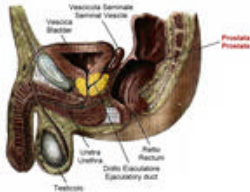
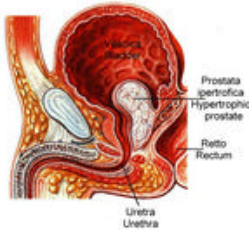


## THE PROSTATE GLAND



The prostate gland

The prostate is a male gland situated below the bladder, in front of the rectum and surrounds the urethra (the duct which allows the seminal liquid to flow out of the penis). The prostate produces part of the fluid which carries spermatozoa during ejaculation. The size and shape of the gland are extremely variable and in an adult man it is usually the size of a chestnut (20g).



A hypertrophic middle prostate lobe causes an obstruction in the urine flow

After the age of 40-45 the action of the dihydro-testosterone hormone mean that the prostate tends to increase progressively in size due to increase in the number of prostate cells. This phenomenon is known as benign prostate hyperplasia or BPH. BPH is not a malignant cancer and does not lead to prostate cancer. However as it affects the central part of the gland and puts pressure on the urethra, it can interfere with normal urinary function. The patient may therefore experience symptoms such as: weak urinary flow, a feeling of incomplete bladder voiding after micturition, an increase in frequency of urination and nocturia.

## PROSTATE CANCER

Under normal conditions, cells produce other identical cells to replace those which are damaged or functioning incorrectly. Neoplasm however is characterised by the uncontrolled growth of abnormal cells. Some tumours are benign (non-cancerous), however others are malignant and can invade and destroy an organ, also extending to adjacent organs or other parts of the body (metastasis).

The most frequent malignant prostate cancer is adenocarcinoma of the prostate.

**Under the age of 40 the risk of developing prostate adenocarcinoma is low but increases progressively with age.** A man has a 15% chance of developing clinically evident prostate carcinoma during his lifetime. The precise cause of this pathology is still unknown.

Recent epidemiological studies show that in the United States **prostate cancer is the most frequent male neoplasm** (244,000 new diagnosed cases in 1995 alone). This figure is continually increasing as the population ages and there is more use of PSA prostate-specific antigen in screening. Prostate cancer **still ranks as the second highest cause of death from tumours after lung cancer** (44,000 deaths in 1995 alone in the U.S.).

As in its early stages, prostate cancer is limited to the gland itself and generally characterised by slow growth, it **can be asymptomatic and remain undiagnosed for years**; in some cases it does not affect the quality of life or the life expectancy of patients even though they remain untreated. **Some prostate cancers however can be very aggressive** and spread rapidly to other parts of the body (particularly the lymphnodes and bones). In these cases, an early diagnosis and the right treatment can be crucial. Unfortunately, with the current level of scientific knowledge, it is not possible to know with certainty whether a prostate tumour will be aggressive or not. Therefore once the prostate cancer is diagnosed, the option is almost always for therapeutic treatment, although inevitably as a consequence this results in the treating of tumours which would not have otherwise impacted on the life expectancy of the patient.

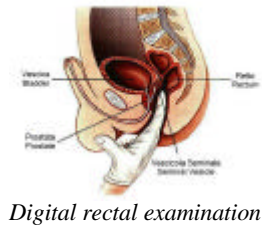
In the U.S. about 20% of subjects with clinical or apparent diagnosis of prostate cancer die despite receiving specific therapy. In Sweden, where prostate cancer is not treated with curatively, 55% of the patients die of the disease. This data highlights that an **early diagnosis and the right therapy mean most patients can be cured and the specific death rate considerably reduced**

Given that all cancer therapies need to be not only effective and well-tolerated, but also ensure an adequate quality of life, **there is a growing interest in the scientific community in other therapies which yield the same results as surgery but with fewer complications and side-effects.**

**AN EARLY DIAGNOSIS OF PROSTATE CANCER**

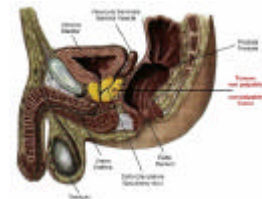
An early diagnosis and the right therapy mean that most patients with prostate cancer can be cured. Unfortunately, most of these patients do not have any symptoms.

