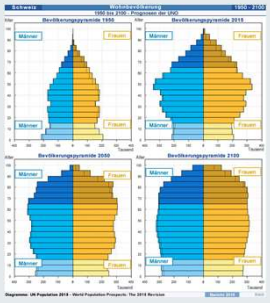
USZ Universitäts Spital Zürich

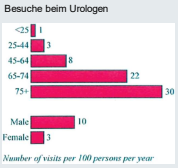
Hausarzt-Symposium Interdisziplinäre Altersmedizin

Urologie im Alter

Alterspyramide Schweiz



50% mehr Prostatakarzinome in den nächsten 10 Jahren.



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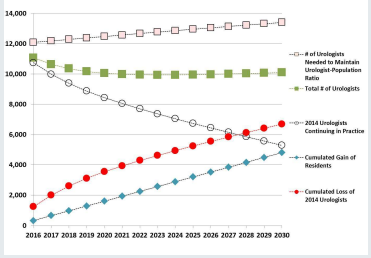
Projecting the Supply of Practicing Urologists in the United States through 2030



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So, Männer sind anders?

- Mann-Sein ist eine gefährliche Sache!
- Die Lebenserwartung des Mannes liegt deutlich unter jener der Frau.
- Männer leben risikoreicher.
- Achten weniger auf ihre Gesundheit als Frauen.
- Haben ein instrumentelles Verhältnis zu ihrem Körper, betrachten diesen als Maschine, die bei Störungen repariert werden kann.

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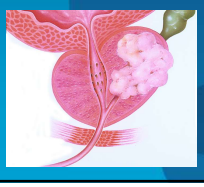
Fortbildung

Moderne Behandlung des Prostata-Karzinoms im Alter 70+

Daniel Eberli, Prof. Dr. med. Dr. rer. nat

Klinik für Urologie, USZ



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Co-Founder	▪ MUVON Therapeutics

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Prostatakarzinom

- Prostatakrebs die häufigste Krebsart überhaupt
- In der Schweiz erkranken pro Jahr 5900 Männer
- Gute Tumorkontrolle dank standardisierten Operationen, guter Ausbildung der Urologen und moderner Technik
- OS wenig beeinflusst (Medien). V.a. High Risk Patienten profitieren

- Screening ?
- Übertherapie ?
- Nebenwirkungen (Blase, Potenz, Darm)
- Psychologischer Stressor

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Prostatakrebs in der Schweiz

Krebs-Neuerkrankungen in der Schweiz (gerundete Zahlen)				
Anzahl Neuerkrankungen pro Jahr (Inzidenz)	Männer	Frauen	Total[$]	% aller Krebsfälle[#]
alle Krebsarten*	20'000	17'000	37'000	100
Prostatakrebs	6'000	---	6'000	16
Brustkrebs	40	5'500	5'500	31

Krebs-Todesfälle in der Schweiz (gerundete Zahlen)				
Anzahl Todesfälle pro Jahr (Mortalität)	Männer	Frauen	Total[$]	% aller Krebstodes-fälle[#]
alle Krebsarten*	9'000	7'000	16'000	100
Lungenkrebs	2'000	950	3'000	19
Dickdarmkrebs	900	750	1'600	29
Brustkrebs	8	1'300	1'400	38
Prostatakrebs	1'300	---	1'300	46

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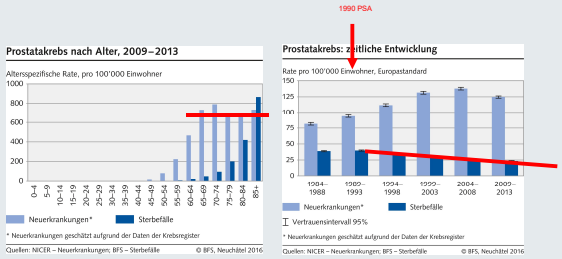
Prostate Cancer in Switzerland



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Herausforderung: Prostatakarzinom

