Ανδρας ηλικίας 60 ετών υποβάλλεται σε τακτικό ετήσιο έλεγχο του PSA από την ηλικία των 50 ετών.
Τα προηγούμενα χρόνια η τιμή του PSA κυμάνθηκε από 0,75 μέχρι 1,35 ng/ml. Η πρόσφατη μέτρηση (χωρίς κάποια ιδιαίτερα ενοχλήματα από το κατώτερο ουροποιητικό) έδειξε 3,3 ng/ml. Το μέγεθος του προστάτη του ήταν 45 ml (διακοιλιακό υπερηχογράφημα) και η δακτυλική εξέταση ανέδειξε συμμετρικό, ομαλό, χωρίς ψηλαφητές σκληρίες και με ψηλαφητή την σπερματική αύλακα προστάτη. Στον πατέρα του (90 ετών εν ζωή) διεγνώσθη προ 2ετίας αδενοκαρκίνωμα προστάτη μετά από μέτρηση του PSA (8,5 ng/ml).
Ο θεράπων ιατρός συνέστησε βιοψία προστάτου, η οποία και πραγματοποιήθηκε (12 τεμαχίδια).

1. Η βιοψία ήταν αρνητική γιά κακοήθεια με παρουσία στοιχείων φλεγμονής
2. Η βιοψία ήταν αρνητική γιά κακοήθεια αλλά υπήρχαν εστίες χαμηλόβαθμης ενδοεπιθηλιακής νεοπλασίας (low grade PIN)
3. Η βιοψία ήταν αρνητική γιά κακοήθεια αλλά υπήρχαν πολλαπλές εστίες υψηλόβαθμης ενδοεπιθηλιακής νεοπλασίας (high grade PIN)
4. Η βιοψία ήταν αρνητική γιά κακοήθεια αλλά υπήρχε μιά εστία άτυπης υπερπλασίας (ASAP: Atypical small acinar proliferation of the prostate)

1. Πότε θα γίνει επανέλεγχος;
2. Χρειάζεται αγωγή με αντιβιοτικά;
3. Θα αξιολογηθεί η αναλογία free/total PSA την επόμενη φορά;
4. Θα αξιολογήσετε την PSA velocity;
5. Θα αξιολογήσετε το PSA doubling time;
6. Θα χρησιμοποιήσετε το PCA3;
7. Θα χρησιμοποιήσετε νομογράμματα/υπολογιστές κινδύνου;
8. Θα ζητήσετε επιπλέον απεικονιστικά στοιχεία;
9. Τι τεχνική θα χρησιμοποιηθεί στην επαναληπτική βιοψία;

The optimal timing of a repeat biopsy procedure is not known and depends among other factors on the outcome of the initial biopsy (e.g. presence of ASAP) and the estimated risk of prostate cancer depending on e.g. rising PSA levels and/or suspicious DRE. The later the repeat biopsy is done, the higher the detection rate

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# When serial prostate biopsy is recommended: most cancers detected are clinically insignificant

**Osama M. Zaytoun, Andrew J. Stephenson, Khaled Fareed, Ahmed El-Shafei, Tianming Gao*, David Levy and J. Stephen Jones**

*Glickman Urological and Kidney Institute, *Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, USA*

Accepted for publication 9 November 2011

We recommend routine delayed interval biopsy every 2–3 years after HGPIN detection in young healthy men, based on studies showing significant cancer diagnosis at these intervals [18]. For patients with ASAP, we recommend repeat biopsy within 6 months. For patients with initial completely normal or benign biopsy findings, the time for further biopsy was tailored according to the risk indicators encountered with each individual case, based on clinical decisions with the staff physician. As noted, for many

International Journal of Urology (2011) 18, 557–568 doi: 10.1111/j.1442-2042.2011.02798.x

Review Article

# Prostate cancer detection after a negative prostate biopsy: Lessons learnt in the Cleveland Clinic experience

Osama M Zaytoun[1,2] and J Stephen Jones[1]

[1]Glickman Urological & Kidney Institute, Cleveland Clinic, Cleveland, Ohio, USA; and [2]Department of Urology, Faculty of Medicine, Alexandria University, Egypt

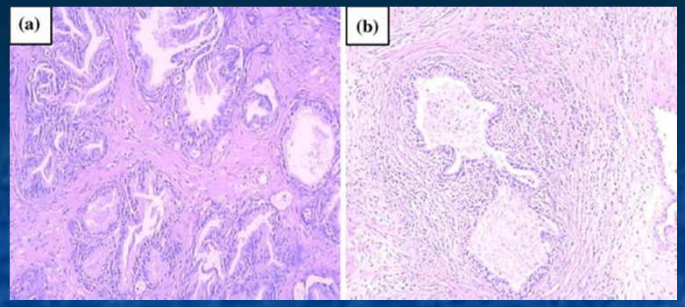
## What is the best time interval between repeat biopsies?

There is no consensus or clear recommendations regarding the optimum repeat PBx scheduling. However, it has been suggested that PCa detection might be influenced by the interval between biopsies.[10,19] This can be attributed by giving adequate time for premalignant lesions to progress into overt adenocarcinoma.