**Digital rectal examination**, which for years has been the only diagnostic technique, reveals changes in the consistency of the prostate tissue and therefore a diagnosis of tumours at later stages. It **does not find the majority of tumours at an early stage of growth**.



Digital rectal examination

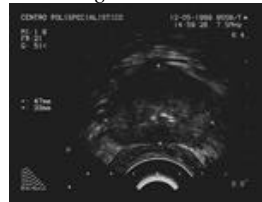
**PSA (prostate-specific antigen)** is a glycoprotein normally produced by the prostate gland. Its concentration in the blood **greatly increases when glandular structures are damaged (prostate cancer, infections, benign prostate hyperplasia)**. Currently the measurement of PSA allows an early diagnosis of prostate cancer. Using PSA means that approximately **70-80% of tumours are diagnosed whilst the disease is still organ-confined** (compared with 20-30% before PSA). This is important as using the most effective therapies about 80% of patients with localised carcinoma can be cured.



Non-palpable tumour

Recommended screening includes PSA measurement and a specialist urological visit every year from the age of 50. Subjects with a family history of prostate carcinoma should enter the screening program at 40.

Prostate gland:



Transversal ultrasound section

**Traditionally a value of 4.0 ng/ml is considered the maximum normal level for PSA. As 20% of patients with a diagnosis of prostate cancer have a PSA value below 4.0 ng/ml, the maximum accepted value in younger subjects below age of 50 (where an early diagnosis and aggressive treatment could be most effective), is now 2.5 ng/ml. On the other hand 70% of subjects with a PSA value above 4.0 ng/ml do not have prostate carcinoma. PSA is an extremely sensitive but unspecific tumour marker. To increase diagnostic accuracy, an urologist can use various parameters: annual PSA increase (PSA velocity), PSA concentration as opposed to gland volume (PSA density), PSA related to the patient's age and the amount of free PSA (which is lower in patients with carcinoma than in patients with benign tumour).**

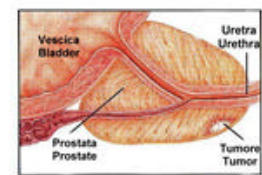


Longitudinal ultrasound section

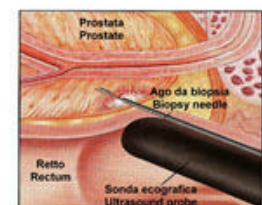
Risk of prostate cancer related to PSA levels	
PSA <= 4,0 ng/ml	5%
PSA between 4,1 ng/ml and 9,9 ng/ml	25%
PSA >= 10 ng/ml	55%

**The value of PSA alone is not diagnostic. To reach an accurate diagnosis of prostate carcinoma further tests such as transrectal prostate ultrasound and ultrasound-guided prostate biopsies are necessary.**

**Prostate ultrasound** is performed by introducing an ultrasound probe into the patient's rectum. Using this method the morphology, the size and the structure of the gland can be evaluated however it is not very sensitive in the screening of tumours. In particular ultrasound **allows** a very thin needle to be guided very precisely inside the gland **to perform multiple biopsies** (removing tiny tissue samples to be used for histological examination).



Combining the information obtained from PSA and the histological outcome of prostate biopsies, as well as of the digital transrectal examination and transrectal ultrasound, **the Specialist must identify patients with clinically localised tumours who are suitable for curative treatment.**



**PROSTATE CANCER STAGING**

When choosing treatment for patients with prostate adenocarcinoma, although factors such as age, and state of health need to be considered, the overriding consideration is the spread (or stage) of the disease. Means of determining the size of the tumour are digital transrectal examination, PSA values and the histological grade (differences between cells from normal ones). Sometimes radiological diagnosis and pelvis lymphadenectomy are also used.

