Zonal Anatomy of Prostate

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Objectives: To analyze qualitatively and quantitatively histological features (histomorphological features) of different zones of normal human prostate and its significance in histopathological diagnosis.

Material and Methods: Thirty normal prostates from men age less than 40 years, who died in traffic accidents, were included in the study. The normal prostatic tissue consisted of four zones i.e. peripheral zone (PZ), central zone (CZ), transitional zone (TZ) and periurethral zone (PUZ). The specimens obtained were examined for qualitative and quantitative analysis of parenchyma (luminal longitudinal dimension, luminal transverse dimensions, acini and epithelial height) and stroma (smooth muscles and collagen fibers). Three random observations were made per slide and mean calculated.

Results: In all zones of the prostate the acini were distributed uniformly with columnar secretory cell lining the acini. Basal cells are found in between secretory cells and the basement membrane. In CZ, the acini were larger and polygonal than in PZ and TZ where acini were comparable and more or less rounded while in PUZ the acini are not developed. The number of acini is down regulated in PZ, CZ and TZ. Height of epithelial cells is more in CZ than in PZ and TZ. Fibromuscular stroma is compact in CZ and TZ and PUZ but loosely woven in PZ.

Conclusions: The variations in size, shape and number of acini in parenchyma and compactness or looseness of stroma were the key features for identification of different zones of prostate. As number of acini was greater in PZ, the higher incidence of adenocarcinoma in this zone was explained. Loosely woven stroma in PZ and compact stroma in TZ also explained the occurrence of adenocarcinoma from the acini of PZ and the benign prostatic hypertrophy in TZ.

Key words: Acini (Aci), Collagen Fibers (CF), Central Zone (CZ), Epithelial Height (EH), Luminal Longitudinal Dimension (LLD), Luminal Transverse Dimension (LTD), Periurethral Zone (PUZ), Peripheral Zone (PZ), Smooth Muscles (SM), Transitional Zone (TZ).

Introduction

The human prostate gland is consisted of several glandular and non glandular regions which are enclosed within a fibrous capsule. The nonglandular component of the prostate is concentrated anteromedially and is responsible for much of anterior convexity of the organ. The glandular component is just like a disc with lateral wings which partially encircle the nonglandular region anteriorly. The term 'prostate' was first used by Herophilus of Alexandria in 335 B. C. to refer to the organ situated in front of the bladder (cited by Oesterling JE 1991).[1] In male it is the largest accessory reproductive gland which surrounds the first part of urethra, *known as prostatic urethra*.[2] Prostatic urethra hugs anterior portion of prostate gland and is divided into proximal and distal segments by an abrupt anterior angulation of 30^{o} in its mid portion. Just distal to this urethral angulation it has a midline longitudinal ridge in its posterior wall, the Verumontanum (crista urethralis). The ejaculatory ducts open in distal urethral segment which also receives about 95% of the ducts of glandular prostate.[3]

Prostate was described previously as consisting of a number of ill defined lobes. However, this terminology has been replaced by the concept of prostate zones and segments. According to Lowsley,[4] the prostate can be divided into five lobes. Anterior to urethra lies the isthmus or the anterior lobe, which contains fibromuscular tissue and scanty amount of glandular tissue. Posterior to the urethra and inferior to the ejaculatory ducts is posterior lobe that is readily palpable by rectal examination. Its ducts end below the ejaculatory ducts in posterior wall of the urethra. The lateral lobes form the major part of prostate on either side of the urethra. Their ducts end in the lateral grooves of the urethra. The middle lobe is present between the urethra and the ejaculatory ducts. It is closely related to the neck of the bladder above. Its ducts open into the urethra above the ejaculatory ducts.[5,6]

McNeal JE (1981) described four basic anatomic zones on the basis of biological and histological concepts. Each zone originates from prostatic urethra and has specific architectural features. These major glandular regions of prostate are labeled as the peripheral zone, the central zone, the transitional zone and the periurethral zone.[5-8]

Peripheral zone forms disc of tissue on the postrolateral aspects of the gland, representing posterior and lateral lobes. It constitutes about 70% of the glandular part of the prostate. Its ducts open into prostatic urethra distal to verumontanum. Almost all carcinoma arise here.

