

# **ΡΙΖΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΚΑΡΚΙΝΟΥ ΤΟΥ ΠΡΟΣΤΑΤΗ**

ΙΩΑΝΝΗΣ ΒΑΡΚΑΡΑΚΗΣ

ΑΝΑΠΛΗΡΩΤΗΣ ΚΑΘΗΓΗΤΗΣ

ΕΘΝΙΚΟ & ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΣΙΣΜΑΝΟΓΛΕΙΟ Γ.Ν

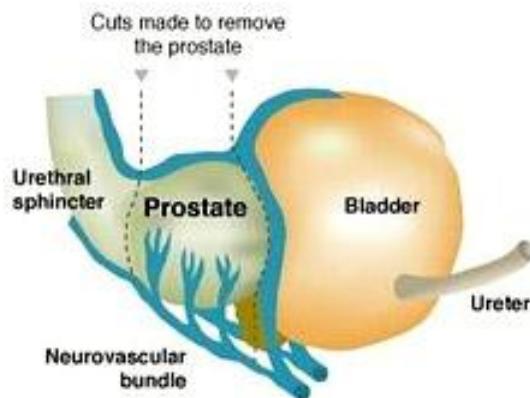


**Dept. Urology, Athens Medical School**

# ΠΙΖΙΚΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ

## RISK STRATIFICATION

	Low-risk	Intermediate-risk	High-risk	
Definition	PSA < 10 ng / mL and GS < 7 and cT1-2a	PSA 10-20 ng /mL or GS 7 or cT2b	PSA > 20 ng / mL or GS > 7 or cT2c	any PSA any GS cT3-4 or cN+
Localised			Locally advanced	



# ΡΙΖΙΚΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ

## EAU GUIDELINES - INDICATIONS FOR RP

In patients with low- and intermediate-risk PCa and a life expectancy > 10 years, RP should be offered. 1b A

In patients with high-risk localised PCa and a life expectancy of > 10 years, RP should be offered in a multimodality setting. 2a A

In selected patients with locally advanced (cT3a) PCa, and a life expectancy > 10 years, RP may be offered in a multimodality setting. 2b B

- Προσδόκιμο επιβίωσης (>10 έτη)
  - Ηλικία
  - Συνοσηρότητα

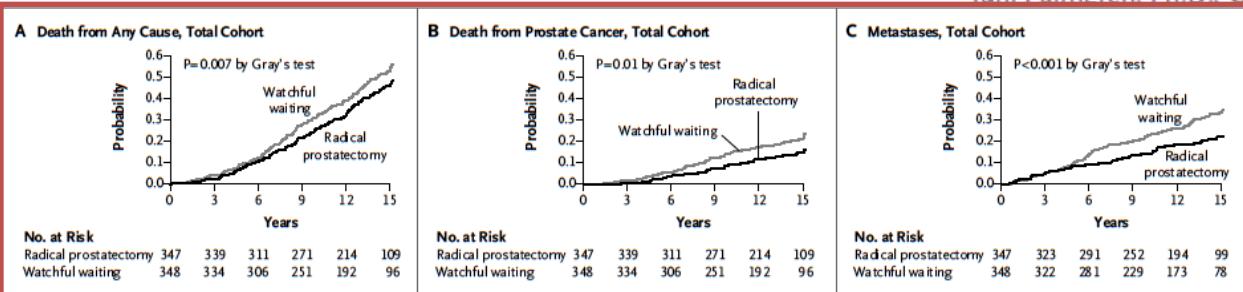
In highly selected patients with locally advanced PCa (cT3b-T4 N0 or any T N1), RP may be offered in a multimodality setting. 3 C





# Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

**benefit for OS & CSS & risk of M+**



SPCG-4

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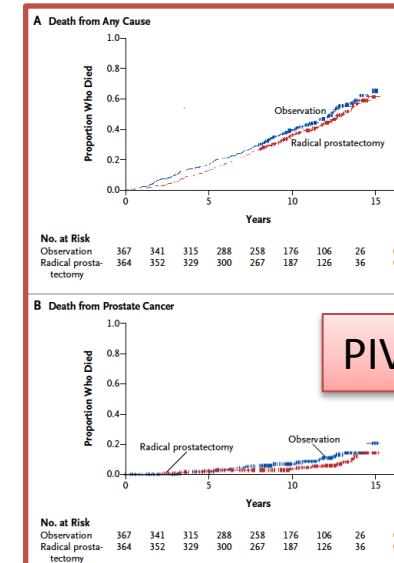
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**Results not reproduced**



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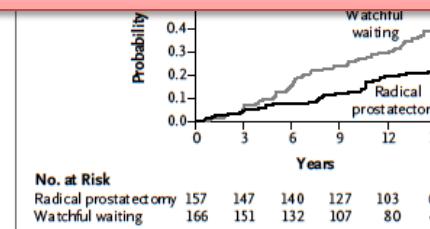
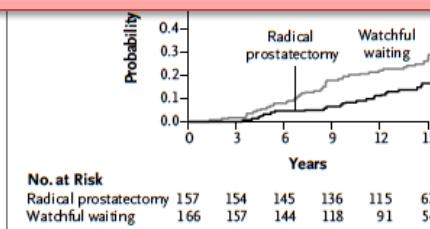
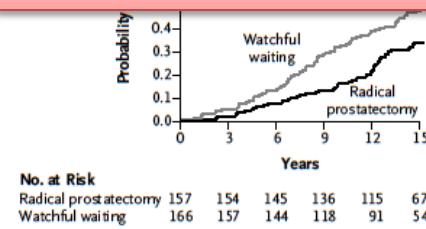
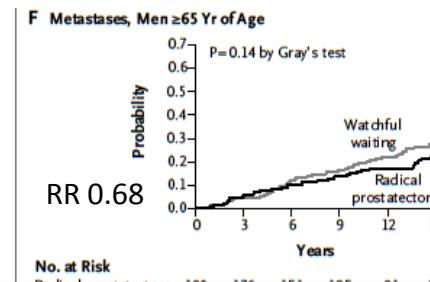
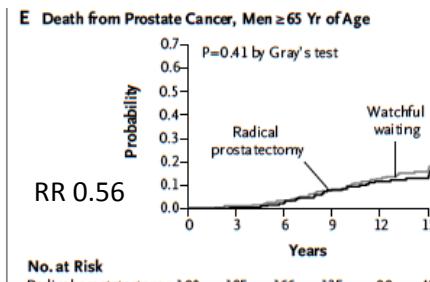
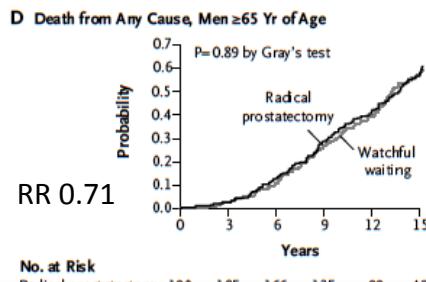
PIVOT trial



