Decennale di
HIGHLIGHTS in
RADIOTERAPIA

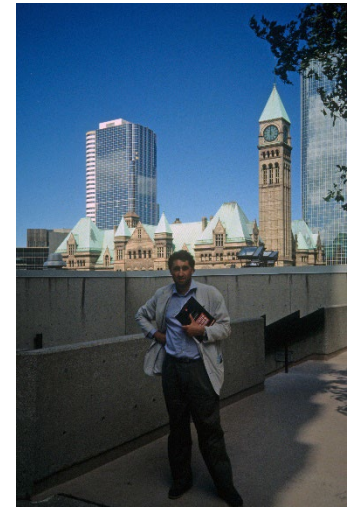
Update degli Studi Practice Changing 2024

Undicesima Edizione

In memoria di Renzo Corvò

Changing landscapes in the treatment of prostate cancer

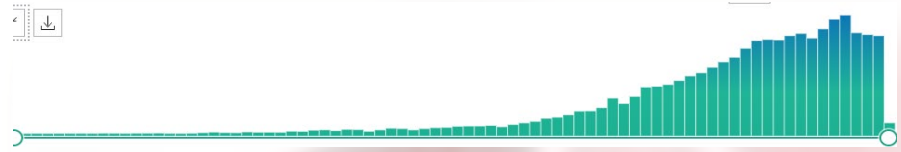
Giuseppe Sanguineti, MD
Radiation Oncology,
IRCCS Regina Elena National Cancer Institute,
Rome, IT
giuseppe.sanguineti@ifo.it



IRE

Disclosures

None



PROSTATE CANCER - Evolving Landscapes

- Patients & Disease

- Treatment Strategies & Combinations

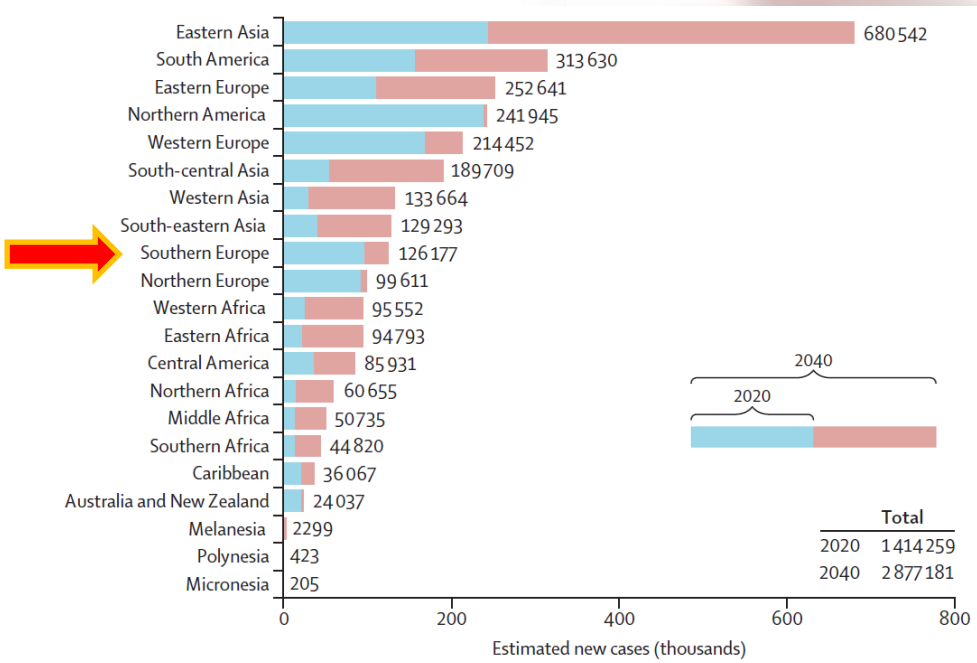
- Technology

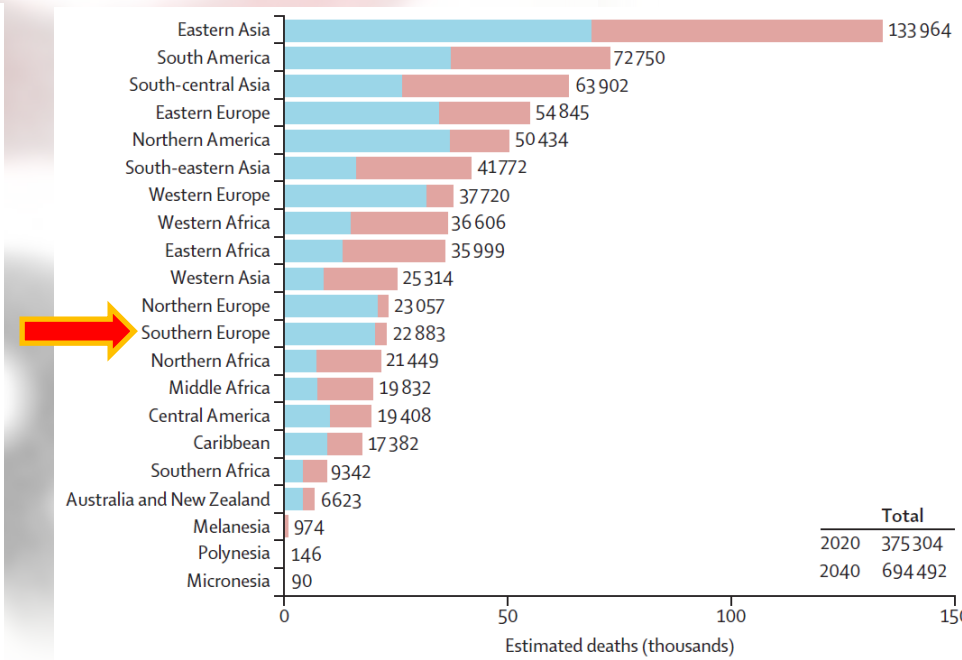
The *Lancet* Commission on prostate cancer: planning for the surge in cases

Nicholas D James, Ian Tannock, James N'Dow, Felix Feng, Silke Gillessen, Syed Adnan Ali, Blanca Trujillo, Bissan Al-Lazikani, Gerhardt Attard, Freddie Bray, Eva Compérat, Ros Eeles, Omolara Fatiregun, Emily Grist, Susan Halabi, Áine Haran, Daniel Herchenhorn, Michael S Hofman, Mohamed Jalloh, Stacy Loeb, Archie MacNair, Brandon Mahal, Larissa Mendes, Masood Moghul, Caroline Moore, Alicia Morgans, Michael Morris, Declan Murphy, Vedang Murthy, Paul L Nguyen, Anwar Padhani, Charles Parker, Hannah Rush, Mark Sculpher, Howard Soule, Matthew R Sydes, Derya Tilki, Nina Tunariu, Paul Villanti, Li-Ping Xie

www.thelancet.com Vol 403 April 27, 2024

- Prostate cancer is the most common cancer in men in 112 countries
- Accounts for 15% of cancers;
- On the basis of data for demographic changes worldwide and rising life expectancy, the number of new cases annually is expected to rise from 1.4 million in 2020 to 2.9 million by 2040



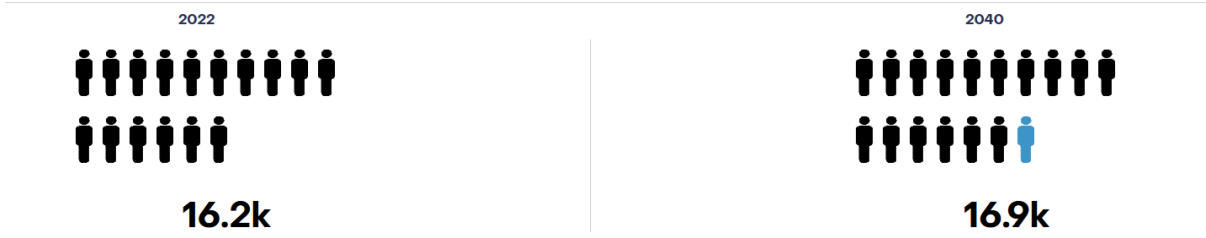


Evolving Landscapes

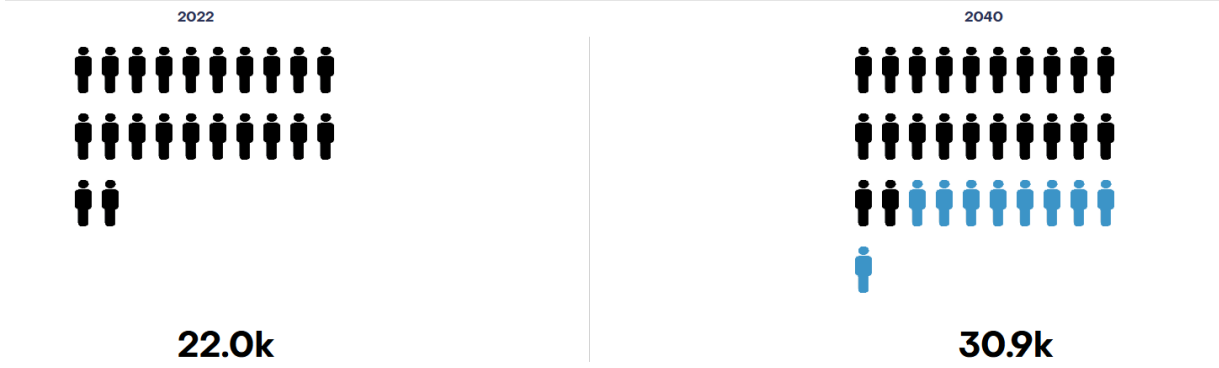
- Diseases & Patients

- Increased incidence over time;
- ≈80% of pts with PCa survive more than 10 yrs regardless stage;
- Most men with localized diz do not die from PCa;
- Increased survival time of M1 pts;
- Elderly and more frail pt population

Estimated number of new patients



<70yrs/old



≥70yrs/old

GLOBAL CANCER OBSERVATORY

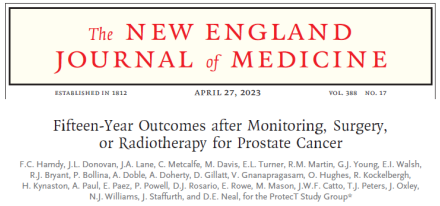
EVOLUTION OF (HOW WE SEE) THE DIZ

PROSTATE CANCER - Evolvi[illegible]dscapes

- Patients & Disease

- Treatment Strategies & Combinations

- Technology



47% of the men in ProtecT who developed metastatic disease initially had low-risk disease…

(Recruitment started in three pilot centers in 1999 and increased to nine centers between 2002 and 2004)

- Old ISUP classification (HR features included in LR)
- Poor detection of csPCa

1966

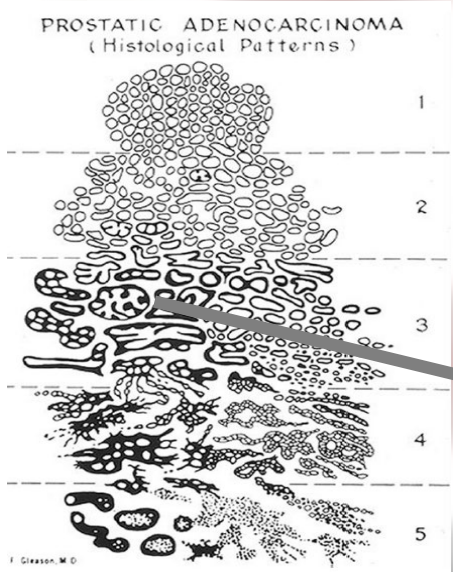


Figure 1. Original Gleason system

2005

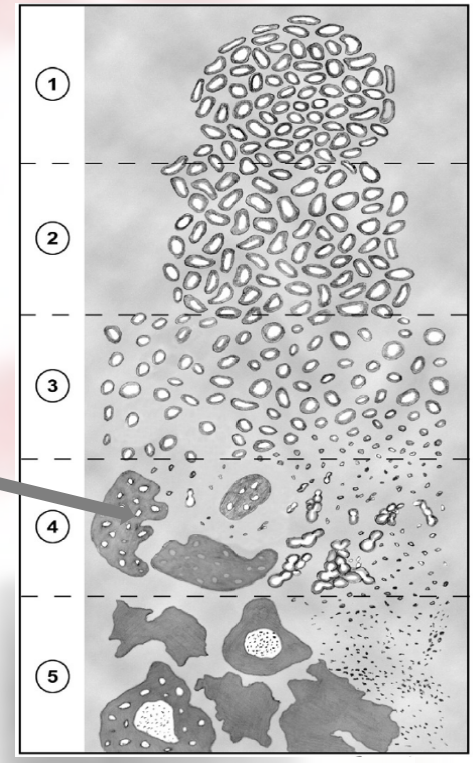


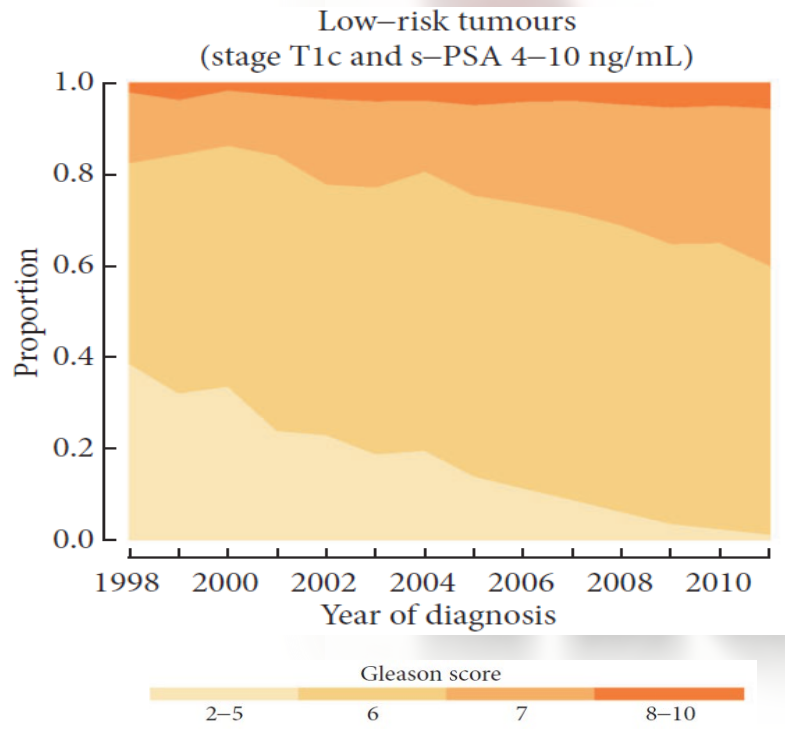
Figure 2. Modified Gleason system. Note cribriform glands are only seen in patterns 4 and 5. Poorly formed glands are also component of pattern 4.

Gleason inflation 1998–2011: a registry study of 97 168 men

Daniela Danneman, Linda Drevin*, David Robinson†, Pär Stattin‡ and Lars Egevad

*Department of Oncology-Pathology, Karolinska Institutet, Stockholm, *Regional Cancer Centre, Uppsala University Hospital, Uppsala, †Department of Urology, Ryhov County Hospital, Jönköping, ‡Department of Surgery and Perioperative Sciences, Urology and Andrology, Umeå University, Umeå, Sweden*

BJU Int 2015; **115:** 248–255



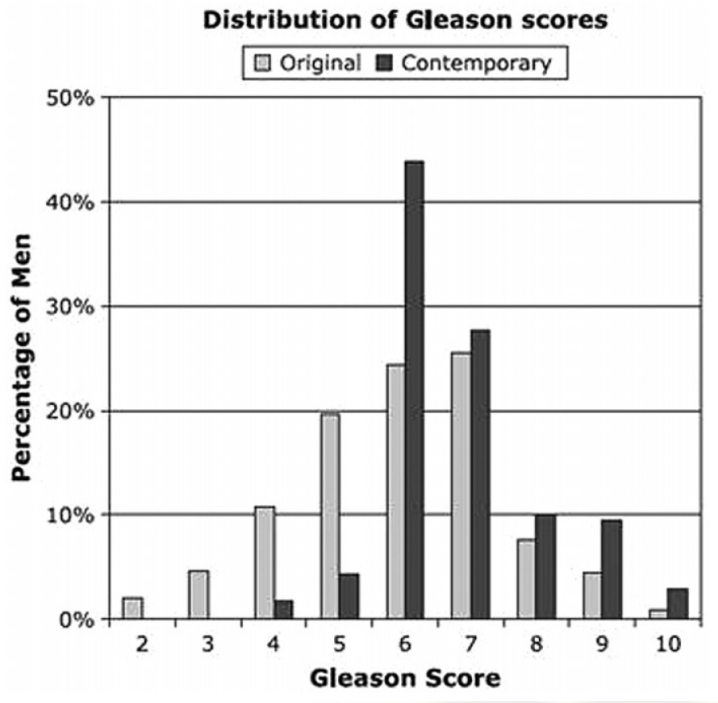
Among stage cT1and iPSA 4–10 ng/mL tumors, GLS 7–10 increased from **16%** in 1998 to **40%** in 2011 ($p<0.001$)

The Will Rogers Phenomenon in Urological Oncology

Ofer N. Gofrit,* Kevin C. Zorn, Gary D. Steinberg,† Gregory P. Zagaja‡ and Arieh L. Shalhav§

From the Department of Surgery, Section of Urology, University of Chicago, Chicago, Illinois

