

PROSTATE BRACHYTHERAPY FOR DOSIMETRISTS

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4/27/08

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PROSTATE BRACHYTHERAPY: GOALS OF TALK

- Discuss prostate cancer treatment options
 - Radical Prostatectomy (RP)
 - External Beam Radiation Therapy (EBRT)
 - Permanent LDR Brachytherapy (PB)
- Review prostate implant dosimetry terminology and technique

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HOW SHOULD PROSTATE CANCER BE TREATED: IS IT EARLY OR ADVANCED?

- 3 major factors predict whether the cancer is in an "early" or "advanced" stage:
 - Clinical Stage
 - PSA
 - Gleason Sum

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CLINICAL STAGE

- T1C: too small to feel on DRE; picked up on routine PSA screening
- T2A/B/C: palpable cancer limited to the prostate
- T3A/B: palpable cancer spread beyond the prostate
- N0/N1: nodal involvement (prostatectomy, surgical sampling) (regional disease)
- M1: bone metastases (bone scan)

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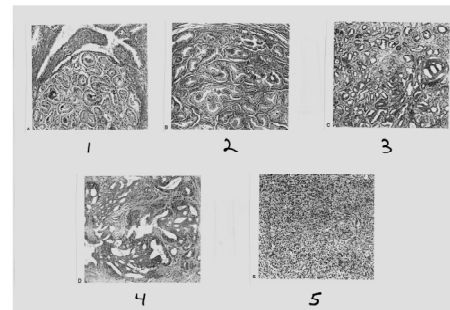
PSA (PROSTATE SPECIFIC ANTIGEN)

- PSA is a biochemical produced by both benign prostate tissue or prostate cancer
- PSA is used a screening test to detect cancer before it can be felt or cause symptoms (like a Pap smear or mammogram)
- Once a prostate cancer has been detected, PSA is the most sensitive test available to monitor the course of the disease

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GLEASON SCORES: MICROSCOPIC APPEARANCE OF CANCER



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GLEASON SCORES

- Most prostate cancers have a primary dominant pattern, and a less prevalent secondary pattern
- Some small volume cancers have only one pattern, such as Gleason 3 + 3 or 2 + 2
- The Gleason Sum is the sum of the score of the primary pattern added to that of the secondary pattern (range 2 to 10)

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PREDICTION OF DISEASE EXTENT

- Using the PSA, clinical stage, and biopsy Gleason sum, the likelihood of localized or metastatic disease can be reliably estimated, along with the likelihood of successful treatment
- The Partin tables, D'Amico tables, and the MSKCC/Kattan prostate nomograms are all useful tools for this purpose

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MSKCC NOMOGRAM

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TREATMENT CONSIDERATIONS

- RP and PB are most appropriate for patients with high probability of localized disease (cancer confined to the prostate, or has spread no more than 1 - 3 mm beyond the prostate)
- More extensive disease is best treated with EBRT +/- hormonal therapy +/- chemotherapy

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PROSTATE CANCER: TREATMENT SUCCESS TERMINOLOGY

- Results are usually reported at specific points in time (5-, 10-, or 15-years) after treatment:
- Biochemical Disease-Free Survival (DFS, bNED):
% of patients with normal PSA after treatment (the most rigorous definition of success)
- Disease-Specific Survival (DSS):
% of patients not dying from prostate cancer (the most important definition of success)

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WHY USE BRACHYTHERAPY? THE "INVERSE SQUARE LAW"

Distance from radioactive source placed in prostate	Radiation Intensity
5 mm (cancer in prostate)	100
15 mm (nearby rectum)	11
25 mm (nearby bladder)	4

- By exploiting the inverse square law, implants are physically able to deliver extremely high doses of radiation to the prostate (14,500 cGy minimum), but substantially lower radiation doses to nearby normal tissues

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WHY ESCALATE THE RADIATION DOSE?

