

# Management of early prostate cancer

## Introduction

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Prostate cancer is the most common cancer in men in the UK (24%) and has a death rate second only to lung cancer (13%) (Cancer Research UK). Incidence of prostate cancer has risen sharply over the last 20 years whereas mortality has only increased slightly. Prostate cancer is more common in older men and has a variable biologic course; therefore a gap between incidence and mortality has always been present due in part to death from intercurrent illness. Although factors such as improved treatment or changes in prostate cancer definition and coding may be responsible for the current rising discrepancy between incidence and mortality, increased uptake of prostate specific antigen (PSA) screening may play a role at detecting cancers that may not have become clinically significant.

PSA screening means that a prostate cancer will often be discovered earlier in its clinical course. Once a prostate cancer is detected a management strategy must be defined. If the cancer is indeed detected early, there are a variety of management options available to patients. The choice of treatment depends on many factors both specific to the disease and on the patient's choice. The references given are intended predominantly to lead the reader to more detailed review articles and overviews.

## Learning objectives

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The activities and content of this module are based around the following learning objectives:

- To understand the detection of prostate cancer and the concept of prostate cancer staging
- To explore the arena of PSA screening and form an opinion on its value
- To gain practical skills in prostate localisation
- To gain an awareness of the different treatment modalities for early prostate cancer and explore the different treatment decisions that a patient can make

This module is designed to give a broad overview of early prostate cancer and to lead the reader to more detailed texts to gain greater understanding. This module aims to show the reader how decisions are made in early prostate cancer management with the use of activities, examples and a discussion forum.

## Prostate cancer screening

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The first available screening test for prostate cancer was the digital rectal examination (DRE). When the posterior wall of the rectum is palpated by a finger, a cancer arising in the peripheral zone of the prostate may be detected. Whilst the majority of prostate cancers develop in the peripheral zone of the prostate, a prostate cancer may be quite advanced by the time it is palpable by a physician's finger, giving the DRE a low sensitivity. This test also has a low specificity with as little as one quarter of men with suspicious nodules on DRE having positive biopsies for cancer [though this could also reflect a low sensitivity on the part of prostate biopsies!] (Bullock & Andriole, 2002)

PSA is a serine protease secreted by epithelial cells lining the ducts of the prostate gland. PSA can be detected in the bloodstream of all men but is found in higher concentrations in men with prostate cancer. The exact cut-off for the normal range of PSA is disputed with more weight

now being given to observing trends in PSA values with PSA doubling times and velocity likely to yield more useful information in the screened population. PSA testing has a relatively high sensitivity but a low positive predictive value resulting in many biopsies taken in men who do not have cancer. Blood tests to detect PSA are widely available and uptake of prostate cancer screening is higher than that of colorectal cancer screening despite more evidence that the latter decreases mortality from the disease (Bunting, 2002).

National guidelines regarding the value of prostate cancer screening vary. In the US annual DRE and PSA screening is recommended by most authorities. In the UK, current guidance is that PSA screening is not justified and PSA testing should only be undertaken after full counselling of the implications of a positive test. In Canada PSA screening is recommended in those at higher risk of developing prostate cancer. There is some evidence that screening may decrease the proportion of patients presenting with advanced prostate cancer. However, there are probably a proportion of men who have prostate cancer detected by screening which would never have become clinically significant and are thus over-treated. The challenge is to detect these men at an early stage.

### **Activity 1 (allow 60 minutes)**

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**Task 1:** Develop your own opinion on prostate cancer screening

**Allow 30 minutes**

- Perform a PubMed search on PSA screening.
- Read a review article on prostate cancer screening.

**Task 2:** Review national and international guidelines on PSA screening

**Allow 30 minutes**

- Review NICE and RCR/BAUS guidance on PSA screening
- Review ACS guidelines for PSA screening

#### **Thinking Point:**

- Would you recommend PSA screening to a 50 year old relative?
- What about a 70 year old relative, or even an 85 year old relative?
- What risk factors would make you more likely to recommend screening?

