

151942

# PROSTATE CANCER

A PRACTICAL GUIDE

EDITED BY

MAY ABDEL-WAHAB

ORLANDO E. SILVA

SAUNDERS  
ELSEVIER

Dedication ii  
Acknowledgements v  
How to use this book ix  
Commonly used abbreviations xi

## **1 History of prostate cancer 1**

## **2 Epidemiology of prostate cancer 9**

Worldwide 9  
North America 10  
Africa 12  
The UK and Europe 13  
Asia 14

## **3 Risk factors 15**

Factors that increase risk 15  
Hereditary prostate cancer 18  
Estimating risk factors 24  
Genetic testing 25  
Current recommendations for high-risk patients 25  
Potential risk factors 28  
Factors that decrease risk 30

## **4 Chemoprevention 33**

5 $\alpha$ -Reductase inhibitors 33  
Selenium 36

Vitamin E ( $\alpha$ -tocopherol) 37  
Selective estrogen receptor modulators 40  
Soy 40  
Lycopene 41  
Major ongoing trials 41

## **5 Prostate-specific antigen and digital rectal examination screening for prostate cancer 43**

Introduction 43  
Digital rectal examination 43  
Transrectal ultrasonography of the prostate 45  
Prostate-specific antigen 46  
New serum markers and novel techniques 52

## **6 Prostate cancer: imaging features 53**

Ultrasound: transrectal ultrasonography 53  
Computerized tomography 54  
Magnetic resonance imaging and magnetic resonance spectroscopy 56  
Nuclear medicine studies 60

## 7 Evaluation of abnormal digital rectal examination or elevated prostate-specific antigen 63

- Digital rectal examination 63
- Prostate-specific antigen 64
- Prostate biopsy 66

## 8 Prostate pathology 70

- Prostatic intraepithelial neoplasia 70
- Prostatic carcinoma 71
  - Adenocarcinoma of peripheral ducts and acini 73
- Immunohistochemistry 80
- Other prostate carcinomas 81
- Sarcoma, lymphoma, and other malignancies 86

## 9 Staging 91

- Clinical 91
- Pathologic 91
- TNM classification 92
- Histologic grade (G) 93
- Radiological evaluation 94

## 10 Prognostic factors and predictive factors in prostate cancer 96

- Serum prostate-specific antigen 97
- Digital rectal examination 98
- Gleason score 98
- Surgical margin status 99
- Tumor ploidy and nuclear morphometry 101
- Histologic subtypes of cancer 101

Number of biopsies of the prostate 101

Molecular prognostic markers 102

*bcl-2* 102

*p53* 102

*pp32* 103

Microvessel density 103

Vascular endothelial growth factor 103

Perineural invasion 103

Transforming growth factor- $\beta$ 1 106

Bone morphogenetic proteins 106

Insulin-like growth factors 106

*Her-2/neu* 107

Interleukin-6 107

Bone sialoprotein 107

E-Cadherin 108

*CD44* 108

Genetic factors 108

Predictors of pathological stage before radical retropubic prostatectomy 108

Bone metabolic markers in advanced disease 109

## 11 High-grade prostatic intraepithelial neoplasia 110

HGPIN demonstrated during a sextant biopsy scheme should be repeated 111

HGPIN demonstrated during an extended biopsy scheme does not warrant immediate repeat biopsy 111

HGPIN and extended repeat biopsy at 3 years 113

Relationship of HGPIN to prostate-specific antigen 113

Testosterone replacement in men with HGPIN 114

## 12 External beam radiation therapy 115

Radiation therapy techniques 115

Radiation therapy dose-response 121

## 13 Pelvic node radiation in prostate cancer 125

Introduction and background: how commonly are lymph nodes involved? 125

Patients who are pathologically node negative 128

Can imaging improve the detection of lymph node metastasis? 129

Treatment of patients with pelvic lymph nodes: a role for radiotherapy? 130

Conclusions 132

Selected papers on the incidence of pelvic lymph node involvement (2006) 132

## 14 Prostate brachytherapy 136

Low dose rate brachytherapy 136

Isotopes 137

Low dose rate brachytherapy as monotherapy 138

Low dose rate brachytherapy in combination with external beam radiation therapy 140

