Soon my name is Mara, Gulshan here at Yale University, Yale Cancer Center, Smilow Cancer Hospital. Welcome you to the third breast CME lecture series. This today we’re really fortunate to have three phenomenal speakers and panelists. We’re going to start with Doctor Regina Hooley, who’s professor of Radiology vice chair in the Department of Radiology in the interim as division Chief for breast imaging, and then we go to Doctor Kristen Knowlton,
Our medical director for Radiation Oncology at Yale at Hamden, and then last but certainly not least, Doctor Tomer Abraham, who is our director of breasts. Microsurgical reconstruction and breast reconstruction here at Yale. The format is that will have three consecutive speakers. I really encourage you to put as many questions as you want into the chat box or the question to answer. Box will try to answer them as much as possible in real time. Some will leave two to the
end for discussion,

and with that I really appreciate everyone taking the time to log in and listen.

This is going to be recorded so you can go back.

If you want or share this with friends and colleagues around the country and around the world,

so with no further ado,

we'll turn it over to doctor Doctor Hooley.

OK, thanks so much doctor Golshan.

It's really great to be here,

so I'm going to start by sharing my slides and let me just get this.

Uhm? Why OK? So?

I'm going to talk a little bit about
breast cancer screening and, you know,

one size no longer fits all these days.

There’s we’re moving towards a

more personalized screening,

so I’m going to review screening

it and show you where it’s going

over the next 20 minutes or so.

My disclosures I am on the Medical

Advisory Board for dense breast dot

Advisory Board for dense breast dot

dash info and that’s where I took

dash info and that’s where I took

some of my tables and figures from.

That’s a website that has a lot

of information on screening.

It’s accurate and it’s for

patients as well as providers.
So I'll start by reviewing the background breast cancer course. Worldwide is the most common cancer in women. It accounts for about 1/4 of all female cancers. About 15% of all female cancer deaths in the US. Lung cancer is number one for cancer related mortality, and interestingly, the rates of breast cancer is rising worldwide at about 6.4% per year. Nobody really knows why, but that adds up.
The World Health Organization reports that in 2018 there were 2,000,000 cases of breast cancer diagnosed worldwide, and by 2040 that’ll rise to 3,000,000, so it is significant. In general, the incidence of breast cancer is more frequent in developed countries, as noted on the blue map on the left, and this is likely due to screening mammography. However, women diagnosed in developing countries, as noted on the map on the right,
more likely to be diagnosed at an advanced age and are more likely to die from the disease. And maybe this is because there is pretend not to be formalized.

Breast cancer screening in these developing countries. When it comes to breast cancer screening and mammography, we’ve certainly come a long way. Screening and mammography was first introduced, probably in the 1960s, and this is a paper from 1967 showing the new technology. At the time there was film screen,
mammography, and zero mammography as well.

Pretty basic stuff that, compared to our standards today.

But even those studies were able to show some cancers.

Of these days, Thomas synthesis or the 3D mammogram digital breast tomosynthesis is becoming the standard of care where we can see explicit detail of the breast tissue as well as.

Small or subtle cancers that are not well seen on the 2D traditional mammogram alone.
Our group at Yale was lucky to be one of the first centers in the United States to get tomosynthesis. I think it was back in 2011 and a few years after that we became fully all of our mammograms were tomosynthesis and we were leaders in publishing led by Doctor Leon Philpotts. And so showing that tomosynthesis is beneficial for screening and diagnosis of breast cancer among all women and among all ages. Some screening mammography has been shown to save lives, multiple randomized control trials, and observation.
ULL studies have shown that breast cancer mortality is increased by about 20 to 40%. Is the only test that has been shown a clear mortality reduction of breast cancer, and this is mostly due to downshifting up stage two and hired a stage one. There are fewer node negative. There are fewer negative invasive cancers, less tumor process, better tumor biology. And among screening detected cancers 75% or stage zero DCIS or stage one and among clinically detected cancer is more than 50% are stage two or higher. And here are some examples of some mammograms in women.
On the left hand side of the screen.

This is a 67 year old woman who had never had a screening mammogram.

She is a palpable 4 centimeter mass.

It’s pirates 5. We know it’s a cancer.

This was a triple negative, high grade cancer and we would think that she would have, you know, regular speeding. Agra fee.

We would have caught this at an earlier stage and smaller size.

On the other hand, in this patient there’s a tiny new group of calcifications there. Linear their branching.

She’s 15-6 years old.
She has a screening mammogram every year, so they’re caught earlier, this was a very tiny 1.5 millimeter grade, two cancer, High Ki 67. So presumably this is a life saving mammogram in this woman. So despite the success of mammography, it is imperfect, particularly limited in women with dense breasts. The overall false negative rate is 10 to 15% in densities is about 10 to 15% in the overall sensitivity is 70 to 90% dense breasts make it hard for
us because of the masking effect where cancers tend to be white spot. So there can be difficult to see with the white fiber glandular tissue versus women with non dense breasts where there’s more fat and less white gland or tissue. And cancers are easier to identify. So screening mammography is very controversial. I think we all know that our patients know that it’s hard to miss the articles in the. And in the press. Over the past decade or so, and screening has become more complicated,
and this step partially because of the United States Protective Services Task Force, who first issued recommendations on screening mammography in 2009 and then reinstated them again, didn’t change them. Basically, in 2015 and basically gave screening mammography, AB, and even a C rating. They basically said that having a annual screening mammogram and women in there. 40S was a C grade, meaning that this service might be. Offered in selected patients.
Depending on some circumstances and then gave screening mammography every two years from age 50 to 74. AB grade and you know when we're in medicine, we generally like A’s that we should be offering this. But you know Decencies and also the changing recommendations didn’t really sit right over all the task force again. Recommended against screening mammogram of women in their 40s. They also recommended against teaching self breast examination they were against. There were against screening women over 74.
the age of 75 and they were really only for screening women every other year in the starting age 50 to 74.

This is very controversial. Patient advocacy groups primary care, oncology, radiology. Perhaps? It was really just about saving money, because it’s certainly the less we screen, the more money we’re going to save on healthcare dollars. And in all fairness. These recommendations are very similar to other countries that have nationalized health services and health programs, but we don’t have that.
here in the United States. So saying that this is what we should do in a country that doesn’t have a full National Health Service doesn’t seem to be fair, and not mentioning that at all doesn’t seem fair. I do want to focus on the fact that we really should be screening women in their 40s, and if there’s one thing that you should take away for anyone who doesn’t believe in screening women in their 40s, we need to screen women in their 40s every year. So, so please take, you know, lock this in from this,
Talk women in their 40s have higher interval cancer rates. They have denser breasts. We know that interval cancers that are diagnosed between having a normal mammogram. These are usually symptomatic. Cancers tend to be more aggressive. Cancers in women have a shorter sojourn time, and they tend to be faster growing. We also know that. There’s higher survival for earlier stage tumors, and, importantly, there’s ethnic differences. Black and Hispanic women have a peak incidence of breast cancer in ages 46 to 47.
so telling having a sweeping statement that says, you know we should only start screening at age 50 is really doing these patients a major disservice. Uhm?

