Breast Cancer Research in Israel: Latest Discoveries and Innovations

National Webinar Transcript

May 4, 2026

Presented by:

SHARSHERET®
The Jewish Breast & Ovarian Cancer Community

In partnership with

ICRF Israel Cancer Research Fund

About Sharsheret

Sharsheret, Hebrew for “chain”, is an international non-profit organization, that improves the lives of Jewish women and families living with, or at increased genetic risk for, breast or ovarian cancer through personalized support and saves lives through educational outreach.

With regional offices in the Midwest, Northeast, Southeast, West, and Israel, Sharsheret serves 275,000 women, families, health care professionals, community leaders, and students. Sharsheret creates a safe community for women facing breast cancer and ovarian cancer and their families at every stage of life and at every stage of cancer - from before diagnosis, during treatment and into the survivorship years. While our expertise is focused on young women and Jewish families, approximately 25% of those we serve are not Jewish. All Sharsheret programs serve all women and men.

As a premier organization for psychosocial support, Sharsheret works closely with the Centers for Disease Control and Prevention (CDC) and participates in psychosocial research studies and evaluations with major cancer centers, including Georgetown University Lombardi Comprehensive Cancer Center. Sharsheret is accredited by the Better Business Bureau and has earned a 4-star rating from Charity Navigator for four consecutive years.

Sharsheret offers the following national programs:

The Link Program

Peer Support Network, connecting women newly diagnosed or at high risk of developing breast cancer one-on-one with others who share similar diagnoses and experiences

- Embrace™, supporting women living with advanced breast cancer
- Genetics for Life®, addressing hereditary breast and ovarian cancer
- Thriving Again®, providing individualized support, education, and survivorship plans for young breast cancer survivors
- Busy Box®, for young parents facing breast cancer
- Best Face Forward®, addressing the cosmetic side effects of treatment
- Family Focus®, providing resources and support for caregivers and family members
- Ovarian Cancer Program, tailored resources and support for young Jewish women and families facing ovarian cancer
- Sharsheret Supports™, developing local support groups and programs

Education and Outreach Programs

- Health Care Symposia, on issues unique to younger women facing breast cancer
- Sharsheret on Campus, outreach and education to students on campus
- Sharsheret Educational Resource Booklet Series, culturally-relevant publications for Jewish women and their families and healthcare Professionals

Disclaimer

The information contained in this document is presented in summary form only and is intended to provide broad understanding and knowledge of the topics. The information should not be considered complete and should not be used in place of a visit, call, consultation, or advice of your physician or other health care Professional. The document does not recommend the self-management of health problems. Should you have any health care related questions, please call or see your physician or other health care provider promptly. You should never disregard medical advice or delay in seeking it because of something you have read here.

The information contained in this document is compiled from a variety of sources (“Information Providers”). Neither Sharsheret, nor any Information Providers, shall be responsible for information provided herein under any theory of liability or indemnity. Sharsheret and Information Providers make no warranty as to the reliability, accuracy, timeliness, usefulness, or completeness of the information.

Sharsheret and Information Providers cannot and do not warrant against human and machine errors, omissions, delays, interruptions or losses, including loss of data.

Liora Tannenbau...: Welcome, and thank you for joining us for tonight's webinar, Breast Cancer Research in Israel: Latest Discoveries and Innovations, with Sharsheret in partnership with Israel Cancer Research Fund. We are excited to welcome Dr. Albert Grinshpun, head of breast oncology at Shaare Zedek Medical Center. I'm Liora Tannenbaum, Director of Sharsheret in Israel.

Before we begin, a few housekeeping items. Today's webinar is being recorded and will be posted on Sharsheret's website, along with the transcript. Participants' faces and names will not be in the recording. If you would like to remain private, you have the option to turn off your video and rename yourself, or you can call into the webinar. We also have closed captioning available. To display live captions on the bottom bar, click on Captions, and then click on Show Captions. You may have noticed that you were muted upon entering the Zoom. Please stay muted during the call. We will hold a Q&A at the end of the presentation. If you have any questions, please type them in the chat box, and we will get to as many as we can during the Q&A.

I want to remind you that Sharsheret is a not for-profit cancer support and education organization and does not provide any medical advice or perform any medical procedures. Our full medical disclaimer is in the chat.

For those of you that don't know, Sharsheret's Israel office is now in its third year. We are so proud and grateful to extend the work that has been done nationally across the United States to those living here in Israel. Since opening our office here, we have supported women, men, and families in a variety of ways and from communities all over the country. In the face of war, instability, and the ongoing uncertainty of daily life, over the past few years, we continue

to emphasize the importance of being proactive about our health wherever possible. Staying on top of medical appointments, resisting the urge to cancel or delay them despite the limited bandwidth so many are feeling is critical. At the same time, tending to our mental health is just as essential, making the effort to stay connected when life feels isolating and offering emotional and practical support when navigating the logistics, anxiety, and complex decision-making that often accompany a diagnosis. Even under ordinary circumstances, these challenges are not simple. We have seen and continue to see how the backdrop of war adds an additional layer of stress, impacting both our health and our sense of control.

