Klinikum rechts der Isar
Technische Universität München

iRM.
Helmholtz Zentrum München

RadioOnkologie 2019:
Was gibt es Neues in der Strahlentherapie?

Prof. Dr. med. Stephanie E. Combs

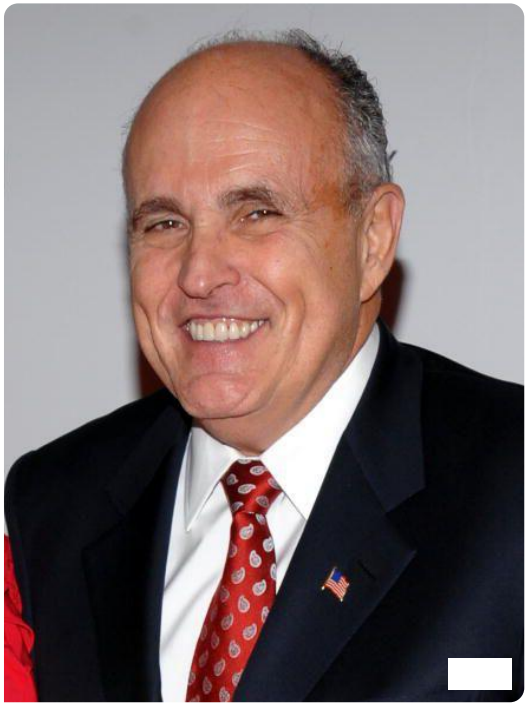
Department of Radiation Oncology
Institute of Radiation Medicine IRM)

CANCER > PROSTATE CANCER

Rudy Giuliani's Battle With Prostate Cancer

PRINT

By Matthew Schmitz, MD | Medically reviewed by a board- certified physician | Updated September 01, 2017

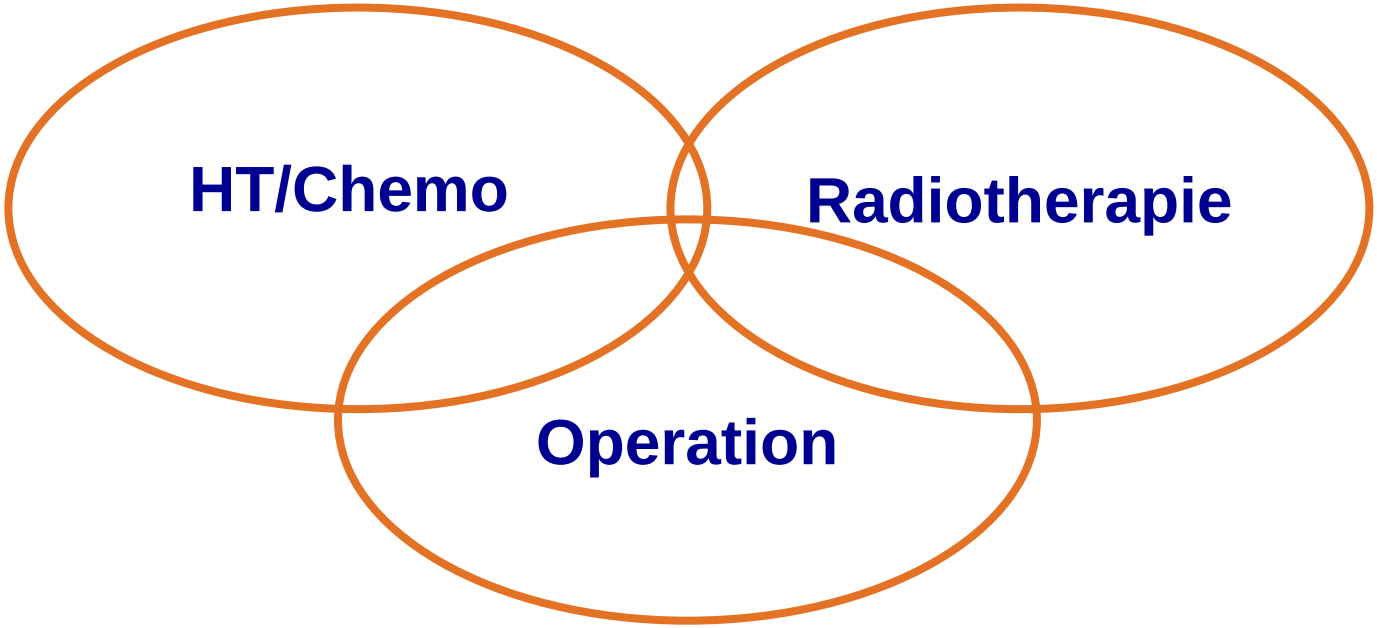


Rudy Giuliani. Dimitrios Kambouris/Getty Images

Rudy Giuliani, former mayor of New York City, was diagnosed with prostate cancer in the year 2000 at age 55. He was diagnosed after undergoing a routine screening PSA test, which showed that his PSA had risen substantially. He subsequently underwent a prostate biopsy, which came back positive for prostate cancer.

In an interview later that year, Giuliani recounted how he had been somewhat confused initially by the "positive" result from his biopsy. Similar to many patients who do not have a medical background, Giuliani was confused by the terms "positive" and "negative" when

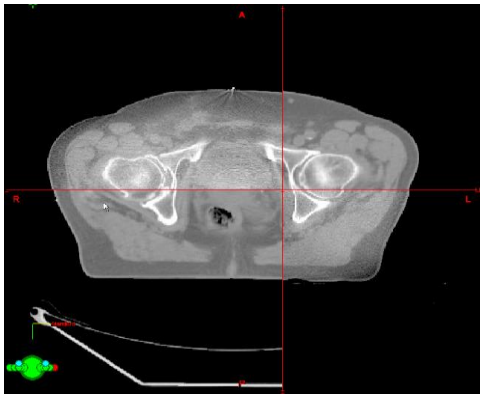
Rolle der Strahlentherapie bei der Behandlung des Prostatakarzinoms

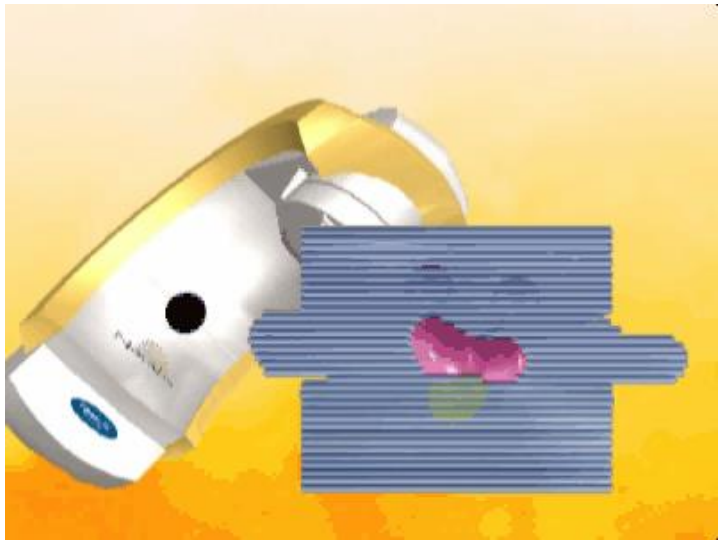


- **50%** aller Tumorpatienten werden mit einer Strahlentherapie behandelt
- Strahlentherapie ist die effektivste (lokale) Tumortherapie zusammen nach der Operation
- Heilungsraten können **>90%** liegen abhängig vom Tumortyp

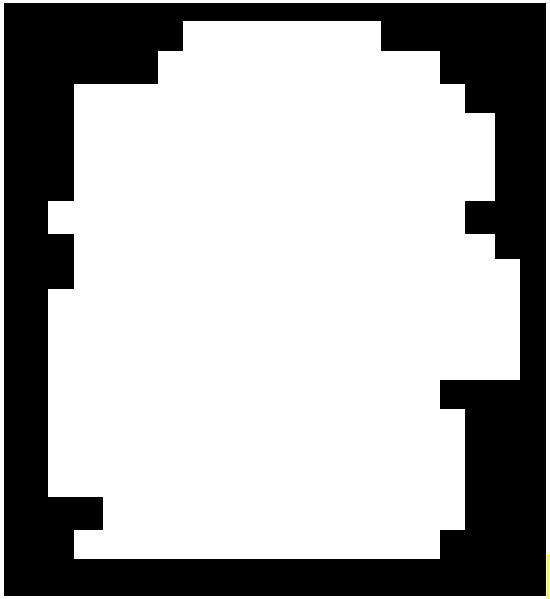
Standard heute: 3D - geplante Strahlentherapie

- 3D - Schnittbildgebung – Computertomographie, MRT etc.
- Patient im „dreidimensionalen Koordinatensystem“
- Festelegung von „Zielvolumen“ und Normalgewebe
- Bestrahlung aus verschiedenen Raumrichtungen
- Strahlen treffen sich im Isozentrum





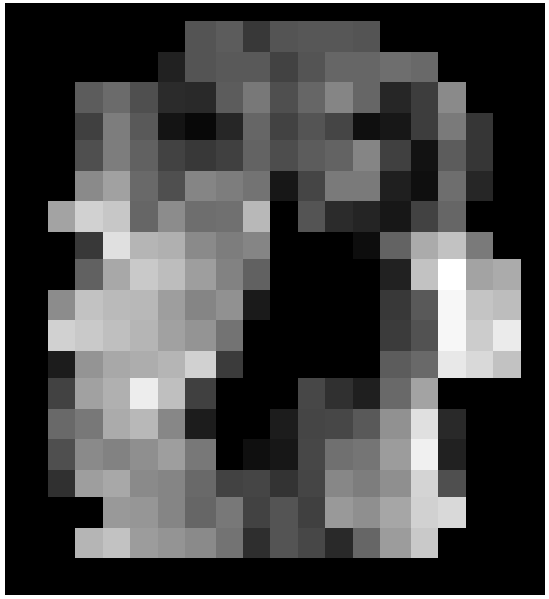
Intensitätsmodulierte Radiotherapie (IMRT)