THE JOURNAL OF UROLOGY®



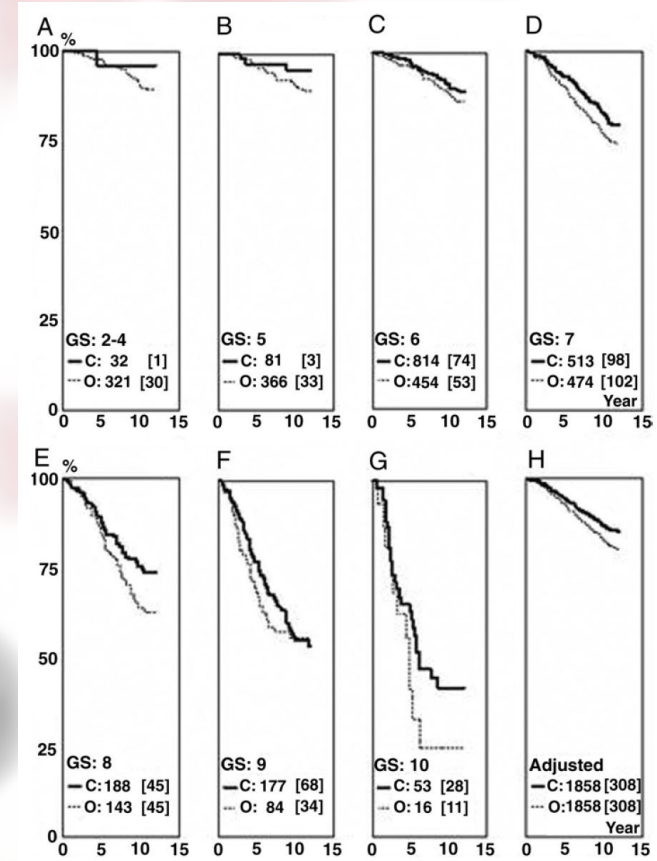
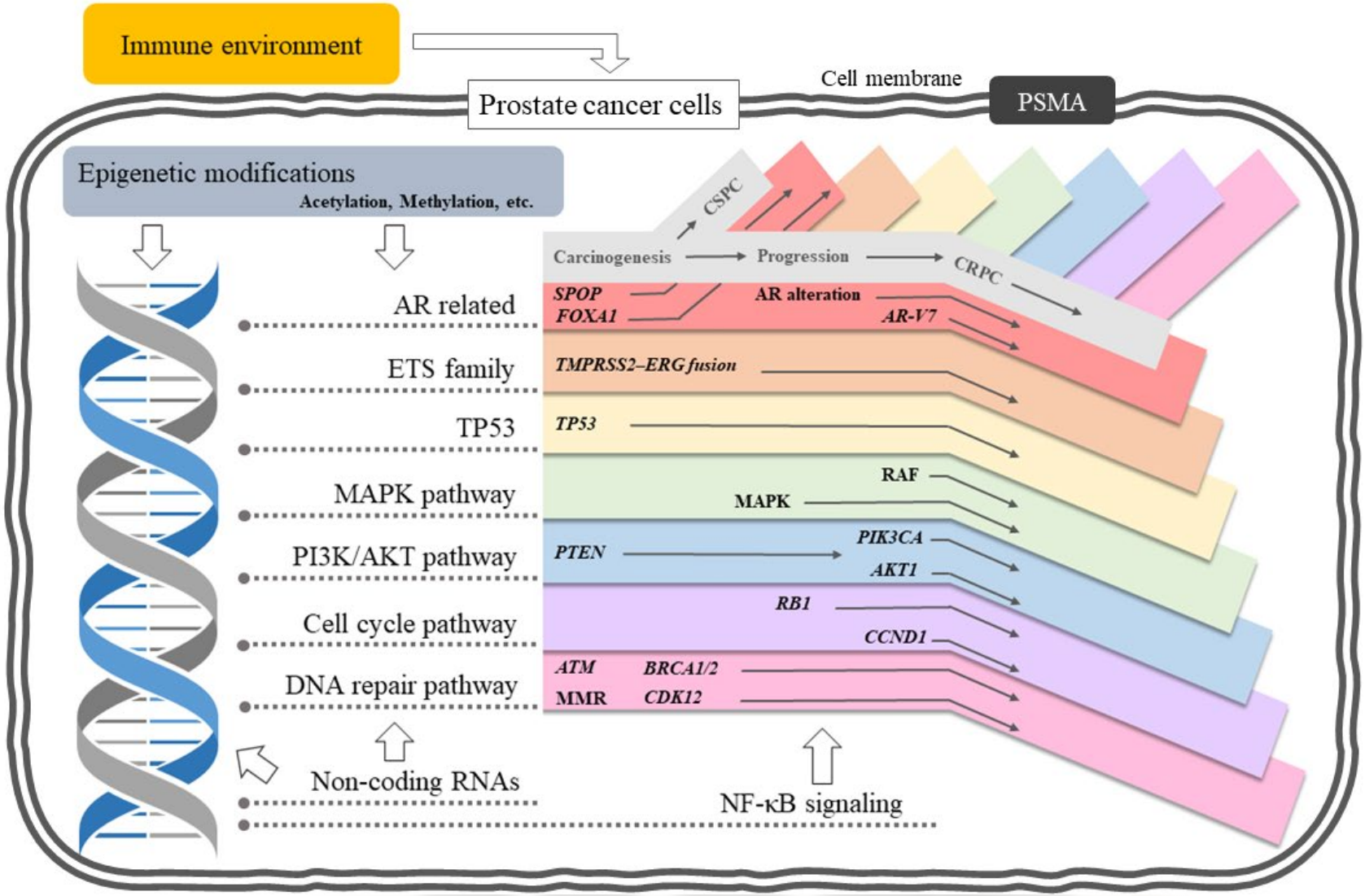
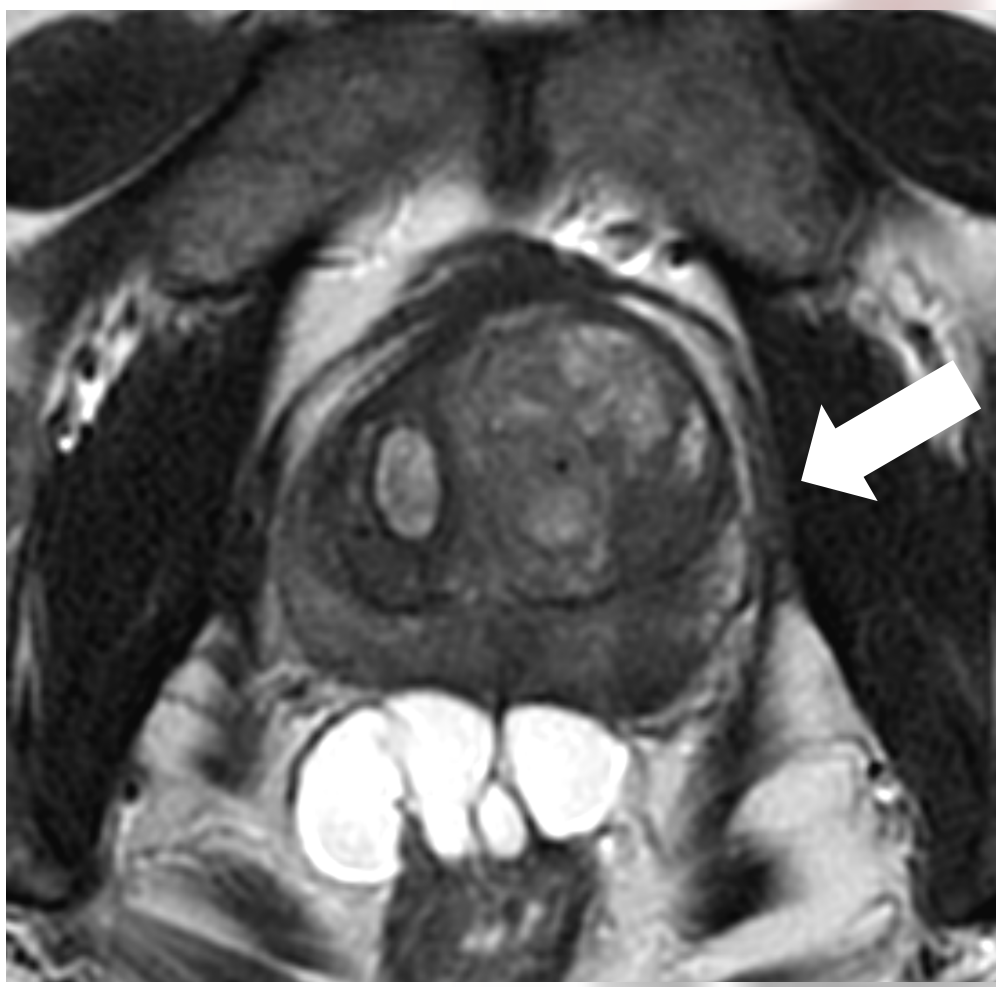


FIG. 2. Cause specific survival curves for patients with biopsy Gleason score (GS) 2–4 (*A*), 5 (*B*), 6 (*C*), 7 (*D*), 8 (*E*), 9 (*F*) and 10 (*G*) by Kaplan-Meier method, and of entire series of 1,858 patients (*H*) by Cox proportional hazards model that adjusted for differences in distribution of Gleason scores between 2 series. Contemporary (C) and original (O) series were standardized to average of 2 distributions of Gleason scores. Horizontal axis shows years since diagnosis. Vertical axis shows percent cause specific survival. Numbers in each panel represent number of patients [number of deaths from prostate cancer]. Reprinted with permission.[7]

MOLECULAR SUBTYPES OF PCa

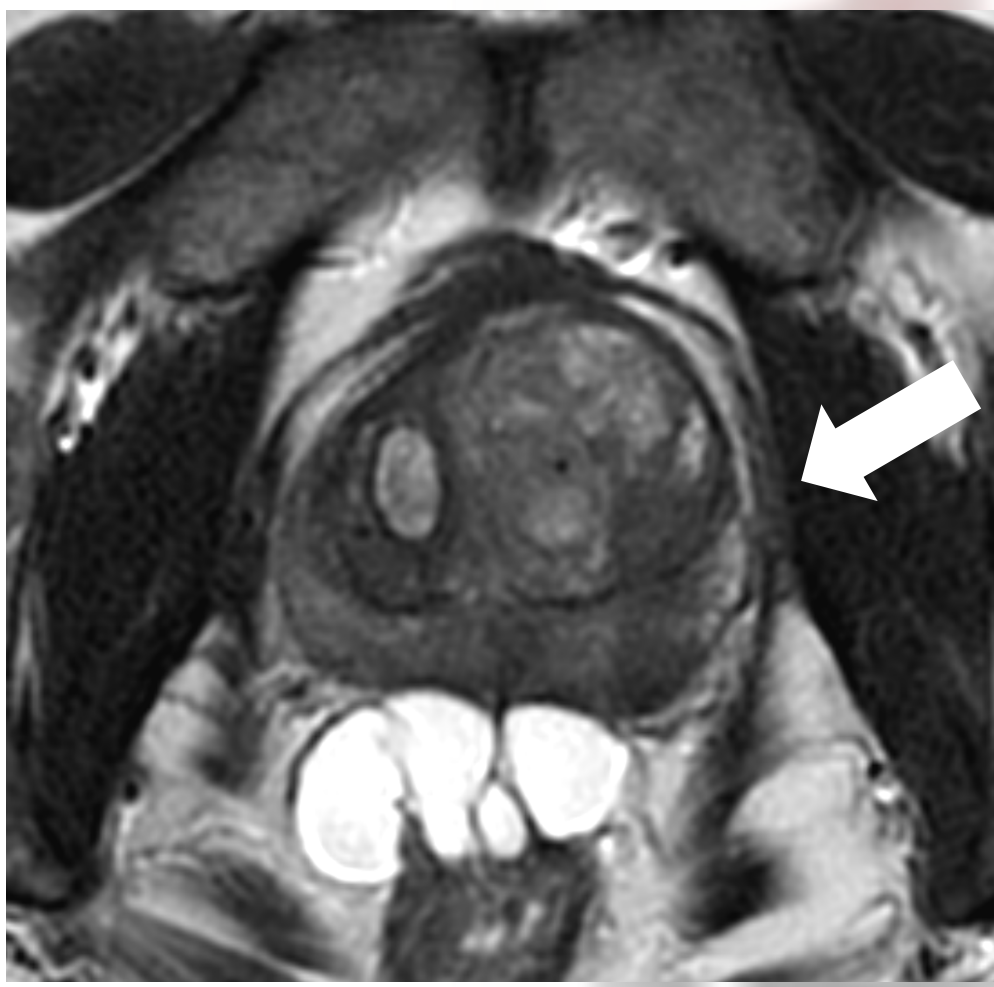


mpMRI



- More accurate definition of GLS
- Higher rate of csPCa w fewer biopsies/less indolent PCa
- Presence/Location of the index lesion(s) (DIL)

mpMRI

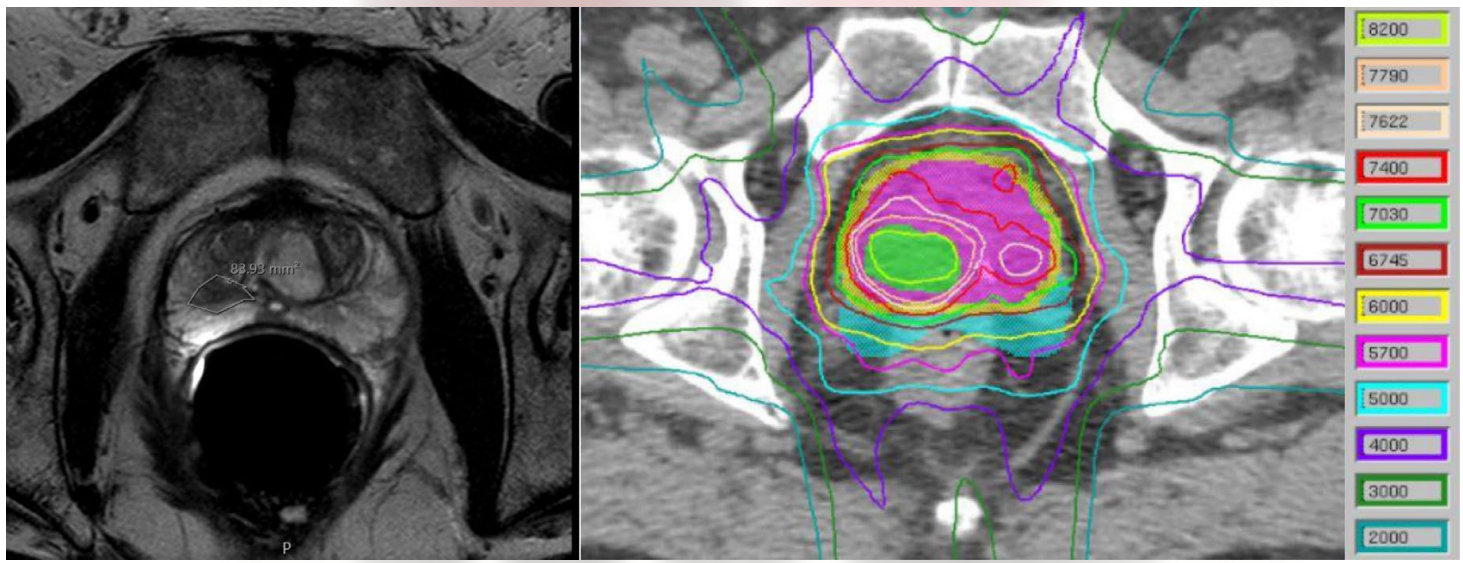


- More accurate definition of GLS
- Higher rate of csPCa w fewer biopsies/less indolent PCa
- Presence/Location of the index lesion(s) (DIL)

- High sensitivity (few FN, high NPV) → ideal to rule out diz
- Low specificity (many FP, low PPV) → suboptimal to support the presence of disease <u>within</u> the DIL

FLAME: **Intraprostatic lesions** were contoured as gross tumor volume (GTV) using T2-weighted, diffusion-weighted imaging and dynamic contrast-enhanced sequences. One or more GTV's could be contoured per patient

DELINEATE: A discrete lesion with a PI-RADS-1 score of at least **3 plus a corroborative biopsy** was required for the lesion to be considered suitable for boosting. Clinicians contoured the maximal extent of abnormality visible on T2 small field of view and/or diffusion-weighted imaging on the prebiopsy diagnostic MRI.



