1 Introduction

Prostate cancer is a disease of ageing men for which the aetiology remains unknown. The incidence rises up to 30 to 40% in men over 80.

The symptoms of localised prostate cancer are indistinguishable from those of benign prostatic hypertrophy. The majority of men over 50 who present with symptoms now have a PSA test and increasingly the test is being done for screening in men without symptoms.

Since PSA testing has become regularly available, more and more men have been diagnosed with potentially curable localised prostate cancer and at an age where radical local treatment is appropriate. While many are referred for radical prostatectomy or external beam radiation using conformal techniques there are a number who are suitable for brachytherapy which has the potential advantages of convenience, effectiveness and relatively low morbidity.

2 Anatomical Topography

The prostate surrounds the urethra from the bladder base to its apex which is near to the external sphincter. The normal gland volume is 20 to 30 cm³.

The majority of tumours start in the peripheral zones of the prostate in the posterior and lateral regions. As the tumour grows it extends into and through the loose capsule of fibrous connective tissue which surrounds the prostate. This may also spread into the seminal vesicles and into adjacent pelvic nodes. The probability of finding disease outside the prostate capsule is related to clinical stage, PSA and Gleason grade.

3 Pathology

The vast majority of prostate cancers are adenocarcinomas. The degree of differentiation is described by the Gleason grading system. Grade 1 is the most well differentiated and Grade 5 the most poorly differentiated. Tumours are often heterogeneous and it is usual to give a combined score for the two most common appearances which varies from 2 to 10. The scoring has a good correlation with outcome; low grade tumours with a Gleason score of 5 or less have good survival with low probability of metastases whereas Gleason scores of 8 to 10 have a high probability of developing metastases within a few years of diagnosis.

4 Work Up

All patients should have
1. PSA.
2. Transrectal ultrasonography to assess volume and stage of the disease.
3. CT or MRI to stage pelvic nodes.
4. Bone scan if PSA greater than 10.
5. Transrectal ultrasound guided biopsy to obtain histological confirmation and Gleason score.
6. Evaluation of urinary outflow by International Prostate Symptom Score and measurement of residual urine and peak flow.

5 Indications, Contra-indications

5.1 Indications for brachytherapy

Patients should have a life expectancy of at least five years. The disease should be localised within the prostate capsule, ie stage T1 and T2. There should be no evidence of metastases in bones or pelvic lymph nodes. The prostate volume should be less than 50 cm³ in order to avoid interference with the pubic arch.

The most significant prognostic features are the presenting PSA, the Gleason score and stage. Patients with a PSA of less than 10, a Gleason score of 6 or less and stage T1C to T2A should do well with brachytherapy alone. Patients with a PSA of more than 20, a Gleason score of more than 8 and T3 disease do poorly and other treatments or additional adjuvant therapy may be indicated. Patients with a PSA of 10 to 20, a Gleason score of 7 and stage T2B to T2C have an intermediate prognosis.

5.2 Contra-indications for brachytherapy

Recent TURP is associated with a higher than usual risk of incontinence and the size of the cavity may also make it very difficult to achieve satisfactory seed placement. For those patients with benign prostatic hypertrophy and a gland volume of greater than 50 ccs but otherwise suitable, three months of neo-adjuvant hormone therapy often reduces the gland volume below 50 cm³.

5.3 Adjuvant hormone therapy

Adjuvant hormone therapy has been shown to be of benefit when given with external beam radiation for locally advanced prostate cancer but this has not yet been demonstrated for earlier disease treated by brachytherapy. Many patients however receive hormone therapy to reduce the volume of the gland before implantation.

5.4 Adjuvant external beam radiation

The risk of extra-capsular disease increases as the prognostic features worsen. For patients with Gleason scores of greater than 6 and PSAs of greater than 10 many have used this as an indication to use external beam radiation first with the seed implant given as a boost. In this case 45 to 50 Gy external beam radiation is followed by 110 Gy with iodine 125 and 100 Gy with paladium. There is no evidence yet, however, that this confers significant benefit.

