



# The isoform [-2]proPSA and the Prostate Health Index (phi) improve the detection of prostate cancer in patients with total PSA between 1.6 and 8.0 ng/mL

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## Objectives.

The benefit of screening for prostate cancer (PCa) using total prostate-specific antigen (tPSA) as the 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) (1, 3). Beckman Coulter recently developed an innovative "Prostate Health Index"  $\pm$  or "*phi*" which combines tPSA, fPSA and [-2]proPSA results (3). This two-center study was set up to confirm previously demonstrated clinical performance of *phi* for the detection of PCa (3). The results of an interim analysis are presented in this poster.

## Material and Methods.

After 6 months of recruitment, 250 men (143 with and 107 without PCa all confirmed by >10 cores biopsies) with tPSA level between 1.6 – 8.0 ng/mL (WHO Calibration) and PCa classified as T1c or T2a from the Hospital Pontchaillou in Rennes and the Hospital Val de Grâce in Paris were enrolled in the study. A tPSA range of 1.6 – 8.0 ng/mL with a WHO-calibrated tPSA Access assay corresponds to a range of 2 – 10 ng/mL with a Hybritech- calibrated tPSA Access assay. Similarly, the classical decision point of 4.0ng/mL in Hybritech-calibrated assay corresponds to 3.1ng/mL with a WHO-calibrated assay. Serum samples from the enrolled patients were prepared within 3 hours of the blood draw then stored frozen at -20°C. The serum concentrations of tPSA, fPSA and [-2]proPSA\*\* were measured with Beckman Coulter Access immunoassays on a Unicel Dxl 800 instrument. The Prostate Health Index was calculated using the following formula: (p2PSA/fPSA)\*<sup>2</sup>tPSA. ROC curves were plotted to compare the clinical performances of *phi* tPSA and %fPSA for the detection of PCa.

## Results and Conclusions.

### [-2]proPSA serum concentration is increased in patients with PCa

In contrast to tPSA, the serum concentrations of fPSA and [-2]proPSA are significantly different in the cohort of patients with PCa compared with the patients without PCa. The concentrations of fPSA were lower in serum of patients with PCa while higher concentrations of [-2]proPSA were detected in this population. As a consequence, the median and mean values of %p2PSA ([-2]proPSA/fPSA\*100) and *phi* were also higher in patients with PCa compared with patients without PCa.

### The prostate health index significantly improves the detection of PCa

The ROC curve analysis showed that *phi* (AUC=0.72) provided significantly ( $p < 0.0001$ ) better clinical performance to detect PCa compared to tPSA (AUC=0.53) and %fPSA (AUC=0.57). The %p2PSA derivation previously used in other studies (2), provides an AUC of 0.72 similar to *phi*. Interestingly, similar results were observed when the analysis was performed in men with tPSA < 3.1ng/mL.

### The prostate health index significantly improves the detection of PCa for men with tPSA < 3.1ng/mL

An analysis on a subpopulation of men with serum tPSA concentration between 1.6 and 3.1 ng/mL was performed (n=105). As shown by the ROC curve analysis, *phi* and %p2PSA are the best parameters to detect PCa (AUC 0.75). In this population of patients with low level of serum tPSA, the clinical performance of *phi* and %p2PSA are significantly greater than tPSA (AUC 0.51) or %fPSA (AUC 0.62).

### The prostate health index improves the detection of PCa in men with tPSA < 8 ng/mL and %fPSA > 25%

When considering the population of men with a tPSA < 8 ng/mL and a %fPSA > 25% (n=24), we observed that *phi*, with a cut-off point at 23, was able to detect 12 out of 14 PCa in this cohort. If the biopsy decisions would have been based on %fPSA information only, none of these 14 PCa would have been detected. This observation is in agreement with previously published results (2).

