Disclosures

Proton Therapy Center

Proton Therapy Dose Deposition

FIGURE 1

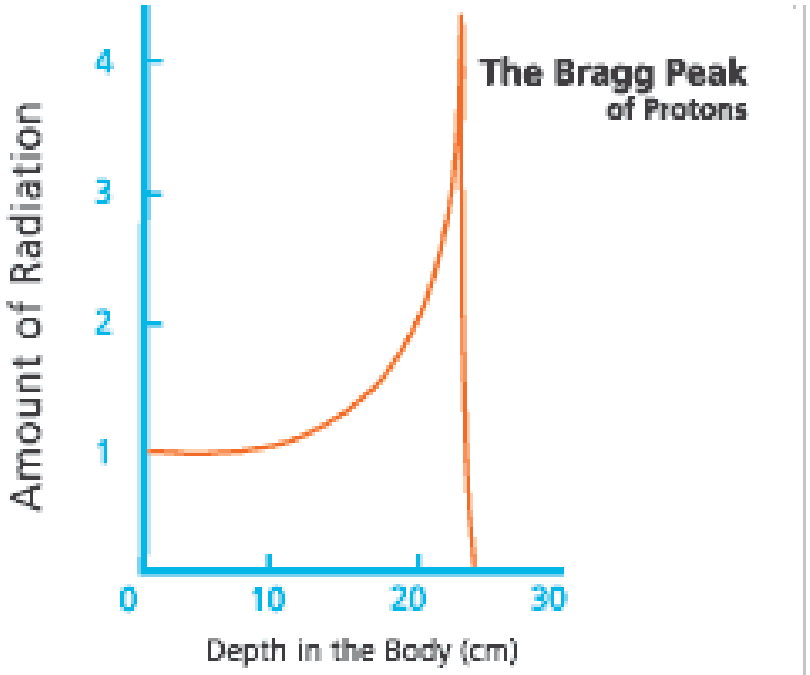
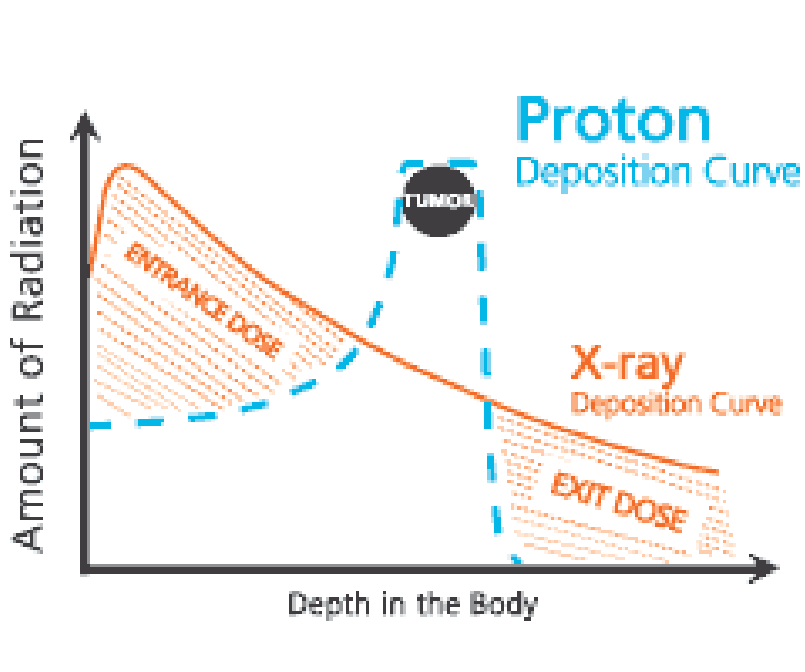
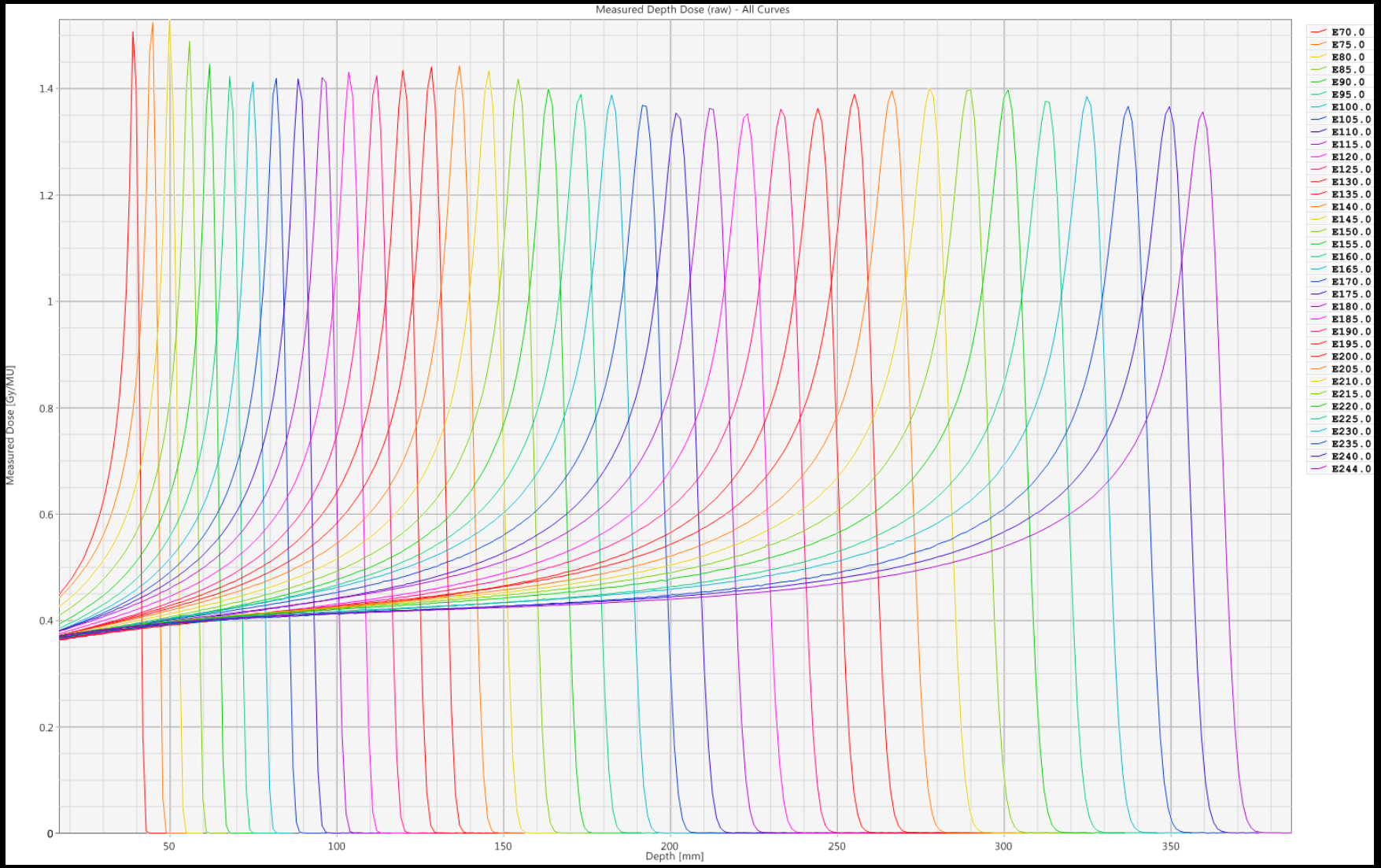
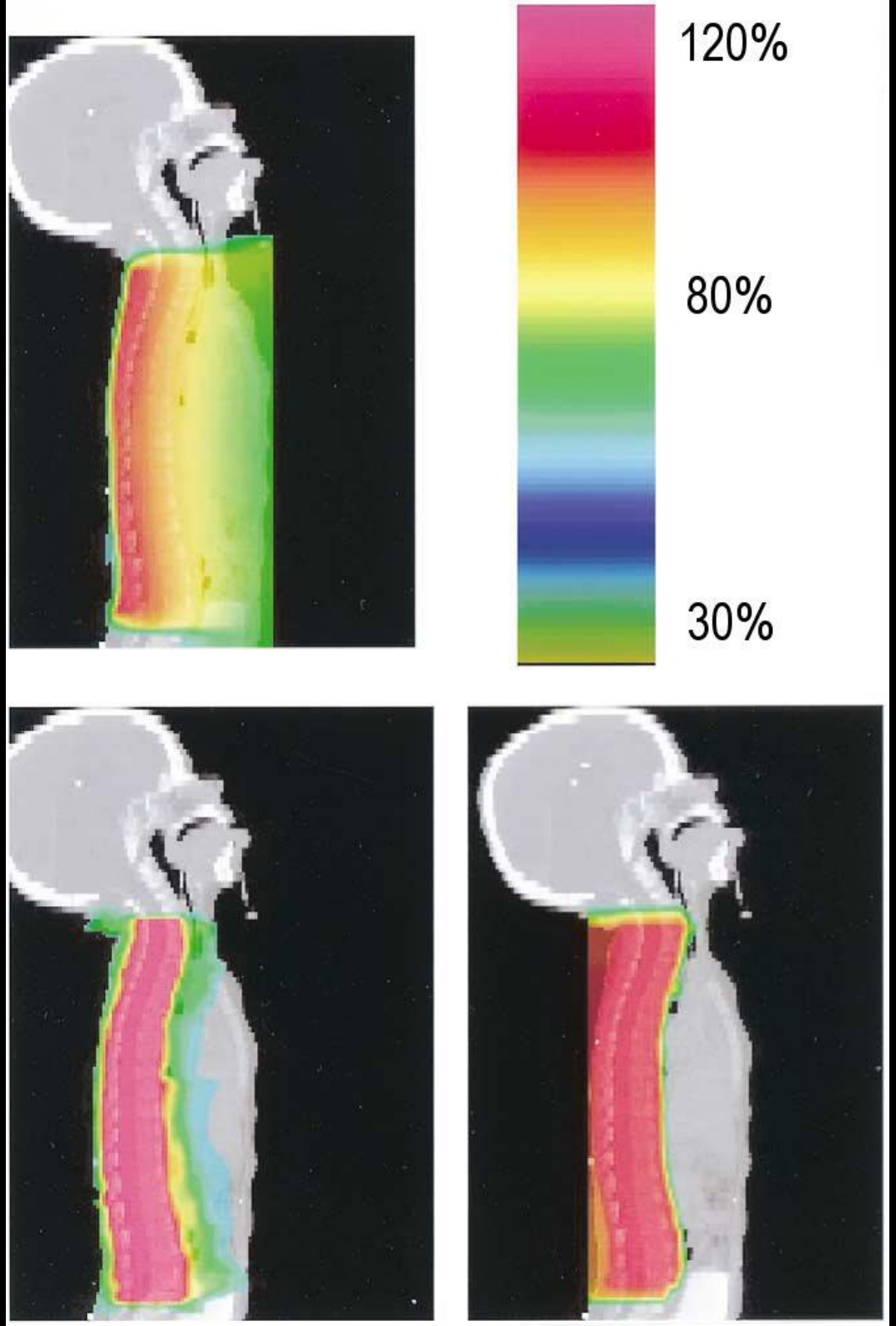


