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The Zonal Anatomy of the Prostate

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Earlier morphologic studies of the prostate, though often extensive, have never systematically delineated its complete structure. Recent comprehensive analysis of 500 prostates has more precisely defined its anatomic composition, identifying previously undetected features and unsuspected complexities. Using a three-dimensional model, these structures and relationships are demonstrated. Four basic anatomic regions are described. The relationship of each to the urethra provides a central anatomic reference point.

1. The *peripheral zone* constitutes over 70% of the glandular prostate. It forms a disc of tissue whose ducts radiate laterally from the urethra lateral and distal to the verumontanum. Almost all carcinomas arise here.
2. The *central zone* constitutes 25% of the glandular prostate. Its ducts arise close to the ejaculatory duct orifices and follow these ducts proximally, branching laterally near the prostate base. Its lateral border fuses with the proximal peripheral zone border, completing in continuity with the peripheral zone, a full disc of secretory tissue oriented in a coronal plane. Marked histologic differences between central and peripheral zones suggest important biologic differences.
3. *Preprostatic region.* The urethral segment proximal to the verumontanum is kinked anteriorly at a 35-degree angle to the distal segment. No major ducts arise in the proximal segment, but the lateral rows of peripheral zone orifices continue. Duct development is aborted here, producing only a small *transition zone* and several tinier *periurethral ducts*. The development of these small ducts is possibly determined and limited by their intimate relationship to a periurethral smooth muscle sphincter that exists only proximal to the verumontanum. These small ducts in a restricted area are the exclusive site of nodular hyperplasia (BPH) origin.
4. The *anterior fibromuscular stroma* forms the entire anterior surface of the prostate as a thick, nonglandular apron, shielding from view the anterior surface of the three glandular regions. Its inseparable fusion to the glandular prostate has probably delayed recognition of the anatomic features described here.

Key words: prostate — anatomy, prostate — zones, prostate — divisions

INTRODUCTION

The prostate gland has traditionally been regarded as an organ that is histologically homogeneous, with relatively simple anatomic structure. This widely accepted concept has been derived largely from the findings of early in-

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vestigators such as Lowsley [1] and Franks [2]. Their studies were extensive and produced valuable information, but they were incomplete in that they did not include a full description of all the tissue components within the normal adult prostate. Lowsley's material, for example, did not include any adult glands. On the basis of data collected entirely from fetal prostates, he subdivided the gland into a system of lobes. Although Lowsley never undertook to determine whether postnatal or pubertal development might produce extensive anatomic changes in the structures he had described, his lobe system became generally accepted as a valid description of adult anatomy. Franks's [2] later observations led him to the conclusion that Lowsley's lobes did not exist in the adult prostate, and this conclusion has been supported by other studies [3,4]. Uncertainty still exists about the interpretation of this discrepancy in findings.

Franks's elimination of Lowsley's lobes led to a still simpler view of prostate anatomy. However, at the same time, Franks drew attention to an additional group of glands that Lowsley had dismissed as not belonging to any of the prostate lobes. These glands formed a tiny group identified by its proximity to the urethra and stated to be important because these glands were the exclusive site of origin of nodular hyperplasia (BPH) in later life. Franks's observations were anatomically incomplete because they were mainly limited to transverse sections through the midportion of the organ and were not supplemented by exploration of more proximal or distal tissues, nor by the use of other planes of section. More detailed comparison of these and other views, attempting to clarify the basis of their differences, is the subject of a recent review article [5].

Not until 1968 were studies initiated to systematically explore the anatomy of the entire adult prostate, using serial blocks through the entire gland in multiple planes of section [6]. A sequence of related investigations [6–8] has disclosed previously unsuspected complexity in the anatomy of this organ. From these recent findings, a three-dimensional model has been constructed of the structure of the entire adult prostate. It demonstrates the exact locations and relationships of a diversity of glandular and nonglandular components and localizes more precisely those areas of greatest susceptibility to disease. The details of this model will be presented together with illustrative examples selected from the prostatic tissue specimens of over 500 autopsies.