# LOW RISK PCa

## Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D.,  
Mirja Ruutu, M.D., Ph.D., Hans Garmo, Ph.D., Jennifer R. Stark, Sc.D.,  
Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D.,  
Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D.,  
Stefan Bratell, M.D., Ph.D., Anders Spångberg, M.D., Ph.D.,  
Juni Palmgren, Ph.D., Gunnar Steineck, M.D., Ph.D.,  
Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D.,  
for the SPCG-4 Investigators\*



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# LOW RISK PCa



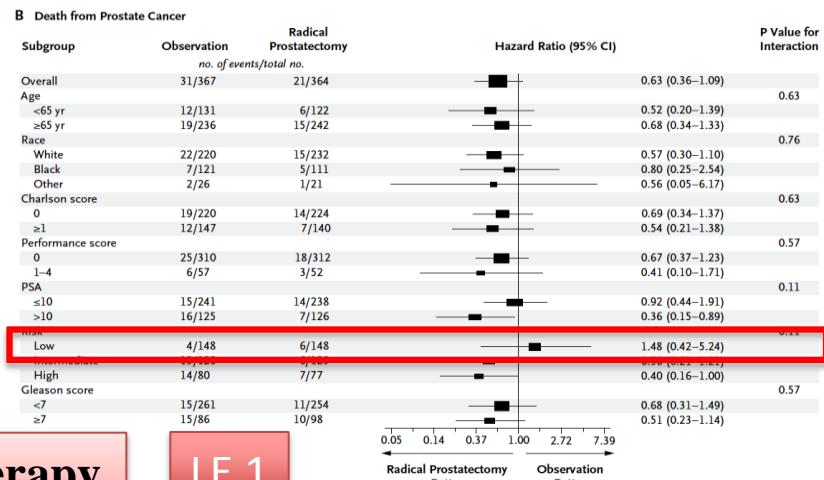
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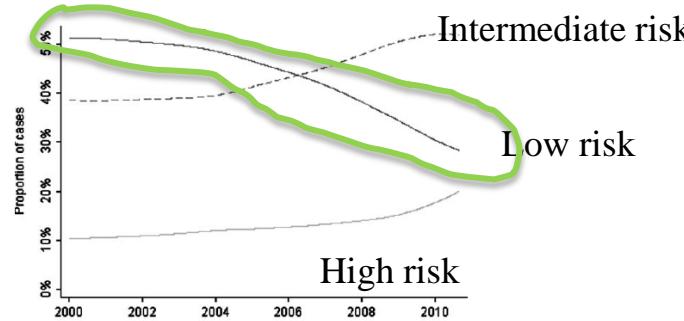


Lack of benefit in low risk Dx from radical therapy

LE 1



Less low risk Pt undergoing RRP



Dept. Urology, Athens Medical School



Reverse Stage Shift at a Tertiary Care Center

Escalating Risk in Men Undergoing Radical Prostatectomy

Jonathan L. Silberstein, MD<sup>1</sup>; Andrew J. Vickers, PhD<sup>2</sup>; Nicholas E. Power, MD<sup>1</sup>; Samson W. Fine, MD<sup>3</sup>; Peter T. Scardino, MD<sup>1</sup>; James A. Eastham, MD<sup>1</sup>; and Vincent P. Laudone, MD<sup>1</sup>

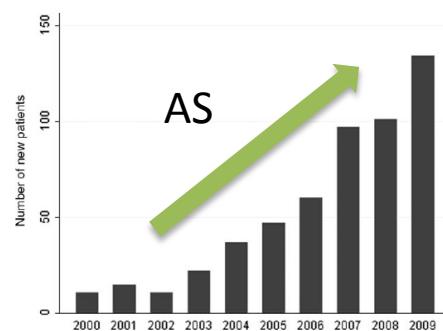


Figure 5. This bar chart illustrates the number of patients enrolled in active surveillance by year.

# INTERMEDIATE RISK PCa

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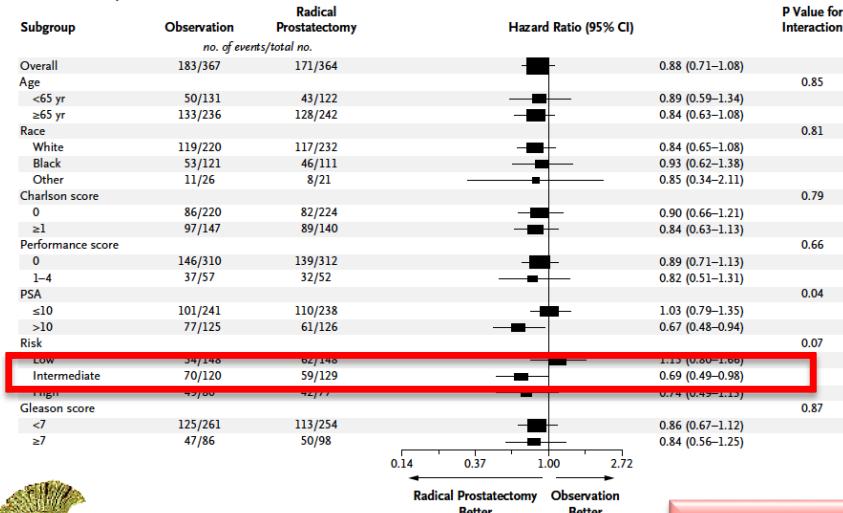
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PIVOT

#### A Death from Any Cause



OS RR 0.71

+LNs 3.7-20.1%  
eLND performed if risk >5%

CSS RR 0.56



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# HIGH RISK PCa



## Radical Prostatectomy for Clinically Localized, High Risk Prostate Cancer: Critical Analysis of Risk Assessment Methods

Ofer Yossepowitch, Scott E. Eggener, Fernando J. Bianco Jr., Brett S. Carver, Angel Serio, Peter T. Scardino, James A. Eastham.

*Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York*

- There is **no consensus** regarding the optimal treatment
- **Not all** high-risk PCa patients have a uniformly **poor prognosis after RP**

	OS	5y CSS	10y CSS	15y CSS
GS 8-10	29%	96%	86%	66%
PSA>20ng/ml		50%	30%	25%

- Provided the tumor is **not fixed** **RP is a reasonable first step** in selected patients with a low tumour volume
- **e-LND** should be performed **in all cases** (risk +LN 15-40%)



# LOCALLY ADVANCED PCa

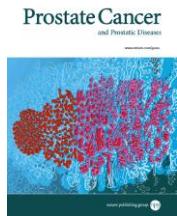
- RP traditionally discouraged because increased risk of +sm, + LN, distant relapse.
- Renewed interest in RP part of multimodality setting assuming LN (-)



## Results of radical prostatectomy in men with locally advanced prostate cancer: multi-institutional pooled analysis.

Gerber GS<sup>1</sup>, Thisted RA, Chodak GW, Schroder FH, Frohmuller HG, Scardino PT, Paulson DF, Middleton AW Jr, Rukstalis DB, Smith JA Jr, Ohori M, Theiss M, Schellhammer PF.

cT3	5years	10years
CSS	90-99%	85-92%
OS	90-96%	76-77%
BFS	45-62%	43-51%



## Predicting prostate cancer-specific outcome after radical prostatectomy among men with very high-risk cT3b/4 PCa: a multi-institutional outcome study of 266 patients

F Moltzahn, J Karnes, P Gontero, B Kneitz, B Tombal, P Bader, A Briganti, F Montorsi, H Van Poppel, S Joniau and M Spahn

CT3b-T4	5years	10 years
CSS	88-92%	87-92%
OS	73-88%	65-71%

- Due to limited evidence, local treatment of cN+ patients, should be discussed on individual basis.



# RP with cN0 → pN1

Immediate versus deferred androgen deprivation treatment in patients with node-positive prostate cancer after radical prostatectomy and pelvic lymphadenectomy

Edward M Messing, Judith Manola, Jorge Yao, Maureen Kiernan, David Crawford, George Wilding, Anthony di'Sant Agnese, Donald Trump, on behalf of the Eastern Cooperative Oncology Group study EST 3886



- Dramatic **improvement** in CSS and OS **in favour of completed RP** vs. abandoned RP in patients who were found to be **N+ at the time of surgery**.

After surgery in pN1 PCa	5 years	10 years	15 years
CSS	84-95%	51-86%	45%
OS	79-85%	36-69%	42%

- Frozen sections** of LN intraoperatively **no longer** recommended



# ROBOT VS OPEN VS LAP



Platinum Priority – Prostate Cancer  
Editorial by Thomas E. Ahlering on pp. 226–227 of this issue

## Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial

Eva Haglund <sup>a,\*</sup>, Stefan Carlsson <sup>b</sup>, Johan Stranne <sup>c</sup>, Anna V. Thorlind Thorsteinsdottir <sup>d,e</sup>, Mikael Lagerkvist <sup>f</sup>, Jan-Erik L. Jonas Hugosson <sup>c</sup>, Peter Wiklund <sup>a</sup>, Gunnar Steineck <sup>a,g,h</sup>,  
on behalf of the LAPPRO steering committee<sup>i</sup>

<sup>a</sup>Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy at the University of Sweden; <sup>b</sup>Department of Molecular Medicine and Surgery, Section of Urology, Karolinska Institutet, Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg, Sahlgrenska University Hospital, Göteborg, Sweden; <sup>c</sup>Department of Clinical Oncology, Sahlgrenska University Hospital, School of Health Sciences, University of Iceland, Reykjavík, Iceland; <sup>d</sup>UroClinic, Stockholm, Sweden; <sup>e</sup>Department of Urology, Skane University Hospital, Lund University, Malmö, Sweden; <sup>f</sup>Department of Oncology and Pathology, Division of Clinical Cancer Epidemiology, Karolinska Institutet, Stockholm, Sweden



Collaborative Review – Prostate Cancer

## A Systematic Review of the Volume–Outcome Relationship for Radical Prostatectomy

Quoc-Dien Trinh <sup>a,b,c,\*</sup>, Anders Bjartell <sup>d</sup>, Stephen J. Freedland <sup>e</sup>, Brent K. Hollenbeck <sup>f</sup>, Jim C. Hu <sup>g</sup>, Shahrokh F. Shariat <sup>h</sup>, Maxine Sun <sup>b</sup>, Andrew J. Vickery <sup>i</sup>

<sup>a</sup>CRCUM, Centre Hospitalier de l'Université de Montréal, Montreal, Canada; <sup>b</sup>Cancer Prognostics, l'Université de Montréal, Montreal, Canada; <sup>c</sup>Vattikuti Urology Institute, Henry Ford Health System, University Hospital, Malmö, Sweden; <sup>d</sup>Section of Urology, Durham VA Medical Center, Durham, NC, USA; <sup>e</sup>Surgery, Departments of Surgery and Pathology, Duke University School of Medicine, Durham, NC, USA; <sup>f</sup>Outcomes and Policy, University of Michigan, Ann Arbor, MI, USA; <sup>g</sup>Department of Urology, David Geffen <sup>h</sup>Department of Urology, Weill Medical College of Cornell University, New York, NY, USA; <sup>i</sup>Department Kettering Cancer Center, New York, NY, USA

In patients who are surgical candidates for radical prostatectomy, all approaches (i.e. open, laparoscopic or robotic) are acceptable because none has clearly shown superiority in terms of functional or oncological results.

1a A

Trifecta differences NS

**Conclusions:** In a Swedish setting, RALP for prostate cancer was modestly beneficial in preserving erectile function compared with RRP, without a statistically significant difference regarding urinary incontinence or surgical margins.

**Conclusions:** Undeniable evidence suggests that increasing volume improves outcomes. Although it would seem reasonable to refer RP patients to high-volume centers, such regionalization may not be entirely practical. As such, the implications of such a shift in practice have yet to be fully determined and warrant further exploration.