Most importantly, if you are currently facing an ovarian cancer or breast cancer diagnosis, please remember that Sharsheret is here for you and your loved ones. Sharsheret provides emotional support, mental health counseling, and other programs designed to help navigate you through the cancer experience. All are completely free and confidential. Our contact information is in the chat box now. We are grateful to Israel Cancer Research Fund for partnering with Sharsheret on this webinar so that together we can amplify the life-saving cancer research being developed here in Israel.

It is now my pleasure to welcome Alan Herman, CEO of Israel Cancer Research Fund.

Alan Herman: Thank you so much. And good morning, afternoon, or evening, depending on where it is that you're joining us from today. I'm Alan Herman, the executive director, CEO of the Israel Cancer Research Fund. It's a true honor to be partnering today with Sharsheret, a true best-in-class organization in the fight against breast and ovarian cancer. The fight against cancer is not theoretical, it's personal, it's urgent, and for many families, it's happening right now in real time. For nearly 50 years, ICRF has been focused on that urgency, backing Israel's most promising cancer researchers. To date, we've invested over $100 million supporting discoveries in Israel that are improving and saving lives around the world.

What makes our model so powerful is focus. We fund bold ideas early when they are just beginning to take shape. We invest in exceptional people, and we do it in one of the most dynamic scientific ecosystems anywhere. Israel brings together scientific excellence, deep collaboration, and a culture that challenges convention and moves quickly. That combination consistently turns breakthrough thinking into real-world impact, and that is exactly what brings us here today.

It's my privilege to introduce one of those exceptional physician scientists. Dr. Albert Grinshpun is a leader in personalized cancer care and translational research. He heads the breast cancer program at Shaare Zedek Medical Center in Jerusalem and leads a translational research lab at the Hebrew University. He trained at some of the world's leading institutions, including Hadassah, the Weitzman Institute, and Dana Farber Cancer Institute. He has authored more

than 30 peer-reviewed publications, including in top journals such as Annals of Oncology and the JAMA Oncology.

I'm proud to say that he is an ICRF-funded scientist. Through a past partnership with the Conquer Cancer Foundation, ASCO, Dr. Grinshpun helped advance a breakthrough idea, a simple blood test designed to detect breast cancer and reduce the need for invasive biopsies. Today, with continued ICRF support through our Clinical Research Career Development Award, he's building on that work, developing a way to detect serious treatment side effects earlier and making sure that patients stay safer while continuing life-saving therapies. This is what friends like you make possible, not just research, but real progress for patients and families who are counting on it.

So please join me in welcoming my friend, Dr. Albert Grinshpun, who represents the very best of what is possible when Israeli science, innovation, and purpose come together for the purpose of changing lives globally. Thank you.

Dr. Albert Grin...: Thank you, Alan. Thank you very much for the kind introduction, and I would like to thank the wonderful teams of Sharsheret and ICRF for organizing this event and for inviting me. And also, I would like to highlight the unique approach of ICRF in funding and supporting physician researchers because for, let's say, standard researchers, there are multiple options of funding and promoting research, but for physicians, there are not many options. And I think ICRF is unique in that it supports translational ideas, which means we see the patient, we think of a problem, then we go, we try to solve the problem, sometimes without even understanding the solution fully, but still we try to get the solution done quickly and go back to the clinic and try to help the patient, and I think that's a great thing. And I would like to thank you, Alan, personally and for all ICRF supporters.

So I'll try to share my screen now successfully. Okay, do you see it now? Okay. So in the 30 minutes that we have, I thought to share with you some ideas and the best... Sorry. Now it moves. And the best idea in sharing and showing what we're doing and what we're trying to do is basically, as I just mentioned, it's coming from the clinic. And so all of our problems starting at the clinic and... There we go.

The first case I wanted to present to you tonight or in the evening... And just want to say happy Lag BaOmer for those who make fire or plan to do fire today. Now they said very strong wind, so be careful, everyone. So the first case is a real patient that I treated a while ago. She's a 65-year-old lady with a metastatic breast cancer. And she was treated with the most amazing drug of the year called Enhertu, which is an antibody drug conjugate. As you see here in the black square, it's an antibody that targets a specific molecule in cancer cells, and it's loaded with chemotherapy, the red circles. The drug basically attaches to the protein, in this case, it's the yellow HER2, and then the cell swallows the molecule, the molecule detaches, the chemotherapy is released, and it eliminates the cancer and destroys the cancer cells.

So the patient was doing great. Her CT scan showed that the cancer is regressing and she felt fine. And then she approached the physician again and she said, "I'm feeling shortness of breath." So as every good doctor, he examined her first, asked her, "Do you have maybe some signs of infection, signs of flu?" She didn't have anything. She did ECG. She had chest X-ray. As you can see, the X-ray is clear, the ECG was clear. Everything was fine. And the doctor said, "Ah, it's probably a viral disease. You can go home," and unfortunately, within two days, she arrived with an ambulance to the emergency room with a severe shortness of breath and was admitted to the intensive care unit with this picture. This is an image from a chest CT scan. As you can see, the normal lung is the black area on top, and all the other areas in the lung marked with red arrows represent a severe inflammation in the lungs that basically was not diagnosed by standard means or standard approach, and the patient was hospitalized for many, many months until she recovered from that episode that was toxicity of the drug. The drug basically damaged the lungs and almost nearly killed the patient.

