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Cancer Detection from Transrectal Ultrasound Guided Biopsy in a Single Center

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1. Introduction

Transrectal ultrasound-guided biopsy of the prostate is the mainstay in the diagnosis of prostate cancer. Cancer detection rates varies from centre to centre and is dependent on various factors including technique, number of cores, prostate volume, PSA levels and digital rectal examination findings.

There are also differences in various ethnic groups with regards to prostate cancer incidence especially in the west where African Americans have a higher incidence. In Malaysia there are three major ethnic groups; Malays (65%), Chinese(25%) and Indians (8%). There is no evidence as yet to show any differences in prostate cancer detection among the three ethnic groups

The Malaysian National Cancer Registry published in 2006¹, ranks prostate cancer as the 4th most common cancer in Malaysian men after large bowel, lung and nasopharyngeal cancer. It constitutes 7.3% of all cancers in men. The overall prostate cancer incidence per 100 000 population (CR) was 7.3 and Age Standardised Incidence (ASR) was 12. By ethnicity Malays had the lowest ASR , 7.7 followed by Indians, 14.8 and Chinese 15.8. In fact Prostate Cancer is the fifth most common cancer among Malay men, fourth among Chinese and the second most common cancer among the Malaysian Indians. Overall , the Age Specific Incidence per 100 000 population increased from 9.7 among men in their 50s to 60.4 in men in their 60s

In an observation by Lim et al¹ from the Malaysian Clinical Research Center, Malaysian Indians have a higher incidence compared to Indians from Chennai, Malaysian Malays have a lower incidence compared to Singapore Malays and Malaysian Chinese have the highest incidence compared to Chinese in other Asian countries. These findings will need to be verified by further research.

It is also postulated that Asians prostate are generally smaller than western counterparts but volume for volume Asians have a higher PSA and part of the reason may be due to higher level of inflammation in Asian prostates.

2. Aims and objectives

The primary objective of this study is to look at a single centre's cancer detection rate and to determine the various factors that may influence cancer detection namely age, PSA levels,

number of cores and prostate volume. The study also aims to determine if cancer detection is higher in Chinese and Indian patients compared to Malay patients as reflected by the national Age Standardised Incidence in the three ethnic groups.

2.1 The secondary objectives include

To determine the detection of prostate inflammation and PIN and its correlation with age, PSA levels, prostate volume and ethnic group within this small cohort of patients.

To evaluate if prostates with malignancy have a strong association with inflammation and PIN.

To determine if malignancy in older patients is more aggressive as reflected by a higher Gleason sum and higher PSA.

3. Materials and methods

671 patients who underwent TRUS biopsies of the prostate from January 2009 to August 2010 were analyzed and the various parameters associated with each biopsy documented. These included patient demographics such as age, race, PSA and previous biopsy history. Prostate parameters included size, digital rectal examinations findings and number of cores taken. The histological parameters looked at were Gleason primary and secondary scores and total percentage of tumour.

Transrectal Ultrasound Guided biopsies were performed by various operators ranging from urological trainees to consultants. There was variability in the number of cores taken where a few operators were following the Vienna nomogram and others were doing a standard 12 core biopsy. Patients who had more than 12 cores were either having a repeat biopsy or had additional targeted biopsies based on ultrasound findings. 95.8% of patients evaluated were undergoing their first biopsy. Prostate volume was assessed transrectally using the BK Hawk Ultrasound. Prostate volume was available for analysis only from January 2010 onwards.

Statistical analysis was with SPSS version 18, Chi square test was used for categorical data and independent t test used to compare means.

4. Results

Between January 2009 to August 2010, a total of 671 TRUS biopsy results were analysed. The mean age of patients presenting for TRUS biopsy at our centre was 68.38 +/- 7years. Overall median PSA was 9 +/- 132.9 ng/mL. The ethnic distribution of patients included 48.1% Malays, 36.7% Chinese, 13.1% Indians and 1.6% of other ethnic origin. Compared to the national demographics there were less Malays and more Chinese and Indians in this cohort of patients. 50.5% of our patients presented with a prostate specific antigen (PSA) level of between 4 to 10ng/mL and 24.7% presented with levels higher than 20 ng/mL.

The majority of patients had a reasonably high prostate volume; 41.6% had a volume of more than 50g while only 17.5% had a prostate volume less than 30g. Overall Malay and Indian patients presented with larger prostates. 90% of Malay and Indian patients presented with prostate volume of more than 30g compared to 66.7% of Chinese patients.