THE PROSTATE AND PROSTATIC URETHRA

In this analysis, four basic anatomic regions have been identified within the prostate. For optimal demonstration of their relationships in three dimensions, three reference planes of section are utilized (Fig. 1). One of these is a sagittal plane (S), which bisects the gland and reveals the lumen of the urethra in the long axis of its entire course through the gland. This sagittal plane alone shows the urethral lumen in its full extent. This view forms an important reference point for localizing the four regions of the prostate, since each of them contacts the urethra along a characteristic segment of its course.

It is anatomically important that the prostatic urethra is not a straight tube; at its midpoint between its distal end (the prostate apex) and the bladder neck, its posterior wall undergoes a sharp anterior kink, beyond which the entire proximal urethral segment pursues an altered course, with an angulation of about 35 degrees anterior to the course of the distal urethral segment. The base

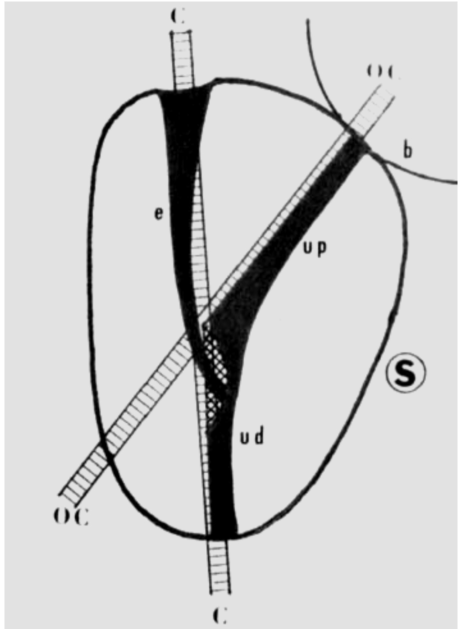

Fig. 1. Diagram of prostate, sagittal plane (S). Relationships to other planes of section, coronal (C) and oblique coronal (OC), are shown by double lines. The verumontanum is crosshatched. The coronal plane follows the ejaculatory ducts (e) and the distal urethra (ud). The oblique coronal plane follows the proximal urethra (up) to the bladder (b).

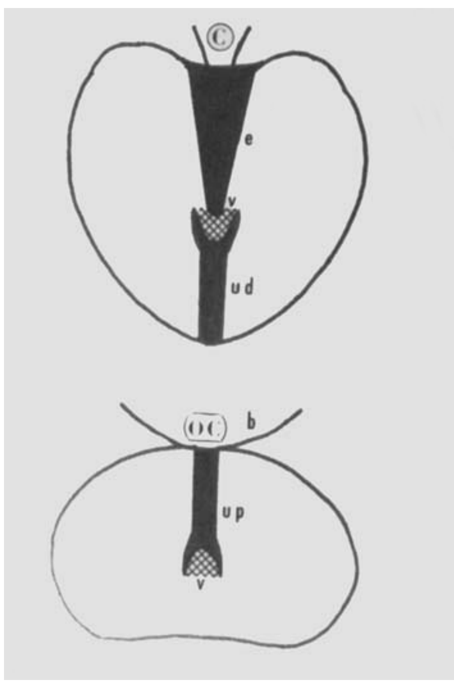

Fig. 2. Diagram showing the contour of the prostate in planes C and OC, with the location of the verumontanum (v), urethra (ud and up), ejaculatory duct stromal core (e), and bladder (b).

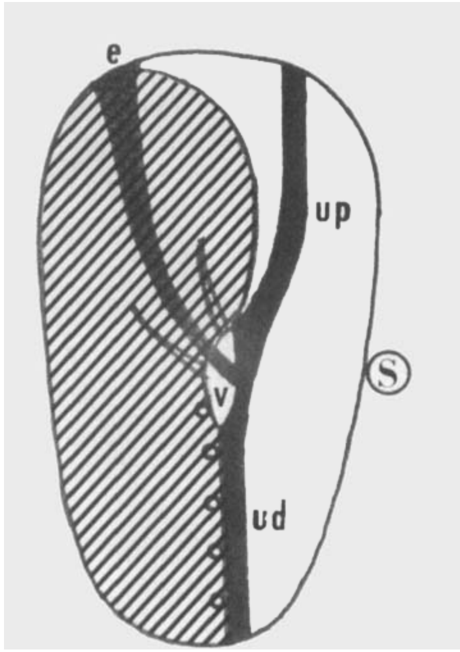

Fig. 3. Sagittal diagram of early embryo prostate traced from a previously published photomicrograph [7] and showing the area of stromal condensation. Laterally developing duct buds (circles) and proximally developing buds (in profile) are shown in relationship to the distal urethral segment and the ejaculatory ducts, respectively. The relationship to the verumontanum (v) and the proximal urethra (up) is also shown.