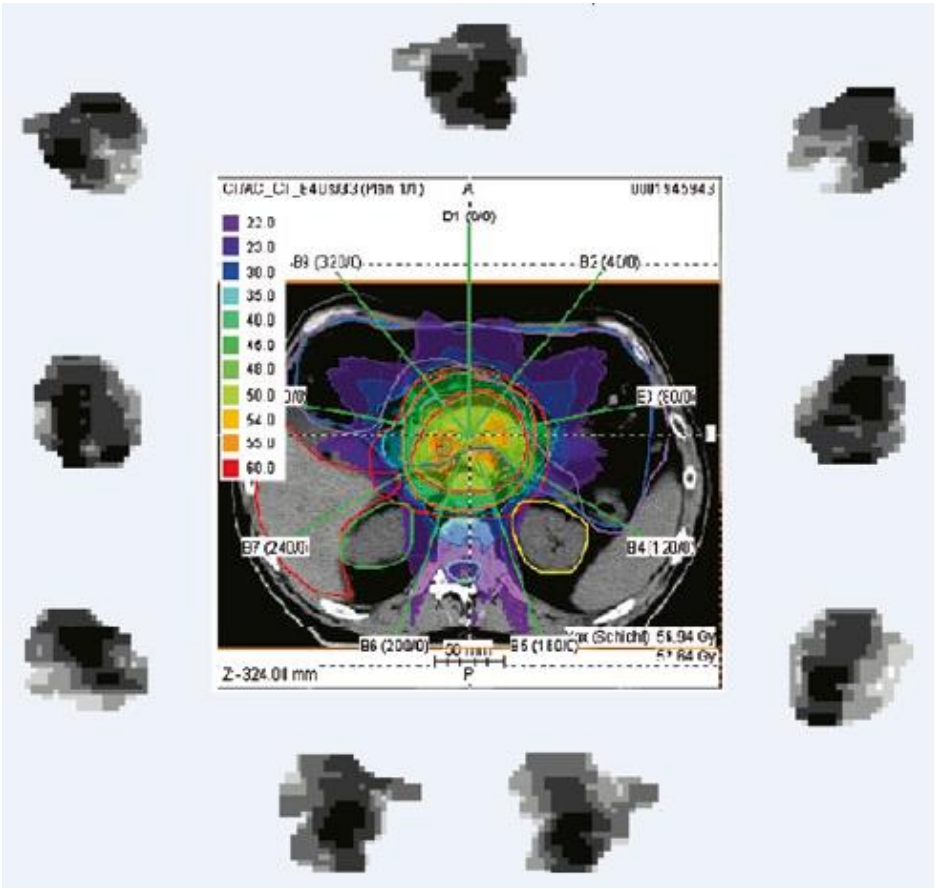
Homogene Dosisapplikation

Hohe Intensität

Niedrige Intensität

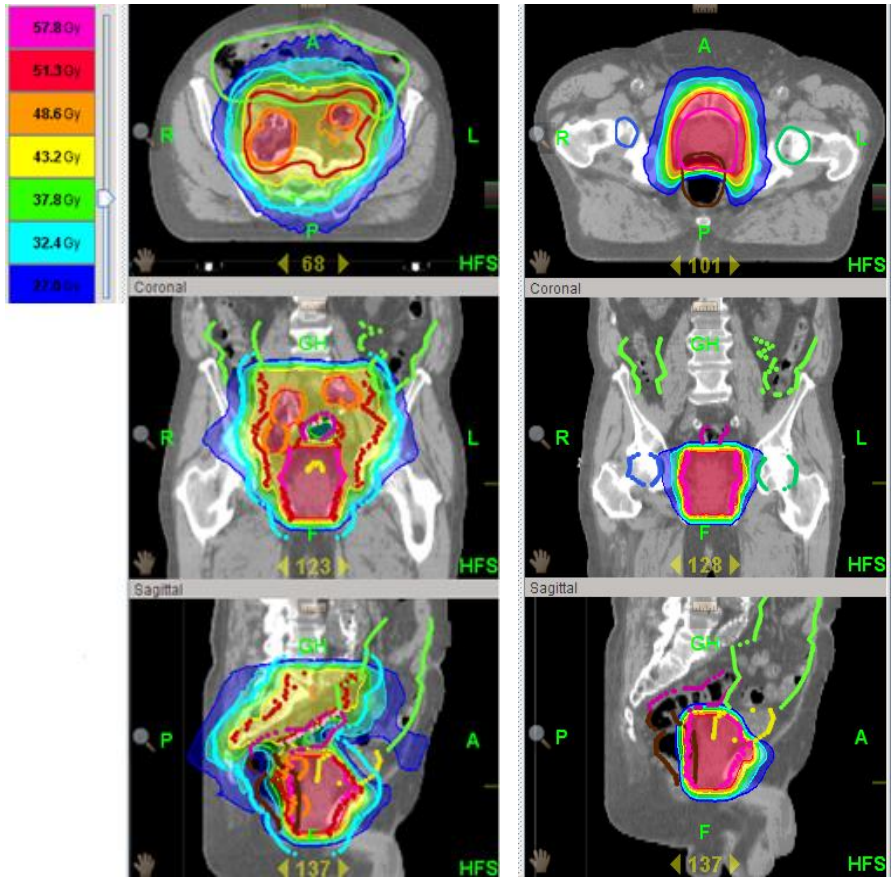


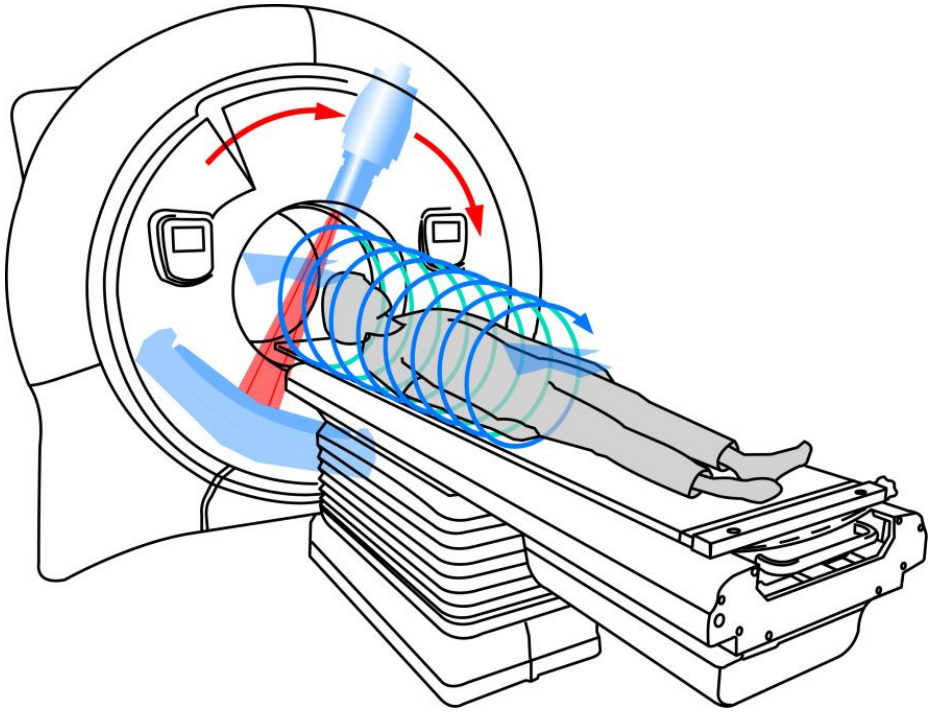
Inhomogene Dosisapplikation bei der IMRT



Bessere Dosiskonformalität
Dosisreduktion an Risikoorganen
Reduktion von Nebenwirkungen
Dosiseskalation

Bestrahlung mit „Tomotherapie“
Seit 2006 am Klinikum rechts der Isar





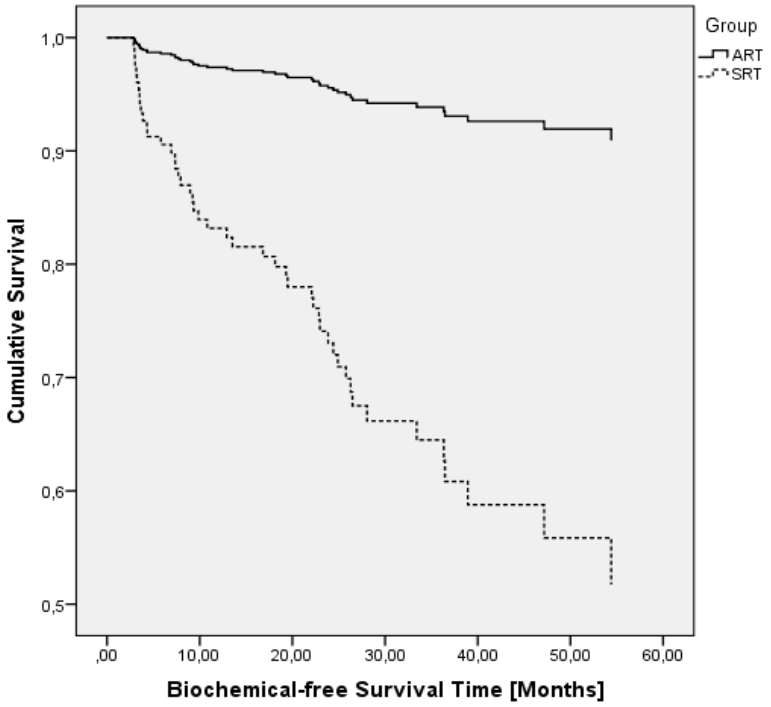
Bestrahlungsplan einschließlich der Lymphabflusswege (50,4 Gy à 1,8 Gy) und SIB (54 Gy à 2,17 Gy), auf PET-positive Lymphknoten, basierend auf der ^{68}Ga-PSMA-PET Bildgebung (links), Bestrahlungsplan ohne Informationen aus dem ^{68}Ga-PSMA-PET (rechts).