EUROPEAN UROLOGY ONCOLOGY 4 (2021) 697–713

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

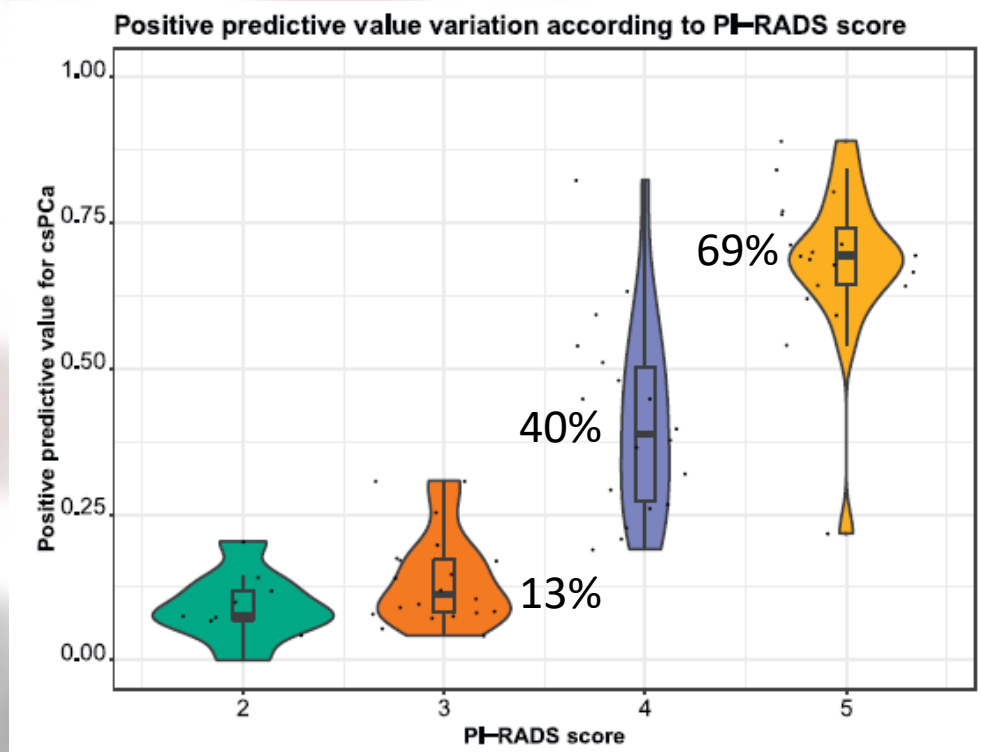
European Association of Urology

Priority Article

Positive Predictive Value of Prostate Imaging Reporting and Data System Version 2 for the Detection of Clinically Significant Prostate Cancer: A Systematic Review and Meta-analysis

Elio Mazzone [a,b,,†], Armando Stabile [a,b,†], Francesco Pellegrino [a,b], Giuseppe Basile [a,b], Daniele Cignoli [a,b], Giuseppe Ottone Cirulli [a,b], Gabriele Sorce [a,b], Francesco Barletta [a,b], Simone Scuderi [a,b], Carlo Andrea Bravi [a,b], Vito Cucchiara [a,b], Nicola Fossati [a,b], Giorgio Gandaglia [a,b], Francesco Montorsi [a,b], Alberto Briganti [a,b]*

[a] Division of Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy; [b] Vita-Salute San Raffaele University, Milan, Italy



- csPCa at targeted biopsies (mpMRI)
- 56 studies, 16.537 pts
- PPVs for csPCa →
- TBx missed ≈6% of csPCa regardless PIRADS

- Systematic biopsies still needed regardless PIRADS
- PI-RADS <4 at low risk of diz – no DIL, unless bx proven

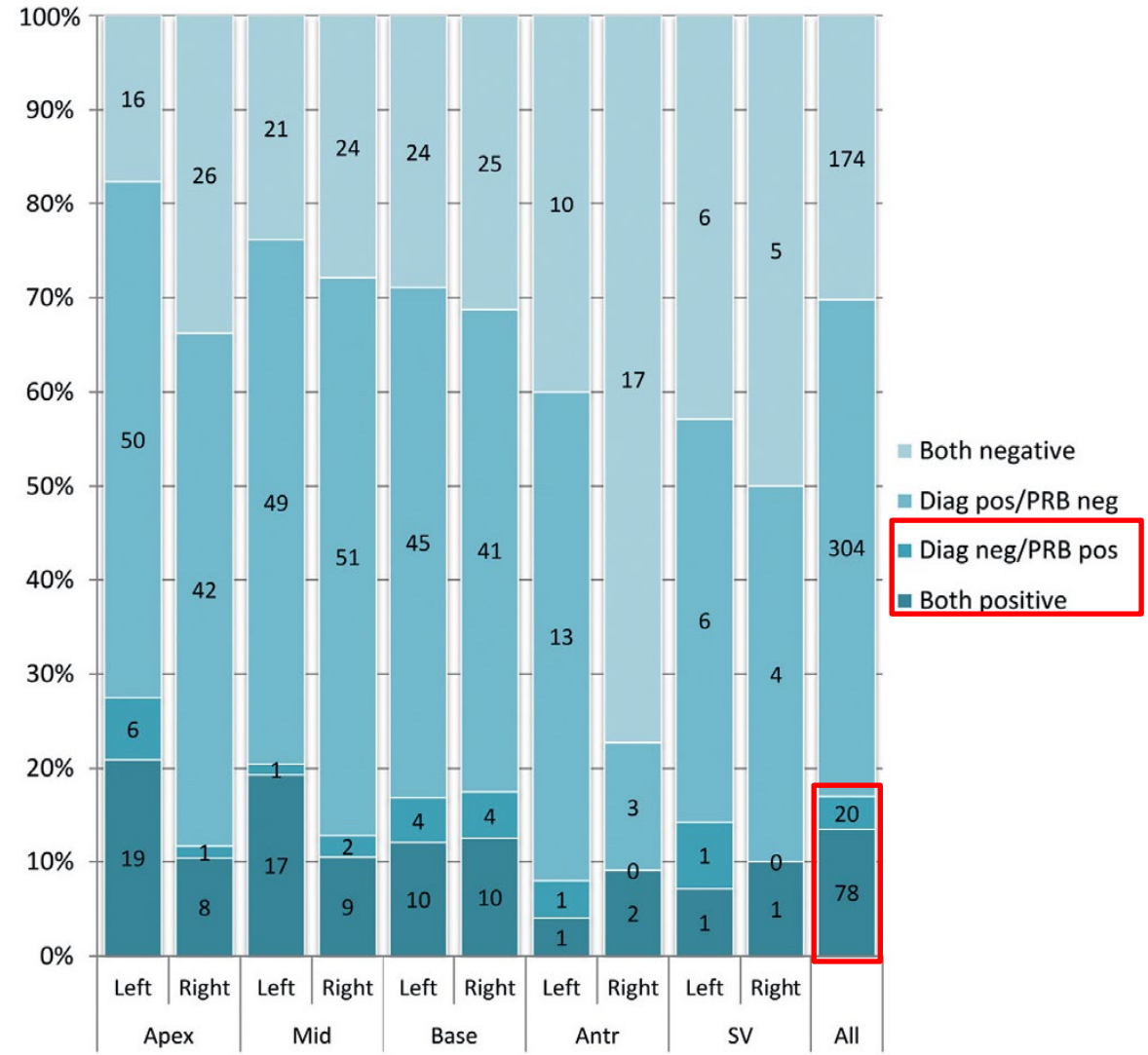
Patterns of Local Failure following Radiation Therapy for Prostate Cancer

Mohamed Jalloh, Michael S. Leapman, Janet E. Cowan, Katsuto Shinohara, Kirsten L. Greene, Mack Roach III, Albert J. Chang, June M. Chan,* Jeffry P. Simko and Peter R. Carroll†

THE JOURNAL OF UROLOGY® Vol. 194, 977-982, October 2015

- Patients with bio fail after definitive RT+/-BT;
- Overall, viable cancer was detected in **65%** of patients at a median of 61 months after treatment;
- Out of 140 pts with mapped results at diagnosis and failure, ≈80% of biopsies positive at failure within the original sextant;
- Of patients who experienced treatment failure, Gleason upgrading occurred in 92 of 197 (47%)

- A sign rate of patients show local diz, of worse grade
- DIL is the main site of failure

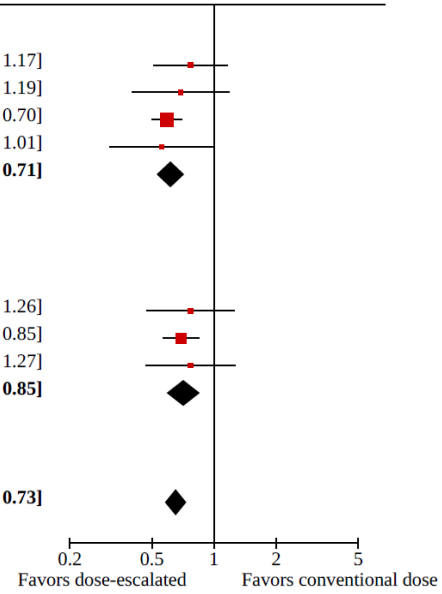


- # RT (whole gland) CF dose escalation:

bNED improv, no effect on DMFS or OS

Analysis 1.15. Comparison 1: Dose-escalated RT versus conventional dose RT, Outcome 15: Time to biochemical recurrence_subgroup analysis (without ADT vs with ADT)

Study or Subgroup	log[Hazard Ratio]	SE	Dose-escalated RT Total	Conventional dose RT Total	Weight	Hazard Ratio IV, Random, 95% CI
1.15.1 without ADT						
Bruner 2019	-0.261365	0.211827	550	542	7.3%	0.77 [0.51 , 1.17]
GETUG 06 trial	-0.371064	0.275976	153	153	4.3%	0.69 [0.40 , 1.19]
Michalski 2018	-0.527633	0.085836	748	751	44.2%	0.59 [0.50 , 0.70]
Pasalic 2019	-0.579818	0.298777	151	150	3.6%	0.56 [0.31 , 1.01]
Subtotal (95% CI)			**1602**	**1596**	**59.4%**	**0.61 [0.53 , 0.71]**
Heterogeneity: Tau² = 0.00; Chi² = 1.63, df = 3 (P = 0.65); I² = 0%						
Test for overall effect: Z = 6.58 (P < 0.00001)						
1.15.2 with ADT						
Creak 2013	-0.261365	0.251569	62	64	5.1%	0.77 [0.47 , 1.26]
Dearnaley 2014	-0.371064	0.103437	422	421	30.4%	0.69 [0.56 , 0.85]
Nabid 2021	-0.261365	0.253586	200	200	5.1%	0.77 [0.47 , 1.27]
Subtotal (95% CI)			**684**	**685**	**40.6%**	**0.71 [0.60 , 0.85]**
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 2 (P = 0.87); I² = 0%						
Test for overall effect: Z = 3.84 (P = 0.0001)						
Total (95% CI)			**2286**	**2281**	**100.0%**	**0.65 [0.58 , 0.73]**
Heterogeneity: Tau² = 0.00; Chi² = 3.44, df = 6 (P = 0.75); I² = 0%						
Test for overall effect: Z = 7.51 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.53, df = 1 (P = 0.22), I² = 34.5%						



Kim et al, Cochrane Database of Systematic Reviews 2023

BT boost – whole gland dose escalation

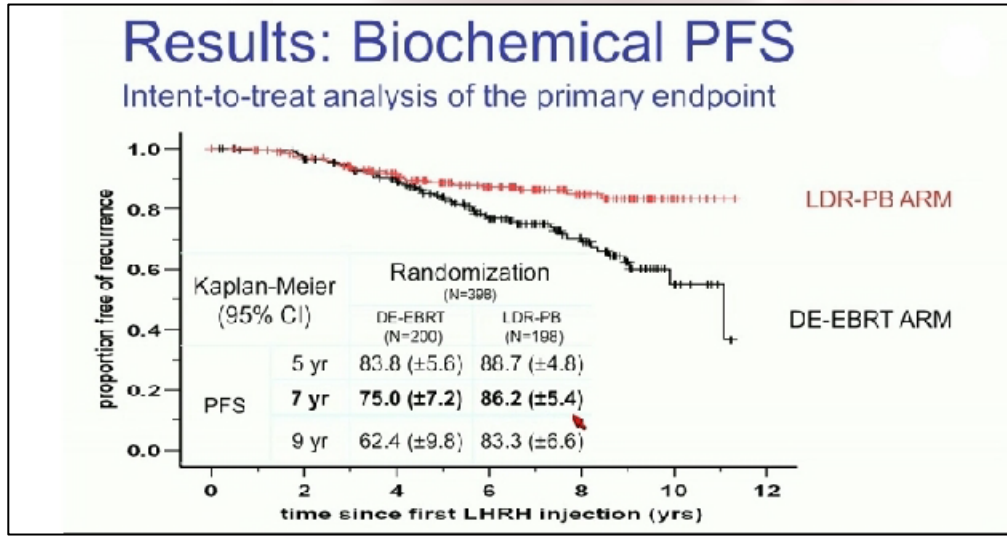
- improved bNED when BT boost (to 115 Gy) is added to WPRT/12 month AD (ASCENDE-RT)(Oh et al, IJROBP 2023)(sign worse GR3 late GU tox)

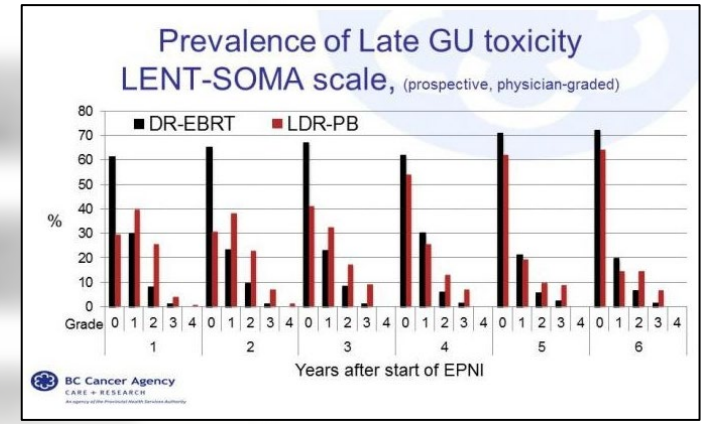
IR (122), HR (276) PCA

EBRT boost 32 Gy

WPRT 46 Gy → 12 month-AD

LDR boost 115 Gy





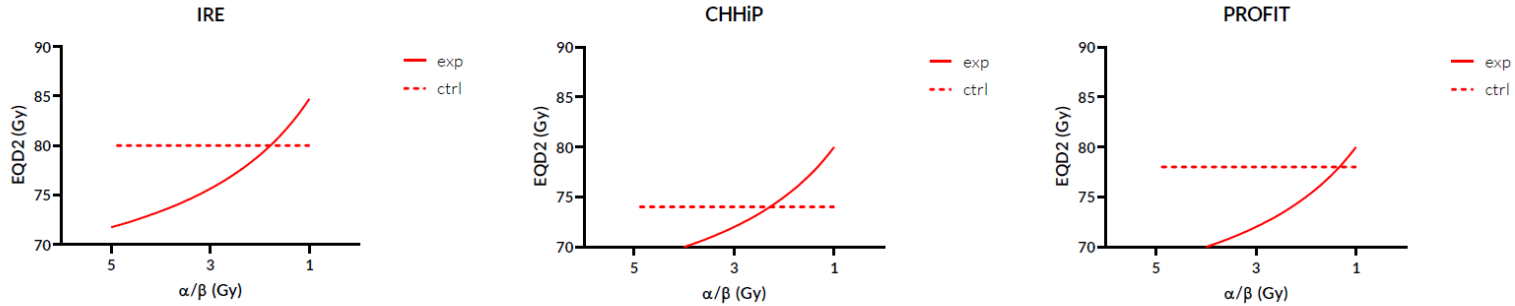
Morris et al, 2015

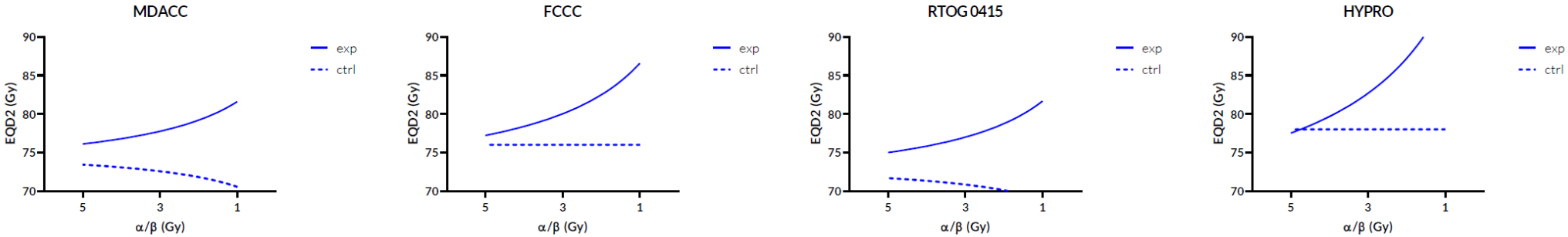
Randomized trials on MHRT

Trial	# pts/ stage/ risk	Schedules	Tech	AD	LQED2Gy α/β=1.5 Gy	LQED2Gy α/β=3 Gy	Median FU (mths)	Outcome (bNED)
CHHiP	3216 T1b-3aN0	74 Gy/37 fxs vs 60 Gy/20 fxs vs 57 Gy/19 fxs	IMRT (few IGRT)	STAD	74 Gy vs 77 Gy = vs 73 Gy	74 Gy vs 72 Gy ↓ vs 68 Gy	62 mths	NON INFERIOR (60 Gy) NOT NON INFERIOR (57 Gy)
PROFIT	1206 Mostly IR	78 Gy/39 fxs vs 60 Gy in 20 fxs	3DCRT /IMRT, IGRT req	STAD permitted bef tmt	78 Gy vs = 77 Gy	78 Gy vs ↓ 72 Gy	60 mths	NON INFERIOR
RTOG 0415	1092 LR	73.8 Gy/41 fxs vs 70 Gy/28 fxs	3DCRT /IMRT, IGRT req	None	70 Gy vs ↑ 80 Gy	71 Gy vs ↑ 77 Gy	58 mths	NON INFERIOR
HYPRO	820 IR/HR	78 Gy/39 fxs vs 64.6 Gy/19 fxs	95% IMRT (94% IGRT)	67%	78 Gy vs ↑ 90 Gy	78 Gy vs ↑ 83 Gy	89 mths	NOT SUPERIOR

