SUMMARY OF SCIENTIFIC BREAKTHROUGHS FROM THE 2019 ASTRO ANNUAL MEETING

THE ROLE OF RADIATION THERAPY IN CANCER CARE



Introduction

Hearing a cancer diagnosis is scary. Overwhelming. Confusing. Many questions flood your mind when you learn you or a loved one have cancer. And trying to learn and understand all the treatment options can be daunting to say the least. At the American Society for Radiation Oncology (ASTRO), our mission is to advance the practice of radiation therapy by promoting excellence in patient care, which includes promoting radiation oncology research and disseminating results to both our members and patients.

For more than 100 years, doctors have been using radiation therapy, also known as radiotherapy, to treat patients diagnosed with cancer. Radiation therapy is often combined with other treatment options, like chemotherapy or surgery, or used as a stand-alone treatment. Radiation therapy is an effective option for many people faced with a cancer diagnosis. In fact, nearly two-thirds of all cancer patients are treated with radiation during their illness.

Radiation therapy targets cancer cells and damages the DNA of the cell. The radiation destroys the ability of the cancer cells to reproduce and repair, causing the cells to die. Once these cancer cells die, the body naturally eliminates them. Normal cells that surround the cancer cells are affected by the radiation treatment as well, but the normal, healthy cells can repair themselves far better than the cancer cells. Advances in radiation therapy have allowed doctors to better target the cancer to reduce the risk of side effects from radiation. Despite the name, radiation therapy does not cause a patient to become radioactive. Radiation therapy treatments allow most patients to continue with their typical daily activities. Side effects vary based on the location and type of cancer, and many patients continue to work or go to school while undergoing treatments.

With radiation therapy, research often focuses on this question: What is the right dose of radiation for each patient? Sometimes more intense therapy is needed, and in others, is it possible to reduce the amount and intensity of treatments while still achieving excellent outcomes for patients? How do radiation oncologists find the right balance between reducing treatment doses to improve patients' quality of life while making sure that the reduced treatment remains powerful enough to stop the cancer from spreading?

The answer is research, where scientists and physicians work together to discover new cancer treatments. Today, radiation oncologists are actively researching safe and effective radiation treatments, including more personalized approaches and studies of lower doses for a variety of cancers.

In an effort to disseminate the latest science related to radiation therapy, ASTRO prepared this pamphlet, which highlights some of the top research presented at our 2019 Annual Meeting.



We encourage you to review all of your treatment options, including radiation therapy, with your primary care physician before determining which option or combination of options is best for you and your lifestyle.

Theodore L. DeWeese, MD, FASTRO Chair, ASTRO Board of Directors

Prostate

Prostate cancer is the most common type of cancer diagnosed in men. The American Cancer Society estimates that one in every six men will develop prostate cancer over the course of their lifetime. Prostate cancer is often curable, with more than 98% of men living more than 10 years after diagnosis. Radiation and surgery are often both equally effective as treatment options.

Study finds weekly high-dose radiation treatment as effective but better tolerated compared to every other day treatments

Stereotactic ablative radiotherapy, or SABR (sometimes called stereotactic body radiation therapy, or SBRT), is increasingly popular for treating some kinds of cancers. SABR differs from conventional radiation in several ways. It delivers a focused beam with a high dose of radiation that pinpoints the tumor without damaging nearby tissues. It's typically used to treat



smaller tumors in the earliest stages of cancer. While conventional radiation treatments are given every day for six weeks or more, SABR treatments can be completed in a much shorter time.

But questions remain about the best frequency of each SABR treatment. For prostate cancer patients, a team of researchers at several Canadian cancer centers studied two schedules of SABR treatment to compare both their effectiveness and the level of side effects associated with each.

The randomized study included 152 patients who received a total of five treatments. About half received the treatments every other day over 11 days, which is a typical course of therapy in many cancer centers. The other half received treatments about once a week over 29 days.

The every-other-day group had more side effects than the weekly group during treatment, but the side effects subsided after treatment, and both groups showed about the same long-term response. "I was happily surprised that the more intense short-term problems experienced by men getting SABR every other day did not linger," said principal investigator Andrew Loblaw, MD, MSc, of the Odette Cancer Centre at the University of Toronto.

At five years after treatment, there was no difference between the two groups in how well their cancer was controlled or in their experience of side effects. Dr. Loblaw says his group plans to combine its data with that of another study in Switzerland to see if the findings are consistent.

The choice of treatment schedule seems to come down to convenience, he adds. "In my experience, patients who have to travel a significant distance to the cancer center or who are working when they are going through treatment find the weekly treatment more convenient and easier to fit into their life."

Radiation may generate immune response as it fights tumors

Can some types of radiation treatment stimulate the immune system to help the body fight cancer? Results of a study, called the ORIOLE trial, spearheaded by Ryan Phillips, MD, PhD, of Johns Hopkins University, suggest that stereotactic ablative radiotherapy (SABR) can help keep prostate cancer from spreading, in addition to shrinking or destroying specific tumors. SABR is a type of external beam radiation therapy that uses a focused beam to deliver a high dose of radiation to a well-defined tumor. This type of treatment is generally best for very small tumors. SABR provides a high dose of radiation in shorter amounts of time and can be completed in one to five treatments.

The study followed 54 patients with oligometastatic prostate cancer — that is, their cancer had spread to one, two or three sites outside the prostate after treatment with surgery or radiation. They wanted to delay starting hormone-suppression therapy, often the next step in treating these types of cases. Previous research has shown SABR to be safe and effective for men with localized or non-metastatic prostate cancer, but patients with oligometastatic disease have been considered incurable.

