U.S. FOOD AND DRUG ADMINISTRATION

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OBSTETRICS AND GYNECOLOGY DEVICES PANEL
OF THE
MEDICAL DEVICES ADVISORY COMMITTEE

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SEVENTY-SECOND MEETING

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TUESDAY
AUGUST 29, 2006

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The Panel convened at 8:00 a.m. in the Montgomery Ballroom of the Hilton Washington D.C. North, 620 Perry Parkway, Gaithersburg, Maryland, Marcelle Cedars, M.D., Acting Panel Chair, presiding.

PRESENT:

MARCELLE CEDARS, M.D.	Acting Panel Chair
DONALD BERRY, Ph.D.	Temporary Voting Member
ELISABETH GEORGE	Industry Representative
LEONARD GLASSMAN, M.D.	Temporary Voting Member
SCOT GOLDBERG, D.O., M.B.	Temporary Voting Member
PAULA HILLARD, M.D.	Member
YULEI JIANG, Ph.D.	Temporary Voting Member
MUSA MAYER	Patient Representative
HUGH MILLER, M.D.	Member
JOANNE MORTIMER, M.D., FACP	Temporary Voting Member
DIANA ROMERO, Ph.D.	Consumer Representative
RUSSELL SNYDER, M.D.	Temporary Voting Member
SHEILA TAUBE, Ph.D.	Temporary Voting Member
JONATHAN WEEKS, M.D.	Member
MICHAEL T. BAILEY, Ph.D.	Executive Secretary
NANCY BROGDON	

FDA PRESENTERS:

ROSELIE BRIGHT, Sc.D.
Office of Surveillance and Biometrics

KISH CHAKRABARTI, Ph.D.
Office of Device Evaluation

NICHOLAS PETRICK, Ph.D.
Office of Science and Engineering Laboratories

ROBERT PHILLIPS, Ph.D.
Chief, Radiological Devices Branch

COLIN POLLARD
Chief, OB/GYN Devices Branch

LAKSHMI VISHNUVAJJALA, Ph.D.
Office of Surveillance and Biometrics

RON YUSTEIN, M.D.
Office of Device Evaluation

SPONSOR PRESENTERS:

VIVIAN DICKERSON, M.D., FACOG
University of California, Irvine

RON GINOR, M.D.
President & CEO, Mirabel Medical Systems, Inc.

SARAH LENINGTON, Ph.D.
Director of Clinical Development
Mirabel Medical systems, Inc.

A. THOMAS STAVROS, M.D., FACR
Radiology Imaging Associates
Denver, Colorado

Sponsor Presenters (continued):

LTC ALEXANDER STOJADINOVIC, M.D.
Vice Chairman, Department of Surgery
Walter Reed Army Medical Center

JOEL I. VERTER, Ph.D.
Statistics Collaborative, Inc.

I-N-D-E-X

P-R-O-C-E-E-D-I-N-G-S

Time: 8:06 a.m.

CHAIRMAN CEDARS: I would like to call this meeting of the Obstetrics and Gynecology Devices Panel to order.

My name is Marcelle Cedars. I am the Chairman of the Obstetrics and Gynecology Devices Panel. I am a reproductive endocrinologist and on the faculty at UCSF Medical Center.

If you have not already done so, please sign the attendance sheets at the doors, and I note for the record that the voting members present constitute a quorum, as required by 21 CFR Part 14.

I would like to ask each of the Panel members to now introduce themselves, their affiliation and their areas of expertise, and also to let you know the mikes we are using today -- If you push it to turn on and then push it again to turn off, and if you could remember, please, to turn it off when you finish speaking, because there can only be four on at a time. Thank you. Why don't we start with Dr. Hillard --

Nancy, I'm sorry.

MS. BROGDON: Good morning. I am Nancy Brogdon. I am not a member of the panel. I am the Director of FDA's Division of Reproductive, Abdominal and Radiological Devices.

DR. ROMERO: Good morning. I'm Dr. Diana Romero, Assistant Professor of Population and Family Health at Columbia University, Mailman School of Public Health. My field of expertise is in reproductive and sexual health, and particularly among low income and other marginalized populations, and I'm on this panel as the Consumer Representative.

MS. MAYER: I'm Musa Mayer. I am the patient representative invited to be on this panel today. I am a breast cancer advocate and 17-year breast cancer survivor, and I have been working with the FDA as a Patient Rep for quite a few years, mostly on the Oncologic Drugs Advisory Committee.

DR. HILLARD: My name is Paula Hillard. I am Professor of Obstetrics and Gynecology and Pediatrics at the University of Cincinnati where I do pediatric and adolescent gynecology.

DR. TAUBE: I'm Sheila Taube. I am the Associate Director of the Cancer Diagnosis Program at the National Cancer Institute and, as such, I oversee a program to develop new diagnostics for cancer.

DR. SNYDER: Russell Snyder. I am the Division head of Gynecology at the University of Texas Medical Branch in Galveston. I am a general OB/GYN with special training in gynecologic pathology.

DR. MILLER: I'm Hugh Miller. I am a maternal fetal medicine specialist in Tucson, Arizona. I don't have any specific breast credentials, but I am interested in the subject.

DR. JIANG: I am Yulei Jiang. I am Associate Professor at University of Chicago, Department of Radiology. My primarily role there is to develop computer diagnoses. I'm not a clinician. I am a researcher.

DR. GLASSMAN: I am Leonard Glassman. I am a diagnostic radiologist in private practice in Washington, D.C. I also run the breast imaging teaching program for the Department of Radiologic Pathology at the Armed Forces Institute of Pathology.

DR. BAILEY: I'm Mike Bailey. I work for the FDA. I am the Executive Secretary of this Panel.

DR. BERRY: Donald Berry, Chairman of Biostatistics at MD Anderson Cancer Center, specializing in breast cancer and screening.

DR. WEEKS: I'm Jonathan Weeks. I am a maternal fetal medicine specialist in Louisville, Kentucky, with Norton Healthcare.

DR. MORTIMER: Joanne Mortimer. I'm the Deputy Director of the Morris UCSD Cancer Center. My area of interest is breast cancer.

DR. GOLDBERG: Dr. Scot Goldberg. I am a diagnostic radiologist in private practice in Newark, Delaware, at the Women's Imaging Center, doing primarily breast imaging and OB/GYN.

MS. GEORGE: And I'm Elisabeth George. I am here as the Industry Rep, and I am a Vice President of Quality and Regulatory for Phillips Medical Systems.

CHAIRMAN CEDARS: Thank you. I would like to ask Heidi Valetkevitch if she would stand, please. This is the FDA press contact, and her contact

information is on the table out front, because she won't be able to stay for the entire day. Thank you.

I would like to remind people to turn off their cellphones, pagers, blackberries, any kind of electrical devices that may sound during the procedure, and then I would like to pass this on to our Executive Secretary.

DR. BAILEY: First, we would like to start off by telling everybody that we only have two additional dates for 2006 for Panel meetings, tentative dates. Those are November 13th and 14th.

I will now read into the record the Deputization of Temporary Voting Members statement and the Conflict of Interest Statement. Today we have two temporary voting statements. I will read the first one.

Pursuant to the authority granted under the Medical Devices Advisory Committee charter dated October 27, 1990, and amended April 20, 1995, I appoint the following as voting members of the Obstetrics and Gynecology Devices panel for the duration of this meeting on August 29, 2006: Russell

Snyder, Sheila Taube, Donald Berry, Yulei Jiang, Leonard Glassman, and Scot Goldberg.

For the record, these people are Special Government Employees and are consultants to this Panel or another panel under the Medical Devices Advisory Committee. They have undergone the customary conflict of interest review and have reviewed the materials to be considered at this meeting.

This was signed by Dan Schultz, Director, Center for Devices and Radiological Health, on 7/25/2006.

The second temporary voting status as follows: Pursuant to the authority granted under the Medical Devices Advisory Committee charter of the Center for Devices and Radiological Health dated October 27, 1990, and amended August 18, 1999, I appoint Dr. Joanne Mortimer to serve as a voting member of the Obstetrics and Gynecology Devices Panel for the August 29, 2006, meeting.

For the record, Dr. Mortimer is a member of the Oncologic Drugs Advisory Committee of the Center for Drug Evaluation and Research. She is a

Special Government Employee who has undergone the customary Conflict of Interest review and has reviewed the materials to be considered at this meeting.

This was signed by Dr. Randall Lutter, Associate Commissioner for Policy and Planning, and was signed on July 27, 2006.

I will now read FDA's Conflict of Interest Disclosure statement:

The Food and Drug Administration is convening today's meeting of the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee under the authority of the Federal Advisory Committee Act of 1972.

With the exception of Industry Representative, all members and consultants of the Panel are Special Government Employees or regular Federal employees from other agencies, and are subject to the Federal conflict of interest laws and regulation.

The following information on the status of this Panel's compliance with Federal ethics and conflict of interest laws covered by, but not limited

to, those found in 18 USC 208 are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this panel are in compliance with Federal ethics and conflict of interest laws under 18 USC 208. Congress has authorized FDA to grant waivers to Special Government Employees who have financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial or conflict of interest.

Members and consultants of this Panel who are Special Government Employees at today's meeting have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their employer, spouse or minor child, related to the discussion at today's meeting.

These interests may include investments, consulting, expert witness testimony, contracts, grants, teaching, speaking, writing, patents, royalties and primary employment.

