

# Prostate Cancer

3DCRT vs IMRT :  
the second debate

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# Take home message



- IMRT allows dose escalation.
- Preliminary data shows IMRT technique improves cancer control while keeping acceptable morbidity in prostate cancer pts.

# Case presentation

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- 60 yom
  - Screening PSA 8/01 - 12.2
  - TRUS bx + 1/6 cores Adenoca, gleason 3+3 involving 25% one rt apex cor
  - On 9/25 on presentation @ MDA
  - Frequency q3 hrs, nocturia x1, no incontinence/hematuria
  - No change in bladder/bowel habit/bleeding/bone pain
  - Erectile function 8/10

# Case presentation

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- Has h/o vasectomy, no TURP/colonoscopy
- No family h/o prostate cancer
- On physical exam
  - No LN/organomegaly/bony tenderness
  - Rectal exam
    - >Normal rectal tone, somewhat enlarged prostate, smooth without nodularity
- Lab
  - Repeat PSA on 10/01 - 13.1

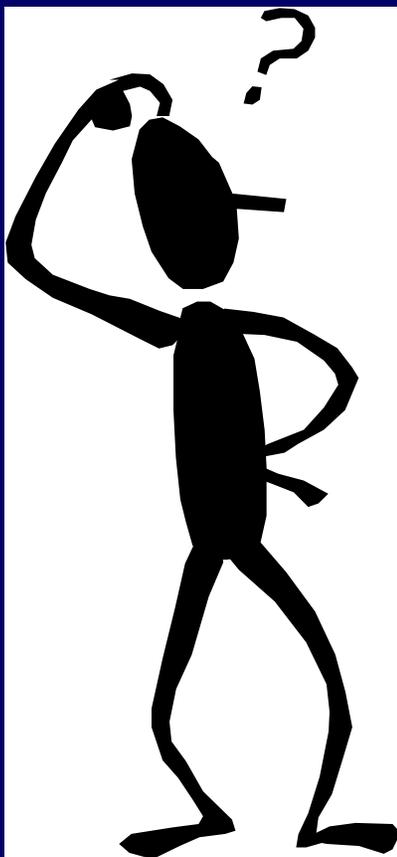
# Case presentation

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- Dx – 60 yom with organ confined CAP T1c stage II, PSA – 13.1, gl 3+3 involving 1/6 cores.

# Questions

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- Prognosis of this intermediate risk group pt.
- Management of this pt.
- Dose escalation with IMRT for this pt.

# Hanks 1984/ASTRO

- Pattern of care study outcome of 574 pts.
- Rslts:

|                | <b>clinical LR @ 4 yrs</b> |           |           |           |  |
|----------------|----------------------------|-----------|-----------|-----------|--|
| <b>Dose</b>    | <b>T1</b>                  | <b>T2</b> | <b>T3</b> | <b>T4</b> |  |
| <b>(Gy)</b>    | (%)                        | (%)       | (%)       | (%)       |  |
| <b>&lt; 55</b> | 10                         | 40        | 38        | 36        |  |
| <b>55-60</b>   | 8                          | 18        | 36        | 10        |  |
| <b>60-65</b>   | 7                          | 12        | 21        | 29        |  |
| <b>65-70</b>   | 6                          | 12        | 11        | 38        |  |
| <b>&gt; 70</b> | 5                          | 10        | 10        | 13        |  |

# Kuban et al 1992

- Post RT 96/309 CAP pts for randomly needle bx.
- Rslts: @ 10 yrs

|             | <b>LF (%)</b> | <b>DFS (%)</b> | <b>DM (%)</b> |
|-------------|---------------|----------------|---------------|
| <b>bx +</b> | 75            | 19             | 71            |
| <b>bx -</b> | 24            | 62             | 35            |
| <b>p</b>    | 0.0001        | 0.0001         | 0.015         |

- Cncl:
- + rebiopsy correlates with LF
- clinical LF is high risk for DM.