**Nomograms which correlate the results of transrectal digital examination, PSA and histological grade, quantify the probability of the pathology being organ-confined or not.** (Partin Tables, Roach III formula)

<http://www.prostatepointers.org/prostate/software/pa.html>

**Computerised tomography (CT) and Nuclear Magnetic Resonance (NMR)** are not routinely used due to their low sensitivity in assessing the localised spread of the disease and the presence of metastases. **They are however suggested for patients who are at high risk of no longer having localised carcinoma** (based on the findings from transrectal digital examination, PSA levels above 20 ng/ml or a histological result showing a very aggressive form).

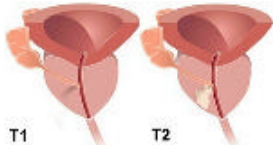
**A bone scan** (to detect possible bone metastases) **is advised for patients with a starting level of PSA above 10 ng/ml.**

**A staging pelvis lymphadenectomy (either laparoscopic or surgical) is indicated where there is a strong suspicion of lymphnode metastases** (based on CT, NMR, PSA levels above 20 ng/ml, very aggressive prostate cancer or pathological transrectal digital examination).

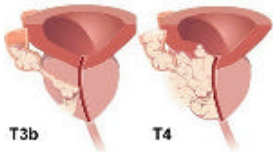
**To clarify the disease for patients the development of the prostate adenocarcinoma is divided into stages** based on the findings of the clinical examination, diagnostic imaging, blood tests and histological results.

### **CATEGORY T**

*Stage T1*: Tumour which is clinically non-palpable and not visible with diagnostic imaging diagnosed by needle-biopsy (performed for a high PSA) or discovered by chance through the histological examination of tissue removed during prostate surgery.



*Stage T2*: Tumour still confined to the prostate gland which does not exceed the capsule but has grown enough to become palpable at digital transrectal examination or visible with ultrasound or other imaging methods.



*Stage T3*: Tumour no longer confined to the prostate capsule (T3a) and/or has invaded the seminal vesicles (T3b).

*Stage T4*: Tumour has infiltrated prostate adjacent structures such as rectum or bladder, the external sphincter or the muscles of the pelvic wall. At this stage specific symptoms can appear.

### **CATEGORY N**

*Nx* Regional lymphnodes cannot be assessed

*N0* No regional lymphnode metastases

*N1* Metastases in regional node of nodes

### **CATEGORY M**

*Mx* Presence of distant metastases cannot be assessed

*M0* No distant metastases

*M1* Distant metastases

**PROSTATE TUMOR  
GRADING**

For each prostate tumour, it is necessary to evaluate the spread (stage) and **the "grading" or histological differences from normal (index for higher or lower aggressiveness of the pathology)**. This evaluation is performed on fragments of prostate tissue taken by biopsy. Normal cells have distinctive features which are lost in tumour cells proportional to the aggressiveness of the tumour.

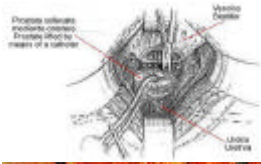
**There are several systems of cell grading; the most common is the summing of Gleason scores. This total ranges from 2 to 10. The lowest values (2-4) indicate a less aggressive disease with slower progression.** A score between 5 and 7 shows a mid range and a value between 8 and 10 indicates that that tumour cells are highly aggressive.

*In particular, the Gleason score total is given by two scores which identify the histological features prevailing in the preparation and the most aggressive states. Each feature is given a score from 1 to 5 where 1 stands for poorly aggressive pathology and 5 for very aggressive.*  
*.<http://comed.com/prostate/GleasonGrading.html>*

**TREATMENT OF  
LOCALIZED  
PROSTATE CANCER**

The choice of treatment for patients with prostate adenocarcinoma must take into consideration several factors such as the age of the patient and general state of health, but above all the aggressiveness of the disease. **When developing a treatment plan it is important that doctor and patient exchange information and discuss the advantages and disadvantages of any possible treatment.**

## SURGERY: RADICAL PROSTATECTOMY



*Retropubic radical prostatectomy performed by abdominal incision*



*Minimally-invasive surgical procedure in laparoscopy.*

**Radical prostatectomy (RP) is a major surgical procedure where the surgeon removes both the prostate gland and the seminal vesicles.** The operation is generally performed through a lower abdomen incision (retropubic RP). Other Authors prefer transperineal access (region between the scrotum and anus) or transcoccygeal posteriorly.

