

1 what the clinical outcome or whether or not a biopsy
2 is going to be used.

3 I think that it would be important to know
4 whether this would be useful in masses that were given
5 sort of a BIRADS 3 or 4 on ultrasound as opposed to a
6 BIRADS 5.

7 DR. CALLAHAN: Right, and,
8 parenthetically, I can say that we do know that where
9 ultrasound would normally have clinically been
10 employed, it appears that it was because a lot of the
11 radiology reports refer to ultrasound results. But as
12 a fact of the protocol, it wasn't required that this
13 be collected or documented or verified. We just do
14 not have that information.

15 So I think the fact is that our enrolling
16 physicians were conducting clinical practice as you
17 described, that those masses that required ultrasound
18 -- and I don't want to speak for our investigators;
19 certainly two of them are here and can add to what I
20 might have to say.

21 DR. CONANT: I agree very much with Dr.
22 Hooley. It seems from looking at your data that

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1 there's a bias from the beginning because some of
2 these patients definitely had ultrasounds, and cysts
3 were seen, and in some cases possible solid masses
4 were aspirated and they were found to be complex
5 cysts, when they were thought to be masses, solid
6 masses, but they still got the IR imaging and they're
7 still included in the data.

8 Then there is a group that didn't get
9 ultrasound factored into the level of suspicion, and
10 biopsy was recommended, and they got IR imaging. So
11 I think even within this data there may be a bias when
12 ultrasound was used and when it wasn't. There wasn't
13 a cut point as ultrasound definitely needs to be used
14 to evaluate or should not be included.

15 I know from just our clinical practice we
16 often, I believe, base our outcome, our category 0
17 through 5, on the ultrasound. We incorporate that
18 into our 0-through-5 bottom line and recommendation.
19 So I am concerned about the same thing.

20 The other thing that is sort of on that
21 line is there were quite a few 0, 1, 2, and 3s
22 included in the data, I believe. Those aren't cases

1 that usually go to biopsy recommended by the
2 radiologist. Now they may have palpable areas, but
3 they don't seem to have been excluded. I may just be
4 missing something here, but they did have IR imaging
5 and they were included in the mass group, I believe.
6 Is that true?

7 DR. PARISKY: Correct.

8 DR. CONANT: Why would a 0, 1, or 2 be
9 included in biopsy? I know sometimes the patient
10 drives at the doctor --

11 DR. PARISKY: One is that the radiologist
12 felt that this was negative, and the surgeon or the
13 patient pursued that something was there. More
14 commonly, that happens with a 2. A 2 means that
15 there's a benign finding, benign finding
16 mammographically. It is still up to the referring
17 surgeon and patient whether or not to remove
18 something. I think you probably have that
19 conversation with women on a daily or weekly basis
20 where they say, "I want it out."

21 DR. CONANT: But if I am looking at it
22 correctly, and please correct me if I'm wrong, the

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1 numbers of 0s, 1s, 2s, and 3s were really quite large.

2 I'm looking at --

3 DR. HOOLEY: I see it's close to being 30
4 percent.

5 DR. CONANT: Yes. Page 29, in answer,
6 response, to Question 9 from the FDA. It's in this
7 white thing. It's about 30 percent.

8 DR. CALLAHAN: Okay, again, I would remind
9 the reviewers that these BIRADS assignments were done
10 by our independent evaluators based on the radiology
11 reports. A lot of times there were zeroes because the
12 radiology reports would say, "Need additional
13 information." That would account for a lot of the
14 zeroes.

15 We do know that there were palpable
16 because the original protocol called for not just
17 mammography, but was "and/or" clinical examination.
18 We had a lot of palpable -- or we had palpable cases
19 enrolled, where in fact they could have a 1 that is a
20 negative mammogram, but a palpable finding that would
21 lead them to go on to biopsy.

22 I think we tried to address the fact that

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1 the BIRADS recommendation and the ACR recommendations
2 for treatment, and what's actually been described in
3 the literature, is in fact that BIRADS in all
4 categories do proceed to biopsy.

5 DR. CONANT: But not on a 30 percent rate.
6 If they were palpable only and not mammographically-
7 visible, they should have been excluded from the final
8 mass category and then not reflected in this group.

