Radiation Therapy

Radiation therapy is a non-invasive treatment for prostate cancer that uses x-rays or gamma-rays to eradicate prostate cancer cells. There are several forms of radiation therapy that may be recommended and each patient receives a customized treatment plan depending on the nature of the cancer, the patient’s unique symptoms and overall health. The Peninsula Prostate Institute offers state of the art radiation therapy technology with an experienced team of doctors, nurses, and technical staff to deliver the highest quality care possible. The various forms of radiation therapy are described below.

External Beam Radiation Therapy

External beam radiation therapy is delivered using an x-ray machine called a linear accelerator (see Figure 1). Treatment is delivered on a daily basis, 5 days per week, for up to 7 weeks. It can be used alone or in combination with interstitial seed brachytherapy as primary treatment for prostate cancer. It can also be used after surgery if it appears that the tumor was not completely removed. It also can be used to shrink tumors that have spread from the prostate to other parts of the body (such as the bones) and relieve pain. The daily treatments take anywhere from 10-30 minutes per day. Patients can select the time of day they would like to be treated and are given the same appointment time each day. One cannot feel the treatment as it is being delivered. The entire course of treatment is delivered in the outpatient setting and patients can usually drive themselves to and from the radiation facility.

Before treatment begins, several steps (taking a few days to a few weeks) are required to create a customized treatment plan for each patient. This usually includes placement of positioning markers (see IGRT section below), as well as a CT and sometimes an MRI scan. Information from the CT/MRI is transferred to a computer in order to create a very accurate virtual 3D model of the body which helps to determine the best radiation beam size, strength and angles to use in order to optimize the treatment plan. A “dry run” session the day before treatment begins is also usually required to verify the parameters set by the computer generated treatment plan.
Intensity Modulated Radiation Therapy (IMRT)

IMRT is an advanced form of external beam radiation therapy. It allows for very high radiation doses to be delivered to areas containing cancer (the prostate, seminal vesicles and lymph nodes) while minimizing dose to the surrounding normal tissues (such as the bladder and rectum). Sophisticated treatment planning computer software is used to test thousands of combinations of radiation beam sizes, strengths and angles to most precisely mold the radiation doses around the target. IMRT treatments usually take 20-30 minutes per day to complete. The radiation oncologists at the Peninsula Cancer Center were some of the first to use IMRT in the Seattle area and also helped to further advance this technology with their pioneering work in image guidance techniques.

Volumetric Arc Therapy (VMAT)

VMAT represents the latest advance in external beam radiation therapy. Like IMRT, it can also facilitate the delivery of very high doses of radiation to cancerous tissue while minimizing dose to surrounding tissues. It also requires sophisticated treatment planning computers and software to optimize the treatment parameters. However, a VMAT treatment can be completed in just 2-3 minutes per day. This technique not only makes daily treatment more convenient, it can also improve patient comfort and tolerance to therapy. Peninsula Cancer Center is the only radiation center to offer this treatment on the Kitsap and Olympic Peninsulas.

Image Guided Radiation Therapy (IGRT)

IGRT describes various techniques used to localize the prostate and other important organs within the body. These techniques play a critical role in accurately delivering radiation dose to
the tumor and minimizing dose to the surrounding normal organs and tissues. The following describes techniques used in the treatment of prostate cancer.

Gold Fiducial Markers – Three small gold markers (see Figure 2) are placed into the prostate under ultrasound guidance using a transrectal approach similar to a prostate biopsy. These markers are placed a few days prior to performing special treatment planning CT and MRI scans. Daily x-ray pictures are then taken prior to each treatment and a triangulation calculation is made similar to the way a global positioning system (GPS) works in order to precisely locate the prostate within the body. Adjustments can be made with 1-2 millimeter accuracy to line up the radiation beam with the prostate. Studies have shown that from day to day, the position of the prostate can vary up to 10-12 millimeters (about half an inch). The gold fiducial marker system can account for these daily position differences. This variability is called *interfracton* motion. The Radiation Oncologists at Peninsula Cancer Center helped to pioneer this technology.