**RP is currently considered to be the "gold standard" in the treatment of localised prostate tumours thanks to the high cure rates obtained and the availability of long-term results** (patients operated over 15 years ago). These factors have made it the favoured therapy for young patients (whose numbers are increasing due to early diagnosis through the introduction of PSA).

**The perfecting of the technique and the diffusion of certain surgical procedures** (e.g. nerve-sparing or saving of neurovascular bundles) **mean that post-surgical complications have been considerably reduced** (at least in the reference centres). **However the frequency of these complications and their impact on the patients' quality of life mean that the selection of patients must be carefully made and they must be informed about the advantages and disadvantages of the method and its relative procedures.**

A few centres have been performing **laparoscopic RP** for a few years. This approach is minimally invasive but still requires long surgery times, even for expert laparoscopists. **It is however very interesting as it minimises some of the disadvantages of traditional surgery** (discharge, removal of bladder catheter) and promotes an earlier return to normal social and working life. It also has a lower level of intraoperative bleeding and fewer infections.

**The survival rates after radical prostatectomy for localised prostate cancer (free from biochemical progression measured by PSA increase) at 5, 10 and 15 years are 83-94%, 53-91% and 40-57% respectively. Tumour grading and preoperative PSA are the crucial factors in oncological outcome.**

**Advantages:** it's a one-step procedure

the complete removal of the gland means:

- the whole tumour is removed from the body and therefore the patient is cured if the disease was confined to prostate
- easier follow-up after treatment. The availability of tumour pathological staging and undetectable PSA reduce patient anxiety at check ups
- associated therapy of disorders caused by prostate hypertrophy

availability of long-term (15 years) results

low costs compared to BT

**Disdvantages:** it's invasive, major surgery

hospitalisation required (6-14 days)

longer anaesthesia than for BT

bladder catheter in situ for 5-14 days

slower return to social and working life (4 weeks)

risk of complications and results highly dependant on skill of surgeon

risk of intra- peri- and post-operative complications reported by major International Centres: globally 7.5 - 18.5%

### **Risk of intra- and perioperative complications:**

operative death rate < 0.5 % and perioperative 0-1.5%  
bleeding requiring blood-transfusion 4-10%  
thromboemboliae 0.7-2.6%  
heart-vascular disorders 0.4-1.4%  
lesion of rectum walls 0.1-2%  
wound infection 0.9-1.3%

### **Risk of postoperative complications:**

sexual dysfunction (impotence) after nerve-sparing mono- or bi-lateral surgery 10-75% (related to age of patient , clinical and pathological stage and to surgical technique)  
minimal urinary incontinence (requiring 1 pad a day) at 18 months 6-17%  
severe or total urinary incontinence (requiring > 2 pads a day or implant of an artificial sphincter) at 18 months 0-12.5%

### **Conclusions - Indications**

**Radical prostatectomy can therefore be suggested for all patients with localised prostate adenocarcinoma and in particular to those with the following features:**

A life expectancy of less than 10 years

no contraindication to major surgery and/or anaesthesia

they have been informed about procedures and possible complications

young patients with aggressive disease (availability of results > 15 years)

patients with obstructions, as the prostate gland which is blocking the urine flow is completely removed

patients where the primary psychological objective after therapy, is undetectable PSA (generally patients whose diagnosis has been reached only after a long process with numerous biopsies and repeated PSA controls for border-line or fluctuating values)

**Radical prostatectomy is however not suggested for patients who:**

are relatively old

are at high anaesthesiologic and/or operative risk

are at high risk thrombo-embolic pathologies

have clotting disorders

are very keen to preserve normal sexual function and perfect urinary continence

need to make a speedy recovery and return to a normal social and working life

Radical prostatectomy is usually proposed as a mono-therapy. However in some cases, and for a variety of reasons, the Specialist may prescribe a neoadjuvant hormone therapy cycle before surgery.