High dose rate brachytherapy 141

High dose rate brachytherapy in combination with external beam radiation therapy 143

High dose rate brachytherapy as monotherapy 150

## 15 Radical prostatectomy 153

Indications 153

History 155

The University of Miami radical prostatectomy 155

Outcome measures for radical prostatectomy 164

Complications 168

Changes in quality of life measures 174

Summary 178

## 16 Post-prostatectomy radiation therapy 179

Adjuvant post-prostatectomy radiation therapy 179

Salvage post-prostatectomy radiation therapy after relapse 181

Choice of postoperative versus salvage radiation 182

Radiation therapy techniques 182

Morbidity of postoperative radiation 183

Role of hormone therapy with postoperative radiation 183

## 17 Cryotherapy for prostate cancer 185

History 185

Cryobiology 186

Patient selection for primary treatment of prostate cancer 187

Cancer-related outcomes after cryosurgical ablation of the prostate 188

Cryosurgical ablation as salvage therapy after radiation treatment 190

Complications following cryosurgical ablation of the prostate 192

## 18 Adjuvant androgen suppression for locally advanced prostate cancer 194

Adjuvant androgen deprivation 194

Neoadjuvant androgen deprivation for locally advanced prostate cancer 196

Neoadjuvant versus adjuvant androgen deprivation 198

Clinically localized prostate cancer 200

Current phase III trials 203

## 19 Prostate cancer recurrence 205

Biochemical recurrence 205

Treatment of biochemical recurrence 208

Local recurrence 210

Treatment modalities for local recurrence after radiation therapy 213

Treatment modalities for local recurrence after surgery 216

## 20 Metastatic prostate cancer 220

Management of bone metastases 220

Spinal cord compression 227

Soft tissue metastases 229

## 21 Endocrine therapy for metastatic prostate cancer 231

Androgen-deprivation therapy 231

Orchiectomy 232

Leuteinizing hormone releasing hormone agonists 232

Leuteinizing hormone releasing hormone antagonists 233

Androgen antagonists (anti-androgens) 233

Complete androgen blockade 234

Complete androgen blockade versus monotherapy 234

Early versus deferred androgen-deprivation therapy 236

Intermittent androgen suppression 236

Androgen antagonist addition 237

Androgen antagonist subtraction (androgen withdrawal) 237

Other endocrine therapy used in prostate cancer 237

Bone mineralization management 238

## 22 Chemotherapy in hormone-refractory prostate cancer 240

- Prognostic factors in hormone-refractory prostate cancer 241
- Historical overview of chemotherapy in hormone-refractory prostate cancer 241
- Single-agent docetaxel 242
- Randomized trials of docetaxel 243
- Toxicity of docetaxel 245
- Estramustine 246
- Docetaxel-refractory patients 247
- Ongoing clinical trials in hormone-refractory prostate cancer 247

## 23 Investigational agents 251

- New cytotoxic agents 251
- Calcitriol (DN-101) 252
- Growth factor receptor antagonists 253
- Anti-angiogenic agents 254
- Proapoptotic agents 255
- Other novel targeted agents 256
- Immunotherapeutic agents 256

## 24 Complications of radical prostatectomy 259

- Hemorrhage 260
- Rectal injury 262
- Oliguria/anuria 263

- Lymphocele 264
- Nerve injury 264
- Cardiovascular effects 265
- Infection 266
- Foley catheter loss 266
- Perineal pain syndrome 267
- Bladder neck contracture 268
- Incontinence 268
- Impotence 269

## 25 Side-effects of treatment 272

- Prostatectomy 272
- External beam radiation 274
- Low dose rate brachytherapy 278
- High dose rate brachytherapy as monotherapy 281
- Cryotherapy 283
- Androgen-suppression therapy 285
- Chemotherapy 288

## 26 Follow-up of patients after treatment of localized prostate cancer 293

- Recurrence after primary therapy 293
- Follow-up protocol following primary therapy 294
- Biochemical recurrence 294
- Predictors of recurrence 295
- Distinguishing local from systemic recurrence 296
- Treatment following recurrence 298