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**BRACHYTHERAPY OR RADIOACTIVE SEED IMPLANTATION-REVIEW**

**INTRODUCTION--THE PROSTATE GLAND**

The prostate gland is located at the base of the penis just below the bladder and in front of the rectum. It produces the fluid that transports semen during ejaculation. The size and shape of the prostate gland vary considerably among men, but it is usually about two inches in diameter (roughly the size and shape of a large walnut).

**CANCER OF THE PROSTATE**

Prostate cancer, like other cancers, is a disease of the body's cells. Normal cells reproduce themselves by dividing--facilitating growth and replacing worn-out and injured tissue. Cancer is characterized by the uncontrolled growth of abnormal body cells. Occasionally, cells grow abnormally into a tumor mass. Some tumors are benign (noncancerous); others are malignant, or cancerous. Cancers invade and destroy nearby tissues and organs or spread to other parts of the body.

Prostate cancer is now the most common type of cancer in males. If not treated early and effectively, however, prostate tumors can start to grow and spread into other tissues such as lymph nodes and bone. Although only a small proportion of prostate cancers progress to this severe stage, the ones that do can spread relatively quickly and are not easily treated or cured. It is most commonly found in the outer portion of the prostate gland. The cancer can grow without symptoms for years, even decades. Prostate cancer is rare before the age of 40, and the risk increases with age. Its cause is unknown.

**GOALS OF PROSTATE CANCER TREATMENT**

Ideally, treatment for any cancer should cure the disease, be easily tolerated, and cause minimal or no problems. This concept is particularly important in prostate cancer for several reasons. Some men have an aggressive form of cancer that can lead to death from this disease. In other men, prostate cancers can grow so slowly that it causes few if any problems during a patient's natural lifetime. However, there is no absolute way to determine if prostate cancer will be aggressive or slow growing. Therefore, for most men whose disease is confined to the prostate, treatment is preferable to waiting and watching, especially since, as our life expectancies continue to increase, even slow-growing cancers could in time become life-threatening.

In other words, the ideal treatment for prostate cancer should effectively arrest or cure the disease particularly in men with aggressive cancer--but cause little, if any, problems--especially for men with slow--growing disease. Furthermore, since many men with prostate cancer are older or have other medical problems that make it impossible for them to undergo radical treatment, a treatment that minimizes trauma and complications is essential.

**HISTORICAL IMPLANTATION**

The idea of implanting radioactive substances into cancers can be traced to Thomas Edison at the turn of the century. Direct implantation into the prostate with radioactive gold was used modestly in the 1950s with marginal success. In the early 1970s, researchers at New York's Memorial Sloan-Kettering Cancer

Center began to implant radioactive iodine seeds (I-125) directly into the prostate, thereby providing internal radiation therapy exactly where it was needed. The term '**brachytherapy**' is the technical way of describing needle implantation. In these early attempts, surgery was performed to expose the prostate gland (which is known as open retropubic surgery) and the radioactive seeds were implanted by the surgeon, essentially freehand, without the aid of imaging techniques now available.

In the early 1980s the open freehand method was abandoned at Memorial Sloan-Kettering and other institutions because success rates were inferior to prostate removal or external radiotherapy techniques. However, in 1985 reports from Denmark showed that an ultrasound directed implant allowed more precise placement of I-125 seeds without an operation or an incision. Since then this new method has been used exclusively and allows very accurate placement of the radioactive agents.

In addition, other radioactive agents are now available, including radioactive palladium and iridium. Iodine and palladium appear to be well suited for prostate implantation. They give off very low energy radiation, or X-rays, that do not significantly travel outside the area of the prostate gland and pose little or no threat to patients or those in close contact with them. Iridium has much higher energy and its use is limited to shorter exposures in special hospital rooms.

### **WHO ARE BEST CANDIDATES FOR IMPLANTATION?**

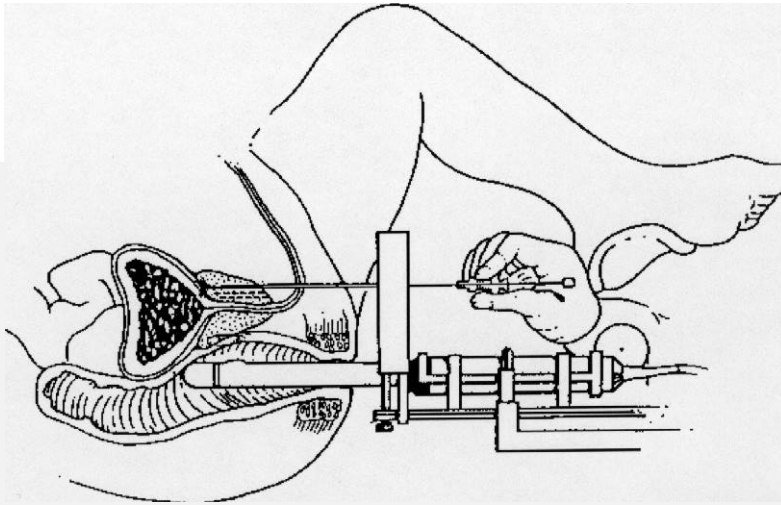
Patients with small prostate tumors localized to the prostate are the best candidates (Stages A and B or any T1 or T2, depending on the staging system used). That means that about **50-60%** of the patients with prostate cancer will fit this criteria. The development of more sensitive tumor detection techniques means that prostate cancer patients are being diagnosed at earlier stages, permitting more patients to become potential candidates for seed implantation.