Central zone is wedge-shaped. It is surrounded by the peripheral zone in its distal part. It comprises of 25% of the glandular prostate that surrounds the ejaculatory ducts. Its ducts open into the prostatic urethra close to the ejaculatory duct. This zone is relatively resistant to carcinoma and other diseases.

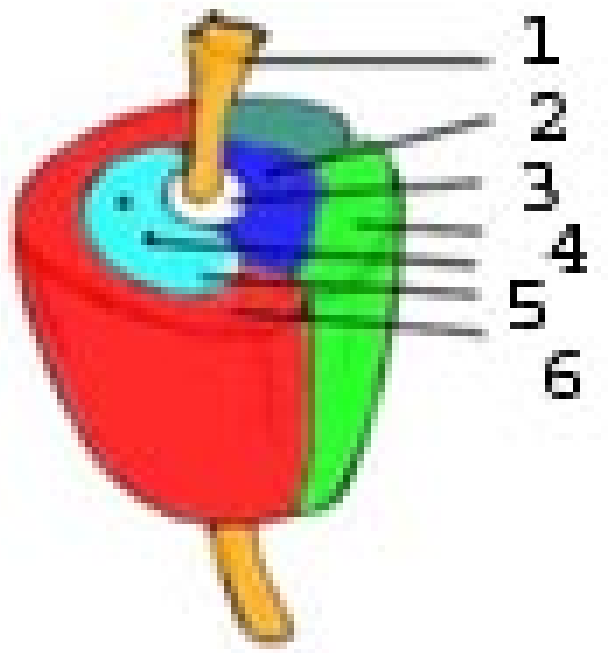

Fig. 1: *A model of Prostate showing arrangement of different zones of prostate. 1 = prostatic urethra, 2 = transitional zone, 3 = periurethral zone, 4 = fibromuscular zone, 5 = central zone and ejaculatory ducts and 6 = peripheral zone. McNeal Classification of Prostatic Zones[9], Manila Genitourinary Clinic Philippines 1999.*

Transitional zone forms two independent lobes of glandular tissue in fibromuscular components of preprostatic sphincter. Its ducts open in postrolateral part of urethra. It is clinically important as it grows with age and is the commonest site where benign prostatic hypertrophy originates.

Periurethral zone is only a fraction of the size of the transition zone. It consists of small ducts and acini which are not completely developed. These are scattered along the proximal urethral segment inside the preprostatic sphincter.

The anterior surface of the prostate is covered completely by fibromuscular stroma hiding from view the anterior surface of the three glandular regions.[3,10]

There is deficiency of information on the morphometry of the normal prostate. The knowledge of normal prostate gland histology will help in diagnosis of different pathological conditions including BPH and allow a more scientifically based selection of medical therapy for men with prostate disease.

Objectives

To analyze qualitatively and quantitatively histological features of different zones of normal human prostate and its significance in histopathological diagnosis of prostatic diseases.

Material and Methods

Thirty normal prostates obtained from unclaimed male dead bodies of less than 40 years of age who died in road traffic accidents and underwent autopsies. The prostates so obtained were further dissected by giving a sagittal incision on anterior aspects of prostatic urethra exposing the verumontanum on the posterior urethral wall. The verumontanum was used as anatomical landmark to excise tissue from different zones of prostate accurately. Around the proximal urethra, the glandular tissue was taken as transitional zone (TZ). Immediately surrounding the urethra within the transitional zone was periurethral zone (PUZ). A coronal section parallel to distal urethra was made to have the tissue from the peripheral zone (PZ). Similarly, tissue collected within the peripheral zone around the ejaculatory ducts was central zone (CZ). The specimens were immediately placed in 10% neutral buffered formalin for 48 hours. Tissues were processed and embedded in paraffin. Five-micron thick sections were made and stained with Hematoxylin and Eosin and Masson's trichrome stain. The sections were examined for quantitative and qualitative analysis of parenchyma and stroma. Three random readings per slide of the following variables of the tissue were taken at 40x. The lumen of acini (maximum longitudinal and transverse dimensions), the height of acinar epithelium was measured by using ocular micro-meter and multiplied by calibration factor. Numbers of acini, smooth muscle fibers and collagen fibers between widely apart acinie were counted. Data collected and analyzed descriptively. Means and standard deviations were computed for all quantitative variables.