So this is the first story that brings us to the first challenge this evening: how can we assess damage or some unwanted side effects of our cancer medications to organs that we don't have a simple blood test for them? We all know that if we have something with our kidneys, we can go to the doctor. He can do a simple blood test that probably costs $1 for a protein called creatinine. We do it. After two hours, we have a result and it says whether our kidneys are fine or not. But the problem, how can we check other organs that we don't have a blood test for them? So this is the first case.

The second case is maybe more interesting. Everything is interesting, but within the most interesting stuff, I brought you the two most interesting. This is a 40-year-old lady that was treated I think six months ago, and she presented with an locally advanced triple-negative breast cancer, which means it's an aggressive breast cancer. She's 40 years old. She didn't do mammography. She just felt a lump, immediately went to the surgeon, the surgeon sent her to mammography. She did everything you see on the left side on diagnosis, her breast MRI. This is a standard breast MRI. And you can see with the blue arrow basically the tumor. The tumor and below the blue arrow you see enlarged lymph nodes, so we call it locally advanced. Basically some of the tumor cells already left the breast and went to the axillary lymph nodes, so this tumor is relatively very aggressive and is being treated with chemotherapy and sometimes with immunotherapy. And she received the standard treatment chemotherapy and immunotherapy for six months.

After finishing chemotherapy after six months, she said, "Wow, that's amazing. I don't feel any lump," and on examination, everything was normal. We did MRI at the end of treatment before surgery, and you can see the MRI on the right side. Basically clearer than that, it's not possible, almost. And the patient wondered, "Wait, why do I need to do surgery if everything is clear," and we said, "No, no, no, no, no, no, no. Everybody's getting surgery these days. This is the standard," and she said, "Okay. Unfortunately I need to do surgery." And she had surgery, and when we got the pathology, when we got the pathological

report from the surgery... I'm bringing you an image from that report, or a similar one. The tumor bed is the area where the original tumor was diagnosed and we put a clip on diagnosis so in case it will disappear from imaging, we will still know where it is located. And under the microscope, the pathologist is calling and saying, "I see a residual invasive cancer," and I'm not going into details, but he said, "It seems that the cancer looks happy and the chemotherapy didn't affect it a lot," which means we eliminated maybe 99% of the cancer cells that were sensitive to the treatment, but the very aggressive, resistant 1% that can lead to metastasis and risk of this patient's life is still there and there is residual invasive cancer.

Luckily, we decided, maybe not luckily, but as standard of care, we send the patient and convinced her that surgery is the next step. And on surgery, that area was removed. Now the tumor is in paraffin in our warehouse, and the patient can continue safely without tumor in her body. But we still know that for patients that have residual invasive cancer, it means that the prognosis for this patient is quite problematic because we gave her five types of different medications for six months and we still had residual cancer, which means this is a high-risk cancer. And after surgery, before letting her go and do whatever she wants, she will still get six months or nine months of additional therapy with a sixth drug in order to prevent recurrence and kill all the cells that might hide somewhere. So it is very important to detect whether there is a residual cancer or not because it affects treatment and affects prognosis.

So the challenges highlighted by this case is basically, how can we detect complete tumor eradication? Because she had the best imaging available in Israel. In Shaare Zedek, we have the best MRI protocols forged by Weitzman Institute scientists and then can detect everything with the best radiologists. But still, you saw it was clean. Clean. Cleaner than that, it's not even possible, and still, there was a tumor there. And the second question is for those that have total tumor eradication, how can we safely minimize the intervention? Maybe we can prevent them from getting surgery, prevent them from getting more chemotherapy, more radiation, et cetera. So these are the two challenges we'll try to answer tonight.

And I will try to show you that perhaps there is one solution for both problems, something related to liquids, and the second is related to biopsies. Sorry. So the liquid biopsy concept was detected many years ago by a Singaporean physician that found that in the plasma, in the blood of women that were pregnant with male babies, he could find Y chromosome in the plasma. And that was a intriguing finding because he said, "Wait, how can we find Y chromosome that comes from the baby in the mother's blood?" And then they followed up after this Y chromosome and they saw that after delivery, after the baby got out, within an hour or two, that chromosome Y DNA disappeared. So basically that shows us until today, this is the ground truth, basically, the circulating nucleic acids or the DNA that comes, for example, from the baby or from a tumor, a different type of a parasite maybe, so that DNA lives in our body for an hour or two. So if we find a piece of DNA in the blood, it doesn't show us historical facts,

it give us recent history. It gives us something that happened in the last two hours.

So as you can see in the illustration, we know that when there is somewhere cancer cells, tumor cells, there is a release of different materials, proteins and DNA, and that is basically circulating in our bloodstream, and we call it circulating tumor DNA, ctDNA. And when we do a simple blood draw from the arm or any location, we can identify these molecules of ctDNA, circulating tumor DNA. And if we detect them, first, we know that there is a tumor; second, we can analyze them and study them in order to get more insights into the biology of the tumor. We can identify mutations there. We can identify dynamic changes, for example, some mutations can be there in the beginning, we can give treatment, resistance mutation can appear, so we can find them later on.

