Yes.
So targeting her 2IN breast cancer has resulted in markedly improved results in treating this disease.
And as this slide shows, there are now eight her two targeting drugs that are FDA approved not including biosimilars or subcube preparations and most with indications in multiple settings and six new drug or disease setting approvals just since 2019.
In this talk, I’d like to focus on recent results with the antibody drug.
conjugate trastuzumab Durcex tecan.

NOTE Confidence: 0.83098558

Include with my personal thoughts about

NOTE Confidence: 0.83098558

application of this particular drug in

NOTE Confidence: 0.83098558

phase one studies trastuzumab dierickx

NOTE Confidence: 0.83098558

tecan had remarkable activity not only

NOTE Confidence: 0.83098558

her two positive breast cancer.

NOTE Confidence: 0.83098558

But as shown here also another her

NOTE Confidence: 0.83098558

two positive tumor types and in

NOTE Confidence: 0.83098558

breast cancer that was assayed as

NOTE Confidence: 0.83098558

her two IHC one plus and two plus

NOTE Confidence: 0.83098558

that were called her two low.

NOTE Confidence: 0.83098558

I’ll return to this group

NOTE Confidence: 0.83098558

in just a few moments.

NOTE Confidence: 0.83098558

Getting back to her two

NOTE Confidence: 0.83098558

positive breast cancer,

NOTE Confidence: 0.83098558

the destiny breast 01 trial was
a single arm phase two trial of trastuzumab Durex tcan for her two positive metastatic breast cancer. All patients had prior treatment. With trastuzumab and TDM, one and 2/3 had prior treatment. With pertuzumab, the median number of prior lines of therapy in the metastatic setting was six, and 92% had visceral metastases. The results showed again remarkable activity in this or two positive population with a confirmed objective response rate of 60.9%, some complete responses and a Disease
Control rate of an astounding 97.3%.

In this heavily pretreated population, the median progression free survival was 16.4 months and the median overall survival has not been reached. At the time of the initial publication, the median duration of response was 14.8 months and again in a very heavily pretreated population. So the results of this trial led to FDA accelerated approval of this agent in December of 2019 for patients with her two positive metastatic breast cancer. Following two or more anti-her two based regiments.

The destiny breast 03 study was
a randomized phase three trial

of trastuzumab dierickx team can

versus TDM one for patients with

metastatic her two positive breast

cancer with prior trastuzumab and

taxane treatment and this once

again showed superior progression

free survival and overall response

benefit across all subgroups.

The confirmed response rates were

almost 80% for trastuzumab Drex Tcan.

Versus 43.2% for TDM one and this

trial led to full FDA approval of

this agent in May of this year.

Phase One expansion result.
Showing here, Debbie one, that there was remarkably high response rates for patients with tumors that were her two negative, but IHC one plus or two plus. This led to a randomized phase three study in this 1 + 2 plus population destiny breast O four of trastuzumab DirectX, tecan versus chemotherapy treatment of physician’s choice. Patients could have had one or two prior lines of chemotherapy for recurrence or or recurrence within six months of adjuvant chemotherapy. This study enrolled 557 patients of which 88% were hormone receptor.
positive but considered endocrine therapy refractory. And 70 to 80% of the patients also had a prior CDK 46 inhibitor. The results showed markedly improved progression free survival compared with chemotherapy, a physician’s choice in the hormone receptor positive group and similarly in all patients. Overall survival as well was improved in both groups by over six months and confirmed objective response rates were remarkably higher for
trastuzumab DirectX tcan in both hormone receptor positive and hormone receptor negative patients as shown here as were the clinical benefit rates and the duration of response. So this these remarkable results in what we’re conventionally her two negative metastatic breast cancer. Patients suggests that it takes very little her to expression for on tumor cells for this drug to have activity against a tumor. And based on the results of this trial, in August of this year the FDA approved a new indication for trastuzumab direct can for patients.
00:05:10.411 --> 00:05:13.828 with what has now been termed quote

00:05:13.828 --> 00:05:16.588 her too low metastatic breast cancer.

00:05:16.590 --> 00:05:18.838 So I would like to share my thoughts

00:05:20.799 --> 00:05:22.797 these studies and an omission from

00:05:22.861 --> 00:05:24.685 the FDA approval of patients who

00:05:24.685 --> 00:05:29.450 have tumors that are hurt to IHC 0.

00:05:29.450 --> 00:05:33.048 So first, regarding the technique of IHC,

00:05:33.050 --> 00:05:35.630 this is not a quantitative assay,

00:05:35.630 --> 00:05:37.814 but rather a qualitative test best

00:05:37.814 --> 00:05:42.171 of an antigen under the conditions of

00:05:42.171 --> 00:05:44.560 the essay and the tissue preparation.

00:05:44.560 --> 00:05:47.068 It might be considered at best

00:05:47.068 --> 00:05:48.740 semi quantitative and conventional.
IHC is subjective as it’s interpreted by the reader’s eye. There are technologies to adapt immunodetection of antigens and tissue for quantitation, including one termed Aqua developed by my Yale colleague David Rim and Bob Camp, but these are generally not used in routine clinical practice. It just so happens that with her two immunohistochemistry, strong staining in formal and fixed paraffin embedded tissue correlates very well with her two gene amplification and performs well at identifying a tumor that is biologically.
NOTE Confidence: 0.901779001818182
00:06:23.920 --> 00:06:24.706 Driven by her,
NOTE Confidence: 0.901779001818182
00:06:24.706 --> 00:06:24.968 too.
NOTE Confidence: 0.80763433
00:06:27.470 --> 00:06:29.170 These original results by
NOTE Confidence: 0.80763433
00:06:29.170 --> 00:06:30.870 Dennis Slayman and colleagues,
NOTE Confidence: 0.80763433
00:06:30.870 --> 00:06:33.880 reported in science in 1989,
NOTE Confidence: 0.80763433
00:06:33.880 --> 00:06:36.390 compare for five different tumors.
NOTE Confidence: 0.80763433
00:06:36.390 --> 00:06:39.407 Her two gene content by Southern blot,
NOTE Confidence: 0.80763433
00:06:39.410 --> 00:06:42.924 her 2M RNA expression by northern blot,
NOTE Confidence: 0.80763433
00:06:42.930 --> 00:06:45.366 and protein expression by Western blot,
NOTE Confidence: 0.80763433
00:06:45.370 --> 00:06:47.665 which is what I want you to focus on,
NOTE Confidence: 0.80763433
00:06:48.918 --> 00:06:50.386 And you can see that even the tumor
NOTE Confidence: 0.80763433
00:06:52.388 --> 00:06:55.769 here with the weakest or almost absent
NOTE Confidence: 0.80763433
00:06:55.769 --> 00:06:57.857 immunohistochemical staining in the 4th lane.
NOTE Confidence: 0.80763433
00:06:57.860 --> 00:07:00.386 That lacks her two gene amplification
NOTE Confidence: 0.80763433
and has low levels of her 2M RNA.

Clearly has her two protein detectable by Western blot.

And I want to make the point that her two IHC result of zero in formalin fixed paraffin embedded tissue is not necessarily her too low null.

And I suspect that there are really likely no breast tumors that are completely her to null.

So what we've learned is that her two positive breast cancer expresses about 2,000,000 molecules per cell, and that level is about 100 times the normal level of her two expression, which is in the range of about...
20,000 molecules of her two per cell.

So rather than refer to breast cancer as her two positive versus her two negative, a more appropriate description in my opinion is her two overexpressing versus her two normal.

Never intending to be quantitative, Mike Press suggested the well known scoring system for her two IHC which is shown here which was designed to allow routine testing in pathology labs giving their ability to swing distinguish.