## BRACHYTHERAPY - PERMANENT IMPLANT



Transperineal insertion of radioactive seeds into the prostate under transrectal ultrasound guidance

**Permanent brachytherapy (BT) is a form of radiotherapy where small capsules ("seeds" about the size of a grain of rice) containing radioactive sources (Palladium  $^{103}\text{Pd}$  or Iodine  $^{125}\text{I}$ ) are implanted into the prostate under ultrasound guidance. This is a minimally-invasive procedure completed in a single operative session lasting about 90 minutes.** The "seeds" are placed in the prostate by means of needles inserted through the perineum (region between the scrotum and the anus).

The ultrasound probe and the needles are extracted after the procedure.

Each "seed" releases a small quantity of radiant energy to a limited region of prostate tissue. This **means the cancer can be treated with an extremely high irradiation dose without damaging adjacent structures**. After a few weeks, the "seeds" will have released most of their energy (time of effective treatment) and will then remain permanently in the patient's prostate in an inactive form and undetected.

The publication of oncological data obtained from patients treated with this innovative implant technique for localised prostate carcinoma has caused a great deal of interest in the scientific community. As a matter of fact **cure rates from the first series of patients treated about 12 years ago are comparable with those obtained with surgery (radical prostatectomy) and higher than results from conventional radiotherapy with external beams** (retrospective comparisons).

**Brachytherapy (BT) can be proposed as an alternative to radical prostatectomy in patients with clinically localised adenocarcinoma.** Each patient has his own particular clinical, physical and psychological features which lead the doctor to suggest the most suitable treatment for him (Brachytherapy, surgery or other forms of therapy for prostate tumour). The following list of the main advantages and disadvantages of this method can help the patient in the choice of treatment.

- Advantages**
- a minimally-invasive procedure which can be performed in day-surgery and in a single step
  - shorter anaesthesia times (about 90 minutes)
  - little or no bleeding
  - very low risk of thrombo-embolic complications
  - removal of the bladder catheter within 24 hours from surgery
  - rapid return to a normal social and working life (in a few days)
  - risk of urinary incontinence 1%
  - in 50-90% normal sexual function is preserved (dependent on age of patient)
  - risk of infection: rare
  - high irradiation doses to prostate whilst sparing adjacent structures
  - oncological results at 12 years comparable with major surgery and superior to conventional radiotherapy with external beams
- Disadvantages**
- no long-term oncological results (15 years after surgery) are presently available and this limits indication in younger patients
  - irritative symptoms on voiding for a few weeks and sometimes up to three months after implant (these can be easily controlled with suitable medical treatment):

increased frequency and nocturia 40% of cases  
acute urinary retention with contemporary bladder catheter 6,5 - 15%  
chronic urinary retention requiring surgical clearing with higher risk in obstructed patients 2,6%

does not allow simultaneous treatment of disorders related to a possible condition of associated prostate hypertrophy

fluctuations in PSA values in the two years after implant can cause anxiety to patients

high cost of the radioactive sources for the health services

### Conclusions - Indications

**BT can therefore be proposed for all patients with localised prostate adenocarcinoma who:**

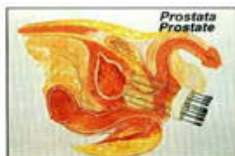
- are relatively old
- are young but with disease in a not so aggressive state
- are at high anesthesiological and/or operative risk
- are at high risk thrombo-embolic pathologies
- have clotting disorders
- require a rapid return to social and working life
- are highly motivated to preserve normal sexual function and a perfect urinary continence.

**BT is however not suggested for patients who:**

- are seriously obstructed (due to high incidence of disorders in the first three months)
- are very young (careful selection whilst awaiting oncological results at 15 years)
- who want undetectable PSA values after treatment to prove its efficacy

**Finally BT is proposed as a mono-therapy for localised prostate tumour with low risk of diffusion outside the prostate. In patients with middle or high risk of extraprostatic disease it is proposed in association with external radiotherapy.**

### BRACHYTHERAPY - TEMPORARY IMPLANT



*Transperineal prostate insertion with multiple catheters in temporary brachytherapy*

Temporary brachytherapy is form of radiotherapy, which like permanent brachytherapy, is characterised by its capability of administering high irradiation doses to well-defined target volumes and with limited involvement of adjacent healthy tissues.