Today's agenda involves a review of a

premarket approval application for a noninvasive device for use a complement to clinical breast examination in asymptomatic women between the ages of 30 to 39. This is a particular matters meeting during which specific matters related to the PMA will be discussed.

Based on the agenda for today's meeting and all financial interests reported by Panel members and consultants, no conflict of interest waivers have been issued in connection with this meeting.

A copy of this statement will be available for review at the registration table during this meeting, and will be included as part of the official transcript.

Ms. Elisabeth George is serving as the Industry Representative, acting on behalf of all related industry, and is employed by Phillips Medical Systems.

We would like to remind members and consultants that, if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial

interest, the participants need to exclude themselves from such involvement, and their exclusions will be noted for the record.

FDA encourages all other participants to advise the Panel of any financial relationships that they may have with any firms at issue. Thank you.

CHAIRMAN CEDARS: Transcripts of today's meeting will be available from Neal Gross & Company. Information on purchasing videos of today's meeting can be found on the table outside of the room.

Presenters to the Panel who have not already done so, should provide FDA with a hard copy of their remarks, including overheads. Karen Oliver -- if you could stand, please -- will collect these from you at the podium.

Next, I would like to invite Mr. Colin Pollard, Chief of the OB/GYN Devices Branch, to make some introductory remarks.

MR. POLLARD: Thank you, Dr. Cedars. Welcome, members of the Panel, distinguished audience.

I first would like to just quickly update you from our last Panel meeting on July -- Our Panel

meeting was in March. On July 28, FDA approved the PMA for the Adept 4% icodextrin adhesion reduction solution. As you know, that device is indicated for use intraperitoneally as an adjunct to good surgical technique for the reduction of post-surgical adhesions in patients undergoing GYN laparoscopic adhesiolysis.

Turning to the agenda, we have convened you here today to deliberate on a premarket approval application, P050003, for the T-Scan 2000 ED from Mirabel.

As Dr. Bailey just mentioned, and as you will hear repeatedly today, the T-Scan 2000 ED is intended to be used as a complement to clinical breast exam for the detection of breast cancer in women ages 30 to 39 who are at average risk for breast cancer. That is women without a significant family history whose clinical breast exam is normal.

The T-Scan 2000 ED is intended to assist physicians in determining which women might be at higher risk for malignancy who should, therefore, undergo further imaging or diagnostic screening.

Our review of this PMA has been led by the

Radiologic Devices Panel -- I mean Radiologic Devices Branch here in the Division of Radiological, Abdominal and Reproductive Devices. We did it this way for a couple of reasons.

One, the Radiological Devices Branch reviewed Mirabel's first generation device, and the underlying technology for the T-Scan 2000 ED, the device before you today, is based on the earlier device, although it is important to note that that was an imaging system, and the indication was different.

Number two, in addition, the Radiological Devices Branch has historically and traditionally been the home branch for all diagnostic devices for breast cancer, regardless of specific technology, as well as for many breast therapeutic devices; and the Branch has extensive experience in the science of electrical impedance, and the Division believed that the scientific expertise residing in that Branch was appropriate for the review of this product. However, FDA also recognized that the T-Scan 2000 ED is intended to be used by gynecologists and other primary care physicians, not radiologists.

Therefore, for us to complete the review of this PMA, we believe it is more appropriate to seek the clinical expertise of physicians such as yourselves here at the Panel, although you can also see that we beefed up the expertise.

So although you will see folks from the OB/GYN Devices Branch here today, including myself and Dr. Bailey, the Panel Exec. Sec., today's FDA presentations will be given by my Divisional colleagues from the Radiological Devices Branch.

So with that, I would like to close, but again thank you for your willingness to review this PMA and participate in today's Panel meeting. Thank you.

CHAIRMAN CEDARS: Thank you. We would now like to proceed with the open public hearing portion of the meeting. Prior to the meeting, we have received three requests to speak in the first open public hearing session.

Prior to hearing from these speakers, I will read the open public hearing statement:

Both the Food and Drug Administration and

the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the open public hearing session of the Advisory Committee meeting, FDA believes it is important to understand the context of an individual's presentation.

For this reason, the FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement, to advise the committee of any financial relationship that you have with the sponsor, its products and, if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging or other expenses in connection with your attendance at the meeting.

Likewise, the FDA encourages you at the beginning of your statement to advise the committee if you do not have any such financial relationship. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

Our first speaker is Dr. Ronald Wapner. Dr. Wapner, if you will please come forward to the microphone.

DR. WAPNER: Good morning. I would like to first thank the Panel for the opportunity to speak this morning. I am Ron Wapner from Columbia University, and I have no financial interest in any companies involved in this area.

I am not an expert in breast disease nor am I an expert in devices like this. I have spent the last 20 years or so of my career involved in screening, and predominantly screening for genetic disorders. I would like this morning to talk a little bit about the paradigm of the screening approach, and then a little bit about some of the lessons we have learned over the last two decades that, I think, are adaptable to the discussion that we will be having today.

I have brought a few slides. So I would like to call your attention to this over here, and just point out the fact that the purpose of a screening device is to take from an entire population

of individuals, all of which have their own individual risk, and be able to identify by some criteria a small subpopulation that has a higher risk.

With that ability to segregate out the highest risk patients, we can then move them forward to additional diagnostic testing or to additional evaluation. Again, there is a significant difference between a screening test, which is only intended to modify risk, and a diagnostic test which is supposed to diagnose a disease. Today we will be talking about a screening test.

Screening tests are usually, if not always, used on entirely healthy patients. Because they are meant to screen entire populations, they should be relatively inexpensive, easy to use, reliable, and then most importantly, the purpose is to identify a high risk group who then can be considered for further evaluation and testing.

The criteria for applying a screening test to any particular disease includes a number of things. First of all, it should be a relatively frequent disease, and also one that has a significant or

potentially fatal outcome, if left untreated.

It doesn't make any sense to screen unless there is some beneficial intervention that can be given to individuals who are identified to have the disorder. There needs to be reasonable sensitivity and specificity of the screening test so that screening would be able to identify an appropriately sized cohort.

There needs to be prompt testing and immediate follow-up available. The benefits need to outweigh both the risks and the costs, and finally, it needs to not only be voluntary, but also there needs to be patient education involved.

From my evaluation, the T-Scan which you will be talking about today fits each of these criteria and makes sense to be used as a screening test in low risk populations for breast cancer.

The second thing is: What have we learned over the past 20 years about screening an OB/GYN population? I just want to spend a few minutes, because I think some of those lessons are appropriately applicable to what we are talking about

today.

The history of prenatal screening for genetic disease is not a short one. It has been not a simple, one-day occurrence. It has been a long evolution, since 1975. That is when screening started and, as you can see, along the way it has been improved by the addition of multiple other additive screening technologies.

The first attempt at screening for genetic disorders came with the understanding that older women had an increased risk of having children with chromosomal abnormalities.

So the first screening paradigm was to take a cohort of women over the age of 35, but even at the time that this screening was recommended in 1979, it was recognized that any particular cutoff for when you move to secondary testing is relatively arbitrary, that there is no significant biologic difference between one population and another, and when you use which type of screening really depends on a number of logistical concerns rather than any biological difference.

Well, although maternal age has stood us for almost now three decades as a screening technique, it was not a very good one. Maternal age as a screening for chromosomal abnormalities has a sensitivity -- that is, a detection rate -- of only 30 percent for a five percent false positive rate. So despite the fact there was only a 30 percent detection rate, it really held us as the main standard, and remains the standard today.

Now along the way, we realized that there were additional screening modalities that could be added. We added alpha fetoprotein. We then went to triple screen with additional hormones and to quad screen.

You can see illustrated here that no one screening modality made a giant leap, and it is the actual addition of subtle and somewhat smaller changes that have now allowed us to be able to identify 30 percent of population having genetically abnormal pregnancies to now 75 or now more recent testing almost 95 percent. But again, this evolution has taken over 25 or 30 years.

The other thing that occurred, and I think is most important, whenever you are thinking about screening tests, we are looking for diseases with a relatively low prevalence, and it is important to point out that with any disorder of a low presence, even a fantastic test will have a very low positive predictive value.

That means that any individual patient put into that high risk group will on their own risk be relatively more likely to be normal than abnormal. Why is this important? Well, it's important --

CHAIRMAN CEDARS: We need you to wrap up, please.

DR. WAPNER: Yes, I will. This is important, because we had to switch our whole entire paradigm, and it became necessary for us to teach our physicians and our patients that a positive screen didn't mean they had the disease. It just meant they were in a high risk group. But we have accomplished that now, and patients and OB/GYN physicians are very, very used to counseling patients with screening tests.

I have two more very quick points, and

I'll be done.

Most recently, we moved to first trimester screening, and that had two additional points that need to be made. First of all, in the first trimester screening relies on two biochemical analytes, and one of the mainstays is free beta HCG. I just want to point out that the detection for a very important part of this screening paradigm for a five percent false positive rate is only 23 percent. So again, screening tests can and are very valuable even at relatively low sensitivity levels.

Finally, the addition of first trimester screening also requires the addition of an ultrasound measurement. We have learned now that fetuses at risk for Down syndrome have increased fluid in the back of their neck.

What this has now done has moved screening from an ultrasound level into the doctor's offices. Doctors are now doing their own ultrasounds. They have been trained, and they have been educated so that it demonstrates the ability to move a screening test into the physician's office.

Conclusion: What have we learned from aneuploid screening that is adaptable to our discussion today?

First of all, individual risk assessment or screening is a very routine part of OB/GYN care and is able to be offered to patients, and patients and doctors understand screening parameters and understand the detection rates, etcetera.