### **Resources required to complete this activity**

#### **Useful websites**

Pubmed

[www.pubmedcentral.nih.gov](http://www.pubmedcentral.nih.gov)

NICE National Institute for Clinical Excellence

[www.guidance.nice.org.uk](http://www.guidance.nice.org.uk)

Royal College of Radiologists (RCR)

[www.rcr.ac.uk](http://www.rcr.ac.uk)

British Association of Urologic Surgeons (BAUS)

[www.baus.org](http://www.baus.org)

American Cancer Society (ACS)

[www.cancer.org](http://www.cancer.org)

## Background reading

Cancer statistics

Available at: [www.cancerresearchuk.org/cancerstats](http://www.cancerresearchuk.org/cancerstats) (accessed on 21/09/2007)

Bullock AD, Andriole GL. (2002) Screening for prostate cancer: Prostate-specific antigen, digital rectal examination and free, density and age-specific derivatives. In: Kantoff PW, Carroll PR, D'Amico AV, (editors). Prostate cancer: Principles and Practice. 1st ed: Lippincott, Williams and Wilkins.

Bunting PS. (2002) Screening for prostate cancer with prostate-specific-antigen: beware the biases. Clinica Chimica Acta. 315: 71-97.

## Prostate cancer staging and localisation

Various staging methods for prostate cancer are available. Generally these divide patients with prostate cancer into risk groups depending on clinical characteristics. One definition of prostate cancer risk groups is given in table 1.

Risk Group	T stage	Gleason Score	PSA value (ng/ml)
Low	T1-2a	≤6	<10
Intermediate	T2b-2c	7	10-20
High	T3a	8-10	>20
Very High	T3b-T4		

Table 1: Table to demonstrate prostate cancer risk groups (NCCN Practice Guidelines in Oncology, 2007)

The prostate can be imaged using a variety of modalities. The most accessible method is trans-rectal ultrasound imaging (TRUS). This is quick, easy and widely available. It also has the advantage of allowing easy guidance for biopsies or treatment. However, TRUS does not provide much information on the structure of the gland or of location of the cancer within the gland.

The prostate can be imaged using computed tomography (CT) but it is difficult to ascertain the position of the apex and base using CT imaging and the internal gland architecture cannot be easily defined. Magnetic resonance imaging (MRI) using an endo-rectal coil is the gold standard for prostate imaging. The apex and base can be clearly defined, the peripheral zone can be defined and extension of the cancer outside the prostate capsule or into the seminal vesicles can be determined with relative accuracy. The location of the cancer within the gland may be visible on MRI but more dynamic imaging modalities such as MR spectroscopy may delineate the cancer more clearly.

## **Activity 2 (allow 30+ minutes)**

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### **Task 1: Reviewing images of the prostate**

Look up [www.prostadoodle.com](http://www.prostadoodle.com) and review CT and MRI images of the prostate.

This website will also teach you post-brachytherapy implant contouring of the prostate gland.

### **Treatments for early prostate cancer**

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There are a variety of treatments available for early prostate cancer. The choice of treatment may be dependant on factors specific to the disease, such as Gleason score or PSA velocity or on factors specific to the patient such as age or prostate gland volume. Many patients will have a choice of management strategies available to them and will be able to choose a strategy based on what most suits their lifestyle and their individual approach to life. However, this makes randomised trials of management strategies in early prostate cancer difficult to recruit for since many men have strong views about which approach best suits them. With careful patient selection, these different treatment approaches should have a disease specific survival of 90% or greater.

#### **Active surveillance**

Active surveillance with selective delayed radical treatment should not be confused with watchful waiting. The watchful waiting approach delays treatment until a patient becomes symptomatic, usually with metastatic disease. When compared to radical prostatectomy, watchful waiting results in a higher incidence of local progression and distant metastases with increased mortality (Bill-Axelsson et al, 2005). In contrast, active surveillance is a policy of carefully selecting patients on the basis of their PSA profile and histopathology and following them up intensively with regular PSA screening and repeat TRUS biopsies of the prostate. There are strict criteria for intervention if there are signs of disease progression. While there is no randomised phase III data for this approach yet, phase II trials show favourable disease free survival results with up to two thirds of patients avoiding active treatment for prostate cancer.

