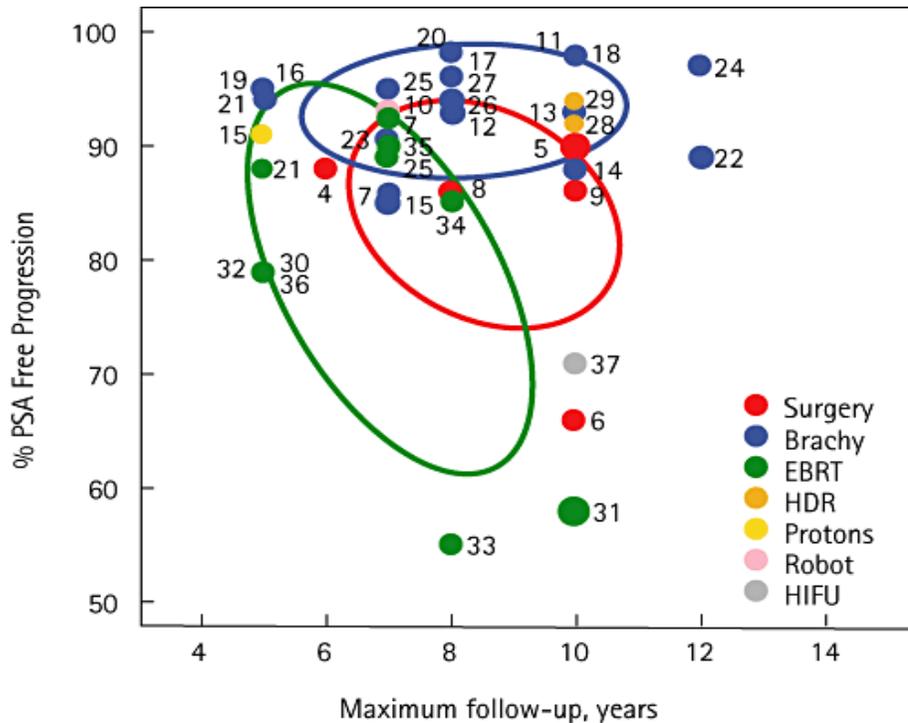


Strahlenbiologische Aspekte bei der SBRT der Prostata

PD Dr. Oliver Blanck

***Leiter Operation, Physik, Forschung und Entwicklung, Saphir Radiochirurgie
Forschungskordinator Stereotaktische Strahlentherapie,
Universitätsklinikum Schleswig-Holstein, Klinik für Strahlentherapie, Campus Kiel
Studienkoordination: u.a. HYPOSTAT***

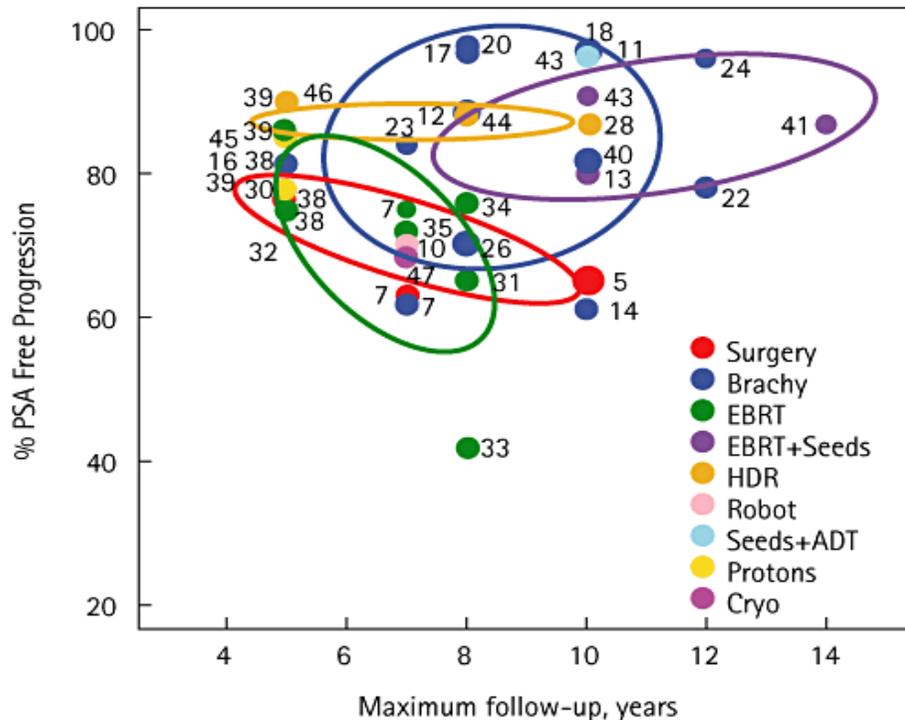
Historische Behandlungsergebnisse: Low Risk PCA



Procedure	No. of patients	Procedure	No. of patients	Procedure	No. of patients
Surgery [4]	336	Brachy [17]	173	Protons [15]	124
Surgery [5]	3283	Brachy [18]	329	Protons [30]	230
Surgery [6]	346	Brachy [19]	586	EBRT [15]	134
Surgery [7]	765	Brachy [20]	173	EBRT [31]	2765
Surgery [8]	1381	Brachy [21]	108	EBRT [32]	421
Surgery [9]	336	Brachy [22]	1345	EBRT [7]	173
Robot [10]	706	Brachy [23]	260	EBRT [21]	108
Brachy [11]	475	Brachy [24]	319	EBRT [33]	485
Brachy [12]	768	Brachy [25]	448	EBRT [25]	281
Brachy [13]	726	Brachy [26]	1444	EBRT [34]	203
Brachy [14]	232	Brachy [27]	319	EBRT [35]	446
Brachy [15]	158	HDR [28]	110	EBRT [36]	227
Brachy [7]	723	HDR [29]	116	HIFU [37]	227
Brachy [16]	273				

Therapieergebnisse (PSA-Progressionsfreiheit) bei Patienten mit **low-risk-Prostatakarzinom** nach verschiedenen Therapieverfahren abhängig vom Follow-up. Die Ellipsen (SDE= standard deviational ellipse) stellen den gewichteten Mittelwert der Studien \pm 1SD dar; SDEs wurden nur für Therapieverfahren mit mindestens vier Datenpunkten berechnet.

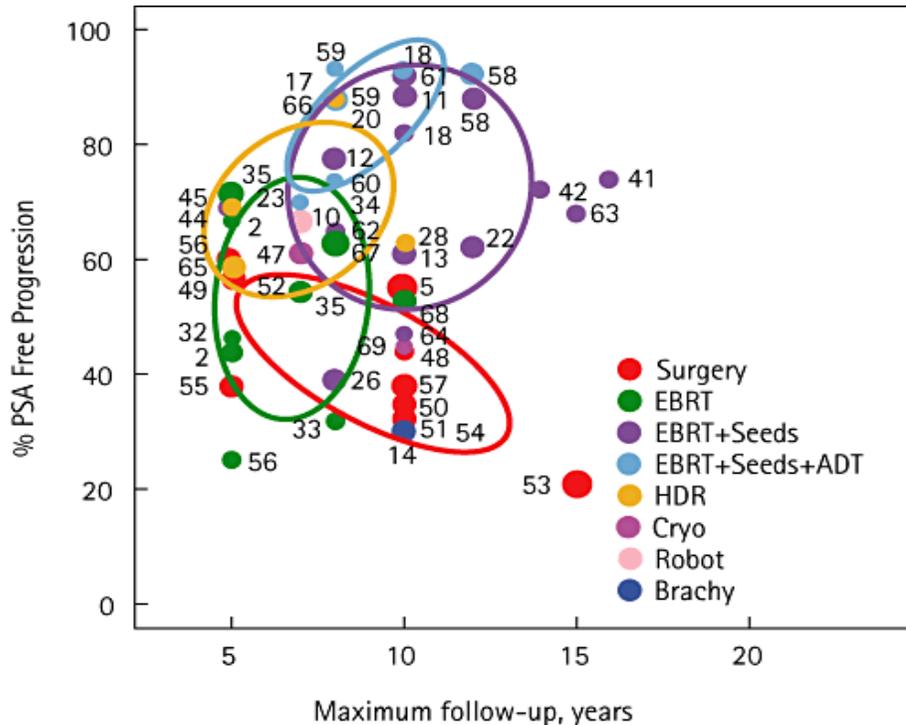
Historische Behandlungsergebnisse: Intermediate Risk PCA