## Conclusions.

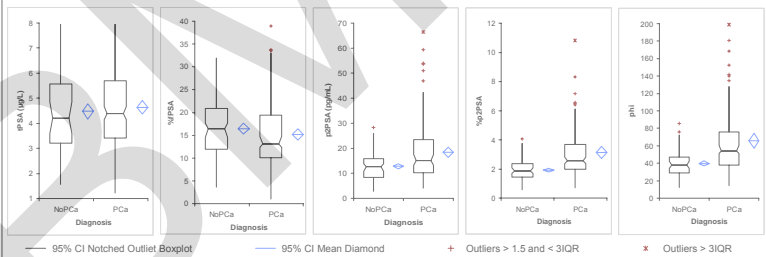
Using this preliminary data set, interim analysis of this two-center study indicates that *phi* has superior clinical performance in detecting PCa in the tPSA range of 1.6 – 8.0 ng/mL (WHO calibration) compared to tPSA or %fPSA. The *phi* index was the best predictor of prostate cancer compared to tPSA and %fPSA in the 1.6 – 8.0 ng/mL tPSA range. The superior clinical performance of *phi* and %p2PSA is also observed for patients with low level of serum tPSA between 1.6 – 3.1ng/mL. We showed that *phi* improves the detection of PCa in men with high %fPSA values. These results indicate that the Beckman Coulter prostate health index could improve significantly the detection of PCa. Further analysis of the results will be required to define the optimal settings for *phi* implementation in routine practice.

## References.

- Sokoll et al. [-2]Proenzyme Prostate Specific Antigen for Prostate Cancer Detection: A National Cancer Institute Early Detection Research Network Validation Study. *The Journal of Urology* 2008;180:539-43
- Mikolajczyk et al. Proenzyme Forms of Prostate-Specific Antigen in Serum Improve the Detection of Prostate Cancer. *Clinical Chemistry* 2004; 50:1017-25
- Jansen et al. Prostate-Specific Antigen (PSA) Isoform p2PSA in Combination with Total PSA and Free PSA Improves Diagnostic Accuracy in Prostate Cancer Detection. *European Urology* 2010; 57:921-27

## Results.

### Descriptive Statistics for PCa vs No PCa groups



Patients (n)	250	Median	PCa n=143	Non-PCa n=107	Significance* (p)
tPSA	4,38	4,38	4,20	0,3913	
%fPSA	13,04	13,04	16,38	0,0347	
p2PSA	15,15	15,15	12,70	0,0005	
%p2PSA	2,55	2,55	1,86	<0.0001	
<i>phi</i>	51,58	51,58	38,18	<0.0001	

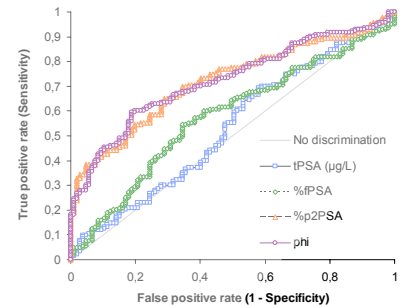
\*: Mann-Whitney test

### Detection of PCa for patients with tPSA > 1.6 and < 8.0 ng/mL

Patients (n)	250
Diagnosis (n)	
No PCa	107
PCa	143

Test	Area ROC	95% CI	p
tPSA (µg/L)	0.53	0.46 to 0.61	-
%fPSA	0.58	0.51 to 0.65	0.3063*
%p2PSA	0.72	0.66 to 0.79	0.0004**
<i>phi</i>	0.72	0.66 to 0.79	<0.0001**

\* %fPSA vs tPSA  
 \*\* %fPSA vs %p2PSA  
 \*\* %fPSA vs *phi*



### Detection of PCa for patients with tPSA > 3.1 ng/mL

Patients (n)	105
Diagnosis (n)	
No PCa	50
PCa	55

Test	Area ROC	95% CI	p
tPSA (µg/L)	0.51	0.46 to 0.61	-
%fPSA	0.62	0.51 to 0.65	0.1538*
%p2PSA	0.75	0.66 to 0.79	0.0396**
<i>phi</i>	0.75	0.66 to 0.79	<0.0415**

\* %fPSA vs tPSA  
 \*\* %fPSA vs %p2PSA  
 \*\* %fPSA vs *phi*

### Phi improves the detection of PCa for patients with %fPSA > 25

Patients	tPSA < 8 and %fPSA > 25	
	PCa	24
Detected PCa	0	12
Non-Detected PCa	14	2



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<sup>†</sup> Not intended as off-label promotion of any Beckman Coulter product

<sup>‡</sup> Not available in the United States