TERAPIE DI SALVATAGGIO NEL CAP: DOPO PROSTATECTOMIA E DOPO RADIOTERAPIA

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[niente da dichiarare]

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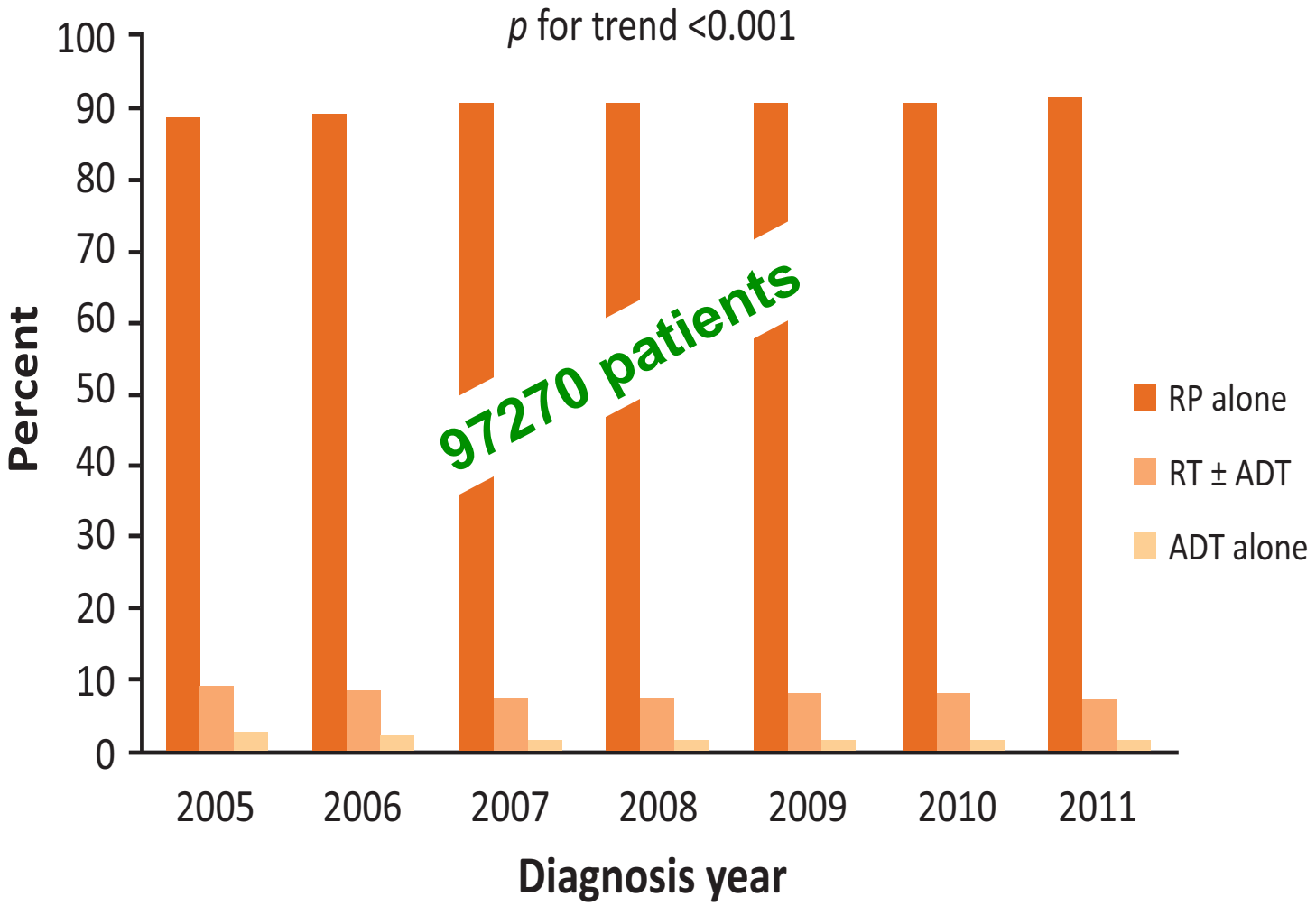
TERAPIE DI SALVATAGGIO NEL CAP: DOPO PROSTATECTOMIA

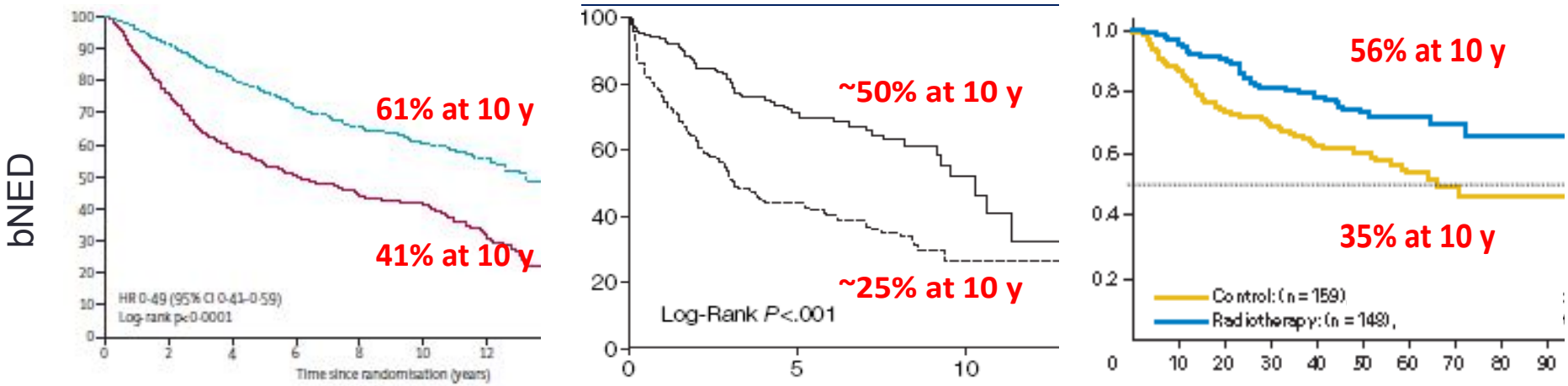
Declining Use of Radiotherapy for Adverse Features After Radical Prostatectomy: Results From the National Cancer Data Base

Helmneh M. Sineshaw [a,†,*], *Phillip J. Gray* [b,†], *Jason A. Efstathiou* [b,‡], *Ahmedin Jemal* [a,‡]



Randomized Trials Adjuvant RT *vs* Observation

EORTC 22911 | SWOG 8794 | ARO 9602



ASTRO/AUA Joint GUIDELINES

Statement	Recommendation
Clinical principle	Counsel men on possibility of recurrence after RP
Clinical principle	Inform men that adjuvant RT can be beneficial
Grade A evidence	Offer men with negative features at RP adjuvant RT

Concerns with Adjuvant RT

"Observation"group did not routinely receive early salvage RT after failure

Table 5: First active salvage treatment for patients who relapsed in wait-and-see group (n=207)

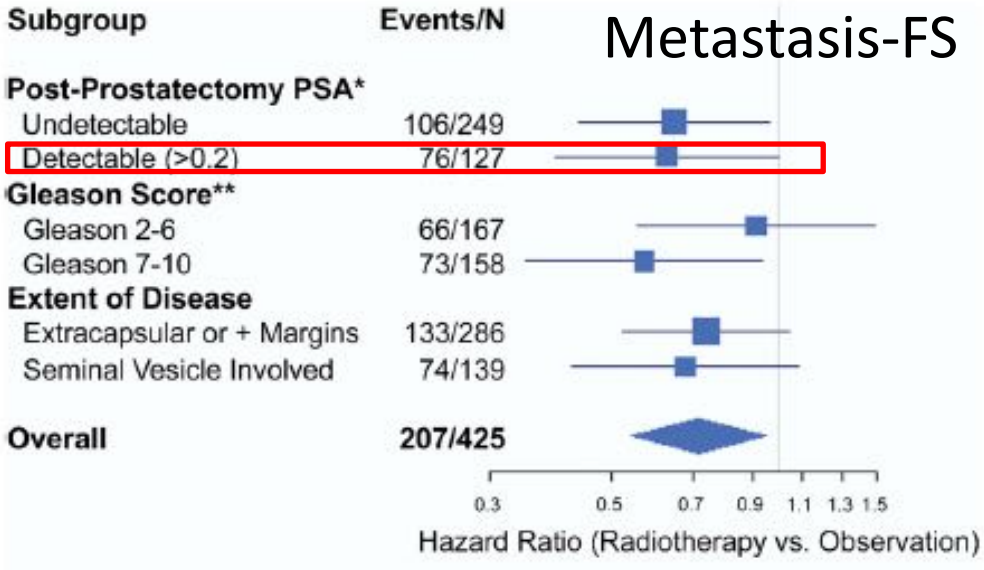
No active treatment (after biochemical failure without clinical failure)	44 (21·3%)
First active treatment for progression → Median time 2.2 years	163 (78·7%)
Pelvic radiotherapy	113 (54·6%)
Surgical castration	1 (0·5%)
Hormonal treatment	45* (21·7%)
Other (eg, estracyt, or hormonal treatment with palliative irradiation)	4 (1·9%)

"If early salvage RT were routinely given, perhaps we would not detect a benefit with adjuvant RT "