- Relevanter Tumor definieren und besser diagnostizieren
  - Autopsiestudien zeigen, dass 60% aller 70-jährigen ein PCa haben!
- Biologisch nicht aktive Tumore nicht detektieren
  - Kosten und psychologischer Stress für den Patienten
- Nebenwirkungen der Therapie und Kosten
  - Therapie mit der besten Wirkung und der kleinsten Nebenwirkungen

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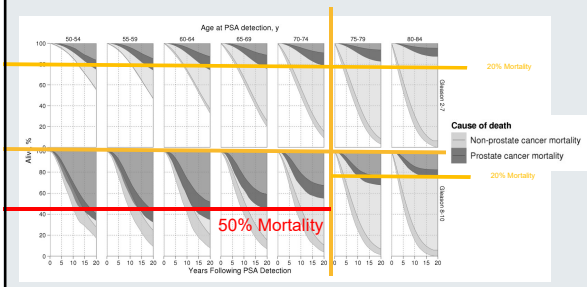
Pca Mortality calculated

Cancer Epidemiology Biomarkers and Prevention, 2011, Volume 20, Issue 5, pp. 740-50, Roman Gulati, et al.,



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ERSPC Studie

Schroder, et al ERSPC, NEJM 2012. 366:981


The NEW ENGLAND JOURNAL of MEDICINE

Prostate-Cancer Mortality at 11 Years of Follow-up

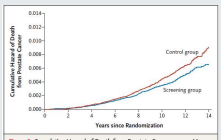

Figure 2. Cumulative Hazard of Death from Prostate Cancer among Men 55 to 69 Years of Age.
Values are not included for centers in France because of the short follow-up period (median, 4.6 years). The Nelson–Aalen method was used to calculate the cumulative hazard of death from prostate cancer.

- 182160 Patienten – Screening vs. non-screening
- 11-Jahre Follow-up
- 29% Reduktion der Prostatakrebs-spezifischen Mortalität
- Kein signifikanter Unterschied im Gesamtüberleben
- Number Needed to Treat: 33 (80 nach 9 Jahren follow-up)

Zum Zeitpunkt der Auswertung sind erst 0.5 % der Patienten in der Kontrollgruppe gestorben. In der Allgemeinbevölkerung ist jedoch eine Mortalität von 5% vorhanden. D.h. 9/10 der tumorbedingten Todesfälle stehen noch aus.

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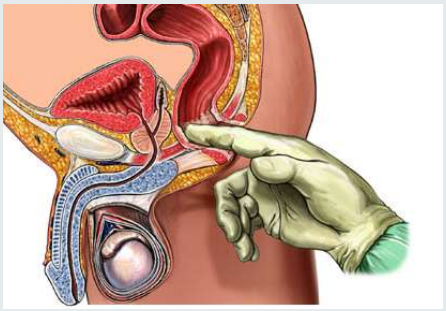
Diagnose – Früherkennung (Screening): DRU



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Diagnose – Individualisierte Früherkennung

- Wunsch des Patienten
  - Risikokonstellation
    - Familienanamnese
    - Ethnie
    - Vorerkrankungen
  - PSA-gestützte Früherkennung → Risikoabschätzung
  - Selbstentscheid des Patienten
    - Aufklärung durch behandelnden Arzt
      - Sensitivität / Spezifität der Methode
      - Konsequenzen (neg. / pos. Testergebnis)

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Easy Access

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Blood markers: Established

Prostate-specific antigen (PSA)

- a blood serum marker
- Best established marker (primary and recurrent cancer)
- Organ, but not cancer specific
- Continuous parameter

PSA level (ng/mL)	Risk of PCa (%)	Risk of ISUP grade ≥ 2 PCa (%
0.0-0.5	6.6	0.8
0.6-1.0	10.1	1.0
1.1-2.0	17.0	2.0
2.1-3.0	23.9	4.6
3.1-4.0	26.9	6.7

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Brief Correspondence

Structured Population-based Prostate-specific Antigen Screening for Prostate Cancer: The European Association of Urology Position in 2019

Giorgio Gandaglia[,†], Peter Albers[‡], Per-Anders Abrahamsson[§], Alberto Briganti[∥,¶], James W.F. Catto[#], Christopher R. Chapple[£], Francesco Montorsi[∥,¶], Nicolas Mottet[¥], Monique J. Roobol[¤], Jens Sønksen[††], Manfred Wirth[‡‡], Hendrik van Poppel[†]*

A single PSA test is useful to stratify surveillance and subsequent risk, but is not enough to prevent PCa mortality. Therefore, structured screening programs based on repeated measurements of PSA over time are needed to produce stage migration and, in turn, reduction in risks of developing metastases and cancer-specific mortality .

