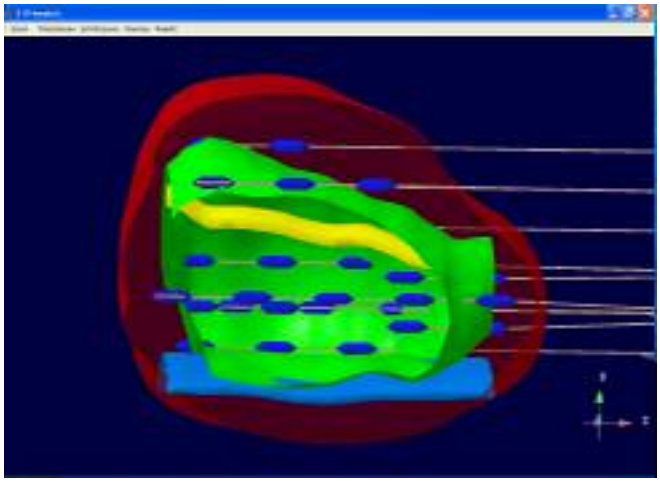
Transperineale Interstitielle Seedimplantation (TPSI) des lokal begrenzten Prostatakarzinoms



Arbeitsgruppe Vaterstetten

An Interinstitutional and Interspecialty Comparison of Treatment Outcome Data for Patients with Prostate Carcinoma Based on Predefined Prognostic Categories and Minimum Follow-Up

Frank A. Vicini, M.D.[1]
Alvaro Martinez, M.D.[1]
Gerald Hanks, M.D.[2]
Alex Hanlon, Ph.D.[2]
Brian Miles, M.D.[3]
Ken Kernan, M.D.[3]
David Beyers, M.D.[4]
Haakon Ragde, M.D.[5]
Jeffrey Forman, M.D.[6]
James Fontanesi, M.D.[6]
Larry Kestin, M.D.[1]
Gyorgy Kovacs, M.D.[7]
Louis Denis, M.D.[8]
Kevin Slawin, M.D.[3]
Peter Scardino, M.D.[3]

[1] Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, Michigan.

[2] Department of Radiation Oncology, Fox Chase Cancer Center, Philadelphia, Pennsylvania.

[3] Department of Urologic Oncology, Baylor College of Medicine, Baylor, Texas.

[4] Arizona Oncology Services, Scottsdale, Arizona.

[5] Grado-Ragde Clinics, Seattle, Washington.

[6] Department of Radiation Oncology, Wayne State University, Detroit, Michigan.

[7] Department of Radiation Oncology, University Hospital, Christian-Albrechts-University, Kiel, Germany.

[8] Oncologic Center, Antwerp, Belgium.

See related editorial on pages 2041–3, this issue.

Presented at the Second Joint International Meeting of the American Brachytherapy Society, the Groupe European de Curietherapie-European Soci-

BACKGROUND. The optimal management of patients with clinically localized prostate carcinoma remains undefined due in part to the absence of well-designed, prospective, randomized trials. The current study was conducted to compare and contrast outcomes with different forms of therapy for patients with prostate carcinoma who were treated at several institutions using predefined prognostic categories.

METHODS. A retrospective study of 6877 men with prostate carcinoma who were treated between 1989 and 1998 at 7 different institutions with 6 different types of therapy was conducted. Five-year actuarial rates of prostate specific antigen (PSA) failure were calculated based on predefined prognostic categories, which included combinations of pretreatment PSA level, tumor stage, and Gleason score. In addition, outcome was calculated using consistent biochemical failure definitions and a minimum, median length of follow-up.

RESULTS. Substantial differences in outcome were observed for the same type of treatment and at the same institution, depending on the number of prognostic variables used to define treatment groups. However, estimates of 5-year PSA outcomes after all forms of therapy for low-risk and intermediate-risk patient groups were remarkably similar (regardless of the type of treatment) when all three pretreatment variables were used to define prognostic categories. For patients in high-risk groups, the 5-year PSA outcomes were suboptimal, regardless of the treatment technique used.

CONCLUSIONS. The current data suggest that interinstitutional and interspecialty comparisons of treatment outcome for patients with prostate carcinoma are possible but that results must be based on all major prognostic variables to be meaningful. Analyzed in this fashion, 5-year PSA results were similar for patients in low-risk and intermediate-risk groups, regardless of the form of therapy. Findings from prospective, randomized trials using survival (cause specific and overall) as the end point for judging treatment efficacy and longer follow-up will be needed to validate these findings and to identify the most appropriate management option for patients with all stages of disease. *Cancer* 2002;95:2126–35.

DOI 10.1002/cncr.10919

Indikation (ABS, ESTRO, EORTC)

- PCa niedrigen Risikos:
  Mono TPSI
- PCa mittleren/hohen Risikos:
  1. EBRT (Dosis),
  2. Dosiseskalation:
     HDR-AL, alt. EBRT+TPSI

TPSI (n = 259)

- Mono TPSI: 218 Pat.
  (∅ Alter: 65,2 ± 6,9 Jahre)
- EBRT + TPSI: 41 Pat.
  (∅ Alter: 65,6 ± 7,1 Jahre)
- „Modified Peripheral Loading“
- Verschreibungsdosis 145/110 Gy
- Bestrahlungsplanung:
  VariSeed™/PSID

Radionuklid

- ^{125}Jod Seeds (RAPID Strand®)
- ^{125}J äquieffektiv ^{103}Pd
- Einzel-Seeds:
  Pulmonale Embolisation
  5,9-36,2 %

TPSI
- Patientenvorbereitung -

- Qualitätsmanagement:
  ABS-, ESTRO- und EORTC-Empfehlungen
- EORTC-QLQ C 30 Questionnaire
- modifizierte RTOG Toxizitäts-Skala, IPSS
- Volumetrie der Prostata
  (Lithotomieposition, 5 mm)
- Erstellen des „Vorplans“

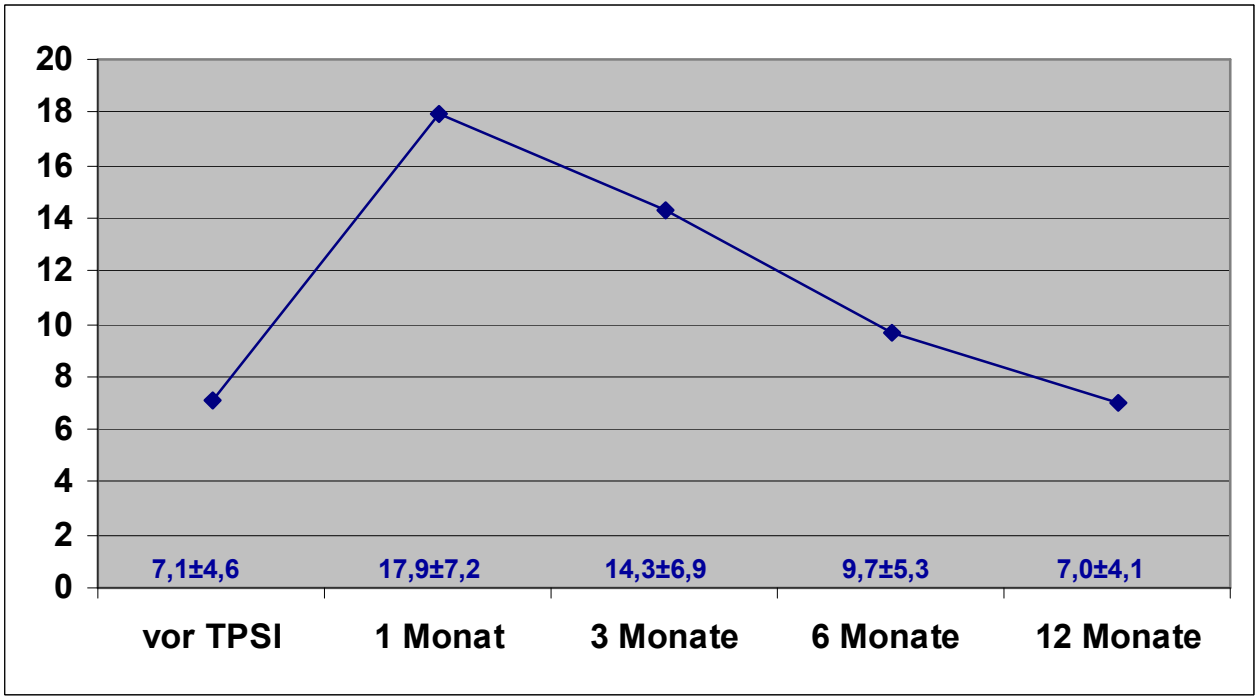
Prä- und Online-Plan

- „Interne Qualitätskontrolle“
- Prostatavolumen (ml):
  32,8 ± 10,3 vs 33,3 ± 10,4
- Seedanzahl:
  49,1 ± 9,5 vs 47,3 ± 10,1
- p > 0,1