Bolla, Lancet 2005

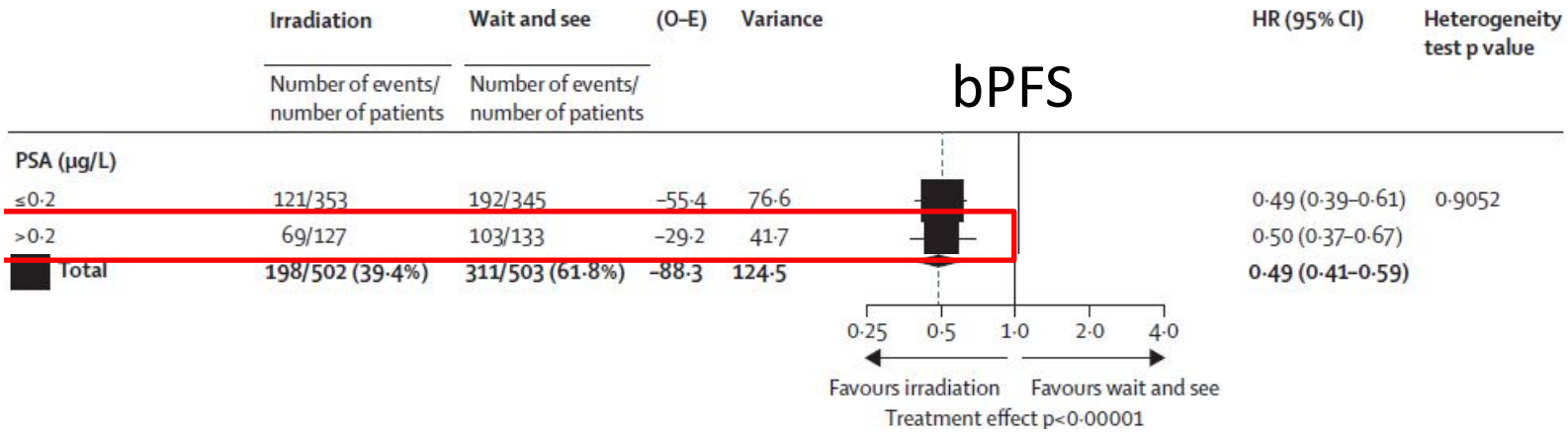
Concerns with Adjuvant RT

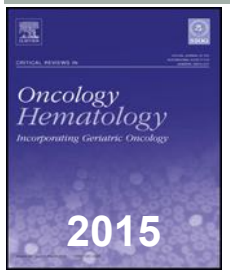
SWOG 8794



30% of men enrolled with a PSA > 0.2

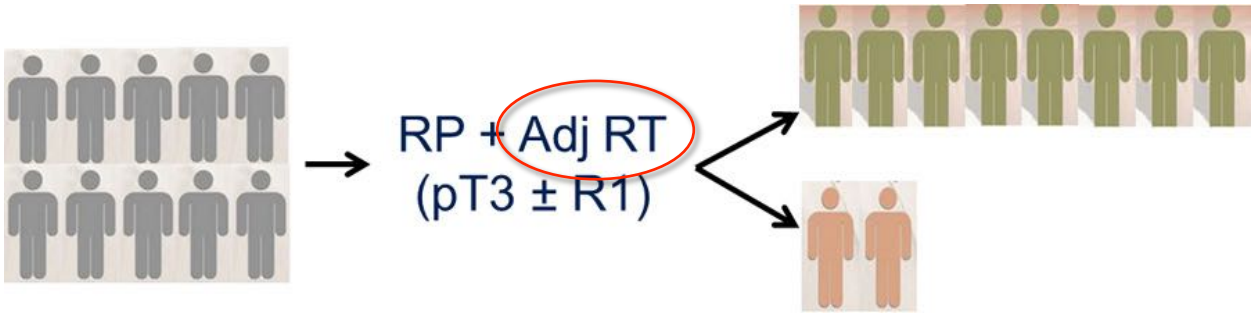
EORTC 22911

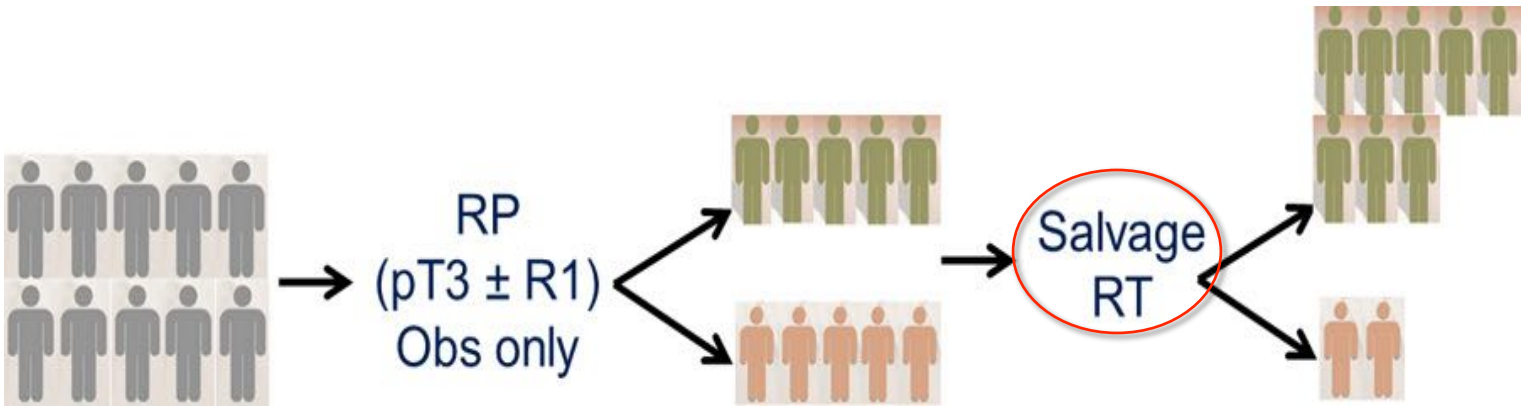




A cast of shadow on adjuvant radiotherapy for prostate cancer: A critical review based on a methodological perspective

Stefano Arcangeli[a,*], Sara Ramella[b], Berardino De Bari[c], Pierfrancesco Franco[d], Filippo Alongi[e]
Rolando M. D'Angelillo[b]





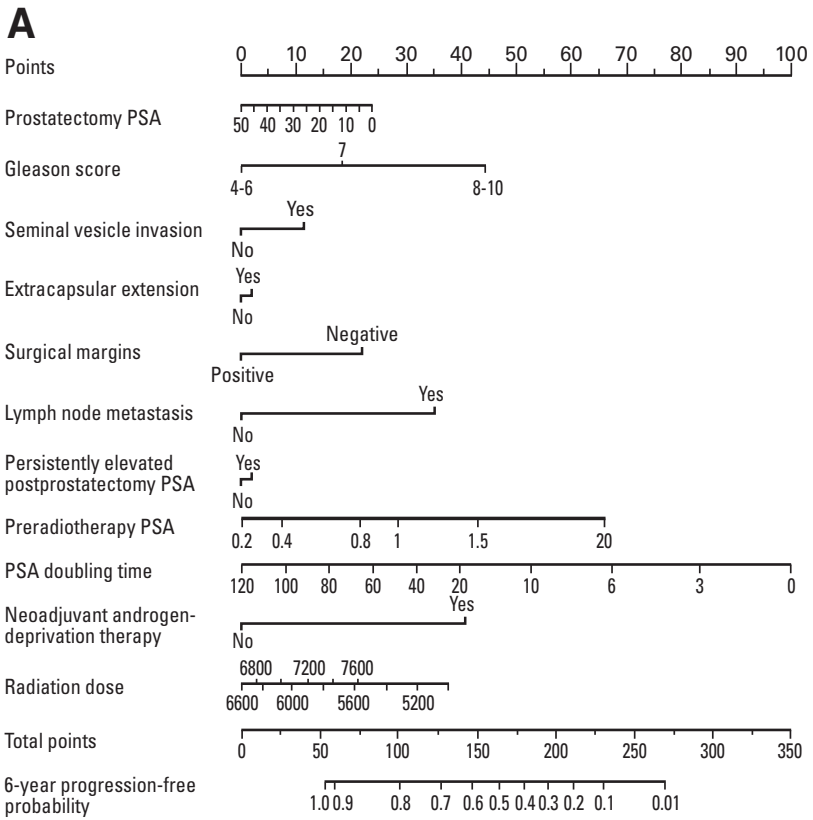
Adjuvant *vs* Salvage RT

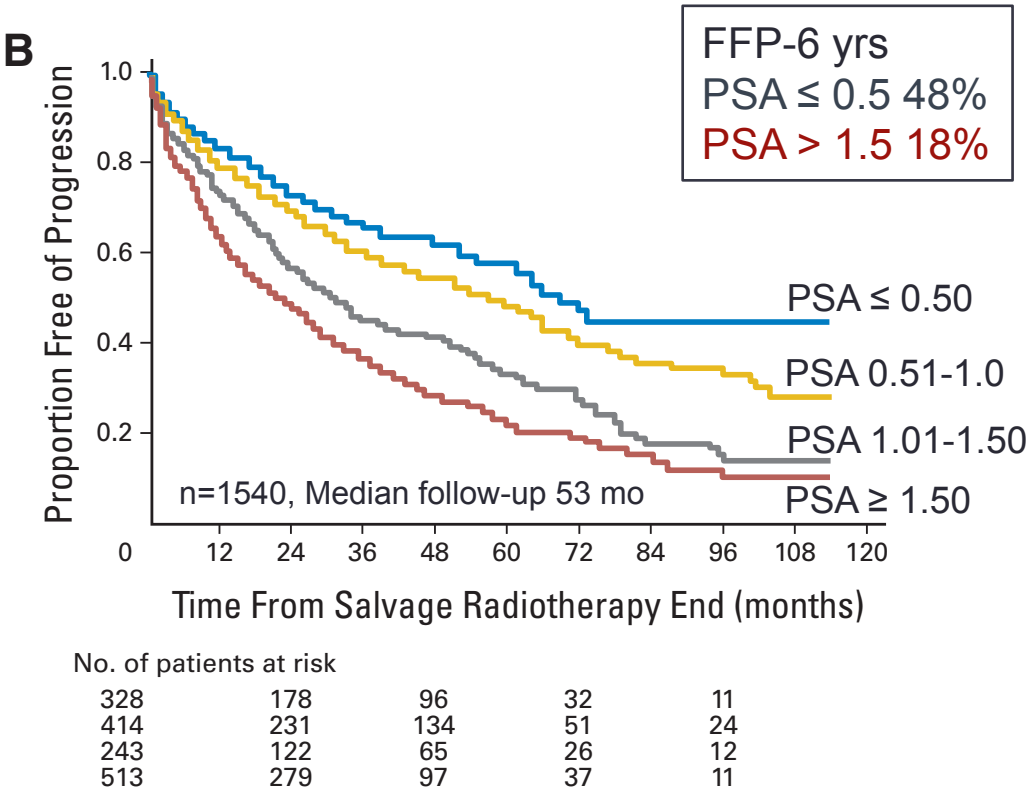
Table 3 Active Randomized Controlled Trials of Adjuvant Versus Early Salvage RT

Trial Name	Eligibility	Arms	RT Dose	ADT	Endpoint
RADICALS: RT and ADT In Combo After Local Surgery MRC-UK	No path criteria	ART vs eSRT PSA cutoff 0.1	66 Gy PB or WP	ADT: none vs 6 mo vs 2 years LHRH or bicalutamide, 150 mg	PCSS
RAVES: RT Adj. Vs Early Salvage Trans-Tasman (TROG)	pT3 or M+	ART vs eSRT PSA cutoff 0.2	64 Gy	No ADT	bPFS
GETUG-17 French Urology Study Group	pT3 or M+	ART vs eSRT PSA cutoff 0.2	64 Gy	ADT 6 mo LHRH	bPFS

Predicting the Outcome of Salvage Radiation Therapy for Recurrent Prostate Cancer After Radical Prostatectomy

Andrew J. Stephenson, Peter T. Scardino, Michael W. Kattan, Thomas M. Pisansky, Kevin M. Slawin, Eric A. Klein, Mitchell S. Anscher, Jeff M. Michalski, Howard M. Sandler, Daniel W. Lin, Jeffrey D. Forman, Michael J. Zelefsky, Larry L. Kestin, Claus G. Roehrborn, Charles N. Catton, Theodore L. DeWeese, Stanley L. Liauw, Richard K. Valicenti, Deborah A. Kuban, and Alan Pollack





No. of patients at risk

328	178	96	32	11
414	231	134	51	24
243	122	65	26	12
513	279	97	37	11

Strategy with a post-op PSA

"Post-op active surveillance"analogy
– Weighing natural history of disease vs. life expectancy

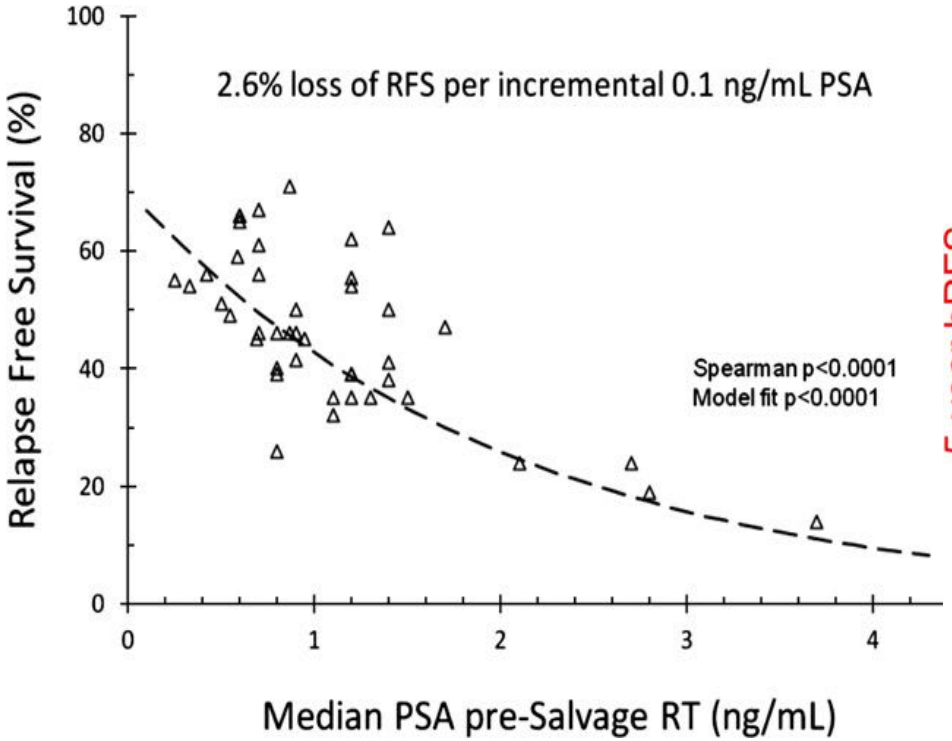
Prostate-Specific Antigen Doubling Time, mo	Risk Estimate, % (95% Confidence Interval)			
	Recurrence >3 y After Surgery		Recurrence ≤3 y After Surgery	
	Gleason Score <8	Gleason Score ≥8	Gleason Score <8	Gleason Score ≥8
5-y Estimate				
≥15.0	100 (98 to 100)	99 (98 to 99)	99 (96 to 100)	98 (90 to 100)
9.0-14.9	99 (70 to 100)	98 (75 to 100)	97 (76 to 100)	94 (63 to 99)
3.0-8.9	97 (81 to 100)	94 (74 to 99)	91 (67 to 98)	81 (46 to 95)
<3.0	92 (70 to 98)	83 (52 to 96)	74 (37 to 93)	51 (19 to 82)
10-y Estimate				
≥15.0	98 (96 to 100)	96 (93 to 98)	93 (80 to 98)	86 (61 to 96)
9.0-14.9	95 (75 to 99)	90 (58 to 98)	85 (49 to 97)	69 (30 to 92)
3.0-8.9	84 (62 to 94)	68 (37 to 89)	55 (25 to 82)	26 (7 to 62)
<3.0	59 (29 to 83)	30 (10 to 63)	15 (3 to 53)	1 (<1 to 55)
15-y Estimate				
≥15.0	94 (87 to 100)	87 (79 to 92)	81 (57 to 93)	62 (32 to 85)
9.0-14.9	86 (57 to 97)	72 (35 to 92)	59 (24 to 87)	31 (7 to 72)
3.0-8.9	59 (32 to 81)	30 (10 to 63)	16 (4 to 49)	1 (<1 to 51)
<3.0	19 (5 to 51)	2 (<1 to 38)	<1 (<1 to 26)	<1 (<1 to 2)

