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 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.
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 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 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,
are 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 pretends 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, of course, 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 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 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, and 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 dense breasts. The overall false negative rate of mammography among all breast 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.

NOTE Confidence: 0.7707585

where cancers tend to be white spot.

NOTE Confidence: 0.7707585

So there can be difficult to see

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with the white fiber glandular

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tissue versus women with non dense

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breasts where there’s more fat and

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less white gland or tissue.

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And cancers are easier to identify.

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So screening mammography is very

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controversial, controversial.

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I think we all know that our

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patients know that it’s hard to

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miss the articles in the.

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And in the press.

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Over the past decade or so,

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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 an 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. 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
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 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,
00:09:44.480 --> 00:09:46.364 talk women in their 40s have higher interval cancer rates. They have denser breasts.

00:09:48.792 --> 00:09:50.944 We know that interval cancers that are diagnosed between having a normal mammogram. These are usually symptomatic.

00:09:54.432 --> 00:09:56.640 Cancers tend to be more aggressive. Cancers in women have a shorter sojourn time, and they tend to be faster growing.

00:10:01.890 --> 00:10:06.760 There’s higher survival for earlier stage tumors, and, importantly, there’s ethnic differences.

00:10:09.630 --> 00:10:12.801 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. 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 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.
00:10:59.361 --> 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 --> 00:11:09.211 this this reflects the patient
00:11:09.211 --> 00:11:12.52 shared decision making with ACOG
00:11:12.52 --> 00:11:13.087 and the American Cancer Society
00:11:13.087 --> 00:11:15.358 has the option also discharge date
00:11:15.358 --> 00:11:17.560 page 40 and says really start
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
00:11:22.241 --> 00:11:24.737 bridge the gap between societies like
NOTE Confidence: 0.83849704
00:11:24.737 --> 00:11:26.950 the American College of Radiology.
NOTE Confidence: 0.83849704
00:11:26.950 --> 00:11:28.640 And the United States Protective
NOTE Confidence: 0.83849704
00:11:28.640 --> 00:11:29.654 Services Task force.
NOTE Confidence: 0.83849704
00:11:29.660 --> 00:11:31.694 Life expectancy is a little bit
NOTE Confidence: 0.83849704
00:11:31.694 --> 00:11:33.050 all over the place.
NOTE Confidence: 0.83849704
00:11:33.050 --> 00:11:34.745 I'm not so sure something
NOTE Confidence: 0.83849704
00:11:34.745 --> 00:11:36.440 magical happens at age 75.
NOTE Confidence: 0.83849704
00:11:36.440 --> 00:11:38.636 I think it's better to limit
NOTE Confidence: 0.83849704
00:11:38.636 --> 00:11:40.100 screening when life expectancy
NOTE Confidence: 0.83849704
00:11:40.164 --> 00:11:41.529 is less than 10 years,
NOTE Confidence: 0.86362046
00:11:41.530 --> 00:11:43.120 because we know these patients
NOTE Confidence: 0.86362046
00:11:43.120 --> 00:11:45.133 are not going to really benefit
NOTE Confidence: 0.86362046
00:11:45.133 --> 00:11:46.948 as much from early detection.
NOTE Confidence: 0.86362046
00:11:46.950 --> 00:11:48.876 So we have healthy patients who
NOTE Confidence: 0.86362046
00:11:48.876 --> 00:11:51.286 might be 76 years old and they
00:11:51.286 --> 00:11:53.046 should still have a mammogram,
NOTE Confidence: 0.86362046
00:11:53.050 --> 00:11:54.850 perhaps, maybe not annually.
NOTE Confidence: 0.86362046
00:11:54.850 --> 00:11:57.100 Perhaps we can even consider
NOTE Confidence: 0.86362046
00:11:57.100 --> 00:11:58.837 every one to two years.
NOTE Confidence: 0.86362046
00:11:58.840 --> 00:12:00.723 And then we have patients who might
NOTE Confidence: 0.86362046
00:12:00.723 --> 00:12:03.128 be 70 or 69 years old or whatever,
NOTE Confidence: 0.86362046
00:12:03.130 --> 00:12:04.434 or not that healthy.
NOTE Confidence: 0.86362046
00:12:04.434 --> 00:12:06.064 And maybe don’t need to
NOTE Confidence: 0.86362046
00:12:06.064 --> 00:12:07.787 have a mammogram as well.
NOTE Confidence: 0.86362046
00:12:07.790 --> 00:12:10.654 And again, as far as the interval goes,
NOTE Confidence: 0.86362046