Procedure	No. of patients	Procedure	No. of patients	Procedure	No. of patients
Surgery [5]	2795	Brachy [22]	554	HDR [46]	109
Surgery [38]	336	Brachy [23]	141	Protons [30]	162
Surgery [7]	211	Brachy [24]	144	EBRT [38]	321
Surgery [39]	354	Brachy [39]	256	EBRT [31]	349
Robot [10]	479	Brachy [26]	960	EBRT [32]	137
Brachy [11]	176	EBRT + seeds [11]	460	EBRT [7]	99
Brachy [12]	535	EBRT + seeds [13]	447	EBRT [33]	218
Brachy [14]	369	EBRT + seeds [41]	119	EBRT [33]	218
Brachy [38]	204	EBRT + seeds [42]	157	EBRT [33]	218
Brachy [7]	199	EBRT + seeds [43]	266	EBRT [39]	305
Brachy [16]	123	EBRT + seeds [7]	105	EBRT [34]	255
Brachy [17]	212	Seeds + ADT [43]	165	EBRT [35]	849
Brachy [18]	425	HDR [28]	188	Cryotherapy [47]	175
Brachy [20]	212	HDR [44]	188		
Brachy [40]	1298	HDR [45]	122		

Therapieergebnisse (PSA-Progressionsfreiheit) bei Patienten mit **medium-risk-Prostatakarzinom** nach verschiedenen Therapieverfahren abhängig vom Follow-up. Die Ellipsen (SDE= standard deviational ellipse) stellen den gewichteten Mittelwert der Studien \pm 1SD dar; SDEs wurden nur für Therapieverfahren mit mindestens vier Datenpunkten berechnet.

Historische Behandlungsergebnisse: High Risk PCA



Procedure	No. of patients	Procedure	No. of patients	Procedure	No. of patients
Surgery [5]	1513	EBRT+seeds+ADT [60]	175	EBRT+seeds [26]	192
Surgery [48]	176	EBRT+seeds+ADT [23]	59	HDR [65]	256
Surgery [49]	235	EBRT+seeds [11]	243	HDR [28]	107
Surgery [50]	288	EBRT+seeds [61]	186	HDR [45]	80
Surgery [51]	265	EBRT+seeds [12]	362	HDR [66]	67
Surgery [52]	188	EBRT+seeds [13]	284	EBRT [67]	1256
Surgery [53]	1061	EBRT+seeds [41]	164	EBRT [32]	57
Surgery [54]	237	EBRT+seeds [42]	124	EBRT [56]	95
Surgery [55]	210	EBRT+seeds [44]	359	EBRT [33]	97
Surgery [56]	134	EBRT+seeds [62]	92	EBRT [68]	296
Surgery [57]	842	EBRT+seeds [58]	284	EBRT [34]	103
Robot [10]	200	EBRT+seeds [17]	127	EBRT [2]	65
Brachy [14]	295	EBRT+seeds [18]	90	EBRT [2]	193
EBRT+seeds+ADT [58]	284	EBRT+seeds [59]	107	EBRT [35]	752
EBRT+seeds+ADT [18]	60	EBRT+seeds [22]	418	EBRT [35]	752
EBRT+seeds+ADT [59]	69	EBRT+seeds [63]	114	Cryotherapy [47]	314
EBRT+seeds+ADT [20]	584	EBRT+seeds [64]	77	Cryotherapy [69]	43

Therapieergebnisse (PSA-Progressionsfreiheit) bei Patienten mit **high-risk-Prostatakarzinom** nach verschiedenen Therapieverfahren abhängig vom Follow-up. Die Ellipsen (SDE= standard deviational ellipse) stellen den gewichteten Mittelwert der Studien \pm 1SD dar; SDEs wurden nur für Therapieverfahren mit mindestens vier Datenpunkten berechnet.

Historische Behandlungsergebnisse: High Risk PCA

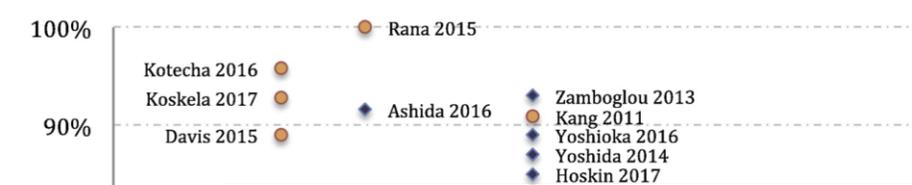
Stereotactic body radiation therapy (SBRT) for high-risk prostate cancer: Where are we now?

Alejandro Gonzalez-Motta MD ^{a,b,*}, Mack Roach III MD FACR FASTRO ^c

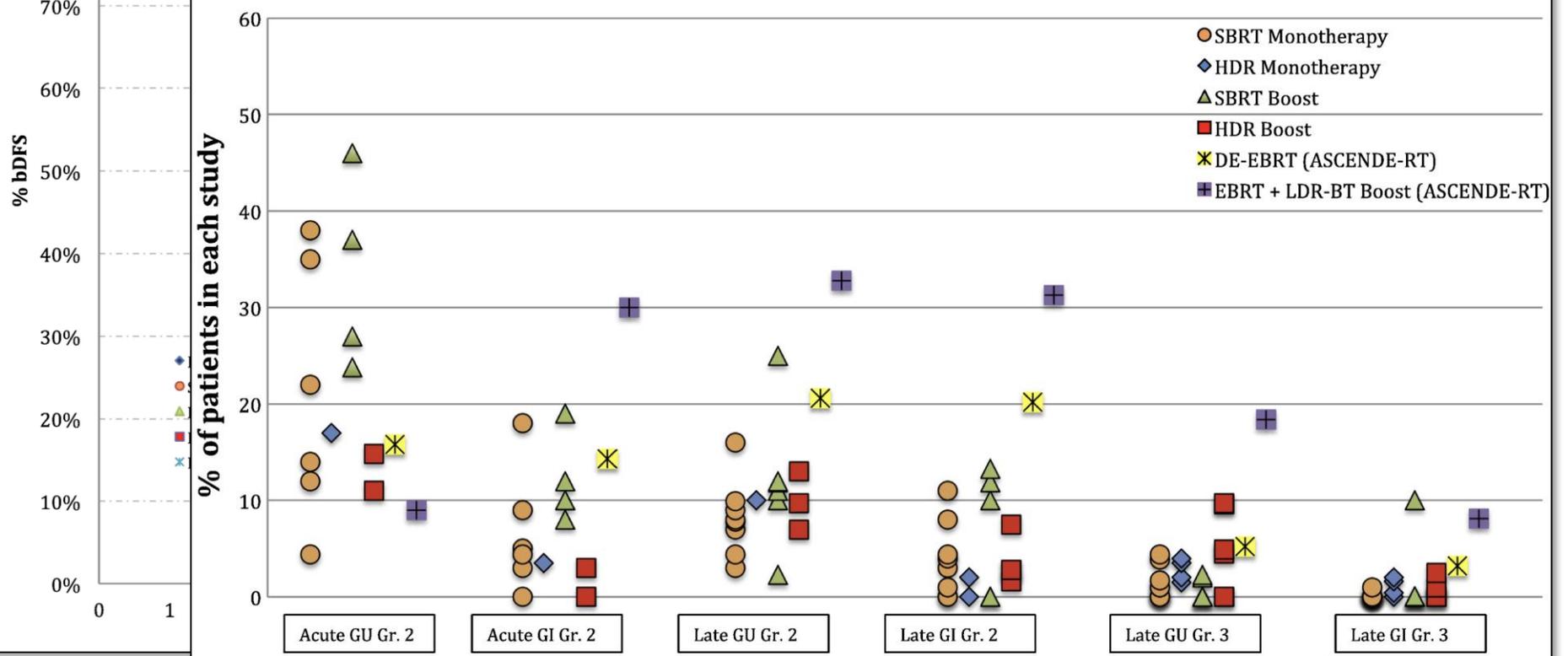
^aUniversidad Militar Nueva Granada, Bogotá, Colombia
^bDepartment of Radiation Oncology, Instituto Nacional de Cancerología, Bogotá, Colombia
^cUniversity of California San Francisco Helen Diller Family Comprehensive Cancer Center, Department of Radiation Oncology and Urology, San Francisco, California