#### **Radical prostatectomy**

Radical prostatectomy (RP) remains the gold standard for early prostate cancer treatment. Open RP is the treatment modality with the longest available follow-up data. RP can also be performed laparoscopically or with robotic guidance. RP is most suitable for younger men with a life-expectancy over 10 years and minimal co-morbidities. RP has the benefit of decreasing the PSA to virtually undetectable levels which more anxious patients may find desirable. RP does carry some risk of side-effects. There is a small risk of operative mortality (approximately 0.5%) which is significant in a cancer which may have remained indolent through the patient's lifetime. There is a risk of impotence which may be lessened by nerve-sparing surgery in selected patients. There is a risk of urinary incontinence approaching 5% which may be lessened in experienced hands. Unlike radiotherapeutic techniques, RP does not carry a second cancer risk which may be important in younger men.

#### **Brachytherapy**

Brachytherapy is the treatment of prostate cancer with radioactive isotopes. These can be temporary high dose rate (HDR) or permanent very low dose rate (vLDR). The technique with the longest follow up to date is vLDR implantation of Iodine-125 or Palladium-103 seeds. The seeds are commonly placed using TRUS guidance but can also be placed with improved gland definition using CT or MRI guidance. Suitable patients have a relatively low gland volume, usually below 60 cc, with no or minimal obstructive urinary symptoms.

Brachytherapy does not carry a risk of urinary incontinence but some patients may require a temporary urinary catheter following the procedure, more commonly in patients with a higher gland volume pre-implant. The risk of impotence may be lower with brachytherapy, particularly if the dose to the penile bulb and neurovascular bundles can be minimised. In contrast to that following surgery, impotence secondary to brachytherapy often responds well to oral potency agents such as Viagra. There is a risk of rectal bleeding which increases as the gland volume increases. The risk of second cancers following brachytherapy appears to be low, though further long-term follow-up is needed. Following brachytherapy patients may experience a PSA “bounce” which can be a cause of anxiety to patients until the PSA drops again.

### **External beam radiotherapy**

External beam radiotherapy (EBRT) can be used alone or with hormonal therapy to radically treat early prostate cancer. The treatment course may range in duration from 4 to 9 weeks depending on the overall dose administered and the dose fractionation scheme chosen. There is data to support a role for dose escalation using EBRT, especially in early prostate cancer. Some series of EBRT show lower survival data than surgical or brachytherapy series but these may be biased due inclusion of patients with co-morbidities making them unsuitable for operative modalities in the EBRT series in addition to patients with more adverse features in whom a strategy incorporating EBRT and 6 months of hormonal treatment may be preferable.

EBRT carries a similar risk of impotence to RP, though again, oral potency agents are likely to be more successful in EBRT patients than RP patients. There is no risk of incontinence and very few patients will require a catheter during or after radiotherapy. There is a risk of rectal bleeding which increases with increased total dose though there is evidence that greater conformation of the radiotherapy to the prostate results in a lower incidence of rectal bleeding (Dearnaley et al, 1999). The second cancer risk following EBRT is a consideration, particularly in younger men with predicted survival over 15-20 years from radiotherapy.

### **Other options**

Other available options for treatment of prostate cancer tend to concentrate on the treatment rationale of partial organ treatment with improved cancer localisation within the organ. The treatment approaches are in the experimental stages at present and rely strongly on the accurate localisation of the cancer within the gland which many investigators may feel is not possible at present with current imaging modalities and the multi-focal nature of prostate cancer. The most available focal modalities are cryotherapy, high intensity focused ultrasound, photodynamic therapy and localised radiotherapy. The current role for these therapies is more likely in the setting of disease recurrence following radical treatment, within clinical trials.