Radixact©-Tomotherapy

- Deutschlandweit 1.
  Installation am Klinikum
  rechts der Isar
- derzeit Inbetriebnahme
- Helikale IMRT
- Vorteilhafte Dosisverteilung,
  Schonung der Risikoorgane
- ab Juni 2018

Zeitpunkt der postoperativen Strahlentherapie beim Prostatakarzinom

- Analyse aus dem Klinikum rechts der Isar
- 253 Patients, medianes Alter age 66 Jahre (42-85 Jahre)
- Nicht eingeschlossen: Patienten ohne PSA-Nadir <0.1 ng/ml
- pT2N0, pT2N1, pT3/4N0 pT3/4
- Vergleich



Adjuvante Strahlentherapie (direkt nach Operation)

Salvage Strahlentherapie (>4 Monate nach OP)

Gesamte Gruppe:
Biochemisches Rezidivfreies Überleben (PSA-Frei) verlängert nach früher Strahlentherapie

Vogel MME et al., submitted

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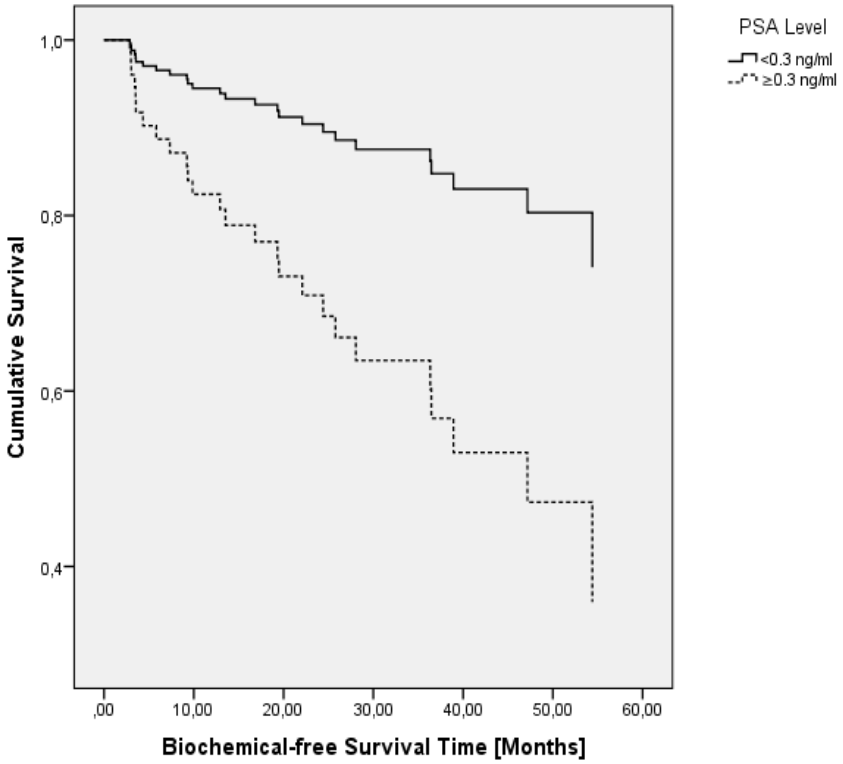


Gesamte Gruppe:
„Eearly Salvage“ Strahlentherapie bei PSA Werten < 3 ng/ml ist vorteilhaft

Vogel MME et al., submitted

Active monitoring, radical prostatectomy, or radiotherapy for localised prostate cancer: study design and diagnostic and baseline results of the ProtecT randomised phase 3 trial

J Athene Lane, Jenny L Donovan*, Michael Davis, Eleanor Walsh, Daniel Dedman, Liz Down, Emma L Turner, Malcolm D Mason, Chris Metcalfe, Tim J Peters, Richard M Martin, David E Neal*, Freddie C Hamdy*, for the ProtecT study group†*

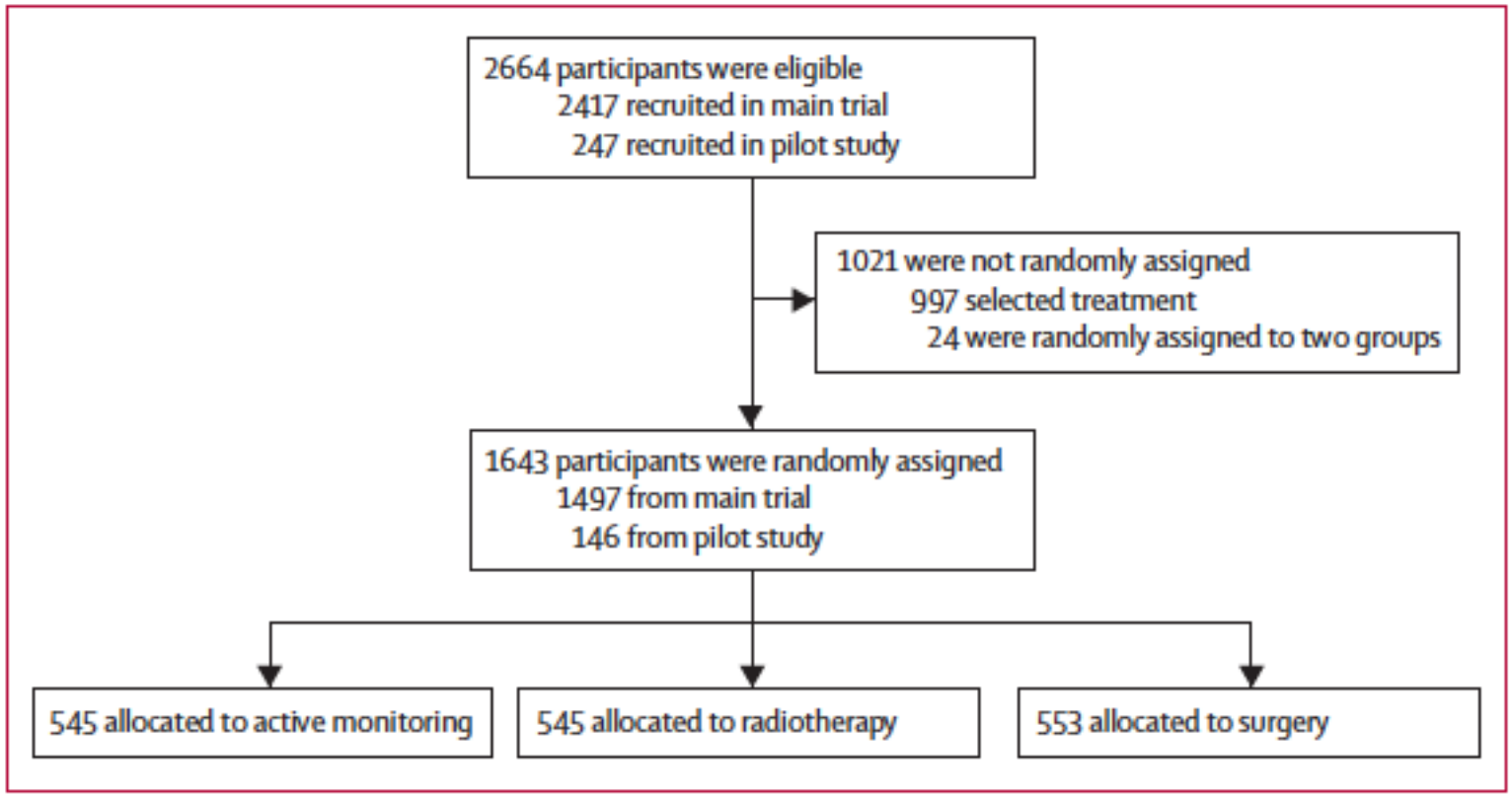
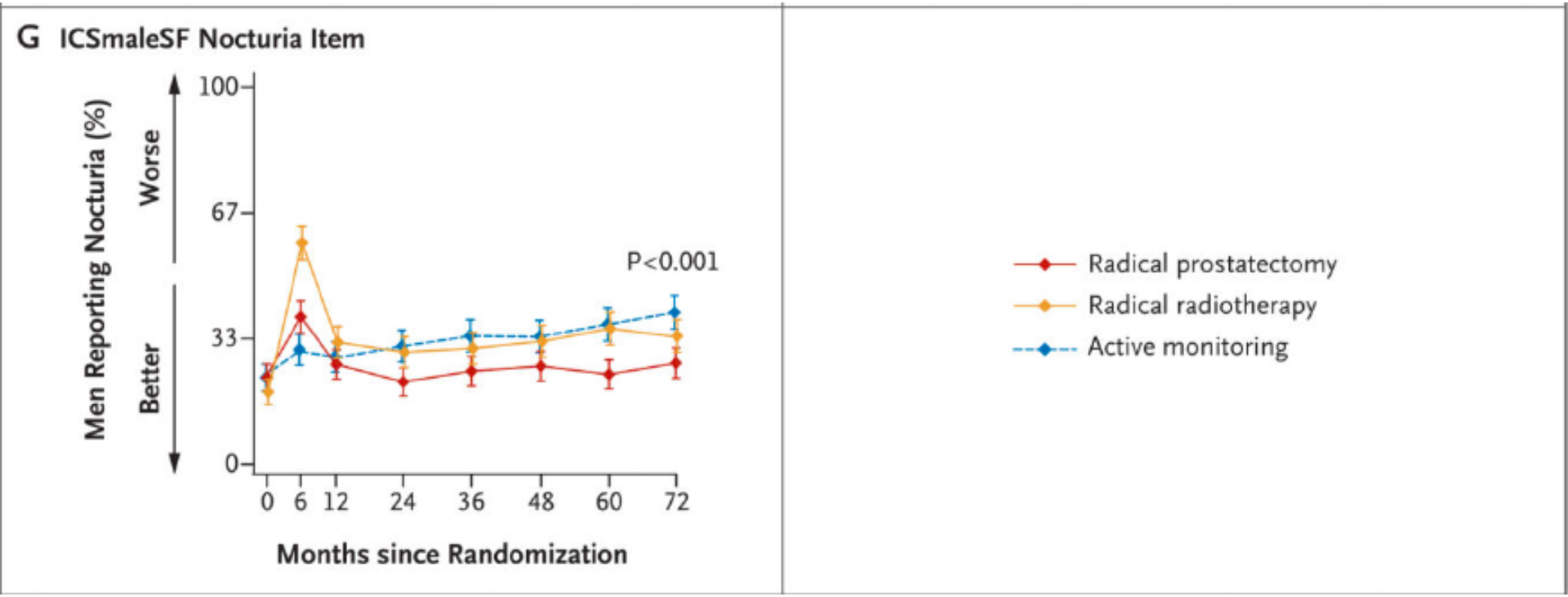