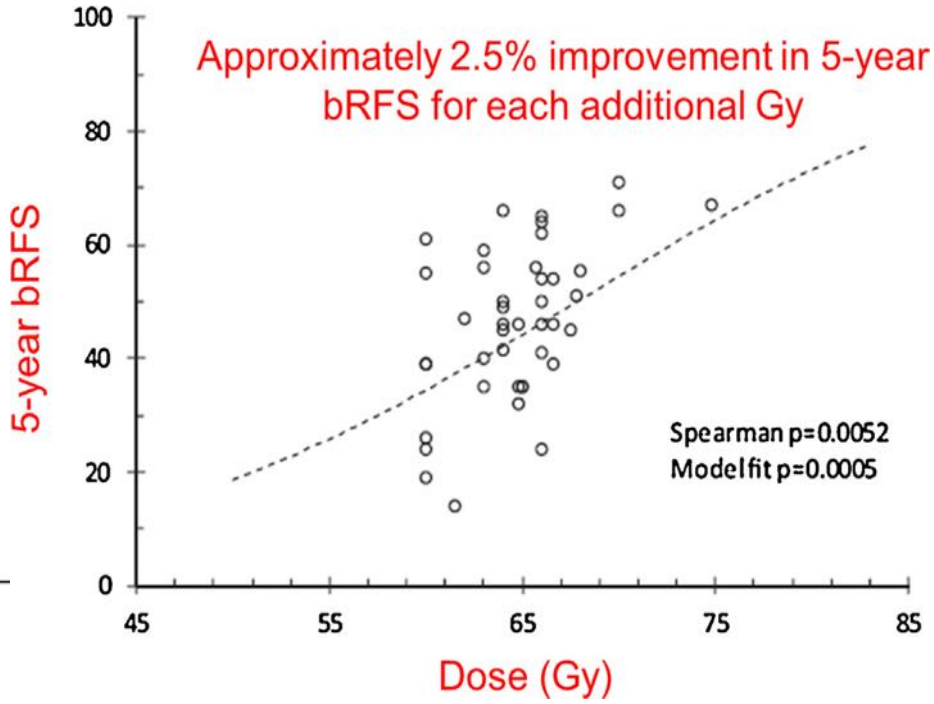
15-y CSS 94%:
BF > 3 y after RP
PSA DT ≥ 15 mo
GS < 8

Freedland, JAMA 2005

Salvage RT: Dose-Response

RT dose above 70 Gy should be administered at the lowest possible PSA





King, Semin Rad Oncol 2013

NEED FOR HIGH RADIATION DOSE (≥70 GY) IN EARLY POSTOPERATIVE IRRADIATION AFTER RADICAL PROSTATECTOMY: A SINGLE-INSTITUTION ANALYSIS OF 334 HIGH-RISK, NODE-NEGATIVE PATIENTS

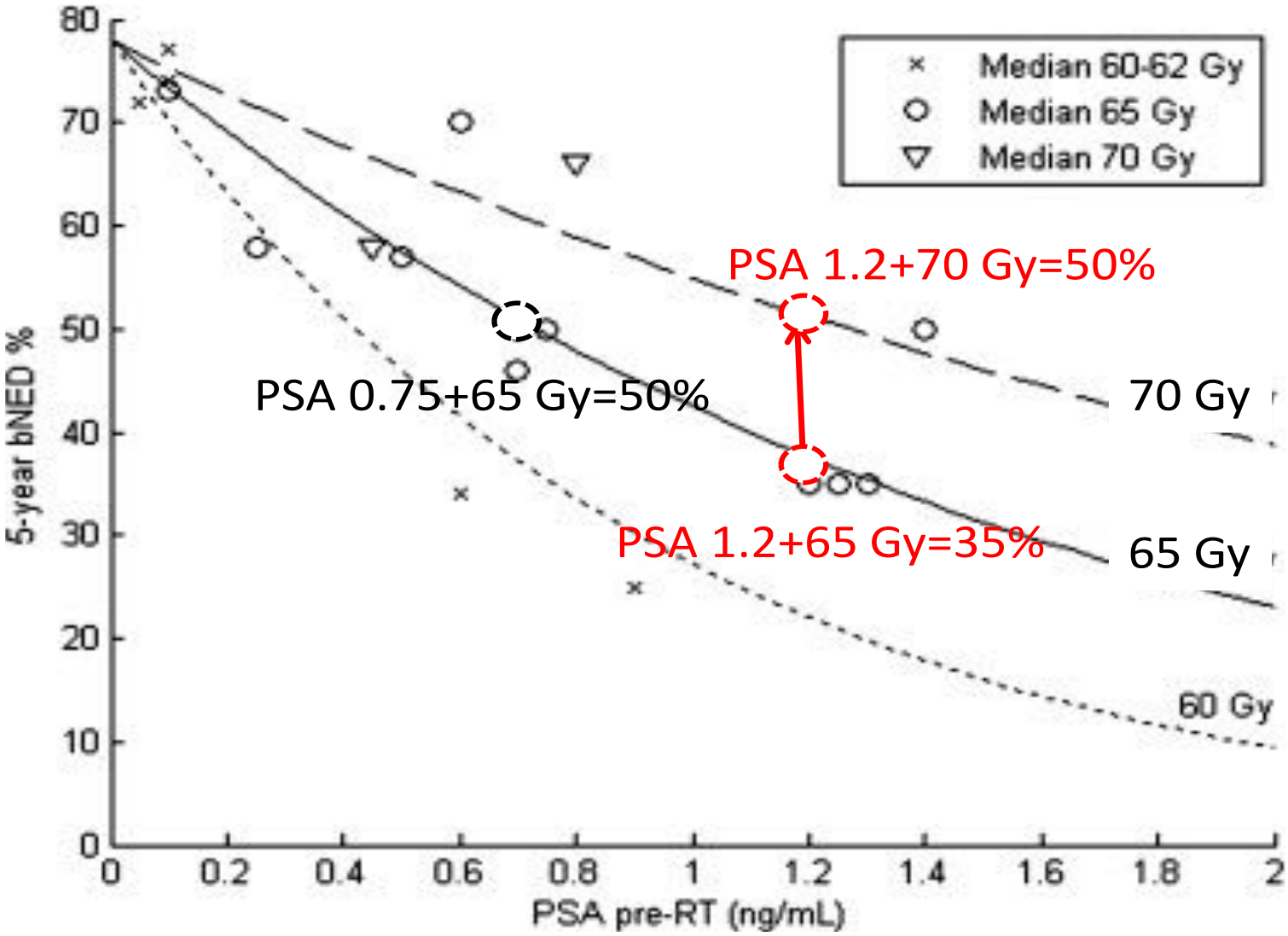
CESARE COZZARINI, M.D.,* FRANCESCO MONTORSI, M.D.,† CLAUDIO FIORINO, PH.D.,‡ FILIPPO ALONGI, M.D.,*§ ANGELO BOLOGNESI, M.D.,* LUIGI FILIPPO DA POZZO, M.D.,† GIORGIO GUAZZONI, M.D.,† MASSIMO FRESCHI, M.D.,‖ MARCO ROSCIGNO, M.D.,† VINCENZO SCATTONI, M.D.,† PATRIZIO RIGATTI, M.D.,† AND NADIA DI MUZIO, M.D.*

Table 3. Multivariate analysis for bRFS and DFS in the whole group

Variable	Comparison	Hazard ratio	95% CI	*p*
bRFS				
Neoadjuvant AD (mo)	Continuous variable			
Initial PSA	Continuous variable	1.00	0.99–1.01	0.60
Pathologic stage	pT2 vs. pT3a vs. pT3b vs. pT4	1.30	0.92–1.83	0.13
Gleason score	Continuous variable	1.48	1.20–1.82	0.0002*
Postoperative PSA	Continuous variable	1.19	1.06–1.35	0.003*
Surgical margins status	Negative vs. positive	1.17	0.67–2.05	0.57
EART dose	≥70 Gy vs. <70 Gy	2.51	1.54–4.88	0.04*
EART dose	Continuous variable	0.93	0.88–0.98	0.002*
Adjuvant AD (months)	Continuous variable	0.99	0.97–1.01	0.50
Adjuvant AD	No vs. yes	0.76	0.38–1.52	0.44
DFS				
Neoadjuvant AD (mo)	Continuous variable	1.06	0.92–1.22	0.36
Initial PSA	Continuous variable	1.00	0.99–1.02	0.39
Pathologic stage	pT2 vs. pT3a vs. pT3b vs. pT4	1.16	0.72–1.88	0.52
Gleason score	Continuous variable	1.63	1.24–2.15	0.0005*
Postoperative PSA	Continuous variable	1.27	1.09–1.47	0.002*
Surgical margins status	Negative vs. positive	0.54	0.25–1.14	0.11
EART dose	≥70 Gy vs. <70 Gy	3.56	1.49–8.46	0.004*
EART dose	Continuous variable	0.91	0.85–0.98	0.02*
Adjuvant AD (months)	Continuous variable	1.06	0.92–1.22	0.36
Adjuvant AD	No vs. yes	0.59	0.20–1.74	0.34

5-y bRFS: +12% if ≥ 70Gy

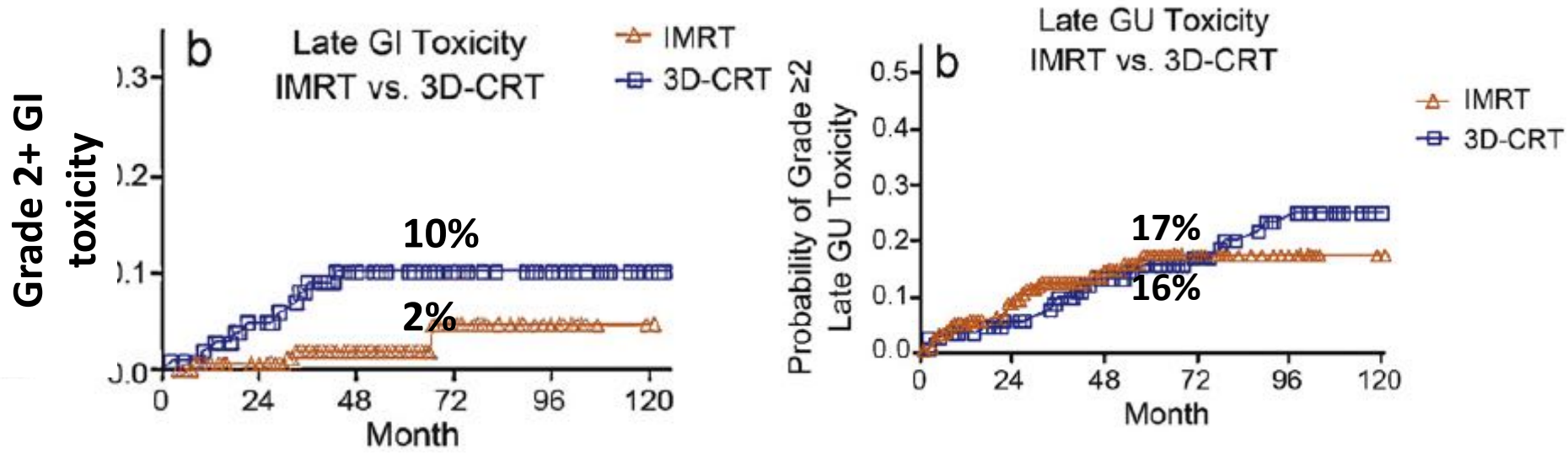
Higher RT doses might compensate for a higher pre-RT PSA



Ohri, IJROBP 2011

Salvage RT: Techniques

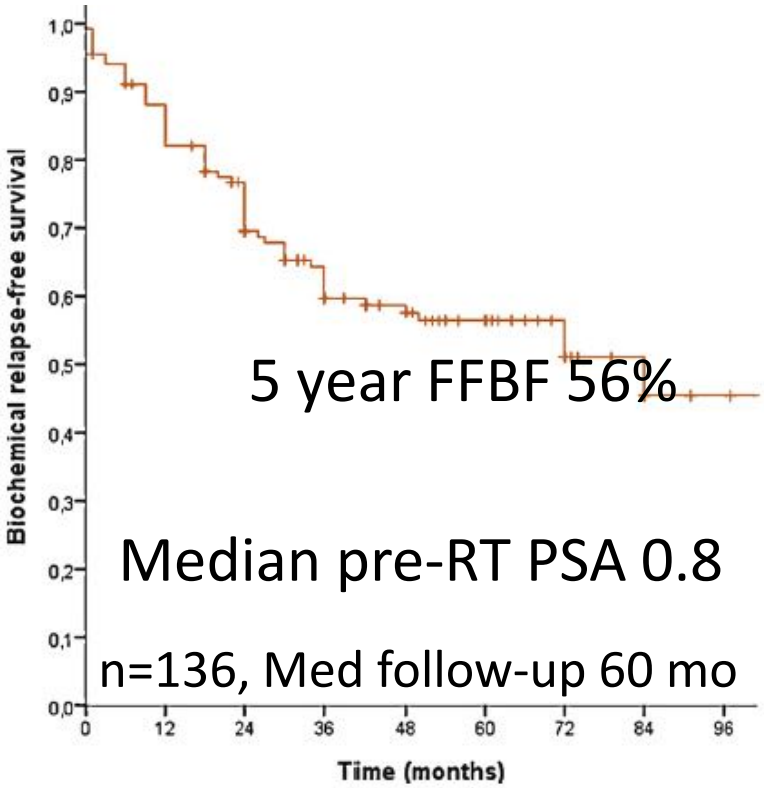
- MSKCC
  - 176 pts IMRT (≥70 Gy); 109 pts 3DCRT (66-70 Gy)
- Treatment primarily to prostate bed alone
- Median follow-up 60 months