Here this graph shows that you know breast cancer in the 40s, accounts for about 20% of all invasive breast cancer, so it is a considerable fraction of the disease burden. So it is very important. So the screening guidelines, as they stand now. Among various organizations,
00:10:50.389 --> 00:10:53.420 looks kind of confusing in this table,
00:10:53.420 --> 00:10:56.258 but it’s pretty.
00:10:56.260 --> 00:10:59.361 Think it’s really pretty straightforward.
00:10:58.200 --> 00:11:02.070 Basically, most organizations
00:11:02.070 --> 00:11:04.434 say you should start at age 40,
00:11:04.434 --> 00:11:06.320 and with the exception of the
00:11:06.320 --> 00:11:07.146 task force were offer it.
00:11:07.146 --> 00:11:09.211 So again,
00:11:09.211 --> 00:11:11.252 this reflects the patient
00:11:11.252 --> 00:11:13.087 shared decision making with ACOG
00:11:13.087 --> 00:11:15.358 and the American Cancer Society
00:11:15.358 --> 00:11:17.560 has the option also discharge date
00:11:17.560 --> 00:11:19.458 annual screening at age 45,
00:11:19.458 --> 00:11:22.241 so the American Cancer Society sort of
bridge the gap between societies like the American College of Radiology. And the United States Protective Services Task force. Life expectancy is a little bit all over the place. I'm not so sure something magical happens at age 75. I think it's better to limit screening when life expectancy is less than 10 years, because we know these patients are not going to really benefit as much from early detection. So we have healthy patients who might be 76 years old and they...
should still have a mammogram,
perhaps, maybe not annually. Perhaps we can even consider every one to two years.
And then we have patients who might be 70 or 69 years old or whatever, or not that healthy.
And maybe don’t need to have a mammogram as well.
And again, as far as the interval goes, most people say annually,
maybe every one to two years the task force being the extreme of every every other year.
So in addition to the variable
mammographic screening recommendations, supplemental screening is also an option for many of our patients. This includes ultrasounds and MRI. There’s also newer technologies such as molecular breast imaging and contrast enhanced mem that are really investigational at this time, but they are on the verge of being offered outside of the screening trials. There are limited screening trials that are going on. So these tools are right around the corner. I believe for more widespread use, widespread clinical use, but I’m only going to review
screening ultrasound and MRI today because of the time constraints.

So breast ultrasound screening is linked to death dense breast notification laws.

We do a lot of breast ultrasound screening in Connecticut because we were the first state to have a breast density notification law which was passed in 2009. Coincidentally the same month that the United States Protective Services Task Force told us that we should stop screening women in their 40s and then we have the Connecticut State saying that we...
should be offering patients with dense breast screening ultrasound.

The restless notification.

Just as an aside, has become quite popular,

I think over 30 states in the United States have breast density notification laws.

There are countries in Europe and South America that are considering breast.

Density notification guidelines as well.

And women with dense breasts do benefit from having a screening ultrasound.

Overall, the cancer detection rate is about two to four per thousand women screen.

This is in addition to the approximate 5 cancers per thousand women.
00:14:02.018 --> 00:14:03.830 screen detected on mammography.

00:14:03.830 --> 00:14:06.616 We know that most cancers detected on screening ultrasound are small and node negative and tend to be early stage, so it’s rational to think that finding these mammographic Leopold cancers at an early stage in smaller size will improve overall mortality.

00:14:08.856 --> 00:14:11.145 screening ultrasound.

00:14:11.150 --> 00:14:13.796 Ultrasound screening is really well accepted by our patients.

00:14:13.796 --> 00:14:15.560 It’s relatively inexpensive. It costs about the same price as a mammogram.

00:14:15.637 --> 00:14:18.206 There’s no Ivy contrast.

00:14:18.206 --> 00:14:20.600 There’s no compression.

00:14:20.600 --> 00:14:22.068 It’s widely available, so it can work.
Which is why we offer it to our patients. It also performs very well in women with dense breast tissue before the mammogram is limited, and that’s because of the contrast on ultrasound. These small cancers on ultrasound tend to be dark or hypoechoic, and dense breast tissue tends to look echogenic or white on the ultrasound, so we can see these little cancers that are draped in the glandular tissue fairly well and they will be mammographic. Leah called because they’re just hiding behind this glandular tissue as well. Breast density is also important,
00:15:12.320 --> 00:15:14.864 so I just want to review this briefly
00:15:14.864 --> 00:15:17.144 because most of our more personalized
00:15:17.144 --> 00:15:19.508 community in the direction that we’re
00:15:19.580 --> 00:15:22.076 going to go to is going to include
00:15:22.076 --> 00:15:24.355 breast density as a factor in what
00:15:24.355 --> 00:15:26.435 kind of screening patients should get
00:15:26.435 --> 00:15:28.577 breast dense breasts is very common.
00:15:28.580 --> 00:15:31.000 It’s seen in about 50% of all
00:15:31.000 --> 00:15:32.725 women in the United States.
00:15:32.730 --> 00:15:34.410 We know there’s an increased
00:15:34.410 --> 00:15:36.540 risk of breast cancer in women.
00:15:36.540 --> 00:15:38.616 It’s a 2/6 times increased risk,
00:15:38.620 --> 00:15:41.030 and it can be confusing.
00:15:41.030 --> 00:15:42.968 When you see what they did,
00:15:42.970 --> 00:15:45.091 you know two times increased risk and
NOTE Confidence: 0.80421704
then we’ll see another article that says four to six times increase risk, and that’s because it really depends on what breast density category you’re comparing. So if you compare women with extremely dense breasts with women with fatty tissue, dense breasts is 4 to 6 times higher than the women with fatty breasts. However, that’s the minority of our patients in the United States. Only about 10% of women have extremely dense breast tissue and only about
10% of women have fatty tissue. So 80% of our patients have heterogeneously dense breasts or scattered fibroglandular tissue. And so if you compare women with heterogeneously dense breasts with fatty scattered fibroglandular, then you have only about two times increase risk. It is considered however, an intermediate risk factor for breast cancer. It limits the mammogram. There are higher interval cancer
rates and worse prognosis for these clinically detected cancers. So that’s why breast density is important and it can only be diagnosed on a mammogram. It can be diagnosed based on a breast exam and if the patient’s breast exam is sort of lumpy and difficult to do. Another option for women with dense breasts is fast MRI screening. It has been proposed for average risk. Women with dense breasts. It is being done clinically in other parts of the country. There’s very little of it done in Connecticut, but for example,
University of Pennsylvania does a lot of fast, summarized meeting for women with dense breasts.
The first study was published back in 2014 by Christiana Cool. She’s a highly regarded radiologist in Germany and showed that with a very fast acquisition time of three minutes, as opposed to about 10 or 15 minutes, we could detect cancers at a very high rate of 18 per thousand, and this has been replicated by other studies as well.
So overall, the cancer detection rate of MRI’s about 15 to 18 per thousand, which is higher than screening ultrasound. That supplemental yield is only about two to four per thousand. But MRI is more expensive and requires Ivy contrast. There’s not a lot of MRI scanners out there as opposed to ultrasound, so it’s not as easy to perform. Patients may not like it as well. Takes longer, but it does work. The two year validation showed there were no interval cancers so it was
NOTE Confidence: 0.81505984
00:18:22.378 --> 00:18:23.988 really catching all those cancers.
NOTE Confidence: 0.81505984
00:18:23.990 --> 00:18:25.685 The sense the negative predicted
NOTE Confidence: 0.81505984
00:18:25.685 --> 00:18:27.867 value was high and the specificity
NOTE Confidence: 0.81505984
00:18:27.867 --> 00:18:29.567 and positive positive predictive
NOTE Confidence: 0.81505984
00:18:29.567 --> 00:18:32.249 value are also very good as well.
NOTE Confidence: 0.81505984
00:18:32.250 --> 00:18:34.226 So here is a 61 year old patient
NOTE Confidence: 0.81505984
00:18:34.226 --> 00:18:36.172 with a pathogenic BRACA mutation
NOTE Confidence: 0.81505984
00:18:36.172 --> 00:18:38.482 and Paris producting something over
NOTE Confidence: 0.81505984
00:18:38.482 --> 00:18:40.810 ectomy with a negative mammogram,
NOTE Confidence: 0.81505984
00:18:40.810 --> 00:18:43.402 and she had a MRI six months later
NOTE Confidence: 0.81505984
00:18:43.402 --> 00:18:46.007 and they saw this little cancer and
NOTE Confidence: 0.81505984
00:18:46.007 --> 00:18:49.178 detected this so it can work in women
NOTE Confidence: 0.81505984
00:18:49.178 --> 00:18:51.590 with dense breasts and this woman.
NOTE Confidence: 0.81505984
00:18:51.590 --> 00:18:54.278 She also had high risk and which is
NOTE Confidence: 0.81505984
00:18:54.278 --> 00:18:57.486 where we do most of our breast MRI in
NOTE Confidence: 0.81505984

34
our practices for high risk screening,
and that’s traditional.
I was screening MRI for high risk patients.
Here’s the list there Braca positive
patients they have some of these
syndromes may have chest radiation,
usually eight years earlier,
part age 30,
an overall lifetime risk of
greater than 20% high risk women.
We recommend that they have an annual
mammogram and MRI beginning around age
25 to 30 and again this is the BRACA
positive patients and another high
risk patients and this is recommended
by the American College of Radiology
and the American Cancer Society.

