Mack Roach III MD
Professor of Radiation Oncology and Urology
University of California San Francisco

UCSF Helen Diller Family Comprehensive Cancer Center

What unusual cases teach us:

The “Art of Radiotherapy” for Clinically Localized Prostate Cancer

UCSF Helen Diller Family Comprehensive Cancer Center

ART (a "broad" definition):

"Art … is the province of every human being. It is simply a question of doing things, anything, well. … whatever his kind of work may be, he becomes an inventive, searching, daring ... He disturbs, upsets, enlightens … Where those who are not artists are trying to close the book, he opens it …". "He does not have to be a painter or sculptor … He can work in any medium. He simply has to find the gain in the work itself, not outside it."

"It is harder to *see* than it is to express …" and … others can often "draw" remarkably well." <u>So then, seeing is the rate-limiting step</u>!

Robert Henri the famous Art Teacher in "Art Spirit"

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Disclosures:

- Full-time faculty from UCSF
- Consulted for almost every drug company providing drugs for treating prostate cancer (most recently Astellas)
- Served on Advisory Board for Accuray
- Up-to Date Prostate Cancer
- NCCN Prostate Guidelines
- No other relevant disclosures

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Goals of this Presentation (40 min.):

1. Data from phase III RCTs ***should*** drive our management of patients with prostate ca. BUT there are limitations due to:
   a) The sparce number of trials
   b) Heterogeneous nature of the disease, but limited eligibility
   c) Limited interventions explored (dose vs volume vs ADT …)
2. Unusual cases can teach because:
   a) Less limited interventions, eligibility and interventions
3. Examples of cases that changed the way I manage prostate ca.:
   a) How aggressive should I be?
   b) PSA? (Low=bad?) High=not bad)? Volume? Large=not so bad?
   c) "The Art of Radiotherapy"

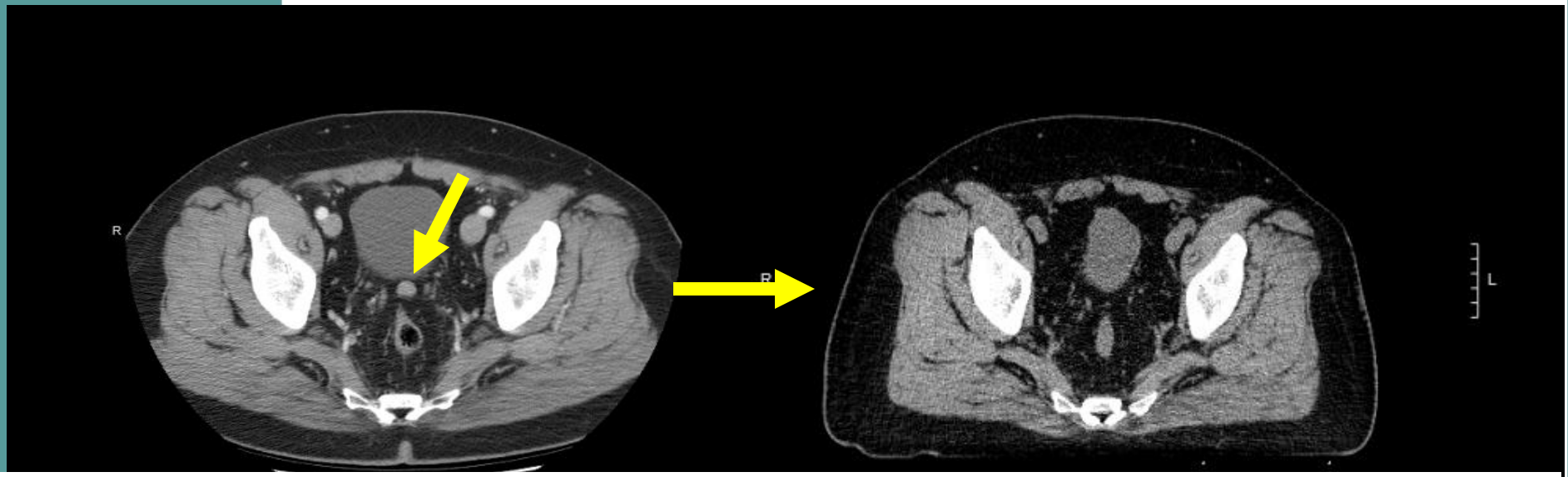
What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #1

61-yo white male with T1c, GS=3+3, PSA 10.2, prostate ca.
Treated with IMRT 79.2 Gy (RTOG 0126) in 2003.

8/1/05 PSA 0.92 **--> 6/29/06 PSA 1.24, T 346 --> 2/14/07 PSA 1.20, T 430 -->**
6/21/07 PSA 2.25 --> 11/9/07 PSA 2.65
5/23/08 PSA 4.85; DRE, Bx and endorectal coil MRI negative
9/15/10 PSA 8.82
11/24/10 MRI/spect: + 8mm hypointense nodule R mid gland toward apex
11/30/10 TRUS/bx: negative
12/21/10 PSA 10.6 and 12/23/10 BS: negative
1/27/11 PSA 11.60 (PSADT 11-12 mos, UCSF PSAs)
2/4/11 CT revealed a + 1.1cm enlarging nodule superior to SV, possibly …



Simulation post NHT

UCSF Helen Diller Family Comprehensive Cancer Center

Quiz case #1

Consider a PSMA+ for a LF only, how would you manage this failure?

A) Intermittent ADT

B) Intensified ADT

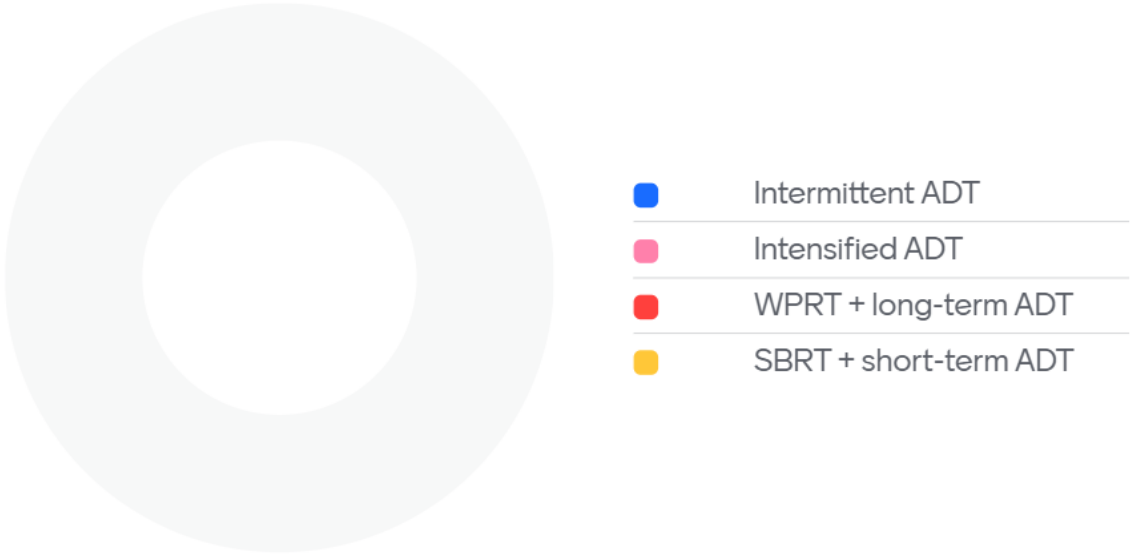
C) WPRT + long-term ADT

D) SBRT + short-term ADT

What unusual Prostate Cancer Cases can teach us

Mentimeter

Consider a PSMA+ for a LF only, how would you manage this failure?



UCSF Helen Diller Family Comprehensive Cancer Center

Case #1 (continued)

Gold seed placed into nodule and Tx NHT then WPRT including PA nodes to 45 Gy (6/8/2011); CyberKnife boost 26 Gy (650 x 4) (7/4/2011) and 2 years of HT. 5 yrs post-treatment (05/23/2016) NED with testosterone 290 & PSA 0.176 ng/ml.

8 yrs post salvage Tx NED (PSA = 0.162 ng/ml (8/30/19), currently alive and well with normal Testosterone

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #1

Lessons Learned:

1. Follow pts especially if the PSA response is suboptimal
2. Node + from outset vs “accessory” prostate tissue vs oligo metastatic Dz?
3. Importance of Image guidance & SBRT motion tracking
4. “If you don’t treat for cure, you won’t cure those you treat” – Phillips

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #2

55-year-old, African-American with a Gleason score of 4+4 T3c, with + SVs and bulky para-aortic and pelvic adenopathy & a pretreatment PSA of 3,900 ng/ml, DX'd early 2001

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Quiz case #2

How would you manage this patient?

A) Doublet with ADT and ARPI

B) Triplet with chemo

C) Extended WPRT + long term ADT

D) Extended WPRT + long term doublet

E) Prostate RT + life long ADT

What unusual Prostate Cancer Cases can teach us

How would you manage this patient?

- Doublet with ADT and ARPI
- Triplet with chemo
- Extended WPRT + long term ADT
- Extended WPRT + long term doublet
- Prostate RT + life long ADT

UCSF Helen Diller Family Comprehensive Cancer Center

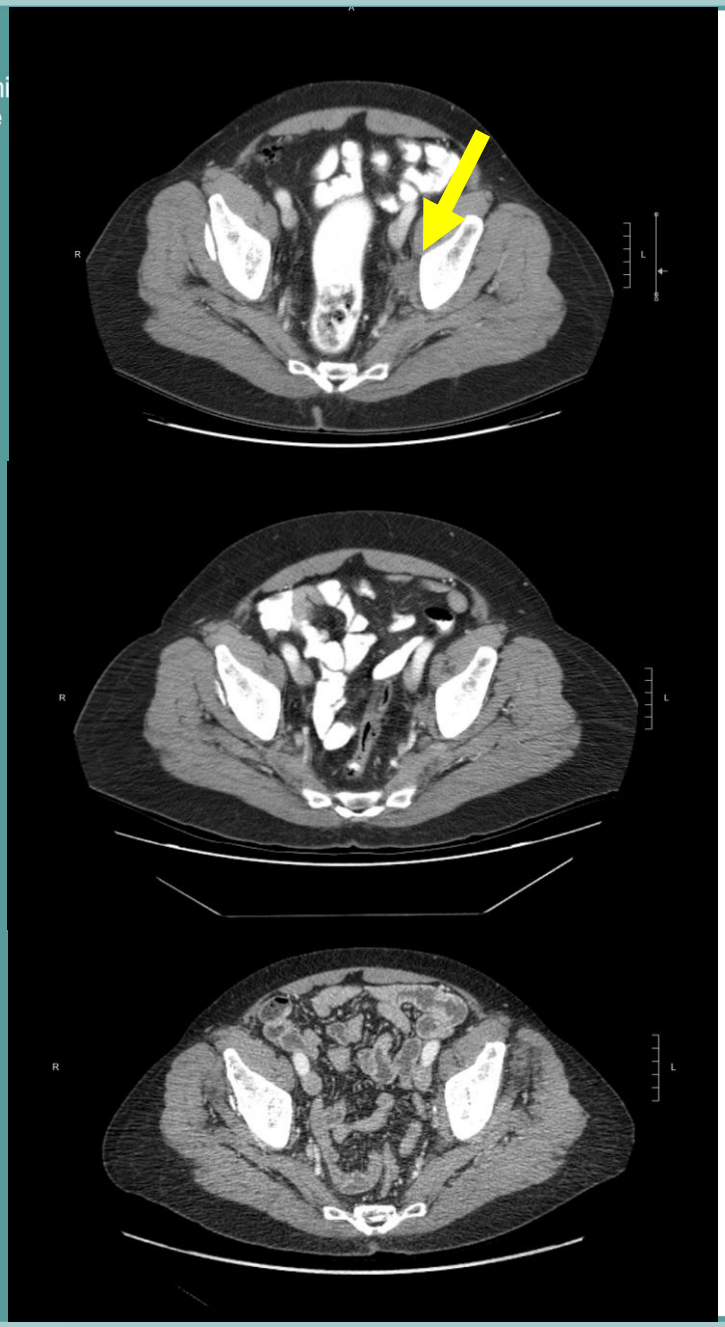
Case #2

Treatment:
NHT + finasteride treated with IMRT 72 Gy to the prostate and para-aortic RT ~ 60 Gy to bulky nodes 4/3/2001 thru 6/4/2001.

