Welcome to Yale Cancer Answers with Doctor Anees Chagpar. 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's a conversation about advances in radiotherapy for cancer patients with Doctor Kimberly Johung. Doctor Johung is an associate professor of therapeutic radiology at the Yale School of Medicine.
Doctor Chagpar is a professor of surgical oncology.

Dr. Johung, let’s have you tell us a little bit about yourself and what it is you do.

Radiation therapy is the use of ionizing radiation to kill cancer cells, one of our main modalities for the treatment of cancer, along with gastrointestinal malignancies.
surgery and of course chemotherapy.

We deliver our radiation from a linear accelerator, a machine that basically, I would say precisely targets high energy X-rays towards tumors, leading to DNA damage in the cancer cells and cell death.

And so I found myself in radiation oncology because I really liked the multidisciplinary aspect of care both within our department we work with physicists who help us devise the plans along with the medical dosimetrist and also a great team of
radiation therapists who deliver the
daily treatments for our patients
and I found myself specializing in GI
cancers mostly because the opportunity
arose when I was early in my career.
Tell us a little bit more about what kinds of GI
cancers you target in particular and
that you work most commonly with and how
does radiation therapy really play into
those patients treatment algorithm?
In the GI tract the
main cancers that we employ radiation
therapy for would be esophageal cancers,
therapy for would be esophageal cancers,
pancreatic cancers, colorectal cancers,
some liver tumors and anal cancers.
And so for some of these cancers, the radiation therapy actually is critical to cure the cancer. We can use radiation therapy in conjunction with chemotherapy to cure anal cancers as well as esophageal cancers. Sometimes surgery is also employed for patients with esophageal cancers. For the other cancers I mentioned, we use radiation therapy as what we would call part of a combined modality treatment program, so along with chemotherapy and surgery to give patients the best outcomes. So for example, in pancreatic cancer,
radiation therapy is often employed prior to surgery to help improve the likelihood of achieving a complete resection of a pancreatic tumor. And then we also use radiation therapy for those patients who may not be candidates for surgery. And we are trying in that instance to provide local control of the tumor and often to control the onset of local symptoms that may be a result of a cancer growing in a particular location. Terrific. So it sounds like radiation therapy has all kinds of utilities for many different cancers in the GI tract. Now at the top of the show,
you had mentioned this new technology RefleXion. Can you tell us a little bit more about what exactly that is and how it plays into the workings of radiation therapy for these patients? Absolutely. So the Reflexion is a linear accelerator, which I mentioned is the machine that directs focused radiation beams towards tumors. And what’s unique about the RefleXion is that it combines PET imaging technology with radiation therapy. So I think to better understand how the RefleXion is novel...
and what the benefits are,

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it’s best to probably first talk

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about what is a PET scan and how

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is that used in combination with

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radiation therapy on the RefleXion.

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So a PET scan is a common imaging technique,

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as you know, used in cancer care.

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These are scans that are

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standard way to image tumors.

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I would say screen for sites of metastases

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and also monitor response to treatment.

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The way a PET scan works is that we first

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inject a radioactive tracer into the patient.

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The radio tracer can be used for

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cancer detection because it’s a

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glucose or a sugar analog that is
00:04:57.724 --> 00:05:00.077 attached to a radioactive marker.

00:05:00.080 --> 00:05:02.460 So that means that active cancer cells will consume more of the radio tracer.

00:05:04.760 --> 00:05:11.495 We call it FDG for the most common type of PET scan and it consumes that FDG at a greater rate than normal healthy tissues.

00:05:14.120 --> 00:05:16.927 So the radioactive signal can be detected and then reconstructed with a CAT scan.