Her two driven her two overexpressing breast tumors from all the others and it turned out that high level protein...
over expression by IHC most of the time
NOTE Confidence: 0.88478821
00:08:24.050 --> 00:08:26.906 correlated with her two gene amplification.
NOTE Confidence: 0.88478821
00:08:26.910 --> 00:08:29.450 And pathologists could relatively easily
NOTE Confidence: 0.88478821
00:08:29.450 --> 00:08:31.482 identify tumors with overexpression.
NOTE Confidence: 0.880442007142857
00:08:33.880 --> 00:08:35.992 David Rimm has found in the
NOTE Confidence: 0.880442007142857
00:08:35.992 --> 00:08:37.892 publication shown here that even
NOTE Confidence: 0.880442007142857
00:08:37.892 --> 00:08:39.584 experienced pathologists don’t have
NOTE Confidence: 0.880442007142857
00:08:39.584 --> 00:08:42.452 a high level of agreement on scoring
NOTE Confidence: 0.880442007142857
00:08:42.452 --> 00:08:44.516 for breast cancers that are not,
NOTE Confidence: 0.880442007142857
00:08:44.520 --> 00:08:46.548 frankly her, too positive.
NOTE Confidence: 0.880442007142857
00:08:46.548 --> 00:08:48.069 In this publication,
NOTE Confidence: 0.880442007142857
00:08:48.070 --> 00:08:50.618 he showed that data from the College
NOTE Confidence: 0.880442007142857
00:08:50.618 --> 00:08:52.055 of American Pathologists surveys
NOTE Confidence: 0.880442007142857
00:08:52.055 --> 00:08:54.550 on a series of about 1400 breast
NOTE Confidence: 0.880442007142857
00:08:54.550 --> 00:08:57.830 cancer cases showed that 19% of the
NOTE Confidence: 0.880442007142857
00:08:57.830 --> 00:08:59.630 cases generate results with less
than or equal to 70% concordance for her two IHC 0 versus 1 plus. And in another series of 170 Yale Cancer Center cases that was distributed to 18 pathologists, there was only 26% concordance between IHC Zero and one plus. In another study, David Rimm’s group used his Aqua method of quantitative immunofluorescence to develop conditions that could more quantitatively measure levels of her 2IN non overexpressing breast tumors. And this plot shows quantitation of her two levels in cases that
are IHC 3 plus shown in Green,
NOTE Confidence: 0.8644511825
2 plus shown in black,
NOTE Confidence: 0.8644511825
one plus shown in red,
NOTE Confidence: 0.8644511825
and zero is shown in blue.
NOTE Confidence: 0.8644511825
And you can see that her two protein
NOTE Confidence: 0.8644511825
was detected in all of these cases,
NOTE Confidence: 0.8644511825
and within the limit of linearity
NOTE Confidence: 0.8644511825
of this particular assay,
NOTE Confidence: 0.8644511825
cases that were called by
NOTE Confidence: 0.8644511825
pathologists 2 + 1 plus or zero
NOTE Confidence: 0.8644511825
are fairly randomly distributed.
NOTE Confidence: 0.8644511825
Doctor Rimm suspects that there may
NOTE Confidence: 0.8644511825
be a small percentage of cases,
NOTE Confidence: 0.8644511825
not more than 10%,
NOTE Confidence: 0.8644511825
that may truly have undetectable
NOTE Confidence: 0.8644511825
levels of her two.
But I actually remain unconvinced so far that there are any truly her two negative breast cancers. Two studies looked at whether there are actually clinical differences in breast cancer behavior between tumors that are her 20 or those that are being called her too. The first study from Canada looked at 319 cases and suggested that her 20 cases compared to 1 pluses and two pluses were actually more likely to be high grade, have lower ER histo score.
be less likely to be PCR positive.

NOTE Confidence: 0.8644511825

Be more likely to be triple negative

NOTE Confidence: 0.8644511825

and have worse overall survival,

NOTE Confidence: 0.8644511825

which is actually counterintuitive

NOTE Confidence: 0.8644511825

to the known association of her

NOTE Confidence: 0.8644511825

two with more aggressive disease.

NOTE Confidence: 0.8644511825

However,

NOTE Confidence: 0.8644511825

a larger study from Dana Farber

NOTE Confidence: 0.8644511825

with over 5000 cases showed that

NOTE Confidence: 0.8644511825

although once again her two

NOTE Confidence: 0.8644511825

zeros seem to be less likely to

NOTE Confidence: 0.8644511825

be hormone receptor positive,

NOTE Confidence: 0.8644511825

they actually showed no difference

NOTE Confidence: 0.8644511825

in disease free survival,

NOTE Confidence: 0.8644511825

distant disease free survival,

NOTE Confidence: 0.8644511825

overall survival or pathologic
NOTE Confidence: 0.864511825
00:11:24.134 --> 00:11:26.546 complete response rates for those
NOTE Confidence: 0.864511825
NOTE Confidence: 0.864511825
00:11:28.330 --> 00:11:30.050 And that suggested that her
NOTE Confidence: 0.864511825
00:11:30.050 --> 00:11:32.739 two low breast cancer is not a
NOTE Confidence: 0.864511825
00:11:32.739 --> 00:11:34.089 distinct biological subtype.
NOTE Confidence: 0.777617024909091
00:11:36.370 --> 00:11:38.895 Finally, the Daisy study actually
NOTE Confidence: 0.777617024909091
00:11:38.895 --> 00:11:41.420 examined the activity of trastuzumab
NOTE Confidence: 0.777617024909091
00:11:41.500 --> 00:11:44.056 direkt can in all breast cancer
NOTE Confidence: 0.777617024909091
00:11:44.056 --> 00:11:46.629 subtypes with three cohorts shown here.
NOTE Confidence: 0.777617024909091
00:11:46.630 --> 00:11:48.650 Cohort 1 being conventionally
NOTE Confidence: 0.777617024909091
00:11:48.650 --> 00:11:50.670 hurt you positive patients,
NOTE Confidence: 0.777617024909091
00:11:50.670 --> 00:11:53.148 Cohort 2 being IHC one plus
NOTE Confidence: 0.777617024909091
00:11:53.148 --> 00:11:55.750 or two plus fish negative,
NOTE Confidence: 0.777617024909091
00:11:55.750 --> 00:11:59.188 what we now call her too low and cohort
NOTE Confidence: 0.777617024909091
00:11:59.188 --> 00:12:02.682 3 being actually her 20 cases and
NOTE Confidence: 0.777617024909091
responses were seen in 33% of the 72.

Were too low cases, but also in 30.6% of the 30s of the 36 her two IHC 0 cases.

So while the IH2 IHC 0 cases were slightly numerically less and the numbers are small,

this study certainly supports activity of this agent in her 20 cases.

So to summarize, I think I’ve discussed that IHC is not a quantitative assay,

that pathologists have difficulty in distinguishing between her two one plus and 0 cases,

that her two IHC breast cancers behave similarly to quote her two low cases,
and that in the Daisy trial there was activity of trastuzumab
dierickx tikan in her two.

cases that is with the small number of cases tested,
really not very different from the activity seen in quote her two low cases.

So I reiterate that her two IHC 0 is not necessarily her to null and I suspect that no breast cancer is completely her to know.

And it’s clear that what we would consider normal levels of her two expression can confer sensitivity to trastuzumab direkt CAD.
So I want to state that I think we know that there is her two expressed and there is her two normal. But I don’t feel that we know for certain that there is any other category but besides those two categories. And so I make somewhat of a provocative statement, but I think I prefer I would propose that perhaps we should not be excluding her 20 IHC patients from potentially benefiting from trastuzumab. I note that this would be off label, but I think scientifically and with support from the Daisy trial,
we could consider this agent for patients with her two zeros that otherwise don’t have any other good treatments for them. That’s my last slide.

Thank you, doctor Digiovanna. That was a fantastic real overview of the evolving definition of her too and positivity. I’m sure that’ll create some provocative hopefully questions in the chat box. And also later in the panel session, we’re going to move on to Doctor Rachel Greenup, who’s our chief of breast surgery.
here at Yale Department of Surgery and Associate Professor of surgery I’m talking about. Dates and breast cancer surgery. Thank you, Doctor Greenup. My name is Ray. Give me one second. I just have to. Re share. Can you see that? OK, great. Thank you for having me. So I’m Rachel Greenup. I’m a associate professor of breast surgery. I’ve been at Yale about a year and a half, and I’m excited to be here with you all tonight.
So I often start with this slide because one of our favorite things about breast cancer surgery is seeing the incredible strides we’ve made in practicing. And by reducing what we do unnecessarily and seeing how it improves patient outcomes. So we stopped doing radical mastectomies in the 1990s, early 2000s, when we learned that lumpectomy with radiation was equally effective. And you can see this picture here, this old black and white photo of this woman who’s really had extensive surgery with resection.
of her pectoralis muscle.

It’s so rare for us to need to do such extensive treatment in 2022. I don’t think the slides are forwarding yet, seeing that.

We're still on the updates and breast cancer. And that’s happening. Let me. Let’s try this again. Can you see that?