And if you compare liquid biopsy, which is a simple blood draw, to a tissue biopsy, a standard biopsy, which means sticking a needle in some organ, so we see that liquid biopsy is basically minimally invasive. Maybe it's not non-invasive, but minimally invasive. It's very easy to access. My daughter, she's doing a course in Magen David Adom. She's going to be 15. I can teach her to take liquid biopsies. I can teach her to take blood from patients. And it's not like doing a liver biopsy, which takes 15 years to train a person to do a liver biopsy. It's rough. It's totally different. We can do repeat sampling. We can do liquid biopsy every week, every hour maybe, which is totally not true for a liver biopsy. We do it once a year. We're not doing it more than that. It gives us real-time monitoring. As I said, if we get circulating tumor DNA, we get information from the last two hours.

In addition, for patients with metastatic disease, the cancer spread to different areas. When we do a standard biopsy, we just get what the needle gets. We get the information from a tissue that's inside the needle, but when we get circulating tumor DNA from the blood, we get circulating DNA molecules from the liver masses and from the lung masses and from the colon masses. Basically we can get a holistic picture and get much more information. And it says here the ability to capture ITH, it's intratumor heterogeneity, which basically says that when we do a liquid biopsy, we get DNA from multiple sources, multiple locations, and we can get a lot of information. And the tumor cell content is usually higher when we do a biopsy of a tumor. And in the blood, it's basically the ctDNA is diluted in the normal circulating DNA, so we need much more sophisticated methods that are getting better and better every year to extract that data.

And just a illustration to show that if there is a lot of tumor, we can measure that in the blood. Instead of CT scan, for example, we can measure that in the blood and see a lot of ctDNA. If we give good treatment or remove surgically the cancer, the ctDNA will drop. And if the tumor will recur or will grow, despite the treatment, we will see the levels of ctDNA going up. So those are potential uses of ctDNA that we... But it enters the clinic, and we use it more and more.

Now, we just spoke about ctDNA, circulating tumor DNA, here in red, but what about normal tissues? Do they shed also DNA? And here we see, if you remember, Dolly the sheep. So Dolly the sheep, she was created from a DNA from a skin of another sheep, and that answers us with a good question. Because if we find normal DNA in the plasma, how do we know its origin? How do we know that that DNA molecule came from the liver or came from the lung, for example? Every DNA molecule in the lung and the liver on the skin contains the entire information for the organism. We can see Dolly here. Dolly was created from a skin DNA from another sheep. The entire sheep was encoded in that DNA.

So how do we know for each molecule, the origin of it? The secret is DNA methylation. DNA methylation, it's a process that... There are methyl groups. This is there for the chemists among us, CH3. This is the most chemistry we will say. These molecules are basically found on the DNA, and their role is to close genes and prevent their expression. We can imagine that every cell contains the DNA, the entire cookbook to create our body, but in the lung, only the genes relevant to the lung are open. All the other genes are methylated. They are locked. In the skin, all the genes that are relevant to the skin are open. All the other genes are locked with the methyl.

And here you can see an illustration, for example, the insulin gene, when it's yellow, it's locked, methylated; when it's blue, it's open. So if we find a piece of DNA with the insulin gene in blue open, it means that that piece of DNA came from pancreas, from the pancreatic beta cells, because in the lung, in the liver, in the colon, these genes are locked. They are not expressed. And if we find, for example, a DNA molecule that encodes for the gene of albumin, which is a liver-specific gene, and it's open, so if it's open, it means this DNA molecule came from the liver. And in all the other organs in the body, this molecule is methylated, which means it's locked.

So researchers from the Hebrew University, [inaudible 00:24:17], and others created basically an atlas of the entire body. And if you find the gene that is unmethylated in the plasma, you can put it in the atlas, and the atlas will tell you what is the tissue of origin for that DNA molecule. And one option is to identify the circulating tumor DNA with mutations, because there are mutations that make the tumor different from our body, and the second technology is the methylation basically, as I just mentioned. And the methylation has several advantages. It's universal. It's basically off the shelf. It's the same methylation for all the organs among all the individuals on the planet. We don't need to find specific mutations for someone's specific cancer. The price is much cheaper than a specific mutation testing. And there is much less need for tissue sequencing. We don't need to take the cancer, find what is unique in the cancer of patient A, and then locate in the blood mutations for patient A. When we use methylation, we can use broadly and use it on the entire public of patients.

So we're back to case one, which was a patient that had severe lung damage from a medication. So I'm showing you my recent blood test, which is not that

recent; it was done in September 2024. And as you can see, just a random blood test. They show creatinine, 1.1, which is normal, luckily, and ALT and alkaline phosphatase, which are liver enzymes. So I can see my liver and kidneys were fine in September 2024. But when we look at all the organs of the body and we say, "Okay, these are all the organs. What can we check with the simplest blood test," we see that for many of them, but not all... We have very simple blood tests. For the liver and the gallbladder, we have liver enzymes, bilirubin. For the kidneys, we have creatinine, et cetera.