6 Target Volume

The volume to be implanted includes the whole prostate within the capsule plus a 2 to 3 mm margin.
The volume is usually defined by transrectal ultrasound with the patient in the treatment lithotomy position. Transverse images of the prostate are taken every 5 mm from base to apex. Superimposed on the ultrasound image is a template matrix. The volume is defined on each ultrasound slice (Fig 20.1) and the images are entered into a dedicated treatment planning system which will determine the exact number and position of seeds required to deliver the prescribed minimal peripheral dose to the margins of the target volume.

Fig 20.1: Transversal endorectal ultrasound of the prostate from the base to the apex with delineation of the prostate capsule.

Where the volume is known accurately the positioning of iodine seeds can be performed interactively in a single step procedure with the aid of online ultrasonography and computer dosimetry.

7 **Technique**

7.1 **Permanent implants**

7.1.1 **Patient Preparation**

The rectum is cleared with an enema before implantation. General or spinal anaesthesia is used.
The patient is placed in the dorsal lithotomy position identical to that used for the transrectal ultrasound volume study. The transrectal ultrasound probe is inserted and attached to a stepping unit and template as for the volume study (Fig 20.2).

The patient is catheterised and 150 cm$^3$ of contrast introduced into the bladder. It is also helpful to place air filled gel in the catheter or urethra so that it is more clearly visible on ultrasonography.

### 7.1.2 Technique

The position of the patient and the prostate is checked with the pre-treatment ultrasound images to ensure that they are in an identical position. To prevent prostate movement two or three stabilising needles are inserted.

The distance from bladder base to template is determined. This is used as a reference for retraction of the needle tip from the base. The radioactive seeds are inserted through 20 cm long 18 gauge needles. These can either be preloaded or loaded with a Mick applicator once correctly positioned within the prostate.

![Ultrasonic template guided technique of seed implantation](image)

*Fig 20.2: Ultrasound and template guided technique of seed implantation: Stepper unit.*

For patients with a pre-plan, the loading pattern indicates the X and Y co-ordinates of each needle, the number of seeds in each needle and the retraction of each needle tip from the reference base plane. It is usual to start implantation with the anterior needles in order to minimise ultrasound interference during the course of the implant.

Each needle is inserted into the preplanned co-ordinate and advanced until it is visible in the ultrasound plane which is set to define the depth (Z co-ordinate). Once the needle is in position the seeds are
deposited in the prostate and the needle withdrawn. A record of each needle inserted must be kept during the implant procedure.

Once the implant has been completed the coverage of the prostate can be checked both by ultrasonography and fluoroscopy. It is usual to keep back a few extra seeds to cover potential cold spots if they are identified. Cystoscopy can be performed at the end of the implant to remove any loose seeds but this is not absolutely necessary as they will usually pass spontaneously. The patient leaves theatre with the bladder catheter in situ and this is usually removed two to three hours later.

7.2 Removable implants

Brachytherapy can be delivered to the prostate with removable implants using implanted catheters afterloaded with Iridium. These are usually given in a number of high dose rate fractions.

The principles of transrectal ultrasound pre-planning and needle placement under ultrasound guidance are similar to those used for permanent seed implants. In the majority of techniques rigid needles are replaced by plastic catheters which are maintained in position by the perineal template. Because the range of radiation in tissue for iridium is so much greater than for iodine or palladium many fewer source trains are required and it is usual to use between 8 and 15 depending on the prostate volume. There should be at least 5 mm between the lowest row of sources and the rectum and the tip of the catheters need to be pushed well up to the bladder base to make sure that this is adequately covered. This can be ensured by cystoscopy which will demonstrate tenting of the bladder mucosa as the tip of the catheter reaches the base. It is possible to place catheters within the seminal vesicles if these are considered to be within the volume at risk.