00:05:19.200 --> 00:05:21.672 So you basically get a three-dimensional image where the amount of tracer uptake would correlate with the metabolic activity or I would say that the tumor activity in that area of the body, basically a PET scan is a whole body scan and it shows us where tumors.
are located in the body and how much
the areas light up on the PET scan
would correlate with how active
cancer cells are in those areas.
So on the RefleXion technology,
which is basically the program that has been incorporated into this Linac,
tracks the PET tracer emissions from cancer cells and that is used to determine where to direct the radiation even if a tumor is moving during treatment.
So the novel technology is combining the PET imaging as a means to guide where and when to deliver the radiation therapy.
NOTE Confidence: 0.93899569
00:06:24.165 --> 00:06:26.240 so that sounds really exciting,
NOTE Confidence: 0.93899569
00:06:26.240 --> 00:06:28.752 but also it seems to kind of make
NOTE Confidence: 0.93899569
00:06:28.752 --> 00:06:30.889 sense that you would have some
NOTE Confidence: 0.93899569
00:06:30.889 --> 00:06:33.031 sort of an imaging modality to
NOTE Confidence: 0.93899569
00:06:33.112 --> 00:06:35.112 direct the radiation therapy to
NOTE Confidence: 0.93899569
00:06:35.112 --> 00:06:37.992 what you wanted to treat prior
NOTE Confidence: 0.93899569
00:06:37.992 --> 00:06:41.480 to this RefleXion technology.
NOTE Confidence: 0.93899569
00:06:41.480 --> 00:06:42.760 How is that being done?
NOTE Confidence: 0.770733589333333
00:06:43.680 --> 00:06:45.717 So what we do for radiation therapy
NOTE Confidence: 0.770733589333333
00:06:45.717 --> 00:06:48.197 is we start with a planning CAT scan.
NOTE Confidence: 0.770733589333333
00:06:48.200 --> 00:06:51.554 This is a three-dimensional image of a
NOTE Confidence: 0.770733589333333
00:06:51.554 --> 00:06:53.918 patient in the position for radiation
NOTE Confidence: 0.770733589333333
00:06:53.918 --> 00:06:56.724 treatment and we use those images to
NOTE Confidence: 0.770733589333333
00:06:56.724 --> 00:06:59.046 define the target volumes being the
NOTE Confidence: 0.770733589333333
00:06:59.121 --> 00:07:01.776 tumor and any at risk areas as well as
NOTE Confidence: 0.770733589333333
the normal tissues that we want to try to minimize radiation dose delivery to. With those CAT scans, we generate a plan to direct the radiation at the sites of interest and we deliver that plan on the Linac with very focused beams that are shaped across the face of the beam to match the shape of the tumor from the angle that the beam is being delivered. We combine that with imaging on the machine on a daily basis, so we can obtain a CAT scan or X-ray imaging to look at the patient anatomy on the day that they come in for treatment and move the patient on the
In order to get the patient in position for treatment.

What this does not help us see is motion that occurs during treatment and that's where this technology really is novel in providing added benefits.

And it sounds like this technology is certainly exciting in the sense that it can see tumors moving, but it also sounds like it might be really expensive.

So I have just a couple of questions. One, how expensive is this and is it covered by insurance? And two, how often do tumors
really move during treatment?

In other words, is this really something that’s necessary for the vast majority of patients or could this simply be an added expense?

So this is currently approved by insurance companies and the cost to the patient would be no different than the cost of a program of radiation therapy that is approved by your insurance company with the added cost to the insurance company of course of the PET scan that would be delivered for treatment planning and during treatment.

But it has been approved by insurance companies and we would of
course make sure that’s authorized prior to proceeding with any treatment. In regards to the tumor motion and how this is beneficial, I think it would be interesting to talk about treatment of a lung cancer to try to envision how the RefleXion technology really provides benefits. So how often a patient’s tumors moves would be very common when we’re considering a lung cancer, for example. So this means that when you’re targeting a lung cancer, you’re basically trying to target a moving target with radiation precisely.
So typically how we would take this into account with radiation therapy is that the radiation field would have to be expanded to encompass the path a lung tumor takes while the patient breathes in order to fully dose the radiation to the tumor. And we also have to take into account not only motion of tumors but also motion of the patient. So a patient may move and even a small amount of motion say millimetres during treatment could move the tumor outside of the high dose radiation region. So we would further expand the radiation field to take into account not only the motion of the tumor but also the motion of the patient.
account that potential motion.

So with the RefleXion they’re calling it biologically guided radiation therapy.