9 DR. CALLAHAN: And they would have been
10 excluded from the final category that could have been
11 evaluated, because if they were palpable and there
12 wasn't a mammographically-apparent lesion --

13 DR. CONANT: Even if on the ultrasound or
14 in retrospect, sometimes you look back at the
15 mammogram. I mean, it just seemed to be included in
16 the end.

17 DR. CALLAHAN: Well, yes, our independent
18 reviewers had to use the mammograms to assign and use
19 an ROI. So I think that is the explanation.

20 CHAIRMAN MEHTA: Dr. Tripuraneni, do you
21 have any questions?

22 DR. TRIPURANENI: Region of interest, when

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1 you had three independent reviewers pick the region of
2 interest, was there significant variability?

3 DR. RUST: One analysis that we did
4 perform, at the request of the FDA, was to determine
5 if there was ever more than a 10-pixel difference
6 between the ROI marker location and the center of the
7 region of interest. We found that that never
8 occurred. So there was never more than the 10-pixel
9 difference.

10 DR. TRIPURANENI: Does the size of the
11 breast have any impact on how it is cooled, on
12 ultimately the results of positivity on the IR?

13 DR. RUST: We did not perform any analysis
14 along those lines.

15 DR. TRIPURANENI: Would it?

16 DR. RUST: That's not a question for a
17 statistician to answer.

18 (Laughter.)

19 CHAIRMAN MEHTA: Do you want someone else
20 from the sponsor to answer the question?

21 DR. TRIPURANENI: Just curious.

22 DR. CALLAHAN: I mean that's a good

1 question. We don't have any data on that, though,
2 that we can report at this time, whether breast size
3 makes a difference. We did not collect that
4 information.

5 DR. TRIPURANENI: You don't have any
6 thermometry about the temperature of the skin on the
7 breast? If you look at the subset analysis with the
8 size of the breast, would there be any difference?

9 DR. CALLAHAN: Again, we didn't collect
10 information about breast size. We only collected
11 information about lesion size. So we don't have the
12 data to address that.

13 CHAIRMAN MEHTA: Dr. Ibbott?

14 DR. IBBOTT: Well, that leads into a
15 question that I have been thinking about for a few
16 minutes. That is, you decided on an equilibration
17 time of, I think, ten minutes. I wonder if that
18 number was selected arbitrarily or if you have some
19 data looking at the effects of things like room
20 temperature or whether the patient ran up the stairs
21 to the clinic before coming in for the exam, things
22 like that.

1 It seems like equilibration time would be
2 important, and I wonder how much effect it has on the
3 exam.

4 MR. SATTERTHWAITE: Let me ask you to
5 restate your question, so we've got it clear here.

6 DR. IBBOTT: Well, the short version is,
7 did you determine the effects of environmental factors
8 such as room temperature on the equilibration process
9 before the IR exam was performed and, if so, what
10 effect that might have on the quality of the exam?

11 MR. SATTERTHWAITE: Okay. Before the
12 trial started, we recognized, in reviewing other work
13 that was done, the problems associated with
14 sensitivity in a device that was an IR imager, and
15 recognized the fact there was a lot of variability for
16 that kind of thing. That was one of the reasons why
17 we both asked for an equilibration and introduced the
18 coolant challenge.

19 The coolant challenge is, we believe, what
20 helped us differentiate ourselves, our diagnostic test
21 from those of the past that have recognized the very
22 issue you are addressing, which is that there would be

1 some variability to that. But doing the coolant
2 challenge allowed us to confirm the kind of
3 characteristics that we looked for.

4 DR. IBBOTT: So, in effect, that excludes,
5 doing the cooling challenge then excludes any impact
6 of differences in the equilibration time? I'm just
7 thinking of different cities. I work in Houston where
8 it's obviously frequently very warm and humid, but at
9 the same time we know how to air condition in Houston.
10 People often complain.

11 So if somebody is coming in out of -- I
12 don't need to go through that. You know what I'm
13 trying to get to.

14 My point is, does the cooling challenge
15 then negate all of those other potential influences?

16 MR. SATTERTHWAITTE: We don't have the data
17 to really address your question so specifically; only
18 to tell you that we recognized the fact that that
19 would be a real issue, and that we needed to do some
20 things that would allow us to try to offset those
21 kinds of problems and think that we probably still
22 could do better, but we think that we have done an

1 adequate job now to be able to identify those things
2 that differentiate.

