BEHANDELOPTIES BIJ GELOKALISEERD PROSTAATCARCINOOM

PIM VAN LEEUWEN, UROLOOG

ANTONI VAN LEEUWENHOEK
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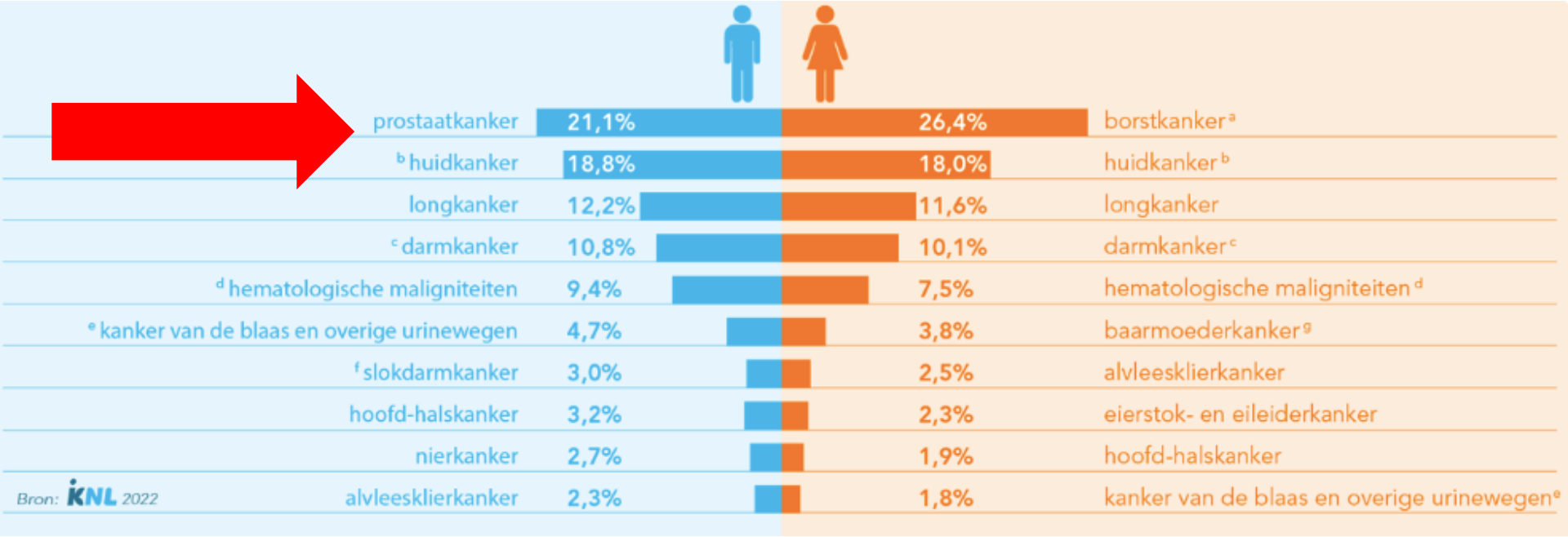
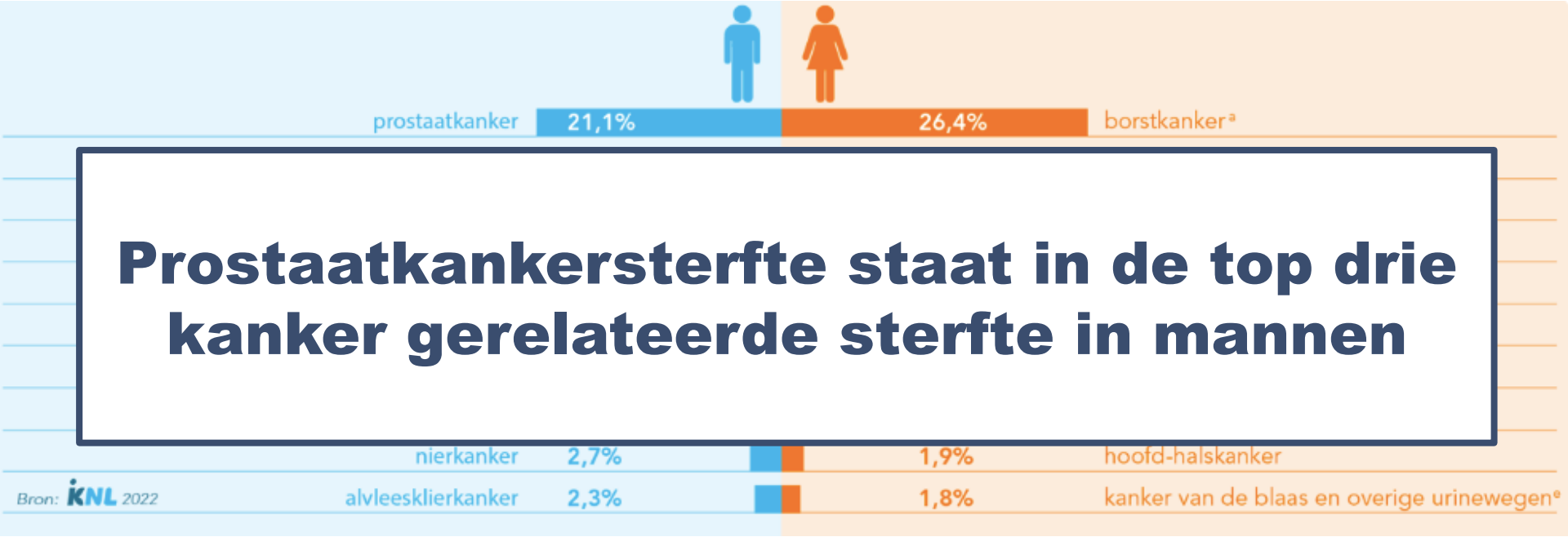
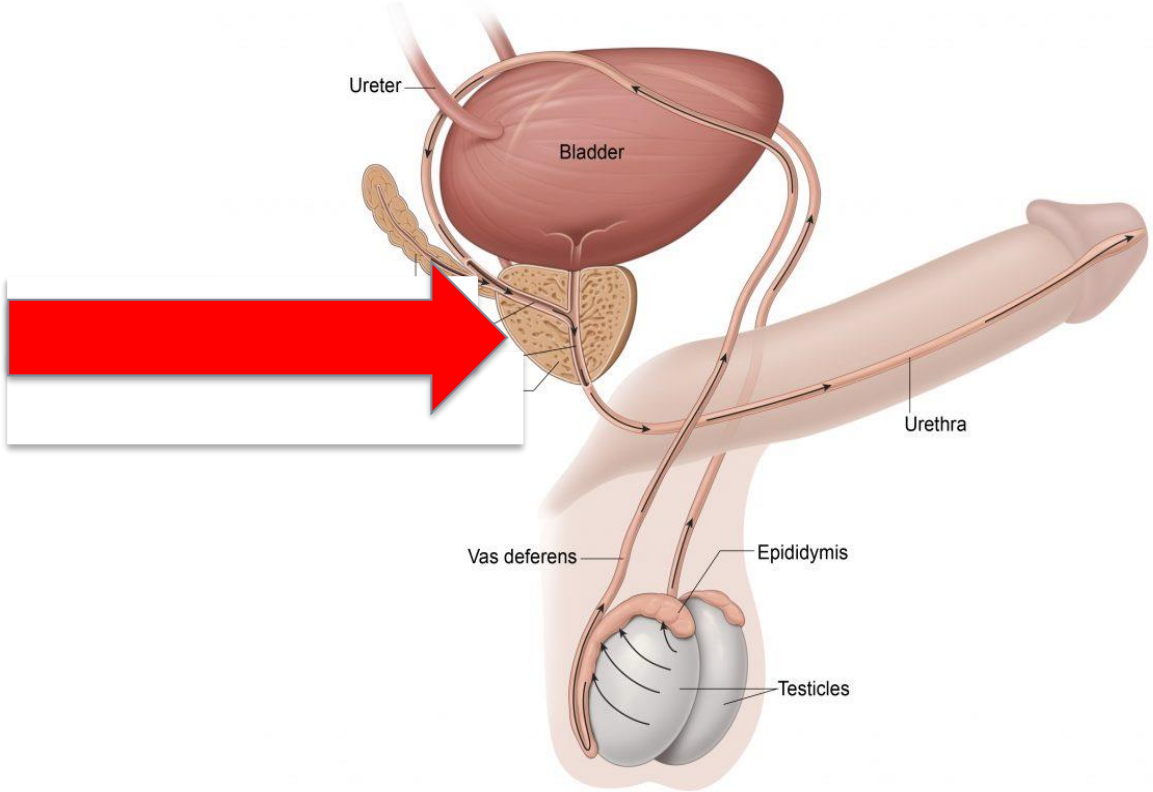
PROSTAATKANKER





Prostaatkankersterfte staat in de top drie kanker gerelateerde sterfte in mannen



DE PROSTAAT

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Er zijn verschillende soorten **prostaatkanker**:

Langzaam groeiende prostaatkanker
Langzaam groeiende kanker geeft pas na lange tijd klachten, of nooit.

Snel groeiende prostaatkanker
Geeft wel (ernstige) klachten, en kan dodelijk zijn. Bij deze soort geeft vroege behandeling een kleinere kans om problemen te krijgen van de ziekte.

PROSTAATKANKER

Prostaatkanker geeft geen klachten

In een verder gevorderd stadium kan **prostaatkanker** pijn in de botten veroorzaken als gevolg van uitzaaiingen.

Vroegdiagnostiek heeft als doel de asymptomatische kanker in een vroeg stadium te vinden zodat **genezing** mogelijk is en de klachten van uitzaaiingen **voorkomen** kunnen worden.

PROSTAATKANKER

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PSA, Prostaat Specifiek Antigeen, is een eiwit dat normaal bij mannen in geringe mate in het bloed aanwezig is.

PSA is een simpele bloedtest.

Een verhoging van het **PSA** kan veroorzaakt worden door prostaatkanker.

>80% mannen leeftijd 55-74 jaar PSA < 3.0 ng/ml

PSA TEST

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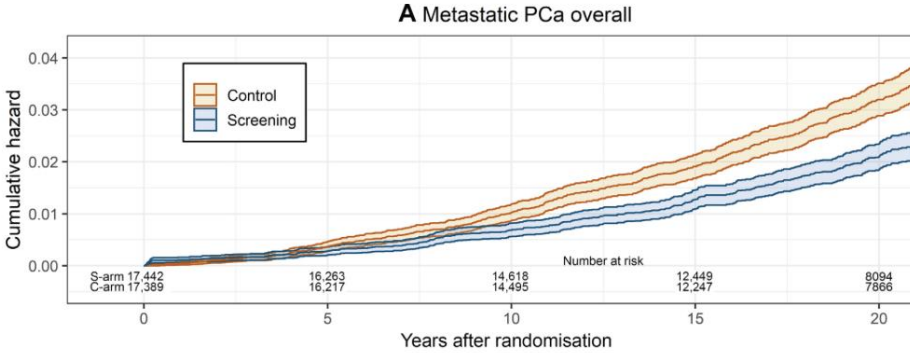
A Detailed Evaluation of the Effect of Prostate-specific Antigen–based Screening on Morbidity and Mortality of Prostate Cancer: 21-year Follow-up Results of the Rotterdam Section of the European Randomised Study of Screening for Prostate Cancer

Ivo I. de Vos [†,], Annick Meertens [†], Renée Hogenhout, Sebastiaan Remmers, Monique J. Roobol, on behalf of the ERSPC Rotterdam Study Group*

Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands



In tegenstelling tot populatiebrede screening is nu geïndividualiseerde (riskbased) vroegdiagnostiek mogelijk. Hierbij worden mannen geselecteerd op basis van risicofactoren.

TIJDEN ZIJN VERANDERD!!!

1. <u>We kunnen overdiagnose verminderen:</u>

   - Beter gebruik van PSA: leeftijd-specifiek PSA, PSA densiteit
   - Risk calculators +/- moleculaire markers
   - **MRI** voor biopten

     …… verminder aantal biopten

     …… diagnose van meer significante en minder insignificante kankers

2. <u>We kunnen de overbehandeling verminderen</u>

   - Toepassen van active surveillance in laag risico prostaatkanker

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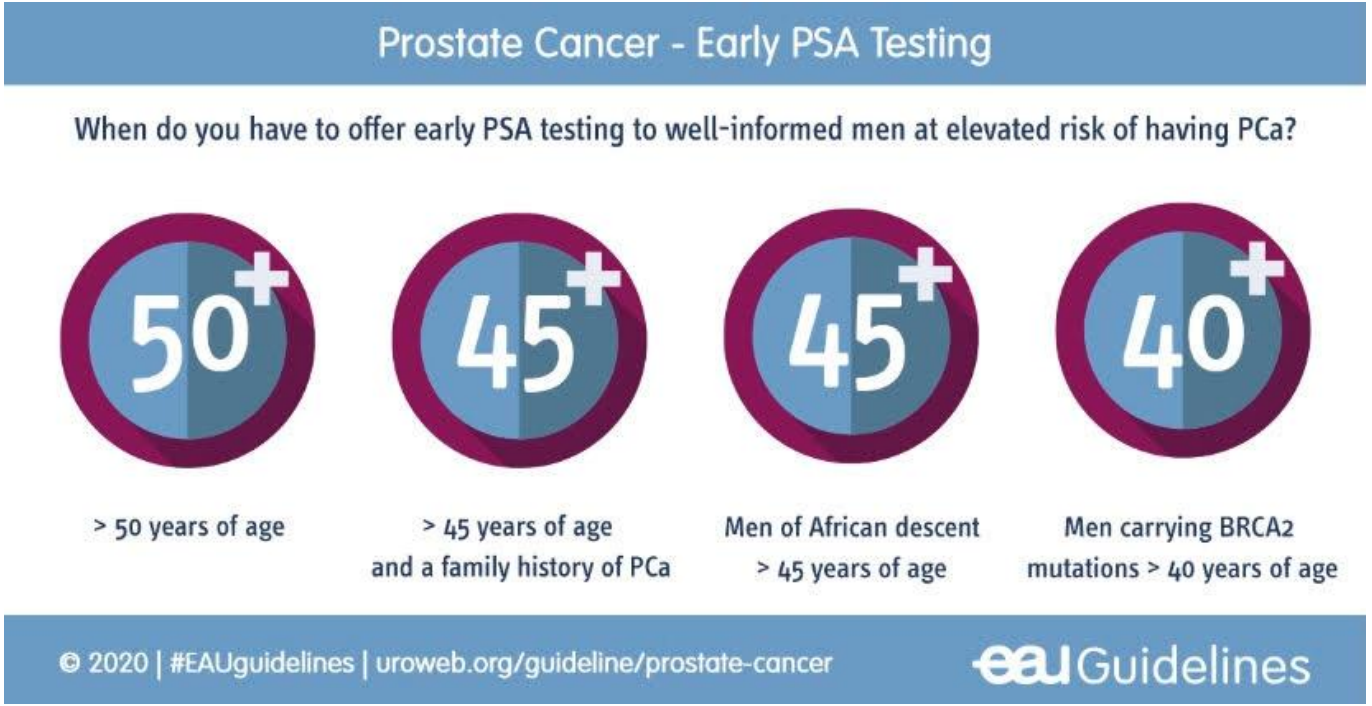

WIE TESTEN?

