SEATTLE PROSTATE INSTITUTE
AT SWEDISH MEDICAL CENTER

About Seed Implantation

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This document is designed as a more detailed companion to the SPI website for readers interested in a discussion of the history, development, and current use of brachytherapy as well as more data regarding the efficacy and potential side effects of the procedure. The SPI medical team established the first ultrasound-guided prostate implant program in the U.S. in 1985. We are proud of our history and have trained many physicians and clinical staff both in the United States and abroad. We have assisted in developing programs at many institutions by performing on-site teaching and would be willing to do this upon request.

This is a general guide to prostate brachytherapy, as described at our center. However, as with many procedures in medicine, variations in approach and technique have been proven in skilled hands to be highly successful in treating men with prostate cancer. The most important factor in selecting a center of excellence, for any treatment in medicine, is the number of procedures they perform.

Prostate seed implants are a type of *brachytherapy*, which translated from latin literally means 'short therapy', describing that the radiation 'seeds' deposit radiation over a very short distance. This is in contrast with standard external beam radiation (historically called 'teletherapy', as 'tele' means 'far' in latin) in which radiation is generated by an external source and aimed from outside-to-inside. In the brachytherapy technique, therefore, the seeds are placed directly within the prostate gland. This allows a very high dose to be delivered to the prostate with a fast drop-off of dose outside the prostate, minimizing the dose to surrounding structures such as the bladder and rectum, penile bulb, hips, and small bowel. Radioactive seeds are about the size of a grain of rice. After delivering their radiation over weeks to months, the seeds are inert and remain in the body.

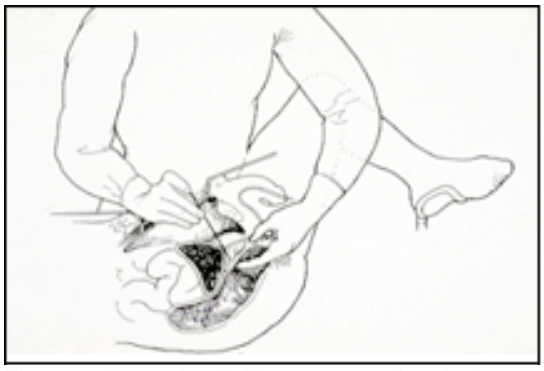

Figure 1. Example of old open procedure before the advent of ultrasound.

The history of seed implants is remarkably long considering that the procedure has become mainstream relatively recently. The idea of placing radioactive material into the prostate for the treatment of cancer has been around since the early 1900's. Modern prostate brachytherapy, however, began to take hold in the 1970's when physicians at New York's Sloan Kettering Memorial Cancer Center first began inserting radioactive seeds into the prostate using an open surgical procedure. With this technique, an incision was made in the abdomen to expose the prostate gland. Using only their hands to guide the surgical needles containing the seeds, the physicians inserted the seeds one by one

into the prostate gland (Figure 1). Without the ability to see inside the prostate, physicians could not ensure that the seeds were being placed evenly throughout the gland The result was that some areas of the prostate would receive clumps of seeds (hot spots) while other areas would receive few or none (cold spots) as illustrated in Figure 2. Predictably, these early procedures did not prove very successful in curing prostate cancer. Consequently, the open surgical technique fell into disrepute and was largely abandoned.

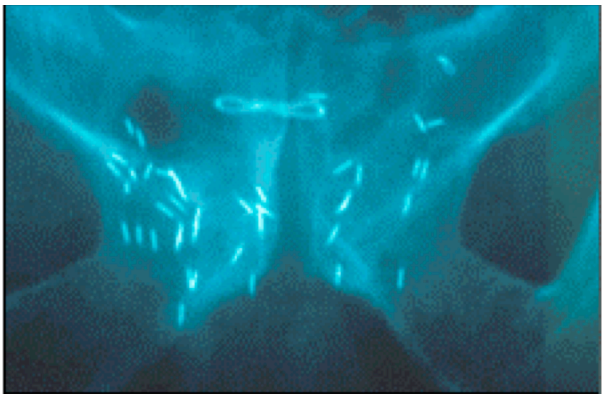

Figure 2. Example of disorganized unevenly distributed seeds after open implant.