3 DR. IBBOTT: Thank you.

4 CHAIRMAN MEHTA: Dr. Hooley?

5 DR. HOOLEY: Yes. I would also like to
6 clarify how you chose the threshold of the index of
7 suspicion. My understanding is that you used a number
8 of subjects and you included all lesions: masses,
9 architectural distortions, and calcifications. You
10 came up with a number of 20.5-something and then
11 applied that to determine mass suspicion. That seems
12 to be incongruent to me.

13 DR. RUST: Okay. The threshold was
14 determined prior to unblinding of the pathology for
15 the original study. The analysis by lesion type that
16 led to a focus on masses was done after unblinding of
17 the original study.

18 We felt that we had no leeway at all to
19 change that threshold after unblinding. So we stayed
20 with that threshold. Even though it was established
21 using masses and non-masses in the dataset, we didn't
22 feel that there were any degrees of freedom in terms

1 of modifying threshold, that we were basically
2 obligated to stick with the algorithm and the
3 threshold that was determined prior to unblinding the
4 original study data.

5 I would like to, if I could, take this
6 opportunity to say that our objective, when setting
7 that threshold, was, as Dr. Sacks stated in his talk
8 earlier, to try to achieve an approximately 99.3
9 sensitivity. When we did that with the training
10 dataset, we attempted to do that with 75 percent
11 confidence by using a simulation procedure, and that
12 is how we came up with that threshold.

13 That was the criterion for establishing
14 the threshold. That criterion was never intended to
15 be a hypothesis to be used for performance evaluation,
16 as I think Dr. Sacks indicated he thought it was. It
17 was simply to set the threshold, and that was it. It
18 was not intended to be used as a performance
19 criterion.

20 DR. GENANT: Just a little bit of a
21 followup on that issue, the threshold, for example:
22 You indicated that you have not performed duplicate

1 measurements or triplicate measures in an individual
2 patient. Yet, when you move from some of the
3 qualitative aspects of imaging to a purely
4 quantitative aspect, where you have a threshold base,
5 it becomes important to know that you have stability
6 of your equipment and that there is reliable
7 reproducibility in some fashion for the equipment
8 itself, whether that be on phantoms or whether it be
9 on -- ultimately, one would like to see some data on
10 patients indicating that it is reproducible.

11 How have you established that the
12 instrument with regard to a threshold base has
13 reliability?

14 MR. SATTERTHWAITE: So I understand the
15 question to be, how do we assure you that this device
16 will operate reliably each time?

17 DR. GENANT: And consistently.

18 MR. SATTERTHWAITE: Consistently. Again,
19 I'll reiterate that we have not tested a patient in
20 more than one imaging session for that kind of
21 reproducibility. But we initiated early on an early-
22 morning system test that the technologist was required

1 to run. They would actually fax the results of those
2 tests into us. But it required temperature sensors to
3 be placed and the cooling system to be turned on in a
4 very specific manner. Then we would measure various
5 factors that assured us that we would have success
6 there.

7 A lot of that, not a lot of that, all of
8 that now is automated and done without technologist
9 intervention. All they need to do is invoke the
10 software that controls cooling and computer imaging,
11 and that takes place.

12 So we believe that we have implemented the
13 tests that will assure us that we have images
14 consistent enough that our algorithm and the
15 application of the coolant challenge will take care of
16 those differences that might exist there.

17 DR. GENANT: But you haven't applied this
18 in any objective fashion to determine whether it
19 actually works? I mean, for example, with a phantom
20 of some sort or --

21 MR. SATTERTHWAITTE: Well, that's true, not
22 with a phantom, but a reproducible test that has --

1 this system here has a number of temperature sensors
2 that are tied to the computer, and the computer
3 monitors all those temperature sensors while this
4 beginning-of-the-day test takes place. Those sensors
5 are located so as to sense the breast chamber and some
6 other areas that we know, if we measure them, we know
7 what they should be consistently, will give us a
8 confidence that that device is going to work like
9 you're suggesting it should.

10 CHAIRMAN MEHTA: Mr. Stern?

11 MR. STERN: Yes, I'm just curious to know
12 if there is a next-generation device on the horizon
13 and if you can say anything about it.

14 MR. SATTERTHWAITTE: I'm sorry, I'm
15 multiplexing here.

16 (Laughter.)

17 Your question specifically again? I'm
18 sorry.

19 MR. STERN: Yes, I was just curious to
20 know if there is a next-generation device on the
21 horizon and if you can say anything about it.