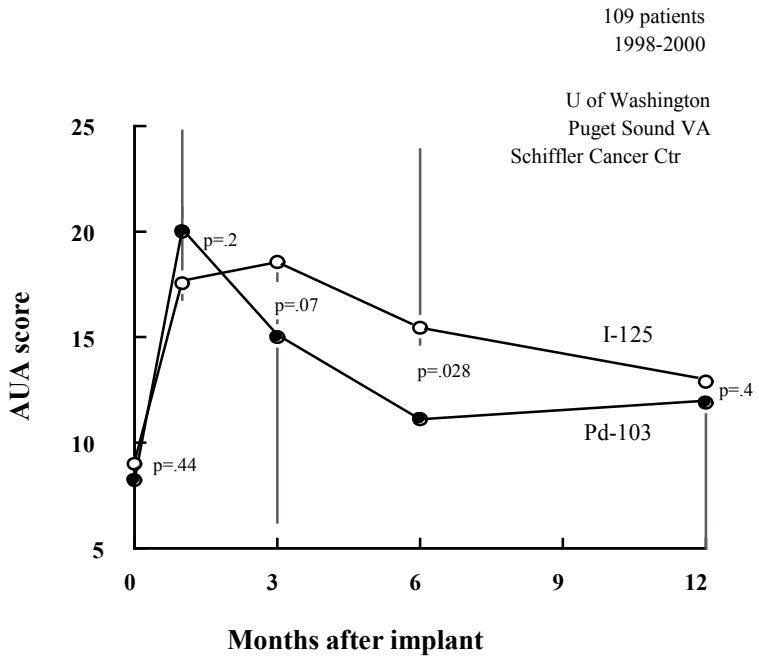
TPSI
- Begleitmaßnahmen -

- Alpha-Blocker (Tamsulosin)
- Gyrasehemmer
- Vortag: Klistier, flüssige Kost
- 500 mg Prednisolon bei Narkoseeinleitung