Finally, we have demonstrated that physicians are very able to integrate many of these new screening paradigms into their practices, including those that involve new techniques.

Again, thank you very much for the opportunity to speak to you.

CHAIRMAN CEDARS: Are there any quick questions from the Panel, clarification questions? If not, thank you, Dr. Wapner.

I would now like to call Dr. Mark Akin to the stand.

DR. AKIN: Good morning. Thank you for allowing me to speak today.

I am Dr. Mark Akin, and a special hello to

those of you I have known from Texas.

I am here today voluntarily to discuss my clinical experience with the T-Scan ED 2000 system and why I believe it is useful, improved breast cancer screening for 30 to 39-year-old women.

I am not being compensated for my time today, and I have no financial interest with Mirabel.

I am an OB/GYN physician in Texas. I have been in private practice for 23 years. My group is known as Austin Area OB/GYN. We have seven OB/GYN physicians and nine nurse practitioners. We are AIUM and ACR certified and perform sonograms and screening mammograms, fine needle aspiration and bone density. We see 350 patients a day in my group.

I am also trained with a Master's degree in biomedical engineering. The T-Scan ED system uses electrical impedance to screen for breast cancer, and so it was only natural for me to have an interest in this research.

I am also the Director of Clinical Research for Austin Area OB/GYN, and I have been the principal investigator for dozens of FDA drug and

device studies. I am the principal investigator who had the largest number of patients in the multi-center trial for the specificity arm of the pivotal study for the T-Scan.

Let me digress for a minute and talk a little bit about 30 to 39-year-old women. Thirty-seven percent of the patients that I see in my practice are in this age range. Most of them have a friend or a relative or a co-worker who has had breast cancer at an early age. They are concerned about their breast health.

They falsely assume that their annual clinical breast exam will allow for a timely diagnosis of breast cancer. They are not given other screening options, as there is no other screening method for breast cancer recommended until age 40.

Unfortunately, women under age 40, the clinical breast exam only detects less than 10 percent of breast cancers that are less than two centimeters in size. In fact, the clinical breast exam is so ineffective that over 70 percent of women find their own breast cancer.

The consequence of not having adequate breast cancer screening for women in this age range results in advanced stage of disease when it is finally diagnosed, and results in higher morbidity and mortality rates. Several thousand women per year in this age range undergo this.

Although only 15 percent of all breast cancers occur in this age group, these cancers account for 40 percent of all years of life lost due to breast cancer. Keep in mind that these patients are at a stage of their life where they frequently have productive jobs, are raising children, and have a significant contribution to society. Clearly, there is a need for improved breast cancer screening in this age group.

In my clinical study of the T-Scan system, 303 of my private patients were asked to voluntarily participate in the pivotal study at the time of their annual checkup. To demonstrate the concern women have for breast cancer, almost all women agreed to participate.

The T-Scan procedure was easily added to

their exam, as it only takes five to 10 minutes. The device is user friendly and has a computer screen that instructs the operator what to do. Only minimal training is required to perform the procedure.

Patient who had a relative who has breast cancer or patients with an abnormal clinical breast exam were automatically excluded from the study. In the T-Scan procedure a sensor probe is painlessly placed against the breast, similar to an ultrasound exam. The device captures nine images of electrical impedance from each breast that are analyzed by the computer.

The technical area is greatly reduced by an algorithm that will not allow images to be recorded if there is inadequate contact of the sensor to the breast or if air bubbles are present.

At the conclusion of the procedure, the computer gives instantaneous results. There is no interpretation required with this procedure. You either get a positive or a negative result. These results at printed on a report. It provides good documentation for the chart or pertinent patient

history and findings, and includes a Gail Model breast assessment.

Patients with positive results were educated to the screening nature of this test. They understood that with a positive result they still had more than a 99 percent chance of having normal breasts. As discussed previously by Dr. Wapner, most patients have come to understand screening tests, particularly those who have had a previous pregnancy, and in my clinical study none of the patients with a positive result expressed undue anxiety over the result, if they received a positive test.

Although the specificity arm of the study was designed only to determine the false positive rate of the screening procedure, patients with positive results were offered further screening options.

In short, the T-Scan breast cancer screening exam can be easily integrated into the annual exam and does not require additional appointments or follow-up phone calls or consultations. As with other breast cancer screening devices such as sonography and mammography, the

procedure can be performed by a trained technician or a nurse practitioner. The equipment is portable and affordable for private practitioners.

In my experience, there was a high patient acceptance, even in the face of positive findings. Subsequent speakers will address the statistical merits of the pivotal study in great detail today, and at the end of the day I hope you will agree with me that the T-Scan ED 2000 system should be recommended for approval, because it offers a significant improvement in the current paradigm for screening of young women to determine those at higher risk for breast cancer. Thank you.

CHAIRMAN CEDARS: Thank you. Are there any questions from the Panel?

DR. GLASSMAN: One question. In your clinical practice, if you have a women between 30 and 39 who did not -- was not part of this study but had a first degree relative with a history of breast cancer, did you screen those patients in some way other than clinical breast exam?

DR. AKIN: Yes, sir. Most of those, at

age 35 we would begin screening with mammography or, if the breast cancer of the first degree relative occurred at a very early age, we would start screening 10 years before that time.

MS. MAYER: Dr. Akin, I think I heard you say that patients in this target population represent 15 percent of cases? Is that correct?

DR. AKIN: Of breast cancers, yes, ma'am.

MS. MAYER: The American Cancer Society breast cancer facts and figures document for 2005, which is based on SEER data, states that that figure is 4.5 percent.

DR. AKIN: I would have to check and see where my reference came from for that.

CHAIRMAN CEDARS: One additional question.

DR. ROMERO: Hi. You mentioned that the women for whom a positive result was reported did not express any undue anxiety. Can you describe how that was measured?

DR. AKIN: By my personal observation of my patients. With all of these procedures, when I explain the procedure to them, I told them in advance

the purpose of the procedure and that even a positive screen would not put them at a risk that they should be concerned about.

Those who had a positive test, obviously, were concerned, but I think they understood clearly that they still had a greater than 99 percent chance of having a normal follow-up exam.

DR. ROMERO: But just so I understand, there wasn't an objective measure or instrument used for that?

DR. AKIN: Well, I don't think one truly exists other than observation.

CHAIRMAN CEDARS: Thank you.

DR. AKIN: Thank you.

CHAIRMAN CEDARS: The next speaker is Ms. Cindy Pearson.

MS. PEARSON: I am the Executive Director of the National Women's Health Network, which is a Washington, D.C.-based national, independent women's health consumer group. We are supported by the dues of our members, as well as foundation grants. We receive no support from industry or any corporate

entity that has a stake in women's health care.

We participate and advocate for good care for women with breast cancer, and for all women, and have done so for over 30 years. During this time, we have concentrated on breast cancer because of its status as the leading killer of middle-aged women and because of women's concerns.

We have taken part in NCI meetings about early screening for breast cancer and FDA OB/GYN devices Advisory Panel meetings about the sensor pad, and tried to advocate and speak out on the issue in many arenas.

We were not contacted by the sponsor in advance of this meeting, and I prepared the remarks I am making today based on the documents that were publicly available on FDA's website yesterday.

We agree that breast cancer in young women is important, whether the numbers are five percent of cases or whatever the numbers are of cases. Women deserve screening that works for them at all ages. The Pap smear isn't a very good screen. This panel has been part of conversations about making that

screen better, but it is there.

Screening without pain, and screening without intrinsic risk is also important to women. So although breast cancer in women under age 39 is rare, it is not nonexistent and, as Dr. Akin said, women are very aware of the risk of breast cancer and eagerly await and ask for and hope for safe and effective screening.

Today the FDA has been asked to approve an expanded indication for this device based on what, in the world of breast cancer screening, is a pretty small sample. I know there are hundreds of women, both in this country and Israel, who took part in the two arms of the study, but it is, in the world of cancer screening, a pretty small sample that also involves a lot of statistical modeling to determine the sensitivity and specificity of the device.

There seem to be pretty significant questions about those levels of sensitivity and specificity, and this is where I want to speak from my training as a consumer advocate, not my training as a statistician, which I don't have.

I just want to say that to consumers, including women of this age group concerned about their risk of cancer, specificity and sensitivity are crucial, because they determine the likelihood that an individual woman will benefit.

Now we started out the morning listening to someone talking about how low -- fairly low numbers can be -- still be a useful test for women. But I want to talk about what does it mean to have a false positive. What does it mean to have a false positive in mammogram screening? What does it mean to have a false positive with the T-Scan screen?

Dr. Akin said to his observation women aren't too worried, because he has already told them you have a 99 percent chance of this being okay. But women don't go from his reassurances or the reassurance of their gynecologist to a quick and easy resolution. They go through more screening. They go through -- Some of them would go through diagnostic tests, and the numbers of those women who have to follow that path to get the ultimate resolution are crucially important.

The data so far aren't very reassuring. It appears as if many, many, many women will receive a false positive and, arguably, few, if any, will benefit.

Now the ease of use of the device, I think, is important to talk about, because this is what women have been agitating for. We want something simple, easy. We don't want to have to go to a special place for our screening. It's great if it can be done in the doctor's office. It's great if it doesn't hurt. It's great if there is a fast response.

All those are wonderful assets and aspects of this technology. However, those same aspects make it all the more important that before it is approved with this new indication the data supporting it are excellent, because its ease of use will lead it to what it has been designed for, widespread use and routine use.