Tolerated treatment well

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center



Serial post RT CT Scans

3/26/01 – (Post ADT) Radiation Oncology treatment CT images showed an interval decrease in the left obturator adenopathy, which currently measures 1.7 x 2.6 cm.

2/18/03 - Previously seen left obturator lymphadenopathy slightly decreased in size, currently measuring 1.0 cm in short axis, with no evidence of new lymphadenopathy.

12/7/09 - No evidence of metastatic disease in the abdomen or pelvis.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #2 (contd.)

PSA Lab Results		
Component	Value	Date
PSA	<0.015	8/5/2015
PSA	<0.015	1/22/2015
PSA	<0.015	7/29/2013
PSA	0.063	6/11/2012
PSA	<0.02	9/29/2004
PSA	<0.02	9/25/2003
PSA	<0.02	3/11/2003
PSA	<0.02	11/8/2002

Currently alive and well 6/2021

with an undetectable PSA!

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

CLINICAL INVESTIGATION

IMPACT OF ULTRAHIGH BASELINE PSA LEVELS ON BIOCHEMICAL AND CLINICAL OUTCOMES IN TWO RADIATION THERAPY ONCOLOGY GROUP PROSTATE CLINICAL TRIALS

George Rodrigues, M.D. M.Sc.,* Kyounghwa Bae, Ph.D.,† Mack Roach, M.D.,‡ Colleen Lawton, M.D.,¶ Bryan Donnelly, M.D.,§ David Grignon, M.D.,** Gerald Hanks, M.D.,†† Arthur Porter, M.D.,‡‡ Herbert Lepor, M.D.,¶¶ and Howard Sandler, M.D.§§

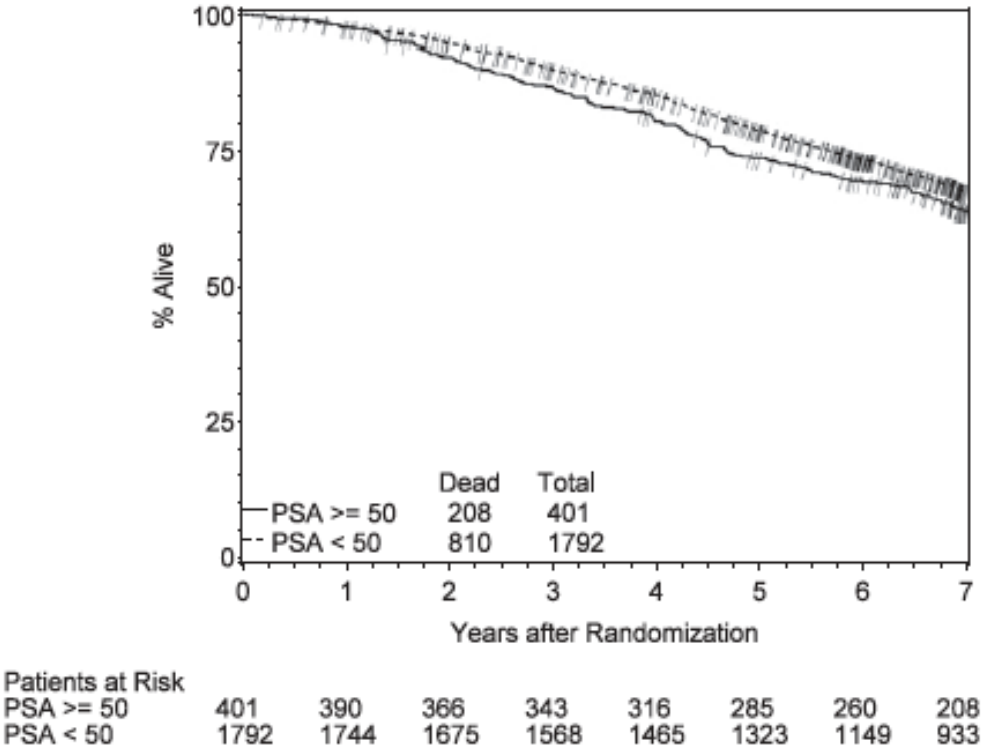


Fig. 1. Overall survival stratified by PSA group.

What unusual Prostate Cancer Cases can teach us

IMPACT OF ULTRAHIGH BASELINE PSA LEVELS ON BIOCHEMICAL AND CLINICAL OUTCOMES IN TWO RADIATION THERAPY ONCOLOGY GROUP PROSTATE CLINICAL TRIALS

GEORGE RODRIGUES, M.D. M.SC.,* KYOUNGHWA BAE, PH.D.,† MACK ROACH, M.D.,‡ COLLEEN LAWTON, M.D.,¶ BRYAN DONNELLY, M.D.,§ DAVID GRIGNON, M.D.,** GERALD HANKS, M.D.,†† ARTHUR PORTER, M.D.,‡‡ HERBERT LEPOR, M.D.,¶¶ AND HOWARD SANDLER, M.D.§§

Table 6. 7-year estimates of OS, DM, and BF rates for 401 patients

Variable	Group	7-year OS rate (95% CI)	7-year DM rate (95% CI)	7-year BF rate (95% CI)
Age	<60	77.5% (61.1, 87.6)	32.1% (17.4, 46.7)	71.3% (56.9, 85.8)
	60-70	67.2% (59.9, 73.4)	18.3% (12.8, 23.8)	66.1% (59.3, 72.9)
	>70	57.5% (49.4, 64.8)	22.0% (15.5, 28.5)	50.3% (42.5, 58.1)
Gleason score	2-6	71.1% (62.3, 78.3)	15.2% (8.9, 21.5)	52.3% (43.3, 61.1)
	7	63.4% (55.3, 70.5)	20.3% (13.9, 26.6)	61.9% (54.3, 69.6)
	8-10	57.3% (47.3, 66.2)	30.0% (21.2, 38.8)	66.9% (57.9, 75.8)
T stage	T1-T2	65.3% (58.1, 71.5)	14.3% (9.4, 19.2)	60.0% (52.7, 66.5)
	T3-T4	63.4% (56.1, 69.8)	28.4% (22.1, 34.8)	61.0% (54.0, 67.9)
KPS	70-90	61.3% (54.6, 67.3)	23.1% (17.7, 28.6)	60.5% (54.1, 66.8)
	100	68.5% (60.6, 75.2)	18.7% (12.6, 24.7)	59.9% (52.3, 67.5)
PSA	50-60	66.2% (55.8, 74.7)	15.3% (8.1, 22.5)	57.3% (47.4, 67.2)
	>60–72.5	61.0% (50.2, 70.1)	10.7% (4.4, 17.0)	59.5% (49.2, 69.7)
	>72.5–90	66.7% (56.4, 75.1)	26.5% (17.9, 35.2)	66.5% (57.3, 75.7)
	>90	62.9% (52.4, 71.6)	32.0% (22.6, 41.3)	57.6% (47.6, 67.5)

UCSF Helen Diller Family Comprehensive Cancer Center

Case #2

Lessons Learned:

1. PSA is over rated!
2. A “nodal phenotype, highly responsive to RT & ADT delayed shrinkage of nodes
3. “If you don’t treat for cure, you won’t cure those you treat” – Phillips

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #3

67-yo white clinical T3b, GS= 4+5, *PSA 1.6ng/ml* adenocarcinoma presents with an abnormal DRE (Sept, 2010)
Bx: Left lat. & mid: GS 4+5=9, predominantly intraductal.

Prostate, left apex: Invasive adenocarcinoma with focal areas suspicious for squamous and sarcomatoid differentiation.

Prostate, left nodule, needle core biopsy:
1. Invasive squamous cell Ca. and sarcomatous differentiation
2. Gleason grade 4+4=8, with prominent intraductal component

CT scan of the abdomen and pelvis was negative.
TRUS from Dec. 2, 2010 revealed a large hypoechoic lesion, left apex to base, with involvement of membranous urethra … with ECE of the left base and involvement of the left SV.

Started on combined ADT in December 2010.

TRUS Feb. (2010) showed a 20% reduction in volume; however, he became obstructed and requires an indwelling catheter.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Original Article

Association of Very Low Prostate-Specific Antigen Levels With Increased Cancer-Specific Death in Men With High-Grade Prostate Cancer

Brandon A. Mahal, MD[1]; Ayal A. Aizer, MD, MHS[2]; Jason A. Efstathiou, MD, DPhil[3]; and Paul L. Nguyen, MD[2]

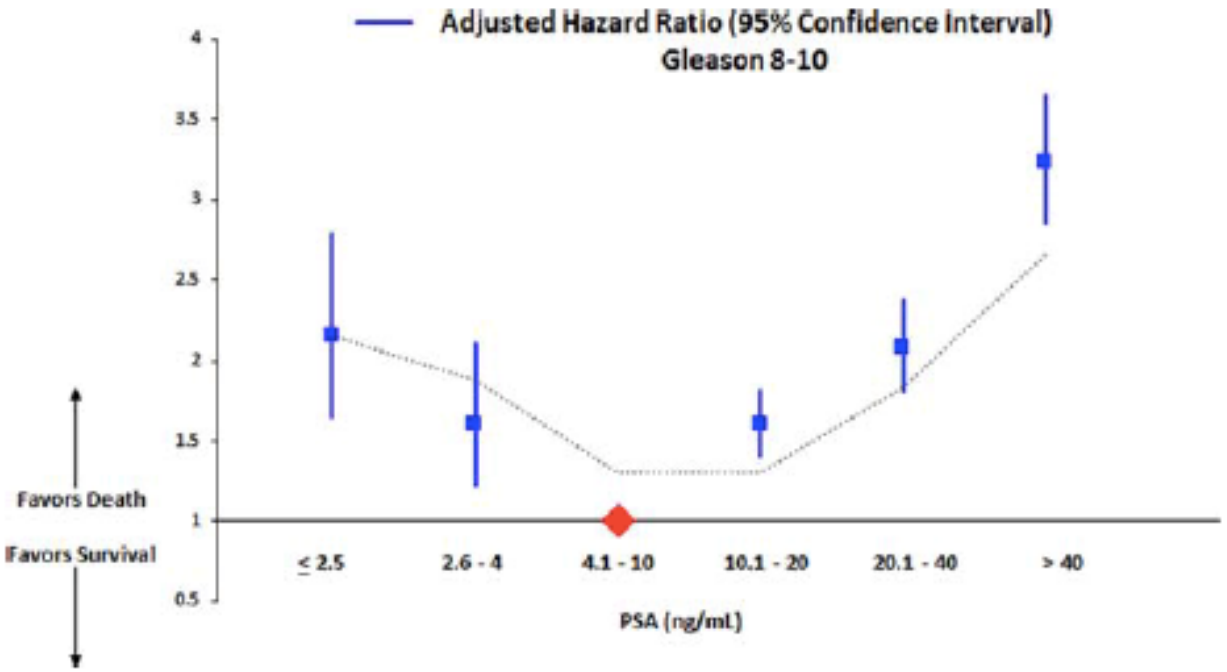


Figure 2. Plot of adjusted hazard ratios and 95% confidence intervals along with the moving average trend line for the association between the PSA level (2.5, 2.6-4, 4.1-10, 10.1-20, 20.1-40, or>40ng/mL) and prostate cancer–specific mortality among men with disease with a Gleason score of 8 to 10 (n= 73,140). A PSA level of 4.1 to 10 ng/mL represents the referent value (1.0). PSA indicates prostate-specific antigen.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #3 (continued)

PHYSICAL EXAMINATION (4/19/11):
On DRE he had a very firm, hard, nodular prostate throughout the gland, small, midline.

Testosterone (4/4/11) < 20 (baseline 400) and PSA of 0.015

MR imaging of the pelvis, 4/22/2011 - the entire prostate is replaced by diffusely abnormally low T2 signal intensity bilaterally, compatible with tumor infiltration.

... predominantly (involves) the left prostate gland, but the right prostate gland is also diffusely infiltrated by tumor. … likely extracapsular extension on the left side. No evidence of SV invasion. The prostate, which measures 3.3 x 3.4 x 4.7 cm bulges slightly anteriorly upon the bladder base and slightly posteriorly upon the rectum.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Quiz case #3

How would you treat this patient?

A) WPRT 45-50 Gy + prostate boost ~30 Gy

B) WPRT 45-50 Gy + BT boost

C) WPRT SIB with “focal boost” (Flame)

D) Prostate SBRT 4-5 Fx

What unusual Prostate Cancer Cases can teach us

How would you treat this patient?

