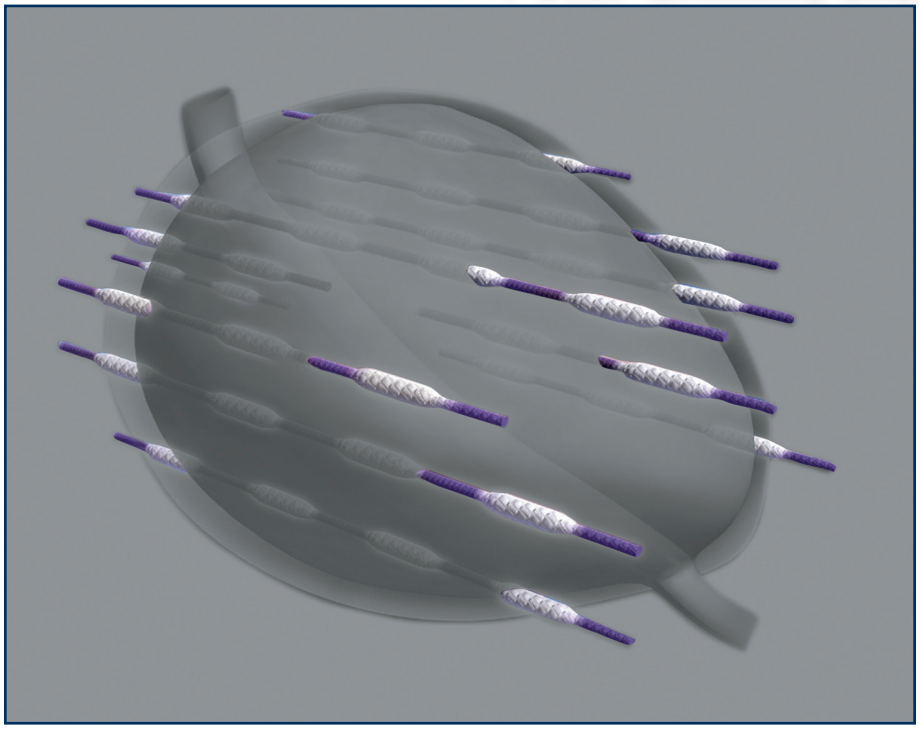
Prostate Brachytherapy Q&A

Peter Grimm, D.O.

Deciding between different types of seeds, knowing the difference between true PSA recurrence and a "bounce," and what to expect from brachytherapy in the long-term.



How does a patient know/decide between the different types of permanent seeds? What are the risks and benefits of Palladium vs. Iodine vs. Cesium?

Historically, permanent seed implantation started with radium needles. These radioactive needles were 2-3 inches long, and were placed into the tissue and remained there for a specific period of time before being removed.

Subsequent developments in implantation resulted in the use of isotopes placed in small titanium tubes ("seeds"), which remained in the prostate permanently.

The first isotopes used in permanent seeds were Iodine-125 and Palladium-103, and more recently, Cesium-131. These isotopes were selected because of their favorable radiation properties.

The advantage of using an isotope with short penetration ability is that the other tissues beyond this short penetration are not affected.

All permanent seed isotopes emit beta radiation, a low-energy radiation that penetrates only a short distance. As these isotopes decay, they emit this beta radiation, and over a short period, return to their basic element (I-125 decays to normal iodine and Pd-103 back to palladium).

The half-life (the period of time it takes for an isotope to be half its strength) is quite short for these isotopes, making them ideal candidates for permanent seed implantation. By placing the seed directly near the cancer, the radiation can effectively destroy the cancer. The advantage of using an isotope with short penetration ability is that the other tissues beyond this short penetration are not affected.

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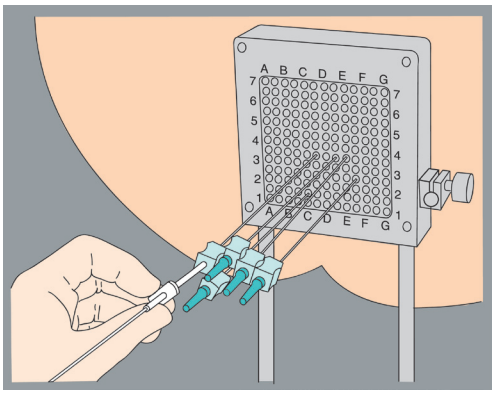

Cancer Control and Isotope Selection

There is no apparent difference in the likelihood of cancer control using the various isotopes. All isotopes deliver a higher dose to the cancer than IMRT or proton therapy. The higher dose to the cancer is the primary advantage of brachytherapy, and higher doses equal better cancer control. I-125 has a half-life of 60 days. Pd-103 has a half-life of 17 days, and Cs-131's half-life is 9.7 days.