So this time period before the indication -- the expanded indication -- is approved is the crucial time period to get the data that are needed.

I saw that the sponsor is involved in a

prospective clinical trial in the United States involving women in the military. That looks really promising. That might be the best avenue for information that can be truly useful to women about the likelihood that average women who volunteer for this will, in the end, benefit.

To the company, I would like to say thank you. I know what you have heard me say sounds pretty negative, but consumer groups and women concerned about breast cancer do appreciate efforts made to make advances in screening, to push the age at which screening is effective back earlier, and to create screening that is not painful and doesn't have its own, albeit it small, risks involved in it. But to the committee, I would say that it is important for you to always remember that need alone is not enough to approve a device.

This device is needed. There does need to be an answer for screening for women under age 40. Effectiveness has to be demonstrated, and to the extent that a device is intended for widespread use for millions of women, the demonstration of

effectiveness really needs to be solid; and poor or ineffective screening is worse than no screening at all.

Thank you for the chance to share my perspective with you.

CHAIRMAN CEDARS: Thank you. Are there any questions from the Panel? If not, thank you very much. Is there anyone else in the audience who would be interested in speaking at this open public hearing? If not, then I would like to move on to the sponsor's presentation.

I would like to remind public observers at the meeting that, while this meeting is open for public observation, public attendees may not participate except at the specific request of the Panel.

The first speaker for Mirabel Medical is Ron Ginor.

DR. GINOR: Hello, everyone. I would like to take a moment while the computer is being set up to thank all of you for being here. I think today is going to be a day of very interesting debate. Some of

that debate, I'm sure, will be more favorable; some will be less favorable. Frankly, we are honored by all of it.

We understand that what we are doing is very important. We have spent a tremendous amount of time and resources trying to offer a reasonable sense of safety and efficacy. We feel we have done so. We feel the experts that are involved are convinced we have done so.

We understand and recognize that our job is to show that to you today, and we look forward to the opportunity of doing that.

By training, most of my work has been in the field of radiation oncology, which is what drew me to a science that involves physics and cancer in this kind of manner, and I look forward to discussing it with you and answering any of the questions that you might have in this regard.

Relatively quickly, I would like to tell you about who will be speaking today. After myself, Lieutenant Colonel Alexander Stojadinovic will be followed -- from the Walter Reed Army Medical Center,

the principal investigator for the entire pivotal study, will be followed by Joel Verter who will address some of the statistical questions which were mentioned a few moments ago, and then a number of members who were asked as an independent expert panel to review our data in preparation for this meeting will also speak. That will include Vivian Dickerson with the gynecological perspective, Dr. Tom Stavros from the reality perspective, and that will be followed with me and some closing remarks.

I don't think there's many people on this panel who don't know as much about the risks of breast cancer as I do, if not quite a bit more. But the fact is, it is the number one killer of women between the ages of 50 and 54 when cancer deaths are concerned.

According to the NCI, the cumulative chance for breast cancer by age 40 is one in 229 women and, as was said, that is not a tremendous amount, but it is also a very significant number in absolute terms when looked at in comparison to the number of cervical cancers we have in America each year or the number of Down syndrome babies that are born each year. Those

numbers are about 10,000 and 5,000. We are talking about roughly 12,000 breast cancers in women under 40 each year.

As you know, women without known risk factors under the age of 40 are not currently offered anything but clinical breast exam. Unfortunately, as you probably also know, more than 85 percent of the women who develop breast cancer did not have a telltale sign of risk which could have been used to offer them additional screening, and that is exactly the folks that we would like to help.

We believe that breast cancer screening in younger women is a need that needs to be addressed. We believe that we have relied on clinical breast exam for too long. We understand that new technologies trying to address this market will ultimately have to undertake study after study after study.

I believe that this study gives as much reassurance of safety and efficacy as is needed to get us to that next step.

In getting to where we are today, we carried out two studies and are in the process of

carrying out a third.

The first was a pilot study to take the known understanding of electrical impedance and its ability to detect cancer and essentially turn it on its head. What I mean by that is that initially electrical impedance was very interesting, because it was physiologically able to identify regions of the breast, regions of any tissue really, that are abnormal and specifically malignant.

The concept was that it was a very high sensitivity tool. We tried and, I believe, succeeded algorithmically to reverse it such that the specificity is now very, very high but offers a sensitivity which is consistent with the sensitivity that we rely upon as clinicians in other screening tools.

We carried a multi-center pivotal trial at 30 centers, including nearly 3,000 patients, which will be the majority of what we discuss today; and we are in the process, as was recently mentioned, in an extensive five-year, multi-center, U.S. Army, Federal government funded study, currently enrolled 2,500

patients, and hopefully we will enroll 15,000 patients over the next five years.

I would like to specify for a moment what the T-Scan is not, and the reason this is so important for me is that the patient advocate that was here before me is exactly correct. I think the worst that could happen is that if women misunderstand what this device does.

What this device does is important. What does it does not is also important, and I would like to clarify that. The device is not a diagnostic test. It cannot tell you that you do not have breast cancer. It is not a substitute for mammography or other imaging, because it is not an imaging device.

It is simply a risk assessment tool like the ones that were discussed by Dr. Wapner before me. It is a method for standardizing and offering a more complete, comprehensive, and documentable clinical breast exam, and it identifies women who are at a level of risk -- and this is important -- which is greater than the standard of care at which we currently offer screening to women.

All of the women that are offered T-Scan are between 30 and 39. They are asymptomatic on clinical breast exam or, as reported by the patient or the physician, their CBE is negative. They have no known high risk factors.

All T-Scan patients are patients that, through risk identification and then ultimately detection, would otherwise be missed, because they would not have been offered further screening based on the fact that they are without risk factors and without symptoms. Currently, those patients are sent home.

This is the indication for use statement. I am not going to take your time to read it to you. I assume by now you have read it several times, and you will probably hear enough about it today. But again, one important element here is that the recommendation following a positive T-Scan is a single imaging event. As opposed to, for example, BRCA, this is not a life long risk assessment, because we are measuring something that is happening physiologically in the breast right now.

This is a relatively simplistic view of what we hope to do on an epidemiological level. We hope to take a large numb er of women, much like was done in the world of Down syndrome, and partition them into two groups, a negative -- T-Scan negative group which will encompass 95 percent or more of the population, and those women will be at lower risk than average, significantly lower risk, and a very small population of roughly five percent of patients who are at increased risk, significantly increased risk, as you will see at roughly five times the risk you would expect to see in women of this age group.

This is a graphic representation of what we hope to do. Before I show that to you, I would like to explain to you a little bit the matrix of this study.

As you see this line right here, which is one in 300, that is roughly the yield of mammograms currently. That is, we currently perform roughly 300 mammograms per cancer detected in the United States.

This line down here, one in 666 -- that is the average risk that patients between the ages of 30

and 39 have when they walk into your clinic. That is why they are currently not getting additional screening.

What I am showing here is a population of 2000 women, and based on published data there would be three cancers there, and this addresses a question that was asked before when Dr. Akin said that up to 15 percent of patients who have breast cancer have it younger. I agree with you that SEER reports a lower number. Where we are concerned is the significant jump that SEER shows with the initiation of the first mammogram.

We believe, and we think everyone believes, that is an indication that there is quite a bit more cancer there that is picked up on that initial mammogram as opposed to an epidemic of cancer at age 40.

By putting the device into the screening regimen, we hope to partition this population of 2000 patients into two populations, one a large "healthy" population -- in this case roughly 1900 of the 2000 patients; and yes, two of the cancers that would have

been missed anyway would have also been missed by our device. But importantly, a small group of women, only 100 women, would have a cancer detected in that group.

These are the women that would be offered further screening. This is the patient that would be helped by T-Scan, and this is a level of risk significantly greater, as you see, than the level at which we routinely offer screening on a day to day basis to millions of women in the United States.

For a few moments, I would like to talk to you about the device. The association between electrical impedance and malignancy has been known for a very long time. It was initially published in a very extensive article by Dr. Morris and Dr. Freit in 1926.

The differences in the conductivity between malignant and normal tissue are relatively easy to assume for those who have an understanding of physiology, especially those with an interest in electrical engineering. But the changes in the water and electrolyte content, the changes in membrane permeabilities, and the changes in the orientation

impacting density of cells -- those of us who read pathology see that as the lack of respect for cellular architecture. Those are the things that the device identifies.

It identifies them on a principle that is essentially relatively simple. That is Ohm's uncomplex law where, if voltage and current are kept fixed, changes in resistance should be measurable. In fact, that is exactly what our device does. It has a very tightly controlled circuit that puts out a very tightly regulated voltage and current. The resistance is provided by the breast, as I will show you in a moment.

We have studied thousands of patients and, therefore, recognize what the normal resistivity of the breast should be, and if the measured resistance in our exam is abnormal, we ask that that patient consider additional screening.

You can look in the RC model at each cell as if it is its own circuit, a resistor and a capacitor. I apologize to those of you who didn't know there was going to be any math today. I promise

that this will not be a large part of my talk.

Essentially, each cell has its own known circuit. When you use low frequencies, as seen here, the electricity following the basic principle of electricity, which is the path of least resistance, will move around each cell and remain in the interstitial spaces which, as you know, are very full of fluid.

When high frequencies are used, the signal will generally cross through the tissue and then give you information also about what is going on intracellularly as well as extracellularly.

When a malignancy takes place, both frequency ranges give you information. The flow of electricity around cells is disrupted by the architectural changes, and the flow of electricity through cells is affected by cellular changes.

