

CONTENTS

Part 1: Tumors of the Prostate Gland

1. The Normal Prostate Gland	3
Anatomy	3
Anatomic models	4
“Capsule”	6
Blood supply	7
Lymphatic drainage	7
Nerve supply	9
Embryology and Developmental Anatomy	10
Histology	12
Immunohistochemical Findings	16
Ultrastructural Findings	18
Prostate Function	19
2. Benign Prostatic Hyperplasia	23
Prevalence	23
Clinical Features	24
Gross Findings	25
Microscopic Findings	28
Immunohistochemical Findings	37
Molecular Genetic Findings	40
Differential Diagnosis	40
Treatment and Prognosis	42
3. High-Grade Prostatic Intraepithelial Neoplasia and Intraductal Carcinoma	
of the Prostate	47
Prostatic Intraepithelial Neoplasia	47
Microscopic Findings	47
Relationship of PIN to Carcinoma	53
Immunohistochemical Findings	54
Differential Diagnosis	55
Clinical Significance of HGPIN	62
Intraductal Carcinoma of the Prostate	63
General Features	63
Microscopic Findings	64
Diagnostic Criteria	64
Molecular Genetic Findings	66
Relationship to Prostate Carcinoma	68
Differential Diagnosis	69

Clinical Significance and Management	70
Workup and Reporting	72
4. Acinar (Usual) Adenocarcinoma of the Prostate	77
Epidemiology	77
Clinical Incidence	77
Mortality	79
Autopsy Prevalence	79
Clinical Risk Factors	80
Prevention	82
Clinical Presentation	82
Clinical Symptoms	82
Digital Rectal Exam	83
Serum Prostate-Specific Antigen	84
Molecular Tests	85
Clinical Staging	86
Gross Findings	90
Location	91
Multifocality	95
Microscopic Findings	95
General Principles of Diagnosing Prostate Cancer	95
Architectural Features	96
Nuclear Features	99
Cytoplasmic Features	104
Intraluminal Contents	108
Stromal Changes	110
Histologic Features Specific for Prostate Cancer	110
Identification of Basal Cells	116
Adenocarcinomas Mimicking Benign Glands	120
Atypical Glands Suspicious for Cancer	123
The Gleason Grading System	133
Historical Background	133
Former Gleason Patterns 1-2	136
Gleason Pattern 3	136
Gleason Pattern 4	140
Gleason Pattern 5	140
Grading Variants of Prostate Carcinoma	146
Grading Prostate Carcinoma Following Therapy	150
Grading Cancers Outside the Prostate and in Metastatic Deposits	152
Reporting Rules for Grading Prostate Adenocarcinoma	152
Needle Biopsy with Different Cores Showing Different Grades	154

Radical Prostatectomy Specimens with Different Nodules Showing Different Grades	154
Prognosis and Grade Groups	155
Grade Group System	155
Correlation of Grade with Serum PSA Levels.	156
Correlation of Grade in Biopsy and Radical Prostatectomy Specimen	156
Change of Grade Over Time	158
Interobserver Reproducibility	159
Treatment	159
Active Surveillance	160
Surgery	160
Radiation Therapy	161
Hormone Therapy	162
Chemotherapy	164
Pathologic Staging, Spread, Metastases, and Prognosis	164
pT2: Carcinoma Confined within the Prostate Gland	165
pT3	167
pT4: Invasion of Rectum or Gross Invasion of Urinary Bladder Neck	175
Perineural Invasion	176
Vascular Invasion	180
Primary Tumor Size	180
pN: Lymph Node Metastasis	182
Distant Metastasis	186
Distant Nonbony Prostatic Carcinoma Metastasis	188
Lung Metastasis	189
Liver Metastasis	190
Treatment Effects on Malignant Prostatic Tissue.	191
Hormonal Therapy	191
Radiation Therapy	193
Cryotherapy	200
High-Intensity Focused Ultrasound	200
Phytotherapy	200
Special Studies	201
Histochemistry	201
Immunohistochemistry	201
5. Variants of Prostatic Carcinoma.	237
Prostatic Duct Adenocarcinoma.	237
Mucinous (Colloid) and Signet Ring Cell Adenocarcinoma	247
Carcinomas with Squamous Differentiation	250
Tumors with Neuroendocrine Differentiation	252
Sarcomatoid Carcinoma	259