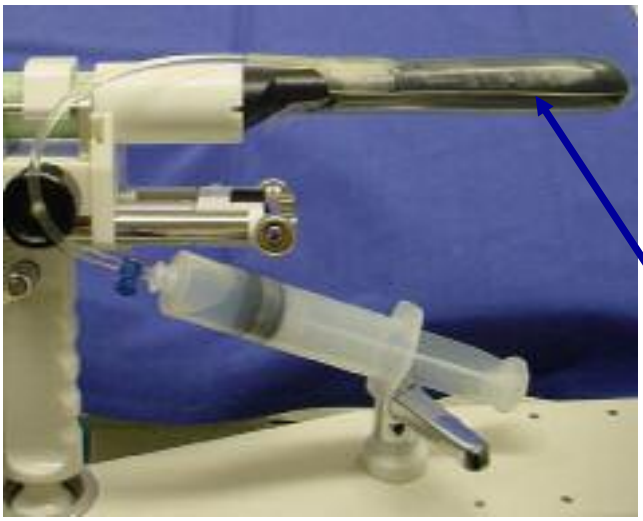
TPSI
- IPSS (n = 100) -

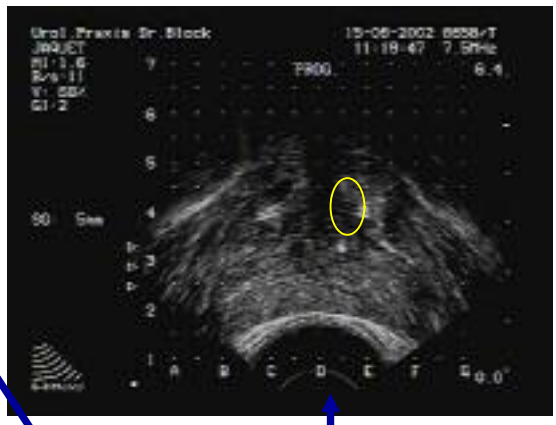


Permanente Seedimplantation
- IPSS: I-125 vs. Pd-103 (Wallner) -

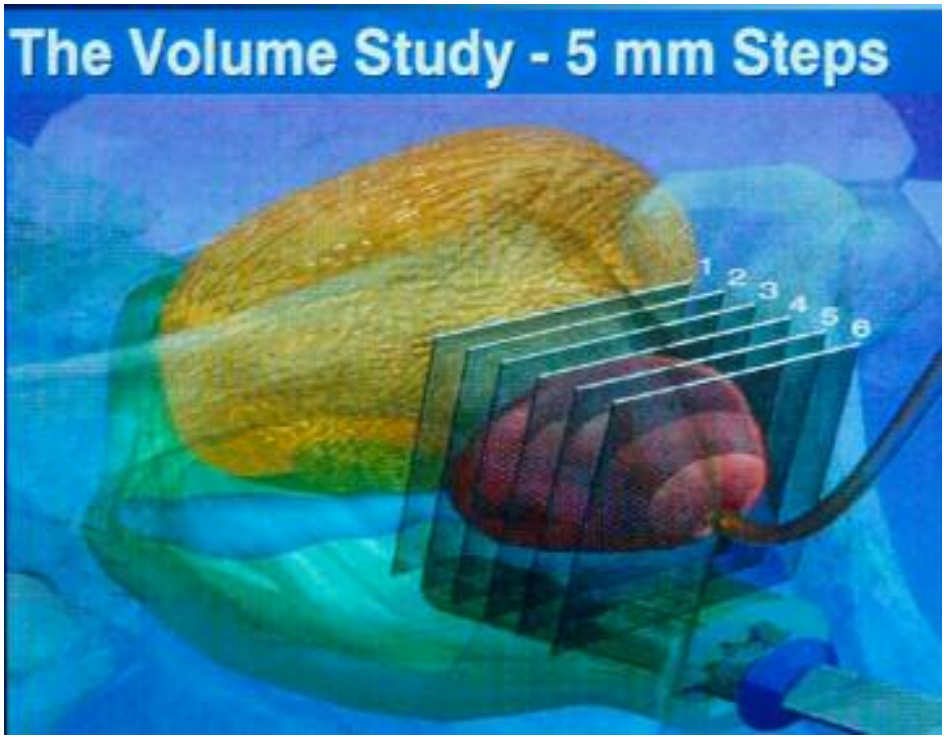


„Brachyballoon“





Elevation ventrale Rektumwand „Brachyballoon“

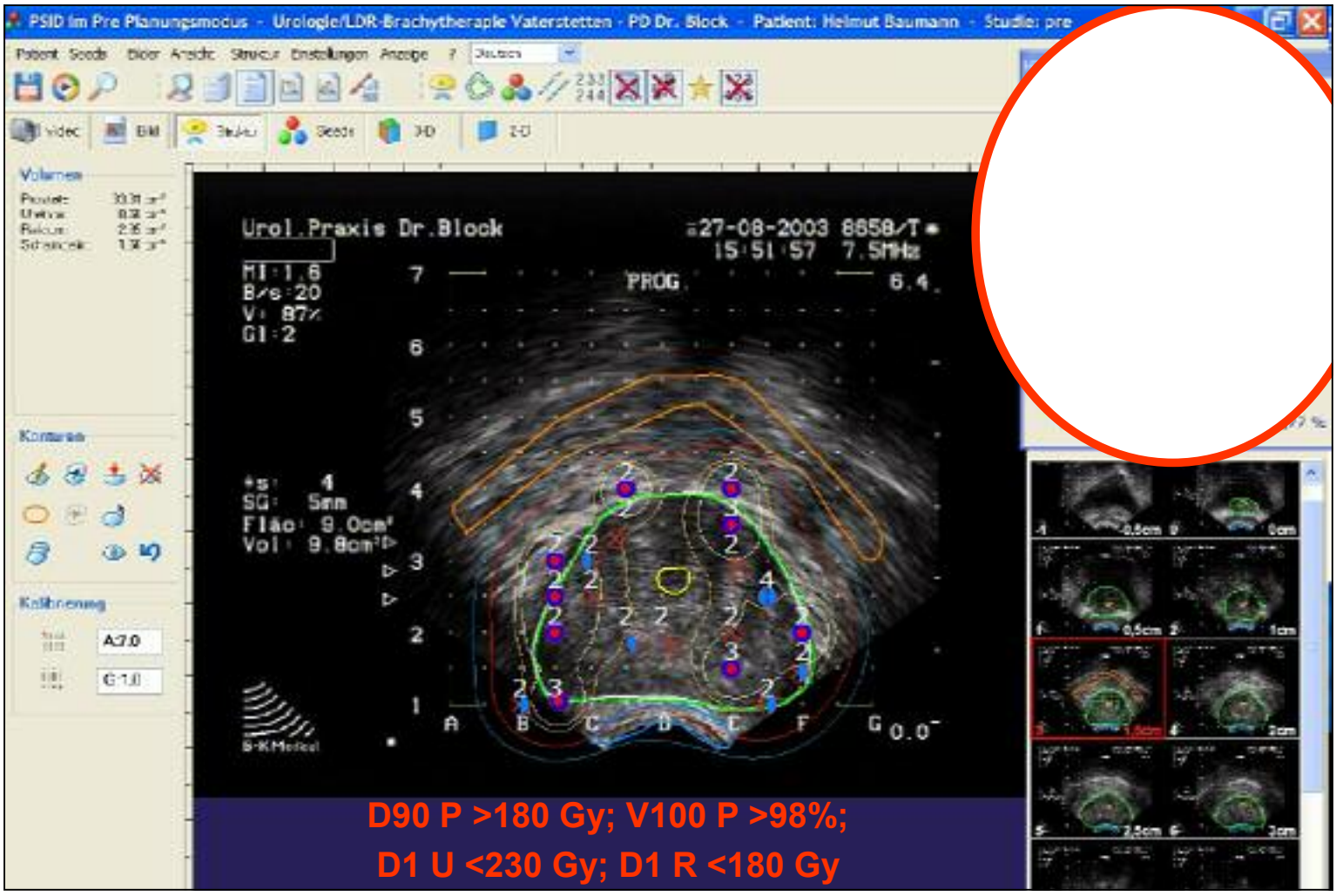


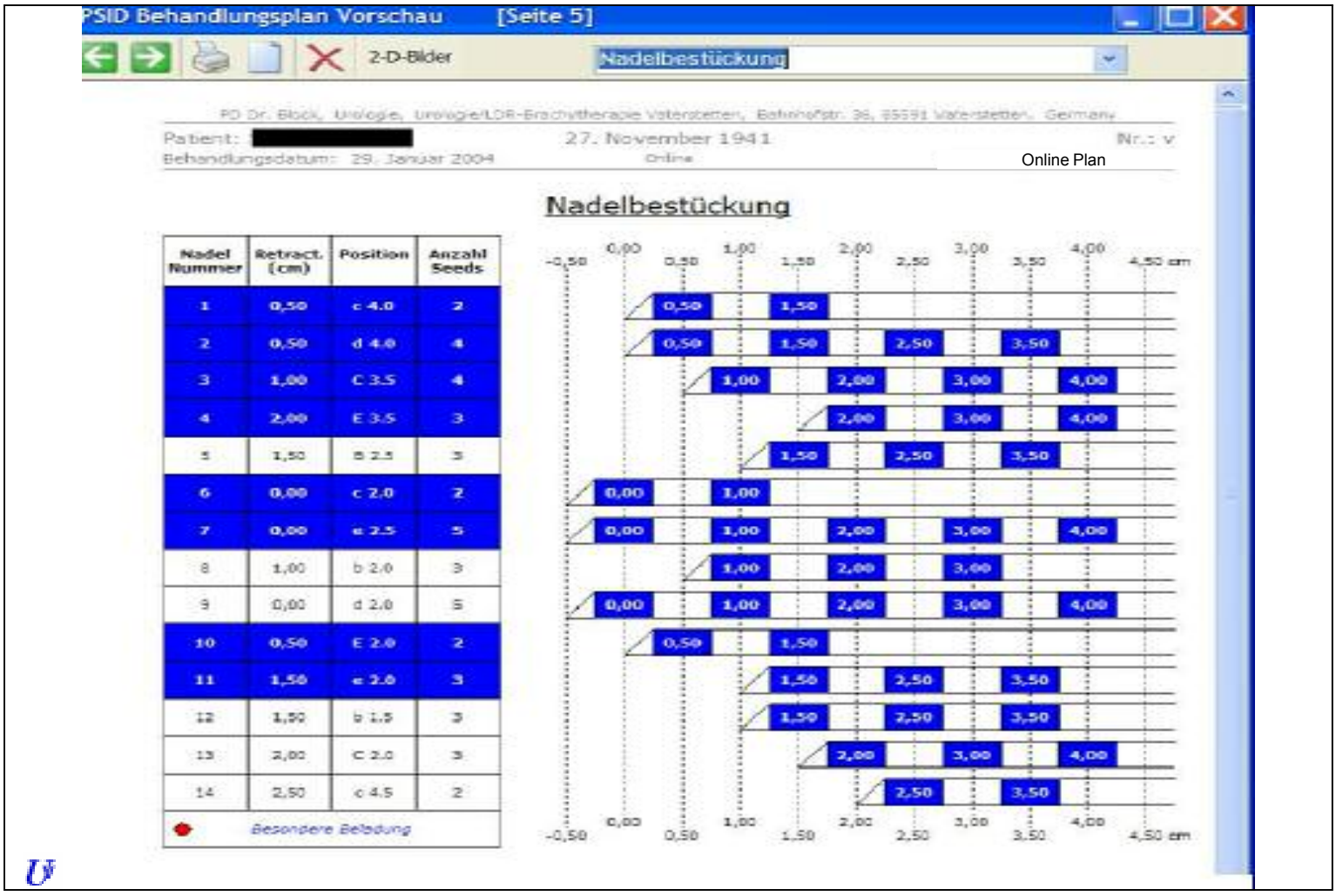
Bestrahlungskriterien

♦ *Prostata* ♦ *Urethra* ♦ *Rektum*

- **Dosis X (Gy)**
  = Dosis,
  die x% eines Organs abdeckt

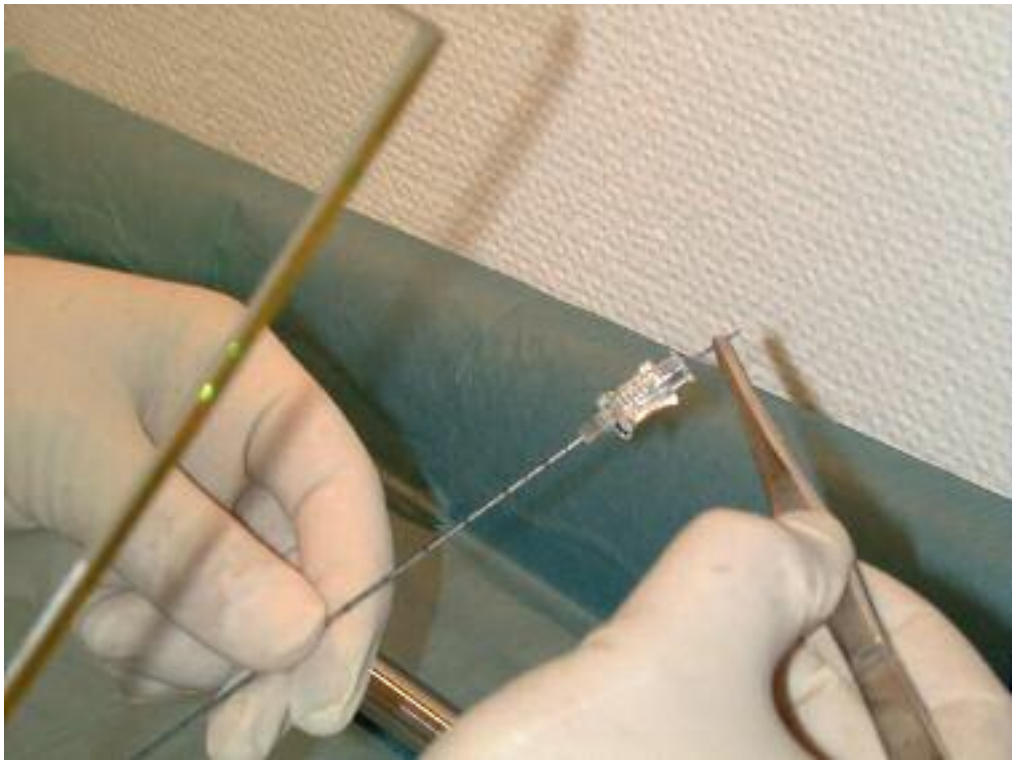
- **Volumen X (%)**
  = Volumen eines Organs, das
  mit x% der Verschreíbungsdosis
  (145 Gy) bestrahlt wird



