# *Brachytherapy for Prostate Cancer*

Who should be thinking about this and why...

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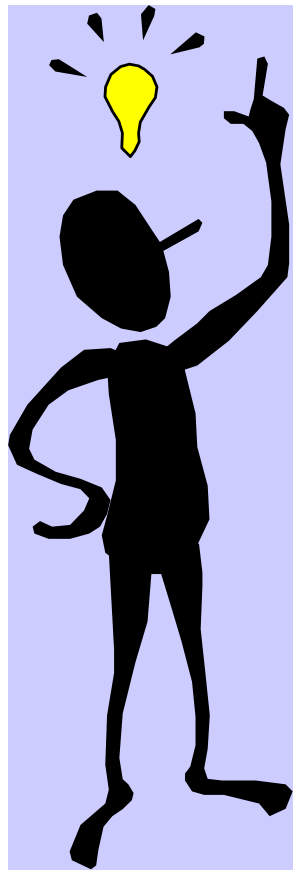
# Many options

- “watchful waiting”？
- Surgery?
- Radiation?
- Seeds?
- Cryotherapy ?
- Hormones?
- HIFU ?
- change my diet?



# This evening's program

- Risk groups:

- Long term (10-15 year) results for brachy
- Selection factors for brachytherapy
- Quality of life post brachytherapy
- How we do it
- FAQ's….

# Prostate cancer risk groups

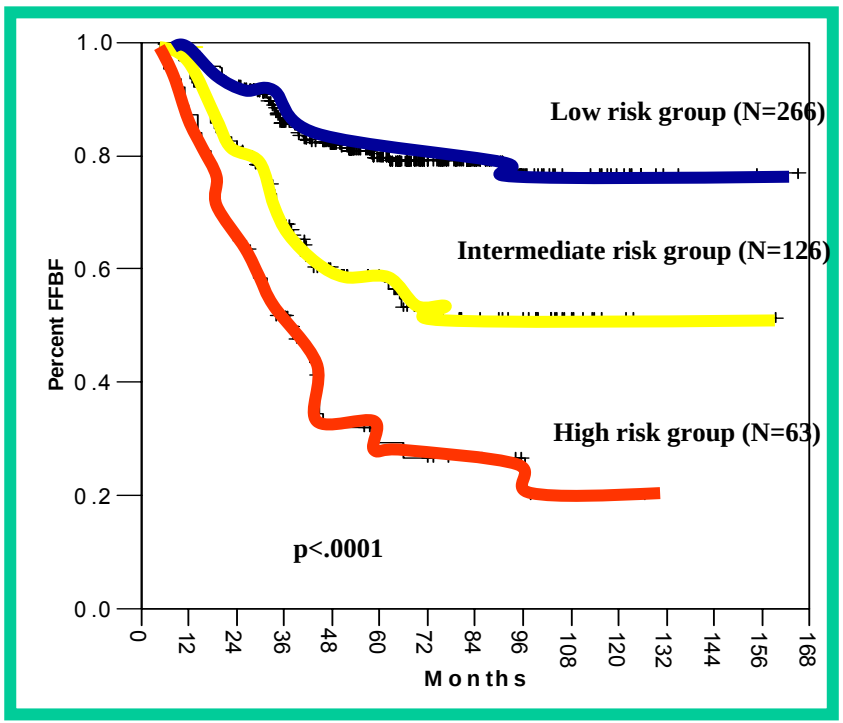
- “Risk groups” not only tell us how we can expect a patient to do (good tumor vs bad tumor) but also what tests need to be done to complete his staging, and also how to approach his treatment

# Risk groups for prostate cancer

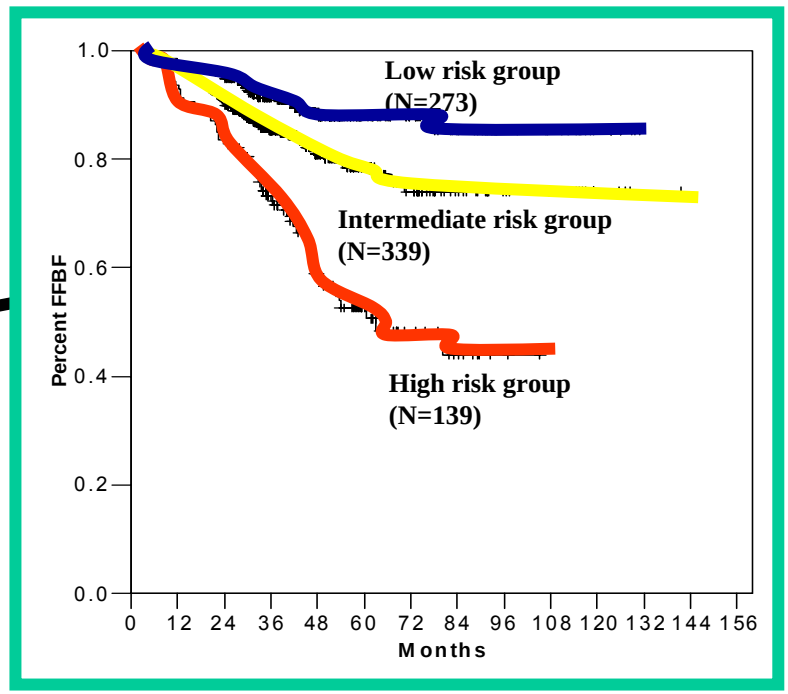
- Low risk (favorable)
  - *T1c/T2a AND Gleason ≤ 6 AND PSA < 10*
  - *metastatic work up not usually performed*
- Intermediate risk
  - *T2b OR Gleason 7 OR PSA 10-20*
- High risk
  - *T3 OR Gleason 8-10 OR PSA > 20*

# Fox Chase Cancer Center Dose Response By Risk Group

## <74 Gy

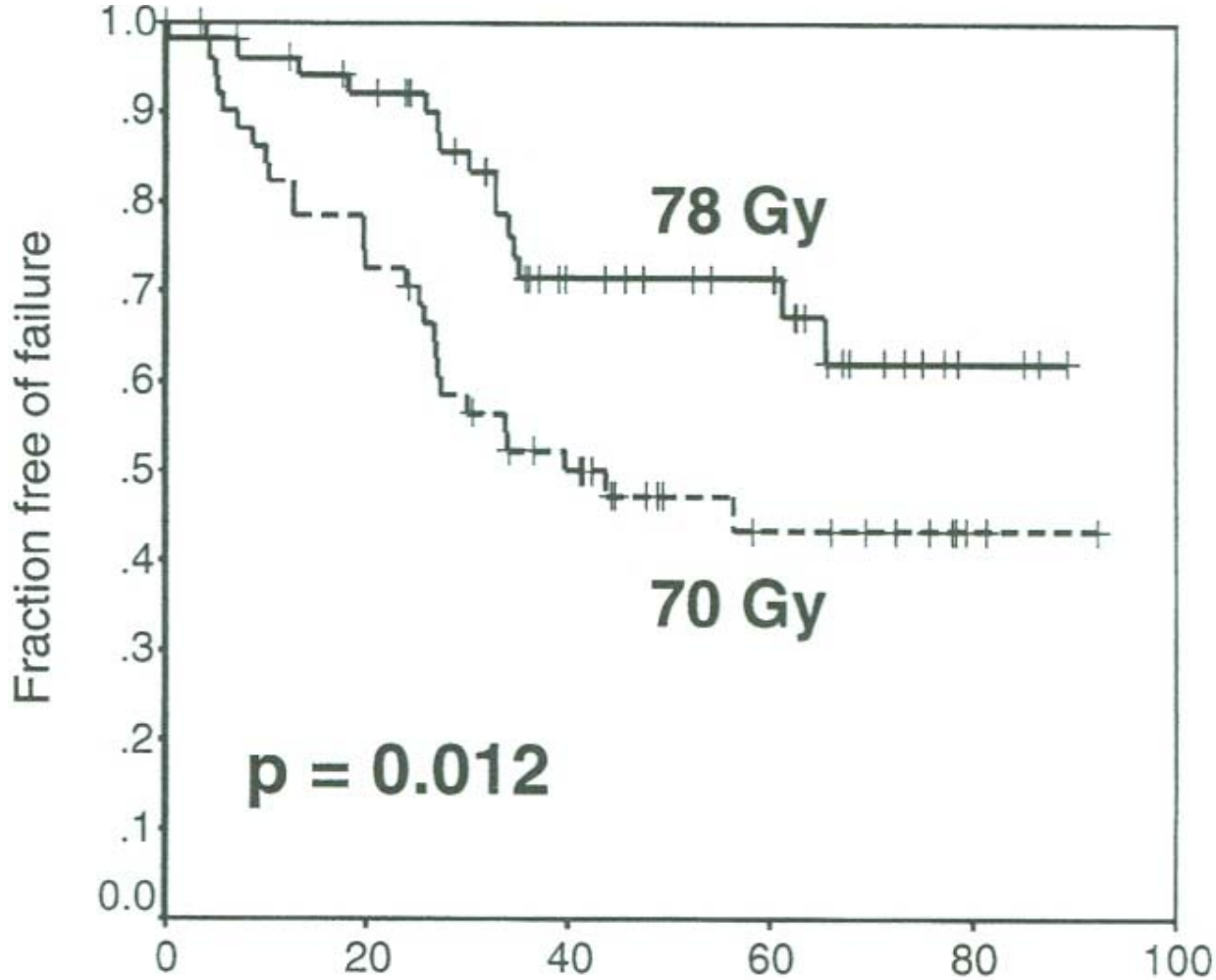



## >74 Gy



# Importance of dose

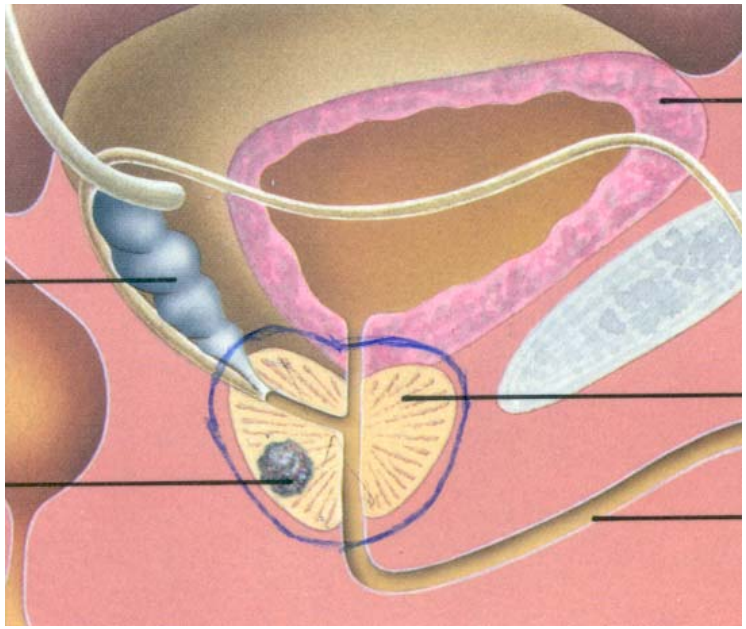
*Pollack et al. IJROBP 2002*



# RT Dose Escalation

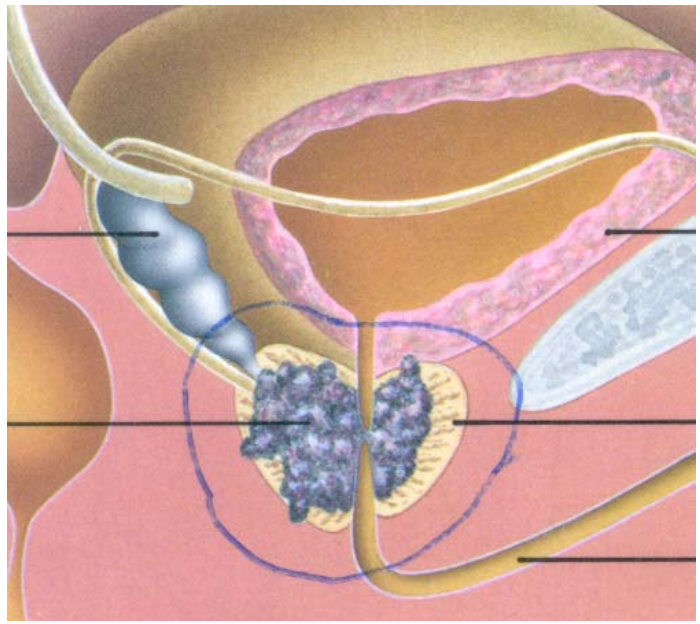
- *favorable risk:* Brachytherapy (145 Gy)
- *intermediate risk:*
  - Combined EBRT and brachy (45 + 110 Gy)
  - high dose EBRT (IMRT) (78 Gy)
  - EBRT + HDR (45 + 3 x 8 Gy)
- *high risk*
  - IMRT (78 Gy)
  - IMRT + BT (45-50 + 110 Gy)

1



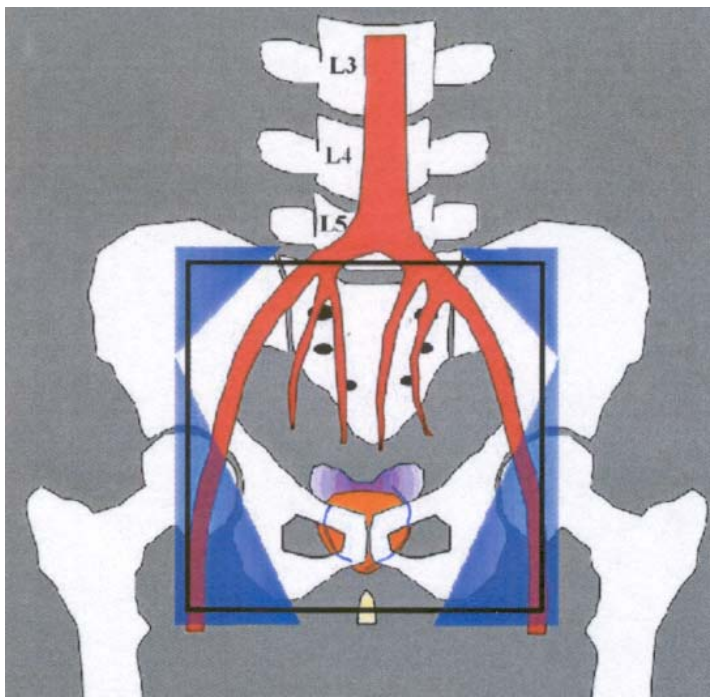
Favorable: brachytherapy

2



Intermediate: external or
Combined RT + BT

3




High risk: LN + prostate

# Characteristics of $I^{125}$/$Pd^{103}$

- Low energy
  - 21-28 KeV
  - Limited tissue penetration
- Low dose rate, continuous
  - $I^{125}$: 10 cGy/hour (60 day ½ life)
  - $Pd^{103}$: 21 cGy/hour (17 day ½ life)

# Why Dose Rate Doesn't Matter for Seeds

Low energy permits:

- An extraordinarily high intraprostatic dose
- Low adjacent organ dose

The very high radiation dose and rapid fall-off overwhelms dose rate effects

# Evidence that seed Brachytherapy delivers the highest dose

- Pickett B. et al.[3]: EBRT vs. Seeds
  - *MRSI data*
    - EBRT: 20% complete metabolic atrophy
    - Seeds: 86% complete metabolic atrophy
  - *Median PSA*
    - EBRT: 0.9 ng/ml
    - Seeds: 0.2 ng/ml

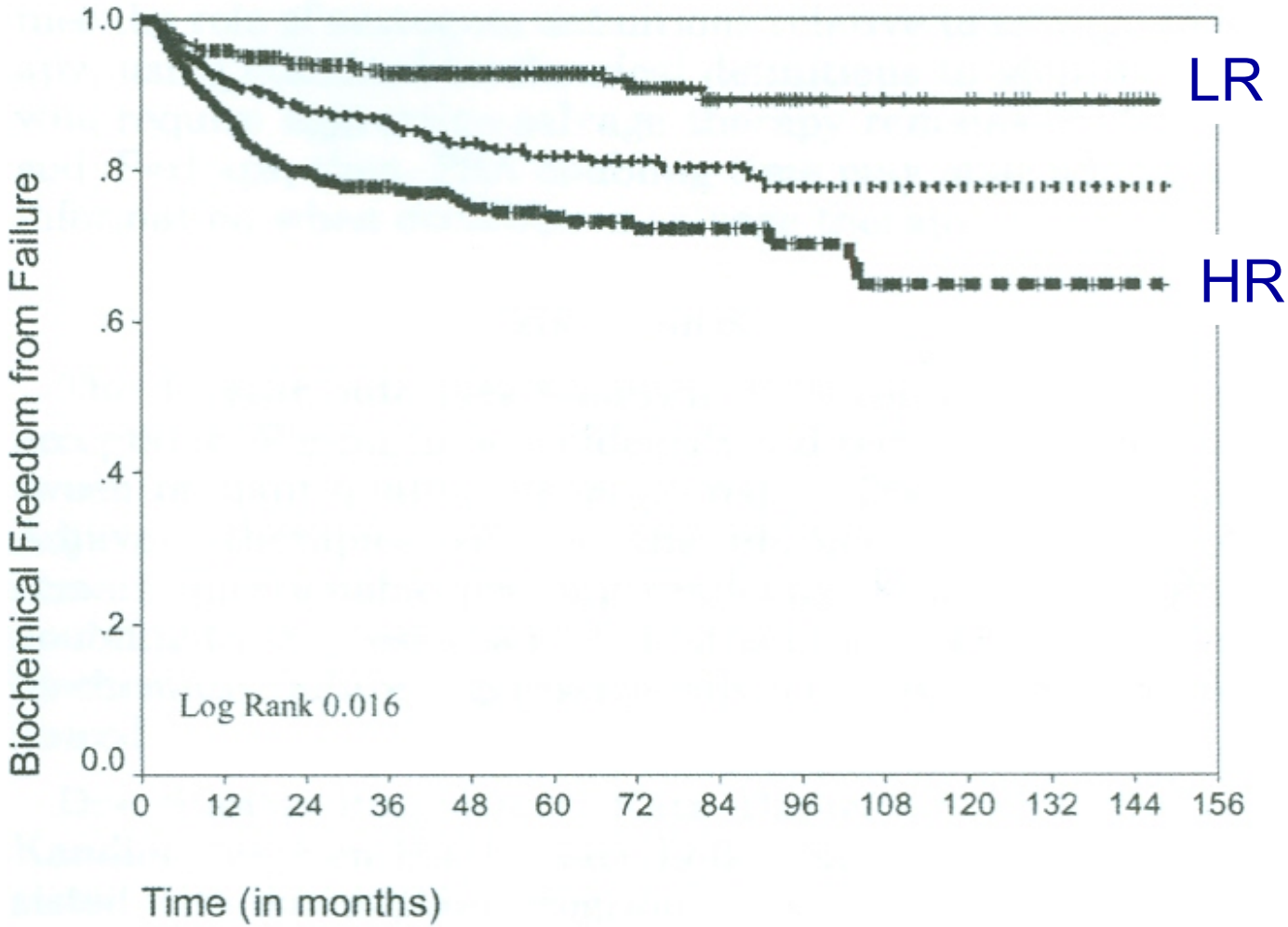
**Pickett B. et al. ASTRO, 2004**

# Long term outcomes

- 12 year results: *Potters et al J Urol 2005*
  - n= 481 low risk
  - 12 yr bNED 91% (ASTRO)
  - 21% NHT, 2% external + BT
  - addition of NHT or RT no difference
  - mean D90: 102%
  - D90 independent predictor of outcome $p<0.0001$

