



PROSTATE CANCER

High Dose Rate Brachytherapy Program



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Prostate Cancer

Prostate cancer is the most common cancer in American men. This year, almost 220,000 men will be diagnosed with prostate cancer. All men are at risk. After the diagnosis, a man and his family face several choices regarding treatment.



"When my doctor said, 'General, you have prostate cancer,' I was thrust into an immediate and fearful state of confusion. I can still recall my inability to move a muscle for what seemed like an eternity after hearing my diagnosis.

As I look back, I am thankful for the many resources available to me: my doctor's skill and the unwavering support of my family and loved ones. But another resource I am most thankful for was the availability of an abundance of information that helped me plan my own fight against this dreaded disease."

General H. Norman Schwarzkopf
U.S. Army (retired)
Commander in Chief
United States Central Command
Operation Desert Shield/Desert Storm

What are my options?

- You should discuss your diagnosis with your physician and your family.
- Your cancer stage, Gleason score, and PSA are important factors.
- Your choice will depend on your health and preferences.
- You may choose from observation, surgery, or radiotherapy.

Is HDR for me?

- This is an alternative treatment to radical prostatectomy, external beam radiotherapy, or permanent seed implantation.
- It is suitable for any localized stage disease (not metastatic disease).
- It may be useful in men with recurrent local disease after surgery or radiation.
- It is suitable for any Gleason score and most prostate sizes.

Pre-Implant Diagnostic Tests

- Blood work
- EKG
- Chest X-ray

Pre-Implant Preparations

- Discontinue Aspirin or NSAIDs (Ibuprofen, Naproxen, or Celebrex)
- Bowel preparation
- After midnight before your procedure, take nothing by mouth

Procedure Side Effects

- Mild to moderate urinary frequency and burning
- Increased intestinal gas and soft bowel movements
- Mild fatigue
- Most of these effects are temporary, and will subside within one month after treatment

External Beam Radiation (IMRT)

- Will begin from one to four weeks after HDR brachytherapy

Follow-up Schedule

- Rectal exams and PSA blood tests will be done regularly

Post-implant Medications

- Flomax or Hytrin may improve urinary flow
- Aleve or Celebrex are anti-inflammatories and can improve urinary flow
- Ciprofloxacin or Bactrim are antibiotics

Diet

- You may enjoy a regular diet after the treatment
- Keep your bowel movements soft. Colace, Metamucil, or other medications may help
- Drink plenty of fluids

Physical Activity

- Avoid strenuous physical activity for the first few days

Radiotherapy

The radiation therapy options for prostate cancer are divided into two categories: external beam radiation, such as three-dimensional conformal radiation therapy or Intensity Modulated Radiation Therapy (**IMRT**), and internal implants, also known as brachytherapy.

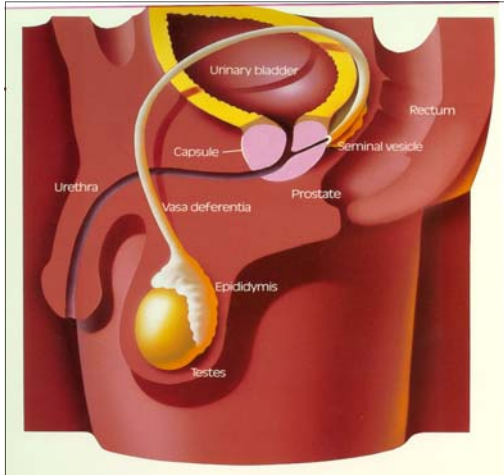
External beam radiation treatments have come a long way since X-rays were discovered in 1895. Modern X-ray treatment machines are called linear accelerators. Your physicians will use advanced computers to design a treatment that is specific to your cancer. These sophisticated machines enable your physicians to treat you quickly, painlessly, and precisely.

The best-known implant technique uses radioactive iodine (^{125}I) or palladium (^{103}Pd) seeds, which are permanently implanted into the prostate. On the other hand, high-dose-rate interstitial implant (**HDR**), uses a high intensity radioactive iridium (^{192}Ir) source. Your physicians will temporarily place an implant apparatus into and around the prostate. A computer-controlled robot called a remote afterloader houses the iridium source, and this machine is connected to the implant apparatus during your treatment. HDR brachytherapy is extremely precise, and can accurately match the size and shape of the prostate gland. HDR allows the radiation to conform to the prostate and tumor. This minimizes side effects because the surrounding normal organs receive minimal radiation.