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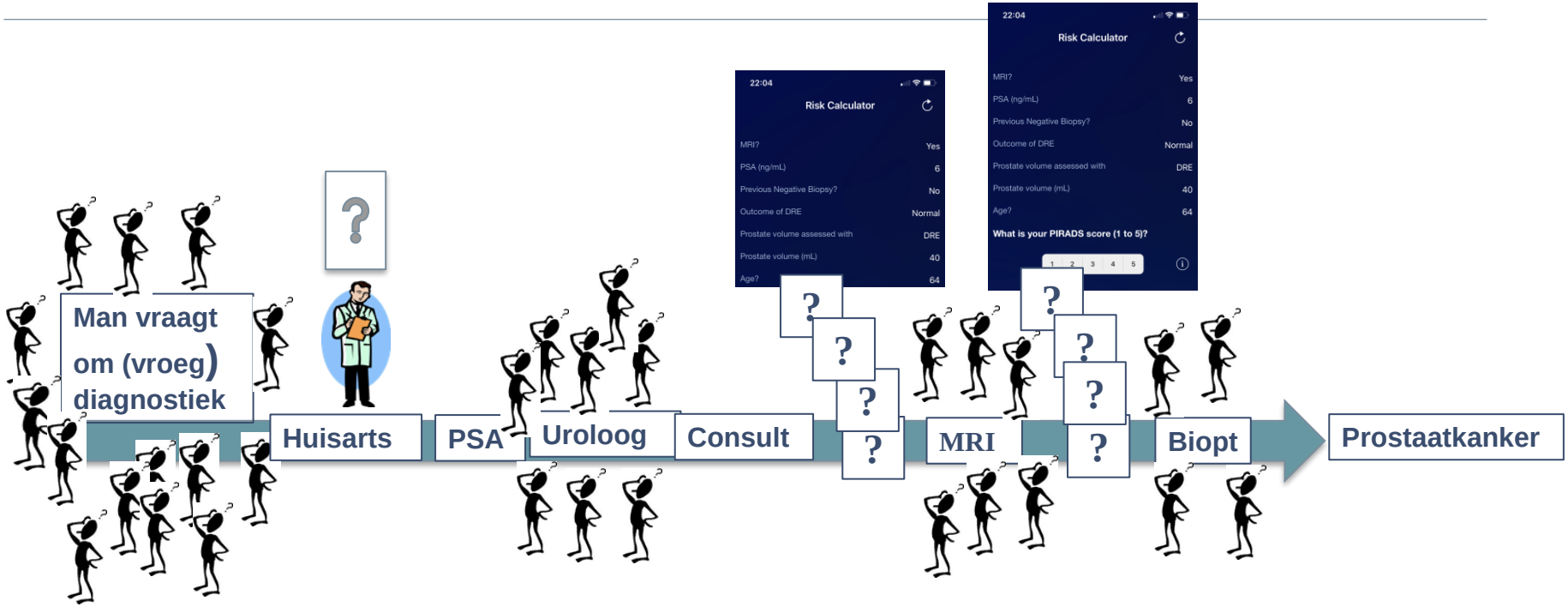
HUIDIGE DIAGNOSTISCH PROCES PROSTAATKANKER



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DIAGNOSE PROSTAATKANKER IS GESTELD, WAT NU?

- TNM
- ISUP
- PSA
- Low risk / intermediate risk / high risk

EAU GUIDELINES:

- Lokale behandeling = curatieve intentie

PROSTAATKANKER

EAU GUIDELINES:

WELKE BEHANDELING PAST HET BEST BIJ U?

- Lokale behandeling = curatieve intentie

  - Active Surveillance
  - Prostatectomie
  - Externe Radiotherapie extern
  - Brachytherapie
  - Focale behandeling (binnen een prospectieve studie)

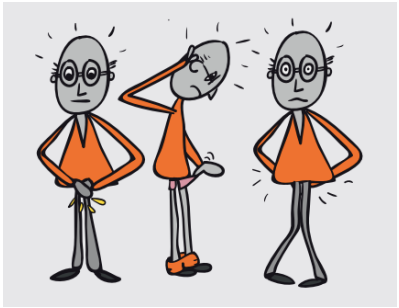
EAU GUIDELINES:

- Lokale behandeling = curatieve intentie
  - Alleen indien geen:
    - T4
    - M1
    - N1 ?

EAU GUIDELINES:

- Lokale behandeling = curatieve intentie
  - Alleen indien geen:
    - T4
    - M1
    - N1 ?

- “In localised disease a life expectancy of at least 10 years is considered mandatory for any benefit from local treatment”



Veel mannen hebben de keuze tussen:

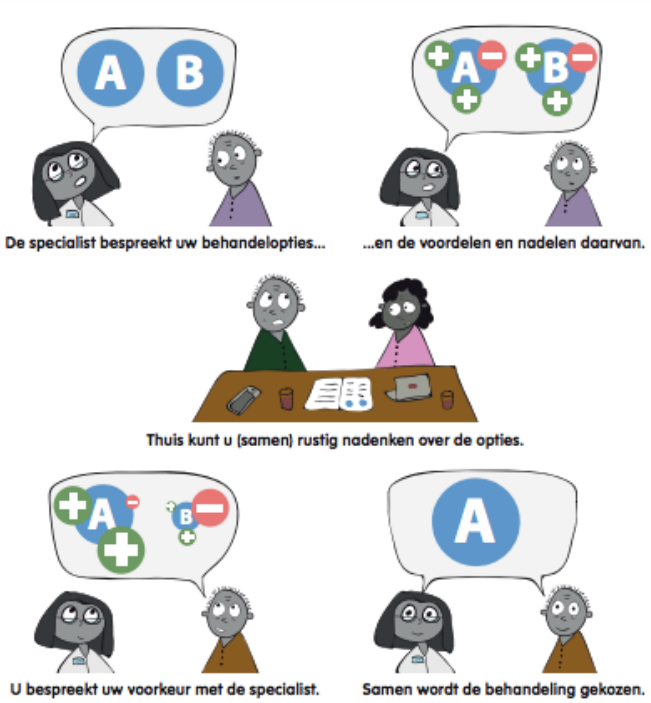
ACTIEF VOLGEN
(de tumor wordt in de gaten gehouden en er wordt pas behandeld als de tumor groeit)

BRACHYTHERAPIE
(inwendige bestraling)

UITWENDIGE BESTRALING

OPERATIE
(radicale prostatectomie)

SAMEN BESLISSEN



	Actief volgen*	Brachy-therapie	Uitwendige bestraling	Operatie
1. Ongewild urineverlies	**7%**	26%	23%	**60%**
2. Gebruik van incontinentie-materiaal	**2%**	14%	11%	**54%**
3. Totale incontinentie	**1%**	2%	2%	**5%**
4. Verhoogde aandrang om te plassen	**24%**	**65%**	48%	29%
5. Diarree	8%	**24%**	16%	**4%**
6. Erectie-problemen	**16%**	28%	56%	**76%**
7. Spanning over kanker	**31%**	15%	**9%**	11%
8. Spijt van de behandeling	**3%**	4%	4%	**3%**
9. Overlijden aan prostaat-kanker	**Minder dan 1 %**	**Minder dan 1 %**	**Minder dan 1 %**	**Minder dan 1 %**

ACTIVE SURVEILLANCE LOW RISK PROSTAATKANKER

- Vast volgprogramma met periodiek serum PSA, MRI, herhaalbiopten.
- Doel: voorkom onnodige behandeling (bijwerkingen) maar behandel op tijd indien nodig

ACTIVE SURVEILLANCE – WATCHFUL WAITING

	Active surveillance	Watchful waiting
Treatment intent	Curative	Palliative
Follow-up	Pre-defined schedule	Patient-specific
Assessment/markers used	DRE, PSA, mpMRI, re-biopsy	Not pre-defined, but dependent on development of symptoms of progression
Life expectancy	> 10 years	< 10 years
Aim	Minimise treatment-related toxicity without compromising survival	Minimise treatment-related toxicity
Comments	Low-risk patients	Can apply to patients with all stages

ACTIVE SURVEILLANCE LOW RISK PROSTAATKANKER

ORIGINAL ARTICLE

Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, C. Metcalfe, M. Davis, E.L. Turner, R.M. Martin, G.J. Young, E.I. Walsh, R.J. Bryant, P. Bollina, A. Doble, A. Doherty, D. Gillatt, V. Gnanapragasam, O. Hughes, R. Kockelbergh, H. Kynaston, A. Paul, E. Paez, P. Powell, D.J. Rosario, E. Rowe, M. Mason, J.W.F. Catto, T.J. Peters, J. Oxley, N.J. Williams, J. Staffurth, and D.E. Neal, for the ProtecT Study Group*

The ProtecT trial: 1999-2009

(*Pro*state *te*sting for *c*ancer and *T*reatment)

82,429 men PSA-tested
2965 prostate cancers detected

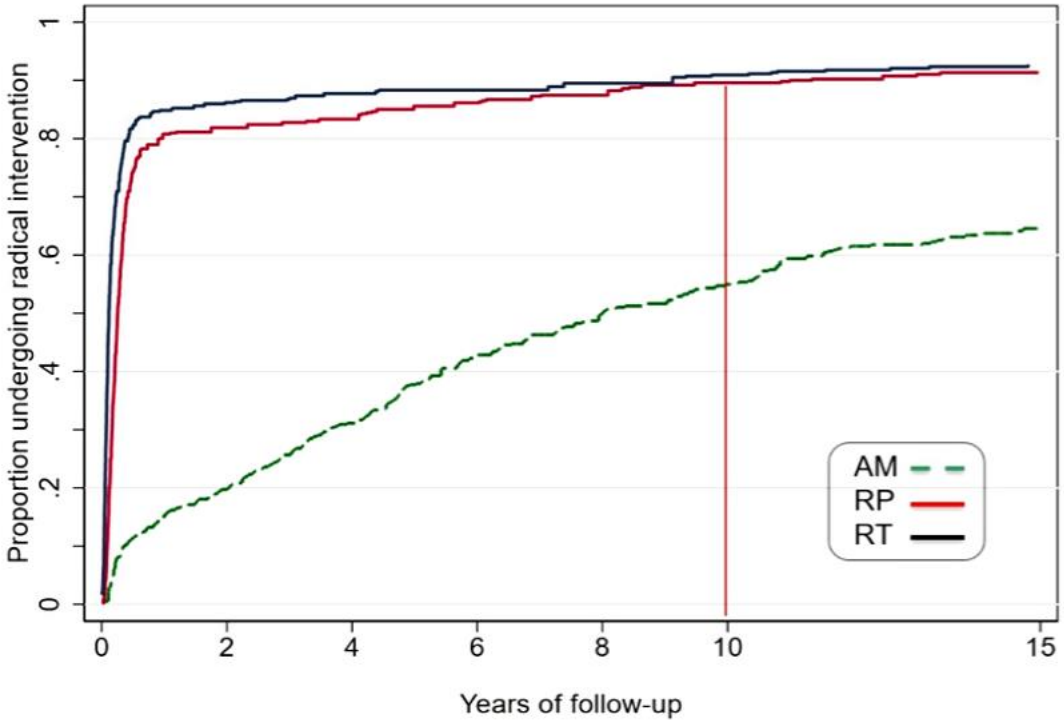
↓

1643 Randomly assigned

↓

545	553	545
Active Monitoring	**Radical Prostatectomy**	**Radical Radiotherapy**

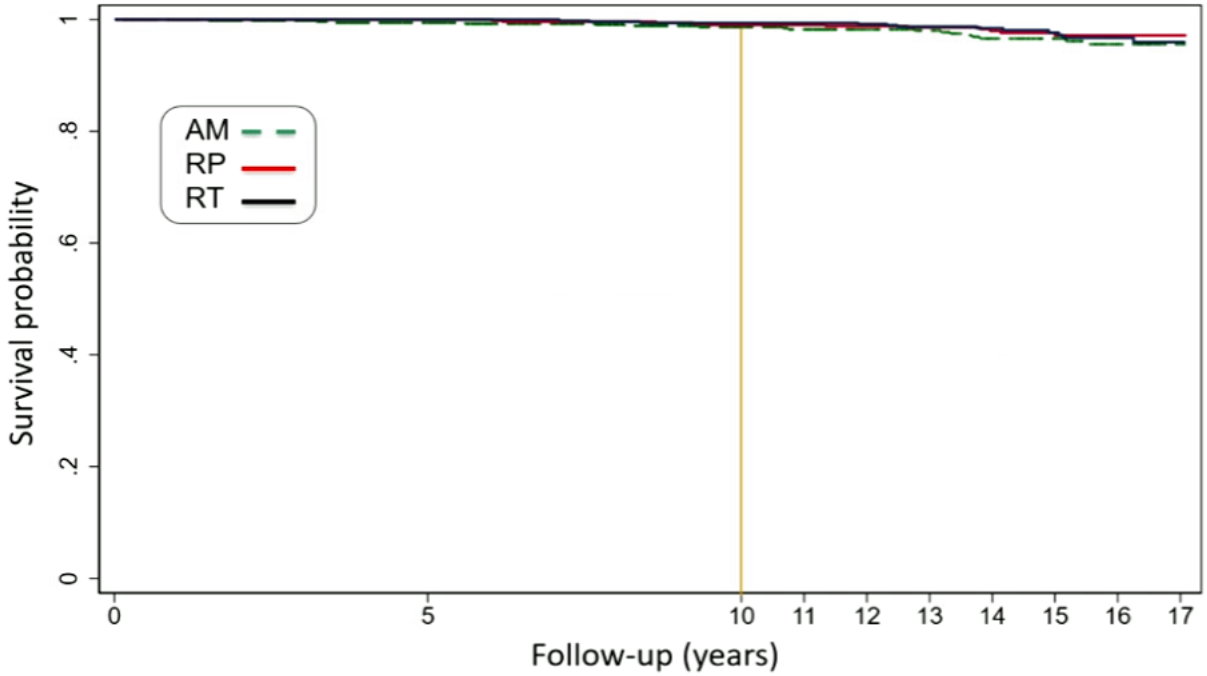
Undergoing radical intervention



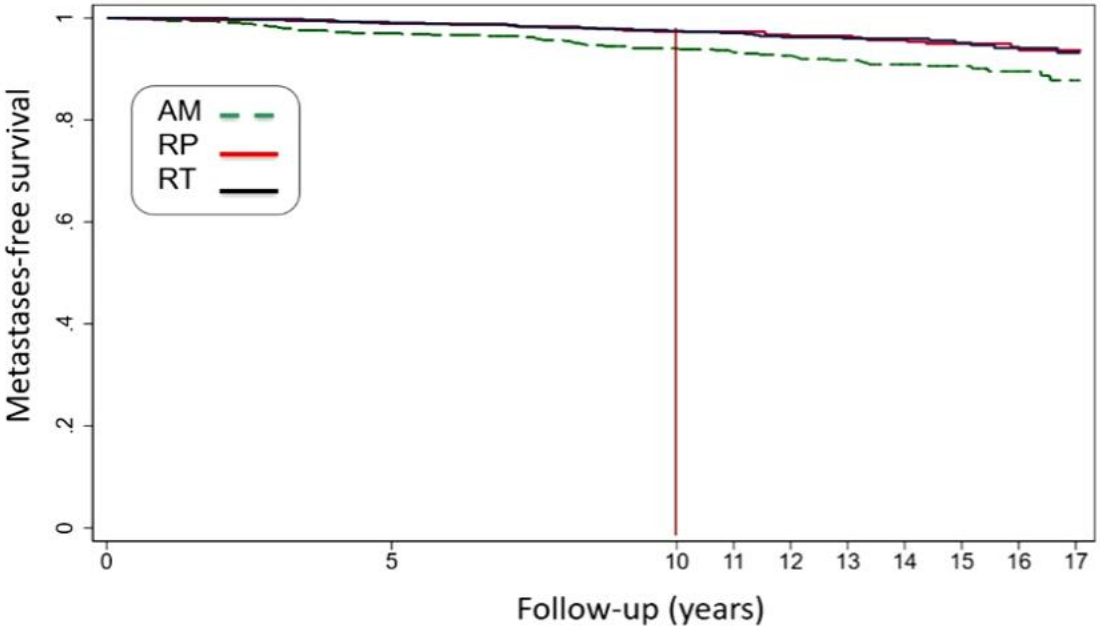
Allocated group	Moved to radical treatment within median 15 years
Active monitoring (%)	333/545 (61)
Prostatectomy (%)	500/553 (90)
Radiotherapy (%)	504/545 (92)

Kaplan–Meier estimates of the Cumulative Probability of Undergoing Radical Intervention during the Follow-up Period, according to Treatment Group.

Prostate Cancer-specific survival



Metastases


Metastases-free survival
0
.2
.4
.6
.8
1
AM
RP
RT
0
5
10
11
12
13
14
15
16
17
Follow-up (years)

WAT ZIJN DE NADELEN VAN UITGESTELDE BEHANDELING?