We also know that it’s reasonable to delay the onset of mammographic screening until the age of 30.

In some of these patients, and that’s because of the radiation risk. These patients are known to have increased radiation sensitivity, particularly the BRACA one carriers and the P53 carriers, as well.

So breast cancer risk evaluation is a growing program. Most more and more breast centers today are offering breast cancer risk assessment.

This is in lieu in in coordination
00:20:07.359 --> 00:20:10.040 with interest in population health.
NOTE Confidence: 0.8335403
00:20:10.040 --> 00:20:12.315 We're doing more screening not
ONLY for breast cancer, but colon,
NOTE Confidence: 0.8335403
00:20:12.315 --> 00:20:15.210 cancer, and other cancers as well.
NOTE Confidence: 0.8335403
00:20:15.210 --> 00:20:18.420 So with breast cancer risk evaluation,
NOTE Confidence: 0.8335403
00:20:18.420 --> 00:20:21.108 there are multiple risk assessment
NOTE Confidence: 0.8335403
00:20:21.110 --> 00:20:23.505 tools that are very available online
NOTE Confidence: 0.8335403
00:20:23.505 --> 00:20:26.410 and the estimated risk can really
NOTE Confidence: 0.8335403
00:20:26.410 --> 00:20:29.014 vary depending on which model you use.
NOTE Confidence: 0.8335403
00:20:29.014 --> 00:20:31.889 Most centers are going for the tire
NOTE Confidence: 0.8335403
00:20:31.890 --> 00:20:34.851 acoustic model that’s most widely
NOTE Confidence: 0.8335403
00:20:34.851 --> 00:20:37.135 breast density into that model.
NOTE Confidence: 0.8335403
00:20:37.135 --> 00:20:41.770 When we think about breast cancer risk,
NOTE Confidence: 0.8335403
00:20:41.770 --> 00:20:44.906 we have to know that risk changes overtime.
NOTE Confidence: 0.8335403
00:20:48.570 --> 00:20:50.790 Unknown risk and change every year.
For example, you can have a patient who is just an average risk and then her sister was diagnosed with breast cancer at age 39, and that’s going to bump up her her risk for breast cancer the following year and overtime the lifetime risk increases decreases, excuse me, but the five and 10 year breast cancer risk is also proportional to age, so it’s complicated and that’s something that I think most breast centers, including our own will be doing within the next 5 to 10 years.
so we’re really moving beyond just starting at age 40 and having a mammogram every year, which is nice and simple, and it’s nice for you know, buzzwords and things like that, advertising to something like this, which looks really complicated, but it’s really not that complicated, so let me just review with you. The first question is, does the patient have at least a 10 year life expectancy? If not, then she would only have breast imaging if there’s a clinically suspicious finding.
The majority of our patients will have a 10 year life expectancy and then we ask, is she under the age of 25? A 75? If not, she’s over age 75 with healthy then maybe she would have an annual or BI annual mammogram. Most of our patients are going to be under the age of 75 and then we’re going to look at the wrist and if she is at high risk for breast cancer then we would recommend annual contrast enhanced. MRI beginning at age 25 or 30 and
mammography beginning at age 30,

Then she would have an annual screening ultrasound in addition to her mammogram.

The majority of our patients that are not going to be increased risk and so then we want to be sure.

That they are under the age of 40.

If they’re not over the age of four.

If they’re not over the age of 40, and we would just tell them to start really screening at 40.

we do the baseline mammogram.

Of course,
we always want to synthesis if it’s available, and if she has dense breast tissue, then we would also offer them screening ultrasound or at some places screening MRI as well. So that’s the algorithm where it stands today. What about the future? There are going to be more screening options. We’re going to have advancing knowledge so it will be better risk assessment and more personalized medicine will have new technology. As I mentioned, molecular breast imaging,
contrast enhanced mammography, and of course AI will be more patient, shared decision making.

We're going to be talking more patience and helping them filter information, medical information and guide their decisions. And of course, health. Health care economics is going to play a part in how we screen our patients as well. And what makes the most sense? Briefly, I'm just going to touch on overdiagnosis. I know that there's some people probably listening and thinking we shouldn't screen so much because of overdiagnosis.
We could talk entire day about overdiagnosis, but I've condensed it into two slides, and here's an example of a case of over diagnosis of 59 year old. She had a mass president or left outer breast stable for five years. It looks just like a little lymph node. And this turns out to be a great two tubular. My cancer probably would have done anything. It’s a low grade cancer and so perhaps this is a true case of overdiagnosis. We know that some screening detected cancers.
may never become clinically evident. They grow very slowly with patients that die of something else before cancer becomes symptomatic. This example would be low grade DCIS in an elderly patient. We might over treat these patients and give him and subject them to potential harm. But the key is we don’t know yet which low grade cancers will become lethal and when they’ll become lethal, and so hopefully more research will be able to. To identify these cancers so that we’ll know more where we need to really treat them. Where we can stand back a little bit.
AI tools and population health and new technology are going to allow us to screen smarter. We’re going to know who needs more and who needs less screening, but it’s going to take a lot of outcome analysis and sufficient data right now. Our data collection is not that great. Most of the cancer registries that collect information on cancer. Breast cancer. Do not look at the method of detection so we don’t know how these cancers are being diagnosed, whether they are palpable or whether they had to mow.
00:25:38.760 --> 00:25:40.734 or that whether they were diagnosis
NOTE Confidence: 0.8449189
00:25:40.734 --> 00:25:42.320 on screening ultrasound or MRI.
NOTE Confidence: 0.8449189
00:25:42.320 --> 00:25:44.861 So the American College of Radiology is
NOTE Confidence: 0.8449189
00:25:44.861 --> 00:25:46.914 working to include method of detection
NOTE Confidence: 0.8449189
00:25:46.914 --> 00:25:49.768 in the BI RADS and then when we do that,
NOTE Confidence: 0.8449189
00:25:49.770 --> 00:25:51.414 hopefully the cancer registries
NOTE Confidence: 0.8449189
00:25:51.414 --> 00:25:53.469 and the national databases will
NOTE Confidence: 0.8449189
00:25:53.469 --> 00:25:55.943 accept this so that we can collect
NOTE Confidence: 0.8449189
00:25:55.943 --> 00:25:57.660 information on new technology and
NOTE Confidence: 0.8449189
00:25:57.660 --> 00:25:59.865 figure out what works and what doesn’t.
NOTE Confidence: 0.8449189
00:25:59.870 --> 00:26:00.833 So in summary,
NOTE Confidence: 0.8449189
00:26:00.833 --> 00:26:02.117 annual screening mammogram beginning
NOTE Confidence: 0.8449189
00:26:02.117 --> 00:26:04.269 at age 40 saves the most lives
NOTE Confidence: 0.8449189
00:26:04.269 --> 00:26:05.689 women with dense breasts have
NOTE Confidence: 0.8449189
00:26:05.689 --> 00:26:07.552 the option to choose supplemental
NOTE Confidence: 0.8449189
00:26:07.552 --> 00:26:09.076 screening ultrasound or MRI,
high risk women benefit from annual MRI in addition to screening mammography. Often this will start before the age of 40 and just one key. If a patient is having a supplement, an MRI in addition to our mammogram, she really doesn’t need a screening ultrasound as well. We know in the future, vascular based imaging may not necessarily require contrast routine breast cancer risk assessment will probably be
available to all women and artificial intelligence will definitely enhance the delivery of breast cancer screening at multiple levels. From effective efficient scheduling to managing and analyzing new data to helping the radiologist read better and faster and more accurately, and also again help us determine who needs what when so that we can really serve our patients very well. So I want to thank you for your time and attention and will be available for questions later. Thanks, thank you Doctor Holy.
00:27:09.910 --> 00:27:11.600 was fantastic. I mean honestly,
00:27:11.600 --> 00:27:13.812 the the amount of work that the
00:27:13.812 --> 00:27:15.166 our breast imaging colleagues
00:27:15.166 --> 00:27:17.511 and yuan in our group and others
00:27:17.511 --> 00:27:19.709 have done is is truly remarkable.
00:27:19.710 --> 00:27:22.552 And there's just so much new excitement
00:27:22.552 --> 00:27:25.614 in the pipeline and kind of figuring out
00:27:25.614 --> 00:27:28.789 what the next steps are going to be great.
00:27:28.790 --> 00:27:32.080 Next, move on to Doctor Knowlton to
00:27:32.080 --> 00:27:35.925 discuss some of the recent changes and
00:27:35.925 --> 00:27:38.845 advances in radiation therapy and.
00:27:38.850 --> 00:27:40.250 The floor is all yours.
00:27:46.440 --> 00:27:48.310 Hope you're on mute still.
00:28:18.350 --> 00:28:20.403 So while we're waiting
00:28:20.403 --> 00:28:23.769 for the slides to pop up.
Regina, what are your thoughts on how to screen an elderly woman after an index cancer? For example, an 85 year old with a newly diagnosed breast cancer after treatment, does she need follow up imaging? This is from Doctor Berger. Really great question. Yeah so generally women you know around 85 or 86 their life expectancy is probably around six or seven years where the benefit of early detection probably is not useful. That said, I think it really depends on how healthy the patient is, maybe she still likes having a mammogram.
love these older ladies of her healthy.
They still want to come in and get
their mammogram maybe every other year.
I just wouldn’t push it,
but there is still some shared decision
making there got it excellent.
Hopefully you see my slides properly now.
I do not unfortunately have as many awesome
52
pictures as our two other presenters. 