RESULTS

The four glandular zones of prostate had its own anatomical and histological features. **In peripheral zone of prostates (PZ),** the acini were distributed uniformly. They were small sized and had rounded contour with epithelial undulations in the lumen. Secretory cells of PZ were columnar with regular luminal border and small more uniform basal nuclei. Basal cells were visible which were markedly flattened parallel to basement membrane. They had slender dark nuclei. Fibro muscular stroma was abundant with loosely woven randomly arranged muscle fibers separated by irregular spaces and numerous collagen fibers (Fig. 2 and 3 Table 1).The mean ± SD of luminal longitudinal dimension (LLD) and luminal transverse dimension (LTD) was 0.1615 ± 0.02114 mm and 0.1424 ± 0.04889 mm respectively. The mean ± SD of number of acini (Aci) were 6.73 ± 0.713. The mean ± SD of height of epithelial cells (EH) was 0.0183 ± 0.00233 mm. The mean ± SD of number of muscle fibers (SM) and of collagen fiber bundles (CF) per high power field were 18.56 ± 3.563 and 19.31 ± 2.477 respectively as shown in (Fig. 4, Table 2).

In central zone of the prostates (CZ), the acini of the CZ were larger than those of PZ and TZ, somewhat polygonal in contour. There were intraluminal ridges i.e. corrugations in their walls. The lumen of the acini was partially sub-

divided by these ridges. Secretory cells in the central zone were irregularly arranged with large nuclei at different levels in adjacent cells. Basal cells were visible. Acini in the CZ were separated by bands of compact smooth muscle fibers but stromal components were less in CZ than PZ and TZ (Fig. 2 and 3, Table 1). The mean ± SD of luminal longitudinal dimension (LLD) and luminal transverse dimension (LTD) of acini was 0.2072 ± 0.02046 mm and 0.1305 ± 0.02985 mm respectively. The mean ± SD of number of acini (Aci) were 3.22 ± 0.331. The mean ± SD of height of epithelial cells (EH) was 0.0279 ± 0.00484 mm. The mean ± SD of number of muscle fibers (SM) and collagen fibers bundles (CF) in CZ per high power field was 13.64 ± 3.244 and 13.84 ± 2.783 respectively (Fig. 4, Table 2).

In transitional zone of prostates (TZ), acini were distributed uniformly. The acini were more or less rounded in shape but not exactly circular in outline as the epithelial border showed undulation. Secretory cells of TZ were columnar regular with smaller basal nuclei. Flattened basal cells with slender dark nuclei were lying parallel to the basement membrane. There were compactly arranged smooth muscle fibers and collagen fibers in the stroma of the transitional zone (Fig. 2, 3 and Table 1). The mean ± SD of luminal longitudinal dimension (LLD) and luminal transverse dimension (LTD) of acini was 0.1481 ± 0.1983 mm and 0.1123 ± 0.02151mm respectively. The mean ± SD number of acini (Aci) HPF was 1.79 ± 0.283. The mean ± SD of height of epithelial cells (EH) was 0.0165 ± 0.0018 mm. The mean ± SD of number of smooth muscle fibers (SM) and collagen fibers bundles (CF) per high power field was 39.21± 1.8435 and 32.01 ± 2.20498 respectively (Fig. 4, Table 2).

In periurethral zone of prostate (PUZ), undeveloped acini were seen. These acini lie within the periurethral fibromuscular stroma. The muscle fibers along with collagen fibers in the periurethral region were compactly arranged (Fig. 2 and 3).