Hormonal therapy alone is also an option for early stage prostate cancer. This is not a curative option but may be a choice in men with a limited life expectancy due to competing co-morbidities and a rising PSA or unfavourable prostate cancer features.

## **Activity 3 (allow 30 minutes plus optional reading for 60-90 minutes)**

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**Task:** Clinical scenarios and management strategies

For this activity, you will consider some clinical scenarios and contemplate which management strategy you may adopt in each situation and what factors may make you change that management strategy. You may wish to read the review articles and overviews referenced for each modality title before commencing this activity. Bear in mind that there are no right answers to these scenarios but certain options may be preferable in certain situations.

**Patient:** Man aged 60, PSA 6, Gleason score 3+3

- What treatment would you recommend?
- How would this change if he was 70?
- What if he was 50?
- What if his PSA last year was 4?
- What if his Gleason was 3+4?
- Would you change your opinion if it was 4+3?

## Resources required to complete this activity

### Background reading

National Comprehensive Cancer Network. Prostate Cancer. Practice Guidelines in Oncology: NCCN Practice Guidelines in Oncology; 2007.

Available at: [www.nccn.org](http://www.nccn.org).

### Active surveillance

Klotz L. (2006) Active surveillance with selective delayed intervention for favorable risk prostate cancer. *Urologic Oncology*. 24: 46-50.

van As NJ, Parker CC. (2007) Active surveillance with selective radical treatment for localized prostate cancer. *The Cancer Journal*. 13:289-294.

Bill-Axelson A, Holmberg L, Ruutu M, et al. (2005) Radical prostatectomy versus watchful waiting in early prostate cancer. *New England Journal of Medicine*. 352:1977-1984.

### Radical prostatectomy

Potter SR, Partin AW. (2002) Surgical therapy of clinically localized prostate cancer: rationale, patient selection and outcomes. In: Kantoff PW, Carroll PR, D'Amico AV, editors. *Prostate cancer: principles and practice*. 1st ed: Lippincott, Williams and Wilkins.

### Brachytherapy

Heysek RV. (2007) Modern brachytherapy for treatment of prostate cancer. *Cancer Control*. 14: 238-243.

### External Beam Radiotherapy

Parker CC, Dearnaley DP. (2003) Radical radiotherapy for prostate cancer. *Cancer Treatment Reviews*. 29:161-169.

Pisansky TM. (2005) External beam radiotherapy as curative treatment of prostate cancer. *Mayo Clinic Proceedings*. 80: 883-898.

Dearnaley DP, Khoo VS, Norman AR, et al. (1999) Comparison of radiation side-effects of conformal and conventional radiotherapy in prostate cancer: a randomised trial. *Lancet*. 353: 267-272.

### Other options

Egger SE, Scardino PT, Carroll PR, et al. (2007) Focal Therapy for Localized Prostate Cancer: A Critical Appraisal of Rationale and Modalities *Journal of Urology*. Available online October 15 2007.

## Discussion Board

The discussion board is a forum in which you can exchange ideas with other participants. This activity relates to the work you will have completed in earlier tasks and provides an opportunity for you to explore the difference in perspectives between the participants.

### Discussion Board

#### When will it take place

For a 3 month period from date of publication of this article.

#### Which discussion thread

Management of early prostate cancer

#### What is expected of you as a participant

This module has provided an overview of the management of early prostate cancer. In particular, consider the following questions:

- What is the PSA screening policy where you practice?
- How do you manage patients with early prostate cancer?
- Are there other issues that affect how your patients with early prostate cancer are managed?

## Summary of this module

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By completing this module you should have a broad overview of early prostate cancer and understand how decisions are made in early prostate cancer management.

### On completion of this module you will have had the opportunity to:

- To understand the detection of prostate cancer and the concept of prostate cancer staging
- To explore the arena of PSA screening and form an opinion on its value
- To gain practical skills in prostate localisation through reviewing CT and MRI images of the prostate
- To gain an awareness of the different treatment modalities for early prostate cancer
- To explore the different treatment decisions that a patient can make

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