CHAPTER TWELVE
BRACHYTHERAPY
Seed Therapy For Localized Prostate Cancer
And High Dose Rate Brachytherapy

By: Drs. Haakon Ragde, Gordon Grado, Frank Critz , Hamilton Williams and Stephen Doggett for seeds and Nisar Syed, Ajmel Puthawala and Aubrey Pilgrim for HDR

This chapter covers the seed implantation (SI) of radioactive pellets or seeds into the prostate. The temporary or High Dose Rate (HDR) procedure will also be covered. These procedures are very popular and there are several sites that perform SI and HDR. Some of the sites use procedures that are slightly different than others. However, they all seem to have similar success rates.

INTRODUCTION

Conceptually, the goal of treating a cancerous tumor anywhere in the body should be twofold: to cure the cancer and minimize negative impacts on quality of life. In the U.S. the mainstays of treatment for prostate cancer confined to the gland itself have been surgical removal and traditional external beam radiation. We believe that brachytherapy or seed implants is a good alternative to surgery or external beam radiation in selected patients.

WHAT IS PROSTATE BRACHYTHERAPY?

Prostate brachytherapy (also called seed therapy, seed implantation, or interstitial radiation) treats prostate cancer by placing radioactive seeds via needles directly into the gland. This allows the delivery of a highly confined dose of radiation directly to the prostate, sparing adjacent healthy tissue from radiation injury, and reducing side effects and complications.

"Brachy-" comes from the Greek word meaning "short" and is used to describe treatment with radioactive sources or materials placed at a short distance to the tumor in comparison to "tele-" (therapy) which refers to external radiation treatments delivered at a distance from the patient and the tumor.

In the late 1980's sophisticated computerized imaging and dosimetry techniques were developed. These techniques permitted correct radiation dose calculation and precise seed placements. Fig. 12-1 is a drawing of an ultrasound guided seed implant. The ultrasound probe is inserted in the rectum which provides visualization of the prostate and the seed placement. Fig. 12-2 shows a CT scan of a patient who has been implanted. Fig. 12-3 shows a computer and ultrasound probe. Fig. 12-3 shows the needle template or guide for seed implants. If you look closely in fig. 12-4 you can see a needle template or guide attached to the top of the ultrasound probe. Fig. 12-5 shows the ultrasound probe inserted into the patient.

In the mid 1980s, Palladium -103, (Pd^{103}) a radioisotope that promised a more aggressive attack on the cancer, became available for needle insertion. The first implantation with this radioisotope was performed by Dr. Ragde in 1987.

Most of the preliminary work-up is performed in a physician's office, and only the actual implant requires a surgical facility. In most centers today the procedure is performed on a cost-effective outpatient or overnight hospital stay, and most patients are able to resume their normal daily activities within 24 to 48 hours.

With a general consensus that PSA measurements after any form of prostate cancer treatment are the most effective way to detect persistence or recurrence of the cancer, no specific treatment method today can lay claim to long-term (15 year) results; the PSA assay has been in clinical use for fewer than ten years. In other words, results with prostate brachytherapy, surgery, and external radiation all are limited to fewer than ten years of PSA follow-up. Seven year data, using serum PSA determinations and repeat needle biopsies as determinants show prostate brachytherapy cure rates equal to the best surgical cure rates reported, but with fewer complications.

WHO ARE APPROPRIATE CANDIDATES FOR SEED THERAPY?

Seed therapy alone will only provide effective radiation to the prostate and a five millimeter-wide surrounding margin. In some patients, who have larger and more aggressive cancers, there is a risk of tumor spread beyond the prostate into the surrounding area. As a result, these patients are not good candidates for interstitial radiation alone. A combination treatment consisting of radioactive seeds and external beam radiation may better address the issue of this "possible locally advanced" disease.

WHAT DOES PROSTATE SEED THERAPY INVOLVE?

Consultation:

Seed therapy is a team effort, involving both a urologist and a radiation oncologist. They will review the patient's records, discuss the different treatments available, consider the complications and costs (quality-of-life costs as well as dollars-and-cents) associated with each treatment, so that the patient and his family can make the best decision based on age, health and life style preference.

