

# SEXUAL DYSFUNCTION AFTER PROSTATE CANCER TREATMENTS

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NEW MEXICO CANCER CENTER  
*New Mexico Oncology Hematology Consultants, Ltd.*

# Disclosures

- No industry financial disclosures
- Practicing radiation oncologist at New Mexico Cancer Center

# Objectives

- Discuss relevant anatomy and pathophysiology of common causes of sexual dysfunction
- Discuss how common prostate cancer treatments could potentially cause sexual dysfunction
- Identify treatments and coping strategies for common causes of sexual dysfunction after prostate cancer treatments

# INTRODUCTION

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# Introduction

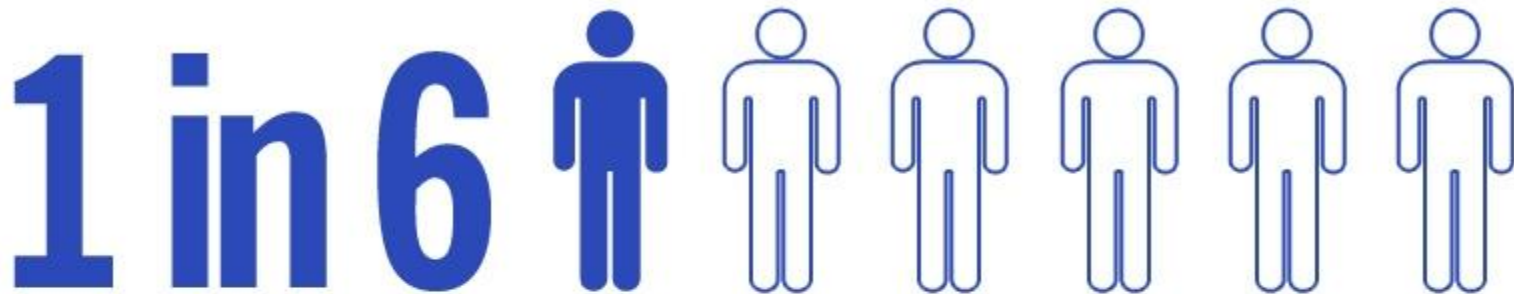
- Prostate cancer is the most common cancer in men in the US and developed world

**1 IN 6**  
MEN WILL BE  
DIAGNOSED  
WITH PROSTATE  
CANCER

Help each one find precision  
treatment. **DONATE** here.

# Prostate Cancer: GET THE FACTS

Other than skin cancer, prostate cancer is the most common cancer in American men.



**men will be diagnosed with prostate cancer during his lifetime.**

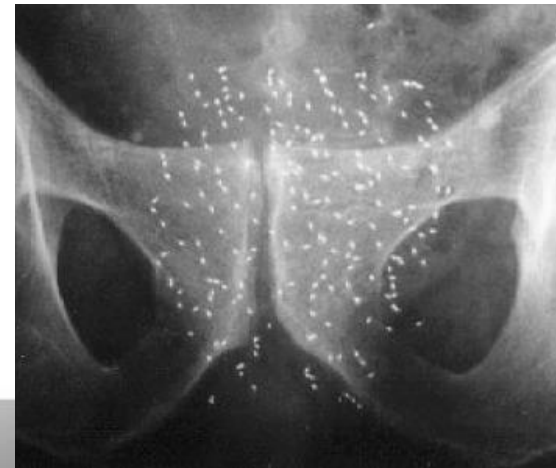


Prostate cancer can be a serious disease, but **most men diagnosed with prostate cancer do not die from it.** In fact, more than 2.5 million men in the United States who have been diagnosed with prostate cancer at some point are **still alive today.**

- Because prostate cancer is a treatable disease with high associated success rates, **quality of life** and **toxicities** are of great importance to prostate cancer survivors.

# Common Treatment Modalities for Prostate Cancer

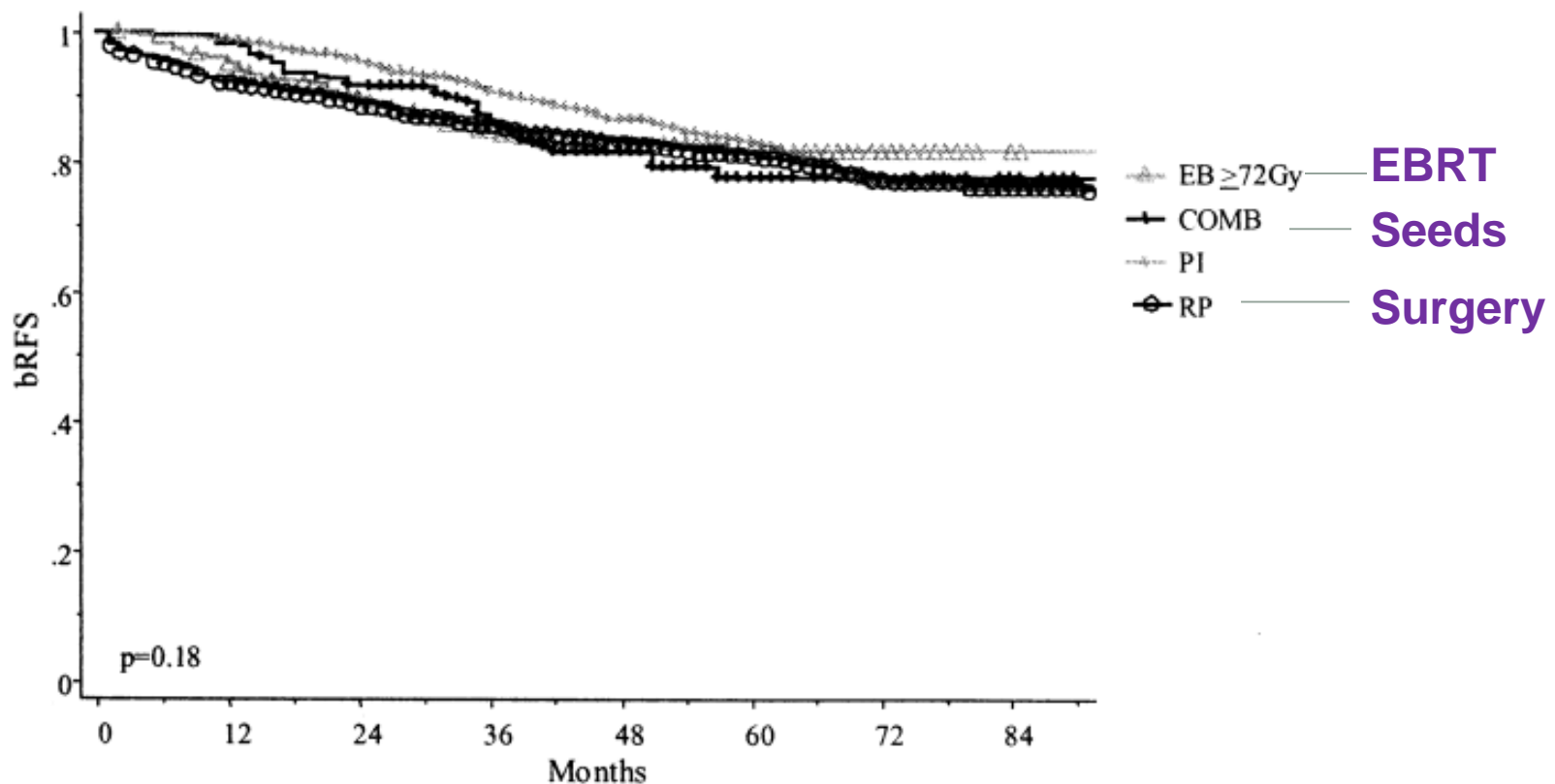
- Surgery
- External Beam Radiation Therapy (X-rays)
- Prostate Seed Implantation (Brachytherapy)





# Retrospective Review: 2991 Consecutive Patients from Cleveland Clinic, Memorial Sloan-Kettering at Mercy Medical Center

- T1-T2 localized prostate cancer, 1990-1998



(b)  
Kupelian et al. Radical Prostatectomy, External Beam Radiotherapy <72 Gy, External Beam Radiotherapy  $\geq 72$  Gy, Permanent Seed Implantation, Combined Seeds/External Beam Radiotherapy for Stage T1-T2 Prostate Cancer. IJROBP 58:25, 2004.