High volume surgeon



# ΕΠΙΠΛΟΚΕΣ RP



Complication	Incidence (%)
Per-operative death	0-2
Major bleeding	1-11.5
Rectal injury	0-5.4
DVT	0-8.3
PE	0.8-7.7
Lymphocele	1-3
Urine leak, fistula	0.3-15.4
Stress incontinence	4-50 / 0-15.4
Impotence	29-100
Bladder neck obstruction	0.5-14.6
Ureteral obstruction	0-0.7
Urethral stricture	2-9

## Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: Surgical, Oncological, and Functional Outcomes: A Systematic Review

Francesco De Carlo<sup>a</sup> Francesco Celestino<sup>b</sup> Cristian Verri<sup>a</sup> Francesco Masedu<sup>c</sup>  
Emanuele Liberati<sup>b</sup> Savino Mauro Di Stasi<sup>a</sup>

Predicted probability of event	RALP	Laparoscopic RP	RRP
Bladder neck contracture	0.010	0.021	0.049
Anastomotic leak	0.010	0.044	0.033
Infection	0.008	0.011	0.048
Organ injury	0.004	0.029	0.008
Ileus	0.011	0.024	0.009
Deep-vein thrombosis	0.006	0.002	0.014
Predicted rates of event	RALP (%)	Laparoscopic RP (%)	RRP (%)
Clavien I	2.1	4.1	4.2
Clavien II	3.9	7.2	17.5
Clavien IIIa	0.5	2.3	1.8
Clavien IIIb	0.9	3.6	2.5
Clavien IVa	0.6	0.8	2.1
Clavien V	<0.1	0.2	0.2



# ΕΠΙΠΛΟΚΕΣ ΣΕ ΕΞΕΙΔΙΚΕΥΜΕΝΟ ΚΕΝΤΡΟ

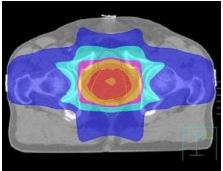
ΕΓΚΡΑΤΕΙΑ & ΣΤΥΤΙΚΗ ΛΕΙΤΟΥΡΓΙΑ ΜΕΤΑ ΑΠΟ ΡΠ

στο **Johns Hopkins**

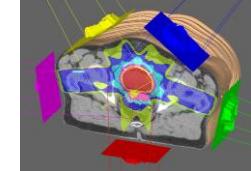
	3 μήνες	6 μήνες	12 μήνες	18 μήνες
<b>Στυτική λειτουργία</b>				
Ικανός	38%	54%	73%	86%
Καθόλου ή μικρό πρόβλημα	49%	64%	76%	84%
<b>Εγκράτεια</b>				
Καμία πάνα	79%	88%	98%	



# ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

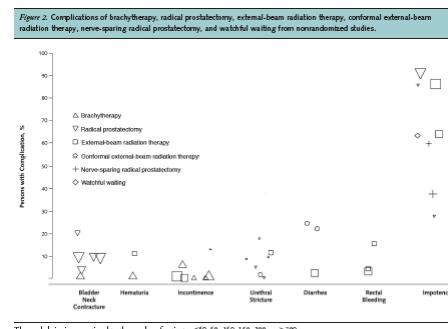


- 3D CRT
- IMRT
- TOMOTHERAPY



- **Intensity-modulated radiotherapy (IMRT)**, with or without image-guided radiotherapy (IGRT), is the gold standard for EBRT.
- **Dose escalation (range 74-80Gy):**
  - No trials showing OS benefit with dose escalation, however consistent improvements in freedom from **biochemical progression** are reported.
- **Hypofractionation (1.8-2Gy)**

## Complications



# XBRT INDICATIONS

Radiotherapy	In low-risk PCa the total dose should be 74 to 78 Gy.	A
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Radiotherapy	In intermediate-risk PCa, the total dose should be 76-78 Gy in combination with short-term ADT (4-6 mo).	A
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Radiotherapy	In patients with high-risk localised PCa, the total dose is 76-78 Gy in combination with long-term ADT (2-3 yr is recommended). In patients with locally advanced cN0 PCa, radiotherapy must be given in combination with long-term ADT (2-3 yr is recommended).	A
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European  
Association  
of Urology

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GUIDELINES

# ΒΡΑΧΥΘΕΡΑΠΕΙΑ

In patients with low-risk PCa, without a previous ~~TURP~~ and with a good IPSS and a prostate volume < 50 mL, LDR brachytherapy is a treatment option.

A



Low risk	5year	10 year		Differences in prostate brachytherapy techniques
RFS	71-93%	65-85%	Low Dose Rate (LDR)	Permanent seeds Uses I-125, Pd-103 or Cs-131 isotopes Radiation delivered over weeks and months Acute side effects resolve over months Radiation protection issues for patient and carers
Complications <b>Urinary retention 1.5-22% (TURP 9%)</b> Incontinence 0-19% ED 40%	High Dose Rate (HDR)			Temporary implantation Ir-192 isotope introduced through implanted needles or catheters Radiation dose delivered in minutes Acute side effects resolve over weeks No radiation protection issues for patient or carers

