- **Intermediate values, found during the course of a benign pathology** (benign prostate hyperplasia, prostatitis) where the total PSA is "falsely positive" and leads to a large number of biopsies being taken that are unnecessary as the result is negative. In these situations, the phi index helps to decide whether to take a prostate biopsy or not and leads to a significant decrease in unnecessary invasive acts.

2. The phi index detects potentially aggressive cancers

Several studies have highlighted a significant correlation between phi and the Gleason score.

3. Phi and PCA3

The interest of phi, PCA3 and their combination is currently the subject of numerous studies. Certain studies put forward that phi has a better performance with regards to the making the decision to take an initial biopsy, and PCA3 for subsequent biopsies. One must be rigorous with the use of these study results, which have been obtained in well-defined populations (clinical, initial biopsy or subsequent biopsies, total PSA, family history of the disease etc.), and sometimes with multi-parameter analyses.

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Key information

[-2]proPSA

- New serum marker
- Almost exclusively expressed by cancerous prostate cells (unlike total PSA)
- Can be measured from a simple blood sample (unlike PCA3)

Phi, Prostate Health Index

- An index calculated from the serum concentration of [-2]proPSA, combined with total PSA and free PSA
- Increase the performance of [-2]proPSA in detecting prostate cancer

Clinical interest of phi

In patients with a serum level of total PSA between 2 and 10 ng/mL (Hybritech Standard)

- To non-invasively identify patients who are highly likely to present with a positive prostate biopsy result
- To detect potentially aggressive cancers (significant correlation between phi/Gleason)
- Potential interest for the monitoring of patients.

In practice
[-2]proPSA and phi calculation

Sample

- 1 mL of frozen serum
- Important: the serum sample must be separated from cells within 3 hours from sample collection.
- The sample must be collected a while after any prostate manipulation such as the digital rectal examination, prostate massage, a transrectal ultrasound or prostate biopsy.

Interpretation

In patients with a serum level of total PSA between 2 and 10 ng/mL (Hybritech Standard).

Phi* index values (Hybritech calibration)	Probability of cancer (at 95% specificity)
0 – 21	8,4% (1,9 – 16,1 %)
21 – 40	21,0% (17,3 – 24,6 %)
› 40	44,0% (36,0 – 52,9 %)

* Calculation includes the simultaneous assaying of [-2] proPSA, free PSA and total PSA (Technique HYBRITECH Beckman Coulter). Total or free PSA results generated by other methods or at other times cannot be used in the calculation.

To find out more about this subject

Find all the necessary details (clinical interest, pre analytical conditions, price, turn-around-time etc.) visit:

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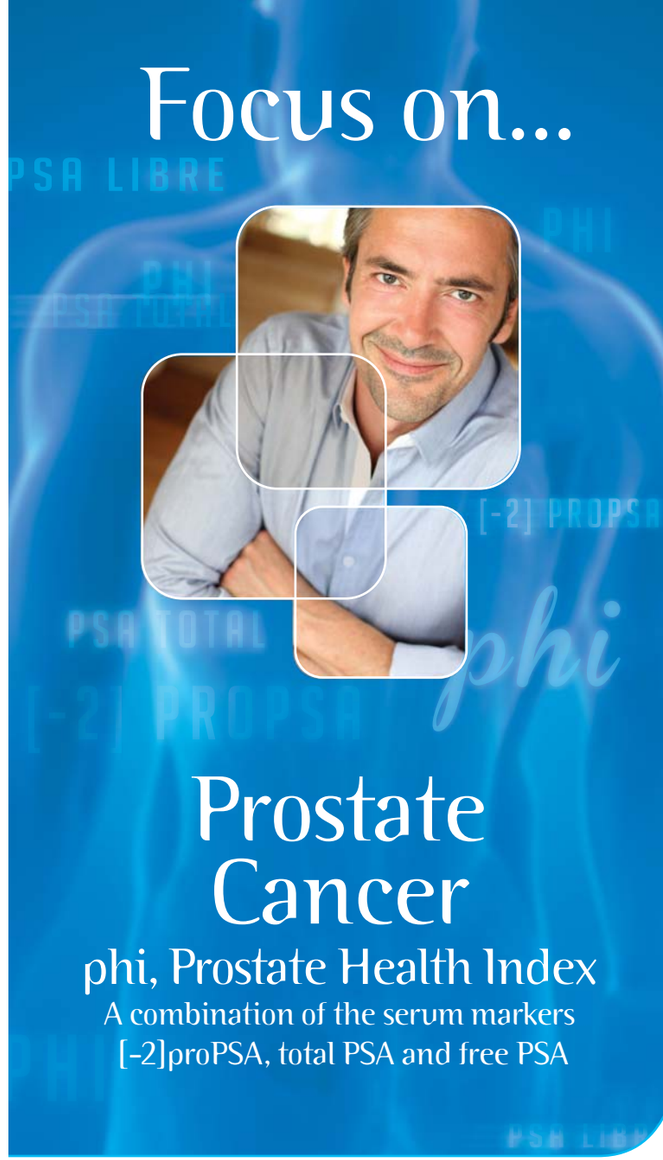

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SPECIALISED MEDICAL PATHOLOGY

*Prostate cancer in the world**

2nd most common cancer in men
900,000 men diagnosed

6th most common cause of death
258,000 deaths

Large increases in the incidence of prostate cancer in many countries worldwide, coupled with little change or small declines in mortality

The developed countries carry the biggest burden of prostate cancer, accounting for nearly three-quarters (72%) of the total

Prostate cancer is suspected when confronted with clinical symptoms, the detection of an anomaly upon digital rectal examination or an increase in serum levels of total PSA.

