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# A Comparison of Total, Free, and % Free PSA for the Serodiagnosis of Prostate Cancer in African-American and Caucasian-American Males

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**Abstract:** Although the major types of non-skin cancer among men are prostate cancer, lung cancer, and colorectal cancer, prostate cancer is the second leading cause of cancer death among men. In 2009, there were 192,280 new cases of prostate cancer and 27,360 deaths from this disease in the USA. It has been suggested that there is a disparity in the incidence and recognition of prostatic cancer between African-American males and Caucasian-American males [1]. One of the most widely used approaches for diagnosing prostate cancer involves measuring prostate specific antigen (PSA) serum levels. One objective of this study was to compare normal (healthy) adult PSA levels in African-Americans and Caucasian-Americans to determine if there is racial/genetic bias. A second objective was the comparison of a manual assay with an automated assay for PSA detection. It was hypothesized that the Diagnostic Automation (manual) assays would be superior to the Beckmann Access (automated) assays for the detection of prostate cancer and that there would be a genetic bias. Tumor marker assays were performed according to the manufacturer's directions. Assays used in this study included total PSA and % free PSA (Diagnostic Automation, Inc. and Beckman, Inc.). A total of 1,056 patient samples and 809 healthy adult male subject samples were tested. We concluded that the manual assay was superior to the automated assay for Free PSA detection but not for total PSA. We also concluded that there was genetic bias for African-American males versus Caucasian-American males.

**Key Words:** Prostate specific antigen, prostate cancer, tumor markers.

## INTRODUCTION

In 2012, there will be an estimated 241,740 new cases of prostate cancer and 28,170 deaths from this disease in the USA, according to the American Cancer Society [2]. This makes prostate cancer the leading non-skin cancer among males in the USA. The prostate is approximately the size of a walnut and is located at the neck of the bladder where it surrounds the urethra. It consists of acinar cells which line the prostatic ducts and glands and stromal support cells. The acinar cells secrete nutrients, enzymes, and buffers into the prostatic fluid which forms a portion of semen. The nutrients supply energy to the sperm, the buffers neutralize the pH of the semen, protecting the sperm from the acidic pH of the vagina, and the enzymes lyse the seminal coagulum following ejaculation, thus permitting the sperm to become motile [3].

The acinar cells are derived from epithelial cells which in turn come from the endoderm. Therefore, the major prostatic cancer is adenocarcinoma. Adeno refers to its glandular nature and carcinoma refers to its embryonic origin in the endoderm [4]. Benign tumors of the prostate are known as benign prostatic hyperplasia or BPH. Benign tumors will remain in situ whereas malignant (cancerous) tumors will eventually invade neighboring tissue and metastasize in blood and lymphatic systems to distant organs. For prostate cancer, the metastasis is usually to the bladder, hipbones, and vertebrae locally, and the lungs distally [4]. Symptoms include difficulty with urination, painful ejaculation, and persistent bone pain. Once symptoms of prostate cancer become noticeable, the tumor is often advanced. The

most widely used approaches for diagnosing prostate cancer involve the use of digital rectal examination (DRE), transrectal ultrasound, prostate biopsy, and prostate specific antigen (PSA) serum levels. Treatment options can include surgery, hormonal replacement, radiation therapy, and chemotherapy [5].

Prostate specific antigen (PSA) is a serine protease and forms a portion of the prostatic fluid. It functions to lyse the seminal coagulum following ejaculation. PSA is highly specific to the prostate. Serum PSA levels are normally very low in healthy males and increase with increasing tumor burden. For these reasons, PSA has been considered an excellent tool for screening, and has been used in combination with other methods for diagnosis, staging, and monitoring for recurrence of disease (relapse). Its one drawback is that serum PSA can be elevated with BPH as well as with prostatic cancer [6].