More recently we’ve been able to reduce the number of axillary lymph node dissections and significantly reduce the rates of lymphedema in women who have small amounts of node positive disease. We have good 10 year data suggesting...
that older women with favorable hormone receptor positive breast tumors can safely forgo radiation. We have good data to suggest that many women with hormone receptor positive breast cancer have little benefit. From chemotherapy above and beyond endocrine therapy. And we have ongoing national and international trials of which doctor Golshan is very much involved looking at women with low grade or low risk ductal carcinoma insight two who can forego usual care for active surveillance and this
00:17:19.393 --> 00:17:22.165 is a comment trial which we are
NOTE Confidence: 0.919685013333333
00:17:22.165 --> 00:17:24.020 currently enrolling at at Yale.
NOTE Confidence: 0.919685013333333
00:17:24.020 --> 00:17:25.868 So many of our patients come to us
NOTE Confidence: 0.919685013333333
00:17:25.868 --> 00:17:28.102 with a breast cancer that was diagnosed
NOTE Confidence: 0.919685013333333
00:17:28.102 --> 00:17:30.252 on screening imaging and you can
NOTE Confidence: 0.919685013333333
00:17:30.252 --> 00:17:32.107 see here a traditional diagnostic
NOTE Confidence: 0.919685013333333
00:17:32.107 --> 00:17:34.102 mammogram with a correlating ultrasound
NOTE Confidence: 0.919685013333333
00:17:34.102 --> 00:17:37.114 showing a biopsy proven breast cancer.
NOTE Confidence: 0.919685013333333
00:17:37.120 --> 00:17:38.660 And I’m going to start with breast cancer
NOTE Confidence: 0.919685013333333
00:17:38.660 --> 00:17:40.520 screening even though Doctor Lewis here,
NOTE Confidence: 0.919685013333333
00:17:40.520 --> 00:17:41.675 I’ll be brief.
NOTE Confidence: 0.919685013333333
00:17:41.675 --> 00:17:44.370 There’s been a lot of opinions over
NOTE Confidence: 0.919685013333333
00:17:44.448 --> 00:17:48.016 several years and as a group we are
NOTE Confidence: 0.919685013333333
00:17:48.016 --> 00:17:49.414 generally recommending screening
NOTE Confidence: 0.919685013333333
00:17:49.414 --> 00:17:52.375 starting at 40 on an annual basis,
NOTE Confidence: 0.919685013333333
00:17:52.380 --> 00:17:53.790 we more recently.
In our American Society of Breast surgeons community, there has been formal guidelines that came forward in 2019 suggesting that women over 25 should undergo formal risk assessment for breast cancer based on personal and family history. These guidelines were really valuable for practicing surgeons and that they included potential recommendations for supplemental imaging, including 3D mammography.
MRI and or screening ultrasound for which yells very well known. When we meet our patients with a breast cancer diagnosis, many of them have options for surgery and this is a black and white illustration demonstrating an A simplest form of breast conservation with lumpectomy versus mastectomy. When we talk about breast conservation, that typically includes language of lumpectomy followed by radiation. But more recently we have identified a subset of lower risk patients for which radiation may not be necessary. We always defer that decision to
our radiation colleagues.
And we typically require support from our radiologist either through wire localized lumpectomy to mark the spot on mammogram or in modern day through localizing devices we have instrumented and operationalized tag localization across our smilo sites. And the data is suggesting that use of these smaller implantable devices that are removed at the time of lumpectomy improve comfort for patients and are associated with higher patient satisfaction scores with reduced rates of margin.
positivity and smaller resections

removal of breast volume.

I think it’s worth discussing all

the controversy around margins.

This really hit the late press even in 2019,

And this was based on the fact that

re excision rates historically

were really high ranging from 15

to 25% and many of women who went

back for second

surgery had close but negative margins,

meaning the second surgery did not

identify residual disease.

So there was a clear lack of consensus

about what was enough and there was
wide variation in clinical practice.

Across the country. Doctor Moran, who leads our breast radiation oncology program was really critical in taking the lead on bringing together experts from a multidisciplinary perspective. They reviewed 33 men and 33 studies in a meta-analysis including over 28,000 patients. And what they found was that certainly positive margins did definitely increase the risk of in-breast recurrence. However, no tumor on ink for invasive ductal cancer was considered a negative margin and that. Age, histology, size did not impact these.
findings and no amount of added radiation or chemotherapy could overcome good surgery. And Doctor Moran, in a partnership with many colleagues from across the country in both surgery and radiation also replicated this process for DCIS, which was really practice changing. And when we estimated the number of surgeries that it saved per year, it was about 25,000. Additional research that came out of Yale looking at margin was the landmark trial by Doctor Ennis Chappar. This was a randomized clinical trial, small numbers,
yet it was one of the few local regional trials done in breast cancer for quite some time. And women were randomized to either having margins resected according to the discretion of the surgeon or routine cavity shave margins and it clearly reduced the rate of margin positivity and the need for re excision by about half and again practice. When we talk about mastectomy, we talk about removing the breast tissue. This can be done with or without reconstruction and we have wonderful.
plastic surgery colleagues that can offer either implant based and or autologous tissue reconstruction. And you'll hear from Doctor Ayalla later in our session, we know that there's been an increasing rates of contralateral prophylactic mastectomy or double mastectomy and that these rates have tripled in the last 40 years. I show this picture always of Angelina Jolie because she has a known Braca 1 mutation and came out publicly talking about her choice for double mastectomy. Yet she's at incredibly high risk, as are our other hereditary
cancer populations.
But this data is really reflecting average risk women who don’t have a high risk of developing cancer on the other side.
We know that when women have their unaffected breast removed and have no hereditary Cancer syndrome, removal of the healthy breast does not add oncologic or survival benefit and is unfortunately associated with a small increased risk of surgical complications.
But we do know many of our patients choose double mastectomy for the benefit of reduced surveillance,
improved symmetry and Peace of Mind.
And so again,
our association of Breast surgery came forward in 2016 with a consensus. Statement saying that we should consider double mastectomy but not recommend it. We are increasingly doing a greater number of sparing mastectomies. We need to think about distance of the tumor from the skin quality, the tumor side. Increasingly we’re realizing that even BRCA mutation carriers can safely have this operation done and the improved aesthetics for some
00:23:32.254 --> 00:23:34.192 women really helps them make it
difficult choice for risk reduction.
A little bit of a plug for our program,
we’re ready to launch a home recovery
after mastectomy program at Yale.
And this is really for a very select
group of patients who live near the
hospital who want to go home for
recovery and who have a a safety
net or support system with family,
friends and a visiting home nurse.
And we’re excited to launch that program
to again improve patient experience
and choice of how they recover after
such a life changing operation.
When we think about managing lymph nodes in the axilla, we have good data from almost a decade ago, the Acas Oxy 11 trial that showed women have a small amount of nodal positivity do not need a full lymph node dissection. We can rely on systemic therapy and radiation to sterilize remaining nodes. And we have a long-awaited data coming soon, hopefully from the Alliance 11202 trials suggesting that women who have upfront biopsy proven nodal disease, who go on to have chemotherapy, may be able to rely
00:24:43.923 --> 00:24:45.803 on radiation further deescalating the
need for completion lymphadenectomy.

00:24:45.803 --> 00:24:48.258 Lastly, I’d like to talk
about genetic testing.

00:24:50.480 --> 00:24:52.490 We had clear NCCN guidelines around
who was eligible for and covered for,
from an insurance perspective,
hereditary cancer screening.

00:25:00.060 --> 00:25:02.480 This study by Peter Beija was the
first to suggest that we were probably
missing a large group of women who
did not meet our historic criteria,
did not meet our historic criteria,
who then went on to have positive
test results and again this prompted.

00:25:19.080 --> 00:25:21.195 Changes in our American Society
Breast surgeons guidelines for hereditary breast cancer testing really endorsing that any patient with a known breast cancer should be offered a genetic testing and that genetic counseling and potential testing should be made available. Finally, we have long-awaited data again from the ECOG 2108 trial suggesting that removal of the primary breast tumor in women with metastatic disease does not improve overall survival. This was a study by Seema Khan and Doctor Golshan was also very involved in this national discussion.
They looked at a secondary outcomes of chest wall disease and patient quality of life. Women went on to have breast conservation or mastectomy with negative margins and systemic. Treatment at the discretion of their treating team. And essentially we found that local regional therapy, including surgery and radiation did not extend survival in women who were diagnosed with newly metastatic breast cancer, but it did have some improvements.
on controlling disease and disease progression locally.

So that’s a whirlwind tour on updates and breast cancer surgery.

I’d be happy to take any questions and thanks for joining us.

Thank you. Doctor Greenup having you here lead our breast surgical program is just absolutely fantastic and all.

the work that you’ve done whether it’s the home recovery from mastectomy.

is so welcome here.

We’re going to move on to doctor.

Kristen Knowlton.

Doctor Kristen Olson is one of our radiation oncologist.
She's also the director of our Smilo site and Hampden and also our NA PVC lead and director here at our Yale New Haven Hospital site. She'll be discussing a radiation oncology.

OK. Here we go. How about now? Not yet. OK, all right.

So hi, I'm Kristen knolton. OK. All right.