1. Obtain a baseline PSA at the age of 45 for risk stratification
   - <1 ng/ml: PSA-testing intervals up to 8 yr
   - ≥1 ng/ml: PSA testing every 2–4 yr
2. Stop PSA testing in men with a life expectancy <10 yr (consider PSA testing only in selected men with above average PSA levels and long life expectancy)
3. In men at risk of significant PCa according to PSA levels consider the following tests to select biopsy candidates:
   - Risk calculators
   - mpMRI
   - Tests based on biomarkers and genetic polymorphisms
4. Consider MRI targeted with concomitant systematic biopsy if the mpMRI is suggestive of PCa
5. Offer active surveillance in well-informed patients with low-risk and selected grade group 2 intermediate-risk PCa

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Next stepts: the electronical nose?

Prostate Cancer

Exhaled-breath Testing for Prostate Cancer Based on Volatile Organic Compound Profiling Using an Electronic Nose Device (Aeonose™): A Preliminary Report

Claire G. Waltman, Tom A.T. Marcelissen, Joep G.H. van Roermund

Department of Urology, Maastricht University Medical Centre, Maastricht, The Netherlands

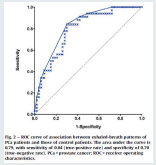

Fig. 2 – ROC curve of association between exhaled-breath patterns of PCa patients and those of control patients. The area under the curve is 0.78, with sensitivity of 0.86 (true positive rate) and specificity of 0.70 (true negative rate). PCa = prostate cancer; ROC = receiver operating characteristics.

Revolutionary non-invasive diagnostics for healthcare

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Dog sniffing PSA

- 2 female dogs trained to detect prostate cancer.
- 900 urine samples 360 with prostate cancer
- Over 90% acurracy

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Blood markers: NEW

The Stockholm 3 study (STHLM3 model)

- A risk-based screening model
- proposed as a first-line screening test
- Combination:
  - PSA
  - single nucleotide polymorphisms
  - clinical parameters
  - plasma biomarkers

Prostate cancer screening in men aged 50–69 years (STHLM3): a prospective population-based diagnostic study

Findings The STHLM3 model performed significantly better than PSA alone for detection of cancers with a Gleason score of at least 7 (p<0·0001), the area under the curve was 0·56 (95% CI 0·55–0·60) with PSA alone and 0·74 (95% CI 0·72–0·75) with the STHLM3 model. All variables used in the STHLM3 model were significantly associated with prostate cancers with a Gleason score of at least 7 (p<0·05) in a multiple logistic regression model. At the same level of sensitivity as the PSA test using a cutoff of ≥3 ng/mL to diagnose high risk prostate cancer, use of the STHLM3 model could reduce the number of biopsies by 32% (95% CI 24–39) and could avoid 44% (35–54) of benign biopsies.

Interpretation The STHLM3 model could reduce unnecessary biopsies without compromising the ability to diagnose prostate cancer with a Gleason score of at least 7, and could be a step towards personalised risk-based prostate cancer diagnostic programmes.

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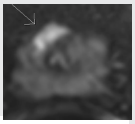
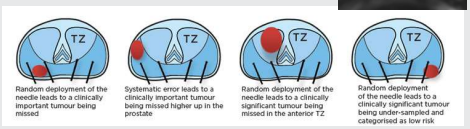
Transrectal TRUS-guided prostate biopsy

- Widely accepted
  - 75-98% of PB today by transrectal approach *Noguchi M et al. A questionnaire survey of patient preparation and techniques for prostate biopsy among urologists in the Kyushu and Okinawa regions of Japan. Int J Clin Oncol 2006;11:390–5*
- Poor sensitivity *Patel AR, Jones JS Curr Opin Urol. 2009 May; 19(3):232-7*
- False negative incidence up to 23%
- Infection in up to 5%
- Difficult sampling of the peripheral and anterior zone





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Accuracy of transrectal biopsy

British Journal of Urology (1997), 79, 415–417

Biopsy Gleason score: how does it correlate with the final pathological diagnosis in prostate cancer?