of the verumontanum merges with the posterior urethral wall just at the point of kinking and along a short distance proximal to it, but the bulk of its tissue is anatomically a feature of the distal urethral segment. The orifices of the ejaculatory ducts, opening onto the midconvexity of the verumontanum, lie entirely in the distal urethral segment.

The course of the ejaculatory ducts forms nearly a direct proximal continuation of the long axis of the distal urethral segment. Consequently, a single coronal section (C) at the proper depth shows both structures throughout nearly their entire combined length (Fig. 2). This plane (C) is utilized as a second demonstration reference plane.

The proximal urethral segment cannot be seen in the coronal plane (C) because of its angulation. However, if the coronal plane is rotated to an angle of 35 degrees around a transverse axis that passes through the point of kinking in the urethra, an oblique coronal plane (OC) is created. This plane, at the proper angle, passes along the long axis of the proximal urethral segment to the bladder neck and transects the base of the verumontanum distally (Fig. 2). This is the third plane utilized for demonstration.

In the embryo, a sagittal section (S) as early as the tenth week of development shows clearly that these anatomic features of the adult urethra—its angulation at its midpoint and its relationship to the verumontanum and ejaculatory ducts—are already established (Fig. 3). Up to the tenth week, the prostatic

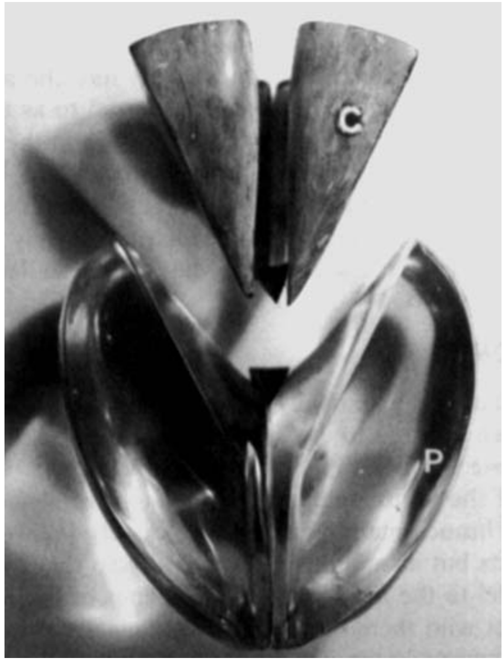

Fig 4. Model of central zone (C) and peripheral zone (P) territories of prostate in coronal view. Zones have been separated for better visualization. Location of verumontanum in relation to each zone is indicated by a triangle.

duct buds have not yet appeared, but mesenchyme has already undergone preparatory condensation selectively in the region that will receive the emerging buds. This area of mesenchymal condensation is greatest along the posterior wall of the distal urethral segment to the verumontanum and then continues proximally in a straight line, surrounding the ejaculatory ducts as far as the base or most proximal border of the gland. By contrast, the mesenchyme anterior to the lower urethral segment, and even more prominently that surrounding the upper urethral segment, is sparsely cellular. This forecasts that duct development in these areas will be absent or limited.

Subsequent duct development follows two major patterns (Fig. 3). The condensed mesenchyme along the posterior wall of the lower urethral segment is penetrated by a double row of duct buds arising from the lateral recesses of the posterior urethral wall. These grow and branch into the receptive mesenchyme mainly in a lateral direction. The condensed mesenchyme surrounding the ejaculatory ducts is penetrated by duct buds arising from a small area on the convexity of the verumontanum, with subsequent growth and branching proximally toward the base of the prostate in close proximity to the ejaculatory ducts and fanning out laterally to them. As the lower urethral segment and ejaculatory ducts form a nearly continuous straight line, it follows that at full development, most of the main ducts of both groups of glands will lie in the coronal plane (C) cut along their common long axis.

