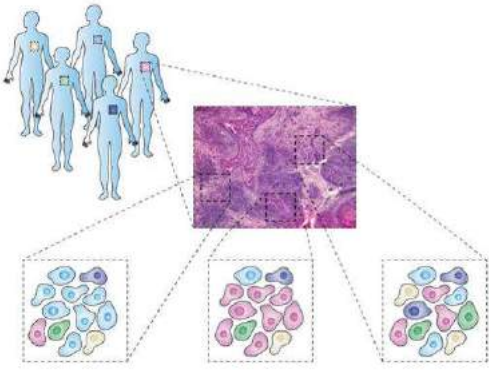


Image by Simona Cristea, Dana-Farber Cancer Institute

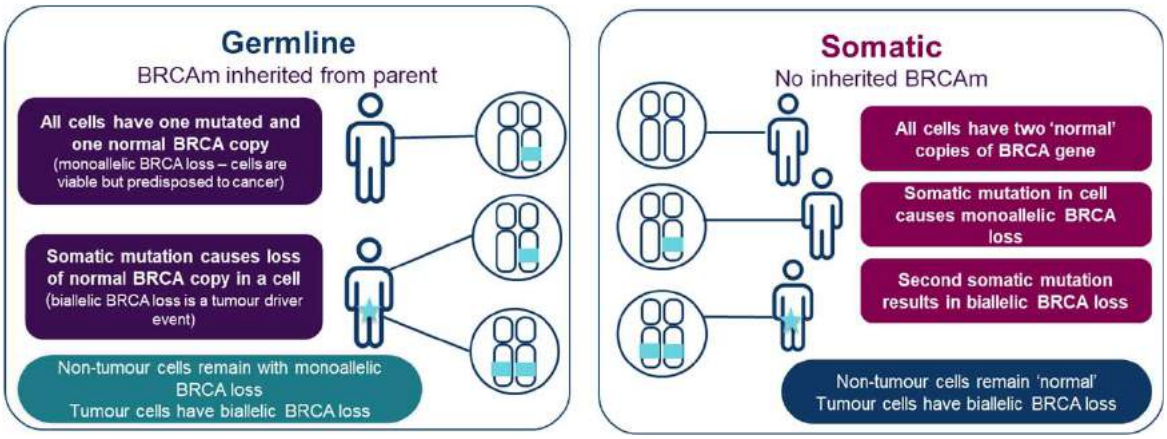
Homologous recombination repair (HRR) gene mutations are a new predictive biomarker

- Mutations in 'HRR genes' can result in cancer cell vulnerability to a class of therapy called PARP inhibitors
- The detection of HRR gene mutations in a person's cancer is a biomarker to predict heightened sensitivity to PARP inhibitors

HRR=homologous recombination repair; PARP=poly-ADP ribose polymerase

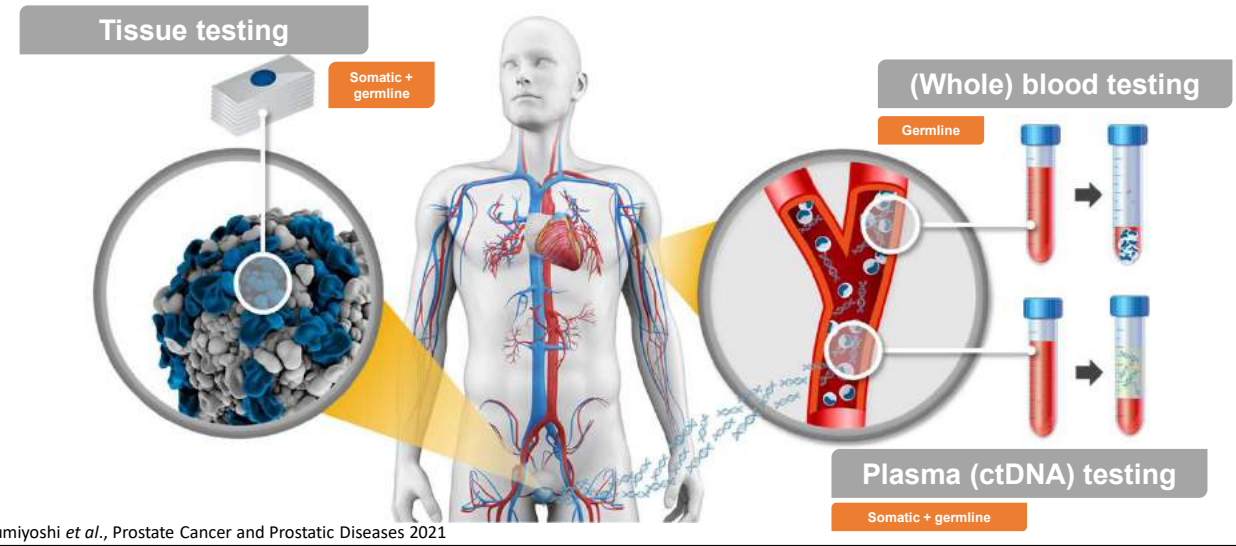
1. Lord CJ, Ashworth A. *Science*. 2017;355(6330):1152-1158; 2. De Bono JS, et al. *N Engl J Med*. 2020;382:2091-102

BRCA2 mutations in prostate cancer can be derived from germline or somatic origin



Jonsson P et al. Nature 2019;571:576–579; Warner EW et al. BJU Int. 2019;123:769–776; Mateo J et al. Eur Urol. 2017;71:417–425.

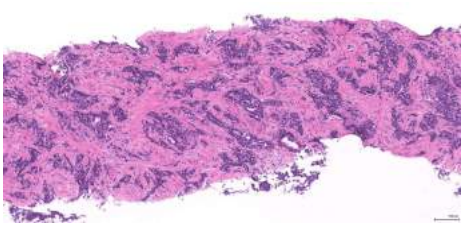
There are several ways to identify gene mutations in cancer

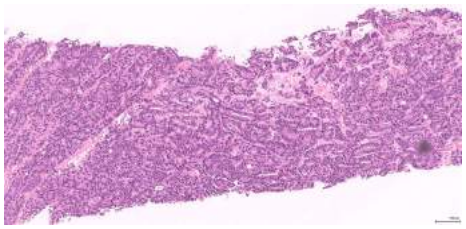


Sumiyoshi *et al*., Prostate Cancer and Prostatic Diseases 2021

Biomarker testing is not always conclusive; more than one test may be required

- Germline tests will miss all the cancer-only mutations
- Tissue tests can 'fail' due to poor quality sample
- Plasma ctDNA tests can 'fail' due to insufficient sample



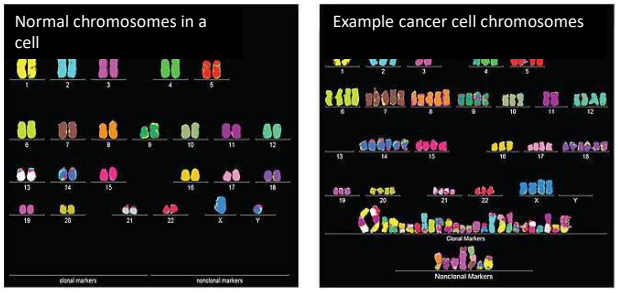


Sumiyoshi *et al*., Prostate Cancer and Prostatic Diseases 2021
Hussain M, *et al*. Presented at ASCO GU 2020; Annala *et al*., Cancer Discovery 2018

Why is biomarker development so confusing?

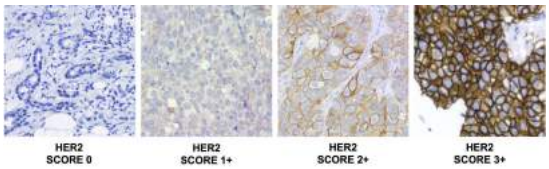
1. Cancer cannot always be 'binarized'

Cancer is a complex ecosystem with redundancies



Why is biomarker development so confusing?

1. Cancer cannot always be 'binarized'
2. <u>Terminology</u> evolves and biomarkers are varied



- E.g. often used interchangeably: **Molecular** versus **Genomic** versus **Genetic**
- Varying mutation reporting standards: **Pathogenic** versus **deleterious** versus **benign**
- Use of **DNA** versus **RNA** versus **tissue immunohistochemistry**

Why is biomarker development so confusing?

1. Cancer cannot always be 'binarized'
2. Terminology evolves and biomarkers are varied
3. No gold standard for validation
4. Clinical trials take a long time
5. Tests compete against each other

How is a patient to understand when a test 'works'?!

Why is biomarker development so confusing?

1. Cancer cannot always be 'binarized'
2. Terminology evolves and biomarkers are varied
3. No gold standard for validation
4. Clinical trials take a long time
5. Tests compete against each other
6. Economic benefit not always clear
7. Explain-ability matters!

Why should we be excited about genomic biomarker testing?

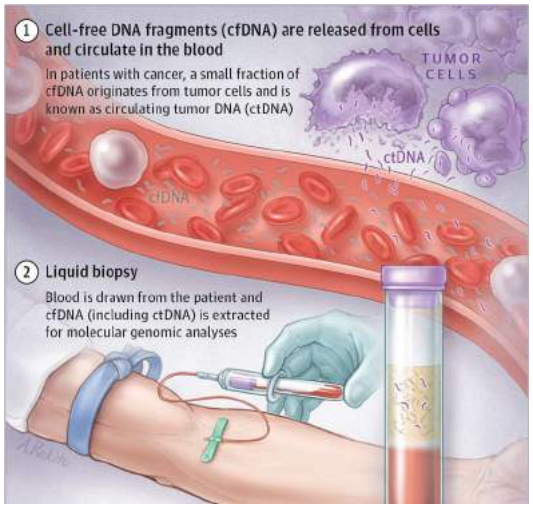
1. New generation of clinicians are trained in genomics
2. Patients and advocates are more comfortable with genomics results
3. Terminology is becoming more consistent
4. Communication is improving (visuals, reports, education)

The need to perform biomarker testing is clear

Our new collective task is to implement practical solutions to test more people with advanced cancers and therefore better treat/manage the subset with 'actionable' mutations

Boutros P. Genome Res. 2015. 25: 1508-1513

Plasma circulating tumour DNA (ctDNA) indicates the presence of cancer



…a minimally-invasive source of material to study the cancer

Analysis of blood plasma ctDNA can tell you about biological characteristics of the cancer

Husain and Velculescu, JAMA 2017; 318:1272-1274

How can blood ctDNA tests help?

- Improve cancer screen in at-risk populations (e.g. inherited cancer)
- Detect residual disease after surgery / radiation
- Estimate the burden of cancer in a patient
- Monitor for response / resistance to therapy
- Identify therapy sensitivity – predict treatment success / failure

How can blood ctDNA tests help?

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- Monitor for response / resistance to therapy
- **Identify therapy sensitivity – predict treatment success / failure**

Blood ctDNA research in the Pacific Northwest

Dr Kim Chi, responsible for collection of over 3000 plasma ctDNA samples

The UBC Vancouver Prostate Centre ctDNA research team – mostly computer scientists / data analysts
Photo: July 2021

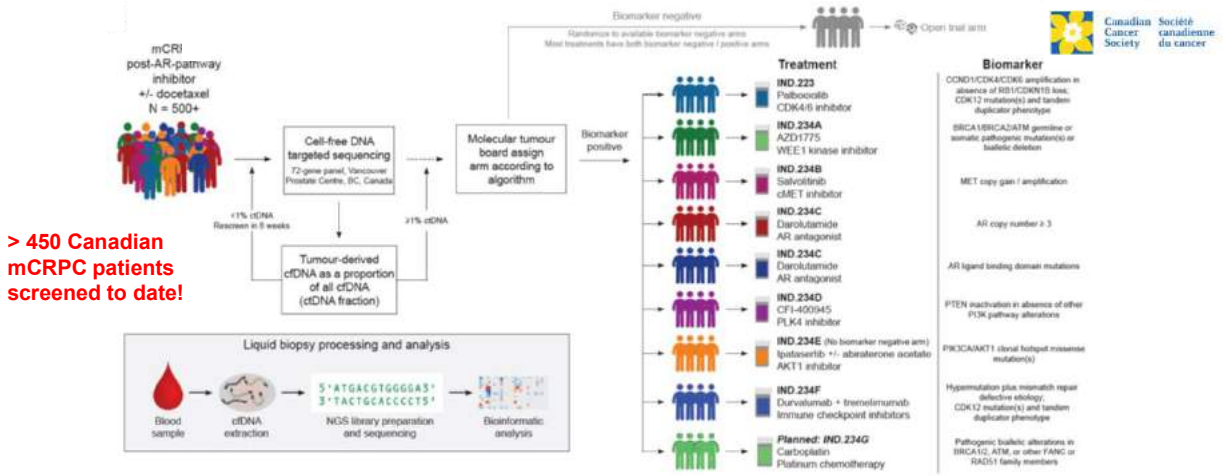
Blood ctDNA research in the Pacific Northwest

Dr Kim Chi, responsible for collection of over 3000 plasma ctDNA samples

It takes time to develop new biomarkers!

- Design new technology in the lab
- Develop new computer software
- Test on synthetic samples
- Pilot tests on patient samples (feasibility)
- Correlative studies (hypothesis generating)
- Prospective clinical validation (hypothesis validating)

The first precision oncology clinical trial testing ctDNA in prostate cancer



> 450 Canadian mCRPC patients screened to date!

Adaptive design, add arms as needed to rapidly test new agents

Kim Chi, Lesley Seymour, many others
ClinicalTrials.gov: NCT03385655

Blood ctDNA research in the Pacific Northwest

Dr Kim Chi, responsible for collection of over 3000 plasma ctDNA samples

It takes time to develop new biomarkers!