IMRT may allow for safer escalation of dose to ~70 Gy

Goenka, Eur Urol 2011

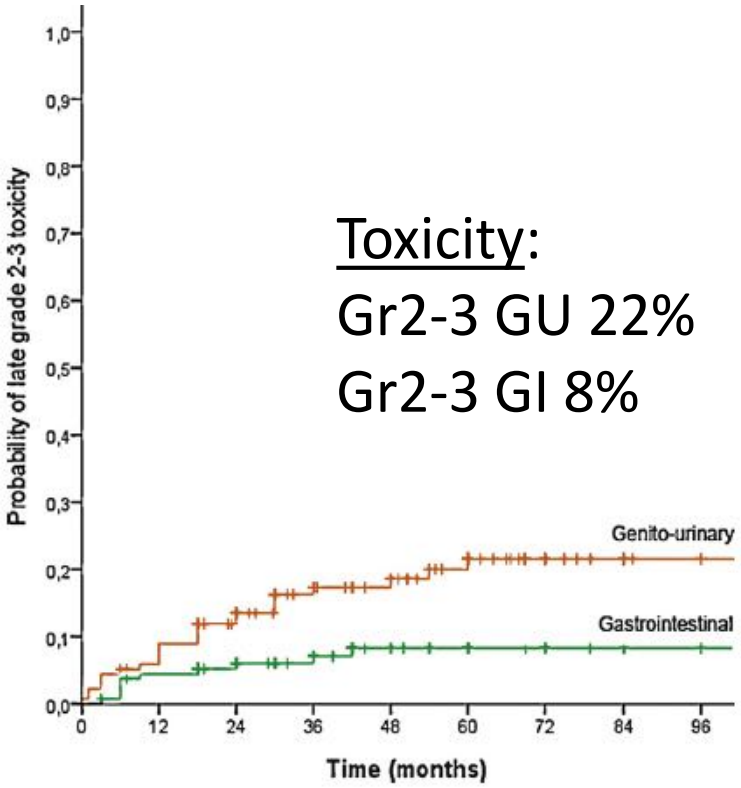
- 76 Gy to prostate bed



5 year FFBF 56%

Median pre-RT PSA 0.8

n=136, Med follow-up 60 mo



Toxicity:

Gr2-3 GU 22%

Gr2-3 GI 8%

High dose IMRT is tolerated with limited G3 tox

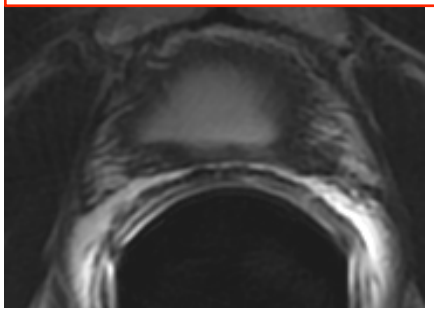
(Smaller, MRI defined prostate bed + 4-7 mm with IGRT)

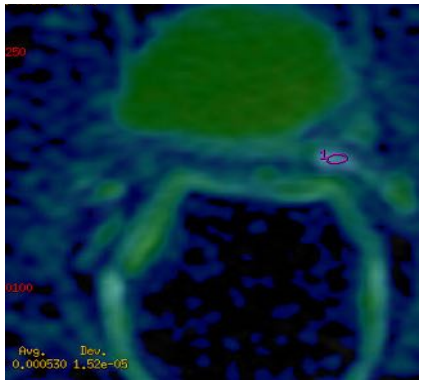
Ost, Eur Urol 2011

^{18}F-Choline Positron Emission Tomography/ Computed Tomography—Driven High-Dose Salvage Radiation Therapy in Patients With Biochemical Progression After Radical Prostatectomy: Feasibility Study in 60 Patients

Rolando M. D'Angelillo, MD,* Rosa Sciuto, MD,† Sara Ramella, MD,* Rocco Papalia, MD,‡ Barbara A. Jereczek-Fossa, MD,§,|| Luca E. Trodella, MD,* Michele Fiore, MD,* Michele Gallucci, MD,‡ Carlo L. Maini, MD,† and Lucio Trodella, MD*

Median PSA before SRT 0.9 ng/mL





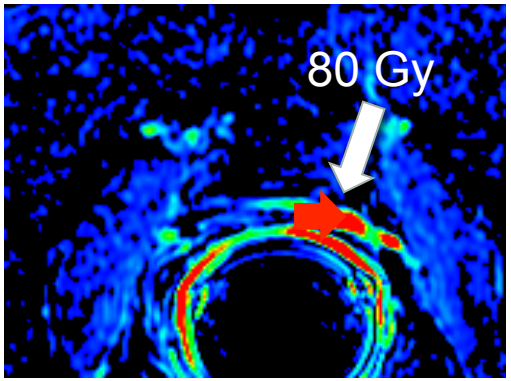
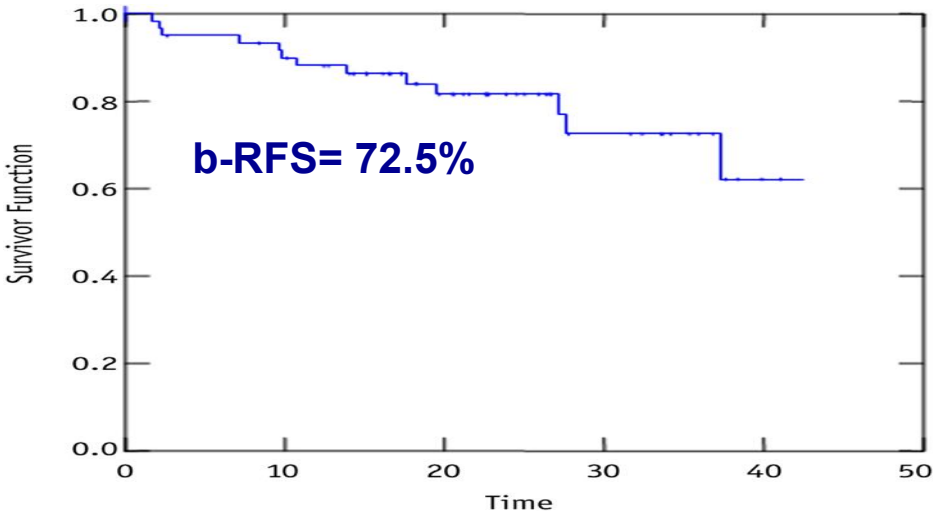


Table 2 Radiation-related toxicity according to Common Terminology Criteria for Adverse Events, version 3.0 (19) (N = 60 patients)

Type of toxicity	Grade 0	Grade 1	Grade 2	Grade 3
Acute toxicity				
Gastrointestinal	35 (58.3)	19 (31.7)	3 (5)	3 (5)
Genitourinary	47 (78.3)	13 (21.7)	0	0
Late toxicity				
Gastrointestinal	49 (81.6)	10 (16.7)	1 (1.7)	0
Genitourinary	54 (90)	6 (10)	0	0

Values are number (percentage).



Salvage RT: Toxicity

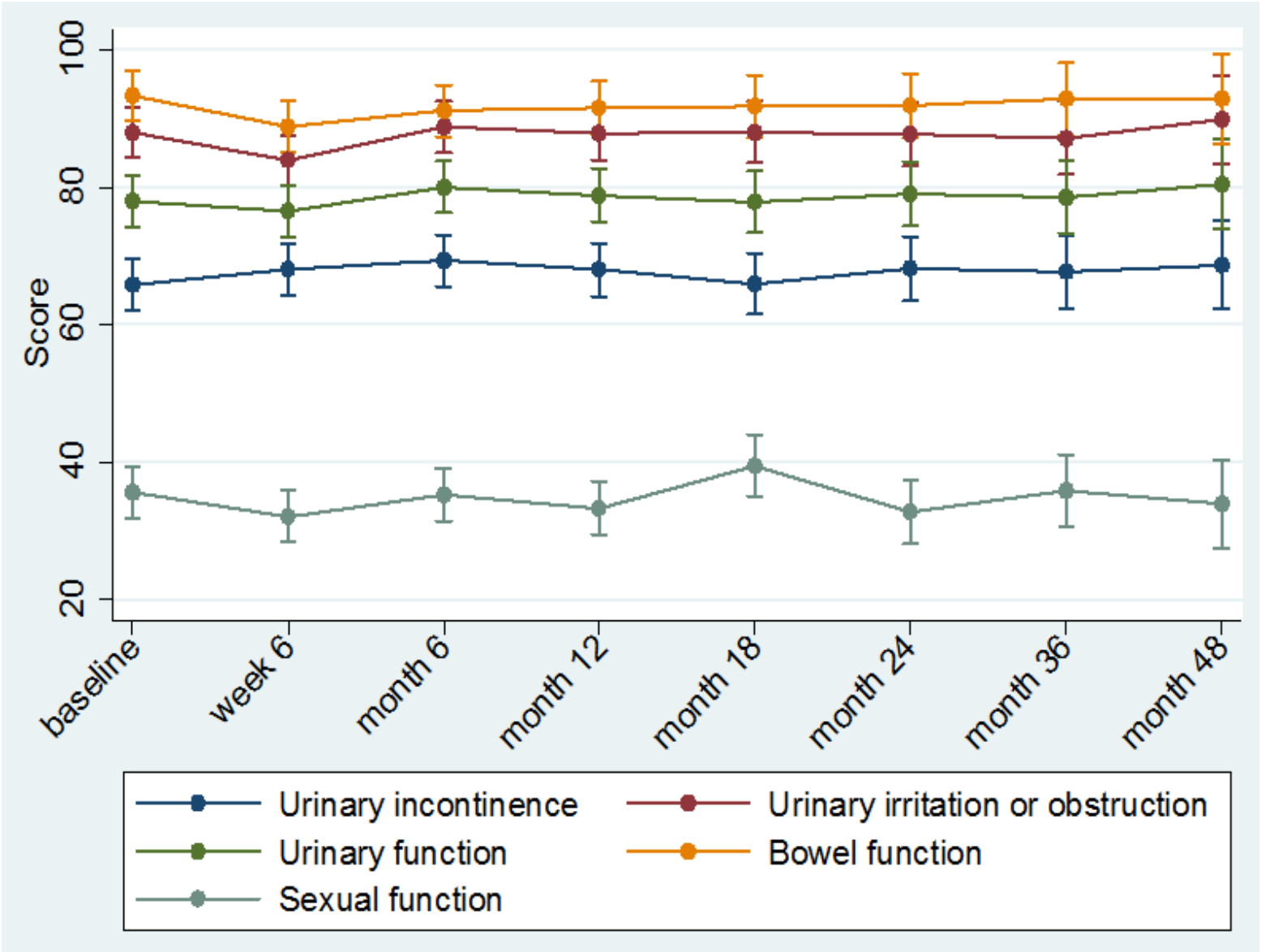
Table 2 Percent of patients reporting specific levels of dysfunction or distress for each quality of life domain

Variable	Baseline (n = 58)	2 months (n = 65)	6 months (n = 64)	12 months (n = 50)	18 months (n = 49)	24 months (n = 44)
Urinary function						
Irritation or obstruction						
Dysuria	2	5	0	0	0	0
Hematuria	0	0	0	0	2	2
Weak stream	2	2	0	0	2	0
Nocturia	9	20	14	10	14	11
Frequency	7	13	5	2	10	7
Incontinence						
Leaking >1 time per day	35	23	22	20	18	20
Frequent dribbling	12	11	6	16	6	5
Any pad use	40	35	35	30	39	27
Leaking problem	9	14	9	10	10	5
Overall urinary problem	7	14	8	10	8	5
Fecal incontinence	2	0	0	2	2	2
Bloody stools	2	2	0	0	0	0
Rectal pain	5	3	2	0	2	2
Overall bowel problem	2	6	3	2	4	7
Sexual function						
Poor erections	62	72	66	67	63	66
Difficulty with orgasm	49	56	48	46	52	59
Erections not firm	62	70	63	67	66	67
Erections not reliable	72	78	77	71	75	77
Sexually active	38	38	33	35	35	28
Poor sexual function	60	69	58	63	64	69
Overall sexuality problem	49	31	44	39	29	40

Post-op IMRT does not clearly worsen continence

Corbin, PRO 2013

Patient reported QOL shows stability at 4 years



Melotek, PLoS One 2015

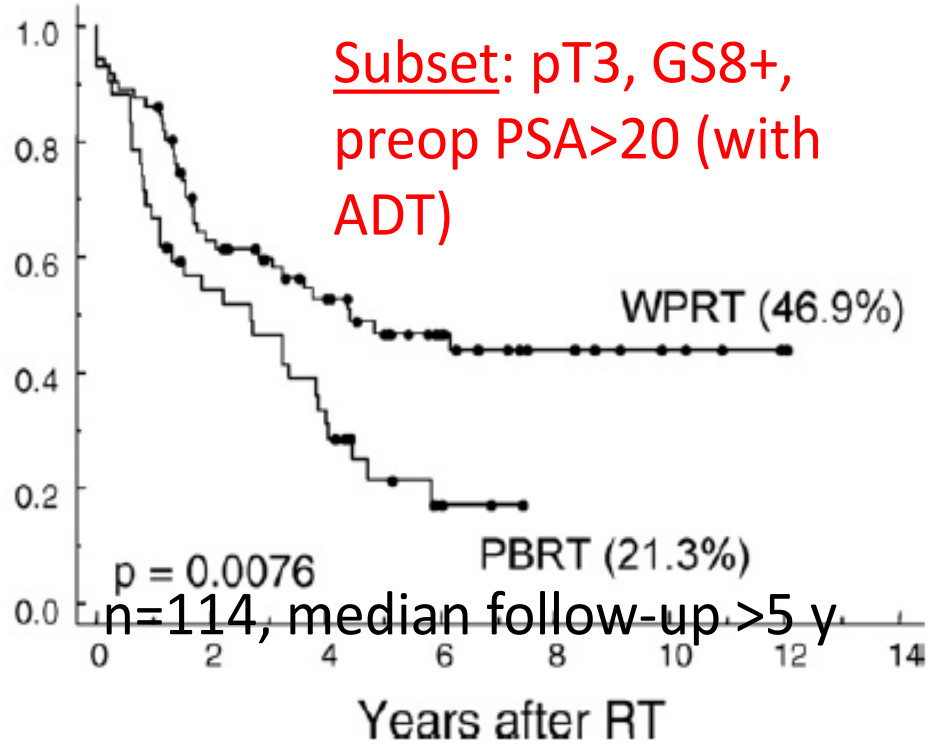
Salvage RT: Volumes

Fig. 3. Examples of consensus contours for patient with apical positive margins and biochemical recurrence.