However, there are several important and clinically very significant to us organs such as the lungs, brain, intestines that we do not have in the clinic any simple measurement to study them and to understand whether there is damage there, for example, intestinal damage. Many cancer medications can cause severe diarrhea, severe damage to the intestinal tract. How do we measure that? Like Hippocrates measured 4,000 years ago, or 5,000 years, I'm not sure, we are asking the patient, "How many times do you go to the toilet?" If he says five, I say, "Okay, that's bad." And then the next day, "How many times," the patient says nine, so I say, "Okay, calculation, nine, more than five. Situation worse." That's it. This is how medicine works for intestinal damage.

For brain damage, the situation is even more complicated. I'm asking the patient, "Who is the prime minister?" He says, "Bibi." I'm saying, "I don't know. Maybe." I don't know if his memory is okay because Bibi is 20 years in the office. "Who is the American president?" He says, "Obama." Okay, something is wrong with his brain. But we really are lacking with precise and accurate methods to measure brain damage, and also, same for the lungs. "Do you have shortness of breath?" "Yes." "Is it worse today?" "No." "Okay. So it's not worse." This is basically how medicine works.

So I'm not showing you today, but our collaborators from the Hebrew University, from Givat Ram, Hadassah Campus, they show that you can take and measure cell-free DNA from different organs as a measurement for damage. If you take patients with a stroke, you can measure brain-derived DNA in their blood. If you take patients with COPD, chronic obstructive pulmonary disease, you can measure lung damage in their lung. You can do the same trick and measure damage from something in something, and you can replace the something with any organ. You can measure damage to the heart, to the pancreas, to brain, lung, liver, et cetera, et cetera, using cell-free DNA. But for some tissues, we don't need the cell-free DNA because for the liver, for example, we can measure the cell-free DNA, but we have super cheap tests. So we don't need to give a million-dollar solution for a $1 problem, but for the lungs, for example, this is what we try to bring to clinic is that we want to create a method that we can measure, literally measure, and get a number of lung damage in patients and, using this method, prevent patients from deteriorate and even die from lung damage that is caused by many new cancer drugs.

And if we take it one step further and we look at a holistic view, you can see here a pie chart that basically summarizes the entire tissues of origin of one

human healthy individual where, let's say, the origin of all the cell-free DNA molecules in a given time point. You see that most of the cell-free DNA comes from what we say blood cells, but we see some liver cells, some endothelial cells, some neurons. In that study, the researchers from the Hebrew University also took younger individuals and older individuals, and you see that the proportions are the same, and basically most of the cell-free DNA in a healthy individual comes from blood cells. But when we take patients that, for example, a patient that has a liver damage, we suddenly see that 60% of the cell-free DNA in his plasma or blood comes from the liver. Or a patient below that has a severe sepsis, a severe systemic infection, over 90% of the cell-free DNA come from granulocytes, the cells that fight bacteria.

So coming back to my patient, you can see here, and this was our publication that we were the first in the world to show that using a blood test, we can measure damage to the lungs. And you can see in part A that this CT scan on day one, a patient that had pneumonitis, lung inflammation from a cancer medication, and below you can see a graph that shows lung-derived, cell-free DNA, and we showed that when she had severe inflammation, she had high level of lung-derived cell-free DNA. When she got treated and she was improved, her situation was improved, the levels of the lung-derived, cell-free DNA went down. And basically now we are doing this research actively and we want to next year implement this blood test that measures lung cell-free DNA in the clinic so we will be able in real time to help monitor patients and not let them deteriorate until they come to the ER with an ambulance and say, "I can breathe. Please help me." But we will be able to detect the damage before it occurs.

And just to summarize this part, we think that cell-free DNA is a promising tool for prediction and even early detection. I'm not showing you all the information, but we have preliminary information to show that before the patient even complains, we can see lung damage because the lung cell-free DNA is going up. The cells in the lung are getting destroyed, they release cell-free DNA, and you can pick it up in the blood test before the patient complains. And now we have, with the general support of ICRF, we work on this project and we want to enhance patient safety by measuring that. And also, we start to think about other sources of cell-free DNA, which can be even more minimally invasive, or even non-invasive. Because if we take, for example, the morning urine, the morning urine contains all the plasma, all the blood that was basically filtered during our night sleep. And I hope everybody's sleeping at least eight hours, so it's going to have a lot of cell-free DNA. And maybe in a few years, we'll have a smart toilet that you go to the toilet and then you get a WhatsApp from the toilet that says, "Please go to your family doctor. You should do a colonoscopy," or something like that. So one day it might happen.

And now we switch gears to patient number two. Just to remind you, the second patient, she had breast cancer, she got treatment, the MRI was clear, and on surgery, she still had cancer there. So what we do with aggressive breast cancers today, we give them neoadjuvant therapy, NAT, which basically a

preoperative treatment. It's basically given mostly to aggressive breast cancers, and with modern treatments, we can lead up to 80% of complete cancer elimination. Here I wrote 75, but we have more data; it's even 80%. And then all patients, they are referred to surgery. So basically today, 100% of patients undergo breast surgery, and then they come to us with the report from the surgery that says no cancer. And then they have the scar, they have axillary damage, they have damage to the hand, the hand lymphedema, and they say, "Doctor, you tried to help me, and I went to surgery," sometimes they even have mastectomy, and everybody's happy. Oh, hey, there is no cancer there, but the patient is left without breast or with axillary damage, and this is why we try to solve.