	AS	RP	RT
Angst	34,30%	28,60%	31,60%
Depressie	14,90%	10,70%	22,80%

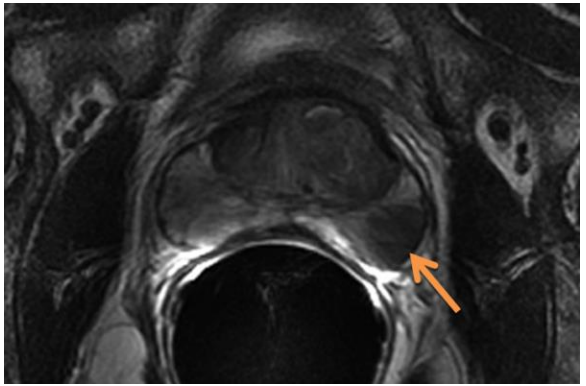
CONCLUSIES ACTIVE SURVEILLANCE

• Slechtere Prostaatkanker Spec Survival	Nee
• Slechtere Overall Survival	Nee
• Risico op metastasen	Ja , 50%

CRITERIA ACTIEVE SURVEILLANCE

- Actieve (uitgestelde) behandeling bij > 10 jaar levensverwachting

- Low risk
  - ISUP 1 prostaatkanker
  - ISUP 2 target biopten geen cribiforme groei
  - ≤ cT2a
  - mT2
  - PSA?



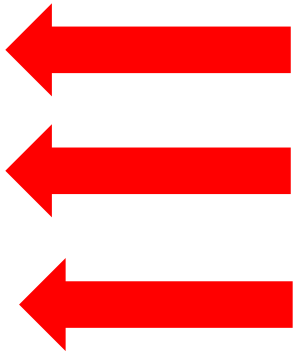
BEHANDELING INTERMEDIATE EN HOOG RISICO PROSTAATKANKER

- Externe radiotherapie +/- hormonale therapie
- Brachytherapie
- Radicale Prostatectomie

EAU – EANM – ESTRO – ESUR – ISUP – SIOG Guidelines on Prostate Cancer

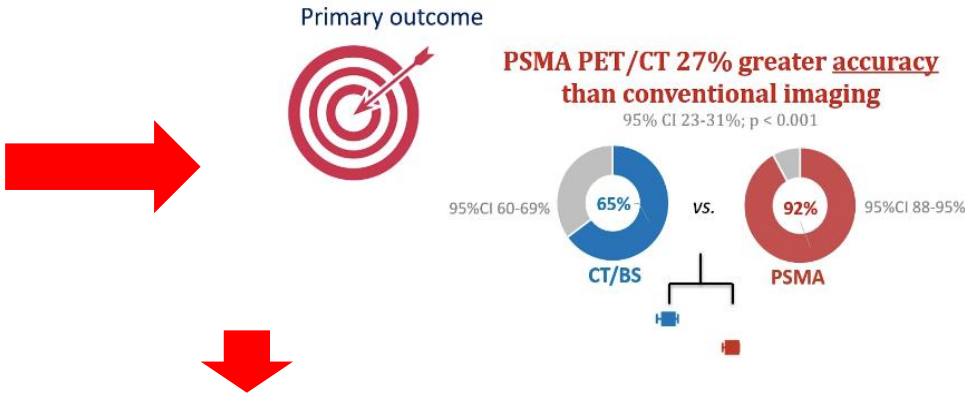
Any risk group staging	Strength rating
Use pre-biopsy MRI for local staging information.	Weak
Low-risk localised disease	
Do not use additional imaging for staging purposes.	Strong
Intermediate-risk disease	
In ISUP grade ≥ 3, include at least cross-sectional abdominopelvic imaging and a bone-scan for metastatic screening.	Weak
High-risk localised disease/locally advanced disease	
Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.	Strong

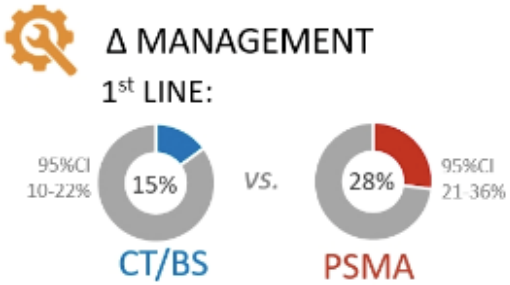
Summary of evidence	LE
PSMA PET/CT is more accurate for staging than CT and bone scan but to date no outcome data exist to inform subsequent management.	1b



Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study

*Michael S Hofman, Nathan Lawrentschuk, Roslyn J Francis, Colin Tang, Ian Vela, Paul Thomas, Natalie Rutherford, Jarad M Martin, Mark Frydenberg, Ramdave Shakher, Lih-Ming Wong, Kim Taubman, Sze Ting Lee, Edward Hsiao, Paul Roach, Michelle Nottage, Ian Kirkwood, Dickon Hayne, Emma Link, Petra Marusic, Anetta Matera, Alan Herschtal, Amir Iravani, Rodney J Hicks, Scott Williams, Declan G Murphy, for the proPSMA Study Group Collaborators**





Hofman et al. Lancet. 2020

KAN PSMA PET/CT DE DIAGNOSTISCHE PLND VERVANGEN?

	Number of men	PER PATIENT ANALYSIS	PER NODE/TEMPLATE ANALYSIS
SENSITIVITY			
Yaxley et al, J Urol, 2019	208	38%	24%
Maurer et al J Urol, 2016	130	65%	73%
Van Leuween, BJU Int, 2019	140	53%	NA
van Kalmthout LWM et al, J Urol, 2020	103	41%	36%
Jansen et al, EJNMI, 2020	117	41%	34%
SPECIFICITY			
Yaxley et al, J Urol, 2019	208	93.5%	99.5%
Maurer et al J Urol, 2016	130	98%	99
Van Leuween, BJU Int, 2019	140	88%	NA
van Kalmthout LWM et al, J Urol, 2020	103	90%	96%
Jansen et al, EJNMI, 2020	117	94%	98%

	Lesion-based accuracy			
	Sensitivity	Specificity	PPV	NPV
Overall	71%	99%	91%	98%
>3 mm	82%	99%	92%	99%

Sensitiviteit is matig

Van Leeuwen et al. BJUI 2017;

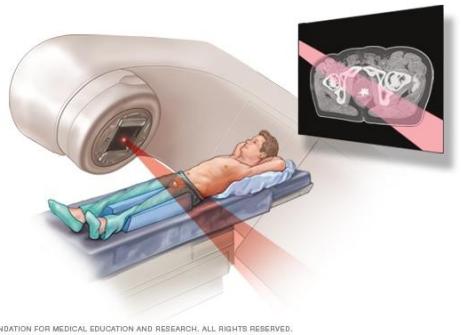
BEHANDELING INTERMEDIATE EN HOOG RISICO PROSTAATKANKER

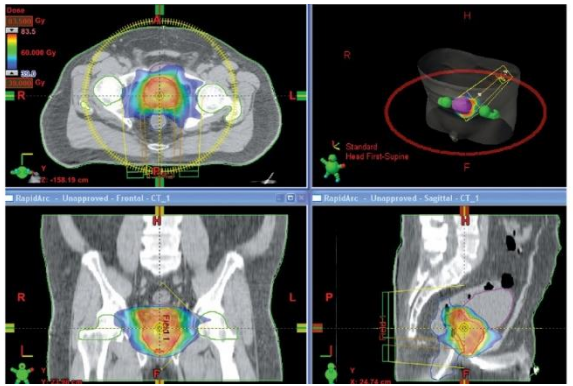
- Externe radiotherapie +/- hormonale therapie
- Brachytherapie
- Radicale Prostatectomie

Prostatectomie
EBRT
brachytherapie

RADIOTHERAPIE, EXTERN (EBRT)

- 64 gray in 20, 74 gray in 28
- Image-guided





RADIOTHERAPIE, EXTERN (EBRT)

- 60 (20) 74 (28) gray
- Image-guided
- Eventueel met hormonen

  Intermediate risk: 6-18 mnd

  High risk: 24-36 mnd

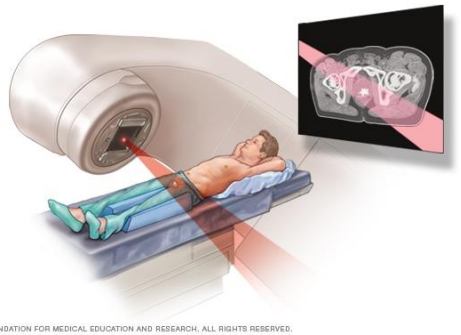
Trial	TNM stage	n	Trial	ADT	RT	Effect on OS
RTOG 85-31 2005 [661]	T3 or N1 M0	977	EBRT ± ADT	Orchiectomy or LHRH agonist 15% RP	65-70 Gy	Significant benefit for combined treatment (p = 0.002) seems to be mostly caused by patients with ISUP grade 2-5
RTOG 94-13 2007 [666]	T1c-4 N0-1 M0	1,292	ADT timing comparison	2 mo. neoadjuvant plus concomitant vs. 4 mo. adjuvant suppression	Whole pelvic RT vs. prostate only; 70.2 Gy	No significant difference between neoadjuvant plus concomitant vs. adjuvant androgen suppression therapy groups (interaction suspected)
RTOG 86-10 2008 [662]	T2-4 N0-1	456	EBRT ± ADT	Goserelin plus flutamide 2 mo. before, plus concomitant therapy	65-70 Gy RT	No significant difference at 10 yr.
D'Amico AV, *et al.* 2008 [663]	T2 N0 M0 (localised unfavourable risk)	206	EBRT ± ADT	LHRH agonist plus flutamide for 6 mo.	70 Gy 3D-CRT	Significant benefit (HR: 0·55, 95% CI: 0.34-0.90, p = 0.01) that may pertain only to men with no or minimal c morbidity
RTOG 92-02 2008 [667]	T2c-4 N0-1 M0	1554	Short vs. prolonged ADT	LHRH agonist given for 2 yr. as adjuvant after 4 mo. as neoadjuvant	65-70 Gy	p = 0.73, p = 0.36 overall; significant benefit (p = 0.044) (p = 0.0061) in subset with ISUP grade 4-5
EORTC 22961 2009 [668]	T1c-2ab N1 M0, T2c-4 N0-1 M0	970	Short vs. prolonged ADT	LHRH agonist for 6 mo. vs. 3 yr.	70 Gy 3D-CRT	Better result with 3 yr. treatment than with 6 mo. (3.8% improvement in survival at 5 yr.)
EORTC 22863 2010 [660]	T1-2 poorly differentiated and M0, or T3-4 N0-1 M0	415	EBRT ± ADT	LHRH agonist for 3 yr. (adjuvant)	70 Gy RT	Significant benefit at 10 yr. for combined treatment (HR: 0.60, 95% CI: 0.45-0.80, p = 0.0004).
TROG 96-01 2011 [664]	T2b-4 N0 M0	802	Neoadjuvant ADT Duration	Goserelin plus flutamide 3 or 6 mo. before, plus concomitant suppression	66 Gy 3D-CRT	No significant difference in OS reported; benefit in PCa-specific survival (HR: 0.56, 95% CI: 0.32-0.98, p = 0.04) (10 yr.: HR: 0.84, 0.65-1.08, p = 0.18)
RTOG 99-10 2015 [669]	intermediate risk 94% T1-T2, 6% T3-4	1,579	Short vs. prolonged ADT	LHRH agonist 8 + 8 vs. 8 + 28 wk.	70.2 Gy 2D/3D	67 vs. 68%, p = 0.62, confirms 8 + 8 wk. LHRH as a standard

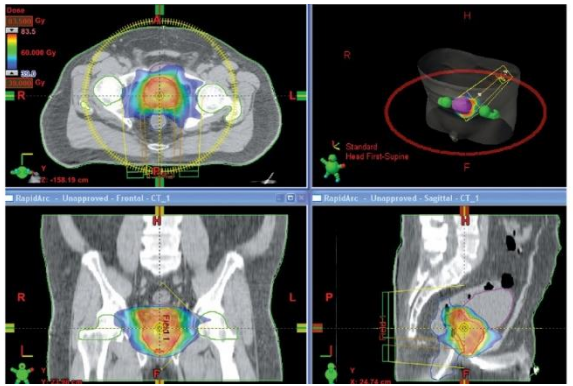
ADT = androgen deprivation therapy; CI = confidence interval; EBRT = external beam radiotherapy in standard fractionation; HR = hazard ratio; LHRH = luteinising hormone-releasing hormone; mo. = months; n = number of patients; OS = overall survival; RP = radical prostatectomy; RT = radiotherapy; wk = week; yr. = year.

Prostatectomie
EBRT
brachytherapie

RADIOTHERAPIE, EXTERN (EBRT)

- cT1a t/m cT3b
- Alle ISUP
- Nadelen:
  - late effecten radiotherapie (leeftijd pt?)
  - blaas, darm, erectiele dysfunctie
  - effecten hormonale therapie





Hypofractionation

HYPOFRACTIONATION *(MODERATE: 19-20X)*

- Meta-analysis, n=7796 (17 studies)

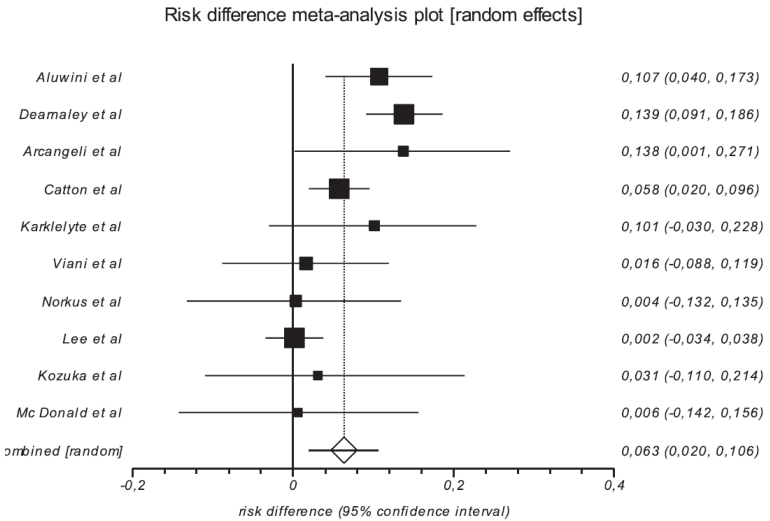
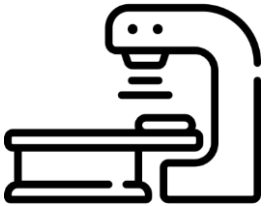


Fig. 2. Pooled analysis of risk of worse acute GI toxicity after moderate HF vs SF radiotherapy.