In serum, prostate specific antigen exists in two forms: free and complexed to alpha-1-antichymotrypsin. Monoclonal antibodies directed at epitopes on free, complexed, and total PSA have been developed and commercial assays exist for each of these [7]. Percent free PSA (% Free PSA) values can be calculated from the free PSA and total PSA results. Normal reference intervals (NRI) are derived for these assays by taking the mean plus or minus two standard deviations ($\bar{x} \pm 2S$) for a set of healthy human subjects. Patient values that fall outside of the NRI are considered to be abnormal. Since a low value for a tumor marker would have no clinical significance, one uses the mean plus two standard deviations ($\bar{x} \pm 2S$) as the "cut-off point" between health and disease. A variety of factors can affect the NRI. Three of the most common effectors are age, gender, and genetics. Examples would include: increasing NRI for cholesterol seen with increasing age, increasing NRI for estrogen seen with females as opposed to males, and decreasing NRI for alcohol dehydrogenase seen in Native-Americans and Asiatics as opposed to Caucasians and Africans [7].

It has been suggested that there is a disparity in the incidence and recognition of prostatic cancer between African-American males and Caucasian-American males [8]. This could be the result of genetic bias or socioeconomic factors. The CDC [9] reported that among all other races, an African-American male has a nineteen percent chance of being diagnosed with prostate cancer and a five percent chance of dying from the disease. In addition, the CDC [10] noted that in 2005 Caucasian males had a higher incidence of prostate cancer than Hispanic males. The UPMC Cancer Center [11] claimed that Asian men had the lowest incidence of prostate cancer among all other races.

Boyles [12] reported that in a study of 1346 adult males (673 with prostate cancer and 673 without prostate cancer), he observed a slight increase in prostate cancer among those individuals who had a history of prior infection with trichomoniasis. He concluded that there may be a link between STD infection and more aggressive prostate cancer. His study suggests the possibility that a discrepancy between the incidence and/or prevalence of STDs could explain an observed difference in the incidence and/or prevalence of prostate cancer between African-American and Caucasian-American males.

Fowke [13] reported that African-American males, among all other racial groups, were more likely to be diagnosed with prostate cancer at a more advanced stage. He compared 121 African-American males with 121 Caucasian-American males with no prior diagnosis of prostate cancer or diabetes. He observed a correlation between obesity, diabetes mellitus, and PSA levels. PSA blood levels (concentrations) were decreased in obese and diabetic males. This association was more prevalent among obese African-American males but was also observed to some extent among obese Caucasian-American males. This finding could also explain an observed difference in the incidence and/or prevalence of prostate cancer between African-American and Caucasian-American males.

Odedina [14] investigated the relationship between prostate cancer knowledge, cultural beliefs and values, and the incidence and prevalence of prostate cancer among African-American males and West African males. According to Odedina, both West African males and recent immigrants from West Africa to the United States have a lower incidence of prostate cancer than African-American males. In her study, she attributed this to their cultural dissimilarities because they have similar genetic backgrounds. She reported that African-American males suffer disproportionately from aggressive prostate cancer which is often detected at a much later stage. Her data demonstrated that African-American males were more fatalistic in their cancer beliefs than other American ethnic groups and hence were more likely to be diagnosed in late stage disease. She raised the possibility that cultural beliefs may contribute to the higher incidence of prostate cancer among African-Americans.

The purpose of this study was to compare African-American males with Caucasian-American males for healthy adult reference intervals (NRI) for PSA and %

free PSA. One addressed the question of racial/genetic bias and the possibility that one should not continue to use the same PSA cutoff values for different genetic/racial subgroups. Additionally two test methods for PSA (manual vs. automated) were compared. It was hypothesized that the new test (manual test) would prove superior to the in-house test (automated test) and that there would be a significant difference between African-American and Caucasian-American PSA NRI.

