Morphometric and DNA Ploidy Study of Benign, Precancerous and Malignant Prostatic Lesions

Thesis

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1. LIST OF ABBREVIATIONS

BPH: Benign prostatic hyperplasia

PIN: Prostatic intraepithelial neoplasia

CaP: Cancer prostate

PI: Proliferation index

GS: Gleason score

GD: Gleason differential

L.I.: Labeling index

T: Value of t-test

F: F ratio for ANOVA

X2: Chi square test

P: P value

P<0.05: Significant at 0.05 level

P>0.05: Not significant

Std: Standard deviation

SPSS: Statistical package for the social science

D.I : DNA index

CV: coefficient of variations

A.S.A.P.: Atypical small acinar proliferation

RRP: Radical Retropubic Prostatectomy

LGPIN: Low grade Prostatic intraepithelial neoplasia

HGPIN: High grade Prostatic intraepithelial neoplasia

FCM: Flow cytometry

ICM: Image cytometry

Π: Pie value

Y-MAX: Maximum Y axis

Y-MIN: Minimum Y axis

X-MAX: Maximum X axis

X-MIN: Minimum X axis

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4. ABSTRACT

Both flow cytometry and static image analysis have been used to determine DNA content (ploidy) of prostate lesions. Quantitative DNA variables were evaluated in prostatic core biopsies from patients with various prostatic lesions. An increase of DNA content was observed from normal to cancerous tissues. **Objective:** The goal is to evaluate the role of the image analyser system in differentiation between benign, precancerous, and malignant prostatic lesions. Also, a correlation will be done between the morphometric and DNA ploidy data.

Study design: The present study included 60 prostatic core biopsies consisting of 20 cases of benign prostatic hyperplasia (BPH), 20 cases of prostatic intraepithelial neoplasia (PIN), 20 cases of prostatic carcinoma and 5 cases as a control. DNA content analysis of sections stained with blue Feulgen stain and nuclear morphometrical analysis of the haematoxylin and eosin stained sections were carried by using the Leica Qwin 500 image analyzer. **Result:** All benign lesions included in this study were diploid (2C) and all the malignant lesions were aneuploid (>4C) except one case which was diploid. The diploid DNA value was significantly higher in the normal group than in all other groups ($p=0.000$); and lower in the carcinoma group than in all other studied groups ($p=0.000$). Also the diploid value was significantly lower in PIN group than in BPH groups ($p=0.000$). The proliferation index (S-phase) value was significantly higher in all groups when compared to normal ($p<0.008$). The aneuploid value was significantly higher in carcinoma group than in all other studied groups ($p=0.000$). The normal group did not show any aneuploid values. The mean nuclear area in carcinoma group was significantly higher than that of normal, BPH and PIN groups ($P=0.000$).**Conclusions:** The DNA ploidy analysis helps to differentiate between normal, BPH, PIN and malignant groups. Distinction

between PIN and cancer could be approached on more objective criteria by DNA and nuclear morphometrical analysis.

Key words: morphometry, nuclear area, BPH, PIN and prostatic carcinoma.

5. INTRODUCTION

Prostate cancer is one of the most common malignancies diagnosed in men and is the most common cancer found in men older than 60 years. Prostate cancer accounts for about 10% of cancer-related deaths in men. A third or more of all men older than 50 years, have a latent form of prostate cancer that may progress to life-threatening prostate cancer (American Cancer Society, 2009).

Environmental factors have been implicated in activating latent prostate cancer. If cancer can be identified in an early or latent stage, the neoplastic process may be reversed (Alsikafi et al., 2001).

Prostate cancer occupies an exceptional position among human malignancies because its prevalence at autopsies by far exceeds clinically manifest carcinomas world wide (Epstein and Yang, 2002).

The number of men with latent prostate cancer is the same across all cultures, races, and ethnic groups, but the frequency of clinically active cancer is markedly different. The American Cancer Society estimates that prostate cancer will be diagnosed in one in six men, and one in 35 will die as a result. More than 2 million men in the United States are living with a prostate-cancer diagnosis, and more than 218,000 men have had the disease diagnosed in 2007 (Diiulio, 2008).

Prostatic intraepithelial neoplasia (PIN) has been identified as a precursor lesion to prostatic carcinoma. PIN involves essentially an atypical proliferation of epithelial cells within acini of the prostate (Zynger and Yang, 2009).

It was agreed at the consensus conference that only the terms low-grade PIN (LGPIN) and high-grade PIN (HGPIN) would be used. Many pathologists no longer report the presence of LGPIN and note only the histologic findings associated with HGPIN (Babaian et al., 2000).

The word morphometry means measurement of Form. The reasons for increasing interest for application of morphometry in diagnostic pathology are its advantage of objectivity, reproducibility and possibility of detecting minor differences or variations in a specimen that would otherwise escape subjective evaluation (Buhmeida, 2006).

Two terms have largely become synonymous, Cytophotometry and cytometry. They are the science that determines the relative optical concentration of intracellular substances in cell populations. The detection of abnormal DNA content in cells has been shown in most cases to be a reliable marker of malignancy, and the degree of DNA ploidy and/or proliferative activity has been related to the biologic behavior of tumors (Isharwal et al., 2009).

Quantitative DNA variables were evaluated in prostatic core biopsies from patients with various prostatic lesions. An increase of DNA content was observed from normal to cancerous tissues (Deitch et al., 1993).

The detection of abnormal DNA content in cells has been shown in most cases to be reliable marker of malignancy, and the degree of DNA ploidy or proliferative activity has been related to the biologic behavior of tumors. Nuclear morphometry allowed the quantitative estimation of an

increase in the nuclear size in different pathological states (Micklos and Freyer, 2003).

Cytophotometric determination of nuclear DNA content undoubtedly provide a powerful diagnostic method for discrimination between low grade and high grade malignant tumors as the incidence of DNA aneuploidy increases with increasing histologic grade and stage of tumors. DNA measurement may be used as an important objective predictor for prognosis, complementary to traditional clinical and morphologic parameters (Markel et al., 1987 and Auer et al., 1989).

6. AIM OF THE WORK

The aim of this work is to evaluate the role of the image analyser system in differentiation between benign, precancerous, and malignant prostatic lesions. Also, a correlation will be done between the morphometric and DNA Ploidy data. In prostatic carcinoma cases, the correlation between the morphometric characteristics, the DNA ploidy status and the conventional histopathological grades will be studied.