In the early 1980s, Dr. Hans Holm of Denmark began applying the new technology of transrectal ultrasound to seed implantation. Along with advances in computerized imaging software, ultrasound technology was a major step forward in the development of prostate brachytherapy.

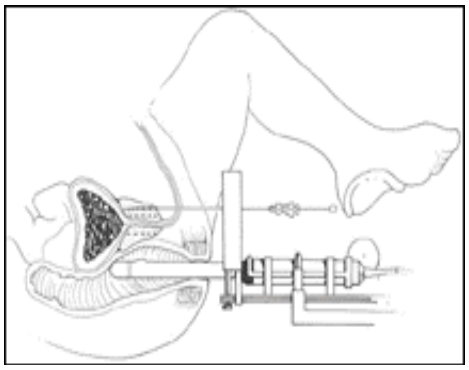

Figure 3. Modern ultrasound guided implantation technique.

Using ultrasound, physicians could now see the seed-bearing needles inside the prostate, thereby better enabling them to deposit the seeds evenly throughout the gland so that the radiation could reach all the cancerous tissue (Figure 3). Equally as important, perhaps, was that open surgery was no longer necessary. By using a rigid template guiding device, the needles could be inserted into the prostate from outside of the body. This transformed what had been major surgery into a 1 hour outpatient procedure with little discomfort and rapid return to normal activities. Unlike the open surgical technique, the more precise ultrasound procedure allowed physicians to achieve the even distribution of seeds that was necessary in order for the radiation to have its maximum therapeutic impact on the cancer cells throughout the prostate.

Building on Dr Holm pioneering work, two Seattle physicians, Dr. John Blasko and Dr. Haakon Ragde introduced ultrasound-guided prostate implantation to the U.S. in 1985. In the years that followed, physicians from around the country and around the world came to Seattle to learn this new and promising technique. Today, hundreds of centers across the U.S. are performing more than 40,000 seed implants a year.

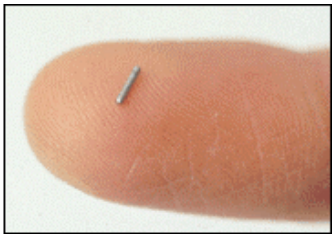

Figure 4. Radioactive Prostate Implantation Seed

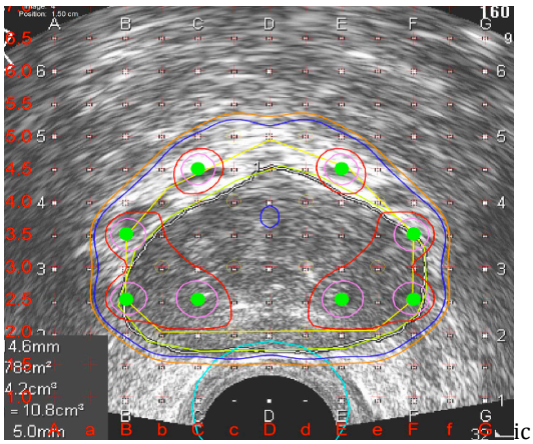

Figure 5. Plan of an implant overlaid on ultrasound image of the prostate gland.

Since the success of an implant depends on the accurate placement of seeds, the first step in treatment process (and evaluation for suitability of an implant) is the volume study. Often therefore we will perform a volume study during the initial consultation (our RN will prepare you for this over the telephone if this will be performed). The ultrasound volume study determines the size and shape of the prostate. This is performed in our office and is a relatively simple procedure. An ultrasound probe in inserted into the rectum and moved along the length of the prostate taking cross sectional images every few millimeters. The software calculates the 3D volume after the staff or physician identifies and contours the prostate on the images (an example ultrasound can be seen in Figure 5). Generally, a size of 60 cc's is the maximum size for a satisfactory implant to be performed. At times, hormone therapy can be initiated two to three months before an implant and the gland will shrink on average by about 30%. The volume study also evaluates the shape of the pelvic bones. At times, even with an average sized prostate gland, 'pubic arch interference' is possible. This makes delivery of seeds through our needles to the anterior prostate difficult because the needles encounter the pubic bone and cannot be advanced into the gland. Often, repositioning can help and a careful evaluation before actually entering the operating room is certainly prudent.