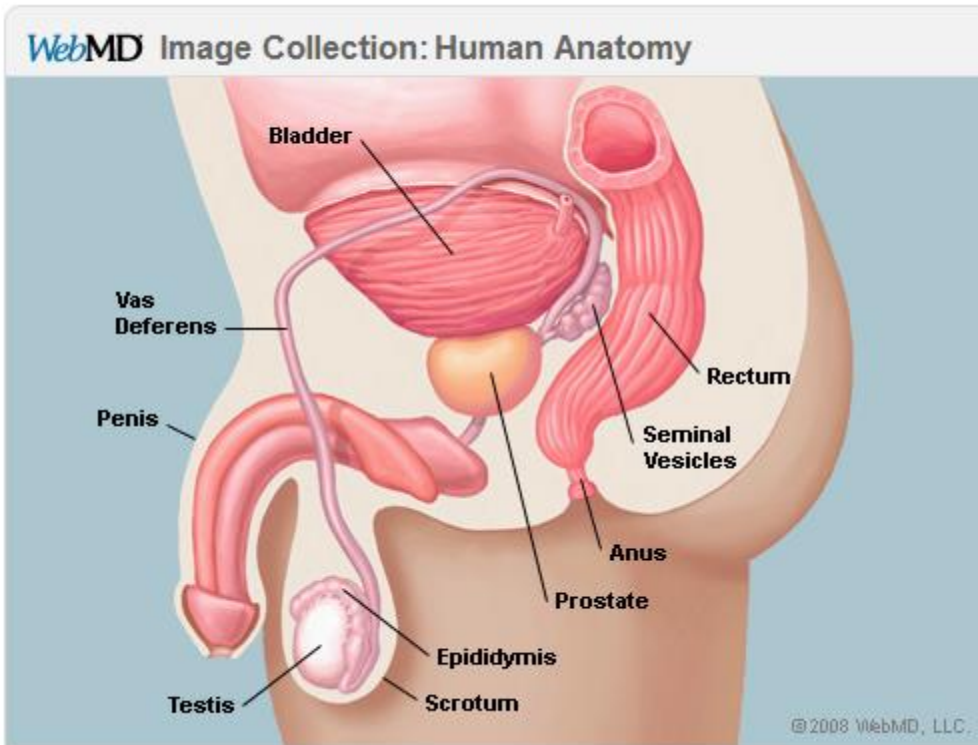
# Sexual Function and Prostate Cancer Treatment

- For many men, survival seems to be the highest valued factor influencing prostate cancer treatment decisions
- Studies have shown that men value maintaining sexual function at levels similar to how they value maintaining urinary function
- Men in good general health tend to place higher value on maintaining sexual function compared to men with more comorbidities
- Inadequate understanding of risk of sexual problems or lack of insight into importance of sexual functioning in one's life may lead to poorly informed decisions about prostate cancer treatment

# ANATOMY

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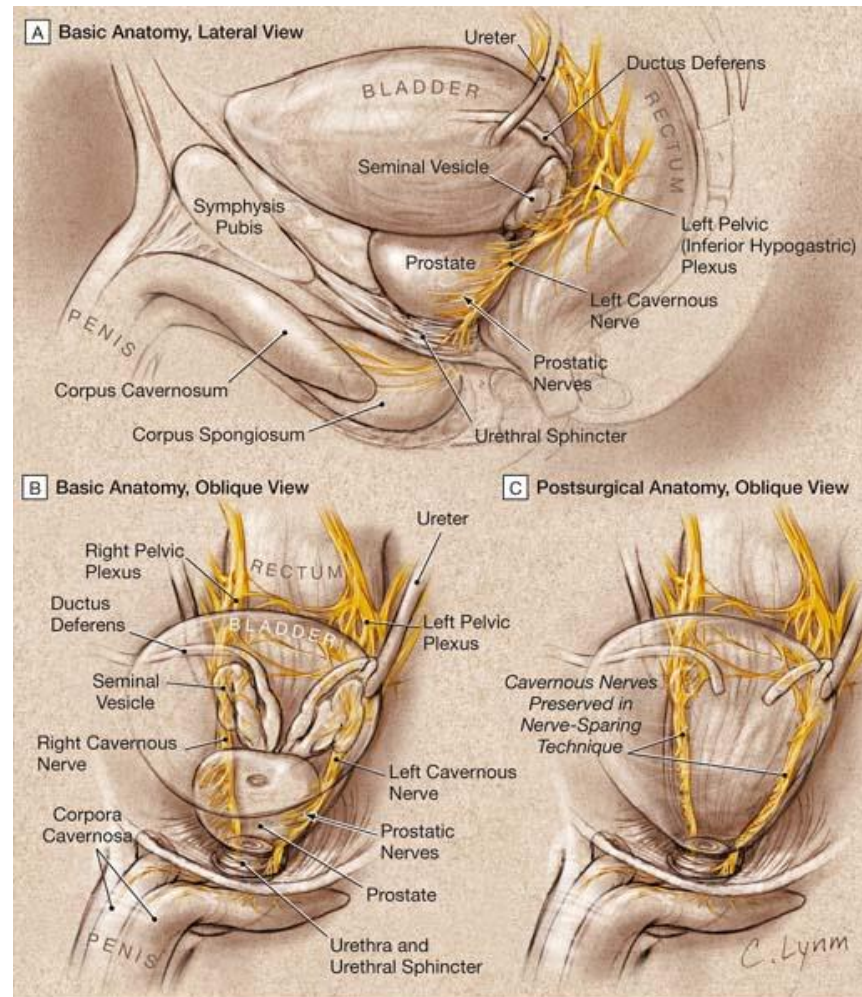
# Where is the Prostate?



## Side View of the Prostate

- Walnut-sized gland below the bladder
- Urethra runs through the center of the prostate, from the bladder to the penis, letting urine flow out of the body.
- Primary role of the prostate: produce fluid for semen, which transports sperm
- Nerves for erections run along back and sides of the prostate

# Neurovascular bundles



# SEXUAL DYSFUNCTION

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# Sexual Dysfunction

- American Foundation for Urologic Disease definition:  
Persistent impairment of couple's normal or usual patterns of sexual interest and/or response
- Many components
  - Physiologic (from medical condition or treatments)
  - Psychologic (depression)
  - Pharmacologic (side effects of medications)

