

# PSA FOR DETECTION, STAGING AND MONITORING OF PROSTATE CANCER

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Screening for prostate cancer has been controversial, primarily because of the lack of hard data to support the premise that early detection leads to better outcomes. Opponents state that prostate cancer is often slow growing and that the widespread use of PSA testing may result in the detection of clinically insignificant tumors that do not require treatment. However, surgical treatment data confirms that prostate cancer is confined to the prostate in only 60% of all PSA detected cancers. This would suggest that these tumors are significant when detected.

PSA does not have sufficient sensitivity when used alone for optimal detection of prostate cancer. Limitations of PSA as a tumor marker are largely due to variable differences in the volume and composition of benign prostate hypertrophy (BPH). However, PSA improves the detection of prostate cancer when combined with digital rectal examination (DRE) and transrectal ultrasound (TRUS). The use of PSA to screen for prostate cancer has led to improved detection of earlier tumors. At present non-palpable, PSA detected prostate cancer is the most common clinical stage. This has led to an increased percentage of organ-confined tumors at surgery. With further studies, PSA may dramatically impact the curability and natural history of men with prostate cancer.

To decrease the death rate from prostate cancer and to spare men from the complications and futility of treating non-localized disease, better methods are needed to insure that cancer is confined to the prostate prior to definitive local therapy. The application of PSA for determining the extent of disease has been the focus of numerous investigations. With serum PSA levels less than 4.0 ng/ml., patients are more likely to have prostate-confined cancer compared to those with significantly elevated PSA levels. However, despite direct correlation between PSA and pathologic tumor stage, studies have shown that PSA cannot accurately predict the final pathologic stage for the individual patient. Therefore, the use of PSA alone is not sufficiently sensitive or specific to use for the determination of tumor stage. Because of this, several investigators have combined PSA level, clinical stage and biopsy Gleason score (a measurement based on the appearance of the prostate cancer cell), to improve the predictive value for estimating pathological stage.

The combination of PSA, clinical stage and Gleason score may be used by the urologist as a guide to better predict pathologic stage and counsel patients who are likely to benefit from definitive local therapy. They may also aid in selecting patients at risk for metastatic disease, who may initially benefit from pelvic lymph node dissection or alternatively, those patients at low risk for disease outside the prostate that may avoid the potential complications of a lymph node dissection.

Serial PSA measurements are the most effective means to monitor patients for disease recurrence following radical prostatectomy. PSA levels decline rapidly to undetectable levels, usually within six weeks. Initial PSA testing should begin at three months. The failure of PSA to become undetectable signifies residual local or distant disease. The time between PSA recurrence and onset of clinical disease is estimated to range from 6 - 48 months. Additionally, early PSA recurrence may be more indicative of metastatic

disease. A PSA doubling time of less than six months may be more suggestive of metastatic disease as well.

PSA has been used to monitor disease actively following prostate irradiation. However, the natural history of benign and malignant irradiated prostatic tissue to manufacture PSA is unknown. In contrast to radical prostatectomy in which PSA can and often declines to undetectable levels, the response of PSA to irradiation is more unpredictable. PSA levels fall more slowly and often may never reach undetectable levels following radiation therapy. The significance of PSA velocity and appropriate nadir (lowest PSA measurement) levels used to connote successful radiation treatment has provoked a great deal of controversy.

Anti-androgen treatment is commonly used for the treatment of patients with advanced prostate cancer. PSA levels typically fall within the first six months following androgen deprivation therapy. The duration of response is usually short with approximately 70% of men having PSA elevations between 6-12 months following hormonal therapy, despite having a good initial response. Serum PSA monitoring following androgen deprivation therapy is useful for identifying disease progression and emergence of hormone-independent prostate cancer. This information will allow the urologist to select alternative treatment strategies.

Many advances have occurred during the last decade in the clinical use of PSA for detection, staging and monitoring therapy in men with prostate cancer. Much of the focus has been on improving the ability of this tumor marker to more selectively detect prostate cancer. New technology designed to detect the presence of gene products may eventually play a role in staging prostate cancer prior to treatment or in monitoring response to therapy.

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