FIGURE 2

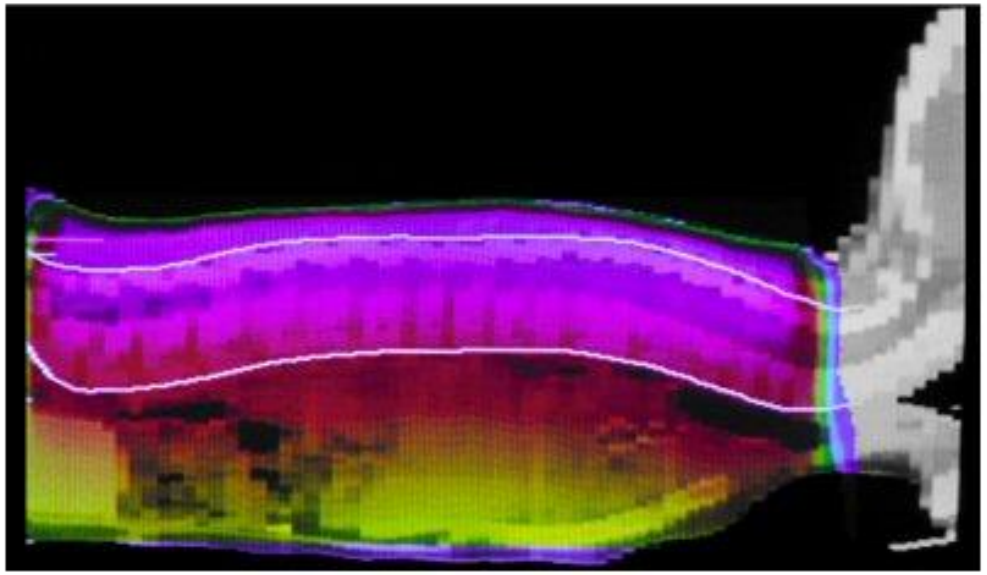


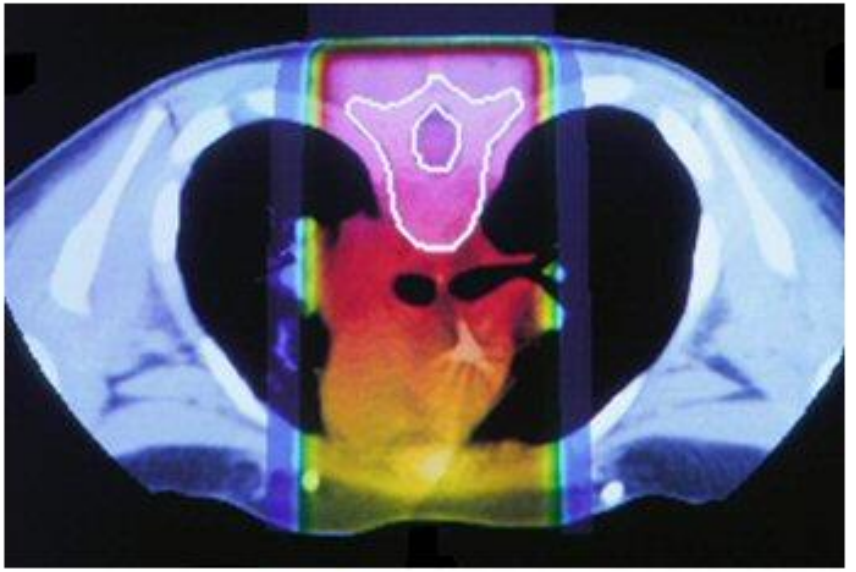
Clinical Bragg Peaks

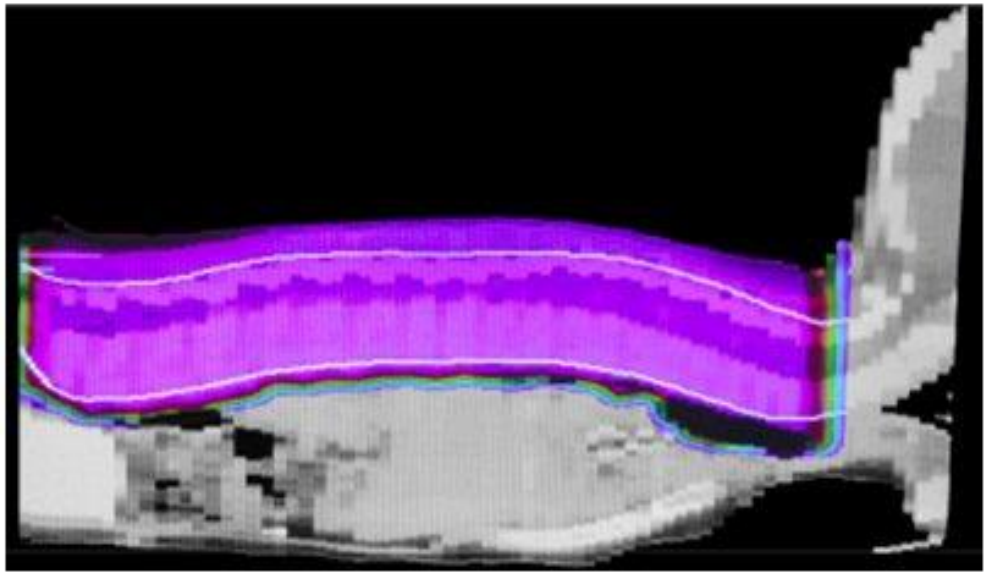


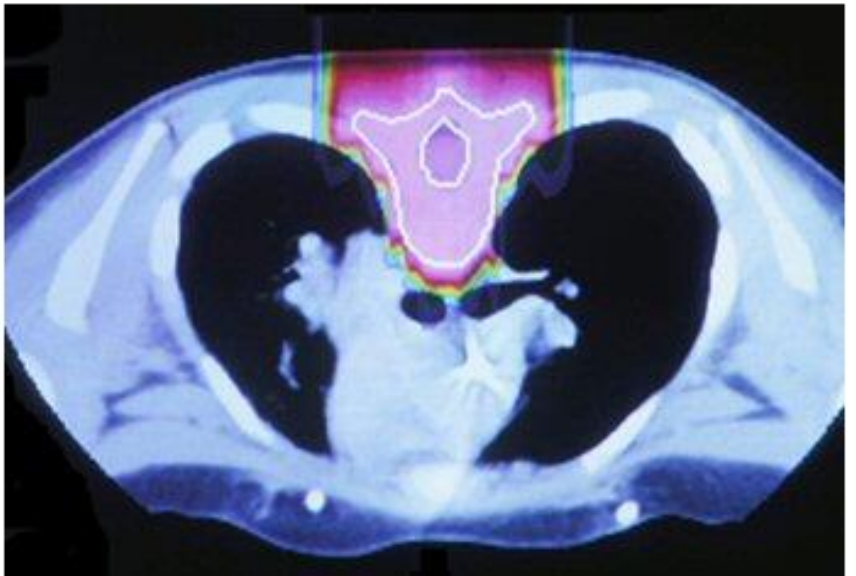

120%
80%
30%

Medulloblastoma Treatment: Photons vs. Protons

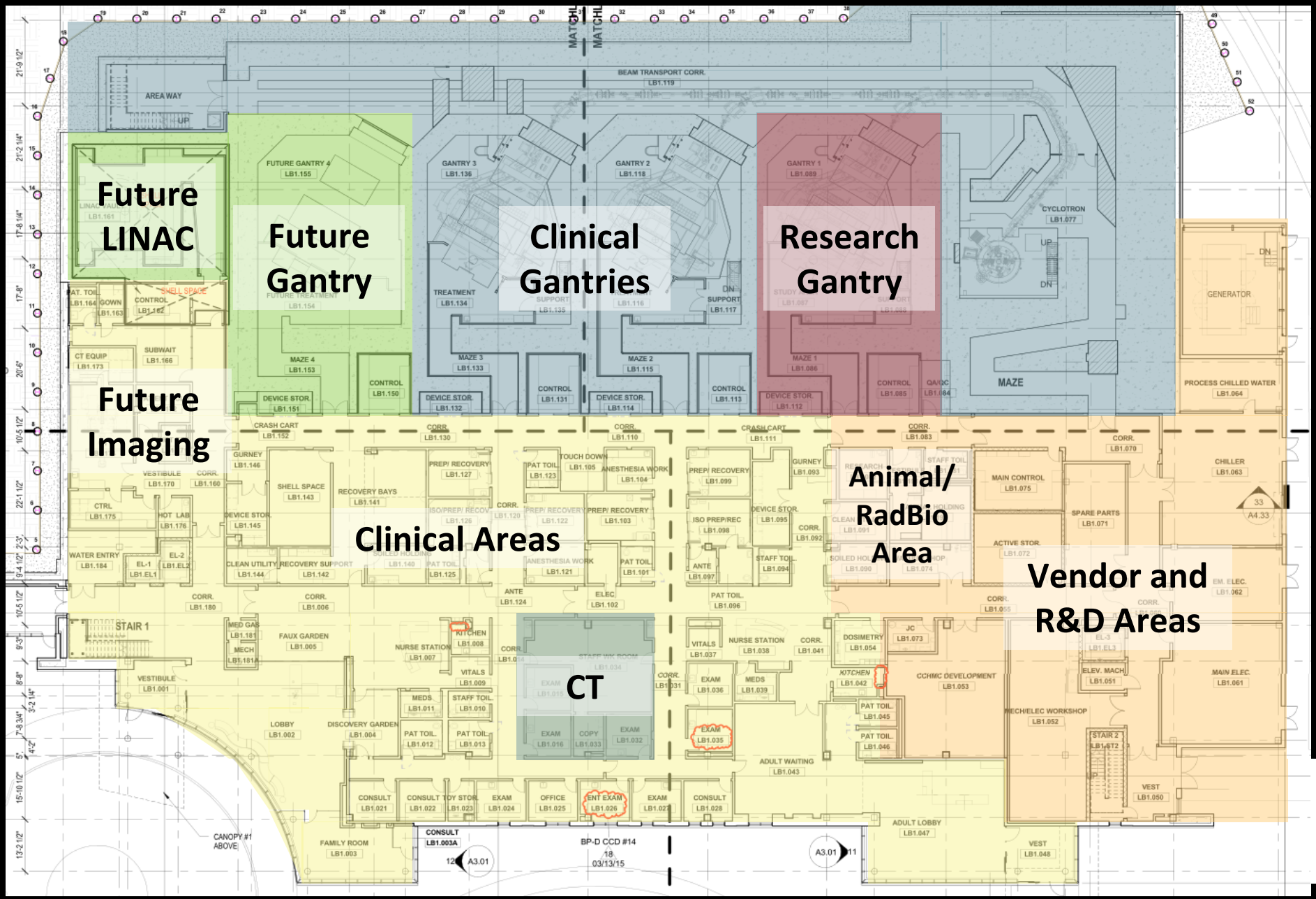


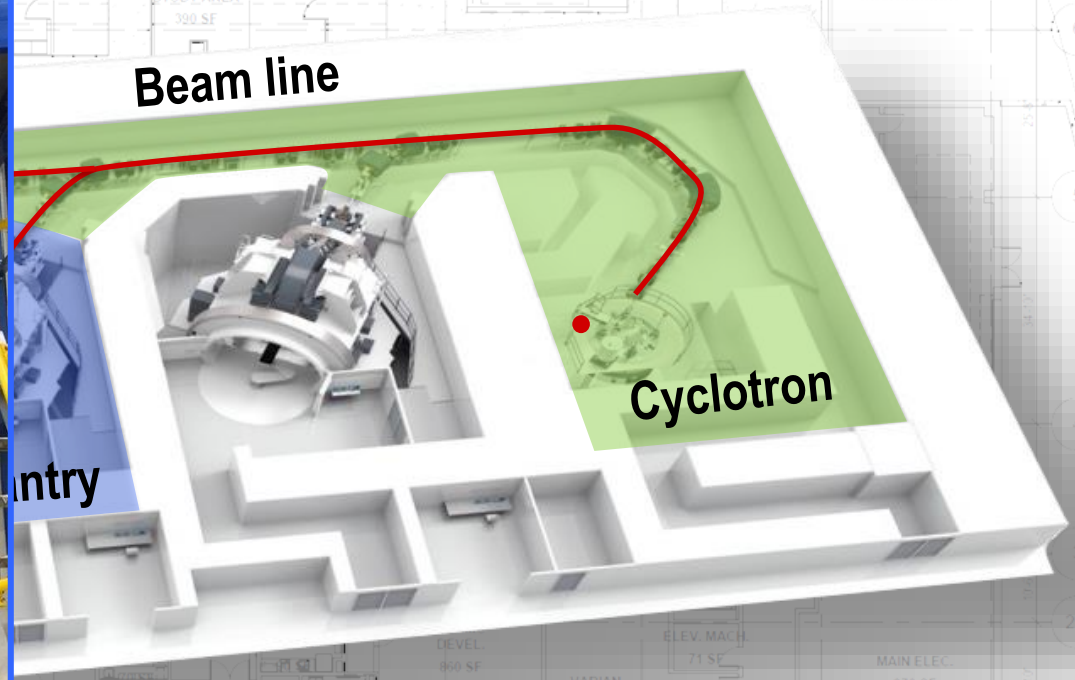


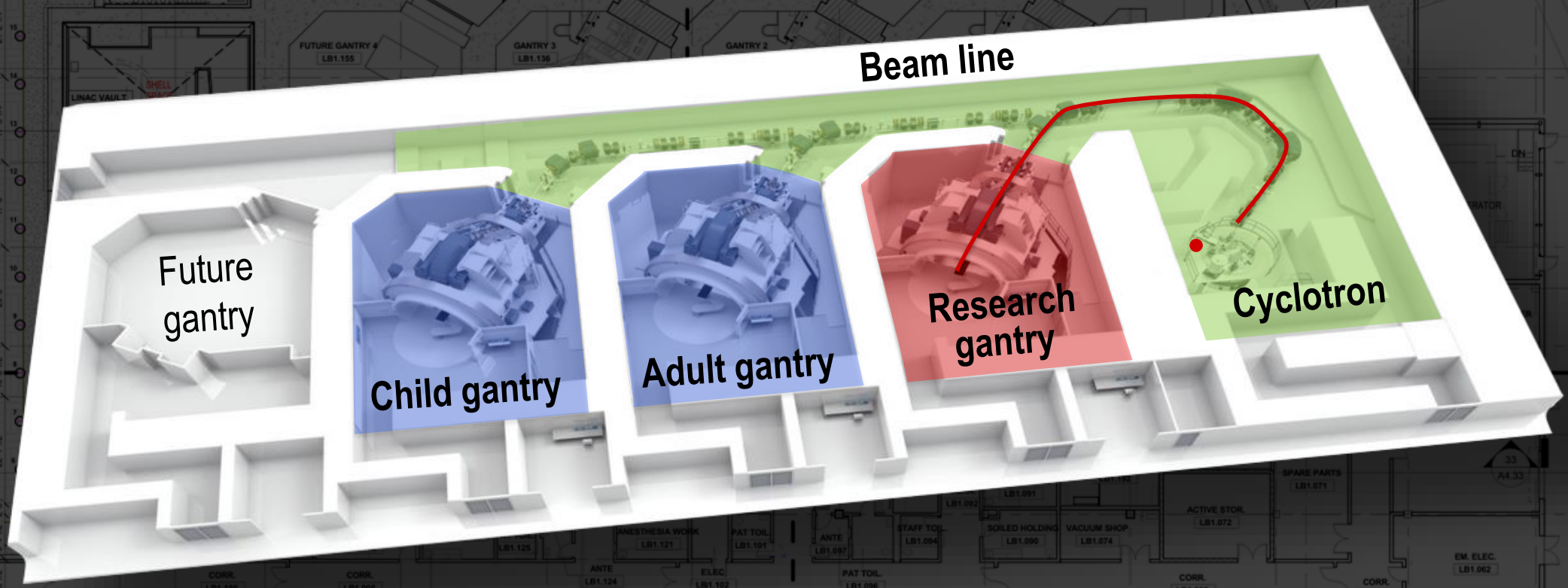




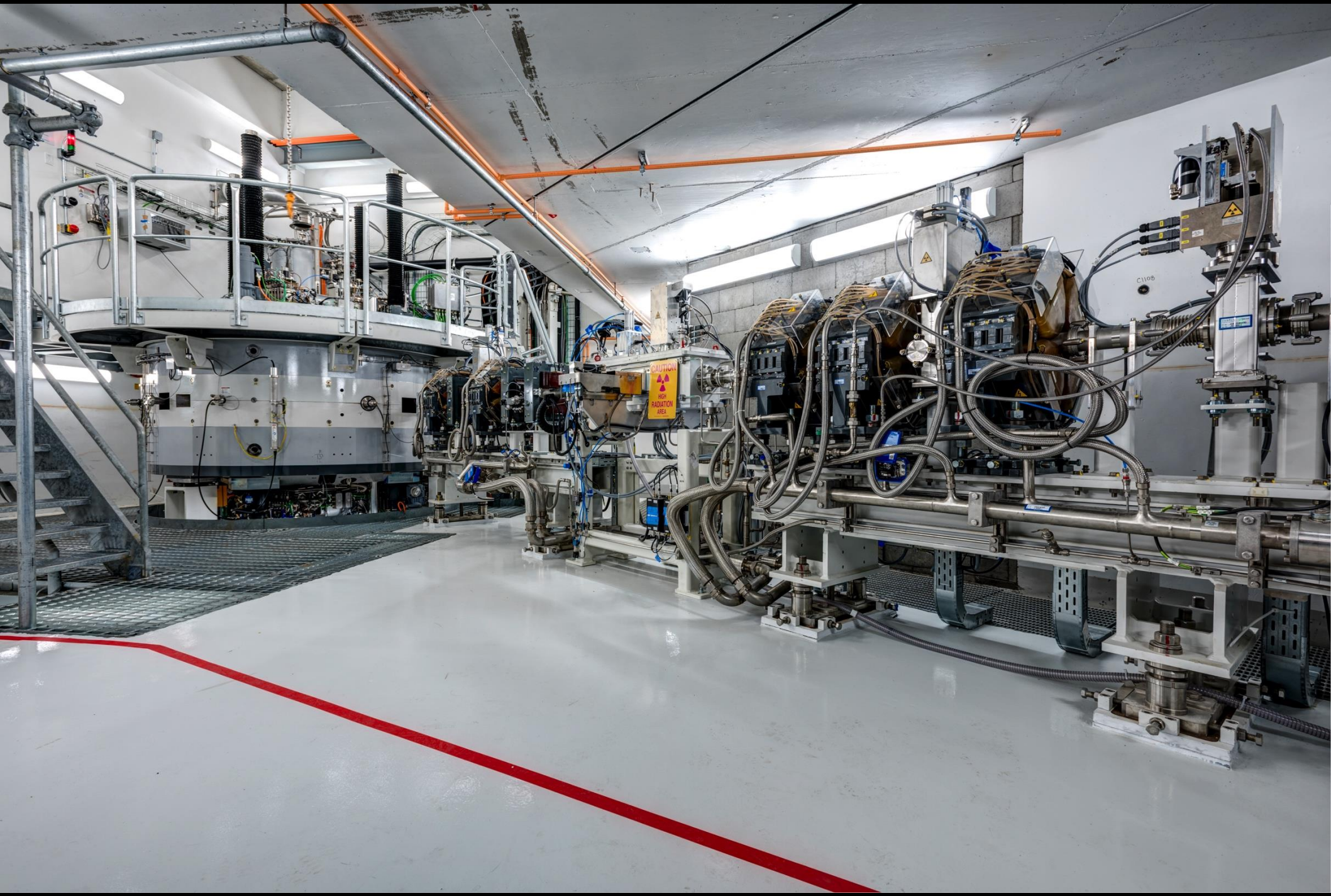
The Proton Therapy Center

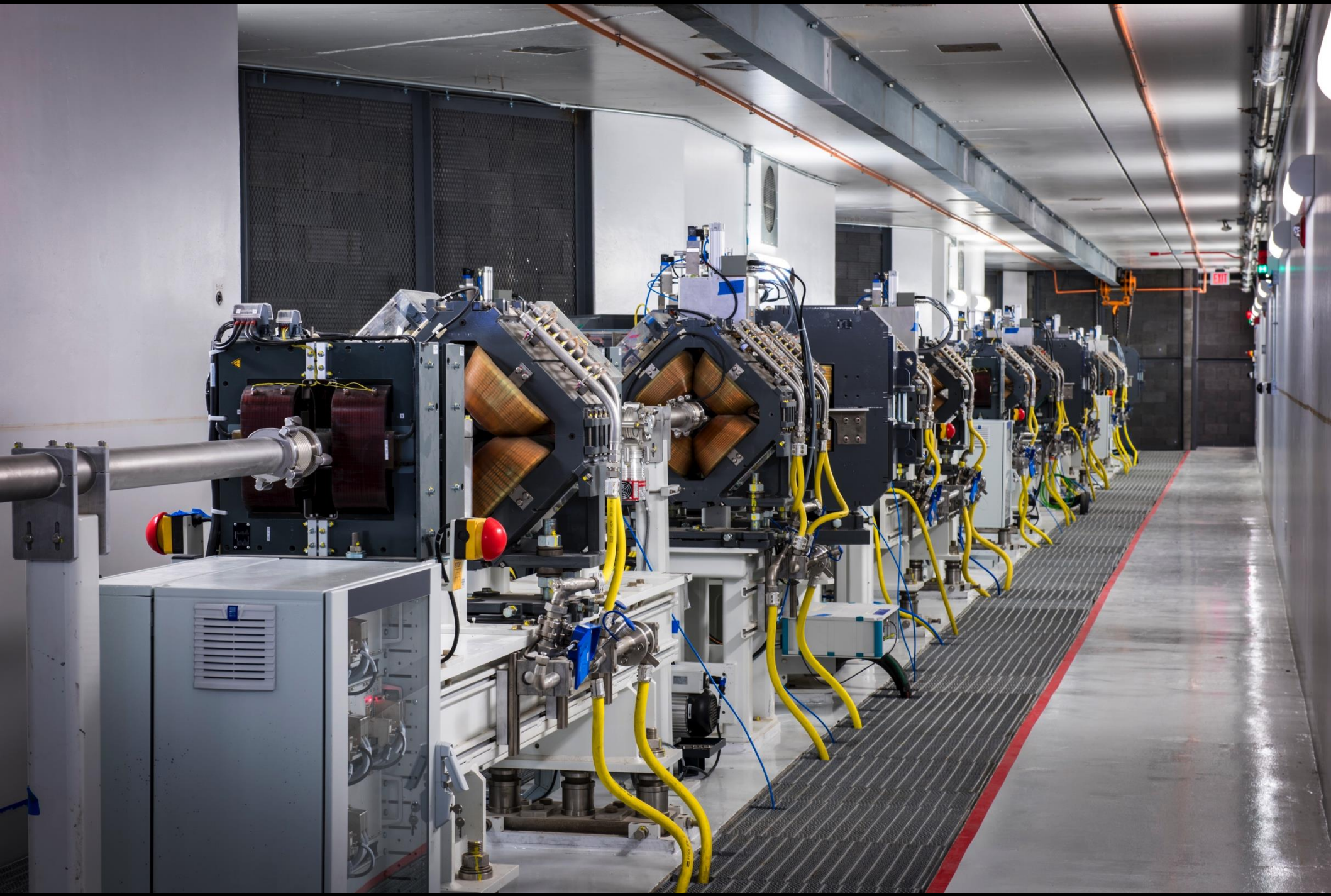



Beam line
Cyclotron

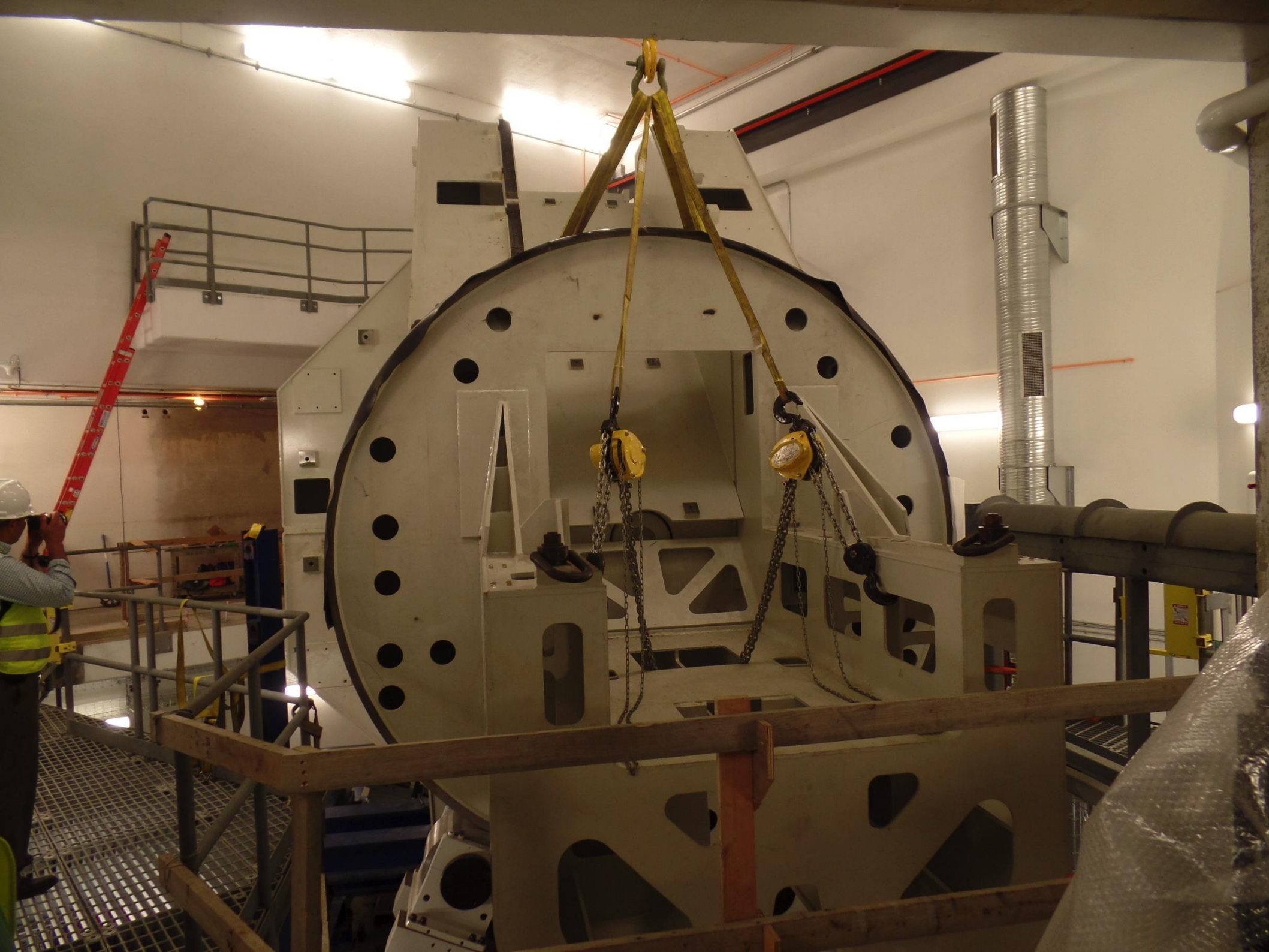


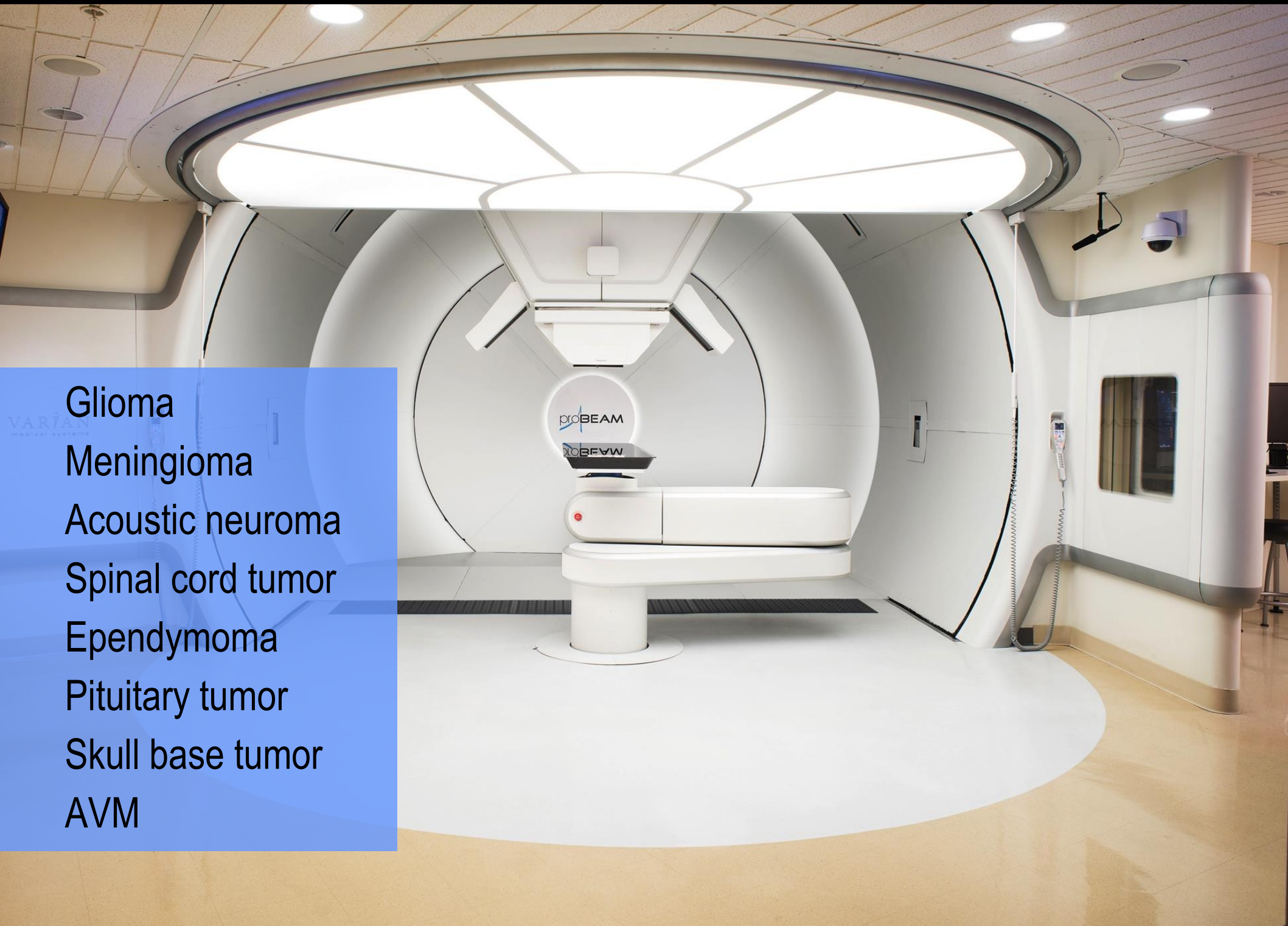
Only research-dedicated proton gantry in the world here at UC - CCHMC!


CAUTION
HIGH
RADIATION
AREA



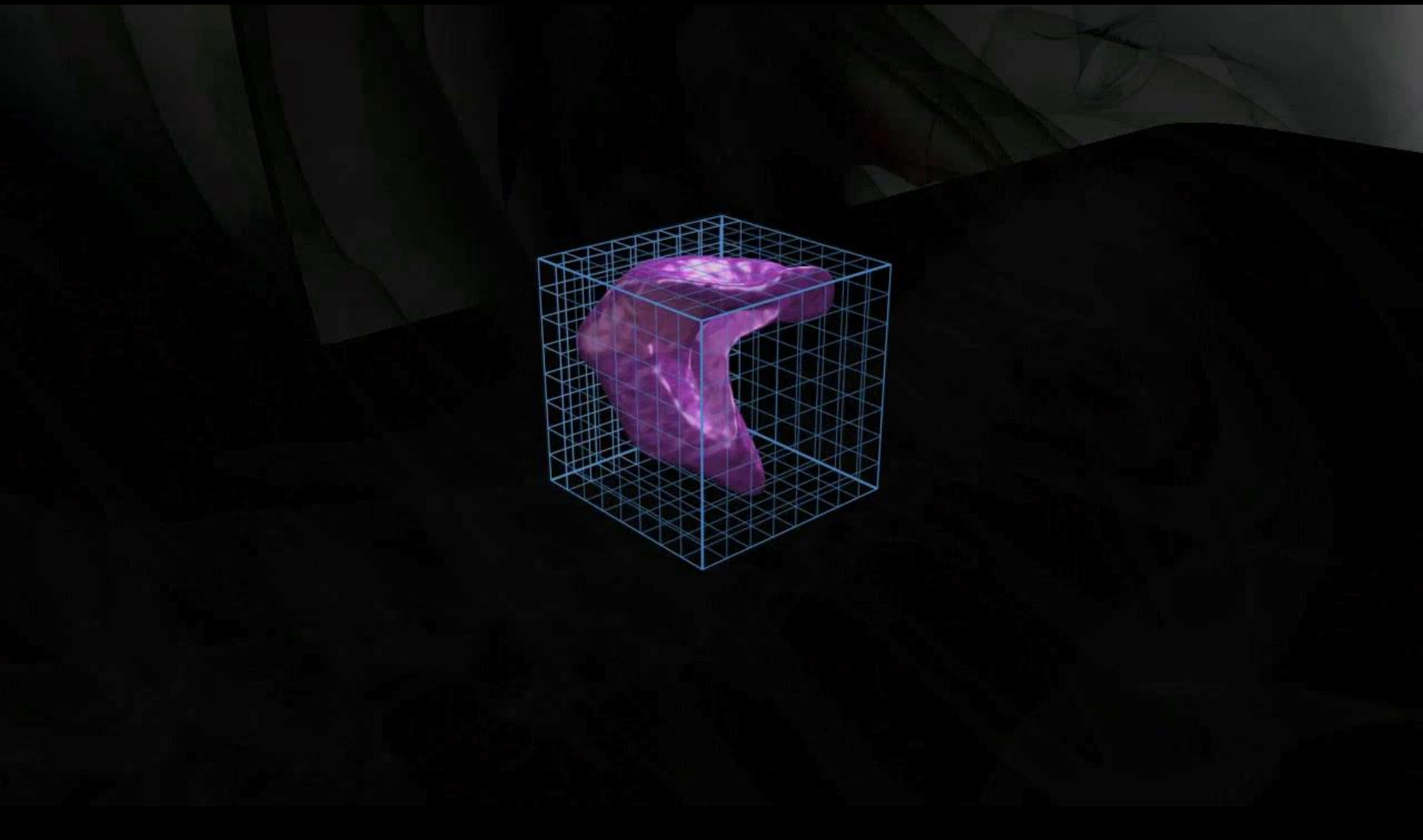

JLG LIFT
ART'S RENTAL





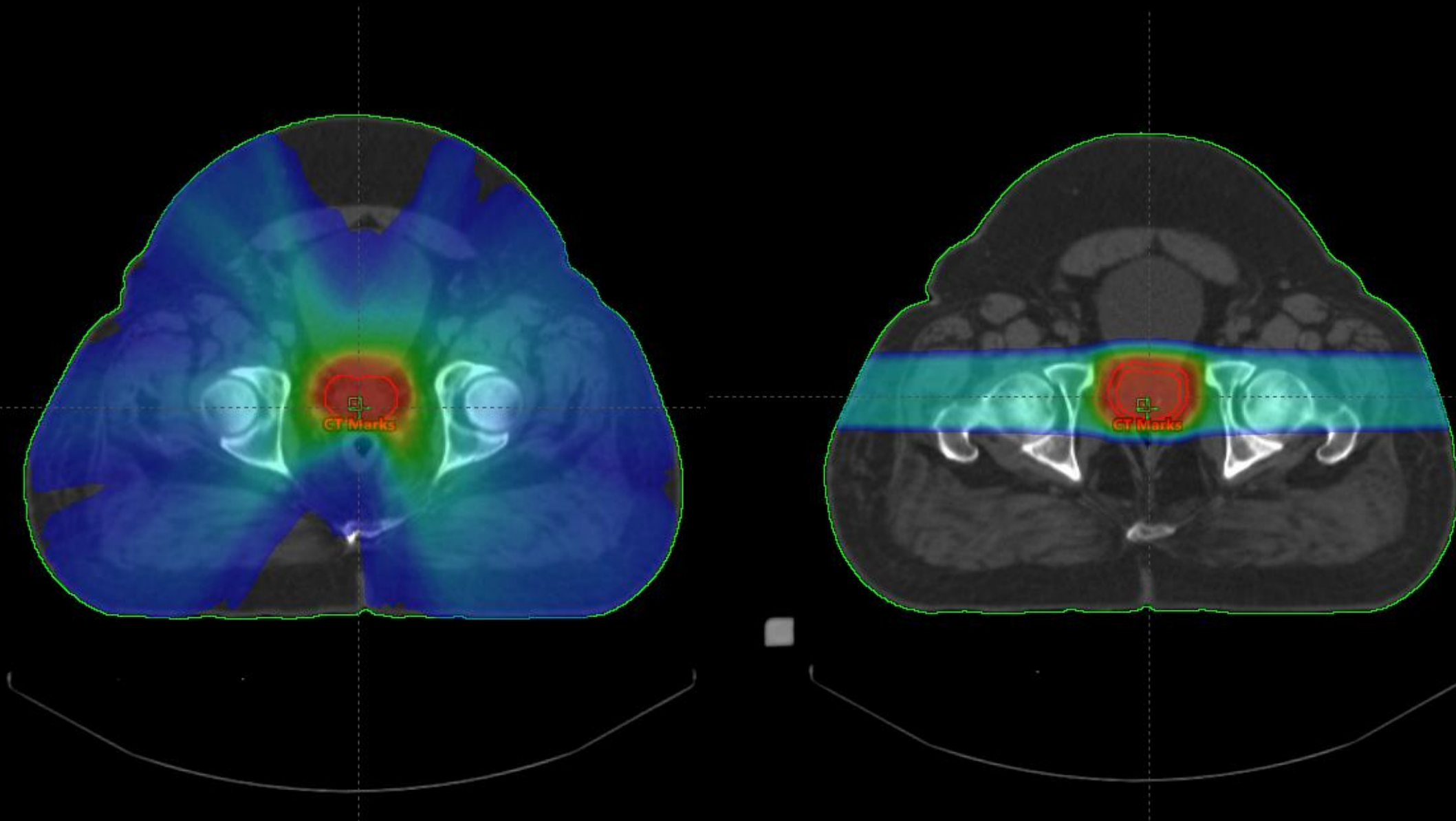
- Glioma
- Meningioma
- Acoustic neuroma
- Spinal cord tumor
- Ependymoma
- Pituitary tumor
- Skull base tumor
- AVM