***Figure 3*: Flow diagram of the randomisation phase of the ProtecT trial**

Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer

J.L. Donovan[#], F.C. Hamdy[#], J.A. Lane[#], M. Mason, C. Metcalfe, E. Walsh, J.M. Blazeby, T.J. Peters, P. Holding, S. Bonnington, T. Lennon, L. Bradshaw, D. Cooper, P. Herbert, J. Howson, A. Jones, N. Lyons, E. Salter, P. Thompson, S. Tidball, J. Blaikie, C. Gray, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, M. Davis, E.L. Turner, R.M. Martin, D.E. Neal[#], and **for the ProtecT Study Group***

[#] These authors contributed equally to this work.



N Engl J Med. 2016 October 13; 375(15): 1425–1437. doi:10.1056/NEJMoa1606221.

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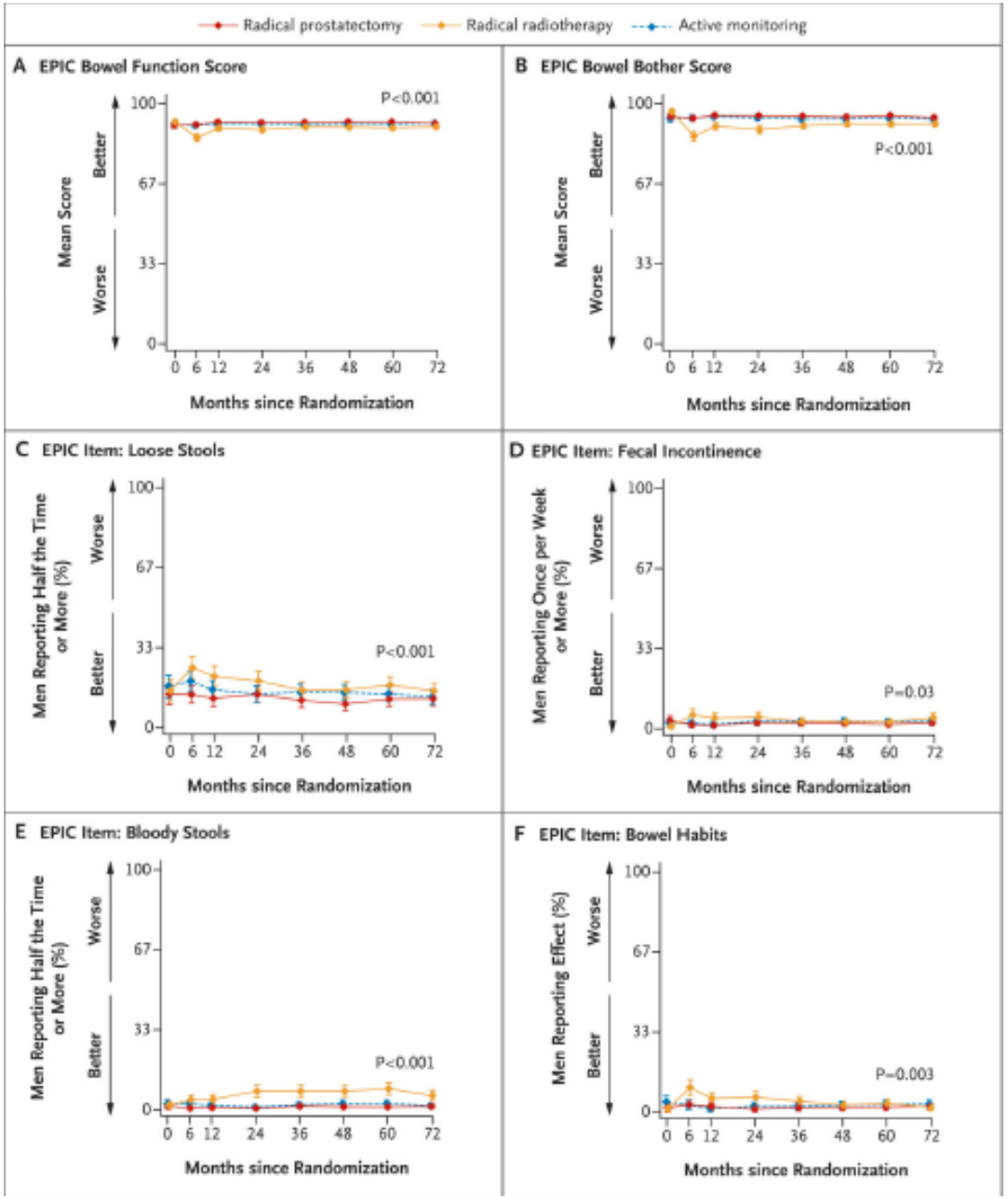
[#] These authors contributed equally to this work.

Evaluation von Darmfunktionen



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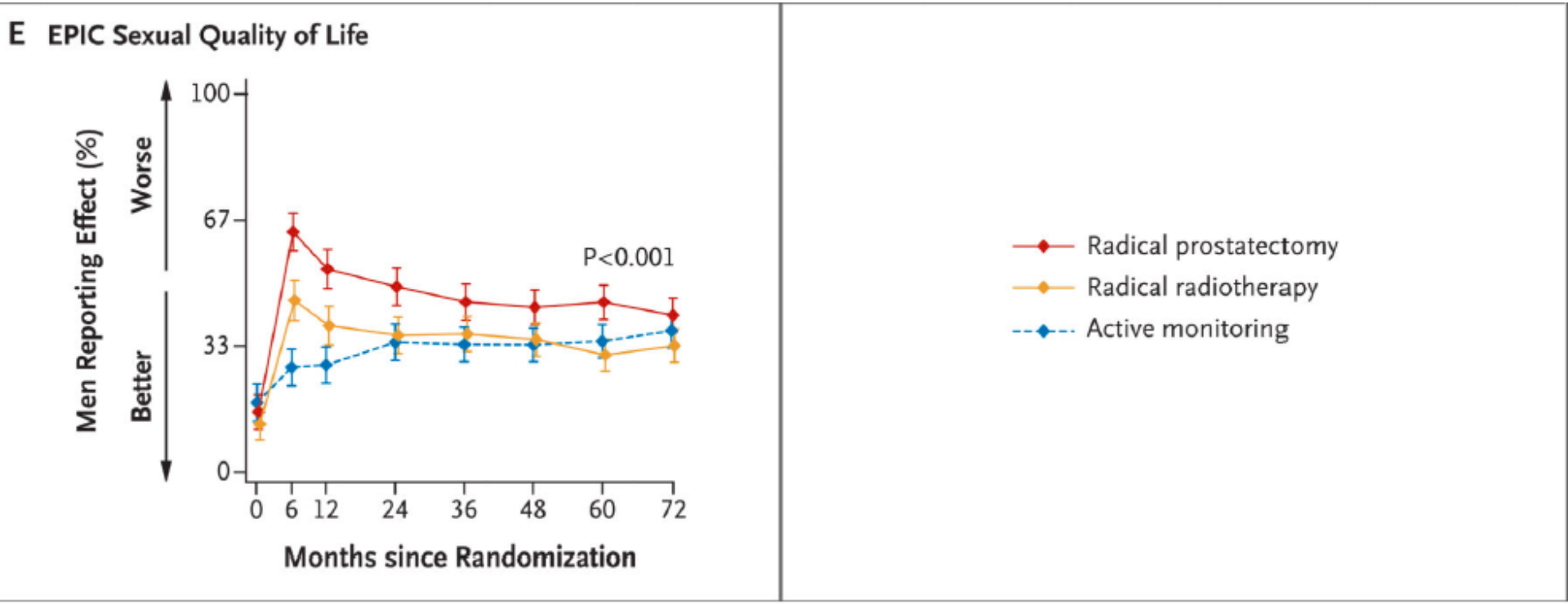