22 MR. SATTERTHWAITTE: I guess we're allowed,

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1 since we have been asked? Is that right?

2 There is a next-generation device. This
3 actually represents some part of the characteristics
4 of the next-generation device in that it is lower than
5 the device that was used in clinical practice but
6 functionally the same.

7 We, indeed, are -- we do have phantom work
8 that is going on right now. We do tests in our own
9 research facility that we think will improve the kind
10 of tests I have already suggested or told you that we
11 are running with the software.

12 MR. STERN: Thank you.

13 CHAIRMAN MEHTA: Ms. Peters, do you have
14 any questions?

15 MS. PETERS: Pretty much just some
16 comments, and I don't know if I'm really addressing it
17 to the Panel or to the presenters here. But in a
18 medical setting you go from your primary care
19 physician who has ordered your mammogram, I mean who
20 has asked you to do your mammogram. If the results
21 come back that there's something suspicious, then your
22 primary care physician says, "Well, I'm going to refer

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1 you to a surgeon" -- this is how a lot of your health
2 groups work -- "refer you to a surgeon to talk about
3 whether you're going to have biopsy or what are your
4 options."

5 So then is this in the realm -- what I am
6 hearing is that this machine is in radiology. So does
7 the radiologist reading a film see something there and
8 suggest to your primary care physician that this can
9 be done to determine whether you should have a biopsy
10 or not or to help in the decision of whether to
11 proceed to biopsy? I'm not sure where this falls in
12 the patient going through the system, the health care
13 system.

14 DR. PARISKY: As I understand, your
15 question is, using a model where a patient is referred
16 for a mammogram and then the primary care physician is
17 the quarterback in directing the patient's care --

18 MS. PETERS: Right.

19 DR. PARISKY: -- and how does that fall
20 in? I think that model is becoming less and less
21 frequent in terms of breast imaging.

22 Your experience in San Francisco, our

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1 experience, I'm sure your experience is the same,
2 where a lot of these decisions are being relegated to
3 the radiologist.

4 I think Dr. Sacks talked about the trauma.
5 I think it is unfair to do a test and send a patient
6 back to her primary care physician, wait for that
7 letter to get to the primary care physician, send the
8 patient back for another test.

9 We try to encompass as many tests as we
10 possibly can. The patient comes to radiology. Now
11 insurance reimbursement, for instance, screening, it's
12 tough to do tests the same day. But if the patient is
13 referred back for diagnostics, I think the prevailing
14 philosophy of most radiologists is to do as many tests
15 as appropriate to come to the right answer.

16 MS. PETERS: So then the radiologist would
17 ask for the patient to come back --

18 DR. PARISKY: Yes, Ma'am.

19 MS. PETERS: -- to have the additional
20 work done?

21 DR. PARISKY: Yes, yes, yes, and actually,
22 by policy and by law, we are the ones that are

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1 instituting the recall. We do the obligatory letter
2 to your clinician, but we have to notify you that
3 there is a problem.

4 MS. PETERS: Okay, it's coming.

5 Then my other concern was, when we were
6 talking about the heat sensitivity of it, in the age
7 range, the majority of your patients were between 40
8 and 60 years old, and that's time where some people
9 are having hot flashes during that time. What impact
10 might that have on the cooling and overall body
11 temperature?

12 DR. CALLAHAN: I think that's an excellent
13 question. It's something that we haven't formally
14 addressed in this investigation, but it is certainly,
15 you know, a question that bears looking at.

16 We do have, I mean as part of the
17 information that's collected, we have the patients, we
18 have all this information about the beginning skin
19 temperature and then throughout time. So it's
20 possible that sort of analysis that you're describing,
21 I mean we could look and see if, let's say, those
22 patients start at a higher temperature perhaps.

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1 One thing I would add to what our engineer
2 said is, for the cooling challenge, the ten-minute
3 equilibration period, part of the protocol is that the
4 room climate control be at a fairly tightly-controlled
5 room temperature, from around 67 to 73 degrees. So
6 we're not saying, have a patient come in and
7 equilibrate at 90 degrees. I mean that's part of the
8 equilibration.

9 CHAIRMAN MEHTA: I'm going to go ahead and
10 ask a question regarding patient consent on this
11 particular study. Obviously, patients were not
12 deriving any direct benefit by participating in this
13 study. So in the consent form and in the consent
14 process, what were the patients told as to the
15 rationale for participating in this study?

