

# RISK FACTORS FOR FAILURE WITH PROSTATE CANCER

by: Gil Lederman, M. D.

There are known risk factors for those diagnosed with prostate cancer. Among the most important prognostic indicators is the aggressiveness of the cancer by histologic appearance. This is evaluated by pathologists reviewing the biopsy under the microscope. Other important features include chromosome studies, the extent of the cancer and as well, the level of the Prostatic Specific Antigen (PSA).

The use of PSA has been important both in detecting cancers early and in following the results of therapy. Now, data reveals the degree of PSA elevation is prognostic.

A recent paper by Hanks et al in The Journal of Clinical Oncology evaluated outcome of external beam radiation based upon pre-treatment PSA levels. One-hundred-twenty patients had a PSA of equal to or greater than 20 nanograms per milliliter. Forty-eight patients had PSAs ranging from 20.0 to 29.9, 39 patients had PSAs from 30 to 49.9 and 33 patients had PSAs ranging from 50 to 191. The average age in these three groups was 69 years.

All patients had diagnosis by biopsy through the rectum. Work-up to determine extent of cancer included physical examination, bone scan, MRI and ultrasound of the prostate.

Radiation was carried out using modern external beam techniques between 1988 and 1993. Total external beam dose ranged between 6900 and 7900 cGy. Follow up time for the groups were 34 months with a range of 4 to 77 months.

The patients were followed at six month intervals with physical examinations and blood tests. Patients were called 'disease free' if there was no evidence of prostate cancer by history, x-rays or blood tests. Biochemical failure was defined as a PSA greater than 1.5 and increasing levels of PSA on two consecutive measurements.

Of patients with PSAs at diagnosis of 20 to 29.9, 88% were free from distant disease at 36 months while biochemically no evidence of disease comprised 64% of patients at 24 months. Of the 39 men with PSAs of 30 to 49.9, 75% were free of distant disease at 36 months but only 45% biochemically had no disease at 24 months. In the third group having pre-treatment PSAs of 50 to 191, there were 33 patients and 85% had no evidence of distant disease at 36 months but only 53% had no evidence of biochemical disease at 24 months.

Free from distant disease means there is no evidence the cancer has traveled into bone or other sites far from the prostate. Biochemical disease-free means there is no evidence of cancer by PSA blood testing. If a man has biochemical failure, that is, a rising PSA level, this would be considered failure of treatment and a harbinger of subsequent metastatic cancer.

The authors noted "The biochemical freedom from disease rate with pre-treatment PSA levels greater than 20 at four years is 28%." It is alarming that 72% of men with marked elevation of PSA treated with external beam radiation therapy only will have incidence of biochemical failure at 48 months after treatment. At this same time, 81% of patients are free of metastases would imply that local or regional failure has occurred or unfound metastatic disease is present and may be causes of failure in men with prostate cancer and high PSAs.

The authors conclude that "The overall rate of failure in these high PSA patients indicates that monotherapy is not optimal and patterns of failure (part-metastatic and part-local/regional) suggest that the two general treatment strategies are indicated."

This same group has found that higher doses of radiation have an effect on biochemically producing no evidence of disease. In fact, they state that "doses greater than 73 Gray "result in significantly improved cancer control in patients with high pre-treatment PSA level."

They, as others have observed before, wrote "There are also strong indications that improved local control may reduce the subsequent development of distant metastases in prostate cancer."

It is for this reason that our current approach is to give high dose radiation via radiation seed implantation followed by external beam radiation therapy. While the radiation seeds are locally emitting radiation to the prostate, external beam delivers dose both to the prostate and surrounding tissues. It is a generally sound approach to boosting radiation dose. This innovative method offers great appeal in dose escalation while shortening the overall course of treatment and minimizing hospital stay.

Addendum:

While this paper looks at conformal or external-type beam radiation for prostate cancer, our data using prostate brachytherapy or seed implantation following by body radiosurgery in comparison to Hanks' data using conformal radiation has shown our approach to have nearly a third more men cancer-free. If one imagines there are nearly 200,000 men a year with prostate cancer, one-third more men would be more than 60,000 lives. It is obvious that technology makes a difference and choosing one's option is critical.

In general, our program is to use Palladium brachytherapy followed by body radiosurgery. Some men with low-risk factors – especially those with a PSA less than 10, Gleason 6 or less – choose monotherapy. The vast majority of patients choose a combined therapy of seed plus body radiosurgery. The rationale is that at 10 years, our data shows about a twelve-point higher cancer-free outcome than seed-alone therapy. We certainly have a much higher rate of cancer-free survival than external beam radiation as described in this paper. We update our data regularly and each man and family interested in this topic can obtain the latest comparison material. It is incumbent for each person to make his own decisions concerning treatment.