E.T. FERNANDES, C.P. SUNDARAM, R. LONG, M. SOLTANI and C.J. IRCOLE

Department of Urology, University of Minnesota, Minneapolis, Minnesota, USA

ACCURACY OF BIOPSY GLEASON SCORES FROM A LARGE UROPATHOLOGY LABORATORY: USE OF A DIAGNOSTIC PROTOCOL TO MINIMIZE OBSERVER VARIABILITY

GRANT D. CARLSON, CHRISTINA B. CALVANESE, HILLEL KAHANE, and JONATHAN I. EPSTEIN

European Association of Urology

Prostate Cancer

Development and Internal Validation of a Nomogram Predicting the Probability of Prostate Cancer Gleason Sum Upgrading Between Biopsy and Radical Prostatectomy Pathology

Felix K.-H. Chun[a,], Thomas Steuber[a,1], Andreas Erbersdobler[c], Eike Currlin[a], Jochen Walz[a], Thorsten Schlomm[a], Alexander Haese[a], Hans Heinzer[a], Michael McCormack[d], Hartwig Huland[a,e], Markus Graefen[a], Pierre I. Karakiewicz[a,*]*

Gleason Upgrade 24-54% reported

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Is a biopsy of MRI-suspicous lesions enough?

Targeted MR/Ultrasound Fusion Biopsy Results		No Cancer	Standard Extended-Sextant Biopsy Results: Low-Risk Cancer: Gleason 6	Low-Risk Cancer: Gleason 3+4 Low Volume[a]	Intermediate-Risk Cancer: Gleason 3+4 High Volume[b]	High-Risk Cancer: Gleason ≥4+3	Totals
	No cancer	439	74	12	12	5	542
Low-Risk Cancer	Gleason 6	38	84	12	10	3	147
	Gleason 3+4 Low volume[c]	17	14	9	19	7	66
Intermediate-Risk Cancer	Gleason 3+4 High volume[d]	14	21	7		4	75
High-Risk Cancer	Gleason ≥4+3	26	13	12	19	103	173
	Totals	534	206	52	89	122	1003

MRI missed 15% of intermediate and high risk tumors

Pinto et all. JAMA. 2015;313(4):390-397. doi:10.1001/jama.2014.17942

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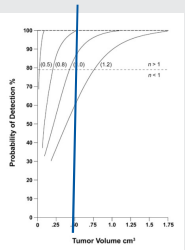
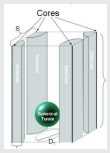
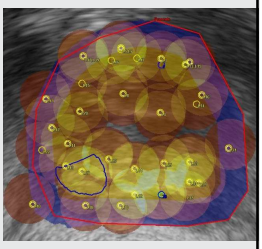
Transperineal template mapping biopsy



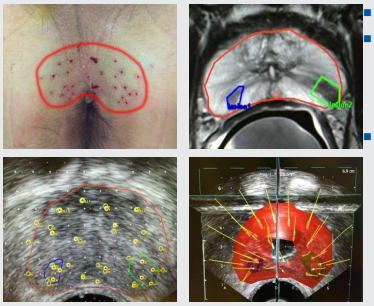




10 mm sampling of the prostate: >90% detection of tumors >0.5cm³

Transperineal prostate biopsy: analysis of a uniform core sampling pattern that yields data on tumor volume limits in negative biopsies