16 Were they, for example, contributing to
17 the development of science? Were the data going to be
18 used for the benefit of women in the future? Could
19 you clarify that for me?

20 DR. HUGHES: Essentially, in the study we
21 made it very clear to the patients that we were not
22 going to use these results for their care. What I

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1 would tell a patient specifically is that we have a
2 new device that we're testing, that it may help us
3 tell what lesions are without having to have surgery
4 done, that we will not have results for them because
5 this was a blinded study, and that they would have
6 this test done and would have no benefit whatsoever,
7 but it may help them or somebody else in the future.

8 Women uniformly in my practice were happy
9 to do this.

10 CHAIRMAN MEHTA: So would it be fair,
11 then, to assume that every patient who signed on the
12 study assumed that their data were going to be used
13 for the benefit of science in the future?

14 DR. HUGHES: I would think so. That's
15 what research is for.

16 CHAIRMAN MEHTA: Okay. Did the 275 women
17 whose data were not initially used, were they informed
18 that the data were going to be cut off because of a
19 timetable deadline, and that only at the behest of the
20 FDA for request of further data would the data be
21 included in the analysis?

22 DR. HUGHES: I'm actually not sure when

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1 the deadline occurred for that. I can't answer that
2 question. I would expect that any data we collected
3 would have been used eventually, whether it was used
4 within this study or not.

5 CHAIRMAN MEHTA: In the initial submission
6 they were not included. It was only when the request
7 was made to get more data were those data dredged out.

8 DR. CALLAHAN: These patients were all
9 enrolled under the same protocol. We continued
10 collecting data for those additional 275 patients, as
11 we had ongoing agreements and enrollment ongoing at
12 those sites, for the additional 275, with the
13 intention, the intention was always to utilize that
14 patient data for analysis purposes.

15 So there was no difference in the consent
16 amongst those. They had IRB approval under the same
17 protocol that was ongoing, and there was never any
18 intention not to use their data or to use it for, you
19 know --

20 CHAIRMAN MEHTA: If the intention was to
21 always to use the data from those 275 patients, why
22 didn't you simply wait until you had those data and

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1 then included them, rather than going back into a
2 cutoff date?

3 DR. CALLAHAN: There were time
4 responsibilities. There were obligations and reasons
5 that we felt like we had collected enough data for an
6 initial submission.

7 We also can, frankly, say that there was
8 always a possibility that additional data would be
9 requested. So by remaining blinded to this, we felt
10 like we had valid cases, the same protocol, the same
11 evaluation procedure, that could have been used to
12 answer questions that arose after review of the first
13 submission.

14 CHAIRMAN MEHTA: Well, my concern is this:
15 This morning you told me that you were planning to
16 enroll 3,000 patients, 600 in each institution times
17 five, and that's not what happened. There were a few
18 hundred at some; there were more at others. It wasn't
19 a 600 times five. Three thousand patients were not
20 enrolled; 2,400 were. Two hundred and seventy-five
21 were cut off from the data and were subsequently used.

22 So I'm just concerned about the entire

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1 consent process of how this all happened.

2 DR. CALLAHAN: We note your concern.

3 CHAIRMAN MEHTA: Any other questions from
4 the Panel? Go ahead.

5 DR. CONANT: I have a few questions about
6 the false negatives and in terms of efficacy. I
7 gather there was one in the summed group of masses.
8 I am wondering if, No. 1, that false negative was read
9 by one, two, or three readers, how many of them felt
10 it was a false negative, and how many other possible
11 false negatives there might have been read by one,
12 two, or, you know, a non-minority number, or that the
13 averages then pulled up above to a positive result?

14 DR. CALLAHAN: Okay, for that particular
15 case, it was read by all three readers. I can tell
16 you that all three got an IOS score close to our
17 threshold, below the threshold but close to the
18 threshold for that case.

19 DR. CONANT: Were there other lesions that
20 were read by at least one, and how many other lesions
21 were read by at least one reader as a negative?

22 DR. CALLAHAN: For our masses, if any of

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1 our total efficacy group of 490 and 105 malignants,
2 any of the other 104 that were read, all the assigned
3 evaluations would have been above the threshold. If,
4 for example, when we looked at our microcalcification
5 cases, when we were looking at all the cases, or in
6 general, if there was one read below the threshold,
7 that was scored as a miss, as a false. If it was, in
8 fact, malignant, it would have been considered a false
9 negative.