Smaller trials from MDACC, IRE, FCCC…

ISODOSE RCT MHFRT

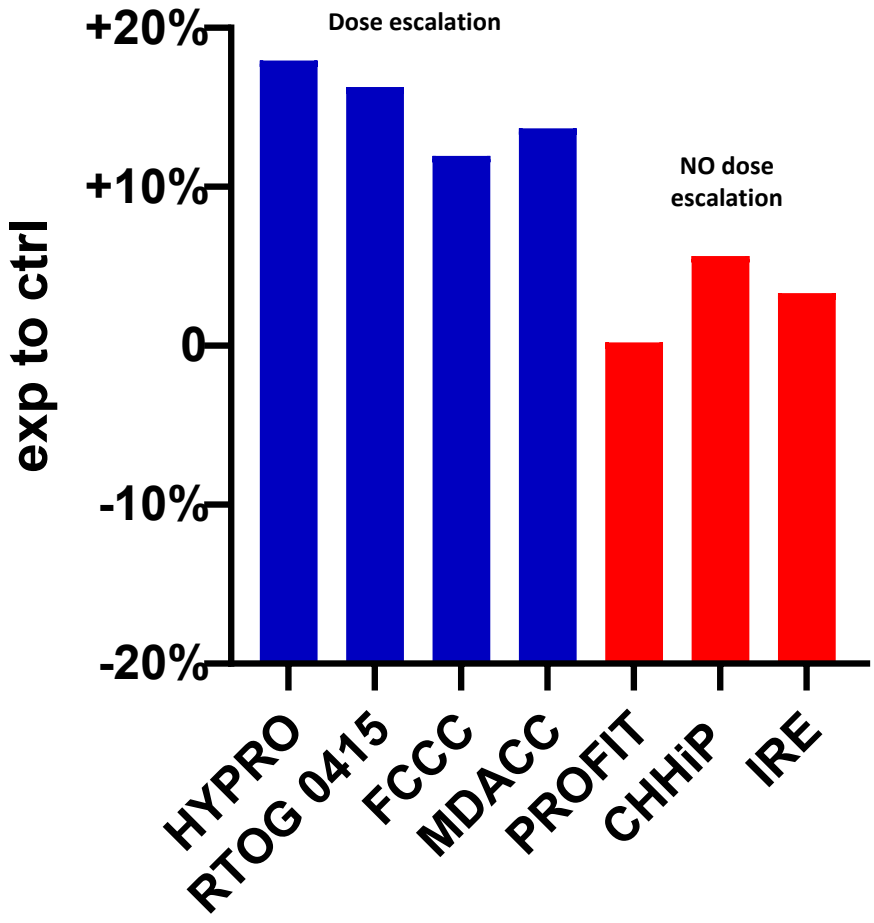




DOSE ESCALATED RCT MHFRT

IRE

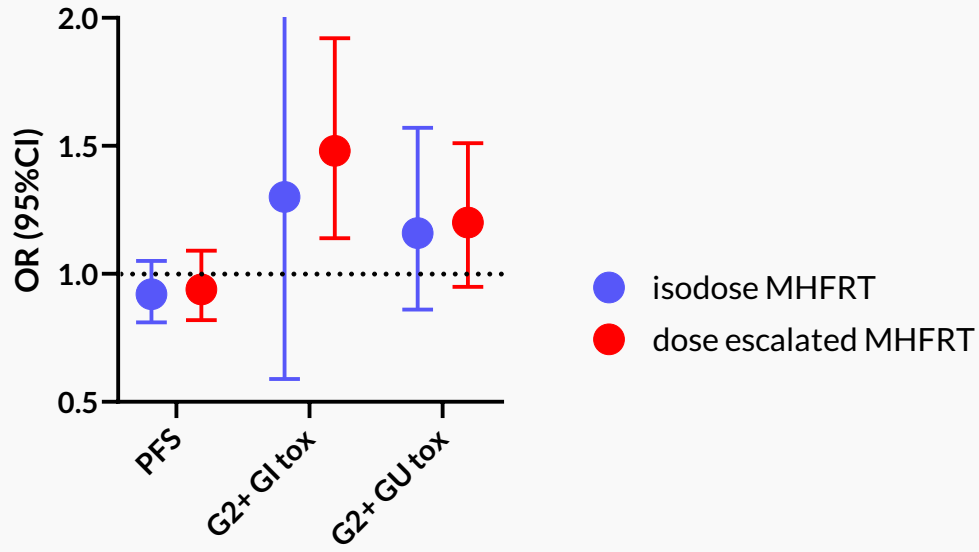
Relative BED advantage compared to control arm (α/β =1.3 Gy)



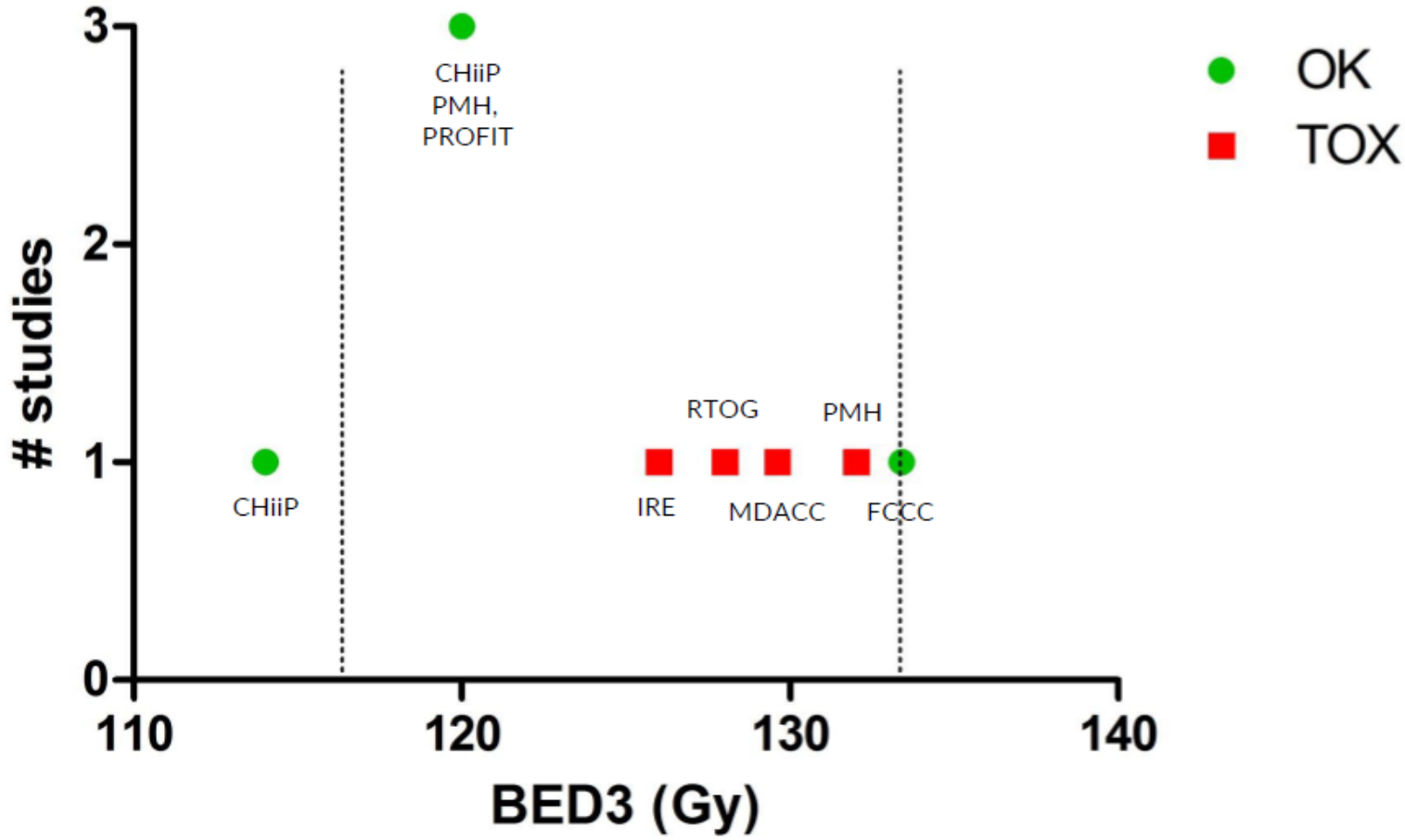
HYpofractionateD RAdiotherapy for Prostate Cancer (HYDRA): An Individual Patient Data Meta-Analysis of Randomized Trials in the MARCAP Consortium

The Lancet Oncology (press)

- Individual patient data were obtained from 7 phase III trials comparing MHFRT vs. CFRT:
- 3 (n=3454) with isodose and 4 (n=2426) with dose-escalated MHFRT
- Median follow-up of 5.4 years (interquartile range [IQR], 4.6-7.2) and 7.1 years (IQR 5.7-8.4) following isodose and dose-escalated MHFRT

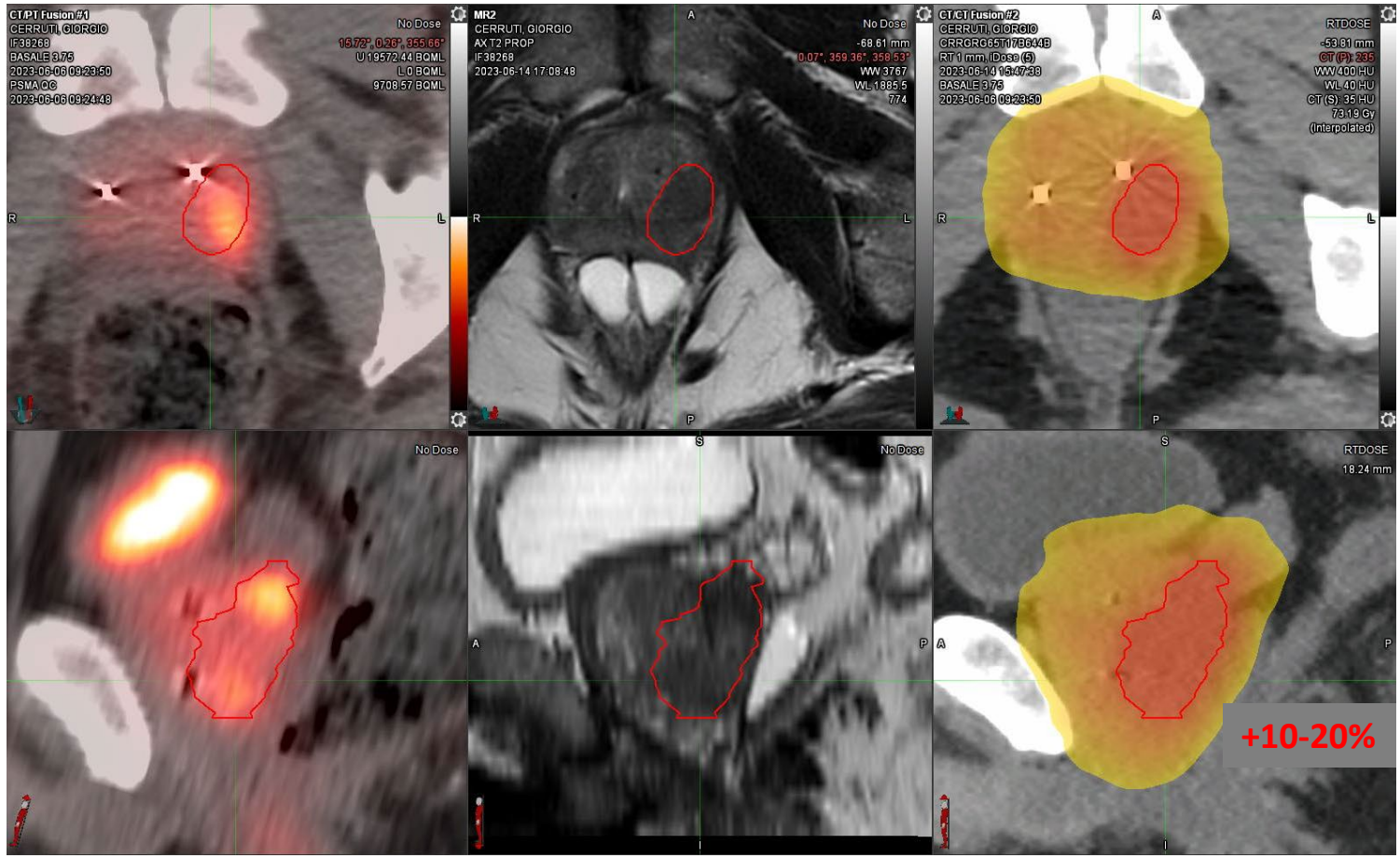


- Isodose regimens, e.g. 60-62 Gy in 20 fractions, should be the standard MHFRT regimen for localized prostate cancer.



BED3 (Gy) by RCT: the red dot indicates a study that found an INCREASE in late tox (either GI or GU) compared to standard fractionation while a green one found no difference in late tox between arms

Is (focal) does escalation a reasonable strategy to (further) improve results?



IRE

RT (selective) dose escalation

Focal Boost to the Intraprostatic Tumor in External Beam Radiotherapy for Patients With Localized Prostate Cancer: Results From the FLAME Randomized Phase III Trial

Linda G. W. Kerkmeijer, MD, PhD[1,2]; Veerle H. Groen, MD[1]; Floris J. Pos, MD, PhD[3]; Karin Haustermans, MD, PhD[4]; Evelyn M. Monninkhof, PhD[5]; Robert Jan Smeenk, MD, PhD[2]; Martina Kunze-Busch, PhD[2]; Johannes C. J. de Boer, PhD[1]; Jochem van der Voort van Zijp, MD, PhD[1]; Marco van Vulpen, MD, PhD[6]; Cédric Draulans, MD, PhD[4]; Laura van den Bergh, MD, PhD[7]; Sofie Isebaert, PhD[4]; and Uulke A. van der Heide, PhD[3]

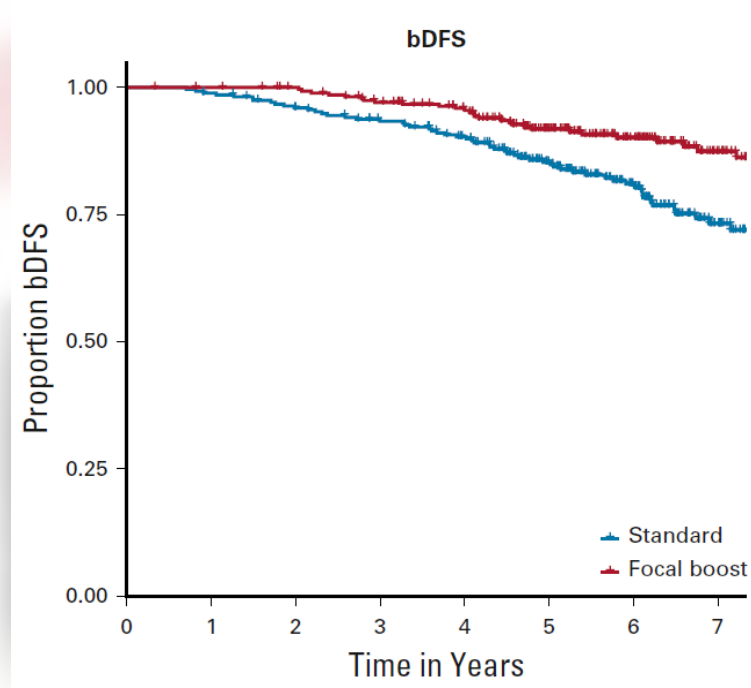
Journal of Clinical Oncology
Volume 39, Issue 7 787

- EB FOCAL BOOST to DIL(s):
  improved bNED with focal boost (level I evidence, FLAME)

- RCT between 77 Gy/35 fxs and an additional boost to the macroscopic tumor of up to 95 Gy;
- 571 patients, IR/HR (15/85%), 65% got also ADT
- Median follow-up of 72 mo

- HR ab 0.5 for bNED, p<.00001
- No diff in DMFS or OS

	Patients (*n*)	
	Standard arm (*N* = 271)	Focal boost arm (*N* = 264)
Local failure	21	7
Regional failure	22	7
Distant failure		
Distant lymph node	13	11
Bone	15	12
Visceral	6	2



Knowledge-Based Assessment of Focal Dose Escalation Treatment Plans in Prostate Cancer

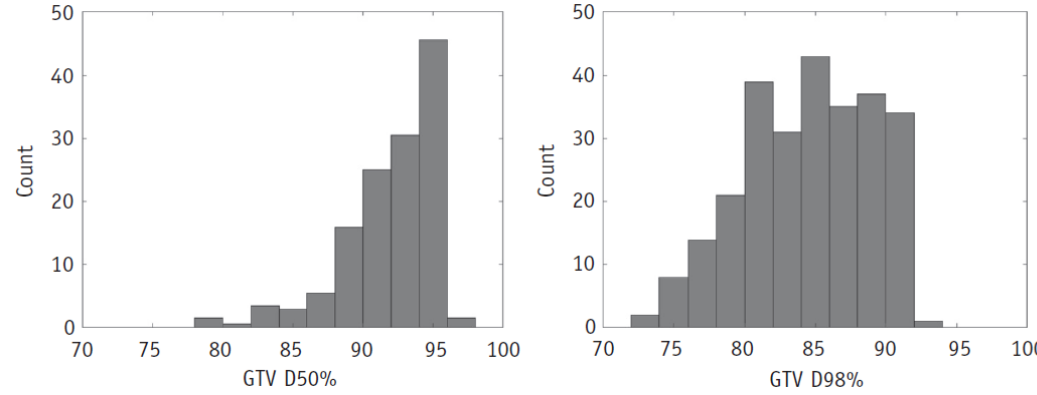
Marcel A. van Schie, MSc,* Tomas M. Janssen, PhD,*
Dave Eekhout, PhD,* Iris Walraven, PhD,* Floris J. Pos, MD, PhD,*
Peter de Ruiter, PhD,* Alexis N.T.J. Kotte, PhD,†
Evelyn M. Monninkhof, PhD,† Linda G.W. Kerkmeijer, MD, PhD,†,‡
Cédric Draulans, MD,§ Robin de Roover, MSc,§
Karin Haustermans, MD, PhD,§ Martina Kunze-Busch, PhD,‡
Robert Jan Smeenk, MD, PhD,‡ and Uulke A. van der Heide, PhD*

**Netherlands Cancer Institute, Radiation Oncology, Amsterdam, The Netherlands; †University Medical Center Utrecht, Radiation Oncology, Utrecht, The Netherlands; ‡Radboud University Medical Center, Radiation Oncology, Nijmegen, The Netherlands; and §University Hospitals Leuven, Radiation Oncology, Leuven, Belgium*

Received Jun 25, 2019, and in revised form Jun 3, 2020. Accepted for publication Jun 26, 2020.

