

the prostate specific antigen (PSA) inter-assay variability.

Material & Methods: Total (tPSA) and free PSA were determined with five different assays in 780 biopsy-referred men. Together with age, prostate volume and digital rectal examination (DRE) status these data were applied to five established online available nomograms for PCa detection and the criteria calibration and discrimination were used to characterize the usefulness of the nomogram models under these conditions.

Results: PCa was found in 455 (58.3%) men and 325 had no evidence of malignancy (NEM). Median tPSA concentrations ranged from 5.5 to 7.04 ng/mL while the median percent free PSA (%fPSA) ranged from 10.6% to 16.4%. Both, calibration and discrimination of the nomograms significantly varied when changing the PSA assays. Median nomogram probabilities, which indicate the PCa risk, ranged from 0.59 to 0.76 when using the same nomogram but different PSA assays. On the other hand, various nomograms resulted in different PCa probabilities with the same PSA assay. Although comparable areas under the curves of the receiver-operating characteristics were found, considerable differences between the five assays were also seen when analyzing the sensitivities and specificities at various nomogram probability cutoffs.

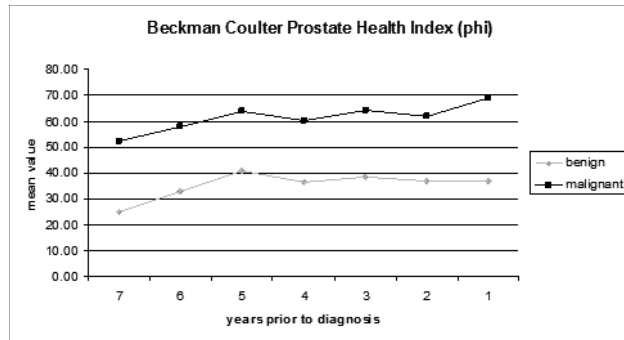
Conclusions: The accuracy of the predicted PCa probabilities by different nomograms is limited by the insufficient interchangeability of the PSA values measured by various PSA assays. A more cautious application of the nomograms is recommended.

985 ACCESS [-2]PROPSA AND BECKMAN COULTER PROSTATE HEALTH INDEX (PHI) AND EARLY DETECTION OF AGGRESSIVE PROSTATE CANCERS

Bektic J., Darte C., Skradski V., Steiner E., Schaefer G., Bartsch G., Horninger W., Klocker H.
Medical University Innsbruck, Dept. of Urology, Innsbruck, Austria

Introduction & Objectives: Prostate specific antigen (PSA) is a useful but nonspecific biomarker for prostate cancer. The aim of this study was to combine the Hybritech [-2]proPSA (p2PSA**) assay with total (PSA) and free PSA (%fPSA) in the prostate health index (Beckman Coulter phi) to enhance discrimination of patients with prostate cancer (PCa) from those without evidence of cancer, and to investigate p2PSA for detecting aggressive PCa.

Material & Methods: The study population included 381 men who had undergone at least one ultrasound-guided prostate biopsy between January 1993 and July 2006, in whom pathologic examination yielded prostate cancer or showed no evidence of prostatic malignancy. Serial PSA, fPSA and p2PSA measurements performed over 7 years prior to biopsy were evaluated and combined using phi ((p2PSA/fPSA) x $\sqrt{\text{PSA}}$). The power of phi to discriminate between cancer and non-cancer was evaluated. The values obtained were correlated with Gleason Scores (GS) and pathological stages of specimens obtained at RP.



Results: Seven years prior to diagnosis the mean phi value was 2-fold higher in PCa compared to non-cancer (52.5 v. 25.0, $p < 0.01$). This difference was significant over all years investigated, remaining almost constant (see diagram). At 90% sensitivity, specificity, positive and negative predictive value were 44.6%, 58.7% and 76.8%, respectively. Using a phi cut-off of 40, cancer sensitivity and specificity were 60.6% and 70.1%, respectively. Moreover, phi distinguished favourable from less favourable GS better than tPSA and %fPSA. Four years prior to diagnosis phi was 51.6, 71.4 and 117.1 in GS ≤ 6 , 7 and ≥ 8 . The difference between organ-confined and non-organ-confined prostate cancer was significant only one year prior to diagnosis.

Conclusions: Combination of [-2]proPSA with established serum markers has promise to increase prostate cancer specificity of tPSA and fPSA. The finding that patients with high phi levels in the years prior to cancer diagnosis correlates with a high risk of aggressive prostate cancer suggests [-2]proPSA is an important predictive marker in PCa screening that warrants further research. **Pending US approval

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THE BECKMAN COULTER PROSTATE HEALTH INDEX (PHI) IMPROVES DIAGNOSTIC ACCURACY IN PROSTATE CANCER DETECTION

Vincendeau S.¹, Ramirez J.², Durand X.³, Deligne E.³, Houlgatte A.³
¹Hospital Pontchaillou, Dept. of Urology, Rennes, France, ²Hia Du Val De Grace, Dept. of Clinical Biochemistry, Paris, France, ³Hia Du Val De Grace, Dept. of Urology, Paris, France

