Support for Yale Cancer Answers comes from AstraZeneca, proud partner in personalized medicine, developing tailored treatments for cancer patients. Learn more at astrazeneca-us.com.Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about radiation oncology with Dr. Henry Park and Dr. Christin Knowlton. Dr. Park is an Assistant Professor of Therapeutic Radiology at Yale School of Medicine and Dr. Knowlton is an Assistant Clinical Professor at Yale and a Clinician in Therapeutic Radiology. Dr. Chagpar is an Associate Professor of Surgery and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.Chagpar Christin, let's start with you, tell us a little bit more about what exactly radiation oncology is, what do radiation oncologists do?Knowlton We treat cancer and some benign conditions, which are noncancerous conditions with radiation.Chagpar Tell us more about radiation. It seems like a pretty scary term to people who have not experienced it.Knowlton Certainly patients do come into their initial consultation nervous about the word radiation because often we are told to avoid radiation from the microwave or from the sun. Our goal and our job is to use radiation to treat the tumor, the lesion that needs to be treated with a highly collimated targeted treatment plan and to spare the healthy tissues nearby and using that technique to limit the toxicity and at the same time increase how effective the radiation can be.Chagpar Are all patients candidates for radiation therapy or only some, how do you decide whether you need radiation for your particular kind of cancer?Park Not all patients are candidates for radiation therapy. Approximately half of patients at some point during their cancer treatment will have received radiation at some point, whether it is for cure or for the intent of symptom control or sometimes both. It really depends on the stage of disease, the location of where the disease is and also the functional status of the patient at baseline, in terms of determining whether or not they may be candidates for radiation.Chagpar Christin, you talked a little bit about using these radiation waves, these beams of radiation to treat cancer and avoid normal tissue. How exactly do you do that? I can 3:00 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3imagine that a lot of patients are worried about how the radiation may affect normal tissue, how it could affect their heart, their lungs and other things that might be in the vicinity of where the cancer is?Knowlton That is very true Dr. Chagpar. I treat breast cancer as my primary field of interest. So, the heart and the lungs that you mentioned are key areas that my patients tend to be concerned about. The first thing is we have to determine what is the best position to treat the patient in so that we can treat the area of interest and best keep the radiation off of the healthy tissues. Then, most patients undergo what we call a CT simulation where we do a CAT scan in the treatment position and that CAT scan is used by the radiation oncologists to plan the radiation. And in those images, we can see the target area or areas, but then, just as importantly, we can see what we call those organs at risk, those that we want to avoid. And then, we use different

techniques; for example, most patients are treated with what we call linear accelerator, which is sort of the work horse of the radiation machines. And in the head of the linear accelerator, there are multiple, multiple small leaves that one can adjust the position of using the treatment planning software to shape the radiation into a very particular shape that is perfect for that patient. Other techniques that we may use for example to avoid the heart, some patients are treated holding their breath, others it is not needed to keep the radiation off the heart or the lungs and so each patient's plan is specifically designed for that patient's body shape, the location of the target that we are treating and the location of the organs at risk.Chagpar But if all of that is based on this CAT scan, the CT simulation, what if the patient moves or is not in exactly the same position as they were during the CT simulation. Are those normal tissues now at more risk?Knowlton That is a really great question. Actually, when the patients come for their radiation, the typical patient, we tell that patient that he or she has a 15-minute time, but he or she will quickly find out that the first bulk of that treatment time, the first 10 minutes is really designed to make sure that the position that the patient is in is absolutely perfect. We start by putting various marks on the patient. Some radiation oncologists may put permanent tattoos on the patient that help with the setup each day because those tattoos are aligned to a laser grid. Also, we can use temporary marks with a little tape over them in lieu of tattoos. For many patients, a mold is made under them and that mold is used every day for treatment. Anything that happens during the CT simulation is replicated during each treatment. The same pillow was placed under their knees, whatever board they are laying on is in the exact same position, their mold is there, their arms, legs, thorax, everything is in the exact same position. So, that is how the patients are set up in the same position each day. But, we also do what is on-board imaging, where we do imaging of the patient whether it is on a daily or weekly or 6:10 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3other