# To summarize

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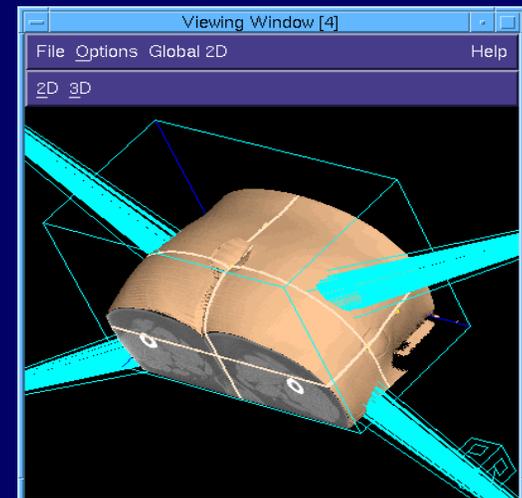
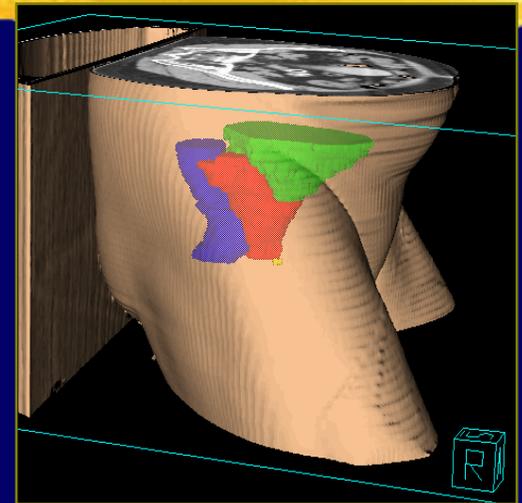
- Failure to achieve LC is followed by subsequent higher DM.

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- Cancer of prostate has a dose response and can be optimized with dose escalation.

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# 3D CRT

- Dose escalation tool is 3D CRT.
- CPT Code 77295
- 3D, computer-generated reconstruction of tumor volume and surrounding critical normal structures from direct CT/MRI data in preparation for noncoplanar/coplanar RT therapy.



# Pollack et al 2002/3DCRT

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- 304 pts with CAP T1-3Nx/N0 randomized to  
> RT dose 70 Gy vs 78 Gy.
- Median pretreatment PSA was 7.8 ng/ml, failure was defined as ASTRO consensus panel.
- RT given initially 4 flds to 46 Gy then 6 flds 3D CRT to boost, dose specified to isocenter. CTV = P+SV with 0.75-1.5 cm margin to block edge.
- No pts received neoad/adj androgen ablation
- Primary end point FFF, secondary end point DM, OS.

# Pollack et al 2002/3DCRT

- FFF/OS results at 6 yrs

| <b>Doses</b>   | <b>PSA</b>  | <b>PSA</b>     | <b>FFF</b> | <b>OS</b>  |
|----------------|-------------|----------------|------------|------------|
|                | <b>≤ 10</b> | <b>&gt; 10</b> | <b>all</b> | <b>all</b> |
|                | (%)         | (%)            | (%)        | (%)        |
| <b>70 Gy</b>   | 75          | 43             | 64         | 83         |
| <b>78 Gy</b>   | 75          | 62             | 70         | 90         |
| <b>p value</b> | ns          | 0.01           | 0.03       | 0.67       |

