Prostate Brachytherapy: A Physician’s Perspective

Jonathan D. Tward, M.D., Ph.D
Co-Leader, Genitourinary Malignancies Disease-Oriented Team
Associate Professor
Department of Radiation Oncology
Huntsman Cancer Hospital
University of Utah
Webpage: [http://goo.gl/BllR6B](http://goo.gl/BllR6B)

Disclosures

• I have served on the following scientific advisory boards within the past 3 years
  – Myriad Genetics
  – GenomeDX
  – Astellas/Medivation
• Principal Investigator for a Myriad Genetics study
• I am a radiation oncologist
A little bit about me...

In Memorium

Peter D. Grimm, D.O.
July 17, 1952 – February 20, 2016
What we will cover:

- Function of the prostate
- History of Prostate Brachytherapy
- Risk Stratification
- Outcomes definitions
- Physician Bias
- Comparative Effectiveness
- Toxicity
- Decline of brachy
- Technical Details
- Wrapup

Anatomy

Male Reproductive Tract

Secretes a milky, alkaline fluid (one of the components of semen) into the urethra at the point of ejaculation.

The fluid nourishes and protects the sperm during intercourse and forms the main bulk of ejaculate volume.
A little History

Hugh Hampton Young

Johns Hopkins

Young’s Transperineal Prostatectomy

1904
Between 1904 and 1926, Young performed only 26 radical prostatectomies.

How did he treat his other prostate cancer patients?

Young’s radium prostate implants:

- 66 in the first 2 years
- 500 between 1915 and 1927, (fractionated radiation therapy)
Some New Methods in the Treatment of Carcinoma of the Lower Genito-Urinary Tract with Radium

Hugh H. Young and William A. Frontz

From The James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Maryland

During the past two years, we have treated with radium sixty-six cases of cancer of the prostate. In forty-two of these, the tumor was extensive, not only the prostate but the seminal vesicles being involved. In nineteen the process was confined apparently to one half of the prostate and the corresponding vesicle, while in four the vesicles were apparently free from invasion.

1917 Young’s First J Urology Article

Intraurethral Radium Application

Young's Radium Applicator
Intrarectal Radium Application

Young’s Radium Map
Barringer Innovations

- Transperineal & Suprapubic implantation
- Transperineal biopsy
- Combined implant & ebrt
- Combined implant & castration
- Screening for prostate cancer
Is Prostate Cancer “Normal”? 

From: Outcomes of Localized Prostate Cancer Following Conservative Management

Fates other than death, should we screen?

Prostate-specific antigen, or PSA, is a protein produced by cells of the prostate gland. The PSA test measures the level of PSA in a man's blood. For this test, a blood sample is sent to a laboratory for analysis. The results are usually reported as nanograms of PSA per milliliter (ng/mL) of blood.
Gleason Grading System

- Describes the appearance of the cancerous prostate tissue
- Gleason Sum
  - sum of the 2 Gleason grades (range 1-5) assigned to the 2 most prevalent glandular patterns of the tumor cells
  - ranges from 2-10
  - modified: includes most malignant grade
- Upgrading may occur depending on specimen
- Intraobserver variability in assigning Gleason sum occurs

Outcomes Definitions

- **Biochemical Failure**
  - After surgery, PSA >=0.2
  - After EBRT, the nadir PSA + 2
  - After EBRT, 3 consecutive rises (defunct ASTRO definition)
  - After Brachy...no agreed upon definition (some like >0.5)

- **Freedom from progression** = not finding any type of evidence of cancer recurrence i.e. biochemical, clinical or imaging
- **Cause-specific-survival** = death from prostate cancer
- **Overall survival** = Death from any cause
Biochemical Failure – Apples and Oranges?

- Surgical Failure (>0.2 after surgery)
- Defunct ASTRO (3 consecutive rises)
- Phoenix Definition (Nadir + 2)
- Nadir >0.5

The Menu... a few years ago

- Diagnostic tools
- Treatments
The Menu...

Now

Diagnostics

RECTAL EXAM $16
Do I know if you have cancer before you do this?

PSA BLOOD TEST $60
Find your cancer 12 years before you need to

BONE SCAN $1500
Great for high risk because you are not needed to be ordered at all

TRUS BIOPSY $300
Have the same black number, different size of the needle open

CT SCAN $400
Great way to give a negative result or one can also check the US with a clear resonance

MRI PROSTATE [PELVIS] $1200
Excellent Small, more than done in the future

AK SCORE $400
More in detail it is not sure to state even more separately

MYSTERY PROSTATE $500
Great way to give a negative result or one can also check the US with a clear resonance

GENOME DX DECLER $350
Great way to give a negative result or one can also check the US with a clear resonance

GENOMIC HEALTH Dx ONCOLOGY $2500
Great way to give a negative result or one can also check the US with a clear resonance

PET SCAN $3000
Great way to give a negative result or one can also check the US with a clear resonance

FRAX SCORE $400
Great way to give a negative result or one can also check the US with a clear resonance

Treatments

EXPECTANCY MANAGEMENT $0.00
Just let us take the tour

ACTIVE SURVEILLANCE $55,000
Getting blood out every 2 years is worth it

SURGERY OLD-DASHED PROSTATECTOMY $15,000
Surgery is the only step at top

ROBOTIC PROSTATECTOMY $25,000
Do better outcome than laparoscopic but it sure brings in the cost