Adenocarcinoma of the Prostate with Pleomorphic Giant Cell Features	260
Miscellaneous Variants	262
6. Basal Cell Tumors and Tumor-Like Conditions	267
Basal Cell Hyperplasia	267
Basal Cell Carcinoma	275
7. Urothelial Tumors and Tumor-Like Lesions	285
Urothelial Metaplasia	285
Urothelial Carcinoma Involving the Prostatic Urethra and Prostate	286
Primary Urothelial Carcinoma	287
Secondary Urothelial Carcinoma	287
In Situ (Intraductal-Acinar) Spread of Carcinoma	288
Invasive Urothelial Carcinoma	290
Grading and Staging of Urothelial Carcinoma in the Prostate	292
8. Miscellaneous Tumors of the Prostate	295
Cystic Epithelial Tumors	295
Oncocytoma	298
Clear Cell Adenocarcinoma of the Utricle/Prostate	298
Renal-Type Clear Cell Carcinoma of the Prostate	298
9. Mesenchymal Tumors of the Prostate	303
Benign Mesenchymal Tumors	303
Leiomyoma	303
Miscellaneous Benign Mesenchymal Tumors	303
Malignant Mesenchymal Tumors	303
Leiomyosarcoma	304
Rhabdomyosarcoma	307
Miscellaneous Malignant Mesenchymal Tumors	311
Mesenchymal Tumors of Uncertain Malignant Potential	312
Solitary Fibrous Tumor	312
Inflammatory Myofibroblastic Tumor	314
Secondary Involvement by Mesenchymal Tumors	316
Gastrointestinal Stromal Tumor	316
Stromal Tumors Arising from Specialized Prostatic Stroma	317
Stromal Tumors of Uncertain Malignant Potential	317
Stromal Sarcoma	324
10. Hematolymphoid Tumors and Tumor-Like Lesions	331
Lymphoma	331
Leukemia	335
Plasma Cell Myeloma	338
Extramedullary Hematopoiesis	338
Signet Ring Lymphocytes	339

11. Miscellaneous Tumors	343
Extragenital Germ Cell Tumors	343
Ganglioneuroma and Nerve Sheath Tumor.	343
Lymphangioliomatosis.	343
Malignant Rhabdoid Tumor.	343
Malignant Mixed Tumor of Salivary Gland Type	344
Malignant Perivascular Epithelioid Cell Tumor.	344
Malignant Melanoma.	346
Ectomesenchymoma	346
Malignant Mesenchymoma	346
Paraganglioma	346
Primitive Neuroectodermal Tumor	347
Wilms Tumor	348
Rare Secondary Tumors	348
12. Tumor-Like Lesions of the Prostate	355
Adenosis	355
Atrophy.	365
Basal Cell Hyperplasia	370
Clear Cell Cribriform Hyperplasia (Cribriform Hyperplasia).	370
Malakoplakia	370
Mesonephric Hyperplasia.	370
Nephrogenic Adenoma	370
Nonspecific Granulomatous Prostatitis	376
Prostatic Urethral Polyps	376
Sclerosing Adenosis	378
Squamous Metaplasia Adjacent to Infarcts	381
Verumontanum Mucosal Gland Hyperplasia	381
Xanthoma.	383
13. Normal Nonprostatic Tissue in Prostate Specimens	387
Seminal Vesicles	387
Colonic Mucosa	387
Cowper Glands.	387
Paraganglia	393
Signet Ring Lymphocytes.	393

Part 2: The Seminal Vesicle

1. Normal Structure and Function of Seminal Vesicle.	399
Anatomic Relationships	399
Blood Supply and Lymphatic Drainage	399
Nerves.	399
Embryology and Developmental Anatomy	399
Gross Findings	399