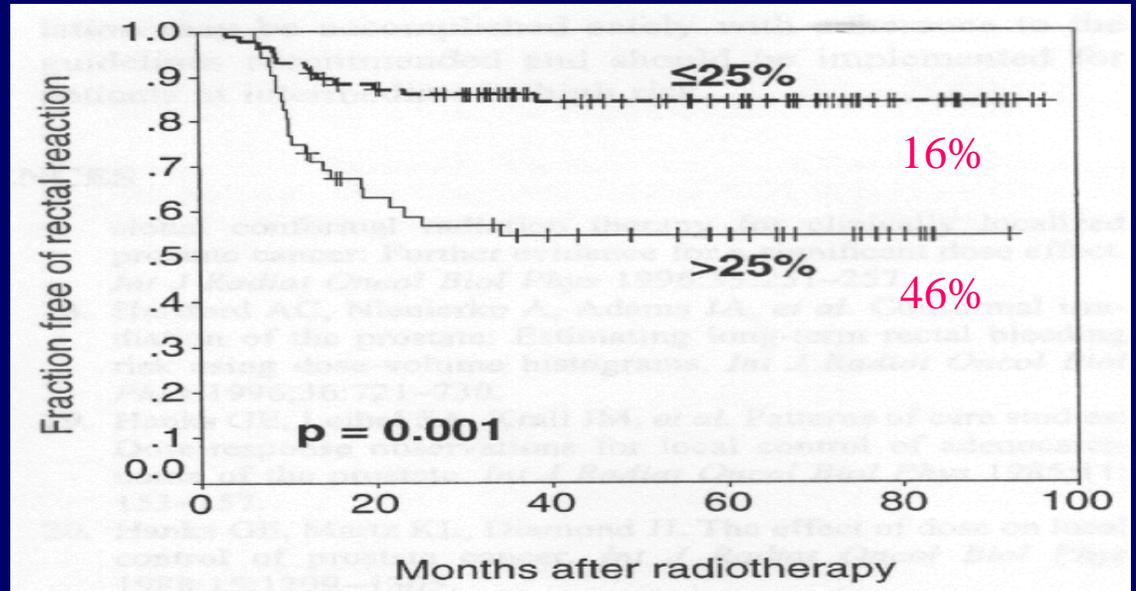
# Pollack et al 2002/3DCRT

- Late toxicity results at 6 yrs

| <b>Doses</b>   | <b>Rectal</b>                     | <b>Bladder</b>                    |
|----------------|-----------------------------------|-----------------------------------|
|                | <b>gr <math>\geq</math> 2 (%)</b> | <b>gr <math>\geq</math> 2 (%)</b> |
| <b>70 Gy</b>   | 12                                | 10                                |
| <b>78 Gy</b>   | 26                                | 10                                |
| <b>p value</b> | 0.001                             | ns                                |

# Pollack et al 2002/3DCRT

- Gr 2 or higher late rectal complications



- Conclusion
  - Dose escalation 8 Gy improved FFF for pts with PSA > 10.
  - However, higher dose increased rectal toxicity.

# Teh et al., 1999

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- IMRT is a new technology in RT that delivers radiation precisely to the tumor while relatively sparing the surrounding normal tissues.
- Combines two advance concepts to deliver 3D conformal radiation
  - inverse treatment planning with computer optimization
  - computer controlled intensity modulation of the radiation beam
- Potential advantages
  - to create multiple targets
  - multiple critical avoidance
  - new accelerated fractionation scheme
- Has potential in radiation oncology in the the 21st century
  - Can be used to spare rectum/bladder in prostate cancer pts

# Zelefsky et al 2002/IMRT

- 1996-2001, 772 pts with clinically localized CAP txed IMRT.
- T1c - 46%, T2a - 26%, T2b - 17%, T3 - 11%.
- T1-2, PSA  $\leq 10$ , gl  $\leq 6$ 
  - favorable - 3 present
  - intermediate - 2 present
  - unfavorable - 0-1 present
- RTOG scale to grade toxicity.
- PTV = CTV+0.5-1.0 cm, CTV = P+SV+0.6-1.0 cm margin  
Isocentric 5 flds, inverse plan, 15 MV, min dose to PTV.

# Zelefsky et al 2002/IMRT

**Table 1.** Clinical Goals for 81 and 86.4 Gy Prostate IMRT Treatment Plans at MSKCC

| <i>Structure</i>       | <i>81 Gy Plan</i>  | <i>86.4 Gy Plan</i>   |
|------------------------|--|---|
| Planning target volume | Maximum dose $\leq 90$ Gy<br>$\geq 90\%$ of PTV must receive $\geq 77$ Gy                | Maximum dose $\leq 96$ Gy<br>$\geq 85\%$ of CTV must receive $\geq 86.4$ Gy |
| Rectal wall            | No more than 30% can receive $\geq 75.6$ Gy<br>No more than 53% can receive $\geq 47$ Gy | Same as 81 Gy plan<br>Same as 81 Gy plan                                    |
| Bladder wall           | No more than 53% can receive $\geq 47$ Gy  | Same as 81 Gy plan  |

