Spooning through the Alphabet Soup of Radiation Therapy Options for Prostate Cancer

SBRT? IMRT? VMAT? HDR? LDR? Radiation therapy for prostate cancer sometimes seems shrouded by a flurry of anagrams. Here, we will decode this alphabet soup so that you can learn the key principles, pros, and cons of these radiation therapy options as you make the highly personal choice of how you wish to treat your prostate cancer.

External Beam Radiation Therapy (EBRT)

External beam radiation therapy is an umbrella term for any sort of radiation therapy that involves passing a ray of radiation through the body. During this process, you lay on a treatment table while a machine shoots beams of radiation toward the cancer.

The most common type of external beam radiation therapy used for prostate cancer is photon radiation. Photons are created on a machine called a linear accelerator or "linac." Photons used in radiation therapy are in the x-ray range of the electromagnetic spectrum, though they are orders of magnitude higher energy than what is used in a typical diagnostic x-ray. Just as diagnostic x-rays travel through you and are not retained in your body, the photons used in external beam radiation therapy do not leave you radioactive. In other words, go hug your family, friends, and pets after EBRT sessions without worry or guilt.

The shape of the radiation beam is adjusted by a system of moving metal blocks called a multi-leaf collimator (MLC), which is built into the machine at a position between the beam and your body so that it can block some of the radiation beam, much in the way one could imagine shadow puppets blocking a portion of a flashlight beam. These metal blocks are controlled by software to move into pre-calculated positions as you are being treated, acting as a sort of morphing radiation shield.

Elizabeth Zhang-Velten, MD, PhD
Keck Medicine of USC
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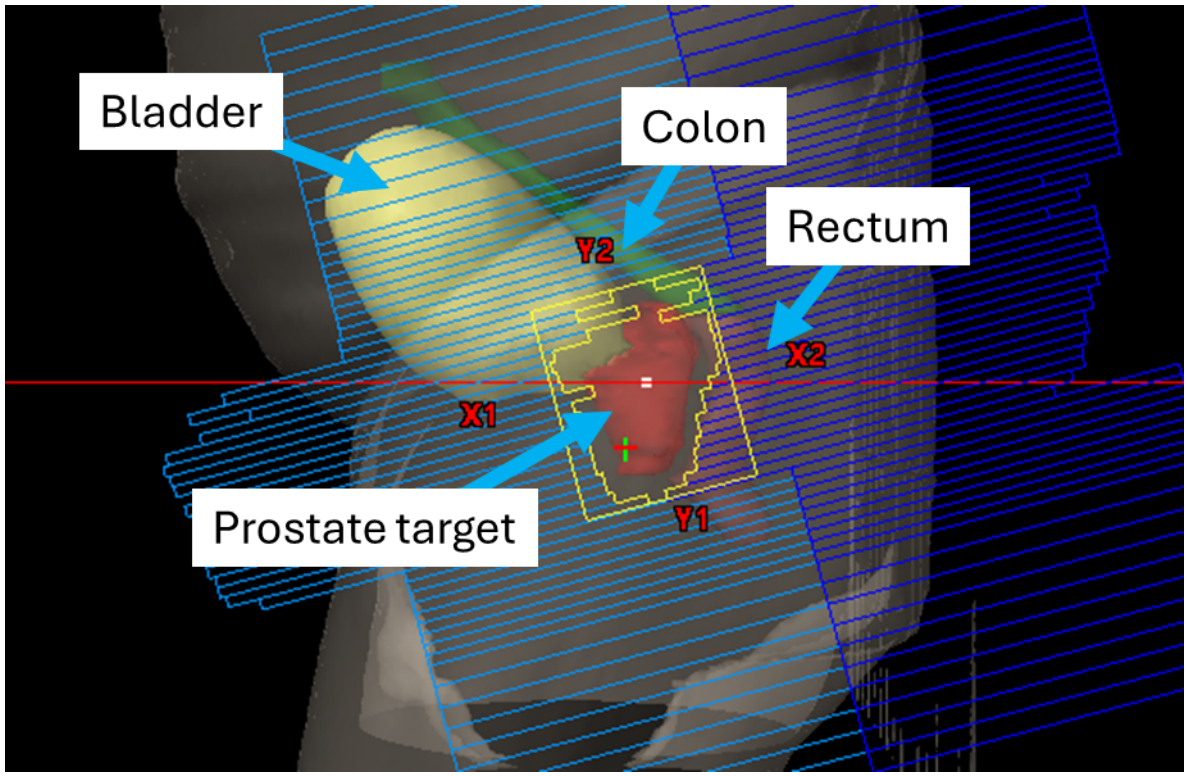