00:12:10.660 --> 00:12:12.416 most people say annually,
NOTE Confidence: 0.86362046
00:12:12.416 --> 00:12:15.549 maybe every one to two years the
NOTE Confidence: 0.86362046
00:12:15.549 --> 00:12:18.033 the task force being the extreme
NOTE Confidence: 0.86362046
00:12:18.033 --> 00:12:20.259 of every every other year.
NOTE Confidence: 0.86362046
00:12:20.260 --> 00:12:22.600 So in addition to the variable
NOTE Confidence: 0.86362046
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 memo 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.
NOTE Confidence: 0.80421704
00:14:02.018 --> 00:14:03.830 screen detected on mammography.
NOTE Confidence: 0.80421704
00:14:03.830 --> 00:14:06.616 We know that most cancers detected on
NOTE Confidence: 0.80421704
00:14:06.616 --> 00:14:08.856 screening ultrasound are small and node
NOTE Confidence: 0.80421704
00:14:08.856 --> 00:14:11.145 negative and tend to be early stage,
NOTE Confidence: 0.80421704
00:14:11.150 --> 00:14:13.796 so it’s rational to think that
NOTE Confidence: 0.80421704
00:14:13.796 --> 00:14:15.560 finding these mammographic Leopold
NOTE Confidence: 0.80421704
00:14:15.637 --> 00:14:18.206 cancers at an early stage in smaller
NOTE Confidence: 0.80421704
00:14:18.206 --> 00:14:20.600 size will improve overall mortality.
NOTE Confidence: 0.80421704
00:14:20.600 --> 00:14:22.068 Ultrasound screening is really
NOTE Confidence: 0.80421704
00:14:22.068 --> 00:14:23.903 well accepted by our patients.
NOTE Confidence: 0.80421704
00:14:23.910 --> 00:14:25.002 It’s relatively inexpensive.
NOTE Confidence: 0.80421704
00:14:25.002 --> 00:14:28.329 It costs about the same price as a mammogram.
NOTE Confidence: 0.80421704
00:14:28.330 --> 00:14:29.798 There’s no Ivy contrast.
NOTE Confidence: 0.80421704
00:14:29.798 --> 00:14:30.899 There’s no compression.
NOTE Confidence: 0.80421704
00:14:30.900 --> 00:14:34.666 It’s widely available, so it can work.
NOTE Confidence: 0.80421704
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,
so I just want to review this briefly because most of our more personalized community in the direction that we’re going to go to is going to include breast density as a factor in what kind of screening patients should get. breast dense breasts is very common. It’s seen in about 50% of all women in the United States. We know there’s an increased risk of breast cancer in women. It’s a 2/6 times increased risk, and it can be confusing. When you see what they did, you know two times increased risk and
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, then the increased risk of developing breast cancer for women with extremely 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 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 been 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 meetings for women with dense breasts. The first study was published back in 2014 by Christiana Cool, a highly regarded radiologist in Germany. She showed that with a very fast acquisition time of three minutes, as opposed to about 10 or 15 minutes for a traditional MRI, we could detect cancers at a very high rate of 18 per thousand. 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
really catching all those cancers.
The sense the negative predicted value was high and the specificity and positive predictive value are also very good as well.
So here is a 61 year old patient with a pathogenic BRACA mutation and Paris producting something over ectomy with a negative mammogram, and she had a MRI six months later and they saw this little cancer and detected this so it can work in women with dense breasts and this woman. She also had high risk and which is where we do most of our breast MRI in.
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 coordination
We’re doing more screening not only for breast cancer, but colon, cancer, and other cancers as well. With breast cancer risk evaluation, there are multiple risk assessment tools that are very available online and the estimated risk can really vary depending on which model you use. Most centers are going for the tire acoustic model that’s most widely used and that also incorporates breast density into that model. When we think about breast cancer risk, we have to know that risk changes overtime. 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, and advertising to something like this, which looks really complicated, but it’s really not that complicated, so let me just review with you. Hence, 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 she has 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 we are not going to be increased risk and so then we want to be sure.

That they are under the age of over 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 at 40,

we do the baseline mammogram.

Of course,
we always want to synthesize 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 of genetics 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 a 59 year old. She had a mass presenter or left outer breast stable for five years. It looks just like a little lymph node. We do tomosynthesis the first time she has atomo exam, and there’s little speculations. 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.
or that whether they were diagnosis on screening ultrasound or MRI.

So the American College of Radiology is working to include method of detection in the BI RADS and then when we do that, hopefully the cancer registries and the national databases will accept this so that we can collect information on new technology and figure out what works and what doesn’t.