Toename gastro-intestinal toxiciteit for HF: 6.3% (2-11%)

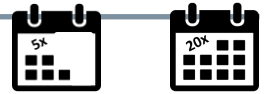
Geen toename genito-urinary toxiciteit



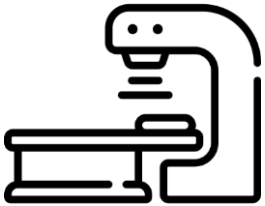
Sinzabakira Clin Trans Rad Oncol 2023

ULTRA-HYPOFRACTIONATION *(>5GY/FRACTION)*

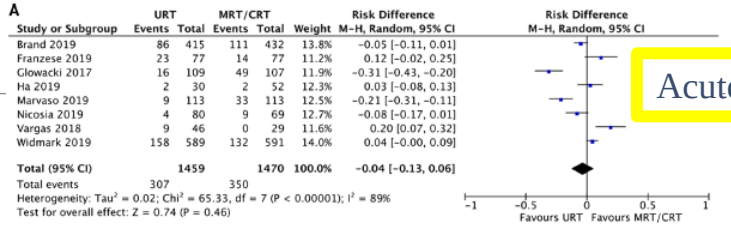
SYSTEMATIC REVIEW, N=2929, 8 STUDIES



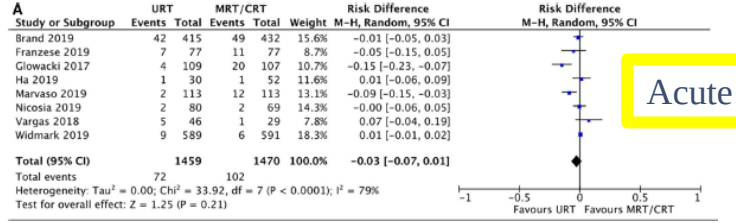
Geen verdere toename acute/late GI/GU toxiciteit



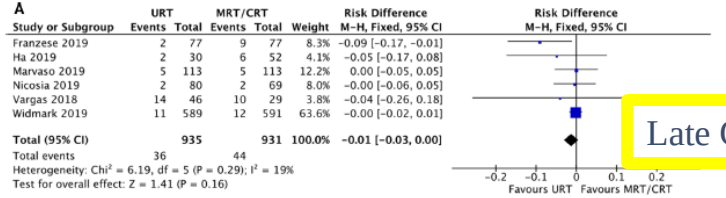
Baccaglini Clinical and Translational Oncology (2022)



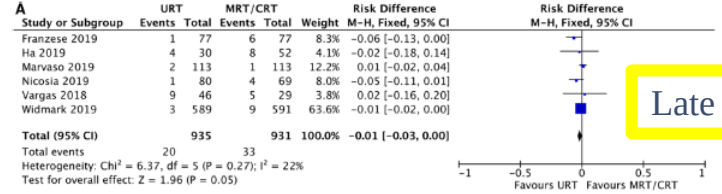
Acute GU



Acute GI



Late GU



Late GI

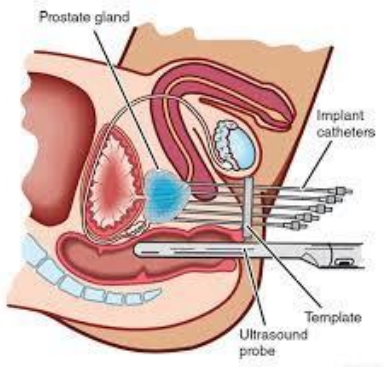
Hormoon therapie

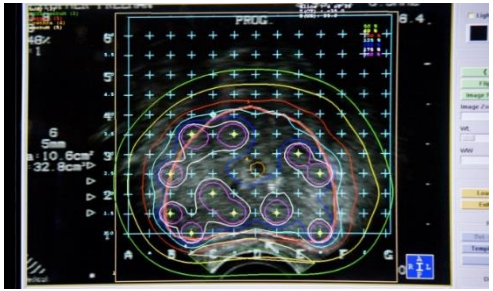
Prostatectomie
EBRT
Brachytherapie

RADIOTHERAPIE, BRACHYTHERAPIE

- cT1b t/m cT2a
- ISUP 1-3
- IPSS < 13, Qmax > 15 ml/sec, niet na turp

- Voor/Nadelen:
  - effect op blaas, geen darm
  - erectiele functie beter
  - Meer acute effecten, maar die verdwijnen deels
  - mn HDR brachytherapie mogelijk minder bijw dan EBRT

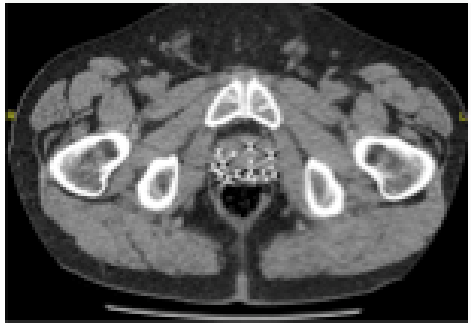




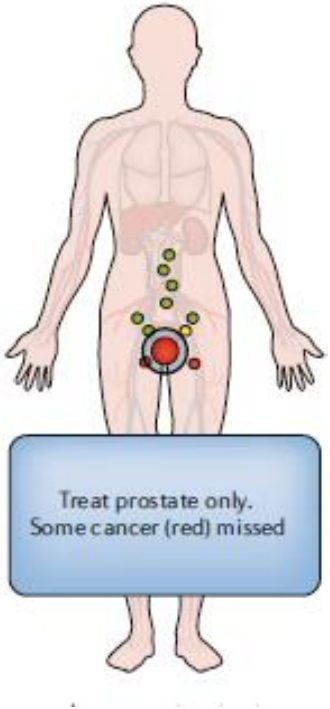
Prostatectomie
EBRT
Brachytherapie

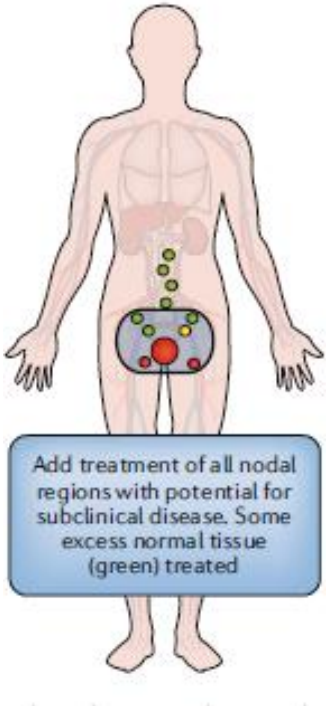
BRACHYTHERAPY LONG TERM (>15 YEARS)

- N=39, 17.8y after brachy, 80yrs
- 13% incontinence
- 33% LUTS
- 8% diarrhea
- 61% ED



Externe Radiotherapie in High Risk Prostaatkanker





Prostate-only radiotherapy (PORT):
Standard of care for clinically node negative (cN0) prostate cancer (PCa) patients

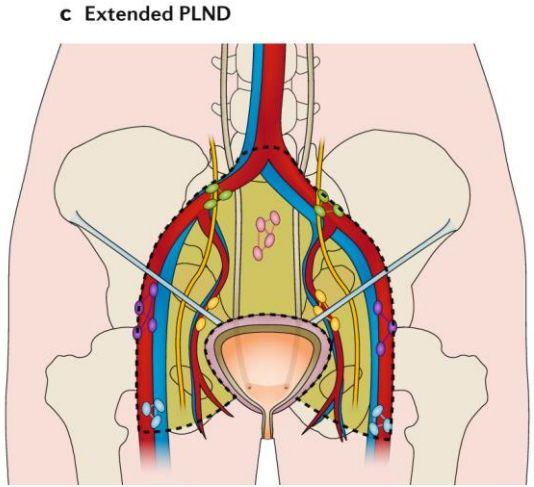
Whole pelvis nodal radiotherapy (WPRT):
Survival benefit in cN0 patients with an increased risk of nodal disease suggested[1]

1. Murthy, V., Maitre, P., Kannan, S., Panigrahi, G., Krishnatry, R., Bakshi, G., ... & Mahantshetty, U. (2021). Prostate-only versus whole-pelvic radiation therapy in high-risk and very high-risk prostate cancer (POP-RT): Outcomes from phase III randomized controlled trial. *Journal of Clinical Oncology*, *39*(11), 1234-1242.

SELECTIE VOOR WPRT OBV KLIERDISSECTIE

- Extended pelvic lymph node dissection (ePLND) gold standard for nodal staging
  - Morbidity
  - Up to 35% of draining lymph nodes outside ePLND dissection template[2]

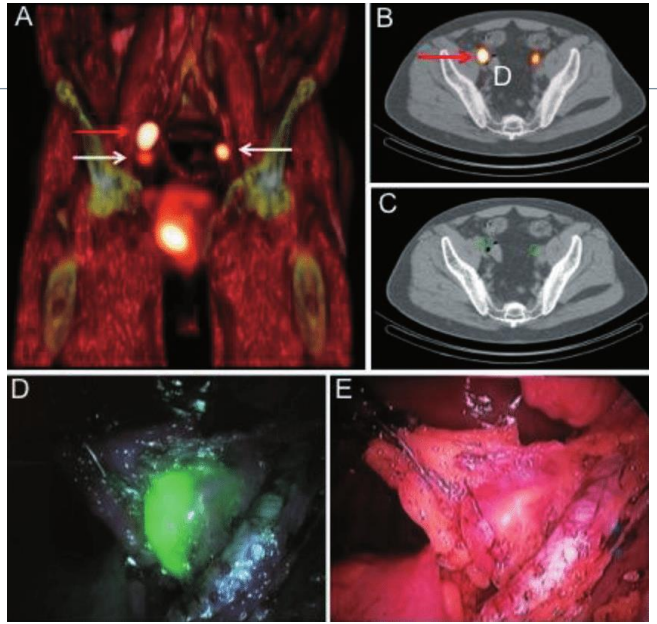
- Alternative: sentinel lymph node biopsy (SLNB)



2. Joniau S, Van den Bergh L, Lerut E, Deroose CM, Haustermans K, Oyen R, et al. Mapping of pelvic lymph node metastases in prostate cancer. Eur Urol. 2013;63:450-8.

SENTINEL LYMPH NODE BIOPSY

- Comparable diagnostic accuracy to ePLND[3]
- Lower complication rate[4]
- Identification aberrant LNs



2. Joniau S, Van den Bergh L, Lerut E, Deroose CM, Haustermans K, Oyen R, et al. Mapping of pelvic lymph node metastases in prostate cancer. Eur Urol. 2013;63:450-8.
3. Wit EMK, Acar C, Grivas N, Yuan C, Horenblas S, Liedberg F, et al. Sentinel Node Procedure in Prostate Cancer: A Systematic Review to Assess Diagnostic Accuracy. Eur Urol. 2017;71:596-605.
4. Acar C, Kleinjan GH, van den Berg NS, Wit EM, van Leeuwen FW, van der Poel HG. Advances in sentinel node dissection in prostate cancer from a technical perspective. Int J Urol. 2015;22:898-909.

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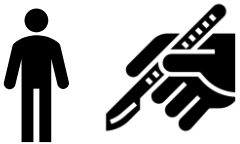
METHODS

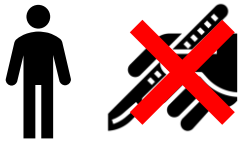
SLNB (N=261)



pN1 → Whole-pelvic radiotherapy (WPRT) + androgen deprivation therapy (ADT)

pN0 → Prostate-only radiotherapy (PORT) + ADT

Non-SLNB (N=267)



→ PORT + ADT

INJECTION

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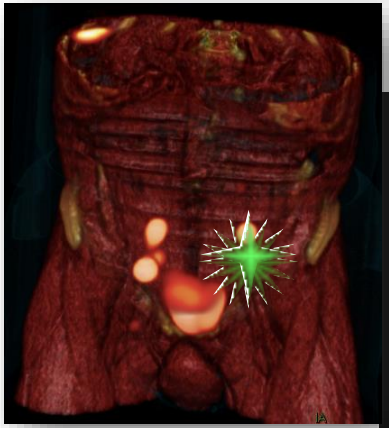
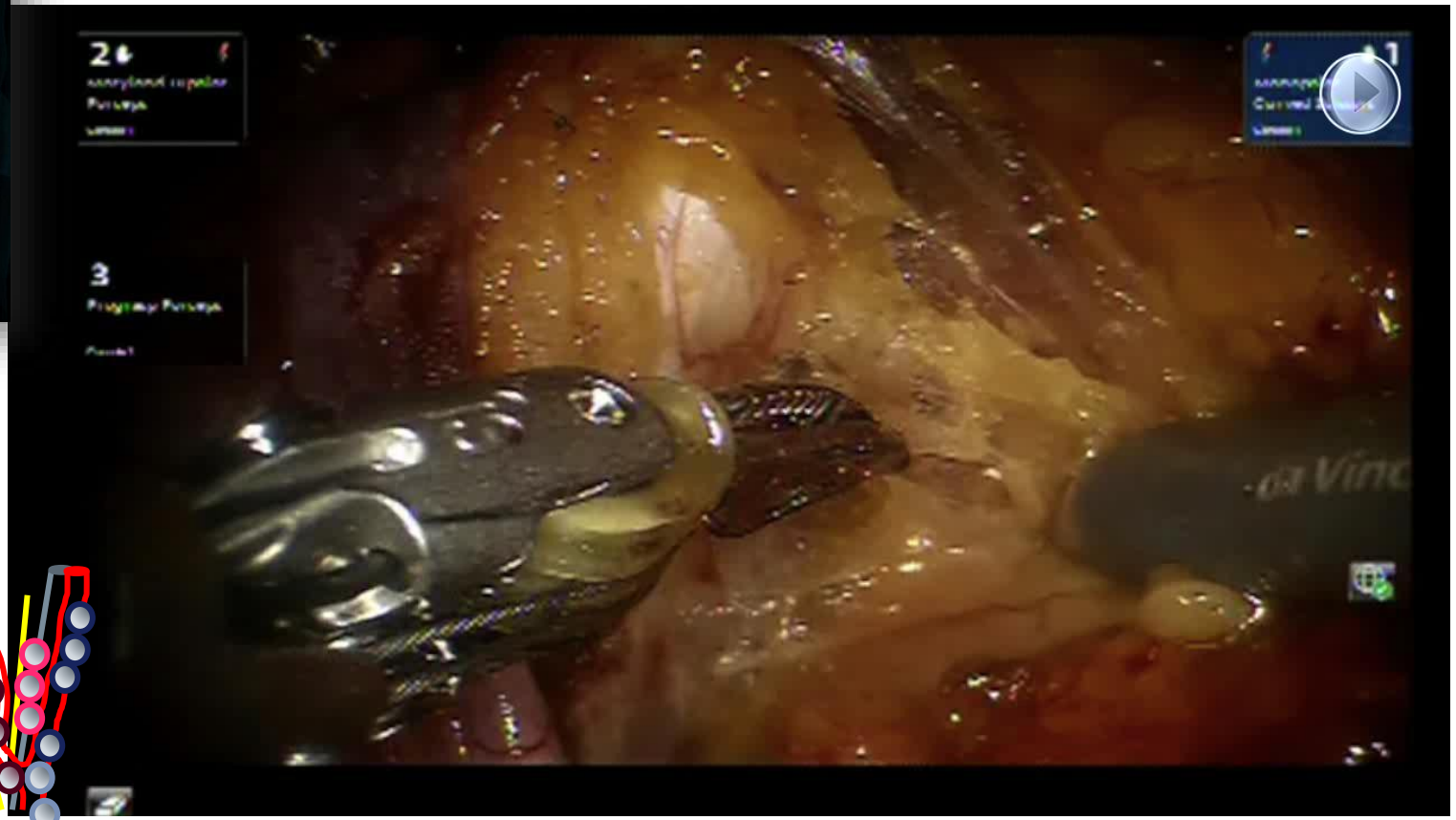
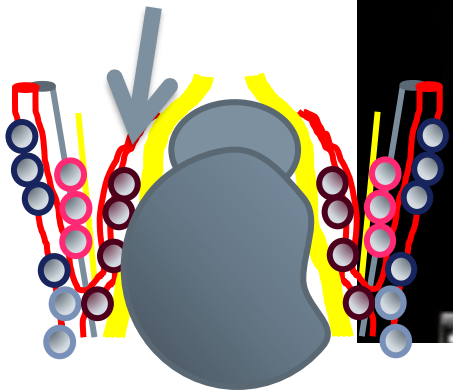
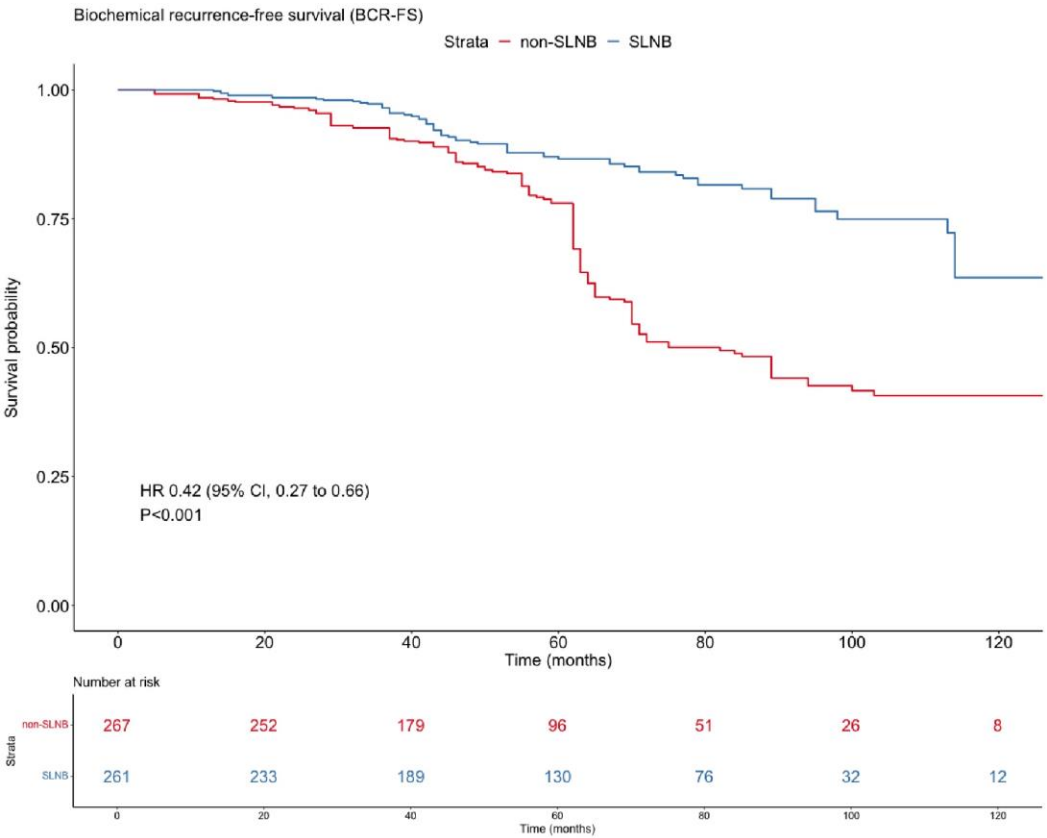