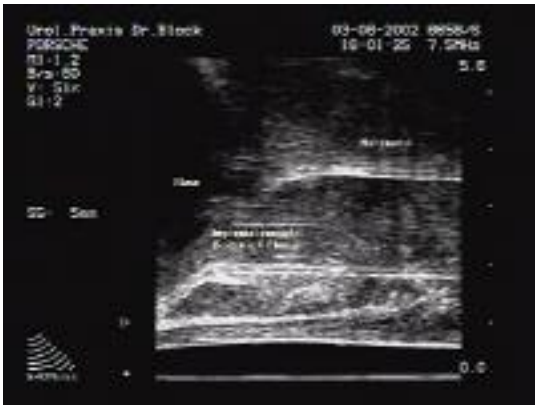


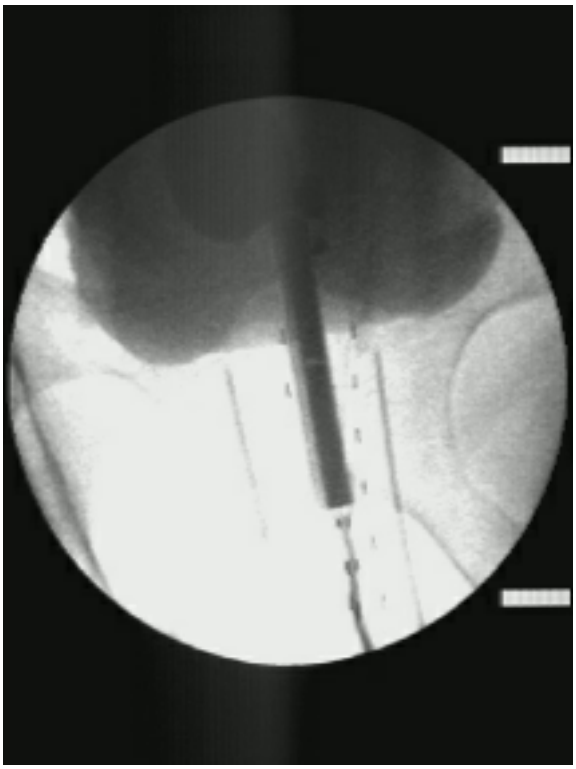
Nadel Nummer	Retract. (cm)	Position	Anzahl Seeds
1	0,50	c 4.0	2
2	0,50	d 4.0	4
3	1,00	C 3.5	4
4	2,00	E 3.5	3
5	1,50	B 2.5	5
6	0,00	c 2.0	2
7	0,00	e 2.5	5
8	1,00	b 2.0	3
9	0,00	d 2.0	5
10	0,50	E 2.0	2
11	1,50	e 2.0	3
12	1,50	b 1.5	3
13	2,00	C 2.0	3
14	2,50	c 4.5	2
	Besondere Belastung		

Einführen der Seeds in Hohlnadel

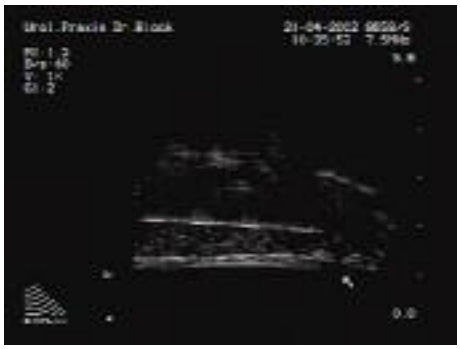


Exakte Identifikation der „0-Ebene“



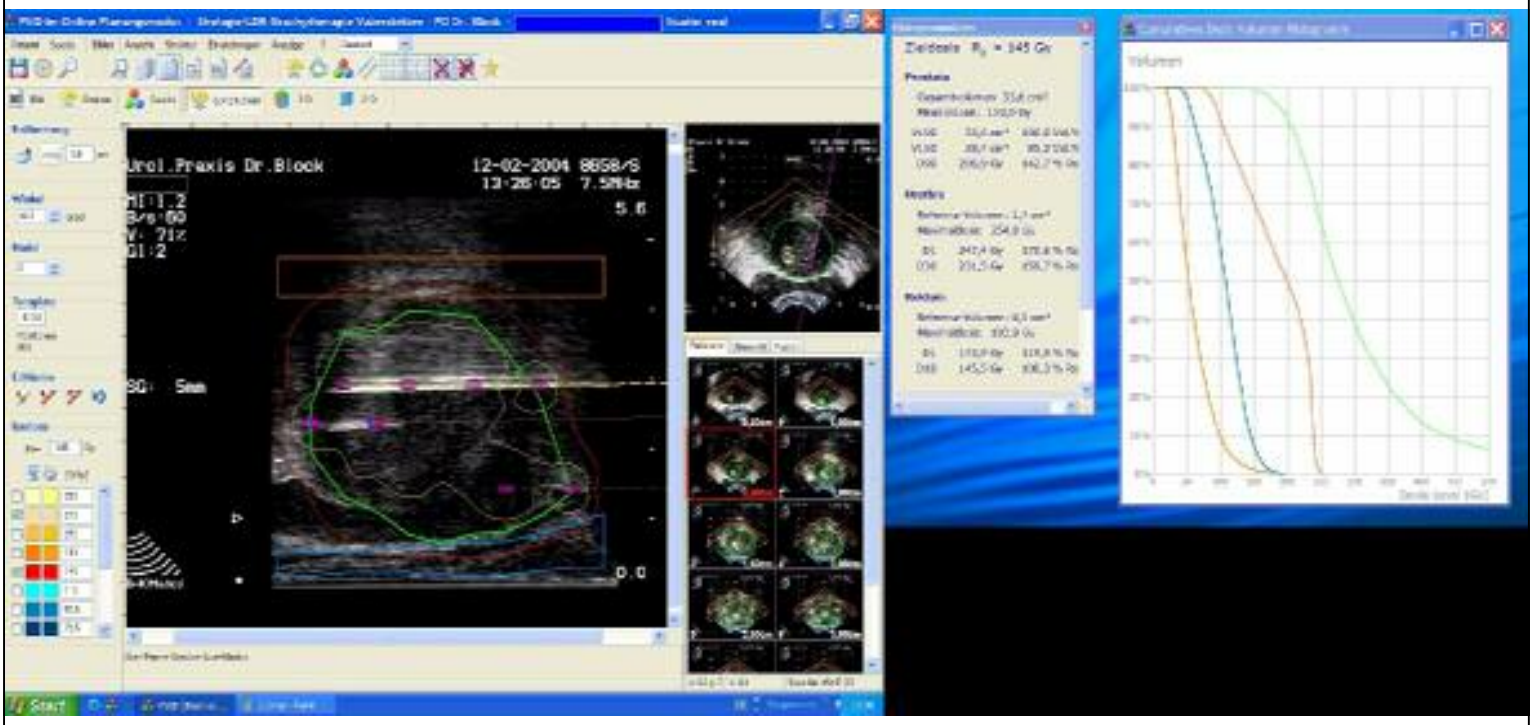


Distanzmessung: Template/Nadelhub
→ schnelle Identifikation der Retraktionsebene

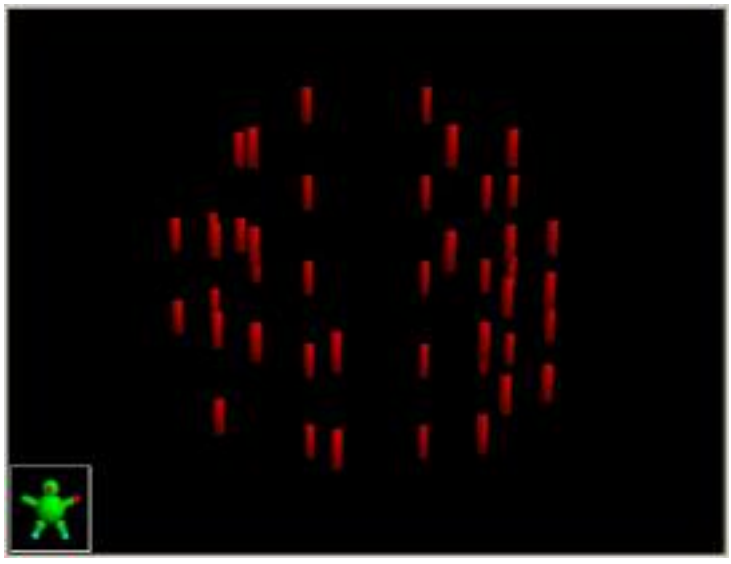


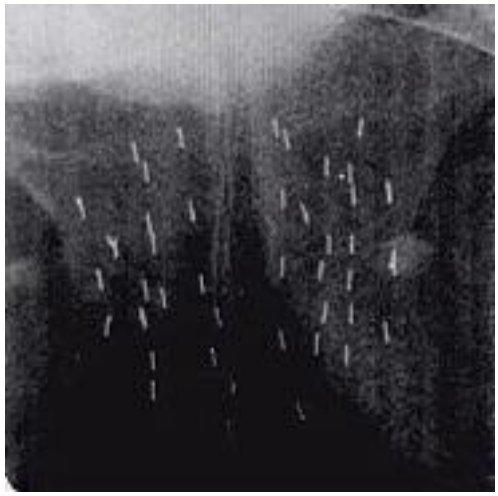
Interaktive Dynamische Realtime Dosisverifikation