Over the years, people have measured and published time and time again the known resistivities of various tissues from blood, muscle, fat, to normal tissue and to cancer breast tissue. These are known figures, and all we try to do is identify parameters

around normalcy and, if patients are outside of those parameters, we indicate that they should consider additional screening.

This is a graphic representation of a manner whereby these changes can be measured, as published in Jossinet. Essentially, he was the father of this technology over the last 20 years or so.

As was mentioned earlier, this technology is based on technology that was extensively reviewed by the FDA, approved after a full PMA in 1999, determined to be safe and effective, determined to have no safety concerns, and determined to have a sensitivity for cancer specifically.

Shortly after approval, a number of studies showed that the device had particularly good sensitivity for the smallest of lesions. Four published articles in RSNA, both in 2003 and a number of other peer review publications showed that the sensitivity for small lesions is best with this technology. That has been known for a very long time.

That is what led the company to recognize that perhaps, instead of focusing on a known

abnormality, it might be possible to screen the entire breast and look for any region that has an abnormality of interest.

The device looks like this. In order to give you an opportunity to envision how it would be used in clinical practice, I will take you through very short slides just to introduce you to the use of the device.

First and most importantly, every patient who is considered for T-Scan must first have a full clinical breast exam, and the device cannot be used on women whose clinical breast exam is abnormal. Those patients, as we all know, deserve further follow-up. There is no question at that point that there is an element of risk because of your finding, and therefore, the device is no longer material.

The device cannot be used in women who are pregnant. Again, it helps identify risk factors, and the result is binary. We do not expect all physicians to learn how to read an image. Much like BRCA or other screening exams, the result is binary.

Once the physician enters the patient's

demographic information, the device requests that these five elements of the CBE are entered into each and every exam: Palpability, nipple discharge, nodal abnormalities, skin changes and pain. This can also be added to by individual physicians who want to search for other things.

If any of these are marked as abnormal, the exam report says please understand that this patient needs additional follow-up, irrespective of the T-Scan result.

We also incorporate the Gail Model Risk Assessment tool in this exam, not because we believe that the Gail Model is an ideal solution for risk screening, especially not in young women. We use it to help the physicians elicit responses of risk that might otherwise not be elicited.

I think we have experienced patients who have significant family histories and didn't know to tell us about it. We hope that this is a way to encourage them to tell us about it and help us identify risk.

Finally, the T-Scan exam itself is

performed. The signal is introduced to the patient through the source. The source is this cylinder which is held in the contralateral hand to the breast that is being examined. The signal then crosses the breast in a manner that I will show you momentarily, and picked up by this transducer.

Essentially, what is created is a circuit where tightly controlled voltage and current leaves the machine, enters the patient, travels up the muscles of the arm, across the pectoralis, is collected by the transducer, and returned to the device, immediately analyzed, and a result is generated.

Please recognize that this area over here, which appears probably like an image, is not an image. It is a way for you to determine at the end of the exam that you have made contact with each of the nine areas, the nipple and the nine areas around it on each breast. There is no diagnostic or screening information in that image. It is not something you can look at and identify a location for something.

The result at the end of the exam is

simply this. All nine regions that were checked are marked, and it will either be green, which is screen negative or screen normal, and red, which is screen positive, and that is the patients that we are interested in helping with this device.

I would like to now invite Dr. Alexander Stojadinovic, Lieutenant Colonel, trained surgical oncologist from Memorial Sloan Kettering, who is the primary investigator of this study and the primary investigator for the Federally funded, multi-center upcoming study as well, to share the results of the pivotal study, unless there are some questions that you would like me to address first. Yes, sir?

CHAIRMAN CEDARS: If we can save the questions until the end of the presenter's presentation.

DR. STOJADINOVIC: Good morning. My name is Alex Stojadinovic. I consider myself privileged to present -- Excuse me? Thank you. Good morning. I consider it a privilege to present before such an esteemed collection of colleagues.

I would like to disclose that my only

disclosure is that of expert testimony, which is not compensated. I have been asked to present this data, because I was a principal investigator at two sites in the specificity arm of the study and at two sites in the sensitivity arm of the study.

I am intrigued by the potential of using individual tissue-specific parameters to assess individual risk as opposed to statistical modeling or family history in an effort to try to optimize the way we choose to follow patients and to select subsequent diagnostic testing.

That having been said, I have undertaken a multi-year, five-year multi-center trial that is ongoing and that is now 2500 patients accrued out of a target accrual of 15,000 patients.

I will state that I am not here in an official capacity and that what I state does not reflect official policy or views of the Department of the Army, Department of Defense or the United States government.

The design of the study was that of a multi-center, prospective, two arm clinical trial.

This was done in consultation with our participating investigators at sites in the United States and Israel and with FDA input and agreement to address a pivotal question, and that is: Can you use a physiologic screening tool to identify breast parenchymal differences that assign risk in an age group of women who are otherwise healthy 30 to 39 in order to try to manage them in an optimal manner?

The primary outcome variable was that of relative probability, which is a calculation. It is a calculation based on estimates of specificity and sensitivity done in the context of the clinical study, and published population based prevalence of disease, not the prevalence of the disease within the study per se.

I recognize that that estimate is impacted by subsequent diagnostic testing sensitivity as well as the prevalence and then incidence of the disease thereafter.

This demonstrates a table of risk factors and then risk multiple from the published literature. I bring your attention to that in order to clarify

the success threshold, which I will get to in a moment.

A standard of care is to assess risk of the disease based on family history, and a risk multiple used is that of 2, which then directs a change in our clinical management, either in terms of more frequent surveillance, selection of diagnostic testing and even perhaps risk reduction intervention.

To give you a basis of comparison, a diagnosis of a typical ductal hyperplasia has a lifetime associated risk of 4, and that of a BRCA mutation of approximately 6. In discussion and concurrence by the FDA, the success threshold for relative probability -- that is, risk of having breast cancer at the time of examination -- was established at 2, which we felt was representative of a standard of care that we currently use in clinical practice.

The specificity arm of the study was performed in the United States and in Israel and included high volume private practice clinics such as that of Dr. Akin, as well as civilian and military, academic and private practice institutions.

The next three slides list the site by principal investigator.

The sensitivity arm of the study was conducted in academic university affiliated institutions as well as private practices in surgical, oncology and radiology in the United States and Israel who have established breast practices and an interest in emerging technologies for the purpose of screening. The subsequent slides list the principal investigators and sites.

As indicated, the principal outcome measure was that of relative probability. That is calculated by estimates of specificity and sensitivity and is dependent upon the published prevalence of the disease in the target population in the literature.

The specificity arm consisted of healthy women undergoing routine well-woman screening, ages 30-39, who specifically had no associated breast related symptoms of palpable abnormality, with the principal interest of estimating specificity.

Because these were healthy women, it was estimated that all positive exams were false

positives. As such, there may have been few, approximately four, women who may have been actually true positives that were overlooked. We deemed that that is actually biasing the estimate against the technology in a very minor way.

The sensitivity arm was different. It was an enriched population of women with an expanded age range of 30 to 45 who were already predetermined to undergo breast biopsy based on a clinically apparent or radiologically apparent abnormality, with the principal aim of defining the sensitivity of the device in order to arrive at the calculation of relative probability.

Specifically, these were pre-menopausal women, and we specified pre-menopausal so that we would assure that the breast tissue milieu was similar between groups based on previously published data.

These were the inclusion and exclusion criteria for the specificity arm. I bring your attention that these were healthy women, asymptomatic undergoing routine annual screening in the age range of 30-39.

Specifically, those that had a palpable lesion were excluded from the protocol analysis, particularly because, I think everyone would agree, we know what to do with a palpable abnormality or a symptomatic patient according to established clinical pathways, and that the intent of the device is to screen healthy women with negative clinical breast examination in an effort to try to determine individual risks. So those with palpable abnormality were excluded.

The sensitivity has similar inclusion and exclusion criteria with important exceptions. In discussion with our colleagues in the FDA and their agreement, we expanded the age range to 45 beyond 39 years of age, focusing only on pre-menopausal women in order to ensure comparability, because published literature supports that impedance changes are more reliant on hormonal differences that occur at the time of menopause and not chronological age per se.

Exclusion criteria are similar. Specifically, once again post-menopausal women were excluded from the analysis.

I would like to discuss briefly the rationale in terms of using an enriched population. It is known that identifying a clinical breast exam negative tumor in young women is unlikely. Most of the women that we see in clinical practice that have cancer in that age group have palpable disease.

Interestingly, initiation of screening mammography at age 40 is not associated with some magical difference in breast parenchyma. The changes that occur are driven primarily by hormonal changes that occur at menopause.

Furthermore, the data on pre-menopausal women ages 40-45 in the sensitivity arm are applicable to the intended use population based on previous study evaluating impedance characteristics in women who are pre-menopausal and those that are post-menopausal.

The other thing that was intriguing to me is, if you expand this population not only to accelerate the enrollment but also it will give you an appraisal of the screening device's performance in women who are undergoing routine annual screening to determine whether it has acceptable performance for

non-palpable radiologically apparent lesions. Thus, post-menopausal women were excluded from the data analysis, as stated previously.

I would like to bring your attention to a derived relative probability calculation. This was a two-arm study design to estimate specifically specificity of the device in the specificity arm, and sensitivity in the sensitivity arm, and utilized what we feel is a conservative estimate of prevalence of cancer in the population at large, not in the study population of 1.5 cancers per 1,000. We will get into this a little bit more in detail later. The calculation is expressed here.