So in summary, annual screening mammogram beginning at age 40 saves the most lives. Women with dense breasts have the option to choose supplemental 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 will become more common. It’s interesting vascular based imaging may not necessarily require Ivy 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,
was fantastic. I mean honestly, the amount of work that our breast imaging colleagues and yuan in our group and others have done is truly remarkable. And there’s just so much new excitement in the pipeline and kind of figuring out what the next steps are going to be great. Next, move on to Doctor Knowlton to discuss some of the recent changes and advances in radiation therapy and. The floor is all yours.

Hope you’re on mute still. So while we’re waiting for the slides to pop up.

The floor is all yours.
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.
00:28:58.668 --> 00:29:00.958 love these older ladies of her healthy.
00:29:00.960 --> 00:29:03.424 They still want to come in and get their mammogram maybe every other year.
00:29:05.520 --> 00:29:07.150 I just wouldn’t push it,
00:29:07.150 --> 00:29:09.439 but there is still some shared decision making there got it excellent.
00:29:13.680 --> 00:29:16.585 Hopefully you see my slides properly now.
00:29:16.590 --> 00:29:18.802 Looks great. OK, great, thank you.
00:29:18.802 --> 00:29:22.084 So my title is as you can see is deescalation of radiation therapy for breast cancer for breast cancer.
00:29:22.084 --> 00:29:23.952 at less is more.
00:29:23.952 --> 00:29:26.960 I do not unfortunately have as many awesome
00:29:26.960 --> 00:29:28.620 At less is more.
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, 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 very much on top of their grammar
and my title may not be correct, 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

54
00:31:01.080 --> 00:31:03.520 doesn’t make sense because we’re reducing the intensity of the radiation.

NOTE Confidence: 0.8602074

00:31:03.598 --> 00:31:05.823 not really reducing the intensity of the radiation.

NOTE Confidence: 0.8602074

00:31:05.823 --> 00:31:07.158 What we do when we are changing the fractionation to a shorter fractionation is we are using newer schemes of radiation.

NOTE Confidence: 0.8602074

00:31:07.160 --> 00:31:10.616 What we do when we are changing the fractionation to a shorter fractionation is we are using newer schemes of radiation.

NOTE Confidence: 0.8602074

00:31:10.616 --> 00:31:12.970 To deliver the same biological effective dose so I do not feel that the free dictionary definition really beats what’s happening in radiation.

NOTE Confidence: 0.8602074

00:31:17.150 --> 00:31:18.770 But the Marian Webster one does.

NOTE Confidence: 0.8602074

00:31:18.770 --> 00:31:21.628 Escalating as I had mentioned with the decrease in number of fractions

NOTE Confidence: 0.8602074

00:31:21.628 --> 00:31:23.583 the free dictionary definition really

NOTE Confidence: 0.8602074

00:31:23.583 --> 00:31:25.839 beats what’s happening in radiation.

NOTE Confidence: 0.8602074

00:31:29.050 --> 00:31:29.050 But the Marian Webster one does.

NOTE Confidence: 0.8602074

00:31:29.050 --> 00:31:32.610 So here we see, this is how we are D.

NOTE Confidence: 0.8602074

00:31:32.610 --> 00:31:34.494 Escalating as I had mentioned with the decrease in number of fractions