Patient Evaluation:

A careful physical exam and review of the patient's records are performed to get a reasonable assurance that the cancer is confined to the prostate. Several additional tests may be required, such as CT scan (to look for evidence of cancer outside the prostate); Urinary Flow Study (a test that measures how well the bladder empties); Cystoscopy (use of an instrument to look inside the bladder and urethra to further evaluate bladder emptying).

A more detailed diagnostic ultrasound of the prostate may be required to evaluate the position of the prostate tumor in the gland, as well as to note any surgical cavity left from previous prostate surgery (such as a TURP).

Additional tests are usually required, such as routine preoperative bloodwork, chest x-ray, and an electrocardiogram. These will aid the anesthesiologist in determining the patient's ability to receive anesthesia.

Personalized Treatment Plan:

This step consists of making a geometric map of the prostate that is derived from an ultrasound scan. This map, also known as a "volume study", forms the basis for an individual patient's treatment plan and is key to a successful implant. It shows the exact volume and shape of the gland, as well as the proposed seed locations. The map is entered into a planning computer to construct a three-dimensional implant model. It also prescribes individual seed strengths, and specifies precise intra-prostatic seed positions, to make certain that the whole gland will be effectively radiated and that the adjacent healthy tissue is spared from radiation injury.

Depending on the width of the bony pubic arch or equipment limitation, prostate glands may need to be reduced before treatment. This may take two to three months, and is readily accomplished by medication that temporarily shuts off testosterone production, to inhibit the cancerous growth and simultaneously shrink the size of the gland. Without pubic arch obstruction we have implanted prostate volumes up to 210 cubic centimeters.

What Radioactive Sources (Seeds) Are Used?

Most commonly Palladium-103 and Iodine-125 (I^{125}) are used. Both are contained in tiny titanium casings which the body can tolerate long-term. Both types of radioactive seeds give off low energy X-rays, with most of the radioactivity released within a short period of time: Palladium 103 in 3 months, and Iodine 125 in 6 months. The main difference between them is the half-life and rate of radiation delivery. Although there is no clinical evidence that one is more effective than the other, some physicians prefer to use Palladium for more aggressive cancers, or select the radioactive isotope based on gland size or shape, or on the basis of past therapy or surgery.

After the seeds are inserted into the prostate they will remain there permanently. Since only a small volume of prostate tissue is radiated by each seed, many seeds have to be inserted to cover the entire gland. This is important because microscopic cancer cells may be present at different sites within the gland even though the biopsy in the general area may have been negative. The number of seeds implanted into the prostate for treatment may vary from 40 to well over 100, depending on the size of the gland.

Although the cumulative effect of the seeds results in high-dose radiation to the gland, the low energy and short tissue penetration of the radioisotopes protect adjacent normal organs and tissue from radiation injury.

Performing the Implant:

The actual implant is usually performed in a surgical facility and takes about an hour to complete. It is most commonly done under spinal anesthesia although general anesthesia may also be used, depending on the preference of the anesthesiologist and the patient.

An ultrasound probe with an attached template guiding device corresponding to the grid on the ultrasound screen, is inserted into the rectum. See figs. 12-3 and 12-4. Video-imaging from the ultrasound is used to guide the insertion of each needle through the perineum into its computer-designated position in the prostate. Each hollow needle may contain several seeds. The individual seeds are then ejected along the path of the needle as it is slowly withdrawn.

When the implant procedure is completed, proper placement is verified by taking an x-ray of the lower abdomen (Fig. 12-2). Before leaving the operating room, a catheter is placed in the patient's bladder to drain the urine.

The Recovery Room:

After the implant the patient will go to the Recovery Room, where he will remain until the effects of anesthesia have worn off. The catheter is usually removed within 24 hours, but it may sometimes be necessary to leave it in longer.

Follow-up Instructions:

Postoperative instructions, covering medications and appointments are given before the patient leaves the treatment facility. Generally there is very little discomfort after the implant, but pain medication is available should it be needed.

Radiation Precaution:

Palladium and Iodine are low energy radioactive isotopes. This means that most of the radiation is shielded by the prostate itself. What little escapes beyond the gland is insignificant and not considered a risk for most people. Small children and pregnant women, however, may be more sensitive to the effects of radiation, and intimate contact, such as hugging and sitting on the patient's lap, should be avoided for the first two months following an Iodine implant and for one month following a Palladium implant.