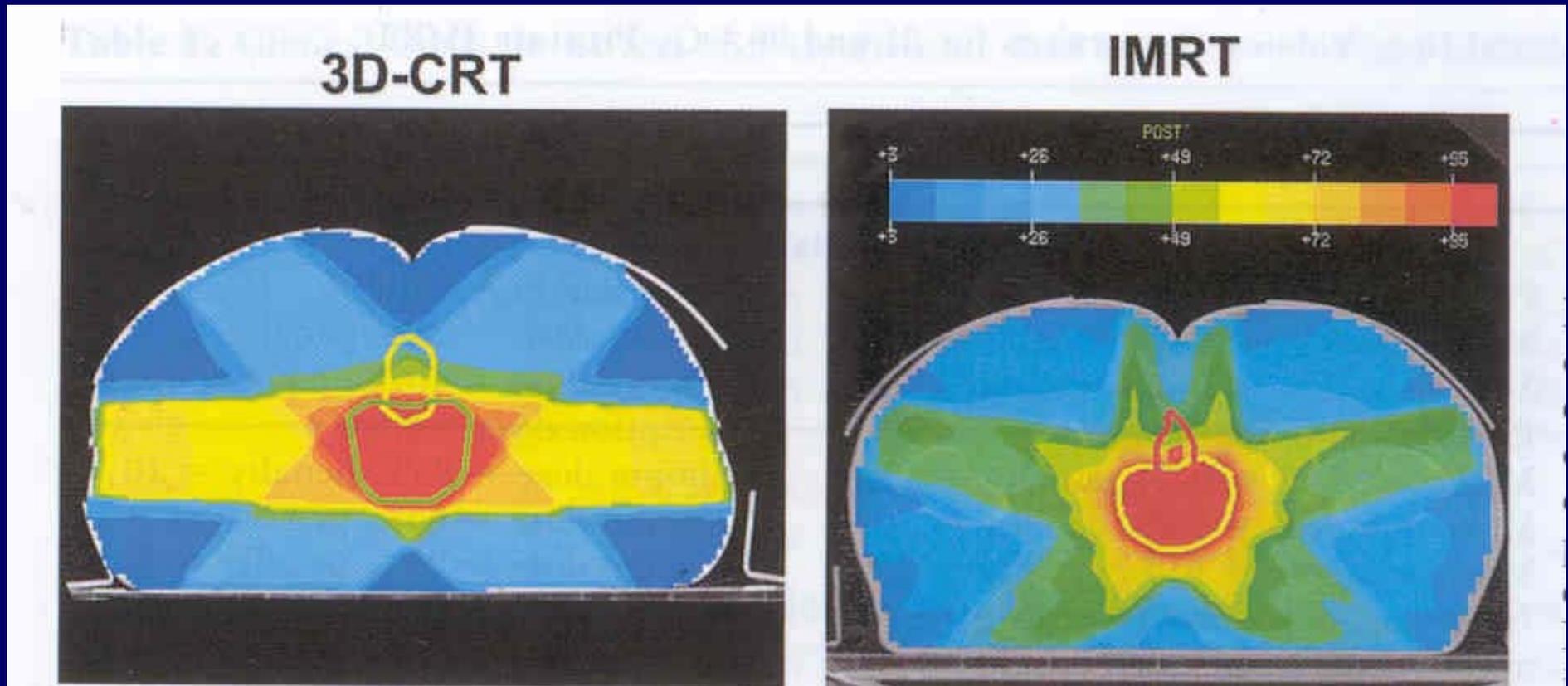
# Zelefsky et al 2002/IMRT

**Table 2.** Optimization Dose and Dose-Volume Constraints for 81 and 86.4 Gy Prostate IMRT Treatment Plans

| <i>Structure</i>     | <i>81 Gy Plan</i>   | <i>86.4 Gy Plan</i>   |
|----------------------|---|---|
|                      | Dose Constraints and Penalties  |   |
| PTV – rectum overlap | Prescription dose = 100%<br>Minimum dose = 98%, penalty = 50<br>Maximum dose = 102%, penalty = 50     | Prescription dose = 100%<br>Minimum dose = 98%, penalty = 50<br>Maximum dose = 102%, penalty = 50     |
| PTV + rectum overlap | Prescription dose = 95%<br>Minimum dose = 93%, penalty = 10<br>Maximum dose = 96%, penalty = 20       | Prescription dose = 84%<br>Minimum dose = 83%, penalty = 10<br>Maximum dose = 85%, penalty = 20       |
| Rectal wall          | Maximum dose = 95%, penalty = 20<br>70% of rectal volume receives <40%<br>maximum dose, penalty = 20  | Maximum dose = 85%, penalty = 20<br>70% of rectal volume receives <30%<br>maximum dose, penalty = 20  |
| Bladder wall         | Maximum dose = 98%, penalty = 35<br>70% of bladder volume receives <40%<br>maximum dose, penalty = 20 | Maximum dose = 88%, penalty = 35<br>70% of bladder volume receives <34%<br>maximum dose, penalty = 20 |

Abbreviation: PTV, planning target volume.