In absence of guidelines regarding the best intervals between biopsies, it seems reasonable that the optimal interval should be tailored according to the risk indicators encountered in each individual case. After a negative PBx session, we usually wait 1 year, unless ASAP was detected.

# Χρειάζεται αγωγή με αντιβιοτικά;

## (type IV asymptomatic inflammatory prostatitis)




**Prostate Specific Antigen Decrease and Prostate Cancer Diagnosis: Antibiotic Versus Placebo Prospective Randomized Clinical Trial**

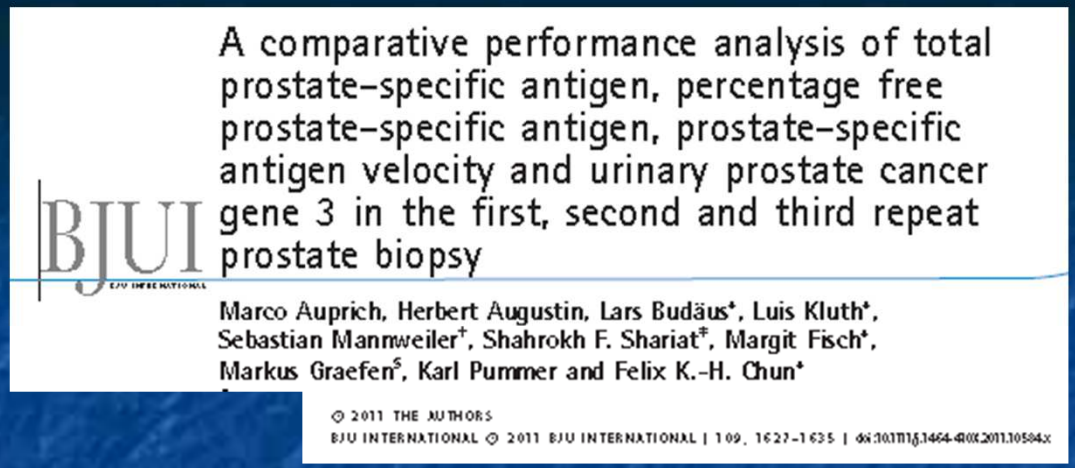
R. M. Stopiglia, U. Ferreira, M. M. Silva, Jr., W. E. Matheus, F. Denardi and L. O. Reis*

0022-5347/10/1833-0940/0
THE JOURNAL OF UROLOGY®
Vol. 183, 940-945, March 2010
Printed in U.S.A.

**CONCLUSIONS**

There was no statistical difference in the decrease in PSA in patients with type IV prostatitis after antibiotics or placebo (59.2% vs 53.1%). There was also no significant difference with respect to patients who had a decrease in PSA and diagnosis of prostate cancer after treatment with antibiotic or placebo (31% vs 26.9%). Thus, this study shows that antimicrobial therapy was no more effective than placebo in reducing PSA, and that the proportion of patients with cancer was similar in both groups (at least a third). More studies and larger samples should be conducted to confirm our data.

Total PSA, F/T PSA, PSA velocity,
PSA density, PSA doubling time, PCA3



A comparative performance analysis of total prostate-specific antigen, percentage free prostate-specific antigen, prostate-specific antigen velocity and urinary prostate cancer gene 3 in the first, second and third repeat prostate biopsy

Marco Auprich, Herbert Augustin, Lars Budäus*, Luis Kluth*, Sebastian Manmweiler†, Shahrokh F. Shariat‡, Margit Fisch*, Markus Graefen§, Karl Pummer and Felix K.-H. Chun*


BJU INTERNATIONAL © 2011 BJU INTERNATIONAL | 109, 1627–1635 | doi:10.1111/j.1464-410X.2011.10584.x

In conclusion, the present findings demonstrate a strong influence of the number of previous repeat biopsy sessions on the performance of established and novel biopsy risk factors.

Total PSA was not a significant risk factor in the overall, first second or ≥ third repeat biopsy session.

PSAV ' s diagnostic potential was reserved to patients at second and ≥ third repeat biopsy.

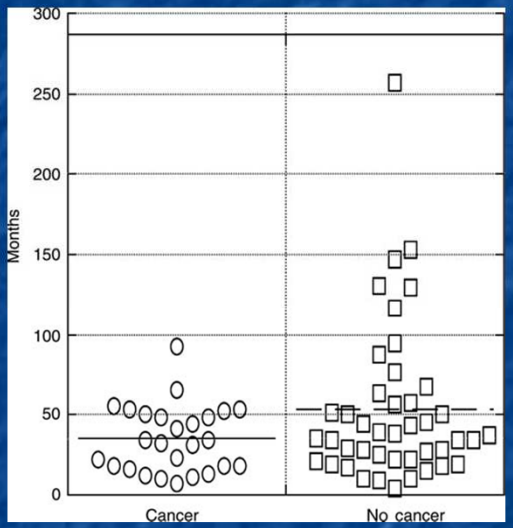
By contrast, %fPSA represented a reliable predictor of PCa across the entire repeat biopsy setting, outperforming tPSA, PSAV and PCA3 at second and ≥ third repeat biopsies.