### **WHO ARE POOR CANDIDATES FOR IMPLANTATION?**

Patients with very large prostate tumors which have extended beyond the prostate capsule or to other organs (Stages C and D or T3 and T4). Patients with very large benign portions of their prostate (**BPH** or benign prostatic hyperplasia) or patients who have had prior prostate surgery (**TURP** or transurethral resection of prostate) may be poor candidates for implantation.

### **HOW IS IMPLANTATION DONE?**

Tiny pellets containing radioactive medication, such as Iodine-125 or palladium are used. Seeds are permanently implanted directly in the middle of the prostate where they give off low-level radiation continuously for up to one year. Using TRUS (transrectal ultrasound) guidance, these seeds can be positioned so that radiation is distributed throughout the entire prostate gland. Since only a small area is irradiated by each seed, relatively little radiation reaches the adjacent normal organs-the colon, which is directly under the prostate gland, or the bladder, lying on top of the gland.



The implant procedure does not require a surgical incision. Instead, the seeds—smaller than grains of rice—are contained in thin needles which are passed into the prostate gland through the skin between the scrotum and rectum. As the needles penetrate through the prostate, they are seen on the screen of the ultrasound machine and can be accurately guided to their final position. While the needles are being inserted the ultrasound probe is in the rectum. When each needle is in its correct position in the prostate, the needle is slowly withdrawn and the individual seeds are injected into the prostate gland. The ultrasound probe and the needles are removed when the procedure has been completed. The numbers of needles and seeds required varies from patient to patient depending on the size of the prostate gland.

#### **Advantages:**

- Preliminary results from centers using I-125 and palladium since 1985 with selected patients shows a very similar disease-free intervals compared to radical prostatectomy and better than external beam therapy. The first implants were done 10-12 years ago so that long term numbers are just becoming available for analysis. 10 to 15 years of follow-up would be needed to have valid results.
- Seed implantation is normally done as an outpatient procedure taking about one hour to perform. The patient usually leaves the hospital the same day as the implant procedure or stays in the hospital for one night and then resumes normal activities within several days.
- Because they are placed at the site of the cancer, the seeds can deliver two to three times more concentrated radiation to the prostate gland than external radiation therapy, which must use a lower dose because it also affects healthy tissue.
- Incontinence occurs in less than 1% of patients who have not had prior surgery.
- Impotence occurs in less than 25% of patients under the age of 70. For patients over the age of 70, impotence occurs more often.
- This procedure is well suited to older patients because it is much easier to withstand than surgery or external radiation.

#### **Disadvantages:**

- There is little information yet on the effectiveness of the implant treatment after 10 years. While the current clinical data show good results through the first five to ten years, younger men are advised more strongly to consider radical prostatectomy.
- It is very common to experience problems with urination after seed implantation. These symptoms

will gradually decrease after 6 to 12 months.

## **The Radioactive Seed Implant: Before, During and After**

### **Before the Implant**

A volume study to determine the location and size of the cancer, will usually be performed about three weeks before the implant. Using a transrectal ultrasound unit, the urologist will locate your prostate and a computer will take several pictures showing the location and size of the cancer. These pictures will assist the medical physicist to determine the number of iodine seeds needed to treat the prostate and exactly where they should be placed.

Approximately one week prior to the implant, you will have blood tests done and possibly an electrocardiogram (EKG) and chest X-ray.

Your doctor will determine which tests are necessary. The test results are used to inform the anesthesiologist of your ability to tolerate anesthesia.

One to two days before the implant, you will be given specific instruction regarding diet and enemas. The enemas will help remove fecal material from your lower bowel and rectum so that the ultrasound image of your prostate will be clear.

### **During the Implant**

The radioactive seed implant procedure is performed in the operating room and lasts about 45 minutes to one hour. You will probably receive spinal anesthesia, leaving you numb from the waist down. You may also receive medication through an intravenous (I.V.) line, which will make you feel drowsy.

An ultrasound probe will be inserted into the rectum to image the prostate on a television monitor. The seeds, usually about 50-80, are then inserted into the prostate with the needles. The needles are inserted through the skin between the scrotum and the rectum and, with the transrectal ultrasound device, are guided with pin-point accuracy directly to the tumor sites. At the end of the procedure, a catheter is temporarily placed in your bladder to drain urine.

### **After the Implant**

After the implant you will go to a recovery room for about two hours, until you have regained the feeling in your legs. While in the recovery room you will have an ice bag placed between your legs to help reduce swelling of the implant area. The urinary catheter is usually removed when you have regained feeling in your legs. Occasionally, the catheter is left in overnight.