INTENSITY MODULATED RADIATION $45,000
Great value for those who want the radiation. Add Image Guidance for $10,000 more

STEREOSPECTRAL BODY MASSING $15,000
Pros: better than UN, pressure to sleeve, poor to trouble

PROTON RADIATION $90,000
Great for those who hit 60 to 62

SEED BRACHYTHERAPY $25,000
Conservative effective, expensive less

HDR BRACHYTHERAPY $35,000
2 sessions must be effective, 4 to 6 weeks away from the atonement

Hormone Therapy $50,000
Who needs a 1000? About the use of chemotherapy and exposure to radiation

Intestinal Home $150,000
Cancer is 7 to 8 steps

Chemotherapy or HRT $30,000
Burns or freeze it, just keep away from you

Biases

Kim et al  Medical Care • Volume 52, Number 7, July 2014

FIGURE 1. Perceptions about current rates of different types of primary therapy for localized prostate cancer by physician specialty. **P < 0.05. *P indicates active surveillance; RR, radiation therapy; RP, radical prostatectomy.
How does specialist multidisciplinary consultation alter the pattern?


Conclusions: Specialist visits influence strongly to prostate cancer treatment choices. In light of these findings, prior evidence that specialists prefer the modality they themselves deliver and the lack of conclusive comparative studies demonstrating superiority of one modality over another, it is essential to ensure that men have access to balanced information before choosing a particular therapy for prostate cancer.

The Effect of Age

NCCN Low, Int, High and Very High (2010-2011)
Enough about bias.... What do the data show?

**Low:**
- T1-T2a
- Gleason score ≤6
- PSA <10 ng/mL

ACTIVE SURVEILLANCE OR ANY TYPE OF MONOTHERAPY:
- Surgery
- EBRT
- Brachy

Enough about bias.... What do the data show?

**Intermediate:**
- T2b-T2c or Gleason score 7 or PSA 10–20 ng/mL

- Active Surveillance (select pts)
- Any type of monotherapy:
  - Surgery
  - EBRT
  - Brachy
- Combined Modality
  - EBRT + ADT
  - EBRT + Brachy
  - Surgery + EBRT
  - Surgery + EBRT + ADT
Enough about bias…. What do the data show?

Schema (primary intervention period)

- **DE-EBRT boost ARM**
- **LDR-PB boost ARM**

**8m of neo-adjuvant ADT**
- LHRH agonist +4 weeks* of NSAA

**EPNI 46 Gy 23# at T-8m**
- prostate, SV and regional nodes

- **DE-EBRT 32 Gy boost**
  - (78 Gy/39 total)
- **LDR-PB boost 115 Gy BT**

- Clinic visits at T+12m T+18m

**How about a prospective randomized trial?**

- q2-m CBC, PSA and TTT
- Clinic visits at T+4m and T+8m
- Assessment of acute toxicity
  - IPSS, QoL
  - CBC, PSA and TTT at T+12m T+15m and T+18m
Results: Biochemical PFS
Intent-to-treat analysis of the primary endpoint

<table>
<thead>
<tr>
<th>Time (yrs)</th>
<th>DE-EBRT (N=200)</th>
<th>LDR-PB (N=198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 yr</td>
<td>83.8 (±5.6)</td>
<td>88.7 (±4.8)</td>
</tr>
<tr>
<td>7 yr</td>
<td>75.0 (±7.2)</td>
<td>86.2 (±5.4)</td>
</tr>
<tr>
<td>9 yr</td>
<td>62.4 (±9.8)</td>
<td>83.3 (±6.6)</td>
</tr>
</tbody>
</table>

Effects on Sexual Function...acute phase

A Prostatectomy
- Nerve-sparing
- Non-nerve-sparing

B Radiotherapy
- Radiotherapy alone
- Radiotherapy plus NHT

C Brachytherapy
- Brachytherapy alone
- Brachytherapy plus radiotherapy, NHT, or both

NHT = neoadjuvant hormone therapy
Effects on Urinary Function...acute phase


Effects on Bowel Function

What about long term effects (urinary)?

Events of interest were procedures for bladder spasm, cystitis, hematuria, incontinence, urinary fistula, ureteral obstruction, benign prostatic hypertrophy (BPH), and urethral stricture/BNC.

Tward et al. submitted
1 randomized trial on side effects...

How often do you have urinary Leakage?

How often do you have pain and burning with Urination?

How often do you have weak stream or Emptying?

1 randomized trial on side effects...

The ability to have an erection?

The quality of erections?

The ability to function sexually?
Time Trends
NCCN Low, Int, High, Very High

Regional Variation
NCCN Low, Intermediate, High Risk 2010-2011
All Risk Groups 2010-2011

Ratio of Surgery to Radiation

Very Regional Differences
Thank You!

The 12 Medical Specialty Stereotypes

- OBGYN: Designs women in their sleep
- Orthopedic Surgeon: Can’t pick up a barbell
- Neurologist: Sleeps in an airport
- Emergency Medicine: Thinks he’s the Chief
- Neurosurgery: logo
- Ophthalmologist: Idea in his head
- Gastroenterology: "It's really, really bad"
- Endocrinology: "Let’s talk about your blood sugars..."
- Radiology: "What do you mean you can’t see it?"
- OBGYN: "I have a simple procedure..."
- Anesthesiology: "It’s just a little gas..."

Questions?