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- Retrospective correlative studies (hypothesis generating)
- Prospective correlative studies (hypothesis validating)

…and now you have to make it scale in an affordable, practical capacity!

Blood ctDNA research in the Pacific Northwest

…and now you have to make it scale in an affordable, practical capacity!

10:56am – 11:20am

Changing Landscape of Metastatic Prostate Cancer

Michael Schweizer, MD

Changing Landscape of Metastatic Prostate Cancer

Michael Schweizer, MD

Associate Professor

University of Washington / Fred Hutchinson Cancer Research Center

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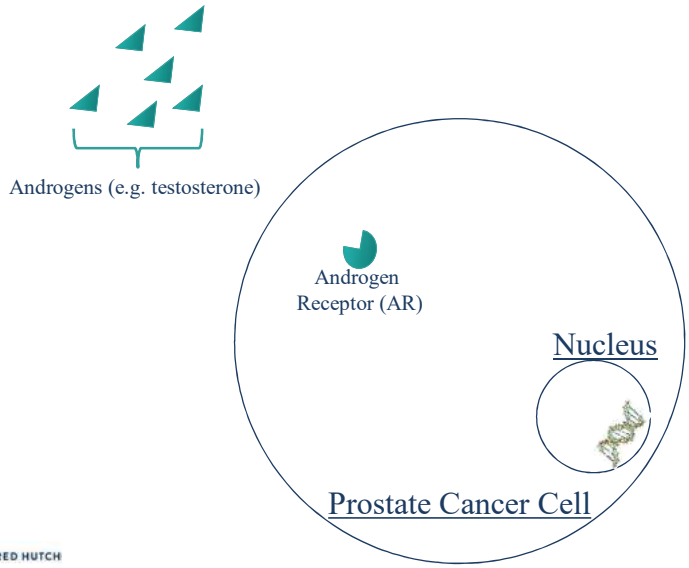
Prostate Cancer Biology



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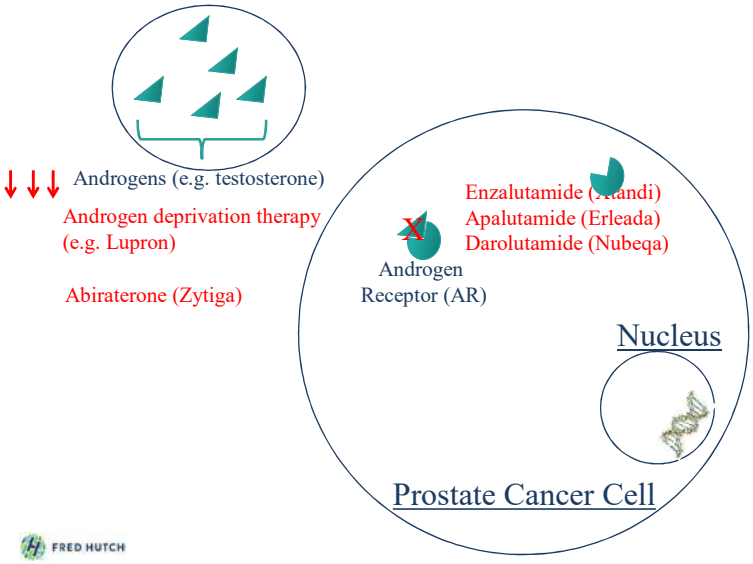
Prostate Cancer Biology



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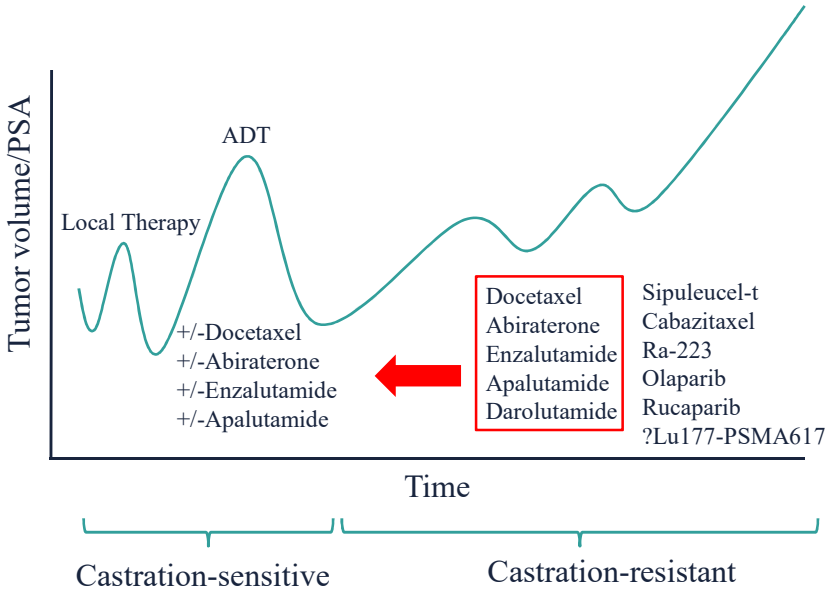
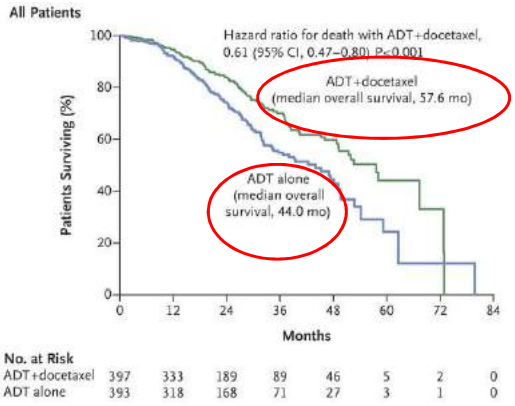
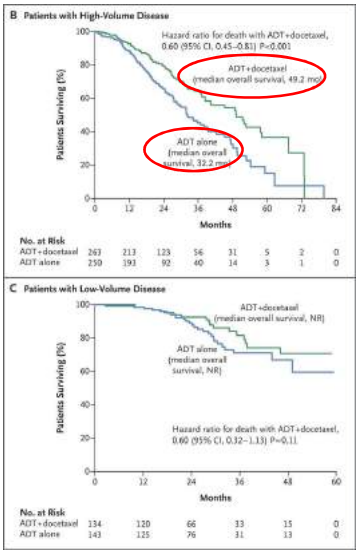
Prostate Cancer Disease Continuum



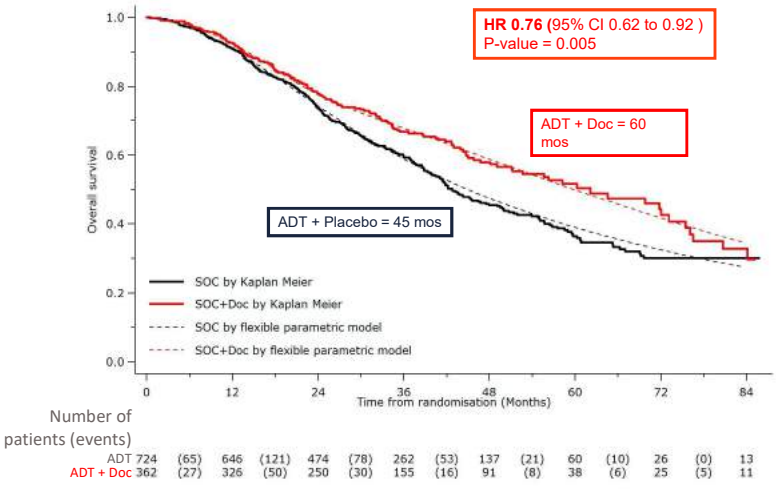
CHAARTED: Docetaxel for Metastatic Prostate Cancer





Sweeney C et al. N Engl J Med 2015; 373:737-46.

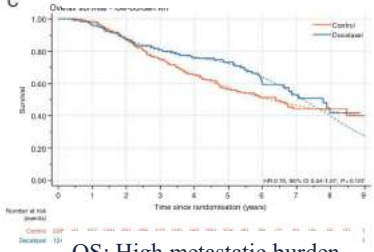
STAMPEDE: Docetaxel for Metastatic Prostate Cancer



James ND et al. Lancet 2016; 387:1163-77.

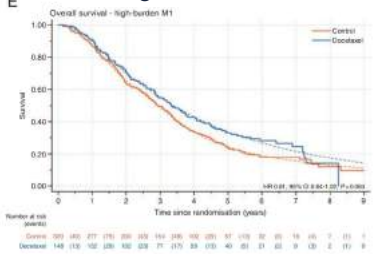
STAMPEDE: Docetaxel for Metastatic Prostate Cancer

OS: Low metastatic burden



HR 0.76, CI: 0.54-1.07, P=0.107

OS: High metastatic burden

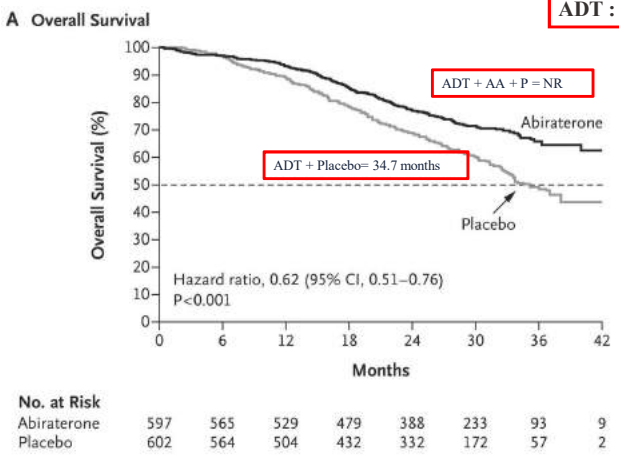


HR 0.81, CI: 0.64-1.02, P=0.064

Clarke NW, et al. Annals Oncol 2019

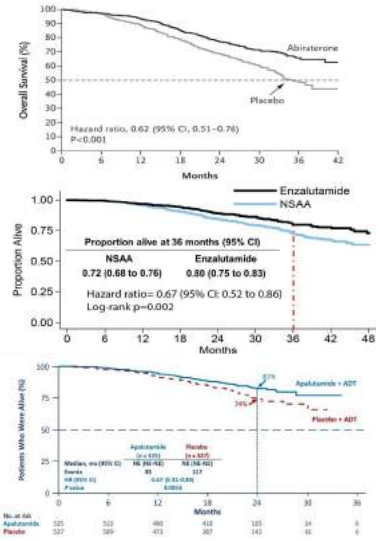
LATITUDE: Abiraterone for Metastatic Prostate Cancer

Survival at three years:
ADT + Abi: 66%
ADT : 49%



Fizazi K et al. N Engl J Med 2017; 377:352-60.

Novel Hormonal Agents in Metastatic Prostate Cancer



Abiraterone

Enzalutamide

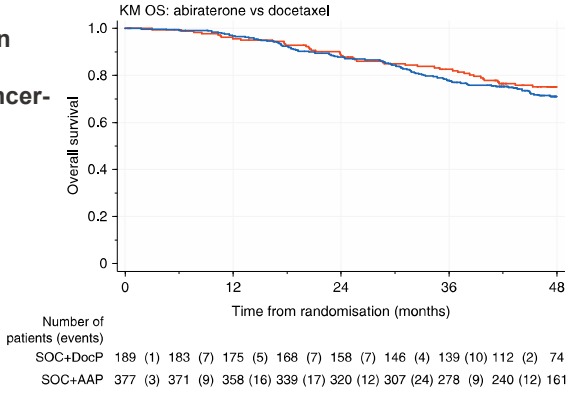
Apalutamide

Fizazi K et al. N Engl J Med 2017; 377:352-60.
Davis ID et al. N Engl J Med. Epub June 2, 2019.
Chi KN et al. N Engl J Med. Epub May 31, 2019.

STAMPEDE: Comparison of Docetaxel with Abiraterone

Not a pre-planned comparison

No difference in OS, MFS, cancer-specific survival, or skeletal related events



Sydes M et al. Ann Oncol 2018; 29(5):1235–48.

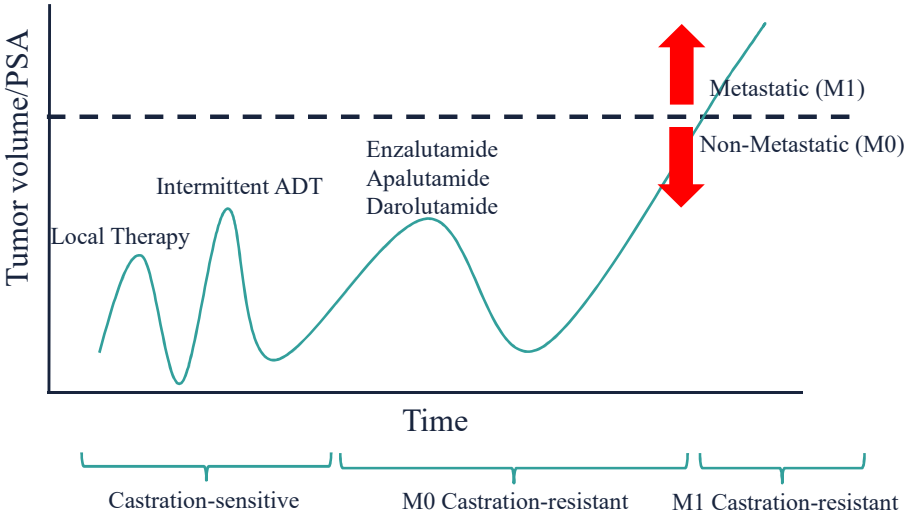
What should we do with all this data?