International Journal of Radiation Oncology biology • physics

- As dose constraints to organs at risk had priority over dose escalation, in the dose-escalated arm, the median tumor D50% and D98% were 93.0 and 84.7 Gy

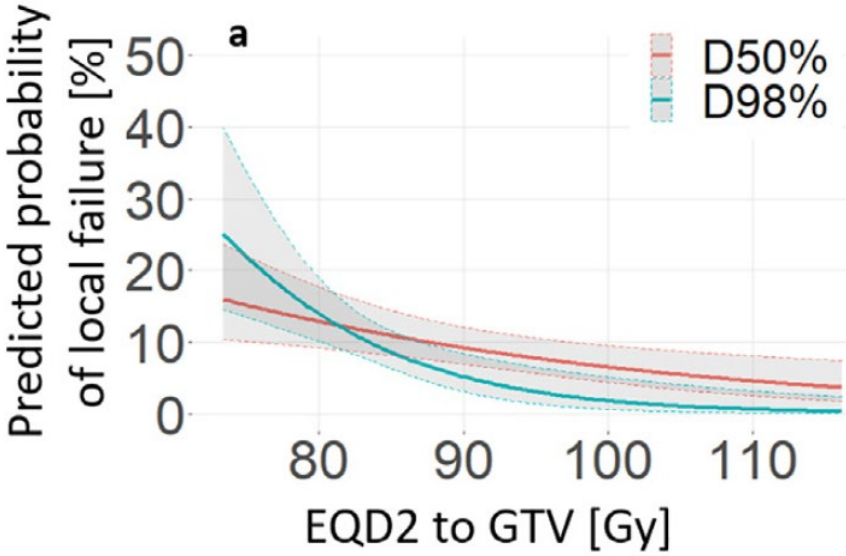


Patterns of Failure Following External Beam Radiotherapy With or Without an Additional Focal Boost in the Randomized Controlled FLAME Trial for Localized Prostate Cancer

Veerle H. Groen [a], Karin Haustermans [b], Floris J. Pos [c], Cédric Draulans [b], Sofie Isebaert [b], Evelyn M. Monninkhof [c], Robert J. Smeenk [d], Martina Kunze-Busch [d], Johannes C.J. de Boer [a], Jochem van der Voort van Zijp [a], Linda G.W. Kerkmeijer [a,d], Uulke A. van der Heide [e,]*

EUROPEAN UROLOGY 82 (2022) 252–257

- The 'coverage' dose (D98%) is more important than 'mean' D (D50%)(hot spots)
- In the dose/response analysis it is important to consider the dose to the GTV rather than CTV



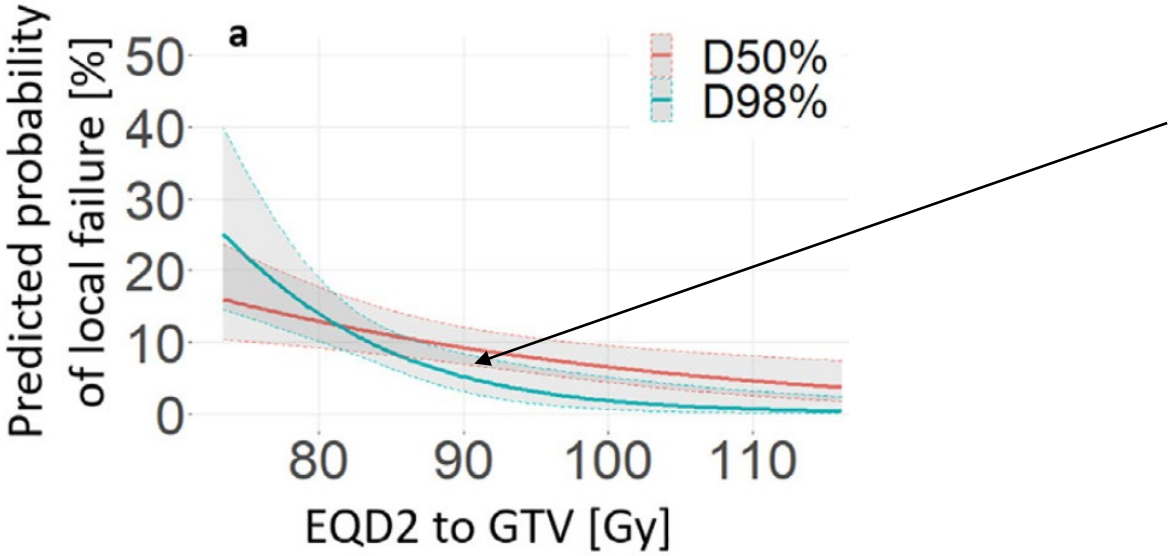
Guricova et al, RO, 2022

Patterns of Failure Following External Beam Radiotherapy With or Without an Additional Focal Boost in the Randomized Controlled FLAME Trial for Localized Prostate Cancer

Veerle H. Groen[a], Karin Haustermans[b], Floris J. Pos[c], Cédric Draulans[b], Sofie Isebaert[b], Evelyn M. Monninkhof[c], Robert J. Smeenk[d], Martina Kunze-Busch[d], Johannes C.J. de Boer[a], Jochem van der Voort van Zijp[a], Linda G.W. Kerkmeijer[a,d], Uulke A. van der Heide[e,]*

EUROPEAN UROLOGY 82 (2022) 252–257

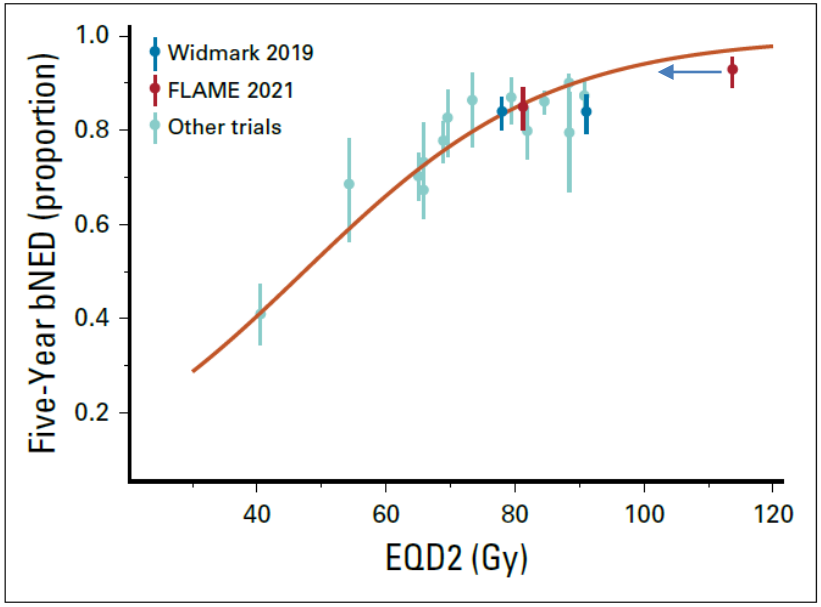
- The 'coverage' dose (D98%) is more important than 'mean' D (D50%)(hot spots)
- In the dose/response analysis it is important to consider the dose to the GTV rather than CTV



Guricova et al, RO, 2022

- Is dose escalation beyond 85-90 Gy EQD2 beneficial?
- Only 14% of pts got a nominal dose >90 Gy (robustness of the finding)
- While FLAME achieved a median D98% of 84.7 Gy (or 94.5 Gy EQD2) to GTV, SABR can safely and tolerably deliver 100–110 Gy EQD2 to the CTV (whole prostate and proximal seminal vesicles)

Correa et al, RO 2022



Vogelius and Bentzen, JCO 2022

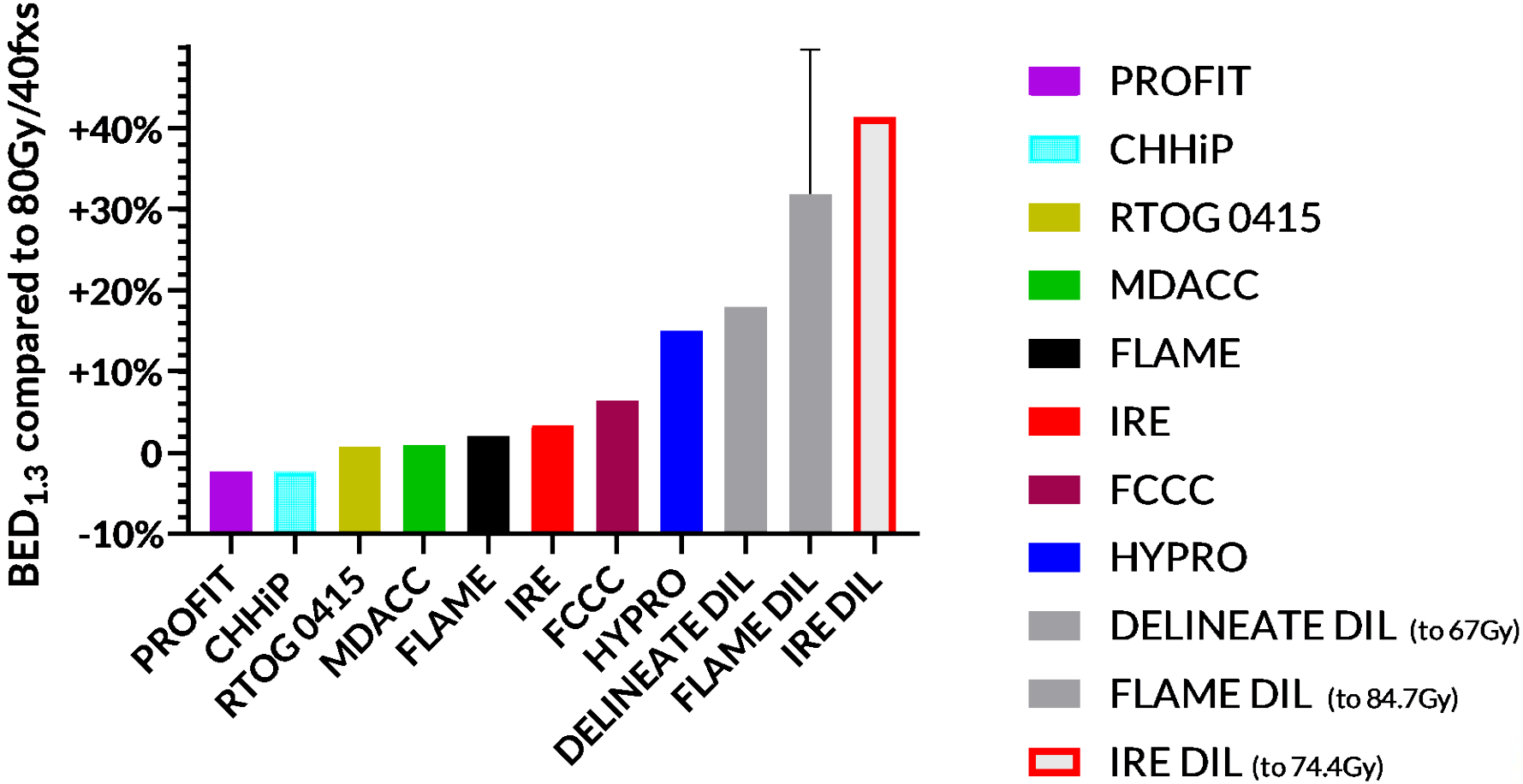
local therapies have NOT maxed out in terms of biochemical relapse-free rate!

- Is dose escalation beyond 85-90 Gy EQD2 beneficial?
- Only 14% of pts got a nominal dose >90 Gy (robustness of the finding)
- While FLAME achieved a median D98% of 84.7 Gy (or 94.5 Gy EQD2) to GTV, SABR can safely and tolerably deliver 100–110 Gy EQD2 to the CTV (whole prostate and proximal seminal vesicles)

Correa et al, RO 2022

Relative BED advantage compared to 80Gy CF

(α/β =1.3 Gy)



IRE

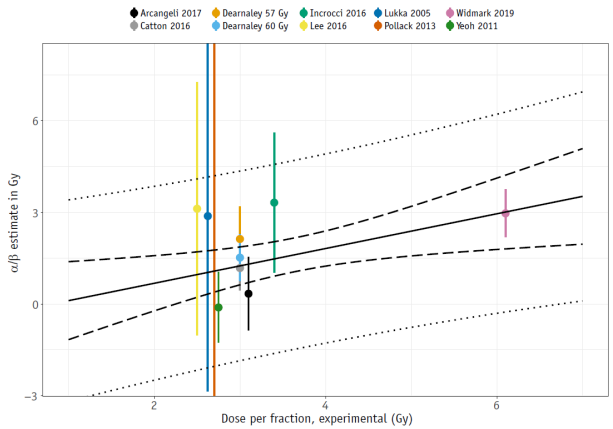


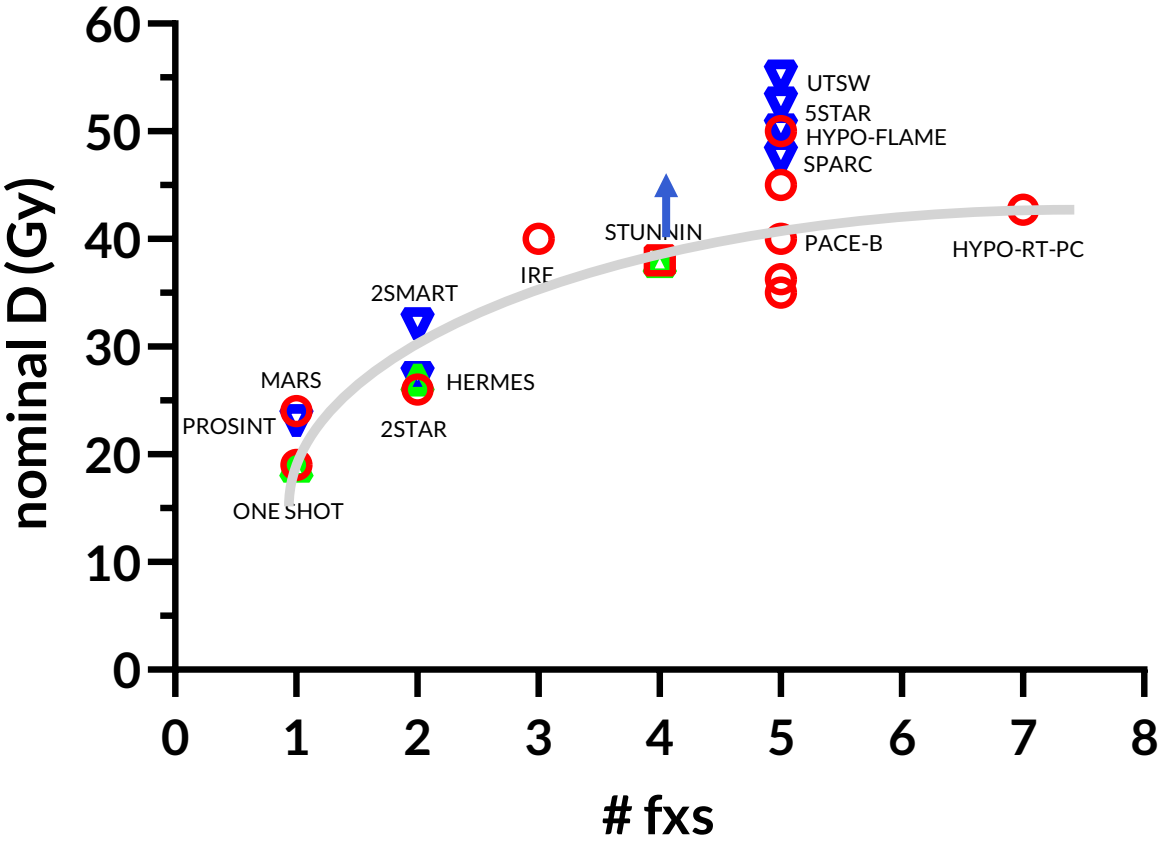
Fig. 2. Estimated α/β value and 95% confidence interval as function of experimental arm fraction size. Linear regression model with 95% confidence (dashed) and prediction (dotted) bounds are shown for the best fitting model with slope = 0.57 Gy/Gy (95% CI, 0.2-0.9 Gy per Gy; $P = .02$). The linear regression is weighted by the inverse variance of the individual α/β estimates from 9 included studies. The 2 experimental arms by Dearnaley et al[9] are included as individual studies and denoted by experimental arm dose rather than date of publication.