So the Smilo network, as we all know,
the Smilow cancer hospital, Yale, New Haven Health Network spans quite a bit of Connecticut and radiation is offered at Rennich Trumbull. We have Derby where, well that is under Griffin Hospital. The physicians who treat patients in the radiation oncology Department are Yale physicians from our department, Hamden, New Haven, Guildford and Waterford. And each site has a representative from what we call the breast team and which means that that person specializes in Breast Cancer Care, attends tumor boards, attends our weekly Recology Center,
radiation oncology.
Eating and breast chart rounds as well.
And all of the sites within the Smilow Cancer Hospital, Yale New Haven Health system have apex accreditation that stands for accreditation programs for excellence.
And that’s under the auspices of Astro, and one could also argue globally, except for Derby, but Derby does also have great accreditation from the American College of Radiology.
So all sites that shows that we
have no clear concrete evidence that we are providing high quality patient centered care at all sites. So the breast team is led by Doctor Marina Mina Moran, she’s a professor in our department. She’s obviously chief of our breast cancer radiation oncology group and she’s also vice chair of the NCCN Breast Cancer panel. And under her leadership the Breast team practices high quality evidence based Breast Cancer Care. And what that really means is that we strive to always provide care that is supported by high
NOTE Confidence: 0.86694515
00:29:31.254 --> 00:29:33.010 quality data with meaningful.
NOTE Confidence: 0.86694515
00:29:33.010 --> 00:29:33.826 Follow up.
NOTE Confidence: 0.86694515
00:29:33.826 --> 00:29:36.274 Also the rest team participates in
NOTE Confidence: 0.86694515
00:29:36.274 --> 00:29:38.527 clinical trials often in conjunction
NOTE Confidence: 0.86694515
00:29:38.527 --> 00:29:40.802 with our medical oncology and
NOTE Confidence: 0.86694515
00:29:40.802 --> 00:29:42.520 surgical oncology colleagues.
NOTE Confidence: 0.86694515
00:29:42.520 --> 00:29:44.770 We hold weekly disease site
NOTE Confidence: 0.86694515
00:29:44.770 --> 00:29:46.120 specific chart rounds.
NOTE Confidence: 0.86694515
00:29:46.120 --> 00:29:47.844 We've adopted systemwide planning
NOTE Confidence: 0.86694515
00:29:47.844 --> 00:29:50.430 goals and objectives and the point
NOTE Confidence: 0.86694515
00:29:50.503 --> 00:29:52.589 of this team approach is that to
NOTE Confidence: 0.86694515
00:29:52.589 --> 00:29:54.463 that to ensure that when patients
NOTE Confidence: 0.86694515
00:29:54.463 --> 00:29:56.591 go to any site where we offer
NOTE Confidence: 0.86694515
00:29:56.600 --> 00:29:58.695 radiation oncology within the smilow
NOTE Confidence: 0.86694515
00:29:58.695 --> 00:30:00.790 cancer hospital system that the
NOTE Confidence: 0.86694515
patient will get similar care.

So in radiation oncology, it's mandated that all radiation plans get reviewed by your peers and it happens weekly.

And in our department, we used to do all sites together. But under me and his leadership, we started to have breast cancer disease teams chart rounds on our own, separate from the rest of the group so that we could really concentrate and delve in deeply into the breast cancer cases.
And she really was ahead of the curve when we started that seven years ago and we were the first disease team in our department to do that subsequently. Now the Gu team and the thoracic team are doing that. So I chose thinking about our talk today, I chose to concentrate on our commitment to de-escalation of care, which is certainly an important emerging strategy in breast cancer treatment. And specifically I chose to concentrate on our clinical trial participation because I do believe that our departments...
00:31:08.319 --> 00:31:10.225 clinical trial participation really
NOTE Confidence: 0.799177013636364
00:31:10.225 --> 00:31:12.395 shows our commitment to embracing
NOTE Confidence: 0.799177013636364
00:31:12.395 --> 00:31:14.518 and helping move forward escalation
NOTE Confidence: 0.799177013636364
00:31:14.518 --> 00:31:17.070 of care and what I mean by that.
NOTE Confidence: 0.799177013636364
00:31:17.070 --> 00:31:19.730 Is either decreasing the dose
NOTE Confidence: 0.799177013636364
00:31:19.730 --> 00:31:22.390 or the number of fractions,
NOTE Confidence: 0.799177013636364
00:31:22.390 --> 00:31:25.570 or maybe even omitting radiation completely,
NOTE Confidence: 0.799177013636364
00:31:25.570 --> 00:31:28.770 but aiming to decrease toxicity
NOTE Confidence: 0.799177013636364
00:31:28.770 --> 00:31:30.690 essentially while keeping
NOTE Confidence: 0.799177013636364
00:31:30.690 --> 00:31:33.897 outcomes the same or even better.
NOTE Confidence: 0.799177013636364
00:31:33.900 --> 00:31:36.570 So an important trial that
NOTE Confidence: 0.799177013636364
00:31:36.570 --> 00:31:38.534 recently closed at our institution,
NOTE Confidence: 0.799177013636364
00:31:38.534 --> 00:31:40.620 but we was open and we enrolled
NOTE Confidence: 0.799177013636364
00:31:40.688 --> 00:31:42.268 a large number of patients.
NOTE Confidence: 0.799177013636364
00:31:42.270 --> 00:31:44.748 It’s called the idea study and it
NOTE Confidence: 0.799177013636364
00:31:44.748 --> 00:31:46.332 stands for individualized decisions
00:31:46.332 --> 00:31:48.156 for endocrine therapy alone.
00:31:48.160 --> 00:31:50.974 And the Pi locally was Doctor Moran
00:31:50.974 --> 00:31:54.326 and this will piggyback a little bit
00:31:54.326 --> 00:31:56.906 on Doctor Greenup’s discussion where
00:31:56.906 --> 00:31:59.705 she mentioned the CLG B9343 study.
00:31:59.705 --> 00:32:03.400 So that study was a well done phase three.
00:32:03.400 --> 00:32:06.270 This trial with over 12 years of
00:32:06.270 --> 00:32:08.655 median follow-up that has shown us
00:32:08.655 --> 00:32:11.767 that patients over 70 with a tumor 2
00:32:11.767 --> 00:32:14.427 centimeters or less estrogen receptor
00:32:14.427 --> 00:32:16.555 positive excised with negative
00:32:16.560 --> 00:32:19.545 margins and negative nodes either
00:32:19.545 --> 00:32:21.933 clinically or surgically tested.
00:32:21.940 --> 00:32:24.226 Those patients if they take endocrine
00:32:24.226 --> 00:32:26.584 therapy they can do very well
00:32:26.584 --> 00:32:28.884
and radiation therapy can safely be withheld in that group. So the idea trial, the goal is to expand on that. We start looking at younger ages, 50 to 69, but this is a single ARM cohort study. So it’s not a randomized trial, it’s a single ARM cohort study to start exploring this. So it’s similar at you know hormonal receptor positive, margins negative, no negative. These patients because they’re younger do need to have some sort of axillary staging,
Sentinel node biopsy or axillary dissection and in order to ensure that it’s a favorable cancer that. Ideally we’ll behave well. The Oncotype recurrence score must be less than or equal to 18. So these patients were enrolled on the single ARM cohort study and they did not receive radiation therapy. They had their lumpectomy with their axillary staging and five years of endocrine therapy and surveillance. And the primary objective is looking at local regional recurrence. And here we have our secondary
objectives looking at the rates of salvage mastectomy and also to see as local regional recurrence associated with endocrine therapy compliance. So this trial is maturing now. It's closed as we said and now the data is gathering. Also at our at Yale, we’re offering the fabric trial that closed even more recently and as we could see a pair fabric stands for study of radiation fractionation on patient outcomes after breast reconstruction for invasive breast cancer. Although ironically the people, the physicians could have stage zero.
but they do put invasive cancer in the trial.

So the question that this is trying to answer is can we decrease the treatment time IE the number of fractions for these patients and possibly the toxicity.

For patients who require postmastectomy radiation therapy in the setting of implant based reconstruction and I highlighted this to let us know that patients had to undergo immediate reconstruction meaning the placement of a tissue expander or an implant either at the time or within 30 days.
So and we see they could have stage zero through stage 3 invasive breast cancer.

Yeah, it was could be ER positive or not, chemo or not.

It was very open but the two arms are arm two is our standard treatment which is 25 fractions for these patients to great per fraction.

And the experimental arm is looking at hypofractionation cutting down the number of treatments.

And in intact breast cancer cases we’ve seen that this can be very successful in actually with as far as controlling the disease locally and also has less toxicity.
So the goal in this trial is to say hey well this also hold up. In the setting of an implant or a tissue expander to be exchanged to an implant. So the objectives for this trial were looking at physical well-being of the patients and patient recorded outcomes using the fact be instrument. They were looking at pain, our mobility, lymphedema and of course we want to look at the clinical outcomes too.
breast cancer specific survival

and interestingly this also wanted

to see was there a difference in

As far as rare radiation oncology,

radiation therapy side effects such as

brachial plexopathy or secondary malignancy.

Now we’re getting to

trials that that are open.

So we have open now at Yale at

essentially all I think of all the sites,

the MA 39 trial also called the Taylor RT,

I’m the local Pi for this trial and here

we see the name a randomized trial of

regional radiotherapy and biomarker low.