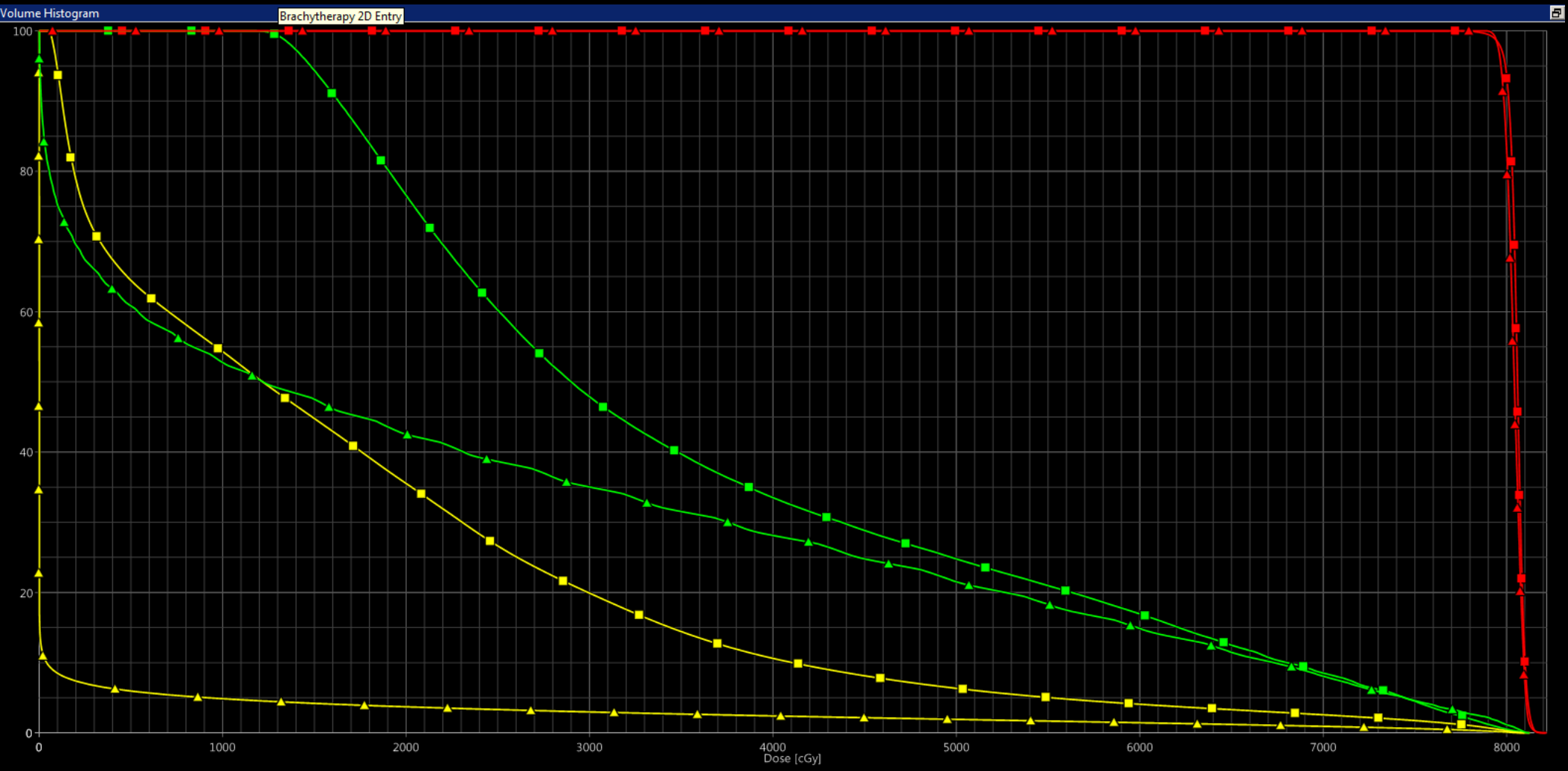
Pencil-beam scanning




PROTON THERAPY CENTER
UHealth

Photon vs. Proton isodose curve

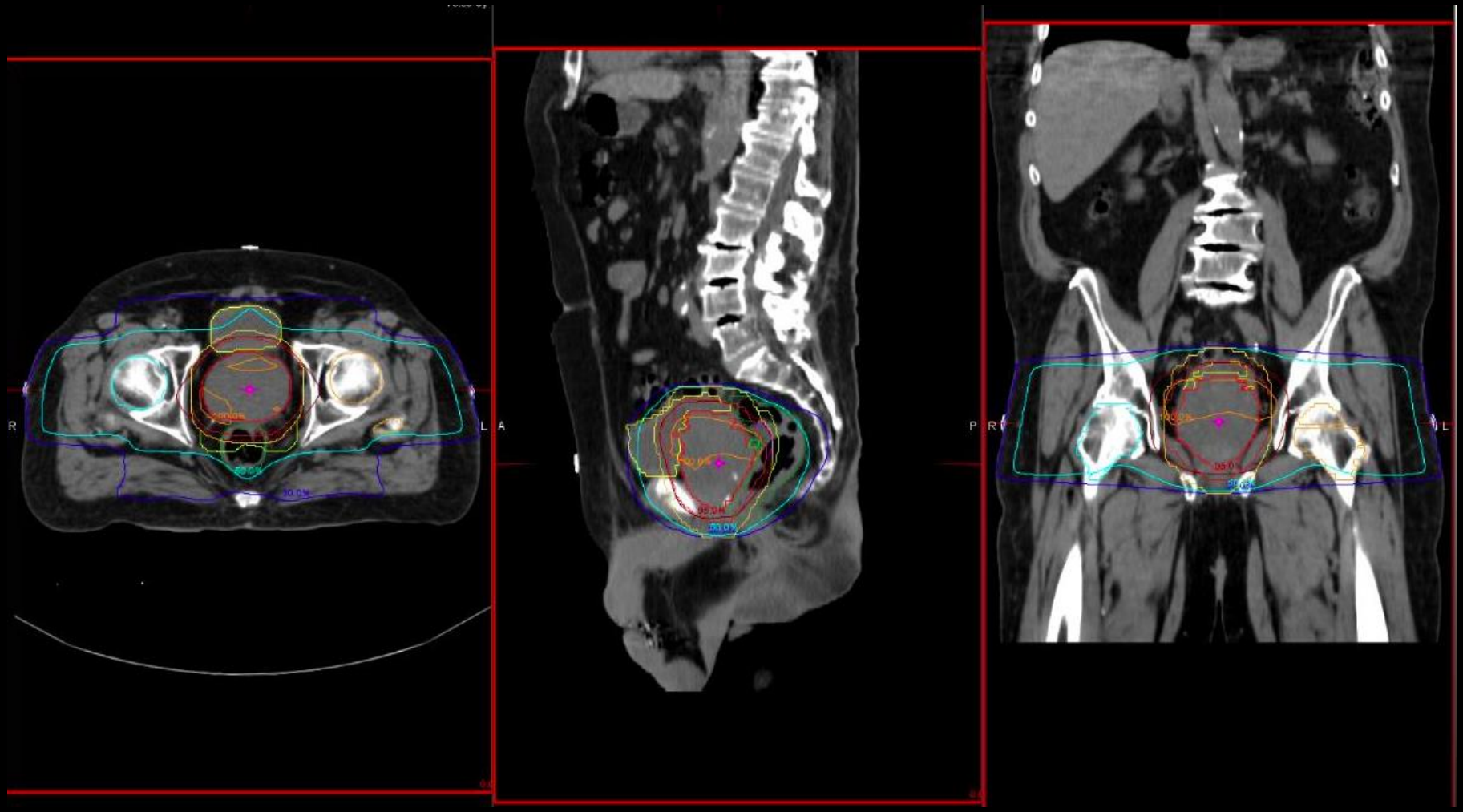




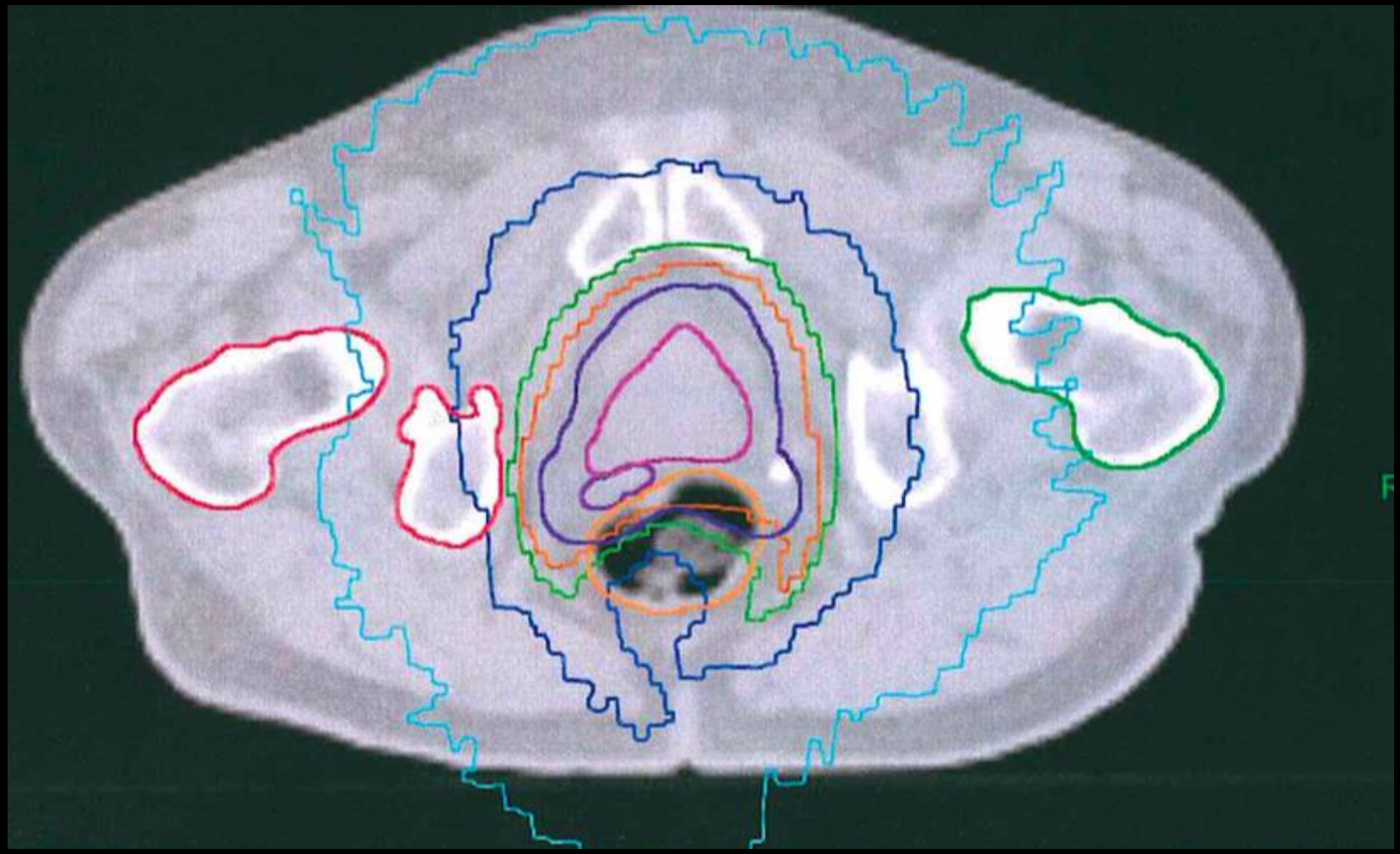
Some structures are unapproved or rejected

w DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [cGy]	Max Dose [cGy]	Mean Dose [cGy]
	Rectum	Unapproved	photon	C1	45.3	100.0	100.0	1162.9	8103.9	3601.4
	Rectum	Unapproved	RO	Chrystal	45.3	100.0	100.1	0.1	8124.8	2405.4
	Prostate	Unapproved	photon	C1	39.2	100.0	100.0	7742.7	8215.7	8056.7
	Prostate	Unapproved	RO	Chrystal	39.2	100.0	100.1	7890.6	8218.5	8040.6
	Bladder	Unapproved	photon	C1	636.5	100.0	100.0	52.1	8128.7	1739.9
	Bladder	Unapproved	RO	Chrystal	636.5	100.0	100.0	0.1	8100.2	223.7