So rather than taking into account the natural motion of the tumor or the motion of a patient with larger treatment fields, the field can be smaller because the PET signal from the tumor is tracked by the RefleXion to guide where and when to deliver the radiation.

So you can imagine it is as if the radiation treatment plan is moving with the tumor.
If the tumor naturally moves, such as in lung cancer or if the patient may wiggle a little bit on the treatment table during treatment. And so if you can narrow the radiation field to just target the tumor and not have to expand the field to account for all of this motion, you might have fewer side effects too, right? The main benefit really is that we can reduce the volume of normal healthy tissue surrounding the tumor and the exposure of those tissues to high doses of radiation and that in turn...
can significantly reduce side effects. And so it sounds like this is novel technology. Has that actually been looked at in terms of studies where you can actually say that there is A-X percent difference in terms of the side effects that patients may have to face. So for example, in the case of lung cancer that there might be less radiation induced pneumonitis or less cardiac toxicity with the use of this new technology versus what we have historically always used. That’s a great question.
So what has been studied so far since this is such a novel technology is that with the PET, with the PET tracking you are in fact delivering adequate dose to the tumor and if anything able to better deliver an ablative dose and full coverage of the tumor while it moves during treatment.

What we have open right now at Smilow is a registry trial. So this is a trial for patients who are being treated on the RefleXion machine, in terms of their tumor type outcomes, in terms of response to treatment and using that data in order to...
understand their response to therapy,

how to predict response,

but also being able to quantify how the delivery of treatment on the RefleXion might reduce the risk of side effects.

Fantastic. Well, we are going to talk more about these interesting breakthroughs in terms of radiation therapy,

but first we need to take a short break for a medical minute.

Please stay tuned to learn more about this breakthrough radiation therapy with my guest,

Doctor Kimberly Johung.

Funding for Yale Cancer Answers
00:13:24.080 --> 00:13:26.040 comes from Smilow Cancer Hospital,
NOTE Confidence: 0.788149961
00:13:26.040 --> 00:13:28.344 where their Prostate and Urologic cancers
NOTE Confidence: 0.788149961
00:13:28.344 --> 00:13:31.028 program is comprised of a team dedicated
NOTE Confidence: 0.788149961
00:13:31.028 --> 00:13:32.993 to managing the diagnosis, evaluation,
NOTE Confidence: 0.788149961
00:13:32.993 --> 00:13:35.558 and treatment of urologic cancers,
NOTE Confidence: 0.788149961
00:13:35.560 --> 00:13:38.470 including testicular cancer.
NOTE Confidence: 0.788149961
00:13:38.470 --> 00:13:42.616 Smilowcancerhospital.org.
NOTE Confidence: 0.788149961
00:13:42.616 --> 00:13:45.121 Genetic testing can be useful for people with cer-
NOTE Confidence: 0.788149961
00:13:45.121 --> 00:13:47.233 tain types of cancer that seem to run in their families.
NOTE Confidence: 0.788149961
00:13:47.240 --> 00:13:49.150 Genetic counseling is a process
NOTE Confidence: 0.788149961
00:13:49.150 --> 00:13:51.060 that includes collecting a detailed
NOTE Confidence: 0.788149961
00:13:51.122 --> 00:13:52.718 personal and family history,
NOTE Confidence: 0.788149961
00:13:52.720 --> 00:13:54.052 a risk assessment,
NOTE Confidence: 0.788149961
00:13:54.052 --> 00:13:57.160 and a discussion of genetic testing options.
NOTE Confidence: 0.788149961
00:13:57.160 --> 00:13:59.786 Only about 5 to 10% of all cancers
NOTE Confidence: 0.788149961
are inherited and genetic testing
are not recommended for everyone.
Individuals who have a personal and or family history that includes cancer at unusually early ages,
more than one diagnosis of cancer in the same individual, rare cancers,
cancer predisposing gene, could be candidates for genetic testing.
Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers such as Yale Cancer Center.
and Smilow Cancer Hospital.

More information is available at yalecancercenter.org.

You’re listening to Connecticut Public Radio.

Welcome back to Yale Cancer Answers.

This is Doctor Anees Chagpar and Doctor Kimberly Johung.