- WPRT 45-50 Gy + prostate boost ~30 Gy
- WPRT 45-50 Gy + BT boost
- WPRT SIB with "focal boost" (Flame)
- Prostate SBRT 4-5 Fx

UCSF Helen Diller Family Comprehensive Cancer Center

Case #3 (continued)

Treated with a "reverse" CyberKnife® SBRT June 15 - July 16,2011, 950 cGy x 2 to 19 Gy to the prostate + SVs.

IMRT was started on June 28 thru July 28, 2011, to a total 52.47 Gy to sentinel lymph nodes, prostate and SVs to 45 Gy.

By the last day of treatment on July 28, 2011, able to urinate without Foley in place and he had only 80 cc residual volume.

PSA was very low (PSA=0.062, 4/20/13). However recent MRI was abnormal, and DRE revealed a normal sized prostate with a palpable nodule in the left apex and mid.

(10/20/14) MRI Fusion Bx:

FINDINGS: … prostate gland was estimated to be 21 cc and transition zone is 6 cc. A isoechoic marginated nodule is seen in the left apex and mid gland posteriorly. Prostatic capsule is bulging posteriorly. ECE was probable if this area is positive for cancer. MRI lesion in the left anterior part is not seen on TRUS.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Reverse Boost SBRT & WPRT*

- SBRT ~ HDR
- No anesthesia
- Less trauma to the gland
- Logistical issues
- Single MRI & CT
- Better anatomic detail (MRI vs CT at start)
- Extrapolation Neutrons 1st vs 2nd (Forman et al.)
- Stimulate the immune system?
- Avoid hot spots in the composite plan
- Anecdotal experience relieving obstruction due to tumor/high volume Dz

* “RBOST-RT”

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #3 (continued)

(10/20/14) MRI Fusion Bx:

FINAL PATHOLOGIC DIAGNOSIS

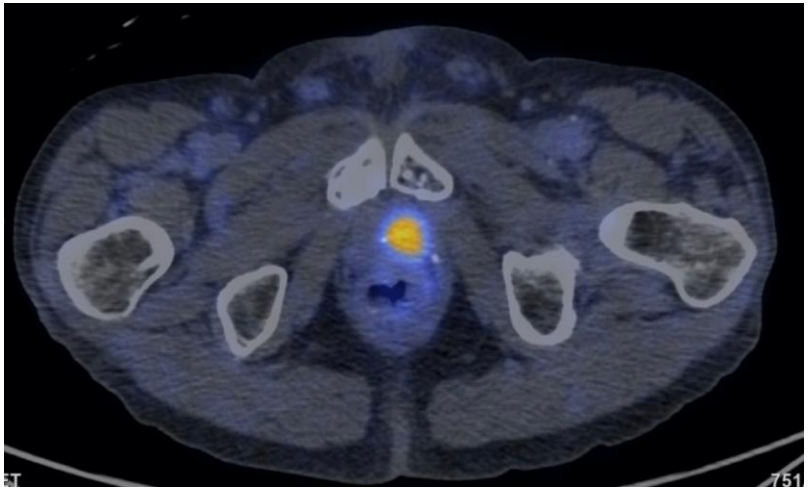
A. Prostate, right apex: Benign tissue with treatment effect.
B. Prostate, right mid: Benign tissue with treatment effect.
C. Prostate, right base: Atypical glands; see comment.
D. Right seminal vesicle: Benign seminal vesicle tissue.
E. Prostate, left apex: Benign tissue with treatment effect.
F. Prostate, left mid: Atypical glands.
G. Prostate, left base: Benign tissue with treatment effect.
H. Left seminal vesicle: Benign tissue with treatment effect.
I. Left TRUS lesion: Benign tissue with treatment effect.
J. Left MRI lesion: GS 4+4=8; in 1/2 cores with adjacent tissue showing treatment effect.

As of 12/1/19: With T < 200 "lethargy" and "belly fat" L3,L4 compression fractures, the patient discontinues ADT

With testosterone gel Testosterone running = "500 to 600 range" with "reduced belly fat" and "PSA = < 0.02 ng/ml" …
"very happy", 10 years out at age 76!

What unusual Prostate Cancer Cases can teach us

9/20/24 (13 yrs later) obstructive symptoms, PSA up to 0.217 ng/mL and PSMA PET shows “hot spot” in the left lobe, Bx GS=4+4 left lobe.

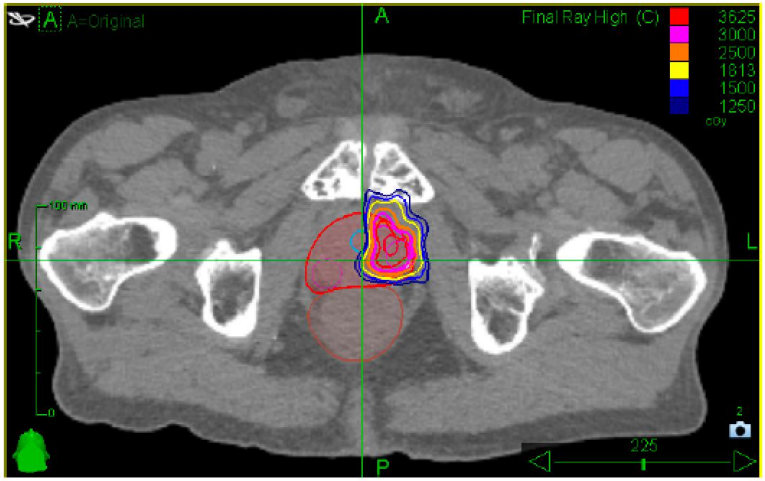


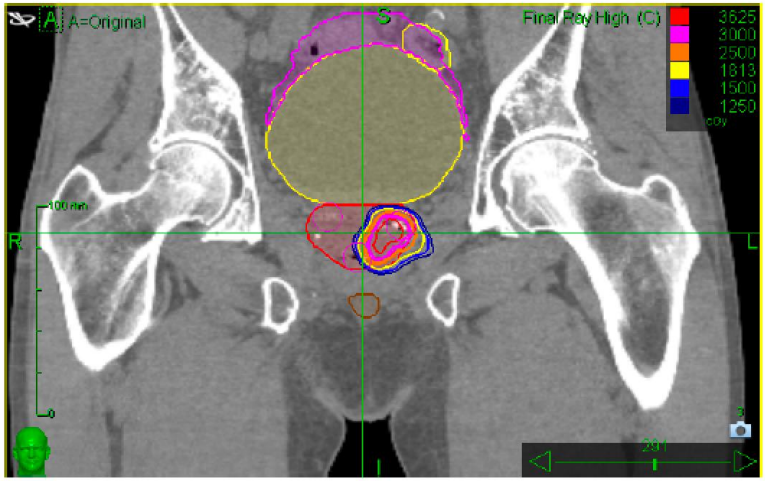
Plan:

SBRT 725 x 5 to the DIL

followed by Adjuvant ADT.

Treatment well tolerated.





UCSF Helen Diller Family Comprehensive Cancer Center

Case #3

Lessons Learned:

1. Obstruction due to high grade tumor may be best treated with reverse SBRT boost.
2. Testosterone replacement may be appropriate in selected patients
3. Long follow-up is needed!
4. “If you don’t treat for cure, you won’t cure those you treat” – Phillips

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Palliation of urinary obstruction from advanced prostate cancer with SBRT.

Boreta, Raleigh, and Roach
UCSF Department of Radiation Oncology

Goal: … institutional experience with SBRT for palliation of urinary obstruction (UO) from locally advanced prostate ca.

Methods: A retrospective review of pts undergoing SBRT for UO … between 2011- 2017.

Results: Three pts were treated with SBRT to the prostate for the palliation of UO. … all had high risk, stage IV disease, Gleason 4+4 or 4+5, T3 or T4, with regional nodal and/or bony or visceral mets. All patients required indwelling catheterization for an avg. 4 mos prior to SBRT. Catheters were successfully removed in all 3 patients, one at the completion of radiation, and the others within 4 wks of completion. With follow-up ranging from 1.2 to 6 yrs, no pts required re-catheterization, and there were no reports of grade ≥3 acute or long-term toxicity.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Palliation of urinary obstruction from advanced prostate cancer with SBRT.

Boreta, Raleigh, and Roach
UCSF Department of Radiation Oncology

	Pt 1	Pt 2	Pt 3
Age	67	52	57
Stage at Dx	T3bN1M0	T4N0M0	T3bN1M1c
Gleason Score	4+5	4+4	4+5
PSA at Dx	1.4	44	0.9
ADT	Y	Y	Y
RT dose	19 Gy/2 F	19 Gy/2 F	38 Gy/4 F
Time from RT completion to Foley removal	Same day	4 weeks	2 weeks
AUA QOL at first fu	Unknown	2	1
Recatheterization	No	No	No

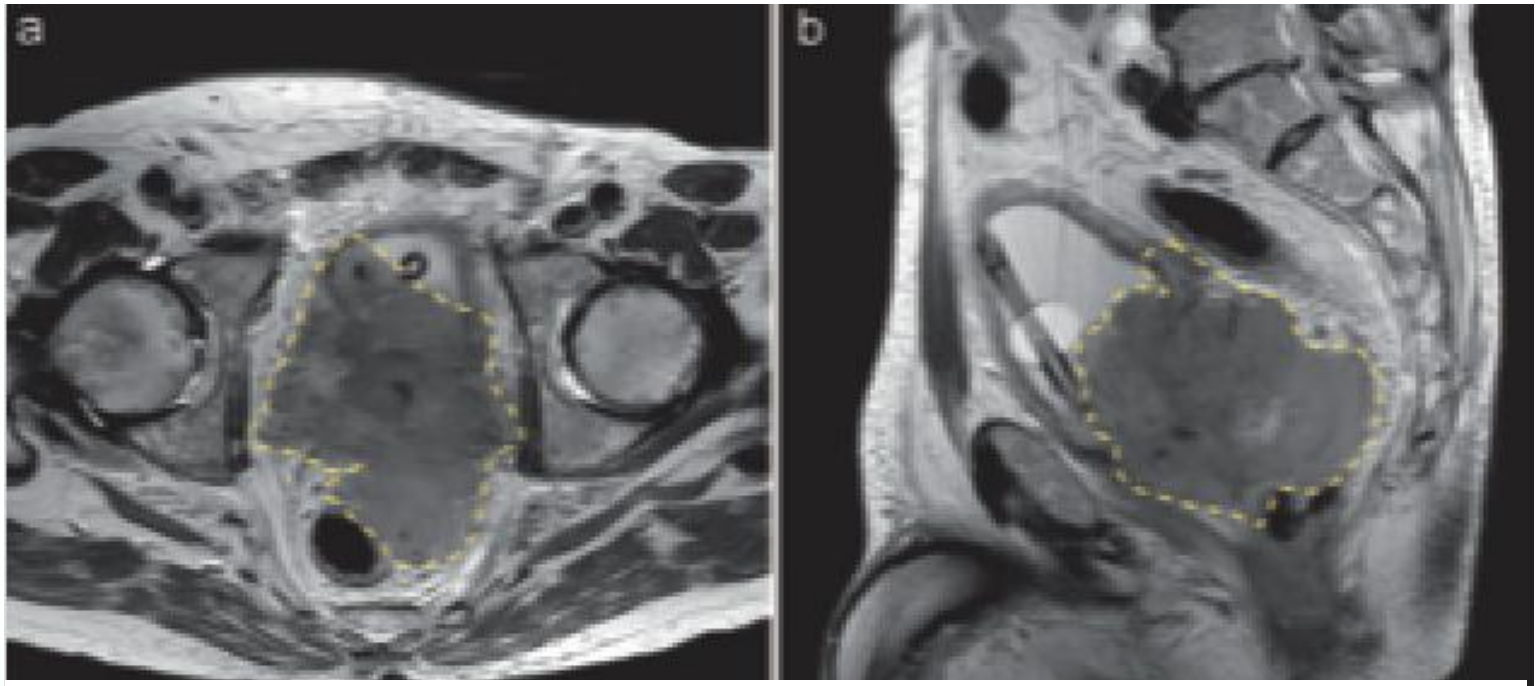
Conclusions: SBRT is an effective treatment to palliate UO from locally advanced PCa, leading to removal of urinary catheters and presumed improved in quality of life. Further investigation is required to establish the optimal dose and fractionation of palliative SBRT for UO from PCa.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #4

75-yo presented a PSA=20 and obstruction requiring a Foley. CT demonstrated an exophytic prostatic mass (~900 cc) & Bx confirmed GS=5+5. PSMA-PET/MRI … prostatic mass abutting the rectum, bladder, bilateral SVs & nodal involvement.