## MATERIALS

The Beckman Access free PSA and total PSA assay kits were acquired from Beckman Coulter (Faulkner, CA). The intended use of the Beckman Access free PSA is for the quantitative measurement of free prostate specific antigen (PSA) in human serum. The assay should be used in conjunction with the Beckman Access total PSA. The intended use of the Beckman Access total PSA is for the quantitative measurement of total PSA in human serum. The assay is also used as an additional test to aid in the management of cancer. Both of the assays are based on the Microparticle Enzyme Immunoassay (MEIA) technology.

The Diagnostic Automation free PSA and total PSA kits were acquired from Diagnostic Automation, Inc. (Calabasas, CA). The intended use of the Diagnostic Automation free PSA test is for the quantitative measurement of free PSA in human serum. The intended use of the Diagnostic Automation total PSA is for the quantitative measurement of total PSA in human serum. The principle of both assays is based upon a solid phase two-site immunoassay. The kits contain a monoclonal antibody with an attached tracer and another one as a capture antibody. The free (unbound) tracers are removed by washing after certain complexes are made. The assay will produce a colorimetric reaction.

The Beckman Access instrument was acquired from Beckman Coulter, Inc. (Faulkner, CA). For the Diagnostic Automation assay kits, everything is done manually. A Stat Fax 2600 microplate washer was acquired from Diagnostic Automation (Calabasas, CA). The Beckman Coulter AD 340 microtiter plate reader was acquired from Beckman Coulter (Faulkner, CA).

## PATIENTS & SUBJECTS

Samples of blood were collected at hospitals (Gulf Coast area) from 1056 male patients seen during a 24-month period of time. All male patients over the age of 18 years for whom an initial PSA test had been ordered by their physician were included. Prostate cancer was found in 155 of the patients; 901 of the patients did not have cancer. The serum was separated from each blood sample, labeled with a code number, and frozen at -20°C. The hospital pathologists sent the researchers a list of the code numbers with the appropriate diagnoses. All other patient identifiers (e.g. name, social security number, and hospital identification number) were removed to protect the confidentiality of the patients. The sera from 809 healthy adult (>18 years of age) male subjects were also acquired from hospitals for the determination of the normal reference intervals for the assays. Of these five hundred and eighty-four (584) were Caucasian-American males, one hundred and eighty-four (184) were African-American males, and forty-one (41) were Hispanic-American males. These volunteer subjects were determined to be healthy by the pathologists on the basis of their clinical presentations and their pathologic/histological examinations. The University of Southern Mississippi Institutional Review Board approved permission for this study to be conducted and the procedures were in accordance with all ethical standards.

## METHODS

The samples of serum were thawed at 37°C and the PSA assay kits for total PSA and free PSA were used according to the manufacturers' instructions. Based on the procedure for the Beckman Access total PSA assay, 150 µL (microliters) of patient's serum were dispensed into each sample well. Then, five drops of the total PSA calibrators and controls were dispensed into the appropriate sample wells. A minimum volume of 250 mL (milliliters) of the MEIA #2 diluent buffer for the Beckman Access total PSA assay kit was also added to the wells. An assay calibration was performed on all new lots of Beckman Access total PSA reagent packs. Once the calibrations were accepted and stored into the Beckman Access instrument, controls were run on the instrument. A minimum of one control per carousel was needed for the run.

Based on the procedure for the Beckman Access free PSA assay, 150 µL of the patient serum was pipetted into each of the wells. Then, five drops of calibrators and controls were dispensed into each appropriate well. A minimum volume of 250 mL of MEIA #2 diluent buffer

was used to properly process each assay run. Calibration was run on all new lots of reagent packs. Once assay calibrations had been accepted and stored into the instrument, controls were run. A minimum of one control per carousel was needed for the run. All of the Beckman Access assay procedures were run on the Beckman Access instrument provided by Beckman Coulter Laboratories.