![Figure 2 – Gold fiducial markers (actual size 4mm)](image)

Calypso® 4D Tracking System – This system is the first of its kind to allow continuous real-time monitoring of prostate position within the body. Small radiofrequency beacons are placed into the prostate (similar to the gold fiducial markers) and can be tracked both *before and during* the treatment session by a radiofrequency panel array placed over the body. The system can be used to line up the radiation beam before each treatment like the gold fiducial system, but it is then left in place during the treatment and continuously checks the position of the prostate at a rate of 10 times per second (see Figure 3). The system alerts the radiation therapists if the prostate moves out of alignment. The treatment can then be paused, the patient re-aligned, and the treatment is then allowed to continue. Studies have shown that, during the time it takes to
deliver a single radiation treatment, significant movement of the prostate can occur (intrafraction motion). The Calypso® 4D tracking system can account for both interfraction and intrafraction motion insuring the precise delivery of radiation with submillimeter accuracy at all times during the treatment. As a result, this system has been shown to help reduce radiation side effects on the bladder and rectum. The Radiation Oncologists at Penninsula Cancer Center were one of the first in the United States to incorporate Calypso® into external beam radiation treatments for prostate cancer.

Figure 3 – Calypso® radiofrequency beacons
Cone Beam CT – This system is another localization technology which utilizes a CT scanner built onto the linear accelerator. Regular CT scans can be used before treatment to help localize the prostate similar to the gold fiducial system. They can also be used to assess bladder and rectal filling which can also help to minimize radiation dose to those organs. This technology can be used for patients treated with radiation therapy primarily, or after prostatectomy in which the tumor was incompletely removed.

Side Effects of External Beam Radiation Therapy

The side effects of external beam radiation therapy can be divided into early (occurring during or shortly after treatment) and late (occurring months or years after treatment) effects. These effects are related to the organs around the prostate. The bladder and rectum sit just above and just behind the prostate, respectively. Typical early effects include bladder and rectal irritative symptoms such as frequency and urgency. Patients may also notice a weaker urinary stream, getting up more often to urinate at night (nocturia), and loose or irregular bowel movements. These effects may be noticed about half way through the course of treatment and slowly increase in intensity until the end of treatment. They usually resolve within a few weeks after completion of treatment. Patients usually meet with the radiation oncology doctors and nurses on a weekly basis during a course of treatment at which time advice and any necessary medication can be provided to alleviate these symptoms. Late effects are much less common than early effects, but
can be more serious and long lasting. Urinary stricture or incontinence are rare, but can occur particularly in patients who have significant urinary problems prior to treatment. Rectal inflammation, called proctitis, can occur, but infrequently becomes serious enough to require treatment. Loss of potency (ability to have an erection) can occur and is directly related to the patient’s age and erectile function prior to treatment. Medications known as PDE-5 inhibitors are often helpful in improving this problem.

Frequently Asked Questions About Radiation Therapy

- **What sort of activity can I do during radiation therapy?** There are no restrictions with regard to physical activity during radiation treatments. Most people can work, drive a car, exercise and carry on their usual daily activities during a course of treatment.

- **Will I feel the radiation while I am under the treatment machine?** No. Receiving radiation treatment is similar to getting a chest x-ray or CAT scan. You do not feel anything while the x-rays are being delivered.

- **Am I radioactive after treatment?** No. X-rays delivered during treatment do not stay in your body. When you leave the treatment room after each daily session, you are not radioactive.

- **Will the radiation treatments make me sick?** No. You will not be nauseated and your hair will not fall out as a result of treatment.

- **How do I know if the treatment worked?** You will undergo regular follow-up visits. Prior to each visit, you should have a PSA blood test which will help your doctor evaluate the status of your cancer. The PSA will drop to its lowest level, or nadir, between 6 and 18 months after treatment and usually is at a level below 1.0 ng/mL. The PSA should remain around that level on subsequent follow-up visits.