On completion of the implant a CT is performed to demonstrate the position of the catheters and their relationship to the prostate capsule. This data can then be used to optimise the dwell position of the sources within the catheters so that the dose to the urethra and rectum can be minimised while at the same time ensuring adequate coverage of the tumour with a boost to sites of macroscopic disease if they are identified.

The tip of the catheters may move in relation to the bladder base between fractions and it is important that there is a means of ensuring accurate catheter position before each fraction. The vast majority of high dose rate removable implants are used as a boost after prior external beam radiation. Patients usually receive 45 to 50 Gy followed by implantation which can either be in a single fractionated course or by two separate implants.

8/9 Dosimetry; Dose, Dose Rate, Fractionation

Fig 20.3: Image assisted treatment planning in prostate cancer. Transverse ultrasound image showing the PTV, urethra and rectum delineated and the dose distribution in a LDR iodine permanent implant. Isodose levels are given for the prescribed dose of 140 Gy as well as for 250 Gy and 110 Gy (compare also Fig 5.13B and 5.16).
Permanent seed implants can be performed either with iodine or paladium. The half life of iodine is 60 days and 17 days for paladium. Both emit very low energy radiation (23 to 27 KeV) so that radiation protection is easily achieved.

The dose prescribed for iodine is usually 145 Gy at the periphery of the target volume and is 125 Gy for paladium. The dose in the centre of the volume is always higher but should be kept to 150% or less than the prescribed dose. This is usually achieved by reducing the number of seeds in the centre of the volume to achieve a modified peripheral loading pattern (Fig 20.3,4).

It is recommended that post implant dosimetry is performed to confirm that the planned dose has been delivered to the target volume. This is best described by measuring the D$_{90}$ which is the dose received by 90% of the target volume and the V$_{100}$ which is the volume that has received 100% of the prescribed dose (Fig 20.3).

**Fig 20.4: Post implant radiograph**

**Fig. 20.5 Treatment Plan for a removable HDR Iridium 192 prostate implant. The isodose lines indicate the dose per fraction.**
10 Monitoring

Patients can be discharged from hospital the same or the following day. The procedure is covered by a seven day course of antibiotics and the patients are encouraged to drink plenty. Voiding symptoms can be helped with an alpha-blocker.

11 Results

11.1 Results

Patients should be followed up regularly with PSA examination. It may take 12 to 18 months for the PSA to gradually achieve its nadir. In approximately 20% of patients there may be a benign rise in PSA at one to two years after treatment which then resolves spontaneously.

The probability of biochemical disease free survival is closely related to the prognostic factors. For patients with PSA less than 10, Gleason score less than 6 and stage T2A or less, 80% are free of biochemical progression at five years. For patients with Gleason score greater than 7 and PSA greater than 20, biochemical disease free survival is 30% or less at five years. There is also good correlation with implant quality as defined by the D90. Biochemical relapse can proceed clinical progression by three to five years. The usual mainstay of treatment for relapsed patients is hormone therapy to which 80 to 90% respond.

11.2 Side effects and complications

Temporary haematuria is common with very occasional clot retention. Patients should also be warned about perineal bruising. All patients develop urethritis which is mostly mild or moderate. This starts five or six days after implantation and may persist at a low level for six to nine months.

Approximately 15% of patients may go into acute retention which requires catheterisation. The majority resume normal micturition after 10 to 14 days but a few need a catheter for a few months. Surgical intervention should be delayed for as long as possible but if there are still obstructive symptoms after 12 months a transurethral incision or channel TURP can be performed. This is safer than a full TURP which carries a significant risk of incontinence.

Urethral stricture occurs in 4 to 5% of patients.
Proctitis occurs in 2%.

Approximately 30% of patients may become impotent but the vast majority respond to Viagra. The amount of ejaculate is often significantly reduced but infertility does not always result.
12 References