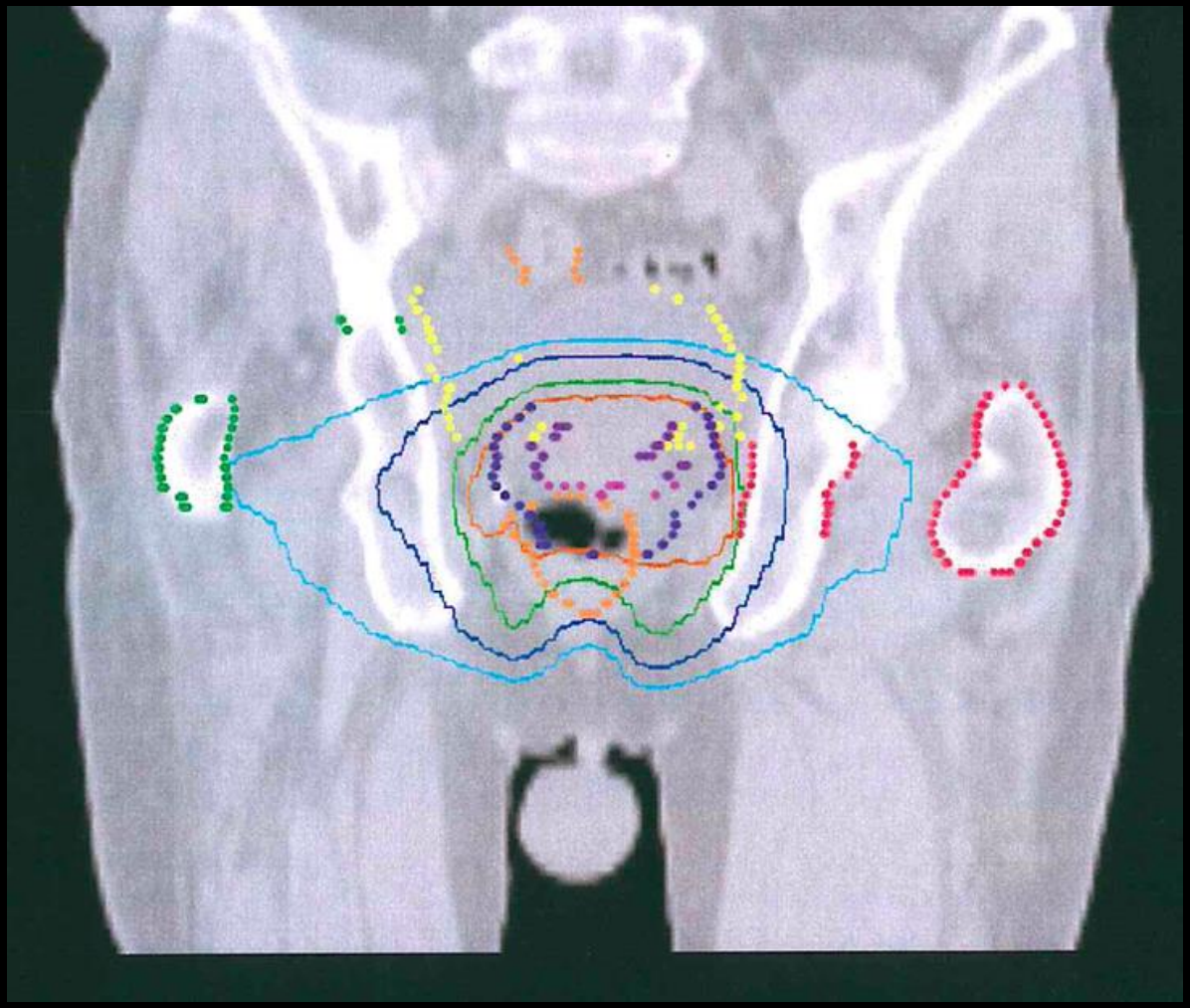
3D confromal radiation



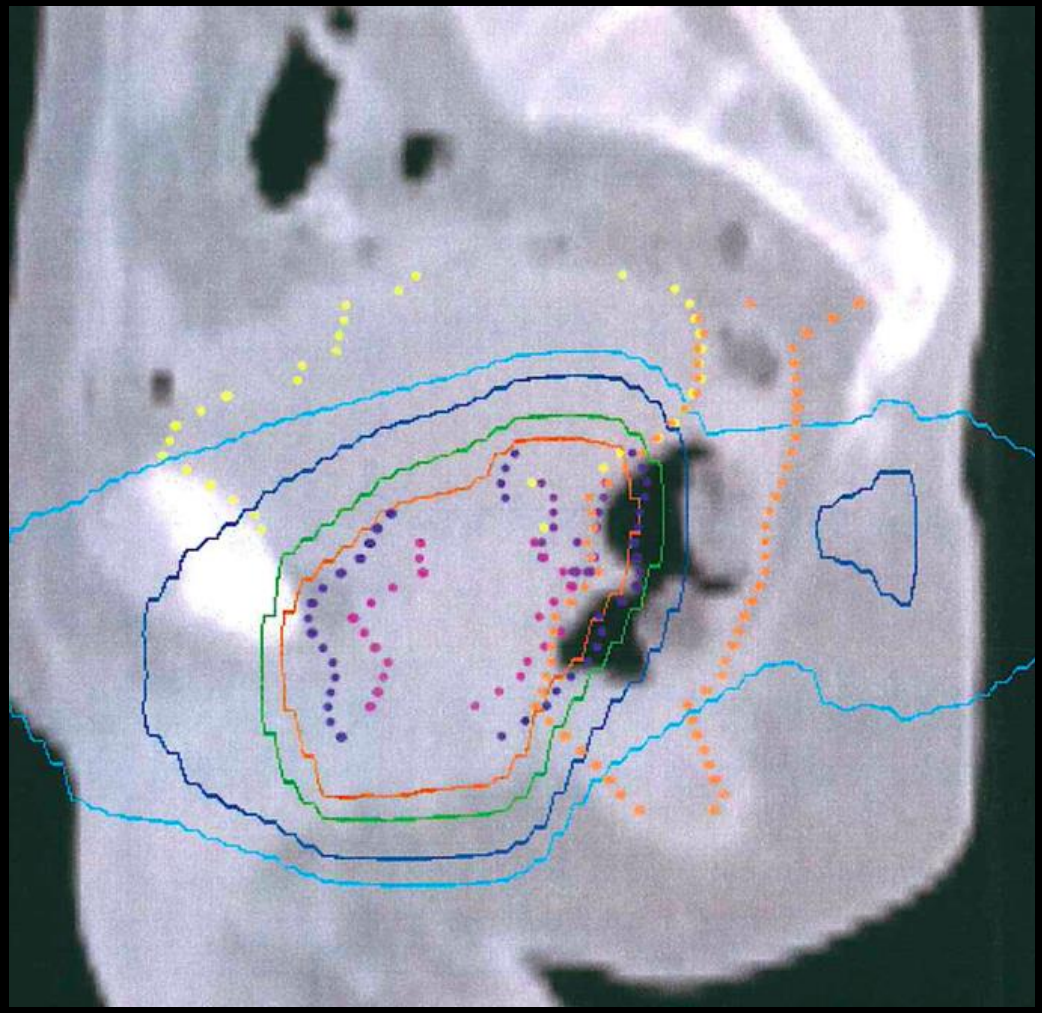
IMRT TOMOTHERAPY
AXIAL



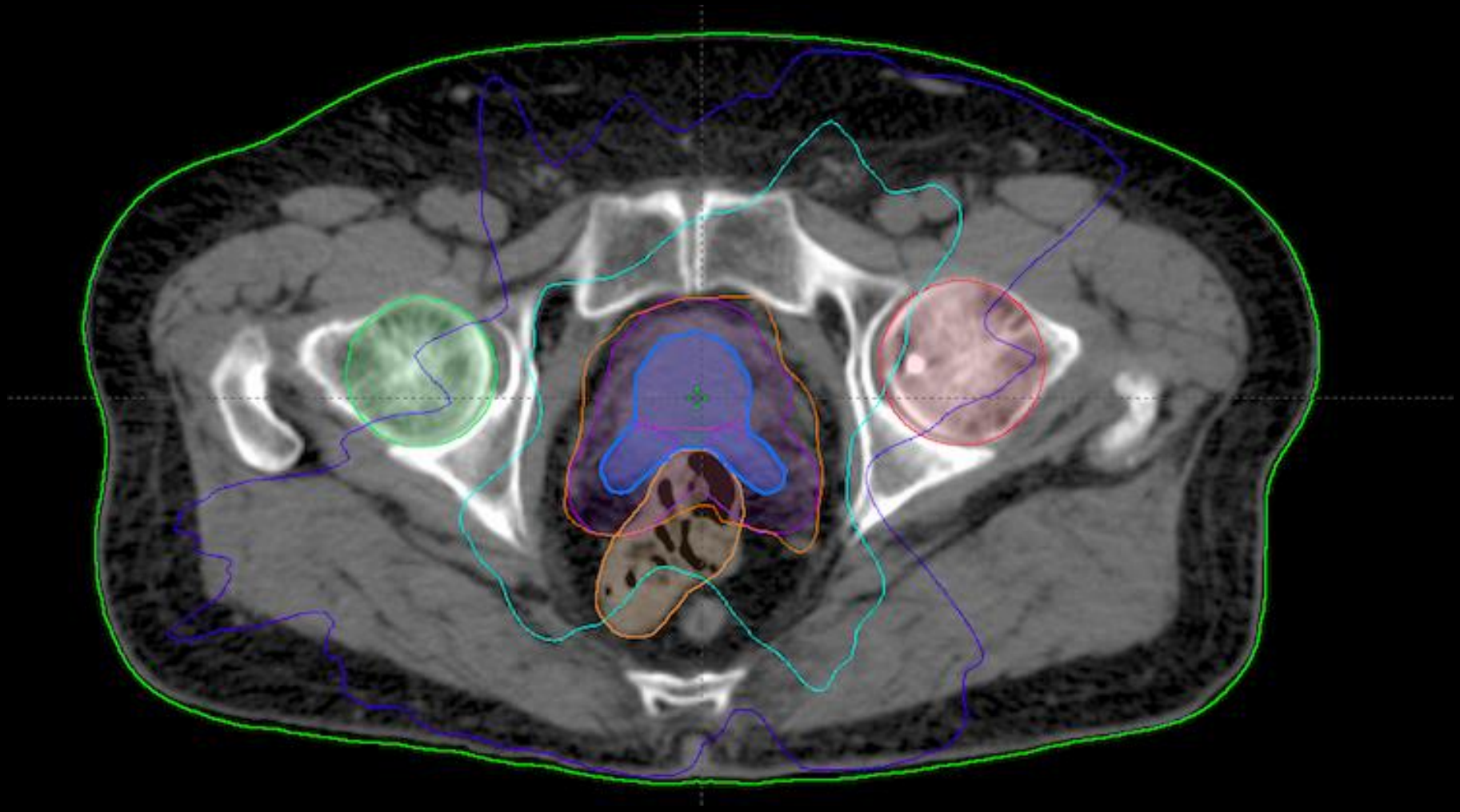
IMRT TOMOTHERAPY
CORONAL



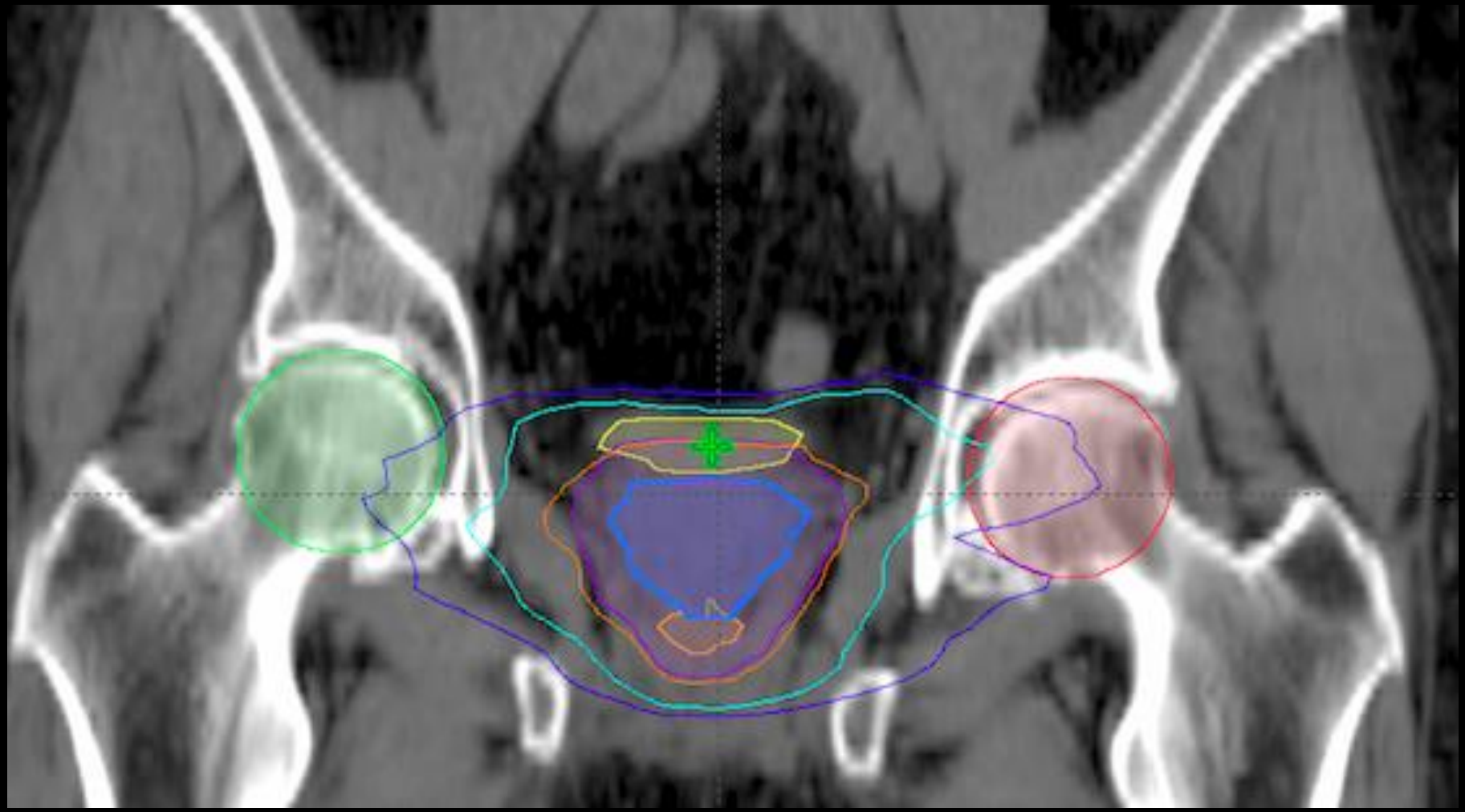
IMRT TOMOTHERAPY
SAGITAL



IMRT TRUEBEM (LINAC)
AXIAL



IMRT TRUEBEM (LINAC)
CORONAL



IMRT TRUEBEM (LINAC)
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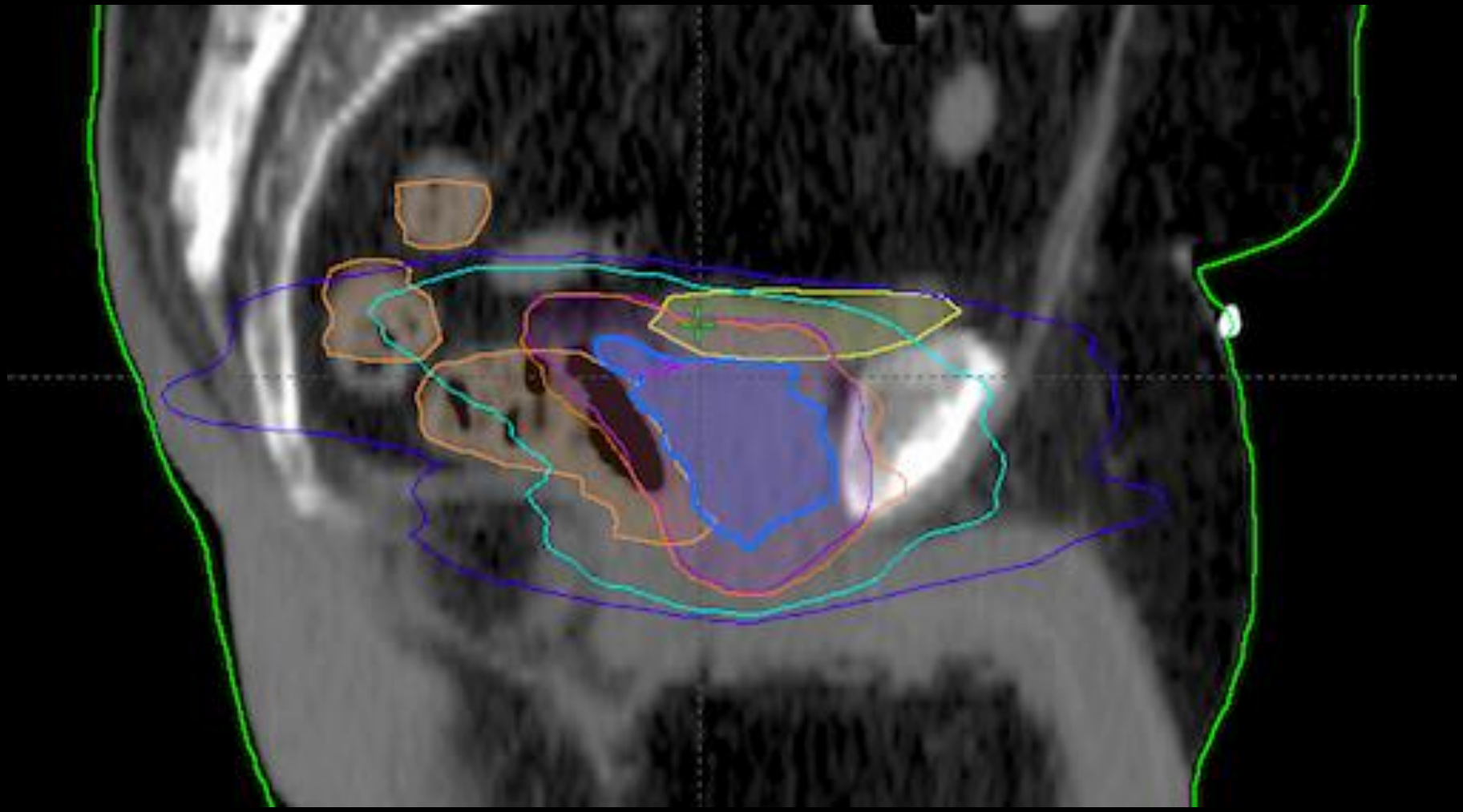

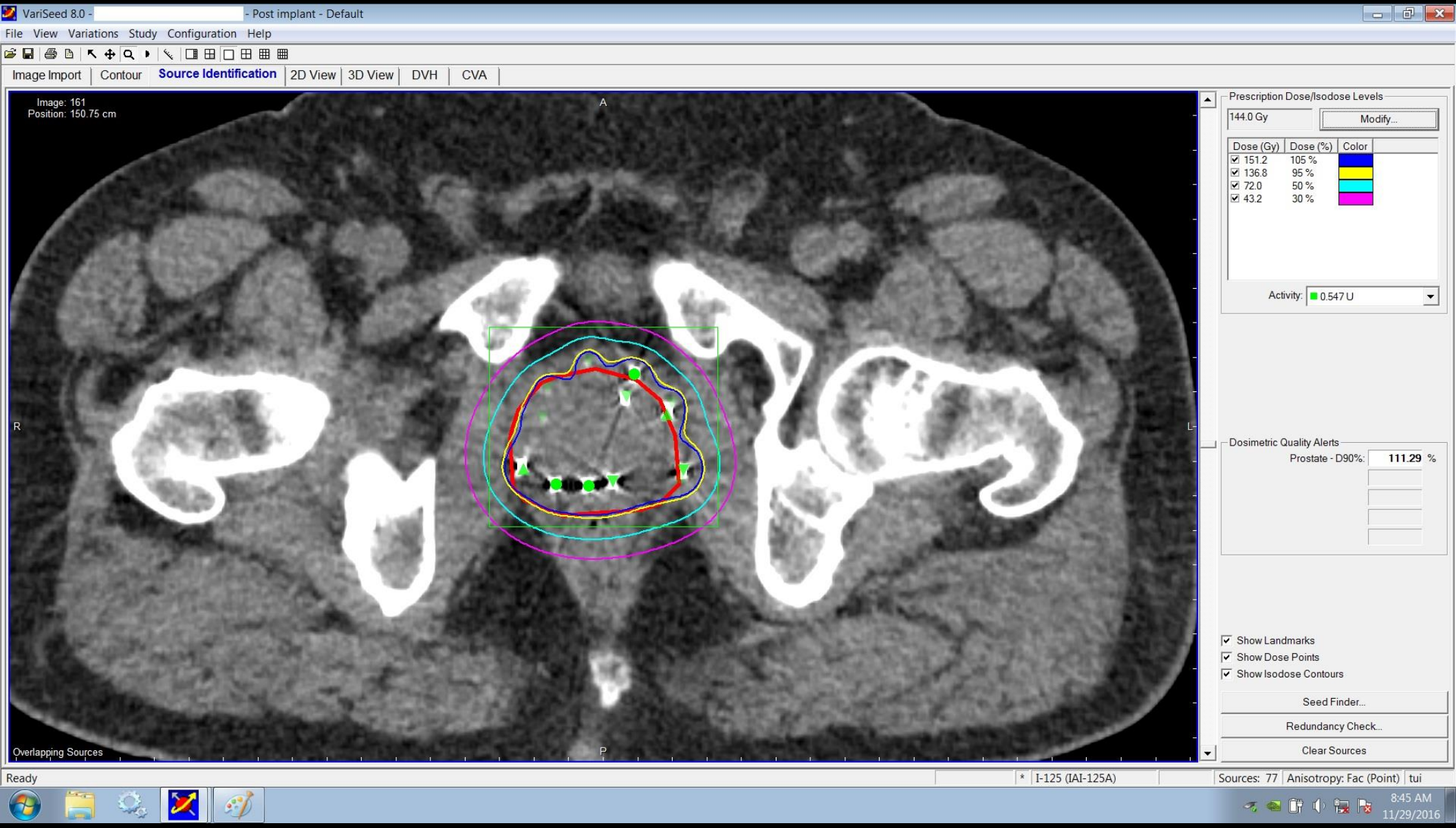
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File View Variations Study Configuration Help
Image Import Contour Source Identification 2D View 3D View DVH CVA
Image: 161
Position: 150.75 cm
A
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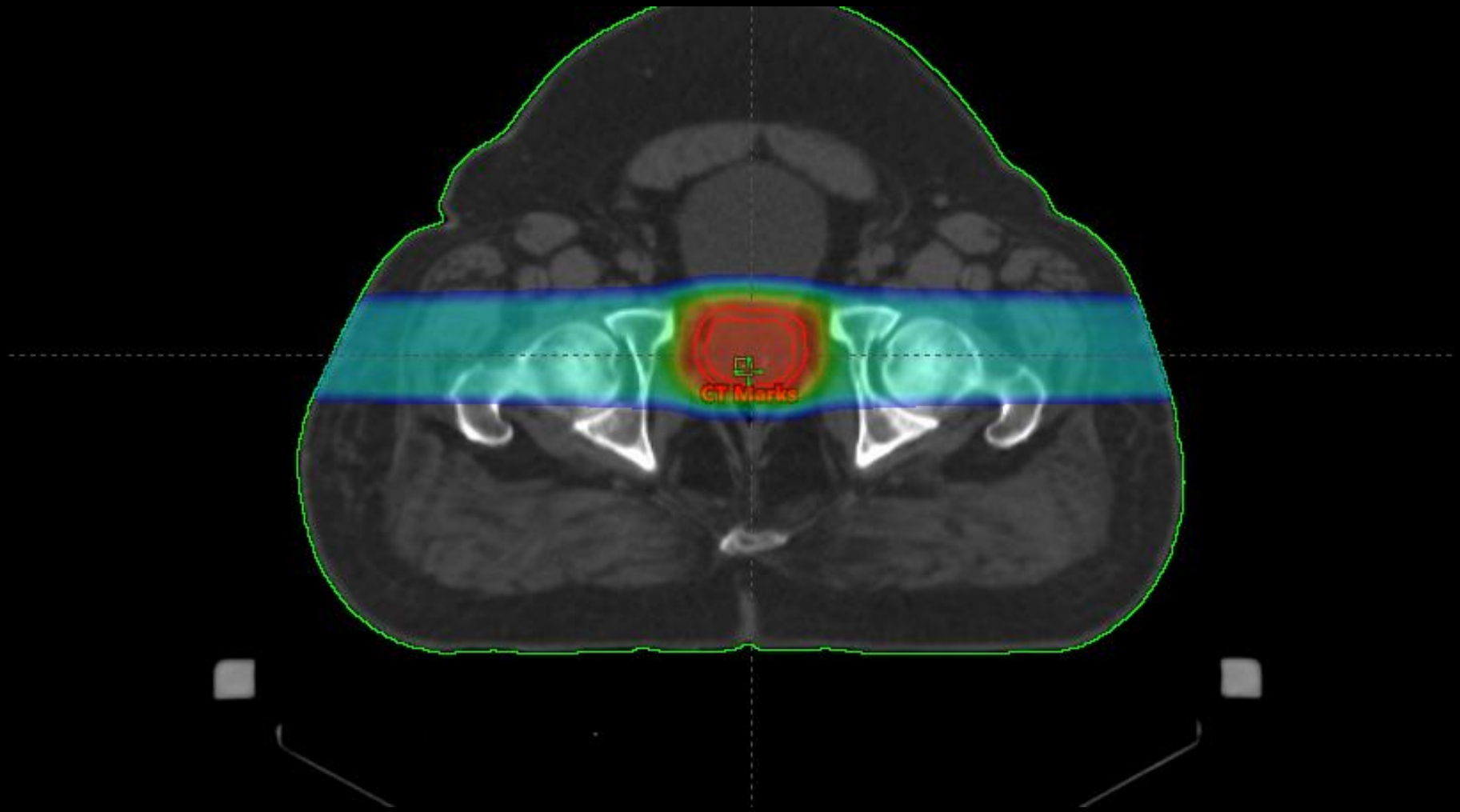
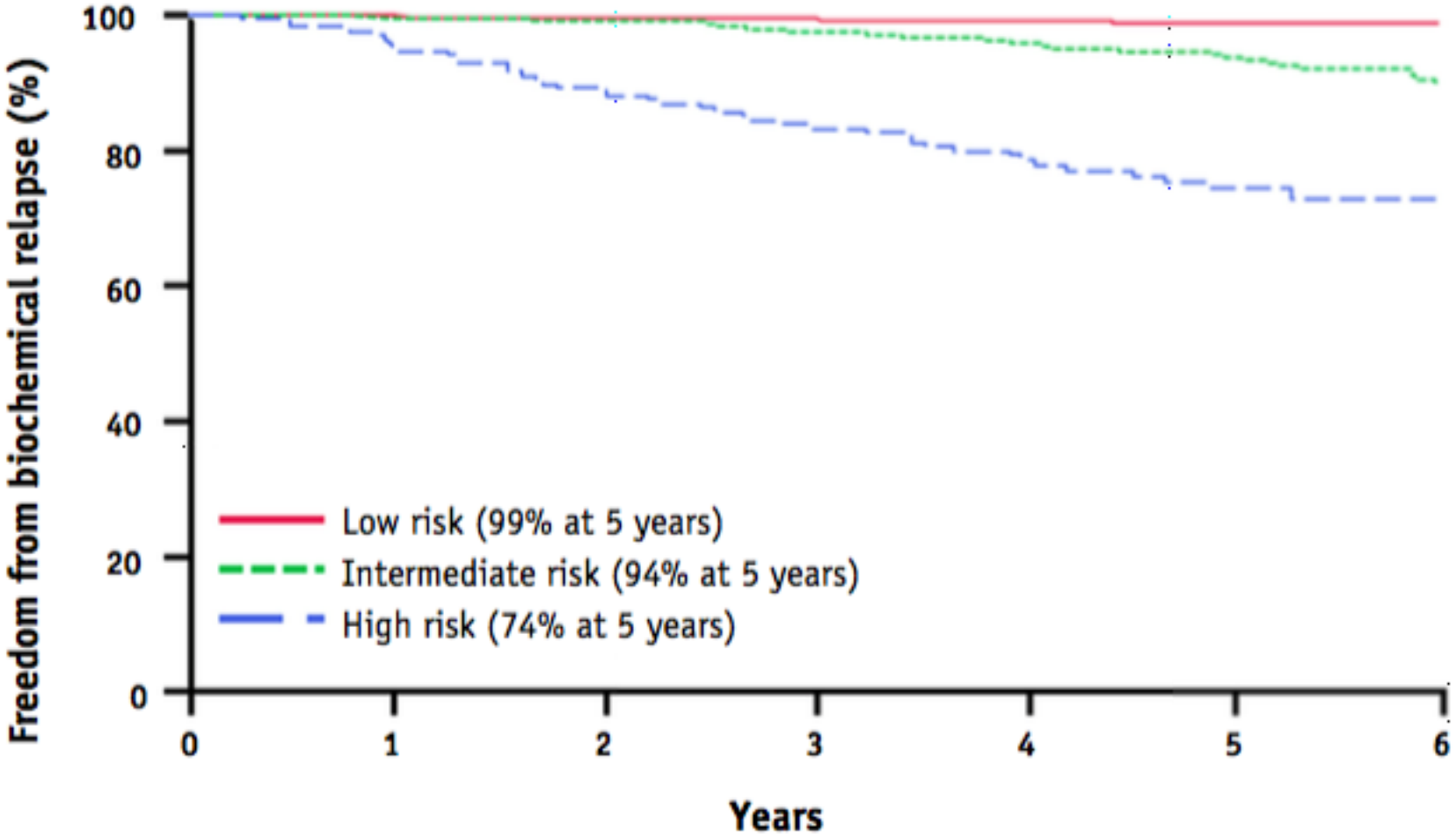
P
Overlapping Sources
Prescription Dose/Isodose Levels
144.0 Gy
Modify...
Dose (Gy) Dose (%) Color
151.2 105 %
136.8 95 %
72.0 50 %
43.2 30 %
Activity: 0.547 U
Dosimetric Quality Alerts
Prostate - D90%: 111.29 %
Show Landmarks
Show Dose Points
Show Isodose Contours
Seed Finder...
Redundancy Check...
Clear Sources
Ready
I-125 (IAI-125A)
Sources: 77
Anisotropy: Fac (Point)
8:45 AM
11/29/2016


GT Marks



Risk Group	1 year No. of pts at risk (%)	2 year No. of pts at risk (%)	3 year No. of pts at risk (%)	4 year No. of pts at risk (%)	5 year No. of pts at risk (%)	6 year No. of pts at risk (%)
Low	512 (99.8%)	508 (99.8%)	486 (99.6%)	436 (99.2%)	316 (98.9%)	153 (98.9%)
Intermediate	527 (99.6%)	521 (99.1%)	489 (97.5%)	442 (95.8%)	322 (93.9%)	157 (90.0%)
High	160 (95.2%)	148 (88.6%)	130 (83.0%)	108 (78.3%)	67 (74.0%)	30 (72.7%)

Fig. 1. Freedom from biochemical failure by risk group.

Table 7 Literature review

Study	No. of patients	Therapy	Median RT dose Gy or CGE	Median F/U years	5-year BCR (%)	G3+ GI toxicity	G3+ GU toxicity
Mendenhall et al (7)	211	Proton therapy	78-82	5.2	LR, 99% IR, 99% HR, 76%	0.5%	1.0%
Slater et al, 2004 (6)	1255	Proton therapy	74	5.3	73%	1%	1%
Spratt et al, 2013 (16)	1002	IMRT	86.4	5.5	LR, 98.8%* IR, 85.6%* HR, 67.9%*	0.7%	2.2%
Vora et al, 2013 (17)	302	IMRT	75.6	7.6	LR, 77.4%† IR, 69.6%† HR, 53.3%†	0%	0.7%
Liauw et al, 2009 (18)	130	IMRT	76	4.4	LR, 97% IR, 94% HR, 87%	2%	2%
Pugh et al, 2013 (19)	291	Proton therapy	76	2.0	- - -	<0.3%	0%
Present study, 2015	1215	Proton therapy	78	5.5	LR, 99% IR, 94% HR, 74%	0.6%	2.9%

Abbreviations: BCR = biochemical control rate; CGE = cobalt-Gray equivalent; F/U = follow-up; GI = gastrointestinal; GU = genitourinary; HR = high risk; IMRT = intensity modulated radiation therapy; IR = intermediate risk; LR = low risk.

* 7-year results.

† 9-year results.

Uof Florida proton vs PortecT

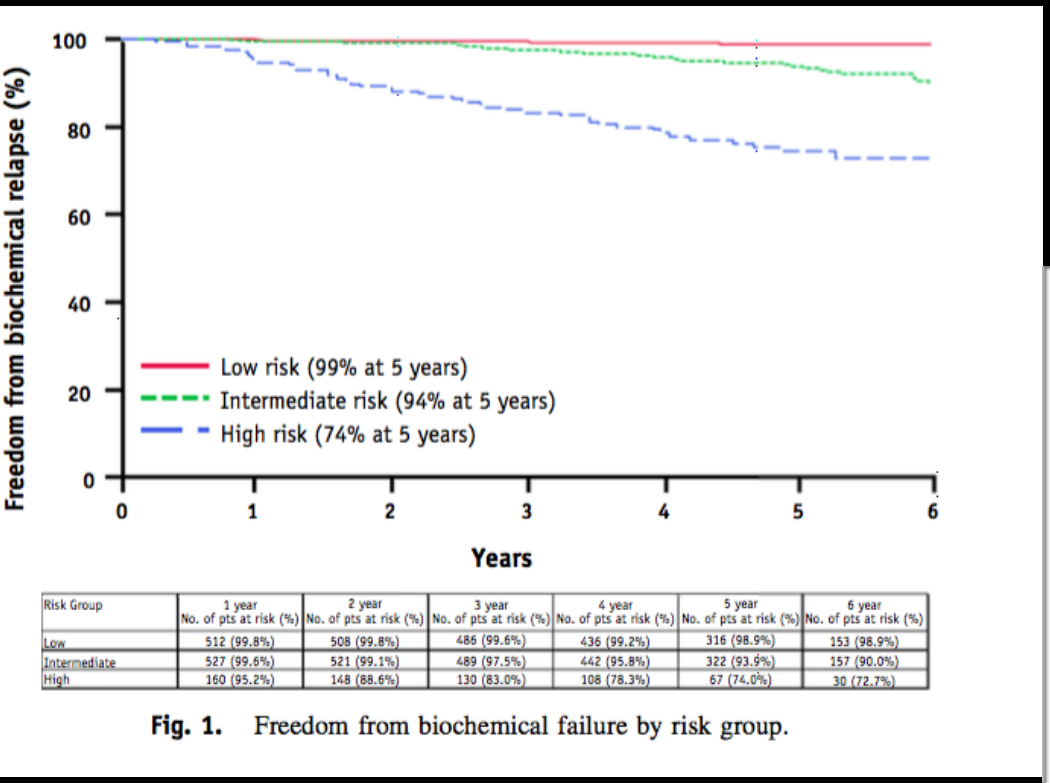


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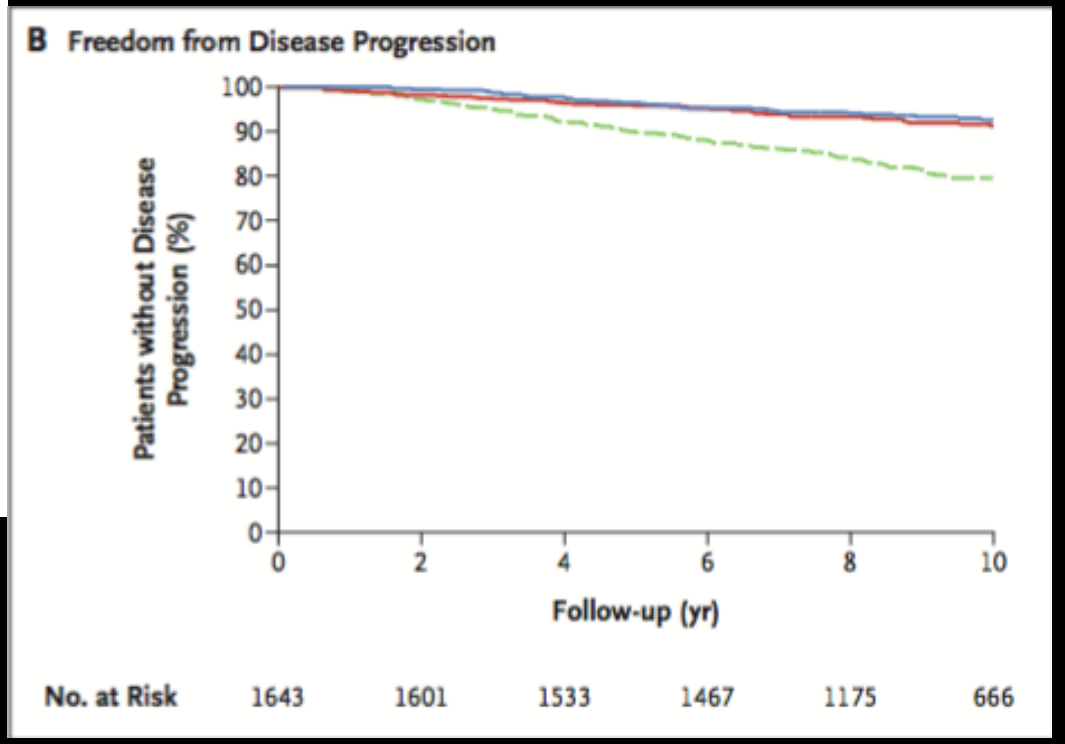
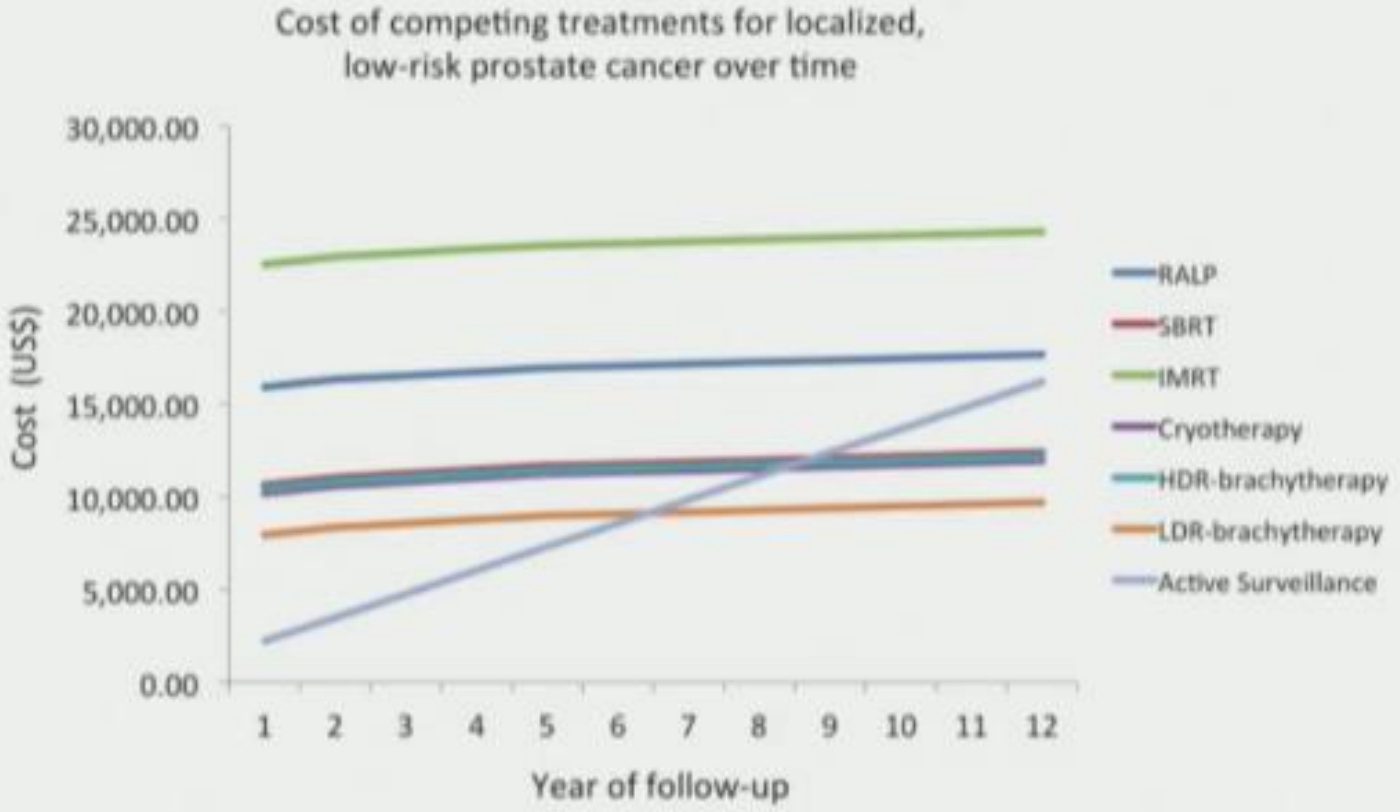
Fig. 1. Freedom from biochemical failure by risk group.