The physician then determines the target volume to be covered by radiation. In general this would include the prostate plus 2-5 mm of tissue surrounding the entire gland. Often the base of the seminal vesicles are included for more advanced cases. These few extra-prostatic seeds allow for a margin to treat potentially microscopic cancer cells outside the prostate capsule. Depending on the clinical risk factors, the physician may include more or less extra-capsular tissue in various areas of the gland.

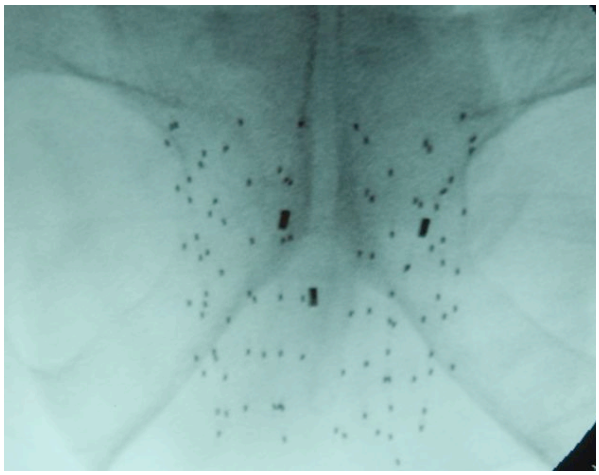

Figure 6. Palladium-103 prostate implant at SPI. Note 3 Calypso beacons present, for external beam tracking.

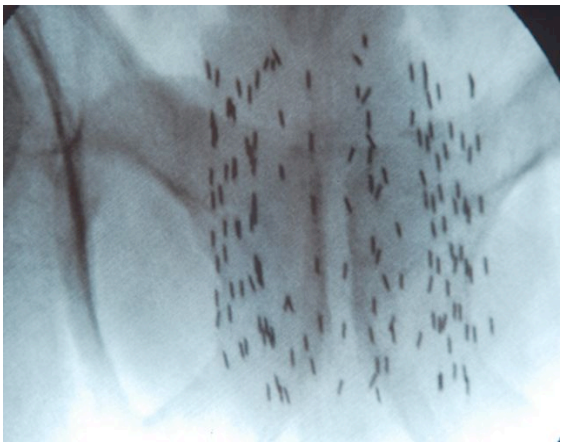

Figure 7. Iodine-125 Prostate implant at SPI. Urethral sparing – modified peripheral loading technique.

Once the volume is determined, elaborate software, a trained radiation dosimetrist, and the physician determine the number, strength, and geometric arrangement of seeds to properly cover the gland (Figure 5). On average, approximately 100-110 seeds are used in a typical implant. The most common radioactive isotopes are palladium and iodine. All of the studies to date show equal efficacy between the two isotopes. Since Palladium has a shorter half-life, it tends to cause more acute urinary symptoms but these resolve more quickly. We use both isotopes, depending on the specifics of one patient's situation and also to some degree the physician's comfort level and preference.

The implant itself is an outpatient procedure. The patient is checked into the preoperative area and meets the anesthesiologist. Then, he is brought into the OR suite, and routine anesthesia procedures are begun (establishing and IV, etc). We typically use a spinal anesthetic in our downtown clinic and general anesthetic in the remaining outpatient surgery centers (exceptions do apply). After positioning the patient, the apparatus is setup and attached to the surgery table. Using a rigid template-guiding device, hollow metal needles containing the seeds are inserted into the prostate from outside the body. At SPI, patients are in the hospital for a total of approximately 5 hours. In the OR, the physician uses live ultrasound guidance to reproduce the images obtained at the volume study and then inserts needles to the correct depth as seen on ultrasound. Then, the hollow needles are retracted while a metal stylet 'holds' the seeds in place. Then both needle and stylet are removed and only the seeds remain. Typical time to perform an implant is just one hour.