Short-term Side-effects:

Side-effects, consisting of some urinary frequency and urgency, and possibly some burning on voiding, are not unusual after the implant. They are caused by the radiation from the seeds in the prostate, and the symptoms may last from a few days to several weeks.

Long-term Side-effects:

Incontinence and impotence, the most dreaded complications associated with treatments intended to cure prostate cancer, occur less frequently after brachytherapy than following surgical removal of the prostate or traditional radiation treatment. The observed impotency rate after seed therapy depends on the patient's age: For those patients who were potent before treatment, and did not receive external beam radiation, those less than 60 years were still potent after treatment; for ages between 60 and 70 years, 20% had erectile dysfunction (ED); above 70 years old between 35 to 50% had ED.

There should be no incontinence if the patient has not had previous surgery of his prostate such as transurethral resection of the prostate (TURP).

CLINICAL RESULTS

As mentioned, PSA is a key indicator in monitoring response to treatment for prostate cancer. Elevation of PSA after treatment may indicate failure to eradicate the cancer, although it may also indicate the presence of metastatic disease. PSA levels may denote the presence of cancer several years before it can be detected on clinical exams. When the prostate is removed surgically, PSA in the serum rapidly decreases to undetectable levels. The radiated prostate, however, continues to produce PSA, but at very low levels.

Dr. Ragde's group in Seattle has reported on 229 consecutive (unselected) brachytherapy patients followed for 12 years. During that time period only 4 patients died from prostate cancer, yielding a cancer-specific survival rate of 98%. This compares favorably with prostate cancer-specific survival rates reported from surgical centers, which range from 83-98%..

In marked contrast to the treatment and recovery times required for surgery and external beam radiation, seed implantation is performed as a one-day outpatient procedure, or—in some cases—as an overnight hospital stay. Most patients are back to their usual daily activities in a day or two.

With a total price tag of about half the cost of a radical prostatectomy, seed therapy should provide substantial saving for patients and third party payers alike.

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Dr. Stephen Doggett's Protocol

Dr. Stephen Doggett practices in the Los Angeles area. He invited me, Aubrey, to observe the seeding of one of his patients. Fig. 12-5 shows the patient and Dr. Doggett preparing to do the seeding.

Before the seeding process a plan had been formulated. This plan was based on the clinical diagnosis and ultrasound images. Just before the seeding, he uses a sophisticated software program called an image registered intra-operative real time treatment planning (IRIRTP) for permanent seed prostate brachytherapy.

Under computer control, the ultrasound provides 5mm image slices of the prostate. The Interplant® IRIRTP from Burdette Medical Systems, Inc. allows the ultrasound images to be entered into the treatment planning computer. Optical probe registration permits precise localization of the ultrasound probe to the template and prostate. Prostate size is precisely documented and errors introduced by prostatic motion are mitigated. The treatment plan is then automatically generated in the operating room on a PC.

Automatic optimization minimizes operator input. Interplant IRIRTP allows real time, pre-implant, three- dimensional superimposition of translucent isodose surfaces over the prostatic anatomy for a simulated micro-dosimetric analysis of radiation exposure to any point in the prostate and surrounding structures.

During the pre-planning stage, Dr. Doggett had determined that he would use 84 PD^{103} seeds. The seeds were placed on the images in the computer. The computer then calculated the placement and dosage of each seed. This prevented any cold spots that were not getting enough radiation. It also calculated the amount of dosage that the urethra and rectal tissue would receive. These computer calculations allowed for the optimum placement of the seeds. Fig. 12-6 shows an ultrasound image of the prostate.

Some brachytherapists use long hollow needles that have been pre-loaded with up to 10 or more seeds. These needles are inserted into the prostate, and using

the ultrasound image, the seeds are then pushed out at specific areas as the needle is withdrawn.

Another system is to place hollow needles in the prostate at areas according to the plan. Fig. 12-7 shows a fluoroscope image of the inserted needles. They then use Mick applicator to insert the seeds. Fig. 12-8 shows a Mick applicator and the seeds housed in the small lead lined carrier. Fig. 12-9 shows the open seed carrier and the cartridges. Each cartridge has 15 seeds.