# Prostate Cancer Treatments Can Cause

- Erectile dysfunction
- Diminished libido
- Abnormal ejaculation

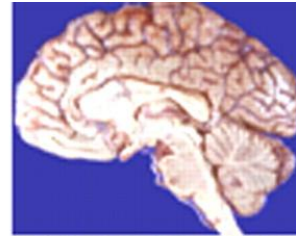


# Normal Physiology of Male Sexual Function



Visual

Tactile

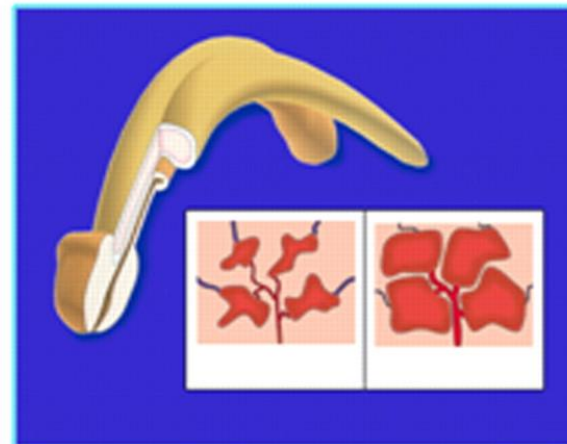


Olfactory

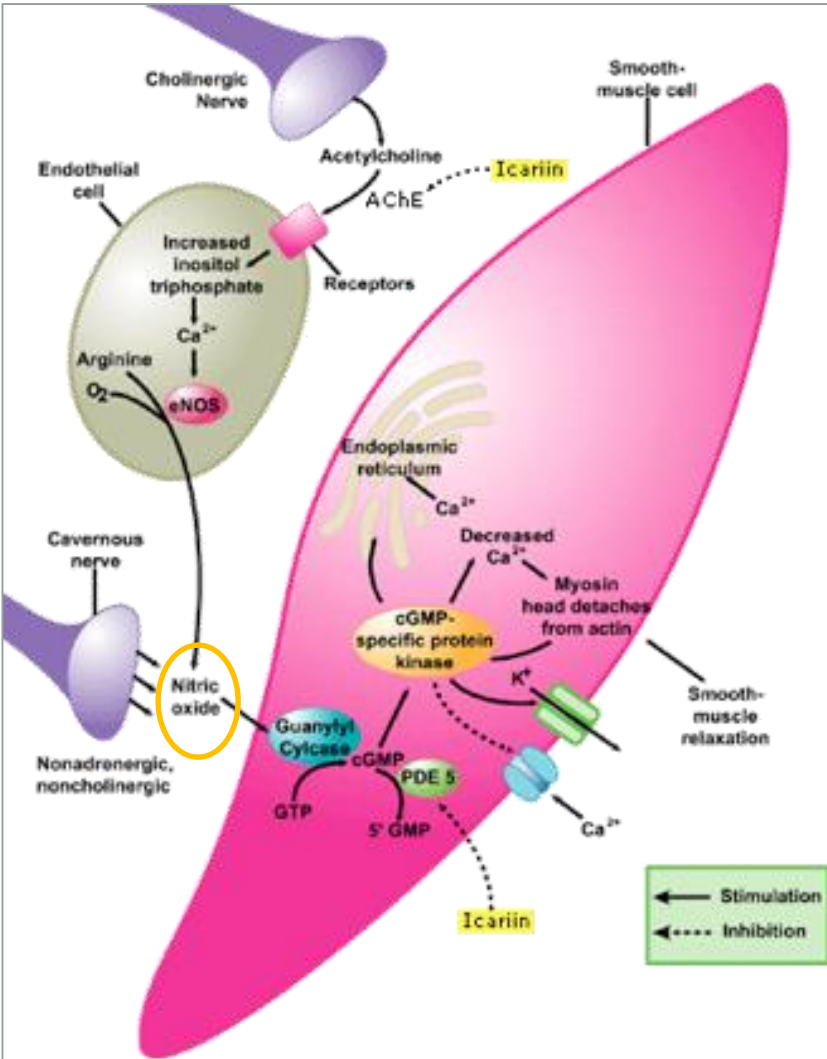
Imaginative

Requires interactions among various systems

- Vascular
- Neurologic
- Hormonal
- Psychologic



# Phosphodiesterase inhibitors (PDE-inhibitors)



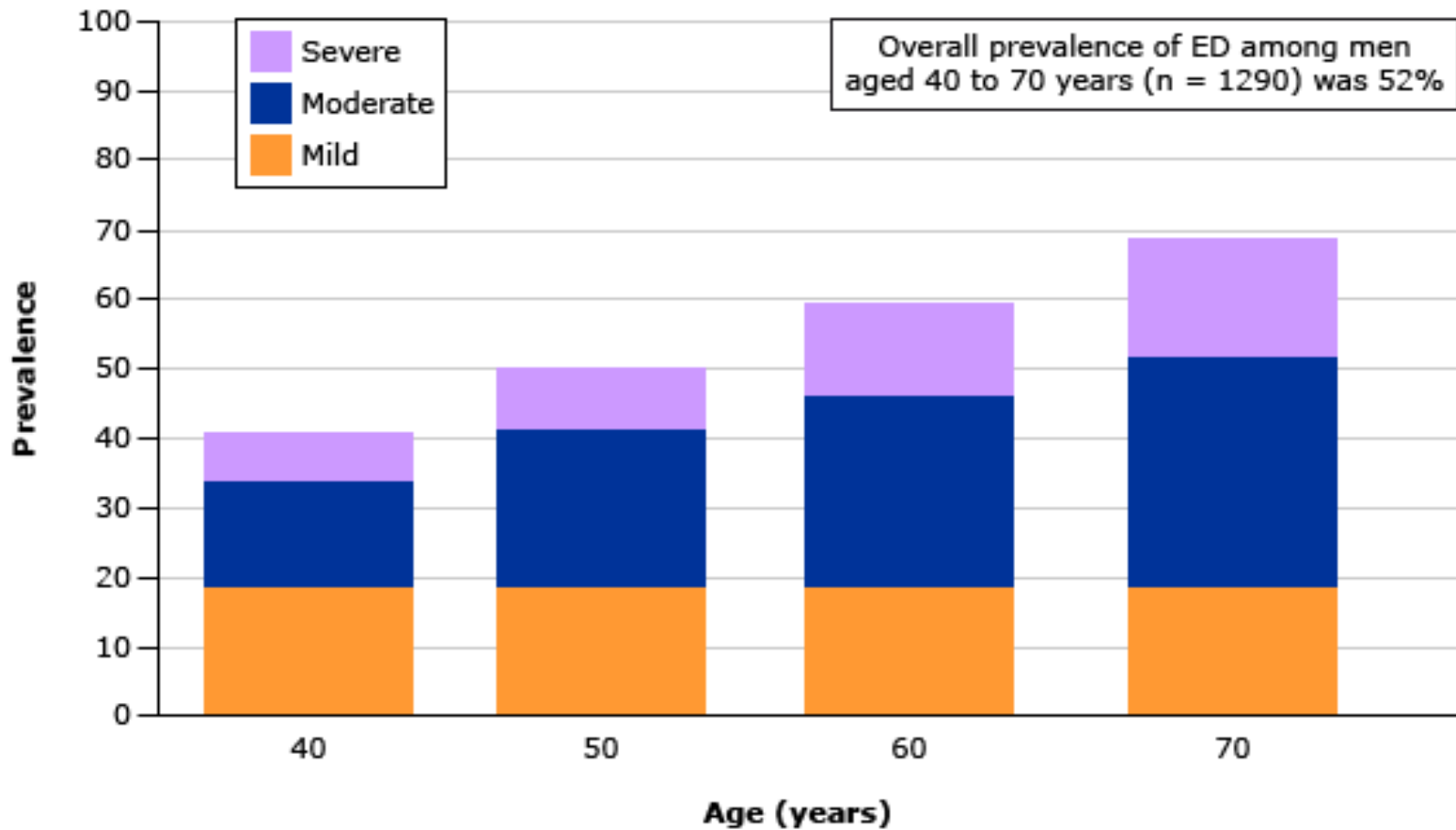
Nitric oxide = improved blood flow = erection

# Common Causes of Sexual Dysfunction

- **Age**
- **Hypertension**
- **Diabetes**
- **Smoking**
- Meds
- Alcohol
- Depression
- Fatigue
- Recreational Drugs
- Relationship Problems
- Systemic Illness
- Testosterone Deficiency

- Massachusetts Male Aging Study in 1994 revealed that sexual dysfunction first emerges for men in early 40s, increases with advancing age
- At age 40, 40% acknowledged some level of impaired sexual function, another 10% had waning sexual prowess or interest with each successive decade
- 9 year longitudinal follow-up of this cohort confirmed age-associated declines in most domains of sexual function
  - Intercourse
  - Erection frequency
  - Sexual desire
  - Satisfaction
  - Orgasm

# Prevalence and severity of ED in the Massachusetts Male Aging Study (MMAS)



# Best Predictors of ED

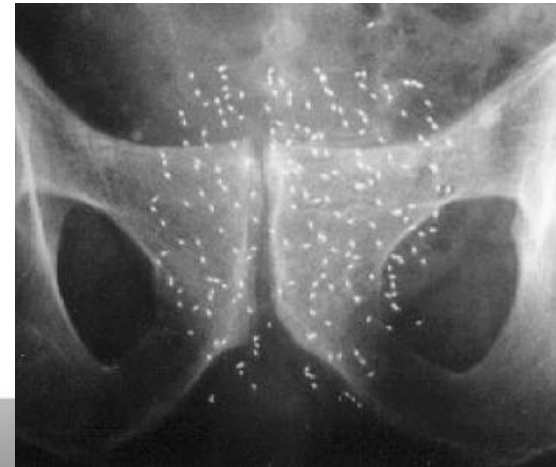
- Diabetes mellitus (type II diabetes)
- Hypertension (high blood pressure)
- Obesity
- Dyslipidemia (high cholesterol)
- Cardiovascular disease
- Smoking
- Medication use

# EFFECTS OF COMMON PROSTATE CANCER TREATMENTS

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# Common Treatment Modalities for Prostate Cancer