Low risk node positive and T3N0
00:36:17.093 --> 00:36:18.758 breast cancer. That’s a mouthful,
00:36:18.760 --> 00:36:21.147 but that’s the official title and the
00:36:21.147 --> 00:36:23.696 question that this is looking to answer is.
00:36:23.700 --> 00:36:26.095 Can we withhold regional nodal
00:36:26.095 --> 00:36:28.490 radiation therapy in patients with
00:36:28.567 --> 00:36:31.612 low volume nodal disease who have a
00:36:31.612 --> 00:36:33.890 favorable breast cancer IE hormonal
00:36:33.890 --> 00:36:35.686 receptor positive and Oncotype
00:36:35.686 --> 00:36:38.890 score of less than or equal to 25.
00:36:38.890 --> 00:36:39.940 And so yes,
00:36:39.940 --> 00:36:42.343 here we see down here PCP one or two
00:36:42.343 --> 00:36:44.467 with low volume nodal disease and
00:36:44.467 --> 00:36:46.796 the definition of what low volume
00:36:46.796 --> 00:36:49.141 nodal disease is changes depending
00:36:49.141 --> 00:36:51.418 on whether axillary dissection was
00:36:51.418 --> 00:36:53.200 PCP one or two with low volume nodal disease and
00:36:53.200 --> 00:36:54.865 the definition of what low volume
00:36:54.865 --> 00:36:57.180 nodal disease is changes depending
00:36:57.180 --> 00:36:58.825 on whether axillary dissection was
00:36:58.825 --> 00:36:60.353 PCP one or two with low volume nodal disease and
00:36:60.353 --> 00:36:62.688 the definition of what low volume
00:36:62.688 --> 00:36:64.393 nodal disease is changes depending
00:36:64.393 --> 00:36:66.064 on whether axillary dissection was
00:36:66.064 --> 00:36:67.996 PCP one or two with low volume nodal disease and
00:36:67.996 --> 00:36:70.306 the definition of what low volume
00:36:70.306 --> 00:36:72.000 nodal disease is changes depending
00:36:72.000 --> 00:36:73.635 on whether axillary dissection was
00:36:73.635 --> 00:36:75.157 PCP one or two with low volume nodal disease and
00:36:75.157 --> 00:36:77.507 the definition of what low volume
00:36:77.507 --> 00:36:79.138 nodal disease is changes depending
00:36:79.138 --> 00:36:80.743 on whether axillary dissection was
00:36:80.743 --> 00:36:82.331 PCP one or two with low volume nodal disease and
00:36:82.331 --> 00:36:84.000 the definition of what low volume
00:36:84.000 --> 00:36:85.608 nodal disease is changes depending
00:36:85.608 --> 00:36:87.240 on whether axillary dissection was
00:36:87.240 --> 00:36:88.880 PCP one or two with low volume nodal disease and
00:36:88.880 --> 00:36:90.501 the definition of what low volume
00:36:90.501 --> 00:36:92.195 nodal disease is changes depending
00:36:92.195 --> 00:36:93.887 on whether axillary dissection was
00:36:93.887 --> 00:36:95.496 PCP one or two with low volume nodal disease and
00:36:95.496 --> 00:36:97.113 the definition of what low volume
00:36:97.113 --> 00:36:98.736 nodal disease is changes depending
00:36:98.736 --> 00:36:10.333 on whether axillary dissection was
00:36:51.418 --> 00:36:53.806 performed or Sentinel lymph node biopsy.
NOTE Confidence: 0.830093063333333
00:36:53.810 --> 00:36:54.896 Only was performed.
NOTE Confidence: 0.830093063333333
00:36:54.896 --> 00:36:57.068 We see here the Oncotype score.
NOTE Confidence: 0.830093063333333
00:36:57.070 --> 00:36:58.990 The patients could not have chemotherapy before the surgery,
NOTE Confidence: 0.830093063333333
00:37:00.530 --> 00:37:00.552 but it is allowed after the surgery.
NOTE Confidence: 0.830093063333333
00:37:03.090 --> 00:37:06.246 And however, when COVID came around,
NOTE Confidence: 0.830093063333333
00:37:06.250 --> 00:37:08.287 they changed it to allow some limited,
NOTE Confidence: 0.830093063333333
00:37:08.290 --> 00:37:10.290 they should say neoadjuvant endocrine therapy allowed because as we know during COVID some patients were placed on endocrine therapy as a placeholder.
NOTE Confidence: 0.830093063333333
00:37:10.290 --> 00:37:12.734 So here we see our primary objectives in May 39,
NOTE Confidence: 0.830093063333333
00:37:12.734 --> 00:37:15.026 during COVID some patients were placed on endocrine therapy as a placeholder.
NOTE Confidence: 0.830093063333333
00:37:15.026 --> 00:37:17.249 So here we see our primary objectives in May 39,
NOTE Confidence: 0.830093063333333
00:37:19.374 --> 00:37:21.100 it’s to compare breast cancer recurrence
NOTE Confidence: 0.830093063333333
00:37:21.100 --> 00:37:23.266 free interval and our secondary
NOTE Confidence: 0.830093063333333
objectives are all our usual suspects, disease free survival, breast cancer specific survival, overall survival, local recurrence, local regional recurrence, free interval. They’re also looking at ARM volume and motility, lymphedema and there are some quality of life questionnaires and here we see the randomization. So arm one, arm two is our standard arm. So if someone had lumpectomy standardly they were and they have regional notes,
they have nodal involvement. Standard arm is whole breast to radiation therapy plus regional nodal RT or in the postmastectomy setting. So the experimental arm that the patients can be randomized to would be following lumpectomy just the whole breast and not including the. Total fields of the patient had a step, they’d be randomized to no radiation therapy and of course. Then we’ll be following them. But as mentioned, this trial remains open and patients can enroll through our department.
And now we are opening this trial soon, Deborah de escalation of breast radiation and RGB R007 and this piggybacks off of the first trial. I talked about the idea trial, I remember that’s the one where that was going to be looking at the withholding radiation therapy for stage one cancers ages 50 to 69, no nodal involvement, ER positive Oncotype less than 18 that was a cohort study. And the patients of course had to go on endocrine therapy. So now this is pushing that forward.
even further to get even more high quality evidence to say hey, can we withhold radiation therapy in this setting and this is a phase three trial. So here we see that see its patients with a T1. So we know that means 2 centimeters or less and 0 hormonal receptor positive. Her two negative Oncotype recurrence score less than 18 just like the idea trial the ages, well here you're allowed. It’s a little bit more with the ages, but the whole point is to expand the ages. And so we’re randomizing to arm one, which is the standard arm, which would be radiation therapy
to the breast plus endocrine therapy or our experimental arm, no radiation therapy plus endocrine therapy.

So while patients of all ages are really allowed to enroll, the point of this is really to start expanding this out to patients that are younger. Umm.

OK. All right.

So thank you. Doctor Knowlton.

Thank you, Doctor Knowlton.

A lot of great trials that have been run at Yale and are currently open and accruing your work and your team with Doctor Moran has been really fantastic.
We're moving on to Doctor John Lewin, who's our chief of breast imaging. And the Espi president coming to talk about some of the latest in breast imaging available not only at Yale but potentially around the country as well. So, Doctor Lewin, the floor is yours.

Thank you. Can you see my screen? Yeah, of course.

So let me go to presentation mode. So let me go to presentation mode. Alright, so thank you. So yeah, I want to talk about what's new in breast imaging and as Doctor Goldstein said, not just the Yale but everywhere because it's kind of interesting to know what's
going on that’s imaging effects everybody whether in primary care or in surgery. So here having just run a meeting on breast imaging, the Society of Breast Imaging meeting here are the hot topics, so as with the rest of the world. The it’s very easy to make a nice paper using AI to read mammograms, That’s what we said five years ago, so it’s not at all clear. The it’s very easy to make a nice paper using AI to read mammograms,
but now that they’re starting to be implemented in clinics, we’re finding railroad real world results aren’t quite what we’d hoped they would be. So it’s going to be a while before we let the computers read screening mammograms even without human intervention. But almost certainly in five years, AI will be used as a second read in most cases. Now the sad thing is, we know from history it will mostly depend on if there’s a payment for the act. That’s what happened with the predecessor of AI, which was called Computer aided diagnosis.
It took off only because it was paid for and it really didn’t work that well. Eventually Medicare said, well, we’re not going to pay for this anymore. It doesn’t actually work. But the same thing will happen with AI. If we can prove that it has merit enough and it gets paid for, it will take off. But that there’s no question AI is going to have everything to do with every part of medicine and certainly radiology and certainly breast imaging. Contrast enhanced mammography is a big deal in meetings and it’s
a large area of research.

But clinical adoption has been slow because there is no billing code.