- **What options do I have if the cancer comes back?** It depends where the cancer comes back. If it recurs in the prostate itself, local treatments such as surgery, seed brachytherapy, and cryotherapy are all possible solutions although each carries increased risk of complications and side effects. If it recurs outside of the prostate (in the lymph nodes or bones, called metastases), systemic treatments which can affect tumor cells anywhere in the body such as hormonal therapy, chemotherapy, and perhaps some newer molecular and immune system therapies, are indicated.

**Brachytherapy**

Prostate brachytherapy is the implantation of small radioactive pellets, or “seeds,” into the prostate (see Figure 5). The radioactive seeds deliver high doses of radiation to a very confined
region, making it possible to deliver a high dose of radiation to tumor cells within the prostate while sparing the adjacent normal organs such as the bladder and rectum. Brachytherapy can be used by itself or in combination with external beam radiation therapy to treat prostate cancer. Physicians at the Penninsula Cancer Center were the first in the Seattle area to use the most advanced technique for prostate brachytherapy known as real-time dosimetry brachytherapy. This technique allows placement of radioactive seeds into the prostate with millimeter accuracy. Older methods of prostate seed implants require a preoperative rectal ultrasound study in which the patient’s position must be matched exactly at the time of implant (up to 1 month later). Matching this positioning in the operating room is often difficult and can result in inaccurate placement of the seeds. Using the real-time technique, patients do not require a preoperative rectal ultrasound in the doctor’s office. This technique also improves the accuracy of seed placement by using a computer system in the operating room to map the prostate gland. The position of each seed can be precisely tracked, ensuring the proper radiation dose within the prostate. Equally important, this technique helps doctors avoid placement of seeds near normal tissues such as the bladder, urethra and rectum, further reducing side-effects. Studies have shown this technique to be superior to the older method of implant known as the “preplanning” technique.

Before the procedure, patients undergo general or spinal anesthesia. A urinary catheter is then placed into the bladder. An ultrasound probe, similar to the one used for the prostate biopsy, is then placed into the rectum. The ultrasound is used to help accurately guide hollow needles through the skin of the perineum (the space between the anus and the scrotum) and into their proper position within the prostate. The seeds are then placed into the prostate through each needle. As each needle is withdrawn, a row of seeds is left behind. The entire procedure is done typically in 45 to 60 minutes. It is performed as an outpatient procedure. Patients are usually discharged with the urinary catheter in place and are given instructions on how to remove it the next morning after the procedure. The first follow-up exam is usually scheduled one month after the procedure. During that visit, a CT scan will be performed to check the position of the seeds and ensure that the prostate has received the proper dose of radiation (see Figure 6).

The seeds give off their radiation according to their half-life and then become inert. They are left in the prostate permanently and do not cause any harm to the body. The radioactive isotopes used for prostate brachytherapy include iodine-125, palladium-103 and cesium-131 which have half-lives of 60, 17 and 9 days, respectively. The amount of radioactivity that escapes the body is exceedingly small. However, as a safety precaution, we recommend that small children and pregnant women do not sit on or next to the patient for 1-2 months. Metal detectors (such as those in an airport) will not pick up the presence of the seeds, but radiation detectors will during the first 5-6 half-lives of the seeds. Radiation detectors are commonly used at border crossings (between the US and Canada/Mexico) as well as international airports (such as the Seattle Tacoma International Airport). Patients are given a medical alert card which describes the type
and date of the procedure as well as the isotope used which should be carried by the patient whenever traveling internationally.