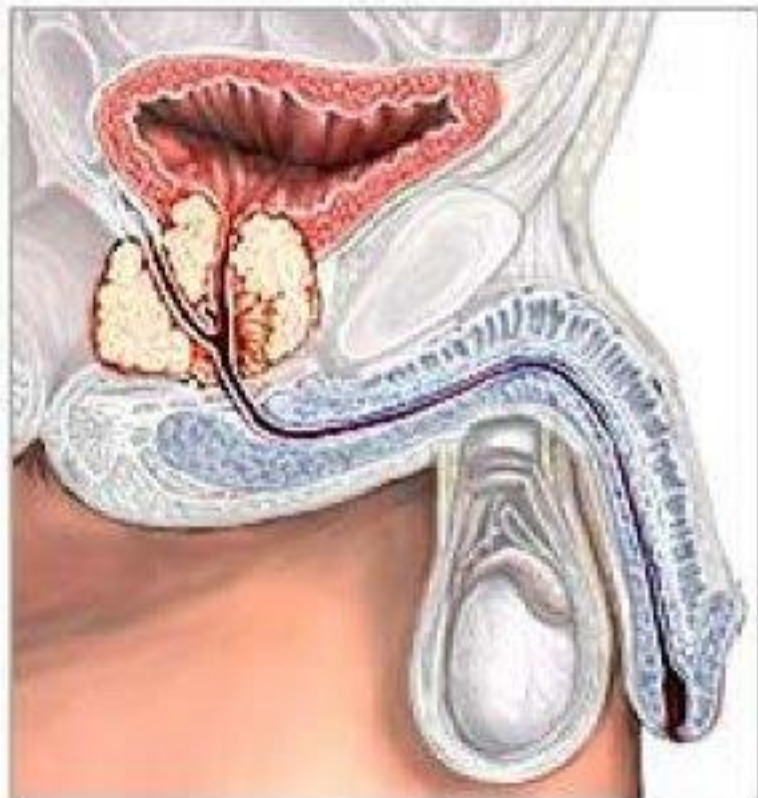
- Surgery (Radical Prostatectomy)
- External Beam Radiation Therapy
- Prostate Seed Implantation (Brachytherapy)



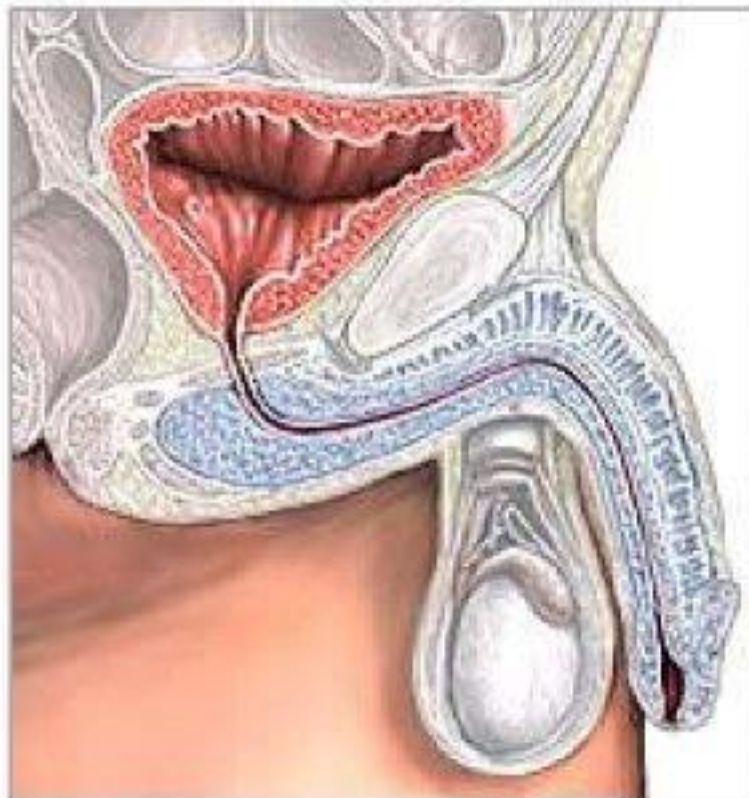


# Surgery

Before



After



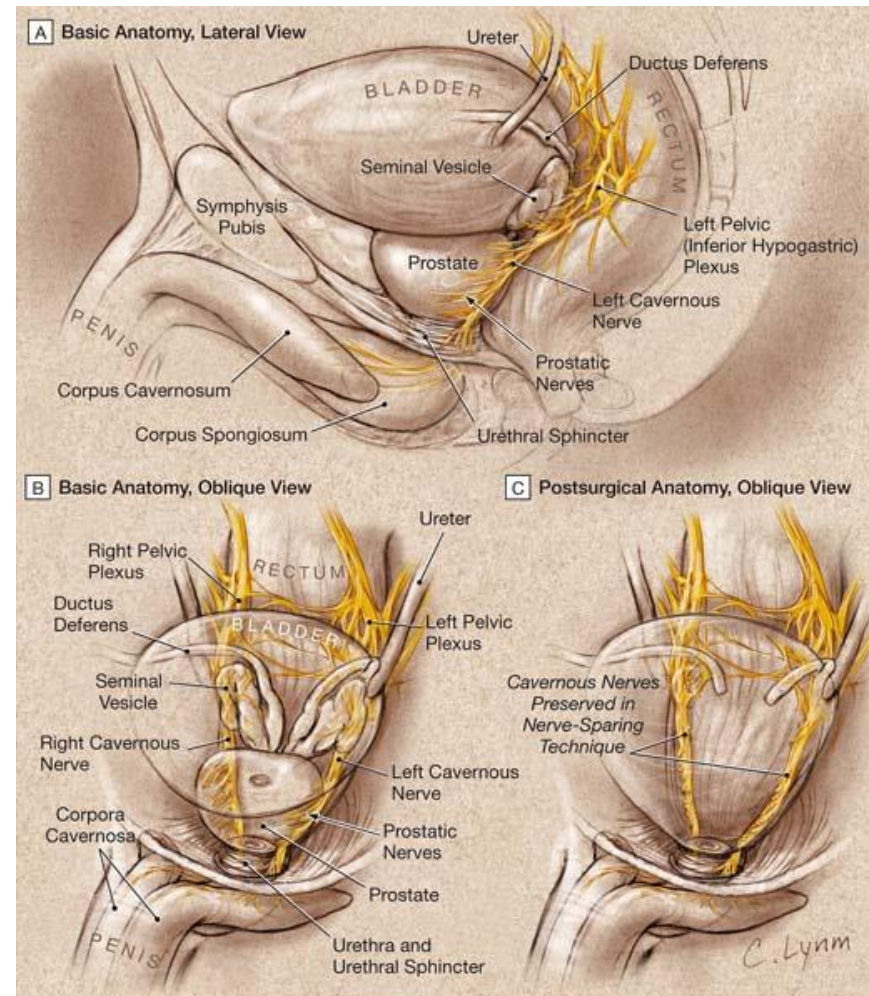
SheerMed

# Surgery



# Nerve-Sparing Approach

- Erectile function after RP depends on preservation of nerves, located within the neurovascular bundles
- Effort to preserve bilateral neurovascular bundles should be made by the surgeon, **as long as cancer control is not compromised**
- Decision to perform nerve sparing surgery based upon visual inspection and palpation of gland and its relationship to neurovascular bundle



# Erectile Dysfunction after Surgery

- Many differing reports of outcomes
  - High potency rates of 76-86% reported by individual surgeons/centers doing nerve-sparing surgery on carefully selected men who then use PDE-inhibitors (sildenafil/Viagra)
  - Another series of 603 patients reported that sexuality problems were a moderate or big concern in 59% of patients 2 months after RP (Sanda – PROSTQA)
    - Although gradual improvement with time, 43% still reported problems 2 years after surgery
  - Recovery of erectile function can be delayed, can continue even beyond 2 years.
  - For men who recover erectile function, available evidence indicates that function can be maintained for at least 10 years

# Erectile Function after Surgery

- Likelihood of regaining potency after RP decreases with increasing age

Decade	Potency Rate after RP (%)
Age 40s	86
Age 50s	80
Age 60s	60
Age 70s	42

# Other Sexual Side Effects from Surgery

- Penile numbness
- Perineal soreness
- Dry ejaculation
- Small decrease in penile length