Wiltshire, IJROBP 2007

Salvage RT: Volumes

STANFORD

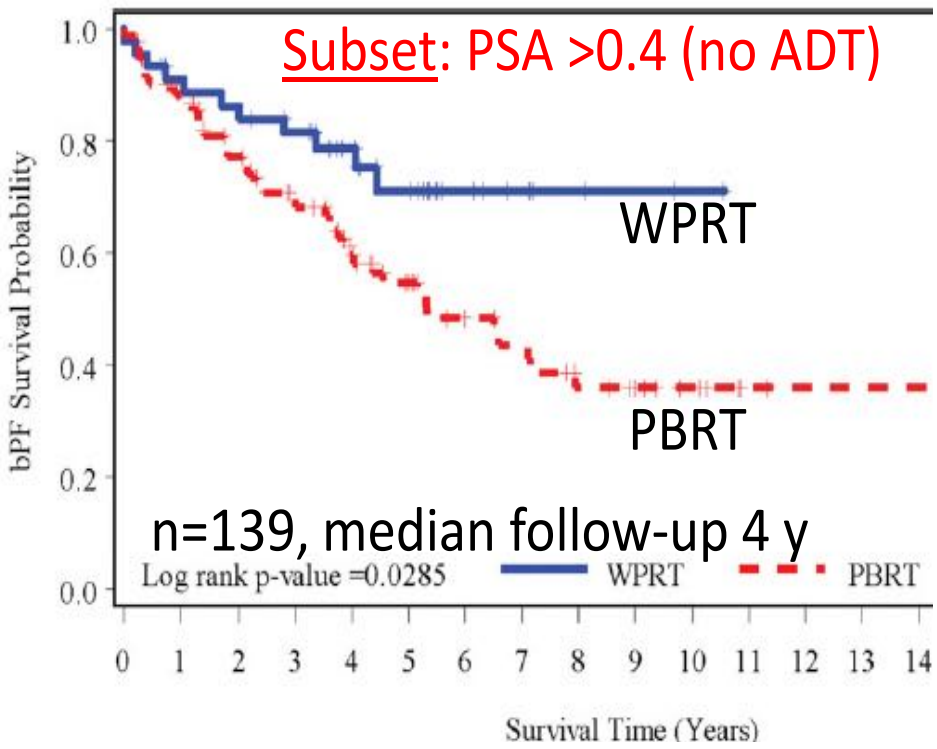


Subset: pT3, GS8+, preop PSA>20 (with ADT)

n=114, median follow-up >5 y

Spiotto, IJROBP 2007

DUKE



Subset: PSA >0.4 (no ADT)

n=139, median follow-up 4 y

Moghanaki, Cancer 2013

Salvage RT ± ADT

Table 4 Active Randomized Controlled Trials of Salvage RT ± ADT

Trial Name	Eligibility	Arms	RT Dose	ADT	End Point
GETUG-16	pT2-4 PSA up to 20	RT alone vs RT w/ADT	66 Gy	ADT 6 mo LHRH	bPFS
RTOG 96-01	pT3 or M+ PSA >0.2 up to 4.0	RT alone vs RT w/ADT	64.8 Gy to PB	ADT 2 y bicalutamide 150 mg	OS
RTOG 05-34	pT3 or M+ PSA 0.1-2.0	RT to PB ± ADT vs RT to WP w/ADT	64.8-70.2 Gy to PB, 45 Gy to WP	ADT 4-6 mo LHRH and bicalutamide	bPFS

Is it practice changing?

GETUG-AFU 16 trial

– 742 N0 pts with PSA-relapse randomised to RT alone vs RT + short-term ADT

- RT 66 Gy prostate bed ± 46 Gy pelvis
- Median follow-up 63 months

	RT (N=373)	RT + ADT (N=369)	HR	95% CI	*P*
5-yr PFS	62%	80%	0.50	0.38-0.66	<0.0001
5-yr OS	95%	96%	0.66	0.36-1.22	0.18

- QoL outcomes by QLQ-C30

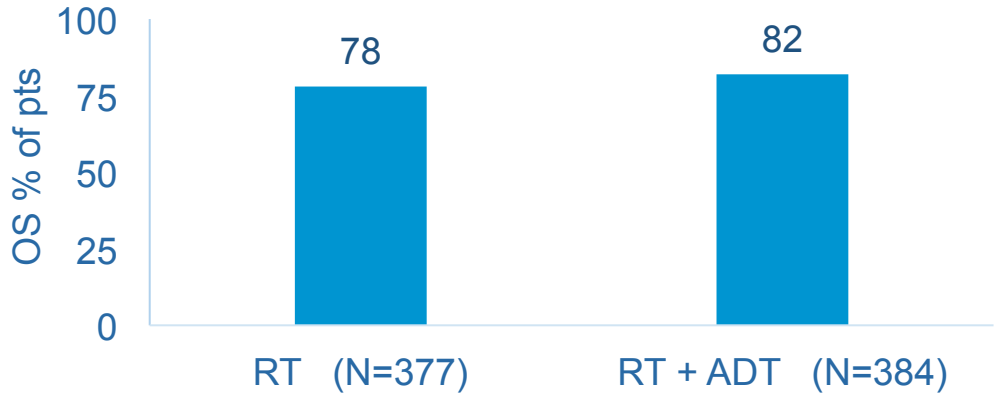
	RT	RT + ADT
Worsened	26%	35%
Stable	56%	48%
Improved	19%	17%

Carrie C. J Clin Oncol 2015

RTOG 9601 trial

– 761 N0 pts with elevated postop PSA (median PSA at study entry: 0.6 ng/ml) randomised to RT or RT + ADT (24 mo bicalutamide 150 mg)

- RT 64.8 Gy to prostate bed
- Median follow-up 12.6 yr



HR: 0.75; 95%CI: 0.58-0.98
P=0.036

	RT (N = 377)	RT + ADT (N = 384)	*P*
12-yr CSM	7.5%	2.3%	< 0.001
12-yr DM	23%	14%	<0.001
10-yr FFP	30%	42%	<0.001
Gynaecomastia	11%	70%	

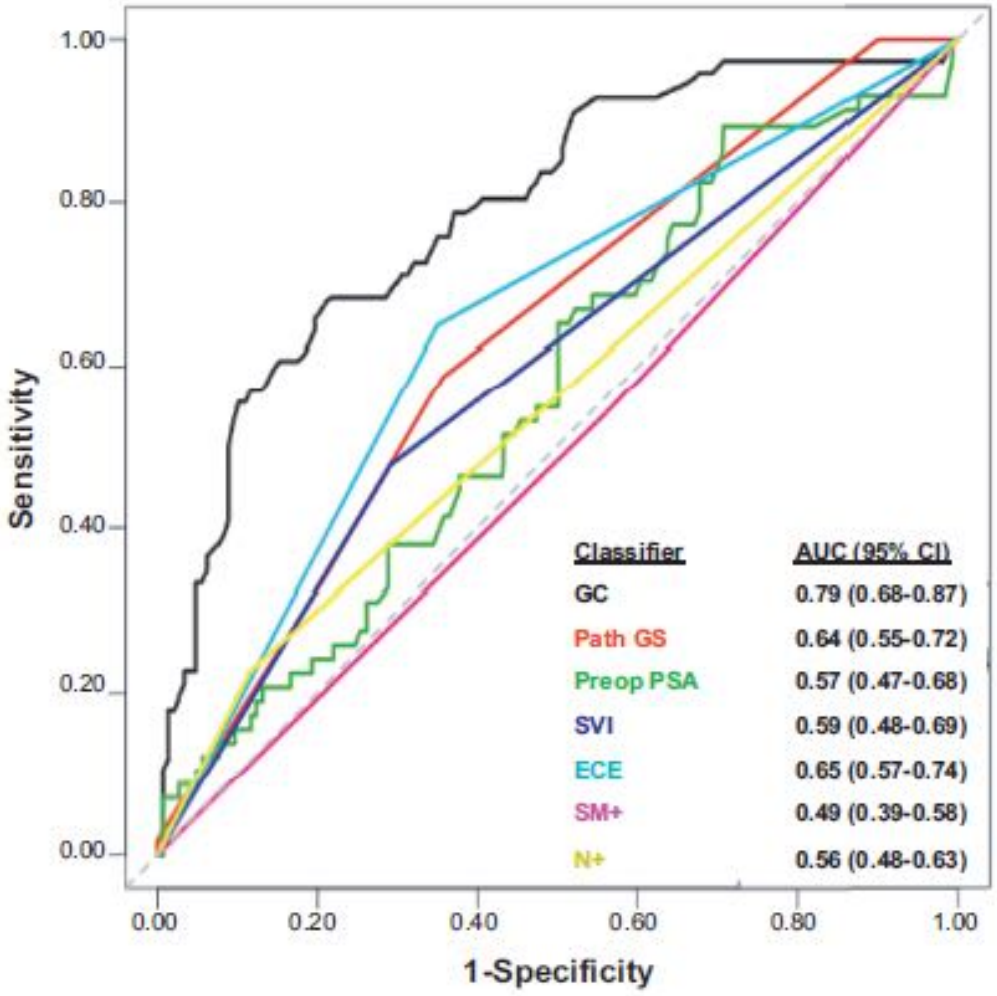
NNT: 17

Shipley WU. IJROBP 2015

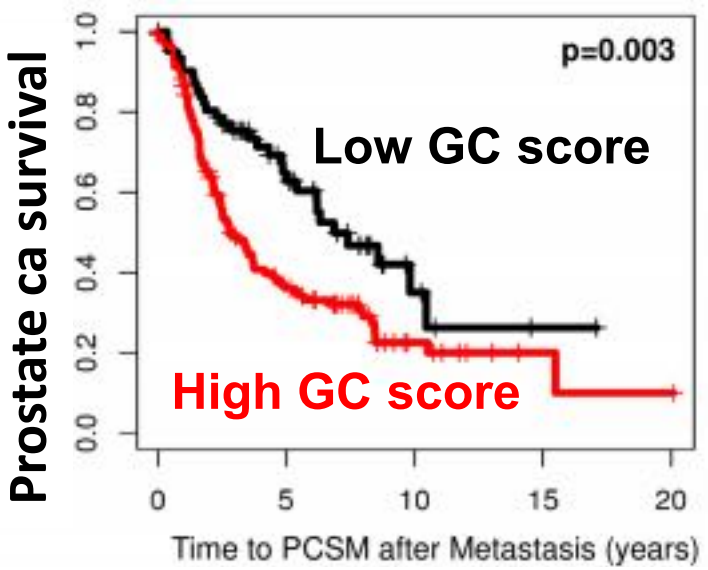
IMAGING for BF

	Recommended?	Comment
Ultrasound and biopsy	No	Moderate sensitivity only; only evaluates prostate bed
CT abdomen/pelvis	No	Low sensitivity with low PSA
Bone scan	*If PSA >10, PSADT<6 mo, velocity >0.5 ng/mL/mo; or sx*	Low sensitivity with low PSA; indeterminate findings possible
RIS (e.g. Prostascint)	Not routinely	Accuracy questionable; does not predict better salvage RT response
PET (C11, F18)	Not routinely	Accuracy low for PSA <2
MRI (Endorectal, DCE, DWI)	*Consider, especially for pT3 and positive margins*	Most favorable sensitivity and specificity (Lymphotropic nanoparticles not approved)

Biomarkers as a (future) variable?