# Zelevsky et al 2002/IMRT



# Zelevsky et al 2002/IMRT

- Results: actuarial PSA free survival
- Median f/u 24 m (6 - 60 m)

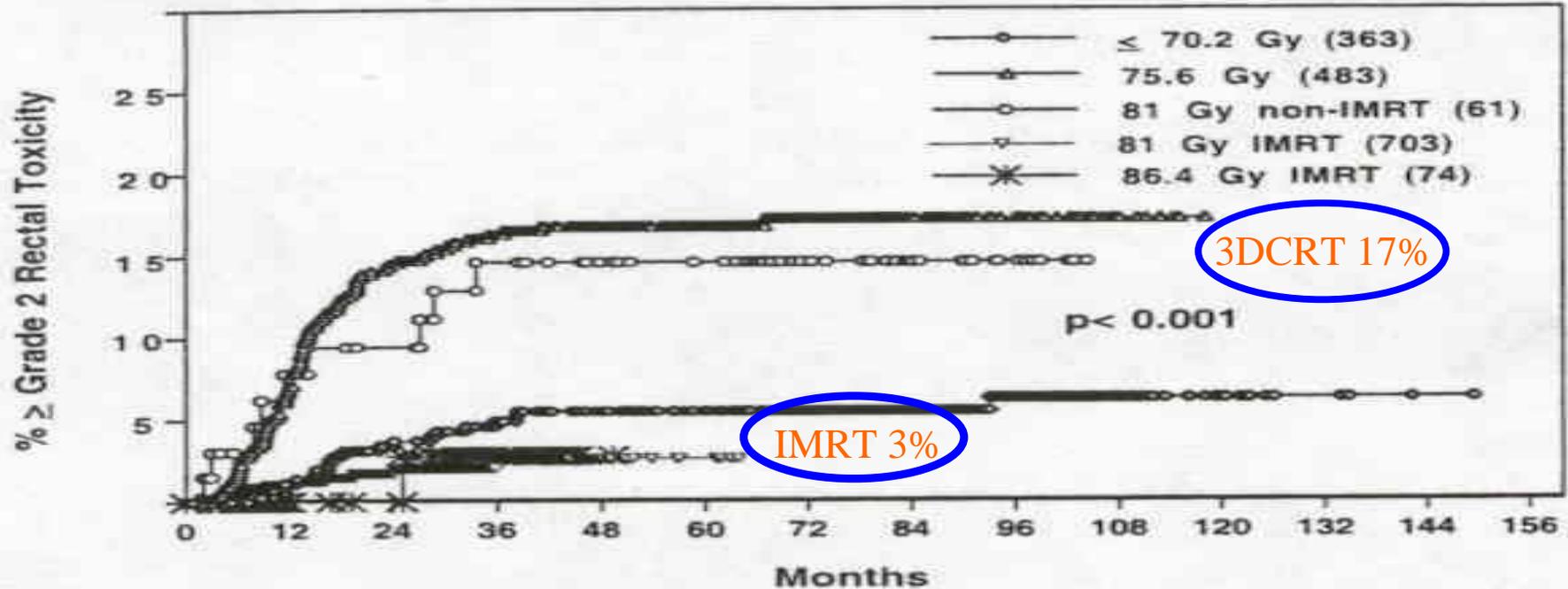
| <b>Risk</b>  | <b>3D CRT</b> | <b>3DCRT</b> | <b>IMRT</b>         |
|--------------|---------------|--------------|---------------------|
| <b>group</b> | 64.8-70.2 Gy  | 75.6-86.4 Gy | <b>81- 86.4 Gy</b>  |
|              | at 5 yrs (%)  | at 5 yrs (%) | <b>at 3 yrs (%)</b> |
| <b>fav</b>   | 77            | 90           | <b>92</b>           |
| <b>int</b>   | 50            | 70           | <b>86</b>           |
| <b>unfav</b> | 21            | 47           | <b>81</b>           |

# Zelevsky et al 2002/IMRT

- Results: acute and late toxicity
- Median f/u 24 m (6 - 60 m)

| <b>Tox</b>   | <b>acute</b>  | <b>late</b>   | <b>acute</b>  | <b>late</b>   |
|--------------|---------------|---------------|---------------|---------------|
| <b>grade</b> | <b>GI (%)</b> | <b>GI (%)</b> | <b>GU (%)</b> | <b>GU (%)</b> |
| <b>0</b>     | 74            | 89            | 33            | 74            |
| <b>1</b>     | 22            | 9             | 38            | 16            |
| <b>2</b>     | 4             | 1.5           | 28            | 9.5           |
| <b>3</b>     | 0             | 0.5           | 1             | 0.5           |

# Zelevsky et al 2002/IMRT



**Figure 2.** Actuarial incidence of grade 2 and higher late rectal toxicity according to dose and mode of treatment delivery.