However, any pictures that were used here were taken from sites that allow use of their photos in this setting.

So when I after the title was submitted, you know D escalation in the setting of, you know, radiation therapy in the setting of breast cancer.

I actually looked up the word deescalation and I think maybe my title is not grammatically correct because Merriam Webster Dictionary does not say that this is a noun in anyway and I tried hard copy and online. It is a will say that it is a verb that can mean to limit to decrease in extent.
Are to decrease in volume or scope.

I was able to find a definition for the noun in the free dictionary, which is a reduction in intensity.

So if we have any people that are very much on top of their grammar and my title may not be correct, I will say however that the title is more in the spirit of the Marian Webster.

Definition where we are in the modern era, aiming to limit the radiation limit, the number of fractions limit the dose that they treatment volumes and also omit radiation when necessary. Really the free dictionary definition
doesn’t make sense because we’re not really reducing the intensity of the radiation.

What we do when we are changing the fractionation to a shorter fractionation is we are using newer schemes of radiation. To deliver the same biological effective dose so I do not feel that the free dictionary definition really beats what’s happening in radiation. But the Marian Webster one does.

So here we see, this is how we are escalating as I had mentioned with the decrease in number of fractions and the decrease in volume of tissue treated an omission of radiation therapy
for appropriate candidates.
And this really does fit the less
is more if we have less radiation
we will have increased compliance.
People will have if the fractionation
scheme is more convenient for them,
whether they have traveled issues
or working issues.
We’re going to have more patients
that will be able to get it with less.
Stress there will be increased
acceptance of the treatment course
increased time for patients to work
or to pursue their hobbies or take
care of their families and increase
00:32:12.608 --> 00:32:13.790 quality of life.
NOTE Confidence: 0.85277045
00:32:15.860 --> 00:32:17.021 So moderate fractionation
NOTE Confidence: 0.85277045
00:32:17.021 --> 00:32:18.956 is now really old news.
NOTE Confidence: 0.85277045
00:32:18.960 --> 00:32:21.676 At this point, we’ve all seen it.
NOTE Confidence: 0.85277045
00:32:21.680 --> 00:32:24.008 This is what it is now.
NOTE Confidence: 0.85277045
00:32:24.010 --> 00:32:25.950 Truly in the United States,
NOTE Confidence: 0.85277045
00:32:25.950 --> 00:32:28.098 the new standard of radiation therapy
NOTE Confidence: 0.85277045
00:32:28.098 --> 00:32:30.426 for the intact breast standard or
NOTE Confidence: 0.85277045
00:32:30.426 --> 00:32:32.928 conventional radiation to the whole breast.
NOTE Confidence: 0.85277045
00:32:32.930 --> 00:32:34.870 It was for several decades,
NOTE Confidence: 0.85277045
00:32:34.870 --> 00:32:36.810 50 Gray and 25 fractions,
NOTE Confidence: 0.85277045
00:32:36.810 --> 00:32:38.970 needed to come for five weeks.
NOTE Confidence: 0.85277045
00:32:38.970 --> 00:32:43.735 And then there would be an optional
NOTE Confidence: 0.85277045
00:32:43.735 --> 00:32:46.203 tumor bed boost of an additional
NOTE Confidence: 0.85277045
00:32:46.203 --> 00:32:48.970 10 to 16 Gray and five to 8.
Actions which many women have received over the years, so that’s six to six and a half weeks of daily treatment. Moderate fractionation for whole breast irradiation therapy, which I’d like to stress in at this time is without including the nodes. This is the new standard where we where the whole breast is being treated in 40 grey and 15 fractions or 42.5 Gray and 16 fractions. That’s really institutional preference. Our institution at Yale we use the 40 grey in the 15 fractions.
00:33:23.504 --> 00:33:25.119 from the start B trial,

NOTE Confidence: 0.85277045

00:33:25.120 --> 00:33:27.260 and for these patients there’s

NOTE Confidence: 0.85277045

00:33:27.260 --> 00:33:29.863 an optional tumor bed boost 10

NOTE Confidence: 0.85277045

00:33:29.863 --> 00:33:31.399 Gray and for fractions.

NOTE Confidence: 0.85277045

00:33:31.400 --> 00:33:33.986 So we’re taking the standard or

NOTE Confidence: 0.85277045

00:33:33.986 --> 00:33:35.710 conventional fractionation of five

NOTE Confidence: 0.85277045

00:33:35.782 --> 00:33:37.806 to six to six and a half weeks,

NOTE Confidence: 0.85277045

00:33:37.810 --> 00:33:39.778 and now it’s become three to

NOTE Confidence: 0.85277045

00:33:39.778 --> 00:33:41.720 four weeks for the patient.

NOTE Confidence: 0.82770544

00:33:43.790 --> 00:33:45.830 And of course there’s some

NOTE Confidence: 0.82770544

00:33:45.830 --> 00:33:48.670 data to back all of this up.

NOTE Confidence: 0.82770544

00:33:48.670 --> 00:33:50.914 These are the three largest trials

NOTE Confidence: 0.82770544

00:33:50.914 --> 00:33:53.181 that have the longest follow-up that

NOTE Confidence: 0.82770544

00:33:53.181 --> 00:33:55.617 are used to backup or support the

NOTE Confidence: 0.82770544

00:33:55.617 --> 00:33:58.039 use of moderate hypofractionation.

