Seattle Prostate Institute Frequently Asked Questions - Brachytherapy

How many other doctors have you trained in the seed implant procedure?

The Seattle Prostate Institute implant team now consists of 25 urologists and radiation oncologists trained here at the Institute in prostate seed implantation. The team meets monthly to discuss cases, improve the technique and improve our understanding of prostate cancer. The Seattle Prostate Institute (SPI) began a state-of-the-art training program here at Swedish Medical Center in March 1997 and have since trained over an additional 750 physicians, physicists and nurses. We are currently training well over 100 physicians and physicists per year from around the world. In addition, SPI hosts an annual Advanced Prostate Brachytherapy Symposium for experienced brachytherapists.

What is Pubic Arch Interference and how do you test for it?

One important determination in deciding whether seed implantation can be technically performed is to evaluate the position and shape of the pubic arch. If the pubic bone, which is shaped like an upside down V or arch, is too narrow, it can be difficult or impossible to place needle in the prostate accurately and completely. SPI has developed an ultrasound pubic arch study that evaluates the position of the pubic bone at the time of the volume study. Occasionally we will also order a CT, which can also do this evaluation. Determining whether the pubic arch will prevent a good implant is obviously valuable. For those patients who have large glands and arch interference, shrinking the gland with hormonal therapy can often make the patient an implant candidate.

Why will the patient have a CT scan and chest x-ray soon after the procedure?

The CT scan is done to confirm the placement of the seeds. The CT allows the implant team to do a post-treatment dose determination. The post implant dosimetry acts as a permanent record of the implant. It also gives the implant team another means of evaluating the quality of the implant. On very rare occasions, additional therapy may be suggested. Also on rare occasion, a "free" seed (a seed that is placed in the needle individually) will be inadvertently implanted in the middle of one of the large veins around the prostate. This seed can travel in the veins, eventually reaching the lungs. Seeds in the lung have not caused any harm to any patient and nor any adverse symptoms. The chest x ray is performed to determine if there is a seed in the lung.

What medications do you prescribe before and after the procedure?

Typically, an alpha-blocker (Flomax, Cardura or Hytrin) is prescribed prior to the procedure. These are medications that relax the internal urethral sphincter muscle, allowing for improved urination. Because it can take a few days with Cardura or Hytrin to reach a proper dose, it may be started several days prior to the procedure. After the procedure, patients typically continue the alpha-blocker for four weeks, longer if necessary. In addition, patients are given an antibiotic and an anti-inflammatory drug such as Aleve. The Aleve helps to reduce the normal swelling, improving the urine flow.

What is the difference between palladium and iodine seeds?

lodine and palladium seeds are nearly identical in their appearance. Both are 0.45 cm long (about the size of a grain of rice) and are implanted in the same way. Both emit low energy radiation. The primary difference between these two isotopes is the rate at which they give off their energy. Palladium gives up 90% of its energy within two months, while it takes approximately six months for iodine to release 90% of its energy. There are advantages to using both isotopes, which is described below in a related question. There is no proof that one seed is better or stronger than another. The doses and seed strengths, in fact, are prescribed to produce the same biologic effect. Often the choice will relate more to the physician's preference and how they were trained and developed their clinical experience.

What dose of radiation will each kind of seed give during its lifetime?

It depends on whether the seed is used as implant alone or in conjunction with external beam. For an implant alone, Iodine delivers 145 Gray (14,500 rads) and Palladium 115 Gy (11,500 rads). When combined with external beam radiation, we can safely give a bit more than ½ the dose for each modality, yielding a very high anti-cancer dose of radiation. Iodine will deliver 110 Gy in this setting and Palladium 90 Gy. The exact definition of how dose is defined has evolved over the years, however this is essentially the same biologic dose we have delivered throughout our brachytherapy experience.

What is halflife? How long will each kind of seed be radioactive after implantation?

Half-life describes the time in which an isotope loses half of its strength. For example, iodine, which has a half-life of 60 days, will be half of its strength at 60 days. 60 days later it will be half of this strength. It takes about six months for iodine to be at about 10% of its original strength, and a year to lose effectively all of it. Palladium has a half-life of 17 days. Within two months it has given up 90% of its energy and has lost almost all of it by six months. Again, there are advantages to both isotopes. Palladium gives up its energy quicker but this does not mean that it is necessarily better or stronger.