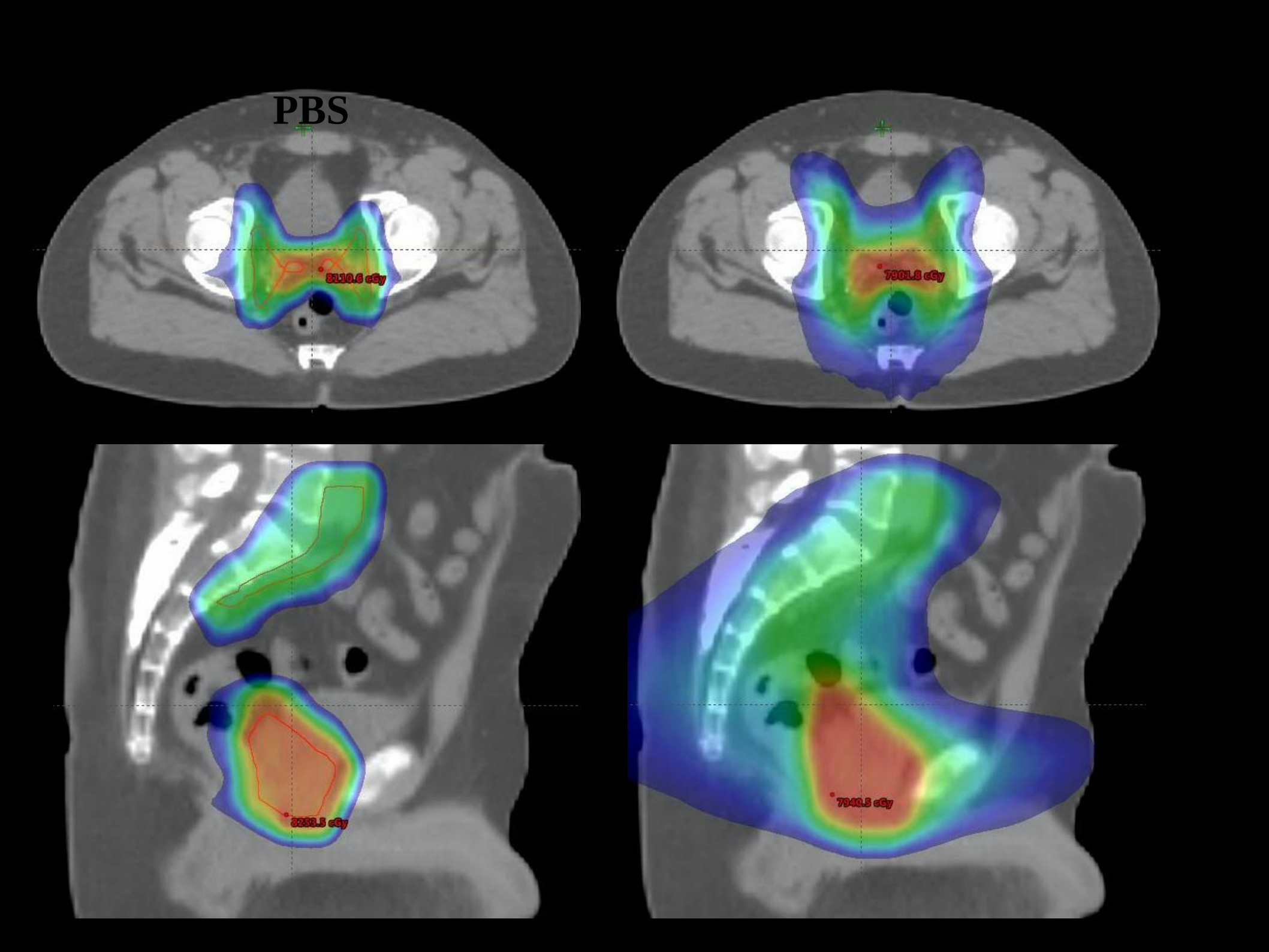
What about cost?



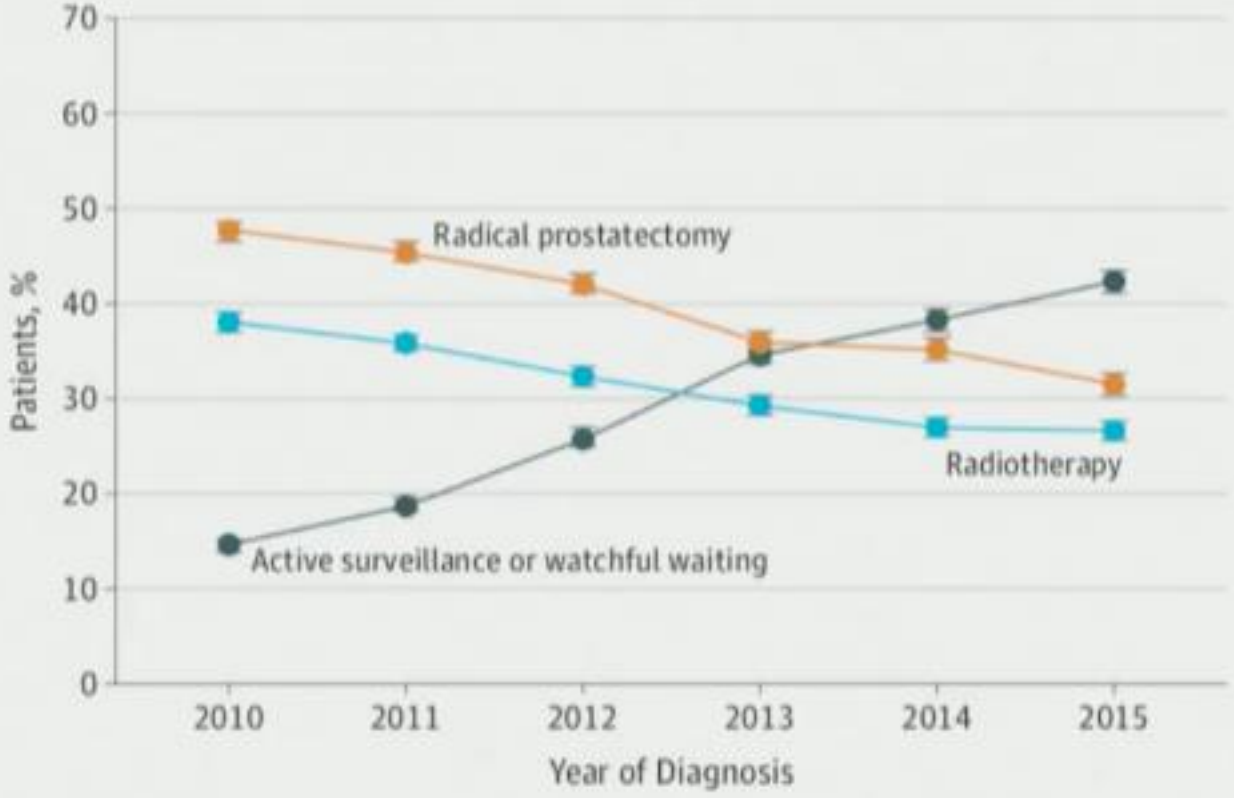
Laviana et al. Cancer. 2016

What's new in 2019

- Increase in the number of restrictions from commercial insurance for the use of proton in prostate cancer
- Increase use of Active Surveillance (AS)
- The use of Prostate MRI
- Decrease number of fractions of radiation treatments with a range of 5-40
- The use of The use of SpaceOrr for rectal sparing
- The use of Genomic Testing (Decipher)


PBS
8110.6 cGy
7901.8 cGy
8253.5 cGy
7940.5 cGy

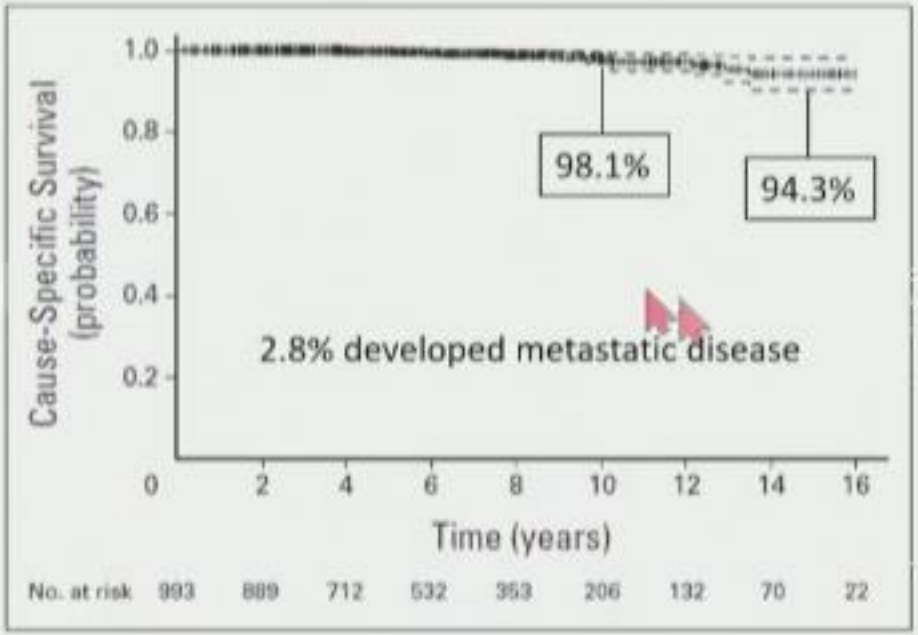
Shifting Patterns of Practice: SEER - Low Risk



40%

Mahal et al. JAMA 2019

When Zero Gy may be the Right Dose



On Surveillance, Untreated:

5 years: 75.7%
10 years: 63.5%
15 years: 55.0%

Klotz et al. J Clin Oncol. 2015

Original Article

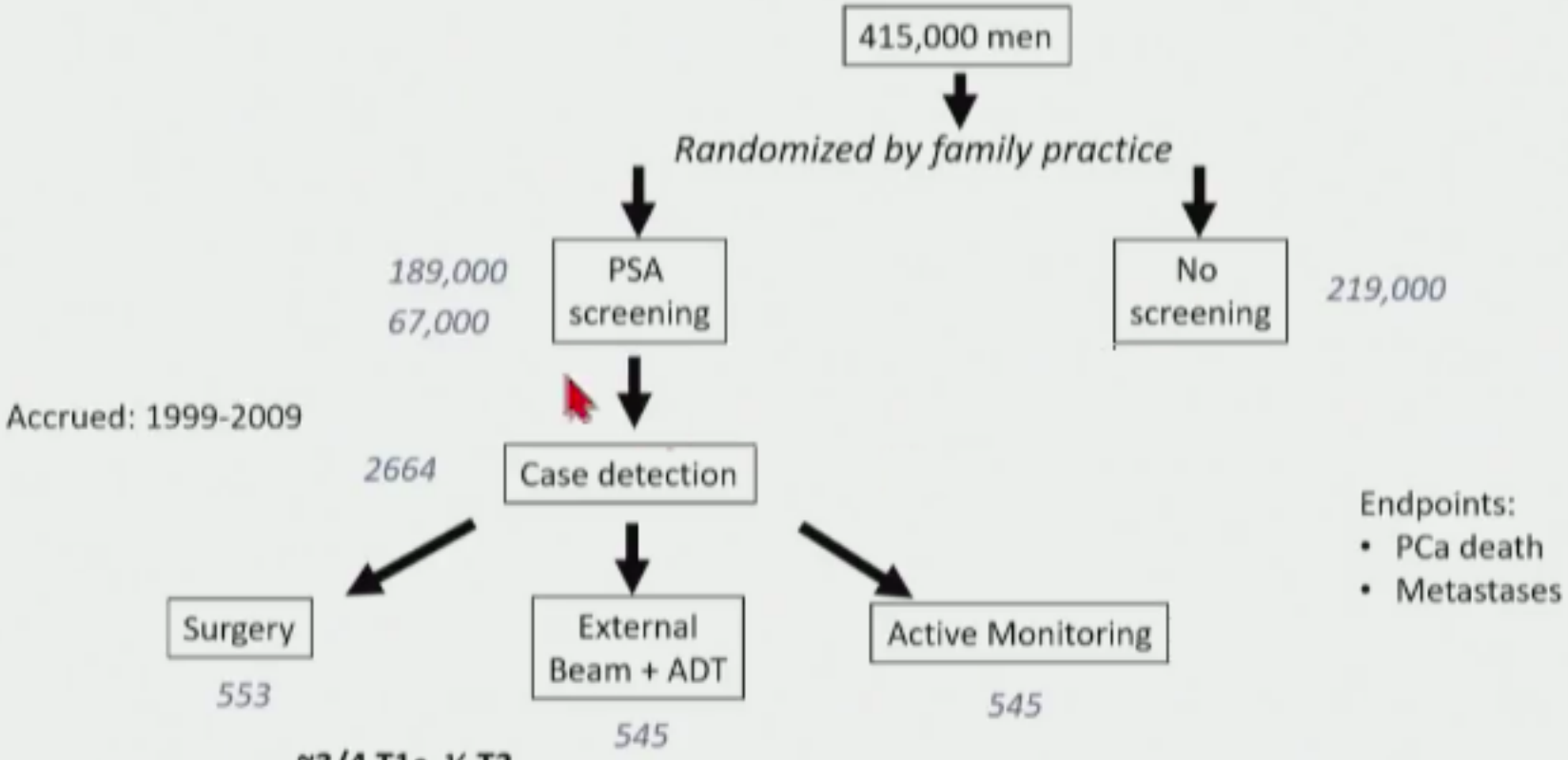
10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

Freddie C. Hamdy, F.R.C.S.(Urol.), F.Med.Sci., Jenny L. Donovan, Ph.D., F.Med.Sci., J. Athene Lane, Ph.D., Malcolm Mason, M.D., F.R.C.R., Chris Metcalfe, Ph.D., Peter Holding, R.G.N., M.Sc., Michael Davis, M.Sc., Tim J. Peters, Ph.D., F.Med.Sci., Emma L. Turner, Ph.D., Richard M. Martin, Ph.D., Jon Oxley, M.D., F.R.C.Path., Mary Robinson, M.B., B.S., F.R.C.Path., John Staffurth, M.B., B.S., M.D., Eleanor Walsh, M.Sc., Prasad Bollina, M.B., B.S., F.R.C.S.(Urol.), James Catto, Ph.D., F.R.C.S.(Urol.), Andrew Doble, M.S., F.R.C.S.(Urol.), Alan Doherty, F.R.C.S.(Urol.), David Gillatt, M.S., F.R.C.S.(Urol.), Roger Kockelbergh, D.M., F.R.C.S.(Urol.), Howard Kynaston, M.D., F.R.C.S.(Urol.), Alan Paul, M.D., F.R.C.S.(Urol.), Philip Powell, M.D., F.R.C.S., Stephen Prescott, M.D., F.R.C.S.(Urol.), Derek J. Rosario, M.D., F.R.C.S.(Urol.), Edward Rowe, M.D., F.R.C.S.(Urol.), David E. Neal, F.R.C.S., F.Med.Sci., for the ProtecT Study Group

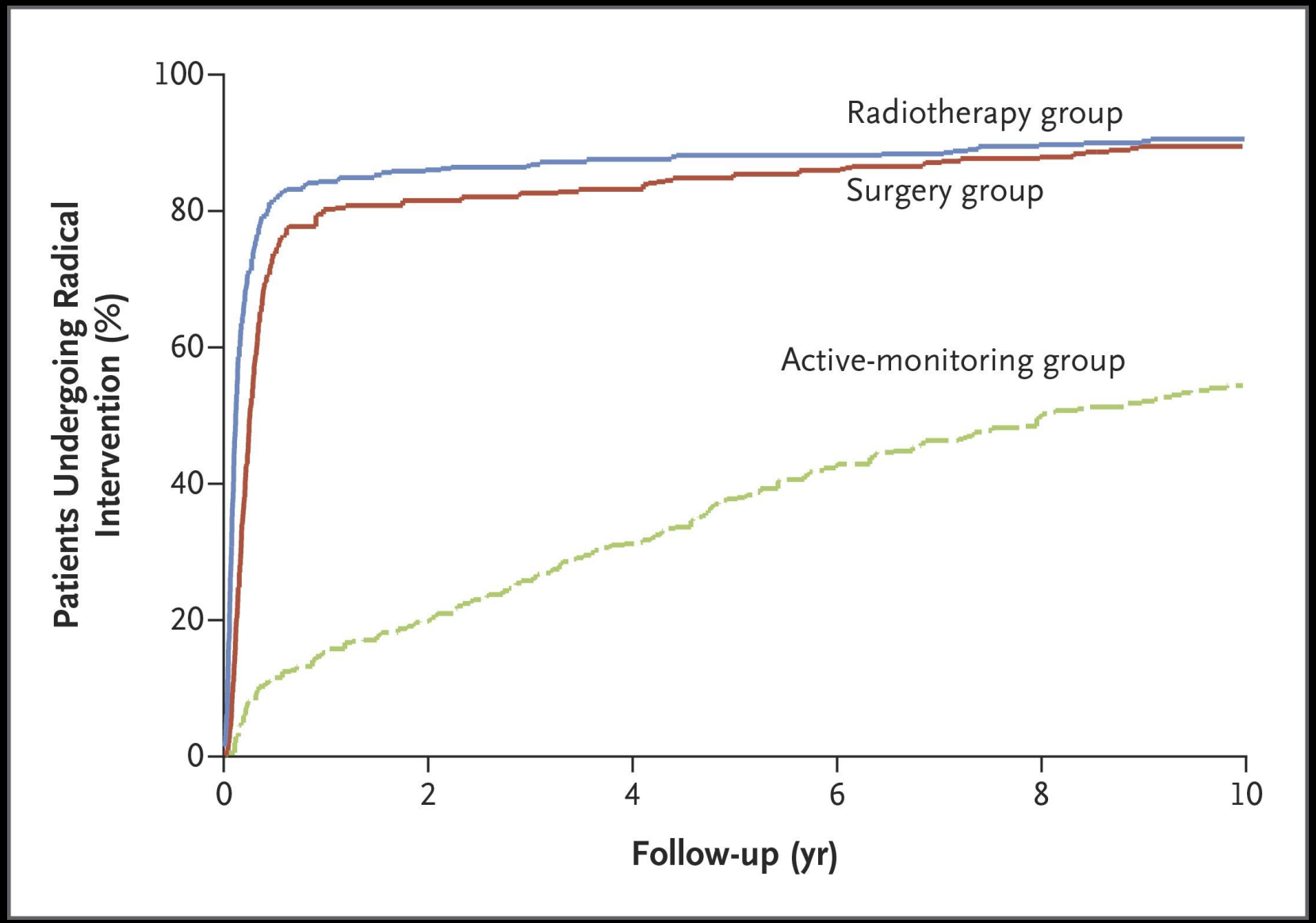
N Engl J Med
Volume 375(15):1415-1424
October 13, 2016

The NEW ENGLAND JOURNAL of MEDICINE

Active Monitoring vs Treatment? – CAP/ProtecT (UK)



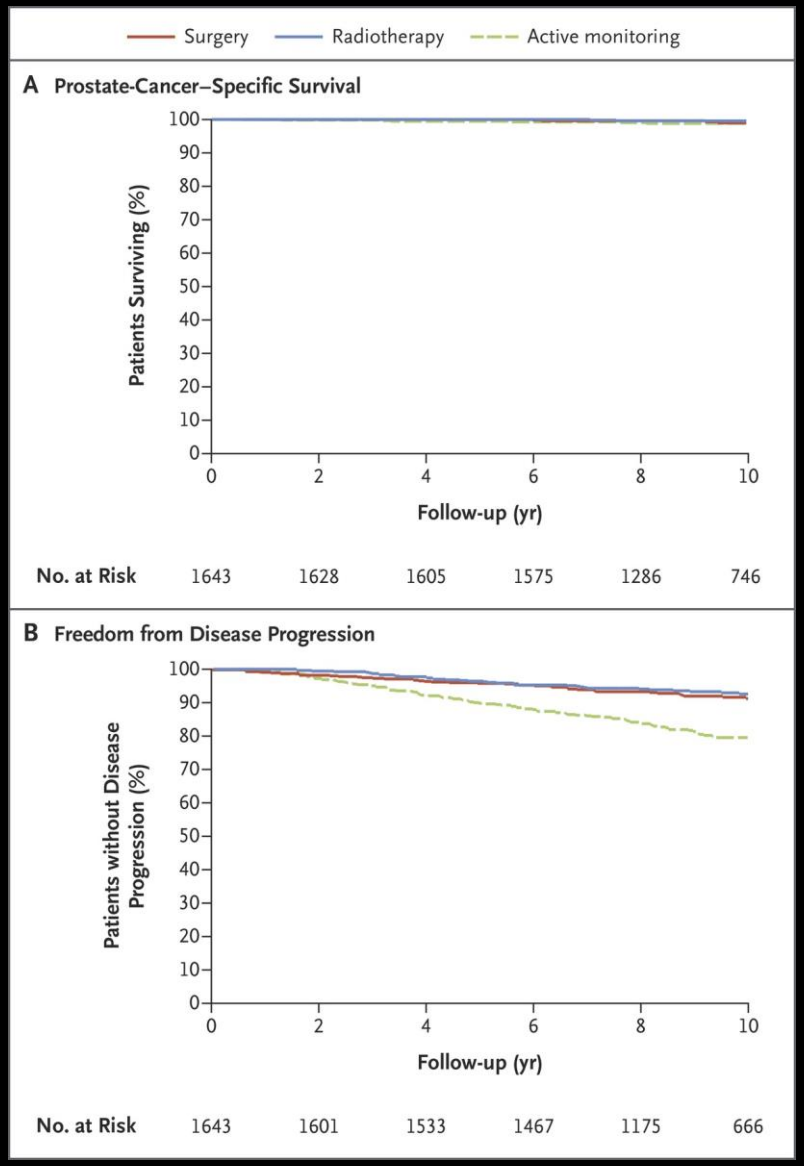
Kaplan–Meier Estimates of the Cumulative Probability of Undergoing Radical Intervention during the Follow-up Period, According to Treatment Group.