Treated with LHRH and abiraterone / prednisone. Following a 4-mo. *PSA decline, PSA began rising and imaging revealed increased primary tumor consistent c/w castration resistance.* Despite carboplatin and docetaxel … MRI demonstrated worse disease and he was switched to carboplatin and cabazitaxel.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Quiz case #4

How would you manage this patient?

A) Chemo and urinary catheter only

B) Chemo + palliative prostate EBRT 30 Gy / 10 Fx

C) Chemo + EBRT (55Gy/20Fx or 70Gy EQD2)

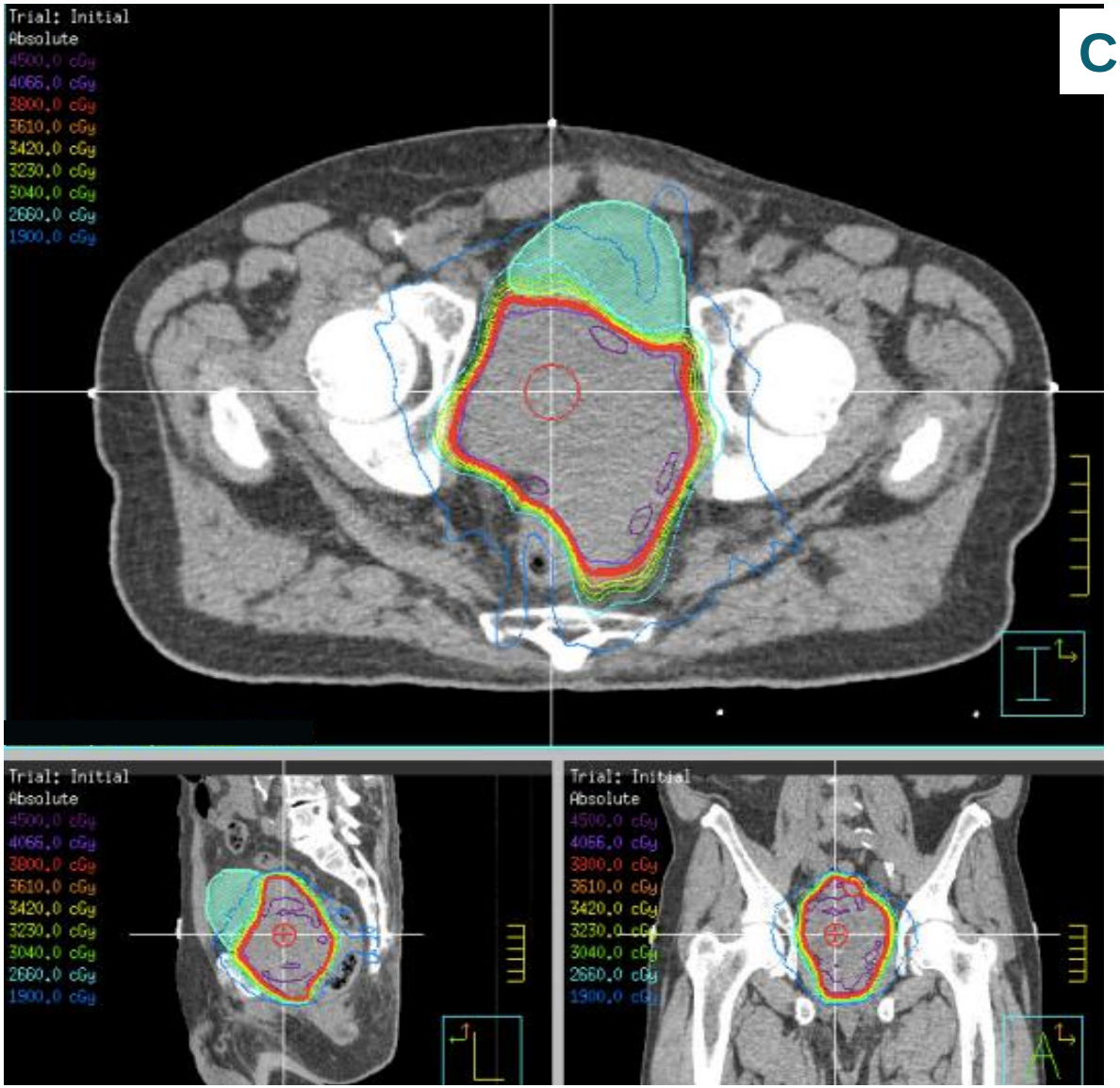
What unusual Prostate Cancer Cases can teach us

How would you manage this patient?

- Chemo and urinary catheter only
- Chemo + palliative prostate EBRT 30 Gy / 10 Fx
- Chemo + EBRT (55Gy/20Fx or 70Gy EQD2)

UCSF Helen Diller Family Comprehensive Cancer Center

Case #4

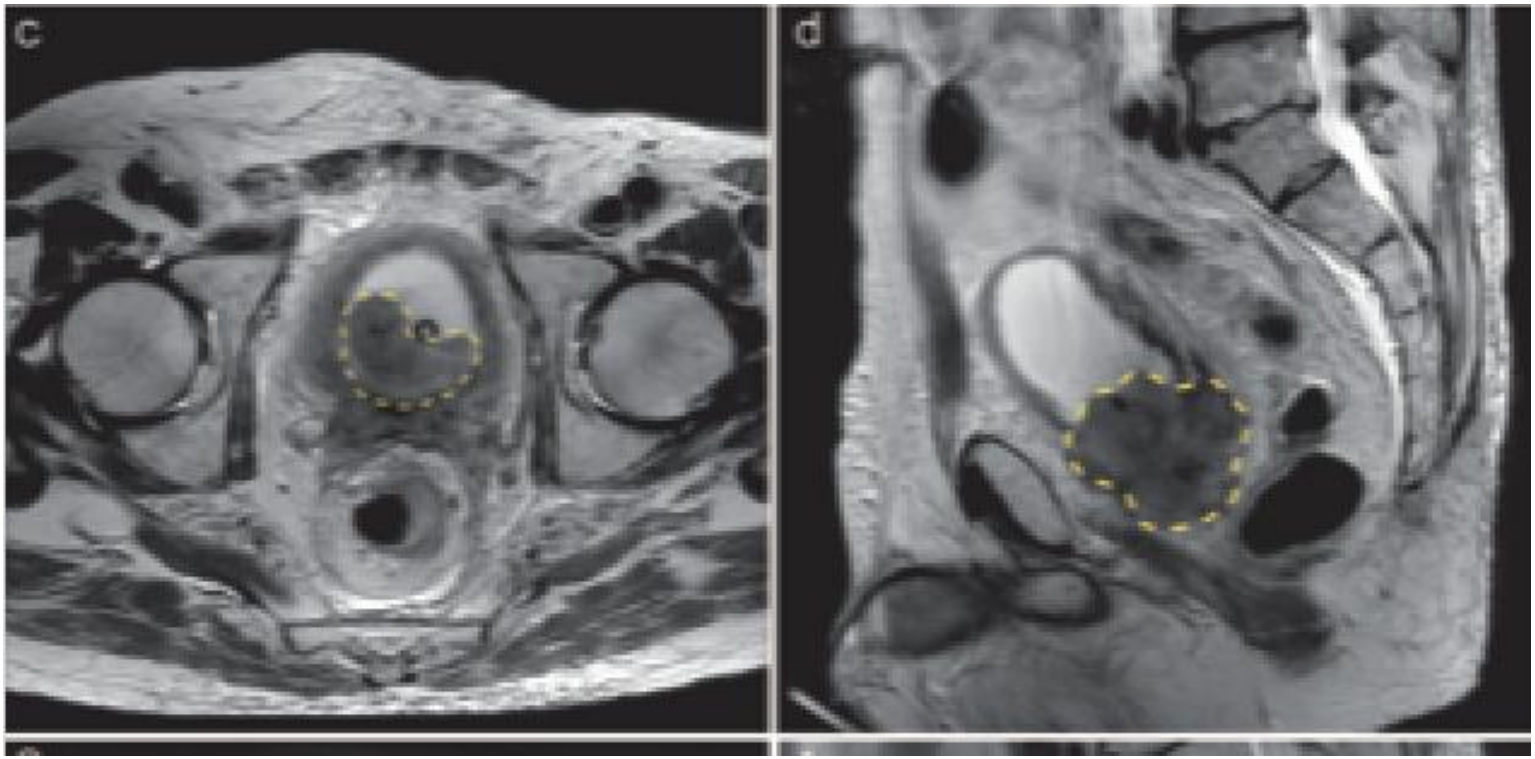


During Cycles 1 and 2, received SBRT 38 Gy to the prostate (9.5 Gy x 4).

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #4



Chemoradiation decreased tumor size & PSA by >90% after 4 cycles.

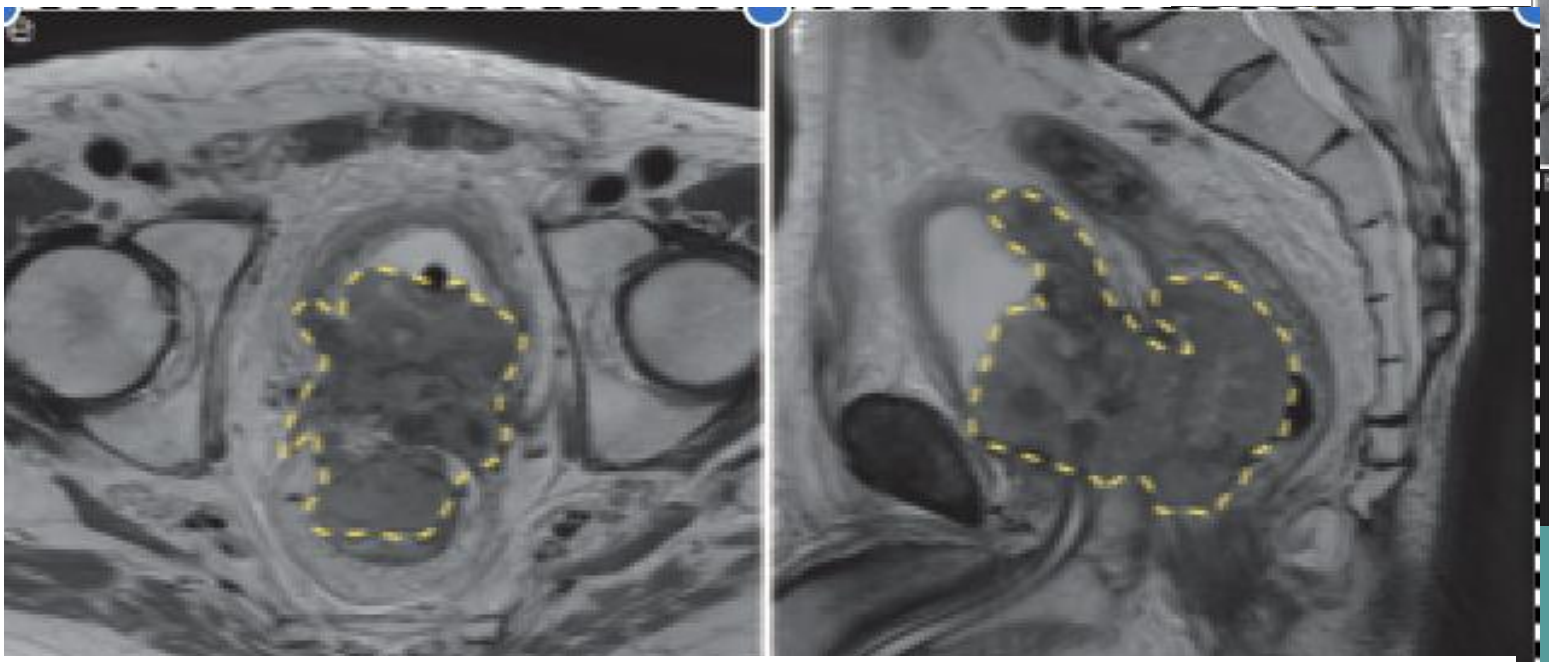
What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