Microscopic Findings	399
Immunohistochemical Findings	402
Ultrastructural Findings	402
Seminal Vesicle Function	402
2. Benign Tumors of the Seminal Vesicle	405
Cystadenoma	405
Fibroadenoma.	407
Leiomyoma.	407
Solitary Fibrous Tumor	408
Peripheral Nerve Sheath Tumor (Schwannoma)	408
Benign Mesenchymoma.	408
3. Seminal Vesicle Tumors of Indeterminate or Low Malignant Potential	411
Epithelial-Stromal Tumor/Mixed Epithelial-Stromal Tumor	411
Adnexal Tumor of Probable Wolffian Origin	413
Smooth Muscle Neoplasm of Uncertain Malignant Potential.	413
4. Primary Malignant Tumors of Seminal Vesicle	415
Carcinoma	415
Adenocarcinoma	415
Squamous Cell Carcinoma.	417
Small Cell Carcinoma.	417
High-Grade Epithelial-Stromal Tumor	417
Primitive Neuroectodermal Tumor	418
Sarcoma	418
Leiomyosarcoma	418
Rhabdomyosarcoma.	419
Angiosarcoma.	419
Fibrosarcoma	419
Liposarcoma	419
Hemangiopericytoma.	419
Germ Cell Tumors, Carcinoid Tumor, and Paraganglioma	420
5. Secondary Malignant Tumors of Seminal Vesicle	423
Prostatic Adenocarcinoma	423
Urothelial Carcinoma of Bladder	423
Miscellaneous Rare Secondary Malignancies	423
6. Tumor-Like Conditions of Seminal Vesicle	427
Benign Cysts.	427
Fibromuscular Hyperplasia.	427
Adenomyosis	427
Atypia in Normal Seminal Vesicle Epithelium.	427
Benign Ectopic Prostatic Tissue	429
Müllerian Stroma	429

Part 3: The Penis and Scrotum

1. Anatomy and Histology of Penis	433
Distal (Anterior) Penis	433
Glans	433
Foreskin	436
Coronal Sulcus (Balanopreputial Sulcus)	438
Proximal Penis (Peneal Body or Shaft)	439
Posterior (Root) Penis	439
Penile Urethra	440
Lymphatic Vessels and Inguinal Lymph Nodes	441
Vascular Supply and Innervation	442
2. Classification of Penile Tumors	445
Histologic Classification of Penile Tumors	446
3. Benign and Precancerous Epithelial Tumors of Penis	449
Benign Epithelial Tumors	449
Penile Horn and Micaceous Balanitis	449
Skin Adnexal Tumors	449
Abnormal and Precancerous Epithelial Lesions	449
Squamous Hyperplasia	449
Lichen Sclerosus	452
Condylomas: Condyloma Acuminatum	462
Unusual Presentations of Condylomas	463
HPV-Positive Flat Lesion	465
Giant Condyloma (Tumor of Buschke-Lowenstein)	466
Penile Intraepithelial Neoplasia	473
Non-HPV-Related PeIN	474
HPV-Related PeIN (Warty/Basaloid Features)	475
Mixed or Coexisting PeIN	487
HPV Genotypes in PeIN	487
P16 in PeIN	488
HPV Genotypes in Invasive Carcinomas and Associated PeIN	491
4. Squamous Cell Carcinoma of Penis: General Features	503
Epidemiology	503
Phimosis	505
Cigarette Smoking	506
Penile Injury, Tears, and Chronic Balanitis	506
Genital Warts	506
Human Papillomavirus	506
Lichen Sclerosus	507
Immunosuppression	507
PUVA Treatment	507

Other Risk Factors	507
Cancer Prevention	508
General Pathologic Features.	508
Sites of Origin.	509
Patterns of Growth	511
Secondary Tumors Associated with Penile Cancer	514
Molecular Genetic Pathology.	514
Routes of Cancer Spread.	516
Local Spread	516
Regional Spread	517
Recurrent Carcinomas	518
Disseminated Cancer	520
Noninvasive and Minimally Invasive Diagnostic Procedures	521
Clinical Evaluation.	521
Ultrasound Evaluation	522
Computed Tomography and Positron Emission Tomography Evaluation	522
Magnetic Resonance Imaging Evaluation	522
Dynamic Sentinel Lymph Node Biopsy.	523
Staging of Penile Carcinoma	523
Treatment of Penile Carcinoma	524
Standard Surgical Treatment	524
Penile-Preserving Therapy	525
Radiotherapy	525
Laser Ablation.	526
Chemotherapy	526
Multimodality Therapy	526
5. Histologic Subtypes of Penile Squamous Cell Carcinoma	543
Non-Human Papillomavirus (HPV)-Related Variants of Squamous Cell Carcinoma	543
Usual Type Squamous Cell Carcinoma	543
Verrucous Carcinoma.	549
Hybrid Verrucous Carcinoma.	556
Papillary Squamous Cell Carcinoma, Not Otherwise Specified (NOS)	559
Cuniculatum Carcinoma	564
Pseudohyperplastic Carcinoma	566
Sarcomatoid Carcinoma.	569
Pseudoglandular Carcinoma	577
Adenosquamous Carcinoma	579
Mucoepidermoid Carcinoma.	581
HPV-Related Variants of Squamous Cell Carcinoma	585
Basaloid Carcinoma	585
Warty (Condylomatous) Carcinoma	593