The patients were randomly assigned to one of two groups: those who were observed but received no further treatment for six months and those who were treated with SABR to the metastatic sites outside of the prostate.

Patients treated with SABR were significantly less likely to experience increases in their levels of prostatespecific antigen (PSA), a marker for the presence of cancer, and they lived significantly longer without any detectable disease progression than patients who received no additional treatment. Just 19% of patients treated with SABR had their disease progress after six months, compared with 61% of those in the observation group. More than half of the patients in the SABR-treated group were still progression-free more than a year after treatment.

The research team also studied what happened to the patients' immune systems by measuring changes in the characteristics of their T cells, a type of white blood cell that is an essential part of the immune system. They found significant changes in the T cells of patients in the SABR group 90 days after treatment, but no change in the T cells of those in the observation group. This response suggests that radiation may spark the immune system to more aggressively fight the cancer.







Long-term hormone therapy may do more harm than good for prostate cancer patients with low PSA

Some men who receive long-term hormone therapy after surgery and radiation treatment for prostate cancer may increase their mortality risk from other causes and their risk of cardiac and neurological problems, enough to offset the cancer survival benefit of the therapy, according to a new study. If they have low levels of prostate-specific antigen (PSA), a protein produced by cells of the prostate gland, after surgery, they may be better off skipping the hormone therapy.

"What we showed for the first time is that a patient's PSA level is a predictive biomarker," said Daniel Spratt, MD, associate professor of radiation oncology at the University of Michigan Rogel Cancer Center. "We found that the lower the PSA, the more harm the patient experienced. The higher the PSA, the more likely the patient was to benefit from hormone therapy."

The study re-examined data from an earlier study of 760 patients treated between 1998 and 2003 at more than 100 centers across North America whose cancer returned following surgical removal of their prostate. Half of them had received both radiation therapy and hormone therapy, and the other half had received just radiation. Overall, the group that received hormone therapy had better survival rates than the group that just received radiation, and that original study helped make hormone therapy an accepted part of prostate cancer treatment.

The new analysis was designed to determine whether a patient's PSA level affected their response to treatment. Researchers divided each group based on their PSA levels after surgery, measured in nanograms per milliliter (ng/mL).

Those with PSA levels higher than 1.5 ng/mL had better survival rates with hormone therapy and radiation therapy than with radiation alone. However, hormone therapy gave no overall survival benefit to men with PSA levels lower than 1.5 ng/mL.

The researchers did further analysis on men with very low PSA levels — less than or equal to 0.6 ng/mL. They found that this group was twice as likely to die from causes other than cancer when hormone therapy was added, with the greatest risk of death for those with the lowest PSA levels (0.2-0.3 ng/mL). These patients were also three to four times more likely to experience a combination of severe heart and neurological problems.

Dr. Spratt called for rethinking treatment guidelines. "We went into this study expecting that men with low PSAs probably would derive minimal benefit from hormone therapy, but we were surprised at the magnitude of harm that these patients experienced," said Dr. Spratt. "A lot of these side effects have been reported over the past few decades, but demonstrating this in a clinical trial to this extent has not been done before. There needs to be a real discussion about the fact that hormone therapy has not been shown to help these men live longer."

Dr. Spratt and his colleagues are currently enrolling post-operative patients with prostate cancer in another study (BALANCE Trial, NRG GU006) that will delve deeper into who might benefit from hormone therapy and who might not, based on genetic testing of their tumors.





Prostate cancer patients get good news: evidence of a cure

Oncologists are understandably reluctant to tell their patients that they're cancer-free — even when posttreatment tests don't show any signs of cancer — if they don't know how likely it is that the cancer might return someday.

But researchers look for ways to confirm that patients can rest easy, and they have found one for the prostate cancer treated with brachytherapy, which is the insertion of radioactive implants directly into the tissue. A long-term study of almost 15,000 patients at seven institutions across the U.S., Canada and Ireland has shown that the results of a blood test four years after treatment can predict, with high levels of certainty, that patients will remain cancer free up to 15 years after treatment.

All the patients had localized prostate cancer and had been treated with low-dose-rate brachytherapy. Most of them had received only brachytherapy, although some had also received radiation through an external beam and/or androgen deprivation therapy, which starves the cancer of male hormones.

The study looked at the patients' test results for prostate-specific antigen (PSA), measured in nanograms per milliliter of blood (ng/ml). While there's no single "normal" PSA reading, the higher the level of PSA in a man's blood, the more likely it is that he has prostate cancer, particularly if the PSA level increases over time. After successful cancer treatment, very low levels of PSA are typical.

The study removed patients whose cancer had returned within four years after treatment and then measured the correlation between the patients' PSA levels at four years and their survival both 10 and 15 years later. "We wanted to see if we could discover a PSA level early in follow-up which would predict for cure at 10 to 15 years after brachytherapy," said Juanita Crook, MD, of the University of British Columbia, the lead author on the study. "We found that 80% of patients had reached a PSA level of 0.2 ng/ml or lower by four years after treatment, and this level was associated with a 99% chance of being free of prostate cancer at 10 years and 97% at 15 years."

The study team suggested that a PSA level of 0.2 ng/ml be adopted as the biochemical definition of a cure for low-dose brachytherapy patients with four years of follow-up. "This standard allows us to reassure patients early on that they are very likely cured, and it also means that they don't need as close follow-up in subsequent years," Dr. Crook said. "It was satisfying to establish this with such a large group of patients."

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