# Zelevsky et al 2002/IMRT

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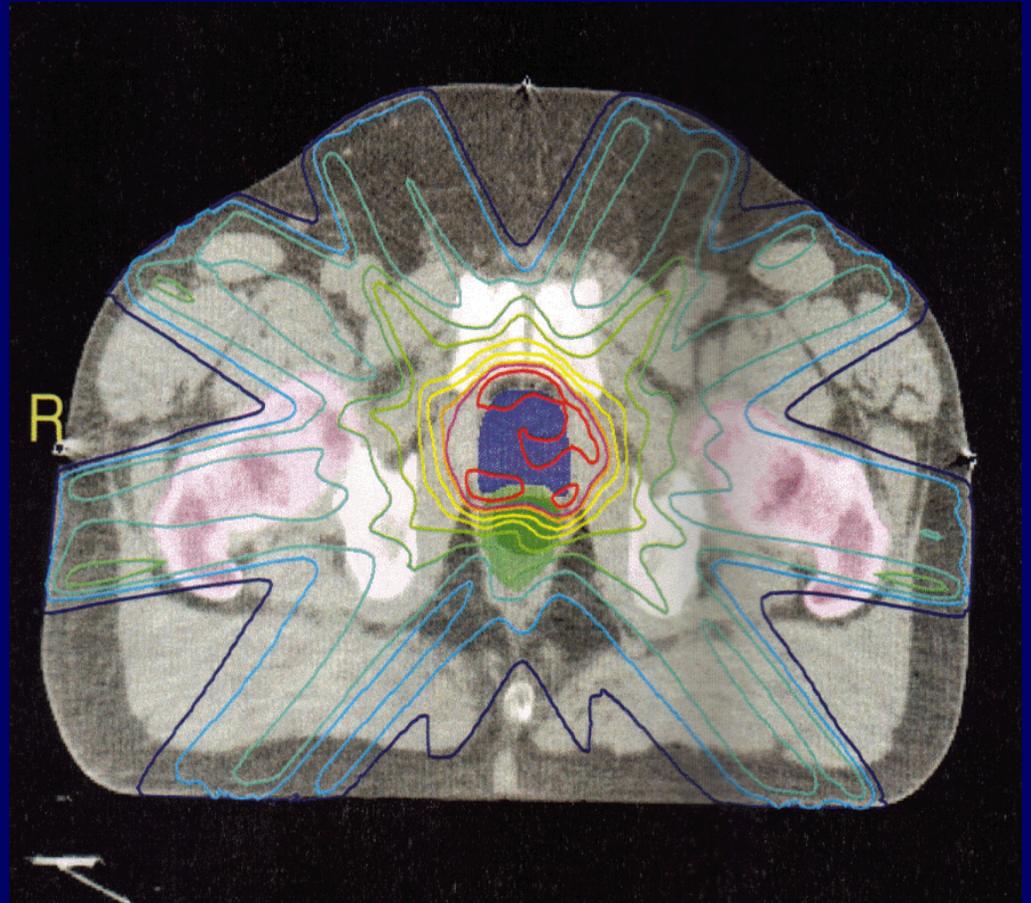
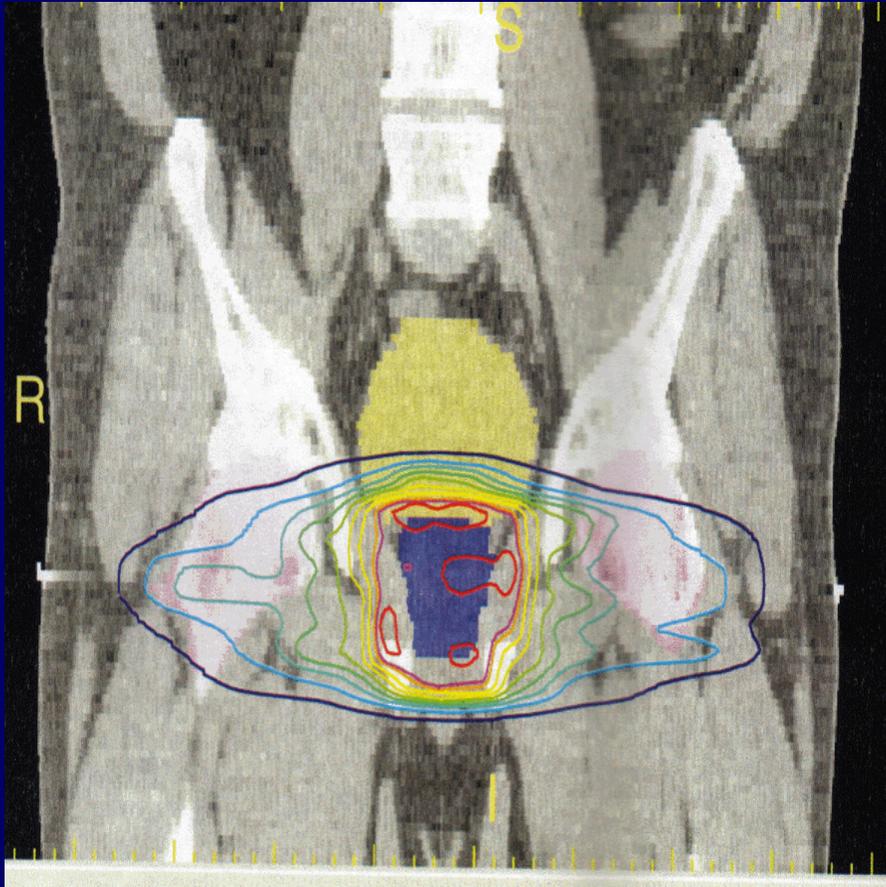
- Conclusion:
- Short term bFS of pts treated with IMRT is comparable with 3D CRT at similar dose level.
- IMRT reduced acute and late rectal toxicity significantly compared with 3D CRT.
- Report confirms the safety of high dose IMRT in a large number of CAP pts.