MLCs in motion: The multi-leaf collimator (represented here by rows of blue rectangles) has leaves that each can be programmed to move in and out of the radiation field to strategically block critical tissues. In the case of prostate radiation, the critical nearby neighbors include the bladder, rectum, and colon.

Your radiation oncologist will obtain a CT scan of you in the "treatment position" (typically laying on your back with your arms on your chest, and with a full bladder and empty rectum) and will draw your specific anatomy on this CT to create a 3D model of your body. This will allow your radiation oncologist and a team behind the scenes including a dosimetrist and medical physicist to create a plan that optimally treats the areas at risk while minimizing dose to normal tissues. Depending on your risk factors, your radiation oncologist may target your prostate (or the surgical bed left behind after a prostatectomy) alone, or potentially add radiation coverage of the lymph node basins that drain the prostate.

3D-Conformal Radiation Therapy (3D-CRT)

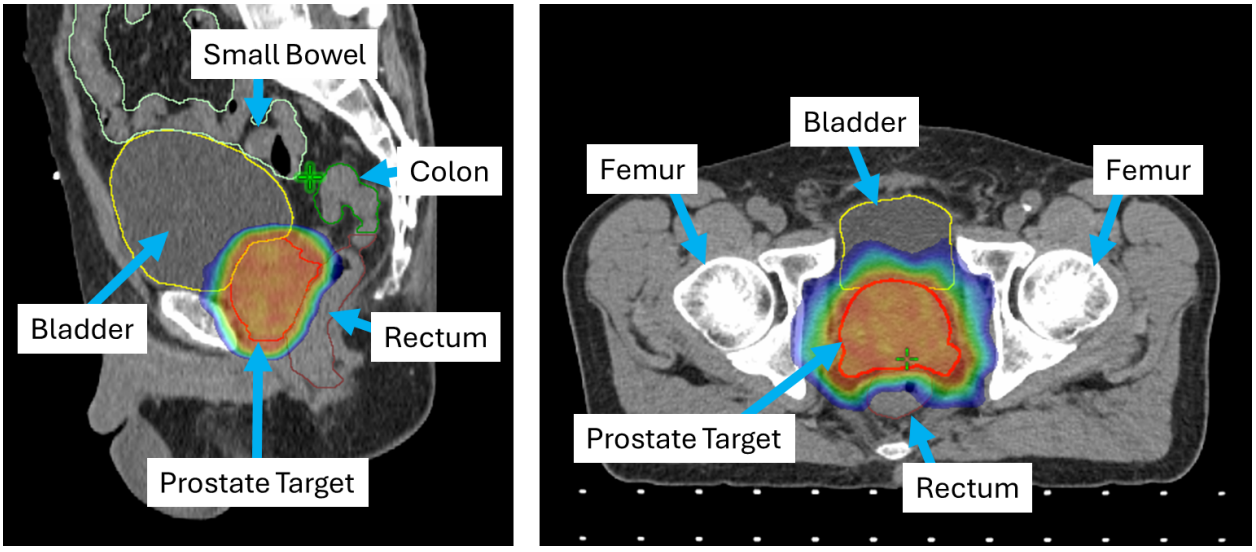
Historically, 3D-conformal radiation therapy was an early type of external beam radiation therapy used for prostate cancer. In 3D-conformal radiation therapy, at least two intersecting beams of radiation are aimed at the patient, and strategic blocking of the radiation beam is designed to reduce dose to normal tissues. 3D-conformal radiation therapy is no longer routinely used for curative treatment of prostate cancer due to the amount of overlapping radiation dose to nearby tissues such as the bowel, bladder, rectum, and femurs. Instead, intensity-modulated radiation therapy and volumetric modulated arc therapy are commonly used for prostate cancer.