In accordance with the assay procedure for the Diagnostic Automation total PSA (Figure 1), 50 µL (microliters) of patient serum, standards, and controls were pipetted into the appropriate sample wells. One hundred microliters of zero buffers were also dispensed into each well. The contents of the wells were thoroughly mixed for ten seconds. Then, the wells were incubated at room temperature (18-22°C) for 60 minutes. After 60 minutes, the incubation mixture was removed and discarded properly. The microtiter wells were washed with the STAT FAX 2600 microplate washer and the wells were thoroughly emptied to remove all residual water droplets. Next, 100 µL of enzyme conjugate were dispensed into each well and gently mixed for five seconds. The sample wells were again incubated at room temperature for 60 minutes. The incubation mixture was emptied at the end of 60 minutes, and the microtiter plates were washed with the STAT FAX 2600 microplate washer. After washing, the plates were thoroughly emptied to remove residual water droplets. Then, 100 µL of TMB solution was pipetted into each well and gently mixed for five seconds. After mixing, the wells were incubated for 20 minutes. Then, the reaction was stopped by adding stop solution to each sample well. Next, the contents of the wells were gently mixed until there was a complete color change from blue to yellow and the microliter plates were read on the Beckman Coulter AD 340 microtiter reader at 450 nm within 20 minutes. The absorbance of the assay was directly proportional to the total PSA in each sample.

In accordance with the assay procedure for the Diagnostic Automation free PSA (Figure 2), 100 µL of patient serum, standards and controls as well as 100 µL of sample diluent were dispensed into appropriate wells. The contents of the wells were thoroughly mixed for ten seconds and the wells were incubated at 37°C for 60 minutes. After incubation, the mixture was removed from the wells and discarded. Then, the microtiter plates were washed by using the STAT FAX 2600 microplate washer and the plates were thoroughly emptied of the residual water droplets. Next, 200 µL of enzyme conjugate reagent were dispensed into each well and gently mixed for five seconds. These mixed samples were also incubated for 60 minutes at 37°C. After incubation, the mixture was also removed and washed with the STAT FAX 2600 microplate washer. Then, 100 µL of TMB stop solution were dispensed into each well and gently mixed for five seconds. Next, the wells were incubated in the dark for 20 minutes. After incubation, the reaction was stopped by adding 100 µL of stop solution to each well. The contents of the wells were gently mixed for thirty seconds until there was a complete color change from blue to yellow and the Beckman Coulter AD 340 microtiter plate was used to read the plates at 450 nm within 20 minutes.

Once the patients' specimens for the Beckman Access total and free PSA as well as the Diagnostic Automation total and free values were obtained, a calculation for the % free PSA was performed. The % free PSA was calculated by obtaining the total PSA and free PSA values. The free PSA value was divided by the total PSA value and that Quotient was multiplied by 100.

Equation 1: (Free PSA/Total PSA) x 100 = % free PSA

**Statistics**

All statistical calculations were performed by using the computer SP software package.

## RESULTS

**Precision**

Quality control samples (included in the kits), analyzed over a 3-month period, were used to determine intra- and inter-assay precision (Tables 1A and 1B). The coefficient of variation results were less than 10% for all but the between run precision, which was less than 20%.

**Table 1A. Comparison of Diagnostic Automation and Beckman Access Assay Precision for Total PSA using Control Sera**

| | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | CV (%) |
|---|---|---|---|---|
| **Within-Run** | | | | |
| Diagnostic Automation | 4 | 3.89 | 0.10 | 2.48 |
| Beckman Access | 2 | 1.00 | 0.02 | 2.00 |
| **Between-Run** | | | | |
| Diagnostic Automation | 52 | 3.87 | 0.71 | 18.30 |
| Beckman Access | 40 | 1.00 | 0.02 | 2.20 |

**Table 1B. Comparison of Diagnostic Automation and Beckman Access Assay Precision for Free PSA using Control Sera**

| Assay | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | CV (%) |
|---|---|---|---|---|
| **Within-Run** | | | | |
| Diagnostic Automation | 4 | 2.25 | 0.09 | 4.10 |
| Beckman Access | 2 | 1.04 | 0.02 | 1.79 |
| **Between-Run** | | | | |
| Diagnostic Automation | 52 | 2.08 | 0.40 | 19.23 |
| Beckman Access | 40 | 1.04 | 0.04 | 3.40 |

**Linearity**

Serial dilutions of abnormal pool samples were used to determine the linearity of the assays (Tables 2A and 2B). The $R^2$ values were greater than 0.99 for all the assays.