Received 22 October 2017; revised 15 November 2017; accepted 17 November 2017

bDFS of High Risk patients treated with SBRT monotherapy, HDR monotherapy, DE-EBRT, EBRT + LDR BT Boost, EBRT+LTADT



Acute and late toxicity in SBRT, HDR, DE-EBRT and EBRT + LDR-BT Boost



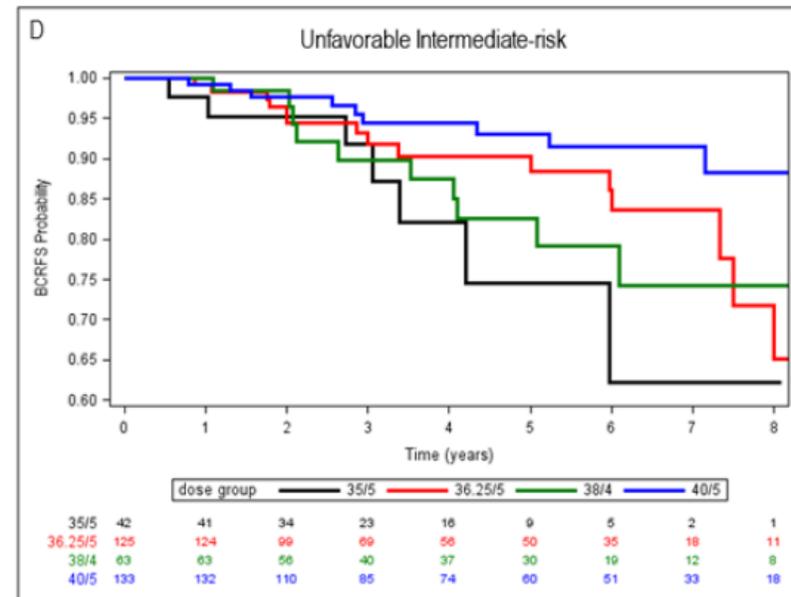
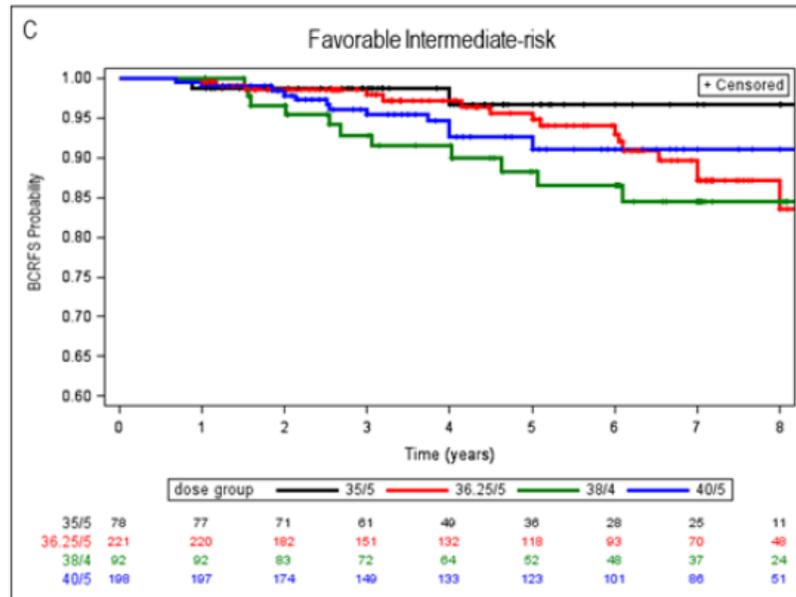
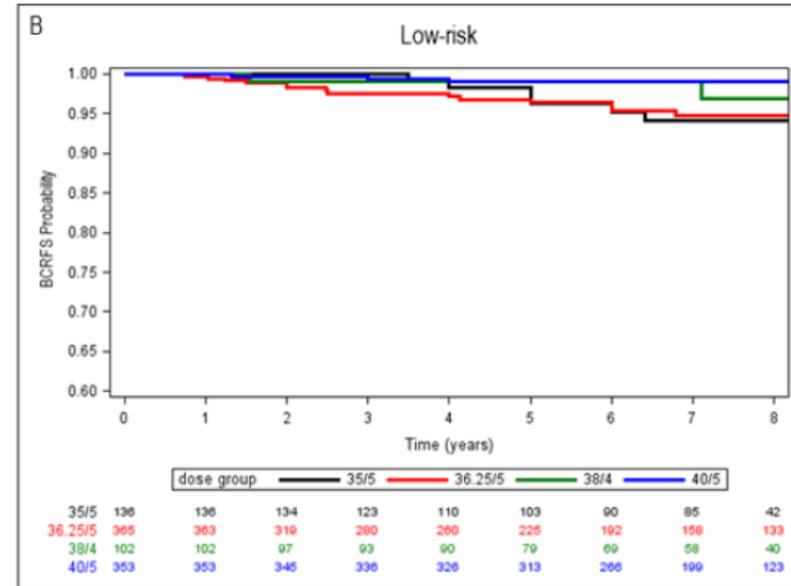
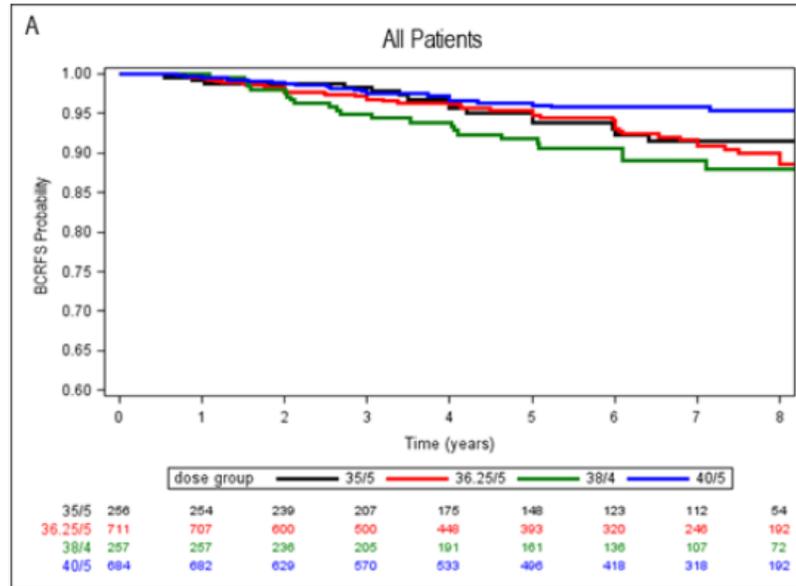
Prostatakarzinom und Strahlenbiologie