Interestingly enough, and our statisticians will discuss this a bit more in terms of what is the relative contribution of prevalence of disease in the target population on the overall relative probability calculation.

This represents a review of representative literature, prevalence in the target population of women age 30-39 who were otherwise healthy and have a negative family history. We selected this one from

Kerlikowske, 1993, because it represented our target population best.

Unlike SEER data, it represents prevalence and not incidence data. It provides data with respect to women in the target population age 30-39 as well as women in that age group who are negative for family history of disease. Our statistician will demonstrate how utilizing this broad range of prevalence in the previously noted calculation affects little of the overall relative probability calculation.

The covariates assessed in Chi score analysis in both study arms are shown here. They include results of clinical breast exam, exposure to exogenous hormones, family history significant as defined by one or more first degree relatives, bra cup size, race and ethnicity.

The bottom line up front: The measured sensitivity in the sensitivity arm was 26.4 percent with confidence interval as shown here; specificity of 94.7 percent with confidence limits demonstrated; and relative probability of 4.95 based on a prevalence of 1.5 per 1,000.

This implies that at the time of exam, a T-Scan positive patient has a relative probability of cancer five times that of a woman from the general population in the target age range.

Data from the specificity arm: Exams were performed on 1946, yielding 1751 per protocol examinations. The majority of exclusions, 171 of 179, were related to age and palpability. For the reasons mentioned, the palpability was excluded, because established clinical pathways already address this definitively.

Age range extending beyond the target population is primarily a military phenomenon. Our IRBs expanded our age range beyond that of the FDA study, because it was suitable for our demographic. Ninety-two percent or more ethnically enriched population, is comprised of young women under the age of 40 who routinely do not undergo annual screening mammography based on age.

These are baseline characteristics. I will quickly take you through the distribution of pre- and post-menopausal women, mean age of 35. Exposure

to exogenous hormones, none; 55.3 percent in the variations that are positive are shown here. The majority of the women, 89 percent, did not have a significant family history of disease in the specificity arm, consisting of 1751 per protocol patients.

Race and ethnicity are demonstrated here. Seventy-eight percent of women were Caucasian. Although not specifically queried in our Israeli sites, a study of their demographics indicates that an overwhelming majority of their population is Caucasian. The distribution of bra cup size is consistent with what we encounter in clinical practice.

We did a Pearson chi-square analysis for relevant covariates mentioned previously. We found no significant difference in the primary outcome, a variable for the specificity arm in terms of menopausal status or exposure to exogenous hormones.

Similarly -- and I would like to note that one proposed indication is for the device to be used as a complement to clinical breast exam, and it was

important to me to understand what the difference in specificity or false positive rate was in those with normal and abnormal clinical breast exams.

These, as you would recognize, were excluded from the analysis, but it is presented here to show that the results are independent of the palpability of the lesion in this subgroup analysis. Additionally, family history did not seem to impact the specificity of the device in the study.

The distribution of ethnicity and bra size as a function of specificity is shown, and shows significant differences in small subgroups of patients here, as well as a function of bra cup size, such that the false positive rate was higher with larger sized breasts as well as with certain ethnic subgroups.

To summarize the specificity arm findings, the specificity in the per protocol population of 1751 patients was 94.7 percent with a 95 percent confidence interval, shown here.

I would like to add that in the range of specificity on the lower end, our pre-specified success criterion was a relative probability at time

of examination of 2 or greater. Even on the lower end of specificity, that particular criterion was met.

The sensitivity arm of the study: 597 examinations were attempted per protocol exams, 390, of which 87 cancers were biopsy confirmed. Exclusions are listed here. Once again, exclusion by age was based on expanded eligibility criteria in military studies, which was relevant to our patient demographic. The post-menopausal exclusions were described to you earlier.

Technical difficulties: Importantly, in this study, unlike the specificity arm, the sensitivity arm investigators were blinded to the test results. Ordinarily, the test gives you a green bar if the examination is screen negative or a red bar if it is screen positive. That binary visual feedback was omitted from the examiners in the sensitivity arm.

As such, any technical difficulties that occur were only encountered at times of periodic quality assurance visits and, as such, these were stacked primarily at a single site and occurred and identified at those sites. That is why that number is

as it is.

To summarize that particular technical exclusion criteria, 65 of these cases or 65 of the 69 cases excluded due to technical difficulties were due to two devices at a single site, and were encountered during quality assurance and monitoring visits. So sites, as I said, were recording blind. This was pre-specified by the FDA during time of study design, and the performance of these devices was not immediately apparent to those conducting the examination. This, obviously, would not happen in clinical practice.

To take you through the baseline characteristics of the 87 cancers in the sensitivity arm comprised of 390 patients, mean patient age was 40 years of age. Exposure to exogenous hormones for purpose of contraception, fertility, and a small group of those for replacement is shown here, 65.5 percent having none.

Family history as well as bra size distribution is shown. Race and ethnicity are represented in this cancer positive group, as well as distribution of clinical breast exam, which was

abnormal in the majority of patients, and then lesion size.

Lesion size cutoff was based on American Joint Committee on Cancer. That is the dividing line between T-1 and T-2 lesions, not only for the implications of clinical palpability but also for indications of biology of disease based on nodal positivity, rates increasing significantly at the T-2 and greater threshold. The distribution is shown there.

Covariate analysis for pre-specified covariates, as indicated earlier, shows sensitivity according to subgroups with age and hormonal exposure showing no significant difference between groups, or for first degree relatives or bra cup size.

Similarly, there is no significant difference across subgroups in the race and ethnicity category. Finally, I would like to bring your attention to this slide. Of interest to me was the performance of the device for smaller lesions, as reported earlier by Doctors Hooks, Jaeger and Kobe, utilizing impedance measurements with a greater

accuracy in smaller lesions.

Although this was not statistically significant, there was a tendency to -- or an increased sensitivity for smaller lesions. Also intriguing was that the results of clinical breast exam was slightly higher for normal lesions, not significant, but suggests that the inclusion of abnormal palpable clinical breast lesions may have had a small bias against the device estimate.

To summarize for the sensitivity arm, the overall sensitivity in our 390 per protocol population was 26.4 percent. The overwhelming majority of these were infiltrating cancers, not in situ lesions, and specifically excluding atypical ductal hyperplasia and lobular carcinoma in situ.

We did not find any statistically significant correlations among our subgroups with regard to sensitivity. Palpability did not affect sensitivity, similar to the finding identified in the specificity arm of the study, and there is a tendency for increased sensitivity for smaller lesions that did not reach statistical significance based on the small

sample size comparisons.

The bottom line, now bottom line is that the sensitivity was 26.4 percent with confidence intervals as demonstrated; specificity, 94.7 percent. This two-arm design allowed for an estimate of relative probability at the time of examination, 4.95, based on a population prevalence in the target population of age 30-39 of 1.5 per 1000, suggesting that a woman with a T-Scan positive examination is at five times increased likelihood of having cancer at the time of examination relative to average risk women in the population of similar age grouping.

To conceptualize this, Dr. Ginor addressed this earlier. If we assume a population model of a million women in the target age range of 30-39 with a negative family history, we would expect a prevalence of 1500 cancers based on Kerlikowske's data, or a risk of one in 667.

This would explain in large part why we don't routinely screen with annual mammography women in that age category who are at average or low risk, because the overall yield of mammograms performed per

cancer detected would be decidedly low, and that this fails to meet the minimal screening threshold of annual screening mammography.

Women of average risk with normal exams subjected to the T-Scan results would, according to a specificity result in this study, have 947,000 negative exams within which would be a clinically unapparent 1100 cancers. The overall risk of cancer in that population on that basis would be one in 861, which is an even lower risk estimate than that demonstrated here, and falls far short of our mammogram screening threshold that we utilize for women who are routinely screened age 40-49.

5.3 percent would be positive screening examinations in which, based on a sensitivity of 26 percent, there would be 400 cancers, yielding a higher risk subgroup with this screening test and a risk of one to 136.

All T-Scan positive cases would otherwise be missed based on the study design of asymptomatic women with normal exam and negative family history.

I would like to bring your attention

briefly to the published literature for the number of mammograms performed or the so called hit rate per cancer detected for women who are routinely screened in this country aged 40-49. This is representative literature that suggests approximately 400 mammograms are performed in women aged 40-49 to detect one cancer with a range of 341 to 593.

Putting that in context of study design and study results: If you consider an average risk women age 30-39 with a negative family history, the risk of cancer is one in 667, and that falls below this screening threshold that we utilize to justify screening with annual mammography in women aged 40-49, assuming a sensitivity of the mammogram of 85 percent.

A standard of care that we utilize is family history in clinical assessment to guide earlier mammographic screening in women that are younger than age 40, and the relative risk is 2, and absolute risk one in 333. That compares favorably with that that we utilize for women in the next decade of life to substantiate annual screening mammograms.

A positive T-Scan as associated with a

relative probability at the time of exam, five times that of the population based comparators, and that the absolute risk for breast cancer is one in 136. That, of course, is assuming for the sake of this example, a 100 percent sensitivity of mammography in that age group, which is not reasonable. So let's look at this final aspect.

So for average risk women who are T-Scan negative and a conservative estimate of mammographic sensitivity of 70 percent, we would perform nearly 1000 mammograms to identify one cancer. The screening threshold, as mentioned, is about 400 mammograms to one in those women who are screened annually in the age group of 40-49 in America.