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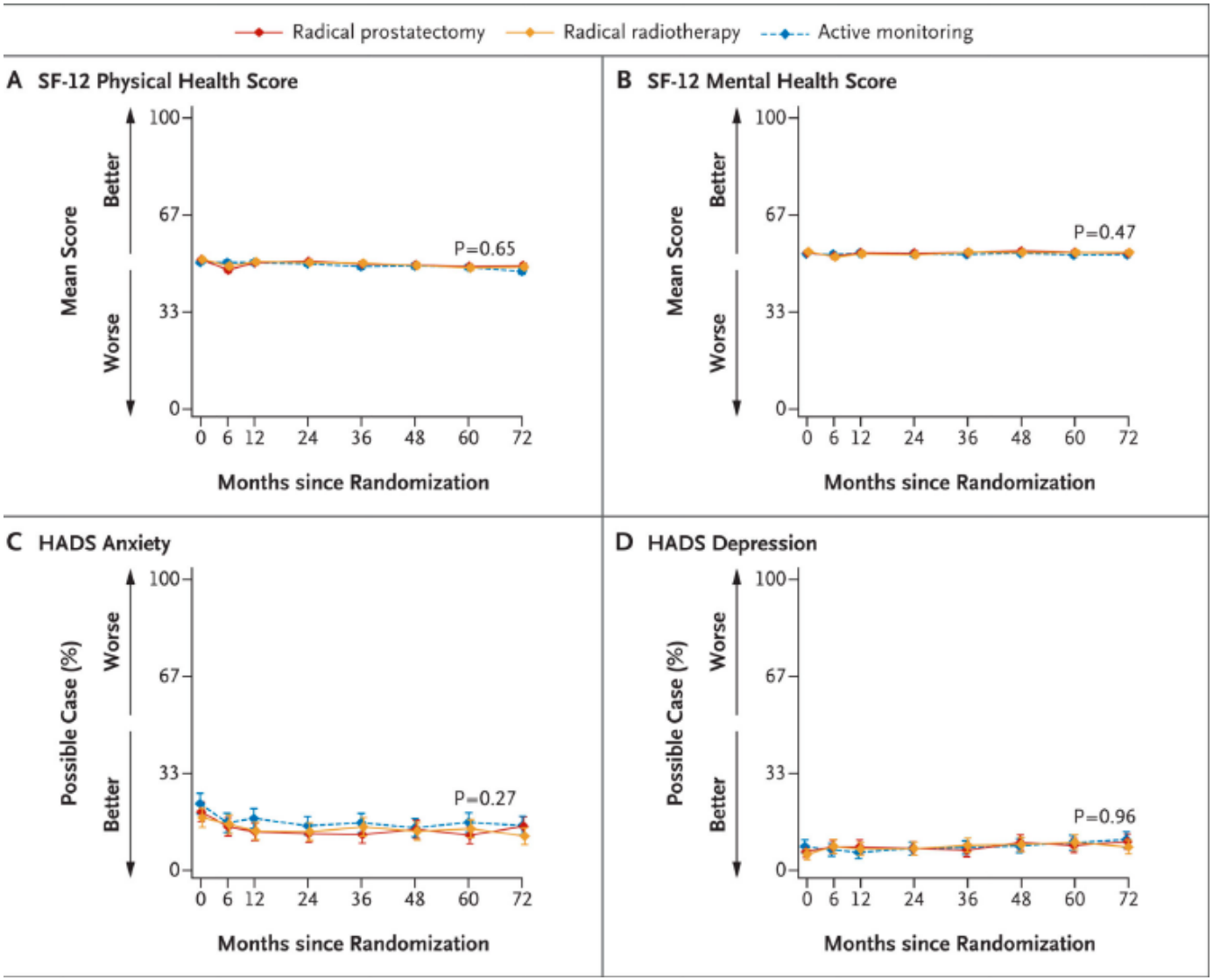
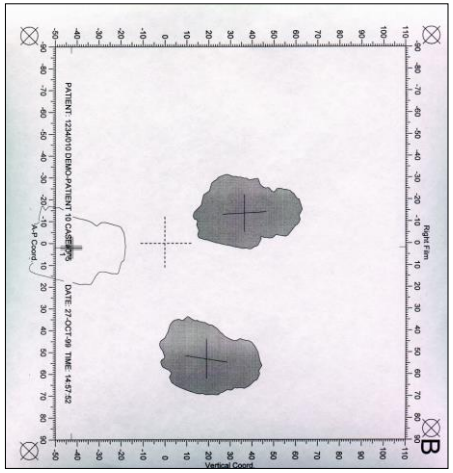
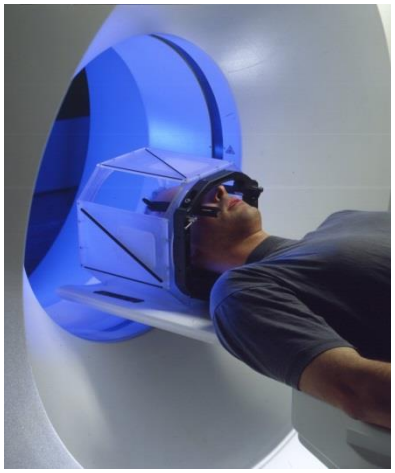


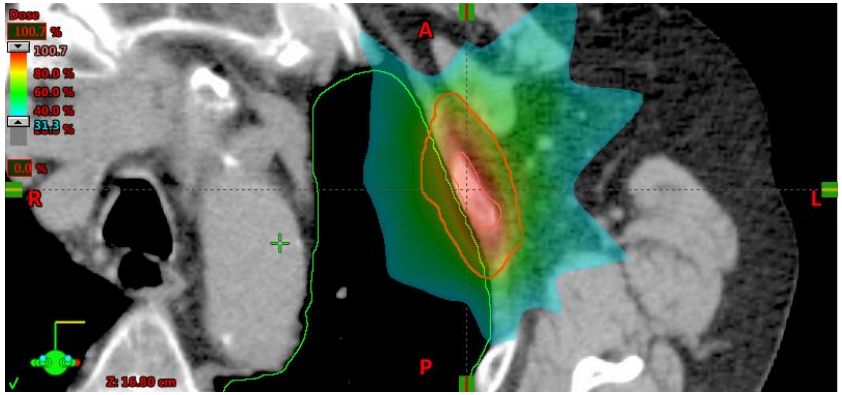
Evaluation von Lebensqualität

N Engl J Med. 2016 October 13; 375(15): 1425–1437. doi:10.1056/NEJMoa1606221.

Stereotaktische Präzisionsstrahlentherapie







- Bestrahlung von kleinen Volumina
- Lymphknotenmetastasen, Knochenmetastasen, Hirnmetastasen

STEREO TAKTUM

Zentrum für Stereotaxie
und personalisierte
Hochpräzisionsstrahlentherapie

Klinik und Poliklinik für
RadioOnkologie und Strahlentherapie

Lokalrezidiv nach Strahlentherapie: Welche Therapieoptionen haben wir?

- Antihormonelle Therapie
- Operative Resektion
- Chemotherapie
- ...

Strahlentherapie mit modernen Techniken der Hochpräzisionsstrahlentherapie

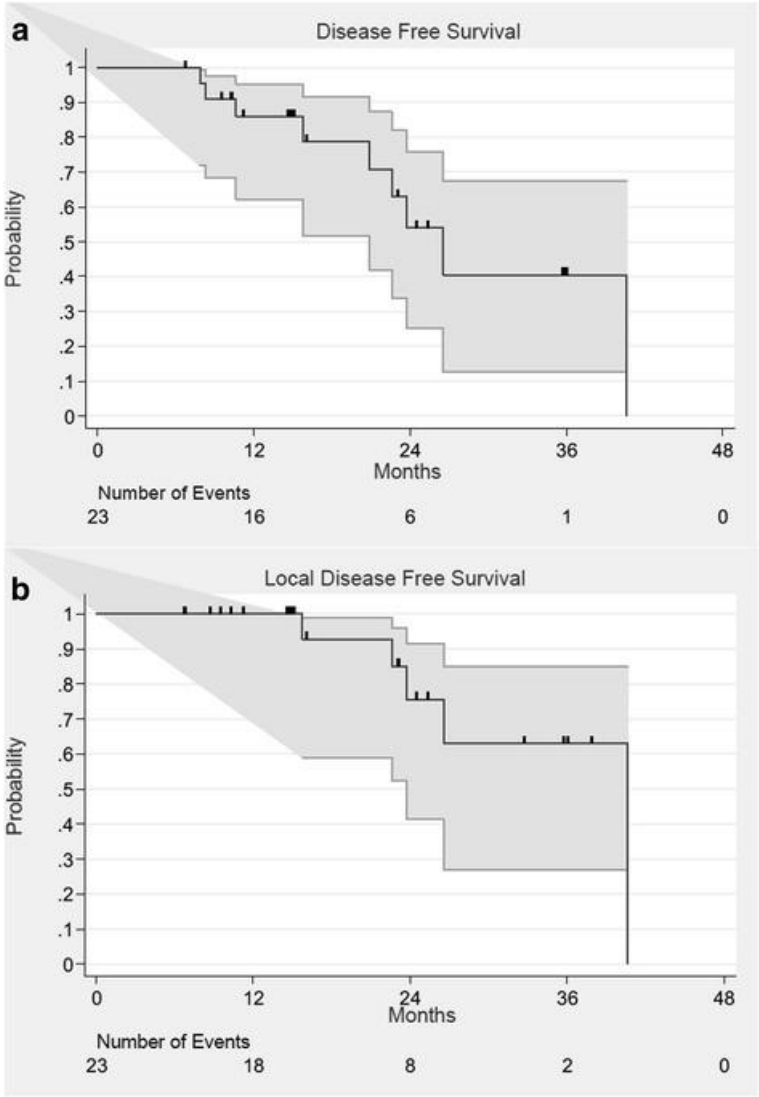
SBRT
Stereotactic Body Radiotherapy
Extrakranielle Stereotaxie

Lokalrezidiv nach Strahlentherapie: Welche Therapieoptionen haben wir?