Dosisregime	Einzel-dosis [Gy]	Gesamtdosis [Gy]	Äquivalenzdosis in 2 Gy Einzeldosis (EQD2)		
			bei $\alpha/\beta = 1,5$ Gy (Tumor) [Gy]	bei $\alpha/\beta = 3$ Gy (Spätreaktionen am Normalgewebe) [Gy]	bei $\alpha/\beta = 10$ Gy (Frühreaktionen am Normalgewebe) [Gy]
Konventionell fraktionierte RT	2	76	76	76	76
Moderat hypofraktionierte RT	3	60	77,1	72,0	78,0
Ultra-hypofraktionierte SBRT - HYPOSTAT	7	35	85,0	70,0	49,6
Ultra-hypofraktionierte SBRT: PACE-B	7,25	36,25	90,6	74,3	52,1
Ultra-hypofraktionierte SBRT: HYPOSTAT-3	9,5	28,5	89,6	71,2	46,3

Brenner und Hall 1999 und Fowler 2001/2002:

- Der α/β -Wert von Prostatakarzinomen ist vermutlich sehr gering (sicher < 3 Gy, vermutlich ca. 1,5 Gy)

Prostatakarzinom und Dosis-Wirkung



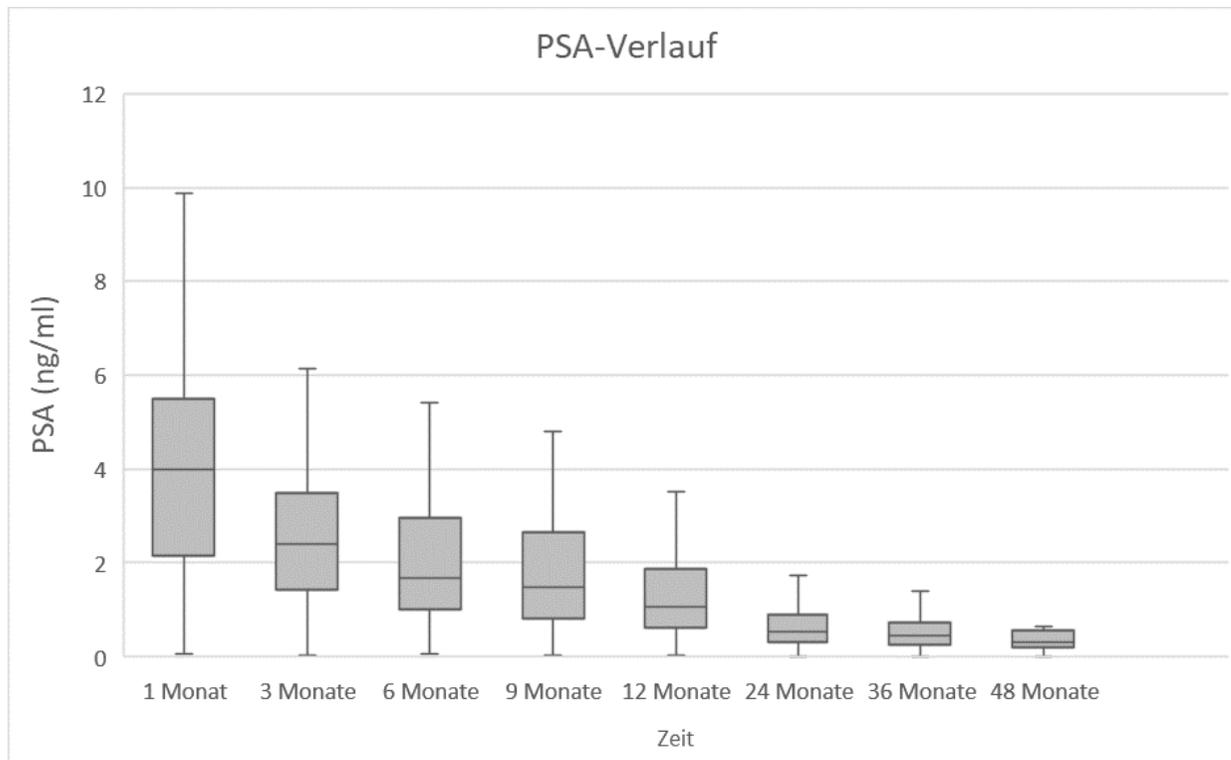
Prostatakarzinom und Dosis-Wirkung

HYPOSTAT I/II (140 Patienten, 10 Jahre)

7 biochemische Rezidive nach median 48,9 Monaten

- 3/76 Favorable, 4/42 Unfavorable Int. Risk

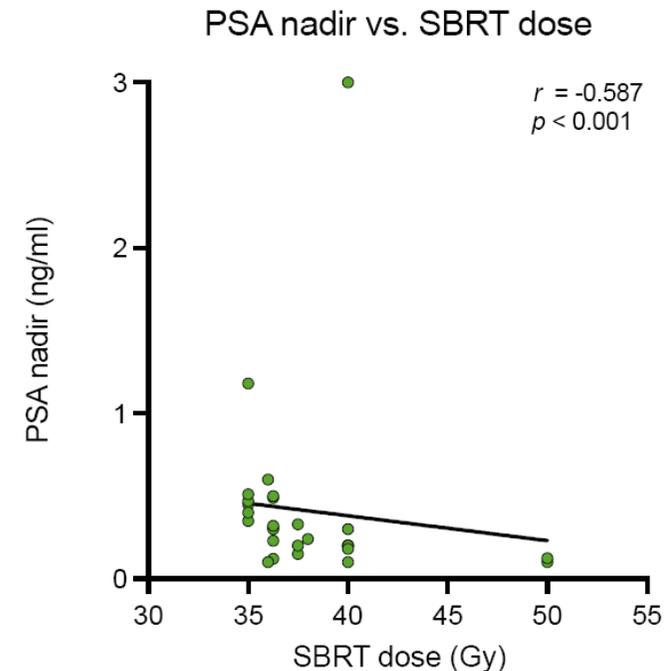
- 3 Lokalrezidive, 4 Metastasierungen



Review Article

Prostate-specific antigen kinetics after stereotactic body radiotherapy for localized prostate cancer: A scoping review and meta-analysis

Cas Stefaan Dejonckheere^{a,b}, Lara Caglayan^a, Andrea Renate Gasmacher^a, Shari Wiegrefe^a, Julian Philipp Layer^a, Youness Nour^a, Davide Scafa^a, Gustavo Renato Sarria^a, Simon Spohn^b, Markus Essler^c, Stefan Hauser^d, Manuel Ritter^d, Marit Bernhardt^e, Glen Kristiansen^a, Anca-Ligia Grosu^b, Constantinos Zamboglou^{b,f}, Eleni Gkika^a