Interaktive Dynamische Realtime Dosisverifikation



„WHAT YOU SEE IS WHAT YOU GET“





Allgemeine Implantationsdaten

- Implantationsdauer: 1,5 – 2 h (Online-Plan, Realtime-Dosisverifikation, Nadelbeladung, flexible Zystoskopie, Strahlenschutz)
- Blasenspülung: 30 – 60 min, danach sofortige DK-Entfernung
- Bei Entlassung: allgemeine Patientenaufklärung

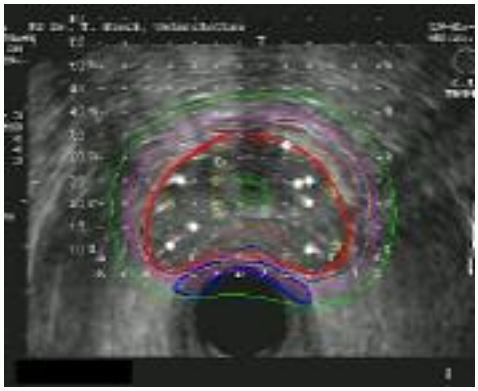
Zielkriterien: CT-Nachplan (Tag 30)

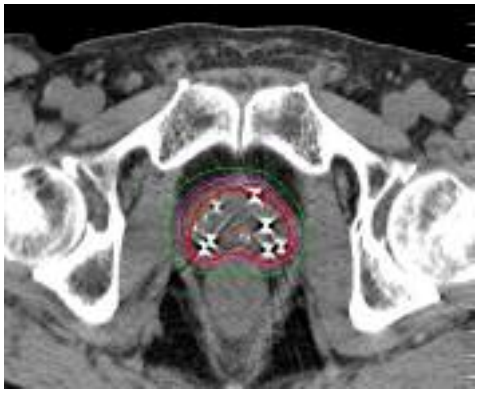
- D90 Prostata >140 Gy = Effizienz
  (Dosis, die 90% des PV abdeckt)
- V100 >85% = Effizenz
  (Volumen der Prostata, das 100% der Verschreibungsdosis – 145 Gy – erhält)
- V150 ≤80% = Toxizität
  (Volumen der Prostata, das 150% der Verschreibungsdosis – 145 Gy – erhält)

Prostatavolumen (PV): CT-Nachplan

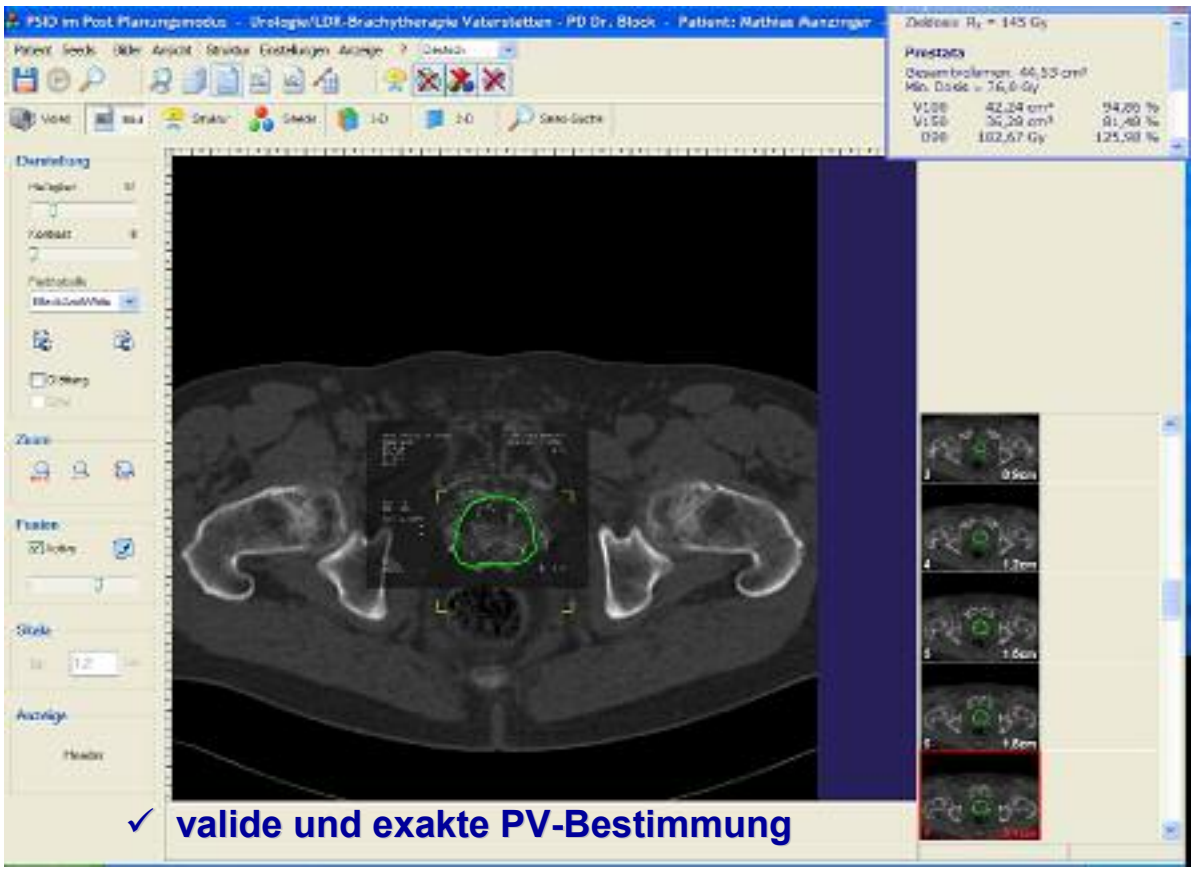
- **TRUS-Volumetrie: Lithotomieposition, 5 mm Inkremente**