We’re talking about a new breakthrough radiotherapy. It’s actually a technique called RefleXion.

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therapists like Doctor Johung to kind of track that tumor as it moves and as a patient moves during therapy with the PET imaging and deliver the radiation therapy more precisely.

So Kim, you were talking earlier on about this technology and you were saying that you actually specialize in GI cancer.

We kind of took a little bit of a detour to kind of get a sense of how this technology might work in terms of lung cancers where you can imagine that as people breathe their tumors might move. Can you talk a little bit more
00:15:51.935 --> 00:15:54.640 about its particular utility
NOTE Confidence: 0.963657975
00:15:54.640 --> 00:15:56.278 in GI cancers?
NOTE Confidence: 0.863470659285714
00:15:57.000 --> 00:15:58.600 Absolutely.
NOTE Confidence: 0.863470659285714
00:15:58.600 --> 00:16:02.430 We did talk a lot about how the RefleXion
NOTE Confidence: 0.863470659285714
00:16:02.430 --> 00:16:04.800 can optimize the treatment of cancers that
NOTE Confidence: 0.863470659285714
00:16:04.800 --> 00:16:06.832 move during treatment.
NOTE Confidence: 0.863470659285714
00:16:06.832 --> 00:16:09.840 And where this comes into play for GI
NOTE Confidence: 0.863470659285714
00:16:09.909 --> 00:16:12.533 cancers would be in the delivery of what
NOTE Confidence: 0.863470659285714
00:16:12.533 --> 00:16:15.719 we call stereotactic body radiation therapy.
NOTE Confidence: 0.863470659285714
00:16:15.720 --> 00:16:18.120 So stereotactic body radiation therapy,
NOTE Confidence: 0.863470659285714
00:16:18.120 --> 00:16:21.680 that’s a mouthful I’ll call it SBRT,
NOTE Confidence: 0.863470659285714
00:16:21.680 --> 00:16:24.230 is a specialized type of radiation
NOTE Confidence: 0.863470659285714
00:16:24.230 --> 00:16:26.862 therapy in which very precise high
NOTE Confidence: 0.863470659285714
00:16:26.862 --> 00:16:29.412 doses or ablative doses of radiation
NOTE Confidence: 0.863470659285714
00:16:29.412 --> 00:16:32.320 can be delivered to small tumors.
NOTE Confidence: 0.863470659285714
00:16:32.320 --> 00:16:36.624 So typically between 1-5 treatments
for tumors that are very localized. And in this situation it becomes very important to precisely be able to track tumors. So we know that stereotactic radiation can be an effective, non invasive way to treat not only early stage lung cancers, but also liver tumors that may not be able to be resected, or metastatic sites with these ablative doses that can be effective without concurrent chemotherapy.
So I did mention the liver tumors and the pancreatic tumors. Those would be primary tumors that develop in those organs. But for metastatic sites, one area where SBR T has very promising data is in the treatment of oligometastatic disease. So tell us more about that, what exactly is oligometastatic disease and how does this work in those patients? Absolutely. So oligometastatic disease would be primary tumors that arise in the colon or the anus and then have...
spread to a limited number of sites, typically under 5 sites.
And what we've seen is that this is a subtype of metastatic disease where patients actually can have very good outcomes that we can see long term survival and this is achieved with definitive treatment of the primary tumor. So that would typically involve chemotherapy, surgery, often radiation therapy to address the primary tumor. And then if a good response is achieved, you can provide local therapy to those one to five limited
sites of metastatic disease. So local therapy can be surgical resection, but when surgery for these metastatic sites is not feasible, particularly if we’re talking about multiple sites of oligometastatic disease, then SBR T or the stereotactic radiation can provide high load rates of local control with minimal toxicity in a way that’s non invasive. And there are other local treatments that can be provided for oligo- metastatic disease such as ablation techniques like microwave ablation or radiofrequency ablation. So in terms of using this
NOTE Confidence: 0.922873391
00:19:04.964 --> 00:19:06.560 technique of RefleXion
NOTE Confidence: 0.922873391
00:19:06.560 --> 00:19:09.980 it sounds like that is really
NOTE Confidence: 0.922873391
00:19:09.980 --> 00:19:13.124 specific to ablating these tumors
NOTE Confidence: 0.922873391
00:19:13.124 --> 00:19:17.800 with SBR T as opposed to microwave or
NOTE Confidence: 0.922873391
00:19:17.800 --> 00:19:20.280 other techniques that you mentioned,
NOTE Confidence: 0.922873391
00:19:20.280 --> 00:19:21.640 is that right?
NOTE Confidence: 0.943815162352941
00:19:21.640 --> 00:19:24.520 Yes, the RefleXion technology with the
NOTE Confidence: 0.943815162352941
00:19:24.520 --> 00:19:26.974 PET tracking or biologically guided
NOTE Confidence: 0.943815162352941
00:19:26.974 --> 00:19:29.716 radiation therapy as we're calling it
NOTE Confidence: 0.943815162352941
00:19:29.720 --> 00:19:33.095 really is to be used in conjunction with
NOTE Confidence: 0.943815162352941
00:19:33.095 --> 00:19:36.005 radiation therapy for the delivery of
NOTE Confidence: 0.943815162352941
00:19:36.005 --> 00:19:38.158 stereotactic body radiation therapy.
NOTE Confidence: 0.943815162352941
00:19:38.160 --> 00:19:41.471 And right now the SBRT is
NOTE Confidence: 0.943815162352941
00:19:41.471 --> 00:19:44.689 approved for the treatment of lung
NOTE Confidence: 0.943815162352941
00:19:44.689 --> 00:19:48.190 tumor sites and bone tumors though we
NOTE Confidence: 0.943815162352941
expect those disease sites to expand.