schedule that is determined to be best for that patient. For some patients, we do port films once a week and those port films will help tell us that the patient and the radiation beams and everything continues to be in the perfect position. Some patients get a mini CAT scan right on the table prior to each treatment. That is called cone beam CT, and other patients can have what we call surface imaging where there are 3 cameras and every moment they are on the table they are viewing the surface of their body, and if the patient moves even out of the treatment position beyond a set parameters of let us say 4 mm, the radiation machine will turn off. So, there are lots of different techniques tailored for each patient to make sure that his or her position is perfect each day for treatment and during the course of the treatment itself.Chagpar Dr. Park, how do you decide which of those myriad of techniques you are going to use to make sure that the dose that you are giving to a patient is going where you want?Park We often use many of them at the same time, and it really depends on the location of the tumor. So, whereas Christin treats breast cancer a lot, I treat head and neck cancer quite a bit and brain cancer. So, for those patients, we often use a mask that is a plastic mask

that then gets customized and shaped to the patient's anatomy so that it dries and hardens over about a 10- to 15-minute period. It is something that you use to keep the patient in place in the shoulder and the head region so that the patient aligns in the same way each time. Then, it really depends after that which structure we want to be avoiding most and which one we want to match to in order to figure out which type of on-board imaging to use each day before we do the radiation treatment.Chagpar It sounds like there are so many tools that you use to really make sure that the treatment that you are delivering is safe. But still, the patients may ask about side effects from radiation and certainly patients who come into the clinic may have had relatives and say, well uncle Harry had radiation 40 years ago and he got burnt, what do you say to the patients about that Christin?Knowlton Well, first of all, I tell the patient that each patient is different and of course the radiation for each location is different, but I also talk to them about some advances that we have made in the modern era if that patient was treated a long time ago, and I offer reassurance and I explain to the patient the techniques that we are going to use to try to keep any acute- and late-term side effects as little as possible.Park There is also a technique called intensity modulated radiation therapy, which is what we use for many areas in the body, including the head, the throat, the lung, the prostate and some other areas as well, where we can really customize the beams and 9:11 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3change the intensity of the beams as it goes around the patient's body to minimize those side effects as much as we can and maximize the dose that we get to the target that we are aiming for.Chagpar So, are there some side effects that the patients can expect regardless of where the tumor is versus other side effects that are very specific to where the tumor might be located?Knowlton Well, most of the side effects are intimately related to the location of the target area; however, fatigue is a universal side effect that whatever site the patient is being treated at, we always tell the patient that he or she should expect to feel some fatigue, usually starting during the course of treatment and continuing for several weeks afterwards. The other side effect that is a late-term effect that is universal is the risk of secondary malignancy, which is the risk of the radiation causing a new cancer, I know that is a very scary sounding one; fortunately, that is extremely rare, but it is something that is universal regardless of site.Park It often takes at least 10 years for that to occur if it even does, and the chance of that happening is much less than 1% in most cases.Chagpar How do you talk to patients about specific side effects that they may have? For example, Dr. Park, you mentioned that you treat head and neck cancers and prostate cancers, what might be some of the radiation side effects that the patients might have when they get radiation for those kinds of cancers?Park So, for head and neck cancer, the most common side effects are often taste changes and saliva changes as well. The patients often will get dry mouth and everything will start tasting funny, either metallic or bland or something like that where it can take away the enjoyment of food temporarily at least. Those side effects tend to take a little while to recover afterwards. The other ones include skin reaction and