A T-Scan woman has a risk five times that of T-Scan negative patients. So this T-Scan positive group we would expect we would have -- based on a 70 percent mammographic sensitivity have to perform 194 mammograms to identify a single cancer, which compares very favorably to the current benchmark utilized routinely.

So to summarize, the findings of this

study based on a success threshold of relative probability of 2 was met, such that a T-Scan positive woman was at five times greater risk of having breast cancer at time of exam relative to population based estimates, and we think that the risk of the disease on that basis and the yield based on -- in terms of mammograms per cancer detected compares favorably with the current standard that we use as part of standard of care to screen in the next decade of life.

I thank you for the privilege of the podium.

My apologies. I would like to introduce Dr. Joel Verter who will present his findings of independent statistical review of the data that I have just briefly outlined for you.

DR. VERTER: Good morning. My name is Joel Verter. I was asked by Mirabel to review their data analysis and comment on some of the potential questions that might be raised.

I also had the opportunity to review the FDA slides yesterday, and I have a few comments on some of their results.

The items that I will try to cover for you this morning briefly are: The enrichment of the sensitivity arm; the estimate of specificity; effects on relative probability of variations in the components; the issue of pooling the data; an issue that's been raised specifically about pooling and subgroup analysis on the Israeli versus the U.S. data; subgroups -- again, those three overlap quite a bit; and then an overall conclusion.

Let's talk first a little bit about the enrichment of the sensitivity arm. Again, as you have heard from previous speakers, the T-Scan is a device to screen women, not to diagnose women. I think it is important in your deliberations this morning and this afternoon to keep remembering that.

The sensitivity arm was needed to calculate an estimate of sensitivity so that the sponsor could estimate the relative probability, which was the standard that the FDA and the sponsor agreed to when the protocol was adopted.

A sensitivity study screening process would involve looking at women 30-39. It would

exclude women with a positive history, family history, and certainly women with a positive clinical breast exam.

All T-Scan women would be identified for follow-up, and those with a lesion would undergo breast biopsy.

In the enrichment arm, without an enriched population, the sensitivity arm would require almost a quarter of a million people in those categories to find the 87 cancers that were being analyzed in the study.

Without going in great detail through everything, the calculation would be roughly this. If we assume the 1.5 per 1000 is the prevalence, assuming our sensitivity, about a 9 percent palpability and a 4 percent with family history, you would wind up with almost a quarter of a million people -- women.

So, therefore, the sensitivity could not be calculated or estimated without some sort of enrichment, which is, I believe, the basis that the FDA agreed to.

Is that out of focus or is it just my

eyes?

As I said, the FDA slide 4, which is in your packet, indicates that -- this has to do with the specificity in some sense. They felt that in the sensitivity arm, they looked at the calculation of specificity. Remember that the specificity arm of the study was designed to calculate specificity. There is no calculation of sensitivity, and the sensitivity arm was meant to calculate the sensitivity. But they have indicated a calculation of specificity and then give a combined outcome.

Let's talk a little bit about the estimate of specificity. As we noted, the specificity arm itself was designed to screen women and come up with an appropriate estimate for that parameter, which we believe it has done.

The data, however, in the sensitivity arm, the way it was collected, contains enough women so that some estimate of a specificity can be calculated. The question for you all is to determine whether that calculation is relevant.

The screening process in the sensitivity

arm, I argue, is not appropriate for a specificity calculation, not so much because of whether this clinical breast exam or other measures -- women with positives exams were in there, but because the paths in which these women have been identified are indicating already that they have some sort of breast pathology.

So the conclusion for us was that the estimate of specificity or the false positive rate from the sensitivity arm will not provide an appropriate and usable false positive rate for the intended screening arm. It should not be considered as an estimate of specificity that is relevant to this discussion.

Let's talk a minute about the components of the relative probability, and then show you what the potential impact of variations in those components are.

Briefly, as you have heard, the prevalence is one component, and it is the assumed rate of prevalence of breast cancer in the population to be screened and, as you have heard from the previous

speakers, careful review of the literature yielded what we believe is a conservative estimate of 1.5 per 1000 or 0.15 percent.

The sensitivity, as you know, is the probability that the results will be positive in a woman who has breast cancer or the true positive rate. The enriched population is, therefore, desirable and necessary to provide some estimate of sensitivity.

Specificity is the probability that the T-Scan device is negative in a woman who does not have breast cancer, i.e., the true negative rate. And as we have noted, the estimate based on the specificity arm, we feel, is very appropriate.

Let's examine for a minute what the potential impacts on the relative probability, again the standard agreed to by the agency and Mirabel at the start of the study.

If we hold the specificity constant, as was observed in the specificity arm, and the sensitivity from the sensitivity arm, our assumption from the literature was a .15 percent prevalence, yielding almost a relative probability of 5, well over

the 2 criteria.

If prevalence is low at the .05 percent, which may be argued at some point today, in fact, the relative probability is marginally increased and basically has almost no effect.

Now let's examine what happens if we hold specificity constant and assume that the prevalence is accurately reflected as .15 percent and vary the sensitivity. I have provided you with three estimates of sensitivity here, none of which is the actual observed sensitivity in the overall arm, but found in a variety of ways.

The 17.6 is the lower confidence limit of our observed 27.4 percent. The 18.9 is limiting it to the 30-39 cohort, and 11.2 is using only women in the United States. As you will observe, although the relative probability varies, in all cases it still meets the criteria set forth by the agency.

Finally, holding sensitivity at the rate observed in that arm and the prevalence at what we agree is -- we argue is the correct one, we varied specificity. The highest observed specificity in that

arm was in women with bra cup sizes A/B, and the lowest was in African American and Asian women. As you can see, on both of those the relative probability again exceeds the pre-specified criteria.

Let me touch for a few minutes on the issue of pooling, which you are going to hear about more. In pooling across sites, we considered the following issues. Many studies, randomized or nonrandomized, are certainly multi-center for a variety of reasons, and the protocols, while often not explicitly stating that they are going to pool across sites, by the very nature of the statement of the hypotheses and their analyses clearly imply that the data are going to be pooled across sites.

Occasionally, and in some PMA presentations, the FDA has asked for the sponsors to look at site to site variability for a number of reasons. Among these are, for example, if you are doing a surgical study or implanting a stent, they want some assurance that the technology and a learning curve is appropriate, and they are not seeing variations that may lead to patient safety.

So it is implied by the protocol. In this study, there was a common protocol used at all sites. The device is the same and the training was the same for all sites. Mirabel monitored the study at the various sites. They saw no evidence that the study wasn't being conducted according to the protocol in a uniform manner at all sites and, very importantly, as you heard before, there is virtually no interpretation of the results here. It is a binary outcome. The device lights up red or green. There is no image to interpret and no data to interpret.

Pooling across the sensitivity arm then -- Again, as I said, the subgroup and pooling issues are intermingled. So you will forgive me if sometimes I am mixing apples and oranges a little bit. But the subgroup analysis issues are to evaluate heterogeneity of response among sites.

We are always concerned about a low power, and that is a legitimate concern. We are also concerned Type 1 error, as we do more and more subgroup analyses, and we are also concerned whether the analyses were post hoc or not, which in this case

they all are. However, I would argue that even under these circumstances, if heterogeneity is suggested by the data, further investigation is warranted and probably should be conducted, but all involved need to do this in a proper manner.

The regulators, the clinical investigators and the sponsor should all encourage this analysis. Why should this be encouraged? I would argue that only through and open and honest attempt to explain any potential heterogeneity can the end user -- and this is very important, that the patient be assured they are getting the best type of medical care.

For the sensitivity argument, there were 15 sites in there and, as you can see, these are the sample sizes of the number of women in the sensitivity arm at each site, very small numbers.

In fact, 60 percent of the sites had only 1 to 4 patients, and only 20 percent had 10 or more, not exactly a sample size in which you would have confidence in looking at heterogeneity. However, since the issue has been raised, I would argue that the first step in looking at heterogeneity, although

the test has very minimal power, is to look at whether the range of sensitivity -- that should be sensitivity -- across sites is different. It is not, and I would certainly agree that it is not an unexpected finding, given the small sample size. But it does argue that you have to be careful about looking for heterogeneity when you do have small sample sizes.

The subgroup analyses, switching back to specificity now, was not pre-specified. No subgroup analyses were pre-specified in the analysis. However, the agency has pointed out three interesting findings: Bra size; ethnicity; and nation.

I bring your attention to the fact that in all cases the specificity is either close to or exceeds 90 percent and, if you recall the previous slide on the variability in the relative probability, anything about 87.5 percent will still yield a relative probability of over 2.

So my conclusion here is that data for all the specificity sites can be pooled.

I will just briefly go through this. In addition, in the sensitivity arm, if we are looking at

the criteria for pooling, one of the criteria one might look at are whether or not there are differences in patient characteristics among the subgroups that you want to analyze. There was no difference based on characteristics that we observed. There were no differences, I mentioned, in the study design or the machine. Medical practices and patient management was similar, and we discussed the fact that there is no room for examiner bias with this machine.

The subgroup analysis of sensitivity: The FDA has noted a possible difference in sensitivity for nations, that the U.S. is 11.5 percent, Israel 32.8. Here I would point the previous slide indicating in the 15 sites there were no differences. To then go in and select groups of sites and look at, I think, is fraught with some danger, and should be very carefully interpreted. I mentioned that. There is a little time issue. So I am going to move on kind of quickly.

I will point out, if the Israeli patients were excluded from both arms, the relative probability for only the U.S. data would still exceed 2. Our conclusion then is that pooling the data from the

sensitivity study is appropriate and justified.