Hamdy FC et al. N Engl J Med 2016;375:1415-1424

The NEW ENGLAND JOURNAL of MEDICINE

Kaplan–Meier Estimates of Prostate-Cancer–Specific Survival and Freedom from Disease Progression, According to Treatment Group.



Hamdy FC et al. N Engl J Med 2016;375:1415-1424

The NEW ENGLAND JOURNAL of MEDICINE

Study Overview

- In the ProtecT trial, over 1600 men with PSA-detected localized prostate cancer were assigned to active monitoring, prostatectomy, or radiotherapy.
- Although more patients assigned to active monitoring had disease progression, overall survival was similar in the three groups.

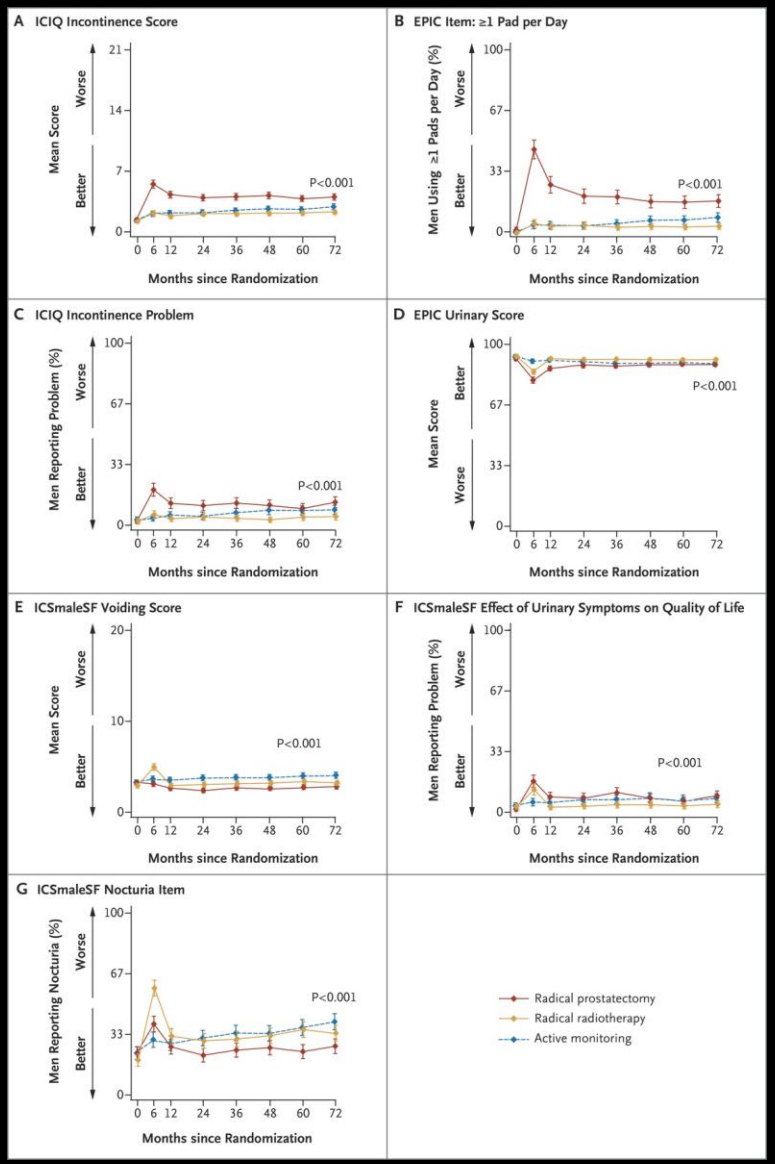
Conclusions

- At a median of 10 years, prostate-cancer–specific mortality was low irrespective of the treatment assigned, with no significant difference among treatments.
- Surgery and radiotherapy were associated with lower incidences of disease progression and metastases than was active monitoring.

Study Overview

- The choice of treatment for PSA-detected, localized prostate cancer is influenced by effects of the interventions on quality of life.
- In the ProtecT trial, patterns of side-effect severity, improvement, and decline in urinary, sexual, and bowel function differed among the treatments.

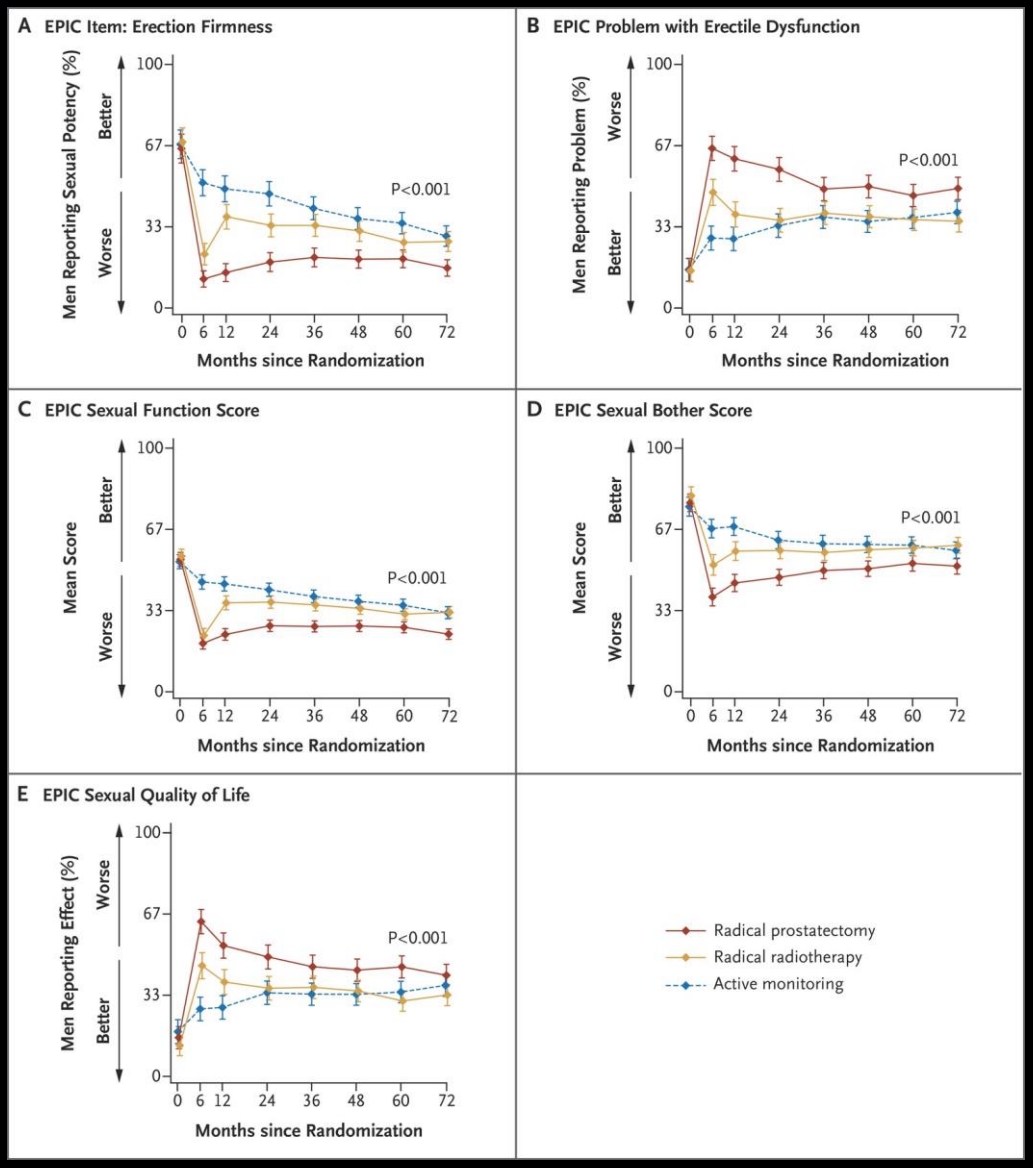
Outcomes for Urinary Function and Effect on Quality of Life.



Donovan JL et al. N Engl J Med 2016;375:1425-1437

The NEW ENGLAND JOURNAL of MEDICINE

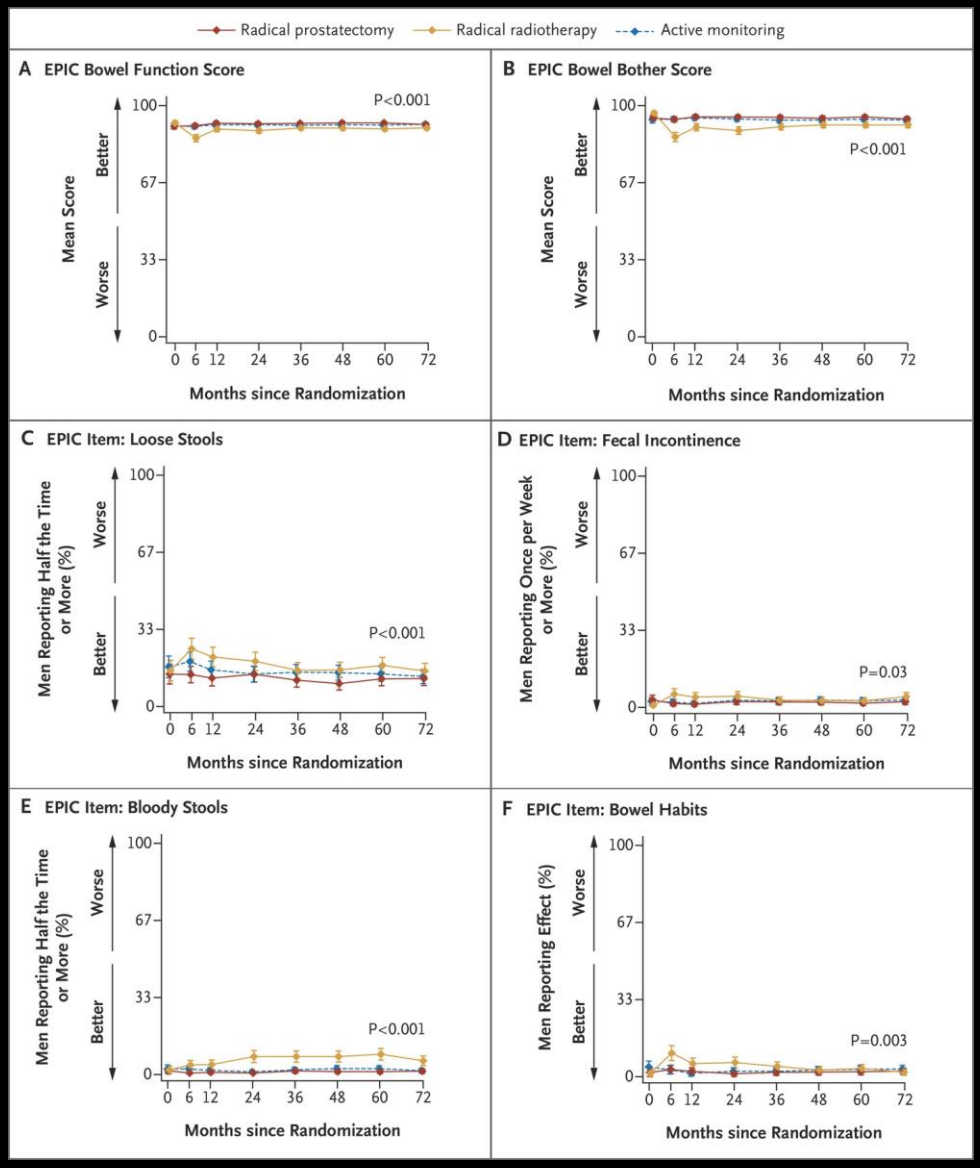
Outcomes for Sexual Function and Effect on Quality of Life.



Donovan JL et al. N Engl J Med 2016;375:1425-1437

The NEW ENGLAND JOURNAL of MEDICINE

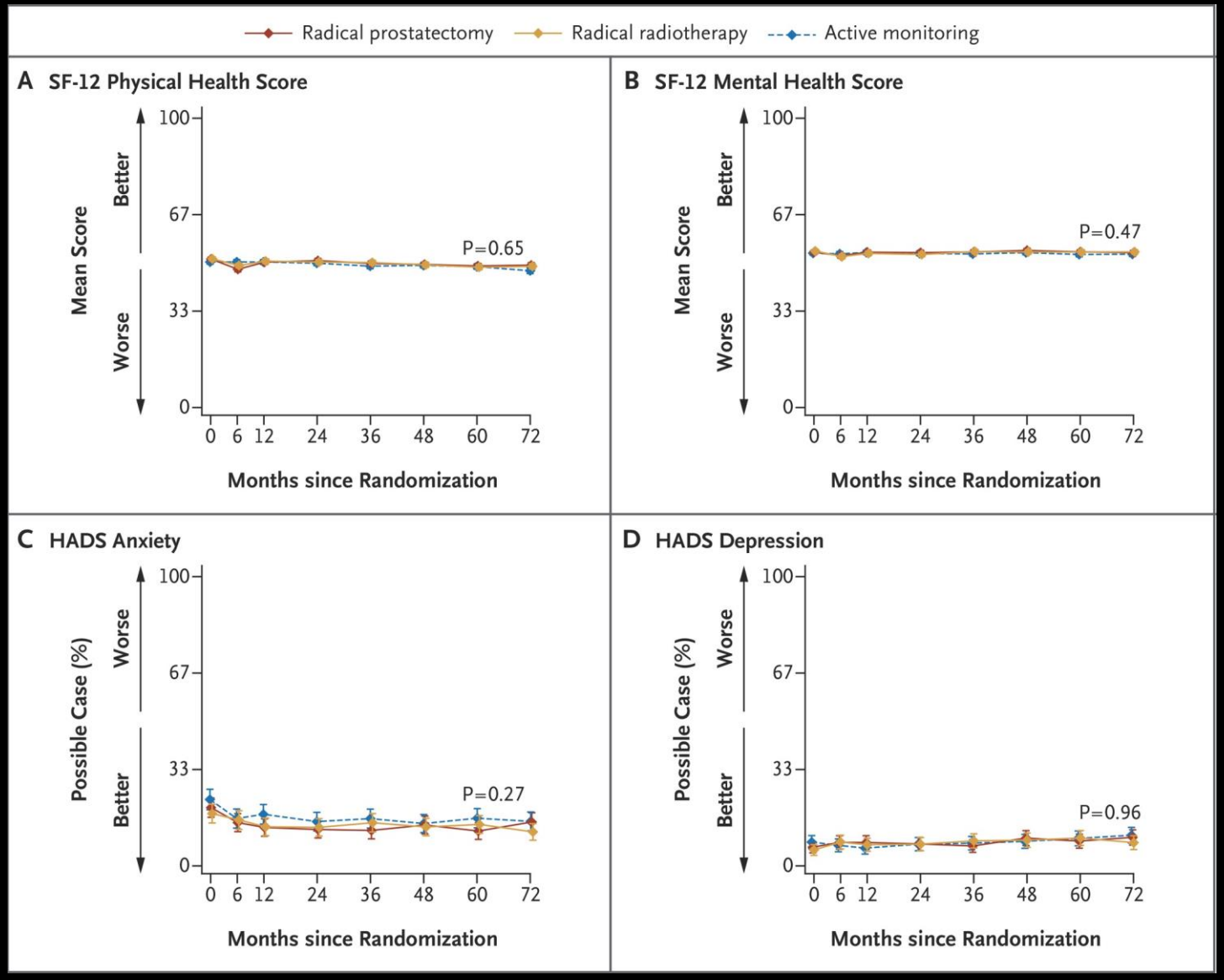
Outcomes for Bowel Function and Effect on Quality of Life.



Donovan JL et al. N Engl J Med 2016;375:1425-1437

The NEW ENGLAND JOURNAL of MEDICINE

Outcomes for Health-Related Quality of Life.



Donovan JL et al. N Engl J Med 2016;375:1425-1437

The NEW ENGLAND JOURNAL of MEDICINE

PortecT trial – number needed to treat

- It was estimated that 27 men would need to be treated with prostatectomy rather than receive active monitoring to avoid 1 patient having metastatic disease
- A total of 9 men would need to be treated with either prostactectomy or radiation to avoid 1 patient having clinical progression.

There is no routine prostate cancer.

The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Rate of Upgrading is not Trivial

- 35% of patients on AS have upgrading of disease on repeat biopsy
- 22-55% are re-/mis-classified
- 50% of men on AS will come to treatment

- mpMRI/US fusion targeted biopsy leads to Gleason upgrading in 32%
  - Detects 80% of index lesions, but misses 53% of non-index lesions with Gleason grade 4, 5
  - MRI remains a crude selection tool with only 85% specificity for high grade cancer

- Further study is needed to assess if advanced imaging/biomarkers can reduce the risk of metastasis in men opting for AS vs immediate treatment

Klotz et al. J Clin Oncol. 2015
Alam et al. J Urol. 2015
Siddiqui et al. Eur Urol. 2013

Summary

- Active surveillance is an evolving strategy
  - It is appropriate in lower-risk, elderly, comorbidities
  - It probably offers the best QOL, lowers costs
  - Needs to be well done
    - ? value of mpMRI, repeat/fusion biopsies, biomarkers = better risk stratification and patient selection
- Unanswered questions:
  - Longer followup needed
  - What frequency of PSA, biopsies, MRI imaging? Should biomarker testing be routine?
  - What should trigger treatment?
  - Is it appropriate in intermediate risk disease? What about younger pts <60?

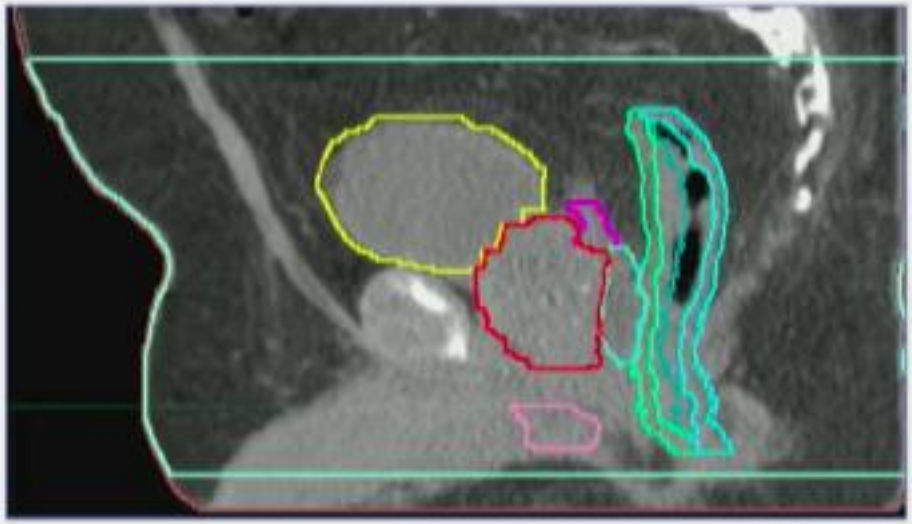
Hayes et al. JAMA 2010; Eldefrawy et al. Urol Oncol. 2011

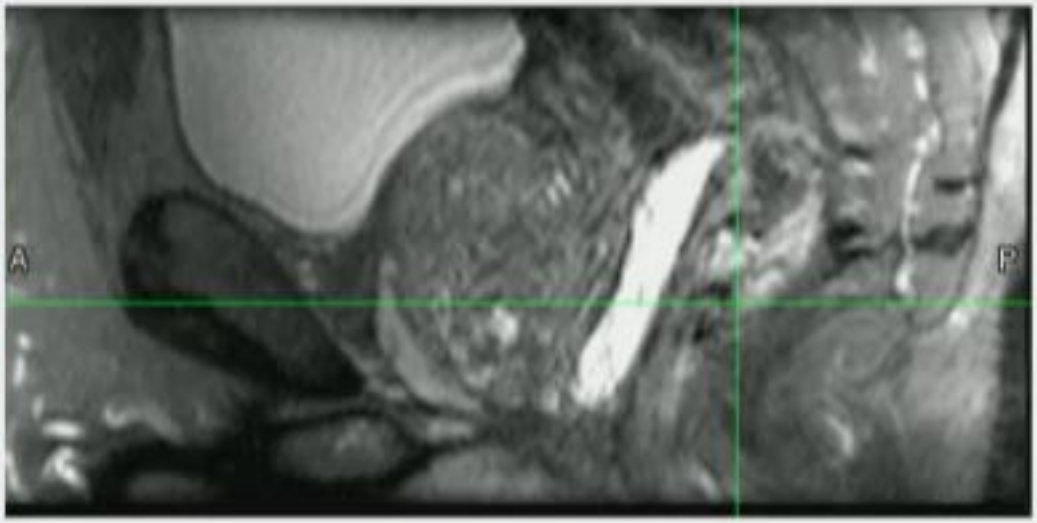
Importance of MultiDisciplinary Care

Treatment	MultiDisciplinary Clinic (n=239)	Individual Practitioners (n=462)	
			p<.001
Prostatectomy (%)	43	56	
External Beam Radiation (%)	7	11	
Brachytherapy (%)	7	10	
Active Surveillance (%)	**43**	**22**	