So when we’re talking about GI cancers and the use of the RefleXion technology, where it really would come into play right now is for the treatment of all oligometastatic disease in the lung or the bone from a primary GI cancer. You know, one would think that if it was good to treat lung cancers where they move and perhaps bone oligometastatic disease just because of the intensity, it sounds like when we’re doing these ablative therapies, it’s really a more intense form of radiation therapy than standard radiation. And so when you’re targeting
these metastatic sites, you want to be more precise about it, is that right?

That’s correct. So when we’re delivering the stereotactic body radiation therapy, each dose of radiation on a particular day can be upwards of 10 times the amount that we would give on a standard radiation therapy program. And so there it becomes extremely important to be very precise with where that delivery of radiation is and to protect the surrounding normal tissues. And when we discussed the ability to reduce the treatment field with...
the use of RefleXion technology.

NOTE Confidence: 0.935818021818182

that benefit in terms of decreasing the

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risk of normal tissue exposure really

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is increased when you’re delivering the

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higher doses of radiation for SBRT.

You know, when we think about

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colorectal cancer, for example,

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it seems that

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we would think that the most common

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place for colorectal cancer to

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metastasize would be to the liver.

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And so is there a reason why

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RefleXion currently isn’t used for

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these oligometastatic sites in the

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liver or did I misunderstand and it

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really is being used in the liver?

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We expect that the RefleXion technology will be used for oligometastatic in the liver because as you mentioned, especially for colorectal cancer, this is often where we see sites of oligometastatic disease and where we’ve seen excellent long term outcomes. So what is in development right now is being able to detect the PET tracer activity from the metastatic site or the tumor site in the liver and be able to differentiate that from the background uptake because there is a certain degree of background uptake in the liver.
track a liver tumor,

one must be able to have a ability to differentiate some slight differences in PET activity or PET uptake between the tumor and the normal tissue.

You really can use this technology when the PET scan is able to show you a spot that lights up that’s very different from normal tissue, and if that degree of separation isn’t always present in the liver, then there might be more work to be done in that area.