THE PERIPHERAL ZONE

Nearly 75% of the glandular tissue of the adult prostate is derived from the double row of duct buds that develop laterally into the mesenchyme posterior to the distal urethral segment. These are referred to as the "peripheral zone." The most proximal orifices of the duct row lie in the recesses lateral to the base of the verumontanum. These more proximal ducts become progressively larger than those near the apex of the prostate, and their branches cover a larger expanse. Hence, they fan out somewhat proximally as well as laterally, and their distal branches come to lie somewhat above the level of the base of the verumontanum (Fig. 4).

THE CENTRAL ZONE

Those ducts that bud proximally into the mesenchyme surrounding the ejaculatory ducts are referred to as the "central zone." Their orifices arise separately from those of the peripheral zone and are clustered in a small circle on the convexity of the verumontanum immediately surrounding the ejaculatory duct orifices. They branch mainly proximally, closely following the course of the ejaculatory ducts but also fanning out laterally so that their most lateral branches run parallel to the most proximal branches of the peripheral zone and lie almost in contact with them. Thus, the two zones are continuous as was the area of condensed mesenchyme into which they grew. The two zones are bound together into a flat disc of tissue that has its greatest extent in the coronal plane (C) (Fig. 4). The central zone glandular tissue completes the proximal quadrant of the disc seen in the coronal plane, constituting nearly 25% of the glandular tissue of the prostate. The geometric center of the disc is at the

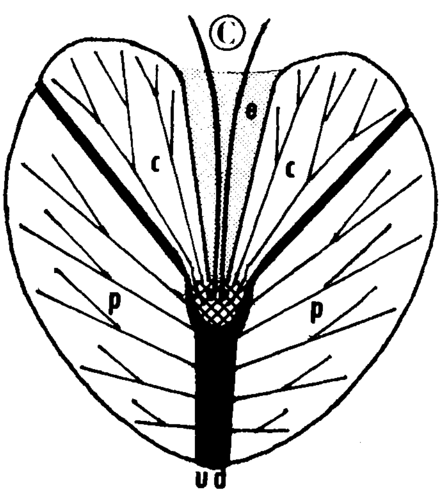

Fig. 5. Coronal plane diagram of the central zone (C) and the peripheral zone (P), with the boundary between them marked by heavy lines radiating from the verumontanum. Relationships are shown to the distal urethral segment (ud), verumontanum (crosshatched), and ejaculatory duct stromal core (e, gray area).

Fig. 6. Gross tissue specimen of a normal prostate, plane C running along the ejaculatory duct core and immediately posterior to the lumen of the distal urethra. The boundary between the central and the peripheral zones is visible, as well as the different texture of glandular tissue between zones. The stroma has been stained black to enhance contrast.

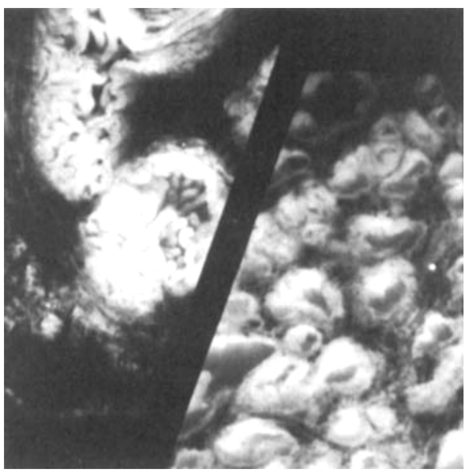

Fig. 7. Gross specimen of Figure 6 magnified 10× to show the acinar architecture of the central zone (upper left) and the peripheral zone (lower right).

upper end of the verumontanum, and *all* of the main ducts of the adult prostate arise at or distal to this point. Anterior and posterior branching of the ducts of both zones occurs to a lesser extent, producing only moderate thickening of the coronal disc in the fully developed organ.

Despite the fusion of the two zones at their borders, an anatomically distinct boundary line remains visible between them in the normal adult gland (Figs. 5, 6). However, more important than this striking anatomic delineation between the two zones are dramatic histologic differences that exist between their glandular tissues. These suggest an important difference in biologic function. The acinar tissue of the central zone consists of large spaces of irregular contour, from whose walls numerous intraluminal ridges or septa project. By contrast, the long narrow peripheral zone ducts branch into small, round, regular acini with smooth, nonseptate walls (Fig. 7). The peripheral zone epithelium is simple columnar and composed of pale cells with distinct borders and basally placed, small, dark nuclei. In the central zone, the cells are strikingly different, with more opaque, granular cytoplasm and less distinct cell membranes. They appear more crowded with variable cell length and an irregular luminal border. Their nuclei, of somewhat larger size and paler staining, are displaced to variable levels from the basement membrane (Fig. 8).

