



PAML Introduces Improved Method for Free PSA

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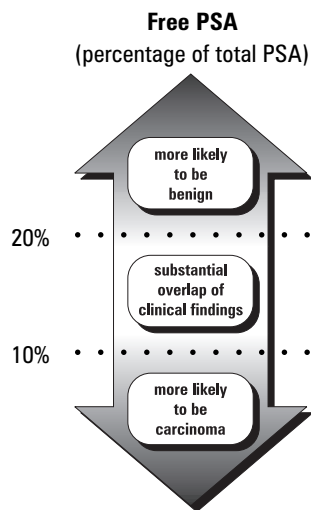
Prostate specific antigen (PSA) is found in the blood in three molecular forms: free PSA, PSA complexed with α -1 antichymotrypsin (PSA-ACT) and PSA complexed with α -2 macroglobulin (PSA-MG). Only the free PSA and the PSA-ACT are immunoreactive, so the sum of these two forms makes up total PSA, as measured by conventional immunoassays.

Extensive clinical studies have shown that measurement of the ratio of free-to-total PSA can improve specificity for distinguishing between benign prostatic hyperplasia (BPH) and prostatic carcinoma in men over the age of 50 with a total PSA of between 4 and 10 ng/mL and a normal digital rectal exam. Note this is a very specific clinical indication for use of the free PSA test. Some recent studies have extended the range, suggesting that the free PSA ratio may be useful in patients with total PSA levels as low as 2.6 ng/mL.

Published studies have reported various cutoffs related to the specificity of free-to-total PSA ratios in detecting prostatic carcinoma. For example, one study showed that if the percent free PSA was less than 10%, the probability of prostatic carcinoma was 70% (with a confidence interval of 60%-80%). If the percent free PSA was greater than 26%, the probability of prostatic carcinoma was 10% (with a confidence interval of 6%-16%). Other studies have showed different percentage figures, but the overall conclusion of the published data is that the higher the percentage of free PSA, the lower the probability of prostatic carcinoma. No percentage of free PSA, however, can conclusively rule in or rule out a malignant diagnosis.

The PAML R&D team has just completed validation of a new, FDA-approved method for measuring free PSA, using the Roche Elecsys immunoassay method. When a free PSA ratio test is ordered, the free PSA and the total PSA will be assayed on the Roche system, to ensure the most accurate free PSA ratio.

PAML will continue to use the Bayer Diagnostics immunoassay method for routine total PSA assays. We recommend using the Bayer method for prostate cancer screening and for serial monitoring of patients with diagnosed prostate cancer. For those patients who may also have a free PSA ratio performed, clinicians should note that the total PSA on the Roche method may differ slightly from the result using the routine, Bayer Diagnostics method. The routine Bayer total PSA method is ultrasensitive, with a detection limit of 0.01 ng/mL and is suitable for following patients post radical prostatectomy.



Selected References

Chen YT, et al. Using proportions of free to total prostate-specific antigen to predict the probability of prostate cancer. *Urology* 1996;47:518-24.

Thiel RP, et al. A multicenter comparison of the diagnostic performance of free prostate-specific antigen. *Urology* 1996;48(6A):45-50.

Catalona WJ, et al. Prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0 ng/mL and benign prostate examination. *JAMA* 1997;277:1452-55.

Catalona WJ, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. *JAMA* 1998;279(19):1542-7.

Polascik TJ, et al. Prostate specific antigen: a decade of discovery – what we have learned and where we are going. *J. Urology* 1999;162(2):293-306.

Grab and Go Facts

- ▶ **The free-to-total PSA ratio is useful in distinguishing prostate cancer from BPH in men over the age of 50 years with a total PSA of from 4 to 10 ng/mL and a normal digital rectal exam. The free PSA ratio may be useful in patients with total PSA levels as low as 2.6 ng/mL.**
- ▶ **Free-to-total PSA ratios of > 20% are more likely to be benign. As the ratio increases, the likelihood of BPH increases.**
- ▶ **Free-to-total PSA ratios of < 10% are more likely to be prostatic carcinoma. As the ratio decreases, the likelihood of carcinoma increases.**
- ▶ **Free-to-total PSA ratios of between 10% and 20% show substantial overlap of clinical findings with both malignant and benign diagnoses.**
- ▶ **No free PSA percentage will conclusively rule in or rule out prostatic carcinoma.**

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Test Information

DESCRIPTION **PSA, FREE**
METHOD ECLIA
ORDER CODE FPSA
CPT CODE 84154, 84153
SPECIMEN 1 mL serum (red-top tube). Collect on ice. Separate serum from cells and put in separate plastic tube. Store and transport refrigerated.
COMMENTS *Minimum amount:* 0.5 mL
Other acceptable specimens: lithium heparin or EDTA plasma.
Unacceptable conditions: heat-inactivated samples, and samples stabilized with azide.
Minimum detectable concentration is 0.03 ng/mL for PSA and 0.02 ng/mL for Free PSA.
Stability: 5 days refrigerated, 3 months frozen.
SCHEDULE Monday – Friday nights
TURNAROUND 1-3 days

RANGES **Total PSA** 0-54 yrs 0.00-2.50 ng/mL
55-59 yrs 0.00-3.40
60-64 yrs 0.00-4.10
65-69 yrs 0.00-5.10
70+ yrs 0.00-5.60

Free PSA (ng/mL)
Free/Total PSA Ratio (%)

Ratios GT 20% suggest benign.

Ratios between 10% and 20% show substantial overlap in benign and malignant conditions.

Ratios LT 10% suggest carcinoma.

The ratio is most clinically useful in the total PSA range 4-10 ng/mL.

This is now an FDA-approved procedure.

For purposes of calculating the PSA ratio, the total PSA and the free PSA were measured by the same analytical method (Roche Diagnostics). This procedure will ensure the most accurate free PSA ratio. PAML's routine total PSA method is from Bayer Diagnostics, and those results may show slight differences from results obtained with the Roche method.

The free PSA ratio is useful in differentiating between benign prostatic hypertrophy and prostatic carcinoma. Serial monitoring of patients should be done with total PSA measurements performed with the routine Bayer method.

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