The last two slides I wanted to talk about is an analysis that the FDA will present using logistic regression. These first two columns are from their slide 17. This is our analysis.

They did a logistic regression using odds ratio and argue that the odds ration is an overestimate of relative probability. What they point out is that the T-Scan is 2.6. I will let them provide their interpretation of it. My interpretation is as follows.

First, there was a slight misclassification of family history. They included some women a family history positive who weren't first degree relatives. When you only use the first degree relatives, you get an odds ratio of 1.5, which is the lowest odds ratio. But more importantly, what this 2.6 odds ratio for the T-Scan indicates is that, even after adjustment for all of these factors, the T-Scan still provides a 2.5-fold increase in the odds of having breast cancer.

They also did the analysis for women 30-

39, and we get the same results there.

So my conclusion from the logistic is that it actually supports the inference that a T-Scan positive woman is at increased risk for breast cancer, even after adjusting for the baseline factors, a two and a half to threefold increase.

My overall conclusion, and I will leave you with this, is that based on a review of the data of both arms of the study, the results meet the conditions for approvability. It was well designed and executed. We feel the sponsor's analysis was very appropriate and to the point, and in all cases met the pre-specified success criteria, and it showed clinical efficacy with, again I emphasize, no safety concerns.

Thank you very much for your time.

I would like to introduce Dr. Vivian Dickerson, Past President of the American College of Obstetrics, Obstetricians and Gynecologists, and Associate Professor of OB/GYN at UC, Irvine. She will speak about the expert panel report.

DR. DICKERSON: Thank you, and good morning. It is my pleasure to appear before you

today.

I would, first of all, like to say that I am pleased to note that I have been promoted. I am now a clinical professor of obstetrics and gynecology at the University of California, Irvine. I am also, as you have heard a Past President of the American College of Obstetricians and Gynecologists, and I recently started a new position as the Director -- Medical Director of Women's Health Care and Programs at Hoag Hospital in Newport Beach, California.

So needless to say, I am here because I believe in what I am about to say, despite the fact that I started a new two job two weeks ago, and three days ago started a demolition/reconstruction on my home. So maybe that's a really good reason to be here.

It is my honor today to speak on behalf of an august panel of experts as well as an individual. I would like to give the following disclaimers. I am not representing the American College of Obstetricians and Gynecologists in my remarks. Furthermore, I am not being compensated for my time here today, nor do I

have any ownership interest in Mirabel Medical Systems or any other associated company.

I would like very briefly to introduce you to the group that made up the expert panel, because they all contributed greatly to the recommendations that I am going to make today.

Dr. Mark Akin, you have already met. You have just now met me.

Dr. Steven R. Goldstein, Professor of Obstetrics and Gynecology at New York University School of Medicine, specializing in ultrasound and other women's imaging.

Dr. Daniel R. Mishell, Professor of Obstetrics and Gynecology, Keck School of Medicine, USC. Dr. Mishell is also the former Chair of that OB/GYN department.

Dr. Lawrence D. Platt, who is Director of the Center for Fetal Medicine and Woman's Ultrasound in Los Angeles. He is also a clinical professor at UCLA, a former Chair of the Department of OB/GYN at Cedars Sinai Medical Center, and the current President of the International Society of Ultrasound and

Obstetrics and Gynecology.

Dr. Ronald Wapner, you have met.

Dr. David Gur, a radiologist, Executive Vice Chair and Professor of Radiology, University of Pittsburgh; and Dr. Thomas Stavros, whom you will meet shortly.

Our surgical oncologist you have also met, Lieutenant Colonel Alexander Stojadinovic.

Our statisticians: Dr. Ralph B. D'Agostino, who is Director of Statistics and Consulting Unit at Boston University; Executive Director of Data Management and Biostatistics at Harvard Clinical Research Institute; Director of Statistics at the Framingham Heart Study. And Dr. Joel Verter, who you have just met.

Our epidemiologist, Dr. Theodore Colton, Professor of Epidemiology and Biostatistics at Boston University School of Medicine and Public Health.

Now that you have met our panel, I will tell you that I have been asked to speak quickly, because we want to allow plenty of time for questions from the panel. Therefore, I will move along at a

fairly decent clip.

Our methodology is as follows: We carefully considered T-Scan breast cancer screening paradigm, and evaluated the design and execution of the pivotal study. We also assessed the issues that have been raised thus far by FDA panels.

We considered if and how T-Scan could be incorporated within the standard of care for young women, the target population, and we have provided all this in a written opinion to you, the Panel.

Our conclusions were as follows: The study was large and well designed. We also felt it was appropriate to exclude post-menopausal women in the study. As you have already heard, the impedance characteristics and indeed many of the clinical characteristics are determined by the relative presence or absence of estrogen, and not by the chronological age of the woman.

We felt it was also, therefore, appropriate to enrich the population in the sensitivity arm with pre-menopausal patients between the ages of 40 and 45. We felt, therefore, that there

were sufficient data presented on safety and effectiveness and that the results were generalizable to the U.S. target population of women 30-39 for the reasons I have already mentioned.

Women identified as positive, we recognize, would otherwise have been missed, as they did not have any other high risk characteristics to identify themselves.

We felt that approval would stimulate further development in an area that, as you have already heard during the public testimony, an area that needs technological improvement.

I would now like to speak briefly just as a gynecologist. I have taken care of patients for 25 years. I am very, very aware of the current lack of effective screening tools for breast cancer in women under the age of 40.

Let's talk about what we have. We have the clinical breast exam and the self breast exam. I am going to speak to the clinical breast exam, because that is what I do. It is the standard of care. It is variable, and it depends on the palpation procedure.

it depends on the tumor size or the lump size, menopausal status or lack thereof, breast density, the examiner proficiency, the breast size, and the frequency with which it is done.

CBE indeed is so variable that the U.S. Preventive Services Task Force has refused to make recommendations for or against its use up to the age of 50 for the detection of breast cancer in women.

Mammography is not recommended, as you know, to average risk women between the ages of 30 to 39. So we have a clinical challenge. Most cancers in this age group are self-detected, approximately 71 percent, and the five-year survival rate in this younger cohort of women is lower than their older counterparts.

Therefore, it is the early detection of breast cancer in young women that is a clinical challenge. Indeed, for me it is more than a challenge. I appreciate the question earlier by Dr. Romero of one of the public speakers who asked about the anxiety levels and about the fear.

I deal with that every day of my life,

because it doesn't just occur with a woman who has gotten a positive exam. It occurs in a woman who recognizes we have nothing to offer her, and every day of my life I am asked by women in their twenties and women in their thirties what is it you can do for me; and as you can see, I really don't have anything that I can absolutely rely on for these women.

So I believe that they are left fearful oftentimes, although I haven't done an objective measure, but I do believe that they are very fearful; and I know that I feel disheartened and without an answer for them, and I feel that an early detection of breast cancer in young women is the challenge, and our ability to identify women at high risk would be so much preferable to them identifying their selves later with a palpable and often fatal lump.

So T-Scan, therefore, fits the bill. It is a screening device, and that is so important for everyone to understand, that while you heard this at the beginning of our presentation, I think it is very important to reiterate it at the end.

It is not a diagnostic device. I, too,

wish that as a 58-year-old woman there was an easy diagnostic device that someone could use in their office that was painless and wouldn't involve squishing and doing all the things that I have to go through every year. I'm happy for mammograms, but I wish there was a diagnostic device. There is no such thing at this juncture.

T-Scan does not promise that to young women. It promises to screen, and it has all of the desirable attributes of a screening tool, and those include reasonable sensitivity, and that is the ability to detect disease when present. You saw the sensitivity data.

The real test of a screening exam is its high degree of specificity, and that is, if the disease is not present, the test is negative; and for all those young women who go home fearful from my office, it would be nice to offer them a test that has as a high a sensitivity as the T-Scan.

Uniform quality and repeatability: You have seen the data to support that. It is easy to perform. It is noninvasive, with low morbidity. It

has high safety. It would be very acceptable to my patients, and it should be widely available, and I am certainly hoping that this Panel will take care of that today.

So what do we have for early risk assessment? The import is to identify women at higher risk, which, therefore, can lead to early detection and diagnosis. And as most of you know, early detection in this patient population would mean less expensive treatment, less aggressive treatment, improved quality of life, and improved long term survival.

I thank you very much for allowing me to appear today. The T-Scan can help us to identify somewhere between 3,000 and 5,000 cancers that would have been otherwise missed using the current standard of care. That is a large number. T-Scan is a safe and effective technology. It addresses an important unmet need in women's health. Thank you.

Sorry. I would now like to introduce Dr. Thomas Stavros, who is the Medical Director of Ultrasound, Radiology Imaging Associates, and the

Director of Ultrasound at the Sally Jobe Breast Center in Denver, Colorado.

DR. STAVROS: Good morning. Thank you for allowing me to express my opinions.

I want to talk today about similarity between breast tissue in women in their thirties and those in their early forties who comprise the enriched part of the sensitivity study. I want to talk about how we would manage positive T-Scans, and I want to talk about the precedent of doing diagnostic workups in women under 30.

I would like to say that, as a radiologist, I do not feel in the slightest bit threatened by this test. I recognize it for what it is, and I view the opportunity to work up these women in their thirties with positive T-Scans as an opportunity to detect cancer earlier, improve the cure rate in an age group where the diagnosis is most devastating, costly to society and the family.

While it is generally true that mammograms become more replaced by fat over age, there is no sudden cutoff point at which a breast is entirely