There is an increasing trend of prostate volume and PSA level with age. None of the patients less than 50 years old had a prostate volume of more than 50g, while 48% of patients older than 70 years old had volume more than 50g. (Table 1)

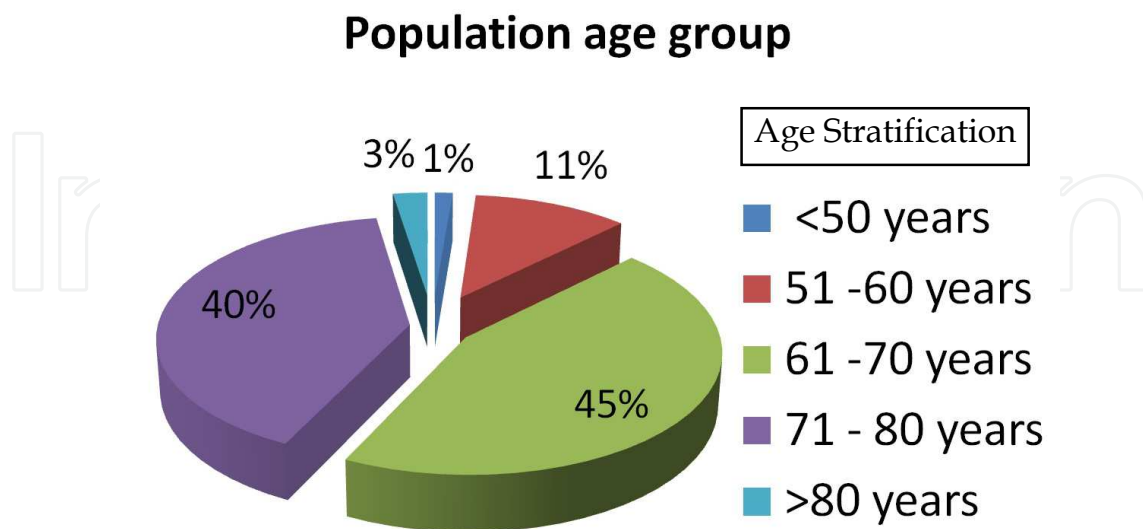


Fig. 1. Stratification of age groups among patients who were biopsied.

Prostate volume (g)	Age stratification (% Patients)			
	<50	50-60	61-70	71-80
<20	0%	17.6 %	4.2 %	2.3 %
20-29	0%	23.5%	8.5%	15.9 %
30-39	100%	5.9%	21.1%	18.2%
40-49	0%	23.5%	25.4 %	15.9%
>50	0%	29.4%	40.8%	47.7%

Table 1. Increasing Prostate Volume seen with Increasing Age

The median PSA of patients younger than 50 years old was 6.8 +/- 4.7 ng/mL , patients 51 to 60 years, 7.96 +/- 177 ng/mL, patients 61 to 70 years , 7.89 +/- 124 ng/mL, patients 71 to 80 years old, 11.0 +/- 127 ng/mL and patients older than 80 years, 26.5 +/- 163ng/mL. (Figure 2) With regards to race, the Malay patients had a median PSA 10 +/- 138.4ng/mL , Chinese patients median PSA 8.55 +/- 113.8 ng/mL and Indians had the lowest median PSA 7.6 +/- 167 ng/mL.