NOTE Confidence: 0.8602074

00:31:34.494 --> 00:31:36.479 the decrease in number of fractions

NOTE Confidence: 0.8602074

00:31:36.479 --> 00:31:38.495 decrease in volume of tissue treated

NOTE Confidence: 0.8602074

00:31:38.495 --> 00:31:40.547 an omission of radiation therapy
NOTE Confidence: 0.8602074
00:31:40.547 --> 00:31:41.870 for appropriate candidates.
NOTE Confidence: 0.8602074
00:31:41.870 --> 00:31:43.907 And this really does fit the less
NOTE Confidence: 0.8602074
00:31:43.907 --> 00:31:46.528 is more if we have less radiation
NOTE Confidence: 0.8602074
00:31:46.528 --> 00:31:48.623 we will have increased compliance.
NOTE Confidence: 0.8602074
00:31:48.630 --> 00:31:50.838 People will have if the fractionation
NOTE Confidence: 0.8602074
00:31:50.838 --> 00:31:52.900 scheme is more convenient for them,
NOTE Confidence: 0.8602074
00:31:52.900 --> 00:31:54.680 whether they have traveled issues
NOTE Confidence: 0.8602074
00:31:54.680 --> 00:31:55.748 or working issues.
NOTE Confidence: 0.8602074
00:31:55.750 --> 00:31:58.042 We're going to have more patients
NOTE Confidence: 0.8602074
00:31:58.042 --> 00:32:01.150 that will be able to get it with less.
NOTE Confidence: 0.8602074
00:32:01.150 --> 00:32:03.285 Stress there will be increased
NOTE Confidence: 0.8602074
00:32:03.285 --> 00:32:05.420 acceptance of the treatment course
NOTE Confidence: 0.8602074
00:32:05.495 --> 00:32:07.625 increased time for patients to work
NOTE Confidence: 0.8602074
00:32:07.625 --> 00:32:10.280 or to pursue their hobbies or take
NOTE Confidence: 0.8602074
00:32:10.280 --> 00:32:12.608 care of their families and increase
NOTE Confidence: 0.8602074
So moderate fractionation is now really old news. At this point, we’ve all seen it. This is what it is now. Truly in the United States, the new standard of radiation therapy for the intact breast standard or conventional radiation to the whole breast. It was for several decades, 50 Gray and 25 fractions, meaning that the patient needed to come for five weeks. And then there would be an optional tumor bed boost of an additional 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.
from the start B trial, and for these patients there’s an optional tumor bed boost 10 Gray and for fractions. So we’re taking the standard or conventional fractionation of five to six to six and a half weeks, and now it’s become three to four weeks for the patient. And of course there’s some data to back all of this up. These are the three largest trials that have the longest follow-up that are used to backup or support the use of moderate hypofractionation. 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 catchy 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 recurrence and overall survival for the patients.

At 10 years they did all 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 adina 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 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,
overall survival at 10 years
NOTE Confidence: 0.82770544
was the same with the 50 Gray,
NOTE Confidence: 0.82770544
and there was a significant
decrease in breast shrinkage,
NOTE Confidence: 0.82770544
breast edema and telangiectasia.
NOTE Confidence: 0.82770544
But age is in the 40 great arm.
NOTE Confidence: 0.82770544
The Canadian trial was interesting.
NOTE Confidence: 0.82770544
That is slightly different.
NOTE Confidence: 0.82770544
so that’s three weeks and a day.
NOTE Confidence: 0.82770544
Subgroup analysis it’s worthy
NOTE Confidence: 0.82770544
of note that they did notice
NOTE Confidence: 0.82770544
increased local regional recurrence.
NOTE Confidence: 0.82770544
In high grade tumors,
NOTE Confidence: 0.82770544
with the Hypo frac with 15.6% of
NOTE Confidence: 0.82770544
patients who received with high
NOTE Confidence: 0.82770544
00:36:23.611 --> 00:36:26.774 grade tumors that had hypo fact
NOTE Confidence: 0.82770544
00:36:26.774 --> 00:36:29.484 experience in local regional recurrence
NOTE Confidence: 0.82770544
00:36:29.484 --> 00:36:32.269 versus 4.7 in the 50 Gray arm.
NOTE Confidence: 0.82770544
00:36:32.270 --> 00:36:32.620 However,
NOTE Confidence: 0.82770544
00:36:32.620 --> 00:36:35.420 I will say that start B did look
NOTE Confidence: 0.82770544
00:36:35.420 --> 00:36:38.742 at that and did not find any any
NOTE Confidence: 0.82770544
00:36:38.742 --> 00:36:40.802 difference in outcomes for the
NOTE Confidence: 0.82770544
00:36:40.802 --> 00:36:41.900 Grade 3 tumors,
NOTE Confidence: 0.82770544
00:36:41.900 --> 00:36:44.612 so we tend to still treat those patients
NOTE Confidence: 0.82770544
00:36:44.612 --> 00:36:45.807 with moderate hypofractionation
NOTE Confidence: 0.82770544
00:36:45.807 --> 00:36:48.057 an in the Canadian trial,
NOTE Confidence: 0.82770544
00:36:48.060 --> 00:36:50.550 there was no significant difference
NOTE Confidence: 0.82770544
00:36:50.550 --> 00:36:53.730 in acute toxicity or cosmetic outcome.
NOTE Confidence: 0.82770544
00:36:53.730 --> 00:36:55.767 So maybe we can tighten things up
NOTE Confidence: 0.82770544
00:36:55.767 --> 00:36:58.411 a little bit more now and the newer
NOTE Confidence: 0.82770544
00:36:58.411 --> 00:37:00.631 regimens that are being brought out
NOTE Confidence: 0.82770544
00:37:00.631 --> 00:37:03.289 there are now called Ultra Hypofractionation.
NOTE Confidence: 0.8578268
00:37:03.290 --> 00:37:05.714 And these once again are in for the
NOTE Confidence: 0.8578268
00:37:05.714 --> 00:37:08.240 setting of whole breast radiation only.
NOTE Confidence: 0.8578268
00:37:08.240 --> 00:37:10.982 We are not yet talking about
NOTE Confidence: 0.8578268
00:37:10.982 --> 00:37:12.810 anything with the nodes.
NOTE Confidence: 0.8578268
00:37:12.810 --> 00:37:14.690 And we have two regiments,
NOTE Confidence: 0.8578268
00:37:14.690 --> 00:37:20.196 Yale has adopted the FAST regimen which
NOTE Confidence: 0.8578268
00:37:20.196 --> 00:37:22.560 we've been using with great success.
NOTE Confidence: 0.8578268
00:37:22.560 --> 00:37:24.810 Patients were randomized to one fraction
NOTE Confidence: 0.8578268
00:37:24.810 --> 00:37:28.560 of radiation per week to a total of
NOTE Confidence: 0.8578268
00:37:28.560 --> 00:37:31.030 so in the fast trial.
NOTE Confidence: 0.8578268
00:37:31.030 --> 00:37:34.180 Patients were randomized to one fraction
NOTE Confidence: 0.8578268
00:37:34.180 --> 00:37:37.626 of radiation per week to a total of