Andy Grove (chairman of Intel) chose the HDR procedure after analyzing all the available forms of treatment, including permanent seeds. He made the analogy that this treatment was like a "smart bomb", whereas permanent seeding was a more crude "carpet bombing" treatment. He wrote about his experience in a Fortune Magazine Article in 1996.

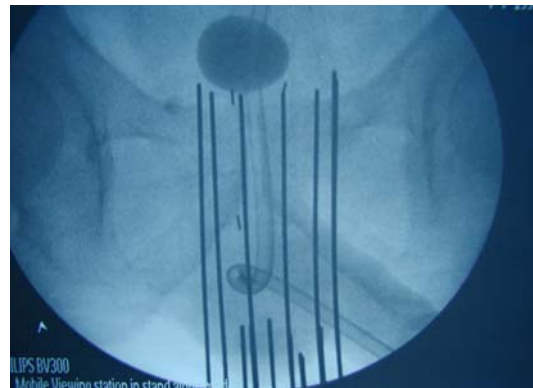
HDR Brachytherapy



HISTORY

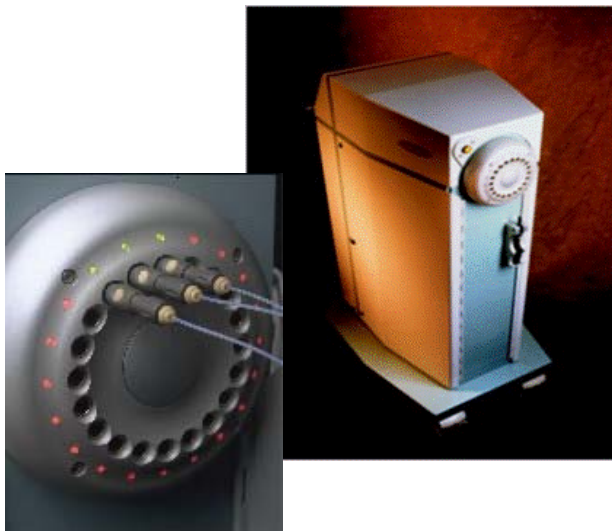
Cancer Care Consultants has been a leader in the field of radiation oncology. Prior to the development of HDR implants of the prostate, our center developed a large experience with low-dose-rate ^{192}Ir for the treatment of prostate cancer. The technique involved surgical implantation of hollow needles into the prostate, either by surgery (laparotomy), fluoroscopy, or by ultrasound guidance. After completion of the operation, the needles were hand loaded with "hot" radioactive iridium-192 ribbons. The loaded implant was left in place for approximately two to three days to irradiate the prostate gland. This technique allowed for near conformal treatment of prostate cancer. Treatments were combined

with external radiation therapy, and thus, the implant served as a radiation boost to the prostate. This technique was initially used in patients with locally advanced prostate cancer, which involved both lobes of the prostate gland (Stage T2b) or that had extended through the capsule of the prostate (Stage T3). The results of this treatment were superior to conventional external beam radiation therapy in patients with similar locally advanced stage. In our series of over 400 patients, a 75% local control rate was achieved, which was superior to conventional external beam radiation therapy, which could only claim a 35% local control rate.



However, this technique exposed nurses and physicians when caring for patients, so equipment was developed to remotely load radiation into patients.

It was called robotically controlled afterloading.



Initially, low-dose-rate radiation sources were utilized; however, with time high activity iridium-192 sources were developed and were used, which shortened treatment time from days to minutes. Since the 1980's, the HDR technique has been widely applied to the treatment of prostate cancer.

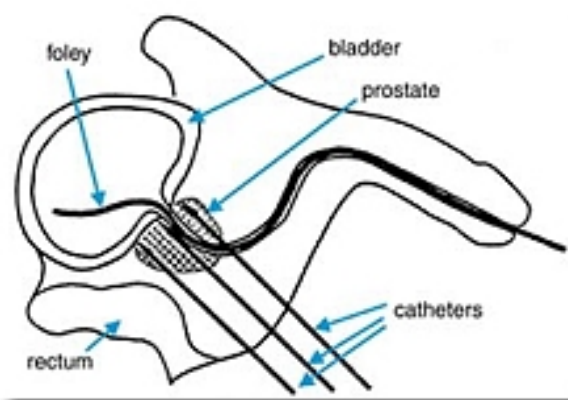
HDR TREATMENT

The HDR treatment begins with the surgical placement of the implant in the operating room under spinal or general anesthesia by an experienced surgical team, which includes a radiation oncologist and an urologist. The patient is placed in stirrups with the legs up, in the so-called lithotomy position. A special template is used which defines the placement and location

of the implant needles. It is placed against the perineum (the flat area between the scrotum and the anus).