<u>How does radiation from seed implantation kill cancer cells? Are there forms of prostate cancer cells that will not be affected by seed implantation radiation? How will the radiation from seed implantation affect healthy cells in the patient's prostate?</u>

There are entire books written on radiation biology and why radiation works. Briefly though, Radiation damages DNA, RNA, and proteins of cells but primarily causes cancer cell death through direct DNA damage. DNA is the instruction manual for a cell to replicate. Cancer cells don't die immediately after radiation. When the cell initiates a replication cycle and tries to divide into two cells, the DNA breaks prevents the cancer cell from dividing properly. The cell ultimately dies. Since prostate cancer cells often divide slowly, the cancer cell may not die for months after the implant. This is why it sometimes takes a long time for the PSA to drop to low levels. Since the cancer cells are most sensitive to radiation at the time of division, it is necessary for cure to have radiation present when this occurs. This is one of the reasons why 'fractionating' external beam radiation is advantageous (the other reason is that it allows normal cells to repair). All cells are sensitive to radiation. Because of the high dose, some normal prostate cells die as result of the implant radiation. Some normal cells remain however, which explains why PSA is still present years later. Normal cells can repair the DNA damage caused by radiation due to specific repair enzymes often lacking in cancer cells. The result of the healthy cells dying is that the prostate function of producing prostatic fluid for ejaculation may be substantially reduced. The presence or absence of an eiaculate, however, does not reflect whether the cancer is cured or not.

Will healthy cells regrow after the radiation is complete?

There is some regrowth of normal cells, but for the most part regrowth is very limited. This regrowth of normal prostate cells is believed to be responsible for PSA values to increase in some patents after treatment.

If the patient had BPH (benign prostatic hypertrophy) previous to seeding, will it go away or return later?

While the gland can shrink with the radiation, often patients have urinary function similar to that prior to the implant. In other words, at this point, seed implantation does not seem to be a good treatment for BPH.

What are the chances the patient will be affected by prostatitis after seeding?

All patients have some inflammation of the prostate (prostatitis) after seeding, which typically resolves as the seeds lose their energy. The presence of prostatitis prior to seeding is always a concern because the prostatitis may be exacerbated by the radiation. Surprisingly, this has not occurred in the patients we have treated. This is not to say that prostatitis symptoms went away after implantation, but that the implant did seem not to have significantly worsened them. Caution is urged with these patients and more study is needed.

$\underline{W}hat$ effect would a TURP, either previous to or after seed implantation, have on treatment?

In some patients, the presence of a previous TURP prevents a technically good implant. In the past, patients with a prior TURP had an increased risk of urinary incontinence of approximately 25% at six years. The majority of this incontinence was minor, requiring a simple pad. In the past several years, we have altered the pattern of seed placement in these TURP patients with the hope of decreasing this risk. Since it takes some time to learn the results, patients with a prior TURP are advised that their risk of incontinence is higher. There are, of course, often very good alternative treatments (radical prostatectomy or external beam radiation).

TURP after the implant also imparts a risk of incontinence. Therefore, a TURP in implant patients is not generally recommended. When a TURP is necessary after implant, someone who understands the problems associated with it should perform it.

What follow up will there be after seed implantation?

The first visit is at 6-8 weeks and thereafter every three months for two years. After two years, visits are recommended every six months. After five years, a PSA is scheduled every six months and a physical exam at least once a year. Alternating these visits between the radiation oncologist and urologist ensures complete care. If the patient has a good internist or family practitioner, we encourage his/her participation as well. Most important is to have a concerned, knowledgeable physician following the course.

Why are urinary difficulties and urinary retention worse at night?

For many men, nighttime urination is a different experience than the daytime, with often a slower stream or difficulty initiating a stream. This phenomenon can be worsened after seed implantation or external beam radiation. The reason for this is unclear. It may be worse at night because there is slightly greater swelling of the prostate at night.

Do you recommend any strategies for alleviating nighttime urinary problems?

Alpha-blockers (Flomax, Cardura and Hytrin) can often help a lot. Finding the correct dose can be a challenge sometimes. Other techniques to improve flow are: walking around, getting into a warm shower or bathtub and urinating, taking Aleve or other anti-inflammatory drugs and avoiding acidic and bladder-irritating foods. Generally, this worsening of the urinary stream at night goes away as the seeds lose their energy.

Should a patient continue to drink fluids throughout the day and evening or should he reduce or stop fluid intake in the evening?