65
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
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, which they have defined as as in that who do not require a boost,
00:38:47.230 --> 00:38:50.446 they had a few sentences about how boosted.

00:38:50.450 --> 00:38:52.090 Difficult in this setting and

00:38:52.090 --> 00:38:53.074 hasn’t been established,

00:38:53.080 --> 00:38:54.725 but that’s really how we

00:38:54.725 --> 00:38:56.370 are approaching it at Yale.

00:38:56.370 --> 00:38:58.930 If we have a patient with early stage

00:38:58.930 --> 00:39:01.306 cancer who does not require a boost,

00:39:01.310 --> 00:39:03.634 and we’re not quite ready for patients

00:39:03.634 --> 00:39:06.224 as young as 50 with just such a

00:39:06.224 --> 00:39:08.220 short term follow-up of 10 years,

00:39:08.220 --> 00:39:10.710 so we are tending to lean

00:39:10.710 --> 00:39:12.880 towards patients 65 and over.

00:39:12.880 --> 00:39:15.638 Although if someone did have a a

00:39:15.638 --> 00:39:17.749 needed transportation need or something

00:39:17.749 --> 00:39:19.894 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
00:39:55.815 --> 00:39:58.090 affects with the 27 Gray arm.

00:39:58.090 --> 00:40:00.520 So overtime I think we’re going
to be very interesting to see what

00:40:00.520 --> 00:40:03.268 happens with that 26 Gray arm.

00:40:03.268 --> 00:40:05.368 And if we get more data,

00:40:05.370 --> 00:40:07.668 more longer term data under our belt,

00:40:07.670 --> 00:40:10.344 that may be something that

00:40:10.350 --> 00:40:12.335 we will be adopting.

00:40:12.335 --> 00:40:13.923 In the future,

00:40:13.930 --> 00:40:15.136 that would certainly be very convenient.

00:40:20.380 --> 00:40:23.425 So, so far we’ve only talked about

00:40:23.425 --> 00:40:25.595 using the HYPOFRACTIONATION in settings

00:40:25.595 --> 00:40:28.374 where just the breast is being treated.

00:40:30.906 --> 00:40:32.590 regional nodal or radiation,
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
The fabric trial that is open at Yale Dr Mina Moran is RPI for that. That’s the study of radiation fractionation on patient outcomes after breast reconstruction and this is randomized as well to hypofractionation. The more standard 50 Gray and patience for this would have the permanent implant or tissue expander. This is not for autologous patients. 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,
NOTE Confidence: 0.8369247

00:42:19.540 --> 00:42:21.997 but there was no difference in local
NOTE Confidence: 0.8369247

00:42:21.997 --> 00:42:23.826 regional recurrence between the 50
NOTE Confidence: 0.8369247

00:42:23.826 --> 00:42:25.626 Gray in the moderate hypofractionation,
NOTE Confidence: 0.8369247

00:42:25.630 --> 00:42:27.420 but there was an increase
NOTE Confidence: 0.8369247

00:42:27.420 --> 00:42:29.210 in grade 3 acute toxicity,
NOTE Confidence: 0.8369247