Very tiny and flexible plastic catheters are placed through the template into the prostate gland. By using an ultrasound placed in the rectum, the physician can watch the placement of the implant. After the catheters have been implanted into the prostate (between 12 and 20), the template is sutured in place.

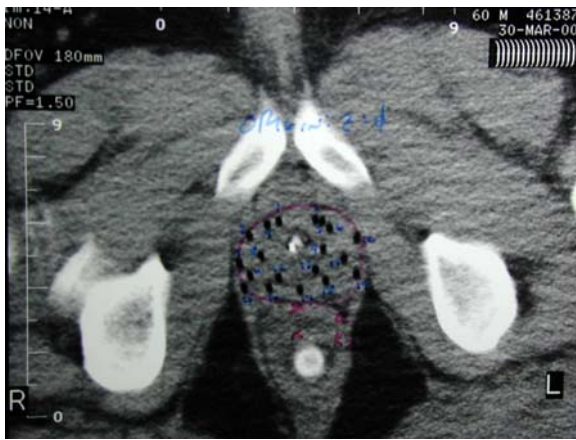


Then, a cystoscope is used to look inside the bladder, to confirm the location of the implanted needles. A

Foley catheter is left in the bladder during the treatment course. The procedure takes approximately one to two hours.

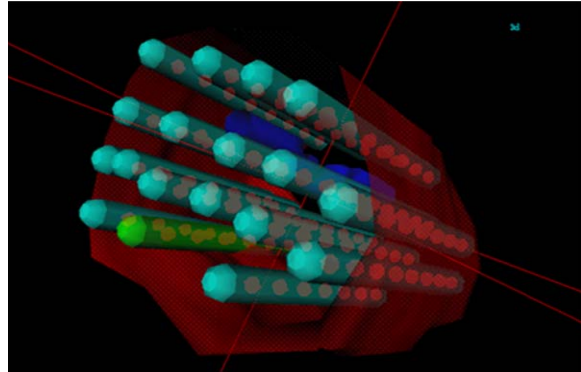
After the anesthesia wears off, there may be a sensation of the plastic catheters and plastic template against the skin. Medications will be provided to ensure comfort. The majority of patients find the procedure only minimally painful.

COMPUTERIZED PLANNING

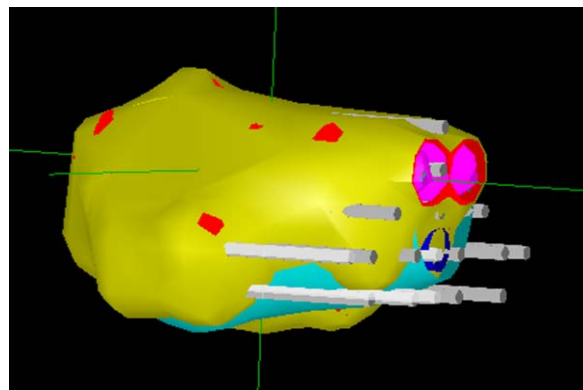


Next, a CT scan is obtained in 5 millimeter slices of the entire pelvis. This takes about 10 minutes and shows the prostate and the plastic catheters. This information is transferred to a special HDR treatment-planning computer. The dose of radiation can be targeted to the tumor in the prostate. High doses are given in three-dimensions to the prostate. This means that the dose is targeted to the tumor, and limits the

exposure to nearby organs (urethra, bladder, rectum). This minimizes side effects.



The dose is conformed to the prostate gland by adjusting the time the source remains within each position of each catheter. This allows the tumor to receive the highest dose. At the same time, we can ensure that the urine passage (urethra), bladder, and rectum will receive the lowest dose. In addition, areas within the prostate gland known to have tumor nodules can be given even higher doses by allowing the source to remain for longer time in those regions.



This ability to modify the dose after the catheters are placed is one of the

main advantages of temporary brachytherapy over permanent seed implants.

You will receive three treatments. For each treatment, you will be taken to the treatment room where the catheters will be attached to the HDR machine. This machine is computer controlled and will transfer a single powerful radioactive source to each catheter one by one. Although you will be alone in the treatment room, you will be constantly monitored with closed circuit TV and intercom.