Finally, PCA3 was highly informative at first repeat biopsy and would have avoided up to 73% of unnecessary biopsies compared with tPSA. However, in contrast to previous studies, this advantage dissipated at second and ≥ third repeat biopsies.

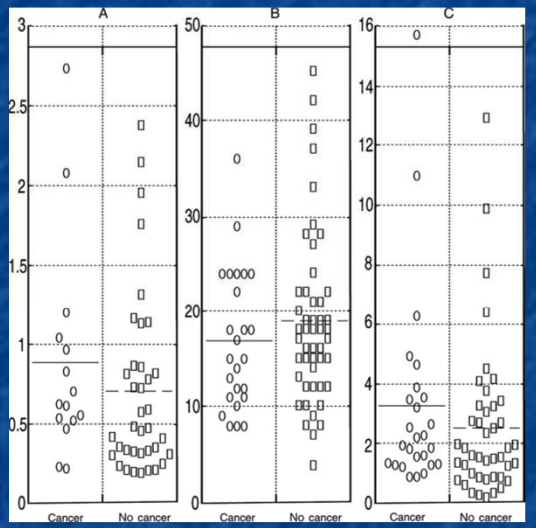
*Jpn J Clin Oncol 2009;39(11)727–731*
*doi: 10.1093/jjco/hyp091*

# PSA Doubling Time as a Predictive Factor on Repeat Biopsy for Detection of Prostate Cancer

**Masashi Shimbo[1], Susumu Tomioka[1], Makoto Sasaki[1], Takayuki Shima[1], Noriyuki Suzuki[1], Shino Murakami[1], Hiroomi Nakatsu[1] and Jun Shimazaki[2]**



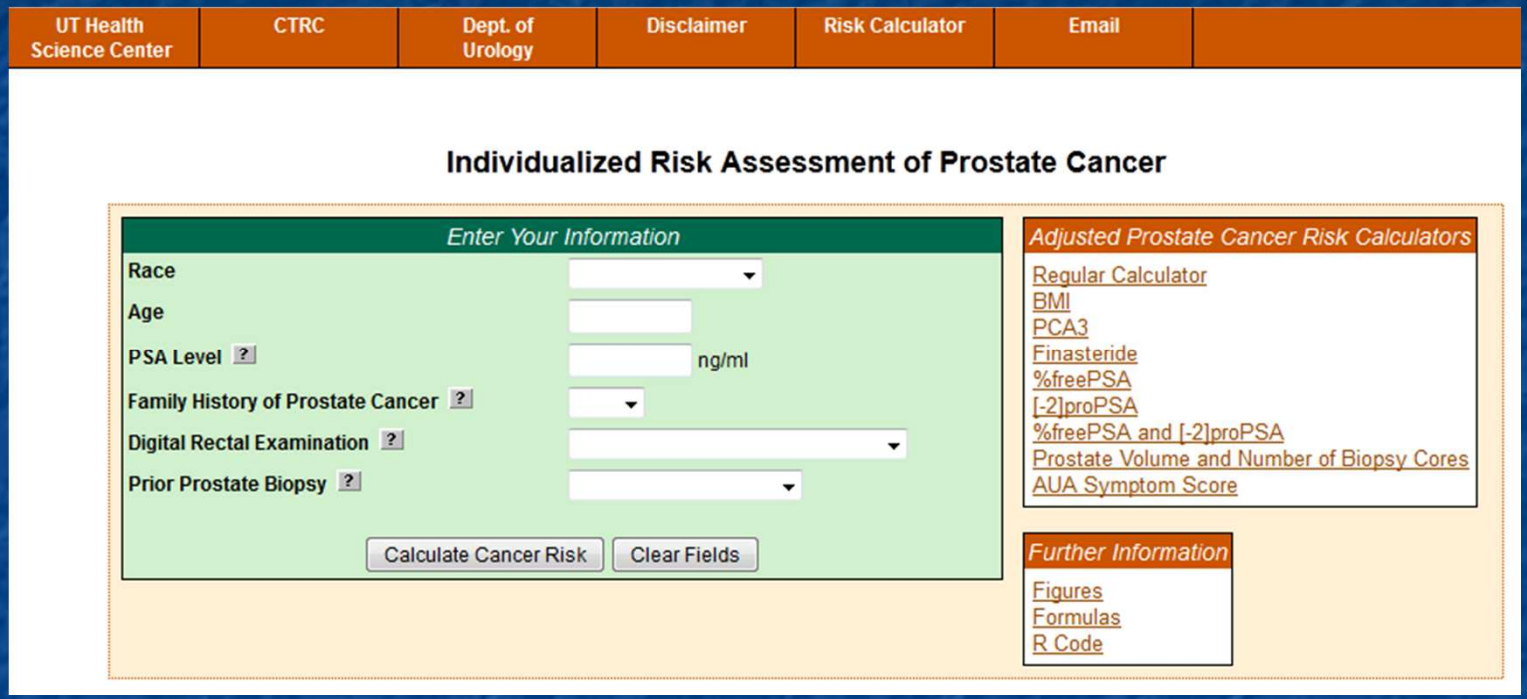

PSA doubling time




PSA transition zone density (ng/ml/volume of transition zone), %Free/tPSA and PSA velocity (ng/ml/year).