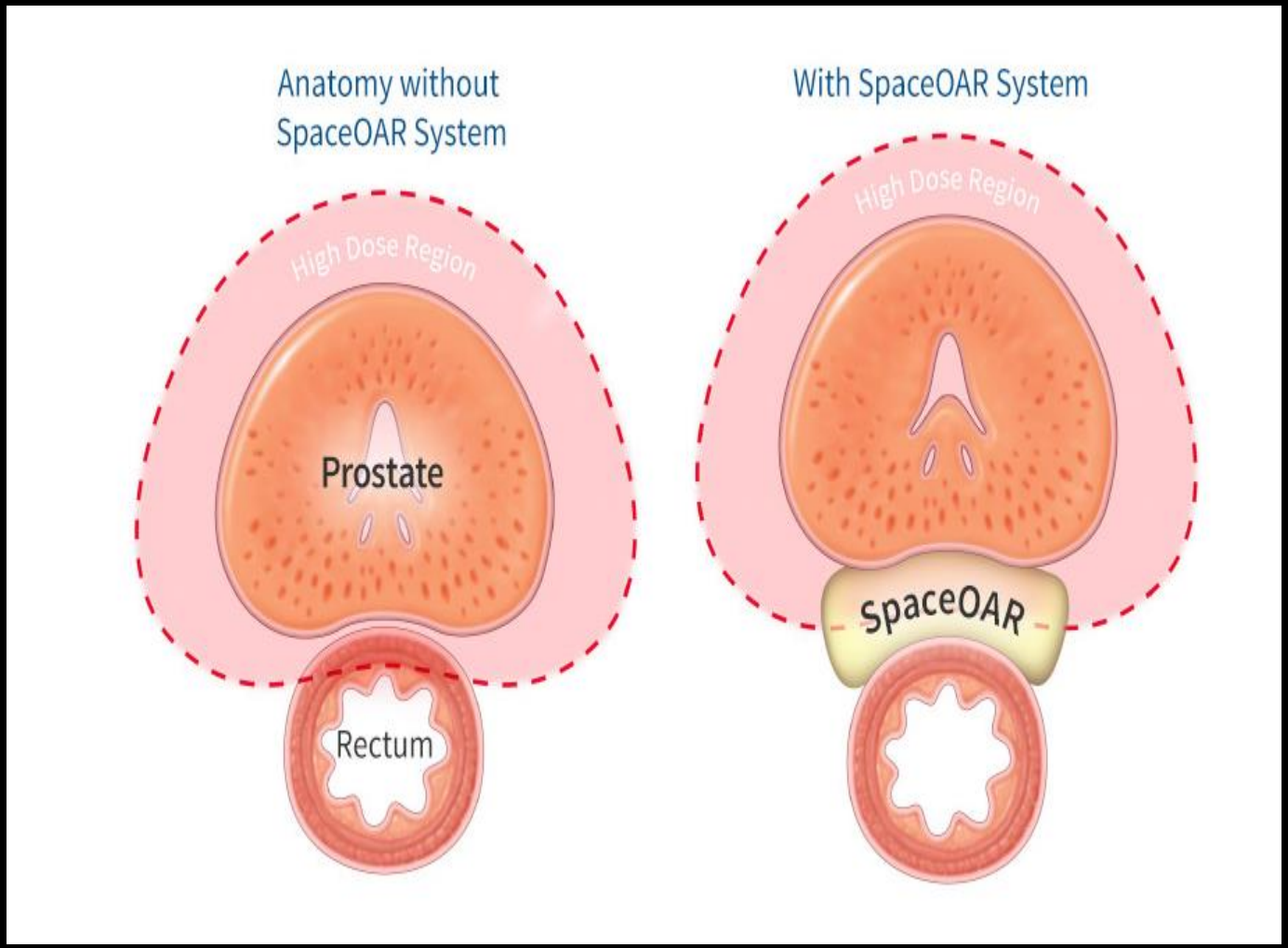
Aizer et al. J Clin Oncol. 2012

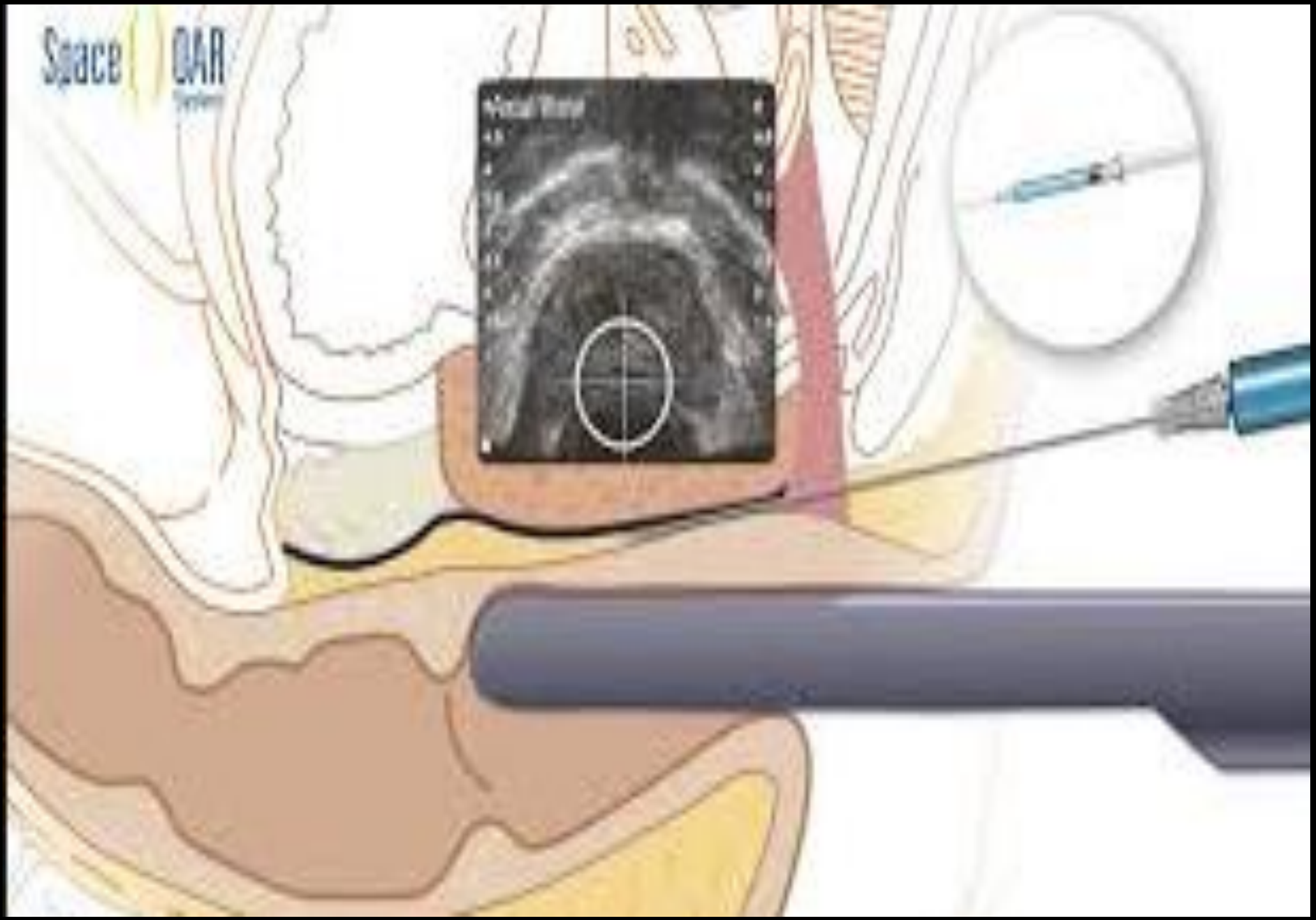
We can decrease toxicity further

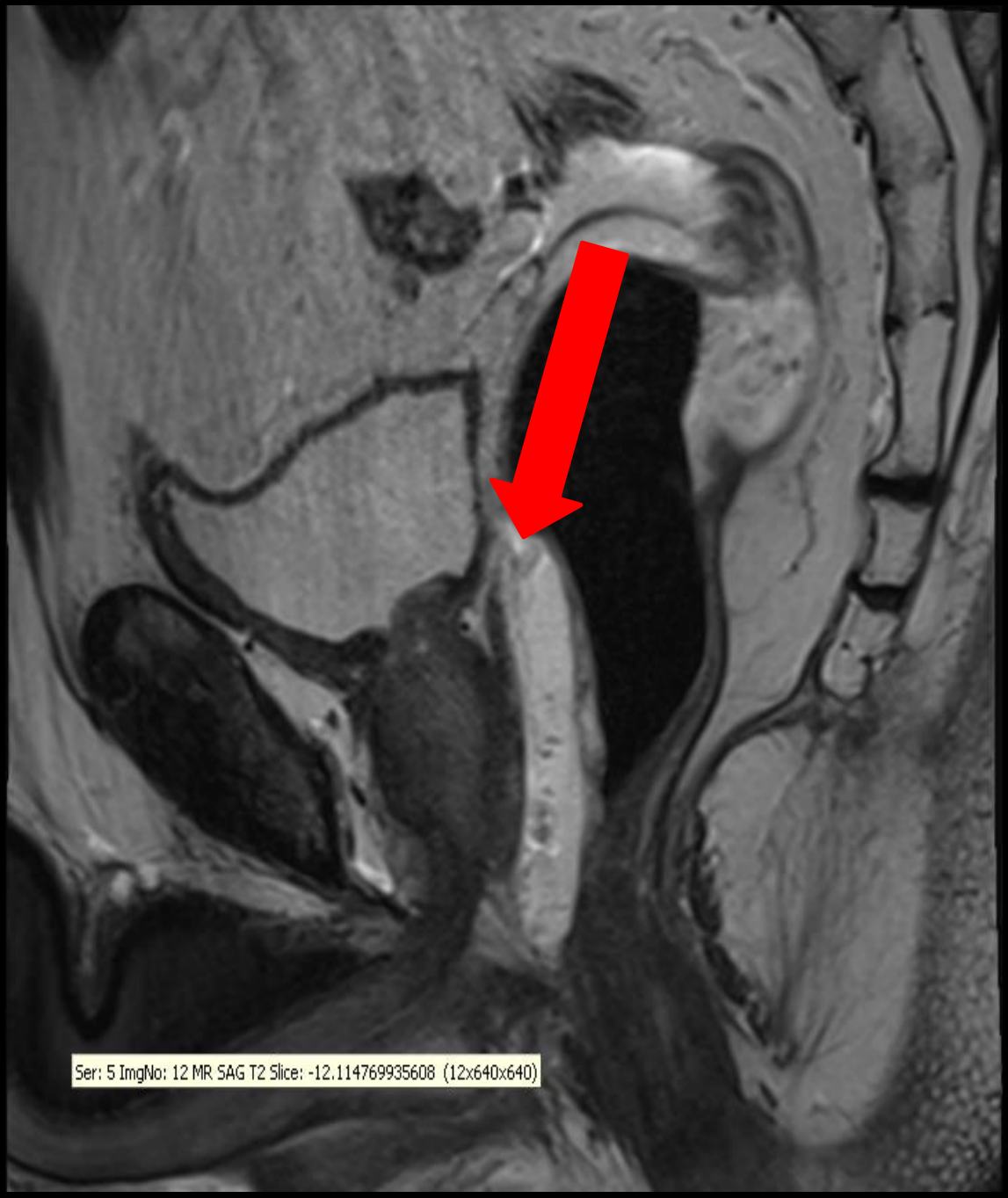




IMRT, VMAT, Proton therapy
Rectal Spacer (Hamstra et al. IJROBP 2017)
Image Guidance
No need for ADT in low risk (RTOG 9408, Jones et al. NEJM 2011)


Anatomy without
SpaceOAR System
High Dose Region
Prostate
Rectum
With SpaceOAR System
High Dose Region
SpaceOAR

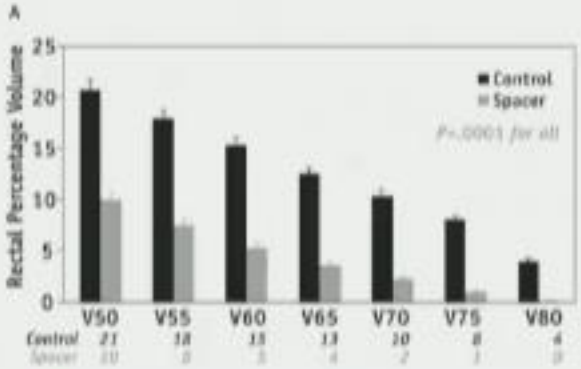

Space OAR


Ser: 5 ImgNo: 12 MR SAG T2 Slice: -12.114769935608 (12x640x640)

Rectal Spacers Reduce Radiation Dose to the Rectum

- An injectable hydrogel to create a rectal-prostate space

CT image MRI image



Reduction In Bowel Dose with Rectal Spacer

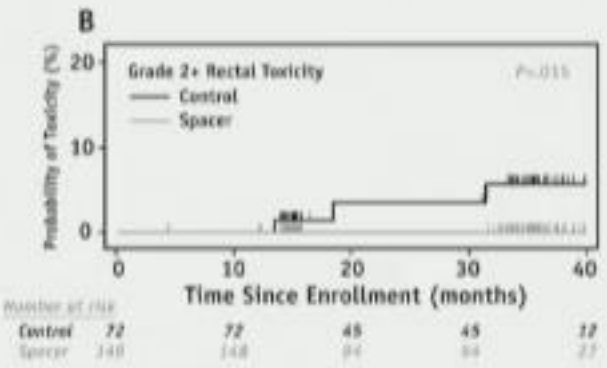
#ASTRO19

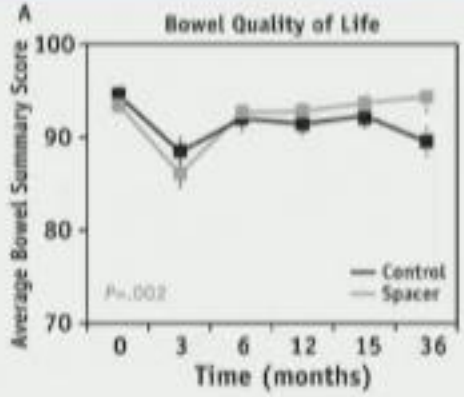
Hamstra DA et al IJROBP 2017; (97):976.

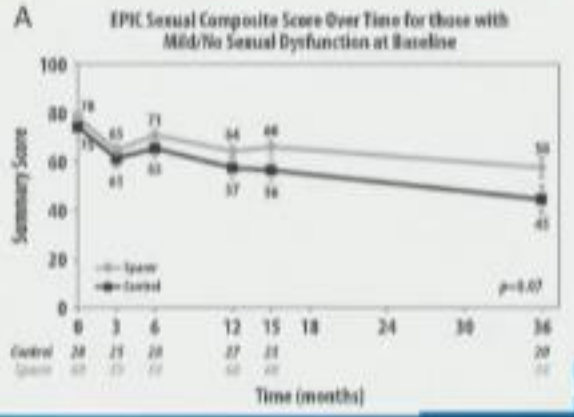
Rectal Spacers Reduce Radiation Dose to the Rectum & Penile Bulb And Subsequent Toxicity

- Reduces both physician-reported and patient-reported bowel toxicity
- Improves patient-reported sexual function among those with good function prior to treatment

Physician-reported Grade 2+ Bowel Toxicity	Patient-reported EPIC Bowel Quality of Life	Patient-reported EPIC Sexual Quality of Life Among Those with Good Baseline Function







Hamstra DA et al IJROBP 2017; (97):976; Hamstra DA et al PRO 2018; (8):e7.

Selecting Patients for Rectal Spacers

- The randomized trial demonstrating benefit enrolled men with low and intermediate-risk prostate cancer
- It excluded men with >50% cores, men on ADT, and men whose disease had extracapsular extension

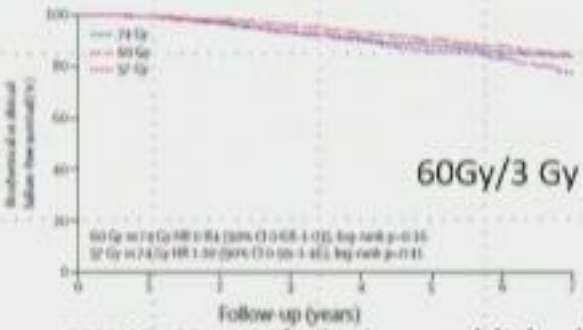
- I use it for men in all risk groups, especially if administering hypofractionation to help achieve bowel dose constraints
- I do not place if men have posterior extraprostatic extension

We can increase convenience
Hypofractionation (CHHiP, RTOG 0415, PROFIT)

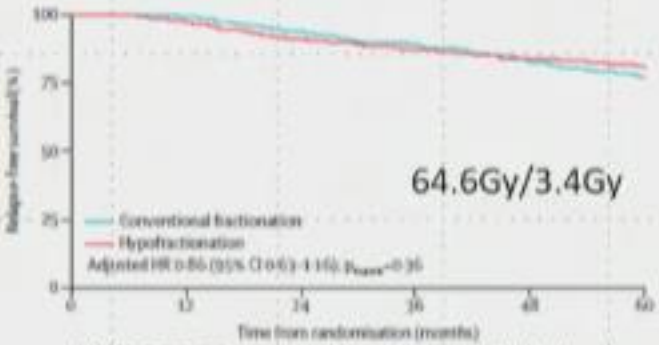
- Patient convenience
- Better resource utilization
- Lower treatment costs
- Potential for therapeutic gain

(Ritter et al. Cancer J. 2009)

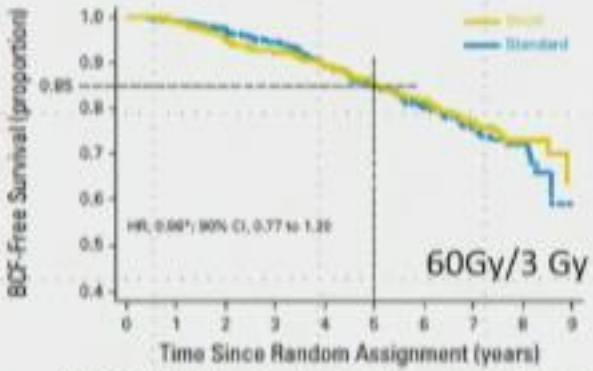
Moderate Hypofxn Provides Similar Cancer Control



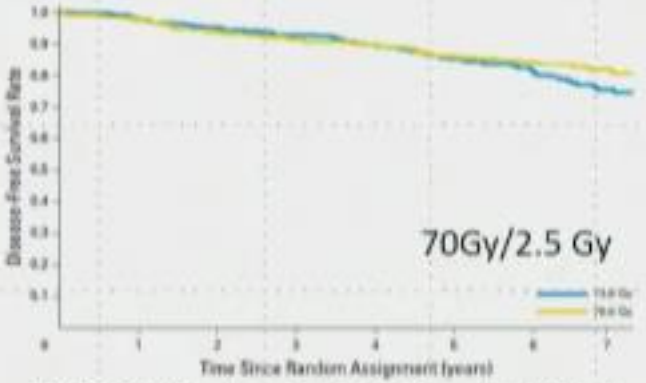
CHHiP: Non-inferiority established for 60 Gy/20 but not for 57 Gy/19



HYPRO: Superiority not established



PROFIT: Non-inferiority established



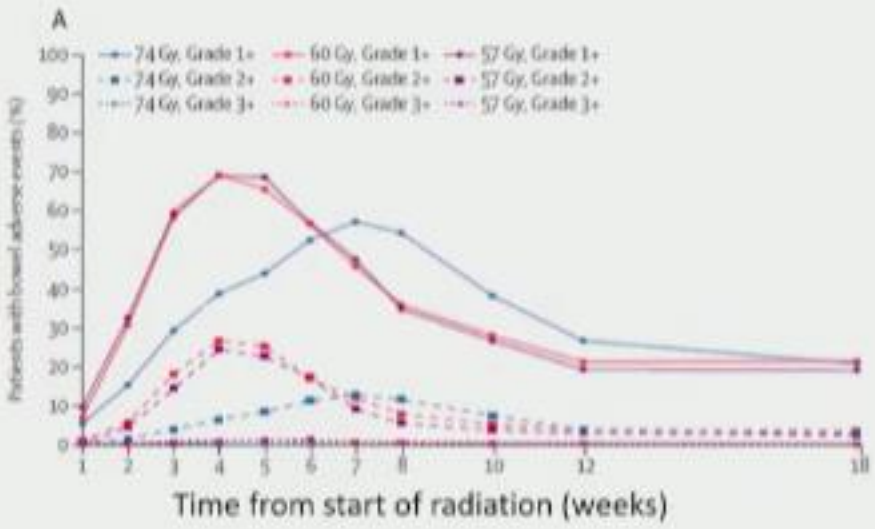
RTOG 0415: Non-inferiority established

1. Dearnaley DP *Lancet Oncol* 2016; 17(8): 1047-1060.
2. Catton C *JCO* 2017; 35(17): 1884-1890.
3. Incrocci L *Lancet Oncol* 2016; 17 (8): 1061-1069.
4. Lee WR *JCO* 2016; 34(20): 2325-2332.

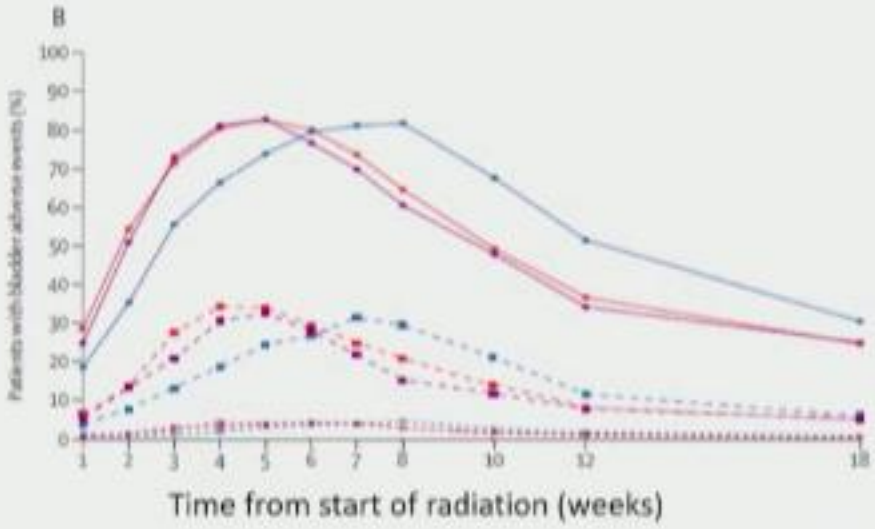
Acute Toxicity Occurs Earlier in Time with Moderate Hypofractionation

- Illustrated by the CHHiP trial

Patients with bowel adverse events



Patients with bladder adverse events



#ASTRO19

Moderate Hypofxn has a Similar Risk of Acute GU Toxicity and Greater Risk of Acute GI toxicity

Trial	Study arms/ EQ2	Acute G2+ GU Toxicity	Acute G2+ GI Toxicity
CHHiP	7400 in 200 cGy/ 7400 cGy 6000 in 300 cGy/ 7700 cGy 5700 in 300 cGy/ 7300 cGY	SIMILAR	INCREASED RISK w/ HYPOFXN 25% vs. 38% (hf) vs. 38% (hf); p<0.0001
PROFIT	7800 in 200 cGy/ 7800 cGy 6000 in 300 cGy/ 7700 cGy	SIMILAR	INCREASED RISK w/ HYPOFXN 10% vs. 16% (hf); p=0.003
HYPRO	7800 in 200 cGy/ 7800 cGy 6460 in 340 cGy (3/wk) /8700 cGy	SIMILAR	INCREASED RISK w/ HYPOFXN 31% vs. 42% (hf); OR 1.6, 95% CI: 1.19-2.14
Italian	8000 in 200 cGy/ 8000 cGy 6200 in 310 cGy/ 8100 cGy	SIMILAR	TREND INCREASED RISK w/ HYPOFXN 21% vs. 35% (hf) p=0.07
RTOG 0415	7380 in 180 cGy/ 7000 cGy 7000 in 250 cGy/ 8000 cGy	SIMILAR	SIMILAR

Moderate Hypofxn has a Similar Risk of Late GU and Late GI Toxicity

- Trials that deliver similar biologic dose

Trial	Study arms/ EQ2	Follow Up	Late G2+ GU Toxicity	Late G2+ GI Toxicity
CHHiP	7400 in 200 cGy/ 7400 cGy 6000 in 300 cGy/ 7700 cGy 5700 in 300 cGy/ 7300 cGy	5.2 years	SIMILAR	SIMILAR
PROFIT	7800 in 200 cGy/ 7800 cGy 6000 in 300 cGy/ 7700 cGy	6 years	SIMILAR	LESS IN HYPOFXN 11% vs. 7%, p=0.006
Italian	8000 in 200 cGy/ 8000 cGy 6200 in 310 cGy/ 8100 cGy	9 years	SIMILAR	SIMILAR

Men Treated with Moderate Hypofxn Report Similar Patient Reported Symptoms

Trials	Study arms/ EQ2	Bowel	Bladder	Sexual
CHHiP	7400 in 200 cGy/ 7400 cGy 6000 in 300 cGy/ 7700 cGy 5700 in 300 cGy/ 7300 cGy	SIMILAR	SIMILAR	SIMILAR
RTOG 0415	7380 in 180 cGy/ 7000 cGy 7000 in 250 cGy/ 8000 cGy	LARGER DECLINE w/ HYPOFXN Not clinically significant difference	SIMILAR	SIMILAR
MD Anderson	7560 in 180 cGy/ 7100 cGy 7200 in 240 cGy/ 8000 cGy	SIMILAR	SIMILAR	SIMILAR
Fox Chase	7600 in 200 cGy/ 7600 cGy 7020 in 270 cGy/ 8400 cGy	SIMILAR	TREND TOWARD WORSE INCONTINENCE	SIMILAR

Moderate Hypofractionation Regimens

- The strongest evidence supports 6000 cGy in 300 cGy fractions over 4 weeks
  - Used in two different RCTs
  - Tested in all risk groups
  - Evaluated in both the presence and absence of ADT
- ASTRO-ASCO-AUA guideline task force group also favored 7000 cGy in 250 cGy fractions over 5.6 weeks

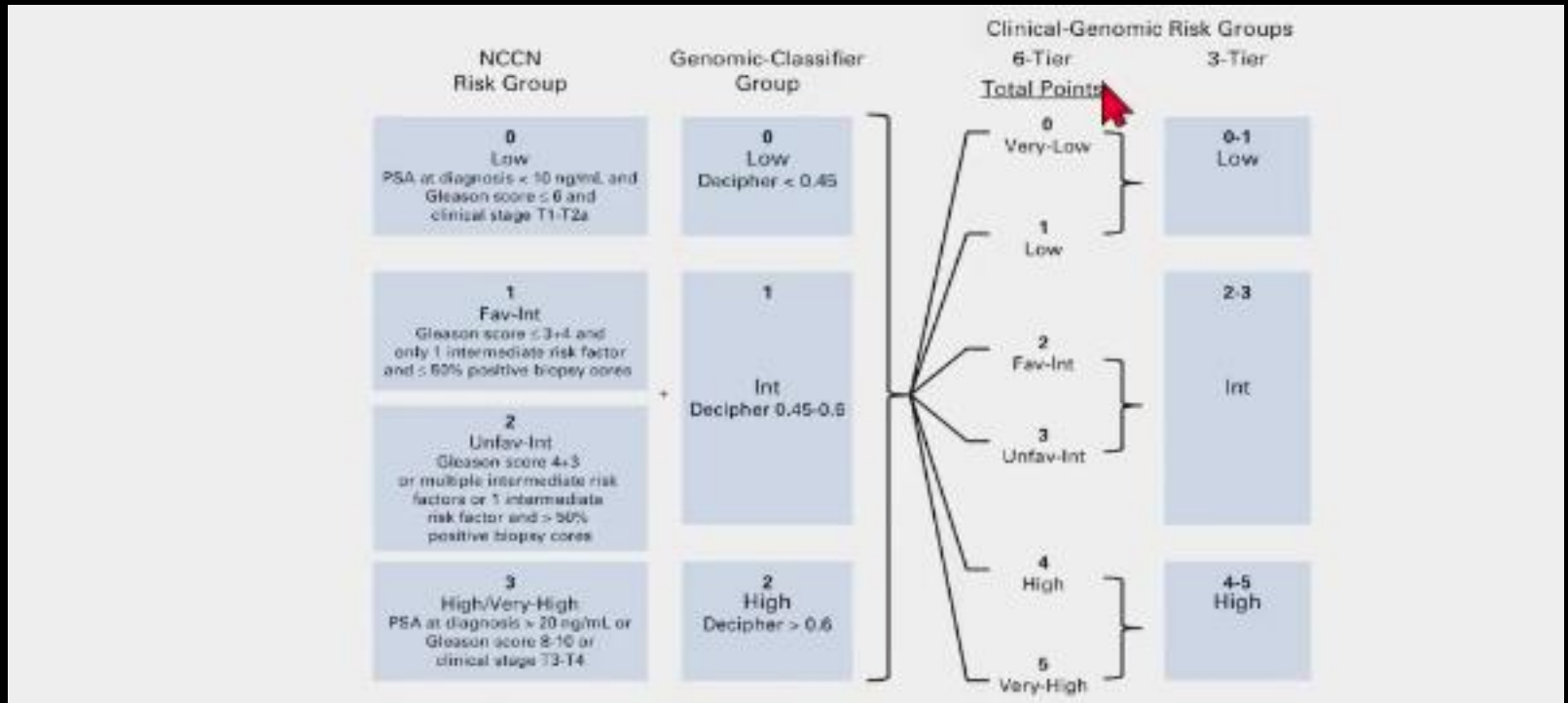
- The HYPRO hypofractionated regimen was not preferred by the task force
  - 6460 cGy in 340 cGy delivered three days a week over 6.4 wks
  - Was associated with greater late grade 3 or higher GU toxicity

Ultrahypofractionation For Unfavorable-Intermediate Risk Disease

- Ultrahypofractionaion is currently NOT recommended by NCCN guidelines for Unfavorable-Intermediate Risk disease.
  - It is only recommended for Low and Favorable-Intermediate Risk Disease.
- ASTRO-ASCO-AUA fractionation guideline conditionally recommends ultrahypofractionated EBRT in low-risk and intermediate-risk disease
  - Enrollment on clinical trials or multi-institutional registries is strongly encouraged for intermediate-risk disease.
- I only treat men with Unfavorable-Intermediate Risk disease with ultrahypofractionation on a clinical trial.