What unusual Prostate Cancer Cases can teach us

Case #4

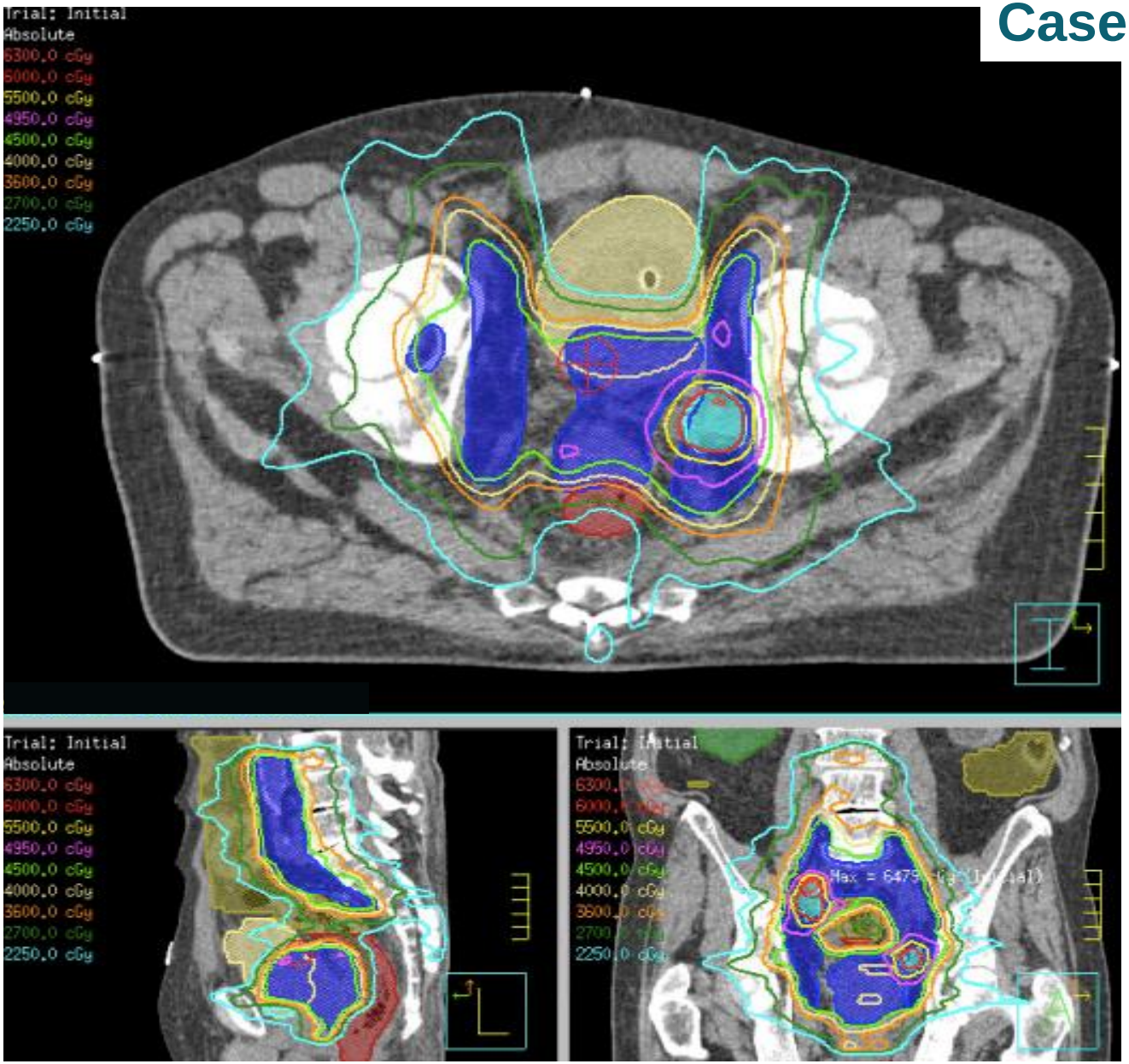
During Cycle 9 - 10 of carboplatin/ cabazitaxel, … pt had a rising PSA with a MRI pelvis revealing enlarging primary, worsening SV involvement and gross rectal invasion, c/w disease recurrence



The pt received re-irradiation to the primary and pelvic nodes with IMRT during Cycles 2 & 3 (45 Gy for 25 fxs) with a simultaneous integrated boost to 50 Gy to the GTV. We re-irradiated the prostate & tx'd nodes with a SIB to 50 Gy to the GTV.

UCSF Helen Diller Family Comprehensive Cancer Center

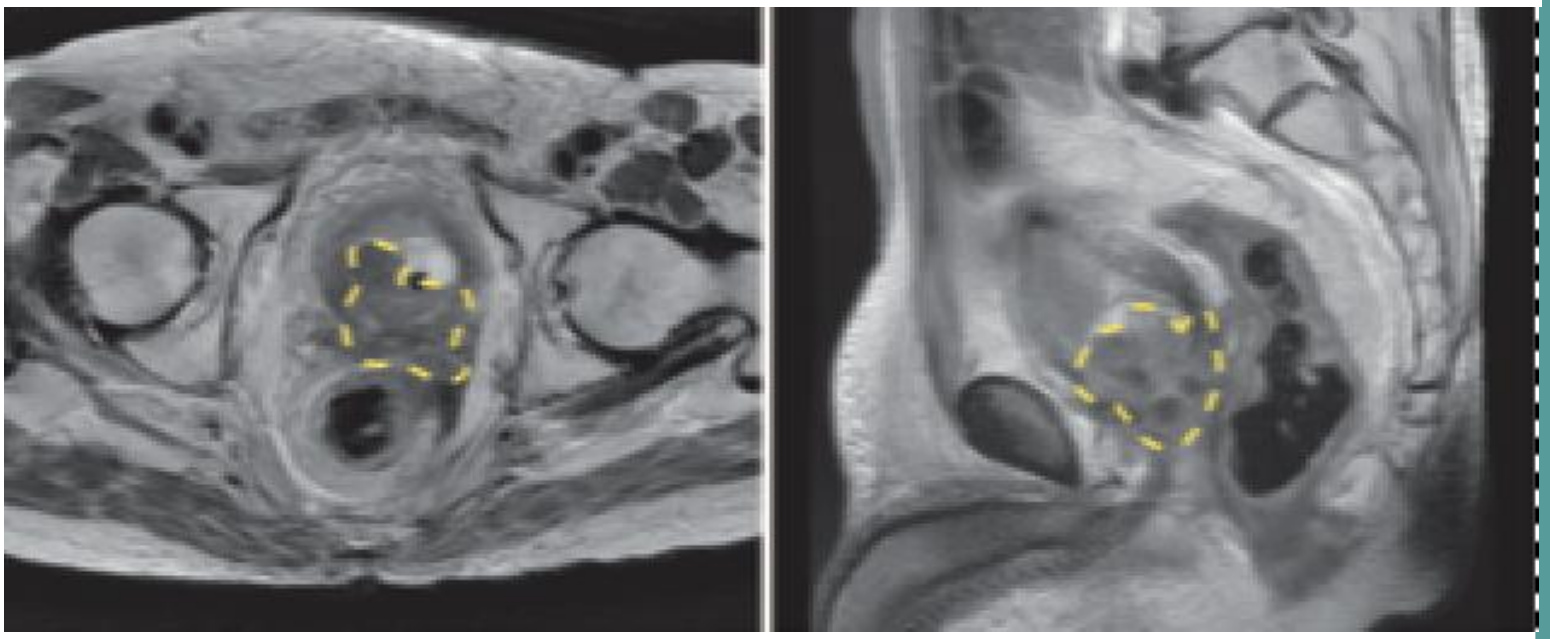
Case #4



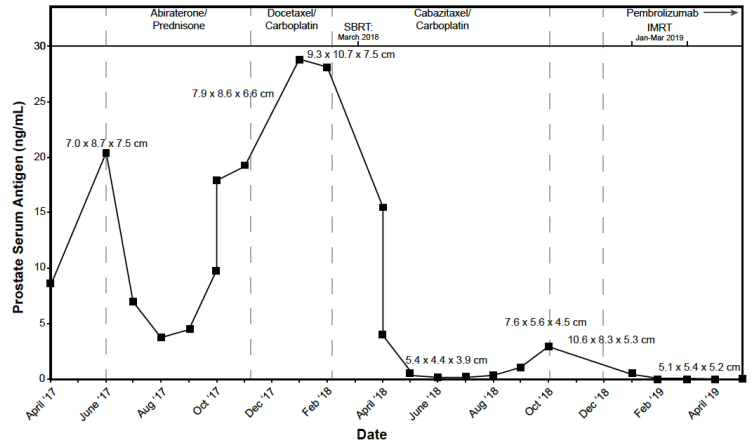
What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #4



Genetic analysis demonstrated MSI & multiple path mutations. *A*fter pembrolizumab (2 cycles) and a boost to tumor the PSA dropped & he underwent a successful voiding trial and remains cath free.



What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #4

Lessons Learned:

1. Tumor size is over-rated
2. MSI high tumors may be extremely sensitive to RT combined with the appropriate drugs.
3. Patients who present to obstruction due to extremely bulky disease may be unique.
4. Don’t undertreat.
5. “If you don’t treat for cure, you won’t cure those you treat” – Phillips

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

What unusual Prostate Cancer Cases can teach us

Local recurrence after radical prostatectomy: characteristics in size, location, and relationship to prostate-specific antigen and surgical margins.

Connolly, Shinohara et al. Urol 47:225-31, 1996

OBJECTIVES:

To define local cancer recurrence after RP … 114 pts with an elevated PSA and negative bone scan, 156 ultrasound-guided prostate fossa biopsies ...

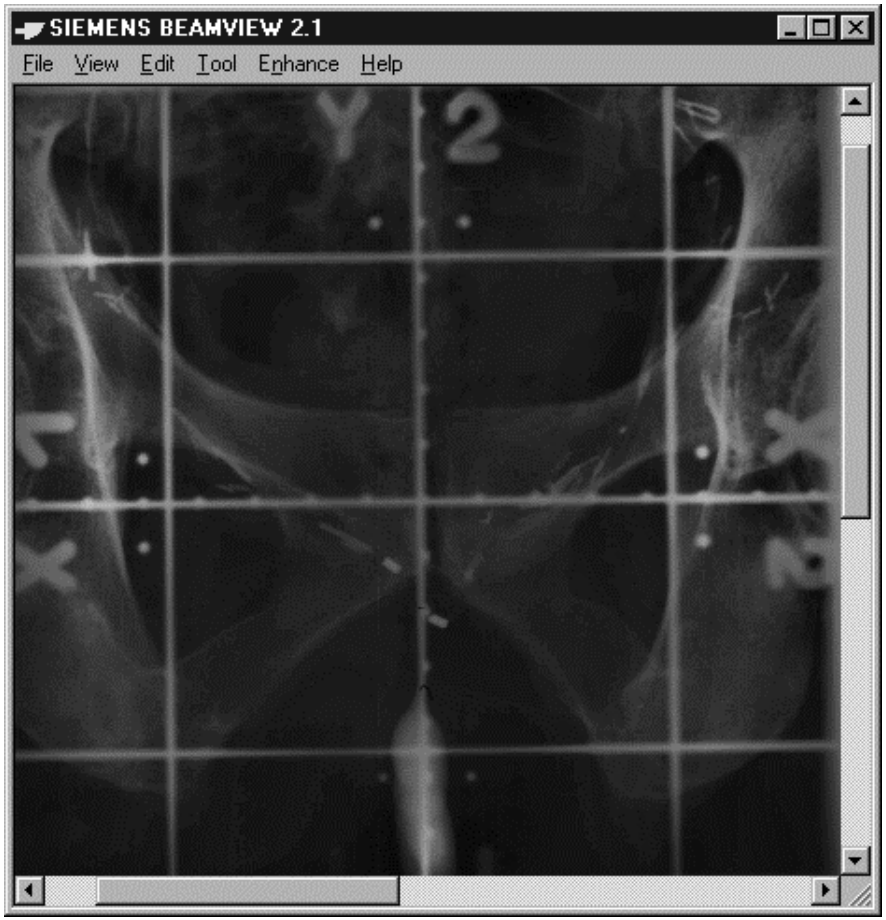
54%, + Bx's proved local recurrences:

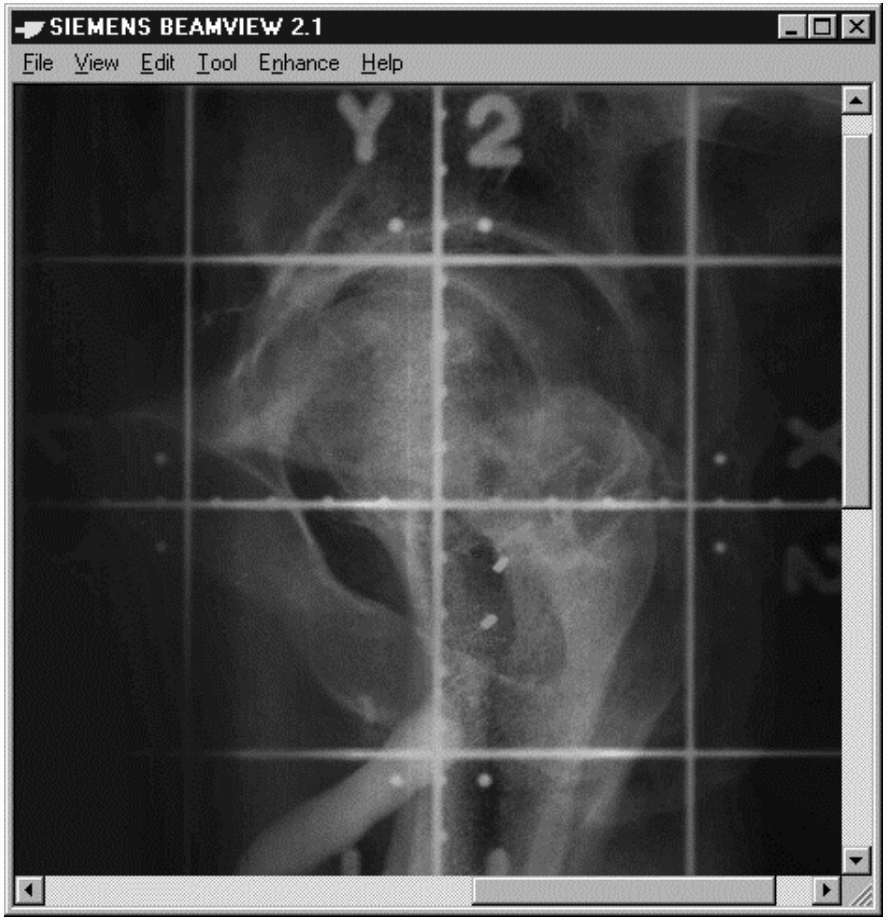
- **anastomotic site (66%),bladder neck (16%)**
- **posterior to the trigone (13%)…**

How?:

Technical Considerations for Post Operative Radiotherapy

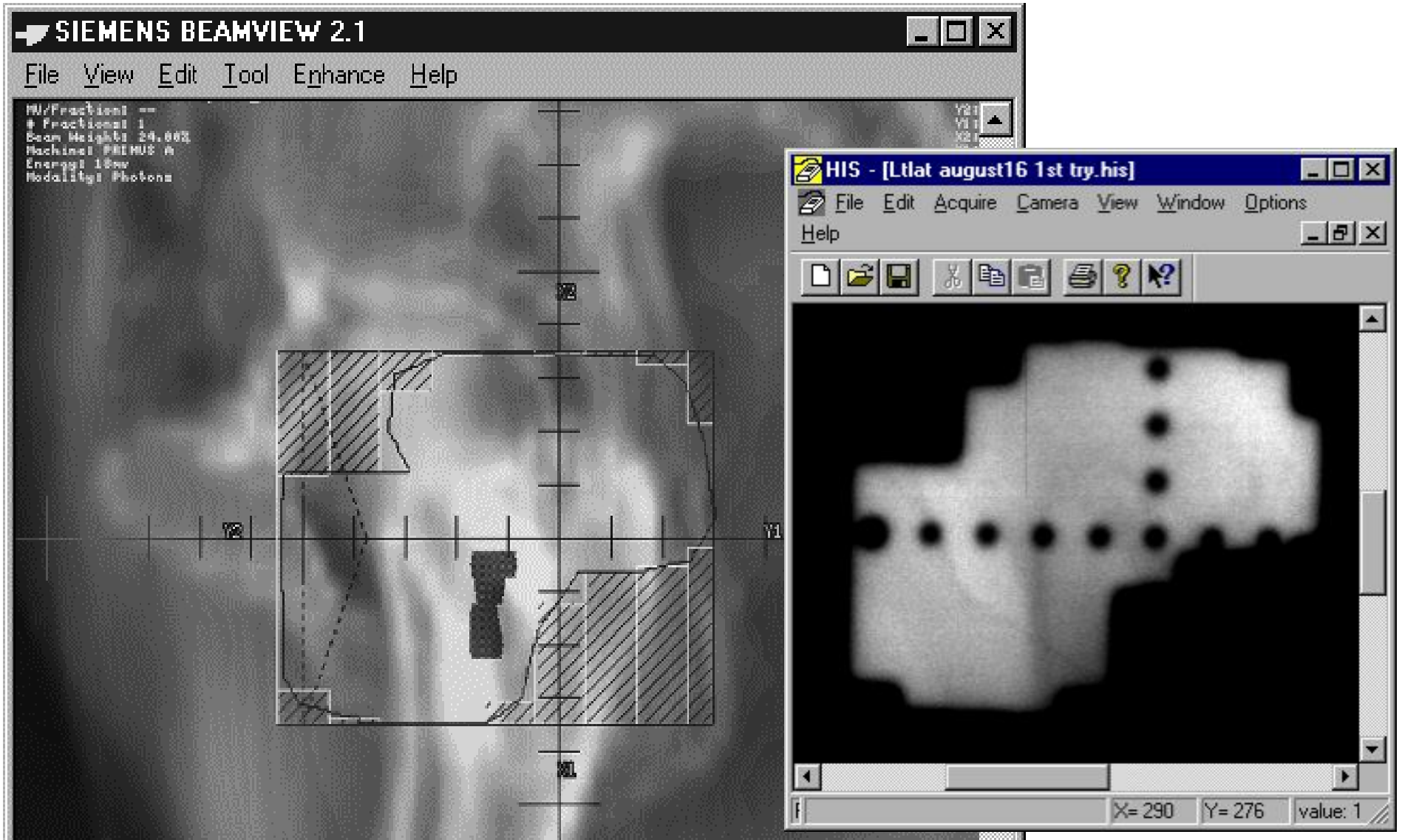
Image Guided Radiotherapy (IGRT) for Localization of the anastomosis





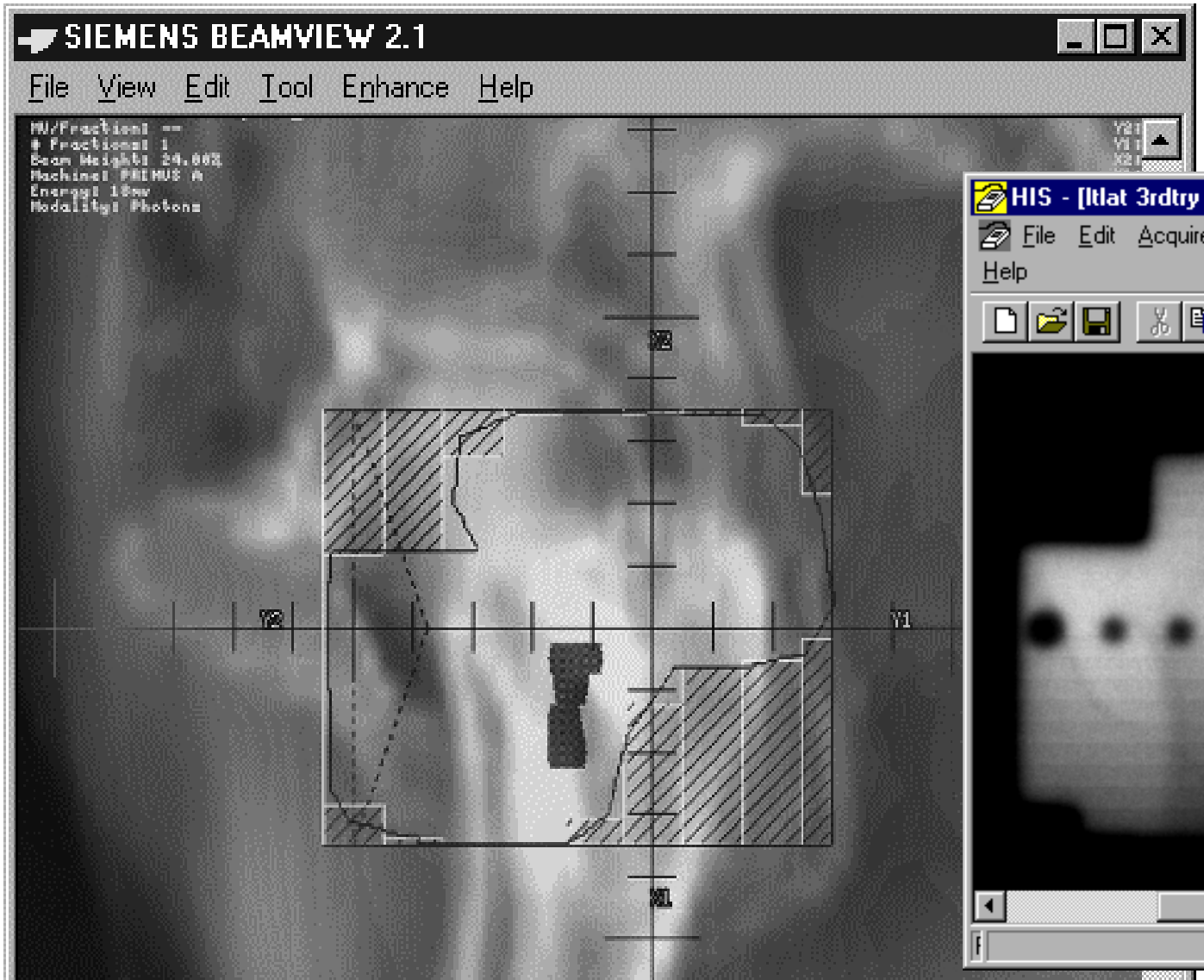
Case #5

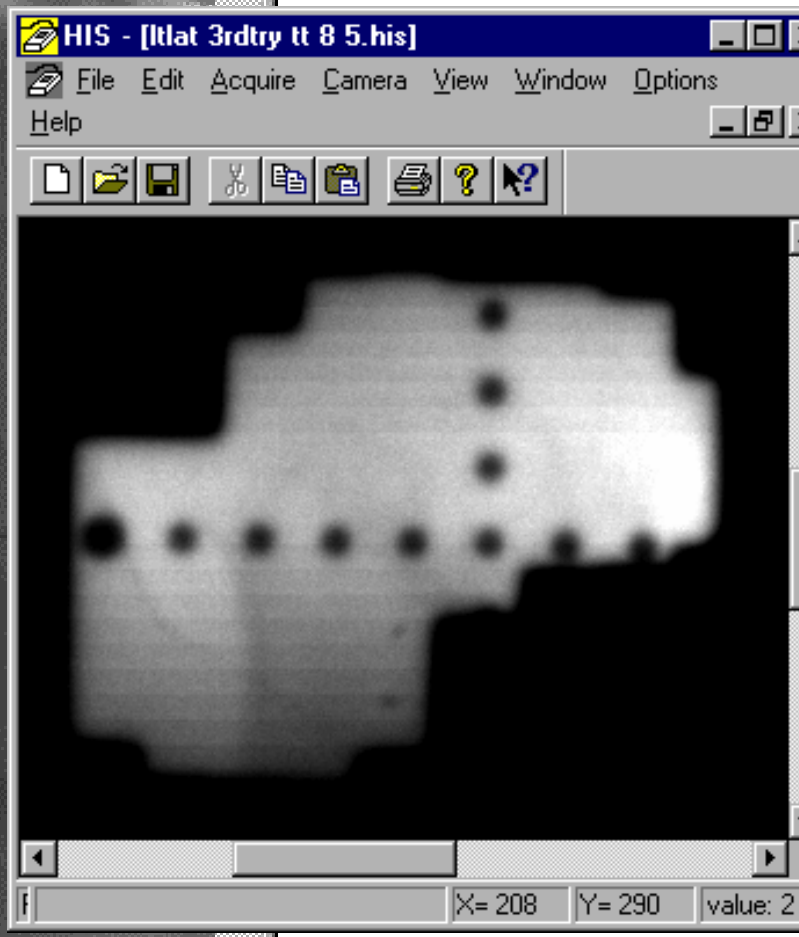
Organ Movement + set-up error?