22-gene classifier for distant metastasis after RP
(RNA micro dissection)

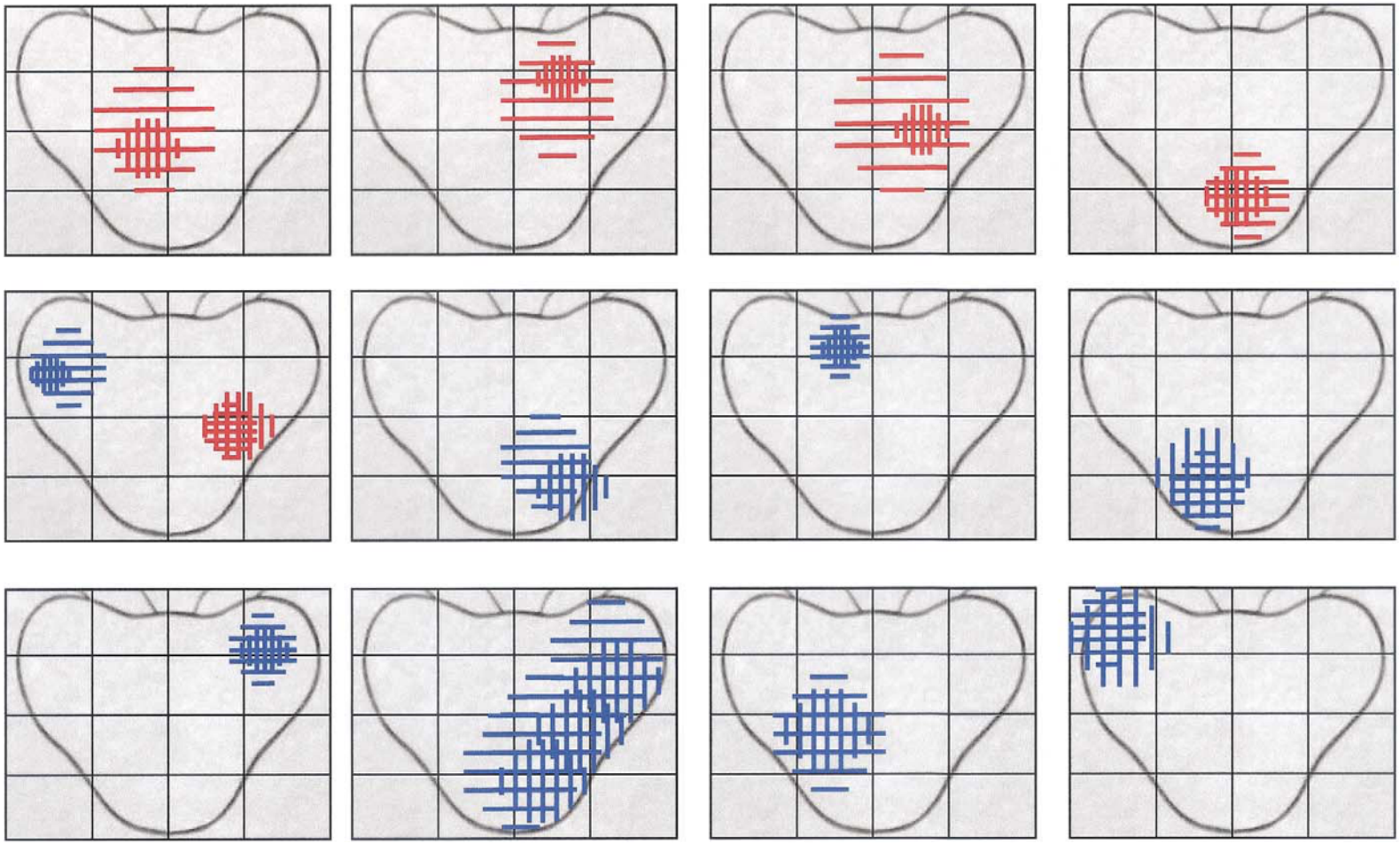


Karnes J Urol 2013

TERAPIE DI SALVATAGGIO NEL CAP: DOPO RADIOTERAPIA

ANALYSIS OF INTRAPROSTATIC FAILURES IN PATIENTS TREATED WITH HORMONAL THERAPY AND RADIOTHERAPY: IMPLICATIONS FOR CONFORMAL THERAPY PLANNING

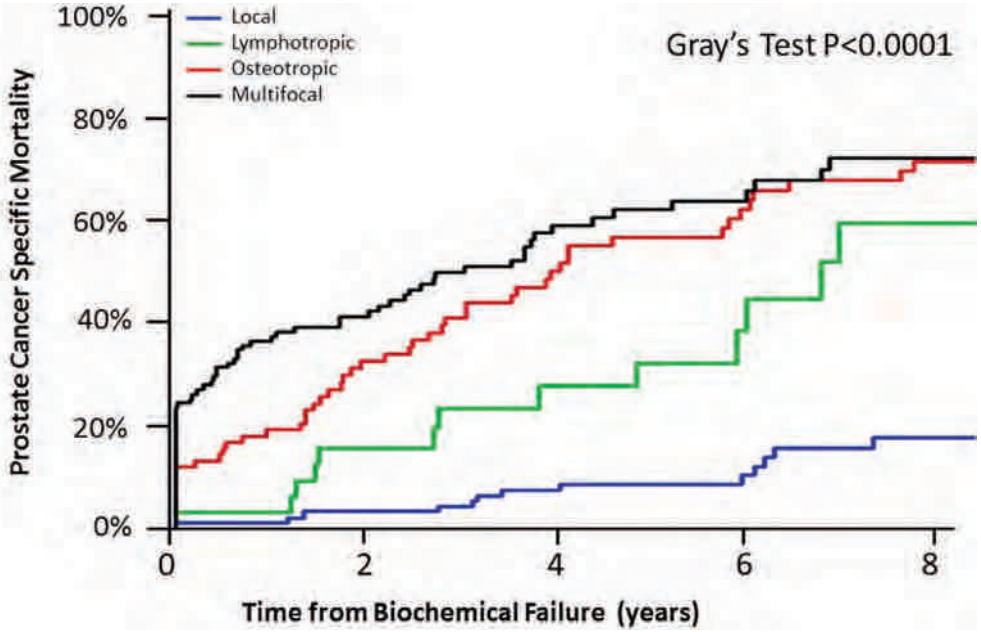
NUMA CELLINI, M.D., ALESSIO G. MORGANTI, M.D., GIAN C. MATTIUCCI, M.D., VINCENZO VALENTINI, M.D., MARIAVITTORIA LEONE, M.D., STEFANO LUZI, M.D., RICCARDO MANFREDI, M.D., NICOLA DINAPOLI, M.D., CINZIA DIGESU', M.D., AND DANIELA SMANIOTTO, M.D.



Anatomical Patterns of Recurrence Following Biochemical Relapse in the Dose Escalation Era for Prostate Patients Undergoing External Beam Radiotherapy

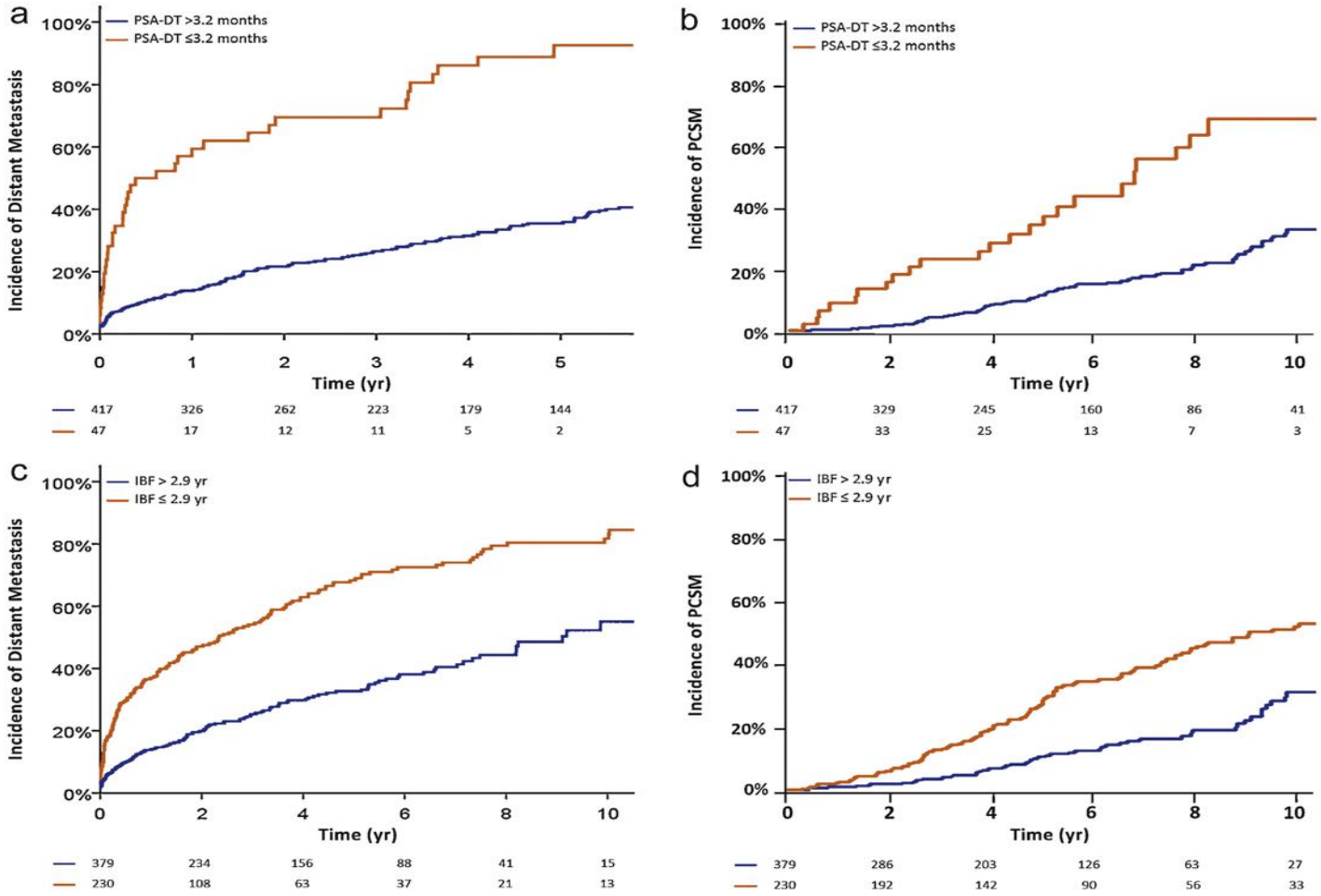
in press *www.jurology.com*

FRS	Low	Intermediate	High	Overall
		8-Yr Incidence		
% Any (95% CI):*				
Local	3.5 (1.8—5.2)	9.8 (7.9—11.8)	14.6 (12.0—17.2)	9.9 (8.6—11.2)
PLNs	0	2.7 (1.7—3.8)	8.3 (6.3—10.5)	3.9 (3.1—4.8)
Abdominal lymph nodes	0.5 (0—1.2)	1.2 (0.1—1.9)	2.9 (1.6—4.2)	1.6 (1.1—2.2)
Thoracic lymph nodes	0	0.7 (0.2—1.1)	0.3 (0—0.8)	0.4 (0.1—0.7)
Bone	0.9 (0.1—1.7)	3.9 (2.6—5.2)	14.2 (11.7—16.8)	6.5 (5.4—7.9)
Viscera	0	0.1 (0—0.4)	1.0 (0.3—1.7)	0.4 (0.1—0.6)