Intensity Modulated Radiation Therapy (IMRT)

Intensity-modulated radiation therapy (IMRT) is a specialized form of radiation therapy in which your radiation oncologist designates the desired dose distribution, and inverse-planning software works backward to determine the shielding configuration and balance of beams intensities to achieve this goal. In IMRT, the metal leaves for blocking the radiation beam are moving in real time while the beam of radiation is on, so that the dose from each of several intersecting beams is finely modulated. IMRT allows dose distributions which would be impossible to achieve with 3D-conformal radiation therapy, such that high dose can "swerve" around critical normal tissues.

Volumetric modulated arc therapy (VMAT)

Volumetric modulated arc therapy (VMAT) is a subtype of IMRT. Here, there is not only continuous motion of the metal leaves for blocking the radiation beam, but also strategic movement of the radiation beam itself in an arc around your body, treating you from all angles of a circle. These two systems are synchronized so that the radiation blocking from the metal leaves dynamically carves the radiation dose in sync with the changing beam angle. VMAT provides the organ-sparing capabilities of IMRT but with greater efficiency, allowing you to complete your treatments in typically a few minutes daily. As a result, VMAT has become the standard method of external beam radiation therapy for prostate cancer.



VMAT for efficient precision: Here, we see two views of the same patient's prostate radiation plan. On the left, we see a sagittal view, where his belly button is facing toward the left side and his tailbone is on the right side. On the right, we see an axial view, which is basically a dresser drawer slice of the body, with the belly button facing the top of the image, the tailbone in the bottom of the image, and the hips and femurs on the left and right of the image. The prostate target receives high dose radiation, with the red color wash representing the prescription dose level. The

radiation oncologist typically prescribes the dose to cover the prostate plus a few millimeters of safety margin given that the prostate position can shift throughout the day depending on bladder and rectal volume. The radiation dose falls sharply even millimeters away from the prostate target; the blue color wash represents 60% of the prescription radiation dose level. The bladder (yellow line), rectum (brown line), colon (dark green), and small bowel (light green) receive minimal dose due to the precision of VMAT as well as the patient's own preparation in coming with a comfortably full bladder and empty rectum.

What kind of treatment schedule would I receive? ***What's SBRT?***

While prostate cancer was historically treated with long courses of radiation (for example, 44 treatments, Monday through Friday, for 9 weeks), patients can now receive treatment in as few as 5 sessions total. This is due to technical advances in radiation oncology that (1) allow better sparing of nearby tissues with techniques such as IMRT and VMAT and (2) ensure crucial accuracy of where the dose is targeted with real-time CTs or MRIs when you are set up for treatment.

As a result, radiation oncologists can safely deliver higher daily doses for many patients. A high daily dose of radiation therapy is delivered in 5 treatments in a technique called **stereotactic body radiation therapy (SBRT)**, which can be quite a convenient option. Alternatively, a "middle of the road" option is hypofractionated radiation, in which a slightly higher daily radiation dose allows the course to be finished in 4 to 5 ½ weeks rather than 9 weeks.

However, one deciding factor in what kind of radiation schedule to use is your urinary symptom burden prior to radiation. This is because the radiation is still expected to overlap with your urethra and the neck of your bladder. If you have significant obstructive symptoms prior to radiation, a risk with high daily doses of radiation is that the prostate could swell, tipping you over into urinary obstruction and even needing a temporary urinary catheter. In this case, your radiation oncologist may recommend the hypofractionated (4 weeks or 5 ½ weeks) or conventionally fractionated (9 weeks) low and slow course of radiation to decrease this risk. Alternatively, your radiation oncologist might first use medications to shrink the prostate (for example, Proscar or even androgen deprivation therapy such as Lupron, depending on the situation). That way, if your urinary symptoms improve greatly with this medical management, a shorter course of radiation with higher daily dose such as SBRT may be safe to do.

What about protons?