So why do we do surgery for all patients? The problem is that post-neoadjuvant therapy imaging has a considerable false negative rate. What does it mean? Basically it means that around 10% of the MRIs that are normal, it's a false negative exam, which means 10% of the women with normal MRI still have cancer. So to date, some consider 10% as too high risk to take for young patient with a breast cancer, so basically 100% of the patients undergoing surgery because we don't want 10% of the patients to have residual cancer.

So what we thought is if we can do a multimodal approach, can we do something to improve the accuracy of the MRI and to minimize that mistake from 10 to 0? Because then if we prevent the false negative rate from 10% to 0, then basically we can avoid surgery in some cases. We can send women and say, "Okay, you got pre-op therapy. Your MRI was clean. We did all the tests. There is no cancer. See you later alligator." That was my recent phrase I heard recently. And in addition, we thought that the second hypothesis is that if there is a residual breast cancer, it means we can do a liquid biopsy and to identify the DNA molecules that are released from that cancer. And if we can find them, it might help us to improve the accuracy of the MRI. And in this study, we use a commercially available test that is called Signatera. And we chose not to use our own test that we cook in our kitchen, but we want to use commercially FDA-approved with all the regulations because if we want to implement it and affect clinical practice, we wanted to use a verified tool.

So basically what does our study contain? It's a prospective study, single-arm interventional, that all the women that have normal breast MRI at the end of treatment, we do a quadrimodal approach, which means four. One, we do MRI. Second, we do a tumor bed biopsy, an invasive biopsy. If the invasive biopsy is clean, we do a liquid biopsy. We basically take blood from the patient, send it to San Francisco, I think they do it there. And also, we have an exploratory step; we collaborate with a company called Ataraxis from New York that they analyze the pathology from that patient. We basically send the photo of the tumor to New York, and it takes for their AI to say whether the tumor is gone or not like three seconds. It's gone or not gone. It's a three-second AI. And we combine these four approaches, and our idea is to take the 10% error into a 0. And when we'll have it, we can safely omit surgery.

So just to show you, this is the Ataraxis, the company that we are collaborating with. So this is from the recent data cutoff that we did in March. We have more patients now, but we haven't analyzed the data. And we are going to present at ASCO in Chicago a poster with updated information in, I think, June 1st, next month. And so in the recent data cutoff, we had 55 patients that were referred to neoadjuvant therapy with different tumor types. And as you can see, some of them, cCR is complete clinical response, which means the MRI was clean. So for example, for HER2-positive patients, 5 out of 12 had clear MRI. For triple-negative, 9 out of 18 had clean MRI.

And then we offered those patients with the clean MRI to go into our pipeline and see whether we can decrease the error of the MRI. And here I show you data from eight patients, and these are the patient numbers, their ages. All of them had clean MRI. The invasive biopsy was clean in six patients, and in two patients it found residual cancer. In fact, in all of the patients that had no tumor on the biopsy, we sent the liquid biopsy, the Signatera, and it was negative in all of the patients, and there was 100% correlation. All the patients were referred to surgery because that's the standard of care. So we can see 100% correlation. It's not a lot. It's just eight patients. And since then we have three more. And the additional three is also, we say, thanks God, 100% correlation.

And the idea is to continue with that study, and in 2027, we want to approach our IRB, our ethical committee in the hospital, and we say, "We want to go to step two of that experiment." The step two of that experiment will be to do the same approach to women. And if they're going to have clean MRI, clean biopsy, clean circulating DNA, and the AI will support us, four different methods, we'll say there is no cancer, the patient will be spared of surgery. Our surgeons, they are not very keen to have that going on, but they are working with us on that, and we want to basically eliminate breast surgery from the most aggressive breast cancers because we have very good systemic therapies.

And this is just the performance for the AI for the first 12 cases. The AI was accurate in 85% of the cases. And the AI is training, so it's getting better, and until next year they have collaborations with other institutions in the US, West Coast, East Coast, so they're also improving their algorithm. So I hope next year it will be much more accurate and will help us in our goal basically to eliminate breast surgery in these patients.

And is our idea, an original one or super bold. No, so that idea was shown in 2019. I remember I saw them presenting that in San Antonio in 2019, and they said, "We're going to have women with normal MRI, and we're going to do a breast biopsy. And if the breast biopsy is normal, we are going to skip surgery." And recently, about six months ago, a team from MD Anderson Texas, they published 50 women that were treated in 2019. 50 women had normal MRI. They had tissue biopsy. They didn't do liquid biopsy back then. I think we are trying to be even more sophisticated. But they showed a normal biopsy. If the biopsy was normal, surgery was canceled. And they show, as you can see here, the breast tumor recurrence rate was 0% at the median follow-up of five years,

which means this approach is feasible, and I think we're going to implement it in a broader patient population, and I think it's going to be implemented safely because we not just doing biopsy, we have the AI with us, we have the ctDNA with us, so I feel it's going to be much more safe.