# ASTRO bNED

*Potters et al, J Urol 2005*



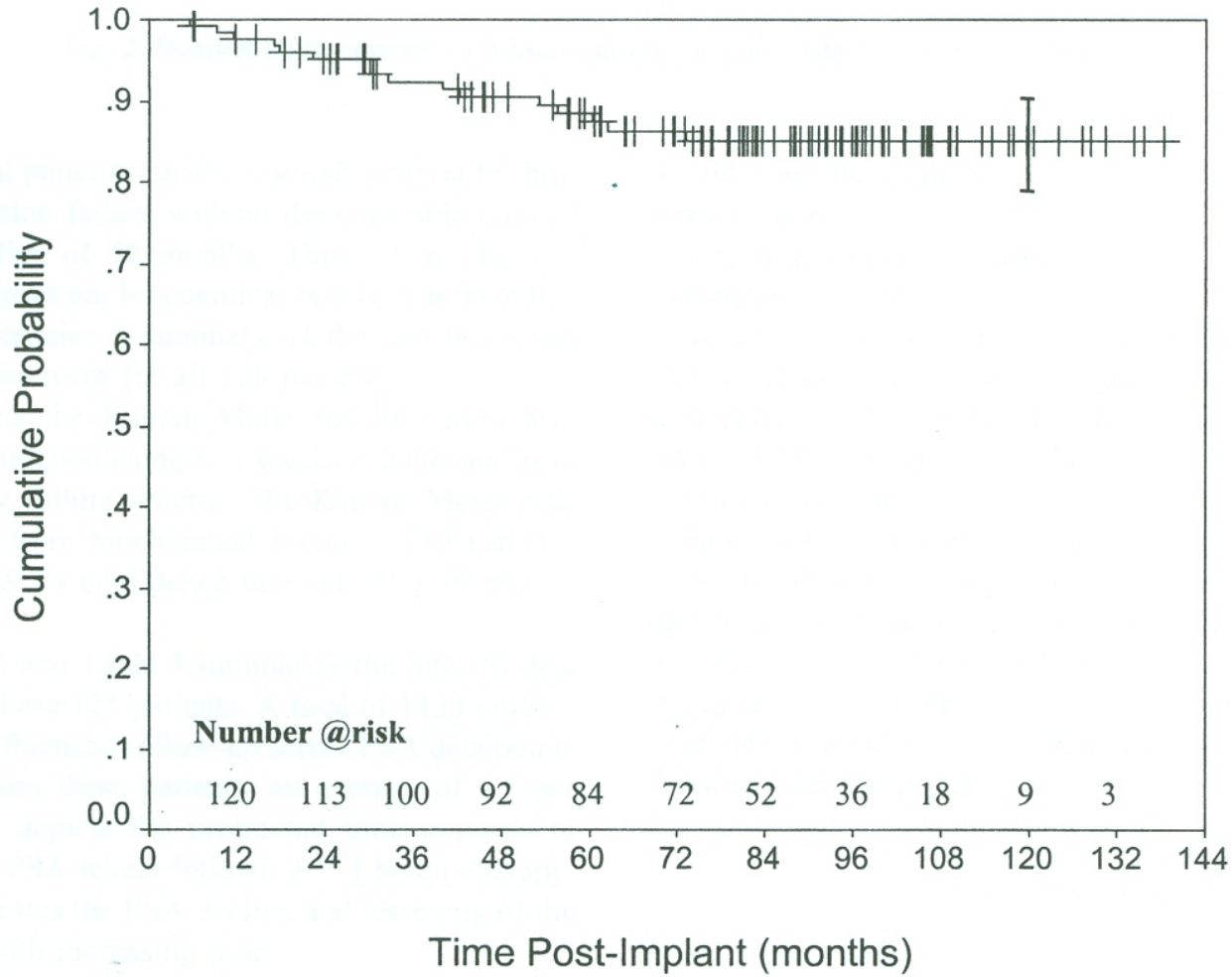
# Long term outcomes

*Grimm et al IJROBP 2001*

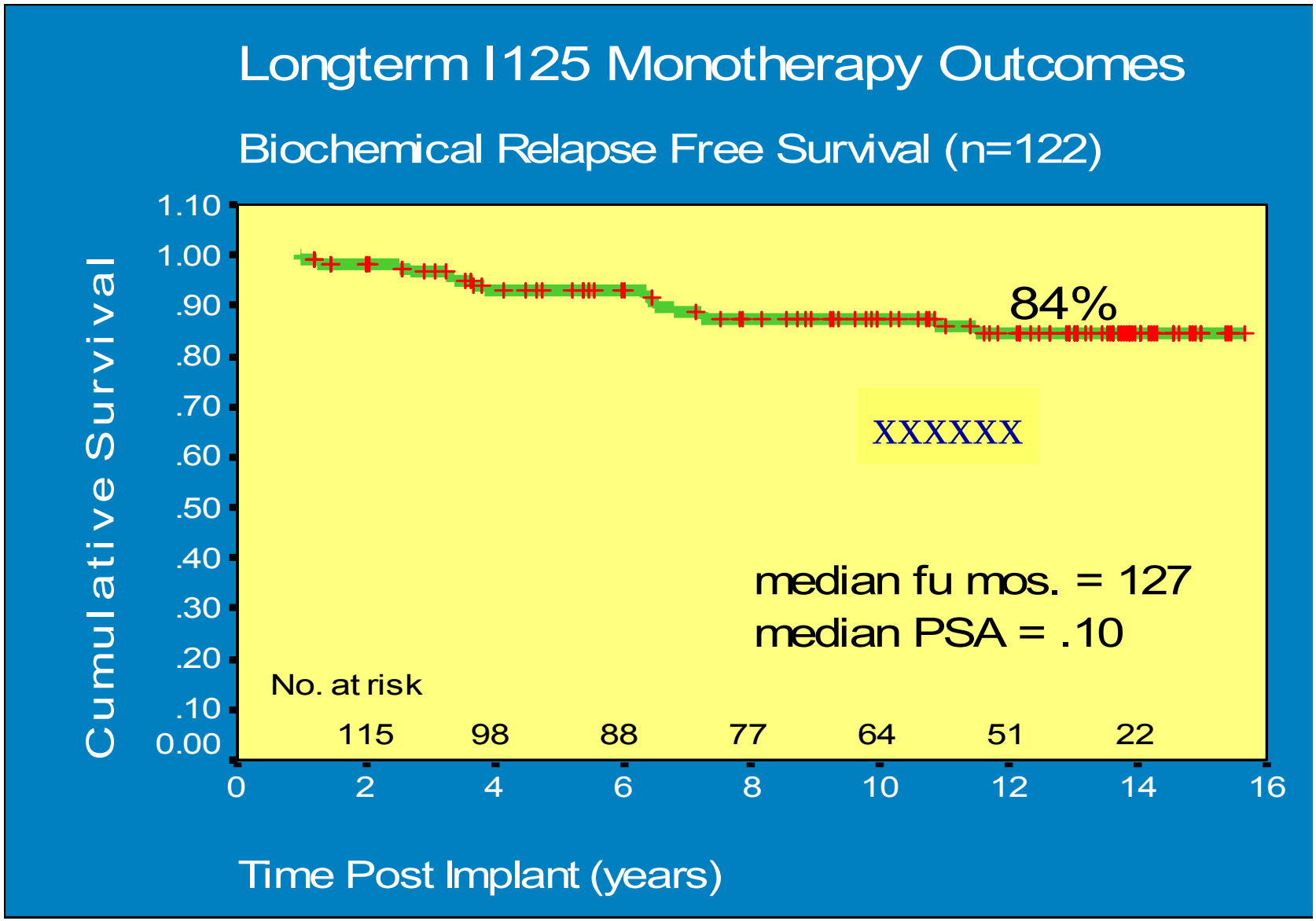
- 10 year results: Iodine 125 brachy
- n= 125 (1988-1990) *mainly low risk*
- 81% PSA < 0.2 ng/ml
- LF 3%, DF 3%
- all failures diagnosed within 8 years

# PSA progression free

*Grimm et al IJROBP 2001*



# $^{125}$I brachytherapy
# 15 Year PSA Results



# Long term outcomes

*Merrick et al IJROBP 2005*

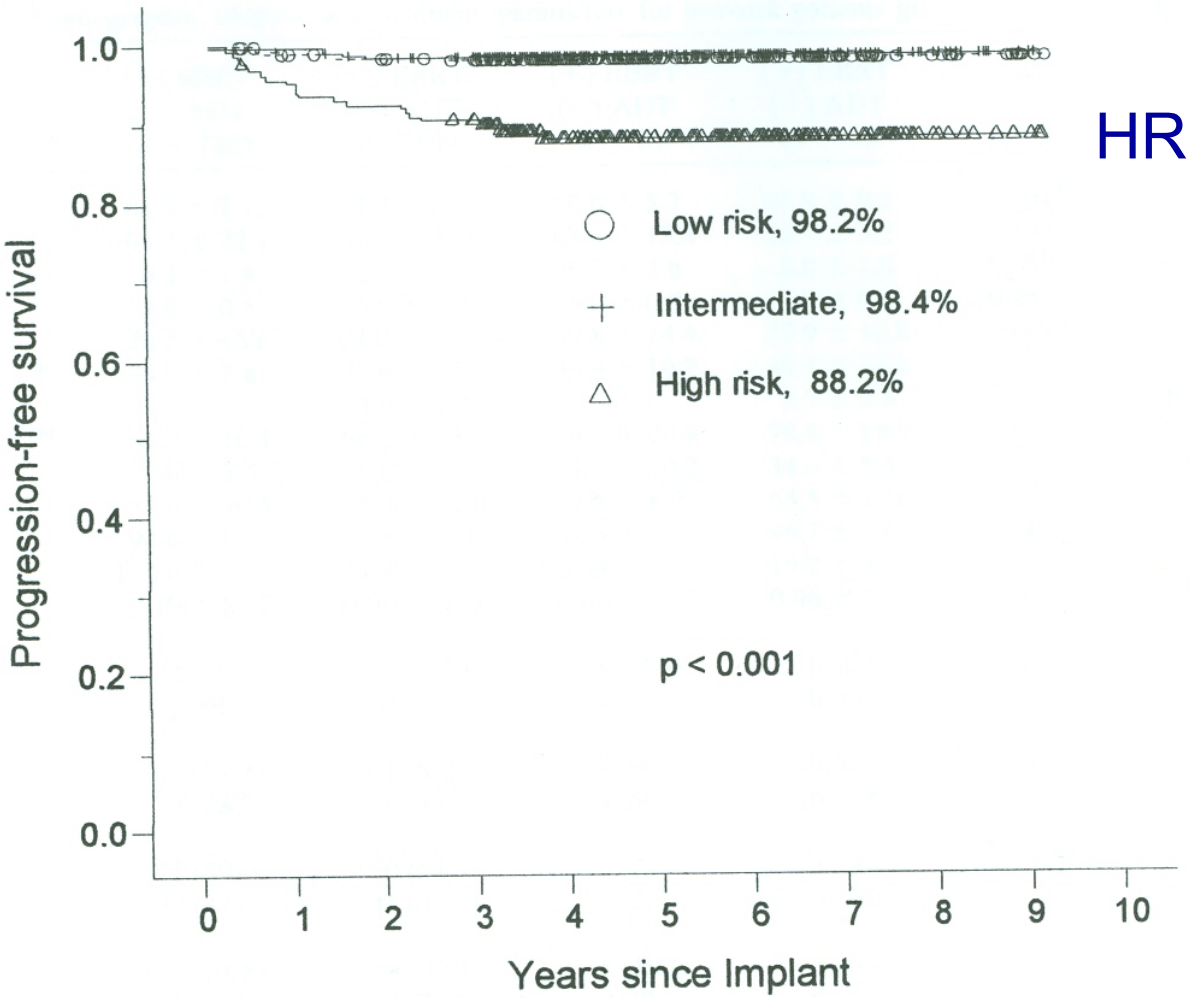
- n= 668 1995-2001
- median follow up 5 years
- low risk 8 year bNED: 98%
- median PSA < 0.1 ng/ml
- addition of NHT or external RT no difference

# progression-free rate

*Merrick et al IJROBP 2005*

LR+IR

HR



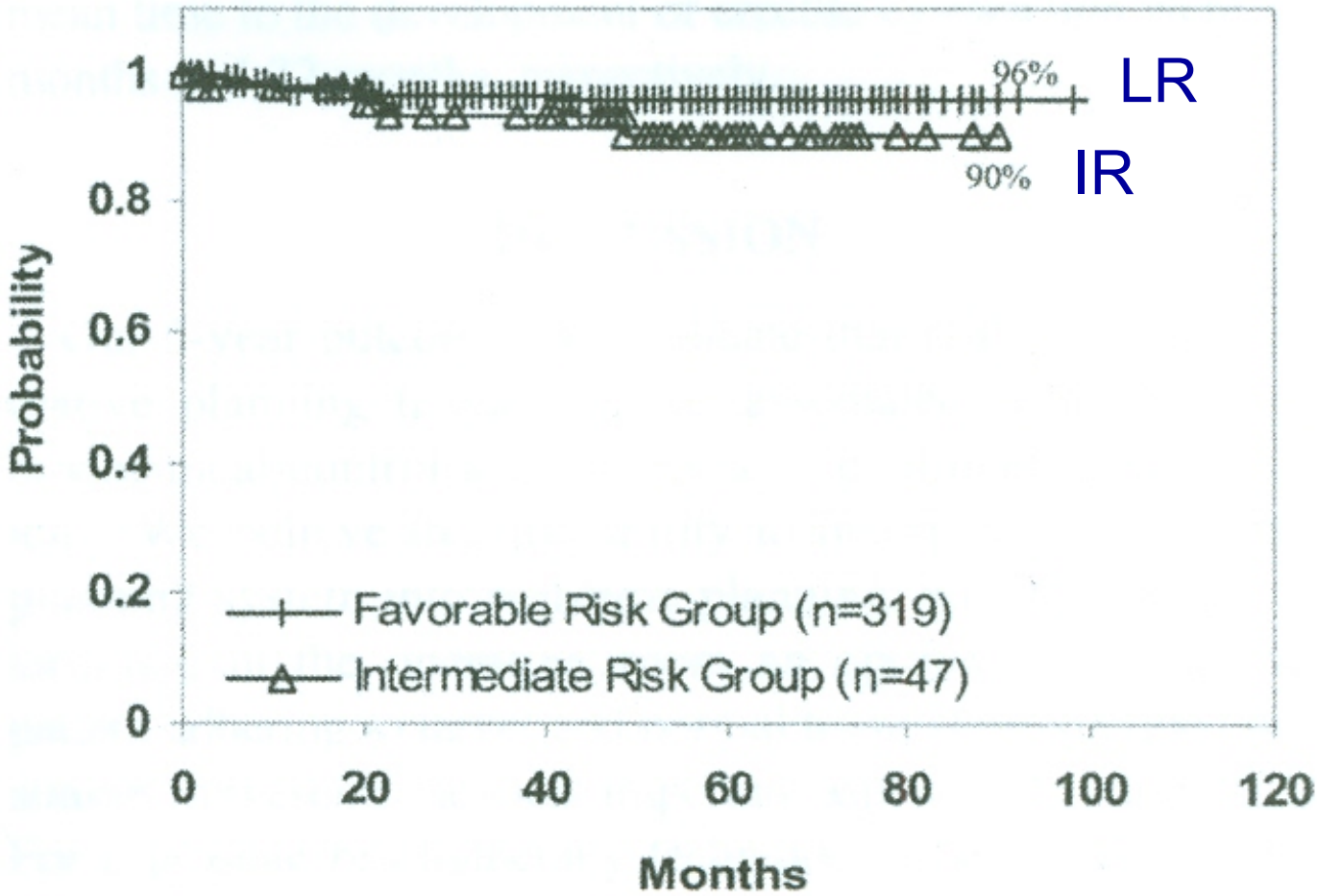
# Brachy vs. IMRT

*Zelefsky et al IJROBP 2007*

- 7 year results for 1126 LR and IR
- BT: 421, IMRT:705
- bNED LR @ 7 years
  - 98% BT vs. 88% IMRT $p<0.001$
- NHT $p=0.5$
- late GI grade 2: 6% vs. 2% (no **Δ** gr 3)
- late GU grade 2: 18% vs. 7% (no **Δ** gr 3)

# nadir + 2 bNED for LR and IR

*Zelefsky et al IJROBP 2007*

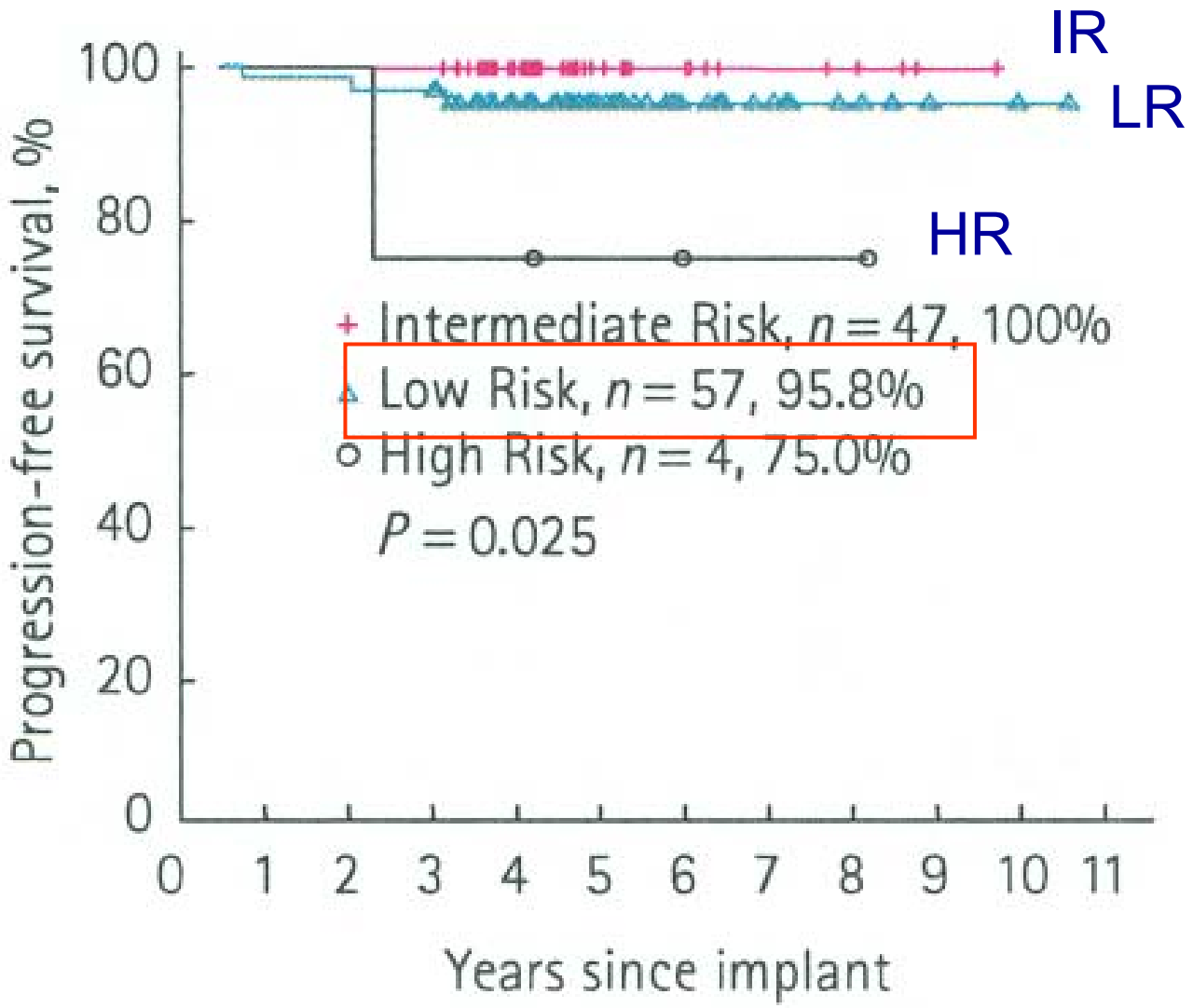


# What about for young men?

*Merrick BJU Int 2006*

- n=108, age ≤ 54 years, 1995-2002
- median follow up 5.3 years
- 8 year bNED for LR 96%
  (PSA < 0.4 ng/ml)
- median PSA for NED 0.05 ng/ml
- no NHT