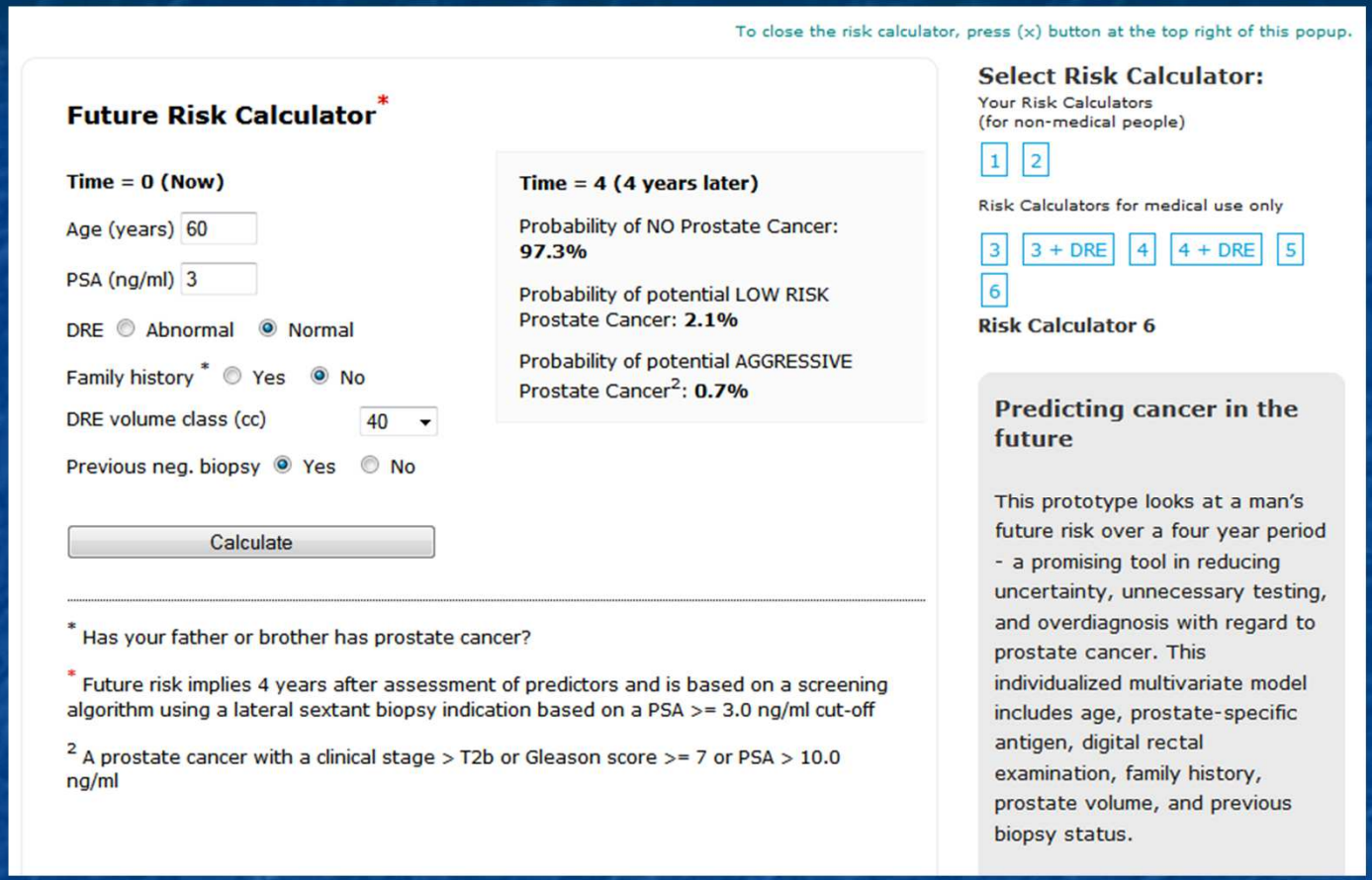
**Methods:** Seventy-seven cases with negative initial prostate biopsy received a repeat biopsy and factors for the detection of cancer were examined.
**Results:** PSA doubling time distinguished a part of cancer cases. Its sensitivity of 30, 50 and 70 months was 36.6%, 30.4% and 10%, respectively. Cancer case did not show PSA doubling time of >100 months in general. Values of PSA transition zone density, %Free/total PSA and PSA velocity were similar between cancer and no cancer cases.
**Conclusions:** PSA doubling time was one of the predictive factors for the detection of prostate cancer and was valuable for avoiding unnecessary repeat biopsy in some cases.