Figure 5 – radioactive seed

Figure 6 – CT scan of the prostate one month after implant

Side Effects of Brachytherapy

As with external beam radiation therapy, side effects from brachytherapy can be divided into early and late effects. Immediately after the procedure, patients may have some perineal discomfort and even some bruising for a few days. The urinary catheter can also cause some irritation which sometimes can be alleviated by application of a small amount of antibiotic ointment around the catheter at the tip of the penis. Patients often experience increased urinary frequency, urgency, weak stream and nighttime urination. These effects are at their greatest for
4-6 weeks after brachytherapy and will dissipate over the following 3-12 months. Medications are provided to help alleviate these symptoms. Late effects (occurring months to years after the procedure) such as urinary incontinence or stricture are rare. Proctitis (rectal inflammation) can also occur, but again rarely requires treatment. The rates of potency after brachytherapy are slightly higher than with external beam radiation, but are again highly dependent upon patient age and erectile function before treatment. Medications known as PDE-5 inhibitors are often helpful in improving potency.

**Frequently Asked Questions About Brachytherapy**

- **How will I feel after a seed implant?** You will have some swelling in the perineal area (the skin between the scrotum and the anus), so you should use a soft chair or couch when sitting. You may also notice some bruising in the same area which could extend up onto the scrotum and even the base of the penis. The swelling and bruising will subside in a few days after the procedure. We recommend that you take a few days off of work and avoid strenuous activity for 3-5 days. You may resume normal activity at that point.

- **Does a prior TURP affect my candidacy for seed implant?** Possibly. Very large TURP defects make it difficult to place seeds in the proper position within the prostate gland. Often times, however, the defect is small enough that, with careful planning using a real-time dosimetry technique, your doctors at the Peninsula Prostate Institute can still effectively deliver treatment to the prostate cancer.

- **How soon after seed implant can I have sex?** You can have intercourse as soon as you feel able. However, we recommend you use a condom for the first 3-4 times or first month after your procedure. Sometimes the ejaculate can be bloody or discolored. Over time, the volume of ejaculate will decrease and could eventually dry up. This is normal and occurs over 3-12 months.

- **How do I know if the treatment worked?** Similarly to external beam radiation therapy, regular PSA follow-up is necessary and the PSA will typically nadir below 1.0 ng/mL in 6-18 months after treatment. In about 25% of men, the PSA could rise briefly and then drop back down to its baseline level. This typically occurs 1-3 years after treatment and is called a “benign PSA bump.”

- **What options do I have if the cancer comes back?** As with external beam radiation therapy, it depends where the cancer returns. A recurrence in the prostate itself is rare (about 3% chance). However, if the cancer does come back in the prostate, surgery or cryotherapy are possible treatment options. A recurrence outside of the prostate (in the lymph nodes or bones) requires systemic treatments such as hormonal therapy, chemotherapy and possibly newer molecular or immune system therapies.
Hormone (Androgen Deprivation) Therapy

Hormone therapy is also called androgen deprivation therapy (ADT) or androgen suppression therapy. Androgens (testosterone and dihydrotestosterone) are produced mainly in the testicles and stimulate prostate cancer cells to grow. Lowering androgen levels often stops or significantly slows the growth of prostate cancer cells, although it does not cure prostate cancer. Over time (usually years), the prostate cancer can develop a resistance to this therapy and begins to grow again. Reducing androgen levels is accomplished mainly by medications, but can also be achieved by removal of the testicles (castration).

Hormonal therapy can be used in several different situations:

- If, at the time of diagnosis, the cancer has already spread beyond the prostate gland
- If the cancer remains or returns after initial treatment with surgery, radiation or cryotherapy
- In combination with radiation therapy as initial treatment for aggressive prostate cancer
- Before seed brachytherapy in order to shrink the prostate to make it possible to place the seeds

Types of Hormone Therapy

Orchiectomy – a surgical procedure in which the testicles are removed. The testicles produce 90% of the androgens and, with this source removed, most prostate cancers will stop growing for a time. This maneuver, however, is permanent.