So just to summarize that part, we try to integrate imaging, regular biopsy, liquid biopsy, and AI to improve the overall accuracy of detection of cancer elimination, mainly in patients with aggressive breast cancers. And ultimately, if we can show that we have nearly zero mistake in detecting residual cancer, we will be able to eliminate surgery in these women. And we believe that the future of breast cancer therapy will emphasize minimally invasive interventions, with a strong focus on improving patient's quality of life. During many, many years, breast cancer therapy was more aggressive and more, let's say, comprehensive in order to improve the outcomes. But I think now in many cancer types, we have excellent outcomes, but the treatment cost, and I mean cost by toxicities and the damage that we leave women with to live for their entire life, is a serious burden, and now that we have excellent treatments, we need to try and focus more on quality of life and to minimize the damage that we unfortunately cause to our patients.

So with that, I would like to thank... Many people ask me why I chose breast cancer and not another type of cancer, and the answer is that unfortunately it's very common, and that's a team sport. It's not like golf. It's like a basketball or a... I think a football team is larger than a basketball team, so it's like a football team. And so I would like to thank our colleagues in my breast oncology unit, in the imaging, surgery, radiation, nuclear medicine, pathology, and everyone, and our funders, and ICRF is the first of them, in supporting us. And thank you, of course, to the patients and the families and caregivers. Thank you very much.

Liora Tannenbau...: Thank you so much, Dr. Grinshpun. We certainly, I think, learned a lot from you today. I know a lot of questions came in ahead and live, so we'll try to get to as many as we can. Please remember that we cannot address any questions that reference uniquely personal situations. I'll go through what we can. One is, would you be able to give some clarity on why triple-negative and HER+ are the focus and not other breast cancers?

Dr. Albert Grin...: Yes, because of the simple fact that today when we give pre-operative therapy for triple-negative and HER2-positive, the pre-operative therapies are very efficient. Nearly 70 or even 80% of the women with HER2-positive breast cancer have total cancer elimination with pre-op therapy. In triple-negative, it's 65%. Unfortunately, the more common type, which is a hormone receptor-positive, the rate in complete tumor eradication is very low. It's like 5 or 10. And there's a global effort to identify how we can increase it, but this is the fact now.

Liora Tannenbau...: Okay. Thank you. I think there are quite a few questions coming in about access to this test in the United States. Do you have any idea-

Dr. Albert Grin...: Yeah, sure. We have many patients that are being treated in parallel in New York and Jerusalem or other places in the US. So many patients, they go to the US to do Signatera. As I mentioned, many liquid biopsies there, I think... I don't know if most, but many liquid biopsy tests are reimbursed by Medicare and all the insurances in the US, and unfortunately, the situation is the opposite in Israel. Nearly none are reimbursed by the Israeli health basket. So I have many patients that they go to the US, they do the liquid biopsy with their insurance, and they go back to Israel. In Israel, you can get all the liquid biopsy test all by out-of-pocket money or by private insurance, like Phoenix, Ayalon, Harel, et cetera, but not from the public health basket. But the access is there. You just need to pay for it, unfortunately.

Liora Tannenbau...: Yeah. Okay, thank you. Another question that came in is how can you tell if the damage there is a result of the cancer or from the treatment?

Dr. Albert Grin...: Okay, so that's a great question because we saw... There is a publication. We saw that if a patient has a metastasis in some organ, you can see damage from the growing metastasis from that organ, so that's a problem. And if a patient has a lot of, for example, lung metastases and also inflammation in the lung, the lung metastases can mask the damage. So that's a problem, and we are aware of it, but that's a challenge we need to address somehow in the future.

Liora Tannenbau...: Keep on working. So another question is should this be standard for stage one, low-grade breast cancer or only advanced?

Dr. Albert Grin...: So now we started from the easiest target, which is the advanced, because in the advanced setting, the patients are getting hit by the entire... Hold on... the full package. They're getting the entire treatment. Usually in stage one or small tumors, they're referred to surgery, and then we discuss whether chemo is needed or not. We have another initiative in parallel in order to eliminate surgery from stage one cancers, which is called cryoablation. It's basically taking a needle, sticking that in the tumor, and the needle becomes very, very cold and destroys, for example, 10 millimeter radius. So then you don't need to do a breast surgery because you destroy it in a 10-minute office procedure. So there is some time until stage one cancers will not be operated.

Liora Tannenbau...: Mm-hmm. Okay, another question, especially I know here in Israel, I know with population screening now being a big topic, could this be used for high-risk BRCA patients who have not yet been diagnosed?

Dr. Albert Grin...: So that's a great question. We tried. I wrote many letters to many companies that do liquid biopsies because in Shaare Zedek, we have the largest or the second-largest BRCA clinic that basically they follow up after mostly young, healthy women with BRCA mutation, and it's called Noga Clinic, and they come every six months to do MRI and everything, and we offer that as a platform for them to test their liquid biopsy test for early detection. And I don't know why... I think it's from commercial reasons, not from academic reasons... we were not able to find a partner for that. But for sure within 5 years or 10, I don't know if

90, but a significant amount of screening will be done using a blood test. There's a blood test called Galleri that is already available in the US and in Israel also. And I was in a birthday, 80, 8-0, 80th birthday of a lady, and her grandson bought her that test as a present for the birthday. It's called Galleri with an I in the end. And they say, "We detect 50 different cancers."