→ exaktere PV-Bestimmung im CT



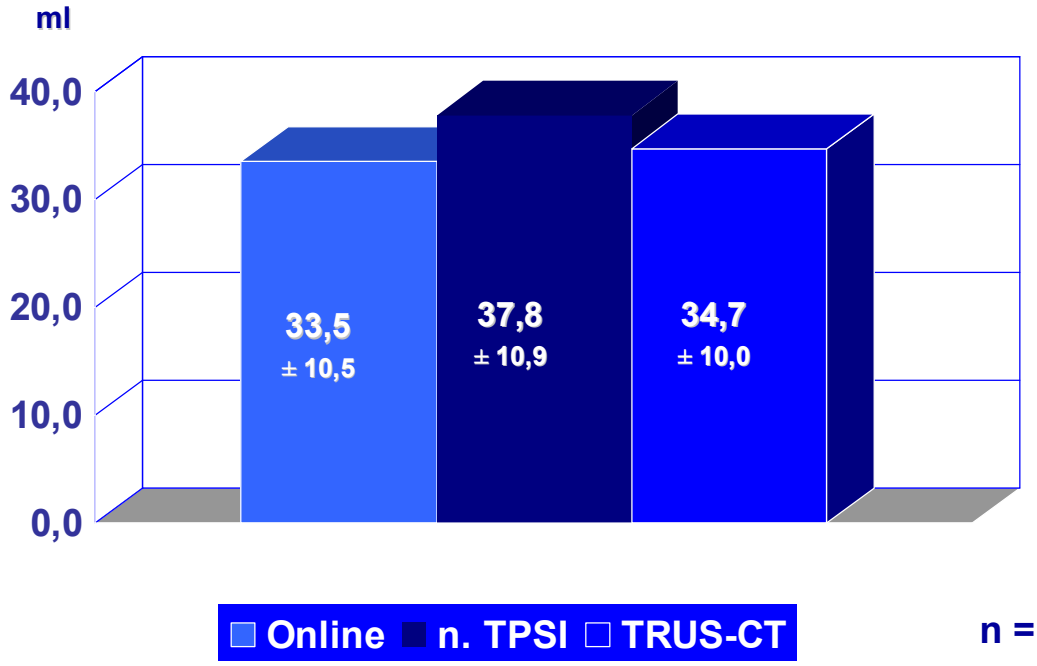


PV: CT-/TRUS-“Image Fusion“



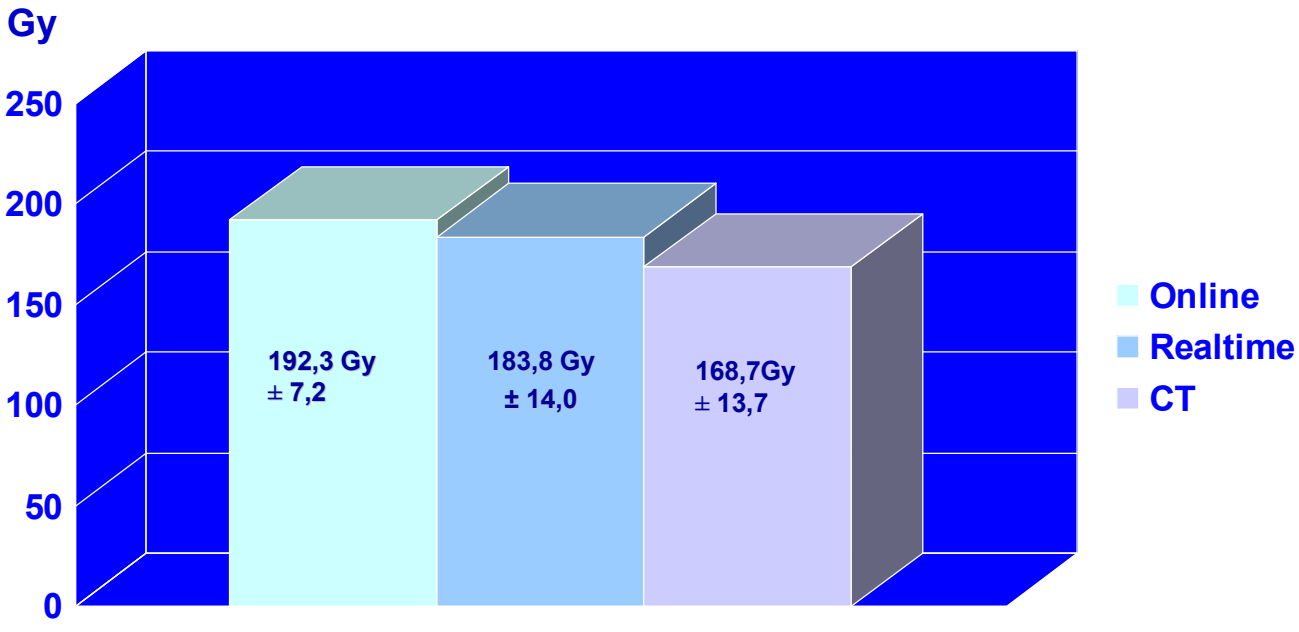
✓ **valide und exakte PV-Bestimmung**

Prostatavolumina (PV)



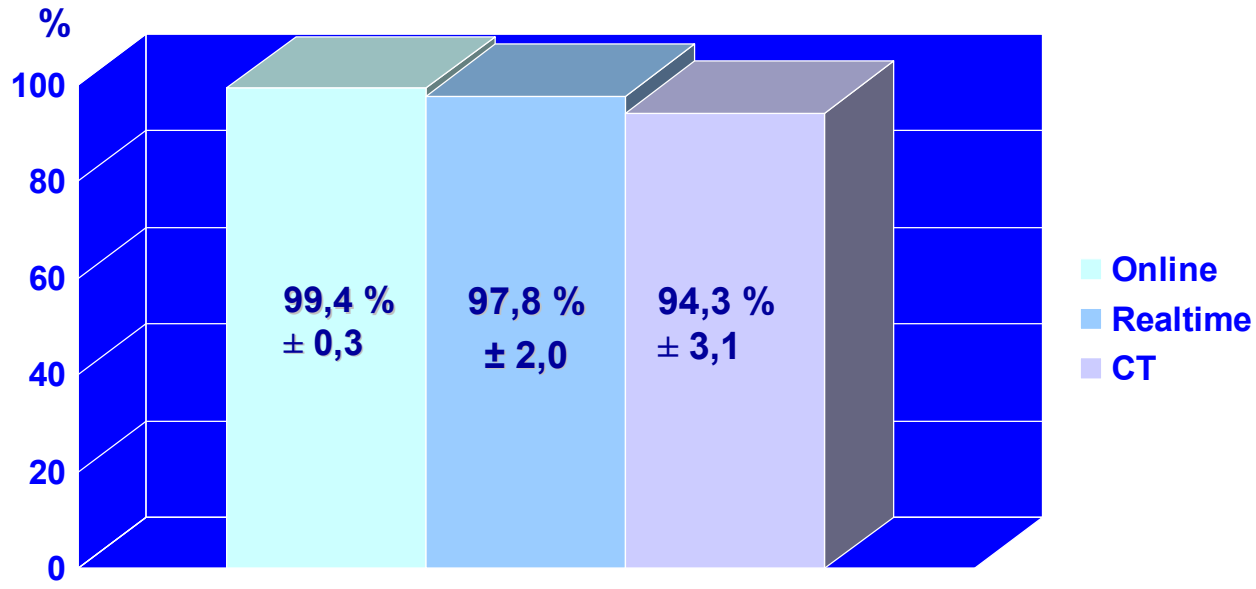
n = 164

Vergleich D90



n = 62

Vergleich V100



n = 62

TPSI-Monotherapie
- mod. RTOG GU Toxizitäts Skala -
(< 3 Monate post impl.)

Grad 1	90,3%
Grad 2	4,6 % (DK <1 Woche)
Grad 3	4,6 % (Pufi > 7 Tage)
Grad 4	0,5%
Grad 5	0 %

n = 218

TPSI-Monotherapie
- Spätkomplikationen -
(> 3 Monate post impl.)

Komplikation	eigenes Kollektiv
Inkontinenz	0 %
Erektionsstörung *	28,1 %

* 100/139 Pat., ≈ 80 % positiver Sildenafil-Effekt

Miktionsbeschwerden

- Irritation ± Obstruktion: 90,3%
- Behandlung:
  Alpha-Blocker-Wechsel (Terazosin 2x5 mg),
  Anticholinergikum,
  testgerechte Antibiose

Retention
- innerhalb von 24 h -

- <7 Tage: 4,6 %; >7 Tage: 4,6 %
- Therapie: EK bzw. Punktionsfistel
- Spontanes Ingangkommen der Miktion:
  4 Pat. (n. 58 - 142 Tagen)
- Interstitielle Laserkoagulation:
  3 Pat. (kontinent, PSA: 0,03-0,9 ng/ml)

Cave: „frühe“ TUR-P

- „Effective Life“:
  ^{125}J: 270 Tage, ^{103}Pd: 90 Tage
- Risiko: Inkontinenz
- Seed-Verlust
- Dosis-Verlust

TPSI + EBRT
- mod. RTOG GU Toxizitäts Skala -
(< 3 Monate post impl.)

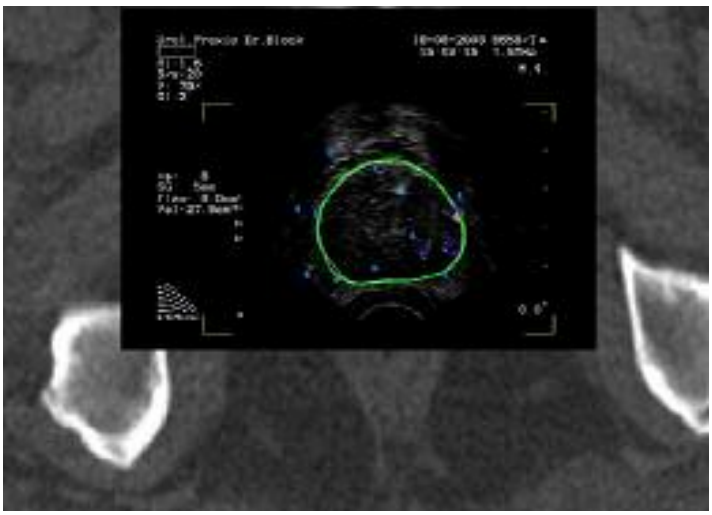
Grad 1	37/41 (90,2%)
Grad 2	2/41 (5,0 %)
Grad 3	1/41 (2,4 %)
Grad 4	0%
Grad 5	1/41 (2,4 %)

n = 41

TPSI + EBRT
- Spätkomplikationen -

Komplikation	eigenes Kollektiv
Inkontinenz	0 %
Erektionsstörung	6/12 (v. 22)