- Higher radiation doses are believed to achieve higher local and biochemical control rates:
- Pt with T1C, GS 6, PSA 6.3 cancer receiving IMRT:

Dose	5-year bNED rate per MSKCC Nomogram
66.6 Gy	81%
72.0 Gy	89%
75.6 Gy	92%
81.0 Gy	93%

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TREATMENT OUTCOME: REPORTED 10 - YEAR RESULTS

	<u>PSA DFS</u>	<u>DSS</u>
PSI alone (I-125)	66 - 85%	88 - 100%
RP	59 - 78%	75 - 97%
EBRT alone	65 - 83%	84 - 85%
EBRT + HDR	73%	92%
EBRT + PSI	70 - 85%	98%

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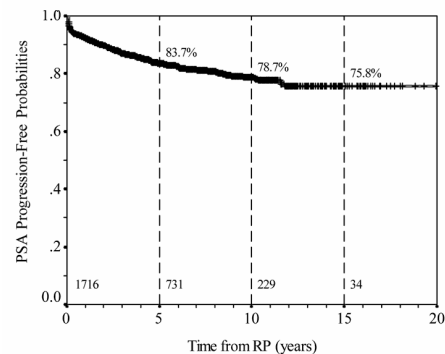
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PROSTATE CANCER: COMPARISON OF TREATMENTS

- The reported 5- and 10-year PSA DFS rates and DSS rates are similar for all 3 major types of treatment, and a large amount of 5- and 10-year data is available
- There is only limited 15-year outcome data available, and to the best of our knowledge, no reliable 25- or 30-year data exist anywhere

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FACTORS TO CONSIDER WHEN COMPARING TREATMENTS

- Most published studies describe the experience of a few treatment experts at a single academic institution, and may not accurately reflect the results obtained in community practice
- Randomized studies comparing these forms of treatment have not been completed due to poor accrual

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REPORTED POTENCY RESULTS

<u>Type of Treatment</u>	<u>Potency Rate</u>
No Treatment	70%
PSI (Seattle, ACS)	50 - 90%
PSI + EBRT (Critz '97)	57%
EBRT (ACS)	40 - 60%
EBRT + HDR Brachy (Martinez '01)	45 - 50%
Nerve-sparing RP: (PCOS '00, WSL, JH)	44 - 66 - 86%
Non-nerve-sparing RP: (ACS, PCOS '00)	10 - 35%
Cryosurgery (UCLA '03)	13%
Hormonal Therapy	10%

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INCONTINENCE AFTER TREATMENT

- Radiation Therapy rarely causes long-term urinary incontinence requiring chronic use of urinary pads or diapers:
 - Implants ~ 1%
 - EBRT ~ 1%
 - RP 7 - 8% (severe), (20-30% mild)

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URINARY IRRITATIVE SYMPTOMS

- Urinary frequency, urgency, urgency incontinence, nocturia, weak urine stream, dysuria, and difficulty emptying the bladder are temporary side effects that should be expected by all patients undergoing PSI and EBRT, although implants produce more intense and longer-lasting symptoms
- These symptoms are not typically seen with RP

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RECTAL PROBLEMS AFTER RADIATION

- EBRT frequently causes long-term rectal symptoms lasting for several years after treatment; less common with PB; very uncommon with RP
- Symptoms can include rectal urgency, several BMs per day, rectal bleeding and discomfort (like hemorrhoids)
- Severe rectal problems such as incontinence of stool requiring diapers are rare (< 1%); colostomy is quite rare (0.1 - 0.6%)

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Relative Advantages/Disadvantages: Dr. Eric Klein's View

	RP	XRT	Brachy	Brachy + XRT
Convenience	++	+	++++	+
Incontinence	+++	+	+	+
Bowel Sx	+	+++	++	++++
Irritative Sx	+	++	++++	++++
Impotence	++	++	++	++

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WHY PATIENTS CHOOSE PB

- Cure the cancer
- Avoid urinary incontinence, attempt to preserve potency, minimize rectal symptoms
- Compared to external beam radiotherapy, complete treatment more rapidly
- Compared to radical prostatectomy, physically recover and return to normal activity more rapidly

