

## Prostate Cancer

### An Overview

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### Introduction

Prostate cancer (PC) is an important health issue. PC is now the most commonly diagnosed malignancy and is the second leading cause of death behind lung cancer in UK men.

### Epidemiology

The incidence of PC is rising. Reasons for this include the changing age structure of our population, heightened awareness of PC and earlier prostate specific antigen (PSA) testing. There is wide variation in the incidence of PC. There is a greater incidence with increasing age, in Western compared to Asian/Eastern countries and African than Caucasian men. Immigration studies documented that the epidemiological PC pattern of the migrants' new residence can be acquired, strongly implicating environmental factors. However associations with environmental factors such as diet (fat intake, lack of vitamins E and D), obesity, occupation (agricultural workers), and sexual activity are inconsistent.

### Prognostic Markers

Early PSA testing has led to greater number of cases of localised disease in younger asymptomatic men. There is some evidence that age specific ranges may improve the sensitivity of prostate cancer detection. One example is shown in Table 1.

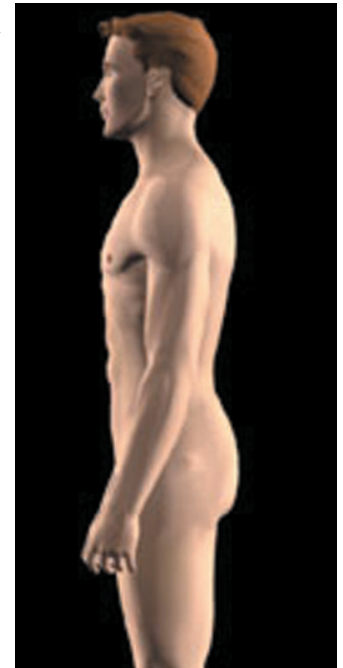
Sensitive reliable prognostic markers are needed to identify those at risk of disease progression and to optimise treatment selection. Currently clinico-pathological factors are used to estimate clinical outcomes using 1) tumour grade (Gleason scoring), 2) tumour stage (Table 2) and

presenting PSA. Gleason summed scores of  $\leq 5$  have the best prognosis and Gleason 8-10 the worst with Gleason 6-7 being intermediate. Average 5-year disease free survivals are highest in T1-2 stage (75-95%) followed by T3 stage (50-70%), T4 (20-50%) and metastatic disease (<30%). PSA values of  $\leq 20$  are correlated with organ confined disease compared to values of  $>30$ . In addition, PSA values are used to monitor responses to therapy as well as to predict treatment outcomes as it precedes clinical evidence of disease recurrence.

In general the usefulness of these factors are enhanced when employed together. Various nomograms have been formulated to predict the extent of disease and likelihood of lymph node disease. Based on a large surgical series, Partin's Tables is one example of a nomogram that correlates clinical T stage, biopsy Gleason score and presenting PSA for prediction of final pathological stage. Newer factors currently being investigated include molecular staging using reverse transcriptase-polymerase chain reaction, markers of cell adhesion and proliferation/apoptosis, growth factors, DNA/nuclear content, tumour suppressor genes, and angiogenesis.

### Surgery

Men with good performance status presenting with early organ confined disease (T1-2, PSA<20)



and possessing a life expectancy  $\geq 10$  years are ideal candidates for radical prostatectomy. Clinical nomograms that estimate likelihood of early organ confined disease can help select appropriate patients for surgery.

Surgical technique has improved substantially. Identification of the dorsal vein complex has allowed radical surgery to be performed in a relatively bloodless field. Understanding of the urethral sphincter and modifications to the vesicourethral anastomosis has improved continence rates up to 90-94%. Sparing of the autonomic plexus to the corpora cavernosa has permitted preservation of sexual function in up to 70-80% overall but preservation of potency does depend on other factors such as preoperative status, age and stage.

Surgical biochemical PSA relapse-free rates for organ confined PC at 5 and 10 years range between 75-80% and 65-75% respectively demonstrating cures. Predictors of recurrence are adequacy of surgical margins, pre-operative PSA values as well as combination of pathological stage and Gleason score. Local recurrences postoperatively may be salvaged with radiotherapy.

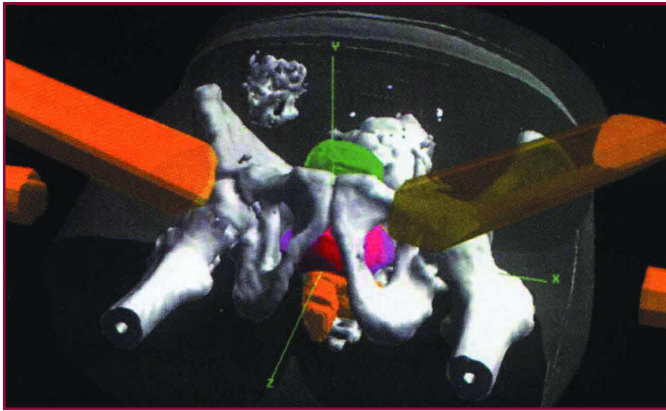


Figure 1 3D patient anatomy for CRFT



Figure 2 MLC housed in the linear accelerator shape radiation fields

## Radiotherapy

For early stage disease (T1-T2), radiotherapy (external beam and brachytherapy or interstitial/implantation methods) is effective and comparable in outcome to radical prostatectomy. For men with locally advanced disease (T3, Gleason 8-10, PSA>20) radiotherapy is more effective than surgery with actuarial 10 and 15-year survivals between 35-45% and 15-30% respectively.

In patients with localised PC, studies suggest a dose-response relationship implying improved outcomes can be achieved by delivering higher radiation doses to prostate (seminal vesicles). In order to maintain acceptable levels of toxicity, escalated doses should be delivered using conformal (CFRT)

or intensity modulated radiotherapy (IMRT).

Technological developments in computing, imaging and medical hardware has permitted CFRT and IMRT. Multimodality imaging with image fusion provides both structural and functional information for radiotherapy planning. CFRT uses 3D reconstructed images of the patient (Figure 1) to shape the high dose radiation volume to the prostate ± seminal vesicles to permit dose escalation and avoid unnecessary irradiation of normal tissues. Multileaf collimators (Figure 2) achieve automatic shaping. IMRT expands the concept of CFRT by enabling the high dose regions to be better shaped around 'concave' targets, increase sparing of normal tissues and allow selective boosting of tumour regions.

Randomised data has demonstrated that clinically relevant side-effects particularly rectal complications, which are dose limiting, can be halved using CFRT compared to conventional unshaped fields. Using IMRT, doses of up to 88Gy have been delivered with minimal side-effects and improved biochemical relapse free rates. Results from completed randomised and long term studies are eagerly awaited.

Whilst the mainstay of treatment for advanced and metastatic disease is androgen ablation, radiotherapy also has a role by providing local control of local-regional masses or bony deposits with symptomatic control in up to 70-80% of cases. Management for these patients can be complex and needs to be individualised.

### Table 1 Age adjusted PSA ranges

Age (years)	PSA range (ng/l)
40 - 50	0 - 2.5
50 - 60	0 - 3.5
60 - 70	0 - 4.5
70 - 80	0 - 6.5

### Table 2 T Staging for prostate cancer

T stage	Description
T1	Not palpable or visible
T2	Confined within the prostate
T3	Through prostatic capsule or involvement of seminal vesicles
T4	Invasion of adjacent structures