The cartridges mount on the Mick applicator as seen in fig. 12-10. The Mick applicator is attached to one of the hollow needles. A long thin wire is used to push a seed into place in the prostate. As the wire is withdrawn, another seed drops down and it is pushed into place. Each seed is placed according to the planned image on the computer screen. The entire procedure took about 45 minutes. The patient had been given a tranquilizer and slept through the entire process.

Burdette Medical Systems says that the Interplant IRIRTP is the first significant technological advance in prostate permanent seed brachytherapy in 15 years. Interplant® IRIRTP is designed to substantially reduce human operator input during the treatment planning process with its attendant error rate. Inaccuracies due to prostatic motion and size changes in the time between planning and surgery are mitigated.

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Radiotherapy Clinics of Georgia (RCOG)
By Drs. Frank Critz and Hamilton Williams
The physicians of the Radiotherapy Clinics of Georgia in Atlanta (http://www.prostRcision.com) have specialized in the treatment of prostate cancer since 1977, beginning the retropubic (open) implantation. When it became apparent in 1979 that the old style retropubic technique was ineffective in curing prostate cancer, Dr Frank Critz, founder of the clinic, began development of simultaneous irradiation, that is, prostate implant followed by conformal external irradiation. During the next 5 years the technique was refined, and in 1984 RCOG began a formal study of simultaneous irradiation which continues to this day.

In 1992, RCOG changed from the retropubic technique to the transperineal ultrasound guided technique. With the improved seed distribution allowed by the transperineal technique we were able to double the dose of radiation given to the

prostate with a greater margin of safety than could be achieved with the open technique. We now have treated more than 3000 men with prostate cancer with simultaneous irradiation, amassing the greatest amount of experience and results in the United States in the process.

While the approach of simultaneous irradiation, performing the implant first then using the seeds as a target for conformal external beam irradiation, made logical sense, it was when PSA was made available for clinical use in 1987 that its true value became apparent. Even in the 1990s, most physicians believed that as long as the PSA was within the normal range after radiotherapy, the patient was cancer free. However, Dr. Critz noted early on that men treated with simultaneous irradiation achieved PSAs not just in the normal range, but they achieved undetectable levels, the same as disease-free men achieve after surgery. Even more importantly, the overwhelming majority of men who achieved these undetectable levels remained cancer-free.

RCOG has pursued a consistent approach for men with prostate cancer since 1984: implant followed by simultaneous conformal irradiation, a process called *prostRcision*. ProstRcision means "excision of the prostate by radiation", and is called such because the men treated with this technique achieve and maintain undetectable PSA levels, 0.2 ng/ml or less, just as often as men treated with radical prostatectomy. In effect, prostRcision is a "radiation prostatectomy", but without the damage to the urination muscles and the sex nerves that happens so often with surgery.

Using the identical nadir goal as required after surgery, achievement and maintenance of PSA nadir $\leq$ 0.2 ng/ml, the 10 and 15 year results of prostRcision are identical to those of Dr. Walsh's radical prostatectomy series.
In conclusion, Radiotherapy Clinics of Georgia offers a unique, time proven approach to prostate cancer backed up by a program of rigorous, ongoing research. We encourage any man with prostate cancer to investigate RCOG.

You can contact the RCOG at (404) 320-1550 / 1-800-952-7687. There is also lots of information at their web site at http://www.prostRcision.com

Editorial Comments from Aubrey:
Does Seeding Cause Sterility
At one of the Seattle conferences, I asked a panel of doctors whether seeding would lead to sterility. One doctor reported that one of his patients, a 70 year old man who had undergone seeding, was mad as hell. He had assumed that he was sterile because of the seeding, but had just learned that he had impregnated his 27 year old girl friend.

Every one is different. In some cases, the seeding does cause sterility. It may also destroy much of the prostate tissue so that there will be very little if any

ejaculate, although the man may still enjoy orgasms. The testosterone level should remain the same after seeding, so the libido should still be intact. The amount of sperm manufactured by the testes should remain about the same, but ordinarily, the sperm needs the prostatic and seminal fluids in order to be effective. The prostate may still be able to produce enough of these fluids in some men for fertilization.

It may be possible that the testes could receive a small amount of radiation from the seeds shortly after implantation, but not likely enough to do much damage. However, sperm are constantly dividing and are very vulnerable during the dividing process. It would probably be advisable not to engage in sex for reproductive purposes for at least three or four months after treatment.