Warty-Basaloid Carcinoma	600
Medullary Carcinoma	603
Clear Cell Carcinoma	606
Lymphoepithelioma-Like Carcinoma	609
Mixed Carcinomas	610
Unclassified Carcinomas	611
6. Prognostic Factors of Penile Squamous Cell Carcinoma	617
Histologic Grade	617
Gleason-Like Scoring System	621
Perineural Invasion	621
Vascular Invasion	621
Depth of Invasion or Tumor Thickness	623
Anatomic Levels of Invasion	623
Anatomic Location	626
Patterns of Growth	626
Front of Invasion	626
Size of Primary Tumor	626
Histologic Subtypes	627
Koilocytosis	629
Positive Resection Margins	629
Urethral Invasion	630
Risk-Group Stratification Systems	631
Current Systems for Stratification	631
Algorithms and Nomograms	632
Molecular Factors and Prognosis	632
Limitations in the Pathologic Evaluation of Prognostic Factors	633
The Prognostic Index	634
7. Other Epithelial and Nonepithelial Tumors of Penis	643
Epithelial Tumors	643
Paget Disease	643
Malignant Melanoma	644
Other Rare Epithelial Primary Tumors	645
Nonepithelial Tumors	645
Mesenchymal Tumors	645
Special Benign Nonepithelial Tumors	646
Special Malignant Nonepithelial Tumors	647
Malignant Lymphoma and Related Lesions	653
8. Tumors Metastatic to Penis	661
9. Tumor-Like Lesions of Penis	669
Cysts	669
Epidermal Inclusion Cysts	669

Mucinous Cysts	669
Median Raphe (Urothelial) Cysts	669
Dermoid Cysts	673
Lymphatic Cysts	673
Verruciform Xanthoma	673
Peyronie Disease	673
Papillomatosis of Glans Corona	676
Lipogranuloma	677
Melanosis Lentiginosis	678
Os Penis	679
10. Tumors of the Scrotum	685
Anatomy and Histology	685
Anatomic Layers	685
Blood Supply	685
Lymphatic Vessels	685
Nerve Supply	685
Benign Epithelial Tumors	686
Condyloma Acuminatum	686
Adnexal Tumors	687
Malignant Epithelial Tumors	687
Squamous Cell Carcinoma	691
Scrotal Intraepithelial Neoplasia	697
Extramammary Paget Disease	699
Basal Cell Carcinoma	700
Malignant Melanoma	703
Miscellaneous Epithelial Tumors	703
Benign Mesenchymal Tumors	703
Angiokeratoma	703
Hemangioma	705
Lymphangioma	705
Leiomyoma	707
Angiomyxoid Tumors	709
Angiomyofibroblastoma	710
Cellular Angiofibroma	710
Other Benign Mesenchymal Tumors	711
Malignant Mesenchymal Tumors	711
Leiomyosarcoma	711
Liposarcoma	713
Malignant Fibrous Histiocytoma	714
Malignant Lymphoma	714
Secondary Tumors	714

Tumor-Like Lesions	714
Verruciform Xanthoma	714
Porokeratosis of Mibelli	716
“Idiopathic” Scrotal Calcinosis and Epidermoid Cysts	717
Sclerosing Lipogranuloma (“Paraffinoma”)	719
Post-Traumatic Spindle Cell Nodule	720
Scrotal Hamartoma Including “Accessory Scrotum”	721
Fibrous Hamartoma of Infancy	722
Smooth Muscle Hamartoma of Dartos	722
Isolated Exophytic Elastoma	723
Scrotal Fat Necrosis	723
Acute Idiopathic Scrotal Edema	723
Polymorphic Reticulosis of Genital Skin	724
11. Penile Cancer Evaluation	743
Frozen Section Evaluation of Penile Cancer	743
Circumcision Specimen	743
Partial Penectomy Specimen	743
Total Penectomy Specimen	743
Lymph Nodes	743
Guidelines for Handling the Resected Specimen	744
Foreskin	744
Foreskin, Coronal Sulcus, and Glans	744
Urethral Margin	744
Shaft Margin	744
Glans	744
Reporting of Resected Specimens of Penile Carcinoma	746
Index	749