Proton beam therapy is unique in that protons have mass, and a lot of it. To visualize how photons versus protons behave in the body, please humor me with a thought experiment. Imagine you have a huge block of Jell-O, the size of a room. If you approach this block of Jell-O with a flashlight, the flashlight beam will go through and through because light doesn't have mass. This

is how photon radiation behaves. Now, if you throw tennis balls at the Jell-O, each tennis ball will enter the Jell-O but will not exit because tennis balls have mass and are being stopped as they interact with the mass of the Jell-O. This is how proton radiation behaves. In other words, protons deposit most of their dose at a specific range of distance from their starting point.

What does this mean for prostate cancer? One study that assessed this was the Prostate Advanced Radiation Technologies Investigating Quality of Life (PARTIQoL) trial. In the PARTIQoL trial, which was presented a major radiation oncology conference in 2024, patients with low-risk and intermediate-risk prostate cancer were randomized to either proton or photon radiation. The patients who received photon radiation received intensity modulated radiation therapy (IMRT) rather than the historic 3D-conformal radiation therapy. The patients were followed for changes in their bowel symptoms, urinary symptoms, and sexual function, as well as whether the radiation was effective at controlling their cancer. Whether patients were treated with photons or protons did not make a difference on quality of life in terms of bowel symptoms, urinary symptoms, or sexual function, and either type of radiation had excellent control of the prostate cancer.

The lack of measurable differences between protons and photons on the PARTIQoL trial is likely because photon radiation has come such a long way in the modern era, with techniques like IMRT and VMAT already achieving excellent dose distributions. Going back to the block of Jell-O analogy, imagine that you have many dim flashlights instead of one bright flashlight. Position those multiple flashlights in a circle around the block of Jell-O so that they are all focused a central point within the block. Their point of intersection will be very bright, but each individual flashlight is contributing very little light to the block. This is how photon irradiation beams are used to achieve high dose to the prostate but minimal doses to normal tissues. All in all, the PARTIQoL trial provides reassurance that patients have two excellent options in protons and photons.

Internal Radiation Therapy (Brachytherapy)

Internal radiation therapy or brachytherapy is a highly specialized procedure in which radioactive seeds are positioned inside the prostate to give very localized radiation dose. Brachytherapy is done in a hospital operating room while you are under anesthesia. You have to be fasting prior to the procedure, and you will need to do bowel preparation prior to the procedure to clean out your colon and rectum (much like you would before a colonoscopy). A rectal ultrasound is used to help see the prostate and medical implements during the procedure. A urinary catheter (Foley catheter) is in place during the procedure, and you'll need to be urinating on your own without the catheter before your radiation oncologist is willing to send you home after the procedure. Most people go home from the hospital on the same day as the brachytherapy procedure.

A major advantage of brachytherapy is that the radiation sources are physically placed within the desired target, such that the tumor can be treated from the inside out. In comparison to EBRT, brachytherapy allows high doses of radiation to tumor without having to shoot beams through bowel, through the bladder, or through the rectum to get there. Challenges of brachytherapy are that it is an invasive procedure, outcomes are very dependent on the technical skill of the radiation oncologist (the procedure should be performed by a radiation oncologist with specialized brachytherapy training and experience), and it can cause urinary irritation and even narrowing of the urethra. Depending on your urinary symptom burden prior to radiation and the shape and size of your prostate, your radiation oncologist may recommend against brachytherapy.

Brachytherapy can be used as the sole treatment for low-risk prostate cancer and favorable-intermediate risk prostate cancer with PSA < 15. For patients with unfavorable-risk intermediate cancer, high risk prostate cancer, and very high risk prostate cancer, brachytherapy may be used as a "boost" to the prostate in combination with EBRT and hormone suppression. A "brachytherapy boost" is used in some patients based on data showing better control of the PSA with the boost as compared to EBRT alone.

There are two main types of brachytherapy which we will discuss: low dose-rate (LDR) and high dose-rate (HDR).