# Conclusions/f/u on our pt

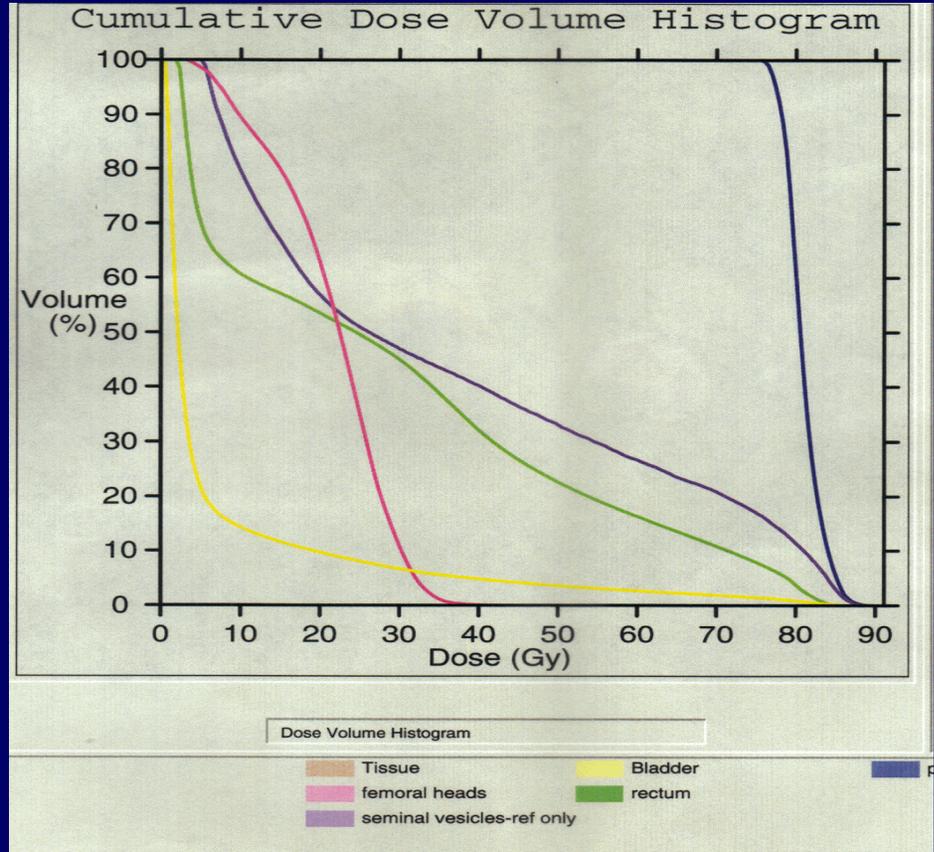
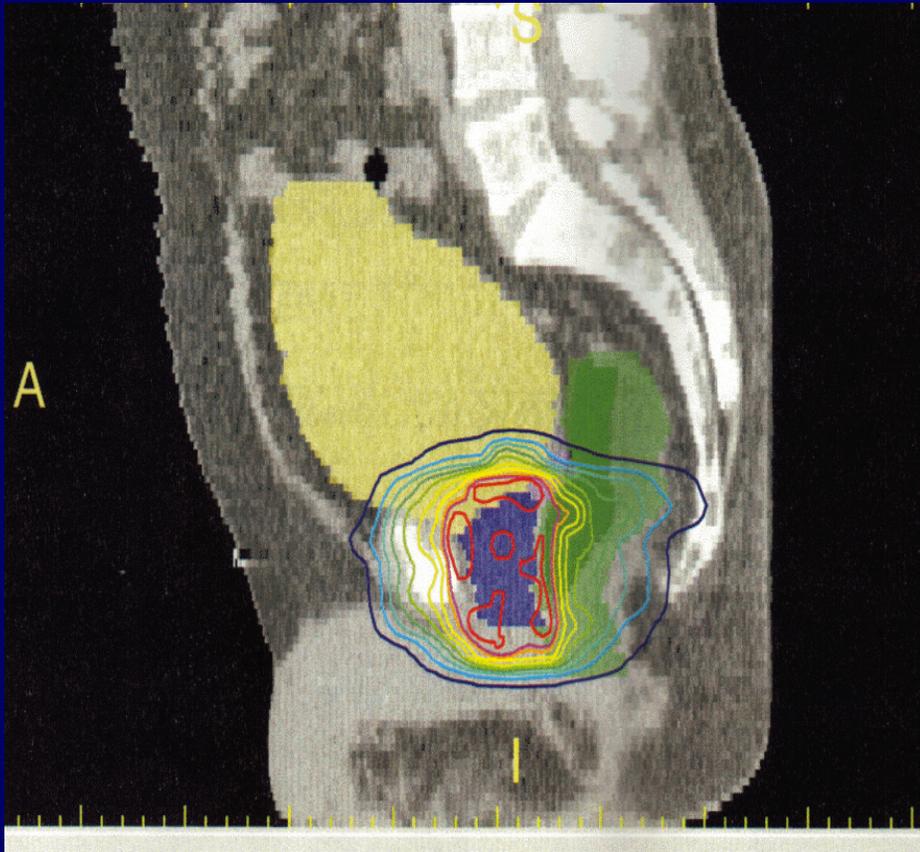
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- After discussing various treatment options
  - RP, EBRT, Implant
- The pt chose EBRT as his definitive local therapy.
  - Pt supine, bladder full, rectum empty, Vac-U-Lok cradel
  - Eight IMRT field technique using 6 MV photon was used.
  - PTV = CTV+1 cm ant/rt/lr lat/inf, 0.5 cm post, 0.75 cm sup, CTV = GTV.
  - He received 75.6 Gy/1.8 Gy via IMRT to P+SV, to isoline encompassing PTV.
  - Critical structures
    - femoral head < 50 % to > 45 Gy
    - bladder < 25 % to > 70 Gy
    - rectum < 25 % to > 70 Gy
  - Received short course of HTx.

# Conclusions/f/u on our pt



# Conclusions/f/u on our pt



## Conclusions/f/u on our pt

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- The pt completed his EBRT on 1/02.
- Last f/u on 4/02
  - Doing well, frequency q4 hrs, nocturia x 2, no hematuria/incontinence/diarrhea/blood.
  - PSA 0.8, DRE – WNL
- Repeat PSA in 3 m, repeat PSA/PE in 6 m.

# Conclusions

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- MDA 3D CRT dose escalation randomized study benefited pts with PSA > 10 ng/ml.
- MSKCC IMRT dose escalation study benefited all subset of prostate cancer pts.



# Conclusions

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- Both MDA/MSKCC studies reduced toxicity with 3DCRT/IMRT technique.
- IMRT reduced GI toxicity more than 3DCRT.



# Conclusions

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- Dose escalation improves bFS in prostate cancer pts.
- IMRT is a superior dose escalation tool.