BEHANDELING

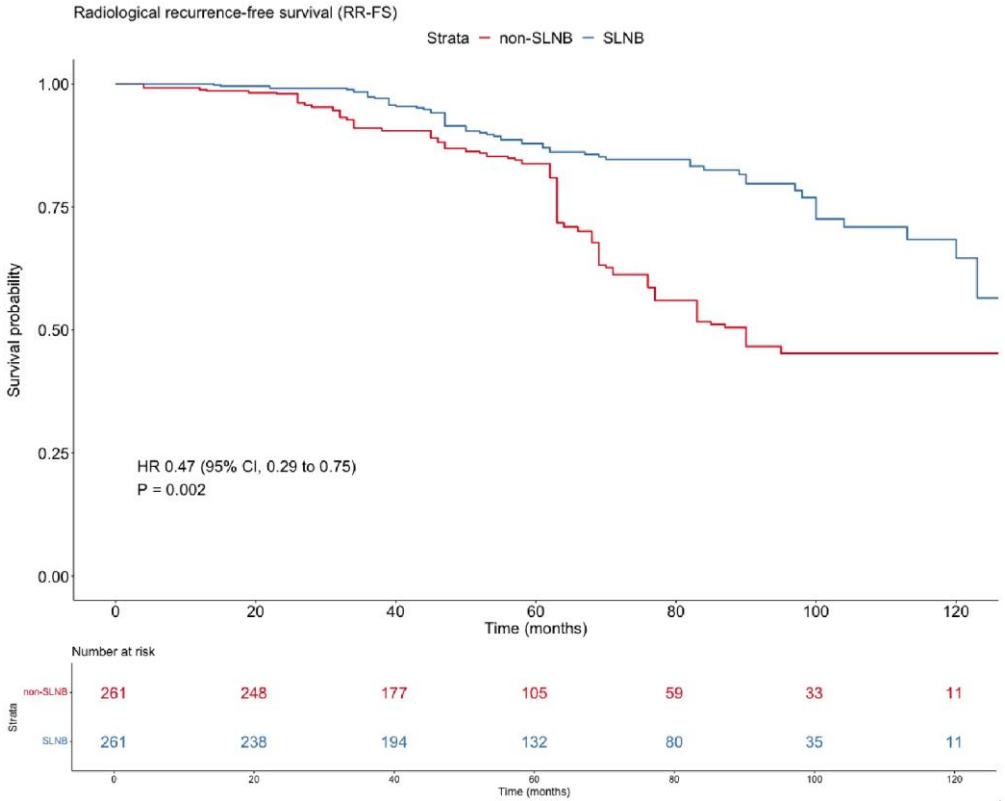
- Radiotherapy technique mostly consistent since 2007
- 75.25-77 Gy on the prostate and seminal vesicles
- WPRT: 52.5-56 Gy pelvic LNs (RTOG guidelines)
- 35-39 fractions
- 6-36 months of ADT



*Adjusted for cT, iPSA, ISUP, ADT duration

Table 1. Propensity score-weighted multivariable Cox regression analysis

	Biochemical recurrence		
Predictor	HR	95% CI	P value
Group			
Non-SLNB	Ref	-	-
SLNB	0.38	0.25 – 0.59	<0.001
cT stage			
cT1-T2	Ref	-	-
cT3-T4	2.35	1.53-3.63	<0.001
Log_2iPSA	1.16	0.95-1.42	0.14
ISUP grade group			
1-2	Ref	-	-
3-5	1.79	1.12-2.86	0.015
ADT duration (months)	0.99	0.97 – 1.00	0.14

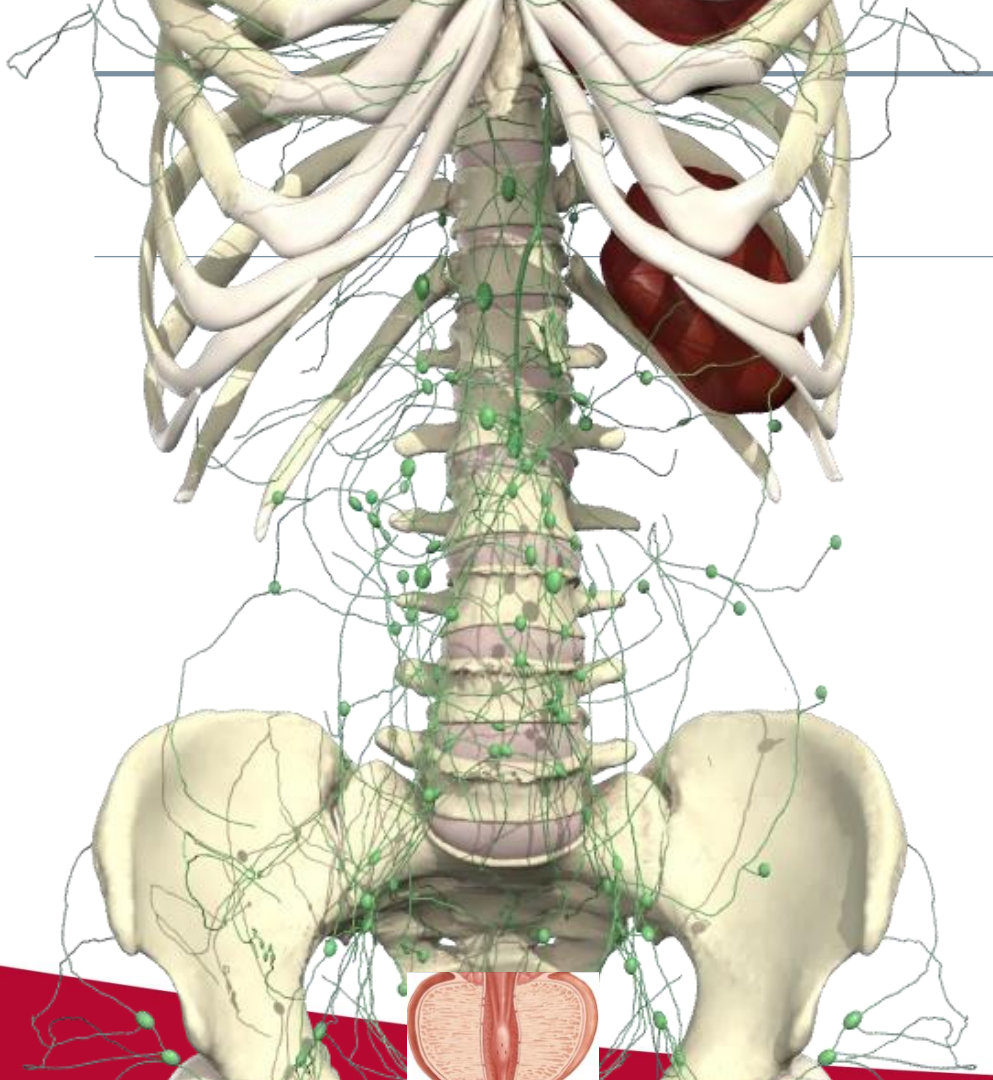


*Adjusted for cT, age, iPSA, ISUP, ADT duration

Table 2. Propensity score-weighted multivariable Cox regression analysis

	Radiological recurrence		
Predictor	HR	95% CI	P value
Group			
Non-SLNB	Ref	-	-
SLNB	0.44	0.28 – 0.69	<0.001
cT stage			
cT1-T2	Ref	-	-
cT3-T4	2.66	1.64 – 4.30	<0.001
Log_2iPSA	1.15	0.94 – 1.41	0.18
ISUP grade group			
1-2	Ref	-	-
3-5	1.97	1.19 – 3.24	0.008
ADT duration (months)	1.00	0.98 – 1.01	0.59

PROSTATECTOMIE



Prostaat

Prostaatweefsel
Prostaatkanker
Neurovasculaire bundel

Lymklieren

Voeren weefsel vocht af
Kanker uitzaaiingen

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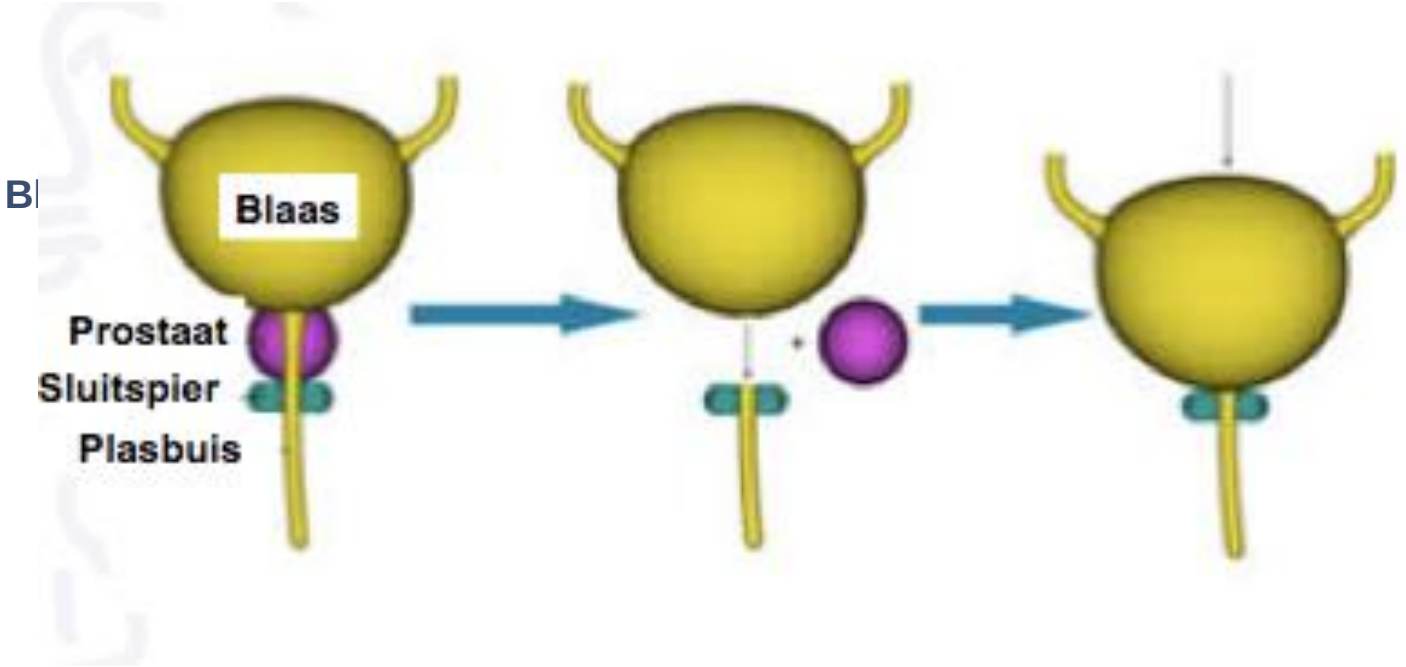
WAAROM ROBOT-CHIRURGIE?

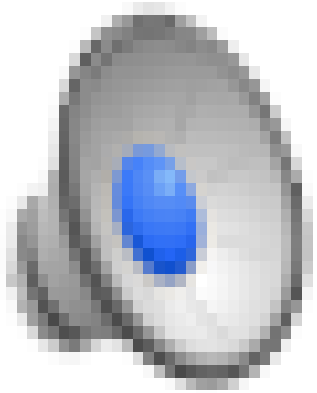
- Minimaaal invasieve chirurgie beter voor de patienten

- Nieuwe technologie
  - Informatiesysteem
  - Beeldvorming

RADICALE PROSTATECTOMIE (OPERATIEF VERWIJDEREN PC)



RADICALE PROSTATECTOMIE

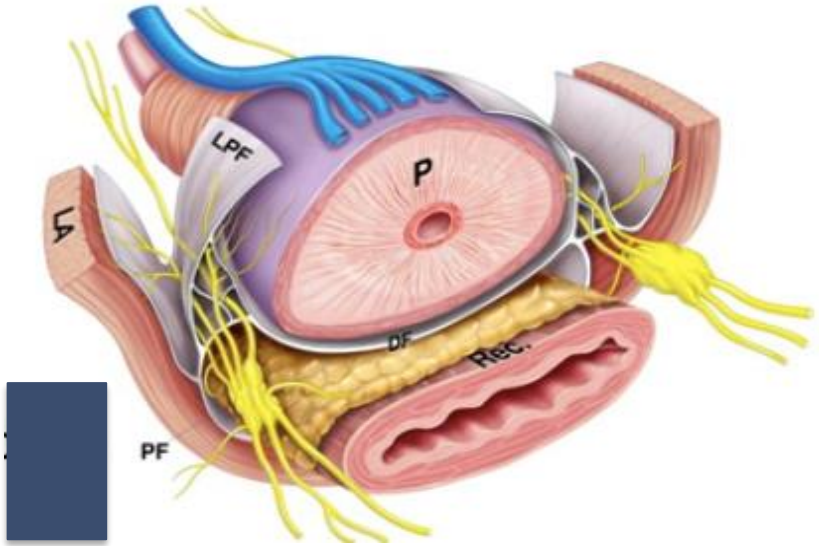


HET DOEL VAN EEN RADICALE PROSTATECTOMIE

- Controle kanker
- Continentie urine
- Potentie

- “Trifecta”

- Zenuwsparing



ERVARING CHIRURG IS MEEST BELANGRIJKSTE!!