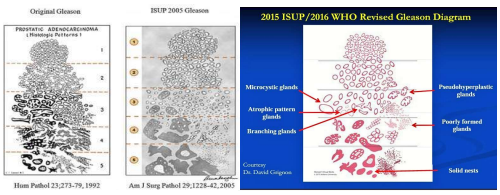
Template mapping fusion biopsy



- 20 cores (template)
- 2 core from each suspicious lesions in mpMRI
- Accuracy for detecting significant prostate cancer >90% *[1]*

1. *Hu Y, et al. A biopsy simulation study to assess the accuracy of several transrectal ultrasonography (TRUS)-biopsy strategies compared with template prostate mapping biopsies in patients who have undergone radical prostatectomy. BJU Intl. 2012 Sep;110(6):812–20*

Gleason Score: Wird immer sicherer!



Changes to make definition of low aggressive Tumors secur.

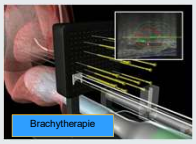
BJU Int. 2015 Feb;115(2):248-55. doi: 10.1111/bju.12671. Gleason inflation 1998-2011: a registry study of 97,168 men. Danneman D1, Drevin L, Robinson D, Stattin P, Egevad L.

Therapie Optionen

Bis 30% Overtreatment

Active Surveillance (Monitoring)

34% der Patienten werden doch behandelt.



Fokale Therapie

Watchful Waiting

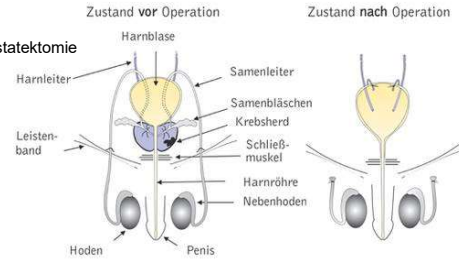
Hormontherapie

Chemotherapie

Fallvorstellung

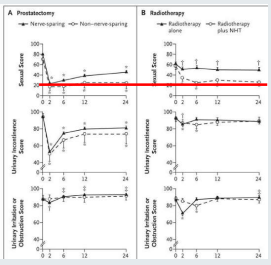
Therapie-Optionen?

Radikale Prostatektomie



Perkutane Radiotherapie

Inkontinenz: ca 10%
Potenzprobleme: ca 50%

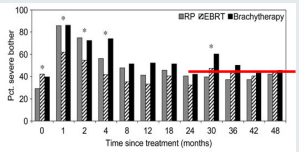


Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors
Sanda NEJM 2008

Long-Term Functional Outcomes after Treatment for Localized Prostate Cancer
N Engl J Med 2013; 368:436-445

At 15 years, no significant relative differences in disease-specific functional outcomes were observed among men undergoing prostatectomy or radiotherapy. Nonetheless, men treated for localized prostate cancer commonly had declines in all functional domains during 15 years of follow-up.

Correlates of Bother Following Treatment for Clinically Localized Prostate Cancer
Gore et all. J Urol 2010



The Robot is efficient

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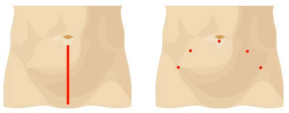
Vorteile DaVinci

- Geringerer Wundschmerz
- Geringerer Verbrauch an Analgetika
- Reduktion der Hospitalisationszeit
- Reduktion der Rekonvaleszenzzeit
- Frühzeitige Wiedereingliederung in Arbeitsprozess
- Schnellere Lernkurve der Operateure
- Kosmetische Verbesserung
- Höhere Kontinenzrate ?
- Höhere Potenzrate ?



Open Surgical Incision *da Vinci*® Prostatectomy Incision

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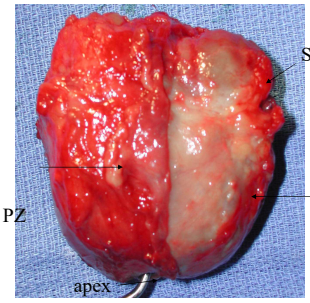
RP-Präparat: die linksseitige PSVF (Denonvilliers ') abgelöst



Fallvorstellung; Älterer Patient in gutem AZ

Im Rahmen von Miktionsbeschwerden wurde ein PSA bestimmt, welches bei 3.94 ug/L ist.