Complications

Short term complications were mentioned earlier. There have been several posts from men who have had seed implants. The complication mentioned most often is urgency to urinate, then not being able to. One reason for this is that the prostate has been severely insulted by the needles and the seeds. When a tissue is injured, the first reaction is swelling. The swelling may be so much that it compresses the portion of the urethra that passes through the prostate. This is similar to what sometimes happens in BPH. One of the best treatments for BPH is Hytrin or Cardura. These drugs help to relax the prostate and makes it easier to urinate.

Spreading Radioactivity

Someone's wife posted a note on the Internet about possible contamination from her husband's radioactive seeds. Dr. Chris Warner answered:

"Mary,
Regarding your sleeping arrangements, I am also a physicist. I work at the Walt Disney Memorial Cancer Institute in Orlando, Fl. I will try to give you a technical answer followed by a practical recommendation. The half-life (the time it takes a radioisotope to deliver half of its dose) of I^{125} is 60 days. After 60 days, 2 months, I^{125} delivers half of its dose. Half of the total external exposure to nearby people will be delivered in the first 2 months. For most of the patients that I have measured who have received I^{125} implants, the surface of the patient will measure approx. 0.0015 Rem/hr to 0.002 Rem/hr; at 3 ft from the patient this drops to 0.0001 Rem/hr. As the I^{125} decays over time this dose rate will decrease.

The exposure limit to non-occupationally exposed people is 0.1 Rem per year. If you were to lay on top of your husband 24 hours a day for a year you would receive an exposure of 3.0 Rem in the first year (30 times the recommended limit). Actually, you probably don't spend 24 hours a day with your husband and you probably don't lay on top of him constantly either. You probably spend about

12 hours a day with your husband and on average are about 3 ft away from him. This would result in an exposure of about 0.1 Rem in the first year. As I said earlier 0.1 Rem is the non-occupationally exposed persons annual limit.

If you were not to sleep with your husband for the first 2 months your exposure would be almost half of this or half of your annual limit. You also have to consider the fact that these annual limits are very conservative and a few years ago this limit was 0.5 Rem per year. If your husband was to receive a Pd^{103} implant, your exposure would be less because the energy of Pd^{103} is less than that for I^{125}.

With all that said, my personal recommendation would be:

If you are not pregnant and are not planning to be in the near future, I would not recommend changing your sleeping arrangements. The exposure to a spouse of a I^{125} Prostate Implant patient would be at or near the very conservative annual limit.

If you are pregnant or are planning to be in the near future, I would recommend modifying your sleeping arrangements for the first two months for the sake of the embryo. I hope this helps."
Chris Warner, M.S., D.A.B.R. Medical Physicist Walt Disney Memorial Cancer Institute Orlando, Florida

Editorial Note: If one is concerned about his radioactivity after seeding, there are a couple of companies who make lead lined shorts for men. In most cases, they are not necessary. I have not heard of anyone causing any problems to any one else because of their radioactive seeds.

Note that with HDR and external beam radiation (XRT), there is no residual radioactivity.

Post Seeding Problems

Here is a letter from Julie about her husband Rudi:

" I'd like to share some problems Rudi is having - 2 months after seeding - Mostly, he's fine. He's only missed one day of work. Recall that he's a cop, patrols the streets, arrests people, spends lots of time where urinary urgency wouldn't be an option. He took cardura because he was having trouble starting his stream and keeping it going but the low blood pressure effect didn't work...he said he felt like he was going to faint when he got out of his police car. So he gave it up and is now taking Aleve. He sleeps through most of the night but I think he's still having trouble urinating in one fell swoop.

The really "bad news" - (everything is relative, when he was contemplating RP, we assumed that intercourse was a thing of the past) - is that when he has an

erection and we have intercourse, it is horribly painful and he feels like he has to urinate. He says he can't tell the difference between an orgasm and urinating. Is this a case of "watch out what you wish for?" Seems like the wires have gotten crossed somewhere. Comments?" Julie

Reason for Painful Ejaculation
Julie mentioned that Rudi had a painful ejaculation. Again, the prostate is a musculo-glandular organ. One of its purposes is to propel the semen out of the penis. To do this it squeezes down and compresses the tissues. Of course if the gland has not healed from the poking and prodding, then squeezing and compressing the tissues around the seeds will let him know that it is still sore.