After the implant, the patient will recover in the recovery room, and if a Foley catheter was inserted, it will be typically removed. On the day after the implant, a pelvic X-ray, a chest X-ray, and a CT scan are taken. The pelvic x-ray provides the physician confirmation about the implant and aids in counting the seeds (Figure 6 and 7). The chest x-ray is often performed to determine if any seeds were deposited into the blood stream and carried to the lungs (this rare event does not appear to cause any harm to patients). Then, a CT scan is obtained with similar intervals as the ultrasound volume study. These two sets of images are then combined in such a way that the physics staff can determine the 'post-plan', or the actual radiation dose received by the prostate and surrounding region. This allows quality assurance and confirmation of a successful implant. In the very rare case that the dosimetry is not ideal, we may repeat the post-implant CT after two to four weeks, allowing for resolution of swelling of the prostate gland (When the gland is swollen, after the procedure, it will underestimate the prostate dose). It would be very rare, in our experience, to still have insufficient dose to the prostate. However if this were to occur, a few doses of external beam radiation could be added to supplement.

Many patients inquire regarding radiation safety. The seeds emit low-energy radiation that is absorbed within a very short distance from the seed. For this reason, only a very small dose would be detectable outside a patient. However, in order to follow the principle of as-low-as-possible radiation exposure (The so-called ALARA rules), we do recommend that patients refrain from prolonged contact with children (such as holding an infant on one's lap for a long time) or contact with pregnant woman. The metal of the seeds is not enough to setup an airport metal detector. However, since 2001 many airports have installed radiation detectors for obvious reasons. We provide patients with a card indicating the procedure and information regarding the radiation used. It is ok to sleep in the same bed as one's partner and to have

one's pet on their laps. The urine itself is not radioactive, unlike when a pill-form of radioactivity is used for thyroid ablation.

Short-term side effects are generally quite limited and include more frequent urination, urinary urgency, slower stream of urine, and some minor skin bruising. Acute urinary retention is rare but possible. For more details please see our handout 'What to Expect from a Seed Implant' and the 'Frequently Asked Questions'. In the first couple days after the implant, one can expect urinary burning and urgency, and some skin tenderness and bruising, worse when sitting down. Some prefer to sit on a 'donut' for a day or two. It would also be common to have a small amount of blood clots pass in the urine. Pain other than this tenderness is very rare, and rarely do patients need more than one or two oral pain medication tablets (if at all). These effects resolve in about a week. Many patients report more frequent bowel movements for a few weeks after the implant, 1-5 times per day instead of once a day. This resolves as the radiation wears off. We do recommend avoiding heavy lifting or strenuous exercise for at least a few weeks after the implant.

Urinary retention is a possible side effect, in about 10% of patients. The risk is higher in patients with a larger prostate gland. We will estimate your risk when we have reviewed your pre-implant urinary symptoms and prostate gland size on ultrasound. Usually 1 week to 1 month after the implant, the radiation can cause swelling that in these patients will obstruct the urine flow, and one will need to have a catheter placed to urinate. This resolves, and is a temporary condition. Often helpful maneuvers to try to urinate when flow is slow or stopped up is to take Advil or other anti-inflammatories (Alleve, ibuprofen, etc) and to get into a hot shower or bath to relax the pelvic muscles. This trick has saved many a patient a late night trip to the urgent care clinic or ER. On average the catheter is removed in 1-2 weeks.