Median age at relapse (range)	70 (58-82)
Initial disease	
T-Stage	T1: 7 (30.4%) T2: 8 (34.8%) T3: 7 (30.4%) NA: 1 (4.3%)
Median PSA	10.38 ng/mL (2.34–57)
Gleason	5: 1 (4.3%). 6: 5 (21.7%). 7: 13 (56.5%). 9 :1 (4.3%) NA: 3 (13%)
Prior RT modality	
External beam radiotherapy	19 (83%)
Brachytherapy	4 (17%)
Median dose of EBRT (Gy) (range)	75.6 (70–75.6)
Residual treatment urinary or rectal toxicities	Yes : 11 (Grade 1 : 7. Grade 2 : 4) No = 12
Median interval from prior RT to salvage (range)	65 months (28 to 150)
Relapse	
Biopsy at relapse	Yes: 19 (83%). No: 4 (17%)
Unilateral positive biopsies	9 (47%)
Bilateral positive biopies	10 (53%)
Number of positive biopsies : median (range)	4 (1–13)
MRI	Yes: 23 (100%). No 0 (0%)
Involvment on MRI	Unilateral: 12 (52.2%) Bilateral: 10 (43%) None: 1 (4%)
Extracapsular invasion on MRI	11 (47%)
Choline PET scan	Yes: 21 (91.3%) No: 2 (8.7%)
Androgen deprivation therapy	Yes: 14 (61%) No: 9 (39.1%)

Leroy T et al. Salvage robotic SBRT for local prostate cancer recurrence after radiotherapy: preliminary results of the Oscar Lambret Center
Radiation Oncology 2017 Jun 9

Lokalrezidiv nach Strahlentherapie: Welche Therapieoptionen haben wir?



SBRT
Stereotactic Body Radiotherapy
Extrakranielle Stereotaxie

Leroy T et al. Salvage robotic SBRT for local prostate cancer recurrence after radiotherapy: preliminary results of the Oscar Lambret Center Radiation Oncology 2017 Jun 9

Lokalrezidiv nach Strahlentherapie

Toxicities	n (%)
Grade 1	13 (56.5%)
Cystitis	9 (41%)
Dysuria	1 (4.3%)
Urethritis	1 (4.3%)
Proctitis	2 (8.7%)
Grade 2	9 (39.1%)
Dysuria	1 (4.3%)
Proctitis	2 (8.7%)
Cystitis	4 (17.4%)
Urethral stenosis	2 (8.7%)
Grade 3	3 (13%)
Cystitis	2 (8.7%)
Neuritis	1 (4.3%)

Dose constraints

Organ-at-risk	Dose constraint
Rectum	V27 < 2 cc
	V12 < 20%
Bladder	V27 < 5 cc
	V12 < 15%
Intra-prostatic urethra	V24 < 30%
	V36 < 1 cc

Leroy T et al. Salvage robotic SBRT for local prostate cancer recurrence after radiotherapy: preliminary results of the Oscar Lambret Center Radiation Oncology 2017 Jun 9

Lokalrezidiv nach Strahlentherapie: Welche Therapieoptionen haben wir?

Study	Number of patients (*n*=)	Median follow-up (months)	Biochemical response rate (%)	1 year BCR-free survival rate	Acute grade 1–2 urinary toxicity (%)	Acute grade 1–2 gastro-intestinal toxicity (%)	Acute grade 3–4 toxicity (%)	Late grade 1–2 urinary toxicity (%)	Late grade 1–2 gastro-intestinal toxicity (%)	Late grade 3–4 toxicity (%)
Olivier	12	34.2	83	79	25	8	0	12.5	0	0
Janoray et al. (13)	10	11.7	90	80	14.3*	9.5*	0	0	0	0
Detti et al. (14)	8	10	88	NA	12.5	12.5	0	0	0	0
Zerini et al. (15)	10	21.3	NA	NA	10	10	0	10	10	0

NA, No Available data.

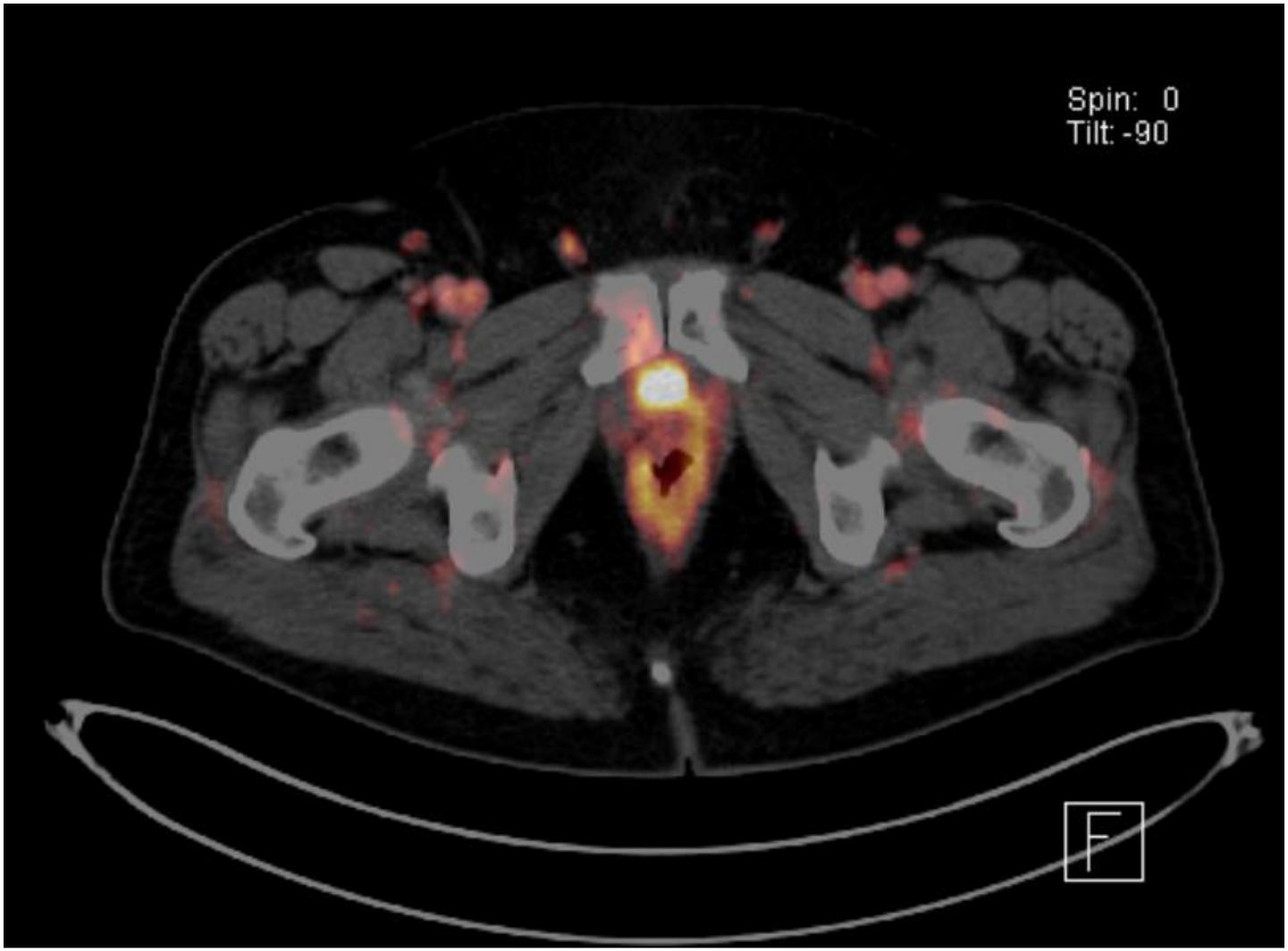
**In this study, the toxicity results were presented for salvage SBRT both on prostate and prostatic bed.*

Olivier J et al. Stereotactic Re-irradiation for Local Recurrence in the Prostatic Bed After Prostatectomy: Preliminary Results Front Oncol. 2019 Feb 15

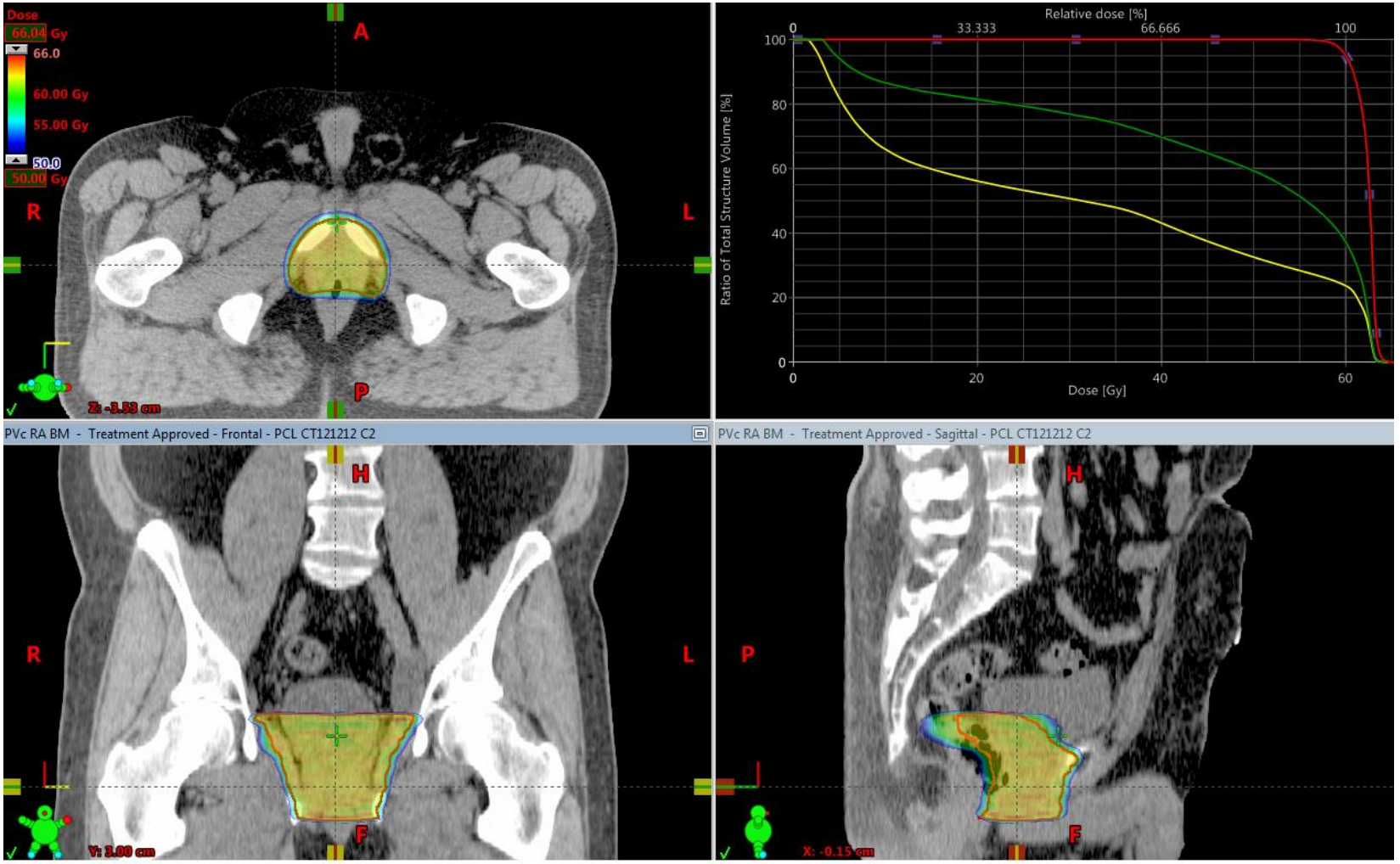
Fallbeispiel aus dem Klinikum rechts der Isar