A patient reads the morning newspaper during his treatment.

The process is painless and will take approximately ten to fifteen minutes. You will hear the afterloader click and whir as the source is directed into each of the catheters. At the end of the treatment, the source will be withdrawn into the afterloader. You will not be radioactive.

You will receive one treatment in the afternoon of the implant day, then you will go to your hospital room for an overnight stay. You may roll from side to side, but not sit upright as that would place pressure on the protruding ends of the catheters.

The next day, you will receive a treatment in the morning. Pre-treatment X-rays will be taken to verify that the implant has not moved overnight. This second treatment requires much less time because most of complex treatment-planning procedures will have already been done.

Six hours after the second treatment, you will receive the third and final treatment. Afterwards, the entire implant apparatus will be removed. Removal of the implant does not require the patient to return to the operating room. During the removal process, there may be some slight bleeding, which can be stopped by applying firm pressure to the perineal area with gauze pads. Most patients are able to go home within hours of the last treatment, and no radioactive sources will remain.

To complete the total treatment course, the patient receives four to five and a half weeks of external beam radiation therapy to the

prostate and extra-capsular tissues. The external beam radiation therapy begins from one to four weeks after the HDR implant.

HDR requires for surgery, anesthesia and hospitalization. In addition, although there are reports in using HDR alone as complete treatment, the current recommendation combines HDR with external beam radiation therapy for a complete treatment.



RESULTS OF THE HDR TREATMENT

Cancer Care Consultants has a large series of patients treated with HDR brachytherapy. As mentioned before, temporary implants are considered particularly effective in the treatment of locally advanced prostate cancer, where other techniques, such as permanent seed implant and conventional radiation therapy, have fallen short.

Our center has excellent results in terms of local control of the prostate tumor, with minimal short term and long term side effects. It should be noted that there are significant difficulties when comparing treatment results between various treatment methods, due to unequal distribution of prognostic factors that are known to determine outcome among patients.

These prognostic factors, that may vary when comparing one study to another include: PSA, Gleason grade, and clinical stage. That said, results of HDR as a boost for locally advanced prostate cancer appears superior to other treatment methods, such as conventional external beam radiation therapy and permanent seed implants. In addition, the results achieved are associated with among the lowest complication rates in radiation therapy. With HDR brachtherapy, there are risks of urethral stricture (usually less than 1%), incontinence (less than 1% in patients who have not received previous prostate surgery), and rectal problems (less than 1%). The risk of impotence is similar to other radiation treatment methods, and is in the range of 18% to 40%.

SUMMARY

HDR brachtherapy offers a flexible, conformal, and precise technique to deliver very high doses of radiation to the prostate with the lowest risk of side effects. HDR is applicable to early stage cancers, as well as advanced cases, with excellent results.



Who are candidates for HDR brachytherapy?

- Excellent alternative to radical prostatectomy, external beam radiation treatment, or permanent seeds
- Any localized stage disease (stages T1-T3b)
- Extra-capsular extension or seminal vesicle involvement
- Perineural invasion
- Any PSA value without evidence of metastatic disease
- Any Gleason score
- **Most** prostate sizes
- After prior transurethral resection of the prostate (TURP)
- Salvage treatment after recurrence of local disease

TEMPORARY vs PERMANENT SEED IMPLANTS

	<u>Temporary</u> ¹⁹² Ir	<u>Permanent</u> ¹²⁵ I, ¹⁰³ Pd
Stages treated	All (T1-T3)	T1 or T2
Symptom duration	Weeks	Months
Conformal treatment	++++	++
Accuracy of tumor targeting	++++	++
Ability to treat tumor beyond prostate capsule	++++	+
Ability to treat tumor in seminal vesicles	++++	++
Ease of radiation control	++++	++
Control of dose to surrounding normal tissue	++++	++
Radiation exposure to family members	No	Yes
Ability to verify dose prior to actual treatment	Yes	No
Need for transrectal ultrasound prior to treatments	No	Yes
Need for external beam	Yes (in present setting)	Sometimes
Ability to treat large prostates	Less difficulty	Can't be done
Need for hospitalization	Yes	No
Radiation dose known at the time of treatment	Yes	Not known until CT scan is done one month later
Ability to treat when a prior TURP has been done	Sometimes	Rarely
Ability to treat when pubic arch is narrow or tight	Yes	No
If procedure cancelled	Can reschedule	Treatment delayed to reorder seeds