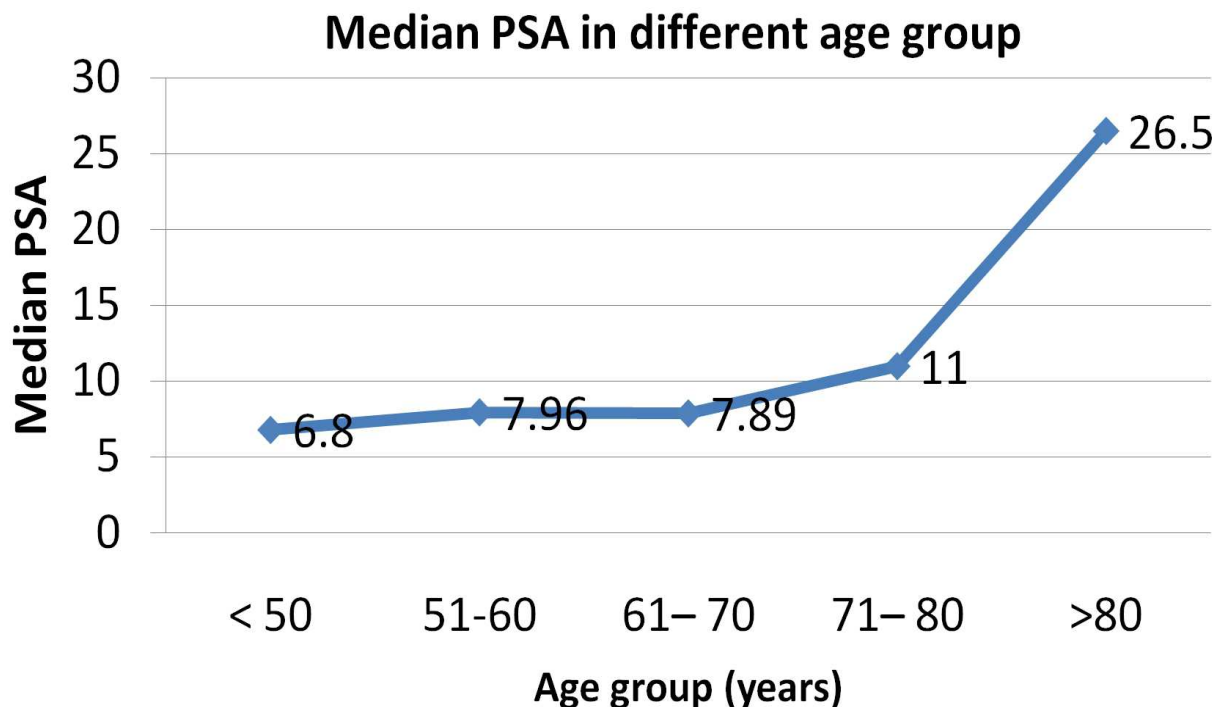


Fig. 2. Increasing PSA with increasing Median Age among the patients biopsied

In a separate cross sectional study done among Malaysian community in 2005², as part of a prostate awareness campaign, the mean PSA of men in their 50s was 1.4 +/- 6.3 ng/mL, men in their 60s, 2.3 +/- 3.8 ng/mL and above 70, 4.3 +/- 11 ng/mL. In the similar study Malays had a mean PSA 2.3 +/- 8.3 ng/mL, Chinese 1.8 +/- 3 ng/mL and Indians 1.3 +/- 1.9 ng/mL. This ethnic variation in PSA in Malaysia is contrary to a separate study by Chia et al³ from Singapore who did not find any PSA variation between the three ethnic groups, however in that study 92.8% of participants were Chinese.

From the 671 biopsies analysed, 29.1% had 6 to 10 cores taken, 46.8% had 12 cores, and 24.1% had more than 12 cores. The TRUS biopsy cancer detection rate at our center was 25.6% and it was almost similar in all the major ethnic groups (Malay-24%, Chinese- 26.2%, Indian 24.4%)($p > 0.05$). Prostate inflammation was identified in 16.8% of our patients, while PIN was seen in 9%. Prostate inflammation was fairly similar in the Malay and Chinese population (Malay-17.4%, Chinese-17.8%) but the Indian population had a lower inflammation rate of 12.8%.

Of the patients who had malignancy, 34.2% had 6 to 10 cores taken, 46.2% had 12 cores and 19.6% had more than 12 cores taken. When compared with patients who were diagnosed with benign disease, the distribution of cores taken was similar; 26.5% with 6 to 10 cores taken, 51.6% with 12 cores and 21.9% with more than 12 cores.

Cancer detection was 0 % in patients < 50 years, 17.6% in those 51 to 60 years old, 20.2% in patients 61 to 70 years old, 32.4% for those 71 to 80 years old and 50% for patients older than 80 years. There was no PIN seen in patients < 50 years old, 4.1% in patients 51 to 60 years old, 11.1 % for those 61 to 70 years old, and 8.3% above the age of 70 years. Prostate inflammation was seen in all age groups ranging from 11% to 19% and lowest (8.3%) in patients older than 80 years (Figure 3)

