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The Prognostic Implications of Prostate Specific Antigen in Patients with Locally Advanced Prostate Cancer Treated with High Energy Neutron Beam Therapy: Preliminary Results

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Abstract

Serial serum prostate specific antigen (PSA) levels were analyzed retrospectively for prognostic implications in seventy patients with locoregional (Stages B2, C, and D1) prostate cancer who were managed with high energy neutron beam therapy. Three groups of patients were identified. Group I included 30 patients whose serum PSA level decreased to the reference range (0-4 ng/ml) following neutron therapy and remained so subsequently. Twenty-eight (93%) remained disease-free, and 2 patients (7%) have failed distantly. All 30 patients (100%) had no evidence of locally progressive disease. This group was categorized as having a good prognosis. The mean time for the serum PSA value to decline to the reference range was 6 months; the calculated mean time to achieve a stable baseline PSA was 53 ±37 days. The follow-up period ranged from 12 to 56 months (median being 21 months). Group II consisted of 13 patients in whom there was an initial decrease in the serum PSA to the reference range followed by a subsequent increase. Six of thirteen (46%) have no overt clinical progression of disease; 7 (54%) have either persistent locoregional or distant metastatic disease. The follow-up period was from 12 to 72 months (median: 39 months). The calculated mean time to achieve a stable baseline PSA for serum PSA in this group was 61 ±21 days. Group III patients had a persistently elevated or rising serum PSA concentration. Of 27 patients in this group, only 9 (33%) have no evidence of disease progression, while 18 patients (67%) have failed already, either locoregionally or distantly. The follow-up period ranged from 12 to 69 months (median: 21 months). The mean time to achieve a stable baseline of serum PSA in this cohort of patients with a poor prognosis was 108 ±76 days.

We conclude that PSA has a predictable prognostic value in patients with locally advanced prostate cancer managed with high energy neutron beam therapy. Rapid normalization of PSA after therapy indicates a good prognosis. Persistent elevation signifies either presence of persistent locoregional disease or development of distant

metastases. Subsequent elevation of the serum PSA concentration after definitive therapy signals progression of prostate cancer.

Key words: Locoregional prostate cancer, high energy neutron radiation therapy, prostate specific antigen.

Introduction

Prostate specific antigen (PSA) is a glycoprotein that is produced exclusively by prostate tissue, making it the first serum tumor marker in all of cancer biology that is organ specific.[1] In recent years, determination of the serum PSA concentration not only has become one of the most important pretreatment evaluations but also a most valuable post treatment tumor marker. Irrespective of treatment, radiation therapy or radical surgery, PSA is the most sensitive tumor marker available for detecting tumor recurrence.[1]

Various authors have published the effect of external photon beam therapy, I^{125} seed implantation and radical prostatectomy on serum PSA concentration values.[2-9] Serial determinations of the serum PSA level has been shown to be useful in identifying patients with progressive cancer following radiation therapy.[10]

High energy fast neutrons were used to treat the patients with locally advanced prostate cancer.[11] We present in this report the results of a retrospective analysis of serum PSA levels subsequent to neutron beam irradiation and its prognostic implications for these patients.

Materials and Methods

Between January 1984 and March 1990, 70 evaluable patients with locoregional prostate cancer (Stage B2, C and D1) were treated with high energy neutron beam therapy at the Neutron Therapy Facility at Fermilab, Batavia, IL. Median age of the 70 patients was 68 years; mean was 65 years, with the range being 49 to 85 years. Tissue diagnosis was made either by transurethral resection of the prostate (27 patients) or by needle biopsy (43 patients). Pretreatment staging evaluation included a digital rectal examination (DRE), a computed tomography (CT) scan of the abdomen and pelvis and a radionuclide bone scan. Clinical stage was assigned to each patient according to the American Urological Association criteria.[12] The Gleason scoring system[13,14] was used

in 62 patients to classify the histologic grade of the tumor. In 8 patients, the tumor was graded according to Mayo Clinic grading system.[15] The tumors were classified into well, moderate and poorly differentiated, depending on the degree of glandular formation. Well differentiated tumors form glands that may be large, intermediate, or small and with papillary configuration. In moderately differentiated tumors only 50-75% form glands, and these may be a cribriform, less papillary pattern. In the poorly differentiated tumor 25% or less of the tumor will form glands and cells are arranged in rows, columns or sheets.[16] There were 9 patients (13%) with Stage B2 (one patient had undergone a staging bilateral lymphadenectomy), 43 (61%) with Stage C and 18 (26%) with Stage D1 disease. Of these 18 Stage D1 patients, 8 had pelvic lymphadenectomy. The general characteristics of all 70 patients are summarized in Table 1.