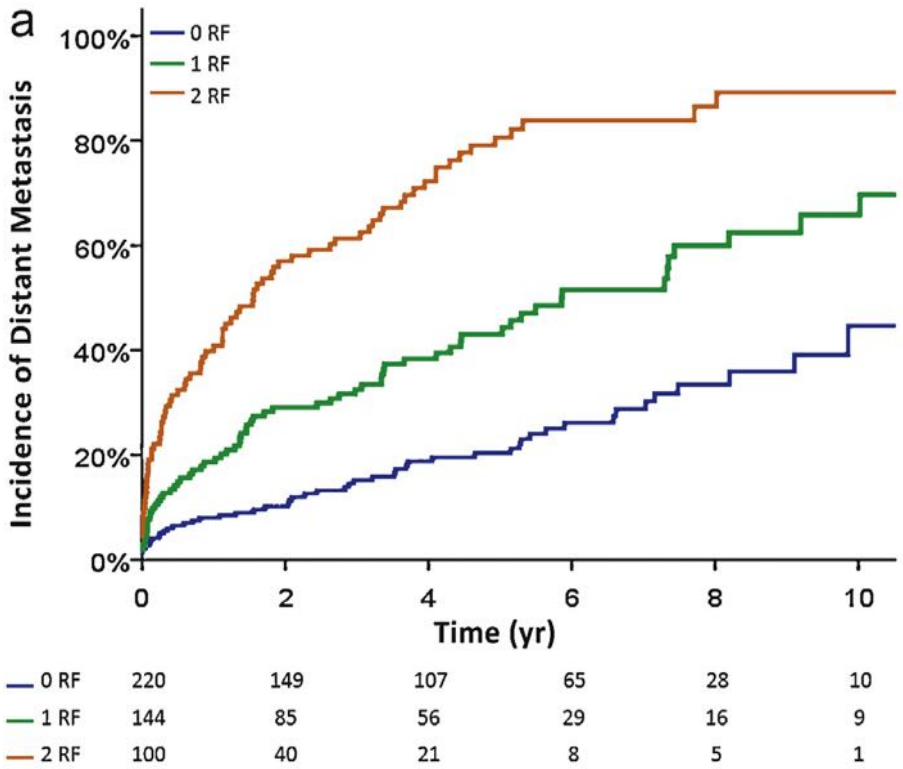


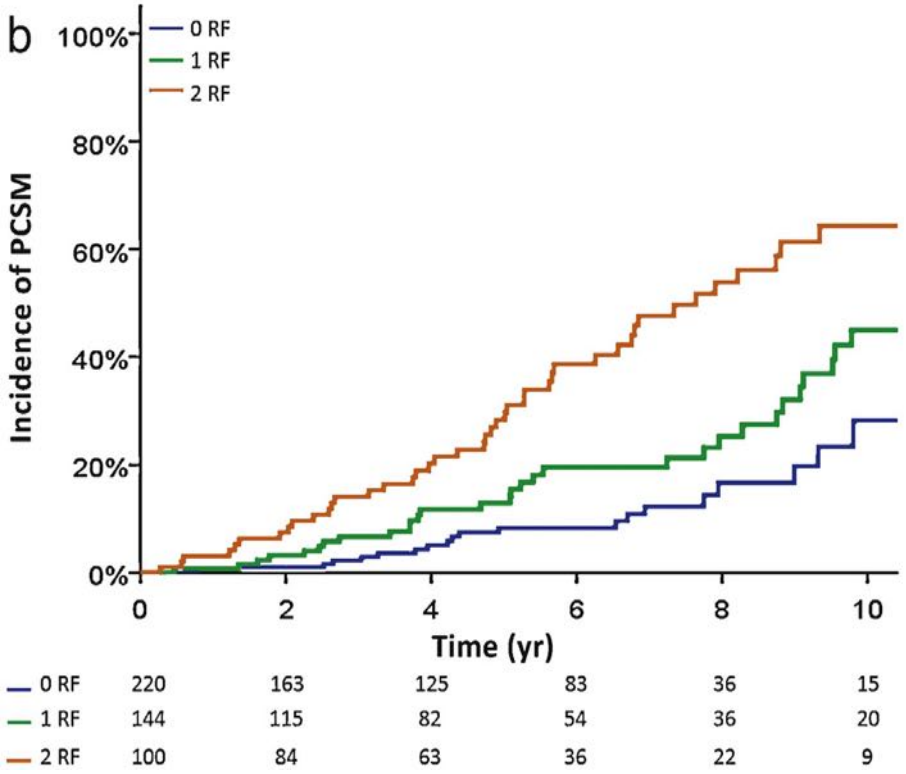
	Univariate*			Multivariate*		
	HR (95% CI)		p Value	HR (95% CI)		p Value
Recurrence pattern:						
Local	1.00	(referent)	—	1.00	(referent)	—
Lymphotropic	4.15	(2.03—8.45)	<0.0001	3.83	(1.57—9.33)	0.0026
Osteotropic	8.11	(4.64—14.20)	<0.0001	8.97	(4.22—19.06)	<0.0001
Multiorgan	9.56	(5.47—16.73)	<0.0001	9.19	(4.49—18.82)	<0.0001
Gleason score:						
6 or Less	1.00	(referent)	—	1.00	(referent)	—
3 + 4	1.01	(0.59—1.73)	0.97	1.49	(0.74—3.00)	0.26
4 + 3	1.86	(1.13—3.05)	0.013	1.75	(0.80—3.83)	0.15
8—10	2.48	(1.57—3.90)	<0.0001	2.20	(1.10—4.41)	0.023
Log PSA	1.03	(0.90—1.17)	0.70	1.00	(0.83—1.20)	0.98
T stage:						
T1c or less	1.00	(referent)	—	1.00	(referent)	—
T2a	1.60	(0.90—2.83)	0.1	1.70	(0.84—3.45)	0.13
T2b-c	1.50	(0.90—2.49)	0.11	1.27	(0.69—2.34)	0.44
T3a	1.24	(0.57—2.68)	0.58	0.71	(0.20—2.52)	0.59
T3b-T4	2.25	(1.39—3.64)	0.0008	1.42	(0.75—2.69)	0.28
Neoadjuvant ADT	1.50	(1.09—2.07)	0.012	0.84	(0.49—1.44)	0.51
Time to BR	0.79	(0.72—0.88)	<0.0001	1.02	(0.90—1.15)	0.77
Age	1.01	(0.99—1.04)	0.25	1.00	(0.97—1.03)	0.88
PSA doubling time	0.98	(0.97—1.00)	0.0079	0.99	(0.97—1.01)	0.17

The Natural History and Predictors of Outcome Following Biochemical Relapse in the Dose Escalation Era for Prostate Cancer Patients Undergoing Definitive External Beam Radiotherapy



The Natural History and Predictors of Outcome Following Biochemical Relapse in the Dose Escalation Era for Prostate Cancer Patients Undergoing Definitive External Beam Radiotherapy





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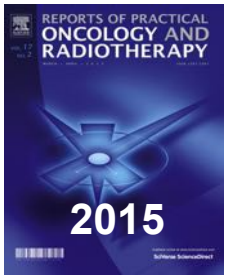
Biochemical recurrence after RT		
In patients with BCR who are candidates for local salvage therapy, prostate mpMRI may be used to localise abnormal areas and guide biopsy.	3	C

undetected cancers range from 12% to 26% and biopsies missed up to 20%

Meeks JJ, et al. BJU Int 2013

Biochemical recurrence (BCR) after RT		
Selected patients with localised PCa at primary treatment and histologically proven local recurrence should be treated with salvage RP (SRP).	3	B
Due to the increased rate of side effects, SRP should be performed in experienced centres.	3	A
High intensity focused ultrasound (HIFU), cryosurgical ablation and salvage brachytherapy are treatment options for patients without evidence of metastasis and with histologically proven local recurrence. Patients must be informed about the experimental nature of these approaches.	3	B



Uroncor consensus statement: Management of biochemical recurrence after radical radiotherapy for prostate cancer: From biochemical failure to castration resistance

Table 1 – Summary of results of local salvage therapy after radical radiotherapy in prostate cancer.

Salvage treatment	Primary treatment	Results	Complications	Observations
Radical prostatectomy	EBRT/BT	BRFS/5 years: 50% (47–82%) BRFS/10 years: 28% CSS/10 years: 70% OS/10 years: 54–89%	Incontinence: 50% (44–77%) Rectal fistula: 2.5% (2–10%) Stenosis: 25% (22–41%)	The treatment with the most extensive clinical experience, largest series, and longest published follow up.
Cryotherapy	EBRT/BT	BRFS/5years: 45% (30–50)% OS/5 years: 73%-85% DFS/5 years: 30–60%	Incontinence: 17% (10–73%) Fistula: 2% (1–10%) Stenosis: 7% (10–45%)	Patients not candidates for RP. Short follow up.
HIFU	EBRT	BRFS/5 years: 40% (30–50%) OS/5 years: 84%	Incontinence: 37% (6–50%) Fistulas: 4% (2–7%) Stenosis: 7% (4–35%)	Very limited experience and short follow up.
Brachytherapy	EBRT and/or BT	BRFS/5 years: 55% (35–70%)	Incontinence: 6% (5–30%) Fistula: 3% (0–6%) Stenosis: 7–8% Rectal ulcers: 2–4% GI Tox gr 4: 2–12% GU Tox gr3: 8–40% GU Tox gr 4:0–6%	Small series and short follow up.

BRFS, biochemical relapse free survival; CSS, cancer-specific survival; OS, overall survival, DFS, disease-free survival; EBRT, external radiotherapy; BT, brachytherapy; RP, radical prostatectomy; GI Tox, gastro-intestinal toxicity; GU Tox, genitourinary toxicity.

European Association of Urology

93.5% of patients are managed with ADT alone as secondary treatment on PSA progression, or with no salvage procedures

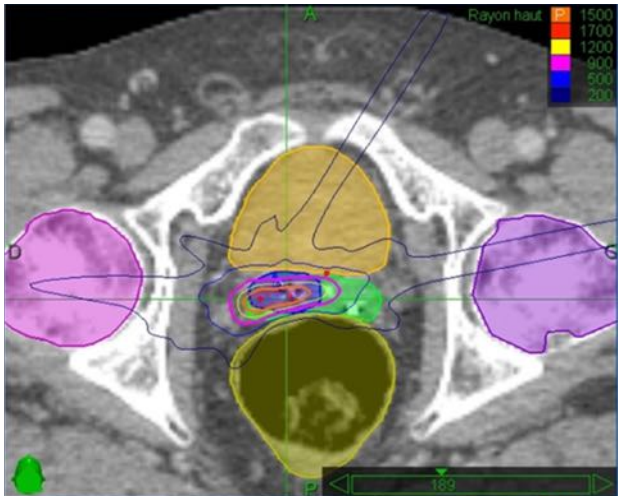
CAPSURE Study, J Urol 2002

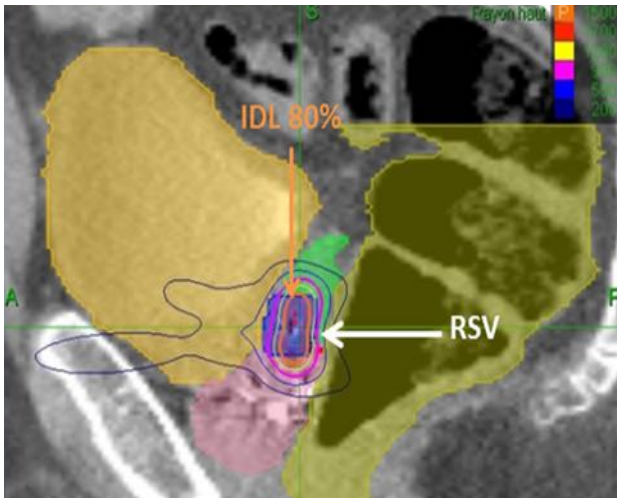
Systemic salvage treatment		
In asymptomatic men with BCR, ADT should not be given routinely.	3	A
Patients with a PSA-DT > 12 mo, should not receive ADT.	3	B
If salvage ADT (post-primary RT) is started, intermittent therapy should be considered in responding patients.	1b	A

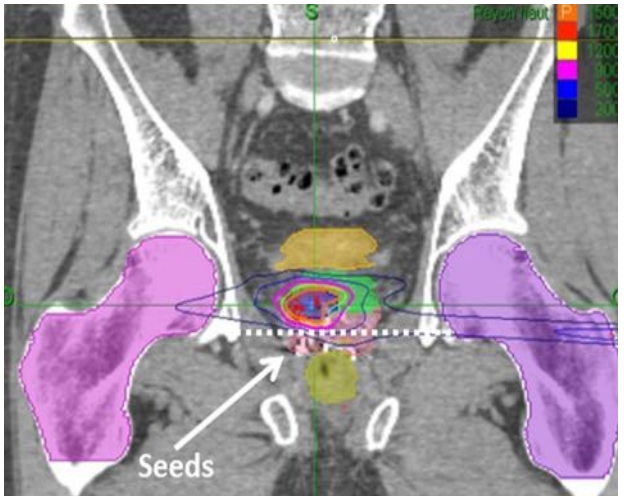
Salvage reirradiation for locoregional failure after radiation therapy for prostate cancer: Who, when, where and how?

Modalités des réirradiations de rattrapage pour les rechutes locales des cancers de la prostate

G. Créhange[a,b], M. Roach III[c,d], É. Martin[a], L. Cormier[e], D. Peiffert[f], A. Cochet[b,g,h], O. Chapet[i], S. Supiot[j], J.-M. Cosset[k], M. Bolla[l], H.T. Chung[m,*]







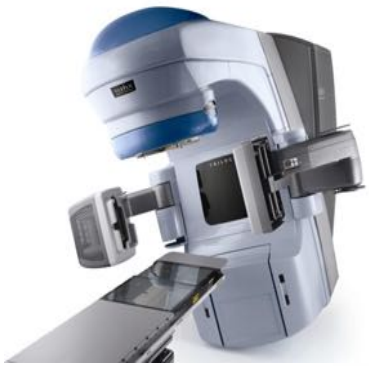
EBRT re-irradiation is not a standard and has rarely been used as salvage treatment for locally relapsing prostate cancer (1.9%)

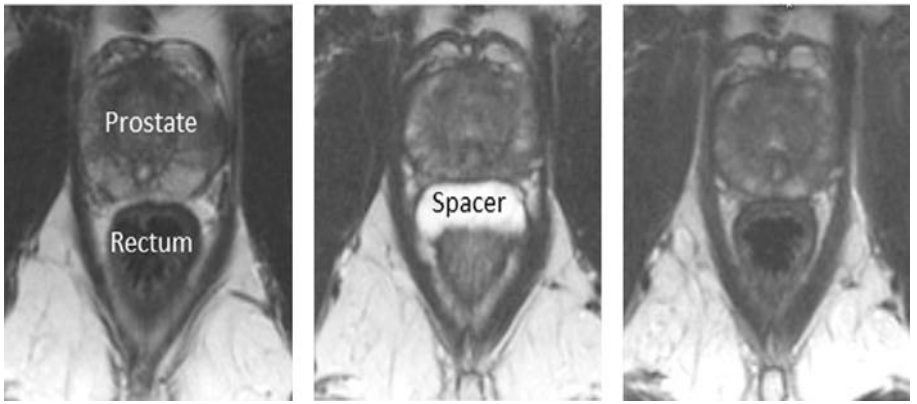
CAPSURE Study, J Urol 2002

Retreatment for prostate cancer with stereotactic body radiation therapy (SBRT): Feasible or foolhardy?