- Prostata-Ca pT3a pN0 (0/16) M0 R1 G2 L0 V0 Gleason 4+3=7 iPSA 9,5 ng/ml
- 19.07.2012: Prostatovesikulektomie + LAE, R1
- bis 31.01.2013: Add. RTx der Prostataloge bis 60 Gy
- PSA-Anstieg auf 0,51 ng/ml im Februar 2019
- 25.03.2019: PSMA-PET: Lokalrezidiv im Bereich der vesikuorethralen Anastomose

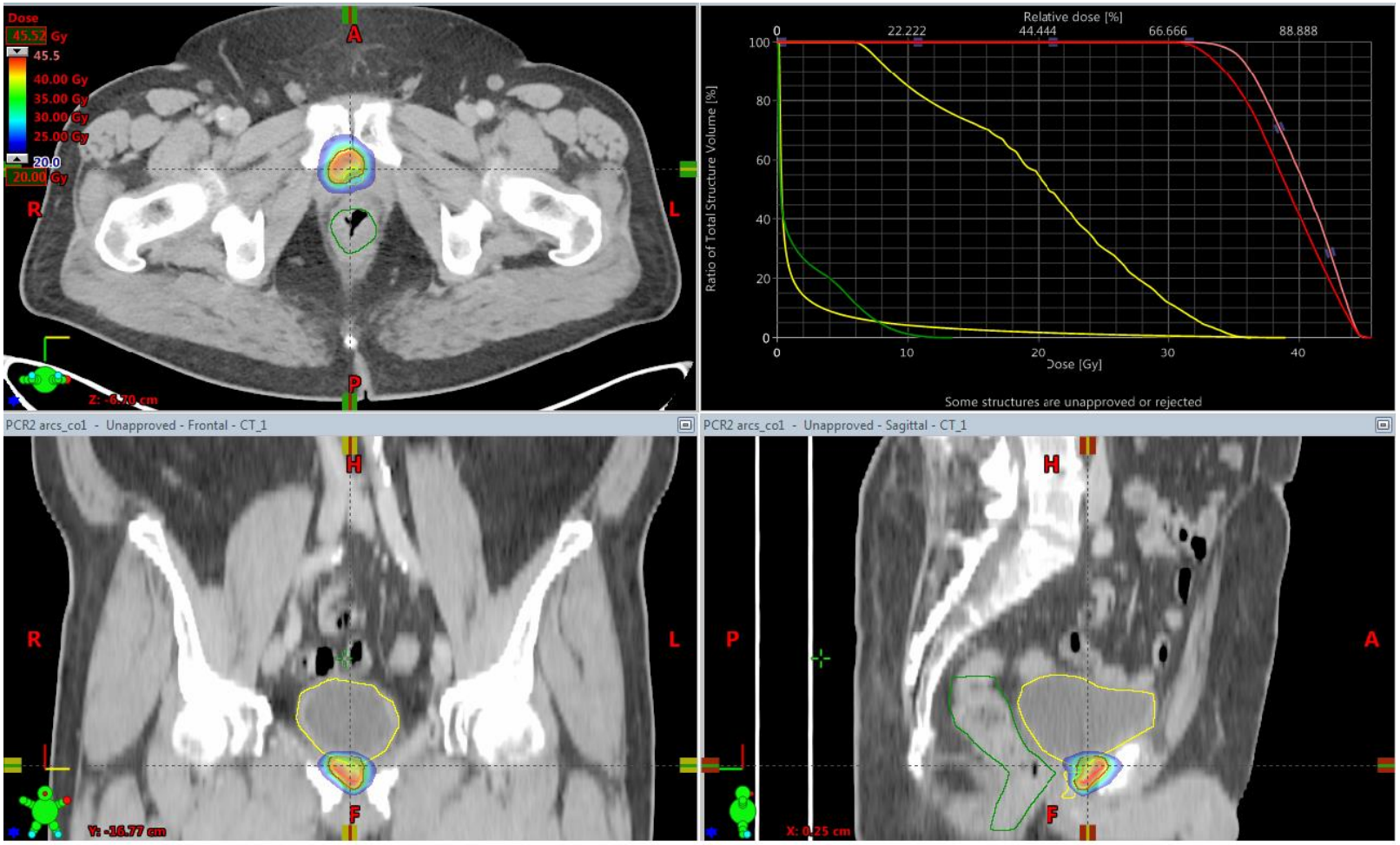
Fallbeispiel aus dem Klinikum rechts der Isar



Vorbestrahlung

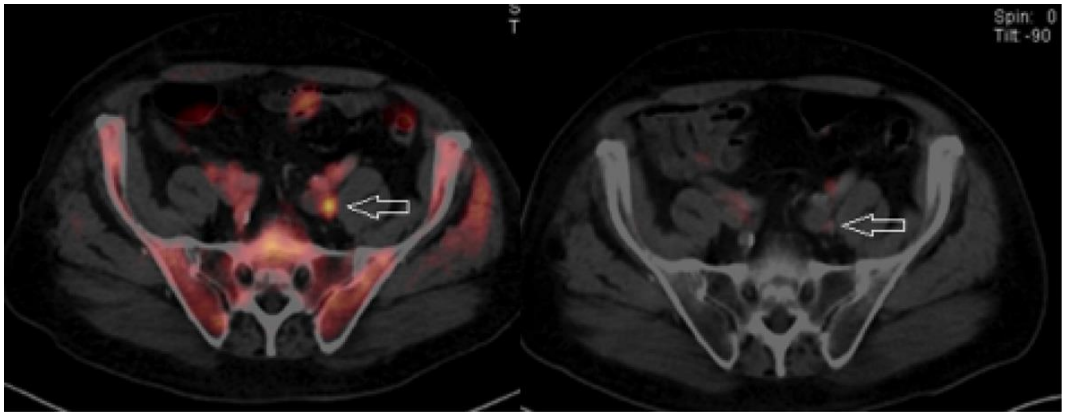


Rebestrahlung mit SBRT bei Lokalrezidiv



Integration of 68Ga-PSMA-PET imaging in planning of primary definitive radiotherapy in prostate cancer

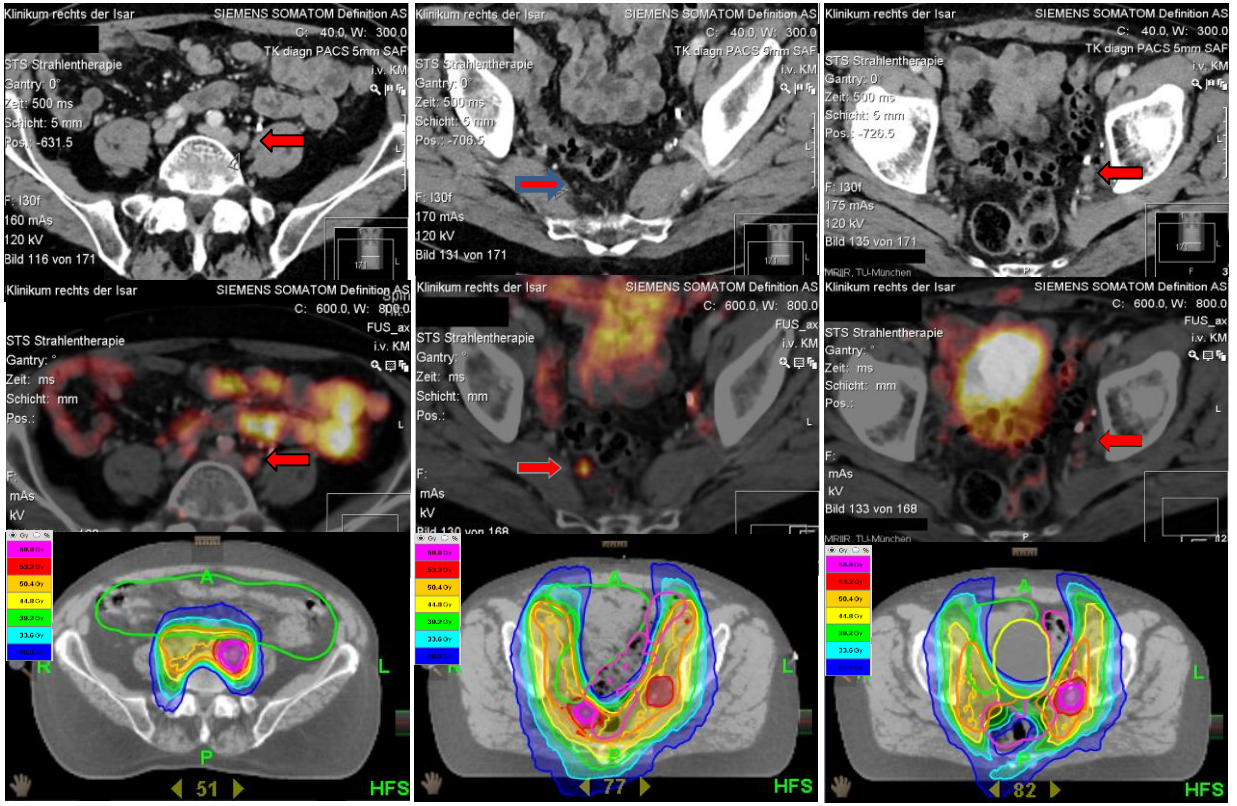
- **^{68}Ga-PSMA-PET Bildgebung** hat einen **großen Einfluss auf die Stadieneinteilung** und somit auch auf die **Bestrahlungsplanung** bei Patienten die primär eine Strahlentherapie erhalten als auch für solche mit PSA-Rezidiv (siehe nächste Folie).
- Bei den **Primärfällen** änderte sich das Tumorstadium in 53.3% und das Bestrahlungskonzept in 33.3% der Fälle. Ein “Down-Staging” erfolgte in 13.3% der Fälle.