Serum PSA Determination

The pretreatment PSA values were known in 59 of 70 (84%) patients. The eleven patients who did not have pretreatment values were treated prior to 1988, when a serum PSA determination was not routinely obtained. However all seventy patients (100%) did have post-therapy levels. Two different assays for measuring serum PSA concentration were used among the referring physicians. The Pros Check PSA Assay, a polyclonal radioimmunoassay (Yang Laboratories, Belleview, Washington, 98004, reference range: 0-2.5 ng/ml)[17] was employed for 10 patients, whereas the Tandem-R PSA Assay, a monoclonal immunoradiometric method (Hybritech Corp., San Diego, CA, 92138, reference range: 0.0-4.0 ng/ml)[18] was used to monitor 60 patients. No attempt was made to directly convert the numerical value from one assay to that of the other, since the relationship between the two assays is not totally linear over a wide range of values.

The first post-therapy serum PSA level was obtained at 3 months after therapy, then every 3 months for 2 years, and once every 6 months as long as it remained within the reference range. More frequent determinations were made if the values started to

increase. Appropriate diagnostic studies (CT scan and bone scan) were recommended to evaluate the patient's disease status either when there was increase in the serum PSA level or when clinically indicated.

Technique of Neutron Beam Therapy

At Fermilab Neutron Therapy Facility; 66 MeV (Mega electron Volt) protons are directed against a beryllium target to obtain high energy neutrons. The physical characteristics of the beam are similar to 6 MeV x-rays.[19] The beam is fixed and horizontal. The prostate cancer patients are treated in a standing position, in an isocentrically located chair which has capabilities of front to back, side to side, and rotational movements. A four field technique was used to treat both the pelvis and the prostate. A total of 14 neutron Gy (45 Gy photon equivalent, 1 Gy = 100 rad) was delivered to the pelvic lymph nodes in 8 to 9 fractions. The usual fields were anterior/posterior measuring 14 X 16 cms and lateral fields measuring 12 X 16 cm. The prostate was boosted with an additional 6.4 to 7 Gy (total dose to the prostate 20.4 to 21 neutron Gy i.e., 61.2 to 63 Gy photon equivalent). The prostate boost fields usually measured antero/posteriorly 10 X 10 cms and laterally 9 X 10 cms. The target absorbed doses were prescribed to an isocenter (dosimetry report ICRU29). The dose variation of ±5% within the target volume was considered acceptable. The overall treatment course was 4 to 5 weeks with 2 to 3 fractions per week. All the patients were monitored as clinically indicated during the treatment course; they were examined for acute side effects, and these were managed appropriately.

Follow-Up

The first post-therapy follow-up was scheduled for one month. Subsequent follow-ups were every 3 months for 2 years, every 6 months for 5 years and annually thereafter. However, more frequent follow-up evaluations and appropriate

investigations, including abdominal and pelvic CT and radionuclide bone scans, were recommended when clinically warranted. During follow-up visits, the specimen for PSA determination was drawn prior to the DRE.

Local response was determined only by DRE of the prostate. Neither a transrectal ultrasound examination nor a biopsy of the prostate was performed routinely for all patients.

Statistical Methods

An attempt to calculate the time of PSA to reach a baseline was made using a linear regression method. The prostate specific antigen values were normalized assuming the initial reading to be 100%. Subsequent readings taken at various intervals following treatment were expressed as a percentage of the initial value. The time to achieve a baseline serum PSA following neutron beam radiation therapy was determined for each subject by a linear regression of logarithm of the normalized value as a function of the elapsed time from completion of the treatment, using standard stastical methods. From two to four readings were utilized to determine the downward slope of the line. The patients who did not have pretreatment PSA values and the patients whose pretreatment values were within the normal range were both excluded for the calculation. The time to reach the normal range calculations were performed for 56 (80%) of the 70 patients.

Tukey multiple comparison method is used to analyze the significance of pretreatment values in relation to the various groups of patients, stage, and degree of tumor differentiation.

Results

Documented preneutron irradiation PSA values were available in 59 of 70 (84%) patients. Three of these fifty-nine patients had normal pretreatment values. All seventy patients had serial PSA determinations subsequent to neutron beam therapy.