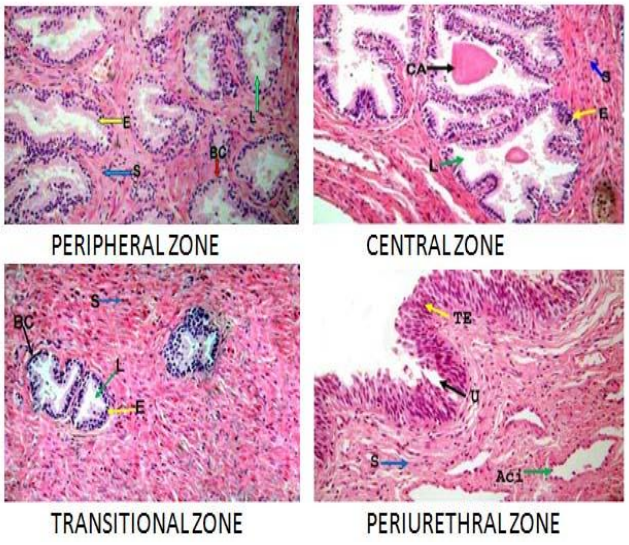

Fig. 2: *Photomicrograph showing comparison of different zones of normal prostate (H and E 40X). Aci = acini, BC = basal cells CA = corpora amylacea, E = epithelium, L = lumen of acini, S = stroma.*

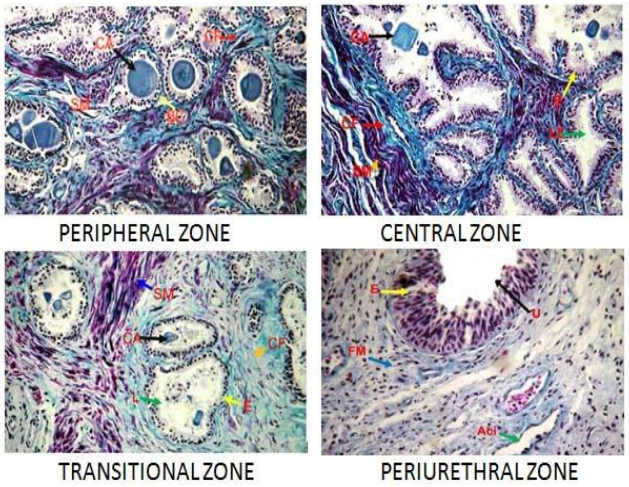

Fig. 3: *Photomicrograph showing comparison of different zones of normal prostate (Trichrome Masson's 40X). Aci = acini, BC = basal cells CA = corpora amylacea, E = epithelium, L = lumen of acini, S = stroma.*

DISCUSSION

The regional anatomy of the prostate was discussed previously with different arguments. It started with concept of lobes and replaced by the modern model of zones. As a result various morphological classifications had been suggested, based upon the studies of glandular morphogenesis, responses to hormones and histopathological findings.[11]

Historically the Vesalius (1543) described (cited by Dauge et al 1999) the prostate as a unique male urogenital organ. In the 19th century, the two descriptions of prostate anatomy were presented, one presented by Cruveilhier and Testut, who explained that the prostate was made of several lobes, whereas Cloquet and Sappey considered it as comprised of one zone. In 1902, Albarran narrated the prostate as the suburethral glands. Following Albarran, certain authors such as Cuneo, in 1911 and Franks, in 1954, again discussed the prostate and attributed the two zones of prostate, one, internal zone that was formed by the Albarran's glands and the other, external zone, concerning the whole prostatic gland. On the contrary, Lowsley, in 1912, reported a homogenous prostate subdivided into five lobes that were embryologically different. McNeal had drawn aside these various descriptions and in agreement with Gil Vernet, had made the proof that the prostate was histologically and anatomically heterogeneous, with four zones, peripheral, central, transitional, and periurethral ones.[6,12]

The four-zone division of prostate was described to have more clinical significance than traditional division of

Table 1: *Qualitative description of different zones of normal prostate.*

Zones	Parenchyma (Acini)					Stroma
	Uniformity	**Shape**	**Size**	**Secretory cells**	**Basal cells**	**Compact/Loose**
Peripheral zone	Uniform	Rounded	Small	Columnar	Present	Loosely woven
Central zone	Uniform	Polygonal	Large	Columnar	Present	Compact
Transitional zone	Uniform	Rounded	Small	Columnar	Present	Compact
Periurethral zone	Nil	Nil	Nil	Nil	Nil	Compact