Luteinizing hormone-releasing hormone (LHRH) analogs – these medications can decrease androgen production by inhibiting the release of testosterone by the testicles. Treatment with these drugs is sometimes called “chemical castration” because they lower androgen levels equally as well as orchiectomy. However, their effects are reversible. LHRH analogs are injected under the skin and are given every 1, 3, 4 or 12 months. The LHRH analogs available in the United States include leuprolide (Lupron, Eligard, Viadur), goserelin (Zoladex), triptorelin (Trelstar) and histrelin (Vantas). When these medications are first administered, they cause a brief increase before causing the desired decrease in testosterone levels. This effect is called a “flare.” The flare can be a problem in men with spread of cancer to the bones. Some patients can experience a short term growth of the cancer causing pain, or even neurologic problems like paralysis if the cancer has spread to the spine. This problem can be avoided by giving drugs called anti-androgens (see below) for a few weeks when starting treatment with the LHRH analogs.

Luteinizing hormone-releasing hormone (LHRH) antagonists – these medications bind to receptors in the pituitary gland reducing the release of luteinizing hormone (LH) from the pituitary which then leads to a reduction of testosterone release from the testes. LHRH antagonists reduce testosterone levels more quickly and do not cause the flare like the LHRH
analogs. The LHRH antagonist available in the United States is degarelix (Firmagon) and is available as a monthly injection.

Anti-androgens – Even after orchiectomy or LHRH analog therapy, a small amount of androgen is still produced by the adrenal glands. Anti-androgens block the body’s ability to use androgens. These drugs, such as flutamide (Eulexin), bicalutamide (Casodex), and nilutamide (Nilandron), are taken daily as oral pills. They are often used (for 2-3 weeks) to block the testosterone flare caused by the initiation of LHRH analogs (see above).

Other androgen suppressing drugs – estrogens were once used frequently for advanced prostate cancer. Due to their side effects (such as blood clots and breast enlargement) and the development of the above mentioned medications, estrogens are now used infrequently.

Ketoconazole (Nizoral) is a medication used to treat fungal infections, but also can block the production of androgens from both the testicles and the adrenal glands by inhibiting a number of enzymatic pathways. It can be used in patients whose cancer has progressed while on the above forms of androgen deprivation therapy. Patients usually must also take a corticosteroid (like hydrocortisone) in order to prevent side effects due to low cortisol levels caused by ketoconazole.

Side Effects of Hormone Therapy

The side effects of orchiectomy, LHRH agonists and LHRH antagonists are similar and are due to a reduction in testosterone levels. These side effects include:

- Hot flashes
- Reduced libido (sexual desire)
- Impotence
- Weight gain
- Breast tenderness or enlargement
- Loss of muscle mass
- Fatigue
- Osteoporosis (decreased bone density)
- Anemia (low red blood cell count)

Risk of developing diabetes and possibly cardiovascular disease is also higher in men treated with ADT.

The side effects of the anti-androgens are similar to the above. However, when these drugs are used alone, libido and potency can often be preserved. When used in combination with LHRH agonists, patients can experience diarrhea and nausea. Anti-androgens can also cause liver inflammation.
Many of the side effects of hormonal therapy can be prevented or treated. Hot flashes can be treated with various over-the-counter remedies as well as certain prescription antidepressants. Breast enlargement can be prevented with a short course (3 treatments) of radiation. Exercise can be helpful in reducing fatigue, weight gain and loss of muscle mass and is highly encouraged. Osteoporosis can be monitored with bone density scans and treated with calcium, vitamin D and other drugs. Anemia is typically mild and usually does not require treatment.

**Intermittent Hormonal Therapy**

When androgen deprivation therapy is used to treat recurrent, persistent or metastatic (spread of tumor outside the prostate) disease, it can be used on a continuous or intermittent basis. All prostate cancer treated with hormonal therapy eventually becomes resistant to this treatment typically over a period of years. Some physicians believe that continuous exposure to hormonal drugs might lead to a faster development of hormone resistance. Therefore, intermittent therapy (e.g. treatment for 6 months, followed by a 6 month break followed by another 6 months of treatment, etc.) has been thought to lengthen the time before the tumor becomes hormone resistant. In addition, another advantage of the intermittent therapy is that the side effects of hormonal therapy can be minimized since the patient is not continuously exposed to the treatment.