The advantage of taking fluids (particularly water) after seed implantation is that it dilutes and neutralizes the urine pH. Concentrated or acidic urine can be irritating. The disadvantage of taking larger amounts of fluid than normal is that it means more urination, possibly increased episodes of urgency and having to get up more times at night. In general, more fluid is not necessarily better. What fluid a patient takes may be more important. Fluids that cause the urine the to be acidic (fruit juices, coffee etc.) should be kept to a minimum if there is irritation upon urination. Everyone is different though, and often even these fluids do not cause any problems, so each patient needs to test them himself and adjust. In medical school there is a maxim, called the resident rule: "Ask the patient what he was doing before this symptom started..... Then tell him to stop doing that". Common sense.

<u>How much radiation will a patient normally receive from EBRT?</u> Do you recommend a specific type of radiation?

A typical dose for pre-implant EBRT is 4500 cGy. All radiation therapy performed today is 3D planned. Most is further refined with IMRT (intensity modulated radiation therapy). The initial fields for this treatment are purposely designed to treat the prostate, seminal vesicles and occasionally the lymph nodes. Standard EBRT is given daily, with multiple non-coplanar fields (which simply means not just right, left, front, back). Sophisticated blocking with mechanical leaves in the head of the machine is customized for each patient to avoid high doses to the

rectum and bladder. Those who do not receive an implant will go on to a final dose of anywhere between 7560 cGy and 81 Gy to the prostate alone.

I have noticed that some implant centers give external beam radiation (EBRT) after the seeding. Should the seeding be done before or after the external beam?

Both approaches are used, and we have done both ourselves. Advantages of performing EBRT after the seeds is that it can allow corrections for occasional misplacement of seeds. One must wait long enough after the brachytherapy in order to avoid significant additive toxicity of simultaneous radiation to the anterior rectal wall. In the past, our center always did the EBRT first, followed by seeds. It was safe and effective, and our published results bolster these facts. Now however, there is new EBRT technology: The <u>Calypso</u>[™] system. Since we need to insert Calypso beacons in the prostate using needles anyways, we decided that both the seeds and beacons could be inserted at the beginning, saving a second procedure.

Why is EBRT given to prostate patients at all?

EBRT is given to deliver a safe but effective dose of radiation to those areas that are at increased risk of harboring microscopic prostate cancer that is outside of the range of the radioactive seeds (the distal seminal vesicles and in some cases the lymph nodes). Generally speaking, the majority of expert brachytherapists feel that low risk and "favorable" intermediate risk patients should receive radioactive seeds alone, while "unfavorable" intermediate risk and high risk patients should receive combination therapy (EBRT and radioactive seeds).

What is Calypso?

•For the first time ever, we can track the prostate's position continuously during the treatment, not just before the beam is turned on. The prostate does move while the beam is in use. Other techniques of IGRT, tomotherapy, proton beam, ultrasound guided radiation and gold fiducials seed placement only check prostate position before the beam is turned on. There are only two modalities that can track the prostate during treatment – the Cyberknife, and Calypso. At the sattelite centers that do not have Calypso, we use the gold seed fiducial marker guided IMRT system. In this case, EBRT is given first, and the radioactive seeds second. We feel that either method is reasonable at the current time.

Will radiation shrink the size of a prostate, and is this good or bad?

Both EBRT and implantation can cause the gland to be become considerably smaller. This is neither good nor bad. As mentioned earlier, the main concern is the effect on urinary function. Most men eventually return to their pre-implant function regardless of the size of the gland.

<u>Under what circumstances would you recommend combined hormonal blockade for seed implant candidates prior to the procedure?</u>

The use of combined or sometimes called complete hormonal blockade (CHB) in treatment is increasing. The advantage for patients with large glands is that it can reduce the size of the prostate, allowing for a technically ideal implant. Several EBRT series have also demonstrated an advantage to using CHB prior to and during treatment. This fact, plus the relatively few side effects of CHB, has prompted the use of CHB in combination with the implant regimens. Low-risk patients receiving seed implantation have high control rates with implant alone and do not benefit much from CHB.

What length of time do you believe is best for a course of CHB prior to seed implantation?

There is much opinion and little information to help decide the appropriate regimen of CHB prior to seed implantation. Our regimen has followed the EBRT and CHB trials that gave CHB for at least two months prior to seed implantation. Patients receiving combined EBRT and seeds receive CHB until the day of the implant. While our regimen stops the CHB the day of the implant, most continue the CHB after implant at least 2 more months. Studies will be necessary to determine if one regimen is superior to the other.

What effect does CHB have on the cancer and how does its inclusion support the SI procedure?