COSTS
At the present time, Pd^{103} costs about $50 per seed; I^{125} is a bit less expensive at about $45 per seed. Up to 100 seeds may be used in a procedure.

At one time, there were only a couple of companies who manufactured the seeds. But the seeds have become so popular that it was difficult at times for the companies to supply all that was needed. Several other companies have now entered the field.

Freshness of Seeds

Someone asked on the Internet about the "freshness of seeds".
Jennifer Cash, Dr. Dattoli's nurse made this reply:

From: <BrachyRN@aol.com>
The Pd-103 seeds are manufactured the day prior to scheduled seeding and air shipped to us the evening before use. The morning of use, they are loaded and recalibrated at that time for dose.

Jennifer>

What Happens To Prostate Post Seeding
Someone posted a note on the Internet asking what happens to the prostate after it has been seeded.

He wrote:
"It is my understanding that the way radiation works is that it adversely effects all cells, but that normal cells are capable of regenerating, whereas cancer cells hopefully do not. Now, if the regenerated cells don't produce PSA just how "normal" are they? Could it be that the new cells are different in other ways too?"

His note was answered by Jennifer Cash:

In regards to functioning prostate tissue after seeding: In our experience, we have been performing seed implants numerous years now, and in the earlier years most of our patients treated underwent routine prostate biopsies between the 1-2 year mark regardless of what their PSA value was. What our pathologists found was residual, viable prostate cells, in addition to radiation fibrosis, and of course, a small subset of patients with residual cancer cells that would be capable of regrowing.

Based on this, we view the effects of radiation therapy of tumor as sterilization rather than complete ablation of normal prostate cells. Also, we have subsequently found, that the consistency of the prostate gland resumes to close to normal within 2-3 years post treatment (not remaining like a lump of charcoal as some believe). Jennifer

Here is another note from Jennifer:

It is very reasonable that after seeding one would expect a PSA nadir of >0 to be normal. We are happy when it drops below the 1.0 value, this has been our best clinical indicator of success. Even though we have a small subset of patients who, when biopsied 1-2 yrs post seeding, had positive biopsies, some of this group went on to have declining PSA's and negative biopsies at later dates. Keep in mind, no treatment has a 100% cure rate!

In reference to the fibrous tissue in the prostate post seeding: Some of the tissue dissolves over time, because, in general, the body does not like scar tissue and, therefore, has the ability to remove some of the scar tissue (just think of other body locations that have had scars and how they diminish over time). Certainly, radiation fibrosis in many patients will persist throughout their life.

We generally see the prostate resume a more normal consistency and size 1-3 years post seeding, and even see a little increase in the size as time passes due to this normalization process and even normal BPH effect with age.
Jennifer Cash e-mail: BrachyRN@aol.com

Other Brachytherapy sites
There are now hundreds of brachytherapy sites. The web site below lists doctors and brachytherapy sites, by state.
http://www.prostatepointers.org/seedpods/seeddocs.html

Here is a site in London:
The Prostate Cancer Charity
Du Cane Road
London W12 0NN
Tel.0181 383 8124 (admin), 0181 383 1948 (helpline)
Fax 0181 383 8126

HIGH DOSE RATE TEMPORARY SEEDS

by Drs. Nisar Syed, Ajmel Puthawala & Aubrey Pilgrim

When 58 year old Andy Grove, CEO of Intel Corporation was told that he had prostate cancer, he was advised to have surgery. But Andy Grove didn't get to be CEO of a multi-billion dollar company like Intel by blindly accepting advice. He wanted to know first hand all of the options, benefits, complications and risks. He began to research and study. After doing considerable research, he decided that the best option was the High Dose Rate (HDR) temporary seed implants or brachytherapy. He went to Swedish Hospital Tumor Institute in Seattle and was treated by Dr. Timothy Mate. After his treatment, Andy wrote an article for Fortune Magazine, May 13, 1996. They featured the article and put Andy's photo on the cover. That particular issue of Fortune sold more copies than any in their history. Because of that article, Dr. Mate has been inundated with patients wanting the same type of treatment.

One location that did low dose rate brachytherapy for over 17 years was at the Long Beach Memorial Hospital near Los Angeles. Dr. Nisar Syed and Ajmel Puthawala treated 536 men with low dose rate (LDR) temporary seeds from 1980 to 1997.