Pat ist 72-jährig.

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Fallvorstellung

1. PSA-Erhöhung unklarer Ätiologie (12/2011)
- V.a. Prostatahyperplasie, DD Malignom

2. Metabolisches Syndrom
- Dyslipidämie, 10-Jahresrisiko nach AGLA 24.7%
- Arterielle Hypertonie
- Übergewicht (BMI 26.5 kg/m2, BU 100cm)

3. Arterielle Hypertonie, Erstdiagnose 1997
- Status nach ACE- Hemmer-induziertem Husten
- Status nach Bradykardie unter Betablockertherapie
- Fundus hypertonicus Grad I-II (10/11)
- cvRF: art. Hypertonie, Dyslipidämie, sistierter Nikotinabusus (kum 12 py)

Fragestellung
Im Rahmen der Vorsorge erhöhter PSA-Wert, anamnestisch abgeschwächter Harnstrahl, Pollakisurie und Nachträufeln. Bitte um weitere urologische Abklärung ggf mittels Biopsie.

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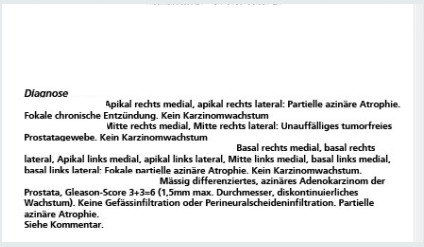
Biopsieresultat



Diagnose

apikal rechts medial, apikal rechts lateral: Partielle azinäre Atrophie. Fokale chronische Entzündung. Kein Karzinomwachstum
Mitte rechts medial, Mitte rechts lateral: Unauffälliges tumorfreies Prostatagewebe. Kein Karzinomwachstum
Basal rechts medial, basal rechts lateral, Apikal links medial, apikal links lateral, Mitte links medial, basal links medial, basal links lateral: Fokale partielle azinäre Atrophie. Kein Karzinomwachstum.
Mässig differenziertes, azinäres Adenokarzinom der Prostata, Gleason-Score 3+3=6 (1,5mm max. Durchmesser, diskontinuierliches Wachstum). Keine Gefässinfiltration oder Perineuralscheideninfiltration. Partielle azinäre Atrophie.
Siehe Kommentar.

- Welche Empfehlung?

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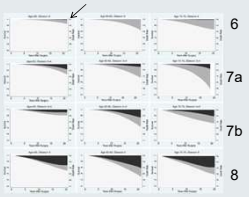
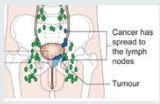
Who should not be treated = Gleason 3+3



Only 3/9957 patients with Gleason 3+3 died of Prostate Cancer

Predicting 20-year prostate cancer specific mortality after radical prostatectomy. Eggener SE, Scardino PT, Walsh PC, Han M, Partin AW, et. all J Urol. 2011 Mar;185(3):869-75. doi: 10.1016/j.juro.2010.10.057. Epub 2011 Jan 15.



14,123 radical prostatectomies examined from 4 Institutions

'Out of over 14,000 cases there was not a single case of lymph node metastases associated with Gleason pattern 3+3 tumour'

Ross H et al. Am J Surg Path 2012

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Fallvorstellung

Active Surveillance
(Aktives Beobachten)
= kurative Therapieoption

Vorgehen:
PSA alle 6 Mt
MRI und Biopsie alle 2-3 Jahre ,bis ca 75 Jährig, dann Watchfull waiting

Was wäre mit Patient Gleason >6 ???