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European Association of Urology

Prostate Cancer

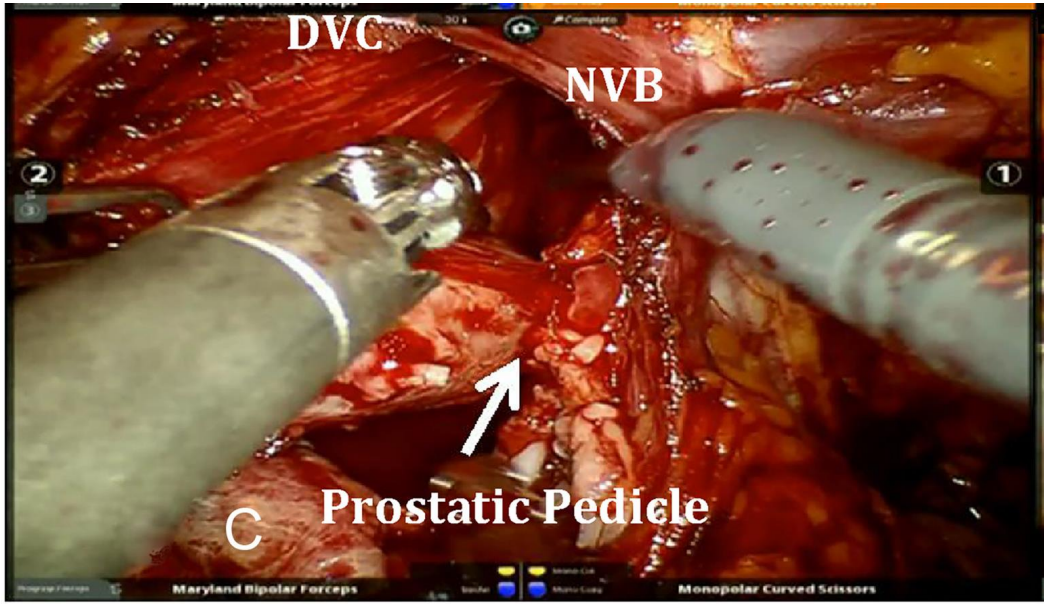
Functional and Oncological Outcomes After Open Versus Robot-assisted Laparoscopic Radical Prostatectomy for Localised Prostate Cancer: 8-Year Follow-up

Anna Lantz[a,b,], David Bock[c], Olof Akre[a], Eva Angenete[c,d], Anders Bjartell[e,f], Stefan Carlsson[a], Katarina Koss Modig[g,h], Martin Nyberg[e,f], Karin Stinesen Kollberg[g,i], Gunnar Steineck[j], Johan Stranne[g,h], Peter Wiklund[a,k], Eva Haglind[c,d]*

- Incontinentie geen verschil
- Potentie geen verschil

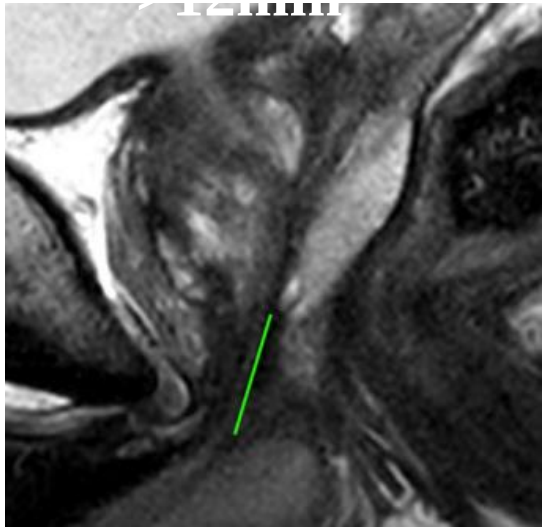
- Robot chirurgie:
  - Minder positieve snijvlakken
  - Beter oncologische uitkomsten (minder recidief)

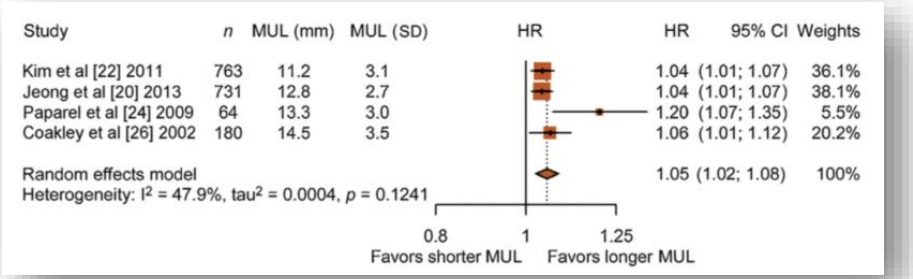
WAT TE DOEN OM BETER TE WORDEN?



SELECTIE VAN DE PATIENTEN VOOR CHIRURGIE

MEMBRANOUS URETHAL LENGTH (MUL) IS CORRELATED WITH POSTOPERATIVE FUNCTIONAL OUTCOME





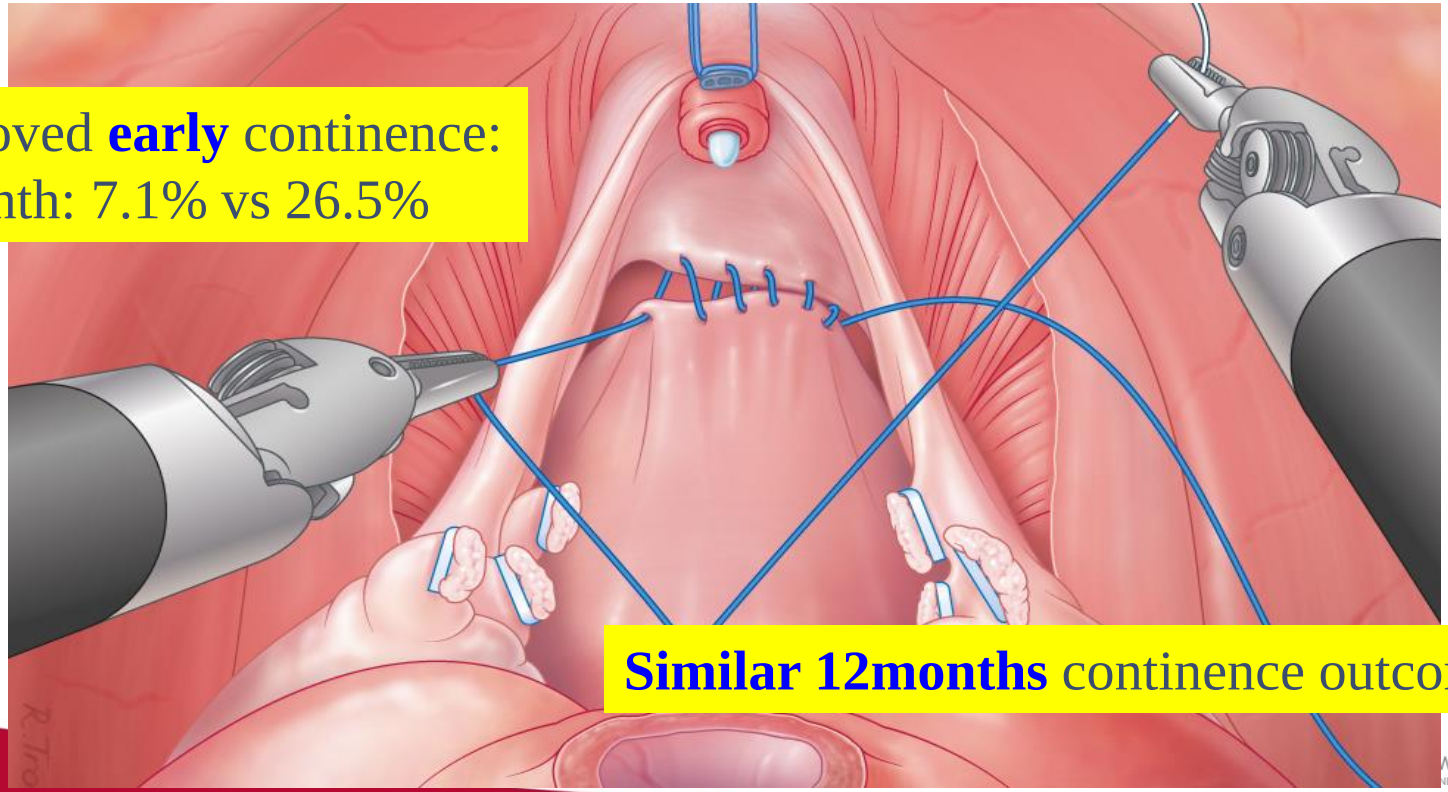
Prediction of outcome
and patient counseling/selection

Grivas, 2018, Mungovan 2016, Veerman 2023

ANASTOMOTIC RECONSTRUCTION CAN IMPROVE CONTINENCE

ANTERIOR + POSTERIOR RECONSTRUCTION ('ROCCO' STITCH)

Improved **early** continence:
1 month: 7.1% vs 26.5%



Similar 12months continence outcomes

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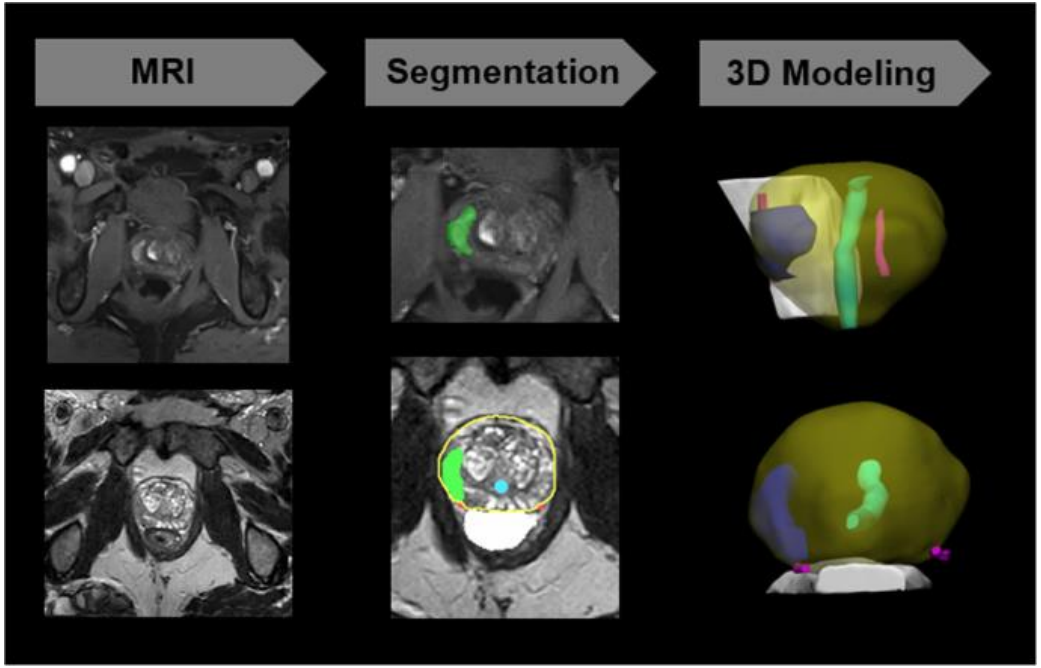
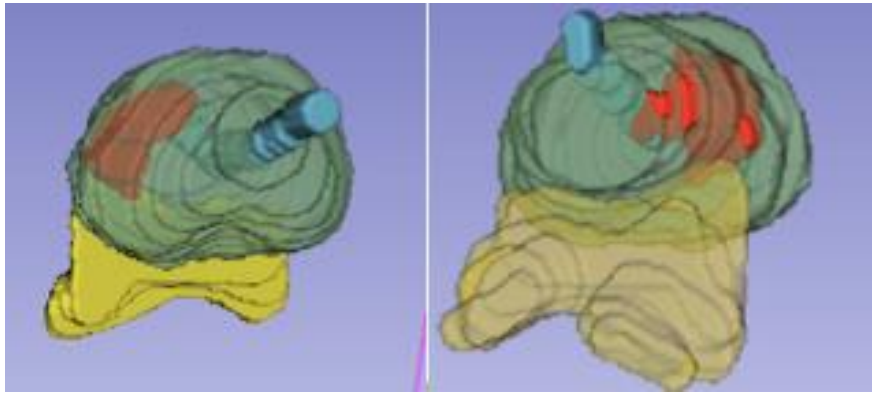
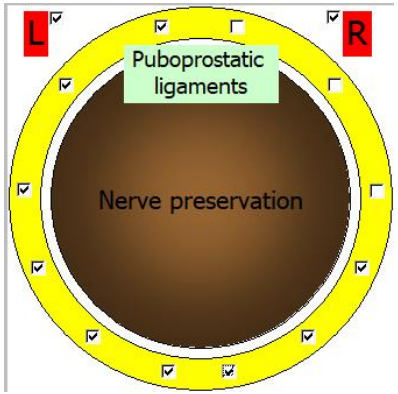
3D MODELLEN



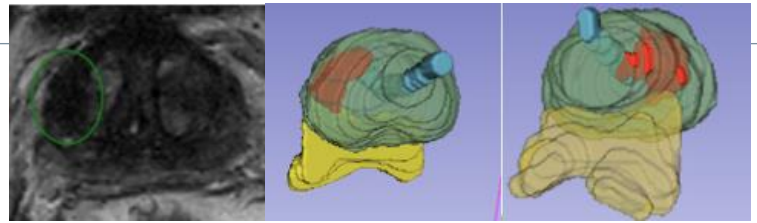
3D MODELLEN

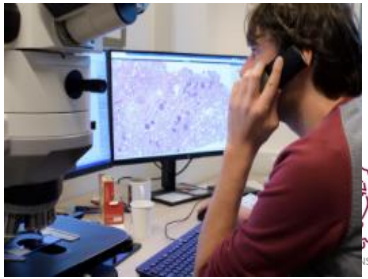




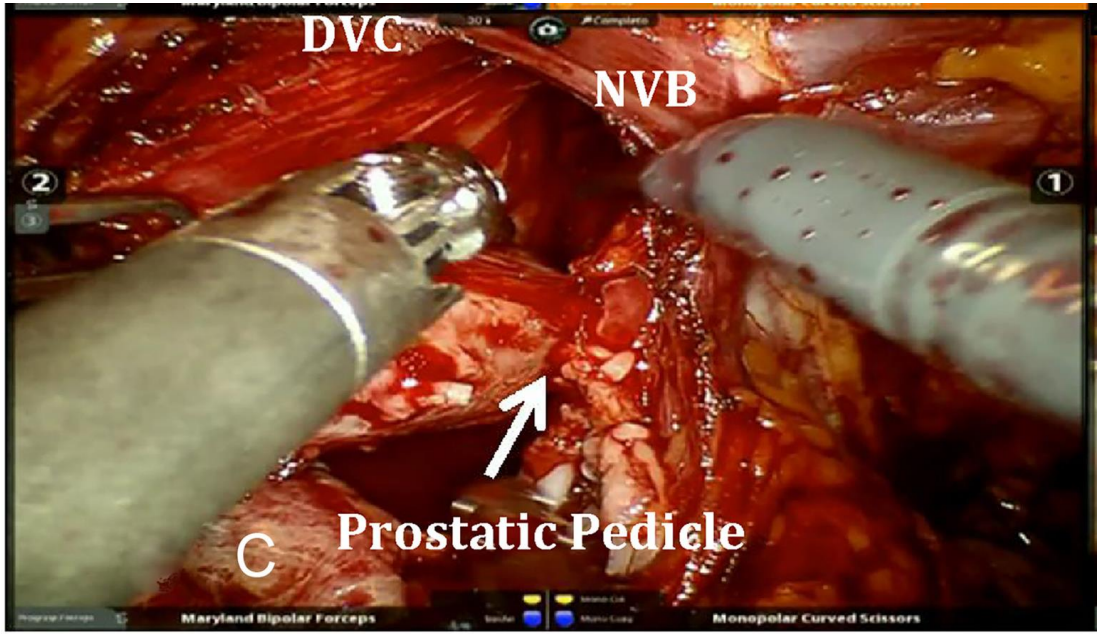
- **3D model leidt tot beleidswijziging zenuwsparing in 26% van operaties**
- **3D model leidt tot betere voospelling van kapseldoorbraak (pT3a)**