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SELECTION CRITERIA FOR TREATMENT WITH IMPLANT ALONE

- High likelihood of localized cancer
- Life expectancy > 10 years
- Prostate anatomy and size suitable for PSI
(Prostate not too large, no prior TURP, no big median lobe, no dense calcifications in the prostate blocking out the ultrasound image deep in the gland)

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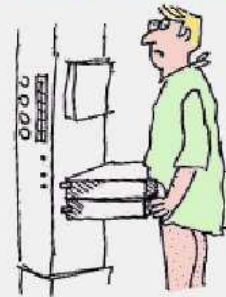
TRANSRECTAL VOLUME STUDY

- The patient lies on his back with his legs up in stirrups
- Ultrasound probe inserted into rectum (similar to the biopsy, but without the needles)
- The volume study determines if the prostate is technically implantable
- As bad as this sounds, it could be worse...

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If Women controlled medicine



The Manogram

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THE IMPLANT DAY

- Patients come to the hospital, are admitted for the procedure, and taken to Pre-Op
- The patient is brought to operating room
- General anesthesia is administered
- Patient is positioned in stirrups
- Ultrasound probe is inserted into rectum; urinary catheter is inserted into the urethra and bladder
- Prostate ultrasound images acquired on computer, dosimetry plan is optimized

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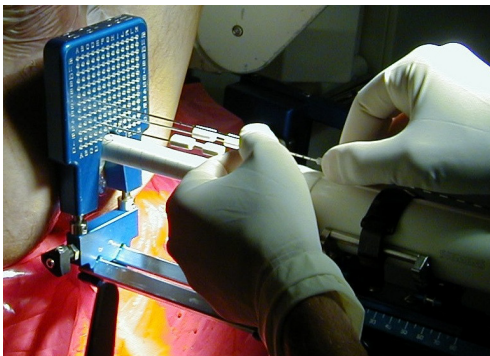
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THE IMPLANT DAY

- Needles and seeds are inserted through the skin behind the scrotum and in front of the rectum (not through the rectum); takes 30 - 60 minutes
- Usually requires about 25 needles (15 - 40), and 110 seeds (65 - 140), depending on size/shape of prostate
- Generally leave a urinary drainage catheter in place for a 2 - 4 days after PSI
- Take post-implant X-ray documenting position of seeds in prostate

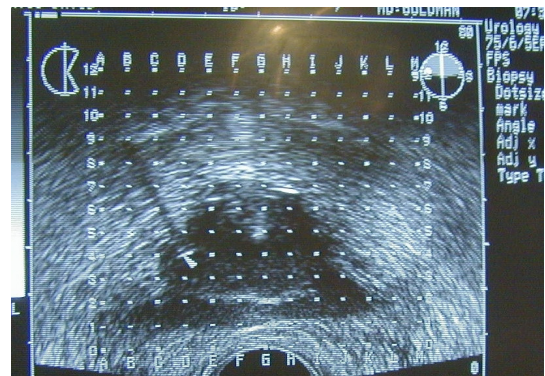
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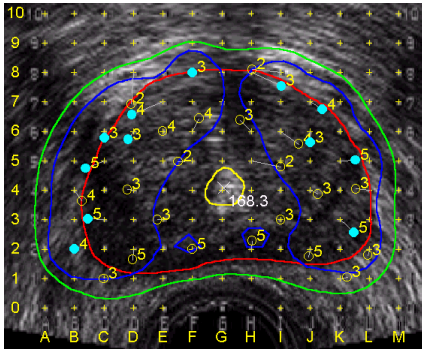
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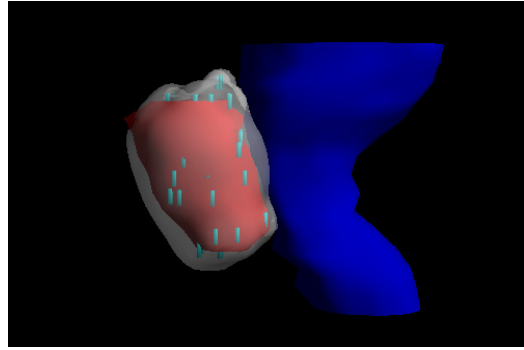
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Real-time Dosimetry at Implant