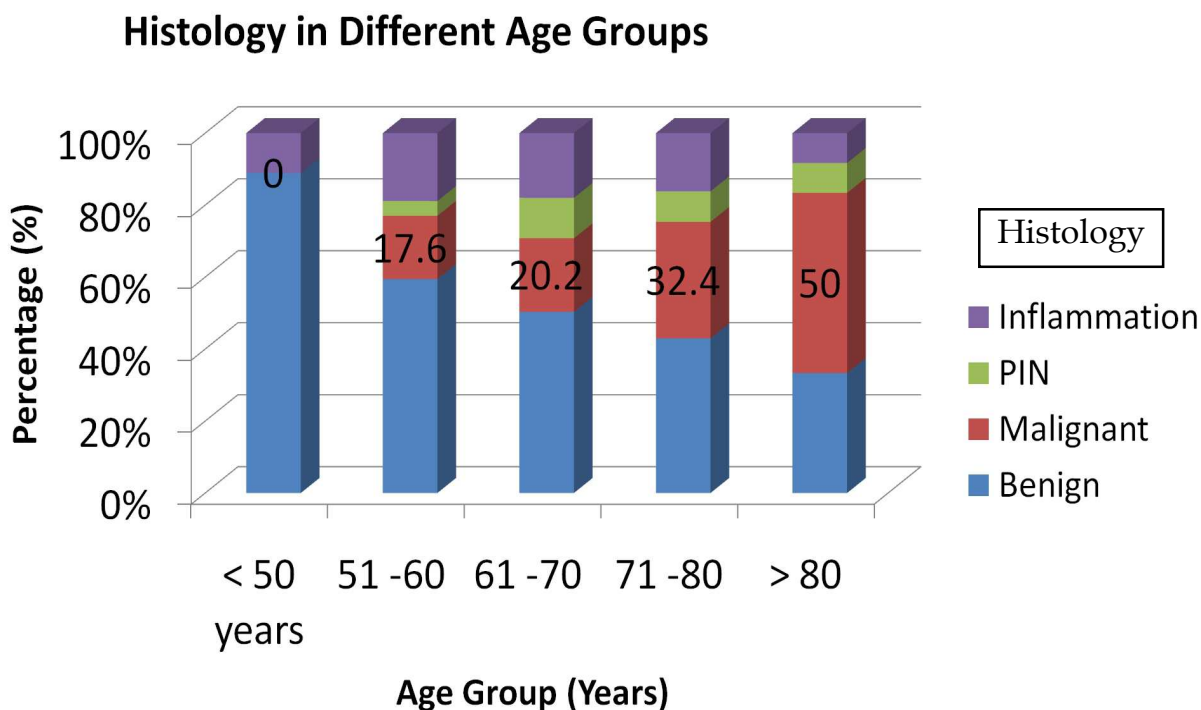


Fig. 3. Variability of biopsy histology based on age stratification. Increasing detection of malignancy with increasing age.

With regards to PSA at presentation, malignancy was detected in 15.3% of patients with PSA 0 to 10ng/ml, 16.2% with PSA 11 to 20ng/ml, 39% with PSA 21 to 50ng/ml and 77.9% with PSA >50ng/ml. Inflammation was seen in 13.8% of patients with PSA 0 to 10ng/ml, 27% with PSA 11 to 20ng/ml, 24.7% with PSA 21 to 50ng/ml and 6.5% with PSA more than 50ng/ml. PIN was seen in 11% of patients with PSA 0 to 10ng/ml, 12.6% with PSA 11 to 20ng/ml, 3.9% with PSA 21 to 50ng/ml and 0% with PSA more than 50ng/ml (Figure 4)

As expected, patients diagnosed with malignancy had a higher median PSA of 26.6 +/- 230ng/ml as compared with benign disease (7.3 +/- 82ng/mL,) inflammation (11.7 +/- 23.7ng/mL) and PIN (8.2 +/- 7.1ng/mL). In our study, the PSA level did not show any correlation with prostate volume.

The higher the prostate volume, the lower the cancer detection. 60% of prostates weighing less than 20g were found to be malignant, 35.3% malignant for volume 20 to 29g, 24% for volume 30 to 39g, 21.4% for volume 40 to 49g and 14.5% for volume more than 50g. PIN was generally not seen in prostates less than 40g. Inflammation however, was seen in 14 to 17% of cases regardless of the prostate volume.

Of the 25.6% of patients with malignancy, 28% of them had a Gleason sum of 6, 24.8% with Gleason 7, 22.4% with Gleason 8, 24.2% with Gleason 9 and 0.6% with Gleason 10. Gleason sum 7 was seen in 30.8%, 19.3% and 28.6% of patients in their 6th, 7th and 8th decade of life respectively. Gleason sum 8 and above was seen in 60.6%, 43.9% and 43.1% of patients in their 6th, 7th and 8th decade of life respectively. Patients above 80 years presented with significantly higher grade disease. 83.3% had gleason sum 8 and above.