Table 2 shows the mean, median and range of pretreatment PSA levels for various stages of prostate cancer. The patients with Stage B2 disease had lower median and mean values (18.9 ng/ml, and 24.2 ng/ml) than patients with Stage D1 disease (median value of 49.8 ng/ml and mean 51 ng/ml) The correlation between the degree of tumor differentiation and the pretreatment PSA value is shown in Table 3. The well differentiated tumors tended to have lower median and mean serum PSA levels (34.5 and 33.5 ng/ml respectively) when compared to the poorly differentiated tumors (50.2 ng/ml and 42 ng/ml). However, since there is no accurate, noninvasive method for determining tumor volume, no attempt was made to correlate the degree of tumor differentiation with the serum PSA concentration per cc of tumor. Table 4 shows patients with pretreatment PSA values grouped retrospectively to predict the prognosis. The patients with lower pretreatment PSA values tended to fall into the group with a good prognosis.

The relationship between pretreatment PSA and group, stage of the tumor, and differentiation of the tumor was examined. Because the pretreatment PSA values were extremely skewed, the data were transformed by taking square roots to obtain an approximately normal distribution. One-way analysis of variance was used to analyze the square-root PSA values. The hypothesis of equal population square-root PSA means for the three groups was rejected ($p = 0.0003$). Tukey multiple comparisons indicated that the Group III population mean square-root PSA was larger than the population means for Groups I and II (95% confidence level). There was no statistically significant difference between the square-root PSA means for the three cancer stages ($p = 0.3600$). There was no statistically significant difference between the square-root PSA means for the three types of tumor differentiation ($p = 0.7880$).

A retrospective review of our post-therapy PSA data distinguished 3 distinct groups of patients. Group I This cohort consisted of 30 patients (43%) in whom the serum PSA level declined to the reference range following neutron irradiation and

remained so on subsequent follow-up. The minimum follow-up period was 12 months, maximum of 56 months and a median of 21 months. Of the thirty patients in this category, ten had received antiandrogen therapy (bilateral orchiectomy in 5 patients and Eulexin + Lupron in 5 patients) immediately prior to the start of neutron irradiation. The mean time for the serum PSA to reach the reference range in these 30 patients was 6 ± 3.8 months. Of the twenty patients who received only neutrons, the mean time for the serum PSA level to reach the reference range was 6.5 ± 4.8 months. In the subgroup of ten patients who had both antiandrogen therapy and definitive neutron therapy, the mean time for PSA to decrease to the reference range was 4 ± 0.7 months.

The local response rate as determined by DRE was 100% (30/30). Two patients (7%) developed distant metastases as determined by radionuclide bone scan (Table 5). Twenty-seven of the thirty patients (90%) are alive; one patient died from prostate cancer, whereas the other two patients died from unrelated causes.

The data from Group I were analyzed further to evaluate the influence of concurrent antiandrogen therapy on the outcome.

Neutron Therapy Only

There were twenty patients in this group; seventeen (85%) are alive NED, with a mean followup of 25 months (range 9 to 56). Of the three men who have succumbed, one died from metastatic prostate cancer 9 months after completion of treatment, one died in an automobile accident 30 months post-therapy, and the third patient died from disseminated transitional cell carcinoma of the bladder at 55 months. Neither of the latter two patients had evidence of residual or progressive prostate cancer.

Combination Neutron & Antiandrogen Therapy

All ten patients are alive. Nine patients (90%) are alive with no evidence of disease, and the other patient is alive with stable metastatic disease at 15 months. The follow-up period ranged from 13 to 38 months (median: 17 months).

The observation of 100% local response (30/30) and 93% (28/30) of the patients being disease-free is an indication of a good prognosis. There was no significant difference in the outcome between the two subgroups (neutron therapy only and combination neutron and antiandrogen therapy). However the mean time for the serum PSA value to decrease to the reference range was 4 $\pm$ 0.7 months in the combined group versus 6.5 $\pm$ 4.8 months in the neutron only group.

Group II: Thirteen patients were contained in this category. In these patients the post-neutron irradiation serum PSA concentration decreased to and remained in the normal range for several months and then began to increase. The average time interval without a detectable increase in serum PSA was 48 months. The median time was 26 months; the shortest interval before PSA started to increase was 9 months, and the longest period was 42 months. The follow-up period for these 13 patients was 12 to 72 months (median: 39 months).