Vogelius and Bentzen, IJROBP 2020

‘‘with extreme hypofractionation, **effective doses may be lower than expected**” and α/β may increase with fraction size

- Is dose escalation beyond 85-90 Gy EQD2 beneficial?
- Only 14% of pts got a nominal dose >90 Gy (robustness of the finding)
- While FLAME achieved a median D98% of 84.7 Gy (or 94.5 Gy EQD2) to GTV, SABR can safely and tolerably deliver 100–110 Gy EQD2 to the CTV (whole prostate and proximal seminal vesicles)

Correa et al, RO 2022



SBRT HOMO

SBRT ETERO

HDR

DIL (HDR or SBRT)

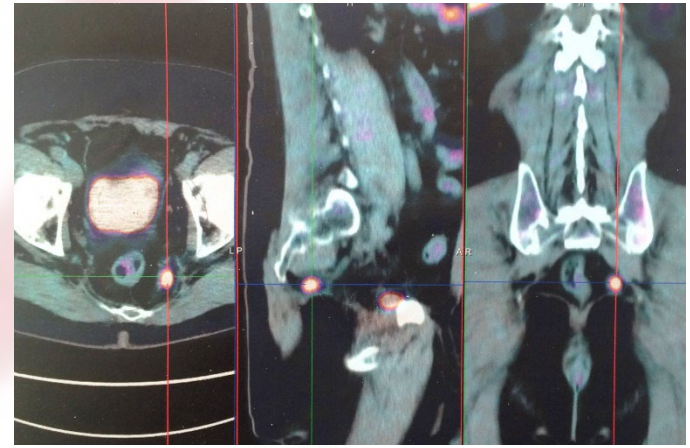
FLAME 77→95 Gy/35 (Kerkmeijer et al, JCO 2021)
HYPO-FLAME 35→45 Gy/5 (Cock et al, RO 2023)
SPARC 36.25→47.5 Gy/5 (Yasar et al, IJROBP 2024)
UTSW 47.7→55 Gy/5 w WPRT to 25 Gy (Hannan et al, IJROBP 2022)
DELINEATE 60→67 Gy/20 (Tree et al, IJROBP 2023)

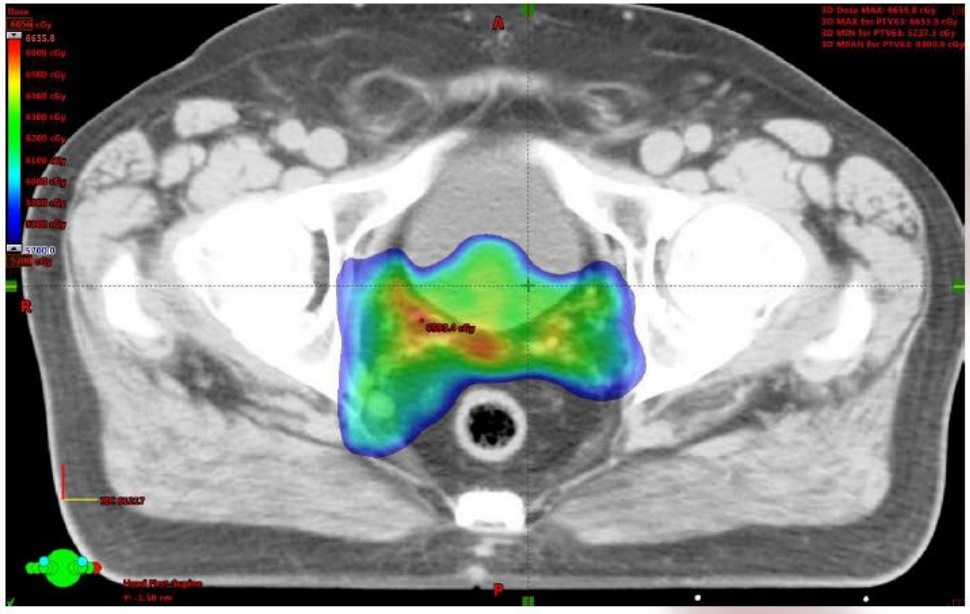
Extreme hypo and the treated volume

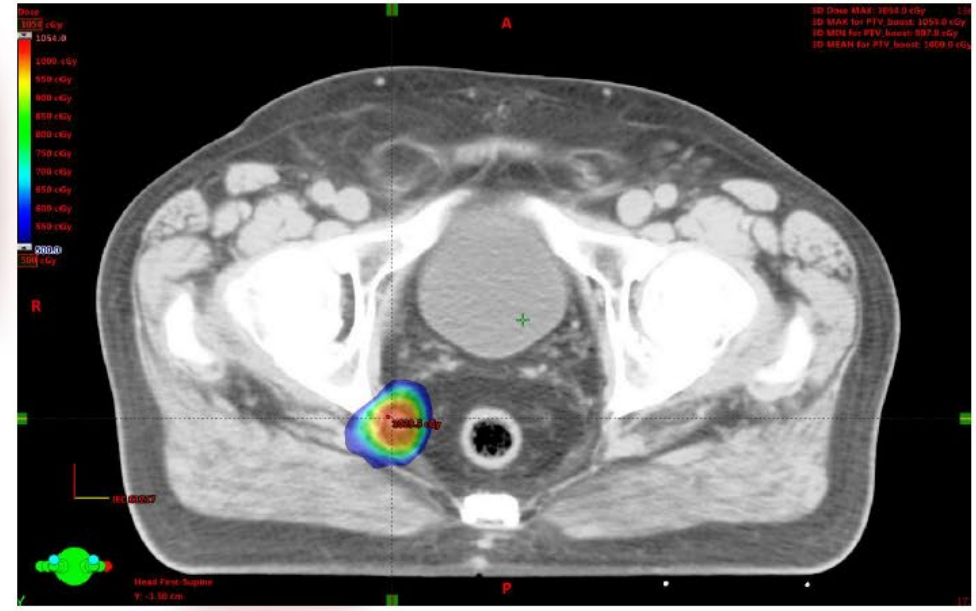
THE CASE OF ISOLATED

NODAL

(PELVIS/LA) FAILURE(S)







WFRT

- Comprehensive elective coverage of the *majority* of (pelvic) lymph nodes at risk
- Highly effective to prevent further nodes

- Somewhat limited efficacy on macro diz, due to limits in the delivered D
- Higher incidence of long term tox
- Long delivery time and hospital workload

MDT

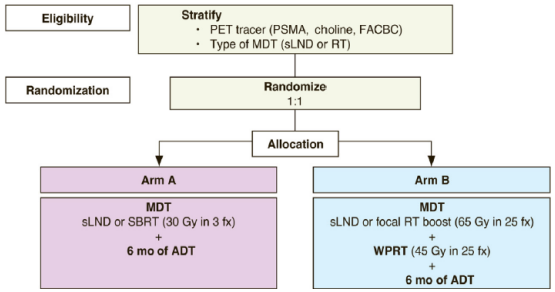
- Highly effective on the treated diz
- Negligible incidence of long term tox
- Possibility of re-SBRT of new lesions
- Short course and limited hospital workload

- Limited to the GTV, higher rate of surrounding failures
- Benefit seen in pts with better prognosis

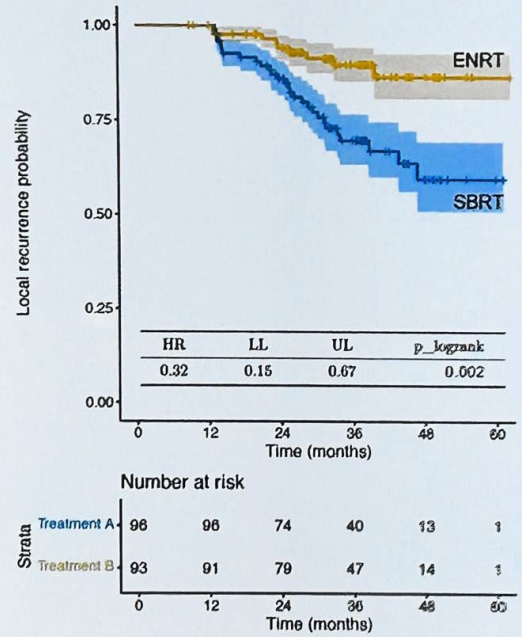
STORM

PEACE V - Salvage Treatment of OligoRecurrent nodal prostate cancer Metastases (STORM): results of a randomized phase II trial

Oligorecurrent PET-detected pelvic nodal PCa with ≤5 nodes



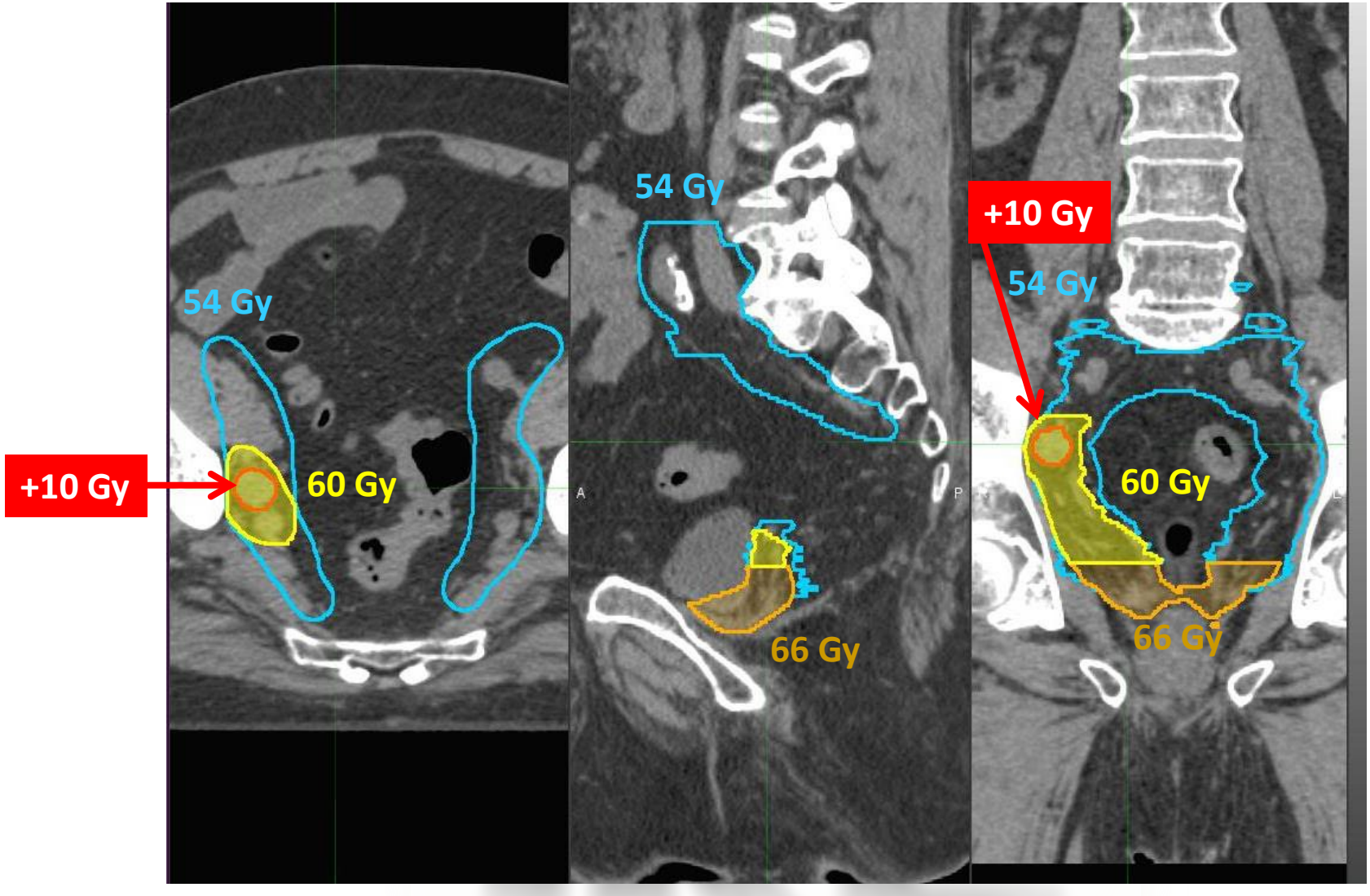
Results: locoregional relapse-free survival



3 year rRFS:

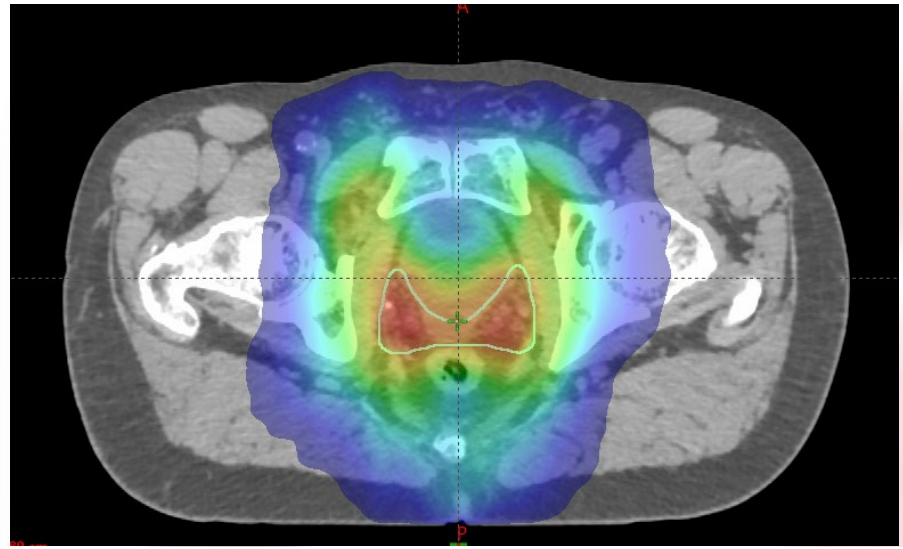
- MDT = **70%** (63%, 77%)
- ENRT = **90%** (85%, 94%)

Zilli et al, 2024

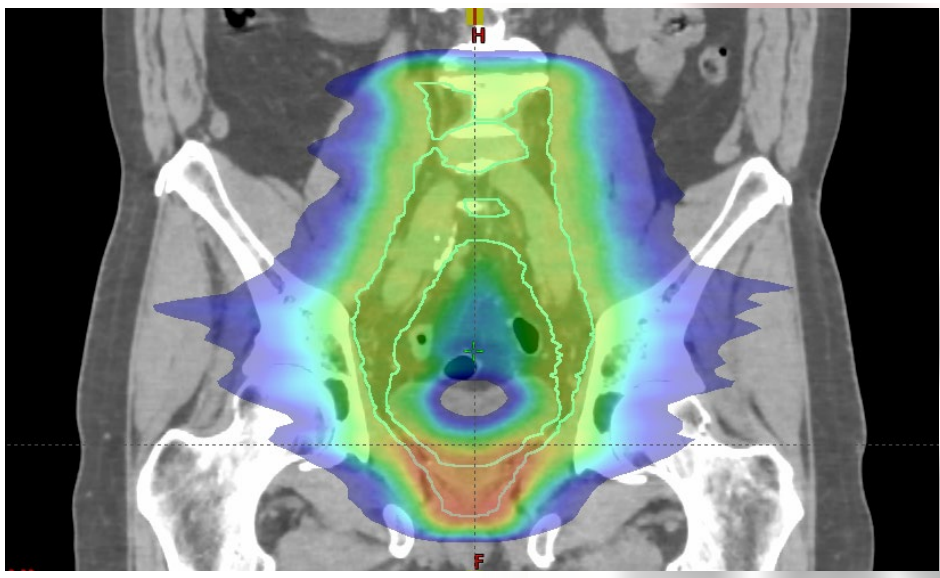


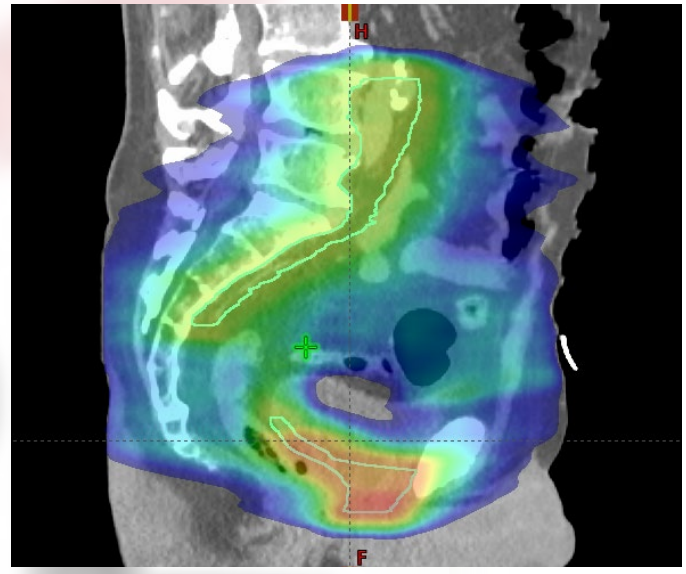
WPRT (30 fxs) → SBRT boost (1 fx)