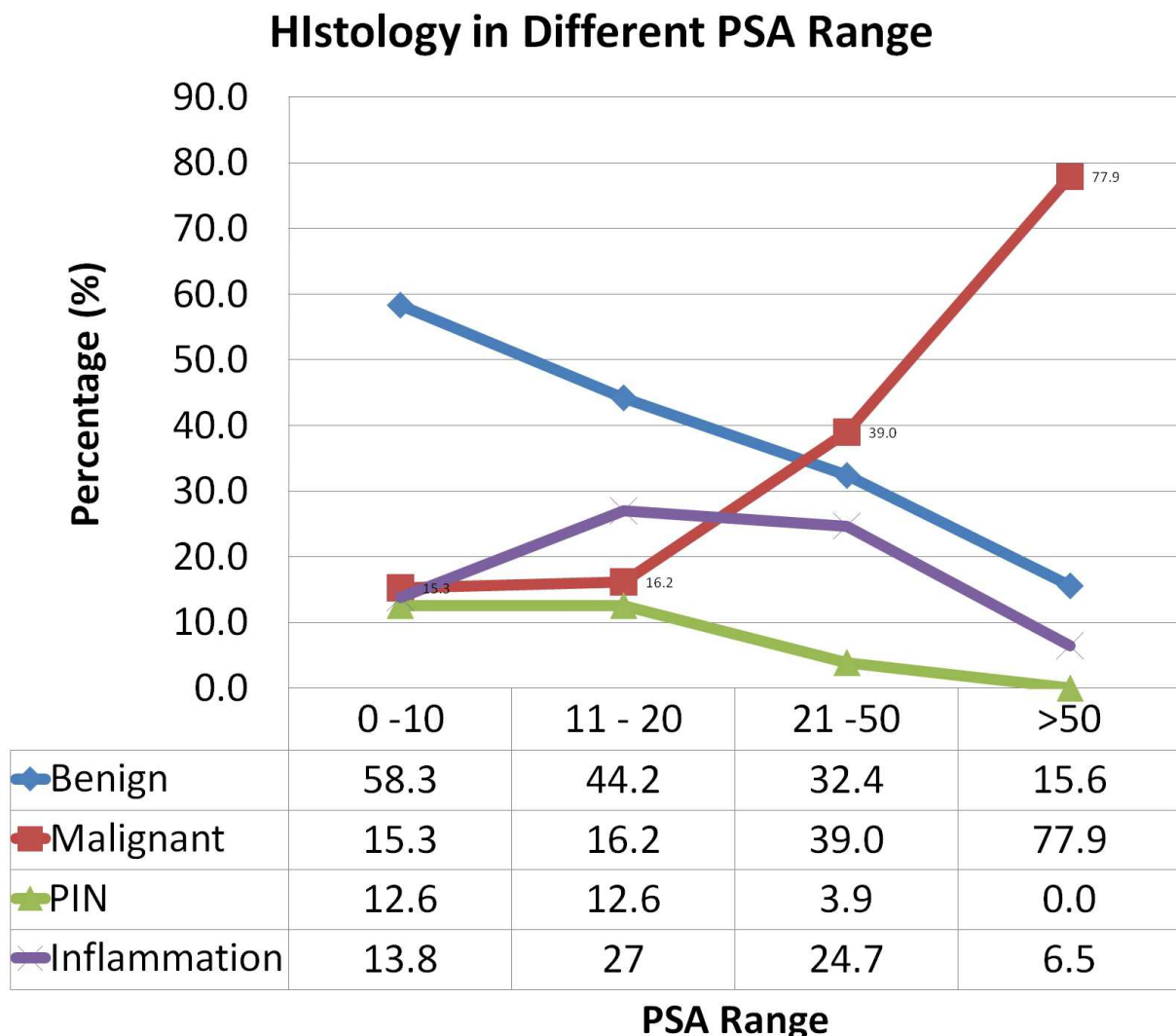


Fig. 4. Line graph shows the probability of detecting various histological diagnosis based on range of PSA at presentation, it acts as a useful guide for the clinician who is doing the biopsy.

5. Conclusion

Cancer detection rate in our center was 25.6% and it appears to be the same among the 3 major ethnic groups. It was noticed that Malay patients presented with a higher median PSA and this is not explained by a large prostate volume as the Indian patients had similarly large prostates but presented with a lower PSA level. Prostate inflammation among Malay patients was similar with that of the Chinese patients. Therefore, it is possible that there may be other factors that could be contributing to the higher PSA among Malays. It was also interesting to note that despite presenting with a higher PSA level, Malay patients had similar cancer detection rate as the other two ethnic groups.