Six patients of the thirteen patients (46%) are alive without documented presence of either local or distant disease (Table 5). The prostate is flat on DRE, and all have a

normal radionuclide bone scan. Three patients died from metastatic disease, but all had a local response. A fourth patient, who died from metastatic malignant melanoma, had local recurrent prostate cancer. One of the thirteen patients (8%) who had local recurrent disease underwent radical prostatectomy. The surgical margins were positive for microscopic disease. He is alive and well with no distant disease, but the serum PSA level is gradually increasing. Of the two other patients, one had biopsy-proven local persistence of tumor and the other patient has developed metastatic disease. Both of these patients however, have clinically stable disease at the present time. Overall, 43 (61%) of the 70 patients (patients in Group I and II) achieved a measurable PSA response following definitive neutron beam radiation therapy.

Group III: A total of 27 patients were in this group; for all men, the serum PSA value remained above the reference range subsequent to neutron irradiation. In two of these twenty-seven patients, the PSA level was slowly decreasing but has not yet reached normal even after 12 months post-treatment, possibly indicating a very slowly regressing tumor. Of the twenty-seven, fourteen (52%) had a normal prostate on DRE; 7 of these 14 (50%) have distant metastases. In two of these patients, the status of local tumor disease is not known, but all are known to have distant metastatic disease. Seven of the 27 patients (26%) have persistent local tumor and these include those two patients whose PSA is still decreasing.. For Group III, only nine patients (33%) have remained clinically stable without documented progression of the cancer (Table 5). In these patients, DRE revealed the prostate to be flat and smooth, and the radionuclide bone scan was negative. The follow-up period for these 9 patients was 14 to 24 months. Altogether four patients have died in Group III, 3 from prostate cancer and one from small cell carcinoma of the lung. The follow-up period for these twenty seven patients ranged from 12 to 69 months with median of 21 months.

Time To Achieve A Stable Baseline PSA Value

The mean time to achieve a stable baseline of serum PSA in Group I patients was 53 ± 37 days. For the men in Group II, the calculated time to achieve a stable baseline was 61 ± 21 days, whereas it was 108 ± 76 days for the Group III patients.

Discussion

Prostate specific antigen is a sensitive tumor marker to monitor the tumor status of patients with prostate cancer. This retrospective analysis was intended to determine the prognostic significance, if any, of post-neutron irradiation PSA levels in patients with locoregionally advanced (B2, C, and D1) stages of prostate cancer.

In our patients, pretreatment PSA values showed a correlation with stage of the disease in accordance with others;[5,7,20] however, this correlation was not statistically significant. Of note in these reports early stage patients (A and B1) were also included. Depending upon the post-neutron therapy serial PSA levels, prognostically there were three groups of patients: Group I: PSA in the reference range post-neutron beam radiation therapy. Group II: PSA initially decreased to the reference range and then became elevated on subsequent followup. Group III: Persistently elevated or rising PSA post-neutron beam radiation therapy.

The patients whose serum PSA concentration reached the normal reference range and remained there, seem to have a good prognosis. On DRE the prostate was considered to be normal in all thirty patients and 90% (28/30) of them were disease-free. The intriguing question is, should all these patients with a stable serum PSA value in the reference range have annual bone scans, CT scans of the abdomen and pelvis, routine prostate biopsies between 18 months to 2 years after neutron beam therapy, or can the serum PSA level alone be relied upon to monitor the tumor status in these patients. GoldRath, and Messing, have reported two patients who had normal serum PSA values despite the presence of locally recurrent disease following radical prostatectomy.[21] The authors concluded that while monitoring PSA is of great value in the follow-up of patients with prostate cancer, it has not yet replaced the more standard means of follow-up.

Similarly we had two patients with a normal serum PSA concentration who developed distant metastatic disease following neutron beam radiation therapy.

In our series the patients with relatively lower pretreatment PSA values, on retrospective grouping, fell into the group with a good prognosis. This finding concurs with observation of Kuriyama et al.[22]; these investigators found that patients receiving antiandrogen therapy who had lower pretreatment levels tend to survive longer than those with higher PSA values. However, in a given individual patient, the prognosis probably cannot be predicted with certainty based on pretreatment PSA value alone, before post-therapy PSA results are available.