**Table 2A. Comparison of Diagnostic Automation and Beckman Access Assay Linearity for Total PSA**

| Assay | R Squared ($R^2$) |
|---|---|
| Diagnostic Automation | 0.9981 |
| Beckman Access | 0.9996 |

**Table 2B. Comparison of Diagnostic Automation and Beckman Access Assay Linearity for Free PSA**

| Assay | R Squared ($R^2$) |
|---|---|
| Diagnostic Automation | 0.9998 |
| Beckman Access | 0.9986 |

**Assay Sensitivity**

Reference intervals for the zero diluent [analytical sensitivity] are given in Tables 3A and 3B. The results range from 0.000 to 0.008 for the manual and automated assays respectively.

**Table 3A. Comparison of Diagnostic Automation and Beckman Access Assay Sensitivity (Analytical Sensitivity) for Total PSA**

| Analytical Sensitivity | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Range (ng/mL) |
|---|---|---|---|---|
| **Assay** | | | | |
| Diagnostic Automation | 19 | 0.00 | 0.000 | 0-0.000 |
| Beckman Access | 20 | 0.00 | 0.004 | 0-0.008 |

**Table 3B. Comparison of Diagnostic Automation and Beckman Access Assay Sensitivity (Analytical Sensitivity) for Free PSA**

| Analytical Sensitivity | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Range (ng/mL) |
|---|---|---|---|---|
| **Assay** | | | | |
| Diagnostic Automation | 20 | 0.00 | 0.000 | 0-0.000 |
| Beckman Access | 20 | 0.00 | 0.002 | 0-0.005 |

**Reference Intervals**

Normal Reference Intervals are given in Tables 4 for healthy, adult African-American and Caucasian-American males.

**Table 4A. Comparison of Diagnostic Automation and Beckman Access Assay Healthy Adult Reference Intervals for Total PSA**

| Healthy Adults | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Range (ng/mL) |
|---|---|---|---|---|
| **Total Males** | | | | |
| Diagnostic Automation | 808 | 1.67 | 2.86 | 0-7.39 |
| Beckman Access | 809 | 1.91 | 6.59 | 0-17.07 |
| **African-American Males** | | | | |
| Diagnostic Automation | 184 | 2.27 | 4.21 | 0-10.69 |
| Beckman Access | 183 | 2.69 | 12.42 | 0-27.53 |
| **Caucasian-American Males** | | | | |
| Diagnostic Automation | 582 | 1.45 | 2.34 | 0-6.13 |
| Beckman Access | 584 | 1.70 | 3.37 | 0-8.84 |

**Table 4B. Comparison of Diagnostic Automation and Beckman Access Assay Healthy Adult Reference Intervals for Free PSA**

| Healthy Adults | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Range (ng/mL) |
|---|---|---|---|---|
| **Total Males** | | | | |
| Diagnostic Automation | 808 | 0.07 | 0.28 | 0-0.63 |
| Beckman Access | 36 | 0.90 | 1.26 | 0-3.42 |
| **African-American Males** | | | | |
| Diagnostic Automation | 184 | 0.12 | 0.43 | 0-0.98 |
| Beckman Access | 10 | 1.56 | 2.24 | 0-6.04 |
| **Caucasian-American Males** | | | | |
| Diagnostic Automation | 582 | 0.05 | 0.23 | 0-1.02 |
| Beckman Access | 26 | 0.65 | 0.43 | 0-1.51 |

A Comparison of Normal Adult PSA values by genetic background and by methodology are given in Tables 5-6.