# PSA ≤ 0.4 ng/ml *Merrick BJU Int 2006*



# Quality of life post implant

# Urinary outcome

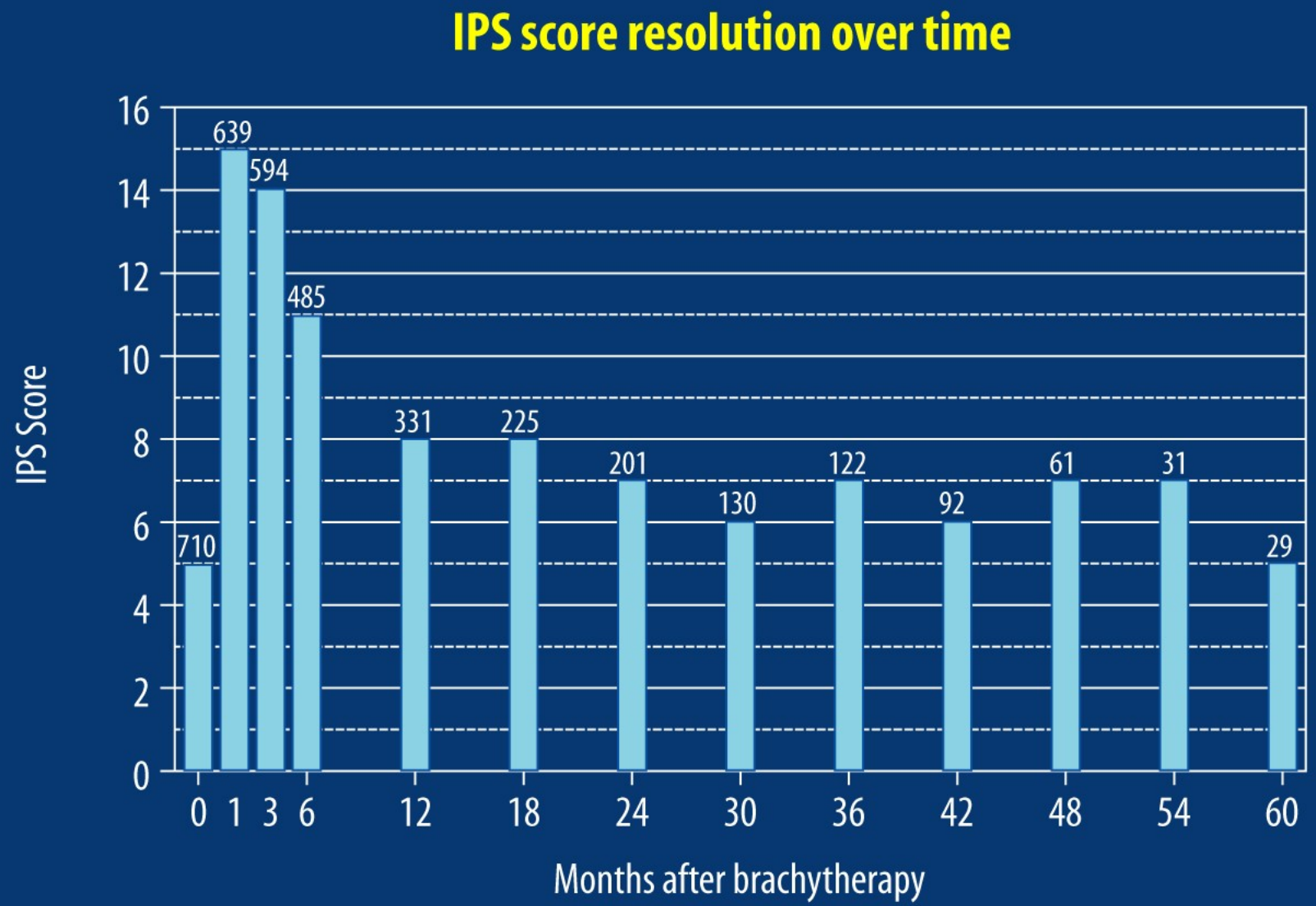
- mild to moderate symptoms expected for 3-6 months
- Quality of life normal by 3 mo
- Symptom score back to baseline by 12 months
- Medication (alpha blockers) may speed recovery
- avoid TURP in first 6 months

# Quality of life post implant

- Catheter rate 15%
  - 10% > 1 week
  - 5% > 1 month
- 1% urethral stricture
- Median IPS score @ baseline 7/35
  - @ 30 mo: 6 and @ 60 mo: 5
- Mild proctitis: 3%, moderate (grade 2): 0.2%

# IPSS: x/35

- Subjective feeling of being "empty"
- Frequency of < 2 hour intervals
- Interrupted stream
- Having to push or strain to start
- Weak stream
- Difficulty postponing urination
- # of times up at night


IPS score resolution over time
IPS Score
16
14
12
10
8
6
4
2
0
639
594
485
331
225
201
130
122
92
61
31
710
29
0 1 3 6 12 18 24 30 36 42 48 54 60
Months after brachytherapy

# Sexual function post brachy

- 85% of men treated at PMH potent pre brachytherapy (16% with pills)
- Ejaculate is reduced (70%) or even absent (20%)
- Medication in the *PDE-5 class* very helpful to preserve erections (may be used prophylactically)
  - Sildenafil (Viagra)
  - Tadalafil (Cialis)
  - Vardenafil (Levitra)

# Potency Rates Following Seed Brachytherapy

| Series | # Patients | Time Point | Incidence |
|---|---|---|---|
| Sharkey | 1048 | 5 years | 85% |
| Stone | 416 | 2 years | 78% |
| Merrick | 209 | 6 years | 92% |
| PMH | 254 | 3 years | 85% |

# IIEF-5: erectile function survey

| | Score | | | | |
|---|---|---|---|---|---|
| **Over the past six months:** | 1 | 2 | 3 | 4 | 5 |
| How do you rate your confidence that you could get and keep an erection? | Very low | Low | Moderate | High | Very high |
| When you had erections with sexual stimulation, how often were your erections hard enough for penetration? | Almost never or never | Much less than half the time | About half the time | Much more than half the time | Almost always or always |
| During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner? | Almost never or never | Much less than half the time | About half the time | Much more than half the time | Almost always or always |
| During sexual intercourse how difficult was it to maintain your erection to the completion of intercourse? | Extremely difficult | Very difficult | Difficult | Slightly difficult | Not difficult |
| When you attempted sexual intercourse, how often was it satisfactory for you? | Almost never or never | Much less than half the time | About half the time | Much more than half the time | Almost always or always |
| The IIEF-5 score is the sum of questions 1 to 5. The lowest score is 5 and the highest score 25. | | | | | |

# Results: self reported IIEF

- 101 completed on-line questionnaire
- Median age: 65 years
- Interval since BT: 23 mo (3-63)
- Median IIEF score 20/25
- PDE-5 use:
  - Sometimes: 25%
  - Always: 30%
  - Never: 46%

# On-line survey: IIEF

- No deterioration in score over time: equivalent scores for men in their first year and beyond 3 years
- More men taking PDE-5's (Viagra, Levitra, Cialis) with longer followup (beyond 3 years 64%)

# What are my chances…

- Important predictors of maintaining potency
  - Smoking ↓↓
  - High blood pressure ↓
  - Diabetes ↓↓
  - Good baseline function ↑↑
- age @ implant 50-59: 92% potent
  60-69: 64%, 70-79: 58%

*Cesaretti et al BJU Int 2007*

# Quality of Life Summary

- Brachytherapy:
  - Less incontinence and impotence than surgery
  - Less bowel injury and impotence than external beam
  - More irritative urinary symptoms than surgery or external beam

# Practical Advantages of LDR Brachytherapy

- Patient viewpoint
  - Eliminate hospitalization
  - One day procedure
  - Rapid return to normal activities
- Technical advantages
  - Eliminates issue of daily prostate motion
  - Efficient use of physician time (1-2 hour procedure)

# Selection factors

- *How do we decide if someone is suitable for brachytherapy?*

# Ontario evidence-based guideline for BT (2001)

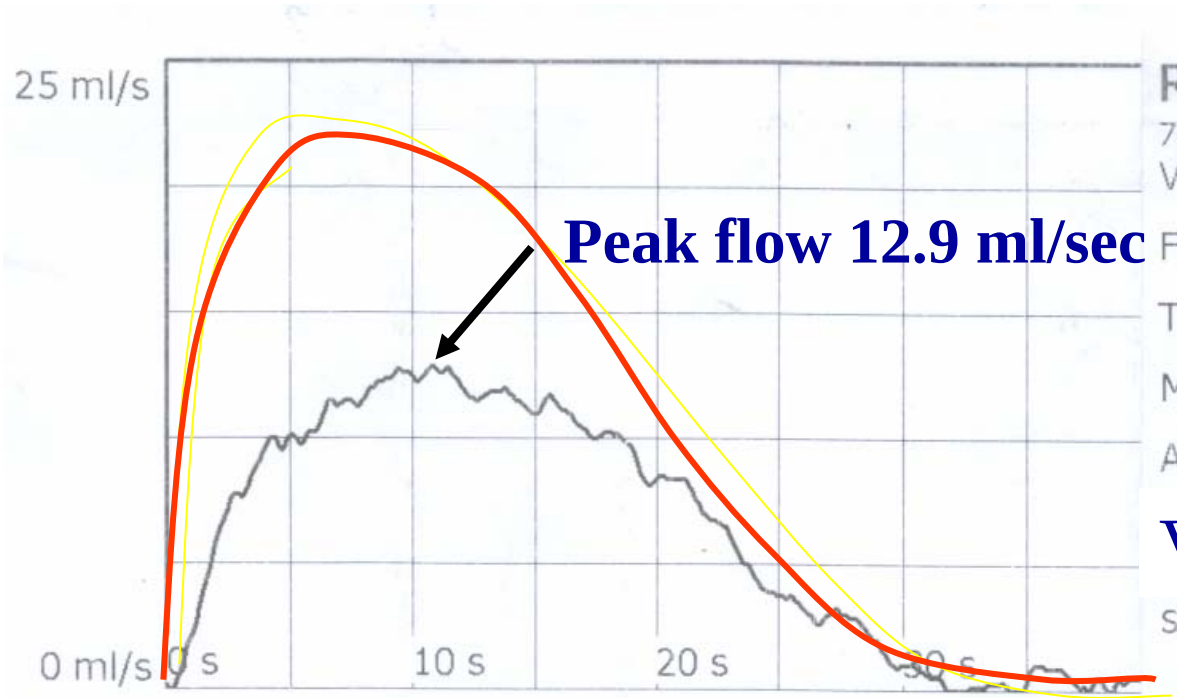
- T1c/T2a
- Gleason $\leq$ 6
- PSA < 10 ng/ml
- no TURP
- Prostate volume < 50 cc

*Walsh: 75% of newly diagnosed PCa in US nonpalpable (T1c)* (NEJM 2002)

# My Criteria for brachytherapy

- Stage T1c/T2a, Gleason $\leq$ 6, PSA < 10
- Prostate size < 60 cc
- "adequate" voiding function
  - IPSS
  - Voiding study
- Preferably no prior TURP

# Voiding study




Results
7-28-2005 3:34PM

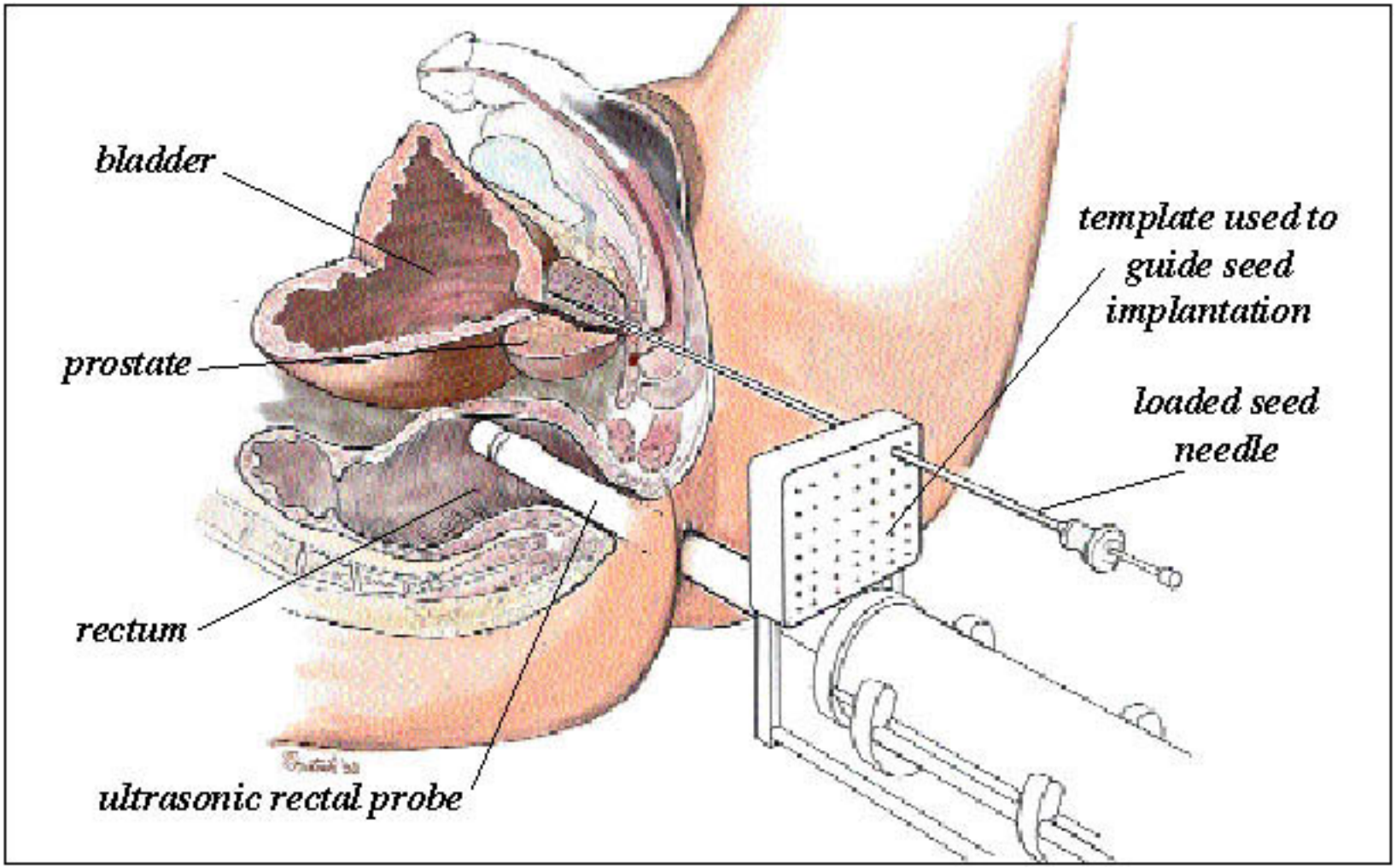
| | | |
|---|---|---|
| Voiding Time: | 44 | s |
| Flow Time: | 35 | s |
| Time to Max Flow: | 10 | s |
| Max Flow Rate: | 12.9 | ml/s |
| Average Flow Rate: | 7.1 | ml/s |

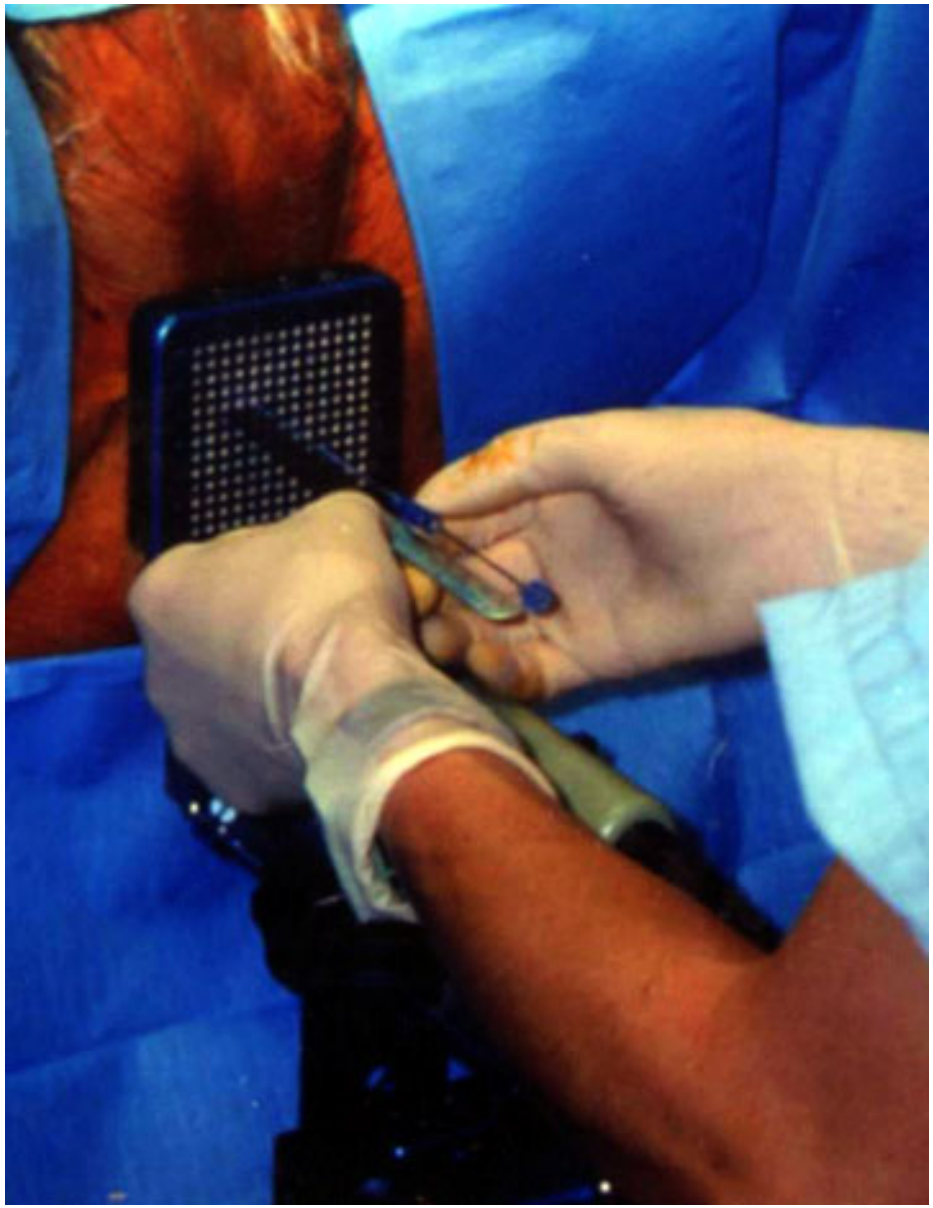
Voided volume: 252 ml

Sensor: Spinning Disc

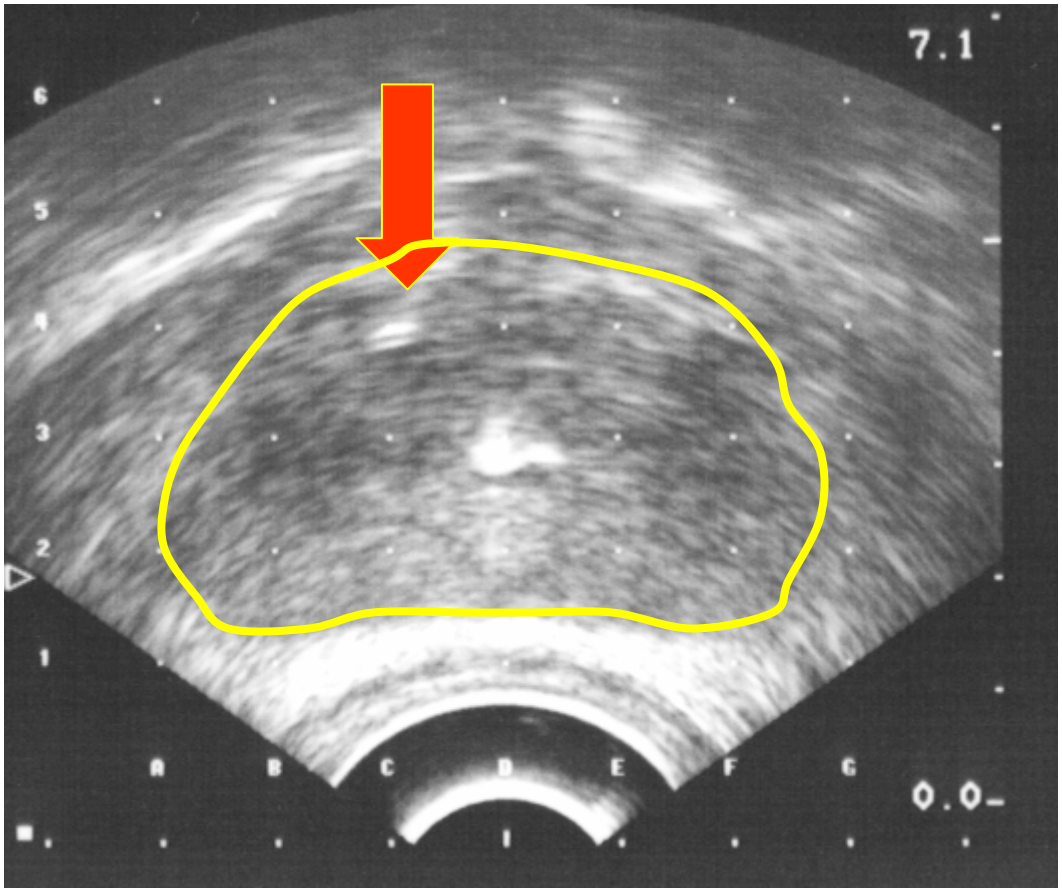
Post void residual 18 cc

# How we do it

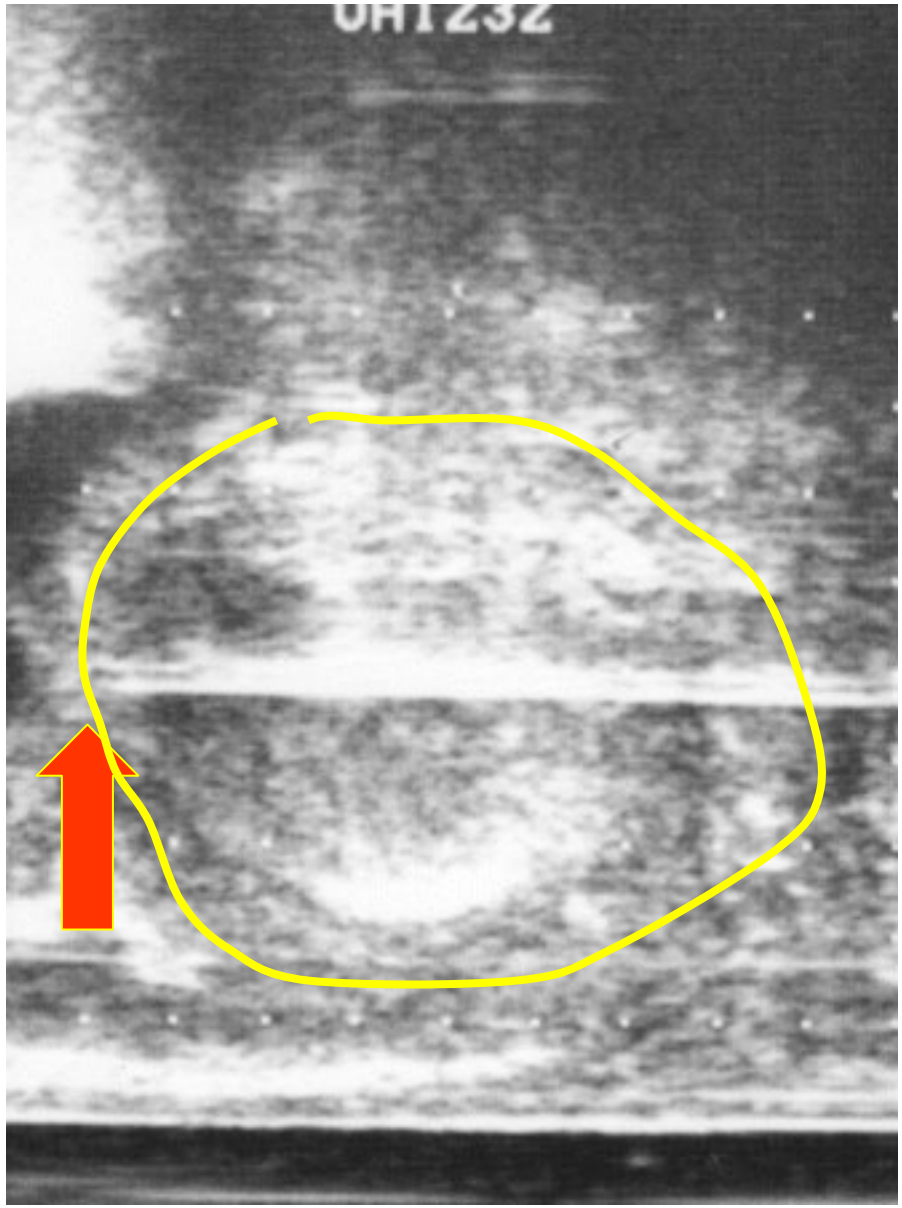

bladder
prostate
rectum
ultrasonic rectal probe
template used to guide seed implantation
loaded seed needle