- Treatment intensification is standard of care for men with newly diagnosed metastatic prostate cancer
  - Docetaxel, abiraterone, enzalutamide and apalutamide are all options
- Outcomes are similar with any of these agents
- My preference is for a novel hormonal agent in men with low-volume prostate cancer
- Consider docetaxel or an NHA in patients with high volume prostate cancer

Biochemically Recurrent Prostate Cancer

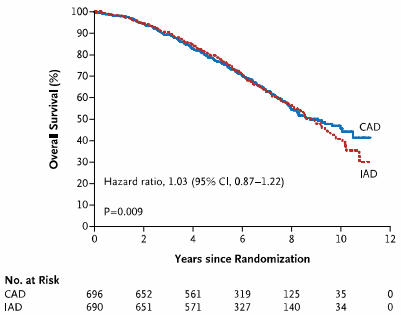
- Defined as a rising PSA after either prostatectomy and/or radiation therapy
- No evidence of metastatic cancer
  - Traditionally defined based on CT and bone scans assessments

Biochemically Recurrent Prostate Cancer



Intermittent vs. Continuous ADT

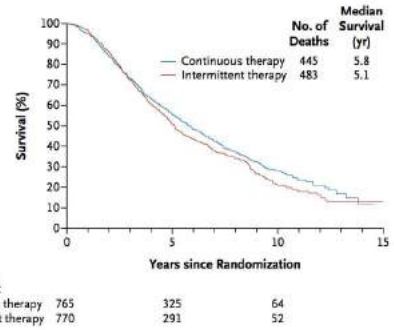
PR7 for BCR



No difference in OS
Improved quality of life

Crook JM et al. N Engl J Med. 2012; 367:895-903.

SWOG 9346 for mHSPC

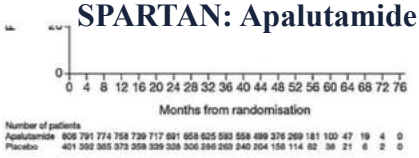


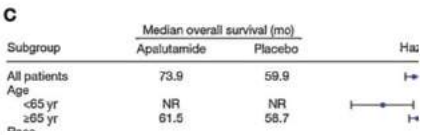
Could not prove that intermittent therapy was equivalent to continuous ADT

Hussain M et al. N Engl J Med 2013;368:1314-25.

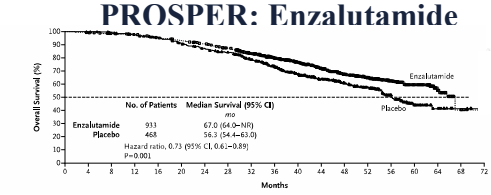
Novel Hormonal Agents Improve Survival in Non-metastatic CRPC

SPARTAN: Apalutamide



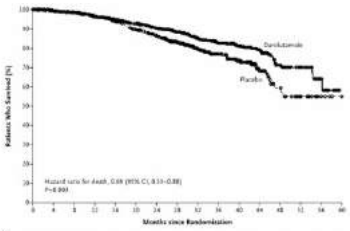


PROSPER: Enzalutamide



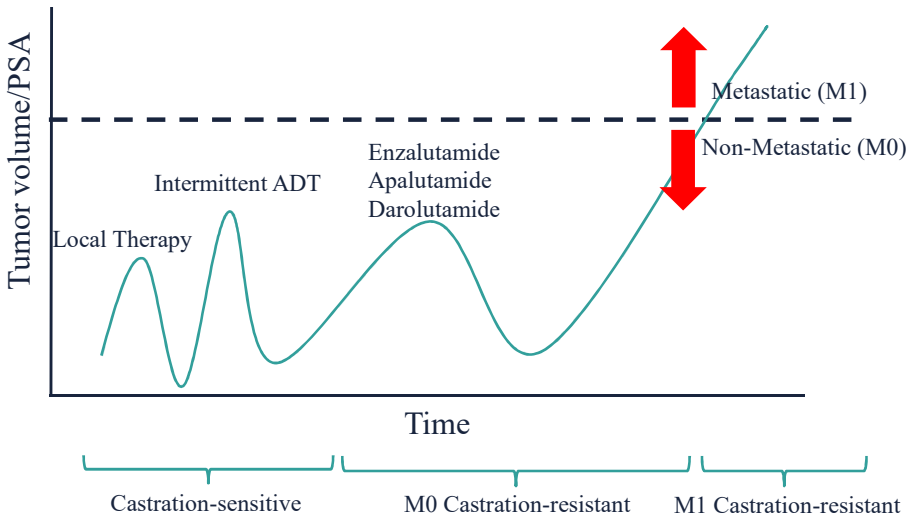
Studies have shown ~1-year median improvement in

ARAMIS: Darolutamide



Smith MR et al. Eur Urol. 2021 Jan;79(1):150-158
Fizazi, et al. N Engl J Med 2020;383:1040-9
Sternberg, et al. N Engl J Med 2020;382:2197-206.

What if we detect metastatic disease earlier?

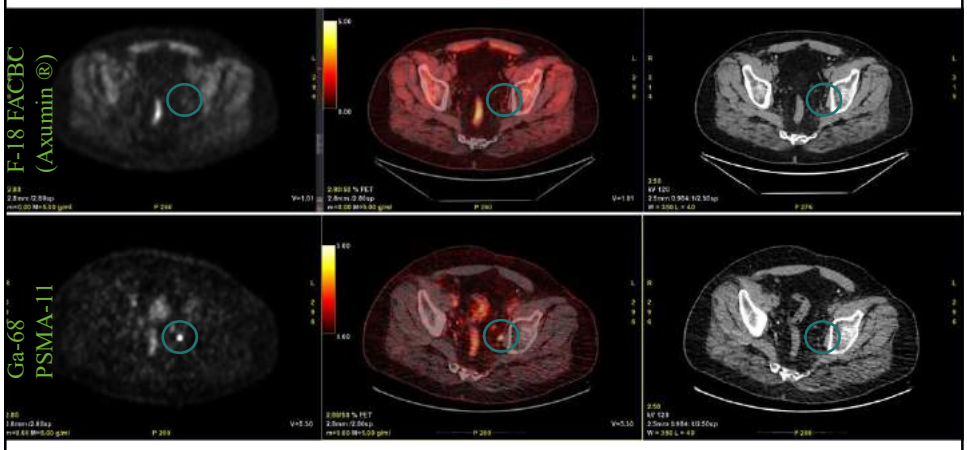


Next-generation PET Imaging

- New PET tracers (e.g., PSMA, Fluciclovin) are more sensitive for detecting metastatic prostate cancer
- PSMA PET imaging is the most sensitive → Ga68-PSMA and ^{18}F-DCFPyL are both now FDA approved
- PSMA 100-1000x higher expression in cancer compared to normal prostate
  - Can also serve as a target for therapies

Lawhn-Heath, et al. Radiology 2021; 299:248–260
Eiber et al. J Nucl Med 2015; 56:668–74.

PSMA PET increases confidence in calling metastases



Images courtesy of Dr. Delphine Chen

Best approach for managing men with low volume metastatic prostate cancer (as defined on PET imaging) is not clear.

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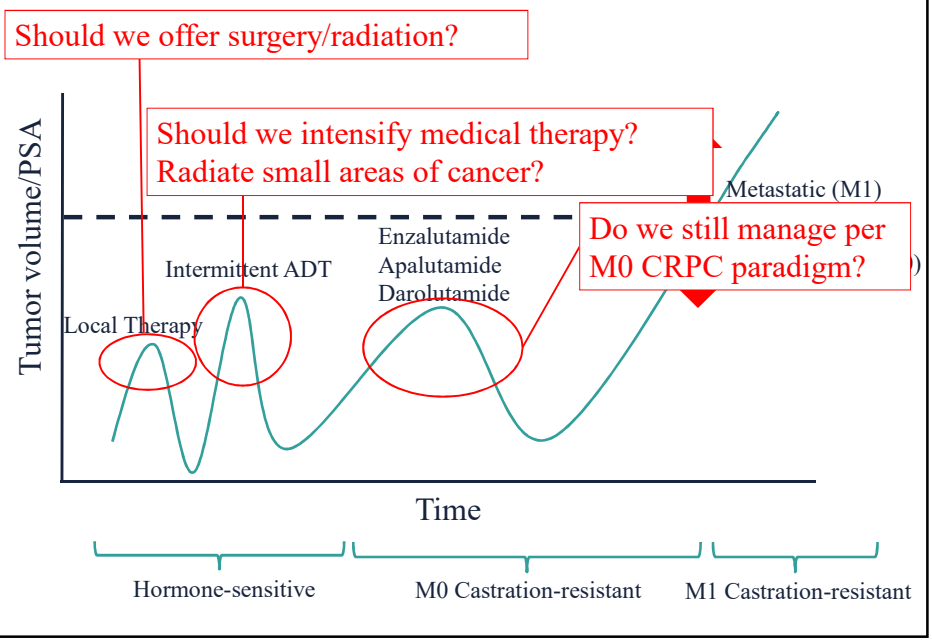
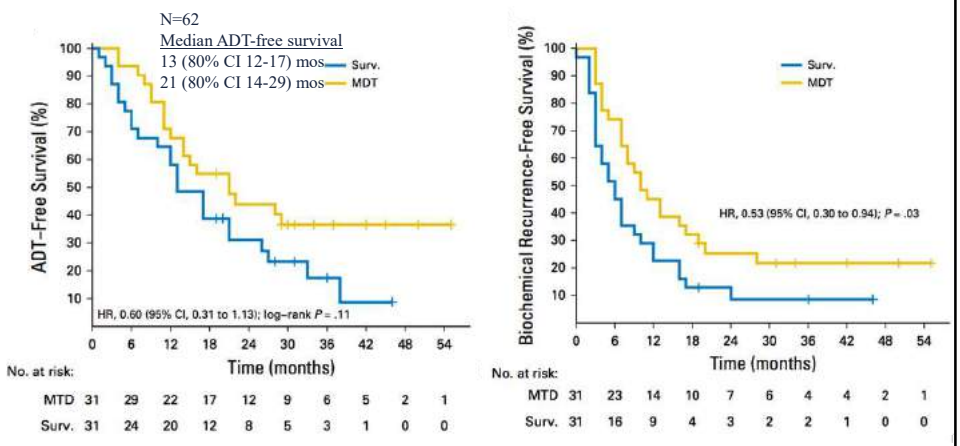
18

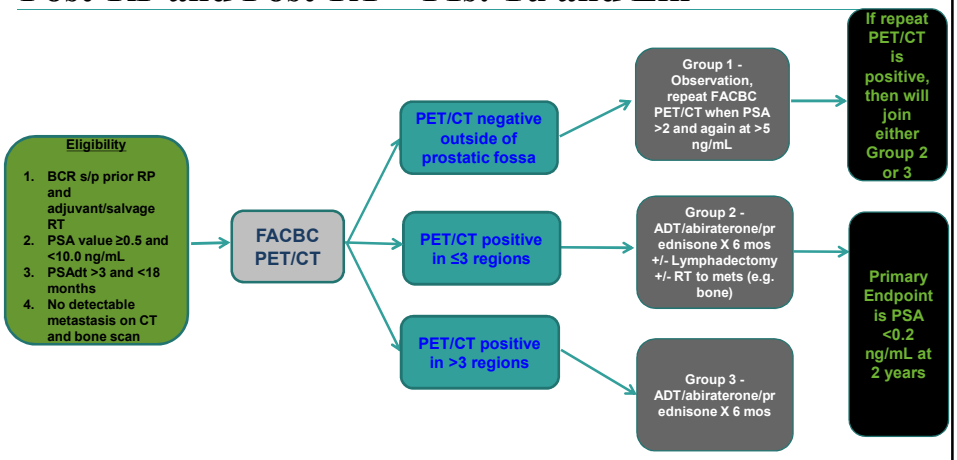


Metastasis-Directed Therapy Identified by Choline PET leads to Improved ADT-free Survival



Ost P et al. J Clin Oncol. 2018; 36:446-53.