**Table 5. Comparison of Normal Adult PSA Values by Genetic Background**

| Total PSA | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Probability |
|---|---|---|---|---|
| **Diagnostic Automation** | | | | |
| African-American Males | 184 | 2.27 | 4.21 | 0.013* |
| Caucasian-American Males | 582 | 1.45 | 2.34 | |
| **Beckman Access** | | | | |
| African-American Males | 183 | 2.69 | 12.42 | 0.288 |
| Caucasian-American Males | 584 | 1.70 | 3.37 | |

| Free PSA | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Probability |
|---|---|---|---|---|
| **Diagnostic Automation** | | | | |
| African-American Males | 184 | 0.12 | 0.43 | 0.038* |
| Caucasian-American Males | 582 | 0.05 | 0.23 | |
| **Beckman Access** | | | | |
| African-American Males | 10 | 1.56 | 2.24 | 0.230 |
| Caucasian-American Males | 26 | 0.64 | 0.43 | |

| % Free PSA | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Probability |
|---|---|---|---|---|
| **Diagnostic Automation** | | | | |
| African-American Males | 184 | 5.29 | 6.21 | 0.014 |
| Caucasian-American Males | 582 | 3.45 | 7.38 | |
| **Beckman Access** | | | | |
| African-American Males | 10 | 5.79 | 9.13 | 0.230 |
| Caucasian-American Males | 26 | 3.76 | 8.94 | |

*p =< 0.05

**Table 6. Comparison of Normal Adult PSA Values by Methodology (paired t-test)**

| | n | $\bar{X}$ (ng/mL) | SD (ng/mL) | Probability |
|---|---|---|---|---|
| **Total PSA - Assay** | | | | |
| Diagnostic Automation | 807 | 1.67 | 2.86 | 0.167 |
| Beckman Access | 807 | 1.91 | 6.59 | |
| **Free PSA - Assay** | | | | |
| Diagnostic Automation | 36 | 0.29 | 0.87 | 0.000* |
| Beckman Access | 36 | 0.90 | 1.26 | |
| **% Free PSA - Assay** | | | | |
| Diagnostic Automation | 31 | 3.55 | 5.59 | 0.000* |
| Beckman Access | 31 | 19.06 | 9.01 | |

*p =< 0.05

There was a significant difference between the values for the two racial groups observed with the manual assay. There was a significant difference between the two assay methods for free PSA and % free PSA. There was no difference between the two assays for total PSA.

**Predictive Values**

Predictive values for prostate cancer in 1056 patients are presented in Tables 7-8. The diagnostic sensitivity for total PSA was less than 50% for both assays and racial groups (Table 7).

**Table 7. Predictive Values of Total PSA for Prostate Cancer in 1056 Patients**

| Assay Method | Sensitivity (%) | Specificity (%) | PV (+) (%) | PV (-) (%) | Efficiency (%) | Cut-Off (ng/mL) |
|---|---|---|---|---|---|---|
| **TOTAL Males** | | | | | | |
| Diagnostic Automation | 10.32 | 93.11 | 20.51 | 85.77 | 80.95 | 4.00 |
| Beckman Access | 18.71 | 87.57 | 20.57 | 86.23 | 77.46 | 4.00 |
| **African-American** | | | | | | |
| Diagnostic Automation | 16.67 | 92.23 | 36.00 | 80.85 | 76.54 | 4.00 |
| Beckman Access | 25.93 | 86.34 | 33.33 | 81.57 | 73.75 | 4.00 |
| **Caucasian-American** | | | | | | |
| Diagnostic Automation | 6.06 | 93.09 | 11.76 | 86.70 | 81.60 | 4.00 |
| Beckman Access | 14.14 | 87.60 | 14.74 | 87.06 | 77.93 | 4.00 |

In contrast, the diagnostic sensitivity for % free PSA was greater than 90% in both racial groups by Diagnostic Automation and greater than 75% in both racial groups by the Beckman Access method (Table 8).