We suspect that the rate of decline of the serum PSA concentration to values within the reference range subsequent to therapy has a prognostic implication, although there are no data yet available to confirm this hypothesis.. However, 6 months appear to be the time limit for the serum PSA concentration level to reach the normal range if complete tumor regression is to be achieved. If longer than 6 months is required, either local persistence or progression of cancer can be predicted. This conclusion is supported by Dundas, et al.[3] These authors prospectively measured PSA in 110 patients with locoregional prostate cancer treated with external photon beam theapy alone or with brachytherapy and hormone therapy. In this series none of the 9 patients (8.3%) who failed had their PSA return to normal, whereas 73% of the remaining (74/101) did so within 6 months of the completion of therapy. Landmann et al.[5] have published the results of PSA values in 71 patients irradiated using conventional photons. They reported that the normalization of PSA levels slowed down beyond 6 months and chances of further decrease remained rather small, similar to our experience. The rate of decrease of the serum PSA value in patients with similar stages (B2, C, D1) treated with photon therapy is not known. The results of a prospective randomized RTOG study (comparing patients treated with neutrons versus photons) are not yet known. The patients with concurrent hormonal manipulation had their serum PSA level decrease to the reference range within 4 months. Leo et al.[23] have

suggested that androgen deprivation therapy in prostate cancer patients may have a direct effect on the serum PSA concentration, independent of the response obtained from any antitumor activity. The combined effect of antiandrogen therapy and neutron irradiation most likely resulted in a more rapid decrease in the serum PSA concentration in these patients. This combined approach may be of consideration for patients with a large tumor burden.

The serum prostate specific antigen decreases to undetectable levels after radical prostatectomy; the half-life was calculated to be 2.2 days by Stamey et al.[9] and 3.2 ± 0.1 by Oesterling et al.[7] Oesterling reported also that all the patients with documented clinical recurrence either local or distant, had an elevated follow-up serum PSA concentration.[7] The rate of change in serum PSA concentration after radiation therapy is variable; Chodak et. al.[4] reported a 50% decline within 4 to 20 weeks after external beam radiation therapy, and Meek et. al.[6] determined the half-life of serum PSA following definitive radiation therapy to be 43 ± 11 days.

The prostate specific antigen half-life is useful information to predict the responsiveness of the tumor. Shorter time for PSA to reach normal range indicates a more rapid tumor regression. In our series, Group I patients had an average time to achieve normal range of 53 ± 37 days as compared to 108 ± 76 days in Group III patients. A prolonged time may suggest unresponsive or progressive disease.

The group of patients in whom PSA started to increase after remaining normal for several months, is interesting. Six of thirteen patients (46%) are clinically well; the prostate is flat on DRE, and the bone scan is normal. However DRE alone without an ultrasonographic examination and/or biopsy of the prostate, in the presence of elevated PSA is not an adequate evaluation to assign a patient to no evidence of disease status solely on the basis of flat normal prostate on digital examination and normal radionuclide bone scan. This view is supported by a publication from Kabalin et al. These authors performed biopsies of 27 prostate cancer patients, 18 months or longer following

definitive radiation therapy. The biopsy results were correlated with the findings on DRE and the serum PSA concentration [10]. Twelve of twenty-seven patients who had elevated PSA (<10ng/ml) had normal prostate on DRE. Of these twelve, ten patients (83%) had positive biopsies. Of the remaining fifteen patients (PSA >10 ng/ml), five had indurated prostates on DRE and all fifteen (100%) had positive biopsies. We can predict that these six patients in our group are likely to manifest either local recurrence or metastatic disease soon. Therefore, these six patients should probably undergo ultrasound-guided prostate biopsy to document the possibility of local recurrence, though the prostate feels flat on DRE; early therapeutic intervention in these patients with adjuvant antiandrogen therapy might be valuable. According to Killan et al.[24,25] an increase in the serum PSA level may preceed an overt clinical relapse by as much as 2 years. Oesterling et al.[7] have reported that subsequent elevation of PSA following radical prostatectomy invariably signals tumor recurrence. However, as of now, there is no consensus on how to manage these patients; a prospective randomized study is indicated to resolve this therapeutic dilemma.

The group in whom the serum PSA level remained elevated had relatively poor prognosis. In our series, only 9 of 27 (33%) have no other clinical evidence of progression of their disease, where 18/27 (67%) have already failed (followup: 12 to 69 months). These 9 patients are most likely to have locally persistent disease. Adjuvant antiandrogen therapy certainly should be considered for these men in Group III.