But when we think on that Galleri, I invite you all to read about that and read the small letters that blood tests can detect only 50% of the cancers, which means if you take 100 people with cancer, the blood test will detect 50 of them. And if you take 100, not patients, 100 individuals that are healthy, one of them will get a report, "You have cancer, sir," and it's a false. So if somebody's doing the test, be willing to get not accurate result. But on the other hand, when I explain about that and patients ask me about the test, "Should I do the test," so I give them this issue.

And also, I'm telling them when we look at that, it's like looking on the picture of the first car where Henry Ford was sitting with the wooden wheel, and instead of lights, they had a small fire that was projecting a small light towards the front. And now we have, not me, but others have Tesla that you get in and it's adjust and gives you the music and puts you the podcast that you like. So the early detection tests that are available today, they're like Henry Ford's first car. In 5 or 10 years, we will have a Tesla blood test. So it will, I think... It's recorded, so I'll take my chances, but I think in 10 years we will eliminate mammography, eliminate colonoscopy, eliminate all the invasive procedures with a simple blood test or even sophisticated toilet that you will go there, do whatever is needed, and it will text you or email you. Sorry.

Liora Tannenbau...: All right. That's certainly optimistic and a great way to be thinking forward. Okay, so I think we have time for another maybe one or two questions. So another question here is, isn't surgery, for now, until we're at the 10-year mark that you just gave us hope for, isn't surgery still the safest option? CtDNA shows a point in time which can change. So [inaudible 00:53:25]-

Dr. Albert Grin...: Today surgery is the safest option. We are still trying to develop how to avoid the safest option by giving another safe option. We have data, as I showed you, from 50 patients that were treated in 2019 in Texas. It was a 100% success. Someone can claim it just 50 patients, which is true. So more studies are needed. Surgeries of course is the standard option, but again, within several years, I think we'll have more data. And there are studies going on in different places on the planet, so I think we'll get more data, and in the future we'll have much less surgery. And now we have 50 medical students coming to our department for rotation. I told them, "You can consider your residency. I would not recommend surgery or breast surgery as a future career."

Liora Tannenbau...: Wow. Okay. All right, another question that came in, if you're already stage four, is there a way to effectively use ctDNA results to help with thinking through treatment plans?

Dr. Albert Grin...: Yes. For stage four, ctDNA is used. I have a few patients that go to the US. They do it as we do just a blood count, so they do liquid biopsy in the US. They did 10, 12 times. In some centers in the US, it's super implemented, like a routine blood test. And it helps to measure the dynamics and predict the success of the treatment. We still don't know enough about making serious decisions. For example, stage-four patient that is on treatment for months, and her or his ctDNA is negative, is it safe to stop the treatment, give him a window of a month, six months, a year without treatment, and then when the ctDNA goes up, restart the treatment? So that's a huge question. Everybody's interested in that. And it is an area of active research, so I guess within a year or two, we'll have answers for that. But still, the liquid biopsies, we are still in the beginning of the revolution. We still don't see all the fruits of that revolution.

Liora Tannenbau...: Okay. One of the questions also that came in ahead of time, since clearly you're so invested and optimistic, I think, about so much of the research, is Israel ahead of their game worldwide for breast cancer treatment and management, would you say?

Dr. Albert Grin...: Of course. Israel is ahead of... And Jerusalem is within Israel. In Israel, there is a phrase, Jerusalem is the belly button of the entire world. So I think in Israel, we have several advantages, and one of the advantages is that we can do... I spent two years in Boston and I saw the huge machine, how it works, amazingly. And in many, many ways, in many, many... even my daily work, I try to resemble what I saw and what I learned in Boston.

I think our advantage is that in Israel, we are much more quicker to implement changes, and we are quicker in doing preliminary and very novel ideas and to try novel ideas and translate novel ideas. I think we can do it faster than in the US. Of course, the numbers are different. If we need a study of 5,000 patients, it's not feasible in Israel. But if we have something very, very novel and we need to do 20 patients, we can do it 10 times quicker than in other places in the world.

Liora Tannenbau...: Mm-hmm. Wow. Okay. One last question. Can you tell us how much it costs for a liquid biopsy in Israel out of pocket?

Dr. Albert Grin...: Now we have an issue. The dollar dropped, so it's very... Things are becoming cheaper here-

Liora Tannenbau...: I know. We all have an issue.

Dr. Albert Grin...: But a liquid biopsy in Israel is between 10 to 20,000 shekels.

Liora Tannenbau...: Okay. Wow. Okay. Thank you. All right, well, as we begin to wrap up, I want to thank Israel Cancer Research Fund and our inspiring speaker, Dr. Albert Grinshpun.

Dr. Albert Grin...: Thanks.

Liora Tannenbau...: This webinar gives me a lot of hope, which is nice to have these days, that there are a lot of treatments around the corner to help us improve and save the lives of more breast cancer patients in Israel and the US and around the globe.

Please take a moment to fill out a brief evaluation survey that is being put in the chat. It really does inform our future programming. Please remember that Sharsheret is here for you and your loved ones in the US and here in Israel. Sharsheret provides emotional support, mental health counseling, and other programs designed to help navigate you through your cancer experience. All are completely free of charge and confidential. Our contact information is in the chat box now. As we come to a close, we put the evaluation link in the chat box once more. Thank you again for joining us today.