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# The Prostate Health Index (*phi*) in Prostate Cancer Risk Assessment

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HOT TOPIC / The Prostate Health Index (*phi*) in Prostate Cancer Risk Assessment



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## Disclosures

- Honorarium: Beckman Coulter

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### Utilization Message

- As you view this presentation, consider the following important points regarding testing:
  - How is the testing going to be used in your practice?
  - When should the tests be used?
  - How will results impact patient management?

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### Prostate Cancer (PCa) Statistics: 2017<sup>1</sup>

- 161,360 new cases
  - 1:7 men will be diagnosed
- 26,730 deaths
  - 1:39 men will die
- >2.9 million men in the US diagnosed with PCa and still alive

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### Advances in Prostate Cancer Diagnosis

- 1970s: Prostate specific antigen (PSA) isolated
- 1986: PSA assay was FDA approved for monitoring
- 1990s: Moved from a monitoring claim to a detection claim

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**PSA Limitations**

- Modest sensitivity / low specificity for PCa
- PSA cannot accurately distinguish between benign and malignant pathology in the total PSA range of 2–10 ng/mL.
- High cost to manage patients
  - Biopsy yields only 22-40% positive cancer rate
  - US ~750,000 negative biopsies

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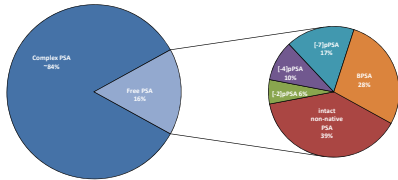
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**PSA Isoforms in Serum<sup>2</sup>**




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**PSA Isoforms in Prostate Cancer**

- Free PSA (fPSA)
  - Men with PCa have a lower %fPSA
  - Calculation of the %fPSA improves the sensitivity and specificity in men with a PSA of 4-10 ng/mL

$$\%fPSA = \frac{\text{free PSA}}{\text{total PSA}} \times 100$$

% Free PSA	Probability of Cancer
→ ≤ 10%	4%
11–15%	25%
16–20%	20%
21–25%	16%
→ >25%	11%

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### PSA Isoforms in Prostate Cancer

- 2proPSA (p2PSA)
- p2PSA is elevated in men with PCa
- Higher specificity than tPSA and fPSA
- Elevations of p2PSA are associated with increased probability of detecting aggressive cancer (Gleason score  $\geq 7$ )
- Prostate Health Index (*phi*)

$$\phi = \frac{p2PSA}{FreePSA} \times \sqrt{Total\ PSA}$$

<i>phi</i> range	Probability of Cancer	95% Confidence Interval
0-26.9	4.8%	5.2-15.4%
27.0-35.9	16.8%	11.3-22.2%
36.0-54.9	33.3%	26.8-39.9%
$\geq 55.0$	60.1%	39.8-61.0%

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### *phi* Specificity for Men with PSA 4-10 ng/mL<sup>3</sup>

Test	All Prostate Cancer		Significant Prostate Cancer*	
	Cut-off <sup>A</sup>	% Specificity (95% CI)	Cut-off <sup>A</sup>	% Specificity (95% CI)
%free PSA	24.1	19.8 (13.9-27.3)	22.7	21.7 (14.3-31.5)
<i>phi</i>	27.0	31.1 (23.5-39.9)	28.6	30.1 (21.0-41.0)

<sup>A</sup>90% sensitivity  
\*per Epstein Histological criteria

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### Prostate Health Index (*phi*)<sup>4, 5</sup>

- Improved diagnostic accuracy over total and free PSA
- phi* provides better risk stratification
- Discrimination between aggressive (GS  $\geq 7$ ) and nonaggressive cancers (GS < 7)

Test	ROC AUC	Specificity @95% sensitivity
Total PSA	0.525	7%
%free PSA	0.648	8%
<i>phi</i>	0.703	16%

Test	Studies N	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic OR (95% CI)
<i>phi</i>	5	0.90 (0.87-0.92)	0.17 (0.14-0.19)	3.06 (1.61-5.84)

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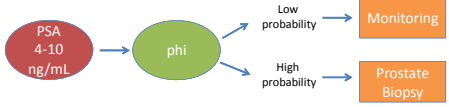
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### Prostate Health Index (*phi*)

- Aid in distinguishing prostate cancer from benign conditions, in men **total PSA between 4.0 -10.0 ng/mL**, and with digital rectal exam (DRE) findings that are not suspicious for cancer.



```

    graph LR
      A[PSA 4-10 ng/mL] --> B(phi)
      B -- Low probability --> C[Monitoring]
      B -- High probability --> D[Prostate Biopsy]
  
```

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### Other Prostate Cancer Biomarkers

- Prostate Cancer Antigen 3 (PCA3)
  - Noncoding mRNA overexpress in cancer tissue and detectable in urine after vigorous DRE.
- 4K™ Score
  - Combines the values of four biochemical markers (total PSA, free PSA, intact PSA, human kallikrein 2) and clinical variables (age, DRE and prior biopsy) to derive a score

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### *phi* vs. PCA3 <sup>6,7</sup>

- 246 men with PSA 0.5–20 ng/mL and scheduled for prostate biopsy.
  - PCa was diagnosed in 110 cases (45%)
- 300 men with PSA 2-10 ng/mL and undergoing first prostate biopsy
  - PCa was diagnosed in 108 cases (36%)

Marker	ROC AUC	Specificity*
<i>phi</i>	0.68	21%
PCA3	0.74	34%

\* @90% sensitivity

Marker	ROC AUC	Specificity*
<i>phi</i>	0.77	40%
PCA3	0.73	40%

\* @90% sensitivity

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### phi vs. 4Kscore <sup>8</sup>

- Both assays have similar diagnostic accuracy for detecting and prostate cancer and high-grade cancers

Marker	AUC All Ca	AUC HG Ca	Cutoff	Biopsies			All cancers		High-grade cancers	
				Performed N	Not performed N	%	Missed N	%	Missed N	%
phi	0.70	0.71		1000	0	0	0	0	0	0
4Kscore	0.69	0.72	<10%	704	296	29.6	83	16.3	28	10.5
			15%	550	450	45.0	153	30.0	58	21.8
PHI			26	915	85	8.5	13	2.5	12	4.5
			39	704	296	29.6	77	15.1	26	9.8

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### NCCN Guidelines for Prostate Cancer Early Detection

PSA >3.0 ng/mL →

- Repeat PSA
- DRE
- Workup for benign disease

→

- TRUS-guided biopsy
- or
- Follow up 6-12 mo with PSA/DRE
- or
- % free PSA, 4Kscore, or PHI

NCCN=National Comprehensive Cancer Network  
TRUS=transrectal ultrasound guided biopsy

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### Ordering phi

```

    graph TD
      A[Total PSA] --> B["<2 ng/mL  
no further testing"]
      A --> C["2-10 ng/mL"]
      A --> D[">10 ng/mL  
no further testing"]
      C --> E["2-4 ng/mL  
Measure free PSA  
p2PSA"]
      C --> F["4-10 ng/mL  
Measure free PSA  
p2PSA  
Calculate %free PSA  
phi"]
    
```

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**Questions or requests...**

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or call Mayo Laboratory Inquiry at 800-533-1710

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