# Treatments

- Sexual counseling for men and their partners may increase the use of and satisfaction with medical therapies.
- Phosphodiesterase inhibitors are most helpful in men who have undergone a nerve-sparing procedure.
  - 84 men presenting with erectile dysfunction following radical prostatectomy

Procedure	Response Rate to Drug
Bilateral nerve-sparing	72%
Unilateral nerve-sparing	50%
Non-nerve sparing	15%

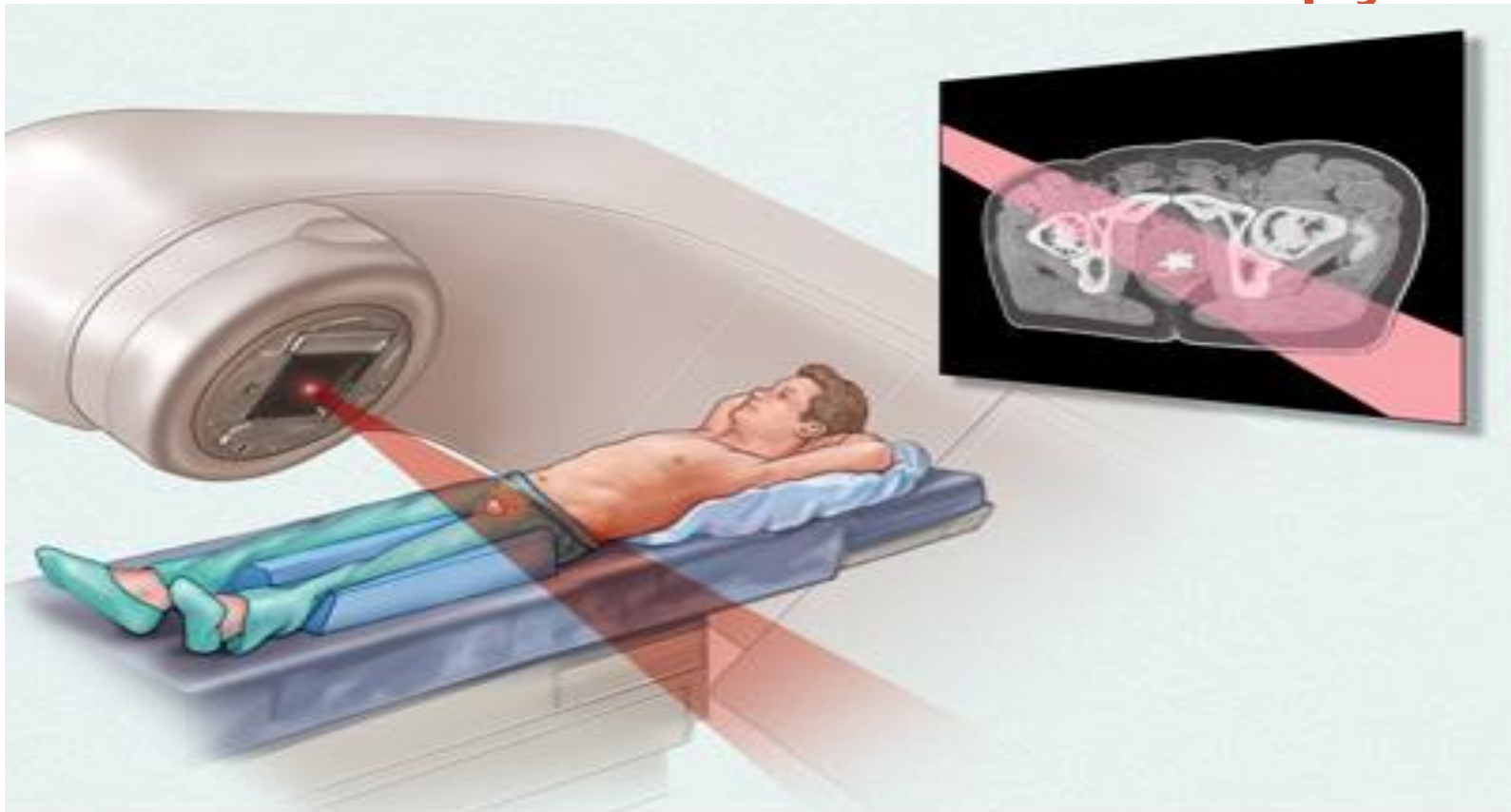
# Response to Medications

- Response to sildenafil increases with time following radical prostatectomy
  - 579 patients s/p radical prostatectomy, 95% of which had undergone nerve-sparing procedures

Time after surgery	% Patients Reporting Benefit from Sildenafil
0-6 months	29%
18-24 months	60%



# External Beam Radiation Therapy

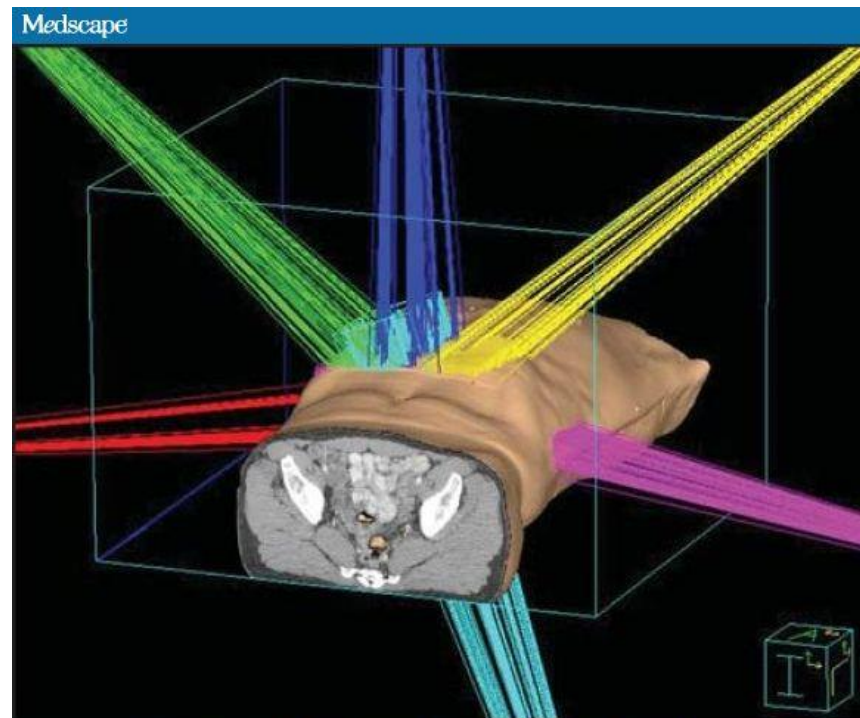


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- Linear accelerator moves around the patient to deliver radiation from different angles
- Treatments are 5 days/week for 8-9 weeks, only 15 min per treatment

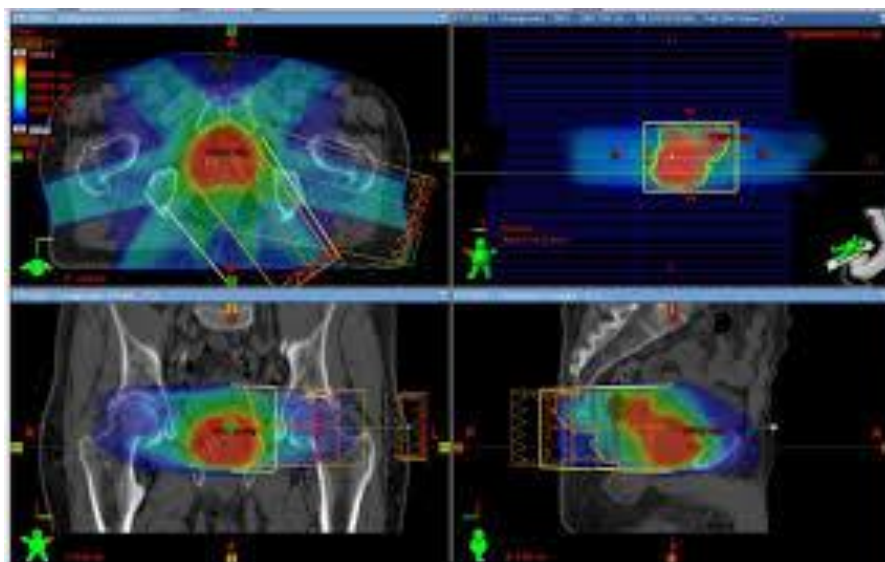
# External Beam Radiation Therapy (EBRT)