There appears to be variation in PSA among the various ethnic groups, however this is an area that will require further research as there may be other confounding factors that would contribute to the differences seen.

The distribution of the number of cores taken was similar between patients diagnosed with malignancy and benign disease. 65.8% patients diagnosed with malignancy had 12 or more biopsies taken compared to 73.5% in patients diagnosed with benign disease. ($p>0.05$) Therefore in this analysis, the number of cores taken did not influence cancer detection rates.

Whether the operator performing the biopsy is an independent factor predicting cancer detection rate was not studied in this analysis. Nathan et al ⁴ suggested significant differences in operators performing transrectal biopsy in the detection of prostate cancer.

It is evident that cancer detection was much better in the smaller prostates, especially when the volume was less than 20g. The diagnosis of malignancy decreases with increasing prostate volume. This is supported by many other studies including a study by Remzi et al ⁵ suggesting a repeat biopsy in prostates with total volume more than 20 ml with a negative first biopsy. This is probably due to easier detection in a smaller volume prostate undergoing biopsy. Reitbergen et al ⁶ found that most important factor responsible for the failure of diagnosis of prostate cancer at the primary screening was prostate volume. Another hypothesis is the higher probability of a smaller prostate with elevated PSA harbouring cancer as compared to a larger sized prostate gland. However, although Chinese patients generally presented with smaller prostates, their cancer detection rate was no higher than the other ethnic groups. It is also interesting to note that PIN was only identified in prostates more than 40g. Inflammation was observed at equal rates in small and large prostates (14 to 17%).

As expected, the cancer detection rate increased with increasing PSA ranging from 15.3% detection for PSA 0 to 10ng/ml to 77.9% for PSA more than 50ng/ml. There was a significant rise in cancer detection with a PSA > 20ng/mL. Prostate inflammation detection was 14%-27% among patients with PSA < 50ng/mL but was significantly less (6.5%) in patients with PSA more than 50ng/ml. This finding does not suggest any correlation between prostate inflammation and malignancy in this cohort of patients. Terekawa et al ⁷ found an inverse relationship between histologic inflammation and prostate cancer in men with PSA 10-50 ng/mL undergoing prostate biopsy.

Detection of PIN was significantly higher in patients with PSA 0 to 20ng/ml compared to higher PSA levels. Within this range of PSA, 12% of biopsies had PIN. The incidence of isolated PIN in prostate biopsies varies in the literature. In urological practice, incidence varies between 4.4-25% ⁸

Cancer detection increased with increasing age averaging 30 to 50% in patients above 70 years old. Patients below 50 years who were biopsied did not have cancer and none had PIN, however 11.1% had prostate inflammation and the rest had benign disease. The lowest incidence of prostate inflammation was seen in patients older than 80 years. These patients also had the highest cancer detection rate.

This study also showed the expected trend of a rising prostate volume with increasing age. From the age of 50 years onwards, there was a 10g increase in prostate volume in every decade and this trend stabilises after the 8th decade of life. Median PSA also notably increased with age. Men older than 80 years old had the highest median PSA, 26.5 ng/mL and when diagnosed with malignancy had a significantly higher grade cancer.

From this preliminary study it appears that there could be some differences in the presentation of prostate disease and PSA distribution in Asian patients as compared to their western counterpart. The patients in this cohort were detected with malignancy at a higher PSA compared to their western counterparts. Further research would be required to explore these differences and to further study the PSA variation between the various ethnic groups.

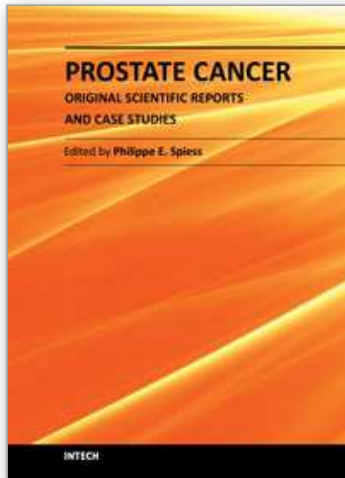
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Keywords: TRUS, Prostate Cancer, Inflammation

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This book encompasses three sections pertaining to the topics of cancer biology, diagnostic markers, and therapeutic novelties. It represents an essential resource for healthcare professionals and scientist dedicated to the field of prostate cancer research. This book is a celebration of the significant advances made within this field over the past decade, with the hopes that this is the stepping stone for the eradication of this potentially debilitating and/or fatal malignancy.

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