**Compared with permanent implant where radioactive sources are implanted in the gland forever, here the radioactive source is temporarily inserted into the gland by means of thin catheters.**

Generally patients undergo transrectal ultrasound to decide the number and position of the catheters through which the radioactive source will be implanted into the prostate. The procedure is carried out under local anaesthetic or analgesic sedation. The catheters are then inserted with a transperineal approach (between the anus and the scrotum) under ultrasound guidance. At the end of the implant procedure, the patient undergoes a prostate CT to set out a treatment schedule. As planning is made after the catheters have been inserted, it is possible to optimise the treatment schedule if the catheters have not been positioned properly.

**The radioisotopes used for temporary brachytherapy are currently limited to Iridium 192 for high dose rate - HDR.**

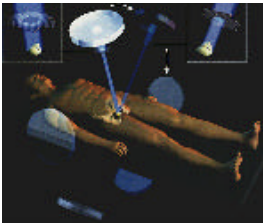


Catheters connected with afterloading device

Radiation **treatment** is carried out in a shielded bunker (to limit the operators' exposure to ionising irradiation) where an afterloading device (a system which loads the sources with a remote device) **can insert a single source (with lower costs) in the chosen positions**, and set the dwell time with a special software. **The procedure can be performed in day-surgery. There are a variety of treatment protocols with a variable number of sessions (ranging from 1 to 8 at weekly intervals) either as a mono-therapy or together with an external beam cycle.**

The higher energy of the Ir-192 compared to the sources used for permanent implants results in a wider dose coverage which is very welcome where there is microinfiltration outside the capsules. The higher energy levels and higher dosage rates (time during which the irradiation is released to the target) raise tolerance issues for healthy adjacent tissues, most of all the rectum. At the present time there are no long term oncological results for this form of Brachytherapy.

### EXTERNAL BEAM RADIO THERAPY



Radiotherapy with external beams

**Through the use of high-energy irradiation released by a linear accelerator, Radiotherapy with external beams damages the malign tumour cells irreversibly** resulting in necrosis (cell death). At a preliminary stage, a treatment simulation is made: the most suitable irradiation beams are studied to obtain high and homogeneous doses to the prostate gland **sparing, as far as possible, surrounding organs (rectum and bladder). The treatment sets out 10-minute daily applications, 5 days a week for a total of 78 consecutive weeks.**

**The irradiation of organs adjacent to the prostate causes the most notable and common short and long term side-effects affecting the genito-urinary and bowel tracts.** Early side-effects are an increase in frequency, nocturia (15% of severe level), burning, urgency, diarrhoea and rectal bleeding (10-15% of severe grade). Generally these side-effects first appear during treatment and are resolved, given application of adequate therapy, within three months of the start of treatment. In the longer term the following side effects can occur: serious radiation-cystitis with bladder contracture, chronic urinary retention (3%) urinary incontinence (2%) sexual dysfunction (40-70%) proctitis (6%) persistent rectal bleeding (< 1%) necrosis of phemur heads.

**From a technical point of view, radiotherapy for prostate tumours can be performed in different ways: conventional, 3D conformational and intensity modulated (IMRT). All the most recent studies show that the "dose" factor in radiotherapy plays an essential role in deciding the probability of patients being cured. The differences between the various radiotherapy techniques are in the dose they can release at prostate level and their ability to save the surrounding structures.**

#### Conventional radiotherapy:

the oldest technique and **the only method which has follow-up results over 10 years after treatment.** As it is used in a relatively wide sweep also involving prostate-adjacent structures, it does not permit the release of very high doses to the gland. **10 years after treatment, the survival rates for biochemical progression-free for localised tumours is about 50-60% (75% stage T1, 66% T2, 30% T3).**

#### 3D conformational radiotherapy:

A treatment which allows, as the therapy proceeds, for the progressive reduction of the irradiated target volume "conforming" it to the size of the prostate. This **allows for much higher dosages than with conventional RT, a greater sparing of surrounding structures and a reduction in side-effects (8% of proctitis, major urinary toxicity about 1%). However no data is available for patients treated for over 5 years.**