Table 2: *Quantitative descriptions of different zones of normal prostate.*

Variables	Peripheral Zone	Central Zone	Transitional zone	Periurethral zone
Luminal longitudinal dimension (mm)	0.1615 ± 0.02114	0.2072 ± 0.02046	0.1481 ± 0.01983	Nil
Luminal transverse dimension (mm)	0.1424 ± 0.04889	0.1305 ± 0.02985	0.1123 ± 0.02151	Nil
Number of acini	6.73 ± 0.713	3.22 ± 0.331	1.79 ± 0.283	Nil
Height of epithelial cells (mm)	0.0183 ± 0.002	0.028 ± 0.004	0.017 ±0.002	Nil
Number of collagen fibers	18.56 ± 3.56	13.64 ± 3.244	39.21 ± 1.84	Nil
Number of smooth muscle fibers	19.31 ± 2.48	13.84 ± 2.783	32.01 ± 2.20	Nil

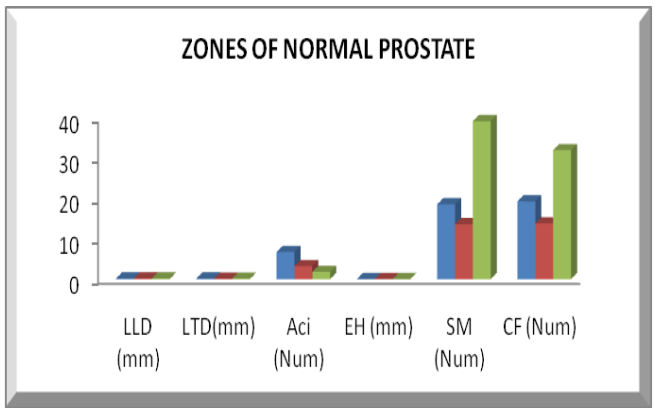

Fig. 4: *Graphical presentation of different zones of normal prostate. mm= millimeter, Num = number.*

prostate. A good knowledge of the normal architecture of the prostate had great practical importance in pathologic diagnosis.[8] The peripheral zone was considered the most common site of inflammation and carcinomas. The central zone was characterized as almost resistant to diseases. The transitional and periurethral zones were considered the main regions involved in benign prostatic hypertrophy. Many workers visualized these zones by dissecting selected coronal plane of sections along the proximal and distal prostatic urethra. They found that peripheral zone was located postrolaterally, the central zone was located at near the base and the transition zone was located along the proximal urethra. Fibromuscular region was concentrated anteromedially[13].

In the present study, it was found that each glandular region had distinct structural features of stroma and parenchyma. Acini and ducts were exactly alike morphologically in all zones. They had comparable caliber, spacing and histological appearance to such an extent that these were not reliably distinguished microscopically. It was also noted that in each zone acini were uniformly distributed and were lined by columnar secretory epithelium of identical appearance between ducts and acini (Fig. 2 and 3). Cells in PZ and TZ were columnar in shape with regular arrangement of more basal nuclei while in CZ, columnar cells with irregular arrangement of nuclei were seen. A layer of fattened basal cells intervene between the secretory cells and the basement membrane throughout the prostate. These histological findings were consistent with McNeal, who in 1988, described the presence of these flattened basal cells, lying parallel to the basement membrane and slender filiform darkly staining nucleus had little or no discernible cytoplasm.[5] It was observed that the acini in PZ and TZ were comparable in dimensions while in CZ the acini were larger. In PZ, the mean LLD (luminal longitudinal dimension) and LTD (luminal transverse dimension) were 0.1615 ± 0.02114 mm and 0.1424 ± 0.04889 mm respectively. The LLD and LTD in TZ were 0.1481 ± 0.01983 mm and 0.1123 ± 0.02151mm respectively. In CZ, the mean LLD and LTD of the acini were 0.2072 ± 0.02046 mm and 0.1305 ± 0.02985 mm