Low dose rate (LDR) temporary seeds involved some exposure to the radioactive seeds for both the doctors and nurses. In 1997, the Long Beach Memorial Hospital installed the computers and equipment necessary to perform high dose rate (HDR) treatments. At the beginning of the year 2000, they had treated over 250 men with HDR.

One of the criticisms usually made about brachytherapy is that there is no long term data. But Dr. Syed has data for 536 patients he has treated with LDR over 17 years. His data is actually better or comparable to surgery for similar stages of tumor. Andy Grove's research showed that the recurrence rate of rising PSA five years after surgery was as high as 31%. It was as high as 27% for external beam radiation therapy (XRT). For permanent seed implants, it was as low as 19% and for HDR it was as low as 14%.

Of course, recurrence depends to a great extent on initial PSA, stage and Gleason score. Overall, Dr. Syed had a progression free rate of 86% with LDR therapy. Progression free may be higher than 94% if the initial PSA and Gleason score was fairly low. The HDR success rates in the 250 patients treated are even better than the 536 treated with LDR.

The HDR procedure is similar to that of the permanent seed implants in many respects. The prostate size and tumor location is plotted and the treatment dose

is generated on a computer. HDR is usually combined with five weeks of external beam therapy and can be used with hormone therapy or as monotherapy depending on initial PSA, tumor stage and its grade.

A couple of very powerful computers are needed for HDR planning and treatment. A lead lined treatment room is required. A robotic machine to contain and insert the Ir^{192} is needed. The machine is under computer control. Fig. 12-11 shows the robotic lead lined housing for the highly radioactive !r^{192} source.

The initial cost of the HDR equipment is much more expensive than that needed for permanent seeds. But the one Ir^{192} source can be used several times and may only need to be replaced about three times a year. Considering that permanent seeds may cost from $40 to $50 per seed, over an extended period, the HDR treatment may be less expensive than permanent seeds.

The patient is placed in the lithotomy position like that shown in fig. 12-5. The ultrasound probe is placed in the rectum and a plastic template is held against the perineum. The template is similar to that shown in fig. 12-3. It has several holes in it to guide the needles. Usually 14 to 16 hollow needles are placed in the prostate under the guidance of the ultrasound probe. Each needle has a short plastic tube attached to the needles. Each plastic tube has a connector so that they can be attached to the tubes from the robotic machine. After the needles are placed, the template is stitched to the perineum. The ultrasound probe is then removed. The needles remain in place in the prostate for the 24 to 40 hour duration of the treatment. This may be the most uncomfortable part of the whole treatment.

Hollow plastic tubes are attached to the robotic machine that houses the Ir^{192} source. See fig. 12-12. A nurse or technician connects the flexible tubes to each needle in the patient. See fig. 12-13. After making sure all the needles are connected, the nurse leaves the lead-lined room and closes the door.

Two video cameras are focused on the patient and the machine. From a separate control room the machine is turned on and controlled by a computer.

There is a single active Ir ^{192} source in the machine. The source is attached to the end of a thin wire that is inserted into each hollow needle in the patient. The source rotates inside the lead lined machine and inserts the source into each plastic tube in turn. The active source is allowed to dwell for a pre-determined time, then withdrawn and placed into another needle until it has been inserted into each of the needles. The treatment takes about 7 minutes, then the patient is wheeled back to his room, then 8 to 12 hours later, the same procedure is repeated.

The diameter of the seed is about 1.1 mm and the length is about 5 mm. (Five mm is a bit less than ¼ inch, so the seed is about the size of a small grain of

rice.) The main difference in the HDR seeds and the permanent seeds is that the HDR seeds have a much higher amount of radioactivity. Another major difference is that the HDR seed is temporarily inserted for a short time under computer control then withdrawn. One reason for using a machine to insert the seeds is because of the high amount of radioactivity.

The computer causes the seed to be inserted for a previously determined amount of time, depending on the pre-planned dose rate. The machine can be programmed to give a tumor in a certain location of the prostate continuous radiation for a predetermined length of time. Under computer control, the dose rate can be adjusted by having the seed dwell for longer or shorter periods of time in certain areas of the prostate. Certain areas such as that around the urethra and the rectal wall can be spared from high doses. A specific dose of radiation can be delivered wherever it is needed.