New FACBC Trial at UW/SCCA for patients who are Post-RP and Post-RT – PIs: Yu and Lin



BCR: Biochemical recurrence; RP: Radical prostatectomy; RT: External beam radiation, proton beam radiation or SBRT; PSA: prostate-specific antigen; PSAdt: PSA doubling time; CT: computed tomography; FACBC: fluciclovine; PET: positron emission tomography; ADT: androgen deprivation therapy

Summary

- Overall shift in more aggressive treatment for advanced prostate cancer
- Treatment intensification is standard of care for men with newly metastatic prostate cancer
- Novel hormonal agents are standard for men with non-metastatic prostate cancer and rising PSA on ADT
- PET imaging is leading us to find metastatic disease earlier
  - Many studies are trying to determine the optimal treatment approach

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THANK YOU

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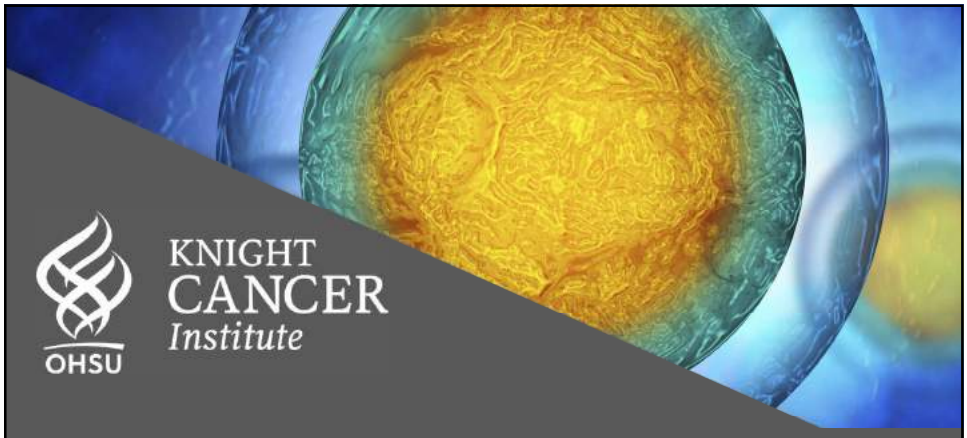
fredhutch.org

11:20am – 11:39am

Prostate Cancer: Breaking News 2021

Alexandra Sokolova, MD



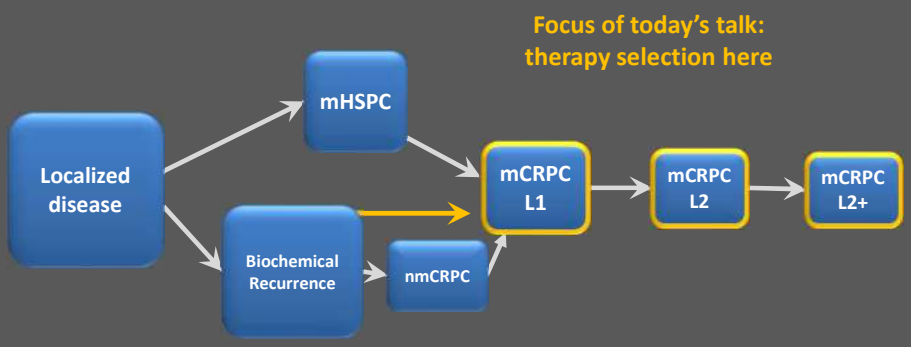
Prostate Cancer: Breaking News 2021

Alexandra O. Sokolova, MD
Assistant Professor, Hematology and Medical Oncology
OHSU Knight Cancer Institute
October 2, 2021

Disclosures

- None

Disease States in Prostate Cancer



mHSPC, metastatic hormone sensitive prostate cancer; nmCRPC, nonmetastatic castration-resistant prostate cancer; mCRPC, metastatic castration-resistant prostate cancer; L, line of treatment.

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Metastatic Prostate Cancer
What is New and What is Important

- Oral Androgen Deprivation Therapy (ADT)
- Germline Testing
- PARP Inhibitors
- Lu-177-PSMA 617

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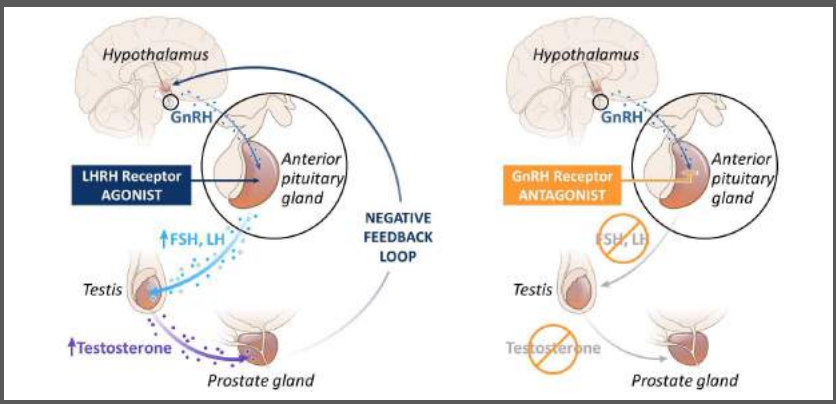
NEW: ORAL ANDROGEN DEPRIVATION THERAPY

KNIGHT CANCER Institute OHSU

Androgen Deprivation Therapy: Agonist vs Antagonist



- Leuprolide
- Triptorelin
- Goserelin

- Degarelix
- Relugolix

Adapted from: Neal S., et al, NEJM 2020

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Phase 3 HERO Study Design

- Primary Endpoint: sustained testosterone <50 ng/dL through 48 weeks

Adapted from: Neal S., et al, NEJM 2020

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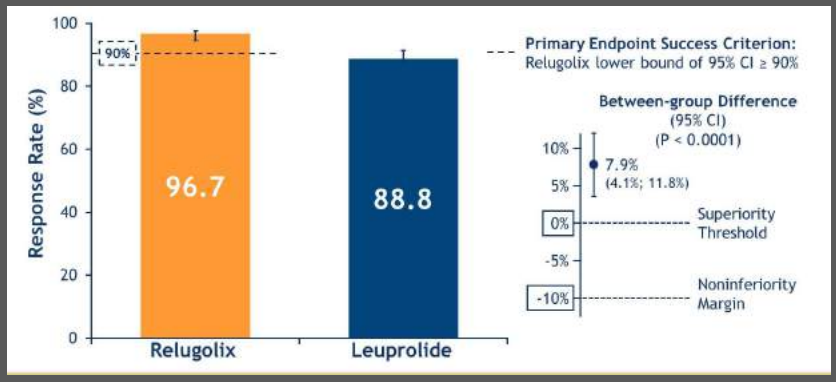
Primary Endpoint Suppressed Testosterone



Adapted from: Neal S., et al, NEJM 2020

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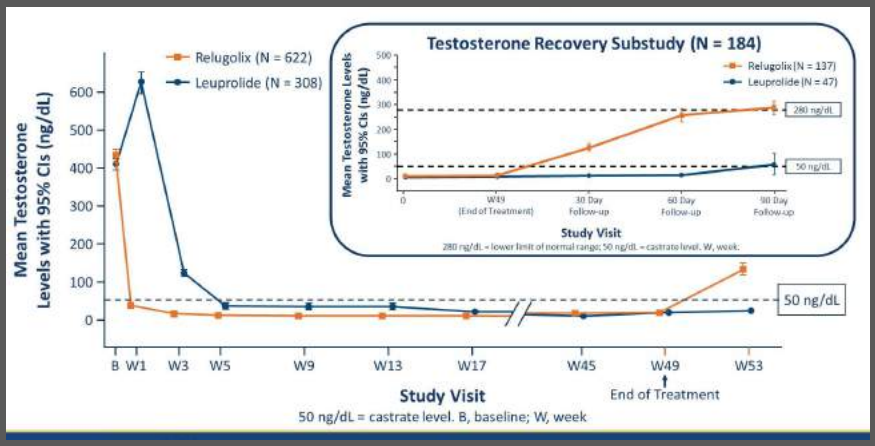
Time Course of Testosterone Suppression



50 ng/dL = castrate level. B, baseline; W, week

Adapted from: Neal S., et al, NEJM 2020

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Adverse Events

	Relugolix (N = 622)	Leuprolide (N = 308)
Hot flush	54.3%	51.6%
Fatigue	21.5%	18.5%
Constipation	12.2%	9.7%
Diarrhea*	12.2%	6.8%
Arthralgia	12.1%	9.1%
Hypertension	7.9%	11.7%

*Adverse events of diarrhea were grade 1 or 2 and did not result in study discontinuation

Adapted from: Neal S., et al, NEJM 2020

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Potential Benefits of LHRH Antagonist

Potential Advantage	Benefit likely	Benefit unclear
Rapid response with lack of flare		
Decreased risk of treatment-induced pain, cord compression, urinary obstruction	High risk mCSPC, avoids anti-androgens	Non-mCSPC (BR), or mCSPC w/out high risk lesions
Fewer Major Adverse CV Events (MACE)		
	Men with history of MI or stroke	Of potential benefit in most
Depth and consistency of testosterone (T) suppression		
• T <20ng/dl at 1yr associated with better outcomes • ~15-25% do not achieve <20ng/dl on agonist therapy • Small studies suggest LHRH antagonists may be superior in this regard	ADT monotherapy such as for BR or adjuvant to XRT	ADT combined with 2nd generation AR signaling inhibitor
More rapid testosterone recovery		
	IADT or ADT adjuvant to XRT	Continuous ADT
Oral administration		
Relugolix	Less travel/exposure (Covid-19)	Men with poor compliance

Adapted from: Mostaghel E., ASCO 2020

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COST

- Relugolix $2300/month
- Degarelix $519/month
- Eligard $481/month

https:// drugs.com
https://endpts.com

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NOT SO NEW BUT IMPORTANT: GERMLINE TESTING

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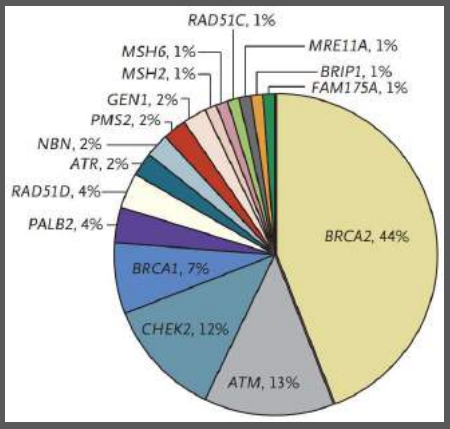
Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer



Distribution of Presumed Pathogenic Germline Mutations

12% with metastatic prostate cancer

vs

5% with localized prostate cancer (Cancer Genome Atlas prostate cancer study)

vs

3% without a known cancer diagnosis (Exome Aggregation Consortium)

Pritchard C., et al. N Engl J Med, 2016

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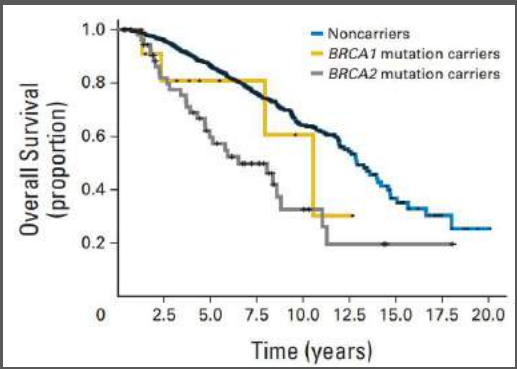
gBRCA Increases Risk of PCa

- *gBRCA2* associated with **4.5**- to **8.6**-fold increased relative risk of PCa
- Pca with g*BRCA 1/2* mutations associated:
  - more advanced stage at diagnosis
  - metastases at diagnosis
  - younger age at diagnosis
  - worse outcomes
  - OS in carriers vs noncarriers 8 vs 13 years



Castro E., et al. J Clin Oncol, 2013

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NCCN Guidelines

Germline Genetic Testing is Recommended for Men With:

I. metastatic PCa

II. localized PCa (high risk, very high risk)

III. intraductal histology

IV. family history criteria

NCCN: Prostate Cancer Guidelines. Version 4.2019 10/05/2019

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NCCN Guidelines

- **IV. Family history criteria:**

- Known germline mutation in the family
- First degree or multiple family members who died from PCa or diagnosed with PCa at <60 yrs
- ≥3 cancers on same side of family consistent with Lynch or Hereditary Breast and Ovarian Cancer syndromes.

NCCN: Prostate Cancer Guidelines. Version 4.2019 10/05/2019

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NEW: PARP INHIBITORS

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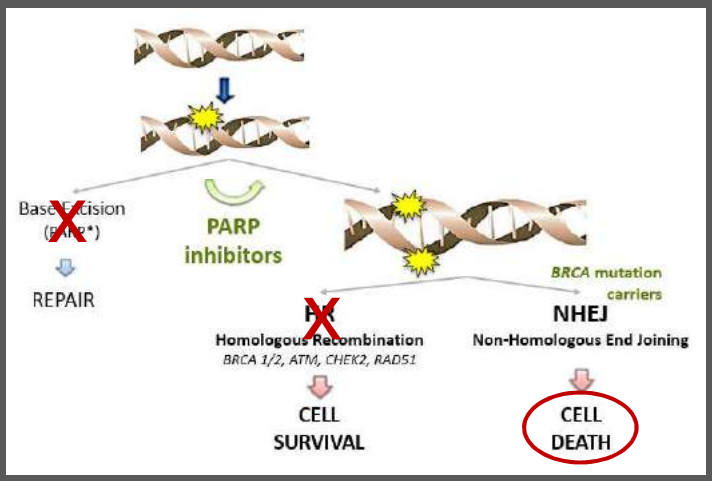
DNA Damage Repair: PARPI



*PARP – Poly-ADP-ribose polymerase

Toss A., et al. J. of Cancer Science and Therapy, 2013

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Phase III Trial of PARPI in PCa: PROfound Study Design

Key eligibility criteria
- mCRPC with disease progression on prior NHA, eg abiraterone or enzalutamide
- Alterations in ≥1 of any qualifying gene with a direct or indirect role in HRR*

Stratification factors
- Previous taxane
- Measurable disease

Cohort A: *BRCA1*, *BRCA2* or *ATM* N=245
- Olaparib 300 mg bid n=162
- Physician's choice‡ n=83

Cohort B: Other alterations* N=142
- Olaparib 300 mg bid n=94
- Physician's choice‡ n=48

2:1 randomization
Open-label

Upon BICR progression, physician's choice patients were allowed to cross over to olaparib

Primary Endpoint

Radiographic progression-free survival (rPFS) in Cohort A (RECIST 1.1 & PCWG3 by BICR)

Key Secondary Endpoints
- rPFS in Cohorts A+B
- Confirmed radiographic objective response rate (ORR) in Cohort A
- Time to pain progression (TTPP) in Cohort A
- Overall survival (OS) in Cohort A

**BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D* and/ or *RAD54L*

Hussain M., et al. ESMO, 2019

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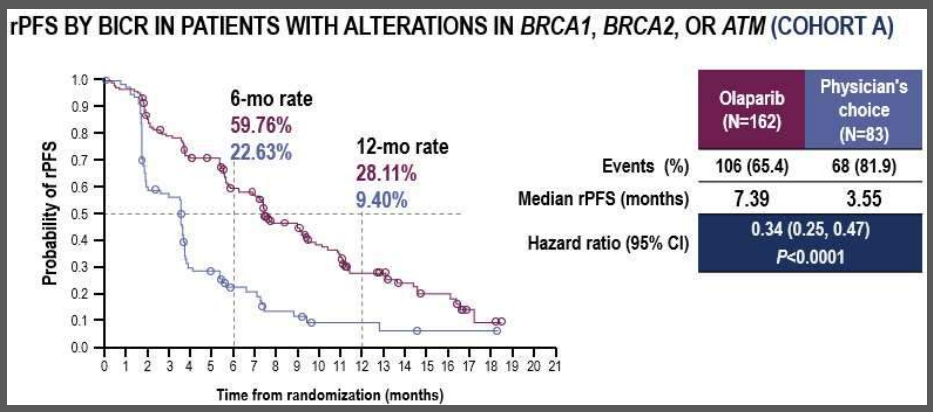
PROfound: Olaparib Improves rPFS*

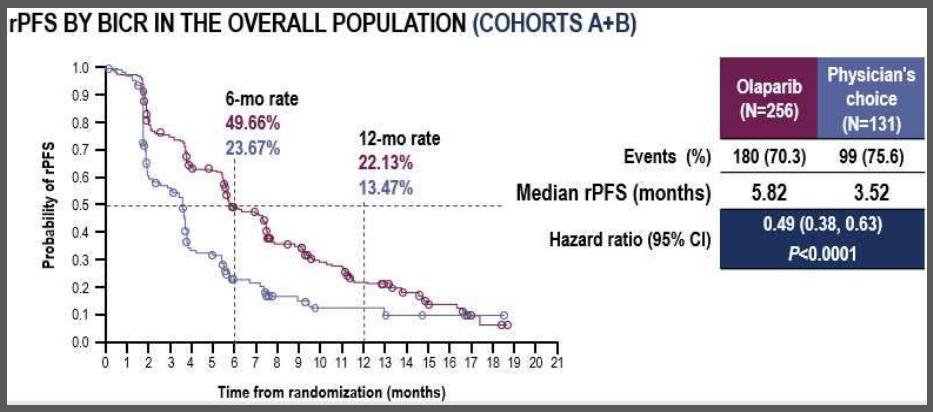


*rPFS – radiographic progression free survival

Hussain M., et al. ESMO, 2019
DeBono., et al. NEJM, 2020

KNIGHT CANCER Institute OHSU

PROfound: Olaparib Improves rPFS*



*rPFS – radiographic progression free survival

De Bono., et al. NEJM, 2020

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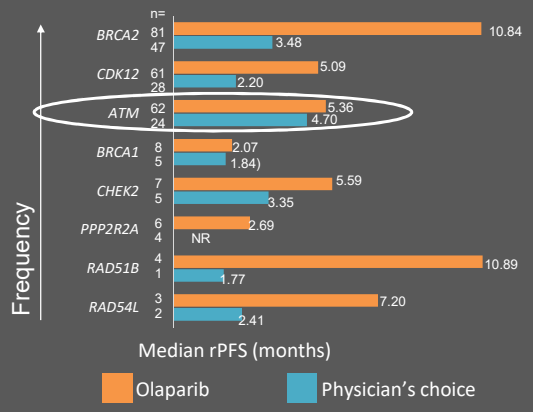
PROfound Gene-by-Gene rPFS



Hussain M., et al. NEJM, 2020

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TRITON 2: Rucaparib in mCPRC with *BRCA1/2*

TABLE 2. Rate of Response to Rucaparib Treatment

Response	Investigator-Evaluable Population (n = 65)	IRR-Evaluable Population (n = 62)
Confirmed ORR, No. (%; 95% CI)[a]	33 (50.8; 38.1 to 63.4)	27 (43.5; 31.0 to 56.7)
Complete response	4 (6.2)	7 (11.3)
Partial response	29 (44.6)	20 (32.3)
Stable disease	25 (38.5)	28 (45.2)
Progressive disease	6 (9.2)	6 (9.7)
Not evaluable	1 (1.5)	1 (1.6)
	Overall Efficacy Population (n = 115)	
Confirmed PSA response rate, No. (5; 95% CI)	63 (54.8; 45.2 to 64.1)	

Abida W., et al. JCO, 2020

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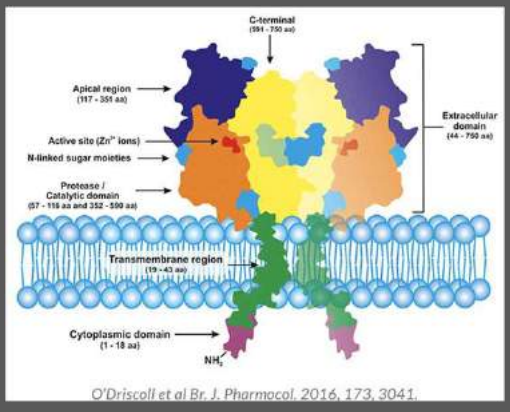
NEW: TARGETING PSMA

KNIGHT CANCER Institute
OHSU

PSMA

- Transmembrane protein
- Highly expressed in prostate cancer
- Relatively restricted normal tissue (*e.g.* salivary and lacrimal glands)



O'Driscoll et al Br. J. Pharmacol. 2016, 173, 3041.

Presented By Michael Morris at 2021 ASCO Annual Meeting

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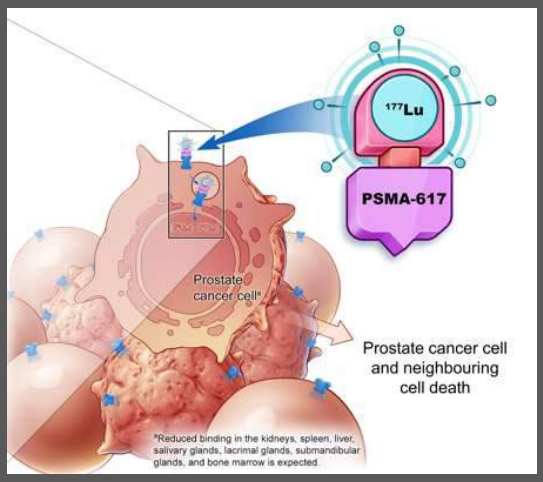
^{177}Lu PSMA-617 Targeted Therapy



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VISION Trial Design

Eligible patients

- Previous treatment with <u>both</u>
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

2:1

Protocol-permitted SOC + ^{177}Lu-PSMA-617
7.4 GBq (200 mCi) every 6 weeks
4 cycles, increasable to 6

Protocol-permitted SOC alone

87% were PSMA+

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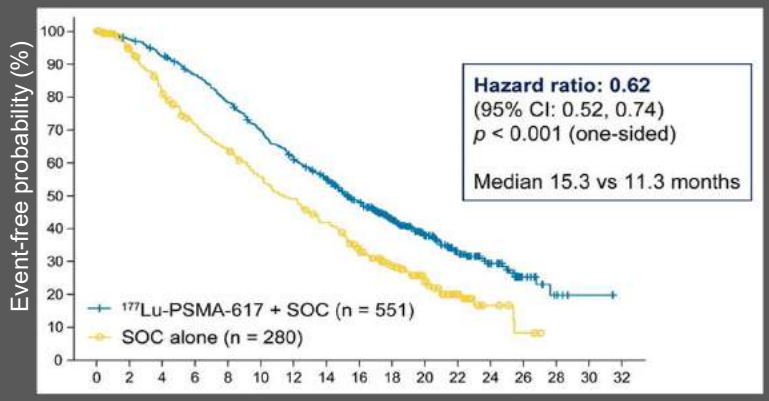
^{177}Lu PSMA-617 Prolonged Overall Survival



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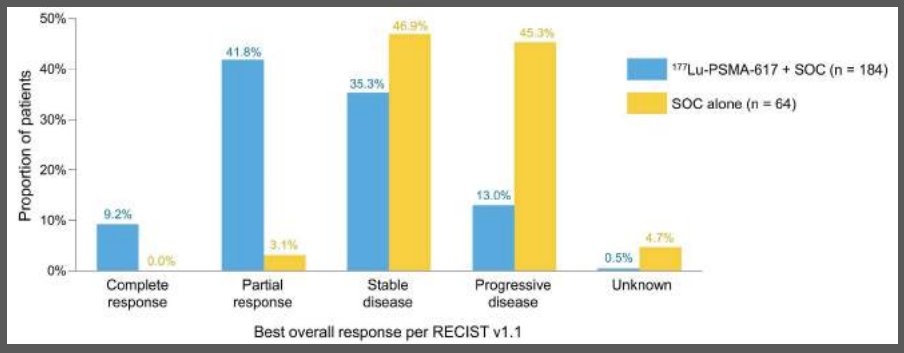
^{177}Lu PSMA-617 Radiographic Response



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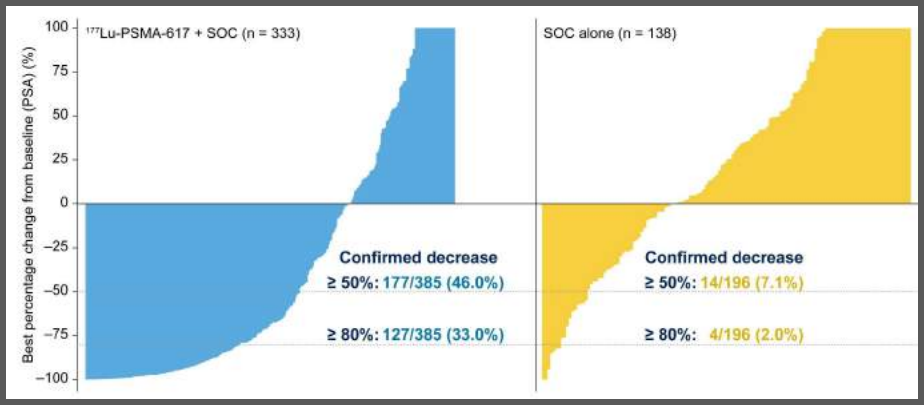
^{177}Lu PSMA-617 PSA Response



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^{177}Lu PSMA-617 Adverse Events

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

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Conclusions

- New FDA Approved Agents:
  - ADT: Relugolix
  - PARPi: Olaparib, Rucaparib
- On the Horizon:
  - ^{177}Lu PSMA-617

THANK YOU

OHSU KNIGHT CANCER INSTITUTE
PROSTATE CANCER RESEARCH PROGRAM

11:39am – 12:05am

Challenges to Sexual Health

Ryan Flannigan, MD

Challenges to Sexual Health

Ryan Flannigan MD FRCSC

Assistant Professor, Department of Urologic Sciences, UBC

Clinical Lead, Prostate Cancer Supportive Care Program Sexual medicine clinic, British Columbia

Director of Male Reproduction & Sexual Medicine research program

Fellowship Director, Male reproduction, Sexual Medicine and Microsurgery Program

Faculty Disclosure

- **Faculty:** Ryan Flannigan
- **Relationships with commercial interests:**
  - **Grants/Research Support:** CIHR, ASRM, CUASF, VCHRI, NFRF, SMSNA
  - **Speakers Bureau/Honoraria:** Paladin Labs, Acerus, Boston Scientific
  - **Consulting Fees:** NA
  - **Other:** NA

Disclosure of Commercial Support

- **This program has received no financial support.**
- **This program has received no in-kind support.**
- **<u>Potential for conflict(s) of interest</u>:**
  - None

Mitigating Potential Bias

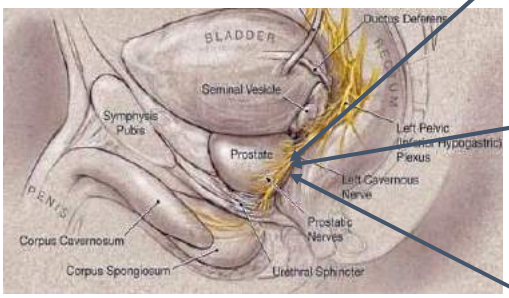
- **No brand names used in discussing penile implant surgery.**

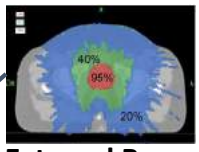
Objectives

1. Forms of sexual dysfunction after treating prostate cancer.
2. Management strategies for sexual dysfunction related to prostate cancer treatment.
3. Accessing resources for patients with sexual dysfunction following prostate cancer treatment.