Ongoing Trials Will Help Us Understand the Role of Ultrahypofractionation

Trial	Planned Accrual	Population	Primary Endpoint	Ultrahypo-fractionated Regimen	Comparator Regimen
HEAT	456	Low and Intermediate	Biochemical or clinical failure	3625 cGy/5	7020 cGy/26
HYPO-RT-PC	1200	Intermediate and High	Biochemical or clinical failure	4270 cGy/7	7800 cGy/39
NRG-GU005	622	Intermediate (Gleason ≤3+4)	HRQOL DFS	3625 cGy/5	7000 cGy/28
PACE B	858	Low and Intermediate (Gleason ≤3+4)	Biochemical or clinical failure	3625 cGy/5	7800 cGy/39 or 6200 cGy/20



Spratt, Daniel E., ..., Pollack A, Stoyanova R, ... *et al.* "Development and validation of a novel integrated clinical-genomic risk group classification for localized prostate cancer." *Journal of Clinical Oncology* 36.6 (2018): 581-590.

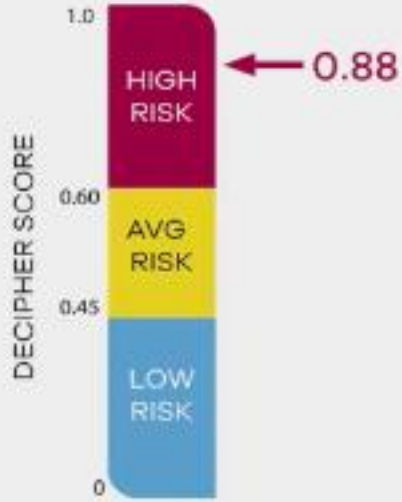
Decipher

Tumor Tissue

RNA Extraction

ZWILCH		
UBE2C	UBE2C	TNFRSF19
TNFRSF19	TNFRSF19	S1PR4
S1PR4	S1PR4	IQGAP3
IQGAP3	IQGAP3	MYBPC1
MYBPC1	MYBPC1	PCDH7
PCDH7	PCDH7	PBX1
PBX1	PBX1	EPPK1
EPPK1	EPPK1	THBS2
THBS2	THBS2	EPPK1
EPPK1	EPPK1	THBS2
	THBS2	RABGAP1

Whole Transcriptome Microarray



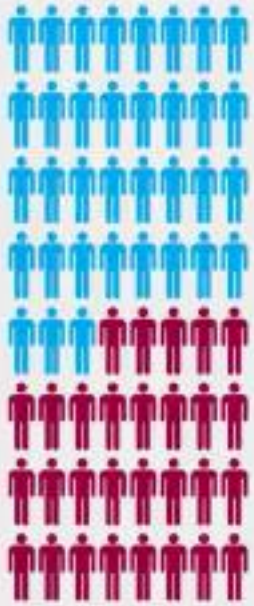
Decipher Score

Decipher Was Developed to Predict Metastasis

MAYO CLINIC

Tumor Registry
639 Post-RP Patients
1987-2001

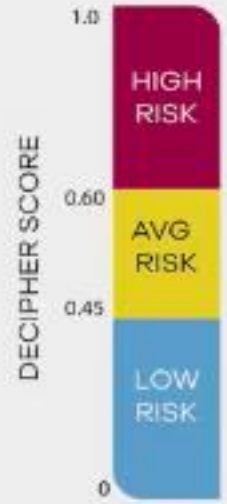
426 No Metastasis



213 Metastasis

Whole Transcriptome Analysis

22 genes across **7** cancer pathways



Decipher Score

Decipher Does Not Incorporate Clinical Features in Predicting Individualized Risk

Prolaris

oncotypeDX
Genomic Prostate Score

Tumor Data

Clinical Features

$$Risk\ \% = \sum_{n=0}^{n=k} bx_n + cy_n$$

Algorithm

% Risk

Individualized Risk

DECIPHER
PROSTATE

Tumor Data

$$Risk\ \% = \sum_{n=0}^{n=k} bx_n + cy_n$$

Algorithm

% Risk

Individualized Risk

Decipher has the most comprehensive data

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2019 Prostate Cancer

Table 1. Available Tissue-Based Tests for Prostate Cancer Risk Stratification/Prognosis

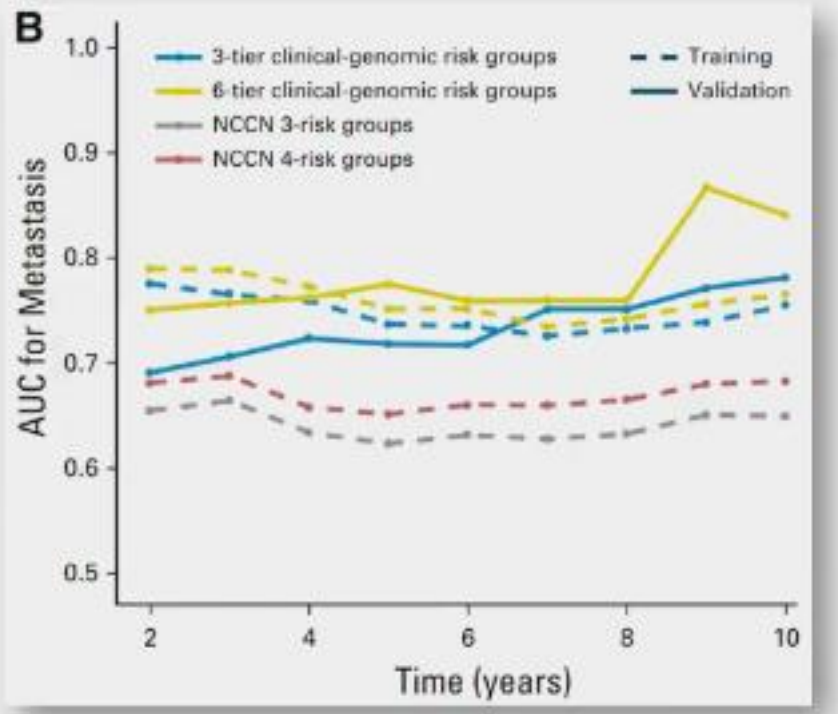
Test	Platform	Populations Studied	Outcome(s) Reported (Test independently predicts)	Selected References
Decipher	Whole-transcriptome 1.4M RNA expression (44,000 genes) oligonucleotide microarray optimized for FFPE tissue	Post radical prostatectomy (RP), adverse pathology/high-risk features	• Metastasis • Prostate cancer-specific mortality • Postoperative radiation sensitivity (PORTOS)	140,143,144,243 ,671,731-743
		Post RP, biochemical recurrence	• Metastasis • Prostate cancer-specific mortality • PORTOS	
		Post RP, adjuvant, or salvage radiation	• Metastasis • Prostate cancer-specific mortality • PORTOS	
		Biopsy, localized prostate cancer post RP or EBRT	• Metastasis • Prostate cancer-specific mortality • Gleason grade ≥4 disease at RP • Adverse pathologic features at RP	

Primary test used and approved for post-RP with adverse path

Also approved for pre-tx Biopsy:
-Very low risk
-Low risk
-Fav intermediate risk

Only test approved for:
-Unfav intermediate risk

AUC of 0.84 to predict metastatic disease



Clinical-Genomic

Zumsteg/MSKCC

D'Amico

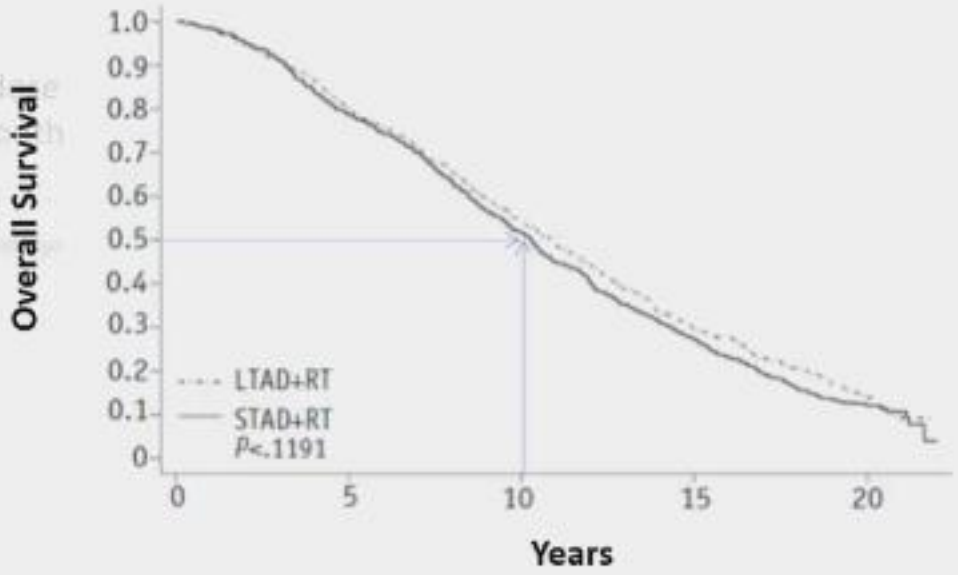
Spratt DE, JCO 2018

Taking a step back (putting the debate aside)

Accepting the reality:

~50% of men die within the first 10 years post-RT

80-90% die of **other-causes**



RTOG 9202

Taking a step back (putting the debate aside)

Trying to reduce this:

~15% distant mets at 20 years

Low dose EBRT
28 months ADT

Minimize Toxicity:

EBRT side effects:

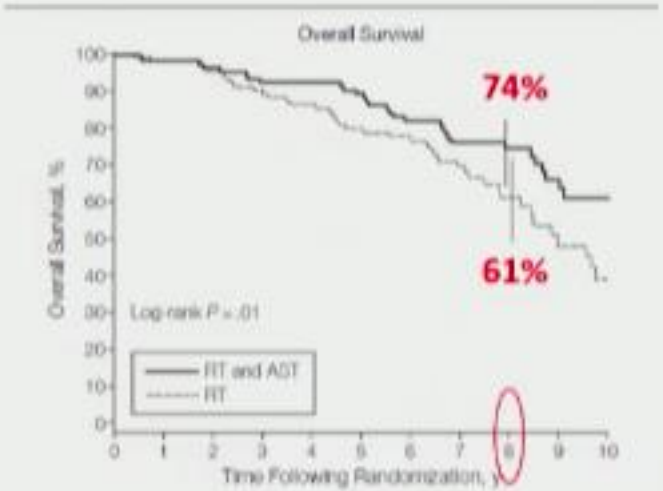
- 1-3% grade 3 toxicity
- 10-20% grade 2 toxicity
- 20-50% loss of erectile function

ADT side effects

RTOG 9202

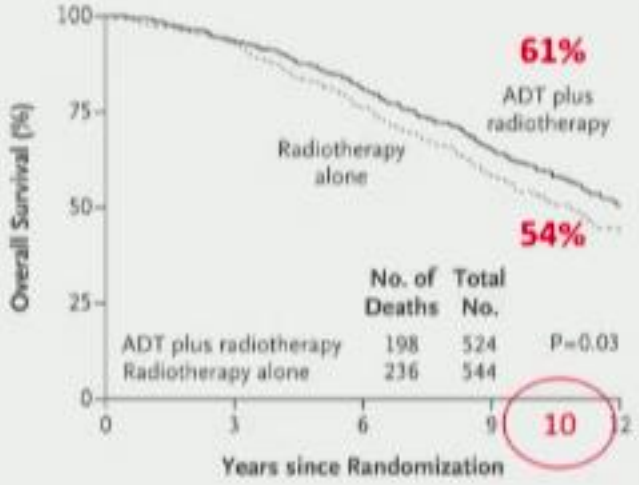
Four to Six months of ADT Improves Survival for Men with Intermediate-Risk Prostate Cancer

Harvard/DFCI 95-096*
70 Gy, +/- 6 mo ADT



Intermediate (73%) & High-risk patients

RTOG 94-08
66 Gy, +/- 4 mo ADT



Intermediate-risk patient subgroup

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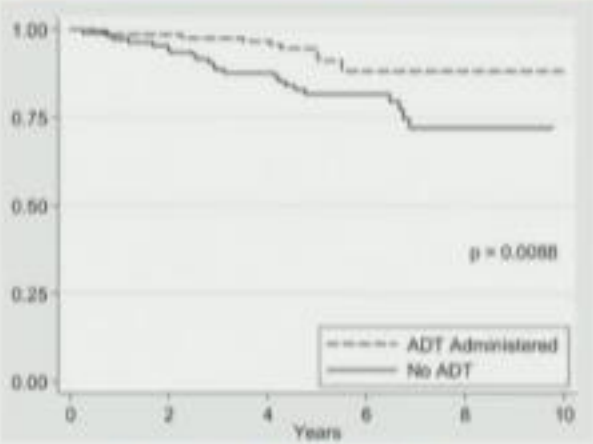
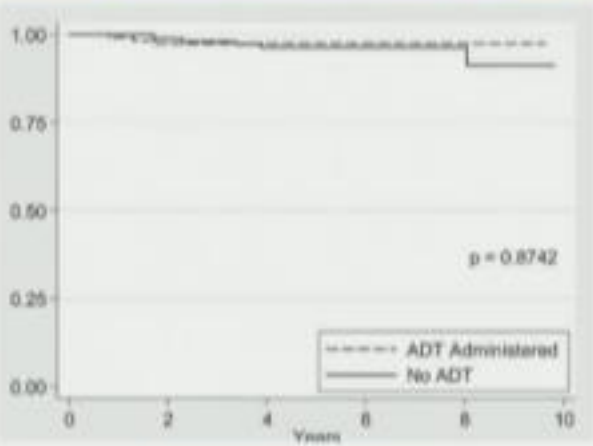
D'Amico AV JAMA 2008, 299 (3):289; Jones CU et al NEJM 2011; 365(2):107.

Men with Unfavorable-Intermediate Risk Disease Appear to Benefit From ADT

- Retrospective analyses suggest Unfavorable-Intermediate but not Favorable-Intermediate Risk disease benefits from ADT

Unfavorable-Intermediate Risk	Favorable-Intermediate Risk





Improved failure-free survival associated w/ ADT

No improvement in failure-free survival w/ADT

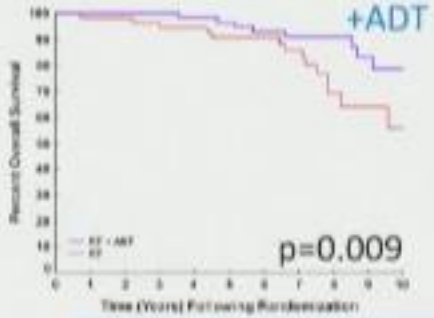
#ASTRO19

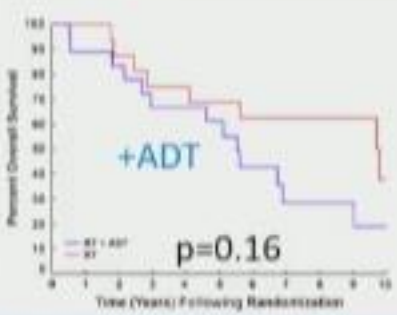
Bian S Annals of Oncology 2012 23(9):2346.

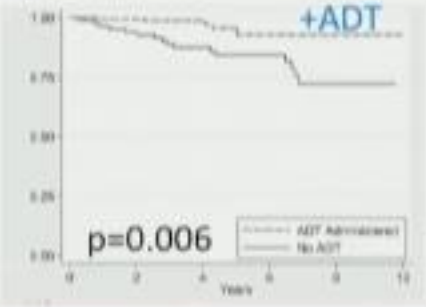
Some Men with Unfavorable-Intermediate Risk Disease May Not Benefit from ADT

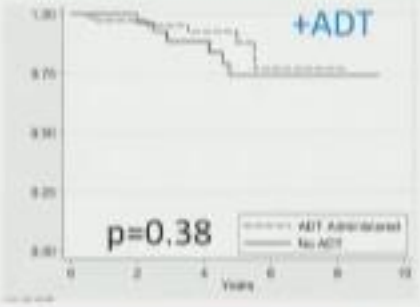
- In post-hoc &retrospective analyses only those men with no/mild comorbidity benefited from ADT

Post-hoc analysis of men with intermediate-risk disease treated on 95-06 (overall survival)		Retrospective analysis of men with intermediate-risk disease treated w/ dose-escalated EBRT (failure-free survival)	
No/mild comorbidity	Moderate/severe comorb	No/mild comorbidity	Moderate/severe comorb









ADT side effects include hot flashes, fatigue, erectile dysfunction, decreased libido, weight gain.

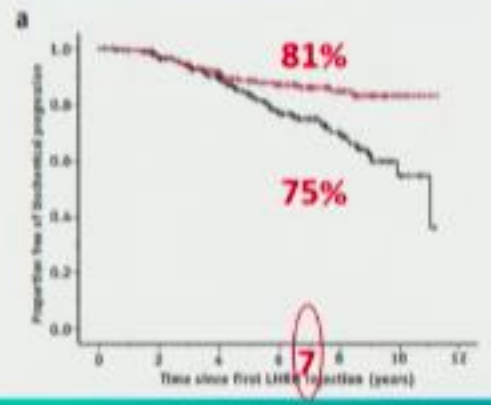
#ASTRO19

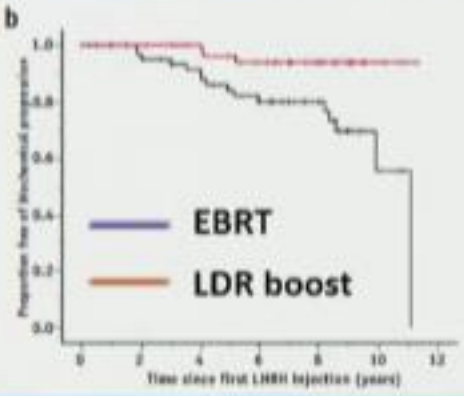
Nguyen PL IJROBP 2010, 77 (4): 1046; Bian S Annals of Oncology 2012 23(9):2346.

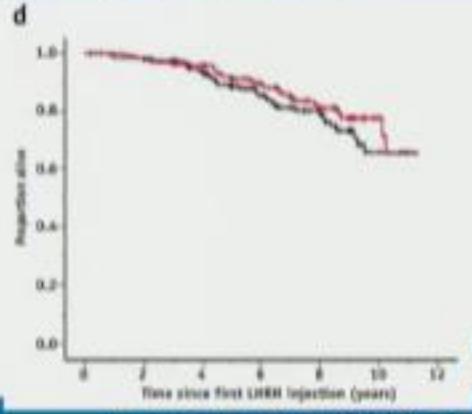
ASCENDE RT Demonstrates Improved Biochemical PFS w/ Brachy Boost

- Men w/ intermediate & high risk prostate cancer received 46 Gy whole pelvic radiation and 12 months of ADT
- Randomized to ^{125}I brachytherapy boost (115 Gy) or EBRT boost (32 Gy)
- No overall survival benefit has been demonstrated

All Patients (biochemical PFS)	Intermediate-Risk Patients (n=122, biochemical PFS)	All Patients (overall survial)







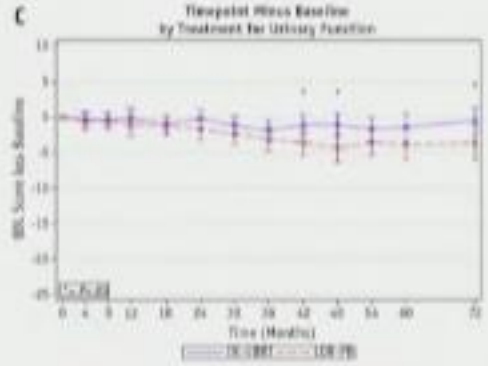
#ASTRO19

Morris WJ et al IJROBP 2017, 98(2): 275.

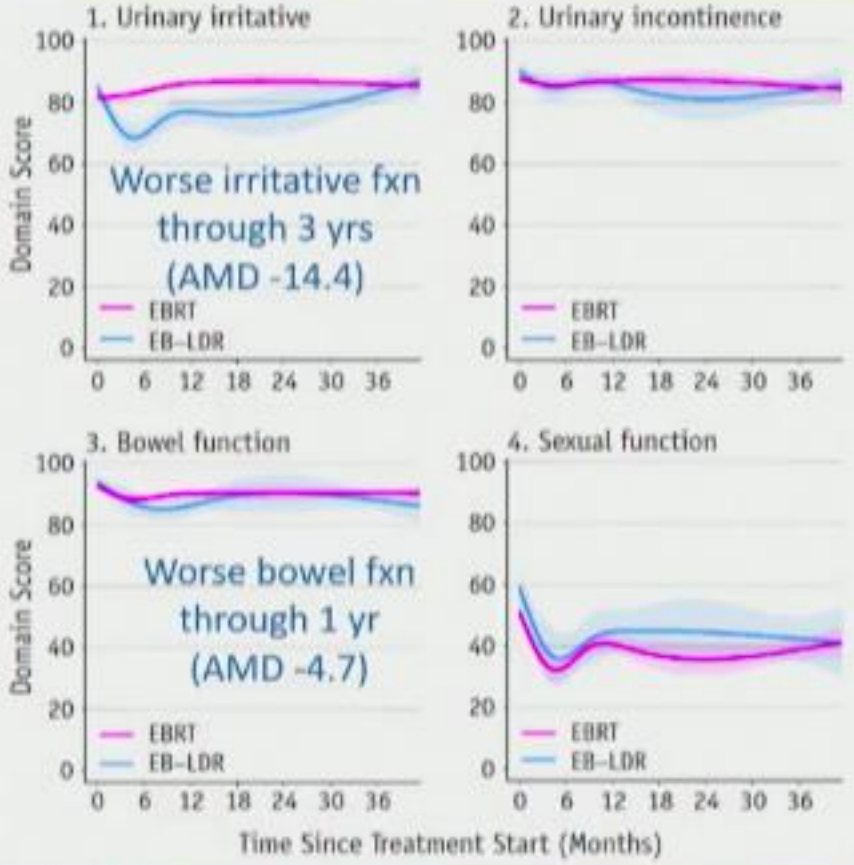
Brachytherapy Boost Increases Side Effects

ASCENDE RT

- Brachy boost increased the risk of physician-reported grade 3 urinary compilations, urinary incontinence and need for catheterization
- Greater decline in patient reported urinary function



Prospective Population-Based Cohort



Rhodda S IJROBP 2017 98(3):581. Lee DJ IJROBP 2018 Annals of Oncology 2012 102(1):116.

Background

- The optimal treatment for high-risk prostate cancer (PCa) remains unclear, with three standard of care options supported by the NCCN and EAU
  - EBRT with 2-3 years of ADT
  - EBRT+BT with 1*-3 years of ADT
  - RP with or without postoperative therapies

- Limited prospective data exist, with only one ongoing randomized study (SPCG-15)

- Numerous retrospective comparisons have been reported
  - Older reports largely did not account for standard of care utilization of ADT with RT, and found large benefits to surgery