- ✓ **TPSI:**
  anerkannte Therapie-Alternative
- ✓ **Äquieffektiv zu RRP und EBRT**
- ✓ **Zunehmende Akzeptanz**
- ✓ **Adäquate Früh- und Spättoxizität**
- ✓ **Hohe Qualitätsanforderungen**
- ✓ **Technisch und zeitlich anspruchsvoll**
- ✓ **TRUS-Image Fusion**
- ✓ **Therapieentscheidung des Patienten**
- ✓ **Effizienz und Toxizität**
  RRP vs. EBRT vs. TPSI



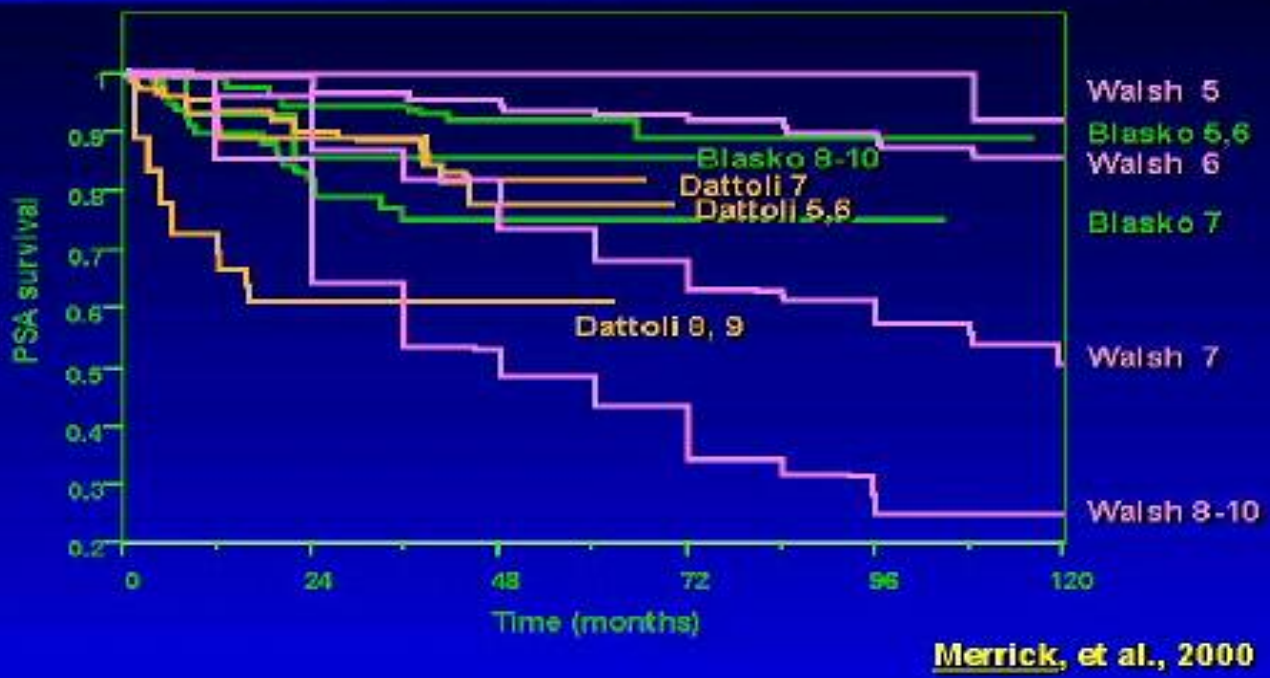
DGU-Kongreß 2003 (Hamburg)

- **„Ergebnisse (der Brachytherapie) vergleichbar RPX“**
- **„In den USA wurden im letzten Jahr mehr Brachytherapien als radikale Prostatektomien gemacht“**

R. Hautmann, Ulm

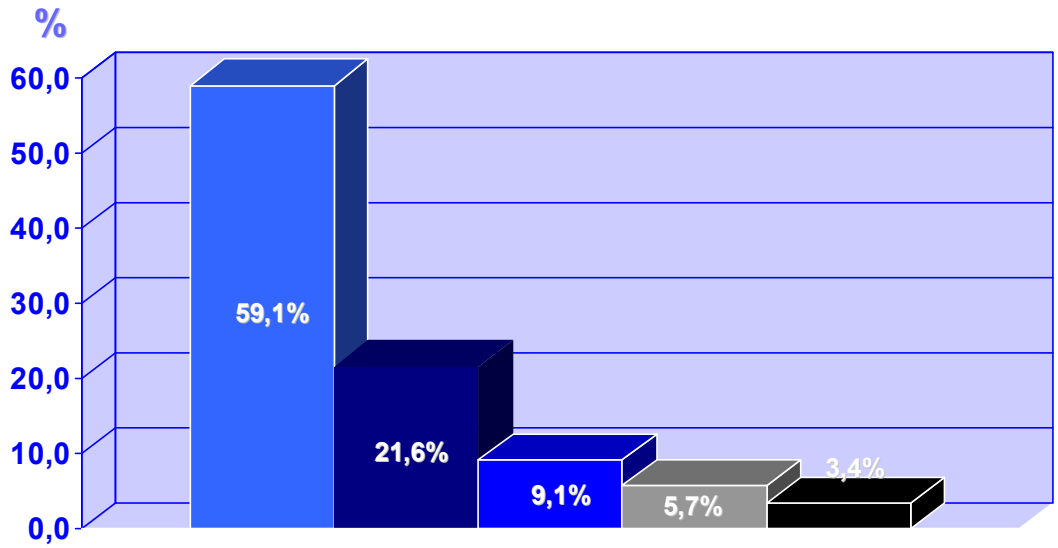
Biochemical (PSA) survival by Gleason score

brachytherapy (Blasko, Dattoli) vs. prostatectomy (Walsh)



Merrick, et al., 2000

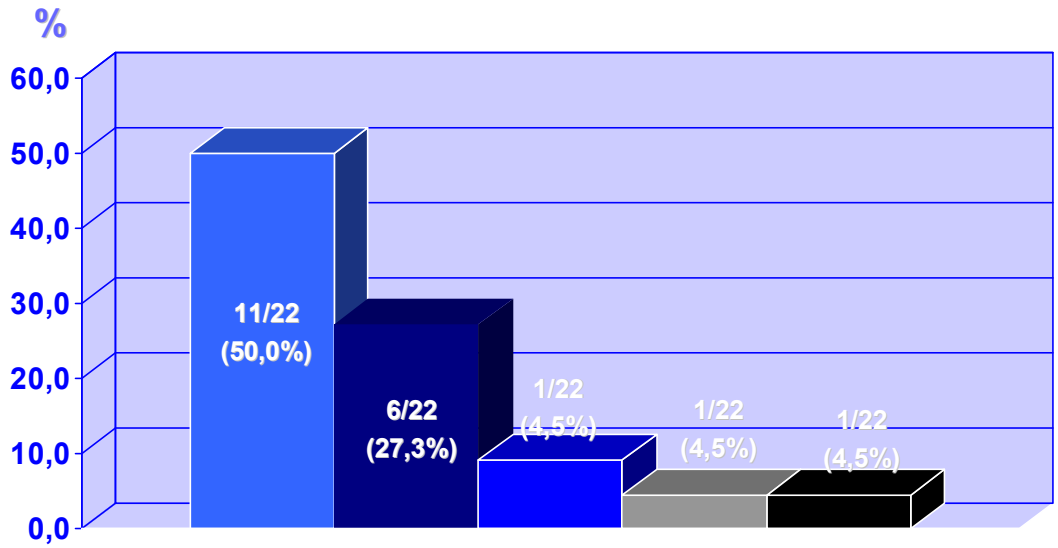
TPSI
- PSA- Verlauf: PSI-Monotherapie -



■ < 0,2 ng/ml
■ < 0,5 ng/ml
■ < 1,0 ng/ml
■ > 1,0 ng/ml
■ PSA-Rez.