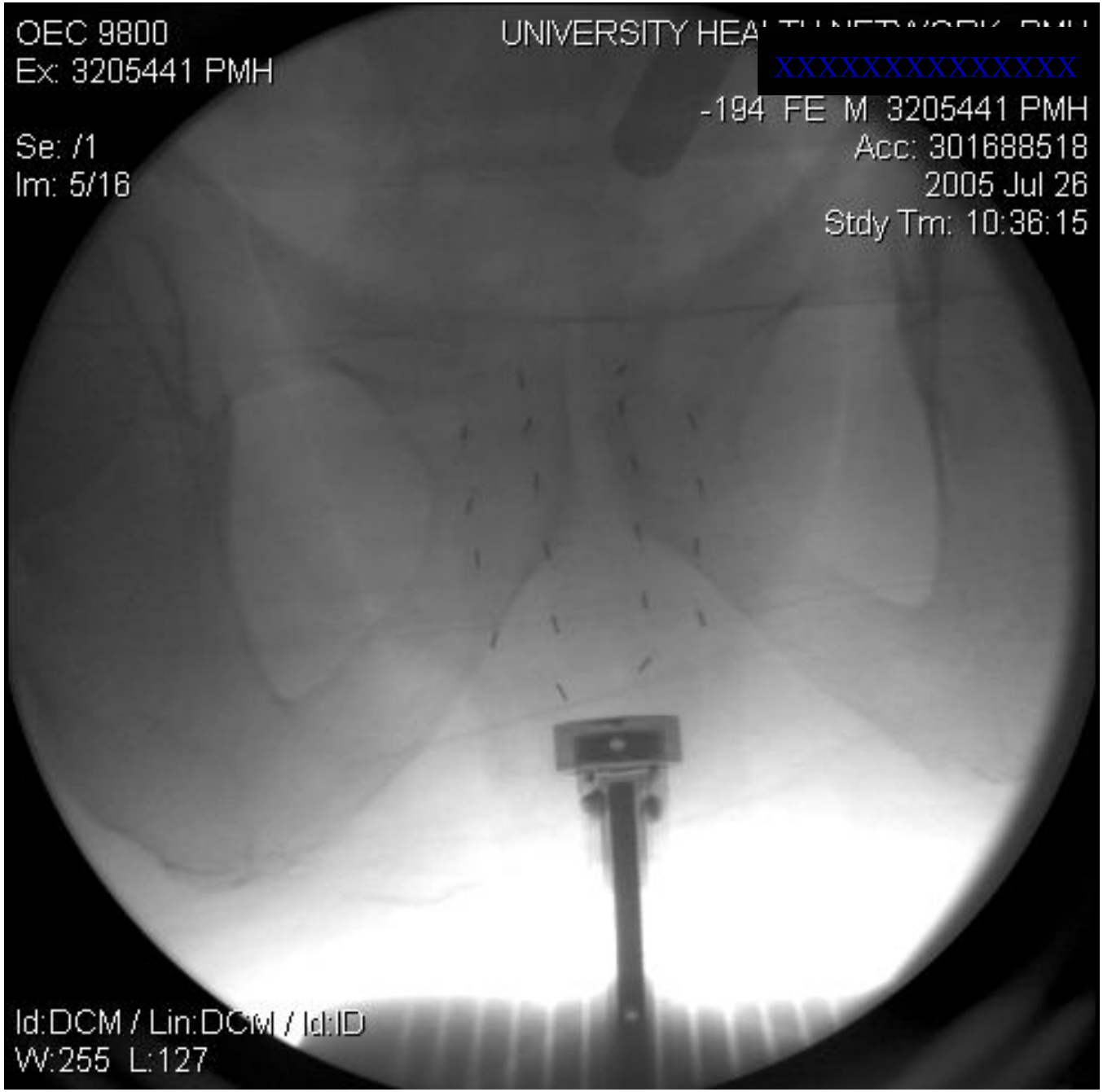
Measuring needle penetration




Needle tip at C4



confirmation of needle position at base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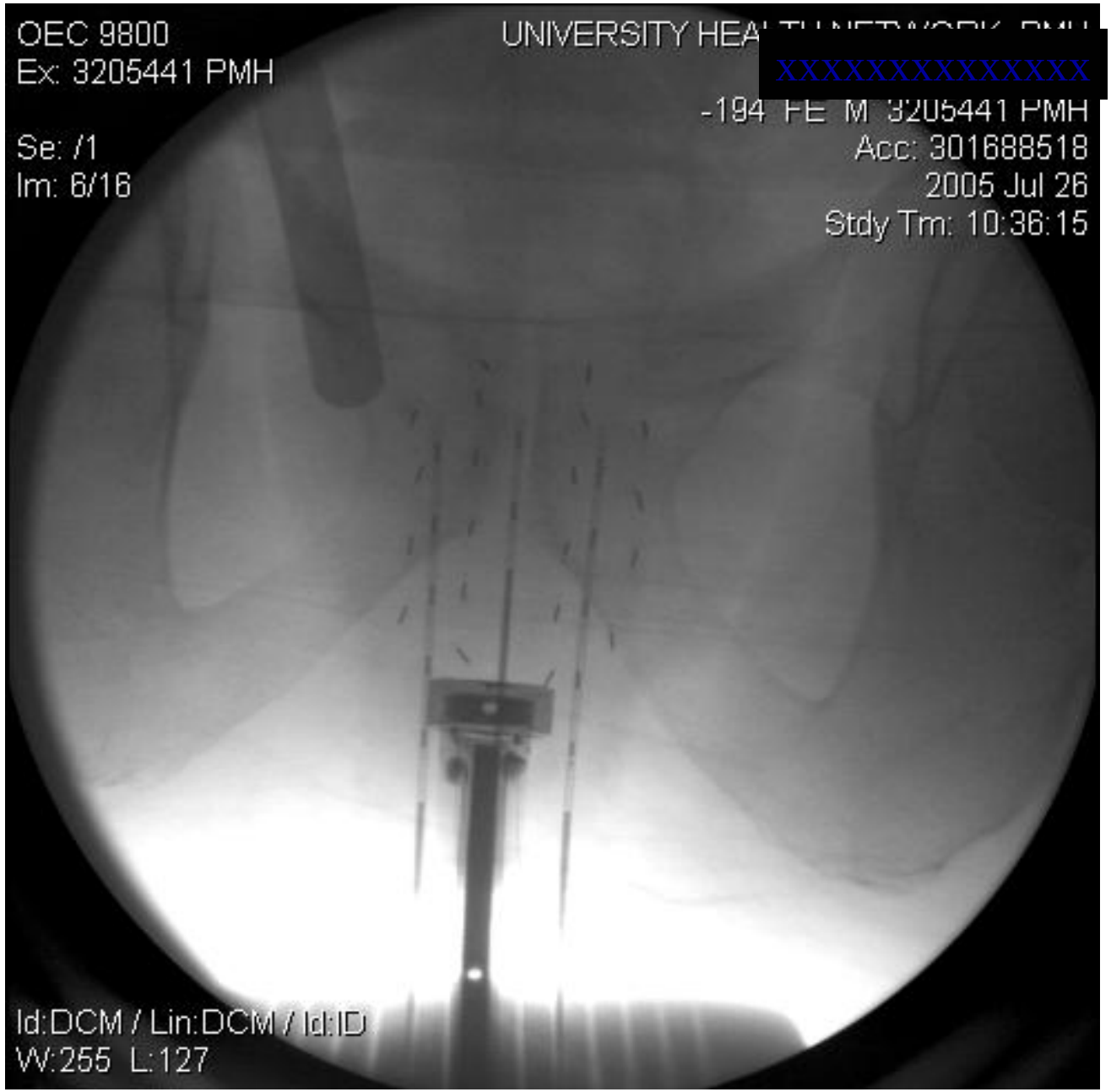
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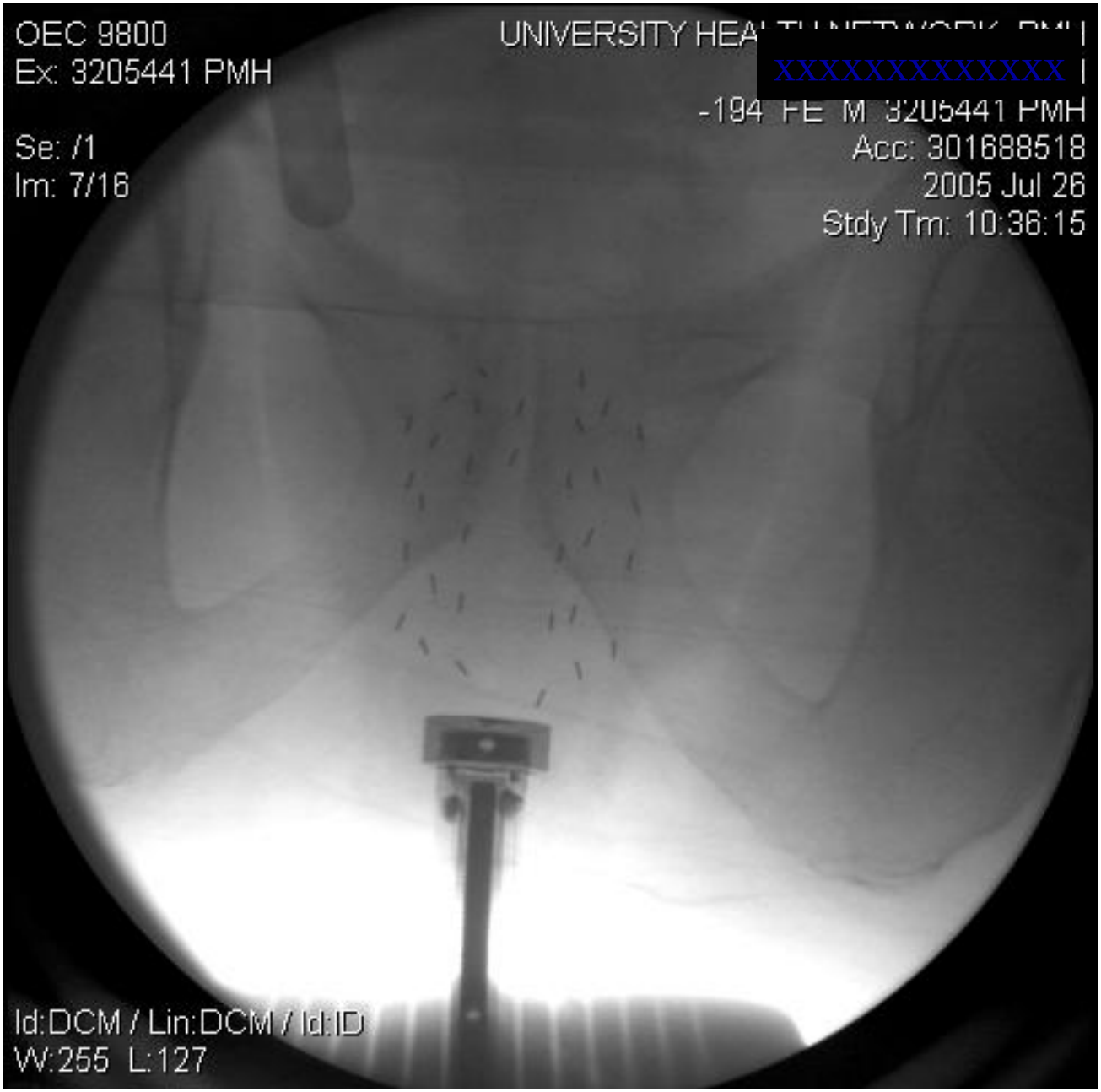
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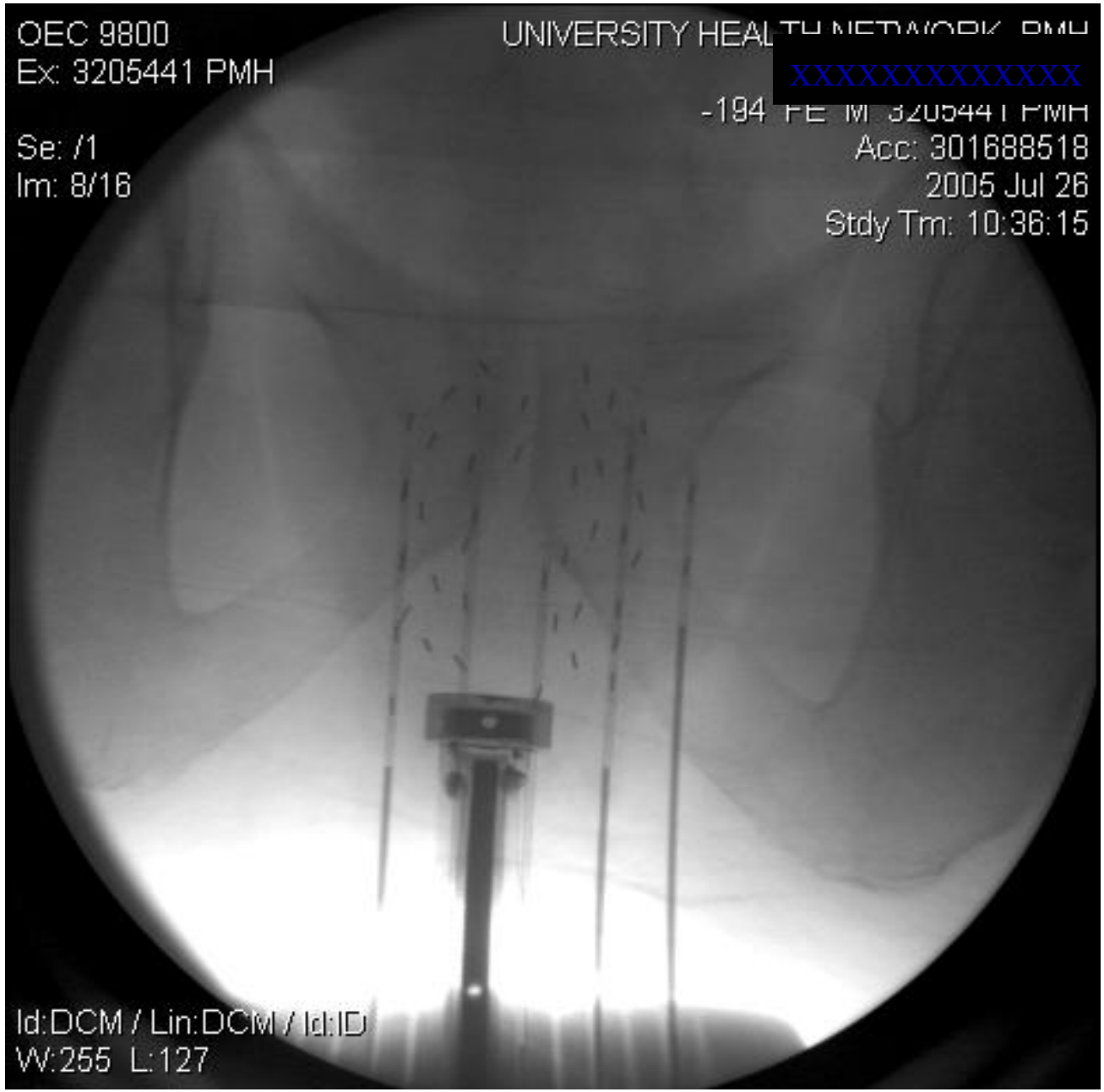
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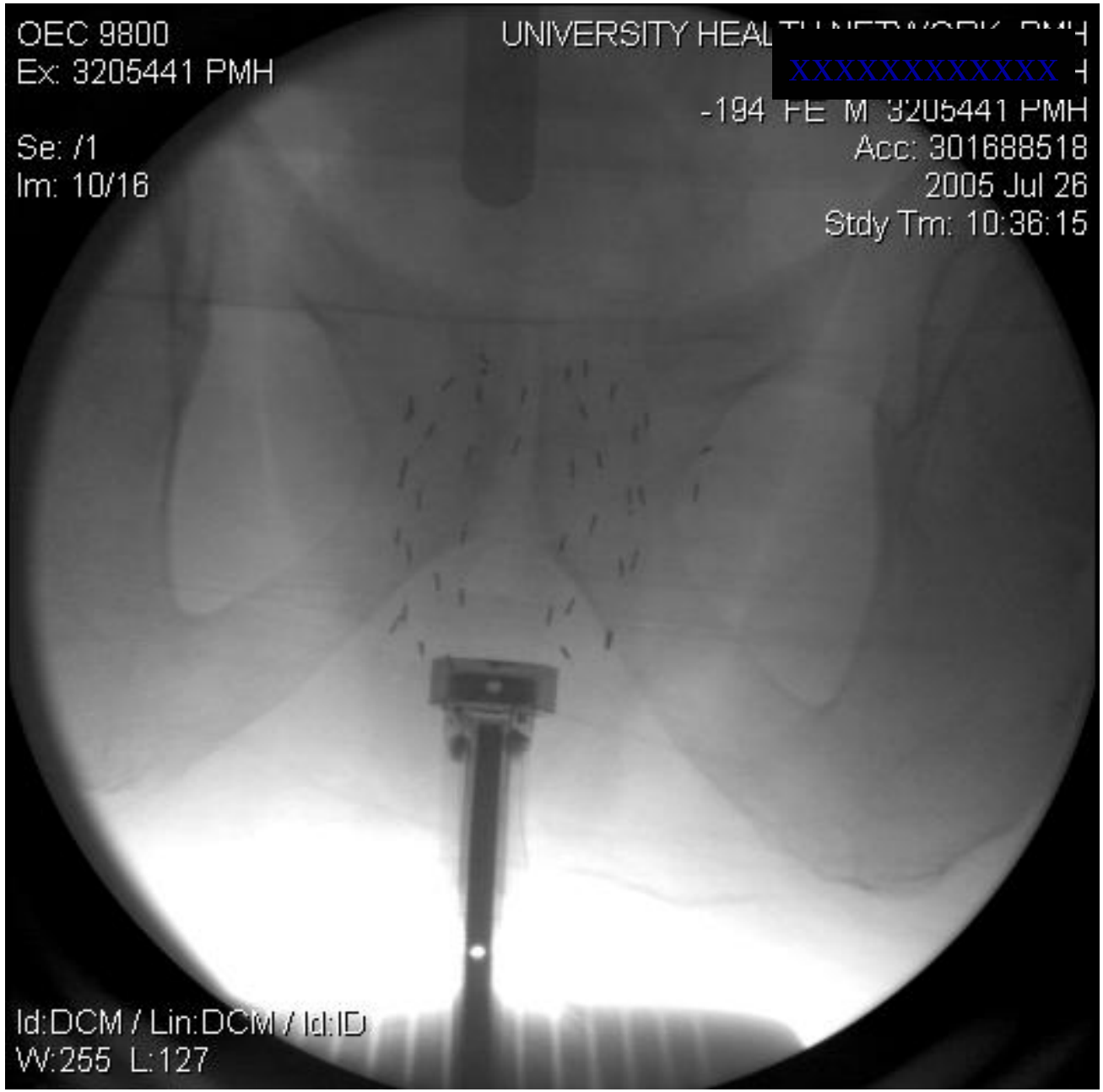