*Source: Cancer Research UK (2008 data)

Digital rectal examination

This examination is essential to identify the volume of the prostate and to search for anomalies such as induration or a nodule. It has also been estimated that approximately 50% of cancers remain undetected. However, this method allows masses to be detected when the total PSA result is "normal".

Within the scope of diagnosing early stage cancer, it is less effective than total PSA alone. It is therefore performed in combination with serum total PSA when confronted with clinical symptoms of the disease.

PSA: Prostate Specific Antigen

PSA is almost exclusively secreted by the prostate gland. It is secreted at a low level by normal tissue and at a raised concentration by benign prostatic hyperplasia and cancerous tissues. As such, it can be said that it is specific to the prostate but not for cancer.

The serum concentration of total PSA is influenced by age, manipulation of the prostate gland and treatments. The retained threshold value is 4 ng/mL (Hybritech standard), however a value below this ensues an, albeit low but not negligible, risk of cancer.

Between 4 and 10 ng/mL, the objective is to diagnose cancers more efficiently, and to better select the patients that should be referred for an initial biopsy, and then a second biopsy in the case of a negative initial biopsy result.
Numerous approaches have been envisaged to reduce false positive (increase specificity) and false negatives (increase the sensitivity):

- **"markers derived" from PSA:** PSA threshold value relative to the patient's age, PSA density and PSA velocity.
- **Forms of circulating PSA:** free PSA/ total PSA ratio and complexed PSA.

None of these approaches has been validated for first-line testing, but they can help in the decision-making process for biopsies.

A rectal examination anomaly or a serum total PSA anomaly requires an urologist to give their opinion on whether a prostate biopsy should be taken or not relative to the risks ensued, the interest associated with diagnosing cancer and initiating treatment.

Ultrasound-guided prostate biopsy sampling

A prostate biopsy is the only way to confirm the diagnosis of prostate cancer. The biopsy is collected by an urologist, who collects a dozen or so samples from all over the prostate gland to find cancerous cells. The degree of aggressivity of these cells is defined using the Gleason score. The more the score is raised, the more the lesion is undifferentiated and so aggressive.

The biopsy is usually well-tolerated, but this remains an invasive act whose morbidity cannot be ignored with 5 - 6% of cases having infection-related complications.

A lot of biopsies are collected unnecessarily and a large number of these biopsies are negative in the presence of prostate cancer.

In the case of suspected cancer and a negative biopsy result, the clinical interest of taking a second biopsy is discussed.

Numerous biological markers have been developed to evaluate the probability of obtaining a positive biopsy result.

PCA3: Prostate Cancer Antigen 3

PCA3 is a more specific genetic marker of prostate cancer than PSA because it is only produced by prostate cancer cells and is not influenced by the volume of the prostate.

Its first indication is as a decision-making tool whether to take a second biopsy in male patients who had a negative initial biopsy result, but where cancer is still suspected. Recent studies show that PCA3 could also help in decision-making for whether to take an initial biopsy.

In practice, we screen for RNA expression within a urine sample collected following prostatic massaging through the use of a molecular biology test.

PCA3 is currently the object of comparison with a new predictive index known as phi, which has the advantage of only requiring a blood sample.

The phi index: Prostate Health Index

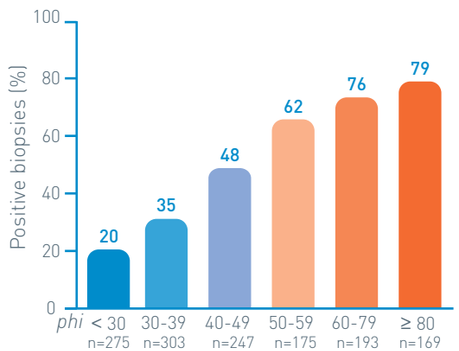
Phi, is an index based on the measurement of a new serum marker for prostate cancer, known as [-2]proPSA. [-2]proPSA is an isoform of PSA, which is strongly expressed in the peripheral zone of cancerous tissues of the prostate and is rarely expressed in the transition zone, which is the main site of most benign prostatic hyperplasia.

It is therefore more specific for prostate cancer than total PSA.

The combination of total PSA and free PSA in the phi calculation gives rise to a considerable improvement in detection specificity of prostate cancer, and as such, significantly reduces the need to perform biopsies.

1. The phi index improves the detection of prostate cancer and better targets the biopsy indications

The higher the phi index is, the greater the risk of having prostate cancer.



Stephan *et al*, Clinical Chem Acta, 2013

The phi index is of particular interest within two different value zones of total PSA:

- **Total PSA values of ‹ 4 ng/mL in patients with a negative digital rectal examination result:** we know that cancers can be diagnosed in this situation. The phi index can be the only raised marker and several months before the diagnosis of prostate cancer is made.