10 DR. CONANT: I guess it comes back to the
11 pooling of the data, because some readers, if there's
12 really one that says -- I mean it's all in the way you
13 run the readers today, but I understand now.

14 DR. RUST: Well, let me clarify how that
15 would show up in the summary data, if it occurred. If
16 one reader had missed, had had a negative for a
17 malignant mass, and there were two other readers that
18 have a positive, then what you would have seen is 1.33
19 missed cancers. So it would show up in our
20 statistics.

21 DR. CONANT: Did that happen often?

22 DR. RUST: It did not happen at all in the

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1 case of masses. All readers on all 104 other masses
2 obtained a positive test result.

3 DR. CONANT: Okay. And then back to that
4 little false negative one, it was a small lesion. I
5 believe -- I have been searching for where I read
6 about that case, but I think it was a 5-millimeter or
7 smaller; I thought it was a 4-millimeter mass.
8 Correct me if I'm wrong, but I thought it was a tiny
9 one.

10 No. 1, I would like to know more about
11 that case.

12 DR. CALLAHAN: It was actually a 1-
13 centimeter mass --

14 DR. CONANT: It was a 1-centimeter mass?

15 DR. CALLAHAN: -- but I'll let Dr. Parisky
16 talk about that.

17 DR. PARISKY: I do have the pathology.

18 DR. CONANT: That's a question: Was the
19 size determined pathologically or mammographically of
20 the lesions?

21 DR. PARISKY: Both. Mammographically, but
22 in the pathology report there's an acknowledgment of

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1 size.

2 DR. CONANT: So for the comparison of
3 grades --

4 DR. PARISKY: Yes.

5 DR. CONANT: -- I mean of sizes here in
6 the data, is that pathologic or mammographic sizes?

7 DR. PARISKY: No, those are mammographic
8 determinations, but in this particular case, which I
9 had a tremendous interest in because you can imagine
10 why, we had a pathological size as well.

11 DR. CONANT: Okay. Then I'm just
12 wondering, your comments, clinically, why there were
13 so few small lesions, two out of all of those cancers.
14 Why do you think that is? I mean, we tend to find
15 small cancers, at least histologically small.
16 Sometimes they look bigger mammographically, but --

17 DR. PARISKY: You're talking about only
18 two lesions below 5 millimeters in size?

19 DR. CONANT: Yes.

20 DR. PARISKY: Yes. I think the majority
21 of mammographic lesions are greater than 5
22 millimeters, the great majority. So we're looking at

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1 people reacting to a 3- or 4-millimeter may very well
2 BIRADS code 3.

3 DR. CONANT: Yes. Well, it might be -- I
4 think if you threw the ultrasound side in there, you
5 would start seeing some more.

6 DR. PARISKY: We would love to throw the
7 ultra -- no, I understand that, but do you react to
8 every 3-millimeter lesion you see if it's, let's say,
9 smooth?

10 DR. CONANT: If it's a change, definitely.

11 DR. PARISKY: No, de novo. You may very
12 well --

13 DR. CONANT: No, I ultrasound them.

14 DR. PARISKY: You ultrasound them. You
15 don't see it ultrasoundographically. You have a
16 decision tree which you're going to follow in six
17 months or needle localize it or maybe do another
18 adjunctive test.

19 DR. CONANT: I'm just asking.

20 DR. PARISKY: And I'm getting back to
21 you --

22 DR. CONANT: So then I've got another

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1 question.

2 DR. PARISKY: Go ahead.

3 DR. CONANT: I'm interested, and I may
4 have missed it in the protocol, how you dealt with
5 that contralateral breast. Because we know there are
6 things lurking in that contralateral breast, and there
7 must have been lots of positives or things that lit
8 up, and it was used as a control --

9 DR. PARISKY: You only light up if you
10 look, and this is not a screening tool. This is a
11 targeted --

12 DR. CONANT: But aren't you using it as a
13 control to the involved breast, and, therefore, can't
14 it cause a problem in calculating? If one's hot, but
15 it's not the one that I'm recommending a biopsy on, my
16 comparison, therefore, may be askew, and --

17 DR. RUST: The theory here is that we are
18 using the entire contralateral breast area, the
19 largest circle you can fit --

20 DR. CONANT: An average.

21 DR. RUST: -- inside it, and average
22 across that as the --

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1 DR. CONANT: Not the quadrant, matching
2 or --

3 DR. RUST: That's right, as the control
4 parameter, and that the effect, if there were a lesion
5 there that would have an effect, there's a small local
6 effect that does not have enough of an effect on the
7 entire breast reading to negate its value as a
8 control. That's the theory.