The proposed biologic difference between central and peripheral zones could be important for understanding prostatic disease, since carcinoma has been reported to arise commonly in the peripheral zone but seldom in the central zone [9].

To explain the existence of these morphologic and proposed biologic differences, it has been suggested that the human prostate is in fact an organ of composite embryologic origin [7]. The central zone is postulated to be part of the Wolffian duct system, while the peripheral zone and urethra are derived from the urogenital sinus. Data compatible with this hypothesis include the close anatomic proximity of the central zone ducts and their orifices to the ejaculatory ducts, a strong histologic similarity between central zone and seminal vesicle epithelium [7], and the relative immunity to carcinoma shared by the central zone with all other epithelia of Wolffian duct derivation. Blacklock [10] has presented morphologic evidence that the human central and peripheral zones are homologous to the cranial and caudal lobes of the rhesus monkey. This could be a significant finding in the search for an appropriate animal model for human anatomy and disease (Figs. 9, 10).

THE PREPROSTATIC REGION

If the embryonic urogenital sinus (adult prostatic urethra) is in fact the source of the duct development of the peripheral zone, it might be expected that this developmental process would continue above the base of the verumontanum into the proximal (preprostatic) urethral segment. Indeed, the double row of lateral urethral orifices that characterizes the peripheral zone does continue along the proximal urethral segment, and the epithelium produced resembles peripheral zone epithelium rather than that of the central zone (Fig. 11). In this segment, the row of ducts is now displaced anteriorly into the oblique coronal plane (OC) but otherwise appears to represent a continuation of the embryonic evolution of the urogenital sinus. However, the adult developmental fate of this tissue is drastically different from that in the peripheral zone, appearing to have become halted not far past the embryonic stage. In the adult, there exist only tiny channels of near-microscopic size and vastly simplified structure, constituting less than 1% of the mass of the glandular prostate. These structures, referred to as the "periurethral glands," do not possess their own periglandular muscularis and are confined in their extent to the immediately periurethral stroma. Rather than expanding laterally away from the urethra, they grow proximally toward the bladder neck, closely paralleling the long axis of the urethral lumen and lying mainly in its oblique coronal plane (OC).

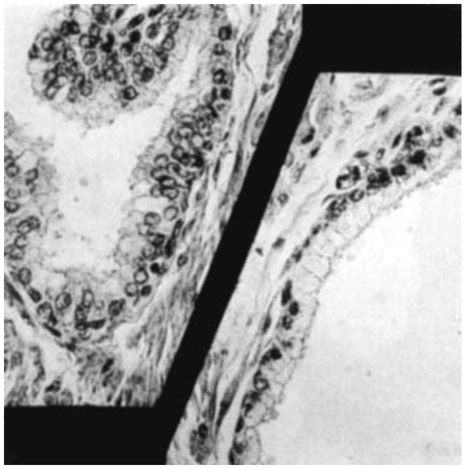

Fig. 8. Photomicrograph contrasting the epithelium of the central zone (upper left) and the peripheral zone (lower right). H & E, 40×.

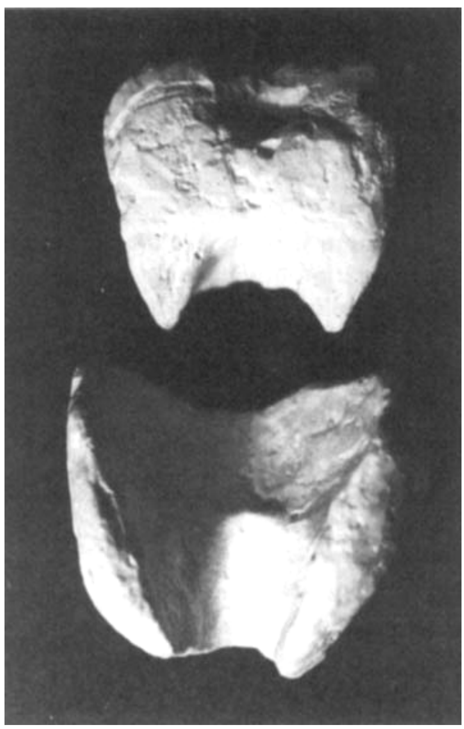

Fig. 9. Plaster cast of a human prostate in coronal (frontal) view with gross dissection of the central zone from the peripheral zone. The central zone is unusually large. It completely surrounds the point of entrance of the ejaculatory ducts into the base of the prostate (circular depression near superior border). The urethra and the verumontanum have been removed.