So it's just like with AI, if we can't get paid for it, it's very hard to get places to buy it when it was conceived and invented. It was about 20 years ago. The idea was that it would save money and we would all be capitated back then. For those of you who are old, enough to remember, we were all told that capitation was the future.
And so the fact that it’s low-cost now was actually slowing its adoption, but you’ll see that it’s a pretty good modality. The thing that’s a big source of top of discussion in our world is labor shortage. So there’s a shortage of technologists all over the country and certainly Yale. And if you have trouble getting them mammogram scheduled, that is why this happened, because of the pandemic and just overall great resignation. Certain number of texts decided they had enough and now...
00:43:45.762 --> 00:43:47.927 we’re training new tax breast
NOTE Confidence: 0.746707799473684
00:43:47.927 --> 00:43:50.220 radiologists are also in great.
NOTE Confidence: 0.746707799473684
00:43:50.220 --> 00:43:53.580 Short supply all over the country.
NOTE Confidence: 0.746707799473684
00:43:53.580 --> 00:43:57.618 And the last thing that is.
NOTE Confidence: 0.746707799473684
00:43:57.620 --> 00:43:59.588 A hot topic in breast imaging is how
NOTE Confidence: 0.746707799473684
00:44:01.205 --> 00:44:03.329 we screen and especially screening
NOTE Confidence: 0.746707799473684
00:44:03.329 --> 00:44:04.753 high risk women and then something
NOTE Confidence: 0.746707799473684
00:44:04.753 --> 00:44:07.119 called personalized screening and
NOTE Confidence: 0.746707799473684
00:44:07.120 --> 00:44:08.632 that’s what I’m going to talk about.
NOTE Confidence: 0.746707799473684
00:44:08.632 --> 00:44:10.900 mammography has been proven to reduce
NOTE Confidence: 0.746707799473684
00:44:10.962 --> 00:44:13.404 breast cancer mortality by seven of
NOTE Confidence: 0.746707799473684
00:44:13.404 --> 00:44:15.032 randomized clinical trials.
NOTE Confidence: 0.746707799473684
00:44:15.040 --> 00:44:16.430 that’s the highest level
NOTE Confidence: 0.746707799473684
00:44:16.430 --> 00:44:17.820 of proof you can have.
NOTE Confidence: 0.746707799473684
00:44:17.820 --> 00:44:19.598 The eighth trial was the Canadian trial,
which was full of problems and actually one nice session and this year’s meeting had to do with people coming forward who are in the Canadian trial in the 1980s and admitting that they did not randomize the patients. Did that have a much impact on anything? No. But it’s interesting because it was clear from the data that they could not have actually randomized patients in that trial. The next big thing that is now absolutely standard of care is tomosynthesis. This evolved from the development
00:44:51.440 --> 00:44:53.144 of digital mammography.
NOTE Confidence: 0.746707799473684
00:44:53.150 --> 00:44:55.286 About 20 years ago and then
NOTE Confidence: 0.746707799473684
00:44:55.286 --> 00:44:57.257 Thomason says got approved shortly
NOTE Confidence: 0.746707799473684
00:44:57.257 --> 00:44:59.157 thereafter and now Thompson.
NOTE Confidence: 0.746707799473684
00:44:59.160 --> 00:45:01.070 This is basically the standard
NOTE Confidence: 0.746707799473684
00:45:01.070 --> 00:45:02.980 anywhere in a large city.
NOTE Confidence: 0.746707799473684
00:45:02.980 --> 00:45:05.302 There’s still places that only do
NOTE Confidence: 0.746707799473684
00:45:05.302 --> 00:45:07.713 2D mammography but Tommy was really
NOTE Confidence: 0.746707799473684
00:45:07.713 --> 00:45:10.471 become the basis so Thomas since this
NOTE Confidence: 0.746707799473684
00:45:10.471 --> 00:45:12.432 definitely find some cancers that
NOTE Confidence: 0.746707799473684
00:45:12.432 --> 00:45:14.676 are not visible on 2D mammography
NOTE Confidence: 0.746707799473684
00:45:14.680 --> 00:45:17.718 and all mammal Yale is done with
NOTE Confidence: 0.746707799473684
00:45:17.718 --> 00:45:20.958 tomosynthesis even if it’s on the mobile van.
NOTE Confidence: 0.746707799473684
00:45:20.960 --> 00:45:22.913 And the other thing which I’m sure
NOTE Confidence: 0.746707799473684
00:45:22.913 --> 00:45:25.605 which I’m sure almost all of you are
NOTE Confidence: 0.746707799473684
00:45:25.605 --> 00:45:27.400 familiar with is supplemental ultrasound,
also called screening ultrasound and this is used for women with dense breast tissue. So dense breast tissue hides cancers on mammography, and it also increases the risk of breast cancer somewhat. But it’s really the fact that the dense tissue can hide a cancer. That has been the push for supplemental ultrasound and the movement started in Connecticut. Screening ultrasound had been done in New York at boutique practices around the country and most probably in some Manhattan. But the movement to screen all
women with dense breast tissue with ultrasound started in Connecticut. And it’s really taken off. And again, a lot of it is economics. In much of the country you would have to pay for your own chain out of your deductible. But in Connecticut it is covered and the most patient can pay under law is $20. So what again is, dense breast tissue, well here is a classic slide that I guarantee you many of your patients are familiar with. So on the left is the rest that is mostly made of fat and in on the
Mammo report we would say that the breast tissue is almost half that is. Really worded, I would say the best issue is best issue. Even if there’s even no lines like you see here, it still makes milk, it still has breast elements, and it can still get breast cancer. But that’s the wording they chose to use. And then the next one up is called scattered fibroglandular tissue tissue, and it looks something like that, where there’s more black than white. This may not be nowadays. It’s a little less dense when you see it.
on digital mammography with processing.

But then the next heterogeneous,

where it’s denser but there’s still at least 25% of the tissue is not dense and then extremely dense and you can see it would be hard to see a cancer.

And because cancers are white, in the middle of all that white tissue and your patients can go online and go to densebreast-info.org formally are you dense?

What’s the name of that website?

And certainly in Connecticut, everybody knows about presidents.

So here’s an old example of just what the problem is.

So here is a digital mammogram.
where there is a cancer and when you when I should listen. 
Eatings the audience is like, well, 
it must be right here, but in fact it was found because it was palpable. 
But it was also visible in Old Town and was enrolled into my first digital. 
Contrast tomography trial and it’s right there shows not only how tricky it is to find breast cancers and dense tissue but also how well certain other modalities can work. 
So that’s why our supplemental and.
Incomes. So in retrospect,
you can see the cancers here,
but you would never be able to pick that out and on this slide to zillions of people, no one. So. I risk screening, which is different than supplemental screening is what I want to talk about. The additional screening for patients who are at high risk and typically that’s due to family history. So the biggest risk factors for breast cancer are gender. If you’re familiar with higher risk and then age, as you get older, your risk goes up. But aside from those, family history is.
The risk factor that is most utilized to determine your risk gene mutations is another source of high risk force. The bracket one and bracket 2 carriers are at very high risk as you all know, but now there are many other mutations, there's check too is a common one that we screen typically high risk patients for so. The other thing that can cause you to be high risk is if you had a previous biopsy with what we would consider a high risk lesion, atypical ductal hyperplasia, fibular carcinoma insight two these are benign lesions.
But they confer an increased risk for the rest of your life of three to four times.

So if you have any risk at all and you multiply by three to four times, you end up high risk.

And the other thing is a history of mental radiation between puberty and age 30.

It’s interesting that you can radiate women after age 30 and not really increase the risk for breast cancer, but between puberty and 30.

A dose of radiation used to treat cancer is a high risk factor.

Personal history of breast cancer makes you more likely to get another breast cancer, and that one’s a little controversial whether
we should do high risk screening for those.

So the guidelines for high risk screening?

Are as follows the most followed guidelines from the American Cancer Society.

And this is where that 20 to 25% lifetime risk comes.

So you calculate the risk using one of the models, and if it’s above 20%, then the Marion County Society would recommend that you consider screening with MRI as well as mammography starting at 30. News from for as long as they’re in good health. Now, this is a lifetime risk.
So you really interpret this that you continue until their lifetime risk falls below that 20% range. But it’s not for everybody. There’s downsides to high risk screening with MRI, and I’ll show you some of those, but keep in mind that 2025% lifetime risk based on family history and genetics or mental radiation or if you have leaf framing, which puts you at a very high risk. Now we’ve talked about the American collector. We talked about the American College radiology and the American collector.
Society breast surgeons.

They have similar recommendations to American Society, but they also include high risk screening for women who have a personal history of breast cancer, especially if they’re young and they have dense breast tissue.