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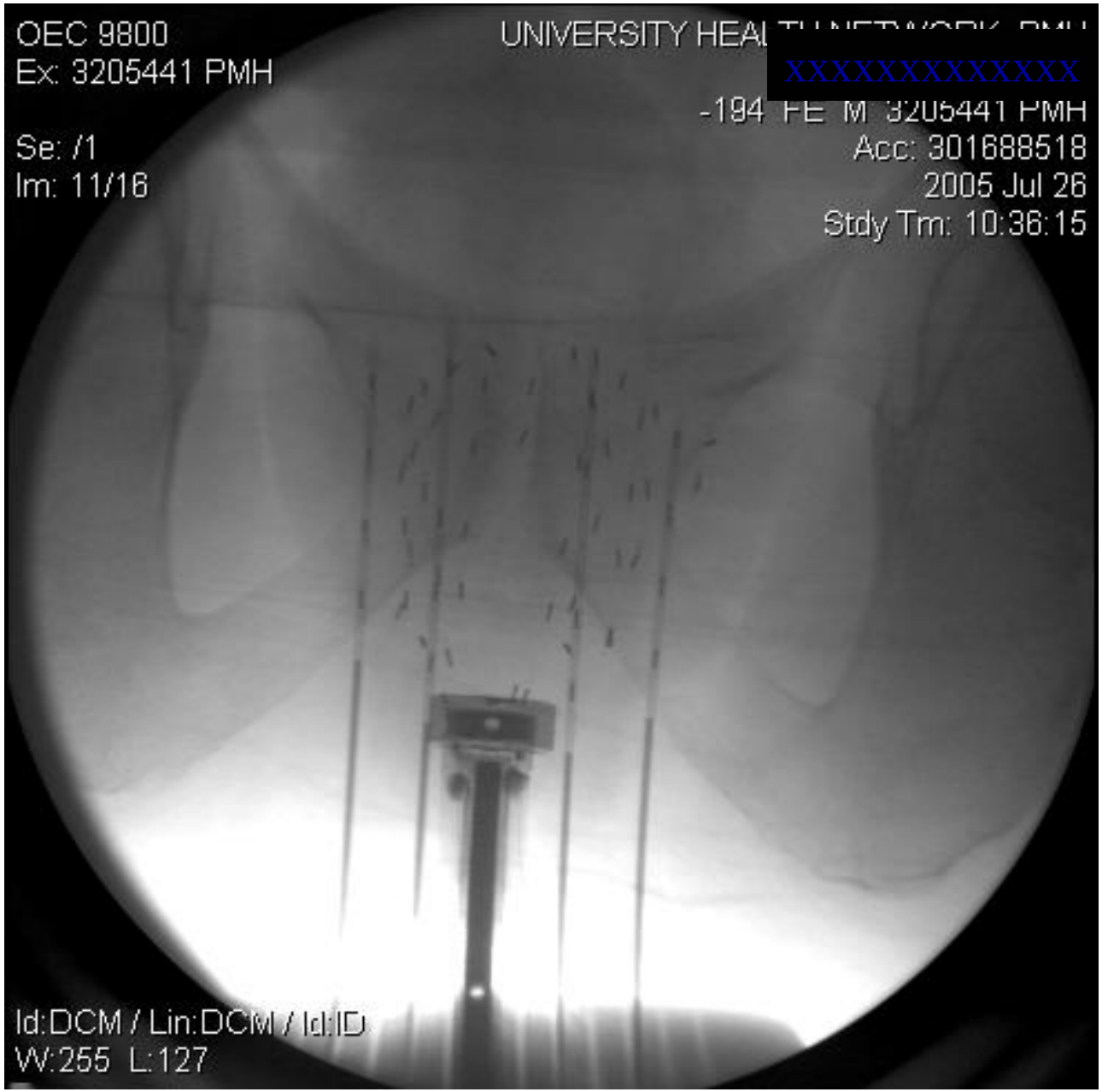
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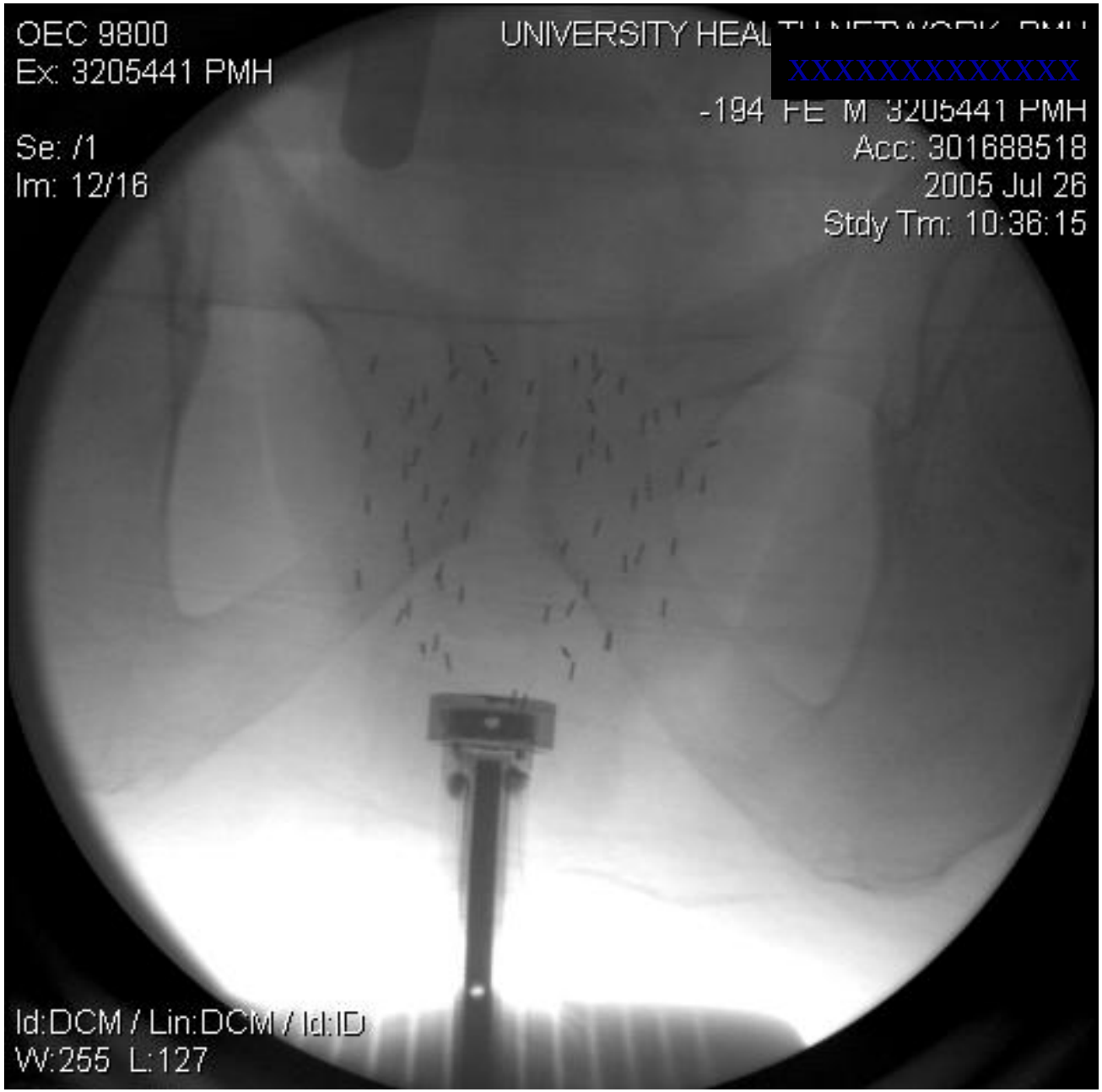
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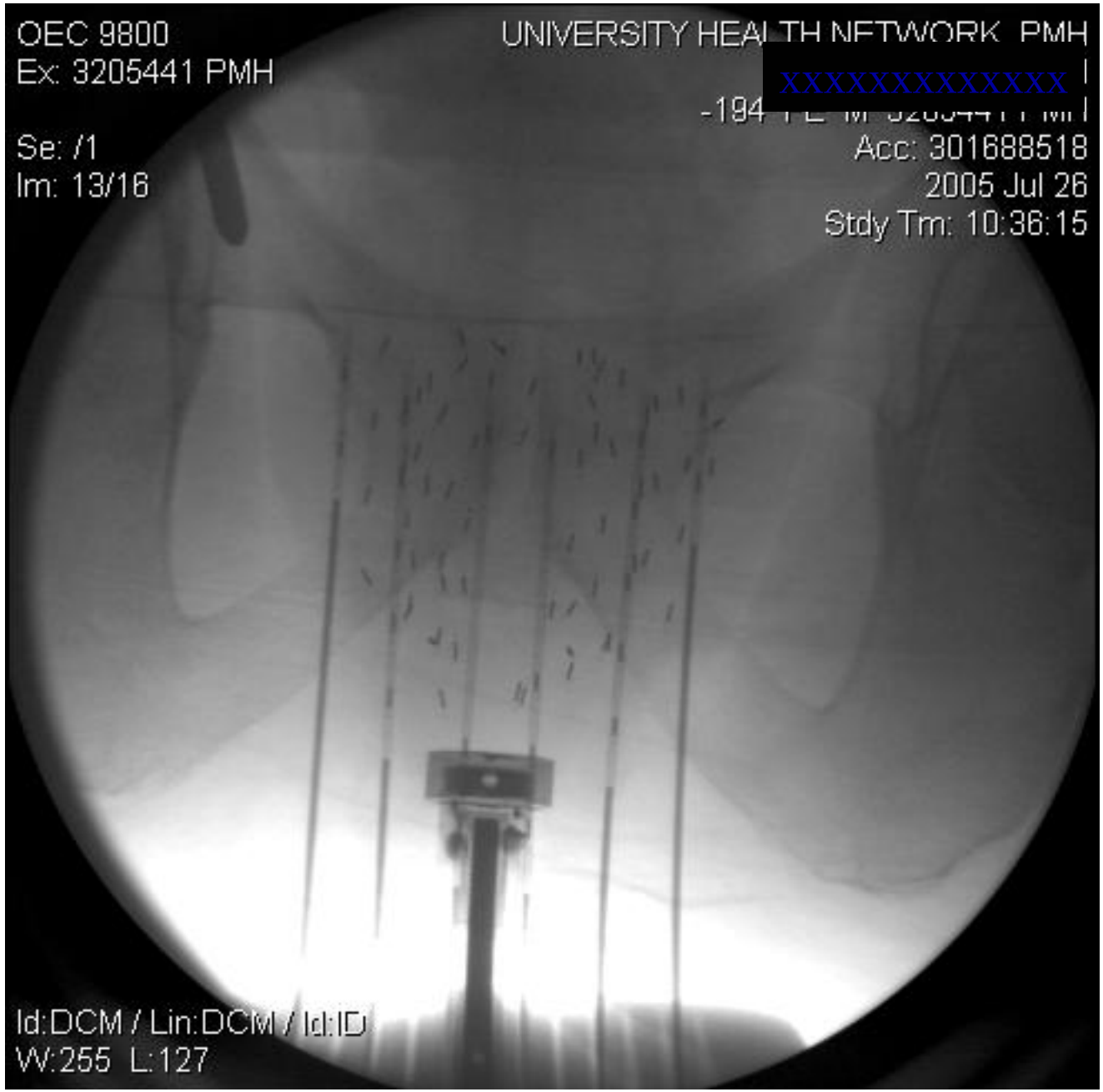
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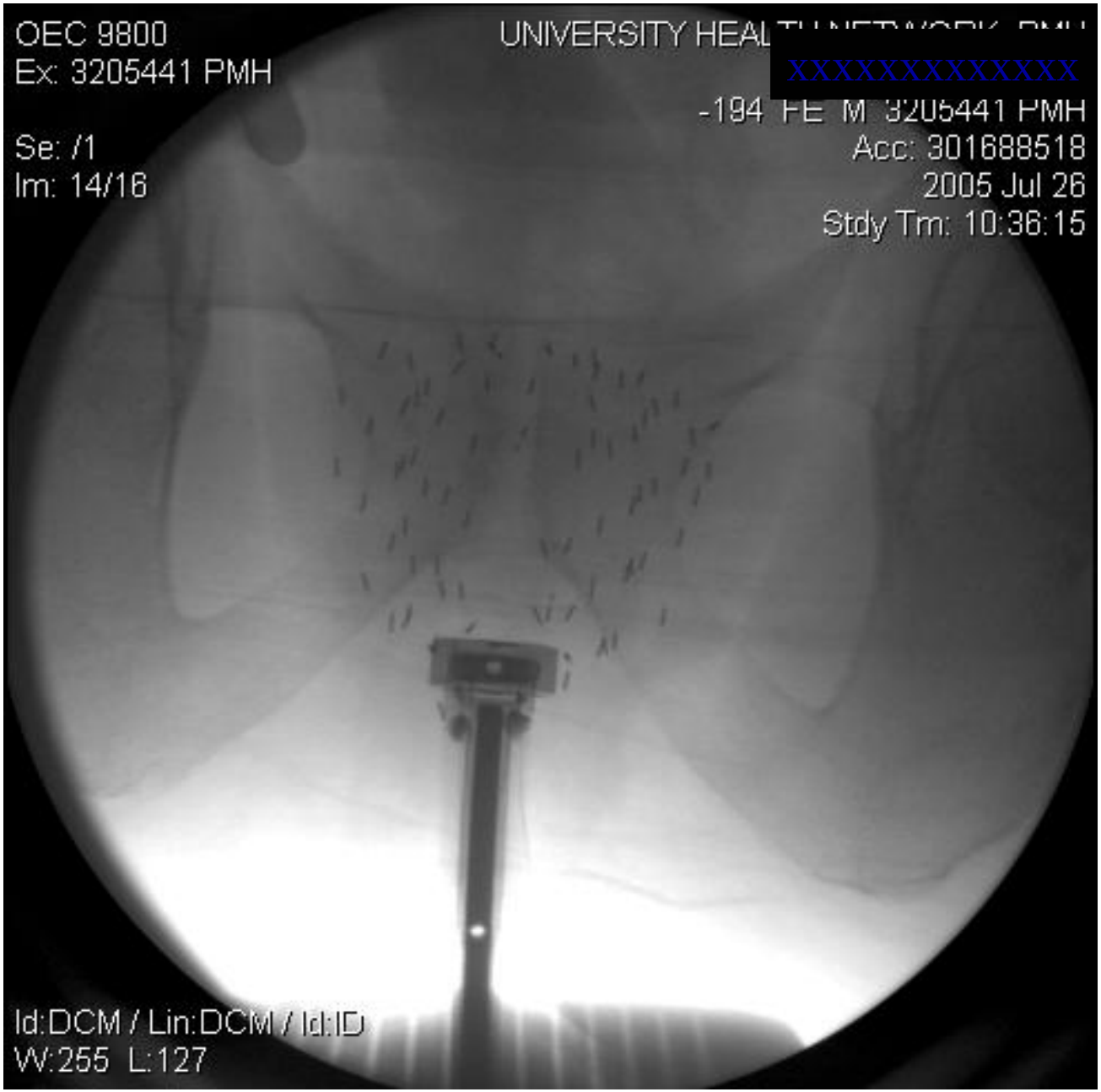
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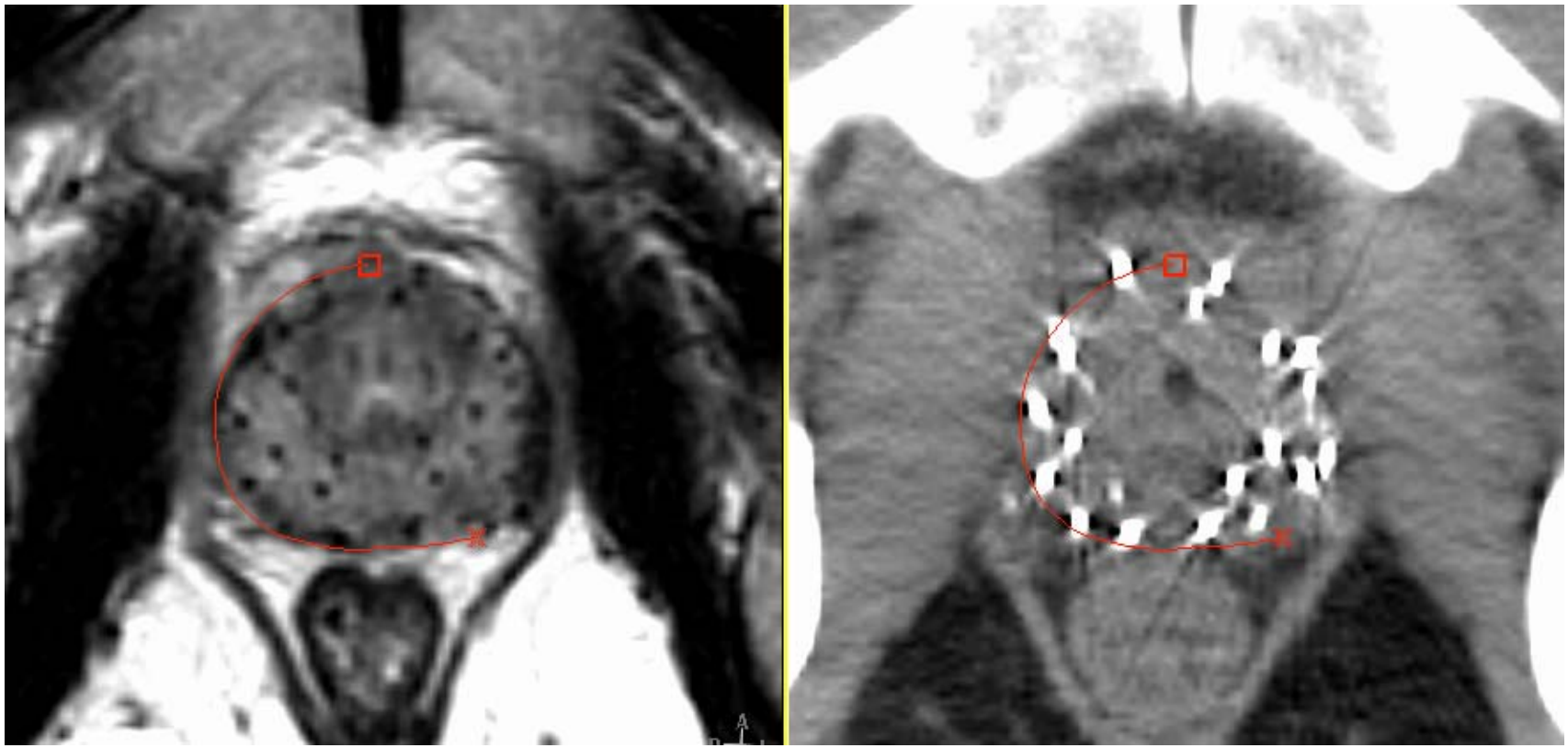
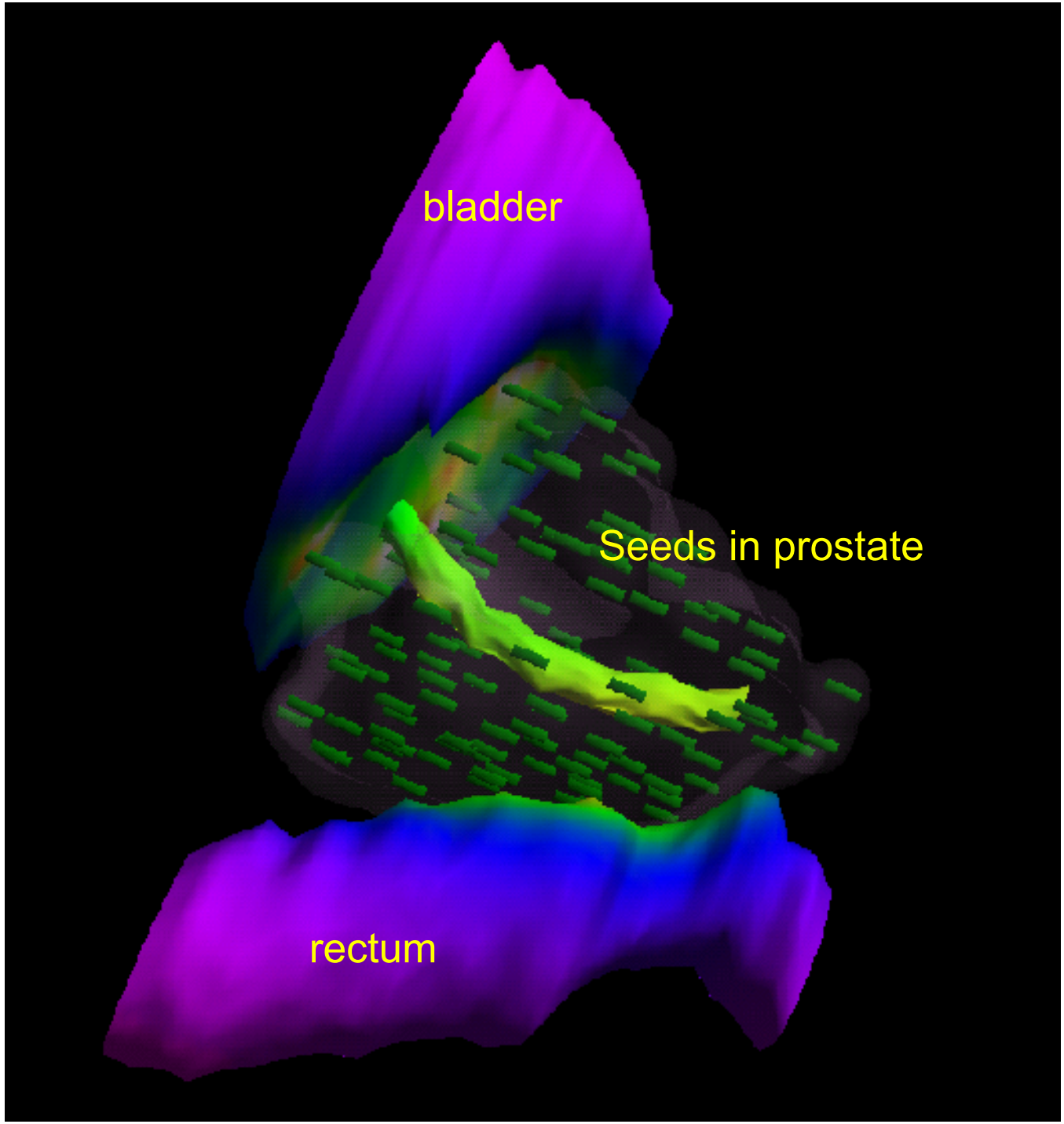
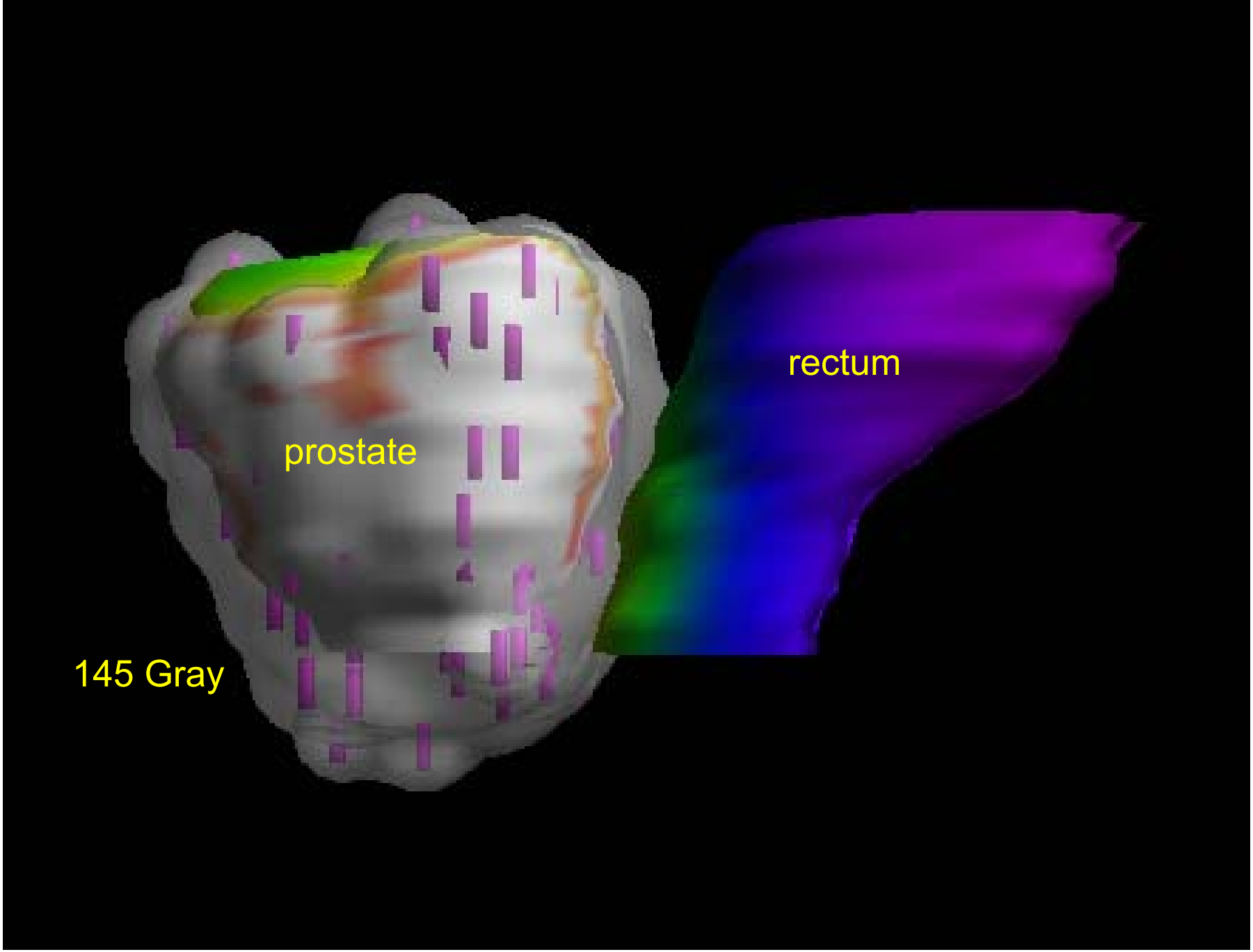
# Post implant dosimetry