Long-Term Complications are rare with this technique. Impotence, incontinence, and rectal injury are possible with any form of prostate cancer treatment. Probabilities of any complication will vary from one patient to another based on their particular case. Regarding impotence, the American Cancer Society estimates, based on age, that 10-30% of men become impotent as a result of seed implantation compared to 40-50% with external beam radiation and 65-90% with standard radical surgery. The ACS reports that nerve sparing prostatectomy results in an impotency rate of 25-30% for men < 60 and 70% for those over 70. At SPI, our experience has largely mirrored the ACS, with the following results: Men less than 60, 10%; Men 60-70 yrs, 15%, Men older than 70, 25%. It is important to recognize that pre-implantation sexual function has a large impact on ones chance of maintaining sexual function following radiation therapy. It is OK to have sexual intercourse after implantation. There is a very slight possibility that a seed could come loose the first time or two after intercourse and be passed thru the urethra. Therefore, it would be prudent the first couple of times to be aware of this and avoid the possibility that this seed could be deposited into one's partner.

Incontinence requiring pads to be worn is rare, seen in approximately 1% of patients. When it does occur, it often is 'stress incontinence', in which there is leakage when a man coughs, sneezes, laughs, etc. This is caused by radiation damage to the bladder sphincter, the valve that constricts to keep urine from leaving the bladder. Rectal complications include painless rectal bleeding in 2% of patients, which increases to 6% with the addition of external beam radiation. This occurs anywhere from 6 to 18 months after treatment. About two in one hundred patients may have more serious rectal problems, which except in the most rare case can be treated effectively.

With surgery, the PSA is expected to go to zero shortly after the procedure as the prostate is removed. In contrast, cancer cells are not killed immediately with radiation. Radiation causes DNA damage and prevents cells from dividing and growing. Often, the cell does not actually die until it attempts to divide, which for prostate cancer can be a significant time. In biologic terms the cells are considered 'functionally dead', because without the ability to divide, they are unable to cause any dysfunction or to spread. With radiation, PSA levels will reach their lowest point (the 'nadir') anywhere from 1 – 4 years after treatment but more typically at about 18 months. Some of the normal, noncancerous, prostate gland will still produce a small amount of PSA as well, since the gland is still present. The PSA values can 'bounce', and this should not be a cause for alarm and in fact is believed by some to be a harbinger of successful cases. The previous definition of failure after radiation from prostate cancer, by the American Society of Radiation Oncology, required 3 rises in PSA before declaring failure. The newer definition is that failure (or recurrence) is defined as a PSA increase of 2 ng/dl over the nadir. For example, if the lowest PSA was 0.3, then values bouncing around this are acceptable but if the PSA becomes 2.3 this is considered clinical failure.

Having introduced the modern ultrasound guided technique of seed implantation in the mid 1980's, we have been tracking the experience of our patients for over 15 years. This shows an overall 85.5% survival rate at 15 yrs for low risk patients, and an almost as favorable 80.3% survival in intermediate risk patients. Together with similarly favorable long term results from other well established prostate brachytherapy centers, the experience of the SPI has clearly established radioactive seed implantation to be as effective, if not more effective, at controlling cancer as surgery and other conventional treatments. In patients with intermediate and high-risk prostate cancer, published series have shown high-quality brachytherapy, often combined with external beam, to be superior to surgery.

Lastly, one should note that these survival numbers are based on treatments over a decade ago. Not only has the technique been further refined since that time, but men presenting in the early 90's generally had much more advanced cancers because PSA screening was not yet widespread. More modern outcome data are better than previous results. For example patients treated from 1995-2001, published by Merrick and colleagues, showed relapse free survival of 98% for low risk patients and 98.4% for intermediate risk patients, and 88% for low risk patients. This is in line with our more recent results as well. To date, there is no evidence that other treatments (surgery, cryotherapy, proton beam therapy, hormone therapy alone) have matched up to these results.

In conclusion, unlike many other cancers, there are a multitude of appropriate treatment options for prostate cancer. This leaves the patient with the ultimate task of making a difficult and often confusing choice. The most important predictor of successful treatment is finding the cancer confined to the prostate alone. Fortunately, because of the widespread use of the PSA test, many more patients are being found with this earliest stage of prostate cancer. When diagnosed with prostate cancer, men should work closely with an experienced physician to select the treatment that they are most comfortable with and they should not hesitate to seek a second, or even third, opinion to help reach a decision.

For more questions please see the "Frequently asked Questions" section and file, and please feel free to contact the Seattle Prostate Institute.