9 DR. CONANT: Okay, that's an interesting
10 theory to pursue. I mean just as the hormonal, the
11 cyclical changes, we know from MRIs that there's
12 significant vascular changes throughout the cycle, and
13 I assume that they are symmetric, but I'm not sure we
14 know that.

15 CHAIRMAN MEHTA: I think we have about 45
16 minutes left in the discussion time. So what I would
17 like to do at this point is to ask Dr. Phillips to
18 sequentially project the discussion points that the
19 FDA would like addressed by the Panel.

20 Copies of these, again, are in the folder,
21 so we can look at these as Dr. Phillips is pointing
22 the questions to us. We can continue the discussion

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1 once the questions have been pointed out.

2 DR. PHILLIPS: Do you want all of them or
3 do you want --

4 CHAIRMAN MEHTA: Well, we could do them
5 one at a time. If you want to project them, maybe we
6 could just use these as discussion points.

7 I don't think that it is necessary to read
8 this out. Everyone can read this, and you have it in
9 your handout. So if you would just take five --

10 DR. SACKS: The record needs it.

11 CHAIRMAN MEHTA: Oh, okay, I guess we need
12 it for the record.

13 DR. SACKS: Yes, the record needs it. All
14 right, go ahead.

15 DR. PHILLIPS: I'll do it.

16 "No. 1, clinical data: (a) The data in
17 Amendment 4 were selected retrospectively from the
18 original PMA dataset, albeit based on lesion-type
19 analyses that were prospectively planned for in the
20 clinical trial protocol. Aren't the data from
21 Amendment 4 applicable for the assessment and
22 determination of the effectiveness of the BCS 2100?"

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1 CHAIRMAN MEHTA: Who on the Panel would
2 like to start either asking questions about this or
3 providing opinions or discussion points about this?

4 DR. GENANT: Well, I've already commented
5 on this, but I could just reiterate it. I mean, I
6 think that these are not valid in and of themselves to
7 document effectiveness. I think they are encouraging,
8 and they're in the right direction, but I think that
9 they do, in fact, represent quantitatively a post hoc
10 analysis and, as such, need to be applied to an
11 independent set of data and show that it's
12 statistically-significant.

13 CHAIRMAN MEHTA: Why don't we ask our
14 statistician, Dr. Toledano, about this as well?

15 DR. TOLEDANO: I was really hoping you
16 wouldn't make me answer this one.

17 (Laughter.)

18 Okay. Prospectively, there was a plan to
19 analyze performance by lesion type. Prospectively,
20 there was no plan to exclude certain lesion types from
21 the indications for use.

22 The current indications for use are based

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1 on masses. You need data and analysis for masses, and
2 that can't come from the data that told you to limit
3 to masses. Sorry.

4 MR. SATTERTHWAITTE: Can I ask a clarifying
5 question?

6 CHAIRMAN MEHTA: I think if the Panel
7 members want a question answered, they will
8 specifically request you to do so.

9 Any other comments from Panel members?

10 DR. CONANT: A quick comment: I would be
11 interested in this prospective data collection,
12 looking at the group of masses already analyzed,
13 sliding the threshold to look at different
14 sensitivities and specificities, and then assigning a
15 threshold to the prospective data collection. Because
16 I think that the threshold was established after the
17 fact and after the analysis, the threshold for the IR
18 numbers.

19 Well, it was from multiple lesion types,
20 and it wasn't specifically for masses. But I think
21 that going back and looking at data you've already
22 accrued and the hard work you've done, and look at

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1 where that threshold may be -- it may be different for
2 masses, as Dr. Hooley mentioned, and then determine
3 that, and make a plan moving forward to gather more
4 data to test that hypothesis.

5 CHAIRMAN MEHTA: Yes, go ahead, Alicia.

6 DR. TOLEDANO: If that recommendation to
7 develop a new threshold based on the indication solely
8 for masses, and using the data available to you, is
9 taken, one suggestion would be to do this with higher
10 power. Your current power for establishing the
11 minimum sensitivity with that threshold is power of 75
12 percent. So you might want to be more certain that
13 you would achieve the necessary sensitivity, perhaps
14 a power of 80 percent, perhaps a power of 90 percent.