- must document the actual dose that the prostate and adjacent tissues receive
- correlate rectal/urethral doses with side effects
- correlate results with the quality of the implant

# MRI-CT fusion




bladder
Seeds in prostate
rectum


rectum
prostate
145 Gray

# *Selected FAQ's*

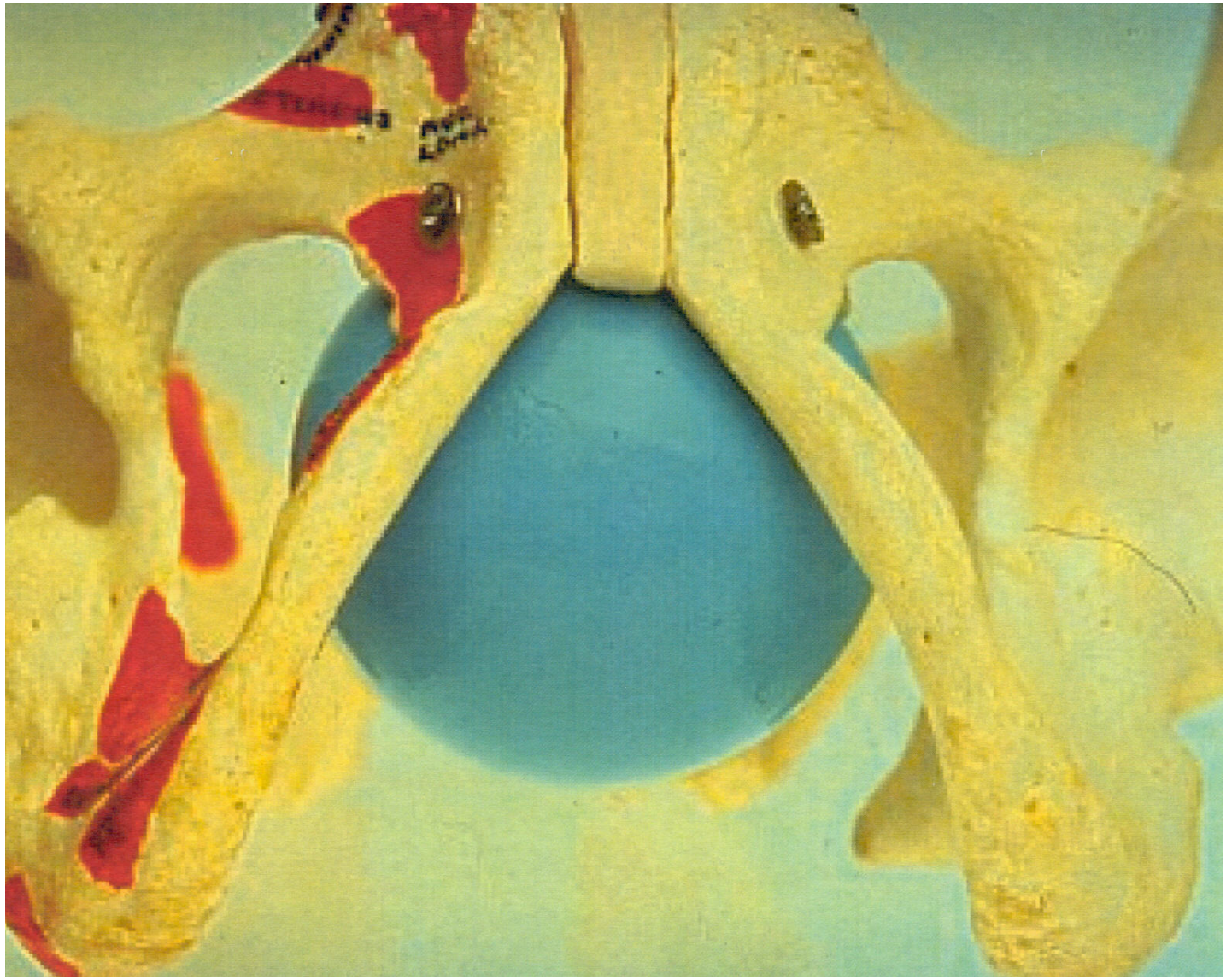
- Why is prostate size important and how big is too big?
- What if I've had a TURP? Is it still possible to have brachytherapy?
- What is seed migration? Where do they go and when?
- Am I radioactive? What is the risk for my (grand)children?
- What is a PSA bounce? What can I expect my PSA to be after brachytherapy?

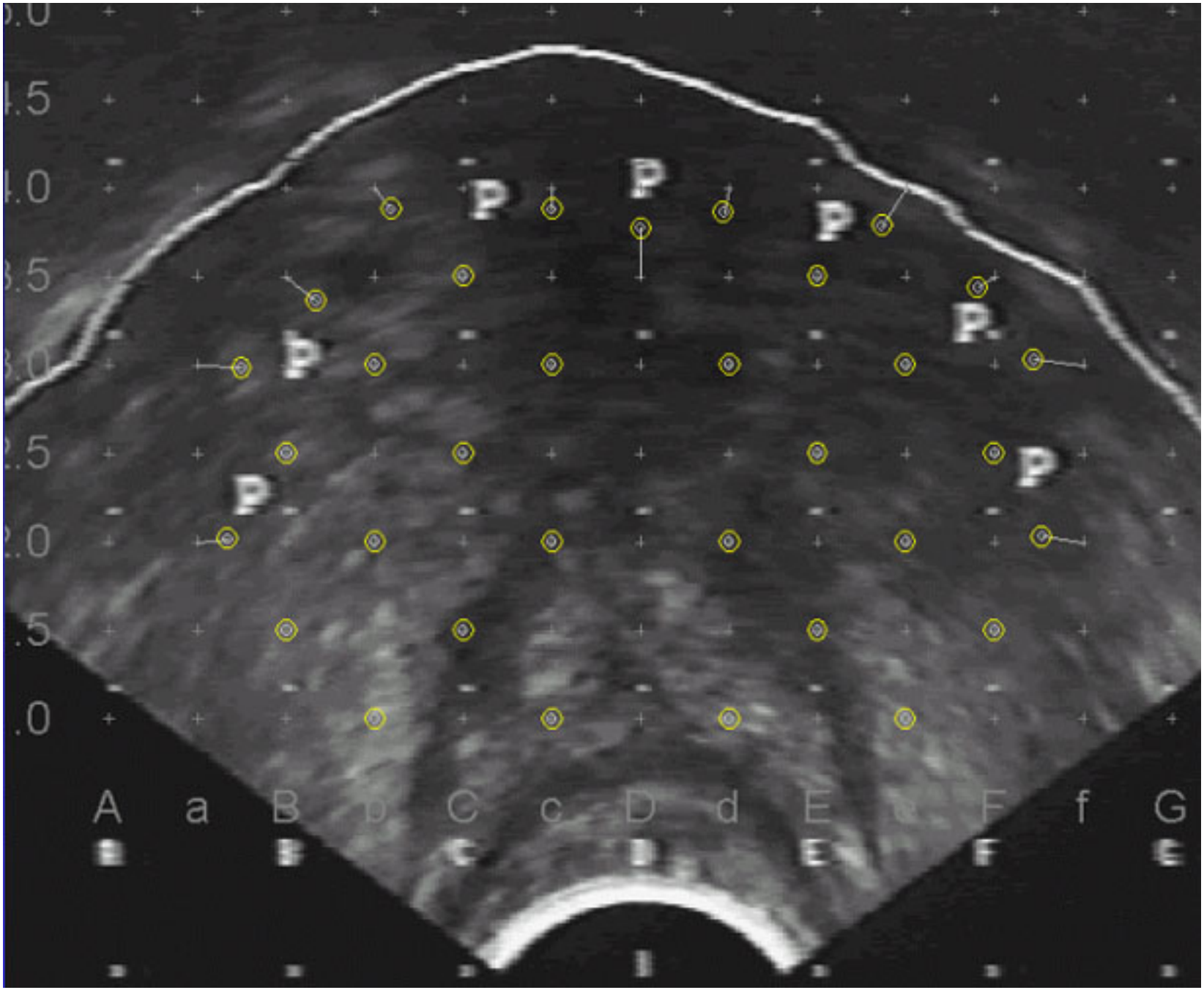
# FAQ #1: Prostate size

- No absolute cut-off for size
- Depends on relationship to pubic arch
- In a small-boned, slim-hipped man, may get PAI @ 40-45 cc, while in large-boned tall individual 65 cc OK
- Hip-position and TRUS probe-angle important

Volume study geometry

# Pubic arch interference

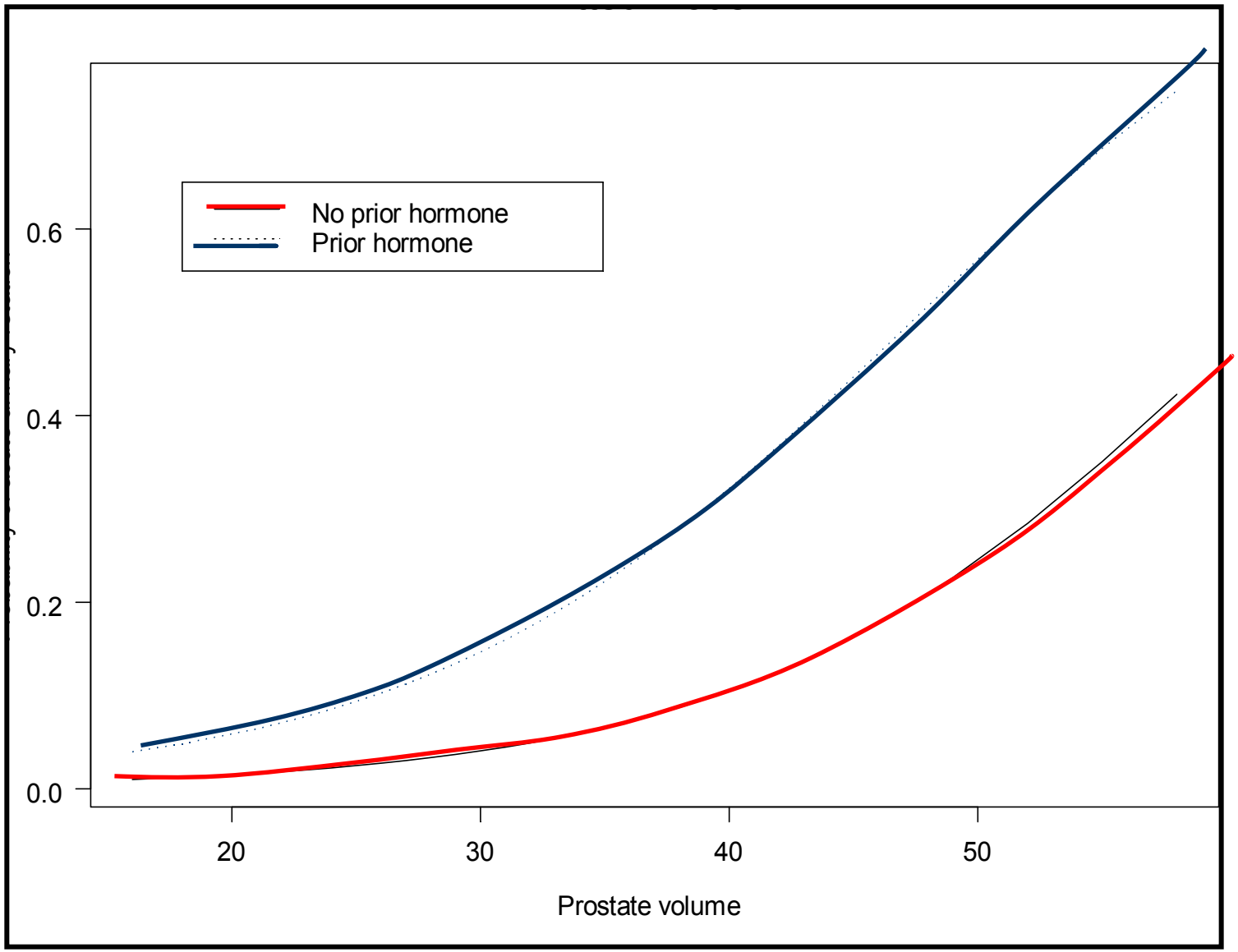



A
a
B
b
C
c
D
d
E
e
F
f
G

# Prostates > 60 cc

- technically difficult b/o PAI
- require larger number of seeds & needles (cost ↑ & ↑ risk urinary morbidity )
- may become good candidate after hormone therapy (3-6 months) to shrink the prostate
- TAB X 3 mo → 46% volume ↓