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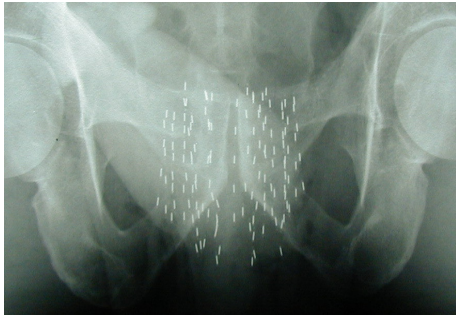
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Post-Implant X-Ray



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THE END OF THE IMPLANT

- After the implant, patients are transferred to the recovery room, go home 1 - 2 hours after the anesthetic wears off
- Implants usually require 2 hours total in OR
- Usually requires ~ 6 hours total from the registration time to discharge from the hospital

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PSI: ACUTE RISKS

- Infection (fewer than 1% require hospitalization or IV antibiotics)
- Bleeding (usually < 15 cc, or 2 tubes of blood, less than 1% require transfusion or operation)
- Pain is mild; ice packs and tylenol are generally all that is required (occasionally Vicodin)

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PSI: THE RADIOACTIVE I-125 ISOTOPE

- The Iodine-125 Isotope:
 - Emits weak X-rays: average energy 28 keV
 - Half-life: 59.6 days
 - 50% of the total radiation dose is delivered during the first 2 months after the implant
 - 25% delivered during months 3 - 4
 - 12.5% during months 5 - 6
 - The remaining 12.5% during months 7 - 20

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AFTER PSI: RADIATION EXPOSURE TO BYSTANDERS

- Radiation exposure rates:
 - 3 feet away from patient after PSI: 0.02 mrem/hr
 - Living in Denver, CO: 0.02 mrem/hr
 - Transatlantic airplane flight 1.00 mrem/hr
- Patients are safe to go out in public without limitation
- The average total radiation dose received by an implant patient's spouse is 14 mRem (or 3% of the 400 - 800 mRem she receives with her annual screening mammogram)

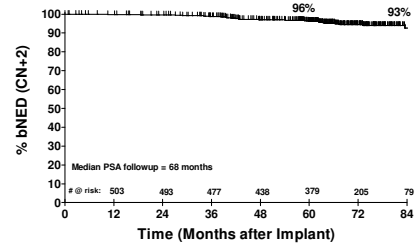
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SACRAMENTO PSI RESULTS

DISEASE-FREE SURVIVAL

511 consecutive low-risk patients treated with I-125 brachytherapy: 01/01/98 through 05/31/02



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SACRAMENTO PSI RESULTS

- 5 - Year bNED rate: 96%
- 5- Year DSS rate: 100%
- 5 - Year OS rate: 98%

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SACRAMENTO PSI RESULTS

- 5 - Year Local Recurrence Rate: 0.4% (n = 2)
- 5 - Year Salvage Prostatectomy/Cryosurgery rate: 0%
- 5 - Year Salvage Therapy Rate: 3% (all treated with hormonal therapy)

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SACRAMENTO PSI RESULTS

PSA typically takes years to fall to a nadir value after PB, compared to only 1 month following RP:

Years after PB	# pts	% with PSA ≤ 0.5	% with PSA ≤ 0.2
1	1220	41%	14%
2	861	48%	19%
3	703	77%	55%
4	549	89%	75%
5	455	90%	83%
6	288	91%	88%

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BRACHYTHERAPY: SUMMARY

PB offers advantages relative to EBRT with respect to treatment convenience, generally fewer rectal symptoms, and possibly better potency for the first few years after PSI

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BRACHYTHERAPY: SUMMARY

PB offers advantages relative to RP with respect to less urinary incontinence, less extensive surgery with a much shorter recovery period, and possibly better potency for the first few years after PSI