#### Intensity Modulated Radiation Therapy (IMRT):

**The most recent technique which should result in, through the use of special software and instruments, a better sparing of healthy tissues surrounding the prostate and for prostate irradiation with very high doses. Preliminary results are very interesting, even though the treatment is much more complex to perform and therefore has a potential margin of error higher than for the above techniques. As this method has only been recently introduced, follow-up is even shorter than for conformational 3D therapy.**

**Advantages & Disadvantages** Generally comparable with those of permanent Brachytherapy. For external radiotherapy no hospitalisation or anaesthesia are requested, although the patients must make hospital visits every day for over two months. Another factor which should not be overlooked is that the long-term oncological results of conventional radiotherapy are inferior to the results from brachytherapy and surgery whilst the follow-up for the most recent methods is too short.

## HORMONE THERAPY

**Prostate carcinoma is hormone-dependent. The main aim of hormone therapy is therefore to inhibit the production and to hinder the action of male sex hormones produced by the testicles (testosterone) and by the adrenals.** This results in a slower neoplastic proliferation and reduces the tumour size. **There are two ways to obtain an androgenic blockade: surgery and pharmacology.**

As most male sex hormones are produced by the testicles, their surgical removal (**orchietomy or castration**) means this can be achieved through a minor day-surgery. However **patients find surgical orchietomy difficult to accept psychologically.**

**Pharmacological castration ("androgenic blockade") is brought about with drugs** which inhibit the testosterone production by the testicles (analog with LH-RH) possibly together with drugs which antagonise the action of male sex adrenal hormones (complete androgenic blockade). **However this treatment is fraught with several side-effects** which are tolerated to different degrees by patients eg: hot flushes, loss of libido, sexual dysfunction and, in some cases, hepatic, cardiovascular or bowel toxicity and osteoporosis.

**The use of hormone therapy on its own to treat localised prostate carcinoma is limited to patients with a life-expectancy of over 10 years, who are unable to undergo surgery or radiation** or refuse these therapies. For patients with life-expectancy below 10 years (optional therapeutic treatment), it can have a significant use in controlling the obstructive symptoms associated with the pathology. The use of the hormone blockade is often suggested to patients where definitive treatment must be postponed. For shorter periods (a few months), this indication has no therapeutic meaning other than to reassure a patient anxious at the thought of starting therapy.

To conclude, hormone therapy can be suggested before and during a surgical or radiating treatment (**neoadjuvant treatment**) for localised tumours with risk of extracapsular extension. The final data from some international protocols, once available, should clarify its impact in terms of survival and quality of life.

## WAITING

**The watchful waiting approach consists of refraining from any form of therapy until clinical signs or symptoms of disease progression appear.**

Although it might seem difficult to take this approach where there is definite evidence of a malign pathology such as prostate adenocarcinoma, there is scientific evidence that **watchful waiting would be the most suitable strategy in patients with life-expectancy below 10 years who have small localised and well-differentiated tumours (which are not very aggressive).**

The majority of patients selected for this approach and with these features would die of other diseases rather than of prostate carcinoma. Doctors should accurately select patients before suggesting "watchful waiting": **in fact survival at 10 years in patients who are "thus treated" drops to 87% for well-differentiated tumours and to 26% in the most aggressive forms.**

Finally, the psychological profile of patients with malign tumours should not be ignored in view of a **possible anxious adverse reaction to a lack of treatment.**

## EXPERIMENTAL TREATMENTS

**Some centres are looking at other treatment strategies.** The aim of this is to reach oncological control of the pathology **with lower invasiveness and reduced morbidity.** **Although these techniques are extremely interesting, no middle or long-term results are available** and it is therefore impossible to assess their safety and efficacy. **These are therefore experimental protocols which can only be suggested in selected cases, for instance as salvage therapies after standard treatments have failed or when they are not suitable.** Cryotherapy and RITA (Radiation-induced thermoablation), which aim to destroy tumour prostate tissue by freezing or temperature increase, fall within this group.