What do we use for risk models? If you see risk models in your radiology report, you want to know where they come from. Well, the oldest model is the Gale model and that was what was used for all the tamoxifen trials.
It is primarily focused on environmental and hormonal factors. It has a family history factor, but it's very coarse. The backup pro and Klaus and Myriad models predict the risk of having a PRC mutation, but they do not predict your overall cancer risk. The one we use for determining high risk screening is the tire cusick model, which is also called Ibis. And it uses multiple factors, and the latest version, which is version 8, includes breast density.
It has a much more complete family history than the GAIL model. It comes with outputs that are five year lifetime and we use lifetime to decide whether people should have an MRI. And the reason is because we're trying to gear these toward young women where we have the greatest chance of having a positive impact, saving as many years of life as possible. The only genes in the model are BRACA one and two. So it doesn't include all the other genes, which is a little problematic because
now many of our patients have genetic panels that show they have mutations in other genes that confer risk. And you cannot have had a personal history of breast cancer. It does not take that into account. So what do you do if you are at high risk? Well, as I said, we do annual MRI and that has to be performed with Ivy contrast. There’s no utility to ordering a non contrast MRI. The patient is months MRI but they don’t want contrast. Then it’s useless. First demography. We do non contrast them right only to evaluate implants.
We do that very rarely these days. Elenium contrast is now very safe. It does this thing called NSF where it was. Horrible disease, but the contrast agent that caused that is off the market and the point where we don’t even do routine crap testing. So. The other so you know for that FF. So that really saves a lot of work. You don’t have to worry about getting pre MRI creatinine deposition of gallium you’ve probably heard about. They could see it in people’s brains who have had multiple MRI with contrast.
that has been essentially eliminated by changing to macrocyclic from linear agents. So with MI, you also should have annual mammography because in studies you find about 9% more cancers if you add the mammogram for the MRI. So by far if somebody says I only want one of these, then they should have the MRI. It’s quite far the better test. But if you want to have the best screening, it’s MRI plus mammography. And typically the mammography is there just like calcifications, which can be a sign of TCS. And if you’re going to have MRI,
there’s no benefit to adding screening ultrasound every study has shown.

So what does it look like if you have a screening cancer?

Well, here’s one that’s about 8 millimeters and they certainly can come smaller at three and four millimeter cancers,

but this is the perfect example.

It’s a patient with very low background enhancement,

a single lesion that’s obvious to everybody,

even without the green circle.

In fact, she’d had a screening mammogram the year before and it wasn’t there, so.

If you knew a little bit spiculated,
it’s a little subtle,
but to us that little tiny bump there means speculation.

This one’s trickier.
This one’s oval and smooth.
And in fact, this one turned out to be a fibroadenomas.
So it’s not that everything that lights up is a cancer.
So the case I showed, of course.
Great if everything looked like that,
but it doesn’t always.
So you will have probably benign.
Comes from these,
so we give you an assessment of probably benign and we recommend a follow up MRI.
We recommend the targeted ultrasound. We cannot always tell a benign from malignant lesion. We have the capability to biopsy under Mr Guidance. The other thing that is sort of the equivalent of dense breast tissue but for MRI is background enhancement. So if the normal tissue lights up like this, and especially if it lights up with a bunch of blobs that are a little bigger than this, which is not uncommon, it could potentially provide a cancer. Even on this pattern, we would be able to see a cancer,
but we're not going to see as many as we see if that. Especially DCIS is what we would lose. So how does DCIS typically present? So it can present as a thing called non mass enhancement. So you see a report and it says there's mass enhancement. We're saying, well it could be DCIS, but it's more likely normal and we have to decide we biopsy this or not. We know that neither one of these is likely to be an invasive cancer and in fact we know that both of them are more likely normal tissue than DCIS.
But if we want to make sure we catch the cancers, we have to have a threshold. When do we biopsy, when do we not? So those are kind of the things that might help you interpret the reports you get. So how good are each of these tests? Well, when you add tomography. For the first thousand patients in the first screening round, I know that well. First of all know that typical screening mammography practice, we will find 2 to 4 cancers per thousand. The yearly incidence of cancer is around two to three in screening age patients. But not everybody shows
up absolutely every year.
So it tends to be a yield of about four.
Adding tomosynthesis in the early studies showed about one to two additional cancers.
Often these were low grade cancers which was a little bit disappointing.
Ultrasound. Was better.
Adding supplemental ultrasound is better than just doing tomosynthesis.
Three to four additional cancers,
Contracts that enhanced mammography and screening studies is a big jump because you’re giving contrast.
So the studies that were done showed eleven additional cancers, but the one that really drives everything is that if you do MRI, you find 14 additional cancers. So what does that really mean? But first of all, where does that really come from? So that 14 number comes from a study called the acronym 6666 trial. And for that trial you did not have to be high risk, you only had to have dense breast tissue 2800 subjects, they had mammography with...
00:57:53.276 --> 00:57:54.869 or without tomosynthesis.
NOTE Confidence: 0.838742302105263

00:57:54.870 --> 00:57:56.886 And then for three years in a row they
NOTE Confidence: 0.838742302105263

00:57:56.886 --> 00:57:58.620 also had supplemental ultrasound.
NOTE Confidence: 0.838742302105263

00:57:58.620 --> 00:58:00.942 That’s where they found about four
NOTE Confidence: 0.838742302105263

00:58:00.942 --> 00:58:02.956 cancers per thousand extra just
NOTE Confidence: 0.838742302105263

00:58:02.956 --> 00:58:03.760 on ultrasound.
NOTE Confidence: 0.838742302105263

00:58:03.760 --> 00:58:04.633 Pretty good yield,
NOTE Confidence: 0.838742302105263

00:58:04.633 --> 00:58:06.379 do you think you found everything?
NOTE Confidence: 0.838742302105263

00:58:06.380 --> 00:58:08.500 But then after three rounds of that day,
NOTE Confidence: 0.838742302105263

00:58:08.500 --> 00:58:09.808 they decided to do one round
NOTE Confidence: 0.838742302105263

00:58:09.808 --> 00:58:11.310 of MRI and lo and behold,
NOTE Confidence: 0.838742302105263

00:58:11.310 --> 00:58:13.428 there were 14 cancers per thousand
NOTE Confidence: 0.783299121578947

00:58:13.428 --> 00:58:16.019 that had been lurking there that were
NOTE Confidence: 0.783299121578947

00:58:16.019 --> 00:58:18.245 not found by mammography and Epstein.
NOTE Confidence: 0.783299121578947

00:58:18.250 --> 00:58:19.050 So what does that mean?
NOTE Confidence: 0.783299121578947

00:58:19.050 --> 00:58:20.255 Are we finding additional cancers
that never would have been found?
No. We’re finding cancers earlier.
So it’s moving the detection point earlier.
So that you’re finding hopefully
We do not want to find 14
That means we’re over diagnosing,
we’re finding too many cancers,
but that’s not what happens.
You find the 14 cancer.
Number and the point is
we’re finding them earlier.
So if you screen with MRI,
you’ll find smaller cancers
and the cancers will all be. Of all different types as far as aggression.
So they have to be aggressive enough that they make their own blood vessels in order to show up on MRI.
So it’s not prone to over diagnosis the way, for example, tomosynthesis seemed to be a little bit.
The feature is called personalized screening and in personalized screening, which we are not doing at this point, but we will be.
As things progressed over the next five years, each patient will get screened.
based on their own risk factors.

That has to mean that some get more screening and others get less.

 Doesn’t do any good if we just screen everybody more.

So it’ll affect how often we say they should be screened and what modalities we use.

We will use the standard risk factors that I mentioned, family history, etcetera.

But also we can use AI to analyze the pattern on their mammogram.

And it’s been shown that with AI you can predict their short term risk very well.
I’m more than just looking at density as we looked at, but if you look at the actual pattern, somehow the computer can tell what their short term risk is. So you might ask well how and they realized we really don’t know. But if you’re looking at short term risk, you’re really looking at not so much as risk but early detection. So in my opinion they’re seeing early signs of cancer, early signs of cancer, late signs of cancer, not super specifically, but enough that if you take those patients where they say hey, this looks like there’s going to be a
cancer here and you do MRI on them. Find that it’s the best predictor of short-term risk, so it’s better than the entire music model. And that is what’s going. So that’s what we have to look forward to.

Screening Murphy is still the only tool that was validated using trials with mortalities and endpoint and it’s still the mainstay of breast cancer screening. But we know it’s far from perfect. Ultrasound definitely finds additional cancers and dense breasts.
And while we don’t have a mortality based trial to prove that it saves lives, clearly we’re finding cancers that would have kept growing, would have been found later with only mammography, understand. MRI is our most sensitive test, but it’s also our most expensive and it also has this reputation of having false positives, which it does. But we’ve come to where we can manage those. We know where our threshold should be and we can do biopsies. And the key to optimizing screening in the future will be matching every patient to the best tests.
and interval for her. And AI will very likely play a role, which means mammography will very likely play a role because it’s from the mammogram that we use the AI to determine risk. So again, a whirlwind tour of what’s going on in breast imaging. So thank you. Thank you, doctor Lewin. That was really comprehensive and so much going on in the world of breast imaging. Last but not least, we have a doctor, Ayela, who’s our newest faculty member,
01:01:43.390 --> 01:01:45.310 joining us from Memorial Sloan Kettering.

01:01:45.310 --> 01:01:48.650 Umm talking about advances in breast reconstruction.

01:01:48.650 --> 01:01:52.085 We're really excited to have a talented microvascular surgeon like you here at Yale.

01:01:52.085 --> 01:01:55.329 Thank you.

01:01:55.330 --> 01:01:56.150 Thank you for the introduction.

01:02:00.200 --> 01:02:01.910 Can you see my screen?

01:02:07.370 --> 01:02:08.622 All right. Well, good evening, everyone. Thank you for the introduction and for the invitation.

01:02:08.622 --> 01:02:09.950 This is a homestretch.