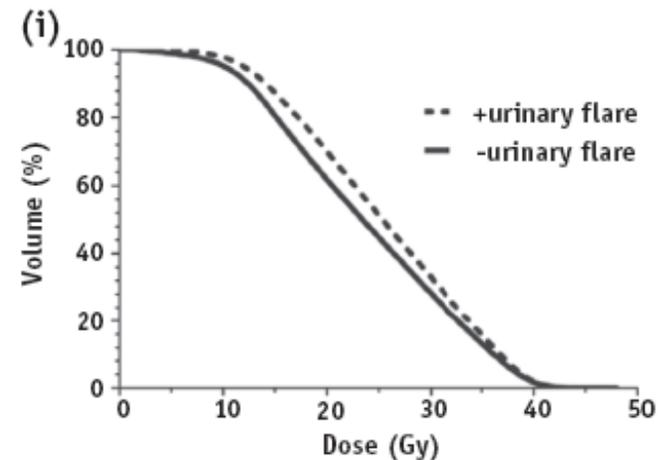
Prostatakarzinom und Dosis-Wirkung

HyTEC Organ-Specific Paper: Abdomen and Pelvis

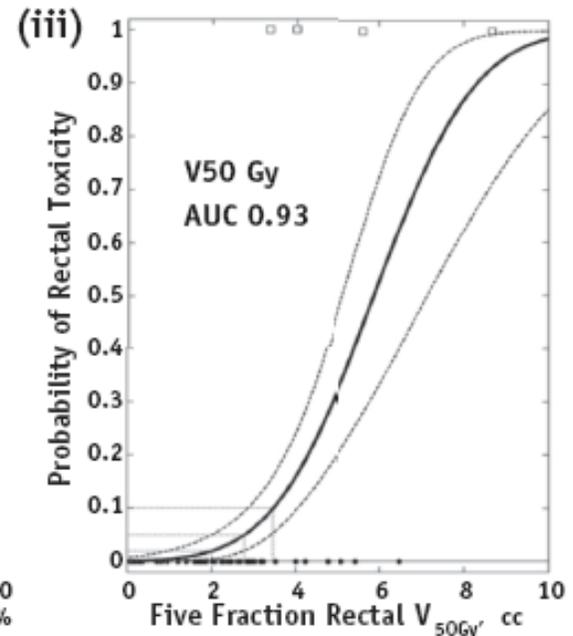
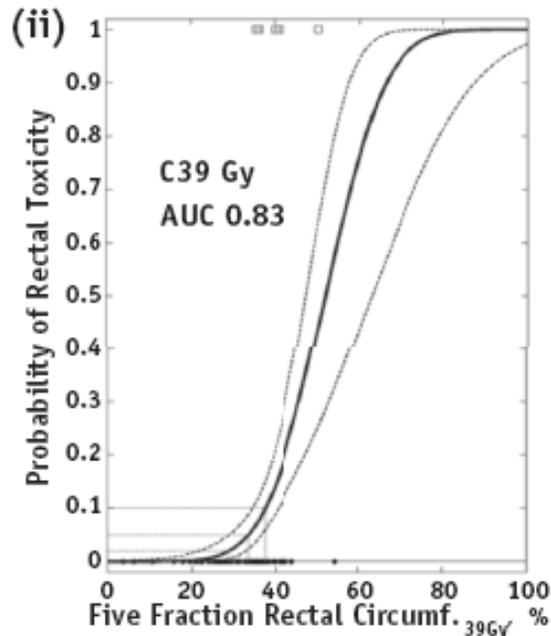
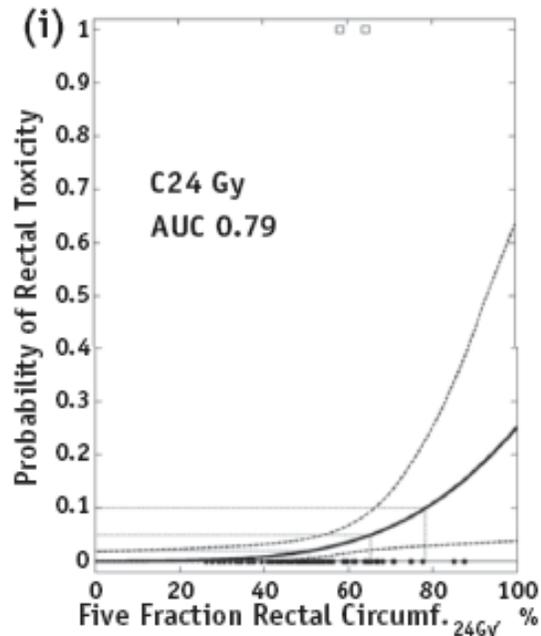
Prostate Stereotactic Body Radiation Therapy: An Overview of Toxicity and Dose Response

Kyle Wang, MD,* Panayiotis Mavroidis, PhD,* Trevor J. Royce, MD, MS, MPH,* Aaron D. Falchook, MD,† Sean P. Collins, MD, PhD,‡
Stephen Sapareto, PhD,§ Nathan C. Sheets, MD,* Donald B. Fuller, MD,||
Issam El Naqa, PhD,¶ Ellen Yorke, PhD,# Jimm Grimm, PhD,**,††
Andrew Jackson, PhD,# and Ronald C. Chen, MD, MPH‡‡

A Bladder dose and late urinary flare



C Rectal dose and grade 3 or higher early (i) or late (ii), (iii) rectal toxicity



Prostatakarzinom und Dosis-Wirkung

Radiation Dose to the Intraprostatic Urethra
Correlates Strongly With Urinary Toxicity After

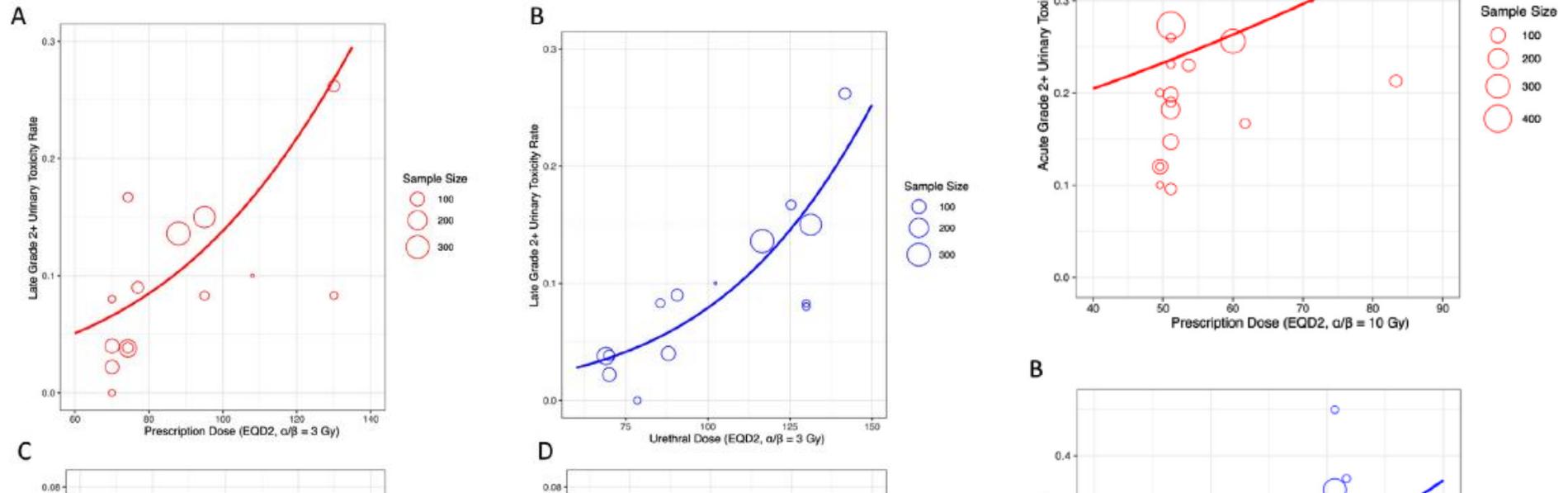


Table 4 Maximum urethral dose metric to toxicity correlation point estimates

Maximum urethral dose metric (5 fraction regimen)	EQD ₂ (Gy, $\alpha/\beta=3$ Gy)	EQD ₂ (Gy, $\alpha/\beta=10$ Gy)	Estimated grade 2+ acute urinary toxicity	Estimated grade 2+ late urinary toxicity	Estimated grade 3+ late urinary toxicity
34.7 Gy (urethral sparing)	67.39	48.0	18.8%	3.4%	0.2%
38.78 Gy (107% of 36.25 Gy)	83.42	57.38	21.5%	5.2%	0.4%
42.8 Gy (107% of 40 Gy)	98.95	66.2	24.4%	7.7%	0.8%
44 Gy (110% of 40 Gy)	103.4	68.7	25.2%	8.6%	0.9%
53.5 Gy (107% of 50 Gy)	146.5	92.3	34.1%	23.5%	4.6%

Abbreviation: EQD₂ = equivalent dose in 2 Gy fractions.