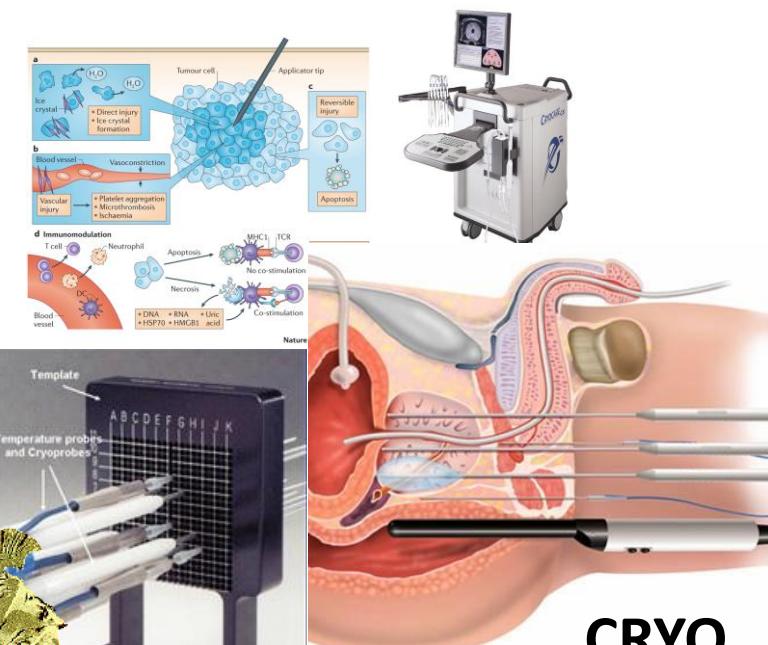


# OTHER FORMS OF RADICAL THERAPY

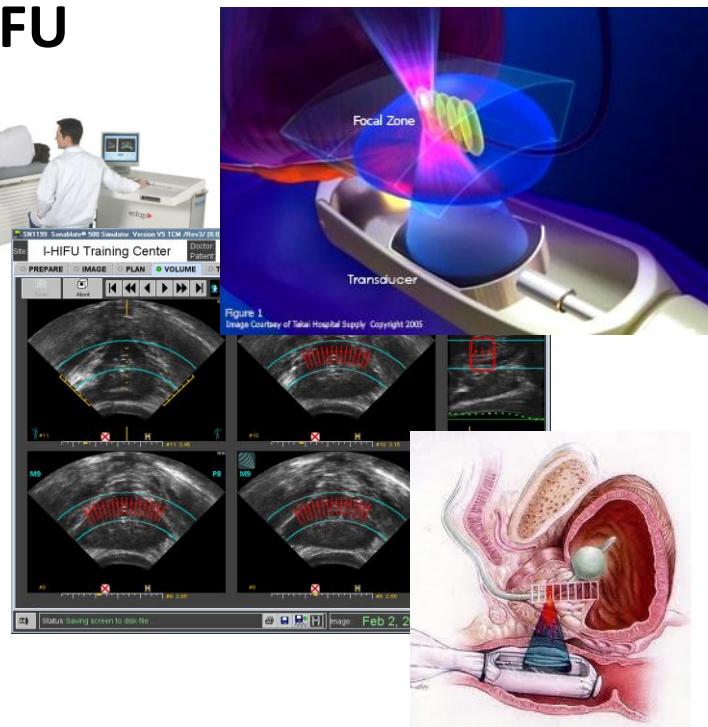
## Cryotherapy, HIFU

In patients who are unfit for surgery or radiotherapy, cryotherapy or HIFU might be an alternative treatment for PCa. The lack of long-term efficacy compared to standard modality should be discussed with patients.

C



## HIFU



## CRYO



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# **ΑΝΤΙΜΕΤΩΠΙΣΗ ΡΙΖΙΚΗΣ ΠΡΟΣΤΑΤΕΚΤΟΜΗΣ ΜΕ ΑΥΞΗΜΕΝΟ ΚΙΝΔΥΝΟ ΓΙΑ ΥΠΟΤΡΟΠΗ**



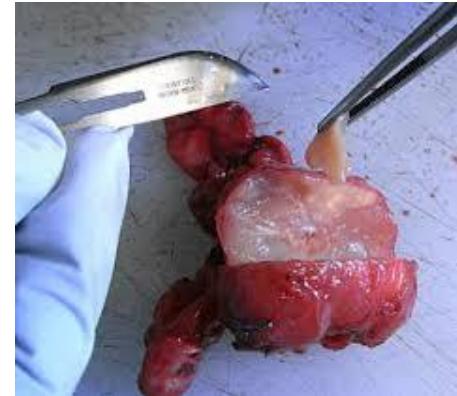
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# ΡΙΖΙΚΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ



## ΚΑΚΑ ΠΡΟΓΝΩΣΤΙΚΑ ΣΗΜΕΙΑ ΜΕΤΑ ΡΠ

- Εξωκαψική νόσος
- (+) χειρουργικό όριο
- Διήθηση ΣΚ
- >GS



ΑΝΤΙΜΕΤΩΠΙΣΗ?