Fig. 10. Plaster cast of rhesus prostate. Gross dissection of the cranial and caudal lobes in a view similar to Figure 9. The urethra remains attached to the caudal lobe. The ejaculatory ducts penetrate the cranial lobe near its center.

This segment of the urethra is related to a unique anatomic feature that may serve to explain the limitation of glandular evolution here. Along this segment alone is found a well-developed cylindrical smooth muscle sphincter, which forms a continuous envelope immediately surrounding the urethral submucosa and completely encircling the urethra from the base of the verumontanum to the bladder neck (Fig. 11, 12). To attain full glandular development, the periurethral ducts would either have to penetrate this cylindrical barrier, or its muscular rings would have to be incomplete. A similar sphincter of striated muscle composition exists along the urethra distal to the verumontanum, but its continuity is incomplete. It consists of semicircular bands that encircle only the anterolateral aspect of the urethra, allowing the peripheral zone ducts to escape around its posterior border and attain full development beyond its confines.

At a single point in the proximal urethral segment, a small portion of the periurethral duct system exhibits a similar escape phenomenon in relation to the smooth muscle sphincter of this region. The most distal of the periurethral duct orifices lies just at the level of the distal margin of the smooth muscle sphincter. Their main ducts consistently escape immediately below the most distal rings of the smooth muscle sleeve to continue development outside its confines. This small duct group, arising at a single point—the junction of the proximal and distal urethral segments—is the "transition zone" (Fig. 11, 12). Developing immediately outside the sphincter, it suffers less space restriction

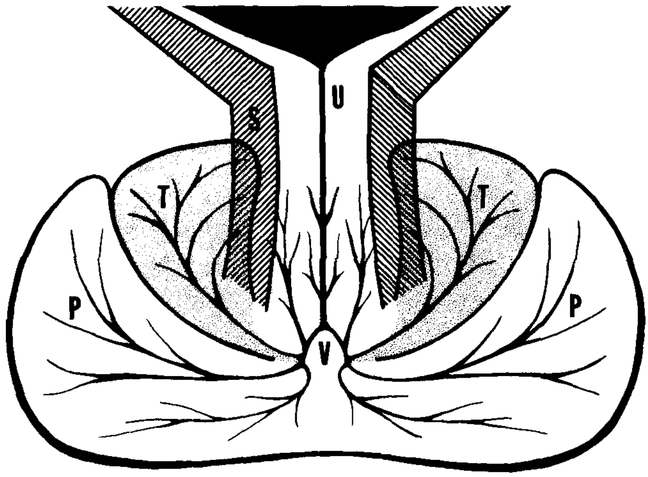

Fig. 11. Diagram of the prostate in OC plane. The most proximal ducts of the peripheral zone (P) radiate laterally from the verumontanum (V). Ducts of the transition zone (T, shaded area) exist from urethra just proximal to the base of the verumontanum, lying between the peripheral zone and the sphincter (S, lined area). Periurethral ducts arising along the proximal urethra are confined to the periurethral stroma (U) and run proximally toward the bladder (black area).