00:42:29.210 --> 00:42:31.000 in the Hypo frac arm,
NOTE Confidence: 0.8369247

00:42:31.000 --> 00:42:33.488 so none of this has really LED for
NOTE Confidence: 0.8369247

00:42:33.488 --> 00:42:36.010 wide adoption of the of hypo frack in
NOTE Confidence: 0.8369247

00:42:36.010 --> 00:42:38.259 the setting of treating regional nodes
NOTE Confidence: 0.8369247

00:42:38.259 --> 00:42:40.669 or post mastectomy radiation therapy.
NOTE Confidence: 0.8369247

00:42:40.670 --> 00:42:42.578 At this point I have done
NOTE Confidence: 0.8369247

00:42:42.578 --> 00:42:44.600 it in very select patients.
NOTE Confidence: 0.8369247

00:42:44.600 --> 00:42:47.204 I think that the rest of our.
NOTE Confidence: 0.8369247

00:42:47.210 --> 00:42:49.802 Group has but it has not yet been
NOTE Confidence: 0.8369247
adopted by the NCC N due to the paucity of data at this point. Although overtime, I’m sure that charm and fabric will provide us with a lot of information. OK. So, another way, besides shortening the treatment course in the number of visits is by decreasing the volume of tissue that we are treating. Actually, you post all probably know, is accelerated partial breast irradiation therapy, and until recently there was a lack of longer term phase. Should say phase three up there.
00:43:26.884 --> 00:43:29.582 I scuse me of longer term phase.

00:43:29.582 --> 00:43:31.917 Three data supporting a PBI.

00:43:31.920 --> 00:43:37.898 We do have these two studies that I put up here that now are have randomized.

00:43:37.898 --> 00:43:41.120 Data giving us their ten year outcomes.

00:43:41.120 --> 00:43:44.189 The NSA BP.

00:43:44.189 --> 00:43:46.586 That looked at whole breast irradiation with standard frack versus.

00:43:46.586 --> 00:43:48.578 Accelerated partial breast irradiation.

00:43:48.578 --> 00:43:51.034 Therapy using either breakey therapy or.

00:43:51.034 --> 00:43:53.920 External beam twice a day for 10 fractions.

00:43:53.920 --> 00:43:57.120 So patients would be done in a week.

00:43:57.120 --> 00:43:58.664 It’s very interesting results.

00:43:58.664 --> 00:44:00.594 So they were really looking.

00:44:00.594 --> 00:44:01.999 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.
00:44:40.620 --> 00:44:41.535 The Florence trial.

00:44:41.535 --> 00:44:43.670 He has gained a lot of attention and that has treated accelerated partial breast irradiation therapy.

00:44:43.734 --> 00:44:45.954 So when we're trading with accelerated partial breast radiation therapy,

00:44:45.954 --> 00:44:47.730 you probably all know that we are really concentrating the radiation therapy on the tumor bed and an expansion,

00:44:47.730 --> 00:44:49.974 and therefore we are leaving more of the well.

00:44:49.974 --> 00:44:51.470 We're leaving the uninvolved breast or a good portion of the uninvolved rest out of the high dose area.

00:44:51.470 --> 00:44:54.438 And by tightening our fields

00:44:54.438 --> 00:44:55.982 you probably all know that we are really concentrating the radiation therapy on the tumor bed and an expansion,

00:44:55.982 --> 00:44:58.565 and therefore we are leaving more of the well.

00:44:58.570 --> 00:45:00.440 We're leaving the uninvolved breast or a good portion of the uninvolved rest out of the high dose area.
like this one can.

Also.

Less dose to the healthy tissues as well,

so the Florence trial used accelerated

30 Gray and five fractions using

and I 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,
00:47:01.130 --> 00:47:03.476 the 6th grade Perfection Times 5
00:47:03.476 --> 00:47:06.249 fractions and that was every other day.
00:47:06.250 --> 00:47:07.042 Using I MRT.
00:47:07.042 --> 00:47:08.890 So we are working with our physics
00:47:08.947 --> 00:47:10.903 department and doing all the safety
00:47:10.903 --> 00:47:12.961 checks and getting our policies and
00:47:12.961 --> 00:47:15.404 procedures in place to start adopting that.
00:47:15.410 --> 00:47:18.570 But we are not on line for that just yet.
00:47:21.220 --> 00:47:23.950 So what about decreasing our the
00:47:23.950 --> 00:47:27.475 amount of tissue that’s treated in the
00:47:27.475 --> 00:47:30.170 setting of regional nodal irradiation?
00:47:30.170 --> 00:47:32.627 Well, there is some ongoing trials that
00:47:32.627 --> 00:47:35.329 we read before this is widely adopted
00:47:35.329 --> 00:47:37.705 to start eliminating our nodal fields.
00:47:37.710 --> 00:47:40.014 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
proven by biopsy,

axillary nodal involvement who received.