- High energy x-rays kill cancer cells
- Normal tissue repairs in between each daily treatment
- Goal: kill cancer cells while sparing as much normal cells as possible

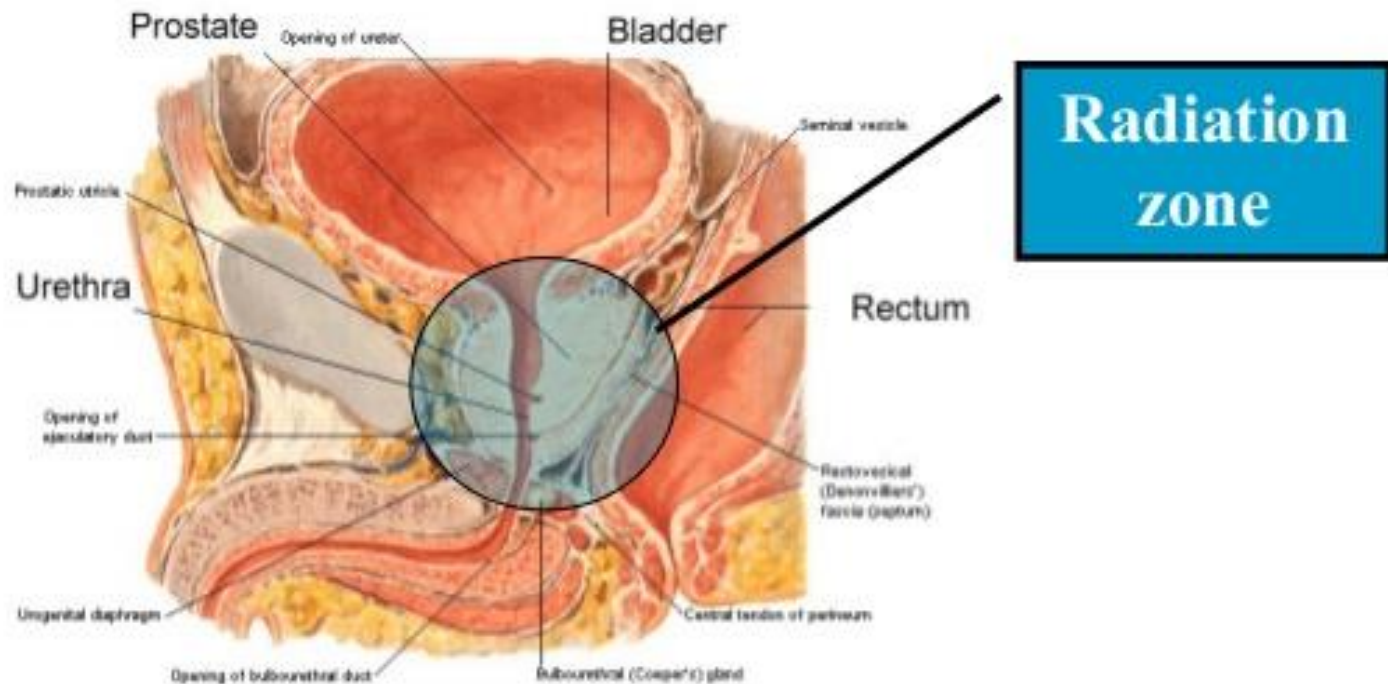


# CT-Guided Simulation (Target Practice)

- CT scan performed and creates a “map” for physician to design treatment to your specific anatomy
- Immobilization devices created to reproduce daily treatment positioning



# Side Effects of EBRT



The structures that will get hit by radiation and have inflammation or irritation: bladder, urethra and rectum

# Mechanism of Injury

- Not entirely well-known
- Vascular damage
- Dose to neurovascular bundles and penile structures

# Erectile Function after EBRT

- 30-45% of men who are able to have erections prior to RT are unable to after therapy
- Frequency increases over time

# Erectile Function after EBRT

- Generally occurs 6 months and beyond
- Risk of erectile dysfunction significantly reduced if penile structures are avoided
- Modern methods of delivering radiation therapy can limit dose to penile structures
- PDE inhibitors have shown to improve symptoms in up to 2/3 of patients with erectile dysfunction after EBRT

# Other Sexual Side Effects from EBRT

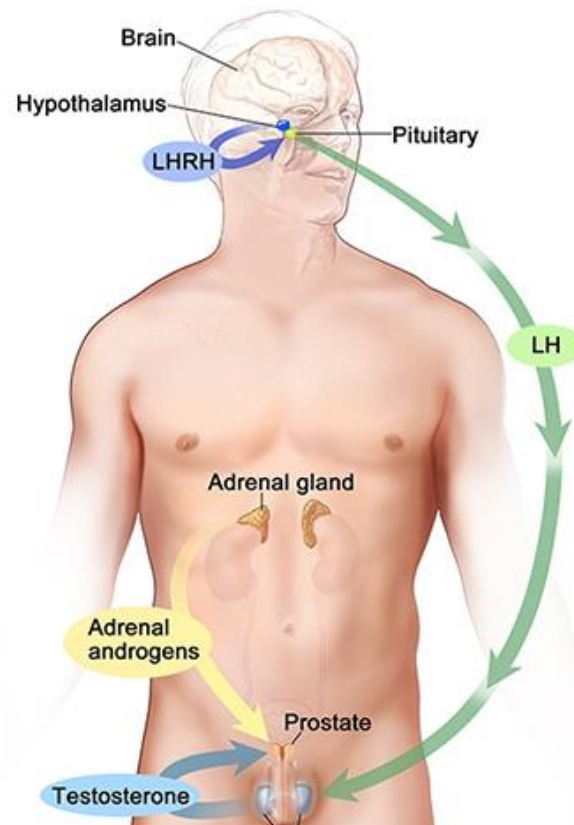
- Less semen ejaculated
- Dry ejaculation
- Weaker, less satisfying orgasms



# Androgen Deprivation Therapy

## Indications

- High risk prostate cancer
- Selected post-op cases
- Recurrent/metastatic disease



1/3 of all men receiving treatment for prostate cancer receive ADT

# Erectile Dysfunction from ADT

- Majority of men receiving ADT develop sexual dysfunction
- GnRH agonist (Lupron) – loss of libido first several months, then erectile dysfunction follows
- Testosterone decreases >95%
- Sexual dysfunction should be anticipated and patients should be counseled before treatment
- Recovery of erectile function possible with short-term ADT
  - Can be delayed
  - Not always complete recovery

# Management

- 44% respond to PDE inhibitors
- Randomized controlled data has shown that exercise improves sexual activity in men undergoing ADT
  - 57 men randomized to “usual standard care” vs. “12 week exercise intervention”
  - Results
    - Standard care group decreased sexual activity
    - Exercise group maintained level of sexual activity
    - At conclusion of study, exercise group had significantly higher percentage of participants reporting major interest in sex (17% exercise group vs. 0% control group)