IRE

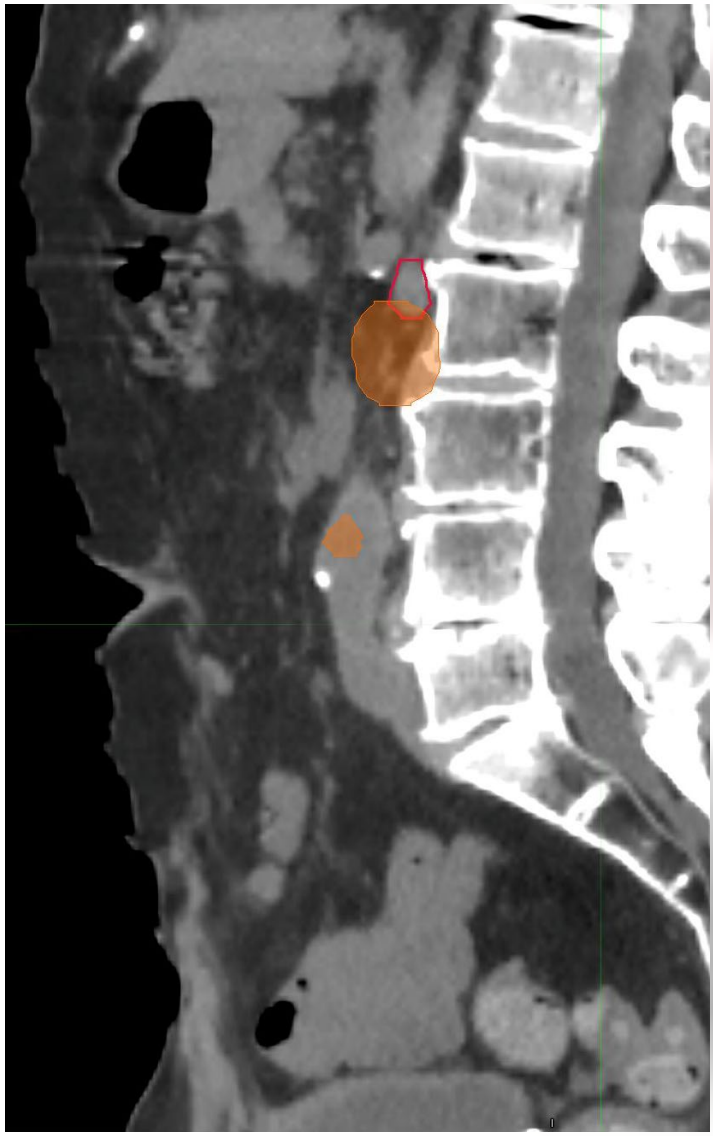


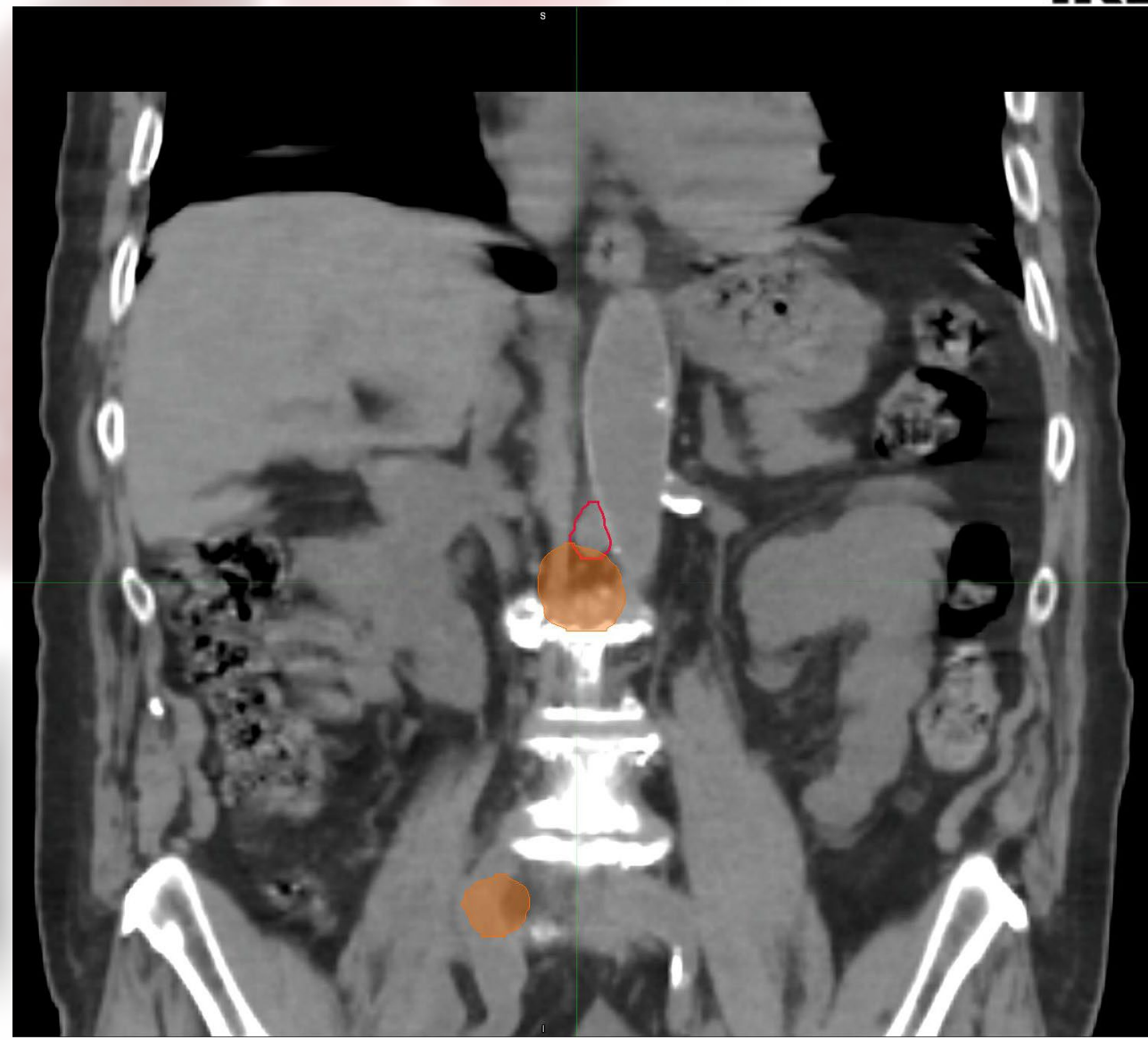
Whole Pelvis: sSBRT to 25 Gy/5fxs



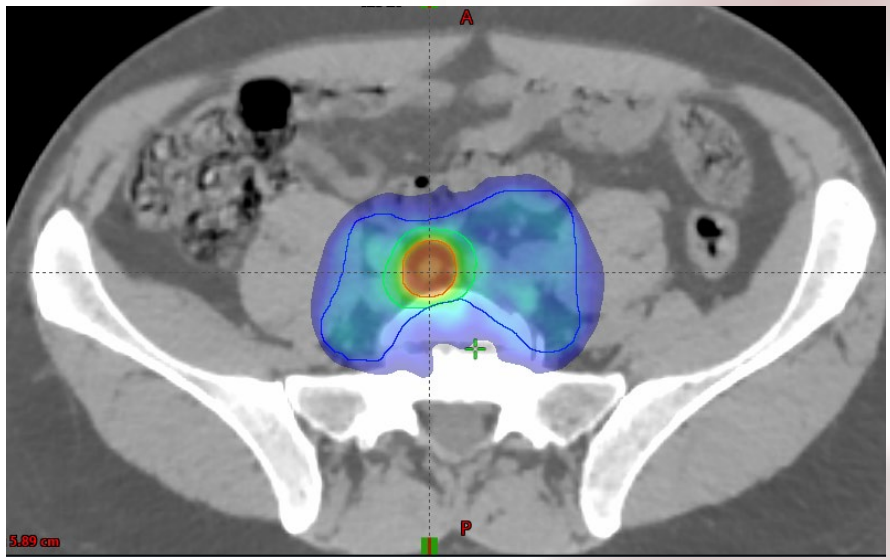


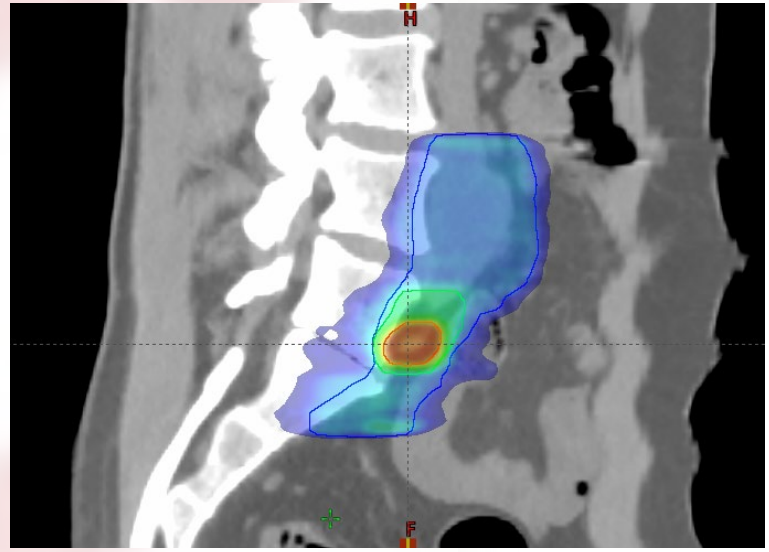
(metachronous) Oligo PD LA N

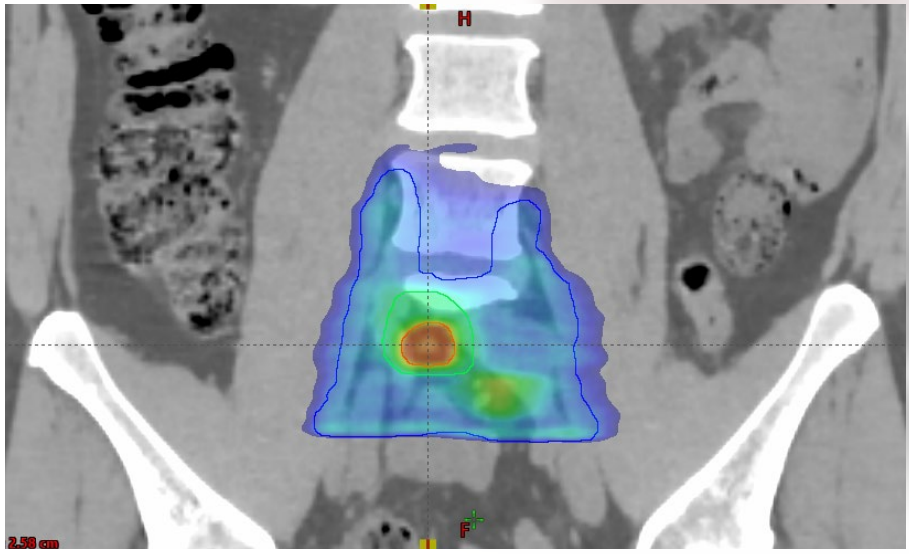




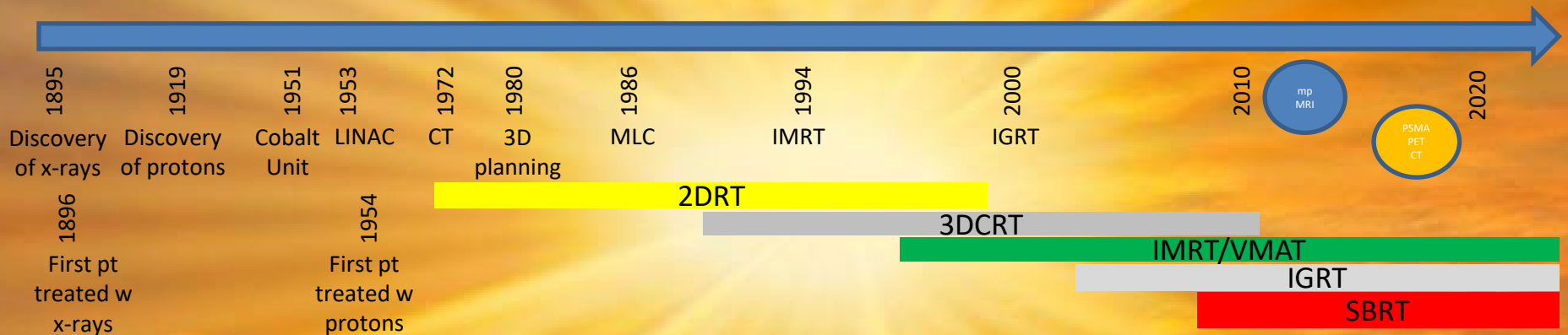
(metachronous) Oligo PD LA N







40/30/25Gy in 5 fxs
30/24Gy in 3 fxs



Radiotherapy improvements allow to deliver dose precisely and accurately to a region of interest within the patient.

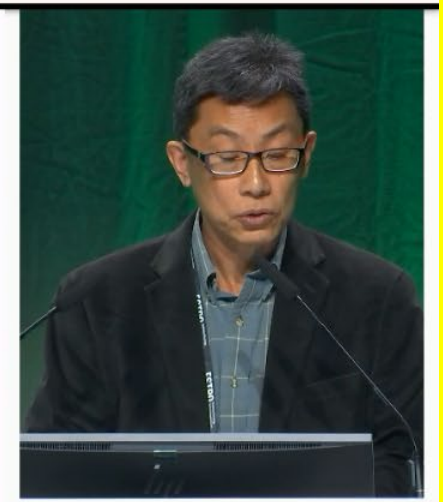
RT consumes only <5% of the total health care budget, whereas the highest proportion of cancer care costs is typically related to drugs and in-hospital stays

Current Indications of RT for PCa

Diz Status	Strata	Ist option	Notes
Localized diz	Very Low	AS	RT if active tmt
	Low	AS	RT if active tmt
	Intermediate fav	RT vs S	
	Intermediate unfav	RT+STAD vs S	
	High	RT+LTAD vs S	
	Very High	RT+AD+ARPI vs S	
N1		AD+ARPI±RT	STAMPEDE Attard et al, Lancet Oncol 2022
M1	Low volume/sync	AD+ARPI±Doce±RT	PEACE-1 Bossi et al, Lancet, 2024
	Low volume/meta	RT vs AD+ARPI	MDT: STOMP/ORIOLE
	High volume	AD+Doce+ARPI	
	CRPC	Combo of systemic tmt	Selected
Adjuvant RT	Dect PSA, pN+/SVI or multiple risk factors	RT±AD	
Salvage RT	Bio fail after S	RT±AD	?ARPI alone

CORE Conclusions

- Overall phase 2 objectives met with a PFS signal in favour (at 20% significance level) of SBRT+SOC
- Results justify larger definitive phase 3 randomised trials;
- Issues with recruitment rate in breast & lung cohorts; if considering Ph 3 would need a trial re-design.
- Phase 3 CORE-prostate (proposal in 2021) was deemed unfeasible due to perceived lack of equipoise i.e. SBRT had become an accepted treatment option
- Biomarker rich & biologically informed randomised trials are still essential to define the group of pts who benefit from SBRT.



Vincent Khoo
United Kingdom

ONE problem is the access to RT – PROSTATE UNITS……*consultation*…….

As cancer organisations (such as the National Comprehensive Cancer Network) and government bodies (such as Cancer Care Ontario) mandate radiation oncology consultation for all newly diagnosed prostate cancer patients

Physician Visits Prior to Treatment for Clinically Localized Prostate Cancer

Thomas L. Jang, MD, MPH; Justin E. Bekelman, MD; Yihai Liu, MS; Peter B. Bach, MD, MAPP; Ethan M. Basch, MD, MSc; Elena B. Elkin, PhD; Michael J. Zelefsky, MD; Peter T. Scardino, MD; Colin B. Begg, PhD; Deborah Schrag, MD, MPH

(REPRINTED) ARCH INTERN MED/VOL 170 (NO. 5), MAR 8, 2010

(SEER DATA) Overall, 42 309 men (50%) were seen exclusively by urologists, 37 540 (44%) by urologists and radiation radiation oncologists, 2329 (3%) by urologists and medical oncologists, and 2910 (3%) by all 3 specialists.
There was a strong association between the type of specialist seen and primary therapy received.

EIN PRESSWIRE by Newsmatics | EIN Presswire | Newsmatics

Robotic-Assisted Surgery: The Superior Choice Over Radiation for Prostate Cancer Treatment, says Dr. David Samadi

NEWS PROVIDED BY
EIN Presswire
Dec 18, 2024, 7:45 AM ET

"When it comes to prostate cancer, precision is everything," says Dr. David Samadi, world-renowned urologist and robotic surgery expert. "Robotic-assisted surgery allows us to remove the cancer with unparalleled accuracy while minimizing damage to critical areas. It's a game-changer for men's health."

Robotic-assisted surgery has demonstrated superior long-term outcomes in cancer control.

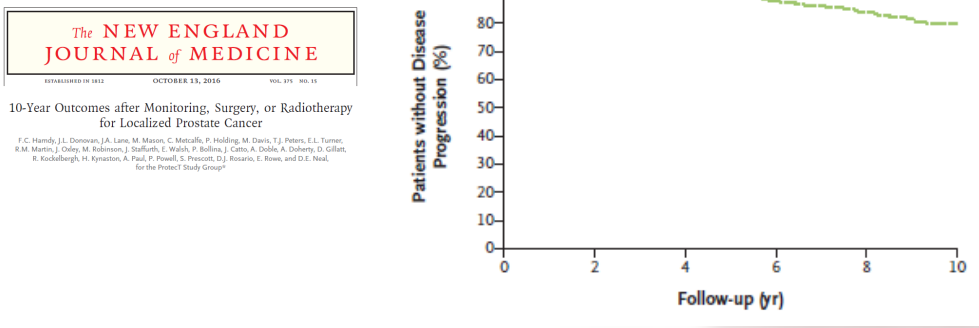
EIN PRESSWIRE by Newsmatics | **EIN Presswire | Newsmatics**

Robotic-Assisted Surgery: The Superior Choice Over Radiation for Prostate Cancer Treatment, says Dr. David Samadi

NEWS PROVIDED BY
EIN Presswire
Dec 18, 2024, 7:45 AM ET

"When it comes to prostate cancer, precision is everything," says Dr. David Samadi, world-renowned urologist and robotic surgery expert. "Robotic-assisted surgery allows us to remove the cancer with unparalleled accuracy while minimizing damage to critical areas. It's a game-changer for men's health."

Robotic-assisted surgery has demonstrated superior long-term outcomes in cancer control.



SBRT
Ultra-Hypofractionation

9.5 Gy x 4 fx
7.25–8 Gy x 5 fx[c]
6.1 Gy x 7 fx[c]

National Comprehensive Cancer Network®


Radiotherapy and Oncology 154 (2021) 207–213
Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com
ELSEVIER

Original Article

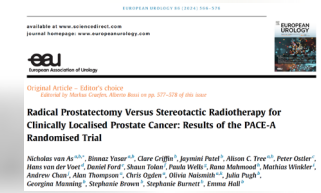
Dose–response with stereotactic body radiotherapy for prostate cancer: A multi-institutional analysis of prostate-specific antigen kinetics and biochemical control

Rebecca G. Levin-Epstein [a], Naomi Y. Jiang [a], Xiaoyan Wang [b], Shrinivasa K. Upadhyaya [c], Sean P. Collins [d],

PSA kinetics.

	All patients	35 Gy/5 fx	36.25 Gy/5 fx	40 Gy/5 fx	38 Gy/4 fx	*p*-value*
nPSA, median (IQR), mean, ng/mL	0.18 (0.10–0.33), 0.34	0.17 (0.10–0.32), 0.31	0.20 (0.09–0.47), 0.39	0.19 (0.12–0.30), 0.33	0.01 (0.01–0.20), 0.30	<0.0001
Time to nPSA, months, median (IQR)	47.7 (24.0–72.0)	44.8 (24.8–62.4)	36.2 (21.2–61.2)	51.8 (28.0–78.0)	38.9 (24.3–60.2)	<0.0001
Achievement of nPSA ≤0.5 ng/mL, *n* (%)	1559 (81.7)	211 (82.4)	541 (76.1)	586 (85.7)	221 (86.0)	<0.0001
Achievement of nPSA ≤0.2 ng/mL, *n* (%)	1001 (52.5)	130 (50.8)	343 (48.2)	347 (50.7)	181 (70.4)	<0.0001

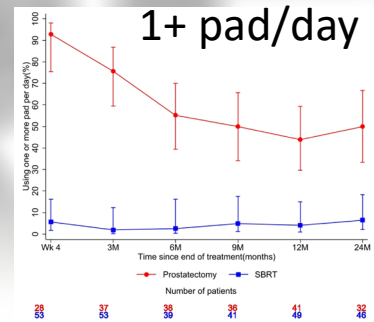
Fx: fractions; nPSA: nadir prostate-specific antigen; IQR: interquartile range.
*p-value derived from multivariate/logistic regression, adjusting for risk group, age, ln(iPSA), T stage, and grade group. Detailed between-group comparisons for threshold values are available in Supplementary Table 4.