NEUROSAFE TECHNIEK





OPTICS IN PROSTATE CANCER SURGERY
DIFFUSE REFLECTION SPECTROSCOPY



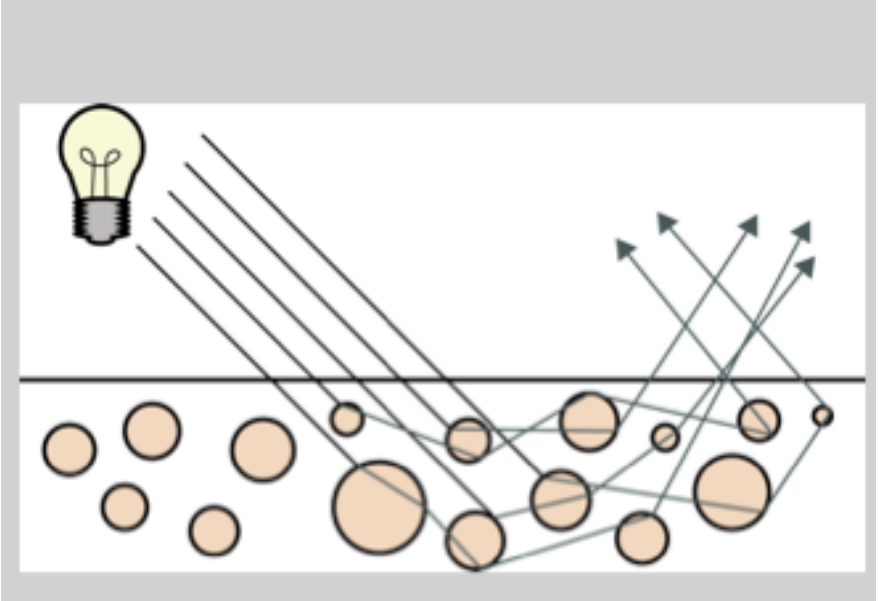
OPTICS IN PROSTATE CANCER SURGERY
DIFFUSE REFLECTION SPECTROSCOPY

Techniek:

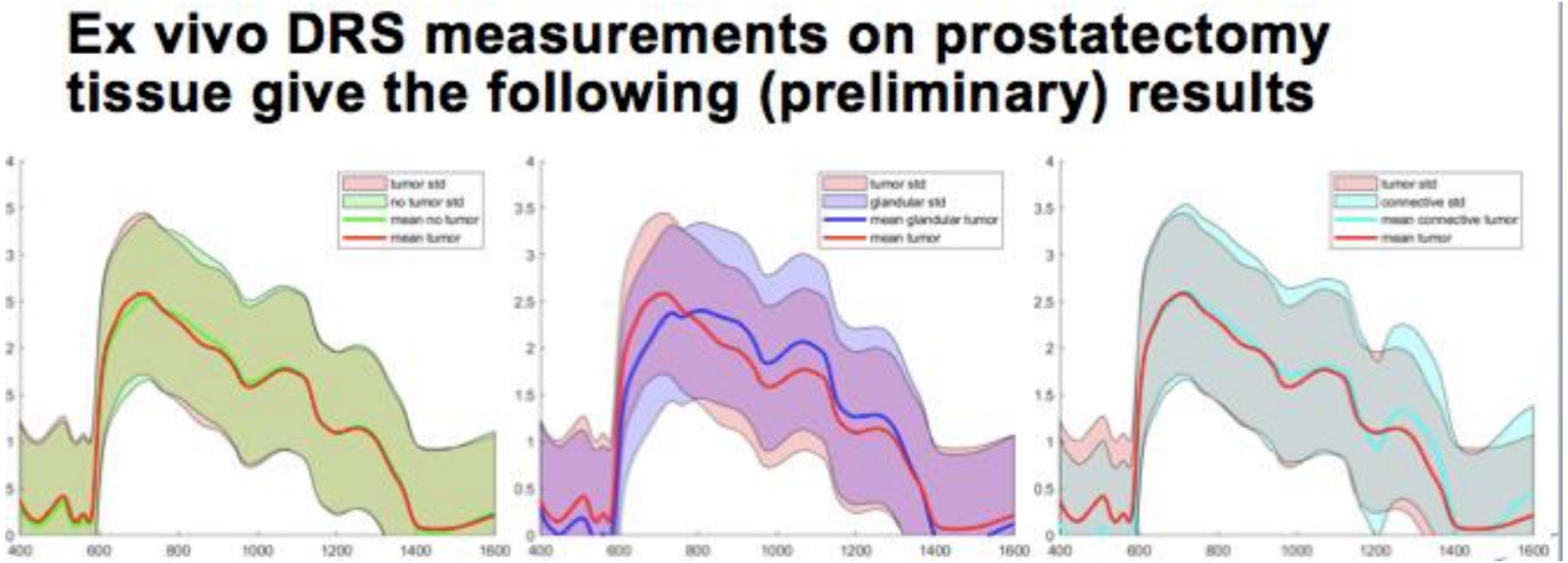
Diffuse Reflection Spectroscopy kan onderscheid maken tussen tumor weefsel en benigne weefsel

Doel:

Reduceren van positieve snijvlakken en dus oncologische en functionele uitkomsten



OPTICS IN PROSTATE CANCER SURGERY
DIFFUSE REFLECTION SPECTROSCOPY



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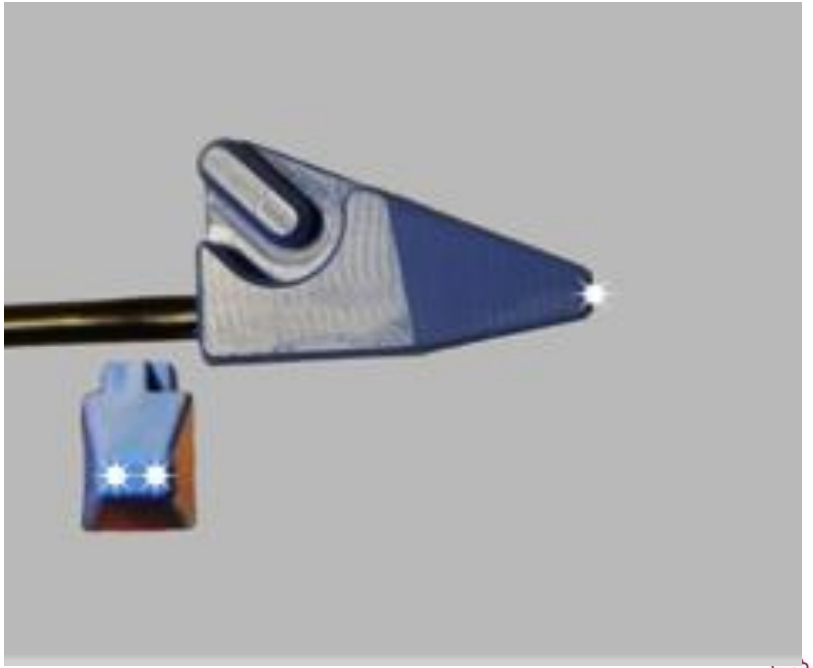
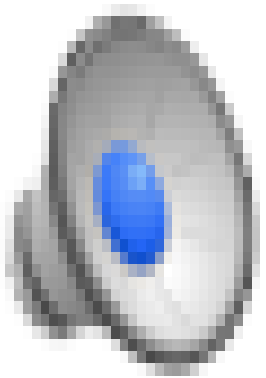
OPTICS IN PROSTATE CANCER SURGERY
DIFFUSE REFLECTION SPECTROSCOPY

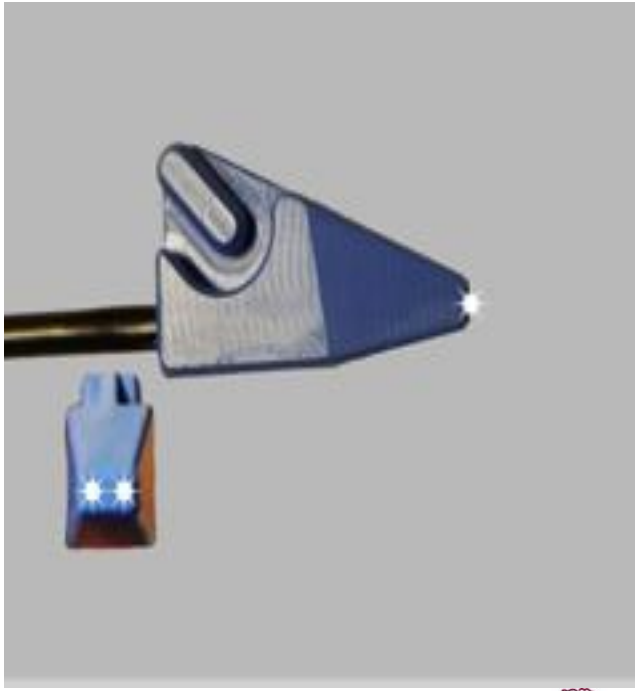
DROP-IN in vivo probe

- Davinci robot chirurgie
- Makkelijk in gebruik



OPTICS IN PROSTATE CANCER SURGERY
DIFFUSE REFLECTION SPECTROSCOPY





PROSTATECTOMIE, KEUZES

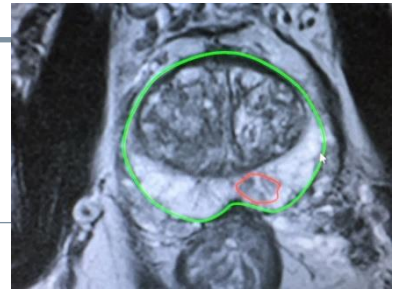
- Continentie
  - Lengte van de membraneuze urethra
  - Zenuwsparing
- Erectiele functie
  - Leeftijd en preoperatieve functie
  - Zenuwsparing

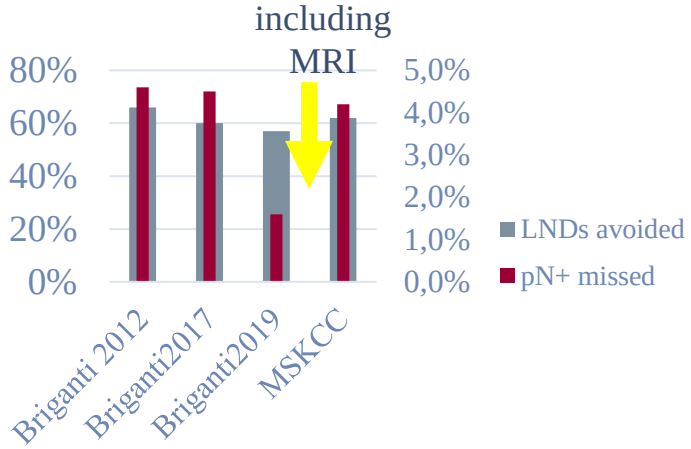
	Actief volgen*	Brachy-therapie	Uitwendige bestraling	Operatie
1. Ongewild urineverlies	**7%**	26%	23%	**60%**
2. Gebruik van incontinentie-materiaal	**2%**	14%	11%	**54%**
3. Totale incontinentie	**1%**	2%	2%	**5%**
4. Verhoogde aandrang om te plassen	**24%**	**65%**	48%	29%
5. Diarree	8%	**24%**	16%	**4%**
6. Erectie-problemen	**16%**	28%	56%	**76%**
7. Spanning over kanker	**31%**	15%	**9%**	11%
8. Spijt van de behandeling	**3%**	4%	4%	**3%**
9. Overlijden aan prostaat-kanker	**Minder dan 1 %**	**Minder dan 1 %**	**Minder dan 1 %**	**Minder dan 1 %**

PROSTATECTOMIE, KEUZES

- Continentie
  - Lengte van de membraneuze urethra
  - Zenuwsparing
- Erectiele functie
  - Leeftijd en preoperatieve functie
  - Zenuwsparing
- **Lymfelklierdissectie**

BRIGANTI 2019





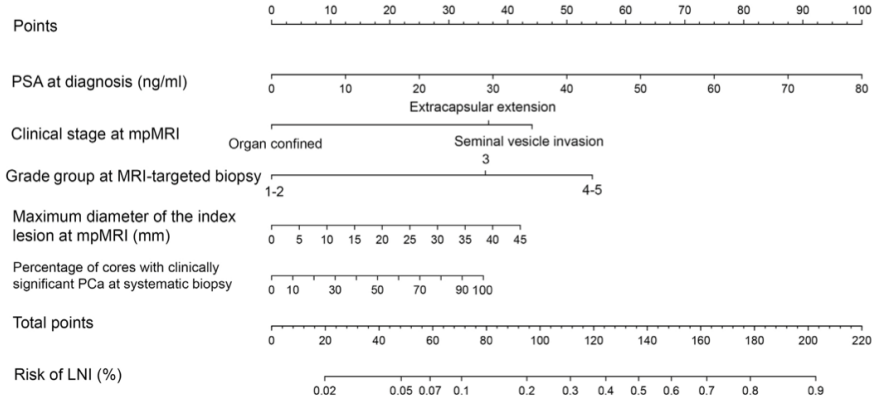


Fig. 1 – Novel nomogram predicting the probability of lymph node invasion (LNI) for patients diagnosed via targeted biopsies and treated with radical prostatectomy and extended pelvic lymph node dissection. mpMRI = multiparametric magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen.

Gandaglia G, Ploussard G, Valerio M, et al. A novel nomogram to identify candidates for extended pelvic lymph node dissection among patients with clinically localized prostate cancer diagnosed with magnetic resonance imaging-targeted and systematic biop-sies. Eur Urol 2019;75:506–14

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TOEVOEGEN PSMAPET

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European Association of Urology

Prostate Cancer

External Validation and Addition of Prostate-specific Membrane Antigen Positron Emission Tomography to the Most Frequently Used Nomograms for the Prediction of Pelvic Lymph-node Metastases: an International Multicenter Study

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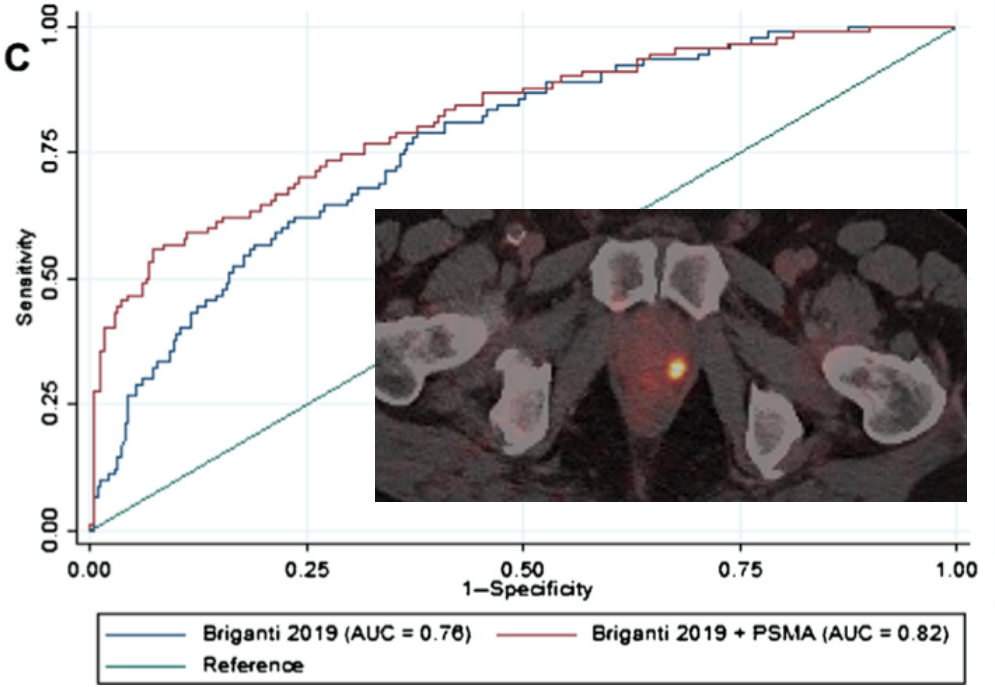
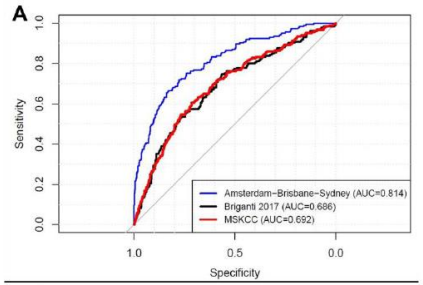


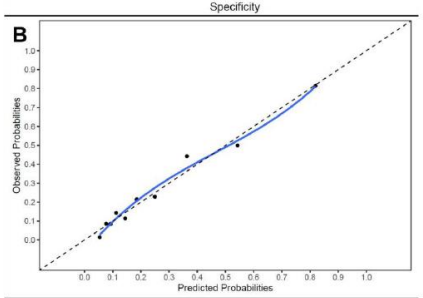
Table 3 – Performance of the different preoperative nomograms in the present population, both with and without the addition of PSMA-PET findings

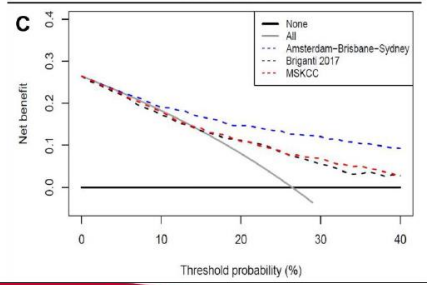
	AUC (95% CI) without PSMA-PET	AUC (95% CI) with PSMA-PET findings
Briganti 2017	0.70 (0.64–0.77)	0.76 (0.70–0.82)
MSKCC	0.71 (0.65–0.77)	0.77 (0.72–0.83)
Briganti 2019	0.76 (0.71–0.82)	0.82 (0.76–0.87)

AUC = area under the curve; CI = confidence interval; MSKCC = Memorial Sloan Kettering Cancer Center; PSMA = prostate-specific membrane antigen; PET = positron emission tomography.
Recalibration of models by re-estimation of slope and intercept does not affect AUCs, and the AUCs given for models without PSMA-PET therefore apply to both the original and the recalibrated model.