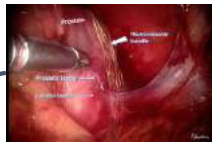
Impact of Prostate Cancer Treatment On Sexual Function

- **Prostate cancer may result in multiple forms of sexual dysfunction impacting both the cancer survivor & their partner.**

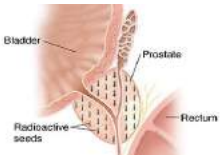




External Beam Radiation



Surgery



Brachy Therapy

https://www.prostatecancertreatment.co.uk/treatment-options/radiotherapy/
https://urology.ufl.edu/patient-care/robotic-laparoscopic-urologic-surgery/procedures/robotic-nerve-sparing-radical-prostatectomy/
https://www.google.ca/search?client=safari&biw=1146&bih=524&tbm=isch&sa=1&ei=NmAlXZuCoHj-gSMyIVo&q=brachytherapy&oq=brachy&gs_l=img.3.0.0i67j0i3j0i67l2j0j0i67j0l2.136049.136696..137851...0.0..0.49.272.6.....0....1..gws-wiz-img.ST-Tbf3ckpI#imgrc=dQWHTSqsIwpK7M:

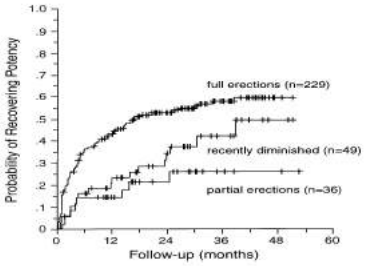
Prostate Cancer Supportive Care

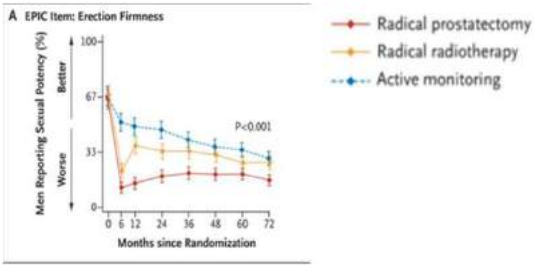
Post-Treatment Sexual Dysfunction

- **Erectile dysfunction**
- Anejaculation
- Dysorgasmia (painful)
- Climacturia
- Penile shortening
- Penile curvature
- Disruption to Intimacy & Masculinity

Sexual Dysfunction by Treatment Modality

- **Radical Prostatectomy**
  - Erectile Dysfunction
  - Penile shortening
  - Peyronie's Disease
  - Anejaculation
  - Dysorgasmia
  - Climacturia
  - Psychosocial impact
    - Masculinity
    - Intimacy
    - Arousal

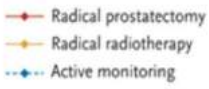


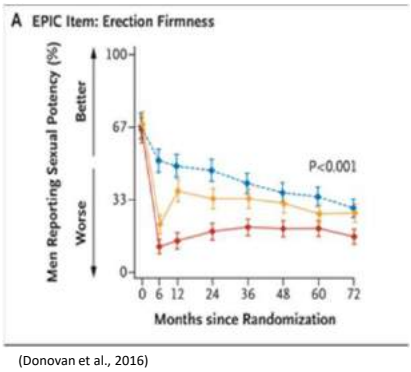


(Donovan et al., 2016)

Sexual Dysfunction by Treatment Modality

- **External Beam Radiation Therapy**
  - Erectile Dysfunction
  - Penile shortening
  - Peyronie's Disease
  - Reduced/Anejaculation
  - Dysorgasmia
  - Psychosocial impact
    - Masculinity
    - Intimacy
    - Arousal (worse if combined with ADT)

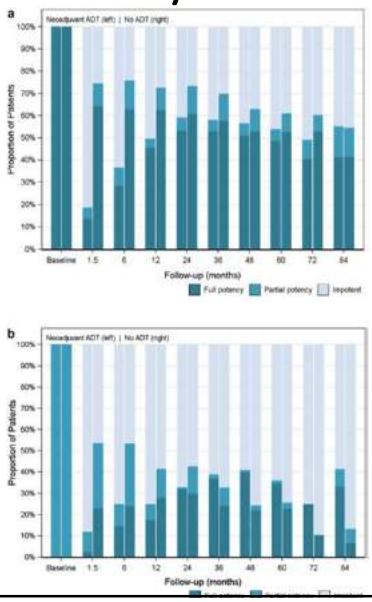




(Donovan et al., 2016)

Sexual Dysfunction by Treatment Modality

- **Brachy Therapy**
  - Erectile Dysfunction
  - Penile shortening
  - Peyronie's Disease
  - Reduced/Anejaculation
  - Dysorgasmia
  - Psychosocial impact
    - Masculinity
    - Intimacy
    - Arousal (worse if combined with ADT)



(Keyes et al., 2015)

Sexual Dysfunction by Treatment Modality

- **Androgen Deprivation Therapy**
  - Erectile Dysfunction
  - Penile shortening
  - Peyronie's Disease
  - Reduce ejaculate volume
  - Reduced orgasmic intensity
  - Psychosocial impact
    - Masculinity
    - Intimacy
    - **Arousal***

APPROACHES to Manage Sexual Dysfunction

- Sexual Adaptation
- Communication
- Refocus intimacy with patient's partner
- Managing ejaculatory dysfunction
- Therapies for improving erectile function
- Work with our sexual health clinicians in our PCSC program

Prostate Cancer Supportive Care

SEXUAL ADAPTATION

Sexual adaptation begins with an awareness of the potential for sex difficulties following any disruption in health.

What is involved in Sexual Rehabilitation?

- Gaining knowledge
- Developing coping or communication skills
- Dealing with feelings of sexual inadequacy
- Understanding societal myths around sexuality
- Adjusting values and beliefs to help support sexual self-view
- Discovering new ways of supporting desired sexual activities and/or behaviors

Enable Communication & Intimacy

- **Communication**
  - Among most predictive factors of sexual satisfaction post-treatment.
  - Communicate what IS working, what is NOT working, thoughts, worries and ideas of how to maintain sexual intimacy
- **Maintaining Intimacy**
  - Couples may maintain all non-sexual forms of intimacy (emotional, intellectual, experiential).
  - Patients may continue to be sexually intimate through touch, external stimulation, devices etc.
  - Not all or nothing

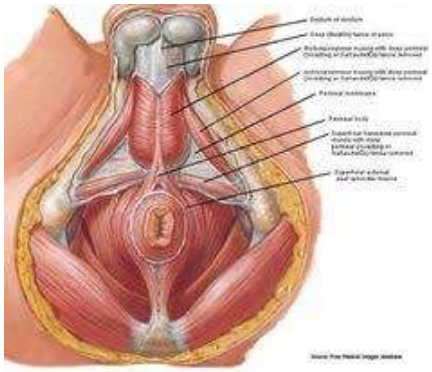
Managing Orgasmic Dysfunction

- **Anorgasmia**
  - Treatment of the inability to achieve orgasm or reduced pleasure has been challenging.
  - Underlying known causes can be treated directly (eg. low testosterone, high prolactin levels, SSRI anti-depressant use).
  - Off-label use of cabergoline has been studied and demonstrated improvement in up to 66.4%.[2]
  - Others have reported improvement with common erection pills (i.e. PDE5i's – eg. Levitra etc).[3]
  - Mindfulness-based techniques
- **Dysorgasmia**
  - ~15% of men post Rx
  - Alpha blockers may help
  - Pelvic floor physiotherapy & biofeedback
  - Time

Clavell-Hernandez, Martin, Wang Sex Med Rev, 2018; [2]Hollander *et al.* Sex Med 2016; [3]Nehra *et al.* J Urol 2005
Image: https://www.medicalnewstoday.com/articles/324112.php

Managing Urinary Leakage During Sexual Activity

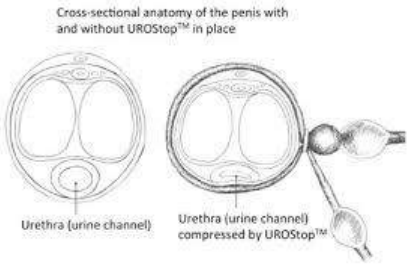
- **Managing leakage of urine during climax or sexual activity (i.e. Climacturia).**
  - Empty bladder prior to sexual activity.
  - Optimize environment (i.e. put a towel down, or perform sexual activity in shower)
  - Pelvic floor physiotherapy to strengthen pelvic floor muscles and urinary sphincter.
  - Bio-feedback to guide pelvic floor muscle strengthening.



Clavell-Hernandez, Martin, Wang Sex Med Rev, 2018

Managing Urinary Leakage During Sexual Activity

- **Managing leakage of urine during climax or sexual activity (i.e. Climacturia).**
  - Penile devices to stop leakage of urine during sexual activity.
    - One study demonstrated significant reduction in leakage, and reduced distress using the 'Urostop device' (Urosciences Inc, NY, USA).

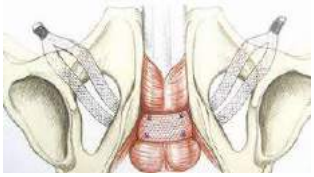


	No Leakage	Small Leakage	Moderate Leakage	Large Leakage	Patient distress	Partner Distress
Pre-Treatment	0%	16%	72%	12%	14%	61%
Post-Treatment	46%	28%	26%	0%	2%	11%

Mehta, Deveci, Mulhall BJUI 2013; Image: https://www.urologyhealthstore.com/shop/men-products/leakage/urostop/

Managing Urinary Leakage During Sexual Activity

- **Managing leakage of urine during climax or sexual activity (i.e. Climacturia).**
  - **Surgery** if urinary leakage is distressing, not managed by conservative methods, or more generalized throughout the day.
    - Male urethral sling
    - Male urinary sphincter



Clavell-Hernandez, Martin, Wang Sex Med Rev, 2018

Erectile Dysfunction & Penile Rehabilitation

Concept that early treatment to encourage penile blood flow and erections, protects the health of the penile tissue resulting in better erectile function recovery

What is involved in Penile Rehabilitation?

- *Stimulate regular erections*
- +/- Oral medications prescribed post treatment
- +/- Intra-cavernosal (penile) injections (ICI)
- +/- Vacuum pump erection device

Studies suggest that Penile Rehabilitation improves erectile function recovery by nearly 3x. (Liu *et al.* J, 2017)

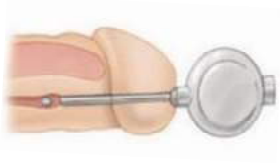
Managing Erectile Dysfunction

1. **Oral Therapies (PDE5 inhibitors)**
   - Typically our first line treatment
   - E.g. Sildenafil, Tadalafil, Vardenafil

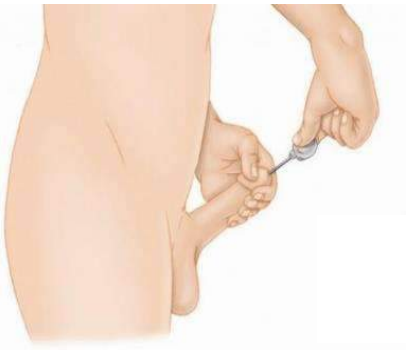
   - **PRO:**
     - Easy to use
     - Can maintain spontaneity.
     - Moderate cost.
   - **CON:**
     - Potential for systemic side effects.
     - Requires some degree of nerve function to be effective.

Managing Erectile Dysfunction

2. **Intraurethral Suppository (MUSE)**
   - Medication self administered in urethra



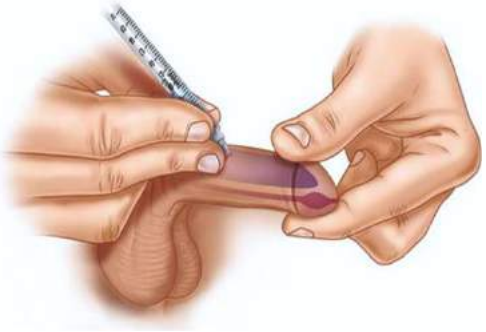
   - **PRO:**
     - Does not require nerve function.
   - **CON:**
     - More expensive per erection
     - Insertional discomfort of pellet
     - May cause some discomfort to partner.



Managing Erectile Dysfunction

3. Penile Injections

- Very effective for most men, works within 5-10 minutes, and ideally lasts for 30-60 minutes
- Requires teaching by our sexual health clinicians



- **PRO:**
  - Relatively cost effective per erection.
  - Does not require nerve function to work.
  - Quite effective in most men.
- **CON:**
  - Requires needle insertion into penis
  - Risk of Priapism if not appropriately supervised.
  - Not as spontaneous

Managing Erectile Dysfunction

4. Vacuum Therapy

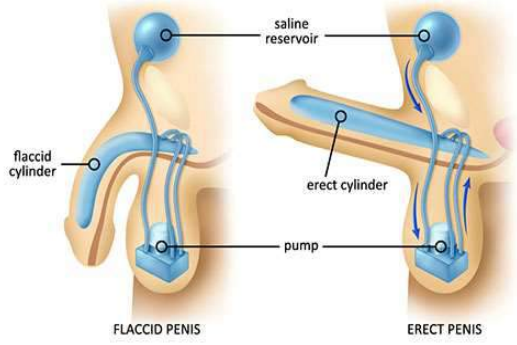
- Effective for non-medical treatment

- **PRO:**
  - Does not require nerve function
  - Does not rely on medication & systemic side effects
- **CON:**
  - Base of penis not rigid
  - Limited with significant penile curve
  - Not as spontaneous
  - Cost of device~$300-500.

Managing Erectile Dysfunction

5. **Penile Implant**
   - ~90% satisfaction rate among men that do not regain erectile function post-therapy

   - **PRO:**
     - Reliable erection
     - High satisfaction rate
   - **CON:**
     - Irreversible
     - Requires surgery



https://myhealth.alberta.ca/cancer-and-sexuality/male-sexuality-and-cancer/overview-of-erection-problems/penile-implant

Accessing a Dedicated Sexual Health Program?

PCSC Sexual Health Program and Clinic

Goal: To provide education, supportive care, medical and surgical therapy to enhance sexual functioning, intimacy, and quality of life.