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BRACHYTHERAPY: SUMMARY

- All effective treatments have relative advantages and disadvantages
- The optimal treatment for any individual patient depends not only on the cancer's characteristics, but the patient's age, overall health, their preexisting urinary and rectal symptoms, potency, and quality of life goals

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IMPLANT DOSES:

- Prescription Doses
- Implants alone:
 - 145 Gy for I-125
 - 125 Gy for Pd-103
- Implant "boosts" combined with 45 Gy EBRT
 - 110 Gy for I-125
 - 100 Gy for Pd-103

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DOSIMETRY TERMINOLOGY: PROSTATE

- Prostate V-100 (the percentage of the prostate receiving 100% of the prescription dose)
- Goal is for >98% on pre-plan; should be >90% on post-PB CT
- Prostate V-150 (the percentage of the prostate receiving 150% of the prescription dose)
- Goal is 40 - 60% on pre-plan and post-PB CT

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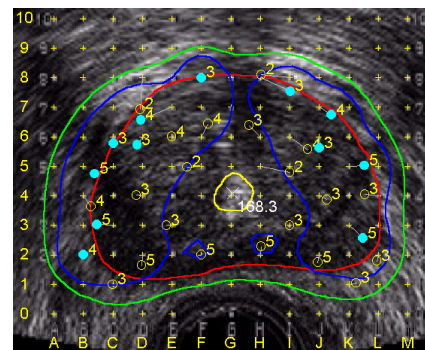
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DOSIMETRY TERMINOLOGY: PROSTATE

- Prostate D-90: the isodose surface that encompasses 90% of the prostate volume
- The ideal dose is controversial:
 - > 120 Gy? > 140 Gy? > 160 Gy? 185 + Gy?
- We aim for 170 - 180 Gy at the end of PB in the OR on our intraop dosimetry computer, 150 - 170 Gy on post-PB CT dosimetry

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DOSIMETRY TERMINOLOGY: RECTUM

- **R-100:** the volume of rectum receiving $\geq 100\%$ of the prescription dose
- Goal should be < 2.5 ml, preferably < 1.00 ml)
- **R-150:** the volume of rectum receiving $\geq 150\%$ of the prescription dose
- Goal should be less than 0.50 ml
- These values should be kept as low as possible! ("You can't be too thin, too rich, or have too low a R-100/R-150")

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TIPS: HOW TO SPARE THE RECTUM

- For the posterior row of needles, only use "seed-spacer-seed" arrangements---"seed on seed on seed" needles, if misplaced posteriorly, can easily overdose the adjacent rectum
- Place the posterior row needles 3 - 5 mm inside the posterior capsule, not right underneath the capsule

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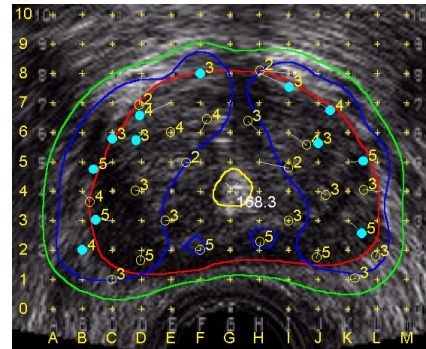
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TIPS: WHERE DOES THE V-150 BELONG?

- Positioning the high-dose region (V-150) in the "isthmus" (between the urethra and the anterior rectum) is a great way to create a rectourethral fistula with permanent colostomy and urinary diversion ("Double-Bag complication")
- Position the high-dose regions anterolaterally, not posteriorly or centrally

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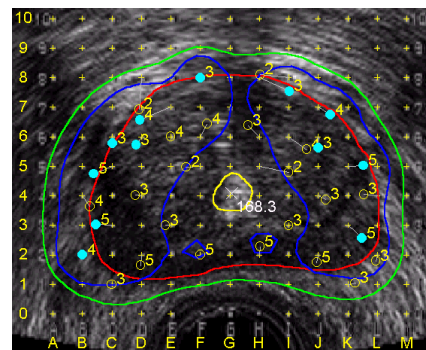
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TIPS: HOW TO SPARE THE URETHRA

- On the pre-plan, keep the urethra D-10 below 190 Gy, and the urethra D-50 in the range of $160-180$ Gy
- Avoid using lots of central needles!
- Central needles are generally loaded with 2 - 4 seeds, and should mainly be used to augment the dose at the apex and base of the gland

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TIPS: SHOULD ALL NEEDLES BE "SEED-SPACER-SEED" LOADS?