Prostatakarzinom und Dosis-Wirkung

Exploring Factors Associated with Late Urinary Toxicity After Prostate Stereotactic Body Radiotherapy: Findings from the PACE-B Study

Table 3 – Cross-fit partialling-out LASSO logistic regression to assess the association between variables of interest and urinary toxicity at 2 yr

Variables of interest	Grade 2+ CTCAE late GU toxicity at 2 yr (n = 357)		IPSS (with imputation) ≥ 7 from baseline at 2 yr (n = 390)	
	Adjusted odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)	p value
Baseline urinary medication (yes)	2.32 (1.09–4.95)	0.03	–	–
Risk group (intermediate)	–	–	0.39 (0.15–1.03)	0.06
Performance status (0 vs 1)	–	–	2.89 (1.14–7.30)	0.03
Baseline IPSS (with imputation)	1.11 (1.05–1.18)	0.001	–	–
Baseline IPSS (without imputation)	1.12 (1.04–1.19)	0.001	–	–
Worst acute grade 2+ CTCAE GU toxicity (yes)	3.15 (1.35–7.36)	0.008	–	–
Worst acute IPSS (with imputation)	1.04 (0.98–1.10)	0.17	1.05 (1.01–1.09)	0.03
Worst acute IPSS (without imputation)	1.04 (0.98–1.11)	0.19	1.05 (1.01–1.10)	0.01
<i>SBRT technique and fiducial use</i>				
CL-SBRT with fiducials (ref)	1 (Reference)	–	1 (Reference)	–
CL-SBRT without fiducials	0.24 (0.09–0.58)	0.002	0.50 (0.17–1.51)	0.22
CK-SBRT	0.19 (0.04–0.80)	0.02	1.93 (0.63–5.89)	0.25
Surrogate urethra Dmax (Gy)	0.91 (0.84–1.11)	0.60	–	–
Bladder trigone D50 (Gy)	0.92 (0.84–1.01)	0.07	–	–
Bladder Dmax (Gy)	–	–	1.28 (0.80–2.04)	0.31

CI = confidence interval; CK-SBRT = CyberKnife stereotactic body radiotherapy; CL-SBRT = conventional LINAC stereotactic body radiotherapy; CTCAE = Common Terminology Criteria Adverse Events; GU = genitourinary; IPSS = International Prostate Symptom Score; LASSO = least absolute shrinkage and selection operator; SBRT = stereotactic body radiotherapy.

D(n) represents the dose (Gy) to (n)% of the structure. Acute period is defined as any point during SBRT and up to 12 wk after. Variables of interest included in the cross-fit partialling-out LASSO logistic regression were selected based on the associations observed in the univariable analysis. Each variable of interest is tested separately using cross-fit partialling-out LASSO logistic regression, with the control variables prespecified in the model summarised in [Supplementary Table 5](#).

Aber ...

Bitte hört endlich auf Eindimensional von Dosis zu sprechen!

Strahlentherapie und Onkologie

<https://doi.org/10.1007/s00066-024-02254-2>

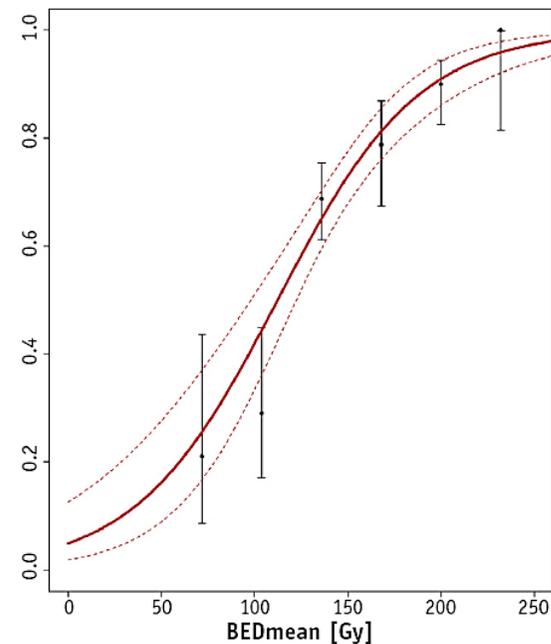
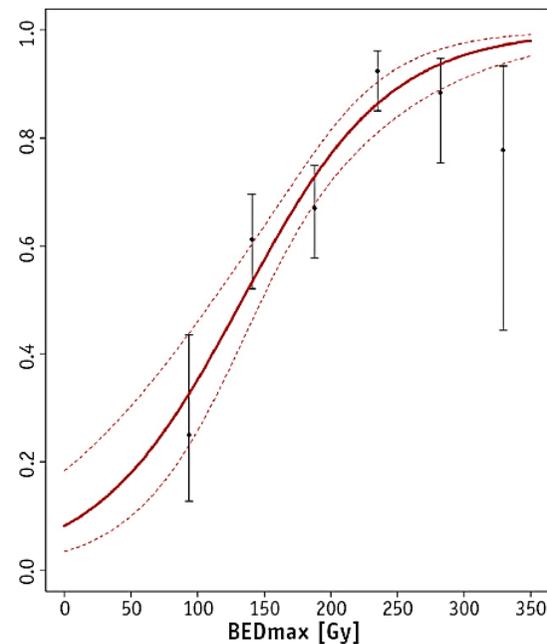
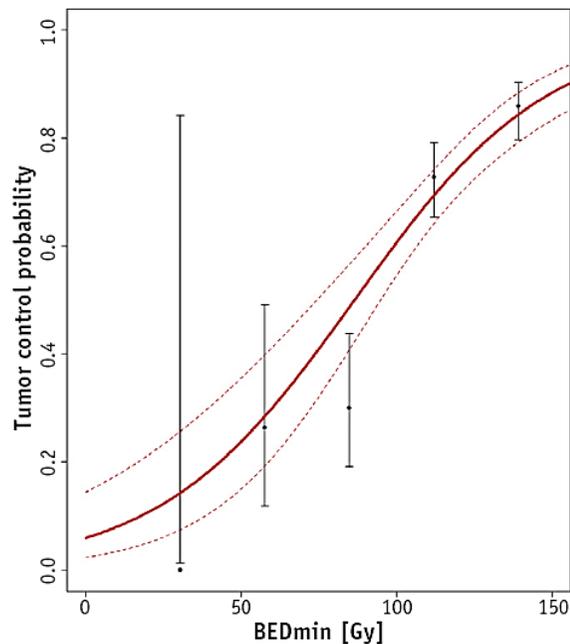
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REV Rainer J. Klement, PhD,* Jan-Jakob Sonke, PhD,[†]
Michael Allgäuer, MD,[‡] Nicolaus Andratschke, MD,[§]
Steffen Appold, MD,^{||} José Belderbos, MD, PhD,[|] Claus Belka, MD,[¶]
Oliver Blanck, PhD,[#] Karin Dieckmann, MD,** Hans T. Eich, MD,^{††}
Frederick Mantel, MD,^{‡‡} Michael Eble, MD,^{§§} Andrew Hope, MD,^{|||}
Anca L. Grosu, MD,^{¶¶} Meinhard Nevinny-Stickel, MD,^{##}
Sabine Semrau, MD,^{***} Reinhart A. Sweeney, MD,*
Juliane Hörner-Rieber, MD,^{†††} Maria Werner-Wasik, MD,^{§§§}
Rita Engenhart-Cabillic, MD,^{|||||} Hong Ye, PhD,^{¶¶¶} Inga Grills, MD,^{****}
and Matthias Guckenberger, MD,[§]