PC SC Prostate Cancer Supportive Care

PCSC Clinical Care Models

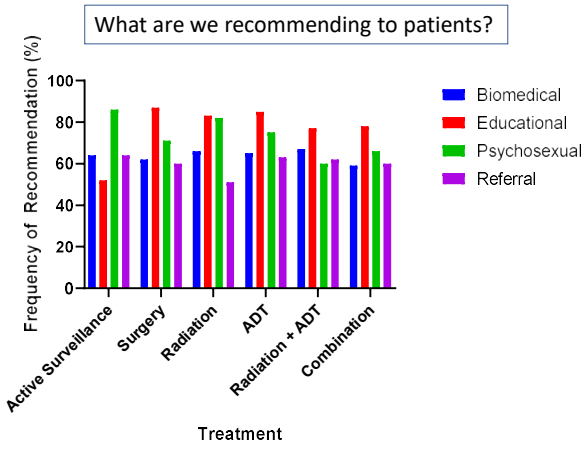
One-on-one Clinic
- Offers 7 face-face or Zoom visits with health care professional for personalized care
- Access to personalized educational resources

Online SHAReClinic
- Initiative in partnership with TrueNTH SHAReClinic created in Toronto
- Offers personalized education online
- Access to message or converse with a health coach for personalized care

Hybrid Online & One-on-one
- Access to online educational resources, but still maintain in-person/telehealth visits

Our PCSC Sex Rehab Clinic Experience

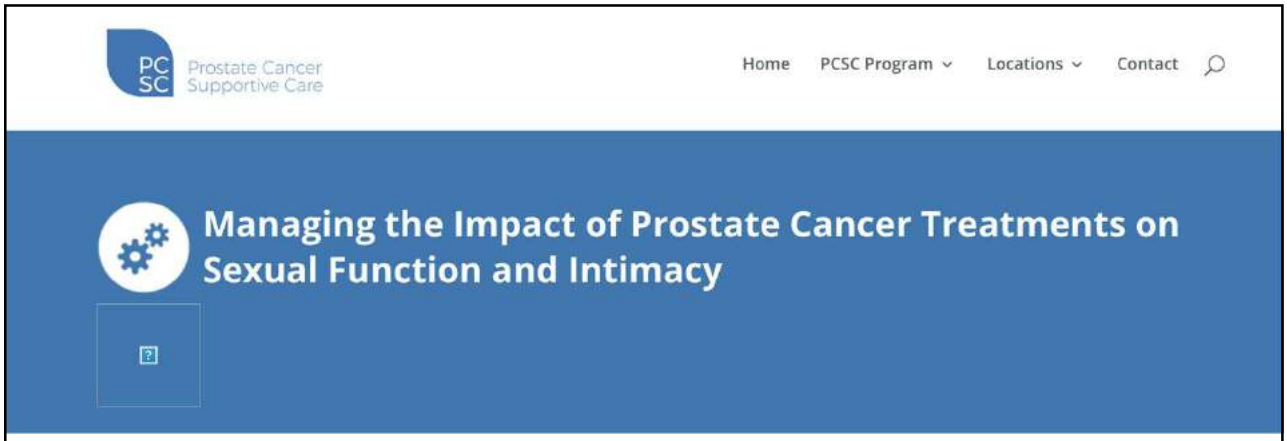
- Between July 2013 and July 2019 –
  - 3391 appointments among 965 patients
- 73.4% attend more than 1 follow up appointment
- Improved self-reported sexual satisfaction, comparing first to last appointment p<0.001



Wong et al. & Flannigan, J Clin Med, 2020
Yuen et al. & Flannigan, in press 2021

Summary

- Prostate Cancer therapy impacts the both the patient and their partner.
- Sexual dysfunction involved biological changes, psychological changes and social changes.
- Various treatments are available.
- Survivorship programs such as the Prostate Cancer Supportive Care program have developed clinics, patient and health care provider resources to facilitate care.
- Online platforms for care are available for patients across BC.



THANK YOU

QUESTIONS?

www.pcscprogram.ca

12:45pm – 1:14pm

Benefits of Exercise for Prostate Cancer Patients

Nicholas Pratap, CEP

Making Exercise a Part of Patient Care

Nick Pratap, BSc Kin, ACSM CEP

Learning Objectives

- Why does weight training need to be a staple for ADT patients?
- What's the right intensity to workout at (low, moderate or vigorous)?
- Does maintaining physical activity help mitigate fatigue related side effects from treatment?
- Should patients with bone metastasis exercise?

As medical professionals lets start asking the questions

- FITT Principle
- Frequency: How often do you exercise?
- Intensity: How hard do you push yourself when exercising?
- Time: How much time do you spend exercising?
- Type: What mode of exercise do you do?

But let's not forget to also ask our patients…

- Are you currently doing any resistance training? (especially if it's a patient on ADT treatment and is older).
- There are many exercise videos out there to get started safely (including our PCSC program YouTube channel). [8]

Is the goal to look like this? NO!

Our goal should be functionality!

ADT Treatment

- As individuals age, we see a steady decline in strength and muscle mass. Muscle mass decreases approximately 3-8% per decade after the age of 30 and this rate of decline is even faster after the age of 60. [1]
- ADT amplifies the process of muscle and strength loss.
- By reducing the rate of muscle decline we:
  - Reduce injury risk
  - Reduce fall risk
  - Reduce fracture risk
  - Allow patients to maintain functionality (ie: getting out of chair)

Will resistance training help patients undergoing ADT?

- Resistance Training Reduces Disability in Prostate Cancer Survivors on Androgen Deprivation Therapy, **Winters-Stone et Al.** [2]
- **Objective:** To investigate whether functionally based resistance exercise could improve strength, physical function, and disability among prostate cancer survivors (PCS) on androgen deprivation therapy (ADT); and to explore potential mediators of changes in outcomes from exercise.
- **Intervention:** PCS were randomized to moderate to vigorous intensity resistance training or stretching (placebo control) for 1 year.

Study 1

- **Results:** Maximal leg strength (*P*=.032) and bench press strength (*P*=.027) were improved after 1 year of resistance training, whereas little change occurred from stretching.
- **Conclusion:** One year of resistance training improved muscle strength in androgen-deprived PCS.

Aerobic Exercise

- Performing physical activity is great for anyone. Whether it's getting out for a nice walk, gardening or playing golf. Some movement is better than no movement!
- However, if we want to see a significant improvement in patient fatigue and other side effects from treatments, training in a higher exercise zone will be adequate.
- How hard should we be exercising?

How intense should we exercise?

- Higher-Intensity Exercise Results in More Sustainable Improvements for VO2peak for Breast and Prostate Cancer Survivors, **Martin et Al**. [3]
- **Purpose/objectives:** To examine peak volume of oxygen consumption (VO2peak) changes after a high- or low-intensity exercise intervention.
- **Sample:** 87 prostate cancer survivors (aged 47-80 years) and 72 breast cancer survivors (aged 34-76 years).
- **Methods:** Participants enrolled in an eight-week exercise intervention (n = 84) or control (n = 75) group. Intervention participants were randomized to low-intensity (n = 44, 60%-65% VO2peak, 50%-65% of one repetition maximum [1RM]) or high-intensity (n = 40, 75%-80% VO2peak, 65%-80% 1RM) exercise groups. Participants in the control group continued usual routines. All participants were assessed at weeks 1 and 10. The intervention groups were reassessed four months post intervention for sustainability.

Results

- **Findings:** Intervention groups improved VO2peak similarly ($p = 0.083$), and both more than controls ($p < 0.001$). The high-intensity group maintained VO2peak at follow-up, whereas the low-intensity group regressed ($p = 0.021$). The low-intensity group minimally changed from baseline to follow-up by 0.5 ml/kg per minute, whereas the high-intensity group significantly improved by 2.2 ml/kg per minute ($p = 0.01$).
- **Conclusions:** Higher-intensity exercise provided more sustainable cardiorespiratory benefits than lower-intensity exercise (for those participants that are able).

RPE Scale

Vigorous: You Can No Longer Talk (RPE: 7-10)

Moderate: You Can Talk (RPE: 3-5)

Easy: You Can Sing or Whistle (RPE:1-2)

Rating of Perceived Exertion (RPE Scale)	
10	Maximal
9	Really, Really, Hard
8	Really Hard
7	
6	Hard
5	Challenging
4	Moderate
3	Easy
2	Really Easy
1	Rest

Exercise Intensity

- When going for walks try interval training (1min fast, 1min slow) and gradually progress.
- Have patients perform the “talk test” to determine if they are pushing themselves hard enough.
- Always monitor for symptoms and take other comorbidities into account which may contraindicate aerobic exercise (ie: unstable CAD, orthopedic issues).

Cancer related fatigue

- One of the biggest side effects of cancer treatment is fatigue.
- Whether its ADT, radiation or chemotherapy, fatigue can leave patients feeling tired to the point they are bed bound.
- Through countless research papers, we are now seeing that movement is the best therapy to combat this fatigue.

Does exercise help combat cancer treatment related fatigue?

- Exercise Prevents Fatigue and Improves Quality of Life in Prostate Cancer Patients Undergoing Radiotherapy, **Monga et Al**. [4]
- **Aim:** To show fatigue prevention and quality of life (QOL) improvement from cardiovascular exercise during radiotherapy.
- **Design:** Prospective enrollment (n=21), randomized to exercise (n=11) and control groups (n=10), with pre- and post-radiotherapy between- and within-group comparisons.
- **Methods:** The interventional group received radiotherapy plus aerobic exercise 3 times a week for 8 weeks whereas the control group received radiotherapy without exercise.
- **Main Outcomes:** Pre- and post-radiotherapy differences in cardiac fitness, fatigue, depression, functional status, physical, social, and functional well-being, leg strength, and flexibility were examined within and between 2 groups.

Study 3 Exercise and Fatigue

- **Results:** No significant differences existed between 2 groups at pre-radiotherapy assessment. At post-radiotherapy assessment, the exercise group showed significant within group improvements in: cardiac fitness (*P*<.001), fatigue (*P*=.02), Functional Assessment of Cancer Therapy–Prostate (FACT-P) (*P*=.04), physical well-being (*P*=.002), social well-being (*P*=.02), flexibility (*P*=.006), and leg strength (*P*=.000). Within the control group, there was a significant increase in fatigue score (*P*=.004) and a decline in social well-being (*P*<.05) at post-radiotherapy assessment.
- **Conclusions:** An 8-week cardiovascular exercise program in patients with localized prostate cancer undergoing radiotherapy improved cardiovascular fitness, flexibility, muscle strength, and overall QOL and prevented fatigue.

Fatigue and Suggestions

- Exercise earlier in the day (ie: morning vs night)
- Break exercise into smaller bouts (3x10min bouts a day)
- Reduce intensity for the day (instead of long 60min at moderate pace, go for a 20min walk instead).
- Try getting up every 1hr and walk around for 5min.
- Take exercise breaks during commercials on TV shows.
- You did too much if:
  - You muscle soreness lasts more than 2 days
  - Cannot complete your ADL's

So what are the ACSM Guidelines?

- Aerobic Training
  - 150min of moderate activity or 75min of vigorous activity a week
  - This can be broken down to 30min a day, 5 days a week
  - Intensity RPE: 3-5 or The Talk Test
  - Issues with THR (220-age): medications can skew these results ie: beta blockers. Low or high fitness levels can also skew results.

As per American College of Sports Medicine (ACSM) guidelines [5]

Aerobic Training Summarized

FITT Principle:

Frequency: Most days of the week

Intensity: RPE 3-5, Talk Test

Time: 30min, (3x10min bouts??)

Type: Walking, swimming, cycling etc

So what are the ACSM Guidelines?

- Resistance Training
  - 8-10 exercises targeting the major muscles of the body (chest, shoulders, legs, back and core)
  - Aim for 2-4 sets of 10-15 reps with a 1min rest period between sets
  - Ideally, you should perform weight training 2x/week on non consecutive days working your way up to 3x/week.
  - COVID had weights flying off the shelves so get creative! Have your patients use soup cans, water bottles as weights and follow along with a program like the one on the PCSC YouTube channel!

As per American College of Sports Medicine (ACSM) guidelines [6]

Resistance Training Summarized

FITT Principle

Frequency: 2-3x/week

Intensity: 2-4 sets,10-15reps

Time: 15-45min

Type: Bodyweight, dumbbells, resistance bands, machines

Exercises and their modifications

Push-Up

Squats

Plank

What about patients with Bone Mets

- When patients have cancer metastasize to bone, the risk of fracture can increase.
- Is it safe to prescribe exercise to patients with bone metastasis?

Study 4 Exercise and Bone METS

- **Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases,** Cormie et Al. [7]
- **Background:** The aim of this feasibility trial was to determine the safety and efficacy of resistance exercise by prostate cancer survivors with bone metastatic disease.
- **Methods:** Twenty men with established bone metastases secondary to prostate cancer were randomly assigned to a 12-week resistance exercise program in which exercise prescription was based on the location of bone lesions (*n*=10) or usual care (*n*=10). Outcomes included safety and tolerance of the exercise program, physical function, physical activity level, body composition, fatigue, quality of life and psychological distress.

Study 4 Exercise and Bone METS

- **Results:** Participants had significant disease load with 65% of participants presenting with two or more regions affected by bone metastases and an average Gleason score of 8.2±0.9. Five participants (exercise=2; usual care=3) did not complete the intervention, three of which were due to advancing disease (exercise=2; usual care=1). No adverse events or skeletal complications occurred during the supervised exercise sessions.
- **Conclusions:** This initial evidence involving a small sample size suggests that appropriately designed and supervised resistance exercise may be safe and well tolerated by prostate cancer patients with bone metastatic disease and can lead to improvements in physical function, physical activity levels and lean mass. Future trials involving larger sample sizes are required to expand these preliminary findings.

Exercise for patients with Bone Mets

- It is safe to exercise this population, however, working with a trained exercise professional can help mitigate injury risk.
- Pain assessment will be discussed with the patient.
- Certain movements and exercises may be avoided.