Choline-PET-CT (links) mit deutlicher Anreicherung eines iliakalen Lymphknotens. ^{68}Ga-PSMA-PET (rechts) bestätigt den Verdacht des Befalls nicht.

Integration der ^{68}Ga-PSMA-PET Bildgebung in die Therapieplanung – *i*RT-Rezidiv-Strahlentherapie beim Prostatakarzinom

68 jähr. Patient
Prostata-Ca, ED 03/2014
iPSA 9.6 ng/ml, pT3a, pN0(0/19), Mx, R0 (1mm), G3, GS 7
03/2014: RPE, PSA Nadir postop. 0.08 ng/ml
08/2014: PSA 0.26 ng/ml



- 54.3 % - Änderung des Therapiekonzeptes / „Stagings“
- 25.8 % - Dosissteigerungen innerhalb der Prostataloge (makroskop. Tumor)
- 37.1 % - Boost auf befallene Lymphknoten
- 14.3% - Indikation RT der Lymphabflusswege

Prostate, 2017

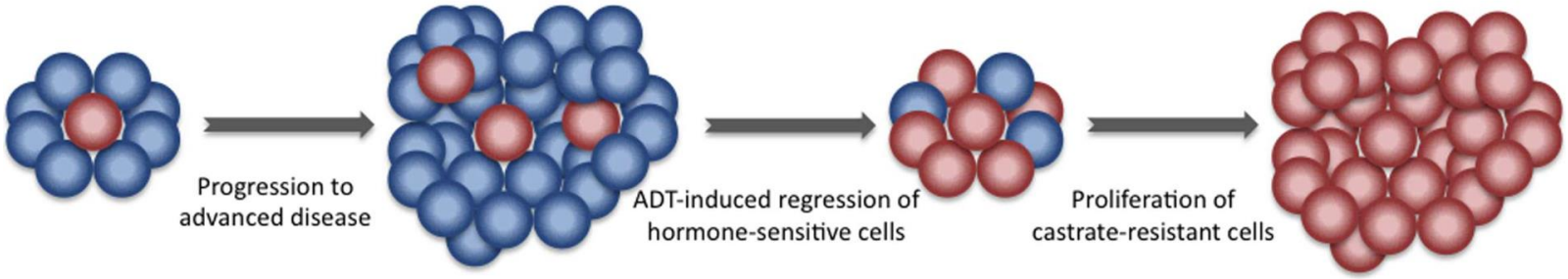
Oligometastasiertes Prostatacarcinom

- Standardtherapie: AHT (PFS, OS)

  Einschränkung der Lebensqualität!

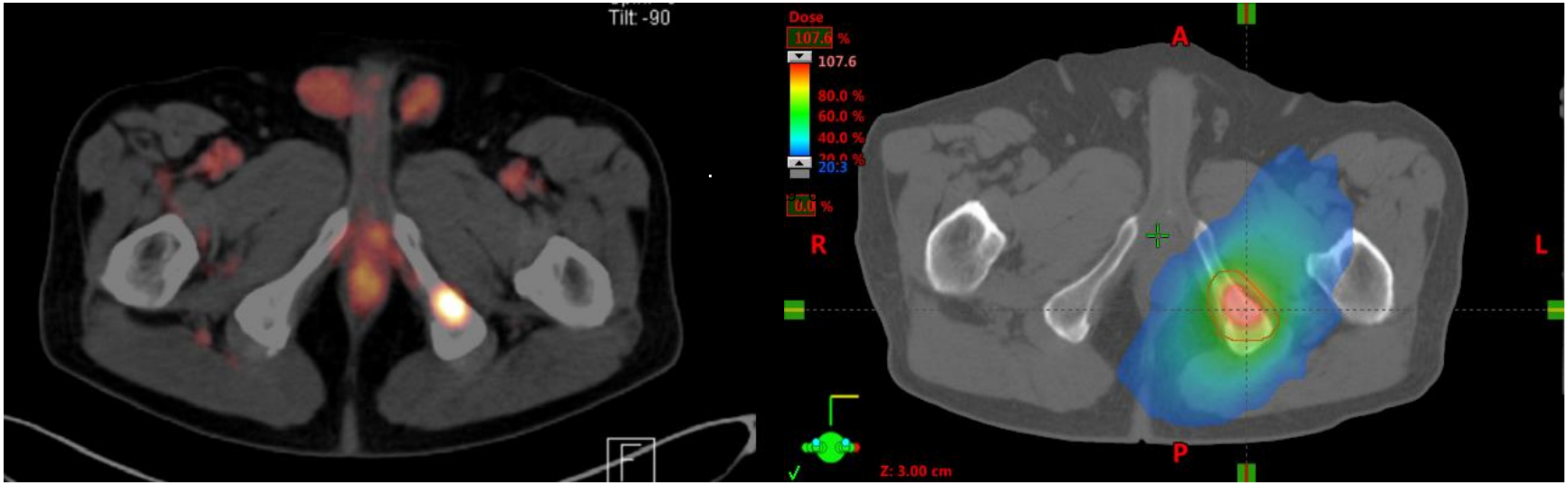
  bei asymptomatischen Patienten „Surveillance-Strategie“?
- Ansprechraten > 80% (im median 18-24 Mo)[1]
- Therapie ossärer Metastasen

  Hoher Tropismus für Knochen[1]
  - Oft einzige Manifestation
  - Skelettale Ereignisse Hauptursache für Morbidität[2]
  - In 40% schmerzhaft
  - In 20% pathologische Frakturen
  - In 5% RM-Kompression



79j. Pat., ED Prostatakarzinom 2009

- Stadium: pT2c pN0 M0 GS7
- 01-10/14 kontinuierlicher PSA-Anstieg 0,22 →1,16 ng/ml
- 10/14: PSMA-PET-CT zeigt fokal intensive PSMA-Expression im li. Tuber ischiadcum (singuläre Knochenmet.)



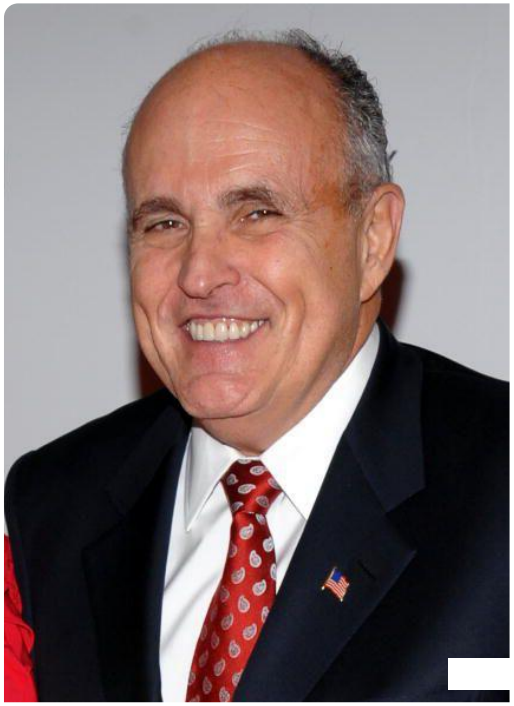
PSA-Abfall <0,01 ng/ml
ohne AHT!

CANCER > PROSTATE CANCER

Rudy Giuliani's Battle With Prostate Cancer

PRINT

By Matthew Schmitz, MD | Medically reviewed by a board-certified physician | Updated September 01, 2017



Rudy Giuliani. Dimitrios Kambouris/Getty Image

Making the Treatment Decision

Giuliani's cancer was diagnosed at an early stage and he was presented with several options for treatment. Upon being presented with his treatment options (which, per Giuliani, were surgery, external beam radiation, brachytherapy, and hormones) he took roughly 2 weeks to weigh his options and make a decision.

Ultimately, Giuliani chose a somewhat unconventional treatment regimen, which included hormonal therapy, radioactive seed implants, and external beam radiotherapy

v.verywellhealth.com/rudy-giulianis-battle-with-prostate-cancer-2782149

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