Neoadjuvant chemotherapy.

Then they would undergo either

lumpectomy or mastectomy.

Sentinel lymph node biopsy,

Sentinel lymph node biopsy converted

Sentinel lymph node biopsy converted to XI section or XI section.

But if they were converted to YPN 0
then these patients were eligible.

Remember,

they had to have T1T3 pathologically

proven N1 disease upfront,

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.

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. 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. Also, a very recent change and what the definition of low volume nodal disease. What is this? Is the updated version here, so 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 for neoadjuvant.

I should have said Neo there,

excuse me.

Neoadjuvant endocrine therapy is now allowed.

Agement chimos 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 or chest wall 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.
00:53:30.252 --> 00:53:33.114 deaths and freedom from local regional
NOTE Confidence: 0.8390835
00:53:33.194 --> 00:53:36.640 recurrence was 98% in the Tamar TR man,
NOTE Confidence: 0.8390835
00:53:36.640 --> 00:53:39.112 90% in the Tamar that actually
NOTE Confidence: 0.8390835
00:53:39.112 --> 00:53:40.348 was statistically significant,
NOTE Confidence: 0.8390835
00:53:40.350 --> 00:53:42.285 there was a statistically significant
NOTE Confidence: 0.8390835
00:53:42.285 --> 00:53:45.225 reduction in the risk of local regional
NOTE Confidence: 0.8390835
00:53:45.225 --> 00:53:48.033 occurrence with the radiation being provided.
NOTE Confidence: 0.8390835
00:53:48.040 --> 00:53:49.850 So you might say, well,
NOTE Confidence: 0.8390835
00:53:49.850 --> 00:53:52.022 this trial should support us doing
NOTE Confidence: 0.8390835
00:53:52.022 --> 00:53:52.746 the radiation,
NOTE Confidence: 0.8390835
00:53:52.750 --> 00:53:54.795 but because the overall survival
NOTE Confidence: 0.8390835
00:53:54.795 --> 00:53:56.840 was not different and although
NOTE Confidence: 0.8390835
00:53:56.914 --> 00:53:58.540 I don’t have it up there,
NOTE Confidence: 0.8390835
00:53:58.540 --> 00:54:00.712 the very low rate of distant
NOTE Confidence: 0.8390835
00:54:00.712 --> 00:54:02.160 recurrence was no different.
NOTE Confidence: 0.8390835
00:54:02.160 --> 00:54:03.604 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. So this could. 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.
00:54:36.832 --> 00:54:39.745 patients for whom a mission of radiation
NOTE Confidence: 0.8390835
00:54:39.745 --> 00:54:42.355 therapy would be certainly acceptable.
NOTE Confidence: 0.8390835
00:54:42.360 --> 00:54:42.678 Also,
NOTE Confidence: 0.8390835
00:54:42.678 --> 00:54:44.268 patients are not going to
NOTE Confidence: 0.8390835
00:54:44.268 --> 00:54:45.540 take the endocrine therapy.
NOTE Confidence: 0.8390835
00:54:45.540 --> 00:54:48.150 They really should get the radiation.
NOTE Confidence: 0.8390835
00:54:48.150 --> 00:54:49.554 Prime two is similar.
NOTE Confidence: 0.8390835
00:54:49.554 --> 00:55:00.930 It’s a little bit behind as far
NOTE Confidence: 0.8390835
00:55:00.930 --> 00:55:02.502 how long it’s been accruing
NOTE Confidence: 0.8390835
00:55:02.502 --> 00:55:04.467 and following out the data.
NOTE Confidence: 0.8390835
00:55:04.467 --> 00:55:08.829 The women can be 65 or older,
NOTE Confidence: 0.8390835
00:55:08.740 --> 00:55:09.330 T2 tumors up to three CM.
NOTE Confidence: 0.8390835
00:55:09.330 --> 00:55:02.502 They must have pathologically
NOTE Confidence: 0.8390835
00:55:02.502 --> 00:55:04.467 negative nodes with Sentinel node
NOTE Confidence: 0.8390835
00:55:04.467 --> 00:55:06.682 biopsy or XI section hormone receptor
NOTE Confidence: 0.8390835
00:55:06.682 --> 00:55:08.829 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 be at the five years where ipsilateral breast tumor recurrence was around 1% in the radiation arm and 4%.