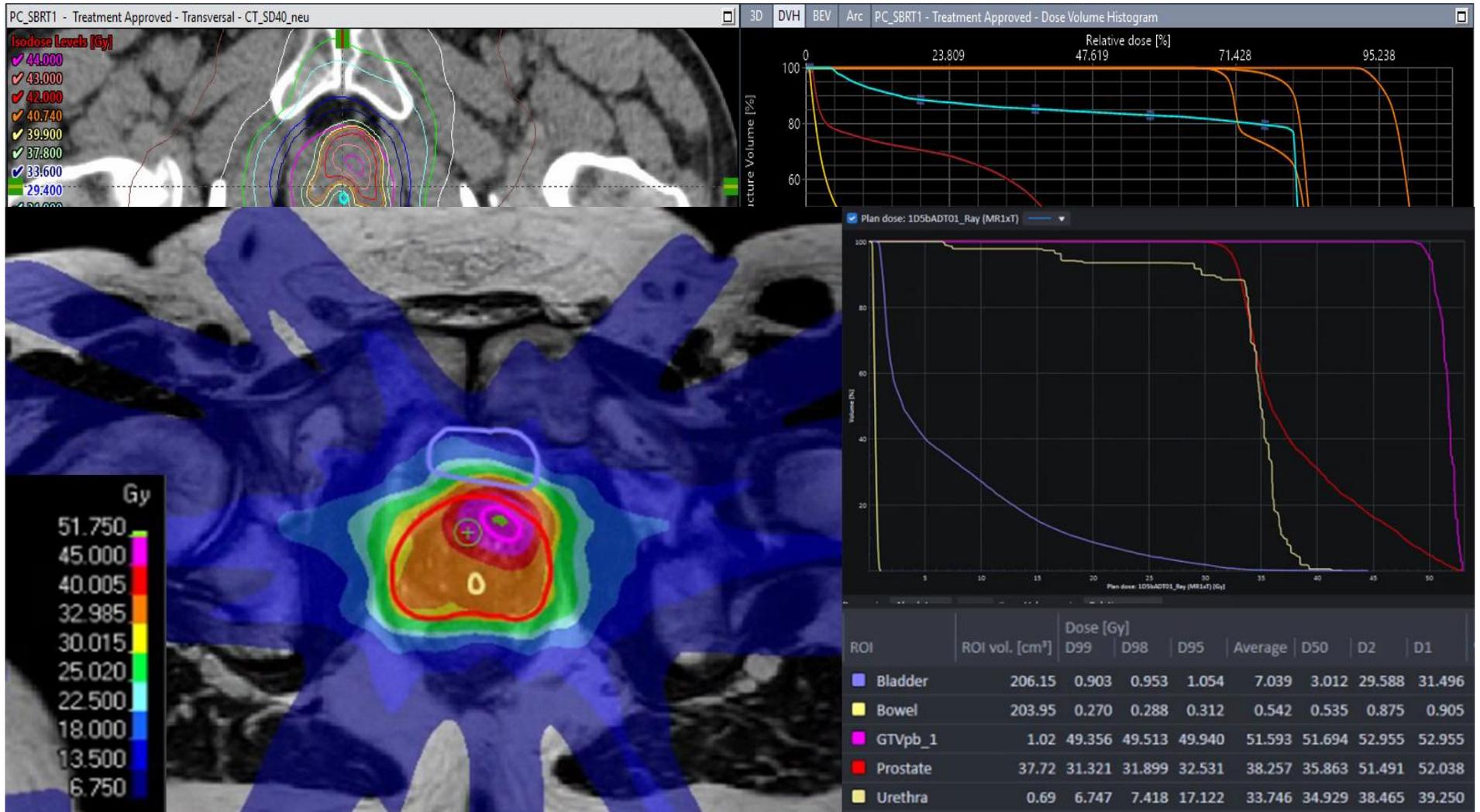
Physics Contribution

Correlating Dose Variables with Local Tumor Control in Stereotactic Body Radiation Therapy for Early-Stage Non-Small Cell Lung Cancer: A Modeling Study on 1500 Individual Treatments



Prostatakarzinom und Dosis-Modellierung

Dosis ist nicht 1D! -> HYPOSTAT, HYPOFOCAL, DESTINATION-1



Prostatakarzinom und Dosis-Modellierung

FLAME Studie

- bDFS signifikant besser
- DMFS nicht signifikant

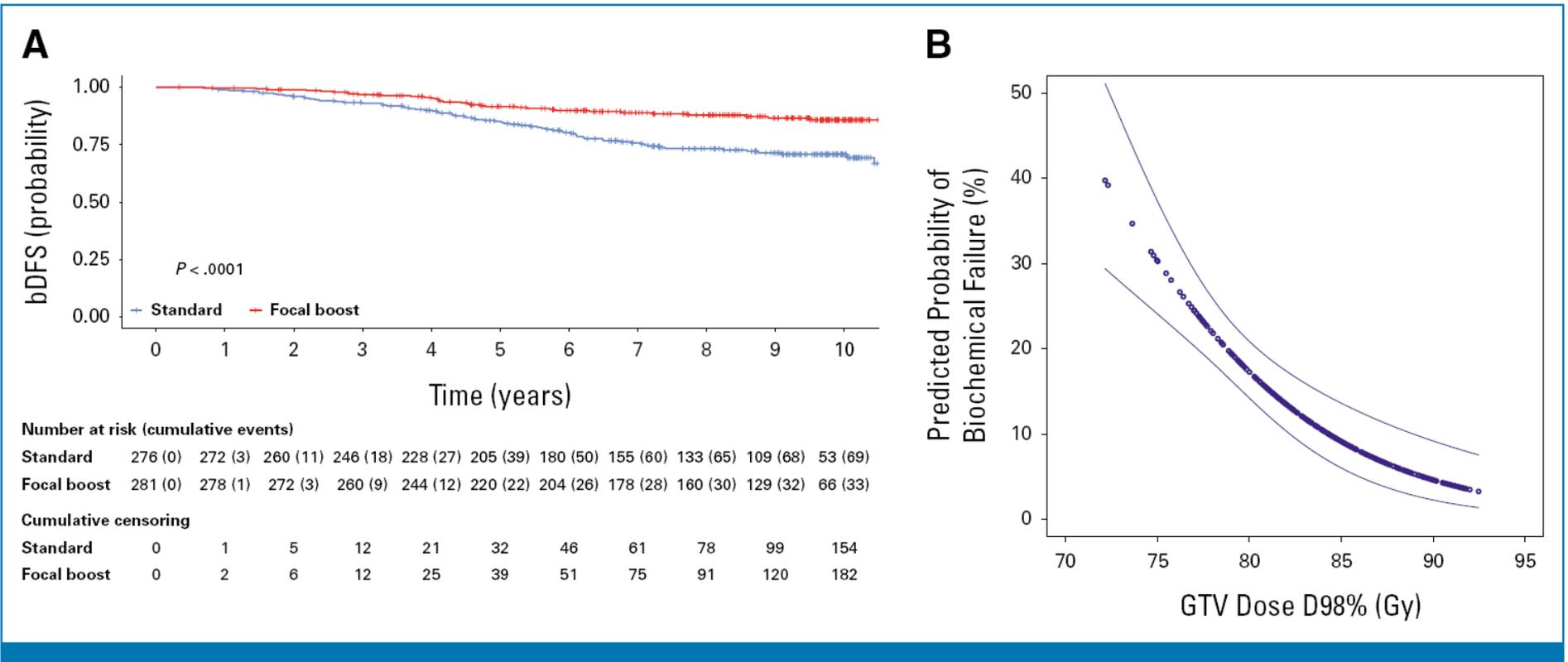
Clinical Trial Updates



Focal Boost to the Intraprostatic Tumor in External Beam Radiotherapy for Patients With Localized Prostate Cancer: 10-Year Outcomes of the FLAME Trial