NOTE Confidence: 0.82770544

00:33:58.040 --> 00:34:02.116 All three trials to start a the start B, and.
There’s no great name for this one. The Canadian Ontario Wayland trial. Depending on who you’re talking about. I learned from this. I need to have make sure that any trials I have have a catch name, but the start a trial and start be were done in England and the obviously the Canadian trial was done in Canada. They all compared their moderately hypofractionated regimens in whole breast radiation therapy to the standard conventional fractionation of welding. I guess we’re going to call that conventional 'cause modern hypo frack is now standard,
but 50 Gray in 25 fractions was the standard arm and all Childs found no significant difference in local and overall survival for the patients. At 10 years they did use a slightly different fractionation scheme to start. A trial, had had patients receiving 41.6 Gray or 39 Gray and 13 fractions over 5 weeks, which is approximately 3 fractions per week. It’s a little bit of. More challenging regimen to schedule, so most institutions are not really using this regiment, but it is interesting that they did.
Note that a significant decrease in the number of patients with breast induration adima intellect until inject ages in the 39 Gray arm compared to the standard frac. The 41.6 Gray arm did not really do any better as far as then the 50 Gray arm as far as acute effects and late term effects as that. Start B, which is what Yale is using. That’s the 50 Gray and 15 fractions. So once a day Monday through Friday, that’s three weeks. So once again their outcomes, local region of occurrence,
00:35:48.976 --> 00:35:50.896 overall survival at 10 years
NOTE Confidence: 0.82770544
00:35:50.896 --> 00:35:53.020 was the same with the 50 Gray,
NOTE Confidence: 0.82770544
00:35:53.020 --> 00:35:54.770 and there was a significant
NOTE Confidence: 0.82770544
00:35:54.770 --> 00:35:56.170 decrease in breast shrinkage,
NOTE Confidence: 0.82770544
00:35:56.170 --> 00:35:57.806 breast edema and telangiectasia.
NOTE Confidence: 0.82770544
00:35:57.806 --> 00:36:01.119 But age is in the 40 great arm.
NOTE Confidence: 0.82770544
00:36:01.120 --> 00:36:02.970 The Canadian trial was interesting.
NOTE Confidence: 0.82770544
00:36:02.970 --> 00:36:04.442 That is slightly different.
NOTE Confidence: 0.82770544
00:36:04.442 --> 00:36:05.914 42.5 in 16 fractions,
NOTE Confidence: 0.82770544
00:36:05.920 --> 00:36:10.169 so that’s three weeks and a day.
NOTE Confidence: 0.82770544
00:36:10.170 --> 00:36:11.602 Subgroup analysis it’s worthy
NOTE Confidence: 0.82770544
00:36:11.602 --> 00:36:13.750 of note that they did notice
NOTE Confidence: 0.82770544
00:36:13.816 --> 00:36:20.713 increased local regional recurrence.
NOTE Confidence: 0.82770544
00:36:20.713 --> 00:36:23.611 In high grade tumors,
NOTE Confidence: 0.82770544
00:36:23.611 --> 00:36:26.713 with the Hypo frac with 15.6% of
NOTE Confidence: 0.82770544
00:36:26.713 --> 00:36:33.613 patients who received with high
00:36:23.611 --> 00:36:26.774 grade tumors that had hypo fact

00:36:26.774 --> 00:36:29.484 experience in local regional recurrence

00:36:29.484 --> 00:36:32.269 versus 4.7 in the 50 Gray arm.

00:36:32.270 --> 00:36:35.420 I will say that start B did look

00:36:35.420 --> 00:36:38.742 at that and did not find any any

00:36:38.742 --> 00:36:40.802 difference in outcomes for the

00:36:40.802 --> 00:36:41.900 Grade 3 tumors,

00:36:41.900 --> 00:36:44.612 so we tend to still treat those patients

00:36:44.612 --> 00:36:45.807 with moderate hypofractionation

00:36:45.807 --> 00:36:48.057 an in the Canadian trial,

00:36:48.060 --> 00:36:50.550 there was no significant difference

00:36:50.550 --> 00:36:53.730 in acute toxicity or cosmetic outcome.

00:36:53.730 --> 00:36:55.767 So maybe we can tighten things up

00:36:55.767 --> 00:36:58.411 a little bit more now and the newer

NOTE Confidence: 0.82770544
Regimens that are being brought out now are called Ultra Hypofractionation. These once again are in for the setting of whole breast radiation only. We are not yet talking about anything with the nodes. We have two regimens, the fast regimen and the fast forward regimen. Yale has adopted the FAST regimen which we've been using with great success. We started using it in the fall of last year, so in the fast trial. Patients were randomized to one fraction of radiation per week to a total of
00:37:37.626 --> 00:37:40.530 28.5 Gray or to a total of 30 Gray,
NOTE Confidence: 0.8578268
00:37:40.530 --> 00:37:43.394 so that’s 5.7 or 6 Gray once a
NOTE Confidence: 0.8578268
00:37:43.394 --> 00:37:45.591 week versus the more traditional
NOTE Confidence: 0.8578268
00:37:45.591 --> 00:37:48.375 50 Gray in the 25 fractions.
NOTE Confidence: 0.8578268
00:37:48.380 --> 00:37:50.440 This fast trial is randomized.
NOTE Confidence: 0.8578268
00:37:50.440 --> 00:37:51.676 It’s well done,
NOTE Confidence: 0.8578268
00:37:51.676 --> 00:37:54.560 and it has 10 years of follow
NOTE Confidence: 0.8578268
00:37:54.660 --> 00:37:56.220 up at this point,
NOTE Confidence: 0.8578268
00:37:56.220 --> 00:37:58.968 and there was no significant difference
NOTE Confidence: 0.8578268
00:37:58.968 --> 00:38:02.541 in normal tissue affects in the 28.5 by
NOTE Confidence: 0.8578268
00:38:02.541 --> 00:38:05.031 ARM compared to the standard fractionation.
NOTE Confidence: 0.8578268
00:38:05.040 --> 00:38:07.168 And that’s why I put that in.
NOTE Confidence: 0.8578268
00:38:07.170 --> 00:38:09.996 Read up there because that is really the arm
NOTE Confidence: 0.8578268
00:38:09.996 --> 00:38:12.932 that we are treating on in the 28.5 Gray arm,
NOTE Confidence: 0.8578268
00:38:12.940 --> 00:38:14.879 because the 30 Gray arm did have
NOTE Confidence: 0.8578268

66
increase in normal tissue effects,

so we're not using that.

For all three dosing fractionation schemes,

however,

local regional recurrence,

distant recurrence,

and overall survival were equivalent,

and this regimen has made it

into the national guidelines.

Now the NCC N guidelines saying

that it may be considered for

patients greater than 50 years of

age with early stage breast cancer,

in that who do not require a boost,
they had a few sentences about how boosted.

Difficult in this setting and hasn’t been established,

but that’s really how we are approaching it at Yale.

If we have a patient with early stage cancer who does not require a boost,

and we’re not quite ready for patients as young as 50 with just such a short term follow-up of 10 years,

so we are tending to lean towards patients 65 and over.

Although if someone did have a needed transportation need or something that still fit this requirement,
we would be open for that.

The Fast forward has not.

It is not yet widely adopted because the data is only going out for five years at this point and that is looking at 26 or 27 Gray in five fractions just Monday through Friday.

You’re done in a week versus the what’s now the more modern.

Then the modern standard hypo fractionation, 40 Gray, and in 15 fractions.

The five year data is promising.

It’s showing non inferiority and local control.