# COMPARATIVE OUTCOMES

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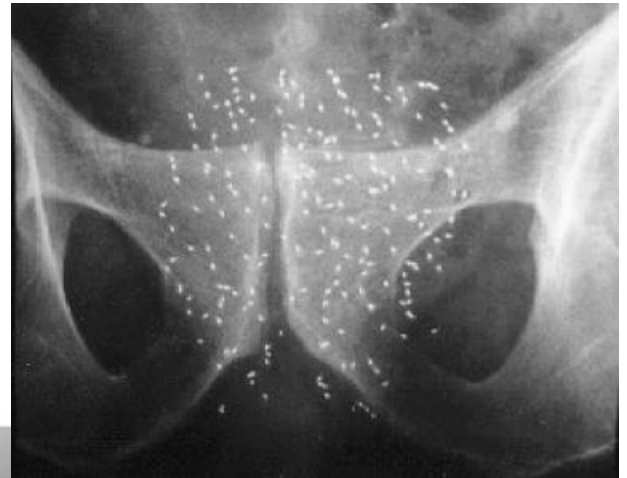
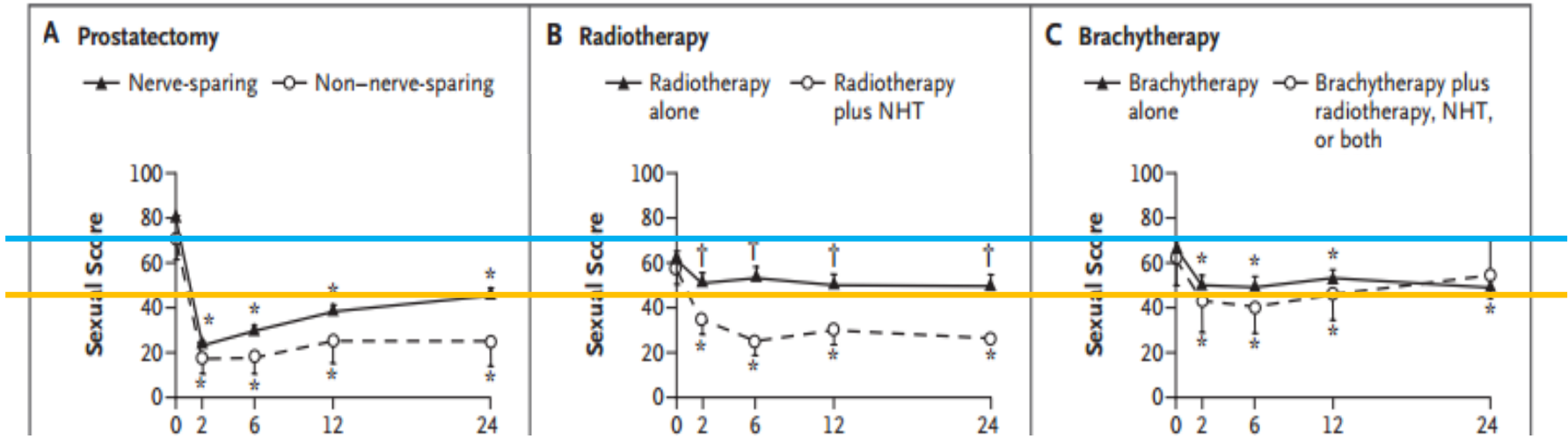
ORIGINAL ARTICLE

## Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

Martin G. Sanda, M.D., Rodney L. Dunn, M.S., Jeff Michalski, M.D., Howard M. Sandler, M.D., Laurel Northouse, R.N., Ph.D., Larry Hembroff, Ph.D., Xihong Lin, Ph.D., Thomas K. Greenfield, Ph.D., Mark S. Litwin, M.D., M.P.H., Christopher S. Saigal, M.D., M.P.H., Arul Mahadevan, M.D., Eric Klein, M.D., Adam Kibel, M.D., Louis L. Pisters, M.D., Deborah Kuban, M.D., Irving Kaplan, M.D., David Wood, M.D., Jay Ciezki, M.D., Nikhil Shah, D.O., and John T. Wei, M.D.

- Multi-institutional study
- Prospectively measured quality of life outcomes
- 1201 pts, 625 spouses/partners

- Sexual Score



# Prediction of Erectile Function Following Treatment for Prostate Cancer

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Meredith M. Regan, ScD

Matthew R. Cooperberg, MD, MPH

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Rodney L. Dunn, MS

Peter R. Carroll, MD, MPH

Martin G. Sanda, MD

**B**ECAUSE MOST PATIENTS SURVIVE early-stage prostate cancer after treatment,<sup>1</sup> health-related quality of life (HRQOL) outcomes have emerged as a major emphasis in treatment decisions. Erectile dysfunction is commonplace after prostate cancer treatment and has signifi-

**Context** Sexual function is the health-related quality of life (HRQOL) domain most commonly impaired after prostate cancer treatment; however, validated tools to enable personalized prediction of erectile dysfunction after prostate cancer treatment are lacking.

**Objective** To predict long-term erectile function following prostate cancer treatment based on individual patient and treatment characteristics.

**Design** Pretreatment patient characteristics, sexual HRQOL, and treatment details measured in a longitudinal academic multicenter cohort (Prostate Cancer Outcomes and Satisfaction With Treatment Quality Assessment; enrolled from 2003 through 2006), were used to develop models predicting erectile function 2 years after treatment. A community-based cohort (community-based Cancer of the Prostate Strategic Urologic Research Endeavor [CaPSURE]; enrolled 1995 through 2007) externally validated model performance. Patients in US academic and community-based practices whose HRQOL was measured pretreatment (N=1201) underwent follow-up after prostatectomy, external radiotherapy, or brachytherapy for prostate cancer. Sexual outcomes among men completing 2 years' follow-up (n=1027) were used to develop models predicting erectile function that were externally validated among 1913 patients in a community-based cohort.

**Main Outcome Measures** Patient-reported functional erections suitable for intercourse 2 years following prostate cancer treatment.

**Results** Two years after prostate cancer treatment, 368 (37% [95% CI, 34%-40%]) of all patients and 335 (48% [95% CI, 45%-52%]) of those with functional erections prior to treatment reported functional erections; 531 (53% [95% CI, 50%-56%]) of patients without penile prostheses reported use of medications or other devices for erectile dysfunction. Pretreatment sexual HRQOL score, age, serum prostate-specific antigen level, race/ethnicity, body mass index, and intended treatment details were associated with functional erections 2 years after treatment. Multivariable logistic regression models predicting erectile function estimated 2-year function probabilities from as low as 10% or less to as high as 70% or greater depending on the individual's pretreatment patient characteristics and treatment details. The models performed well in predicting erections in external validation among CaPSURE cohort patients (areas under the receiver operating characteristic curve, 0.77 [95% CI, 0.74-0.80] for prostatectomy; 0.87 [95% CI, 0.80-0.94] for external radiotherapy; and 0.90 [95% CI, 0.85-0.95] for brachytherapy).

**Conclusion** Stratification by pretreatment patient characteristics and treatment details enables prediction of erectile function 2 years after prostatectomy, external radiotherapy, or brachytherapy for prostate cancer.

JAMA. 2011;306(11):1205-1214

www.jama.com

- At 2 years after prostate cancer treatment:
  - 37% of all patients reported functional erections
  - 53% of patients with functional erections prior to treatment reported functional erections
- Factors associated with functional erections 2 years after treatment
  - Pretreatment sexual function
  - Age
  - Pretreatment PSA
  - Race/ethnicity
  - BMI
  - Intended treatment details
- PDE inhibitors effective in 68% of men who tried it after treatment





# Psychosocial / Lifestyle Interventions

- Exercise
- Diet
- Stop smoking
- Limit alcohol intake
- Reduce stress
- Kegel exercises
- Communication
- Counseling