## Κινδυνος

- BY
- Παραμονή υψηλού PSA

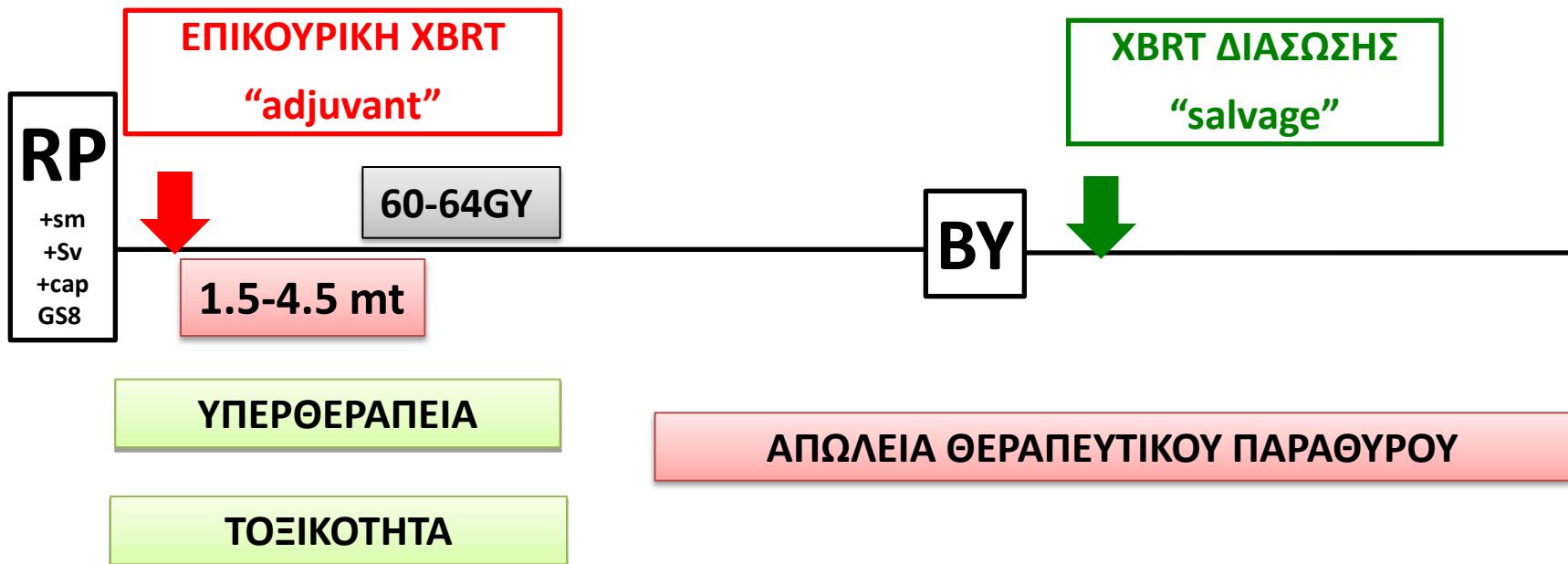




# ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ



## ΠΟΤΕ ΚΑΤΑΛΛΗΛΟ ΤΙΜΙΝΓ;



# ΕΠΙΚΟΥΡΙΚΗ ΑΚΘ vs. ΠΑΡΑΚΟΛΟΥΘΗΣΗ

3 προοπτικά τυχαιοποιημένες μελέτες – LEVEL 1b

Study	N	Median FU	Biochemical PFS	Mets	Death (%)	
EORTC 22911 Bolla et al			<b>Van Popel 2011 EAU Vienna</b> FU>10years	MF NS	OS NS	
SWOG 8794 Thompson et al			<b>Thompson et al J Urol 2009</b> 12.6 years	MF p<0.016	OS p<0.023	
ARO 96-02 Wiegel et al			<b>GUIDELINE STATEMENT 2013 (ASTRO &amp; AUA)</b> <b>ADJUVANT XBRT IN PT WITH ADVERSE PATHOLOGIC FEATURES</b> <ul style="list-style-type: none"><li>• SV</li><li>• +SM</li><li>• EPE</li></ul>			



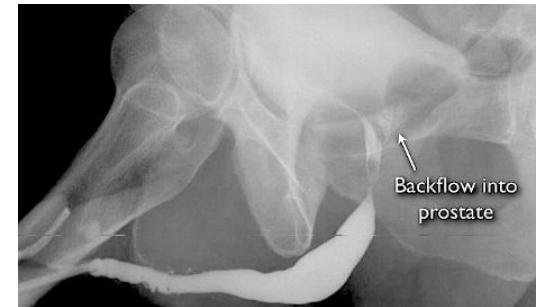
# ΜΕΙΟΝΕΚΤΗΜΑΤΑ ΕΠΙΚΟΥΡΙΚΗΣ ΑΚΘ: ΤΟΞΙΚΟΤΗΤΑ

Toxicity	Grade 2	Grade 3	Grade 4	Any significant >G2
<b>Overall GU toxicity</b>	12.4%	2.3%	1%	15.9%
Cystitis	4.7	0.5	0	
Hematuria	4.7	0	0	
Urinary stricture	4.7	1.3	1	
Urinary incontinence	4.7	0.5	0	
<b>Overall GI toxicity</b>	9.5%	0.2%	0%	9.8%
Proctitis	8.2	0	0	
Chronic diarrhoea	3.7	0	0	
Small bowel obstruction	0.2	0.2	0	
<b>Leg oedema</b>	1.5%	0%	0%	1.5%
<b>Erectile dysfunction</b>				
<b>Secondary malignancy</b>				



# ΜΕΙΟΝΕΚΤΗΜΑΤΑ ΕΠΙΚΟΥΡΙΚΗΣ ΑΚΘ ΤΟΞΙΚΟΤΗΤΑ

- SWOG 8794
  - **Urethral stricture** 24% vs. 12%
  - **Total incontinence** 6.5% vs. 2.8%
  - **Rectal complications** 3.3% vs. 0%
- EORTC 22911
  - **More frequent grade II toxicity**
  - Marginally more grade III toxicity 4.2% vs. 2.6%
  - **No grade IV toxicity**
- ARO 96-02
  - **Only 1 grade III bladder toxicity** (3D conformal planning)



x2



# ΜΕΙΟΝΕΚΤΗΜΑΤΑ ΕΠΙΚΟΥΡΙΚΗΣ ΑΚΘ: ΚΙΝΔΥΝΟΣ ΥΠΕΡΘΕΡΑΠΕΙΑΣ

- Κέρδος ΚΥΡΙΩΣ σε ασθενείς με (+) ΧΟ
- Β.Υ όχι σίγουρη σε (+) ΧΟ

## ΤΙ ΓΙΝΕΤΑΙ (-) ΧΟ & EPE

### Prostatectomy Alone

#### Prostatectomy Gleason Score 6

Capsular penetration, negative margin

90%

Capsular penetration, positive margin

75%

#### Prostatectomy Gleason Score 7

Capsular penetration, negative margin

62%

Capsular penetration, positive margin

35%



# The Impact of Anatomical Radical Retropubic Prostatectomy on Cancer Control: The 30-Year Anniversary

Jeffrey K. Mullins, Zhaoyong Feng<sup>f</sup>, Bruce J. Trock, Jonathan I. Epstein, Patrick C. Walsh, Stacy Loeb



- The **most common finding** among the 3 adverse pathologic findings for XBRT (SV, EPE, +SM) is the presence of **-SM & EPE**

## Immediate Adjuvant Radiation Therapy Following Radical Prostatectomy Should Not Be Advised for Men with Extraprostatic Extension Who Have Negative Surgical Margins

Patrick C. Walsh <sup>a,\*</sup>, Nathan Lawrentschuk <sup>b</sup>



- SWOG subanalysis of pt EXP & (-) SM never performed 
- ARO 96-02 pt EXE & (-) SM received **no significant benefit** from ADJ XBRT 



EORTC 22911 significant **reduction of BFS** but **no reduction in OS** 

Dept. Urology, Athens Medical School, J. Varkarakis



## Declining Use of Radiotherapy for Adverse Features After Radical Prostatectomy: Results From the National Cancer Data Base

Helmneh M. Sineshaw <sup>a,†,\*</sup>, Phillip J. Gray <sup>b,†</sup>, Jason A. Efstathiou <sup>b,‡</sup>, Ahmedin Jemal <sup>a,‡</sup>

<sup>a</sup>American Cancer Society, 250 Williams Street NW, Atlanta, GA, USA; <sup>b</sup>Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA



100.000 ασθενείς

ΕΞΑΤΟΜΙΚΕΥΣΗ ΘΕΡΑΠΕΙΑΣ



### ADJUVANT XBRT : WHO SHOULD RECEIVE IT

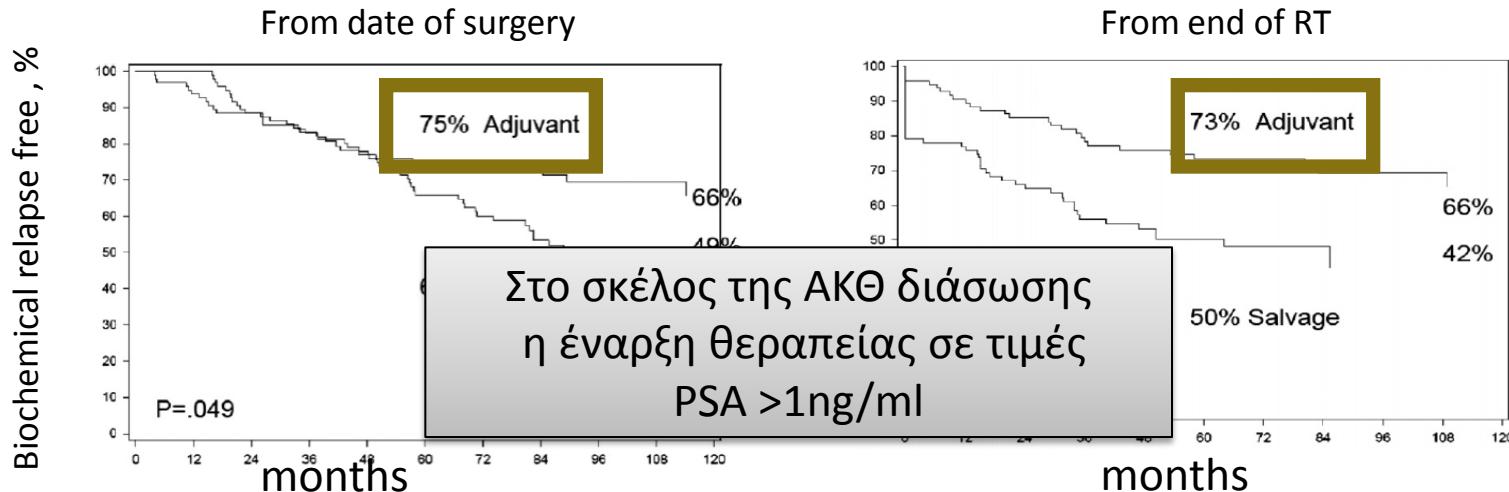
NO	YES	Marginal Benefit
<ul style="list-style-type: none"><li>• EXE &amp; (-) SM</li><li>• &gt;70y unless very healthy &amp; HG or (+) SM</li><li>• Bladder neck <b>contraction</b> or significant <b>incontinence</b> and marginal indications</li></ul>	<b>GS≥7 &amp; (+)SM</b>	+SV  ARO-9602 NO benefit BFS EORTC better BFS NO OS



# ΕΠΙΚΟΥΡΙΚΗ ΑΚΘ vs. ΑΚΘ ΔΙΑΣΩΣΗΣ

## A Multi-Institutional Matched-Control Analysis of Adjuvant and Salvage Postoperative Radiation Therapy for pT3-4N0 Prostate Cancer

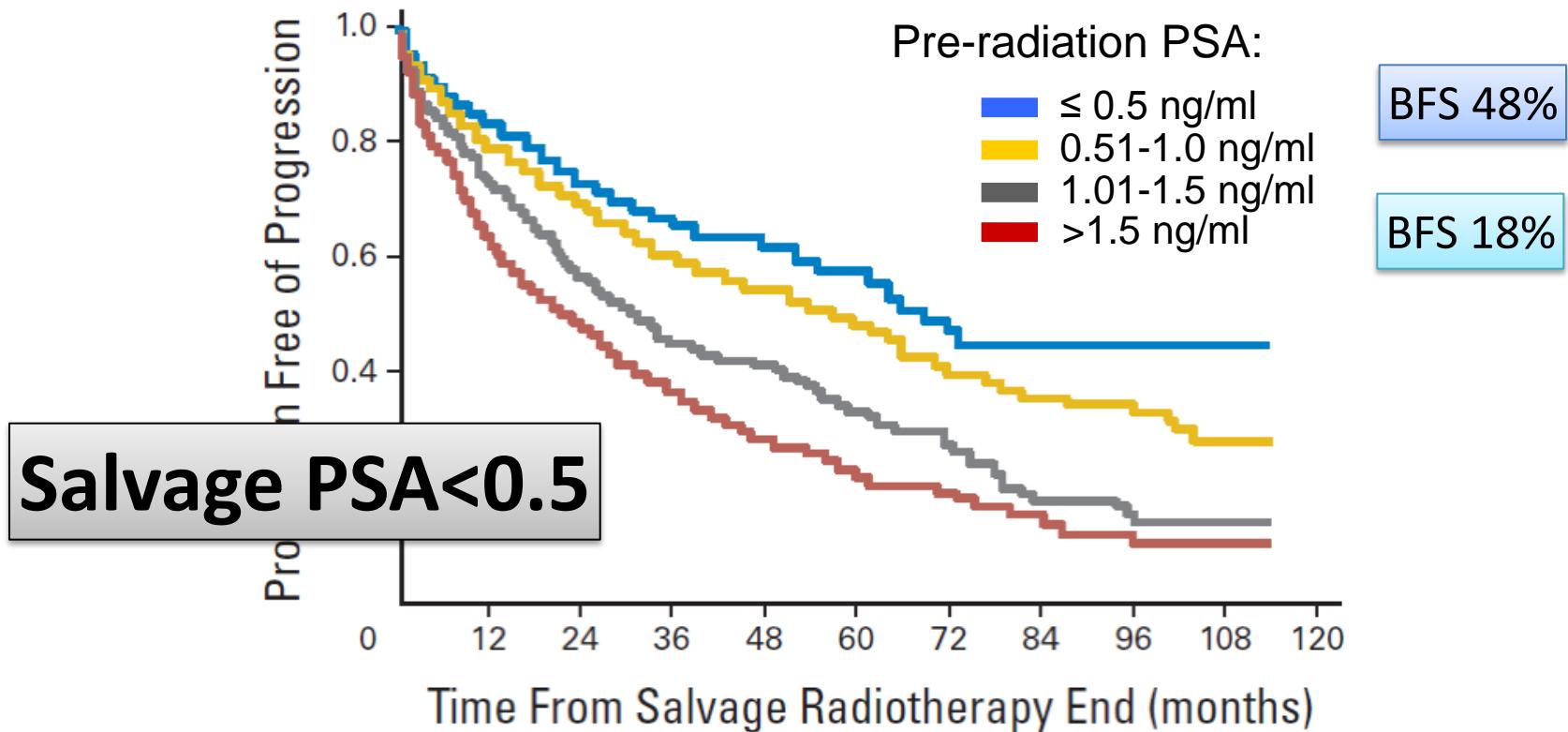
Edouard J. Trabulsi, Richard K. Valicenti, Alexandra L. Hanlon, Thomas M. Pisansky, Howard M. Sandler, Deborah A. Kuban, Charles N. Catton, Jeff M. Michalski, Michael J. Zelefsky, Patrick A. Kupelian, Daniel W. Lin, Mitchell S. Anscher, Kevin M. Slawin, Claus G. Roehrborn, Jeffrey D. Forman, Stanley L. Liauw, Larry L. Kestin, Theodore L. DeWeese, Peter T. Scardino, Andrew J. Stephenson, Alan Pollack