There are increased normal tissue
NOTE Confidence: 0.8578268
00:39:55.815 --> 00:39:58.090 affects with the 27 Gray arm.
NOTE Confidence: 0.8578268
00:39:58.090 --> 00:40:00.520 So overtime I think we’re going
NOTE Confidence: 0.8578268
00:40:00.520 --> 00:40:03.268 to be very interesting to see what
NOTE Confidence: 0.8578268
00:40:03.268 --> 00:40:05.368 happens with that 26 Gray arm.
NOTE Confidence: 0.8578268
00:40:05.370 --> 00:40:07.668 And if we get more data,
NOTE Confidence: 0.8578268
00:40:07.670 --> 00:40:10.344 more longer term data under our belt,
NOTE Confidence: 0.8578268
00:40:10.350 --> 00:40:12.335 that may be something that
NOTE Confidence: 0.8578268
00:40:12.335 --> 00:40:13.923 we will be adopting.
NOTE Confidence: 0.8578268
00:40:13.930 --> 00:40:15.136 In the future,
NOTE Confidence: 0.8578268
00:40:15.136 --> 00:40:17.548 that would certainly be very convenient.
NOTE Confidence: 0.8369247
00:40:20.380 --> 00:40:23.425 So, so far we’ve only talked about
NOTE Confidence: 0.8369247
00:40:23.425 --> 00:40:25.595 using the HYPOFRACTIONATION in settings
NOTE Confidence: 0.8369247
00:40:25.595 --> 00:40:28.374 where just the breast is being treated.
NOTE Confidence: 0.8369247
00:40:28.380 --> 00:40:30.906 What about in the setting of
NOTE Confidence: 0.8369247
00:40:30.906 --> 00:40:32.590 regional nodal or radiation,
NOTE Confidence: 0.8369247

70
or post mastectomy radiation therapy?

There is a growing body of maturing data and accruing data in this setting that we may see in the future that we are more widely adopting.

The hypo fractionation for these patients as well.

One trial that’s ongoing right now is the RT charm trial.

And it’s looking at moderately hypofractionated post mastectomy radiation therapy for patients who’ve had breast reconstruction comparing with the standard 50 Gray and patients can have autologous reconstruction implant reconstruction immediate.
00:41:10.217 --> 00:41:14.956 or delayed to be on this trial.

00:41:14.960 --> 00:41:18.152 The fabric trial that is open at

00:41:18.152 --> 00:41:21.858 Yale Dr Mina Moran is RPI for that.

00:41:21.860 --> 00:41:23.990 That’s the study of radiation

00:41:23.990 --> 00:41:25.694 fractionation on patient outcomes

00:41:25.694 --> 00:41:27.199 after breast reconstruction

00:41:27.199 --> 00:41:29.219 for invasive breast cancer,

00:41:29.220 --> 00:41:31.520 and this is randomized as

00:41:31.520 --> 00:41:32.900 well to hypofractionation.

00:41:32.900 --> 00:41:33.306 Plus,

00:41:33.306 --> 00:41:35.742 the more standard 50 Gray and

00:41:35.742 --> 00:41:38.090 patience for this would have

00:41:38.090 --> 00:41:40.715 permanent implant or tissue expander.

00:41:40.720 --> 00:41:43.480 This is not for autologous patients.

00:41:43.480 --> 00:41:45.830 There is some published data.
That one can find, for example, this trial out of China by Doctor Wang. It’s a randomized trial of standard fractionation versus moderately hypofractionated patients in post mastectomy radiation therapy. I read every word in the article. I can find nothing that really discuss is if reconstruction was used and the median follow-up is not that long at 58.5 months, but there is an. These were a little bit high. These were some high risk patients as well.
00:42:18.465 --> 00:42:19.536 for everybody T3T4,

00:42:19.540 --> 00:42:21.997 but there was no difference in local

00:42:21.997 --> 00:42:23.826 regional recurrence between the 50

00:42:23.826 --> 00:42:25.626 Gray in the moderate hypofractionation,

00:42:25.630 --> 00:42:27.420 but there was an increase

00:42:27.420 --> 00:42:29.210 in grade 3 acute toxicity,

00:42:29.210 --> 00:42:31.000 in the Hypo frac arm,

00:42:31.000 --> 00:42:33.488 so none of this has really LED for

00:42:33.488 --> 00:42:36.010 wide adoption of the of hypo frack in

00:42:36.010 --> 00:42:38.259 the setting of treating regional nodes

00:42:38.259 --> 00:42:40.669 or post mastectomy radiation therapy.

00:42:40.670 --> 00:42:42.578 At this point I have done

00:42:42.578 --> 00:42:44.600 it in very select patients.

00:42:44.600 --> 00:42:47.204 I think that the rest of our.

00:42:47.210 --> 00:42:49.802 Group has but it has not yet been

NOTE Confidence: 0.8369247
00:42:49.802 --> 00:42:52.251 adopted by the NCC N due to the
NOTE Confidence: 0.8369247
00:42:52.251 --> 00:42:54.289 paucity of data at this point.
NOTE Confidence: 0.8369247
00:42:54.290 --> 00:42:54.984 Although overtime,
NOTE Confidence: 0.8369247
00:42:54.984 --> 00:42:57.413 I’m sure that charm and fabric will
NOTE Confidence: 0.8369247
00:42:57.413 --> 00:42:59.449 provide us with a lot of information.
NOTE Confidence: 0.8805183
00:43:01.670 --> 00:43:04.724 OK. So, another way,
NOTE Confidence: 0.8805183
00:43:04.724 --> 00:43:06.914 besides shortening the treatment course
NOTE Confidence: 0.8805183
00:43:06.914 --> 00:43:10.113 in the number of visits is by decreasing
NOTE Confidence: 0.8805183
00:43:10.113 --> 00:43:15.768 One way that’s been around for awhile.
NOTE Confidence: 0.8805183
00:43:15.770 --> 00:43:18.008 Actually, you post all probably know,
NOTE Confidence: 0.8805183
00:43:18.010 --> 00:43:19.510 is accelerated partial breast
NOTE Confidence: 0.8805183
00:43:19.510 --> 00:43:20.260 irradiation therapy,
NOTE Confidence: 0.8805183
00:43:20.260 --> 00:43:22.420 and until recently there was a
NOTE Confidence: 0.8805183
00:43:22.420 --> 00:43:24.370 lack of longer term phase.
NOTE Confidence: 0.8805183
00:43:24.370 --> 00:43:26.884 Should say phase three up there
The NSA BP 39 that looked at whole breast irradiation with standard frac versus accelerated partial breast irradiation using either breakey therapy or external beam twice a day for 10 fractions. So patients would be done in a week. It’s very interesting results, so they were really looking at in ipsilateral.
Breast tumor recurrence.

At 10 years it was found to be 4% and the accelerated partial breast irradiation and 3% in the whole rest of radiation arm.

But based on their statistical analysis, even though there's just that 1% difference, it did not meet the criteria for equivalence, so API was not bound to be equivalent to whole breast or radiation therapy.

That being said, in the discussion the authors discuss how with that 1% difference in lower risk patients, this still does perhaps leave the door open for a PBI for low risk patients.
The Florence trial.
He has gained a lot of attention and that has treated accelerated partial breast irradiation therapy.