# PCPT risk calculator




*http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp*

# ERSPC risk calculator




*www.prostatecancer-riskcalculator.com*

Θα ζητήσετε επιπλέον απεικονιστικά στοιχεία;

Modern imaging studies (including multiparametric MRI, multiparametric TRUS, or an MR/US fusion technique) might have an even more relevant role in visualising clinically significant cancers to facilitate precise sampling from a suspicious area in the repeat prostate biopsy setting

**Contemporary Role of Systematic Prostate Biopsies: Indications, Techniques, and Implications for Patient Care**

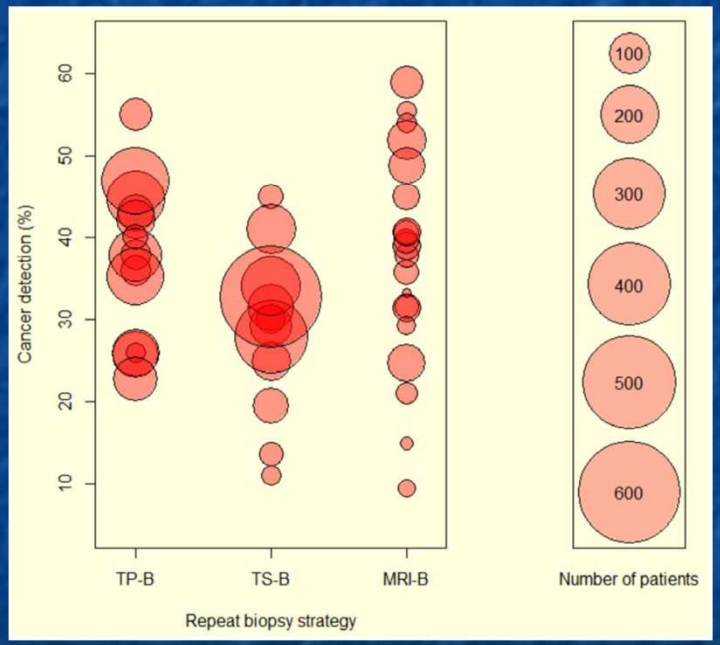
*Osamu Ukimura[a,b,*], Jonathan A. Coleman[c], Alex de la Taille[d], Mark Emberton[e,f], Jonathan I. Epstein[g], Stephen J. Freedland[h], Gianluca Giannarini[i], Adam S. Kibel[j], Rodolfo Montironi[k], Guillaume Ploussard[l], Monique J. Roobol[m], Vincenzo Scattoni[n], J. Stephen Jones[o]*

*European Urology 2013*

# Repeat Prostate Biopsy Strategies after Initial Negative Biopsy: Meta-Regression Comparing Cancer Detection of Transperineal, Transrectal Saturation and MRI Guided Biopsy

Adam W. Nelson[1], Rebecca C. Harvey[2], Richard A. Parker[2], Christof Kastner[1], Andrew Doble[1], Vincent J. Gnanapragasam[1,3]*

PLOS ONE | www.plosone.org 1 February 2013 | Volume 8 | Issue 2 | e57480




Conclusions: In the re-biopsy setting, it is unclear which strategy offers the highest cancer detection rate. MRI-B may potentially detect more prostate cancers than other modalities and can achieve this with fewer biopsy cores. However, well-designed prospective studies with standardised outcome measures are needed to accurately compare modalities and define an optimum re-biopsy approach.

## Τι τεχνική θα χρησιμοποιηθεί στην επαναληπτική βιοψία;

extended biopsy (EPBx; 10–12 cores) saturation biopsy (SPBx; 20 cores)

EAU Guidelines: Most studies of repeat prostate biopsy following extended initial prostate biopsy indicate that up to 30% of patients have cancers that were not previously identified.

*Campos-Fernandes J-L, Bastien L, Nicolaiew N, et al. Prostate cancer detection rate in patients with repeated extended 21- sample needle biopsy. Eur Urol 2009;55:600–9.*
*Zaytoun OM, Moussa AS, Gao T, Fareed K, Jones JS. Office based transrectal saturation biopsy improves prostate cancer detection compared to extended biopsy in the repeat biopsy population. J Urol 2011;186:850–4.*

# Συνιστώμενη τεχνική στην επαναληπτική βιοψία;

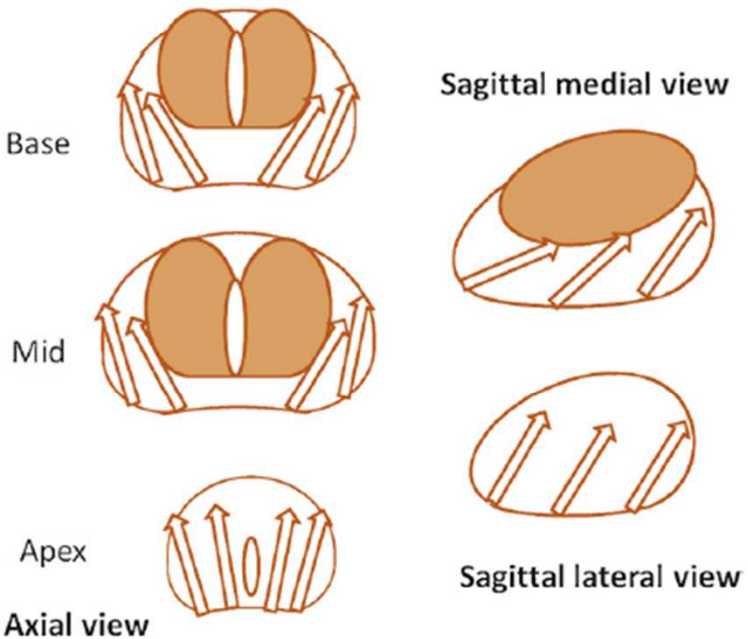



**Fig. 1 – Recommended scheme for initial prostate biopsy. A lateral and medial sextant pattern with 12 cores (extended) covers the entire peripheral zone (PZ) of the prostate to maximise diagnosis of the most frequent cancer located in the PZ.**