Complete hormonal blockade (CHB) results in significant cancer cell death. It also reduces the number of normal cells. It unfortunately does not kill all the cancer cells by itself. Since radiation is more effective when there are fewer number of cells it needs to kill, CHB is attractive as additional treatment, especially in those situations in which there is a bulky cancer or a high chance of disease outside the gland. The morbidity of CHB is relatively low and short term compared to, for example, chemotherapy.

What effect will SI have on PSA readings after the procedure and for how long might the procedure affect PSA readings?

PSA readings initially can actually be higher than original PSA if done shortly after the implant. This is probably due to the trauma of the procedure. Typically, PSA levels gradually fall over the first year. We have seen PSA levels continuing to fall over several years. Patients should be aware that often PSA levels could artificially increase and then subsequently decrease. We have seen this particularly at twelve to twenty four months from the implant. This is called the PSA "Bounce" and is well described in the literature.

<u>What PSA level should be hoped for over the long term? What is a good level of PSA after seeding?</u>

Most of the literature supports the observation that patients achieving a PSA level less than 1.0 have a better prognosis. We have, however, many patients who have stable PSA readings above 1.0. It has been speculated that the PSA rises to this level because of regrowth of normal prostate cells, similar to the way BPH can increase PSA. A stable PSA is probably more important.

<u>When should PSA be checked after SI and how often should it be repeated? If PSA rises, what would the options be at that point?</u>

We generally recommend the PSA be done at each follow up visit. Usually the PSA is done at three-month intervals for the first two years after implant and then every six months thereafter. If the PSA should rise, we increase the interval of the PSA to establish a trend over three or four readings. Decisions or conclusions about the cancer should never be made on one PSA reading. The most important thing to do if the PSA continues to rise is to establish if there is in fact cancer. See the above question about PSA levels. If there is a suspicion, the next step is to determine if it is in the prostate or not. Typically, bone scan, MRI, and biopsies are the first steps.

Should a patient have a biopsy after seed implantation?

The value of a biopsy after seed implantation is controversial and in practice, biopsy is rarely done unless there is clinical concern for recurrence. Radiation can cause prostate cancer cells to appear quite abnormal. This has been particularly noted if the biopsy is done before two years. An unskilled pathologist may interpret a biopsy as cancer, while a skilled pathologist may interpret it as severely damaged and dying cancer cells. Obviously the cancer interpretation has serious ramifications. We fortunately have a very skilled pathologist who is an expert in this area. If we do a biopsy, we usually do it at or after two years. Prior to two years, the pathology interpretation has little value.

What is the likelihood of blood in the urine and passing blood clots after the procedure?

It is very likely that blood and/or clots will be noticed in the urine immediately after the procedure. This usually resolves within twenty-four hours. Occasionally it lasts longer or occurs spontaneously some time after the implant. It usually resolves relatively quickly. If it persists, then an evaluation is appropriate.

Do you recommend Kegel exercises before or after SI?

Kegel exercises are exercises of the external urinary sphincter, the muscle which allows us to control the urine when we have the urge. This muscle can be impaired or weakened naturally, or

as a result of the implantation. Kegel exercises can increase the strength of this muscle, allowing for more control of urgency often associated with the implant. It doesn't hurt to do them and they may help.

What part does age play in loss of potency or incontinence after SI?

We have noticed that men over 70 have a slightly greater chance of impotency. This may be part of the natural aging process. We have not found that age is related to the risk of incontinence.

<u>What kind of physician typically performs the radioactive seed implantation procedure and in what kind of setting?</u>

Radioactive seed implantation is usually performed in an outpatient hospital setting by a team of physicians consisting of a urologist, radiation oncologist and a radiation physicist. A spinal anesthetic or general anesthetic is used. Some centers perform in their hospital operating rooms. Both outpatient and inpatient settings are acceptable.

What are the side effects from radioactive seed implantation?

Complication rates with radioactive seed implants are less than those of radical prostatectomy or external beam radiation. After a radioactive seed implant, fewer than 1% percent of patients who have no had prior surgery (i.e. TURP) will become incontinent. About 20-25% of the men will become impotent with another 25% partially impotent. As a result of the implant procedure, some men experience mild discomfort in the groin area for two to three days, which is managed very effectively with mild analgesics. Some blood may be seen in the urine and sperm for a few days after the procedure. This is normal and stops after two to three days.

The effects of the radiation from the seeds usually begin one to two weeks after seed implantation. The main symptoms are urinary difficulties such as frequency, urgency or slight pain. These can last for 2-6 months. These can usually be controlled with simple medications. Occasionally, a temporary catheter is necessary.