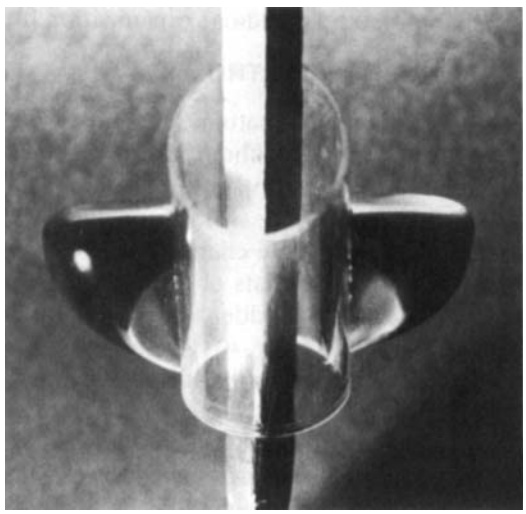

Fig. 12. Model of the preprostatic area in frontal view as seen from the bladder neck. The sphincter (clear cylinder) surrounds the proximal urethra (white). The verumontanum (gray) is at the lower border of the illustration. Transition zones project laterally from the sphincter and progressively increase in area with proximal distance from the verumontanum.

than the other periurethral ducts and achieves more nearly full glandular development. Though it shows considerably more duct branching and acinar proliferation than the other periurethral ducts, it nevertheless remains of small size, constituting less than 5% of the mass of the glandular prostate. In its developmental expansion, its ducts fan out laterally and ventrally, but its main direction of growth is proximally toward the bladder neck, nearly parallel to the course of the other periurethral ducts. Hence, though it is histologically similar to the peripheral zone, it is anatomically separate except for a narrow, usually anatomically distinct boundary line at its lateral border. The greatest expanse of the transition zone lies entirely in the oblique coronal plane (OC) of the other preprostatic structures—the sphincter and periurethral glands—which comprise the third main subdivision of the prostate, the "preprostatic region."

The location and orientation of growth of the transition zone are therefore intimately related to that of the cylindrical sphincter. The medial border of the transition zone usually lies in apposition to the external fibers of the sphincter throughout most of its length. Many of the more medial of the transition zone ducts and acini actually penetrate into the sphincter and lie embedded between its fibers. In this location, their periacinar muscularis characteristically fails to develop.

Though insignificant in size and probably in functional importance, the *transition zone* has great significance for adult pathology. The transition zone and other periurethral glands are the exclusive site of origin of BPH. Of these two gland groups, the transition zone almost invariably produces the most numerous and the largest nodules, especially from that part of its mass lying near to or within the sphincter. It has been hypothesized that the pathogenesis of BPH derives from inductive interactions between these tiny groups of glandular tissue and the preprostatic stroma, which is essentially a foreign stroma of sphincteric rather than prostatic glandular organization [8].

THE ANTERIOR FIBROMUSCULAR STROMA

The fourth and last of the main anatomic regions of the prostate is entirely nonglandular and is apparently without importance for prostatic function or pathology. Nevertheless, it makes up about one third of the bulk of the tissue within the prostatic capsule [8] (Fig. 13). It considerably increases the total thickness of the gland and produces the characteristic convexity of its anterior surface on external inspection. It consists of a thick sheath of tissue, continuous with the detrusor muscle at the bladder neck. Surrounding and blending with the internal bladder neck sphincter, it sweeps distally as an apron of muscular tissue, forming the entire anterior surface of the prostate and contacting the urethra again at its distal end—the prostate apex. In its course, it fans out laterally to merge with the capsule along the entire anterolateral border of the glandular prostate. As it passes in front of the distal urethral segment, it incorporates on its inner surface the semicircular bands of striated sphincteric muscle characteristic of this region and continuous with the striated muscle of the external sphincter distal to the prostate apex.

The greatest anatomic significance of this tissue is that it completely shields from view the anterior aspect of all the tissue of the previously described glandular regions (Fig. 14, 15). It is tightly adherent to these three regions along its inner aspect, and its fusion to them makes adequate gross dissection almost impossible. Largely for this reason, the complexities and exact anatomic relationships of the three above-described regions of the glandular prostate may have been delayed in their discovery.

Fig. 13. Plaster cast of the anterior fibromuscular stroma dissected free from the glandular prostate and seen in oblique view. Depression near the superior border of the illustration is the bladder neck. Width of the tissue shield tapers distally toward the urethra (not visible) as it emerges from the prostate apex.