AMSTERDAM-BRISBANE-SYDNEY NOMOGRAM







Initial PSA-value

Initial PSA-value, at the time of performing prostate biopsies

0 — 500 — 5.2 ng/mL

Highest Grade Group from systematic biopsies

Highest biopsy Grade Group according to ISUP, derived from systematic prostate biopsies

No malignancy / no systematic biopsies performed | GG 1 | GG 2 | **GG 3** | GG 4 | GG 5

Highest Grade Group from MRI-targeted biopsies

Highest Grade Group according to ISUP, derived from MRI-targeted prostate biopsies

No malignancy / no MRI-targeted biopsies performed | GG 1 | GG 2 | GG 3 | GG 4 | GG 5

Total number of systematic biopsies taken

0 — 30 — 12 biopsies

Number of systematic biopsies with Grade Group 2 or higher

0 — 30 — 2 biopsies

Radiological T-stage on MRI

No tumor visualized on MRI | T2: Organ-confined disease | T3a: Extracapsular extension | T3b or higher: At least seminal vesicle invasion

Lymph-node status on PSMA PET/CT

N0 | N1

Meijer & Vis

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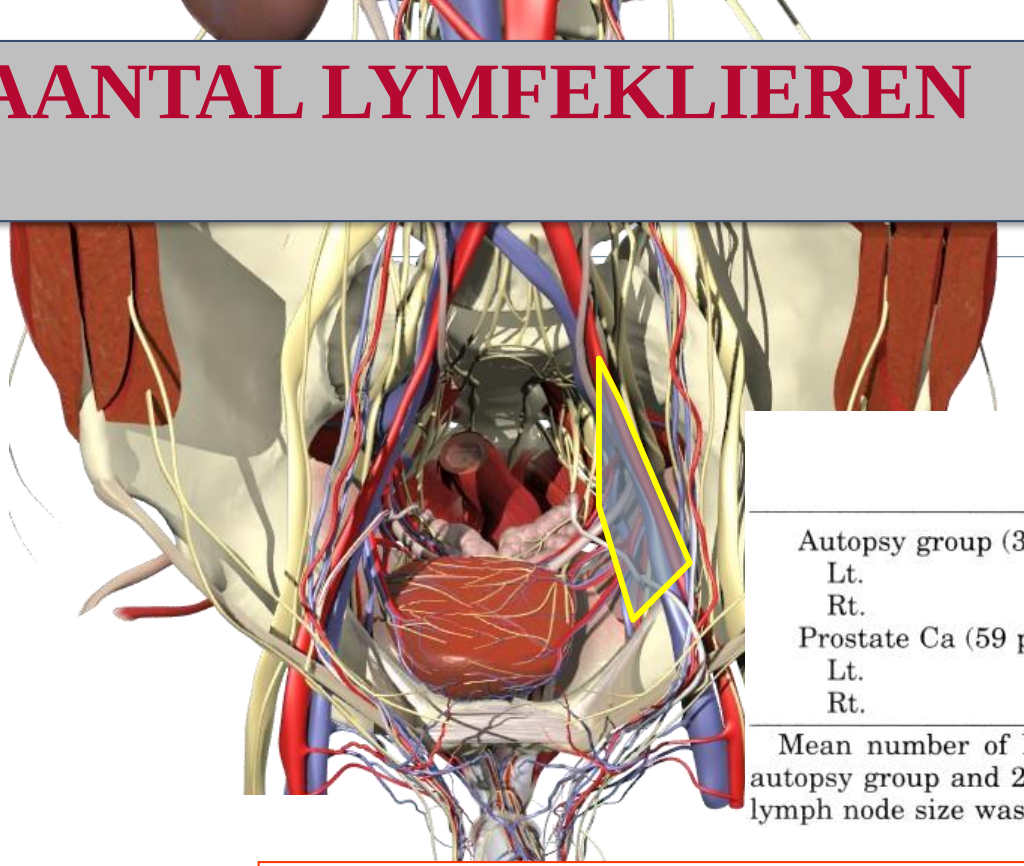
AANTAL LYMFEKLIEREN



20-22 nodes (bilateral)

	No. Lymph Nodes	
	External Iliac	Obturator
Autopsy group (30 cases):		
Lt.	5.7	4.8
Rt.	6.5	5.7
Prostate Ca (59 pts.):		
Lt.	4.3	5.3
Rt.	4.1	5.8

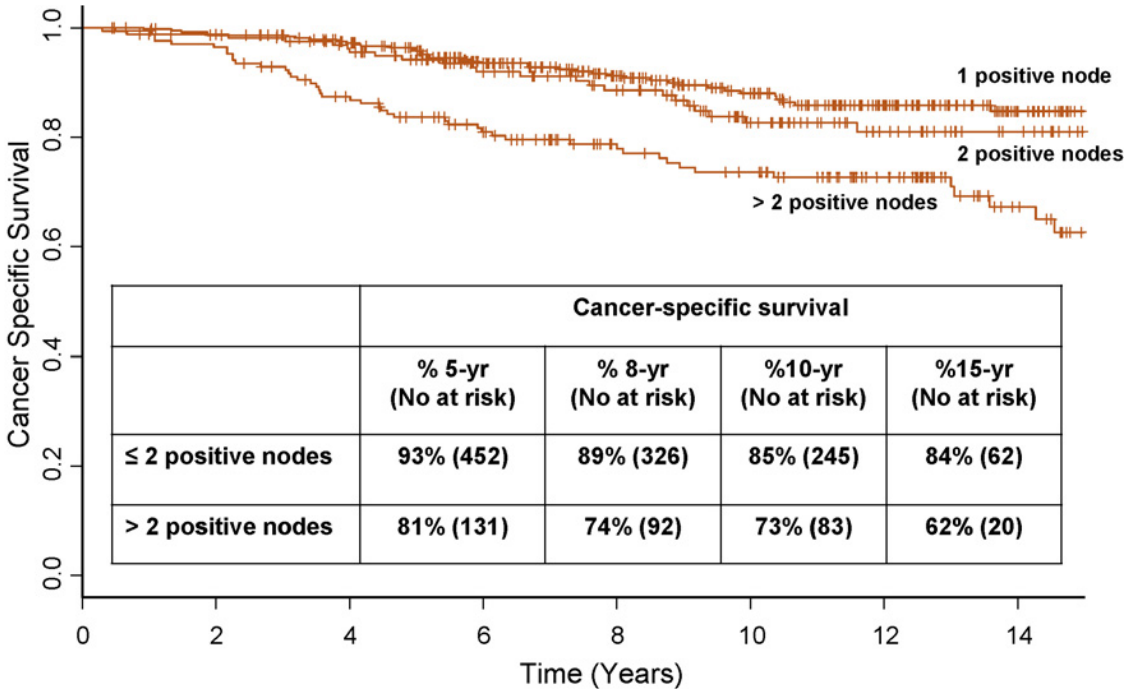
Mean number of lymph nodes removed was 22.7 (range 8 to 56) in the autopsy group and 20.5 (range 10 to 37) in the prostate cancer group. Mean lymph node size was 4.3 and 13.7 mm., respectively.

Lymph node dissection included all nodal and fibrofatty tissue between the external and internal iliac arteries from the bifurcation of the common iliac proximally to the circumflex iliac vein and endopelvic fascia distally. Lymphadenectomy also included removal of tissue in the obturator fossa and surrounding the obturator nerve.

Weingartner et al., J Urol 156:1969, 1996

NUMBER OF POS. NODES

EXTENDED LND, N=703



	Cancer-specific survival			
	% 5-yr (No at risk)	% 8-yr (No at risk)	%10-yr (No at risk)	%15-yr (No at risk)
≤ 2 positive nodes	93% (452)	89% (326)	85% (245)	84% (62)
> 2 positive nodes	81% (131)	74% (92)	73% (83)	62% (20)

(Briganti et al., Eur Urol 55:261, 2009)

EXTENT OF LND

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European Association of Urology

Platinum Priority - Prostate Cancer – Editor's Choice
Editorial by Axel Heidenreich on pp. 605–606 of this issue.

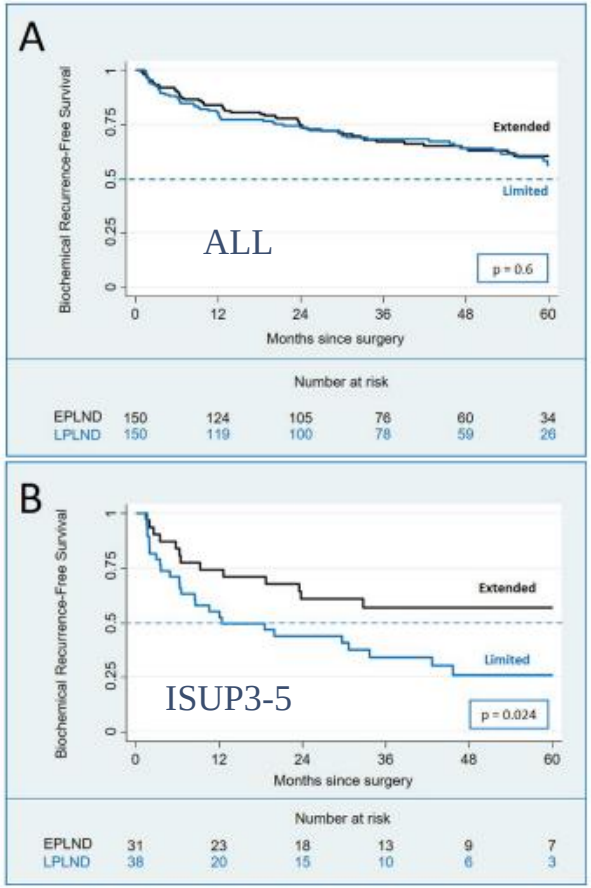
N=300

Extended Versus Limited Pelvic Lymph Node Dissection During Radical Prostatectomy for Intermediate- and High-risk Prostate Cancer: Early Oncological Outcomes from a Randomized Phase 3 Trial

Jean F.P. Lestingi[a,], Giuliano B. Guglielmetti[a], Quoc-Dien Trinh[b], Rafael F. Coelho[a], Jose Pontes Jr.[a], Diogo A. Bastos[a], Mauricio D. Cordeiro[a], Alvaro S. Sarkis[a], Sheila F. Faraj[a], Anuar I. Mitre[a], Miguel Srougi[a], William C. Nahas[a]*

Median: 17 vs 3 nodes removed

RCT confirms that EPLND provides better pathological staging, while differences in early oncological outcomes were not demonstrated.



Lestingi JFP, Guglielmetti GB, Trinh Q-Det al. Extended versus limited pel-vic lymph node dissection during radical prostatectomy for intermediate- andhigh-risk prostate cancer: early oncological outcomes from a randomizedphase 3 trial.Eur. Urol.2021;79: 595–604

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1 WHO MAY BENEFIT FROM EPLND
N=27.690, SEER

- Older, ISUP>3, nr of nodes removed

frontiers in Oncology
ORIGINAL RESEARCH
published: 26 January 2022
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Identifying the Candidates Who Will Benefit From Extended Pelvic Lymph Node Dissection at Radical Prostatectomy Among Patients With Prostate Cancer

OPEN ACCESS
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Reviewed by:

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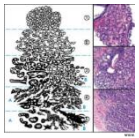

TABLE 2 | Cox multivariate analyses of prognostic indicators for OS in the entire cohort and PSM cohort.

Variables	The entire cohort		PSM cohort	
	HR (95%CI)	p-value	HR (95%CI)	p-value
Age (continuous)	1.043 (1.020–1.065)	<0.001	1.046 (1.016–1.076)	0.002
Gleason score at biopsy				
≥8 vs. <8	1.654 (1.21–2.261)	0.002	2.020 (1.32–3.091)	0.001
Clinical T stage				
T3 vs. T1–T2	1.327 (0.693–2.543)	0.394	1.145 (0.460–2.85)	0.770
Percentage of positive cores (continuous)	1.011 (1.004–1.018)	0.002	1.012 (1.004–1.021)	0.006
PSA (continuous)	1.003 (0.988–1.018)	0.698	1.001 (0.981–1.020)	0.957
Lymph node invasion				
Yes vs. N0	2.036 (1.464–2.831)	<0.001	1.753 (1.136–2.705)	0.011
NRN (continuous)	0.963 (0.941–0.986)	0.002	0.961 (0.935–0.987)	0.004
NRN				
≥12 vs. <12	0.517 (0.356–0.752)	0.001	0.458 (0.300–0.697)	<0.001

OS, overall survival; PSM, propensity-score matched; NRN, Number of removed nodes; HR, hazard ratio; CI, confidence interval.

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Patient selection and inclusion
1. Untreated biopsy-proven prostate cancer eligible for surgical treatment with curative intent
2. Risk of lymph node invasion >5%, any clinical T and any N

PSMA PET/CT

miM1 OR
PSMA nonavid
prostate cancer

→ Exclusion

miM0

Randomisation
Block randomisation per side, ratio 1:1

Arm A: control
RARP + ePLND

Arm B: intervention
PSMA miN0: RARP without ePLND
PSMA miN1: RARP + ePLND

Primary endpoint
Biochemical recurrence within 2-yr post-surgery

Secondary endpoints
- Number of ePLNDs indicated and performed
- Total number of lymph nodes removed and relative number of nodes with cancer
- Adverse events after surgery graded according to Clavien Dindo
- Diagnostic accuracy measures
- Adverse events after PSMA PET/CT
- Androgen deprivation therapy (ADT) free survival
- Metastasis free survival
- Initiation of salvage treatment (date of initiation and type of treatment)
- QoL measured using EQ-5D questionnaire: at baseline and every 12mo following primary treatment
- Patient reported outcomes assessed by EPIC-26: at baseline and every 12mo post-treatment
- Productivity losses assessed by PCQ: 3mo, 6mo post treatment and every 6mo thereafter
- Total medical costs per patients assessed by MCQ; 3mo, 6mo post treatment and every 6mo thereafter

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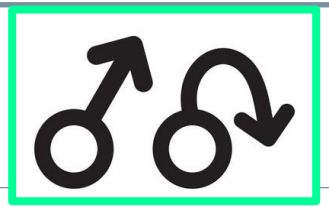
CONCLUSIES



- Behandeling gelokaliseerd prostaatkanker afhankelijk van risico groep
- Active surveillance de voorkeur bij laag-risico prostaatkanker
- Actieve behandeling op basis van te verwachte bijwerkingen
- Selectie van de juiste patiënt voor de juiste behandeling is de uitdaging

VRAGEN?

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