mouth sores. So, this is not a very easy treatment to go through, yet we reserve radiation for patients who really need it, and that is the case for radiation in general is that we do not take these side effects lightly and we know that radiation can have some side effects, but at the same time, we try to use it in very selective patients who really would benefit from it more than be harmed by it.Chagpar What about for prostate cancer?Park For prostate cancer, the rectum and the bladder are nearby, so the bladder itself can cause increased urinary frequency, sometimes during the day and sometimes at night. In the rectum, it also can cause more loose stools as well and more frequent trips to 11:55 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3the bathroom. We do a special technique called SpaceOAR, which is a gel that can be inserted before the prostate radiation that can create some space between the rectum and the prostate, and therefore our rectal doses are much lower than they used to, and we are seeing this in clinical practice that the patients who are getting prostate cancer treatment tend to have quite a bit less rectal side effects than they used to.Chagpar And Christin, what about breast cancer, what are the side effects that people can anticipate after radiation for breast cancer?Knowlton I do tell the patients as we discussed that they will experience fatigue, all the patients who receive radiation for breast cancer will get some sort of skin changes within the radiation field. We have a lot of modern techniques that keep that less than in the past; for example, we use a technique called field-in-field that is similar to the IMRT technique that Dr. Park was talking about, that can better shape the radiation dose and can help limit the hot spots and the cold spots too, which is also important to help make the radiation be as effective as possible. We also have some updated lotions that we prescribe. I do prescribe a steroid cream for some of my patients to use every day during radiation treatment and for up to 1-2 weeks afterwards. A large phase III trial did show that there was not necessarily a decrease in the number of patients that had skin reaction, but there was a decrease in the intensity of it, and patients do find that this lotion is helpful. So, the skin reaction and the fatigue are pretty much universal. And I have to say, for most of the patients that is pretty much all that we see. There are other things that we see, some of them are extraordinarily rare as Henry was saying in less than 1%, but things that we do tend to see sometimes in the clinic can be some cosmetic changes in the breast over time, you can get some contracture of the treated breast where it gets a little bit smaller than the other side. We certainly are seeing it to be much less severe than in the past, I think because of this field-in-field technique where the hot spots are really being limited. Also, there has been a shift in the dosing paradigm for breast cancer patients, previously patients who kept their breast were treated for 5-6 weeks, and now we are treating them for 3-4 weeks and the side effects from the more modern treatment to the skin and the cosmetic side effects have been less.Chagpar That is so interesting, and we are going to pick up on that and learn more about different radiation techniques and how those may influence and lessen the side effects from radiation right after we take a short break for a medical minute. Please stay tuned to learn more about radiation treatment and its side

effects with my guests, Dr. Henry Park and Dr. Christin Knowlton.14:39 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3Support of Yale Cancer Answers comes from AstraZeneca, a science-led biopharmaceutical company dedicated to partnering with leading scientific companies, organizations and the community to improve outcomes for advanced cancer patients. More at astrazeneca-us.com.This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable. And as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient-specific treatments. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.Chagpar This is Dr. Anees Chagpar, and I am joined tonight by my guests, Dr. Henry Park and Dr. Christin Knowlton. We are talking about radiation therapy. A therapy that many cancer patients will have to face and the potential side effects. Right before the break, Christin, you had mentioned that there are treatment advances in radiation oncology where in the past patients who were treated with radiation for breast cancer had 6 weeks of treatment and now that has diminished somewhat down to 3 or 4 weeks, is that right?Knowlton Yes, that is correct.Chagpar But is that as effective, I mean it is one thing to say the side effects are less, certainly people would love to get out of therapy earlier I would imagine, but is it as effective?Knowlton Yes it is, and I am not just saying that, that is based on well-done phase III randomized trials. Any sort of major change that one would make in radiation treatment or anything really that anybody doses in radiation treatment is bolstered or backed up by evidence. Evidence-based practice is the way that we like to practice. So, in the literature, there are 3 large trials – the START-A, the START-B and what we colloquially call the Whelan trial done in Canada with large numbers of patients, where they were randomized to the more traditional course of radiation spanning the 5-6 weeks and the other group was randomized to a hypofractionated course of 3-4 weeks. Interestingly, however, in the hypofractionated course, those patients received a slightly higher dose of radiation per day and if you do the equations to determine the biological effective dose of the fractionation over the 5-6 weeks versus the fractionation over the 3-4 weeks, they were biologically equivalent, but that is not enough, we still need to follow the patients over time. So, these trials have follow-up now, median – meaning half the patients have even been followed longer for over 10 years, showing an equivalency in the outcomes as far as breast cancer recurrence in both arms, and in fact, the hypofractionated course, which is what we call the shorter course, there was a statistical trend towards better outcomes. There was a statistical trend towards less 17:56 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3side effects, and quality of life studies performed with questionnaires on the patient showed a statistical improvement in quality of life, patient perceived quality of life, in the shorter course arm.Chagpar Christin, staying on breast cancer for a minute, some pa-