01:02:09.950 --> 01:02:11.750 Thank you for the introduction and for the invitation.

01:02:11.750 --> 01:02:13.190 I’ll be talking about strategies and
comprehensive breast reconstruction.

So we’ll briefly discuss the background, why do we choose reconstruction, some options after both breast conservation and mastectomy surgery and a couple of new directions that we hope to be exploring at Yale for our patients. That it’s been almost 25 years since the government has mandated healthcare payer coverage for all breast reconstruction, including contralateral procedures to achieve symmetry and any treatment after sequella of mastectomy. However, they’re really still continues to be less than a 50% rate of women.
who are seeking breast reconstruction.

And upon additional surveys we have found that common reasons not to choose reconstruction are to avoid additional surgery belief that reconstruction is either not important or not available or potentially. A fear of breast implants, especially surrounding the current media state.

We have found over and over that patients who do undergo reconstructive procedures have very high rate of satisfaction and very, very good and improved quality of life.
And reconstruction is we can be performed concurrently with both breast conservation methods as well as after mastectomy. It's important to note for our patients that reconstruction is safe and it does not affect the risk of local disease recurrence. This is very advantageous in many respects, and there's tons of literature and numerous algorithms to help us decide the optimal incisions and resection patterns. But I think it's simplest to tell patients that large breasts generally
undergo therapeutic reduction.

Small breasts with small masses undergo tissue rearrangement with a lift,

Small breasts with a large mass may need volume replacement in the form of a local tissue flap.

So here's a schematic of an oncoplastic reduction for a larger breast.

We usually use this incision pattern, the wise pattern and this is a patient who had a upper outer tumor for resection and we approached this using again that traditional wise pattern incision.

We were able to reduce and lift the breast after the tumor was
01:04:22.080 --> 01:04:24.360 removed and she here she is postop,
01:04:24.360 --> 01:04:27.100 good contour, good symmetry.
01:04:27.100 --> 01:04:29.356 Small breasted patients who are losing
01:04:29.356 --> 01:04:31.716 a significant amount of their volume
01:04:31.716 --> 01:04:33.706 may need replacement with tissue.
01:04:33.710 --> 01:04:35.957 Often we take this from the back.
01:04:35.960 --> 01:04:37.031 So for example,
01:04:37.031 --> 01:04:39.173 this woman had a upper intermedial
01:04:39.173 --> 01:04:41.628 quadrant tumor and would have definitely
01:04:41.628 --> 01:04:43.658 had an aesthetic contour deformity.
01:04:43.660 --> 01:04:45.442 It doesn’t have quite enough tissue
01:04:45.442 --> 01:04:46.965 to rearrange and she definitely
01:04:46.965 --> 01:04:48.375 does not lean a lift,
01:04:48.380 --> 01:04:49.717 nor does she want to be smaller.
01:04:49.720 --> 01:04:52.240 So the plan is to replace this volume with
a thoracodorsal artery perforator flap, taking just the skin and the fat. Of the back and sparing the muscle. And this is her post-op healed good contour, no volume loss. So options after mastectomy, there are two traditional arms we know about. Of course for total breast volume replacement implant or autologous based. We decide on the best arm together with the patient after discussing her unique factors such as plans for radiation. Implants are still the most popular choice. A certain subset of patients, small breasted minimal tosis,
can have an implant placed directly at the time of mastectomy, but it is still definitely more common for this to be done in two stages. This allows the mastectomy skin to heal and in cases of limited skin will allow us to expand the pocket to the desired volume. The prosthetics have traditionally been placed underneath them also, but now there’s a large movement to place them above the muscle and these implants of course include silicone or saline still in the market. The pros of course is you
have one operative site,
NOTE Confidence: 0.771689783
you’re only operating on the chest.
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Compared to the autologous group,
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it is a reduced operative time and
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there is more rapid post-op recovery.
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But the cons is we’re doing unilateral
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reconstruction is very difficult to obtain
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symmetry to the contralateral breast.
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The patient does have to
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come back very frequently,
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sometimes over the course of several
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months for tissue expansion visits,
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and they do require at least two operations
NOTE Confidence: 0.771689783
to achieve reconstructive completion.
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With radiation there is potential
NOTE Confidence: 0.771689783
for increasing complications and
01:06:29.058 --> 01:06:30.831 sometimes in very thin patients who
01:06:30.831 --> 01:06:32.833 have low BMI and we are putting
01:06:32.833 --> 01:06:34.498 the implant above the muscle,
01:06:34.500 --> 01:06:35.910 the implants can be visible,
01:06:35.910 --> 01:06:39.640 palpable or you can see rippling.
01:06:39.640 --> 01:06:40.621 Natalie, this option,
01:06:40.621 --> 01:06:42.583 great options for patients who want
01:06:42.583 --> 01:06:44.171 their own tissue natural appearance
01:06:44.171 --> 01:06:46.362 and feel often are very good options
01:06:46.362 --> 01:06:47.997 in unilaterally constructions to match
01:06:47.997 --> 01:06:49.928 the tosis of the contralateral breast.
01:06:49.928 --> 01:06:52.091 And I think this is usually the
01:06:52.091 --> 01:06:55.700 better option in the setting of
01:06:55.700 --> 01:06:56.058 However,
it does require an experienced microsurgeon
and we're operating on two sets of body.
So this does necessitate a longer operative
time and a longer recovery upfront.
So there's a lot of discussion about
the optimal timing of reconstruction.
Immediate reconstruction is
definitely always preferred,
so patients do not have to wake up flat.
But a lot of plastic surgeons are
wary of the effects of radiation
on their final reconstruction,
whether that is an implant or
if it is a flap.
And we've also found that patients
can be very overwhelmed with their
recent cancer diagnosis and they want to defer thinking about their choice of final reconstruction until all of their adjuvant therapy can be completed. So we find that we can mitigate all of these concerns by placing a tissue expander at the time of mastectomy to maintain the breast pocket, make sure that the patient does wake up with some sort of breast mound. And then we have the patient complete their cancer treatment including adjuvant radiation, chemo, whatever is needed with the expander.
in place the entire time.

And then in these cases it’s preferred that the tissue expander should be placed in the pre pectoral plane above the muscle, avoiding the morbidity of elevating the pectoralis muscle. It allows much faster, much more comfortable. Extension for the patient so they can be fully expanded, healed, go on to adjuvant therapy more quickly. And then on the patient’s own timeline, the expander can be exchanged electively, so patients have time to discuss again, choose if they want to continue and replace this expander with a permanent implant,
or at this point they can remove the prosthesis and put in their own tissue. This patient shown here, she underwent expander placement, fully expanded in a few weeks, completed all of her radiation and then came back, I believe six months later for autologous reconstruction. So we figured out a really good way to use our own tissue to create healthy warm breasts, restoring blood flow in and out of this new breast mound. And we tell patients that they’re
going to feel like a breast,
which is true to others,
but not necessarily the patient.
Often patients are very disconcerted
with the numb feeling in their chest.
So now we’re working on strategies
to improve sensory recovery after
mastectomy concurrently with
autologous tissue reconstruction.
I really like the way one
of my partners put it.
We have to hook up the plumbing
and the electricity to make
the reconstruction complete.
So to offer truly comprehensive
breast reconstruction,
we must be able to also offer options
to prevent and treat sequella of
axillary dissections under radiation.
As we know, lymphedema is very devastating to patients quality of life and we have not yet found a curative treatment. We do offer hope to offer preventative options such as immediate lymphatic reconstruction or also known as lymphatic mapping to identify which nodes are important for armed drainage. For patients who already develop
develop any sort of lymphedema,

NOTE Confidence: 0.870645268888889

they do have patent lymphatic

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channels in their arm.

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We can bypass these scarred lymphatics

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with serial lymphatic ovular anastomosis.

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This is a really easy outpatient procedure.

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And for those who are a little

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bit more advanced,

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I have no channels left in their arm.

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Lymph node transplant can often be performed.

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So we use the omentum as a good donor

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side to prevent donor site lymphedema.

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But with the use of referral synthetic

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mapping we can also take select

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groin lymphatics along with the

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abdominal flap for whole holistic
breast and axillary reconstruction.

So very grateful to join Yale, be a part of this multidisciplinary team focused on cancer eradication and really improvement of quality of life for our patients.

So thanks for the opportunity to discuss our approach to comprehensive breast reconstruction tonight.

Thank you, Doctor Ayala. Wow.

Thank you, everyone for, you know, 5 phenomenal presentations and the audience for sticking with us through this evening.

There are a couple of questions that...
01:10:43.562 --> 01:10:44.879 actually came in through the chat,
NOTE Confidence: 0.8691891
01:10:44.880 --> 01:10:45.940 not sure they can actually
NOTE Confidence: 0.8691891
01:10:45.940 --> 01:10:47.335 be seen by the audience.
NOTE Confidence: 0.8691891
01:10:47.335 --> 01:10:49.000 I’m going to ask our panel.