Low dose-rate (LDR) brachytherapy

LDR brachytherapy involves the permanent placement of radioactive seeds such as Iodine-125 or Palladium-103 into your prostate gland. These radioactive seeds have a half-life on the scale of weeks. As the seeds undergo radioactive decay, localized radiation is released inside your prostate. The distribution and amount of the radioactive material is chosen so that all the dose is delivered to the prostate over the course of several months.

Although it's an invasive procedure, LDR brachytherapy is convenient as it can be completed in a single OR session. One potential disadvantage of LDR brachytherapy as compared to HDR brachytherapy is that the prostate is still a soft gland rather than a brick wall – that is, a few seeds could possibly move within the prostate after implantation. If there is significant migration, there could be risk of underdosing a portion of the prostate. Additionally, LDR brachytherapy does intentionally leave radioactive seeds inside your body. Depending on the type of radiation source that was implanted, you may be measurably radioactive at a close distance. You may be advised to avoid holding children on your lap and sleeping with direct contact of your pelvis against your partner.

High dose-rate (HDR) brachytherapy

High dose-rate (HDR) brachytherapy involves placement of hollow needles into your prostate. These needles are not radioactive, but they serve as channels for a radioactive source to be launched into pre-calculated positions within the prostate. Your radiation oncologist chooses a radioactive source with a fast decay rate so that the radioactive source only has to dwell for a short period of time in each position within the hollow needles – hence the term "high dose-rate" brachytherapy. After only minutes, the radiation delivery is completed. The radioactive source is withdrawn from your body, and the hollow needles are removed.

One important thing to note is that, if brachytherapy is being used as the only treatment (e.g. if you have low-risk or favorable intermediate-risk prostate cancer), two HDR sessions in total are needed to ensure effective treatment. This means an additional hospital visit as compared to LDR. This practice is based on data that show that one HDR session (even with higher total dose) is not as effective as two HDR sessions. The reason behind this finding is felt to be that, on any given day, different cells within the prostate tumor are in different phases of the cell cycle. As a result, some cells will be more vulnerable to radiation than others during the minutes that HDR brachytherapy is given. The two HDR session are spaced a week apart to account for this; cells that were in a less vulnerable phase of the cell cycle during the first session will have moved onto a different phase in the interim and will be picked off by the second HDR session.

Considerations and deliberation

Is the right option surgery or one of the radiation therapy options discussed above? There is no one-size-fits-all solution for this personal decision. Radiation therapy has its pros and cons. Here are some pieces of the puzzle that have been tie-breakers for some men.

Side effects of radiation versus surgery

A key difference between radiation and surgery is the effect on urination. Prostatectomy results in urinary leakage, at least temporarily, and you would have to do pelvic floor exercises to gradually regain urinary continence. Radiation therapy meanwhile causes irritative, obstructive symptoms (going to the bathroom more often during the day and at night, urgency, incomplete bladder emptying). In someone who already has significant urinary symptoms due to a very large prostate, prostatectomy may be helpful to both treating the prostate cancer and also removing the obstruction that is the prostate.

Another notable difference is that prostatectomy should not cause issues with the rectum or colon. However, radiation therapy results in some overlapping dose to the rectum and colon. This typically results in diarrhea for which many men have to take Imodium. If you have Crohn's

disease or ulcerative colitis, radiation therapy could even cause a flare. After radiation is completed, men have a small chance of something called radiation proctitis, which is a chronic wound of the front of the rectum, right behind where the prostate lives, which can cause bleeding, discomfort, and diarrhea.

Will hormone suppression be recommended in combination with your radiation? If so, are you willing to take it?

Radiation therapy may be a "package deal" with a period of hormone suppression, especially in someone with high-risk or unfavorable intermediate-risk prostate cancer. Some men undergoing radiation with hormone suppression find that the side effects of the hormone suppression are more bothersome than the side effects of the radiation. Some men choose prostatectomy over radiation in order to be able to avoid being committed to hormone suppression.

Final thoughts

That's a lot of alphabet soup. Overall, the abundance of techniques and technologies within the realm of radiation therapy highlights how far prostate cancer treatment has come in the past decades. There are options now! Talk to a radiation oncologist so that you can make the choice that's right for your personal scenario.