References

Volpi, E., Nazemi, R., & Fujita, S. (2004). Muscle tissue changes with aging. *Current opinion in clinical nutrition and metabolic care*, *7*(4), 405. [1]

Winters-Stone, K. M., Dobek, J. C., Bennett, J. A., Dieckmann, N. F., Maddalozzo, G. F., Ryan, C. W., & Beer, T. M. (2015). Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: evidence from a randomized controlled trial. *Archives of physical medicine and rehabilitation*, *96*(1), 7-14. [2]

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Monga, U., Garber, S. L., Thornby, J., Vallbona, C., Kerrigan, A. J., Monga, T. N., & Zimmermann, K. P. (2007). Exercise prevents fatigue and improves quality of life in prostate cancer patients undergoing radiotherapy. *Archives of physical medicine and rehabilitation*, *88*(11), 1416-1422. [4]

American College of Sports Medicine. (2013). *ACSM's guidelines for exercise testing and prescription*. Lippincott Williams & Wilkins. [5][6]

Cormie, P., Newton, R. U., Spry, N., Joseph, D., Taaffe, D. R., & Galvao, D. A. (2013). Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. *Prostate cancer and prostatic diseases*, *16*(4), 328-335. [7]

PCSC Program YouTube Channel: https://www.youtube.com/channel/UC7i3mvOwfELhHlfBSO9zvxA/featured [8]

1:14pm – 1:44pm

What is Self Care? Some Keys to Optimizing Our Well-Being

Monica Hu, RCC

Integrated Self-Care

In the context of stress patterns and responses

Monica Hu, *MA, RCC, Prostate Cancer Supportive Care Program, BC*

Prostate Cancer Supportive Care

Objectives

- Define, and better understand, integrated self-care and impact on quality of life
- But first… with the goal of empowering us in our self-care choices/efforts:
- Consider differences in the types and patterns of stress in the context of dealing with prostate cancer and how these impact us and our stress reactions
- Introduce the working and contribution of human regulatory systems to help us understand when/how/why we are in different states, and how this affects our quality of life and self-care choices

Integrated Self-Care

- Integrated self care is based in a systems approach - the consideration of the inter-related impacts and functioning of various systems or realms that affect the whole person
- These factors do not work autonomously but play inter-related roles, for example as risk factors, perpetuating factors, or protective factors
- Each of these realms affect health, wellness, mental health, resilience and coping
- The overall combination has a lot to do with our experience of quality of life

But first…

Stress Patterns & Characteristics

"PATTERN" Stress/ Challenge:	Predictable Vs Unpredictable	Moderate Vs Extreme	Controllable Vs Prolonged

Consider some of the stressful aspects of your experience with prostate cancer and the types and patterns of stress that they have been for you.

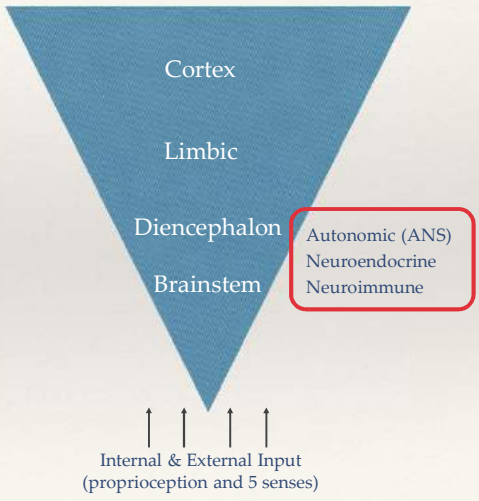
These patterns have an impact toward developing: tolerance/resilience or sensitization/vulnerability and this influences the states we are in more often.

Which gives us clues and to how and why our self-care choices matter.

But first… understanding regulatory systems and states.

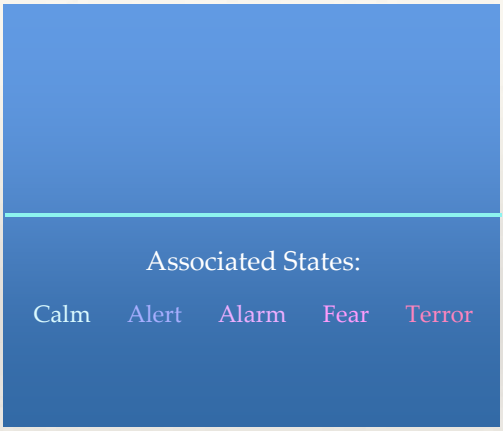
Our Brain & Regulatory Systems

- The purpose of our RSs is to maintain homeostasis (body temp, blood sugar levels…)
- The data for this RS work, incl. signals of threat or safety, are assessed by faster, more primitive parts of our brains first…
- And create impacts on our functioning via states…



Autonomic Nervous System (ANS)

Parasympathetic Nervous System: "Rest & Digest"



Sympathetic Nervous System: "Fight or Flight"

STATE	Calm	Alert	Alarm	Fear	Terror
Dominant Brain Area(s)	Cortex	Cortex (Limbic)	Limbic (Diencephalon)	Diencephalon (Brainstem)	Brainstem
Adaptive Behaviour	Reflect/ Create	Hyper-vigilant/ Avoid	Freeze/Com ply	Flight/Disso ciate	Fight/ Faint (Collapse)
Cognition*	Abstract (creative)	Concrete (routine)	Emotional	Reactive	Reflexive

*Functional IQ also varies with the shifts in states

All functioning of the brain (thinking, feeling), and much of the functioning of our body (heart, stomach, lungs…) depends on the state we are in.

The 'States' seen in cats…

Calm

- Limbs everywhere
- Head on its side
- eyes half-closed

The 'States' seen in cats…

Alert

- Eyes open, focused
- head upright

The 'States' seen in cats…

Alarm

- Instead of 'splayed out' limbs, now limbs are drawn in to body
- Head also drawn in somewhat
- Eyes bigger, rounder, pupils fairly normal

The 'States' seen in cats…

Fear

- Ready to bolt, legs prepared under body, low centre of gravity, balanced
- Ears beginning to flatten
- Eyes fully open wide and round; pupils dilated

The 'States' seen in cats…

Terror

- Makes body as large as possible (to deter predator)

States are reflective of the assessment of internal/external challenges or level of threat.

With no internal needs unmet (e.g. hunger, body temperature within limits) and no external challenges/threats, we will be in a state of calm. In this state we have the most access to the 'smartest' part of our brain.

How do our states impact our functioning in various domains?

STATE	Calm	Alert	Alarm	Fear	Terror
Dominant Brain Area(s)	Cortex	Cortex (Limbic)	Limbic (Diencephalon)	Diencephalon (Brainstem)	Brainstem
Adaptive Behaviour	Reflect/ Create	Hypervigilant/ Avoid	Freeze/Comply	Flight/Dissociate	Fight/ Faint (collapse)
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*Functional IQ is also reduced with the shifts in cognition

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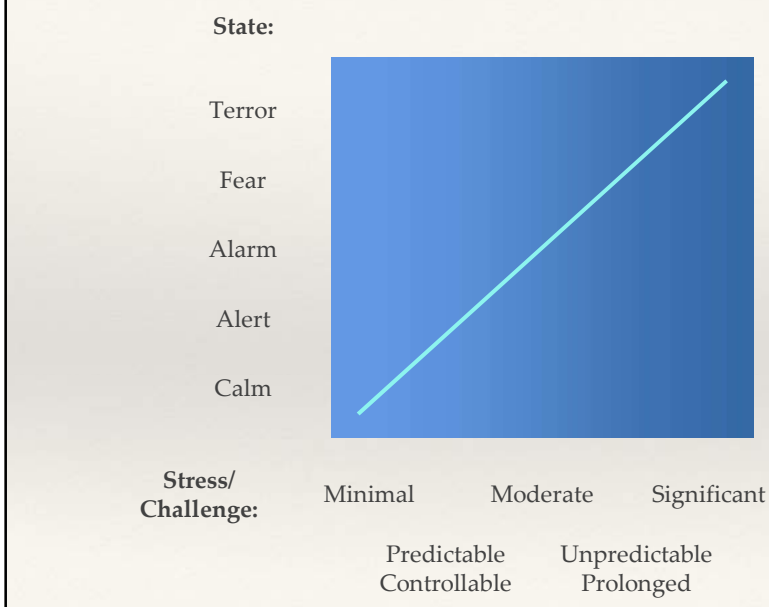
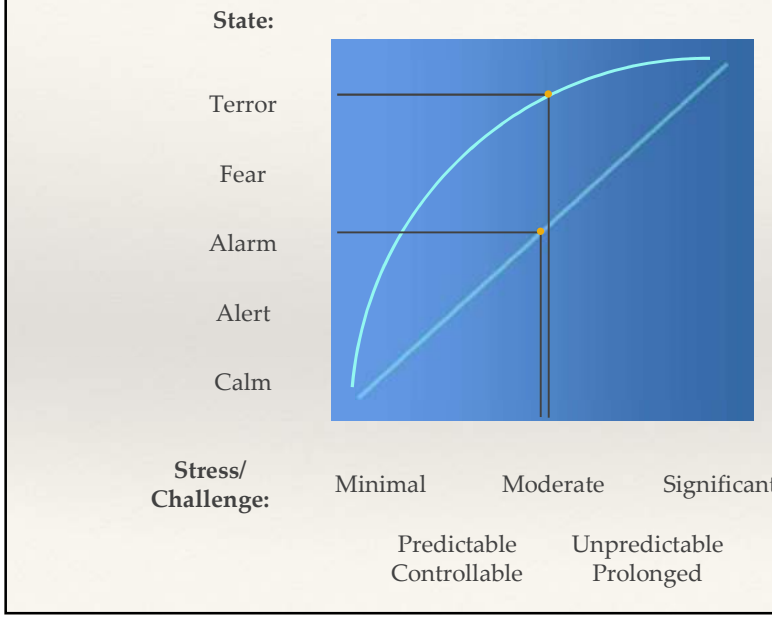
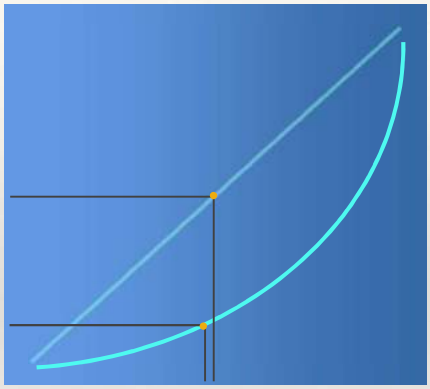
Stress Response



Sensitized Stress Response



Resilient Stress Response



Stress Patterns & Characteristics

"PATTERN" Stress/ Challenge:	Predictable Vs Unpredictable	Moderate Vs Extreme	Controllable Vs Prolonged

Impacts on developing:

tolerance/resilience or sensitization/vulnerability

Which gives us clues and to how and why our self-care choices matter.

Working with States

- Consider stress source and patterns:
  - unpredictable, extreme, prolonged -> sensitization
  - predictable, moderate, controllable -> resilience
- Calming/relaxation techniques to calm nervous system
- Employ routines to provide predictability
- Consider the situation in component parts, and
- Focus on things that are in your control

Realms of Integrated Self-Care

- Body: physical, somatic
- Mind: thoughts, cognition
- Emotions: feelings, affect
- Spirit/Beliefs: meaning, purpose, values
- Relationships: all levels (community to intimate)
- Environment: surroundings, nature
- Lifestyle: behaviours, nutrition, sleep

Questions to ask yourself

- In which realms do I have stress/challenges?
- What are my symptoms, and in which realms are they?
- In which realms do I have factors I could change?
- In which realms do I have protective factors?
- Which realm(s) are drawing my attention?
- What stress response states am I often in? How does this show up in my body/mind/emotions/behaviours/relationships/environment/lifestyle?
- What do I need? What do I long for when I listen deeply?
- Where can I make a difference now?

Where can I make a difference now?

- Understand the human mind's biases toward wanting to definitively resolve and focus on threats and potential threats (and how this may relate to your experience with prostate cancer)
- With this in mind, find a balance that feels right to you with choosing to focus on things that make a difference to your quality of life now

Self-Care Ideas

- Exercise: cardio, strength, stretching, integrated (exercise to the point of sweating is 'medicine'!)
- Do something Creative: cooking, art, gardening, writing…
- Practise deep breathing, relaxation, meditation, mindfulness
- Enjoy the beauty of nature, fresh air, sunshine
- Learn to enjoy change; try something new
- Discuss your feelings with family/friend, therapist
- Have/develop self-compassion
- Be open-minded and intellectually curious; maintain perspective
- Do things that engage your senses (find things for each of them)
- Seek out and learn new coping/stress management skills

Self-Care Ideas continued

- Stay connected, maintain relationships; be kind/attentive
- Eat healthy/nutritious foods; learn new recipes; try new ingredients
- Practice good sleep hygiene; maintain routines
- Take care of your environment, declutter, organize
- Limit alcohol; avoid unhealthy substances
- Cultivate gratitude for small things
- Listen to or play music
- Limit unhelpful mental habits such as worrying; seek out skills for this
- Allow yourself to play, dance, sing…
- Take time for yourself; make time for contemplation/reflection
- Don't ignore red flags, engage professional help as needed

In Summary

- Reflect on the types of stressors in your life and how you experience them
- With the understanding of how they affect your internal states and functioning and ultimately your quality of life,
- (My hope is that you) see the power you have via conscious and educated integrated self-care choices to influence your quality of life today

"It's the little things that matter, and gather together to make profound differences."

–Based on Chaos Theory/The Butterfly Effect (Lorenz, 1963)

Acknowledgements

- Cat photos: https://www.cbc.ca/life/pets/do-you-speak-cat-common-feline-postures-decoded-1.5256356
- Neurobiology: Dr. Bruce Perry, Dr. Dan Siegel and so many others

Resources

- bccancer.bc.ca/health-info/coping-with-cancer
- cancer.net/survivorship/

Thank you

Q & A

Save the Date!

22nd Annual

Pacific Northwest Prostate Cancer Conference

Saturday, October 15th 2022