Since seed implants are generally outpatient procedures, you can go home after you have recovered from the anesthesia. Because you may feel a little weak, it is recommended that you do not drive for at least 12 hours.

You may resume eating and have visitors as soon as you wish, but you should avoid heavy lifting or strenuous physical activity for the first two days you are home. After that, you will probably be ready to return to your normal activity level.

### **Possible Side Effects**

There is surprisingly little discomfort after the implant, although mild soreness is expected between the legs for one to two days. If you do feel discomfort, your doctor can provide you with pain medication.

After the implant, you may experience some slight bleeding or burning beneath the scrotum, or blood in the urine. These side effects are caused by the needles used to place the seeds. The seeds themselves, the catheter and other instruments used during the procedure also can contribute to these side effects. It is normal for some blood to appear in the urine draining from the catheter, which may continue for several days. While this slight bleeding is no cause for alarm, if it should become severe or there are large blood clots, call your urologist. Drinking plenty of water helps prevent blood clots and flushes the bladder.

Some patients have difficulty urinating just after the implant and may need to have a catheter left in the bladder until the swelling from the implant subsides. Most patients are given special medications around the time of the implant to improve urinary flow (called alpha-blockers, such as Flomax, Cardura or Hytrin).

Other side effects that may occur after the implant, such as frequent or uncomfortable urination, are generally due to the radiation from the seeds in the prostate. These symptoms will gradually decrease as the seeds lose their strength within 6 to 12 months after the implant. Drinking plenty of fluids and avoiding caffeine may help to relieve these symptoms. As with all medical procedures, there is a small chance that there could be longer term, or even permanent, side effects. Your physician will discuss these risks with you.

### **Radiation Safety**

Many patients are concerned about whether an implant poses any potential dangers of radiation exposure to their family and friends. Iodine-125 and palladium (one of the radioactive materials used in seed implants) emit a very low energy radiation that does not travel far; in fact, the vast majority of the radiation does not go beyond the prostate itself.

Very small amounts of radiation, however, can reach other people either from a seed being passed in the urine or if a tiny amount of radiation escapes from the prostate and travels a short distance through the air. Because the amount that might escape is so small, it is not considered a risk for most people, and there are no restrictions on a patient's travel or physical contact with other adults. Small children and pregnant women, however, may be more sensitive to the effects of radiation. It is usually recommended that additional precautions be taken for these people when around the patient for the first two months following the implant.

### **Suggested Follow-Up Schedule**

After a seed implant, follow-up with your urologist and radiation oncologist should be done on a regular basis. Both physicians will work together to provide you with the best care possible. The follow-up schedule usually includes a visit every three to six months for the first five years, to check for seed placement and treatment progress. Physical examination, blood tests and transrectal ultrasound examination will be performed periodically.

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### **WHAT'S NEW:**

#### **BRACHYTHERAPY USING HIGH DOSE RATE AFTERLOADING WITH IRIIDIUM**

High dose rate remote afterloading brachytherapy involves the placement of an intense radiation source directly into or around a tumor for a brief period of time.

#### **High dose rate remote afterloading (HDRL) technique for prostate cancer works as follows:**

Under a spinal anesthetic, 15-25 small diameter, flexible plastic needles are inserted through the skin beneath the scrotum (the perineum) into the prostate. This is done with ultrasound guidance to help direct the placement of the needles. This procedure takes approximately 1-1 1/2 hours. The needles are fixed to the perineum by a plastic plate that is kept in place with temporary sutures. For most patients, the needles and template are only minimally painful and usually patients are more aware of the bladder catheter, which is placed during the procedure, and kept in place until the next day.

The process of planning the radiation treatment begins after the needle insertion. First, patients are taken to radiology where a CT scan of the prostate is obtained of the entire prostate. On each of these CT images, we identify the capsule of the prostate, the course of the urethra, and the position of the rectum. Each of the implanted needles are identified and numbered. This information is then entered into the HDR treatment planning system where we individually optimize the dose of radiation to the patient's prostate and tumor, taking into consideration the position of the patient's normal tissues.

Once the plan has been approved, the patient receives the first of three HDR treatments. They are taken to a special treatment room where each of the needles is attached to the HDR machine via connecting cable. The HDR machine is under computer control and transfers a very intense radioactive source to each implanted needle as determined by the dosimetry plan. The treatment is painless and takes approximately 5-8 minutes. The current protocol specifies the delivery of three HDR treatments. This is given **on** the **afternoon** of the implant day and the remaining two are given the day after in the morning and afternoon. Following the last HDR treatment, the template, needles, and bladder catheter are removed. Once the patient is able to void, he is discharged from the hospital.

The second phase of treatment is the delivery of external beam radiation. The intent of the external beam radiation is to deliver additional radiation to the prostate itself. This also has the added benefit of delivering additional radiation to the prostate and adjacent areas to ensure that any local extension of cancer is covered. The current protocol specifies 20 external beam radiation treatments given for a period of four weeks.

HDR therapy in the USA started 4-5 years later than seed implantation programs. Therefore, data from HDR treated patients is too early to determine how effective it might be, but early information is quite favorable.

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# Decision Tree for Brachytherapy