The doses prescribed for each of these is slightly different because of their half-lives. A typical implant of I-125 alone will receive a dose prescription to the periphery of the gland of 145 Gy, Pd-125 Gy and Cs 100-115 Gy. While these doses appear to be very different, their biological effects are quite similar. It should be noted that 120 Gy of IMRT radiation would be needed to reach the equivalent dose of a permanent seed implant.

Isotope and Side Effect Profiles

While the cancer control rate among isotopes is similar, the short-term side effect profiles of the isotopes are modestly different. Cs-131 patients, because the energy is given up over a very short time, have a tendency to experience slightly more intense effects of frequency of irritation in the first several months, when compared to Pd-103 and I-125. The long-term effects appear to be similar; therefore, the primary selection may be physician preference.

Technical Differences

Palladium and Iodine are supplied as connected seeds, whereas Cesium is not available as a connected product. Studies have demonstrated that connected seeds almost completely eliminate seed migration and improve dosimetry. Iodine is also available in a thinner connected seed model, which has been demonstrated to decrease the immediate discomfort and bleeding that some patients experience.

Cancer Grade and Isotope Selection

A common belief exists that for high-grade cancers, isotopes that give off energy quicker (such as Pd-103) may be better. However, studies have not yet proven this, and in one study, both iodine and palladium had similar cancer control rates for all grades. At our center, we typically prescribe I-125 for Gleason 4-7 and Pd-103 for Gleason scores 7-10, with personal choice for Gleason 7.

How can a patient know/decide between permanent seeds (above), and temporary seeds (HDR)? What are the risks and benefits?

Both treatments are designed to give a higher dose to the prostate than IMRT or other external beam approaches, and both work well. Each has its own advantages and disadvantages. An advantage to permanent seed implant is that it is usually a single outpatient procedure, requiring only about an hour of operating room time.

A temporary implant is done in an operating room in a similar fashion, but the patient remains in the hospital for several days with plastic needles in the perineum and prostate. During the hospitalization,
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a radioactive seed on a wire is directed through the needle and into the prostate. A computer-based system decides where and how long the seed stays in each position in the prostate, and the treatment is usually done several times over a two-day period.

Temporary seed treatments are usually accompanied by a five-week course of IMRT as well, so it can take a few months to complete the entire process. Some centers perform two HDR treatments, but this of course requires two hospitalizations.

The decision to have either permanent or temporary seeds should first begin with treatment success. Both are quite successful, but the data for HDR is more limited, and the number of experienced practitioners is limited as well.

After seeding - when a patient has a rise in his PSA, how can he know if it is PSA recurrence (cancer-related) - or PSA bounce/bump (not cancer-related)? How can you distinguish one from the other?

PSA levels can actually increase immediately after a permanent seed implant. The earliest we recommend checking PSA levels is six weeks after the procedure, then every three months for the first two years, every six months for up to five years, and then annually.

It may take years for the PSA to reach its lowest level. If the PSA has not progressed on three successive readings, the patient is considered disease-free. A small fluctuation or increase in PSA level is not necessarily indicative of a problem with prostate cancer, but rather, may only reflect normal laboratory fluctuations.

The PSA trend is more important than the absolute PSA value. We have a small number of patients with PSA levels above 1 ng/ml who have been stable for years. After the first year, PSA levels slowly decline over several years, and then stabilize. It is not uncommon, when the PSA is below 1 ng/ml, for slight fluctuations to occur. These small variations do not necessarily mean the cancer is present.

What PSA level should be expected over the long term?

A lower PSA is always better. However, our long-term studies have demonstrated that if the lowest PSA is less than 1ng/ml, that patient has over a 90% likelihood of being disease-free in ten years.

More important than the absolute number is the pattern of PSA. Because every man is different, there is no set standard for absolute PSA. The important thing is that it is stable and non-rising. *(continued on page 12)*

Dr. Peter Grimm is director of the Prostate Cancer Center of Seattle.

In the late 1980s he pioneered, with his partners, a low-dose brachytherapy technique known as seed implantation for prostate cancer.

Grimm and his colleagues have treated over 10,000 patients and trained over 6,000 physicians from around the world in prostate brachytherapy.

He developed six U.S. patented devices that have led to continuous improvements in the equipment widely used in prostate implantation.

In 2010, he received the highest award in the Brachytherapy profession, the President award from the American Brachytherapy Society, for his outstanding achievements and contributions.

What is a PSA bounce?

About one-third of permanent seed patients experience a PSA "bounce" (also referred to as a spike, blip or bump), which means the PSA temporarily goes up and then declines. It happens, on average, between 18-24 months after the implant in approximately 30% of patients after seed implantation.