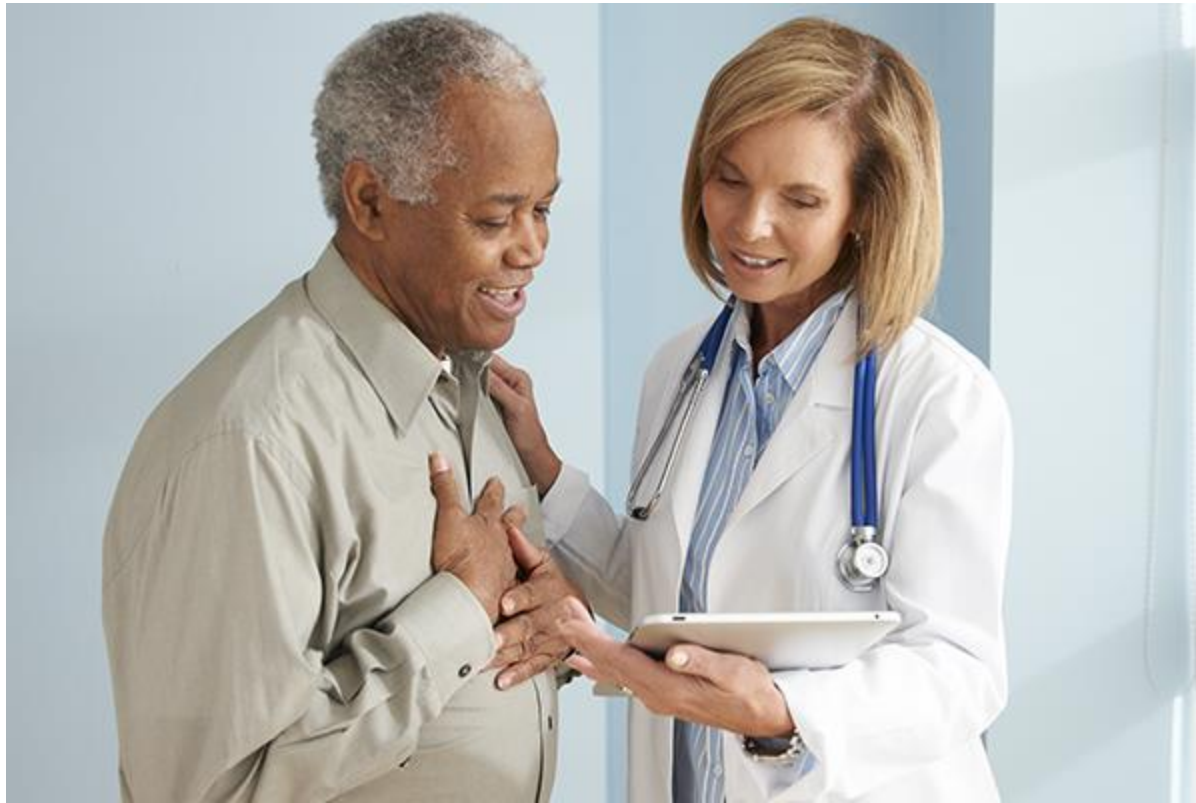
# Treatment options

1. Treat reversible causes
2. Pharmacologic intervention
3. Procedural/surgical interventions

# Conclusions

- Sexual dysfunction is common in all men and increases with age
- Prostate cancer treatments including surgery, radiation therapy, and androgen deprivation therapy are associated with sexual dysfunction
- Age and pre-treatment sexual function are the best predictors of probability of erectile function after cancer treatment
- Many treatment options with differing degrees of invasiveness are available for treatment of sexual dysfunction after prostate cancer treatment

# Talk to Your Doctor



# For More Information

- American Cancer Society (ACS)
  - [www.cancer.org](http://www.cancer.org)
  - Sex and Men with Cancer (all cancers, not limited to prostate)
- National Cancer Institute (NCI)
  - [www.cancer.gov](http://www.cancer.gov)
- Center for Disease Control and Prevention (CDC)
  - [www.cdc.gov/cancer](http://www.cdc.gov/cancer)
- Prostate Cancer UK
  - [www.prostatecanceruk.org](http://www.prostatecanceruk.org)
  - Prostate Cancer and Your Sex Life booklet



# Thank You



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Albuquerque  
Gallup  
Silver City

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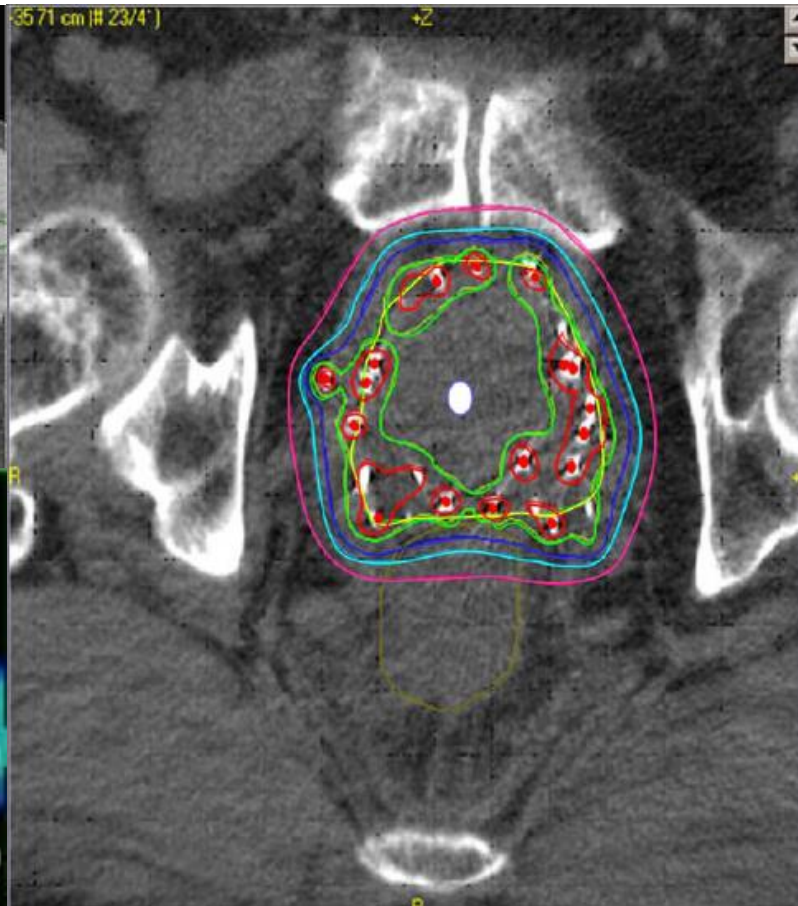
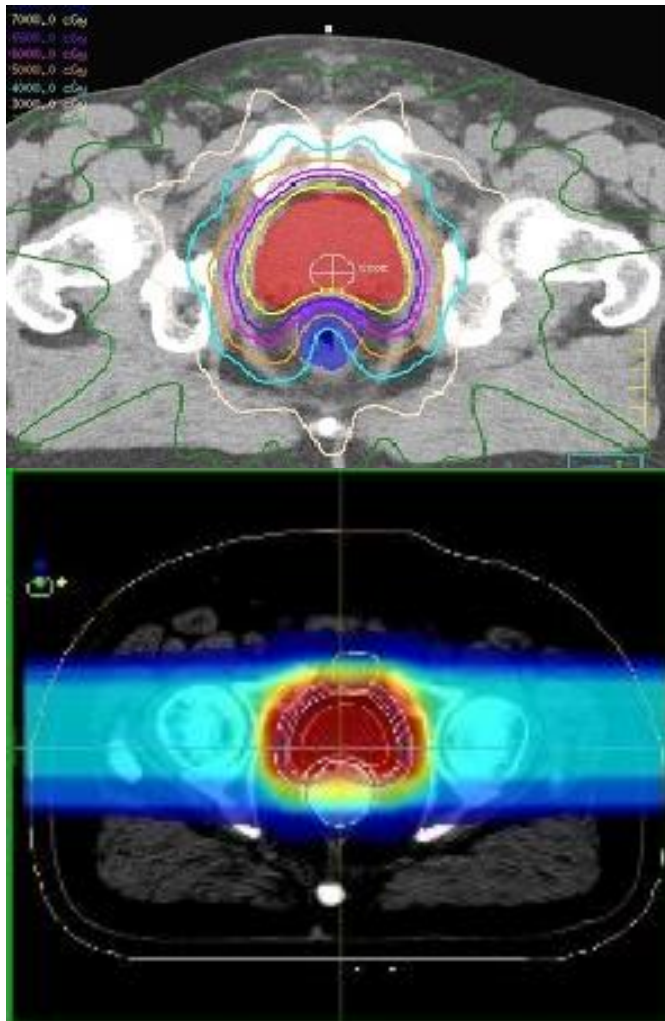
SEPTEMBER IS NATIONAL  
PROSTATE CANCER  
AWARENESS MONTH

**MOVEMBER**  
CHANGING  
THE FACE  
OF MEN'S  
HEALTH





# IMRT vs. Protons vs. Seeds



Axial Isodose  
Distribution:  
Peripheral  
Loading and  
Urethral  
Sparing

Yellow	Prostate
Olive	Rectum
Blue	Urethra
Red	290 Gy
Green	217.5 Gy
Dark Blue	145 Gy
Cyan	116 Gy
Pink	80 Gy

# Can erectile dysfunction from XRT be prevented?

- Possibly
  - MSKCC – sildenafil vs. placebo, prospective double blind randomized trial
    - Daily administration during and after XRT showed improved overall sexual function vs. placebo
    - First randomized trial to demonstrate utility of PDE-inhibitor as rehabilitation strategy in prostate cancer XRT patients
  - RTOG 0813 – tadalafil vs. placebo, perspective double blind randomized trial
    - No difference after 1 year