tients may ask about something called accelerated partial breast irradiation, some form of radiation therapy that can be given over a week. How about that?Knowlton Yes accelerated partial irradiation is offered and it is delivered over a 1-week time with a relatively high dose of radiation in the morning and then again in the afternoon for a 5-day period. So, you are coming in for the 10 fractions. It can be delivered in 2 ways, it can be delivered externally using the linear accelerator with external beam irradiation or another common way is to have a sort of brachytherapy -- I will explain what that means in a moment, but a device inserted into the breast that remains in the breast for the week of treatment. What brachytherapy means is that a radiation source is actually placed within the patient's tissues and that applicator that is within the breast remains within the breast for the week and the source is inserted into the patient's breast through that applicator. Accelerated partial breast currently does not have any published phase III data behind it. There are multiple retrospective trials and registry trials; however, we are still waiting for the large phase III data that has been accumulating and now being followed over time, because particularly for breast cancer, you need to follow these patients over time, especially the type of patient that would be perhaps eligible for accelerated partial breast irradiation because at early stage favorable breast cancer can recur 10 to 12 or more years out, so you need to follow these patients for that period of time to really make sure that this type of treatment is as effective as the traditional external beam treatment and we are not quite there yet.Chagpar And the other thing that the patients may ask about is intraoperative radiation therapy. Some centers are doing a one-shot radiation and you are done right at the time of surgery, how about that? Is that backed by evidence and is that something that you recommend?Knowlton There is some evidence behind it; however, there are proponents of intraoperative radiation therapy and there are those that still are not quite ready to embrace it yet. They feel that the length of time which is just a couple of years that these patients have been followed is way too short to start universally adopting this technique.Chagpar Dr. Park, what about in the field of prostate cancer? I mean, people talk about all kinds of different techniques for prostate cancer, brachytherapy, stereotactic-type 20:55 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3procedures for brain cancers? Tell us more about some of the other specialized techniques in the cancers that you treat.Park Absolutely. In prostate cancer, we are probably about 5 years behind breast cancer in terms of hypofractionation. There have been trials now with slightly shorter follow-up, more in the 5- to 7-year range now but are showing similar results overall, that instead of 9 weeks of once-a-day treatment 5 days a week, we may be able to go down to about 5-1/2 to 6 weeks in some cases, sometimes even as little as 4 weeks and in some very selective cases as little as 5 sessions total in a process called SBRT, stereotactic body radiation therapy. So, the idea behind it is that you can increase the dose per fraction or each time you come in and come in a fewer number of times. The idea behind it being to increase patient convenience and to limit the side effects caused by the treatment while not compromising on the effectiveness of the treatments. But it is quite sub-

tle in terms of figuring out who are good candidates for those treatment, but this is an area of a lot of research going on right now, about trying to figure this out for prostate cancer. Whereas, in brain and in lung cancer, this has been more well established for a long time and anywhere between 1 and 5 sessions of high-dose radiation may be possible to potentially cure patients with these diseases.Chagpar What about brachytherapy for prostate cancer? There are people who talk about having seeds implanted, how does that work?Park Seeds can be implanted through brachytherapy which is an internal radiation therapy. This is done in the operating room where seeds are placed in a very conformal way to be sure that you are getting the dose internally, from inside the body out instead of coming from the outside to the inside of the body. This is something that can be used in some patients, but with the advent of IMRT and with SBRT, overall the need for brachytherapy in prostate cancer has been declining in this country overall, and there are fewer and fewer people doing it because the side effects are getting much less from prostate IMRT generally, so we are much better able to spare the normal organs around the prostate than we used to be. So, the theoretical advantage of brachytherapy coming from inside the prostate whereas coming from the