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 R T arm and then .9% in the R T 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,
to be 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. 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.

Thank
you so much Doctor Knowlton wow
three really fantastic talks and I
really appreciate everyone’s time and
effort in our audience for listening
and putting in some questions.
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
in the United States and maybe where we're going and be great to hear about that. Sure, so uh, MRI has shown that contrast enhanced screening has the highest cancer detection rate, right? So because cancers are vascular, and so you know, that's the way it's going with contrast, enhanced mammography, and even like in the breast imaging which all require. You know Ivy contrast. There are some studies looking at MRI and diffusion weighted images,
Some people say that they 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.

Who knows.

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 out there should be aware of,
01:00:36.770 --> 01:00:39.242 for you know for those that end up
01:00:39.242 --> 01:00:40.866 getting implants for reconstruction
01:00:40.866 --> 01:00:43.226 with the implant associated anaplastic
01:00:43.226 --> 01:00:46.710 large cell lymphoma, which is, you know,
01:00:46.710 --> 01:00:51.168 gotten some press in the last year or two.
01:00:51.170 --> 01:00:53.744 Dial yeah, so first of all the the presence
01:00:53.744 --> 01:00:56.332 of a textured implant which is obviously
01:00:56.332 --> 01:00:59.009 for somebody who’s not a plastic surgeon.
01:00:59.010 --> 01:01:00.720 Maybe a little bit challenging.
01:01:00.720 --> 01:01:03.107 So if there’s any concern you know,
01:01:03.110 --> 01:01:05.494 have the patient go back to the plastic
01:01:05.494 --> 01:01:08.221 surgeon so you know because we are at
01:01:08.221 --> 01:01:10.041 this point considering removing them
01:01:10.041 --> 01:01:12.645 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

know doing anti estrogen therapy.

But have you also seen the converse

You know 5 plus years of anti

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 patient's comorbidities, we may do a fast regimen of once a week, or you may do the moderately hypofract. 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 that when you said maybe try antiestrogen therapy for a month or two. Is there kind of a cut off where you would say if they went with antiestrogen and decided to stop and wanted to come back to you to...
NOTE Confidence: 0.8348222
01:03:56.280 --> 01:03:57.800 radiation where you’d feel comfortable.
NOTE Confidence: 0.8677446
01:03:58.580 --> 01:04:00.090 Well, that’s a good question.
NOTE Confidence: 0.8677446
01:04:00.090 --> 01:04:01.956 You know two or three months
NOTE Confidence: 0.8677446
01:04:01.956 --> 01:04:03.700 I wouldn’t even blink an eye,
NOTE Confidence: 0.8677446
01:04:03.700 --> 01:04:05.460 especially if they were taking
NOTE Confidence: 0.8677446
01:04:05.460 --> 01:04:07.519 endocrine therapy for the bulk of
NOTE Confidence: 0.8677446
01:04:07.519 --> 01:04:09.415 that I have done up to six months.
NOTE Confidence: 0.8677446
01:04:09.420 --> 01:04:11.526 I have done it, but at that point we
NOTE Confidence: 0.8677446
01:04:11.526 --> 01:04:13.781 may ask the patient to have another
NOTE Confidence: 0.8677446
01:04:13.781 --> 01:04:15.740 Mamo before starting the radiation.
NOTE Confidence: 0.8677446
01:04:15.740 --> 01:04:17.552 And sometimes I’ll bring those patients
NOTE Confidence: 0.8677446
01:04:17.552 --> 01:04:19.349 up in our multidisciplinary tumor board.
NOTE Confidence: 0.8677446
01:04:19.350 --> 01:04:22.005 I did have one patient where it was a
NOTE Confidence: 0.8677446
01:04:22.005 --> 01:04:24.170 year out, but she was substantially high.
NOTE Confidence: 0.8677446
01:04:24.170 --> 01:04:25.670 Risk enough that I presented,
NOTE Confidence: 0.8677446

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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
01:04:58.165 --> 01:05:00.360 joining us for this series of three

01:05:00.360 --> 01:05:02.236 breast CME’s here at Yale and and

01:05:02.236 --> 01:05:03.908 look forward to continuing them

01:05:03.908 --> 01:05:05.588 in the next academic year.

01:05:05.590 --> 01:05:07.767 So with that thank you so much.

01:05:07.770 --> 01:05:09.320 Have a great weekend. Thank

01:05:09.320 --> 01:05:10.310 you, thank you.