Case #5

Organ Movement + set-up error?





UCSF Helen Diller Family Comprehensive Cancer Center

Case #6

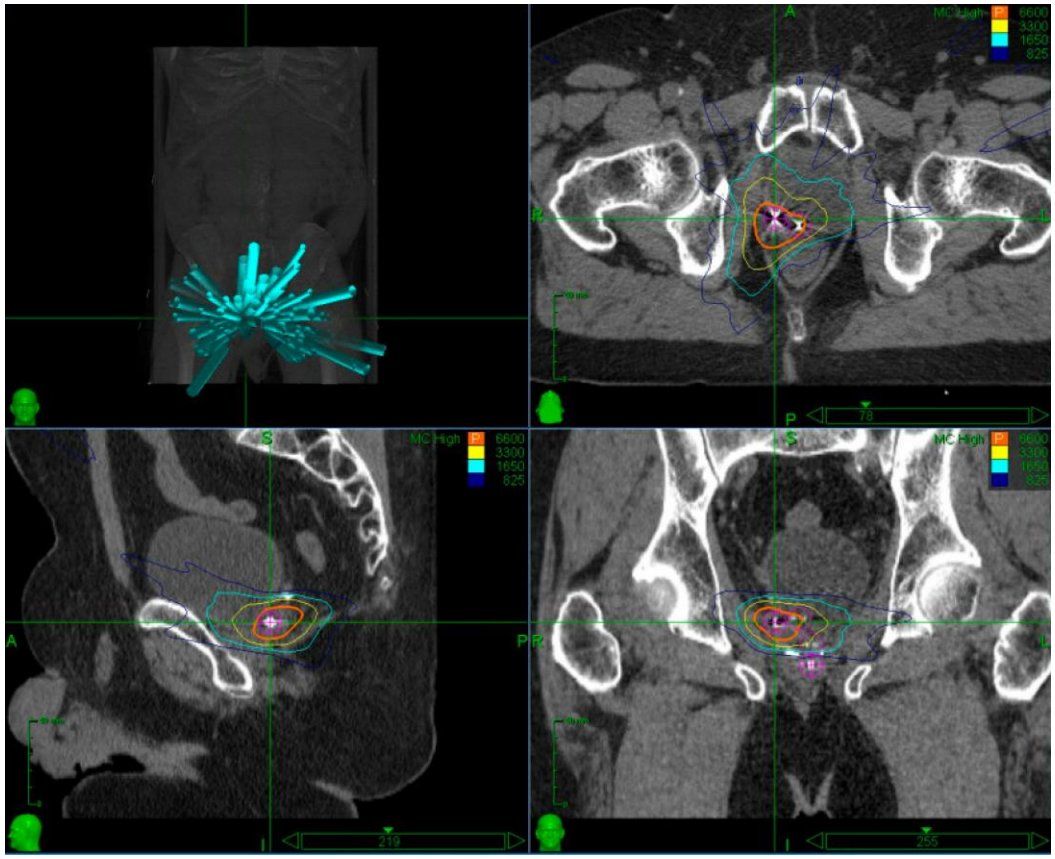
3/10/2004

53-yo white male s/p RP 11/3/2003 for a PSA 49, pT3bN0M0, GS = 4+5 involving 70% of the specimen, with ECE and multiple positive margins 0/2 + nodes.
PO, PSA 6 ng/ml … Jan. 2004 9 ng/ml. Met. w/u neg. post PSA is down to 1.07.
ROS: mild urgency … incontinence. DRE, induration on his left anastomotic area.

SRT 72 Gy + NHT (6/17/2004) + ADT for ~ 2 yrs. PSA < 0.02 ng/mL thru 10/23/06.

65 y.o. PSA had risen to 4.34 ng/mL, by 1/20/16.
BS 2/8/16 negative
TRUS - hypoechoic lesion at posterior right bladder neck Bx + GS 5+4 adeno ca.

66 Gy in 33 fractions to the lesion on 06/21/2016 with adjuvant ADT

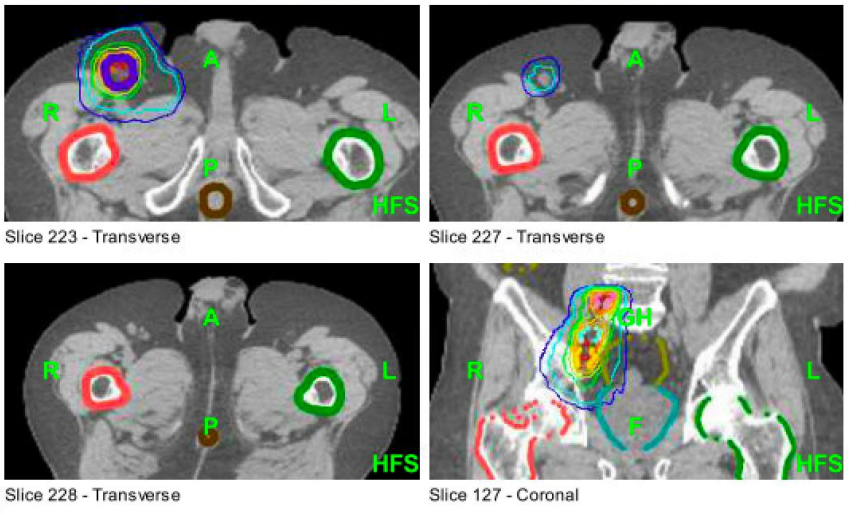


What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Case #6

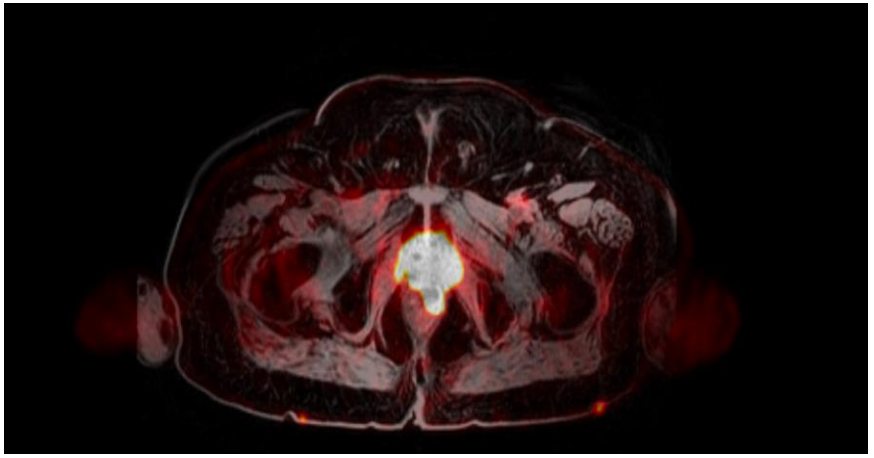
67 y.o. PSA up to 0.3 ng/mL 8/28/17 … 4.065 3/22/18.
PSMA PET on 5/7/18 showed PSMA-avid + the right inguinal, common and external iliac & aortocaval lymph nodes
Apalutamide added (5/2018).
Tx: 7/9/2018 to 8/10/2018, 60 Gy/25 fx to PET-avid pelvic & PA nodes



8/10/18 PSA = 0.048; 11/16/18 PSA = 0.111 … 10/04/22 PSA = 2.2 ng/mL.

PSMA PET 07/2022 c/w recurrence in bed. Bx: Urinary bladder tumor, transurethral resection: 1. Prostatic adenoca., GS 5+5, in urinary bladder lamina propria

PSMA PET 06/03/2024: … tracer avid prostatic lesion invading the bladder and abutting the rectum … Tracer avid right pelvic sidewall node … encasing both ureterovesicular junctions w/ hydronephrosis … 9/24/24 PSA = 7.86 ng/mL



What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

What unusual Prostate Cancer Cases can teach us

European Association of Urology

EUROPEAN UROLOGY

Dose-intensified Versus Conventional-dose Salvage Radiotherapy for Biochemically Recurrent Prostate Cancer After Prostatectomy: The SAKK 09/10 Randomized Phase 3 Trial. Ghadjar et al. Eur Urol , 2021

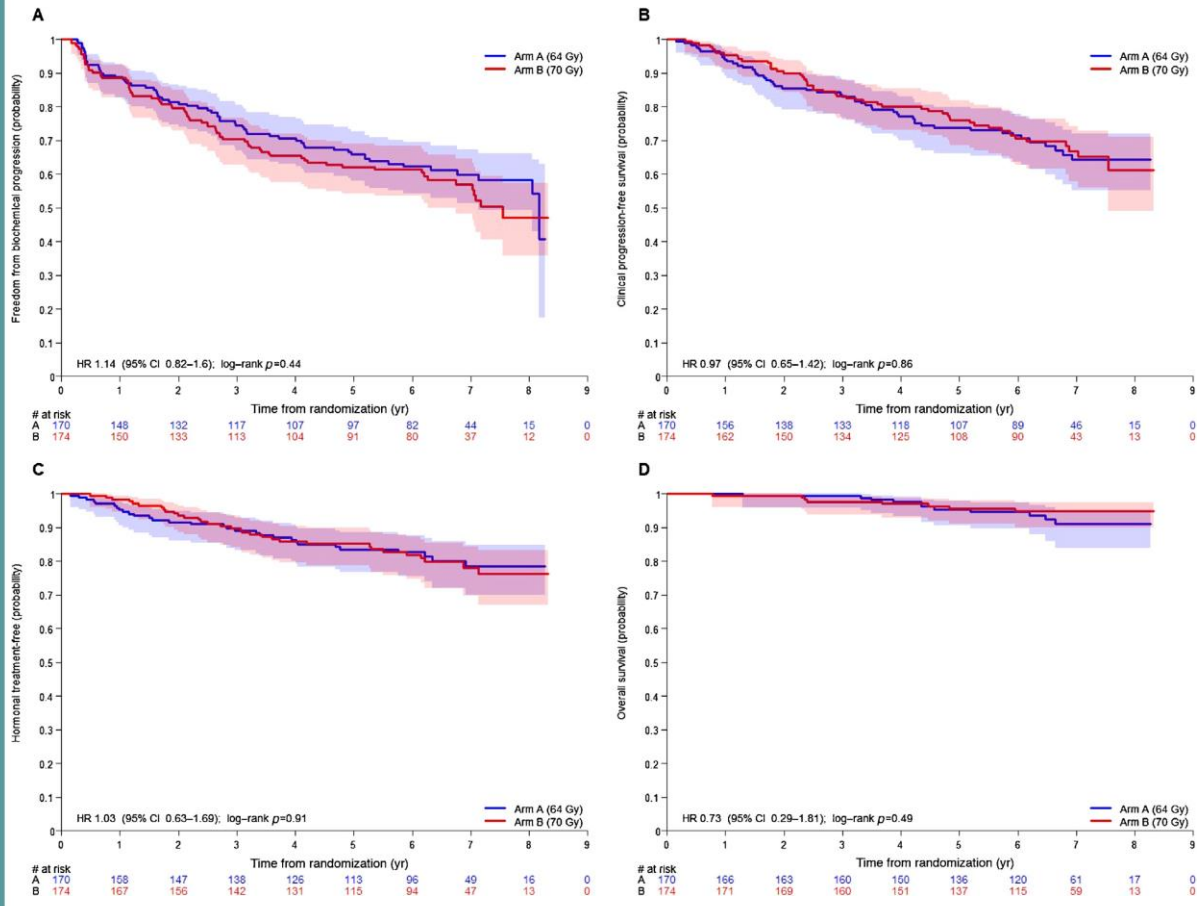


Fig. 2 – Kaplan-Meier analysis of:

(A) biochemical progression–free,

(B) clinical progression–free,

(C) hormonal treatment–free, and

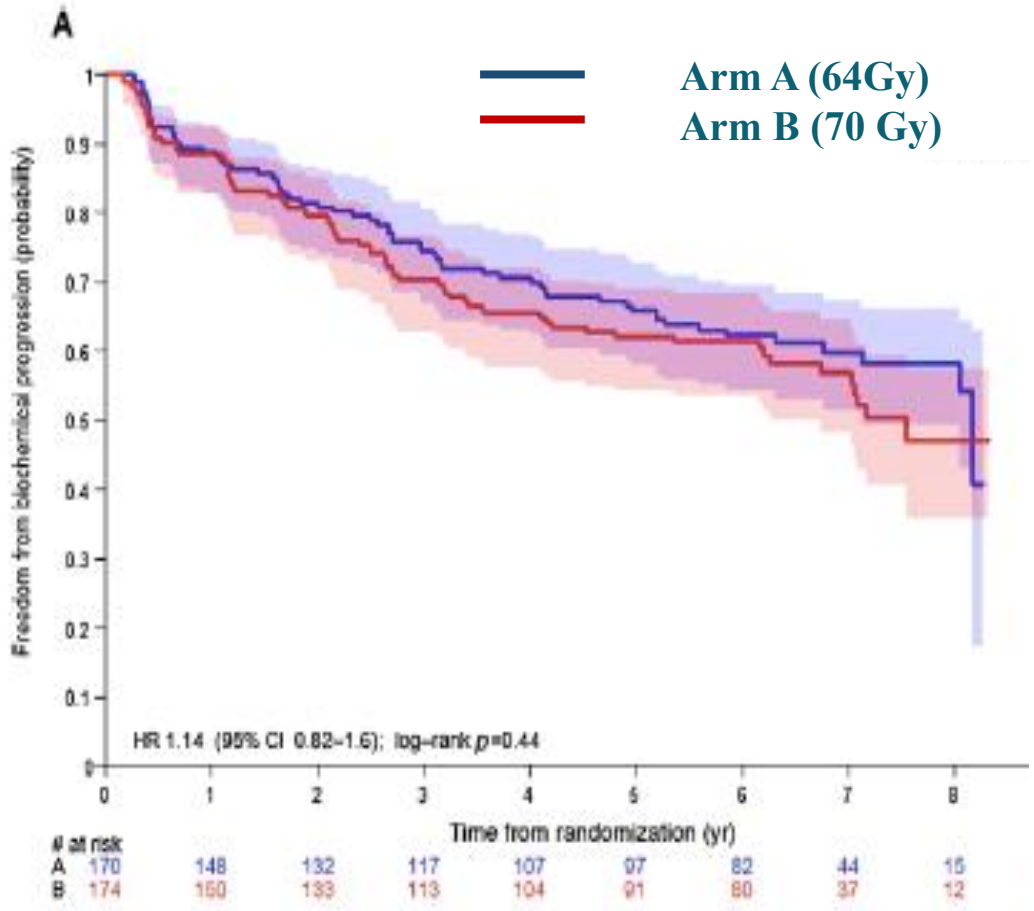
(D) overall survival.

HR = hazard ratio; CI = confidence interval.

UCSF Helen Diller Family Comprehensive Cancer Center

Dose-intensified Versus Conventional-dose Salvage Radiotherapy for Biochemically Recurrent Prostate Cancer After Prostatectomy: The SAKK 09/10 Randomized Phase 3 Trial

Ghadjar et al. Euro 2021



Problems:

1. Dose only critical if low risk of region/distant Dz (50% failure)
2. No image guidance
3. No ADT
4. No WPRT
5. Short follow-up with PSA values and endpoints (<0.0 vs 0.4ng/ml)
6. QA ?
7. 71 vs 63 BNED (70 vs 64Gy) despite 17 vs 11 regional failure

Wha
unu
Pros
Can
Cas
teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Dose-intensified Postoperative Radiation Therapy for Prostate Cancer: Long-Term Results from the PKUFH Randomized Phase 3 Trial. Li et al. IJROBP

PURPOSE: … 72 Gy … compared with … 66 Gy ... previous study … no … diff. in bPFS … current analysis 7-year ...

METHODS & MATERIALS: … pT3-4, positive surgical margins, or a PSA increase >/=0.2 ng/mL … 72 … or 66 Gy …

RESULTS: … 2011 and November 2016, (n=144) … no difference in 7-year bPFS between … 72- and 66-Gy cohorts ...
… Gleason score (8-10), the 72-Gy cohort had … improvement in 7-year bPFS (66.5% vs 30.2% … P = .012).
… multiple positive surgical margins, the 72-Gy cohort had … improvement in 7-year bPFS compared with single positive surgical margin (82.5% vs 57.5%; HR, 0.36; P = .037).

CONCLUSIONS: … pts with … GS (8-10) or multiple positive surgical margins might benefit from the 72-Gy ...

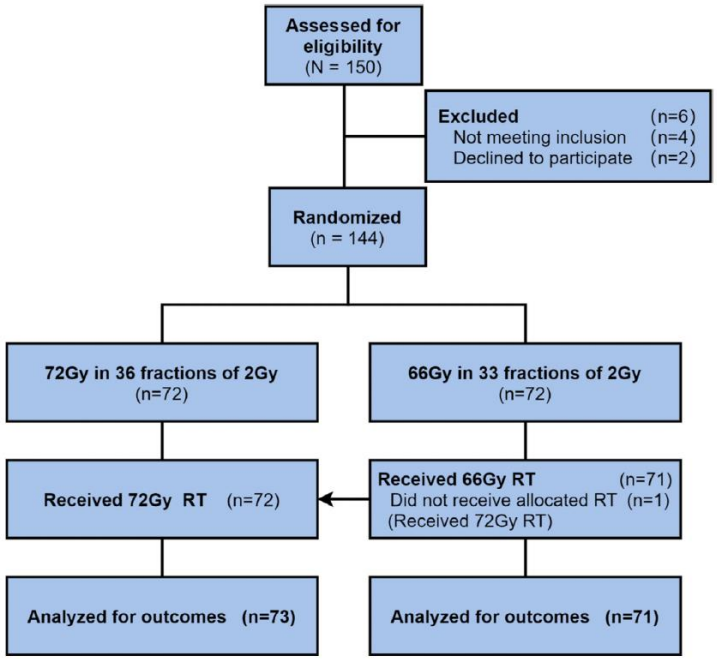
What unusual Prostate Cancer Cases can teach us

CLINICAL INVESTIGATION

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
www.redjournal.org

Dose Intensified Postoperative Radiation Therapy for Prostate Cancer: Long Term Results From the PKUFH Randomized Phase 3 Trial.

Li *IJROBP* 118:697-705, 2024



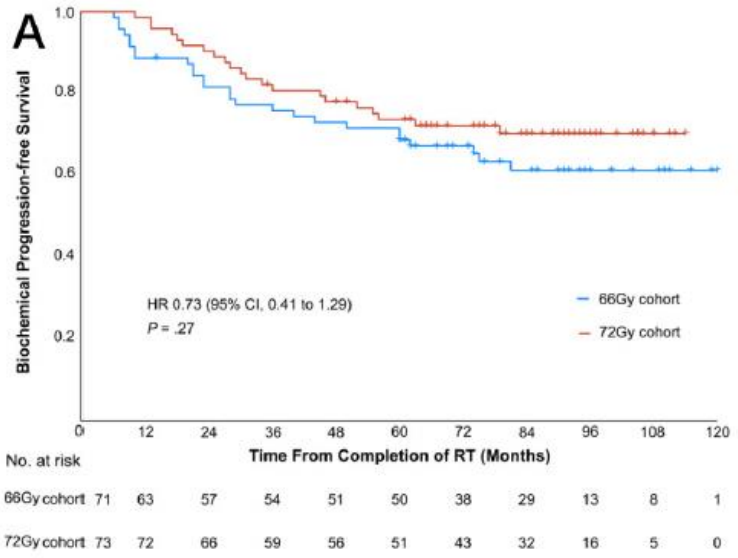


Fig. 1. CONSORT diagram for the PKUFH randomized trial. *Abbreviation:* RT = radiation therapy.

UCSF Helen Diller Family Comprehensive Cancer Center

CLINICAL INVESTIGATION

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
www.redjournal.org

Dose Intensified Postoperative Radiation Therapy for Prostate Cancer: Long Term Results From the PKUFH Randomized Phase 3 Trial.

Li *IJROBP* 118:697-705, 2024

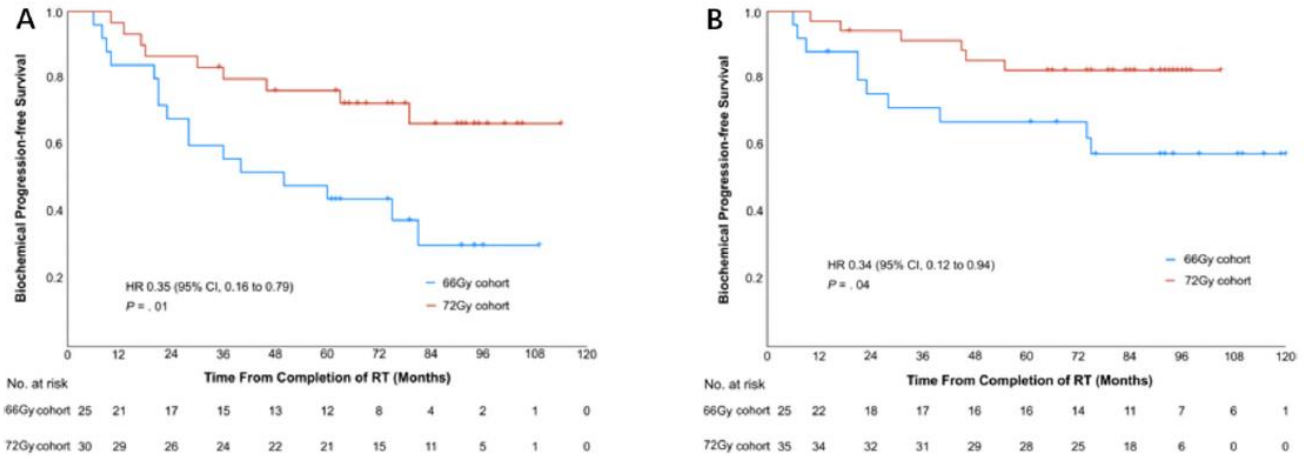


Fig. 4. Kaplan-Meier estimates and cumulative incidence curves. (A) Biochemical progression-free survival in GS ≥ 8 subgroup. (B) Biochemical progression-free survival in multiple margins positive subgroup. *Abbreviations:* HR = hazard ratio; RT = radiation therapy.

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Lessons Learned:

Cases #5 & 6

1. Target motion and set-up errors are common
2. Targeting the anastomosis is critical to accurate dose escalation.
3. Don't "under dose" due to "guidelines" built on poor trials with short follow-up.
4. Long follow-up is needed.
5. "If you don't treat for cure, you won't cure those you treat" – Phillips

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

Daily Electronic Portal Imaging of Implanted Gold Seed Fiducials in Patients Undergoing Salvage Radiotherapy After Radical Prostatectomy. Schiffner, … and Roach

Total positioning errors (set-up and movement)

Total Fractions (163)	RL	IS	AP
# Shifts Negative	92	77	88
# Shifts Positive	71	86	75
Systematic Error (Mean, mm)	0.2	1.2	-0.3
Standard Deviation (mm)	4.5	5.1	4.5
% Shifts > 5mm	14.1 %	38.7 %	28.2 %
Range	- 16.5 to 22.3	- 9.4 to 12.7	- 11.6 to 9.9

What unusual Prostate Cancer Cases can teach us

UCSF Helen Diller Family Comprehensive Cancer Center

ART?

"The undercurrent and motive of all art is an individual … idea"

"The object isn't to make art, it's to be in that wonderful state which makes art inevitable."

From "The Art Spirit" by Robert Henri

"Art is never finished, only abandoned"

Leonardo Da Vinci

What unusual Prostate Cancer Cases can teach us

"Seeing is the rate limiting step"

"An artist cannot, not do art"

Mack Roach III

UCSF Helen Diller Family Comprehensive Cancer Center

Conclusions:

1. Data from phase III RCTs should drive our management of patients with prostate ca. there are severe limitations due to:
   a) The limited number of trials
   b) Heterogeneous nature of the disease, but limited eligibility
   c) Limited interventions explored (dose vs volume vs ADT)
2. Unusual cases can teach because:
   a) Unlimited interventions, eligibility and interventions
3. Examples of cases that changed the way I manage prostate ca.:
   a) How aggressive should I be?
   b) PSA? (Low=bad?) High=not bad)? Volume? Large=not so bad?
   c) "The Art of Radiotherapy"

What unusual Prostate Cancer Cases can teach us

"Not everything that counts can be counted, and not everything that can be counted counts."

Albert Einstein (Sign hanging in his office at Princeton)

“Count what you can count and hope that it counts!”

Mack Roach III

UCSF
University of California
San Francisco
advancing health worldwide™