The pre-planned dosage is given in three or four fractions over 24 to 40 hours depending on the tumor size, PSA and Gleason grade. This doesn't mean that the man will be attached to the machine for this entire length of time. It takes only a few minutes for a fraction of the dose to be delivered. After the fraction is delivered for the planned time, the machine pulls the seed back into its lead safe. The Ir^{192} radiation in the source seed lasts for a long time, so it can be re-used several times.

The machine is lead lined so that no radiation escapes when the seeds are stored inside. Once the seeds are safely back in the machine, as a precaution, an operator enters the room with a Geiger counter to make sure that there is no radiation still present. The tubes are then disconnected from the man and he is returned to his hospital room to wait for the next fraction. The fractions are given about every 8 to 12 hours. The template and hollow needles will remain attached to the man for the duration of the full treatment time of 24 to 40 hours.

While disconnected from the machine, the man can roll over in bed from side to side, but he is not allowed to get out of bed. Since there is no residual radiation from the treatment, the man can have visitors between the short treatment times.

If necessary, about two weeks after the HDR treatment, the patient may be given a series of external beam radiation therapy (XBRT) to the pelvic region. The amount of radiation received from the temporary seeds may be 2200-2800 centigray (cGY) depending on the initial PSA, stage and Gleason. The follow up XBRT may be 4000 to 4500 cGy.

They may use hormones with HDR in patients who have locally advanced disease, T2 or T3, high PSA (more than 15) and high grade Gleason score (8, 9 or 10). In these situations they give two to three months of androgen blockade before irradiation, and in some patients who are at a high risk of recurrence and

distal metastases the androgen blockade or hormone treatment may continue for one to three years.

Complications

In the 536 patients that Dr. Syed treated with low dose radiation (LDR), 237 of them said that they had no erectile dysfunction (ED) or impotence before treatment. At a one year follow up, 71 patients of the 237 (30%) said that they were having ED problems. But as in all radiation treatments, with time, the number of men with ED will increase.

Only six patients treated with LDR had an incontinent problem, four had urethral stricture, or constriction of the urethra that made it difficult to void, and eight had severe proctitis. However, these types of complications are almost completely avoided by using HDR, since it gives the radiation oncologist much better control for radiation dose delivered to critical structures like bladder, urethra and rectum.

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Other HDR Brachytherapy sites

Here is a note posted to the Internet by Joe Armon, armon@ibm.net (Joe Armon):

> For a very simple explanation of the HDR process, check out the site of one of the manufacturers of HDR afterloaders, Nucletron. Go to http://www.nucletron.com/clin_ap/prostate.htm
>
> There are two HDR treatment centers that have excellent websites, Tulsa (CTCT) and Oakland (CETMC). They are by no means the only two centers, just the two web sites that give outstanding explanations and illustrations of temporary brachytherapy.
>
> http://www.brachytherapy.com/prost-brachy.html
>
> http://www.cetmc.com/prostate.html

What Should You Choose

Andy Grove said about doctors, "There is no good gatekeeper in this business. Your general internist is not; the field of prostate cancer is a complex and

changing specialty. Neither is a urologist; urologists have a natural preference toward surgery, perhaps because urologists are surgeons and surgery is what they know best. Any other treatment is deemed experimental even if it has just as much data associated with it. My review of the data led me to conclude that there are viable alternatives."

Andy Grove strongly recommends that a man should consult the Partin tables to get an idea of his risks. He said, "...I think these tables ought to be posted on the walls of every urologists office. They should be viewed as the point of departure for a prostate cancer patient's bill of rights."

One thing that Andy demonstrated so very well is that it is your body, your disease and you must take charge. You must do your homework and decide what is best for you. Another point that Andy made was that, even though we only have about ten years of data for this procedure, it looks very good. Even if the cancer recurs at the end of ten years, who knows, maybe by that time we will have found other and better treatments. Maybe by then we will have found the magic bullet.

Andy is still doing well. He is now working with Michael Milken's CaP CURE organization, helping to raise funds for prostate cancer research.
You can reach CaP CURE at 310-458-2873

HDR is also used to treat cancers of the lung, genitourinary systems, breast, esophagus, pancreas and others.