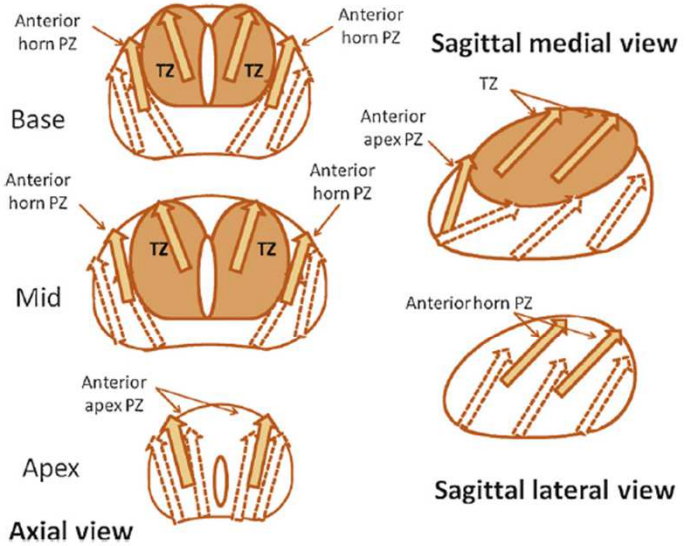


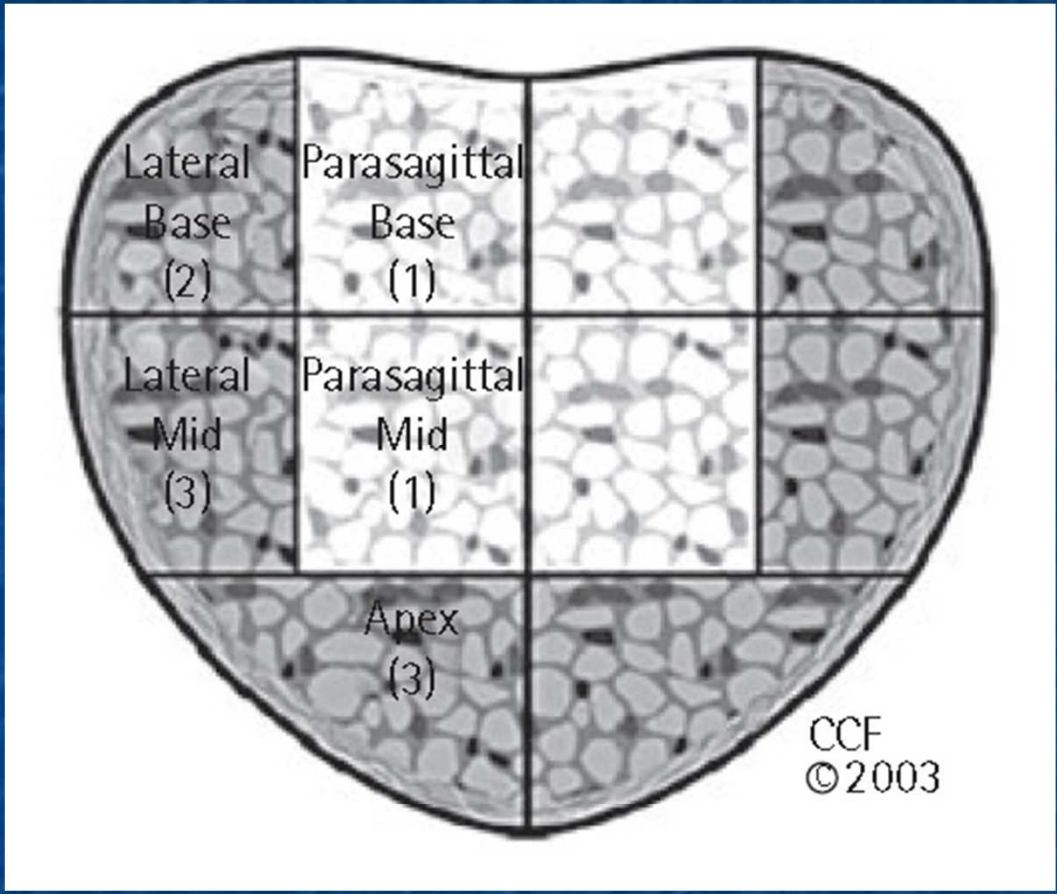

**Fig. 2 – Recommended scheme for repeat prostate biopsy. The anterior apex peripheral zone (PZ), anterior horn PZ, and anterior transition zone are the recommended locations in which significant cancers likely missed on initial biopsy (dotted arrows) are potentially located. These anterior biopsies (yellow arrows) require the technique of needle placement into the middle of the prostate before firing the biopsy gun, with consideration of the advanced needle length of 22 mm (typically, including the proximal 17-mm part of the tissue sampling area and the distal 5-mm part, where the tissue is not sampled).**
PZ = peripheral zone; TZ = transitional zone.