The magnitude of this PSA rise can range from just a few tenths of a point to as many as 10 points! No one knows exactly why these bounces occur. Some speculate that it may be due to a mild infection, prostatitis (inflammation) or cells which are dying and releasing PSA. The information we have thus far indicates that if the PSA bounces, it does not seem to predict whether a patient will fail. In a study we conducted, patients experiencing a PSA bounce actually did slightly better than their counterparts who did not experience a bounce.

It is important to note that the PSA test can change between the laboratories performing them - therefore, it is valuable to have the test consistently performed by the same laboratory. In addition, sexual activity should be avoided for two days prior to the test.

If the PSA bounce occurs, what should I do?

The bounce is generally a short-term phenomenon. If a PSA reading is up, the normal course of action is to repeat it, either monthly or after three months.

Younger patients have a tendency to have higher bounces. This could be due to the fact that younger men have more normal, healthy prostate cells to begin with, and when that larger number of cells dies, they produce a bigger, temporary PSA bounce.

In other words, a man in his 40s who experiences a PSA bounce will likely have a bounce that's much greater than a bounce a man in his 70s would have. The advice for both groups of men is not to worry. Get re-tested monthly over a three-month period, and the PSA should be back down.

What if my PSA rises? Is it a bounce or not?

If the PSA rises, the first assumption should be that it is a benign bounce or laboratory error. A bounce can be seen for 4-6 months or longer, so patience is important. Since benign conditions such as bacterial prostatitis can also cause the bounce, treatment is usually instituted with the assumption that an infection is causing the problem.

A consistent rise over time, however, can mean the treatment has not worked, and that cancer cells are growing somewhere. If your doctor determines a true rise, the challenge is to find out where the cancer has recurred. There are three different possibilities: (1) disease is outside the prostate, (2) disease is inside the prostate, or (3) cancer is growing both inside and outside of the prostate.

True recurrence in the prostate after permanent seed implantation is rare, and is less than 1% for low- risk disease. A slow rise in PSA can suggest a local recurrence. A rapid rise in PSA usually means the disease is outside the gland. A biopsy is necessary to determine if it is a true local recurrence. The pathology must be read by an experienced radiation pathologist. *(continued on page 13)*

Once a newly diagnosed patient knows his risk stratification (D'Amico, NCCN, CAPRA, Shades, etc.), how can he use this information in his treatment choice, specifically regarding seed implants?

Low-Risk men are the most likely to not have PSA recurrence after treatment. In this group, seed implantation appears to be the most successful, compared to surgery or IMRT.

Which Intermediate-Risk men should consider seed implants?

All should consider it, as it is the most successful treatment, compared to surgery or IMRT. Surgery will fail more often, because it doesn't treat microscopic disease beyond the prostate. IMRT fails because the dose to the gland is insufficient in many patients. Seeds treat both, and give approximately two times the dose to the gland compared to IMRT. If you want to get ultimate control, you have to treat the disease inside the gland AND the microscopic disease beyond the gland. Brachytherapy does both. Many intermediate patients can be stratified to a Low-Intermediate risk group, and can have an implant alone. These are patients with only a small number of positive biopsies.

Would High-Risk men benefit from seed implants? Which ones?

These men would not benefit from implant alone. They need combined treatment with hormone therapy, EBRT and seeds.

Does risk level change the seed implant procedure?

It does not substantially change it in low or intermediate-risk patients. As the grade increases (7-10), the distance the cancer will extend beyond the gland is wider, so we increase the field size in those patients.

Recent literature seems to show men at highest risk have the best PSA control with seed implant (high dose in prostate), combined with IG/IMRT to mop up any cancer around the prostate and in the seminal vesicles (and possibly pelvic lymph nodes). Is this consistent with your views?

I completely agree. Seeds, IMRT or surgery do very poorly alone, compared to a combined approach with seeds, IMRT and hormone therapy.

For a man with Intermediate-Risk who might be a candidate for adding IMRT, would it make sense to do seed implants first and then monitor the PSA, hoping the cancer was local and controlled, and then do IMRT if a recurrence is found?

For most intermediate cases (categorized as Low-Intermediate), the control rate with a standard seed implant alone is 90-95%. EBRT and seeds for High-Intermediate Risk has a 80-90% control rate. It is important to distinguish between these two groups. I do treat some patients in this high intermediate group with implants alone, even though I think they may need combined treatment. However, I use a slightly different plan, using more seeds and a wider implant volume. Obviously, it is possible to do an implant in all of these patients, and then watch to see if they fail treatment, hoping it will work and relying on a mop up. The problem is that the mop up IMRT dose to actually get high control is going to be very similar to a full course of RT. So as you can see, some may escape more aggressive therapy, but those who fail really pay a large price. If you increase the failure rate, you would also increase the complication rate overall. Since the morbidity of a primary implant or combined implant and IMRT are so low (<1% incontinent, 0% death, 0% infection), why take the chance? ◆