Introduction & Objectives: The benefit of screening for prostate cancer (PCa) using total prostate-specific antigen (tPSA) as biochemical marker is a matter of intense debate due to the relatively low clinical specificity of tPSA leading to serious drawbacks such as overdiagnosis and overtreatment. New biomarkers that could improve the specificity for PCa detection are highly desirable. Previous studies showed that a molecular isoform of PSA ([-2]proPSA) could improve the clinical specificity for the detection of PCa compared to tPSA and free PSA (fPSA). Beckman Coulter recently developed an innovative "prostate health index" or "phi" which combine tPSA, fPSA and [-2]proPSA results. The clinical performance of phi for the detection of PCa is under evaluation in a two-center study.

Material & Methods: After 3 months of recruitment, 129 men (79 with, 50 without PCa all confirmed with >10 cores biopsy) with tPSA level between 2 – 10 ng/mL and non-suspicious digital rectal examination (DRE) from the Hospital Pontchaillou in Rennes and the Hospital Val de Grace in Paris were enrolled in the study. The serum concentrations of tPSA, fPSA and [-2]proPSA were measured with Beckman Coulter Access immunoassays on a DxI800 instrument. Interim analysis using ROC curve was used to compare the clinical performances of phi with the %fPSA taken as a gold standard for the detection of PCa.

Results: Combining the two cohorts for tPSA-range 2 – 10 ng/mL, the area-under-the-ROC curves (AUC) analysis shows that phi (AUC=0.67) provided significantly better ($p=0.05$) clinical performance relative to %fPSA (AUC=0.57).

Conclusions: Using this preliminary data set regrouping a limited number of patients, interim analysis of this two-center study indicates that phi may have superior clinical performance in detecting PCa in the tPSA range of 2 – 10ng/mL compared to current gold standard biomarker of %fPSA. These results will have to be confirmed with the final analysis at the end of the study incorporating a larger number of patients.

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POTENTIAL CLINICAL VALUE OF CIRCULATING DJ-1 IN PATIENTS WITH PROSTATE CANCER

Loran O.B.¹, Veliev E.I.¹, Okhrits V.E.¹, Lisitskaya K.V.², Eremina L.S.², Kovalyov L.I.², Kovalyova M.A.², Shishkin S.S.²
¹Russian Medical Academy of Postgraduate Education, Dept. of Urology, Moscow, Russia, ²Bach Institute of Biochemistry Russian Academy of Sciences, Dept. of Biochemistry, Moscow, Russia

Introduction & Objectives: Serum prostate-specific antigen (PSA) is widely used for the early detection of prostate cancer but lack of its specificity warrants the search for additional biomarkers. Dj-1 is a product of oncogene Dj-1 that cooperates with H-Ras and transforms cells by increasing cell proliferation and resistance to cell cycle arrest. Dj-1 protects the tumor cells against oxidative damage and inhibits hypoxia-induced apoptosis. Over-expression of Dj-1 has been reported in several cancer cells, including prostate cancer (PCa). The aim of the study was to estimate the serum concentrations of Dj-1 in patients with PCa and benign prostatic hyperplasia (BPH).

Material & Methods: We measured serum Dj-1 levels in 24 untreated men with verified PCa and in 12 patients with histologically confirmed BPH. Median patient age in group of men with PCa was 64 years (range 55 to 73 years), in group of men with BPH - 67 years (range 59 to 74). The mean level of PSA in PCa group was 12,83 ng/mL, in BPH group - 3,84 ng/mL. 14 PCa patients had Gleason score <7, 10 PCa patients had Gleason score ≥ 7 . For quantitative measurements of serum Dj-1 levels, the Human Dj-1/PARK7 ELISA kit (Abnova) was used. Every sample was run in duplicate and the mean calculated for data analysis.

Results: The mean serum Dj-1 concentration was 18,5 ng/mL (range 2,5 – 110 ng/mL) in BPH patients and 55,3 ng/mL (range 9,0 – 122 ng/mL) in PCa patients, thereby serum Dj-1 levels were elevated in PCa patients compared with BPH subjects ($p=0,002$). If the Dj-1 concentration $\geq 14,0$ ng/mL was defined as the threshold for PCa diagnostics, the sensitivity and specificity would be 80% and 85%, respectively. In patients with Gleason score <7 the mean serum Dj-1 concentration was 40,9 ng/mL (range 9,0-88,5), and in patients with Gleason score ≥ 7 it was 67,5 ng/mL (range 15,0-122,0 ng/mL), so higher grade tumours were significantly associated with higher plasma Dj-1 levels ($p=0,038$).

Conclusions: In patients with PCa, serum Dj-1 levels correlated either to the presence of malignancy ($p=0,002$) and Gleason score ($p=0,038$). These tentative results suggest that DJ-1 can be considered as potential diagnostic and prognostic biomarker of PCa.