**Contemporary Role of Systematic Prostate Biopsies: Indications, Techniques, and Implications for Patient Care**

*Osamu Ukimura [a,b,*], Jonathan A. Coleman [c], Alex de la Taille [d], Mark Emberton [e,f], Jonathan I. Epstein [g], Stephen J. Freedland [h], Gianluca Giannarini [i], Adam S. Kibel [j], Rodolfo Montironi [k], Guillaume Ploussard [l], Monique J. Roobol [m], Vincenzo Scattoni [n], J. Stephen Jones [o]*

*European Urology 2013*

# Επαναληπτική βιοψία κορεσμού



# Διορθική ή διαπερινεϊκή επαναληπτική βιοψία;

ELSEVIER

Urologic Oncology: Seminars and Original Investigations xx (2012) xxx

UROLOGIC ONCOLOGY

Original article

## Transperineal template-guided prostate biopsy for patients with persistently elevated PSA and multiple prior negative biopsies

Boris Gershman, M.D.[a,*], Anthony L. Zietman, M.D.[b], Adam S. Feldman, M.D.[a], W. Scott McDougal, M.D.[a]

[a] *Department of Urology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA*
[b] *Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA*

Received 4 December 2011; received in revised form 28 December 2011; accepted 3 January 2012

**Abstract**

**Objective:** To evaluate the use of transperineal template-guided prostate biopsy for patients with persistently elevated PSA despite multiple negative prior biopsies.

**Materials and methods:** A retrospective review was performed of patients with at least two prior prostate biopsies who underwent transperineal template-guided biopsy. Electronic medical records were reviewed to obtain relevant clinical, laboratory, and pathologic data.

**Results:** A total of 34 patients underwent transperineal template-guided biopsy. Patients had a mean of 3.7 ± 1.6 (range 2–8) prior biopsies, including prior negative transurethral resection (TUR) biopsy in 6 (17.6%) patients. Prostate cancer was detected in 17 (50%) of the 34 patients. Of these, 14 (82.4%) patients had cancer in the anterior prostate, 9 (52.9%) patients had cancer in the apical prostate, and 16 (94.1%) patients had cancer in either the anterior or apical prostate. Gleason score was 3+3 in 9 (52.9%) patients and 3+4 or greater in 7 (47.1%) patients. The mean number of positive cores was 4.5 ± 3.0 (range 1–11). Of the 17 patients with a diagnosis of cancer, 7 underwent radical prostatectomy, 7 underwent radiation therapy, 1 elected active surveillance, and 1 was deciding between surgery and radiation therapy; 1 patient received palliative chemotherapy for synchronous metastatic pancreatic carcinoma. Patients in whom cancer was detected had significantly smaller prostate volume, higher PSA, higher PSA density, and greater PSA velocity.

**Conclusions:** Transperineal template-guided prostate biopsy is an effective technique for detecting cancer in patients with persistently elevated PSA despite multiple negative biopsies. It improves sampling of the anterior and apical prostate, and should be included as part of the diagnostic algorithm to reduce extensive repeat biopsy. 

# TUR-P αντί γιά επαναληπτική βιοψία;

*6.4.5* ***Diagnostic transurethral resection of the prostate (TURP)***

The use of diagnostic TURP instead of repeat biopsies is a poor tool for cancer detection (38) (LE: 2a).

Urology. 2003 Nov;62(5):883-7.

**Detection of prostate cancer by TURP or open surgery in patients with previously negative transrectal prostate biopsies.**

Zigeuner R, Schips L, Lipsky K, Auprich M, Salfellner M, Rehak P, Pummer K, Hubmer G.

Department of Urology, University Hospital, Karl-Franzens-University, Graz, Austria.

**Abstract**

**OBJECTIVES:** To evaluate retrospectively the effectiveness of transurethral resection of the prostate (TURP) in diagnosing prostate cancer in patients with obstructive voiding symptoms and a history of negative transrectal prostate biopsy but elevated prostate-specific antigen (PSA) and/or abnormal digital rectal examination (DRE).

**METHODS:** In 1189 consecutive patients undergoing TURP or open prostatectomy between 1994 and 2000 for obstructive voiding symptoms, we identified 445 patients (37.4%) with at least one previous set of transrectal prostate biopsies because of an elevated PSA level and/or abnormal DRE findings. The probability to detect prostate cancer by TURP (n = 423; 95%) or open surgery (n = 22; 5%) was investigated overall, as well as related to patient age, PSA level, DRE findings, number of previous biopsies, time from biopsy to surgery, and weight of resected tissue.