  mono LHRH → 22% volume ↓



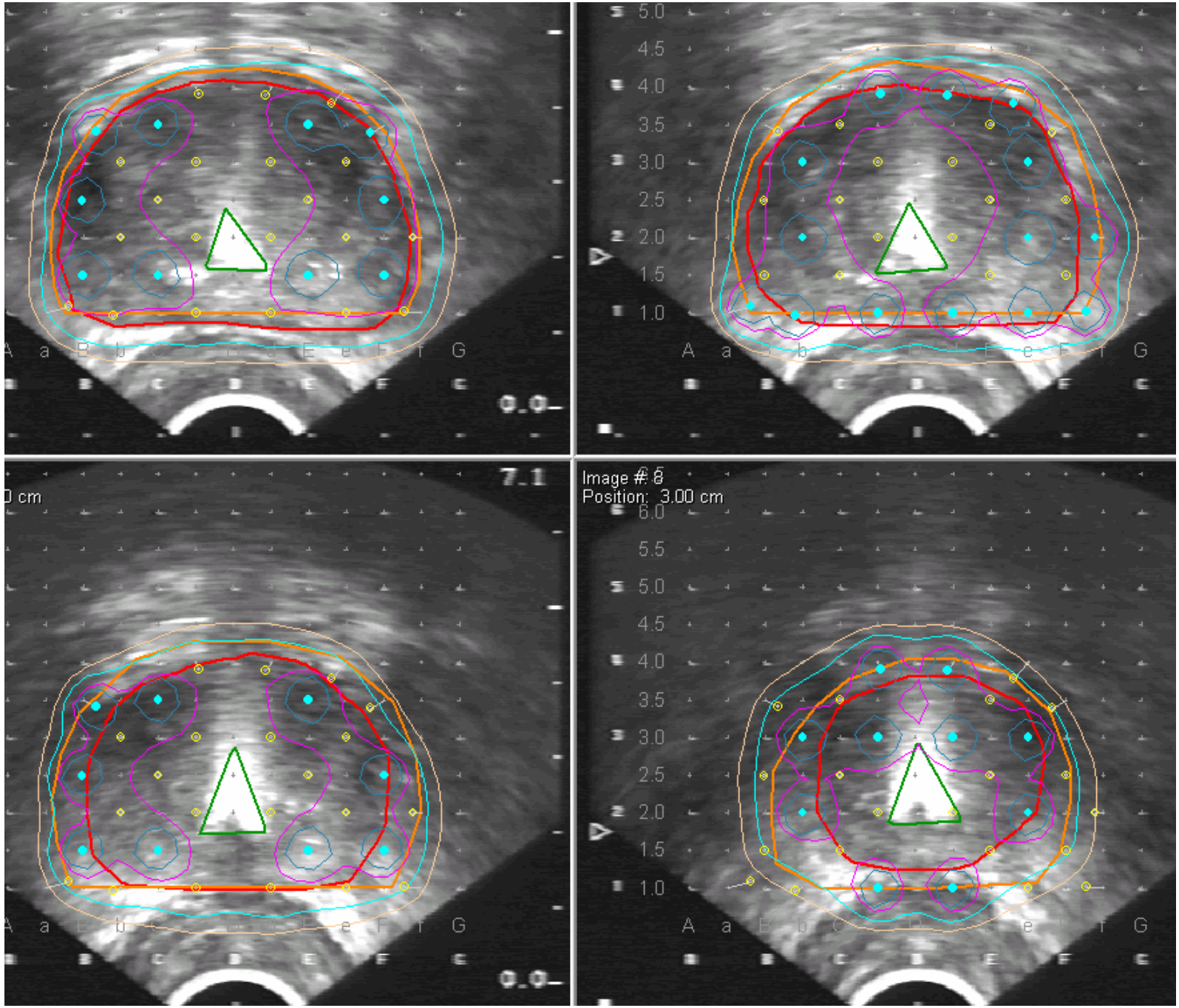

# Risk of catheter according to hormone use & prostate volume

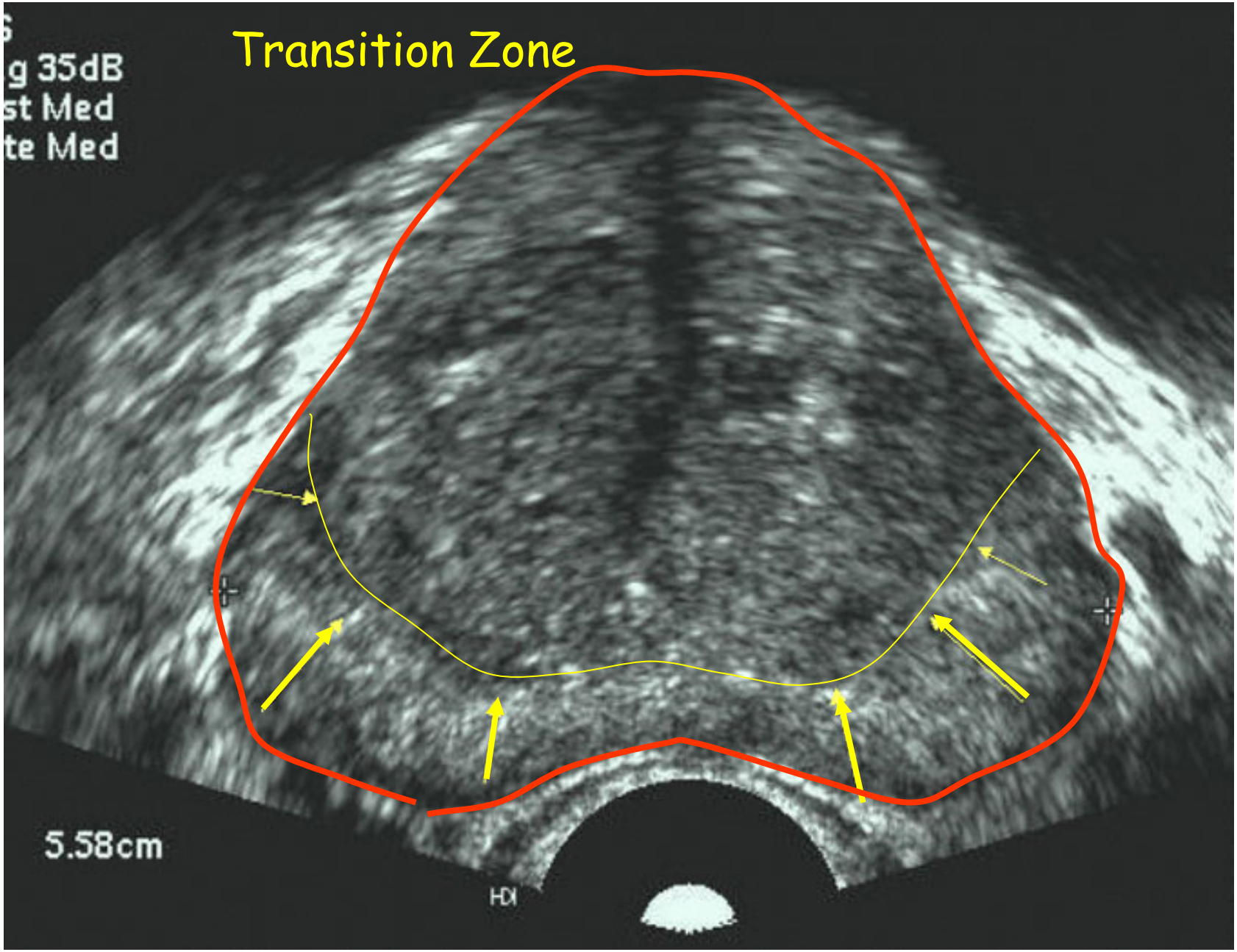
# FAQ #2: Prior TURP

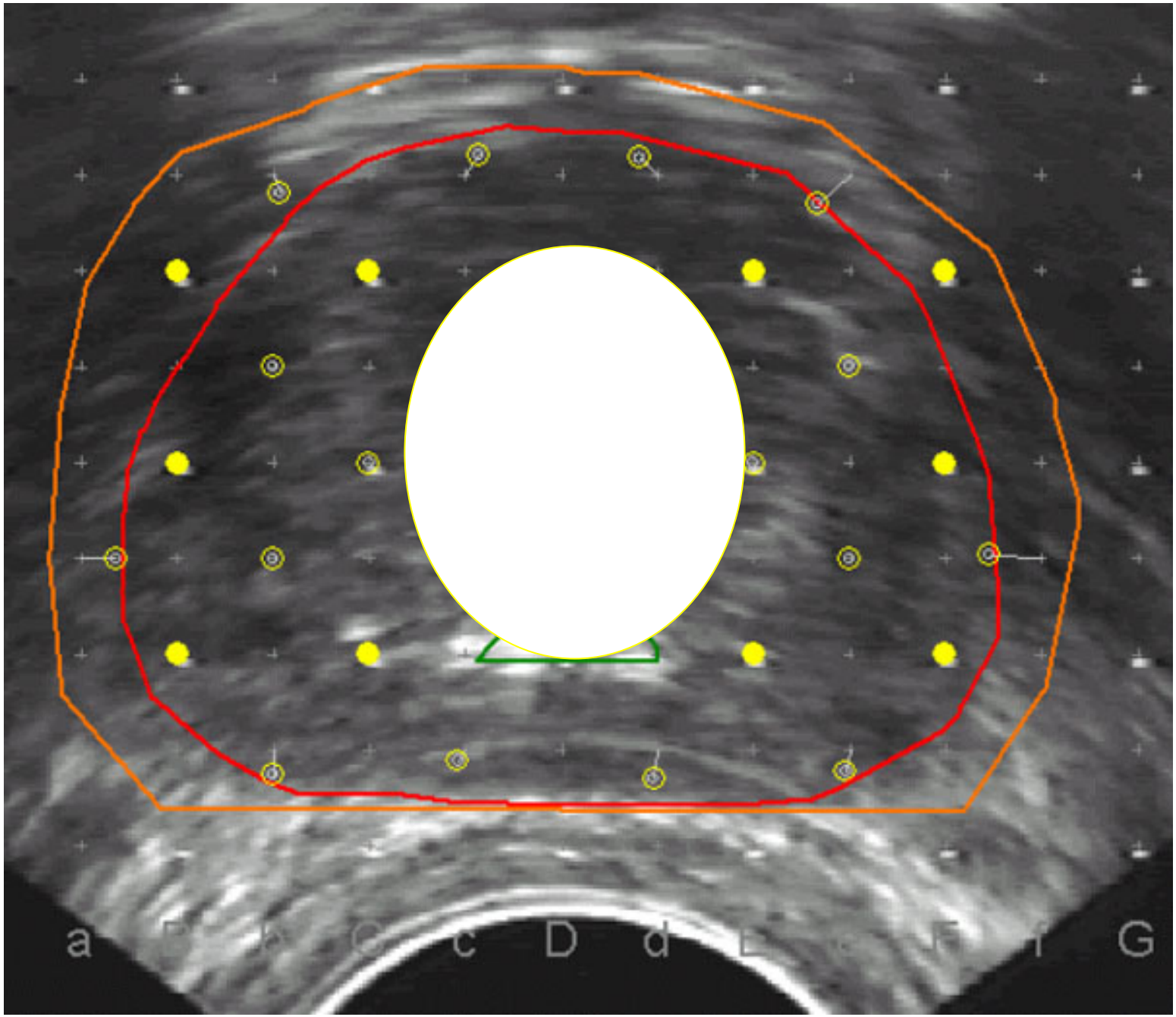
- large TURP defect → seed loss and poor dosimetry
- possible ↑ risk of urethral necrosis, stricture, urinary incontinence
- exclude those with large or poorly healed TURP defect
- small TURP OK with peripheral loading
- allow minimum 3 months for healing

# Previous TURP

- Depends on amount of tissue removed and how long ago
- Earlier reports suggested an ↑ risk of incontinence after brachytherapy
- Recent literature reports equivalent urinary QOL to non TURP patients *Merrick et al IJROBP 2004*


5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
A a B b C D E e F f G
0.0
7.1
Image # 8
Position: 3.00 cm
6.0
5.5


Transition Zone
g 35dB
st Med
te Med
5.58cm
HDI


a
c
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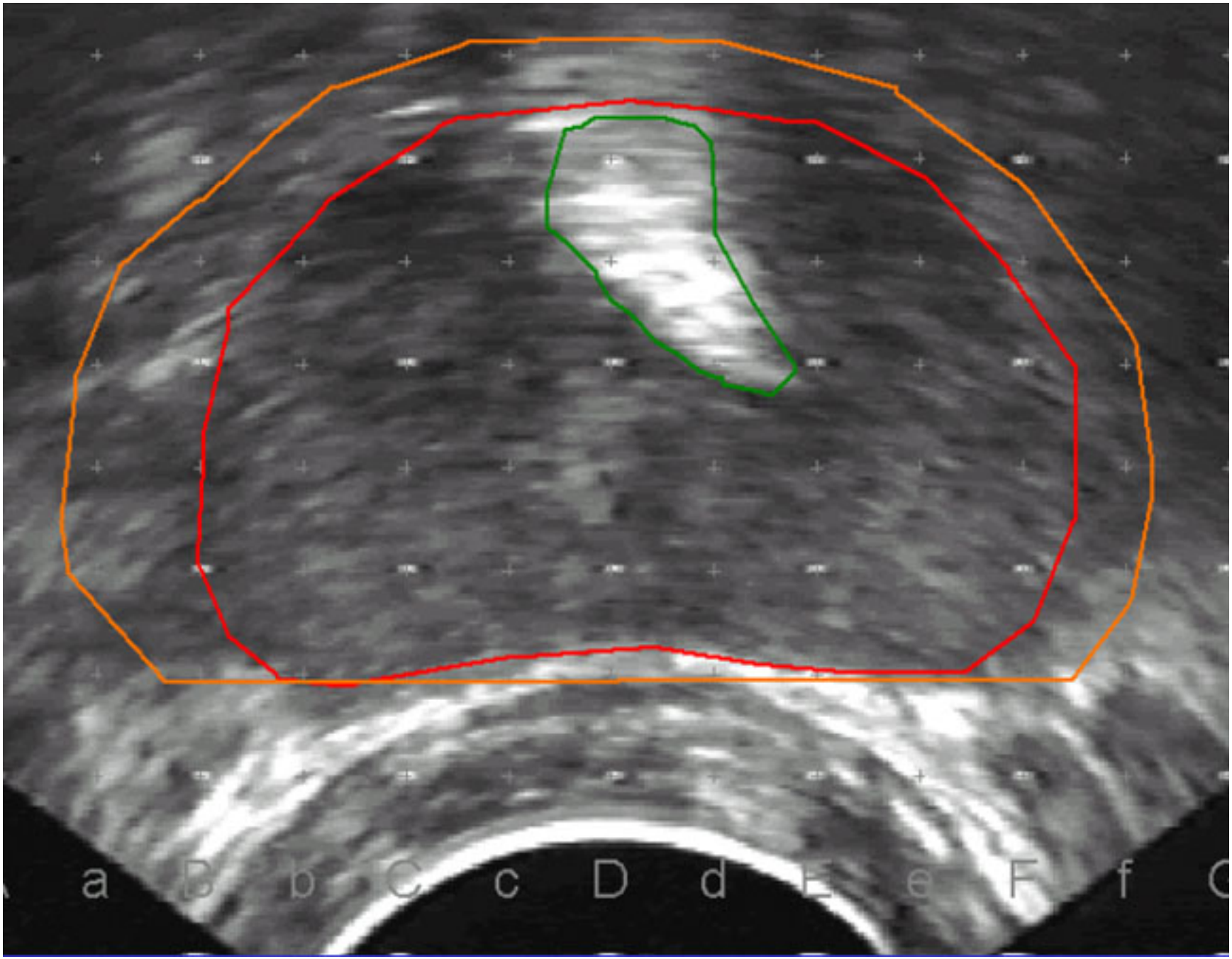
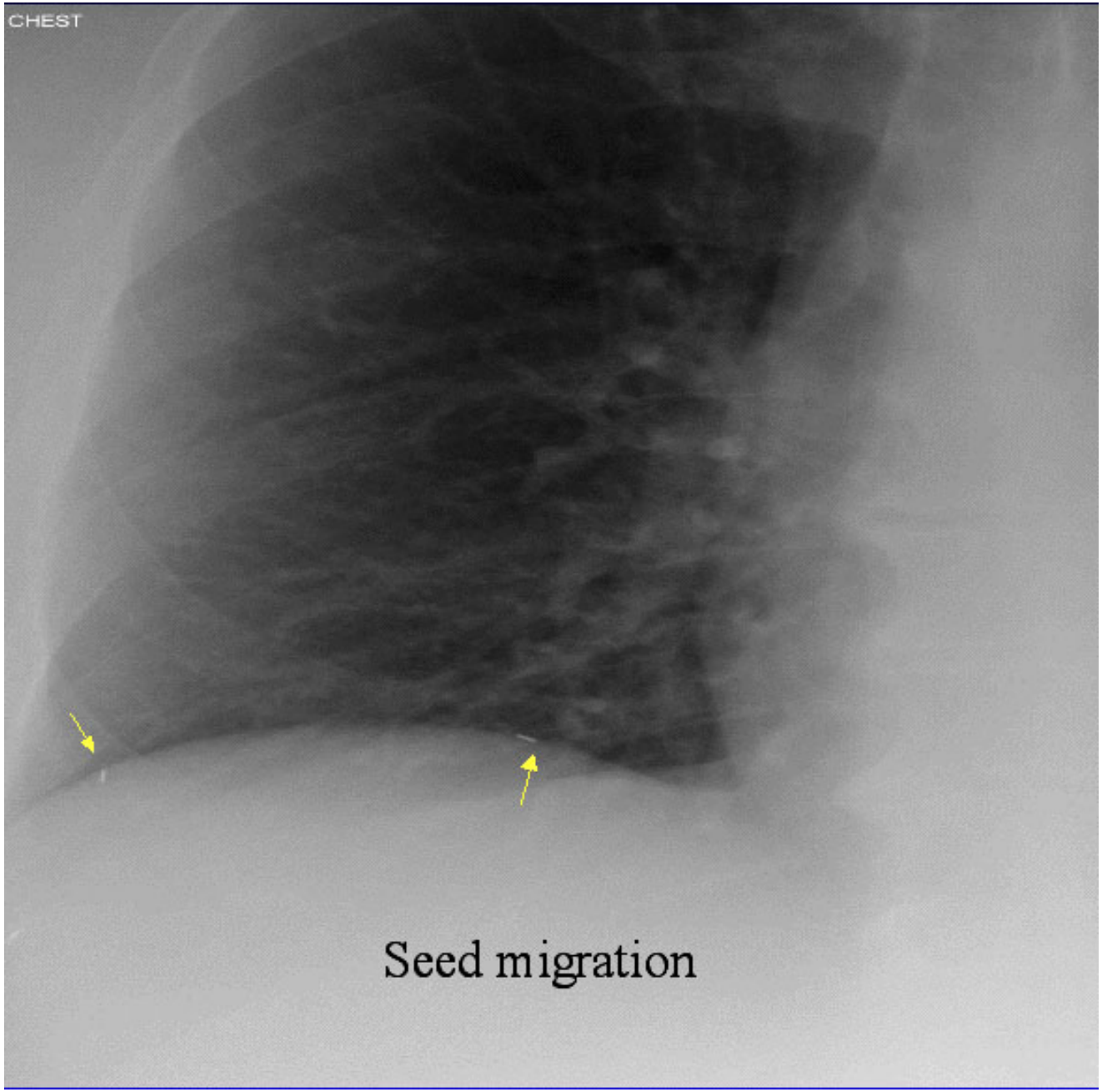
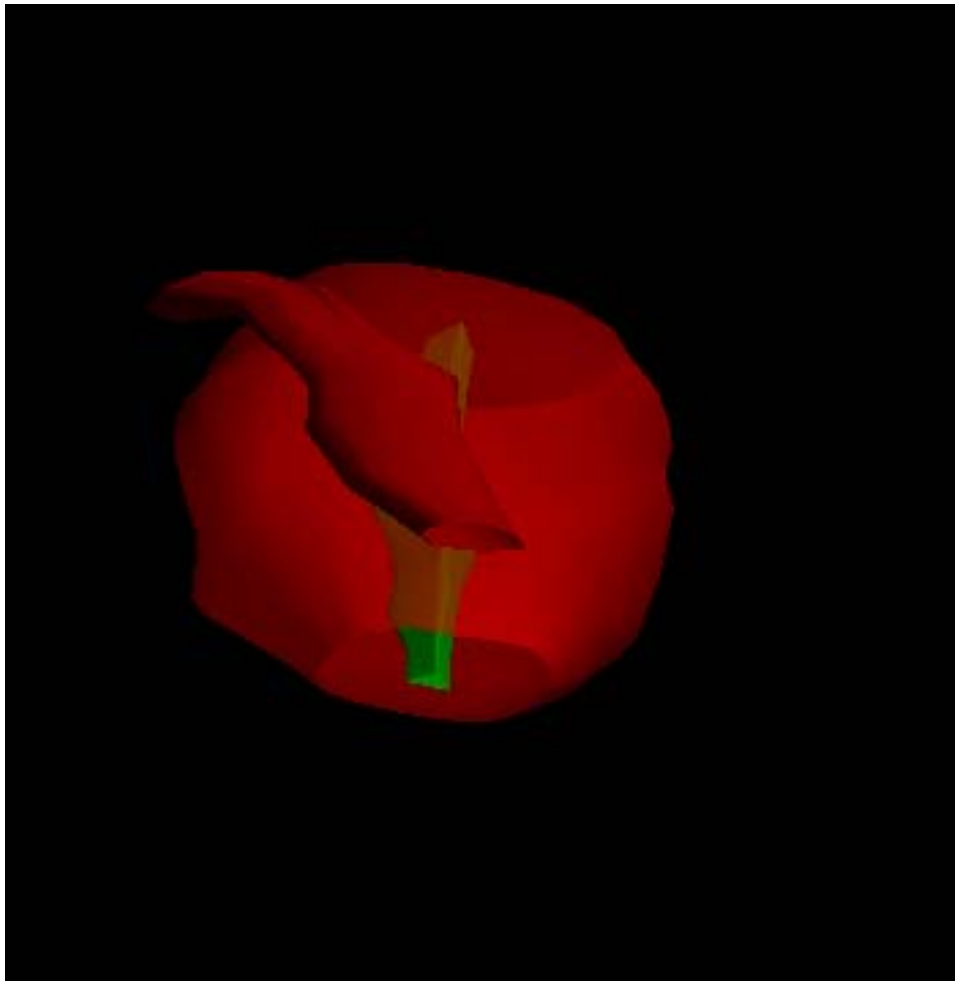