**Table 8. Predictive Values of % Free PSA for Prostate Cancer in 1056 Patients**

| Assay Method | Sensitivity (%) | Specificity (%) | PV (+) (%) | PV (-) (%) | Efficiency (%) | Cut-Off (ng/mL) |
|---|---|---|---|---|---|---|
| **TOTAL Males** | | | | | | |
| Diagnostic Automation | 97.25 | 4.27 | 13.23 | 91.18 | 16.41 | 25.00 |
| Beckman Access | 80.00 | 33.33 | 5.13 | 97.37 | 35.34 | 25.00 |
| **African-American** | | | | | | |
| Diagnostic Automation | 95.00 | 8.00 | 19.10 | 87.50 | 24.19 | 25.00 |
| Beckman Access | 100.00 | 30.00 | 4.50 | 100.00 | 32.25 | 25.00 |
| **Caucasian-American** | | | | | | |
| Diagnostic Automation | 98.15 | 3.13 | 11.74 | 94.12 | 14.16 | 25.00 |
| Beckman Access | 75.00 | 33.75 | 5.36 | 96.43 | 35.71 | 25.00 |

The diagnostic specificity for total PSA was greater than 80% for both assays and both racial groups (Table 7). However, the diagnostic specificity for % free PSA was less than 50% for both assay methods in both racial groups (Table 8).

It is important to note that the Diagnostic Sensitivity of a test is the proportion of individuals with the disease who test positively with the test. Diagnostic Specificity of a test is the proportion of individuals without the disease who test negatively with the test. Predictive Value + is the fraction of positive tests that are true positives. Predictive Value – is the fraction of negative tests that are true negatives. Diagnostic Efficiency of a test is the fraction of all test results that are either true positives or true negatives [15].

## DISCUSSION & CONCLUSIONS

Based on the findings of this study, the hypothesis that there would be genetic bias was accepted. In contrast, the hypothesis that the manual test would be superior to the automated test was rejected for Total PSA assays and supported for % Free PSA assays. Analytical parameters were acceptable for all the assays. The normal reference intervals were slightly higher than those cited

by the manufacturers. There was a significant difference between the NRI of African-American and Caucasian-American adult males for Total PSA, Free PSA, and % Free PSA by the manual assay. A comparison of normal adult PSA reference intervals by methodology showed significant difference for Free PSA and %Free PSA, but not total PSA. The Beckman Access results were typically slightly higher than the Diagnostic Automation results.

Using the decision values established by the manufacturers, one obtained diagnostic sensitivities of <50% for Total PSA by both methods. This has been reported in the literature. While our values were in line with those of other researchers, they were disappointing. It is speculated that this may be due to inclusion of patients with prostate cancer who may have been diagnosed and were undergoing treatment. Alternatively the patients may have been diagnosed earlier in the course of the disease. The diagnostic sensitivities for % Free PSA were excellent with a Diagnostic Automation value of 97% and a Beckman Access value of 80%. The other predictive values were as expected and there was no significant difference between the values observed in African-American and Caucasian-American males.

Fowler proposed that there was a genetic bias due to high concentrations of high-grade prostatic intraepithelial neoplasia (HGPIN) that was found more often in African-American males than in Caucasian-American males. This study's data are partially supported by his results [1] [8]. Fowke [13] observed a lower PSA level among diabetic and obese males and especially among African-American males. This introduces the intriguing possibility that dietary considerations may play an important role in the epidemiology of prostate cancer. Fowke's work also partially supports our study's findings. Since there was no data collected on social/lifestyle behaviors for our study, we cannot exclude a social contribution to the observed findings of different PSA NRI among different genetic/racial groups (African-American vs. Caucasian-American males).

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