So when we're trading with accelerated partial breast radiation therapy, you probably all know that we are really concentrating the radiation therapy on the tumor bed and an expansion, and therefore we are leaving more of the well. We're leaving the uninvolved breast or a good portion of the uninvolved rest out of the high dose area. And by tightening our fields.
Like this one can. Also. Less dose to the healthy tissues as well, so the Florence trial used accelerated partial breast radiation therapy 30 Gray and five fractions using MRT approach versus whole breast and standard fractionation. So at 10 years with their randomized trial, there was no significant difference in ipsilateral breast tumor recurrence. It was 2.5% in the whole breast versus 3.7% in the accelerated partial breast irradiation therapy. But based on their statistical analysis, this was not.
Statistically different, there was also significantly less acute in late term toxicity with the accelerated partial breast radiation therapy, so they partial breast irradiation therapy has made it into the national guidelines. It’s been there for a little while, but on the most recent iteration, the Florence Regiment is listed as the preferred regimen, and it is recommended that the Astro guidelines where I’ve put a reference on here. As many of you may know, Astro has published guidelines regarding
who is suitable for accelerated partial breast irradiation therapy, and there are three groups, suitable cautionary and basically do not treat unsuitable. So here at Yale, we are working. We do treat accelerated partial breast irradiation therapy. Although not very often for suitable cases, just because the hypo frack is so works out so well and you’re really not saving the patient much time. However, we are in the process of gearing up to start offering treatment in the manner that was used in the Florence trial,
the 6th grade Perfection Times 5
fractions and that was every other day.
Using I MRT.
So we are working with our physics
department and doing all the safety
checks and getting our policies and
procedures in place to start adopting that.
But we are not on line for that just yet.
So what about decreasing our the
amount of tissue that’s treated in the
setting of regional nodal irradiation?
Well, there is some ongoing trials that
we read before this is widely adopted
to start eliminating our nodal fields.
In certain cases we need some
more guidance on that in, especially in the post mastectomy setting you know who, when the patients have involved, knows, who can we really skip treating the regional nodes and still ensure that we have excellent outcomes? This trial, the NSA BP 51 it was open at Yale for a while and it was very challenging to accrue to, and it was nationally quite difficult to accrue too so really long trial may not name. Maybe that was part of it that it’s a bait. You can read the name there, but basically what it does is it took patients who had pathologically
00:48:21.523 --> 00:48:23.020 proven by biopsy,

00:48:23.020 --> 00:48:25.310 axillary nodal involvement who received.

00:48:25.310 --> 00:48:26.276 Neoadjuvant chemotherapy.

00:48:28.691 --> 00:48:30.140 Then they would undergo either

00:48:30.140 --> 00:48:32.550 lumpectomy or mastectomy.

00:48:32.550 --> 00:48:33.996 And they could have Sentinel

00:48:36.290 --> 00:48:39.320 lymph node biopsy,

00:48:39.320 --> 00:48:42.616 But if they were converted to YPN 0

00:48:42.616 --> 00:48:45.598 then these patients were eligible.

00:48:45.600 --> 00:48:46.065 Remember,

00:48:46.065 --> 00:48:48.855 they had to have T1T3 pathologically

00:48:48.855 --> 00:48:50.910 proven N1 disease upfront,

00:48:50.910 --> 00:48:51.942 neoadjuvant, chemo,
and then rendered YPNO in the axilla.

So arm one was omission of regional nodal irradiation therapy, with so lumpectomy patients would only have the breast treated high tangents. Not allowed.

Mastectomy would have no radiation.

An arm two, which was I call it the yes regional nodal radiation therapy would treat in though that arm the whole breast and the chest wall would receive radiation plus regional nodal irradiation which was defined on the trial as internal mammary nodes. Une dissected axilla.
And the superclass. So you’re either getting a very limited radiation or basically the full boat. And I think that some people when I mean I know when I talk to patients about the trial one, either want one arm or the other, and many people were reluctant to let go of the regional nodal radiation therapy. So I personally was not able to accrue anyone to the trial when I spoke with them. And I think that that was a problem kind of nationwide, but it’s now closed to accrual.
They've obviously reached their goal, which is great. And I am not aware of any preliminary results at this time. Another trial this is open at Yale and we are actively accruing. So please we would love to have your patience on this trial. The MA 39 also called Taylor RT. This is different. This is not really looking at response to chemotherapy. It is looking at omitting regional nodal radiation therapy for patients who have a more favorable cancer as far as biomarker risk is concerned.
So the inclusion criteria have changed extremely recently within the last eight weeks. Initially when we open the trial, only T1 or T2 patients were allowed on the trial, but now patients with T3 disease are allowed. Also, a very recent change and what the definition of low volume nodal disease is. If the patient had lumpectomy or mastectomy an axillary dissection, they can have one to three positive nodes if they have lumpectomy or mastectomy plus Sentinel.
Lymph node biopsy only.

They can now have one to two positive nodes.

That’s a change.

And a huge change is that the archetype score when this trial opened had to be 17 or less to enroll patients.

Now patients with an archetype score of 25 or less are eligible.

They cannot have had neoadjuvant chemotherapy.

They’ve also made it amendment allowing Neoadjuvant endocrine therapy is now allowed.
Agement endocrine therapy is allowed.

Patients are randomized, similar to the other one.

The no regional nodal radiation arm that no RNI, so those patients would have to have whole breast irradiation if they had lumpectomy, but no radiation.

If mastectomy and then yes, I would be whole breast irradiation depending on their surgery and regional nodal.

And like the other trial, regional nodal means internal mammary nodes.
Une dissected axela in the superclass.

And the primary endpoint is breast cancer recurrence free interval,

but of course they’re over looking at.

You know, local recurrence,

distant recurrence, side effects,

and lymphoedema risk as well.

So the last way to limit or deescalate the radiation therapy is to just not do it.

Those patients were 70 years of age or older T1 tumors.

That’s the kind of most straightforward.

I think that a lot of us now are familiar with the CL GB 9343 trial.

I can, you know,

memorize this one in my sleep.

Those patients were 70 years of age or older T1 tumors.
They could be clinically or pathologically node negative had to be hormone receptor positive and lumpectomy with negative margins. I put the negative margins in red because for this trial negative margins was defined as no tumor on Inc. The patients were randomized to tamoxifen alone or whole breasts or radiation therapy using a moderate hypofractionation course plus tamoxifen. At 10 years you could see the overall survival was the same 67% in Tamar T and 66% in the Tam arm with a lot of those deaths being non breast cancer.
deaths and freedom from local regional recurrence was 98% in the T amar TR man, 90% in the T amar that actually was statistically significant, there was a statistically significant reduction in the risk of local regional occurrence with the radiation being provided. So you might say, well, this trial should support us doing the radiation, but because the overall survival was not different and although I don’t have it up there, the very low rate of distant recurrence was no different. The breast cancer specific
mortality was not different, so the radiation was not doing anything to prevent those more. One could argue more meaningful outcomes. This is used for two in support of omitting radiation therapy for women that meet the criteria. If I see patients and I have a 71 year old patient who is very who I feel has a life expectancy exceeding 10 years or then we talk about hey, maybe we should do the radiation so. But it is good fodder for discussion and it can help to find those.
patients for whom a mission of radiation therapy would be certainly acceptable.

Also, patients are not going to take the endocrine therapy. They really should get the radiation. Prime two is similar.

The women can be 65 or older, T2 tumors up to three CM. They must have pathologically negative nodes with Sentinel node biopsy or XI section hormone receptor positive and their definition of a
negative margin is 1 millimeter.

They live had some limits that the CL GB trial did not.

The tumor could be grade 3 or have elvii, but you could not have.

Both an once again must have adequate their Bay and we see similar results at the five years.

It almost mirrored the CLG at the five years where ipsilateral breast tumor recurrence was around 1% in the radiation arm and 4% in the no radiation arm with no difference in overall survival.