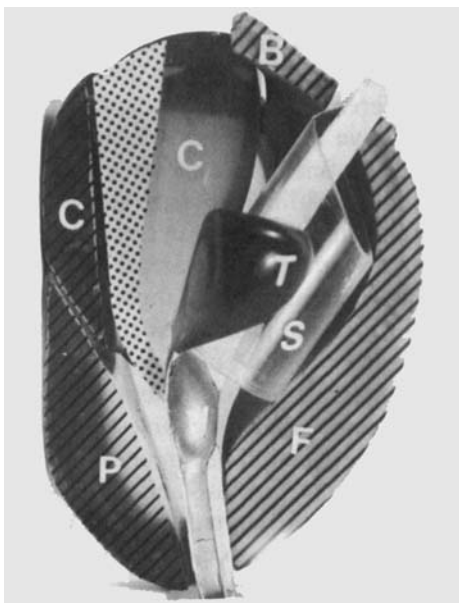

Fig. 14. Three-dimensional model of prostate anatomy, side view. Sagittal cuts (lined areas) have removed the near side of the fibromuscular stroma (F), bladder neck (B), central zone (C), and peripheral zone (P). The transition zone (T), sphincter (S), and urethra with the verumontanum (V) are seen in full. Periurethral ducts are hidden behind the transition zone. Ejaculatory ducts (stippled) traverse the center of the central zone.

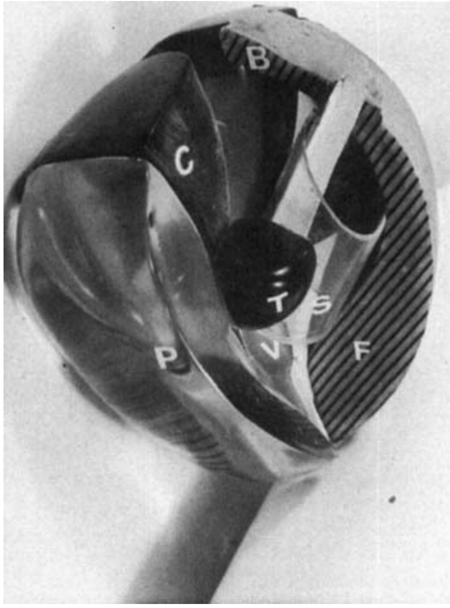

Fig. 15. Three-dimensional model of prostate anatomy, 3/4 view. The near side of the fibromuscular stroma and the bladder neck only were removed by sagittal cut. Same symbols as in Figure 14.

CONCLUSIONS

The prostate gland is an anatomically heterogeneous organ, composed of four separate regions. They differ markedly in their tissue composition and show highly significant differences in their susceptibility to different pathologic conditions. These regions have not previously been fully characterized, nor their boundaries adequately defined, because they are tightly welded together within a single capsule and are difficult to separate by dissection. In addition, one of the regions, the nonglandular fibromuscular stroma, though it is of no pathologic interest, forms the entire anterolateral one third of the gland and shields from view the anterior aspect of the three glandular regions.

A coronal section through the prostate at the proper depth follows the course of the distal half of the prostatic urethra and exposes the two largest glandular regions in their plane of greatest extent. Their ducts arise exclusively from the distal prostatic urethra along its course from the base of the verumontanum to the apex of the gland. The larger region, the peripheral zone, forms nearly 75% of the glandular prostate and is the site of origin of almost all carcinomas. The smaller region, the central zone, is of quite different glandular composition and is relatively immune to cancer. Its anatomic location is closely related to the course of the ejaculatory ducts as they extend proximally from the verumontanum.

An oblique coronal section through the prostate at the proper depth follows the course of the proximal half of the prostatic urethra from the base of the verumontanum to the bladder neck. This plane exposes in its greatest extent a fourth region, which is characterized by minimal gland development—less than 5% of the glandular prostate—and also by prominent blending of the epithelial and stromal components of the glandular tissue with periurethral smooth muscle elements of sphincteric, nonprostatic function. This tissue admixture represents a downward intrusion of bladder-neck-related stroma into the proximal portion of the glandular prostate. This region is the exclusive site of origin and BPH and is almost completely immune to carcinoma. Even within this region, there is a gradient of susceptibility to BPH. Its focus of most frequent nodule formation coincides with an area where the larger of two glandular components in this region, referred to as the transition zone, penetrates between the fibers of a cylindrical smooth muscle sphincter that surrounds the entire proximal prostatic urethra.

Further elucidation of the biologic differences between the three glandular regions and the features associated with their differential susceptibility to disease could provide valuable information about the pathogenesis of prostatic carcinoma.

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