- Don't be afraid to load lateral needles with "seed-on-seed-on-seed-on-seed" arrangements--they push the dose out laterally, and deliver extremely high doses to the peripheral portion of the prostate where the cancer volume is greatest
- Think "Peripheral Loading"
- Try to avoid putting needles outside the prostate: seeds that end up in periprostatic veins float away and embolize to the lungs

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TIPS: WHY ARE THE PRE-PLAN AND POST-PB CT DOSIMETRY VALUES SO DIFFERENT?

- The prostate volume identified on CT is typically 20 - 30% larger than the US or MRI prostate volume (overestimates size of prostate)
- Greater volume + same activity = lower V-100, D-90, etc.
- V-100 is usually about 5 - 10% lower on the post-PB CT than on the US pre-plan; D-90 is usually about 20 Gy lower; V-150 shows little change

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WHAT ABOUT CRYO OR HIFU?

- So far, cryosurgery and HIFU haven't produced better bNED outcome than standard 3DCRT, and the results are inferior compared to dose-escalated IMRT, or PB:

Modality (program)	# pts	median f/u	5-yr bNED
HIFU (Blana, Europe)	140	6.4 yrs	63% (low, int risk)
Cryo + AD	590	5.7 yrs	61%
3DCRT (MDAH 70 Gy)	151	8.7 yrs	59% (low + int risk)
3DCRT (LL, MGH 70.2)	197	5.5 yrs	60% (low risk)
IMRT (MSKCC)	279	5.0 yrs	85% (low risk)
PB (Sacramento ROC)	586	5.7 yrs	96% (low + int risk)
PB (MSKCC)	146	4.0 yrs	88% (low risk)
PB (Wheeling/Pug Sound)	122	5.7 yrs	97% (low risk)

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WHAT ABOUT PROTONS AND 3DCRT?

- Protons appear to be more effective than conventional-dose 3DCRT:

Modality (program)	# pts	median f/u	5-yr bNED
3DCRT (MDAH 70 Gy)	151	8.7 yrs	59% (low + int risk)
3DCRT (LL, MGH 70.2)	197	5.5 yrs	60% (low risk)
Protons (LL, MGH 79 Gy)	195	5.5 yrs	80% (low + int risk)

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WHAT ABOUT PROTONS, IMRT, and PB?

- However, protons do not appear to be more effective than dose-escalated IMRT or PB:

Modality (program)	# pts	median f/u	5-yr bNED
Protons (LL, MGH 79 Gy)	195	5.5 yrs	80% (low + int risk)
3DCRT (MDAH 78 Gy)	151	8.7 yrs	78% @ 8 yrs (low + int risk)
IMRT (MSKCC)	279	5.0 yrs	85% (low risk)
PB (MSKCC)	146	4.0 yrs	88% (low risk)
PB (Wheeling/Puget Sound)	170	5.7 yrs	98% (low + int risk)
PB (Sacramento ROC)	586	5.7 yrs	96% (low + int risk)
PB (Grimm, Seattle)	125	6.5 yrs	87% @ 10 yrs (low risk)

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PROTON CONCLUSIONS

- Dose escalation does work!
- Protons are clearly better than conventional-dose 3DCRT (81% vs 60%)

BUT:

- Protons appear to be no better than high dose 3DCRT and IMRT (81% vs 78 - 85%),

AND:

- Protons may be inferior to PB (81% vs 96 - 98%)

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PROTONS, IMRT, AND PB: CONCLUSIONS

- **The inverse-square law is still more powerful than the Bragg Peak!**

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