Karolína Menne Guricová, MSc¹; Cédric Draulans, MD, PhD²; Floris J. Pos, MD, PhD¹; Linda G.W. Kerkmeijer, MD, PhD^{3,4}; Evelyn M. Monnikhof, PhD⁵; Robert J. Smeenk, MD, PhD³; Martina Kunze-Busch, PhD³; Hans C.J. de Boer, PhD⁴; Jochem R.N. van der Voort van der Zyp, MD, PhD⁴; Karin Haustermans, MD, PhD^{2,6}; and Uulke A. van der Heide, PhD¹

DOI <https://doi.org/10.1200/JCO-25-00274>



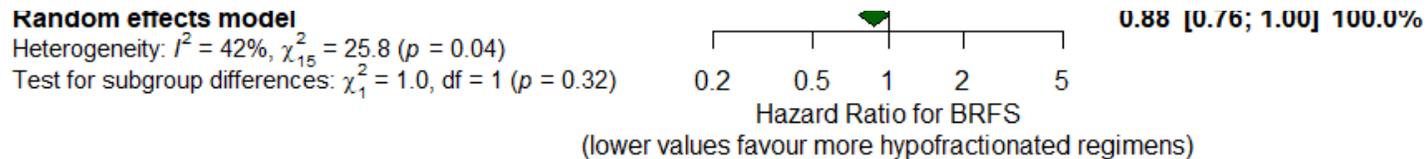
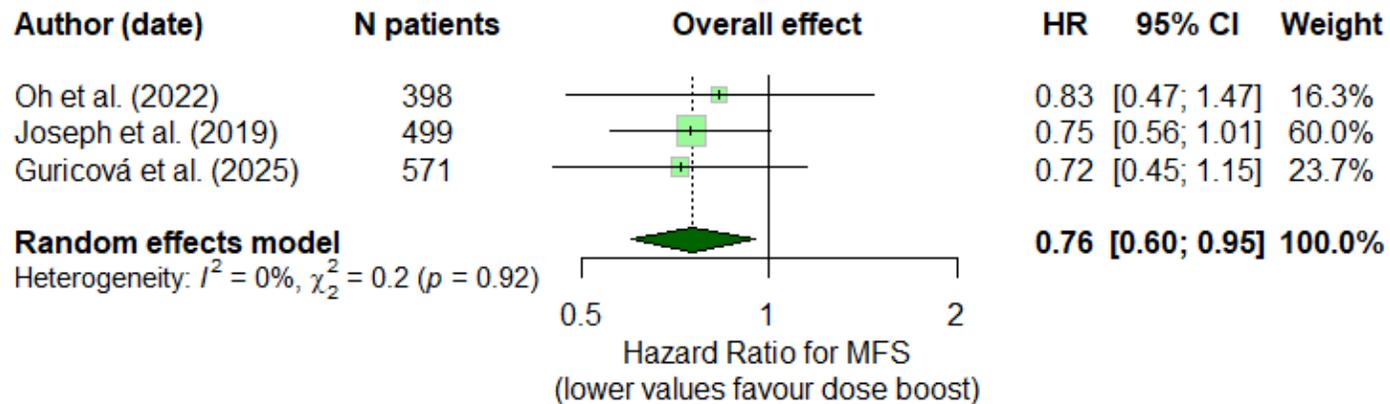
Zusammenfassung

To SBRT or not to SBRT?

Efficacy and Side Effects of Hypofractionated and Dose-boosted Radiotherapy for Localised Prostate Cancer: A Systematic Review and Meta-Analysis

To Bo

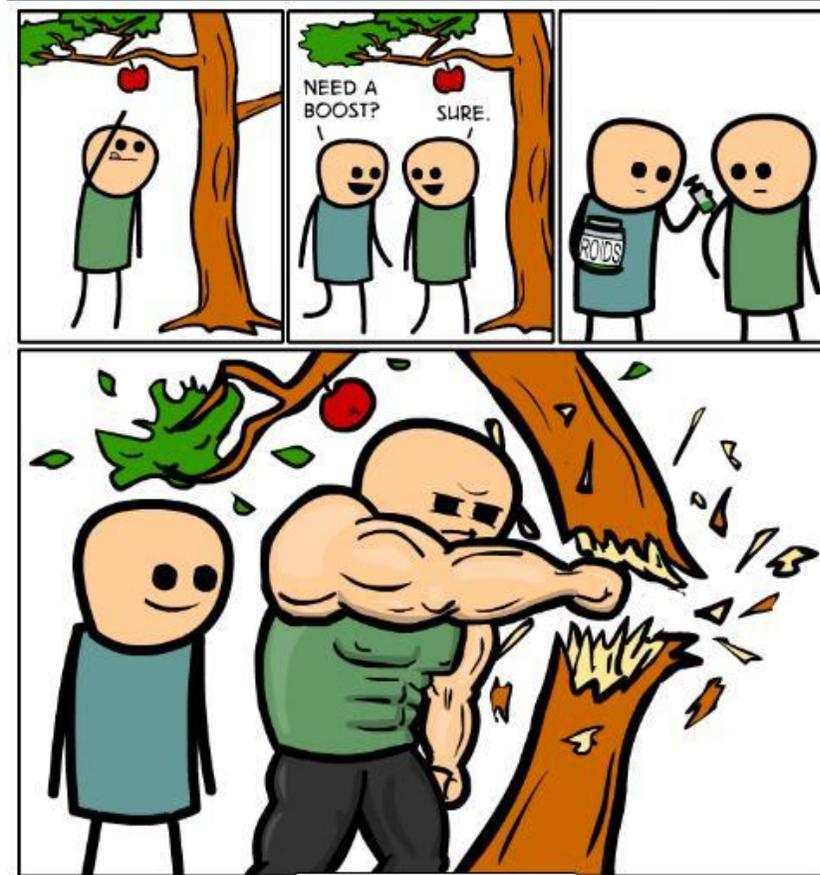
Author (date)	N patients	EQD2 difference ($\alpha/\beta = 1.5$ Gy)	Overall effect	HR	95% CI	Weight
Oh et al. (2022)	398			0.83	[0.47; 1.47]	16.3%
Joseph et al. (2019)	499			0.75	[0.56; 1.01]	60.0%
Guricová et al. (2025)	571			0.72	[0.45; 1.15]	23.7%
Random effects model				0.76	[0.60; 0.95]	100.0%



Zusammenfassung

- **Mit deutlicher Langzeitevidenz:** Eine Dosis-Wirkungsbeziehung für den Therapieerfolg und die Nebenwirkungen ist Risiko- und Nebenbedingungs-abhängig (z.B. Fav./Unfav., IPSS) auch bei der SBRT deutlich zu erkennen (*PACE-B vermutlich optimal*)
- **Mit wachsender Evidenz:** Ein fokaler Dosis-Boost in der Prostata scheint einen Benefit zu bringen (*bessere Wirkung bei gleichen Nebenwirkungen*), jedoch ob das auch für die SBRT gilt, ist unklar (*Studien laufen, Langzeitdaten werden noch eine Weile brauchen*)
- **Ohne Diskussion:** Wir müssen die Prostata SBRT besser dokumentieren und berichten, besonders in Publikationen und Studien (*mindestens nach ICRU 91, jedoch bleibt das SIB-Konzept und der Technikvergleich weiter eine Herausforderung für sich*)

To SBRT Boost or Not to SBRT Boost ...



... at Least Report the Methods Correctly!