There was a recent update.
at the San Antonio Breast Conference, however, that paper has not followed showing similar results as CLG be at 10 years with ipsilateral breast tumor recurrence around 10. In the know in the, I miss those up in the no RT arm and then .9% in the RT arm. So I think that Prime 2 once that paper comes out, you know we may start offering for younger women or women with some larger tumors. Omission of radiation therapy. Now this is my last slide before I get into the thank yous in the summaries, and these are trials that I'm not that familiar with.
To be frank with you, there seemed to be more surgical trials, but I thought they were worth just springing up. We have the comet trial open at Yale. The PI is doctor Golshan, and that if I’m understanding correctly, looks at. You know what’s considered a lower risk DCIS grade one and grade two and looking at endocrine therapy alone with surveillance in lieu of surgery, an obviously, if we don’t do surgery. We’re not coming to the radiation.
so in a way this would be part of omitting radiation and the Lord trial is somewhat similar as well. I’m for my homework. I feel I need to learn a little bit more about these trials, so I’ll give you guys some homework too, but I felt that it would not be complete without bringing it up, but I think it’s interesting you know the question that seems to be being asked if I’m is, can screen detected low risk DCIS be managed by an active surveillance strategy rather than. Surgery.
So in summary, we are seeing you know in real time and working further towards a deescalation of radiation therapy for appropriate patients in regard to the number of treatment visits infractions, the volume of tissue treated, and the appropriate emission of radiation therapy, and I'd like to thank you if you have any questions about any of the references or would like to discuss further. That's my contact info, thanks.
you so much Doctor Knowlton wow
three really fantastic talks and I
really appreciate everyone's time and
effort in our audience for listening
Please feel free to put in.
More questions will be happy to answer
them and while we wait for those I have
a couple just listening to the talks.
Maybe I'll start with Doctor, Doctor
Hooley and a little bit about the contrast.
Enhance image Ng for screening and
how you can do that without contrast.
Potentially I was.
You know like more,
but you know you know where we're
00:58:23.846 --> 00:58:26.723 at in the United States and maybe

00:58:26.723 --> 00:58:28.359 where we're going and

00:58:28.360 --> 00:58:30.760 be great to hear about that.

00:58:30.760 --> 00:58:33.455 Sure, so uh, MRI has shown that

00:58:33.455 --> 00:58:35.504 contrast enhanced screening has the

00:58:35.504 --> 00:58:37.560 highest cancer detection rate, right?

00:58:37.560 --> 00:58:39.560 So because cancers are vascular,

00:58:39.560 --> 00:58:41.008 and so you know,

00:58:41.008 --> 00:58:43.960 that's the way it's going with contrast,

00:58:43.960 --> 00:58:44.870 enhanced mammography,

00:58:44.870 --> 00:58:47.600 and even like in the breast

00:58:47.600 --> 00:58:49.460 imaging which all require.

00:58:49.460 --> 00:58:51.040 You know Ivy contrast.

00:58:51.040 --> 00:58:53.410 There are some studies looking at

00:58:53.481 --> 00:58:55.876 MRI and diffusion weighted images,
or some people who say that some people will never happen.

Some people say that it will perhaps somehow happen that you could do MRI with diffusion, weighted imaging or some other technique that some really smart people are going to invent and figure out some sequences where we can look at vascularity without Ivy contrast injection. Likewise, there are also some ultrasound products out there. Randy Butler participated in an auto acoustics ultrasound study that was the optoacoustic. Ultrasound equipment was just
FDA approved last January and it’s basically looking at heating lasers and heating lights. Laser light and heating the blood vessels and looking determining oxygenation within the blood vessels. And she published a couple of articles. Common radiology, which is our top journal showing the vascularity within tumors and superimposing that over a traditional ultrasound so that is vascular based without without contrast and there’s some other. New ultrasound techniques.
Also that are a little bit different that measure.

They can measure vascularity as well,

so those are the ones that right now are.

Active you know, and we could see it.

You know, in five or ten years or maybe sooner.

Well, actually opt acoustics is already out there, so you have to wear fancy space classes and stuff.

Awesome, thank you a question for Doctor Abraham.

What are some of the signs or indications that you know clinicians
01:00:34.277 --> 01:00:36.767 there should be aware of, for you know for those that end up
01:00:36.770 --> 01:00:39.242 getting implants for reconstruction
01:00:39.242 --> 01:00:40.866 with the implant associated anaplastic
01:00:40.866 --> 01:00:43.226 large cell lymphoma, which is, you know,
01:00:43.226 --> 01:00:46.710 gotten some press in the last year or two.
01:00:46.710 --> 01:00:51.168 Dial yeah, so first of all the the presence
01:00:51.170 --> 01:00:53.744 of a textured implant which is obviously
01:00:53.744 --> 01:00:56.332 for somebody who’s not a plastic surgeon.
01:00:56.332 --> 01:00:59.009 Maybe a little bit challenging.
01:00:59.010 --> 01:01:00.720 So if there’s any concern you know,
01:01:00.720 --> 01:01:03.107 have the patient go back to the plastic
01:01:03.110 --> 01:01:05.494 so you know because we are at
01:01:05.494 --> 01:01:08.221 this point considering removing them
01:01:08.221 --> 01:01:10.041 sort of prophylactically and then any change,
particularly a delayed ceroma, is what is classically referred to. So you know in breast surgery seromas are not uncommon, but you know, at the time of surgery or immediately following. Postmastectomy radiation, but if there is a saroma that develops and delayed fashion to 310 years after an implant is placed at sign for concern. Thank you and maybe a last question. For doctor Knowlton. You know, I I, you know, often we see patients that are over the age of 70 small your positive
breast cancers and you know with the LGB data that you showed you know undergoing breast conservation and forgoing radiation and you know doing anti estrogen therapy. But have you also seen the converse where some would just prefer to do a short course of radiation as opposed to putting themselves through? You know 5 plus years of anti estrogen therapy. I guess like if we bias a patient one way or the other when they get to you, how is that discussion go that I see this every week?
I would say every week.

So and you know, I listen to the patient. Many of them come in with some biases against the endocrine therapy. So that doctor Google doesn’t do much justice. So I talked to them about data showing that you know at least half of patients really don’t get any of these. You know, join aches or hot flashes and that’s placebo. Patients got the same amount. Maybe they should just give it a try. I discussed the benefit of helping prevent breast cancer in the contralateral breast. An IV after I finish my spiel,
it's attempting to get them to be
more open to AI or.
Tim, sometimes they will try it
and we’ll check back in with each
other in two to three months.
And if they’re still taking it in,
tolerating it super,
or if they’re not,
then I have come back and done the
radiation at that point or even,
or some if they might give my
initials feel an they still tell
me I’m not by I’m not going to
take it no matter what I say, OK,
I hear you and then we would either.
Do you know?

Depending on the characteristics of the tumor and the patients comorbidities,

we may do a fast regimen of once a week,

or you may do the moderately hypo frack.

The 15. Plus or minus a boost,

so I certainly do see that quite often every week.

Ann and maybe just to finish off on on

that when they said maybe try anti estrogen therapy for a month or two.

Is there kind of a cut off where you would say that if they went with

anti estrogen and decided to stop

and wanted to come back to you to
radiation where you’d feel comfortable.

Well, that’s a good question. You know two or three months, I wouldn’t even blink an eye, especially if they were taking endocrine therapy for the bulk of that I have done up to six months. I have done it, but at that point we may ask the patient to have another Mamo before starting the radiation. And sometimes I’ll bring those patients up in our multidisciplinary tumor board. I did have one patient where it was a year out, but she was substantially high. Risk enough that I presented,
or at our multidisciplinary tumor board we got.

Breast imaging no evidence that not. There's nothing suspicious on that, and I did offer radiation, but beyond six months I would really want to have a multidisciplinary discussion about that.

Thank you and again thank you all so much for these three wonderful presentations. I learned so much in the course of the last hour and a half and the great thing is that this is recorded so others could go back and be able to look at that.

Really thank the audience for their participation.
01:04:58.165 --> 01:05:00.360 joining us for this series of three breast CME’s here at Yale and

01:05:00.360 --> 01:05:02.236 look forward to continuing them

01:05:02.236 --> 01:05:03.908 in the next academic year.

01:05:03.908 --> 01:05:05.588 So with that thank you so much.

01:05:05.590 --> 01:05:07.767 Have a great weekend. Thank you, thank you.