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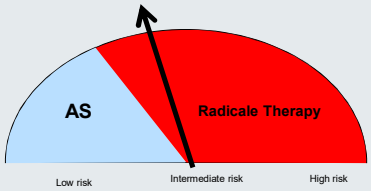
Therapeutical Options for Prostate Cancer Gleason 3+4=7



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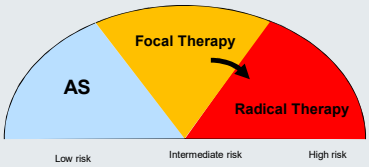
Therapeutical Options for Prostate Cancer Gleason 3+4=7



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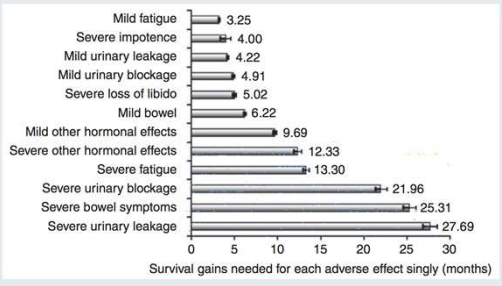
Patients are willing to trade sruvival over side effects!



Survival gains needed to offset persistent adverse treatment effects in localised prostate cancer
King MT et all, Br J Cancer. 2012 Feb 14;106(4):638-45

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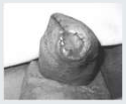
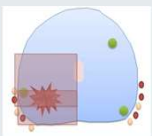
Fokale Therapie; Neuer Ansatz fürs Prostatakarzinom

Lernen von anderen Tumoren.
- Penis
- Niere



Konzepte bei der Prostata:
- Ganzes Organ behandeln
- Hemiablation = die Hälfte
- Index-lesion: es genügt die aggressiven Herde zu behandeln



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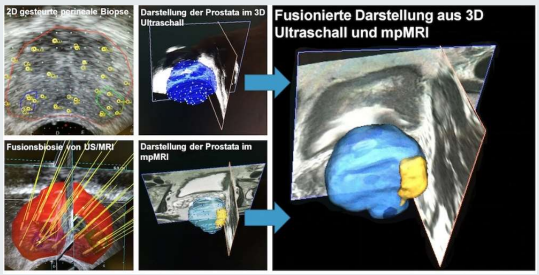
3D-MRI-Fusionierte Biopsie



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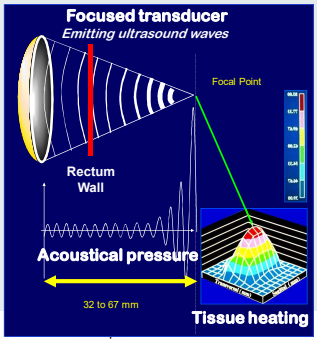
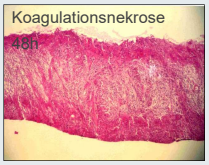
HIFU Prinzip





- Focal Treatment of Prostate Cancer with

Focal·One®

ROBOT-ASSISTED PROSTATE TUMORECTOMY

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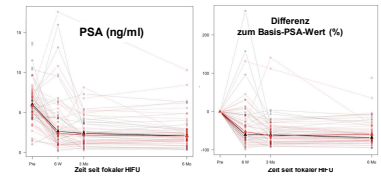
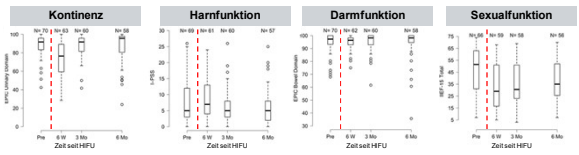
HIFU: Geringe urogenitale Nebenwirkungen





Ergebnisse USZ

Initial Bx → HIFU

56% Tumor frei

PCa

13% Beobachten

13% 2. HIFU

12%
- Radikale Operation
- Bestrahlung

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Rules of Thumb

- 6000 Pca Fälle jedes Jahr. 1500 versterben
- Nur Männer Screenen die noch lange leben (Min 10 Jahre), am Besten um 50J.
- Ziel Verhinderung von Tod, Schmerzen durch Metastasen
- MRI ist in 85% korrekt. 15% der Tumore werden übersehen.
- Biopsie mit MRI 95% Sicherheit der Diagnose.
- Bei Gleason 3+3 Tumoren Active Surveilance
- Roboter OP sehr gute Tumorkontrolle. Nebenwirkungen
- Fokale Therapie: Gut für kleine Tumore im Alter.

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Vielen Dank für Ihre Aufmerksamkeit!

Fragen?

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