**RESULTS:** The mean number of preoperative negative biopsies per patient was 1.6 (range 1 to 8). The mean patient age was 69 years (range 48 to 89). The median PSA level and resection weight was 8.64 ng/mL and 32 g, respectively. Ninety-seven patients (21.8%) had abnormal DRE findings. Overall, prostate cancer was detected in 35 patients (7.9%). The cancer incidence was 5.5% (19 of 348) in patients with a normal DRE compared with 16.5% (16 of 97) in patients with an abnormal DRE ($P < 0.001$; Fisher's exact test). The cancer rate was also related to age; other subgroups showed no statistically significant differences regarding cancer incidence.

**CONCLUSIONS:** In patients with previously negative biopsies, the diagnostic yield of TURP is low. Therefore, TURP for diagnostic purposes only cannot be recommended. However, in patients with an abnormal DRE and obstructive symptoms, surgery should be preferred over alternative treatment options.

# Ενδείξεις γιά επαναληπτική βιοψία του προστάτη

While the need for an initial prostate biopsy is determined on the basis of the PSA level and/or a suspicious DRE, the indications for a repeat biopsy according to different organizations are:

EAU: Rising and/or persistently elevated PSA; suspicious DRE; atypical small acinar proliferation (ASAP); and extensive (multiple biopsy sites) prostatic intraepithelial neoplasia. High-grade PIN as an isolated finding is no longer considered an indication for repeat biopsy. In the case PIN is extensive (i.e. in multiple biopsy sites), this could be a reason for early repeat biopsy, because the risk of subsequent prostate cancer is slightly increased.

*Heidenreich A, Bellmunt J, Bolla M, et al., European Association of Urology. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. Eur Urol 2011;59:61-71.*

NCCN: ASAP in biopsy: extended pattern repeat biopsy (within 6 mo), with increased sampling of the ASAP site and adjacent areas. HGPIN multifocal (≥2 cores): extended pattern biopsy within the first year. Patients with prior negative biopsies, yet persistently rising PSA values should undergo repeat biopsy based on risks and benefits discussion.

*NCCN Guideline Version 2012 Prostate Cancer Early Detection; http://www.nccn.org*

NICE: Men should decide whether to have a rebiopsy following a negative biopsy, having had the risks and benefits explained to them.

*National Institute for Health and Clinical Excellence, Clinical Guideline 58, Prostate Cancer 2008; http://www.nice.org*

ITALY: It is recommended that a biopsy be repeated after a prior negative biopsy when the prior sampling is inadequate (<6 cores sampled, no prostatic tissue, and in the case of thin or bad readable cores); PSA persistently >10 ng/ ml; PSA velocity >0.75–1 ng/ml per year; or ASAP or HGPIN at first biopsy.

*Systematic Development of Clinical Practice Guidelines for Prostate Biopsies: A 3-Year Italian Project Anticancer Res 2007;27:659-66*

Canadian Urological Association: ASAP lesions are cancerous until proven otherwise and should undergo repeat biopsy. Repeat biopsy may no longer be indicated for HGPIN lesions in the era of extended core biopsy, unless the patient has an increase in PSA or change on DRE .

*Canadian Urological Association Guidelines 2010 on Prostate Biopsy Methodology. Can Urol Assoc J 2010;4:89-94*

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# When serial prostate biopsy is recommended: most cancers detected are clinically insignificant

Osama M. Zaytoun, Andrew J. Stephenson, Khaled Fareed, Ahmed El-Shafei, Tianming Gao*, David Levy and J. Stephen Jones

*Glickman Urological and Kidney Institute, *Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, USA*

Accepted for publication 9 November 2011

## CONCLUSION

- In men with two prior negative prostate biopsies, prostate cancer detection remains low regardless of clinical indication or transrectal biopsy protocol; most cancers identified are clinically insignificant, suggesting the threshold to repeat biopsy after more than one negative session should be very high.

International Journal of Urology (2011) 18, 557–568 doi: 10.1111/j.1442-2042.2011.02798.x

Review Article

# Prostate cancer detection after a negative prostate biopsy: Lessons learnt in the Cleveland Clinic experience

Osama M Zaytoun[1,2] and J Stephen Jones[1]

[1]Glickman Urological & Kidney Institute, Cleveland Clinic, Cleveland, Ohio, USA; and [2]Department of Urology, Faculty of Medicine, Alexandria University, Egypt

In total, 70% of PCa is detected on initial PBx; therefore, we believe that optimization of the initial PBx intuitively reduces the likelihood of facing a "repeat biopsy dilemma".

*6.4.4* ***Sampling sites and number of cores***

On baseline biopsies, the sample sites should be as far posterior and lateral as possible in the peripheral gland. Additional cores should be obtained from suspect areas by DRE/TRUS. These should be chosen on an individual basis.

Sextant biopsy is no longer considered adequate. At a glandular volume of 30-40 mL, at least eight cores should be sampled. The British Prostate Testing for Cancer and Treatment Study has recommended 10 core biopsies (36) (LE: 2a) More than 12 cores are not significantly more conclusive (37) (LE: 1a).