I can imagine that another metastatic sites where it would be really helpful
to be very precise about targeting
radiation therapy would be the brain.
And so is it the same kind
of consideration for using
this technology in the brain,
the idea that there might not be that
difference in terms of resolution
between background and signal exactly.
So we often don’t use PET scans in order
to detect brain metastases for that very
reason that you mentioned Doctor Chagpar.
And thankfully brain metastases
or primary brain tumors typically
don’t move as much during treatment.
So we have other ways when we’re
delivering high doses of radiation or
stereotactic radiation to make sure the patient doesn’t move during treatment such as immobilizing the patient very precisely on a different platform for stereotactic radiation delivery, which is called the Gamma Knife that we do have at our Cancer Center. So we’ve talked a little bit about using this technology for targeting these oligometastatic sites for ablation particularly in the lung and in bone. Does it have any utility in the GI tract for treating primary cancers for example?
will be coming into development because GI cancers by nature will move with respiration or with normal movement of the gut or the organs within a patient. And so I think that being able to more precisely differentiate, as you mentioned, the pet uptake or activity from a tumor to those background organs will be critical to moving forward with using this technology to treat primary GI cancers.

What about for other tumors? I mean, you mentioned that for lung cancer, it seems to make sense to use this. I would imagine that this is now being used for primary lung cancers.
00:25:05.560 --> 00:25:07.282 Is that right? And is it being

00:25:07.282 --> 00:25:08.879 used for any other cancers?

00:25:09.520 --> 00:25:11.830 So currently we're focusing on early

00:25:11.830 --> 00:25:14.169 stage lung cancers for patients who

00:25:14.169 --> 00:25:15.994 are not surgical candidates where

00:25:15.994 --> 00:25:18.838 we do see excellent outcomes with

00:25:18.838 --> 00:25:21.074 stereotactic body radiation therapy.

00:25:21.080 --> 00:25:22.778 And so that would typically be

00:25:22.778 --> 00:25:24.680 3 to 5 treatments to the lung.

00:25:24.680 --> 00:25:25.928 Outside of that,

00:25:25.928 --> 00:25:28.840 the focus is on oligometastatic disease.

00:25:28.840 --> 00:25:31.180 And right now we are limited

00:25:31.180 --> 00:25:32.520 to treatment of metastatic

00:25:32.520 --> 00:25:34.480 sites in the lung and the bone.

00:25:34.480 --> 00:25:36.810 We can use the RefleXion

NOTE Confidence: 0.932816983703704
technology to deliver treatment

without the PET guidance as well.

And there are benefits to treatment

on the RefleXion outside of the

biologically guided radiation therapy.

So this would include basically

any tumor site and we can deliver

intensity modulated radiation therapy

using the RefleXion machine.

So intensity modulated radiation therapy

is different from stereotactic radiation

in that we are now delivering small

doses of radiation on a daily basis,

typically over the course of weeks.

And the reason for the small doses over days,

every day over weeks rather is that
that allows the normal tissues to heal in between each treatment. So while we are taking into account tumor motion, it is less critical because we do have the time in between each treatment for normal tissues to heal. The benefit of the RefleXion technology is that we do have high quality imaging on the RefleXion machine such that we can use a CAT scan or a high quality CAT scan or a pair of X-rays in order to align the patient for those daily treatments on the RefleXion.
So not only can the RefleXion deliver the biologically guided radiation therapy with PET guidance, but also can be used to deliver more standard radiation therapy such as IMRT. And so in terms of using the reflection without the PET, is that with continuous imaging, how is the RefleXion without PET any different than a standard linear accelerator? Well, one of the benefits of the RefleXion actually is the ability to treat multiple tumor sites at the same time. So typically we’ll go back to the example of the oligometastatic sites, right.
So if you were not to use biologically guided radiation and you are treating multiple tumor sites at the same time, this would typically require one treatment plan for the first site and then realigning the patient and treating the second site. But the RefleXion is able to simultaneously deliver treatment to those two sites at the same time. And if you were to be treating a tumor in the lung that’s moving, it would be able to track and treat those two tumors at the same time.
to treat multiple sites simultaneously
and also that the while the RefleXion
does provide the typical radiation
we have found that the quality of
the imaging that we take before each
treatment is delivered is of a higher
quality such that we are bit better
able to discern borders between normal
tissue structures and the tumor and
make sure that the patient is aligned
with millimeter precision for treatment.
Doctor Kimberly Joung is an associate professor of therapeutic radiology at the Yale School of Medicine. 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.

We hope you'll join us next week to learn more about the fight against cancer here on Connecticut Public Radio.

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