Stefano Arcangeli[a,*], *Linda Agolli*[b], *Vittorio Donato*[a]

- **precisely targeted** ionizing radiation beams
- that deliver **high doses**
- to **ablate** malignancies or lesions
- **anywhere** in the body
- in **1-5 fractions**/stages
- by **accurately conforming** the high dose region to the target volume and **sparing** surrounding normal tissue and structures





ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOTHERAPY, FOR ISOLATED RECURRENT PRIMARY, LYMPH NODE OR METASTATIC PROSTATE CANCER

Barbara Alicja Jereczek-Fossa, M.D., Ph.D.,*† Giancarlo Beltramo, M.D.,‡ Laura Fariselli, M.D.,§ Cristiana Fodor, M.Sc.,* Luigi Santoro, M.Sc.,‖ Andrea Vavassori, M.D.,* Dario Zerini, M.D.,* Federica Gherardi, M.D.,*† Carmen Ascione, M.D.,*¶ Isa Bossi-Zanetti, M.D.,*† Roberta Mauro, M.D.,*† Achille Bregantin, M.Sc.,‡ Livia Corinna Bianchi, M.D.,‡ Ottavio De Cobelli, M.D.,# and Roberto Orecchia, M.D.*†

Table 2. Patient and CBK-SRT treatment characteristics (n = 34 patients/38 lesions)

Characteristics	P (n = 15)	A (n = 4)	LN (n = 16)	M (n = 3)	All lesions (n = 38)
Pre–CBK-SRT PSA [median (range)] (ng/mL)	3.51 (1.69 – 22.9)	6.60 (0.47 – 10.11)	1.77 (0.22 – 15.50)	10.7 (0.30 – 38.3)	3.20 (0.22 – 38.3)
[^{11}C]choline PET/CT before CBK-SRT					
Yes	13 (87%)	2 (50%)	16 (100%)	3 (100%)	34 (89%)
No	2 (13%)	2 (50%)	0	0	4 (11%)
Biopsy of target lesion					
Yes	15 (100%)	3 (75%)	1 (6%)	0	19 (50%)
No	0	1 (25%)	15 (94%)	3 (100%)	19 (50%)
Fiducial marker in target lesion					
Yes	14 (93%)	3 (75%)	9 (56%)	0	26 (68%)
No	1 (7%)	1 (25%)	7 (44%)	3 (100%)	12 (32%)
Localization in previous RT volume					
Yes	15 (100%)	4 (100%)	8 (50%)	0	27 (71%)
No	0	0	8 (50%)	3 (100%)	11 (29%)
ADT added to CBK-SRT					
Yes	5 (33%)	2 (50%)	12 (75%)	2 (67%)	21 (55%)
Pre-ADT PSA					
n	5	2	12	2	21
Median (range) (ng/mL)	3.27 (1.90 – 43.0)	6.67 (3.41 – 9.94)	3.74 (0.90 – 17.1)	11.25 (5.40 –17.1)	4.31 (0.90 – 43.0)
CBK-SRT data					
Median total dose (Gy)	30	30	33	36	30
Dose/fraction	6	6	11	12	7.5
No. of fractions	5	5	3	3	4.5
Mean overall CBK-SRT duration (d)	5	6	5.5	3	5.1

ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOTHERAPY, FOR ISOLATED RECURRENT PRIMARY, LYMPH NODE OR METASTATIC PROSTATE CANCER

Table 3. Treatment outcome (n = 34 patients/38 lesions)

Outcome	P (n = 15)	A (n = 4)	LN (n = 16)	M (n = 3)	All lesions (n = 38)
Acute toxicity of CBK-SRT (for all lesions)					
All urinary toxicity*	5 (33%)	1 (25%)	1 (6%)	0	7 (18%)
Grade 1	2 (13%)	1 (25%)	0	0	3 (8%)
Grade 2	2 (13%)	0	0	0	2 (5%)
Grade 3	1 (7%)	0	1 (6%)	0	2 (5%)
All rectal toxicity					
Grade 1	0	1 (25%)	0	0	1 (3%)
Late toxicity of CBK-SRT (for all patients)					
All urinary toxicity*	3 (20%)	0	4 (30%)†	0	7 (21%)†
Grade 1	1 (7%)	0	2 (15%)	0	3 (9%)
Grade 2	1 (7%)	0	1 (8%)	0	2 (6%)
Grade 3	1 (7%)	0	1 (8%)	0	2 (6%)
All rectal toxicity	0	1 (25%)	1 (8%)†	0	2 (6%)†
Grade 1	0	0	1 (8%)	0	1 (3%)
Grade 2	0	1 (25%)	0	0	1 (3%)
Follow-up duration [median (range)] (mo)	9.5 (3 – 28.9)	23 (3.9 – 30.6)	21.9 (4.3 – 35.4)	13.7 (3.9 – 20.2)	16.9 (3 – 35.4)
Biochemical response to CBK-SRT in lesions treated with CBK-SRT only, with no neoadjuvant and/or concomitant systemic therapy					
n	9 (60%)	2 (50%)	4 (25%)	1 (33%)	16 (42%)
Complete response (substantial PSA reduction)‡	6 (67%)	1 (50%)	2 (50%)	–	9 (56.25%)
Partial response (partial PSA reduction)‡	2 (22%)	–	1 (25%)	1 (100%)	4 (25%)
Stable PSA	1 (11%)	–	1 (25%)	–	2 (12.5%)
Progression§	–	1 (50%)	–	–	1 (6.25%)
Disease progression	5/15 (33%)	2/4 (50%)	5/16 (31%)	2/3 (67%)	14/38 (37%)
Site of progression					
In CBK-SRT field	1 (7%)	2 (50%)‖	0	0	3 (8%)
Out of CBK-SRT field	4 (27%)	1 (25%)	5 (31%)	1 (33%)	11 (29%)
Biochemical only	0	0	0	1 (33%)	1 (3%)
PFS					
30-mo PFS (%) (95% CI)	22.2 (0–58.2)	33.0 (0–68.7)	63.5 (36.6–90.3)	0 (—)	42.6 (21.6–63.7)
Median PFS (95% CI) (mo)	13 (10, >30)	14 (10, >30)	>30 (—)	11 (6–16)	17 (13, >30)

Salvage image-guided intensity modulated or stereotactic body reirradiation of local recurrence of prostate cancer

[1]D ZERINI, MD, [1,2]B A JERECZEK-FOSSA, MD, PhD, [1]C FODOR, MSc, [1,2]F BAZZANI, MD, [1,2]A MAUCIERI, MD, [1,2]S RONCHI, MD, [1,2]S FERRARIO, MD, [1,2]S P COLANGIONE, MD, [1,2]M A GERARDI, MD, [1,2]M CAPUTO, MD, [1]A CECCONI, MD, PhD, [1]F GHERARDI, MD, [1]A VAVASSORI, MD, [3]S COMI, MSc, [3]R CAMBRIA, MSc, [3]C GARIBALDI, MSc, [3]F CATTANI, MSc, [2,4]O DE COBELLI, MD and [1,2,5]R ORECCHIA, MD

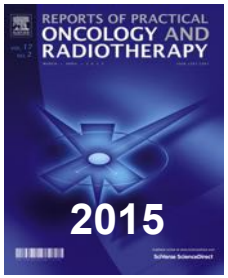
Characteristics	Prostate, $n = 22$	Prostate bed, $n = 10$
Pre re-EBRT PSA (ng ml^{-1})		
Median (range)	3.9 (0.8–16.9)	2.3 (0.7–51.8)
Biopsy of the target lesion		
Yes	13	6
No	8	4
Unknown	1	0
ADT added to re-EBRT		
Yes	8	3
Type of ADT added to radiotherapy		
Complete androgen blockade	3	2
Luteinizing hormone releasing factor alone	2	1
Antiandrogen alone[a]	3	0
re-EBRT data		
Median total dose (Gy)	25 (25–30)	25 (15–25)
Dose/fraction	5 (3–6)	5
Number of fractions	5 (5–10)	5 (3–5)
Mean overall re-EBRT duration (days)	10	9
Median (days)	10	9

Acute toxicity	RT fractionation			Number of patients
	30 Gy (6 × 5 fr), number of patients 5	25 Gy (5 × 5 fr), number of patients 25	30 Gy (3 × 10 fr), number of patients 1	
GU G1	0	5	1	6
GU G2	1	1	0	2
GI G1	0	3	0	3
GI G2	0	1	0	1

Late toxicity	RT fractionation		Number of patients
	30 Gy (6 × 5 fr) number of patients 5	25 Gy (5 × 5 fr) number of patients 25	
GU G1	2	5	7
GU G2	0	1	1
GI G1	1	4	5

Number of patients	Outcome	Radiotherapy concomitant with androgen [illegible]n therapy	
		Yes (number of patients [illegible]	[illegible]tients, 21)
13	No evidence of disease		10
3	Biochemical relapse		2
4	Clinical [illegible]	2	2
1		0	1
7	[illegible]static relapse	2	5
4	Dead[a]	3	1

2-yrs tumor control in 50% of patients



PATIENT WITH BIOCHEMICAL FAILURE (BF) AFTER LOCAL RADIOTHERAPY TREATMENT

AFTER RT+/-HT DEFINITION:

PSA NADIR + 2ng/ml *

POOR PROGNOSTIC FACTORS: RISK OF METS

Stage at Diag ≥ T 3, N1

- PSA at diagnosis > 20 ng/ml
- Gleason at diagnosis ≥ 8
- Interval to BF ≤ 2years
- PSADT ≤ 10- 12 months
- No biochemical control after RT+/-HT

COMPLEMENTARY TESTS *(Only if treatment will be initiated)*

1. CT – Bone Scan if:
   - PSA>20 ng/ml
   - PSADT < 10-12 months
   - Patient diagnosis: High Risk
2. MRI if local salvage therapy considered
3. CHOLINE PET (if considering local salvage therapy and if prior tests negative)
4. Prostate biopsy (PB) (if considering local salvage therapy and if prior tests negative)

THERAPEUTIC MANAGEMENT

I. LOCAL RELAPSE AFTER PRIMARY RT - MO

LOCAL SALVAGE THERAPY: INDICATIONS

1. Age < 70 years
2. Life expectancy > 10 years
3. Lack of relevant urinary/intestinal comorbidities
4. Absence of risk factors for metastasis:
   - Low/intermediate risk at diagnosis
   - PSADT > 10-12 months
   - Late BCR > 2 years
   - PSA value at rescue < 10 ng/ml
   - Positive PB

SBRT re-irradiation ?

II. BCR - MO

NOT CANDIDATES FOR LOCAL SALVAGE AND CANDIDATES FOR SURVEILLANCE AND DELAYED HT

1. Patients who do not meet scenarios I-III
2. Patients con Low/intermediate risk
3. PSADT > 10-12 months
4. Late recurrence > 2 years
5. Age > 75 years or life expectancy < 5 years

FOLLOW UP PROTOCOL

1. PSADT <10-12 months: every 3-6 months
2. PSADT >10-12 months: every 6-12 months

III. BF - MO

CANDIDATES FOR IMMEDIATE HT

- Pts. with high-risk PCa, < 70 years and/or
- PSADT ≤ 6 months
- Early relapse < 2 years
- No biochemical control after treatment:

IV- BF – M1: HORMONOTHERAPY

TYPE OF HT

1- IHT: in absence of rapidly progressing or highly symptomatic disease

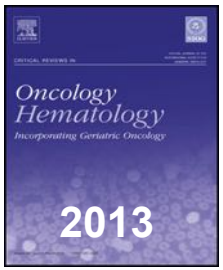
2- IHT SCHEME:

- Induction phase: 6-12 months (PSA nadir as low as possible and always < 4 ng/ml)
- Restart with PSA >10 ng/ml

…more in

Management of Biochemical Recurrence After Primary Treatment of Prostate Cancer: A Systematic Review of the Literature

Sanoj Punnen [a], *Matthew R. Cooperberg* [a], *Anthony V. D'Amico* [b], *Pierre I. Karakiewicz* [c], *Judd W. Moul* [d], *Howard I. Scher* [e], *Thorsten Schlomm* [f], *Stephen J. Freedland* [d,*]



Salvage therapy of intraprostatic failure after radical external-beam radiotherapy for prostate cancer: A review

Filippo Alongi [a], Berardino De Bari [b,*], Franco Campostrini [c], Stefano Arcangeli [d], Deliu Victor Matei [e], Egesta Lopci [f], Giuseppe Petralia [g], Massimo Bellomi [g], Arturo Chiti [f], Stefano Maria Magrini [b], Marta Scorsetti [a], Roberto Orecchia [h], Barbara Alicja Jereczek-Fossa [h]