In summary, the data of this retrospective review of patients with locoregional prostate cancer undergoing definitive neutron beam radiation therapy indicate:

1. PSA is a sensitive tumor marker to monitor the disease status in patients with prostate cancer, and has prognostic implications following neutron beam radiation therapy.
2. Serum PSA values within the reference range by 6 months

post-neutron therapy indicate good prognosis.

3. When PSA remain persistently elevated or becomes normal and then subsequently rises, either local recurrence or distant spread of cancer is to be expected.

4. Appropriate therapeutic strategies need to be developed for those patients with elevated serum PSA values subsequent to definitive neutron beam radiation therapy.

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TABLE 1

General Characteristics of 70 Patients

Characteristics	# of Patients (%)
Age (in years)	
Range 49-85	
Median 68	
Mean 65	
Stage of the Disease	
B_2	9 (13%)
C	43 (61%)
D_1	18 (26%) 8 surg. staged (44%)
Pathological Differentiation	
Well differentiation (Gleason Score 3-5)	12 (17%)
Moderate differentiation (Gleason Score 6-7)	26 (37%)
Poor differentiation (Gleason Score 8-10)	32 (46%)
Diagnosis	
TURP	27 (39%)
Needle Biopsy	43 (61%)
Concomitant Antiandrogen Therapy	10 (14%)

TABLE 2

Pre-Neutron PSA Levels Versus Various Stages of Prostate Cancer

Stage	Pre-Tx Level Avail - # Pts	Pre-Tx Level Not Avail - # Pts	Mean (ng/ml	Median (ng/ml)	Range (ng/ml)	Total (# Pts)
B2	8 (89%)	1 (11%)	24.2	18.9	3.4-50.9	9
C	36 (78%)	7 (16%)	44.0	29.0	0.5-248	43
D1	15 (83%)	3 (17%)	51.0	49.8	1.7-127.1	18
Total	59 (84%)	11 (16%)				70

TABLE 3

Pre-Neutron PSA Levels Versus Degree of Tumor Differentiation*

Differentiation	Pre-Tx Level Avail. - # Pts	Pre-Tx Level Not Avail. - # Pts	Mean (ng/ml)	Median (ng/ml)	Range (ng/ml)	Total (# Pts)
Well Diff. (Gleason Score) 3 - 5	8 (67%)	4 (33%)	33.5	34.5	1.7-100	12
Mod. Diff. (Gleason Score) 6 - 7	23 (88%)	3 (12%)	41.0	48.4	4.5-127.1	26
Poor Diff. (Gleason Score) 8 - 10	28 (88%)	4 (13%)	42.0	50.2	0.5-248	32
Total	59 (84%)	11 (16%)				70

*Tumor volume not available: as a result, the serum PSA concentration per cc of tumor could not be computed.

TABLE 4

Pre-Treatment PSA Levels Versus Various Groups of Patients

Group	Pre-Tx Level Avail - # Pts	Pre Tx Level Not Avail - # Pts	Mean (ng/ml)	Median (ng/ml)	Range (ng/ml)	Total # Pts
I	27 (90%)	3 (10%)	26.9	27.9	1.3-127	30
II	8 (62%)	5 (38%)	25.1	29.0	8.1-62.7	13
III	24* (89%)	3 (11%)	66.2	60.2	5.2-248	27
Total	59 (84%)	11 (16%)				70

*PSA is still decreasing in two patients.

Group I: PSA in the reference range post-neutron beam radiation therapy.

Group II: PSA initially decreased to within the reference range and then became elevated on subsequent followup.

Group III: Persistently elevated or rising PSA post-neutron beam therapy.

TABLE 5

Disease Status in Different Post-Neutron Groups of Patients

Group	# Pts	Loc. Response # Pts. (%)	Persist.	D.M. Only	D.M. + Local Dis.	# Pts Dis. Free
I	30	30 (100%)	0	2 (7%)	0	28 (93%)
II	13	9 (69%)	4 (31%)	3 (23%)	0	6 (46%)
III	27*	14 (52%)	7* (26%)	7+ (26%)	4 (15%)	9 (33%)
Total	70	53 (78%)	11 (16%)	12 (17%)	4 (6%)	43 (61%)

*PSA still decreasing in 2 patients.
+Local disease status not known in 2 patients.
Persist = Persistence
DM = Distant Metastases
Dis. Free = Disease Free

Group I: PSA in the reference range post-neutron beam radiation therapy.
Group II: PSA initially decreased to within the reference range and then became elevated on subsequent followup.
Group III: Persistently elevated or rising PSA post-neutron beam therapy.