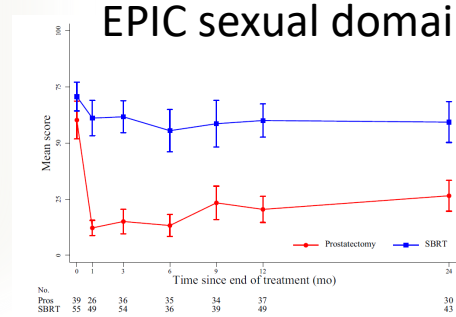

EUROPEAN UROLOGY 86 (2024) 568–576
available at www.sciencedirect.com
journal homepage: www.europeanurology.com
eau European Association of Urology
EUROPEAN UROLOGY

Original Article – Editor's choice

Radical Prostatectomy Versus Stereotactic Radiotherapy for Clinically Localised Prostate Cancer: Results of the PACE-A Randomised Trial

Nicholas van As [a,b,*], Bisnaa Yasar [a,b], Clare Griffin [a], Jaymini Patel [a], Alison C. Tree [a,b], Peter Ostler [c], Hans van der Voet [d], Daniel Ford [e], Shaun Tolan [f], Paula Wells [g], Rana Mahmood [h], Mathias Winkler [i], Andrew Chan [j], Alan Thompson [k], Chris Ogden [l], Olivia Naismith [a,b], Julia Pugh [a], Georgina Manning [a], Stephanie Brown [a], Stephanie Burnett [a], Emma Hall [a]

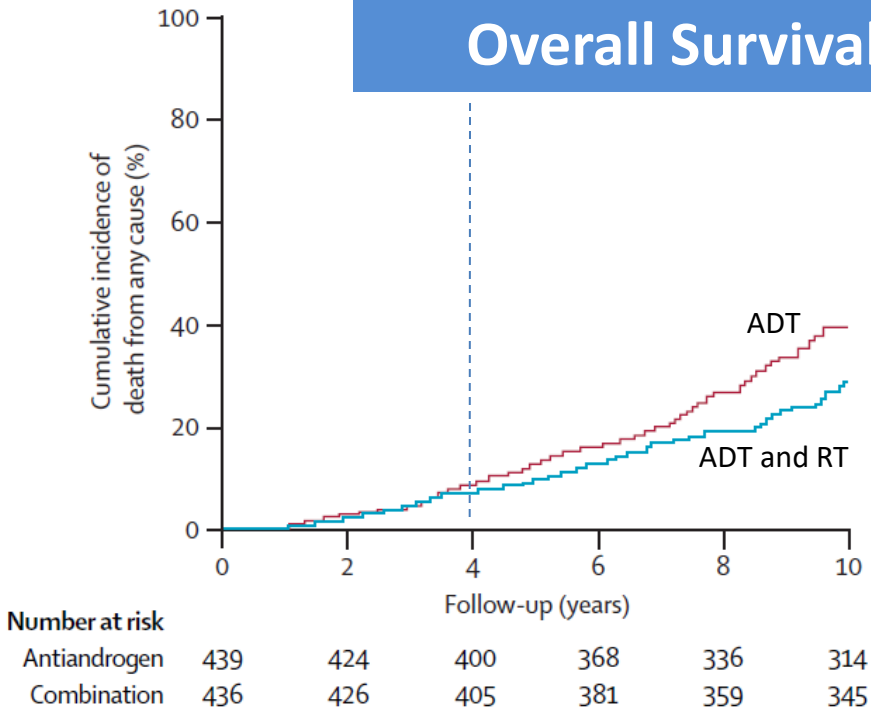




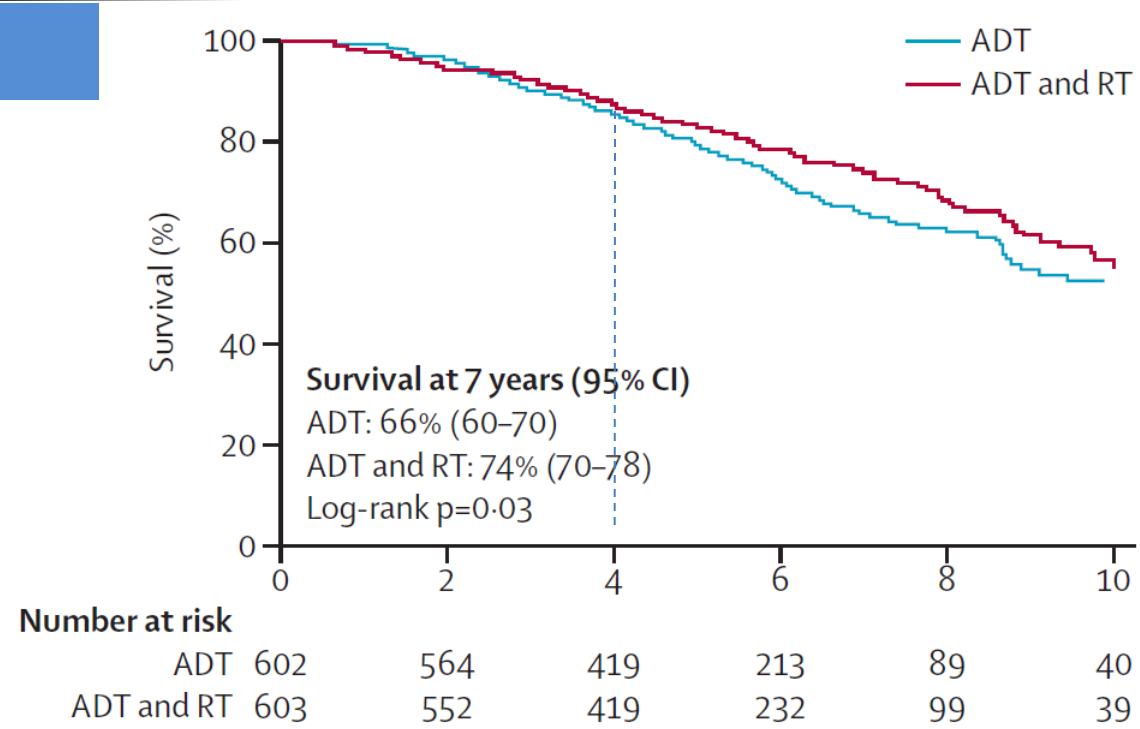
RCT on LTAD+EBRT

Trial	# pts	pts	Doses (Gy)	AD	Outcome	Toxicity
SPGC-7/ SFUO-3	875 (1996-2002)	T1b-2 (G2-3) T3 (any G) (UICC 1992) pN0 PSA≤70 (20% int risk)	70+Gy PORT	(LHRH+)AA	Median FU 7.6 yrs HR-OS: 0.68, p=0.004 Abs improv at 10 yrs: 9.8%	Worse urinary, diarrhea, ED
NCIC/MRC	1205 (1995-2005)	T2 and PSA>40 T2 and PSA>20 and GLS>8 T3 or T4 N0-x	65-69 Gy PORT 45 Gy WPRT (72%)	LHRH or orchx	Median FU 6.0 yrs HR-OS: 0.77 (p=0.03) Abs improv at 7 yrs: 8%	Worse mild GI tox

Overall Survival



Widmark et al, Lancet 2009



Warde et al, Lancet 2011

- **Loco(regional) RT improves overall survival**
- **Effect through reduction (in second wave) of DM**

The NEW ENGLAND JOURNAL of MEDICINE

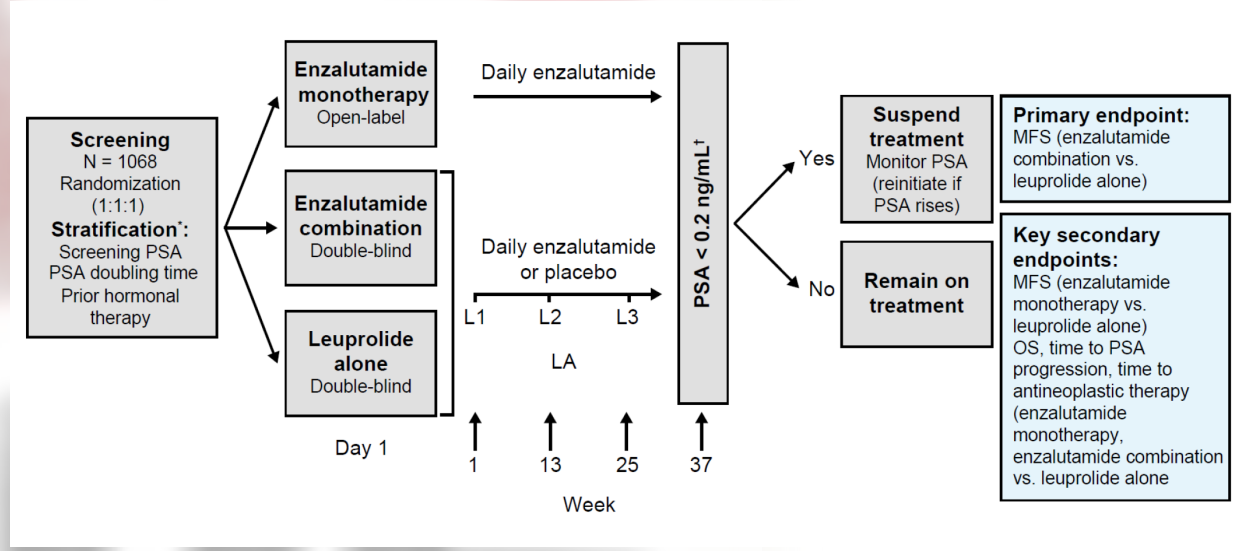
ESTABLISHED IN 1812 OCTOBER 19, 2023 VOL. 389 NO. 16

Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer

S.J. Freedland, M. de Almeida Luz, U. De Giorgi, M. Gleave, G.T. Gotto, C.M. Pieczonka, G.P. Haas, C.-S. Kim, M. Ramirez-Backhaus, A. Rannikko, J. Tarazi, S. Sridharan, J. Sugg, Y. Tang, R.F. Tutrone, Jr., B. Venugopal, A. Villers, H.H. Woo, F. Zohren, and N.D. Shore

HR bio recurrence after RT and/or SURGERY (PSADT≤9 mths or PSA>1ng/ml)

≈25% previous RP
≈25% previous RT
≈50% previous RT+RP



The NEW ENGLAND JOURNAL of MEDICINE

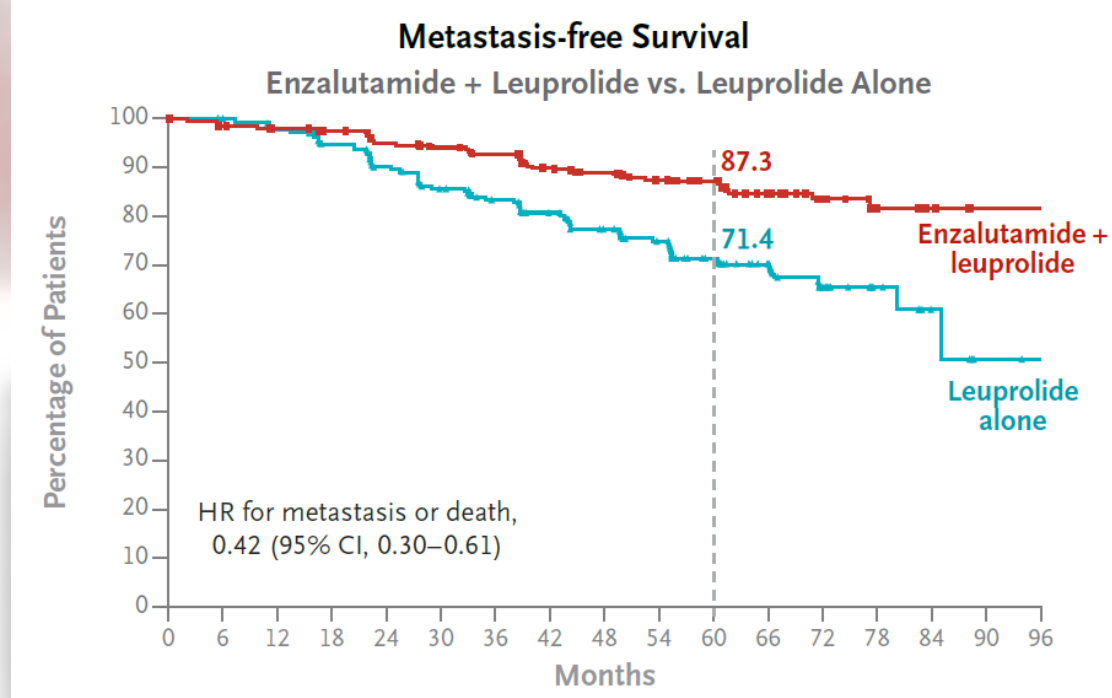
ESTABLISHED IN 1812 OCTOBER 19, 2023 VOL. 389 NO. 16

Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer

S.J. Freedland, M. de Almeida Luz, U. De Giorgi, M. Gleave, G.T. Gotto, C.M. Pieczonka, G.P. Haas, C.-S. Kim, M. Ramirez-Backhaus, A. Rannikko, J. Tarazi, S. Sridharan, J. Sugg, Y. Tang, R.F. Tutrone, Jr., B. Venugopal, A. Villers, H.H. Woo, F. Zohren, and N.D. Shore

HR bio recurrence after RT and/or SURGERY (PSADT≤9 mths or PSA>1ng/ml)

≈25% previous RP
≈25% previous RT
≈50% previous RT+RP



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 19, 2023 VOL. 389 NO. 16

Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer

S.J. Freedland, M. de Almeida Luz, U. De Giorgi, M. Gleave, G.T. Gotto, C.M. Pieczonka, G.P. Haas, C.-S. Kim, M. Ramirez-Backhaus, A. Rannikko, J. Tarazi, S. Sridharan, J. Sugg, Y. Tang, R.F. Tutrone, Jr., B. Venugopal, A. Villers, H.H. Woo, F. Zohren, and N.D. Shore

HR bio recurrence after RT and/or SURGERY (PSADT≤9 mths or PSA>1ng/ml)

≈25% previous RP
≈25% previous RT
≈50% previous RT+RP

Patients were excluded if…. after radical prostatectomy they were considered by the investigator **to be a candidate** for salvage radiation therapy.

Prostate Cancer–Specific Survival Following Salvage Radiotherapy vs Observation in Men With Biochemical Recurrence After Radical Prostatectomy

Salvage radiotherapy alone was associated with a significant 3-fold increase in prostate cancer–specific survival relative to those who received no salvage treatment….

….**this was limited to men with a PSADT < 6 mths**

Trock et al JAMA 2008

Darolutamide plus androgen-deprivation therapy (ADT) in patients with high-risk biochemical recurrence (BCR) of prostate cancer: A phase 3, randomized, double-blind, placebo-controlled study (ARASTEP).

Alex Chehrazi-Raffle, Alicia K. Morgans, Jürgen E. Gschwend, Neal D. Shore, Ashley Ross, Felix Y Feng, Thomas A. Hope, Lucia Trandafir, Iris Kuss, Marie-Aude Le Berre, Heikki Joensuu, Karim Fizazi; Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, CA; Dana-Farber Cancer Institute, Boston, MA; Universitätsklinikum rechts der Isar, Technical University Munich, Munich, Germany; Carolina Urologic Research Center and Genesis Care/Atlantic Urology Clinics, Myrtle Beach, SC; Northwestern Medicine, Chicago, IL; Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA; Radiology School of Medicine, University of California at San Francisco, San Francisco, CA; Bayer Consumer Care AG, Basel, Switzerland; Bayer AG, Berlin, Germany; Bayer HealthCare SAS, Loos, France; Orion Corporation, Orion Pharma, Espoo, Finland; Gustave Roussy, University of Paris-Saclay, Villejuif, France

'…RP alone if ART/SRT was not **appropriate**…'

PRESTO: A Phase III, Open-Label Study of Intensification of Androgen Blockade in Patients With High-Risk Biochemically Relapsed Castration-Sensitive Prostate Cancer (AFT-19)

Rahul Aggarwal, MD[1]; Glenn Heller, PhD[2]; David W. Hillman, MS[3]; Han Xiao, MD[2]; Joel Picus, MD[4]; Mary-Ellen Taplin, MD[5]; Tanya Dorff, MD[6]; Leonard Appleman, MD[7]; Douglas Weckstein, MD[8]; Akash Patnaik, MD[9]; Alan Bryce, MD[10]; Daniel Shevrin, MD[11]; James Mohler, MD[12]; Daniel Anderson, MD[13]; Arpit Rao, MD[14]; Scott Tagawa, MD[15]; Alan Tan, MD[16]; Susan Halabi, PhD[17]; Katharine Dooley, MPH[3]; Patrick O'Brien, BS[3]; Ronald Chen, MD, MPH[18]; Charles J. Ryan, MD[19]; Scott E. Eggener, MD[9] and Michael J. Morris, MD[2]; on behalf of the PRESTO Study Investigators

J Clin Oncol 42:1114-1123

'Previous adjuvant or salvage radiation was required unless **contraindicated** per treating investigator discretion'


FUTURE