Αναδρομική Πολυκεντρική μελέτη 2299 (192) pts

# ΑΚΘ ΔΙΑΣΩΣΗΣ

## Σημασία PSA προ ΑΚΘ



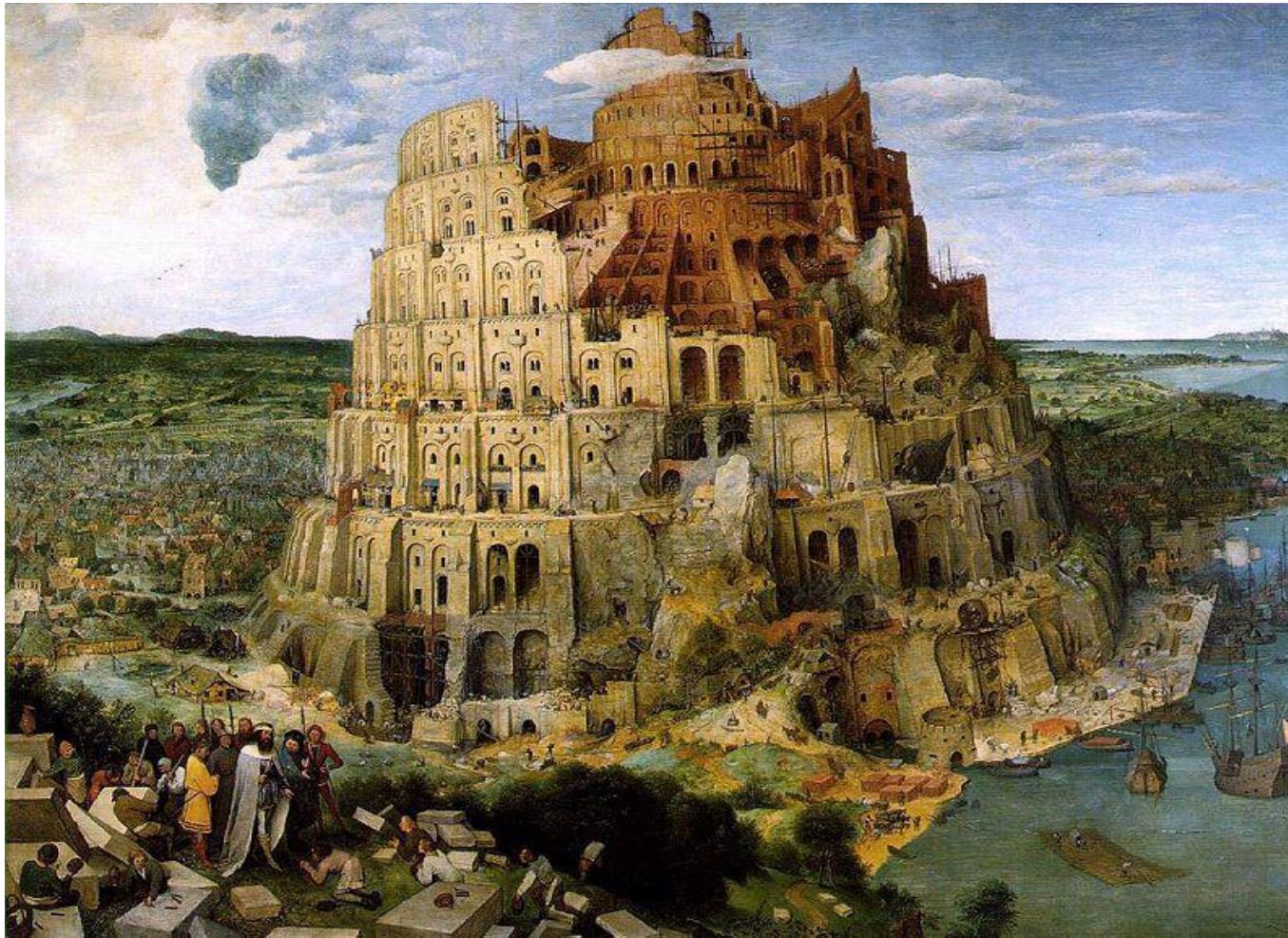
6-year progression-free probability decreased from  
48% (PSA<0.5 ng) to 18% (PSA >1.5 ng/ml)



# **ΣΥΜΠΕΡΑΣΜΑΤΑ**

- **Πρόβλεψη Βιοχημικής Υποτροπής**
  - Ομάδες Κινδύνου (Κλινικά στοιχεία, Παθ/κή εξέταση)
- **Επικουρική ΑΚΘ**
  - Καλύτερα αποτελέσματα όσον αφορά την BY κυρίως σε ασθενείς με (+) ΧΟ & HIGH GRADE νόσο
  - Αυξημένη νοσηρότητα
- **ΑΚΘ Διάσωσης**
  - PSA<0.5ng/ml





# ΕΥΧΑΡΙΣΤΩ



Dept. Urology, Athens Medical School, J. Varkarakis