n = 87
median: 29,9 Monate
mittel: 30,2 Monate

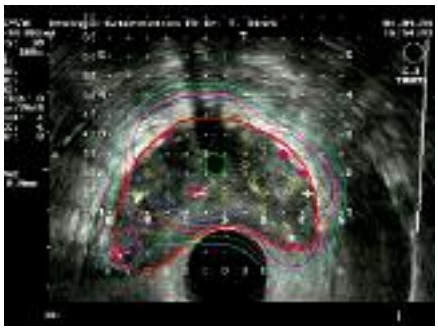
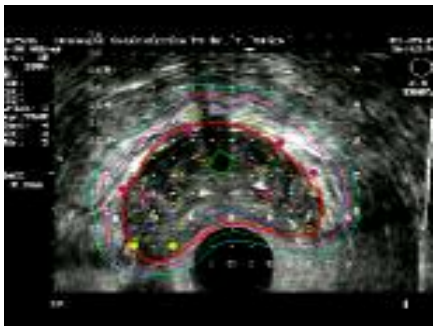
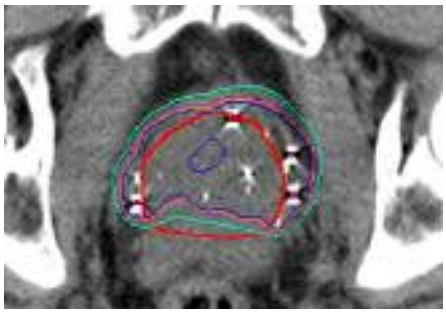
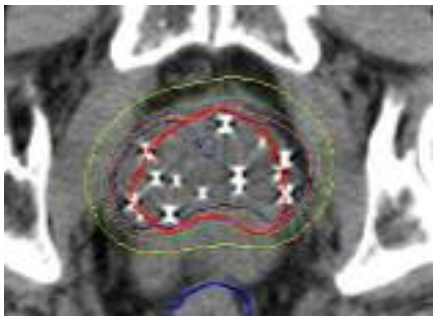
TPSI
- PSA- Verlauf: PSI + EBRT -



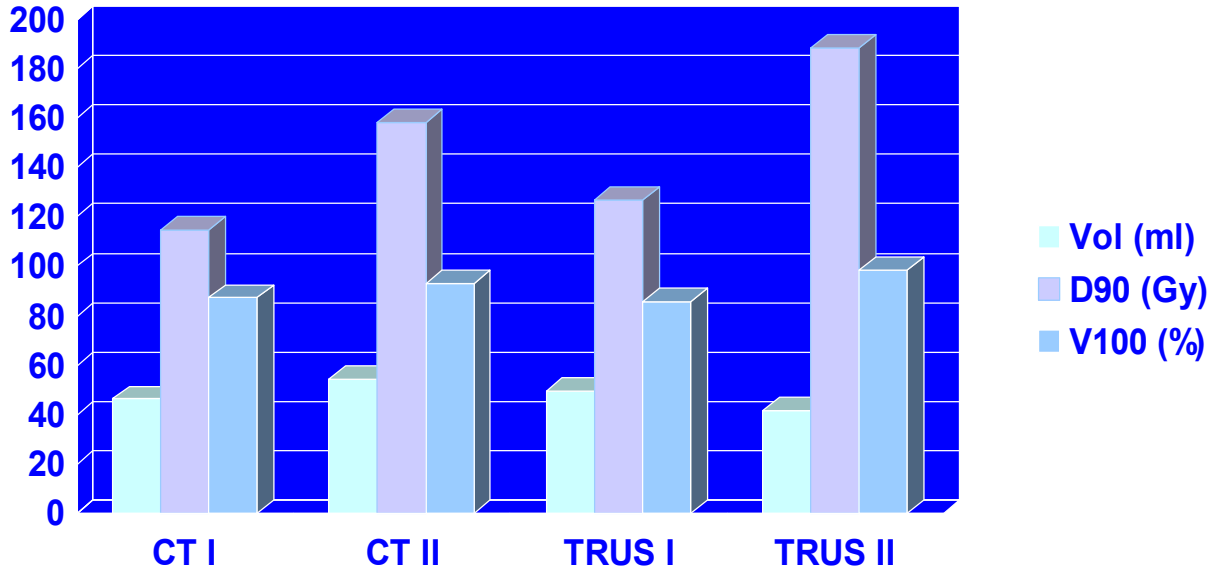
■ < 0,2 ng/ml
■ < 0,5 ng/ml
■ < 1,0 ng/ml
■ > 1,0 ng/ml
■ PSA-Rez.

n = 22
median: 29,9 Monate
mittel: 27,2 Monate

Qualitätssicherung bei TPSI
- „Nachspickung“ -

Dosimetrie nach „Nachspickung“

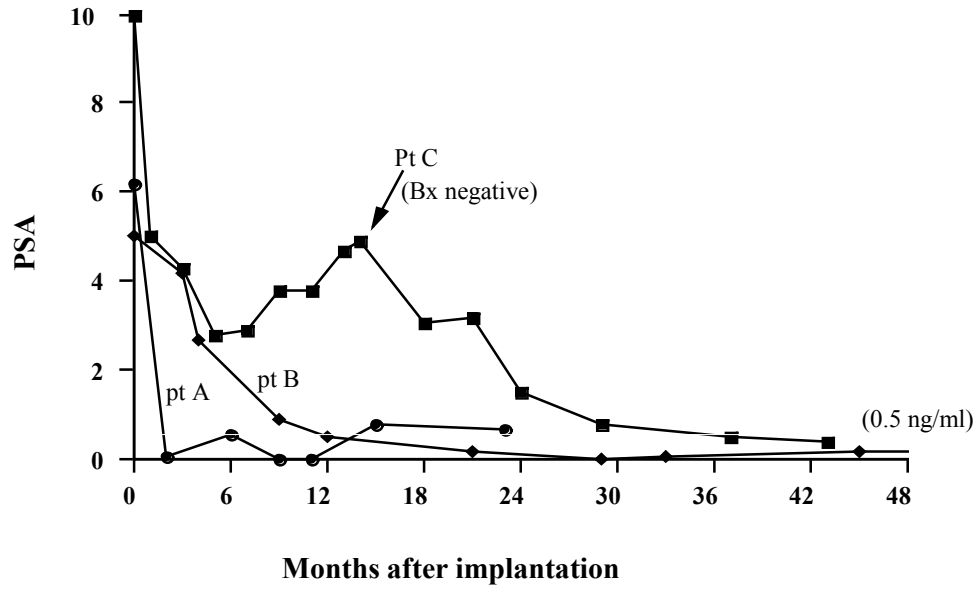


Qualitätssicherung bei TPSI
- „Nachspickung“ -

- **Quellenfehllage (0,0–1,0 cm; median 0,3 cm)**
- **Verlust an Dosis (1-13 %)**
- **Ausgleich:**
  zusätzliche Quellen (0–10; median 8) 10
  ⇒ D90 >140 Gy, V100 > 94%

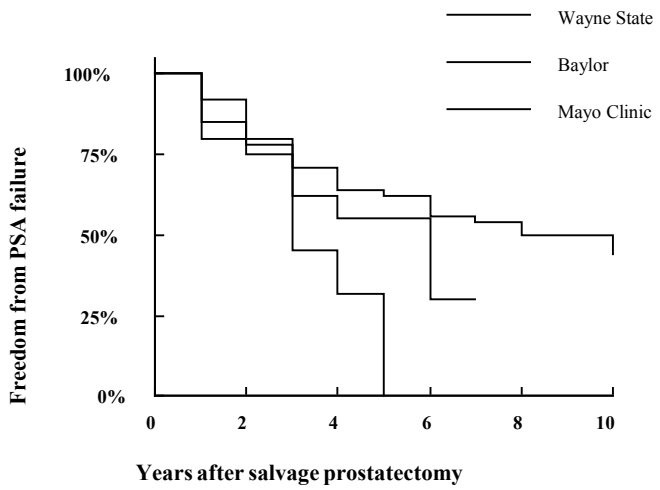
Cormack et al., IJROBP 2000

A multitude of post-implant PSA patterns



K. Wallner, Seattle, 2002

Salvage prostatectomy



K. Wallner, Seattle, 2002

Seed Migration Conclusions - SPI 2003 -

- **Lung Migration** Significantly Decreased with linked seeds
- **Pelvic Migration** Significantly decreased with linked seeds over loose Two stage/linked significantly better than linked conventional technique
- **Variance** Significantly improved with Linked seeds More Study necessary

Seed Migration to Lung Linked vs Loose Seeds

Loose Seeds	**109/472**	**23%**
Linked	**13/528**	**2 %**
		P=0.002

Seattle Prostate Institute 2003

Some current regimens - SPI 2003 -

Investigator	1st modality	EB dose	Isotope	Imp dose	Gap
Blasko, etc	EB	45 Gy	I-125/Pd-103	90/80 Gy	2-6 wks
Critz	Imp	45 Gy	I-125	80 Gy	3-6 wks
Wallner, Merrick	EB	44	Pd	86 Gy	0-2 wks
Wallner, Merrick	EB	20 Gy	Pd	113 Gy	0-2 wks
Dattoli	EB	41 Gy	Pd	80 Gy	2-6 wks
Stock	Imp	60 Gy	Pd	80-90 Gy	8 wks
Dattoli	EB	20 Gy	Pd		0-1 wk