<u>What are the advantages of non-surgical seed implantation as compared to other treatment options?</u>

Seed implantation is associated with lower rates of impotence and incontinence compared to traditional treatments, such as radical prostatectomy and external beam radiation. For most patients, seed implantation is a one-time, non-surgical, low-impact procedure. Patients can return to normal activity, including work, within one to three days with little or no pain. Radical prostatectomy patients remain in the hospital for 4-10 days and require weeks of recovery at home. External beam radiation patients must visit a radiation treatment center almost daily over a seven to eight week period.

What kind of patient is best suited for seed implant therapy?

This procedure is an alternative for men who have early-stage prostate cancer. Seed implant alone is used for patients who have a low risk of disease outside the gland. External beam radiation plus seed implantation is used in situations in which there is a greater risk of disease outside the prostate. Seed implantation is also an attractive option for men whose poor health precludes radical prostatectomy.

<u>D</u>oes the radiation from seed implants pose any danger to organs or tissue surrounding the prostate?

Because seeds are implanted with pinpoint accuracy, they pose little risk to surrounding organs or tissue, therefore having low complication rates. The radioactive isotopes used in this procedure (iodine and palladium) decay over a period of a few months. The organs nearby the prostate, that may receive significant dose, are primarily the bladder and rectum.

How effective are seed implants compared to conventional therapies?

According to our latest 15-year publication, the longest to date, low risk patients were free from prostate cancer recurrence 85.7% of the time, and intermediate risk patients 83.6%. This is equal to surgery. Lower complication rates are noted with seed implantation as compared to patients undergoing radical prostatectomy and even external beam radiation. The results from today's radiation implant procedures are expected to be better than that of 15 years ago.

What soreness, discomfort or pain should I anticipate having after the implant? How long will it last? What medications are available to deal with any discomfort or pain?

After the implant, there typically is some soreness underneath the scrotum. Occasionally patients describe feeling like they are "sitting on a golf ball". This is due to the slight swelling and bleeding associated with he surgery. It gradually resolves. Most patients require only mild analgesics like Tylenol Extra Strength. Narcotic pain medications are rarely required.

Is there any chance of infection? If so, what should I do about it?

There have been no major infections in our patients. However, with all surgical procedures there is always a chance. Therefore, all of our patients take an antibiotic for about a week after the implant. Occasionally patients develop urinary tract infections or prostatitis months or years after the implant and require antibiotic therapy.

How long will it take for the effects of Lupron and Casodex to wear off?

Patients of course respond differently to these hormonal agents. Typically, it takes from one to six months for the symptoms (hot flashes, tiredness, etc.) to wane.

<u>When should a patient expect to resume normal activities? How soon after should a patient be able to begin strenuous exercise? How long should I wait before going back to my exercise routine?</u>

The insertion of the needles causes some trauma to the vessels surrounding the prostate. Therefore, immediately after the implant, any exercise or activity that puts pressure on the prostate should be avoided. We recommend that patients do not lift heavy objects or do vigorous exercise for at least three to four days after the implant. Very vigorous exercise after this period may cause some minor bleeding in the bladder. This is not harmful, but we ask the patients to limit their exercise until the bleeding stops. Activities such as bike riding, horseback riding, motorcycle riding in which there is pressure on the prostate should be avoided for at least six months. The repetitious jarring of the prostate with these activities can cause some swelling and impair urination.

How long should I wait before trying to engage in sexual intercourse?

In the past we recommended that patients wait at least two weeks before intercourse and use of a condom with the initial few encounters. This was based on our concern that a seed might fall out in the semen. This event has occurred in only one patient to date and therefore we feel that patients can engage in sexual activity any time after the implant. Occasionally blood in the semen or slight pain at climax with the first ejaculates is fairly common. Of note is that the semen is not radioactive.

<u>Are there any nutritional changes that I can make in my diet to improve the health of my prostate?</u>

Many patients tell us of nutritional supplements that either improve their function or reduce their PSA levels. Unfortunately, there have been no good studies that we are aware of that support one regimen or another. Most of them do no harm however and therefore we have no objection to their use.

After brachytherapy how concerned should I be about scatter radiation exposure to family members?

While there has never been a report of harm to someone near an implant patient, we feel it is prudent to observe some precautions and avoid exposure to young children and pregnant

women. The seeds lose their energy quite quickly. Waiting two months before close, prolonged contact is prudent. Patients can have normal contact time such as brief hugging, sitting at the dinner table, sitting on airplanes, etc. before the two months. Simply keep a modest distance such as 4- 6 feet if the contact is going to be more than several hours.