outside is less than it used to be.Chagpar Christin, it sounds like there have been all of these advances, I mean you are changing the doses, you are changing techniques, you are trying to minimize side effects, you are increasing patients satisfaction and convenience, are there other clinical trials ongoing, I mean is this the end of the line or are there more exciting things on the horizon?Knowlton Well, some of the exciting things on the horizon for breast cancer are centered around trying to figure out who does not need the radiation.23:51 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3Chagpar So, can we get rid of it altogether?Knowlton Well, we are not quite there yet. But we are trying to determine which patients are in the low enough risk category with evidence behind it that we can forego the radiation and not sacrifice the outcome. For example, as I think that you know and many of your listeners may know, a large trial called the CALGB 9343 included women over 70 with early stage estrogen receptor positive breast cancers who had undergone lumpectomy with negative margins and with pathologically or clinically negative nodes, and typically patients that have a lumpectomy are treated with radiation, and that has been the standard of care for actually a few decades now based on large randomized trials from the past. However, this trial, the CALG 9343 followed these women out now for over 10 years and it was a phase III well-done trial where one group had the radiation therapy, the other did not. The caveat, they all had to take what we call endocrine therapy, a pill, for at least 5 years following the treatment that helps to prevent the cancer from coming back, but really the advantages from the radiation for that group were very minor and it is safe in those patients to withhold the radiation therapy, but of course not every patient that comes in is over 70 and their cancer does not necessarily meet all of those criteria. So, we certainly are still offering radiation to the majority of women who receive lumpectomy. So, some exciting trials; for example, there is the Prime 2 and some other trials that have expanded that cohort of patients down to the age of

65; however, we have only been following those patients for about 5 years now median follow-up, and like we talked about for breast cancer, that is not quite long enough. It is looking favorable; however, we need to follow those patients out longer before we can universally adopt telling women 65 and up with these favorable characteristics that they can withhold breast cancer, radiation.Chagpar What about in your field Dr. Park, any exciting clinical trials in either head and neck cancers or prostate cancer?Park Absolutely. So, on one end, with early stage breast cancer, there is a movement towards decreasing the amount of treatment that is needed. But in some other cancers, including head and neck cancer, there is a need to sometimes increase how aggressive we are in curing these cancers. So, sometimes chemo and radiation and surgery are not enough to cure patients with some of these more advanced cancers that have a tendency to come back often. So, immunotherapy is something that is being used a lot in patients really with all sorts of cancers at more advanced stages when we are realizing there we're not quite getting the outcomes good enough yet. So, when you combine that with chemotherapy and/or radiation therapy, ongoing trials right now that have been looking at immunotherapy and in trying to use that to the 26:55 into mp3 file https://cdn1.medicine.yale.edu/cancer/2018-YCA-1014-Podcast-Park-Knowlton_344286_5_v1.mp3advantage of the patient. And I think it has a lot of appeal to it given that patients would like to have their own immune systems work against their cancer and help fight the cancer along with the radiation and the chemotherapy that may also be needed.Chagpar What about in prostate cancer? Are there advances and clinical trials looking at radiation or avoiding radiation in that setting?Park In prostate cancer, the trials are more looking right now at hypofractionation and if we can decrease the need for as many sessions of radiation going forwards. It is similar to early stage breast cancer where for most prostate cancers, we are doing quite well overall in terms of outcomes, so most patients whether they get surgery or radiation therapy tend to do pretty well for the most part and few patients overall die of their prostate cancer among the total number of patients who get prostate cancer. So, we are trying more and more to decrease the dose and also even the need for any therapy at all for some patients. We often do active surveillance for people with low-risk prostate cancer where we believe that the benefit of treating them may actually be outweighed by the risks of treating them, and we are more and more cognizant of the fact that our treatments are not always necessary in prolonging life or in improving quality of life, and if we do not achieve either of those goals, then there is no point in the treatment. So, we try to be very cautious of giving treatments without a very good reason to do so.Dr. Henry Park is an Assistant Professor of Therapeutic Radiology at Yale School of Medicine and Dr. Christin Knowlton is an Assistant Clinical Professor at Yale and a Clinician in Therapeutic Radiology. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber, reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.