(Table 2, Fig. 4). It was observed that in PZ and TZ the acini were smaller and rounded in shape as compared to the acini in CZ where acini were polygonal in shape and larger than the other two zones of the prostate (Fig. 4). It was found that there were more acini in PZ 6.73 ± 0.713 than in CZ 3.22 ± 0.331 and in TZ 1.79 ± 0.283 of prostate (Table 2 and Fig. 4). McNeal also noted that acini were down regulated from peripheral zone to central and then transitional zone.[3]

In PZ, mean epithelial height (EH) was 0.018 ± 0.002 mm and in TZ, mean epithelial height (EH) was 0.017 ± 0.002 mm, while in ZC, mean epithelial height (EH) was 0.028 ± 0.004 mm (Table 2, Fig. 4). These results were consistent with the findings of McNeal and Sugandh Shetty who observed the same morphological dimensions of the prostatic morphology.[3,14]

In PZ, the stroma was loosely arranged with muscle bundles and collagen fibers separated by indistinct spaces. The mean number of interacinar smooth muscle fibers and the collagen fibers bundles in PZ were 18.56 ± 3.56 and 19.31 ± 2.48 respectively. In TZ, stroma had more compact smooth muscles fibers with collagen fibers. The mean number of interacinar smooth muscle fibers and the collagen fibers were 39.21 ± 1.84 and 32.01 ± 2.20 respectively. Similarly, in CZ more compact arrangement of smooth muscle fibers and the collagen fibers were seen. The mean of interacinar smooth muscle fibers and collagen fibers was 13.64 ± 3.244 and 13.84 ± 2.783 (Table 2, Fig. 4). There was a morphological contrast demarcating the boundary between CZ and PZ but it was less consistent between the PZ and TZ of the prostate (Fig. 2 and 3). McNeal reviewed the stroma of the prostate at different times and his findings were more or less the same.[3,5,9]

Conclusion

From above discussion it can be suggested that the parenchymal components of the prostate varies in the size, shape and the number of acini in different zones. The acini were down regulated from NPZ to NCZ and NTZ respectively. These key features were helpful in the identification of different zones of normal prostate. As number of acini was greater in NPZ, the higher incidence of adenocarcinoma in this zone was explained. Loosely woven stroma in NPZ and compact stroma in NTZ also explained the occurrence of adenocarcinoma from the acini of NPZ and the benign prostatic hypertrophy in NTZ.

References

1. Oesterling JE. The origin and development of benign prostatic hyperplasia. An age – dependent process. J Androl 1991; 12(6): 348-55.
2. Cancer Bacup. The Prostate [On Line] Available from URL:http://www.cancerbacup.org.uk. 2009 [cited on 2009, July 03]
3. McNeal JE. Normal histology of the prostate. Am J Surg Pathol 1988; 12 (8): 619-33.
4. Kirby RS. The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology 2000; 56 (5 Suppl 1): 3-6.
5. McNeal JE. The zonal anatomy of the prostate. Prostate 1981; 2 (1): 35-49.
6. Dauge MC, Delmas V, Potier M. The anatomic lobulation of the prostate, a controversial description. Morphologie 1999; 83 (260): 5-14.
7. Grenier N, Devonec M. Imaging of normal, hyperplastic and inflammatory prostate gland. J Radiol 2006; 87 (2): 165-87.
8. Ma J, Huang S, Zhang C, Shao Q. Observations on prostate histology in 50 young and middle aged men. Its implication on clinical pathological diagnosis. Zhonghua Bing Li Xue Za Zhi 1999; (2).
9. McNeal JE. Anatomy of the prostate: an historical survey of divergent views. Prostate 1980; 1 (1): 3-13.
10. Allen KS, Kressel HY, Arger PH, Pollack HM. Age – related changes of the prostate: evaluation by MR imaging. AJR Am J Roentgenol 1989; 152(1): 77-81.
11. Timms B. Prostate development: a historical perspective. Differentiation 2008; 76 (6): 565-77.
12. McNeal JE. Anatomy of the prostate: an historical survey of divergent views. Prostate 1980; 1 (1): 3-13.
13. Villers A, Steg A, Boccon-Gibod L. Anatomy of the prostate: review of the different models. Eur Urol 1991; 20 (4): 261-8.
14. S. S. Transrectal Ultrasonography (TRUS) of the Prostate. *eMedicine Urology* 2008.