a
B
b
C
c
D
d
e
F
f

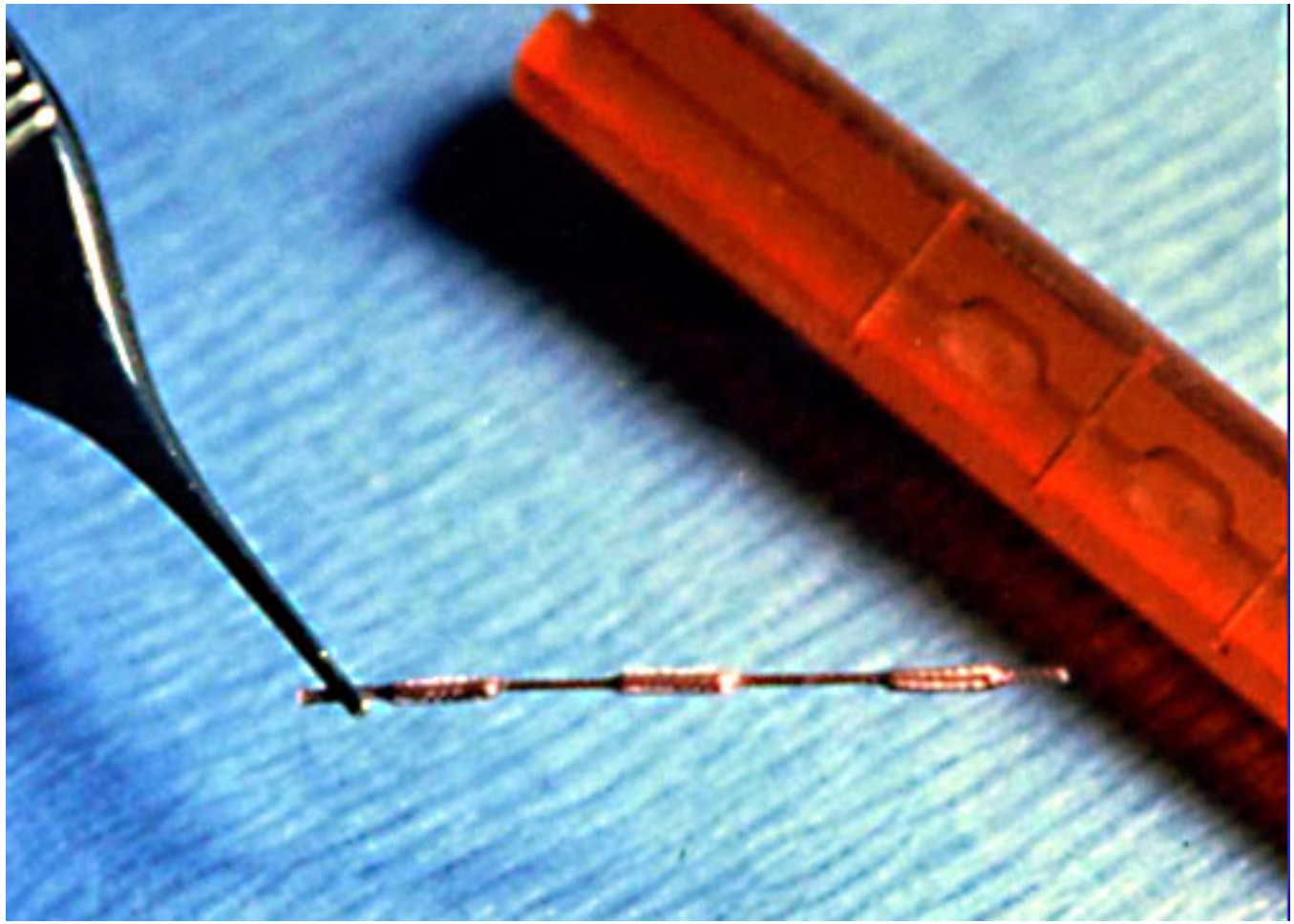
# FAQ #3: Seed "migration"

- Refers to a seed traveling through the blood stream to the lungs
- Occurs in 10-20% of men following brachytherapy using loose seeds (3% if stranded seeds)
- Usually only 1 seed, rarely > 2
- Passing a seed in the urine or in the ejaculate is not considered "migration"


CHEST
Seed migration



Dorsal vein



“Rapid Strand”

# FAQ #4: Radiation Safety

- Iodine 125 has a half life of 2 months
- In the first 2 months half the dose is delivered to your prostate
- In these first 2 months we recommend to keep a 6’ (2 m) distance from babies, pregnant women and small children
- No risk to non-pregnant adults in work or home environment

# Radiation safety

- 44 men given dosimeters for self and household for 6 months following implant
  - Calculated lifetime dose to spouse 0.1 mSv
  - 94% of room monitors showed no exposure *Michalski et al IJROBP 2003*
- Av exposure @ 30,000' is 3-4 μ Sv/hr or 0.05 mSv for 2-way trans-Atlantic flight

# Radiation Safety

- Dose rate measurements @ skin surface and at 30 cm (n=636 pts) indicate that lifetime dose @ 30 cm distance is < 5 mSv limit
- 19 days of direct skin contact required to reach 5 mSv limit *Dauer et al Brachytherapy 2004*

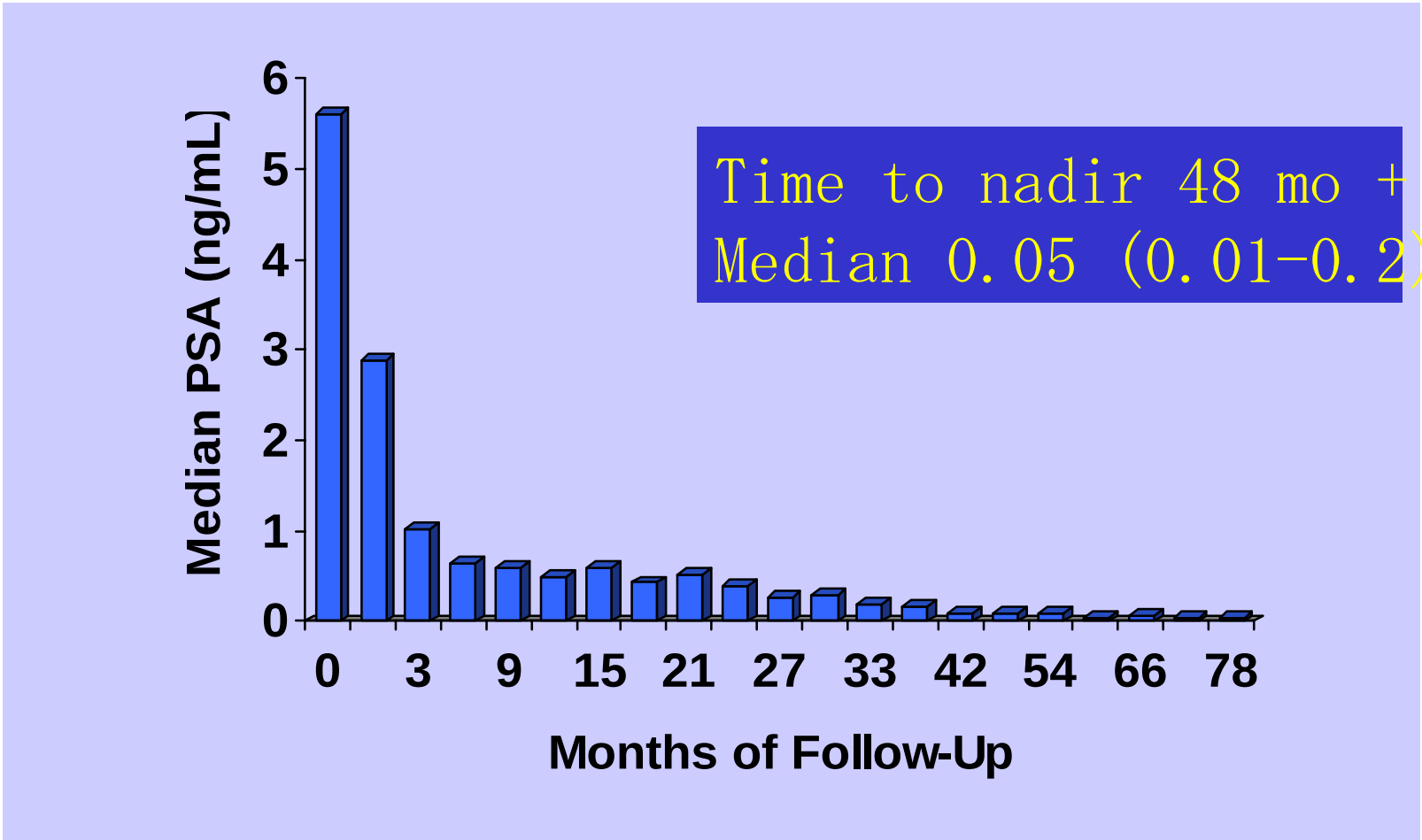
# Recommendations

- Still advise 2m distance from babies, pregnant women and small children for 2 mo
- If frequent contact with toddlers, recommend use of lead-lined “underwear” (available on loan)
- Avoid sleeping in “spoon position” for first 2 months

# FAQ #5: What should my PSA be after brachytherapy?

- Program @ PMH began March 1, 1999
- 985 implants performed
- Median age 65 (45-83)
- 2/3 T1c, 1/3 T2a
- Gleason 6: 92%
- Follow up > 24 months in 724

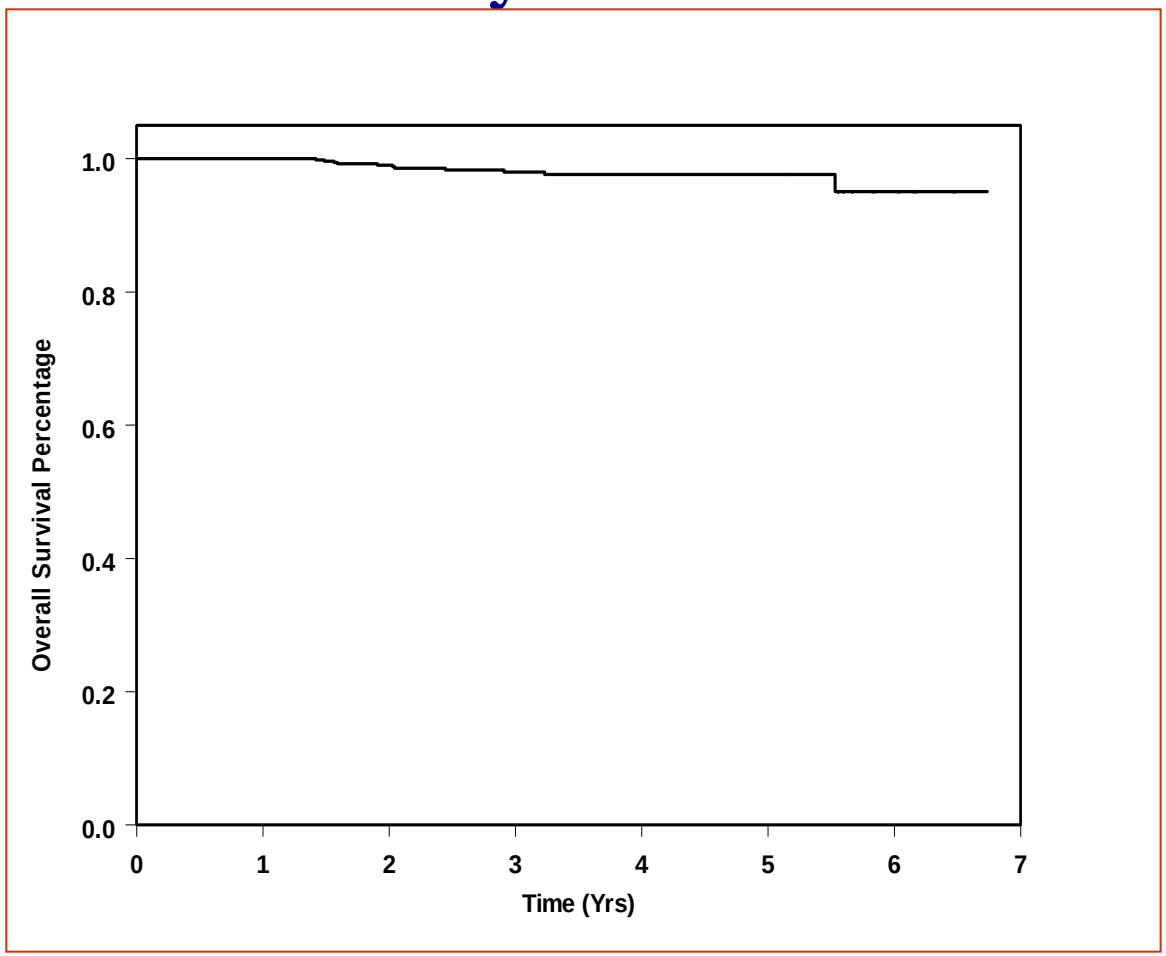
# Median PSA after brachytherapy



# PSA results @ PMH

- Median PSA @ 30 mo: 0.30 ng/ml
  36 mo: 0.18 ng/ml
  48 mo: 0.06 ng/ml
  60 mo: <0.05 ng/ml
- 13 men have had a recurrence:
  4 distant (bone 2, lymph nodes 2)
  5 recurrences in prostate (0.5%)
  4 rising PSA (beyond 36 mo)

# Actuarial DFS: 95.3% @ 5 yrs



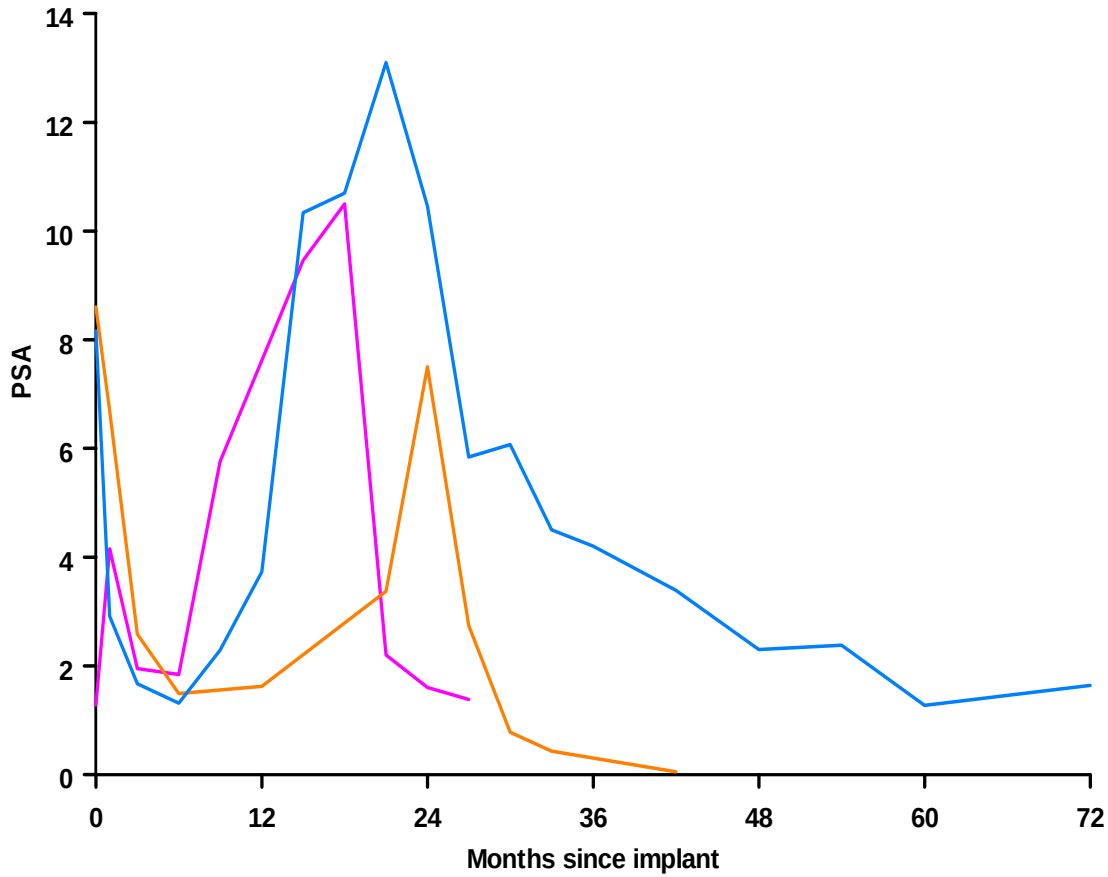
# FAQ #6: What is a PSA bounce?

- 35-40% of men will experience a PSA bounce after brachytherapy
- Consists of 1 or more increases in the PSA reading which then spontaneously decreases again without other treatment or intervention

# PSA bounces

- most start @12-24 mo (6-30)
- Average duration 8 mo
- 15% will ↑ > 2 ng/ml
- 78% resolved by 36 mo
- Tend to occur in younger men who are sexually active
- Double bounces can occur

# 3 sample bounces

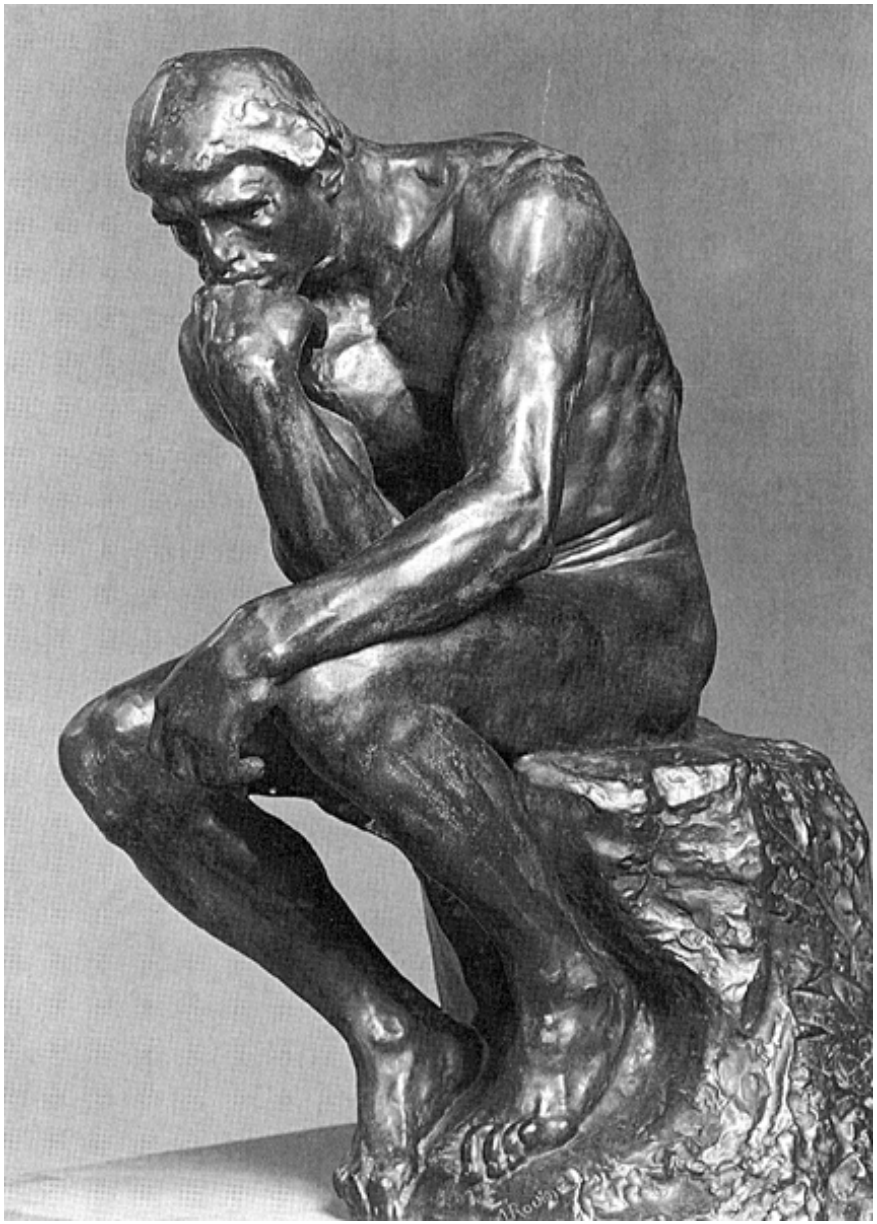


# Permanent seed implants: Conclusions

- Highly effective treatment for early stage prostate cancer
- PSA unreliable in first 3 years
- > 15 years experience demonstrates excellent, durable results
- Proper technique on appropriately selected patients yields very low morbidity

# Permanent seed implants: Conclusions

- More irritative urinary symptoms
- Longer period of uncertainty of outcome b/o PSA bounce etc
- Surgical result quicker in terms of PSA/pathology report



So, who are you going to call?