15 CHAIRMAN MEHTA: Any further discussion on
16 this point? Any comments from the Panel members?

17 (No response.)

18 You can go to 1(b) then.

19 DR. PHILLIPS: "1(b) The additional data
20 in Amendment 5 consists of 78 masses. Are these
21 additional data by themselves sufficient for the
22 assessment of determination of effectiveness of the

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1 BCS 2100?"

2 CHAIRMAN MEHTA: Should we start from the
3 other end of the table this time? Any views from
4 anyone? Prabhakar?

5 DR. TRIPURANENI: I think a simple answer
6 is no. We just don't have enough number of patients
7 to actually confirm the data. I think that Dr. Sacks
8 has quite nicely shown that the variability is quite
9 large. I don't think that by just looking at this
10 small number of patients, compared to the bigger
11 picture, that one can draw a conclusion on the
12 effectiveness.

13 CHAIRMAN MEHTA: Alicia?

14 DR. TOLEDANO: Given that it is too small
15 and that you would need more patients, we should also
16 consider one of the points raised by Dr. Sacks, that
17 the key measure of diagnostic accuracy here is
18 specificity, establishing specificity.

19 So we don't need to worry about area under
20 the ROC curve. That blends sensitivity and
21 specificity. We're not concerned about sensitivity
22 too much. We're not concerned about AUC too much.

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1 We're concerned about, can you be specific?

2 So when you consider how many patients you
3 need data on, look at adequate power to establish
4 specificity. That's just a comment.

5 CHAIRMAN MEHTA: Any other comments on
6 1(b)?

7 (No response.)

8 Hearing none, we can move on to 1(c).

9 DR. PHILLIPS: "1(c) When combined,
10 Amendment 4 provides 84 percent -- in other words, 412
11 -- of the masses, and Amendment 5 provides 16 percent,
12 or 78 of the masses. What is the validity of
13 combining these data to assess and determine the
14 effectiveness of the BCS 2100?"

15 CHAIRMAN MEHTA: Anyone? I'll put in my
16 two cents, and then we'll have Alicia give the
17 statistical version of this.

18 (Laughter.)

19 I don't think you can make a yes by
20 combining two noes.

21 Alicia?

22 DR. TOLEDANO: Not valid.

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1 CHAIRMAN MEHTA: Okay, we can move to
2 Question 2 then.

3 DR. PHILLIPS: Question 2 is the same
4 series of questions but related to safety. "2(a) The
5 data in Amendment 4 were selected retrospectively from
6 the original PMA dataset, albeit based on lesion-type
7 analyses that were prospectively planned for it in the
8 clinical trial protocol. Are the data from Amendment
9 4 applicable for the assessment and determination of
10 safety of the BCS 2100?"

11 CHAIRMAN MEHTA: Perhaps we could have our
12 radiology experts comment on the safety aspect of this
13 device.

14 DR. CONANT: Well, I'm still concerned
15 about the false negatives certainly in terms of safety
16 and the false sense of security potentially for
17 lesions read as negative. I don't think I have the
18 data to really base that on right now from the limited
19 numbers. So I'm not sure that I can really address
20 safety at this point.

21 I mean, no adverse effects, that's really
22 great, but I'm more concerned about prolonged followup

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1 of malignant lesions, delaying diagnosis. I think
2 with larger numbers, there is potential for even --
3 well, I'm not sure what would happen with larger
4 numbers.

5 CHAIRMAN MEHTA: Well, I guess the safety
6 question has three components to it: the false
7 negative component, the false positive component, and
8 the actual physical safety of the device itself.

9 I suspect in this particular component, if
10 we start by limiting to physical safety, we might get
11 to a quick answer, and then address the other aspects
12 of it.

13 Any concerns about physical safety or
14 performance safety, mechanical safety of the device?

15 (No response.)

16 So the false negatives appear to be a
17 concern. There is a question about false positives
18 later on. We can defer to later.

19 Do other people on the Panel have concerns
20 about the false negative rate and its implications for
21 patients? Please go ahead and state your concerns, if
22 you have them.

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1 DR. GENANT: Well, to the extent that we
2 don't feel that we have compelling data for the
3 overall effectiveness of the device, and that false
4 negatives are a concern, and this carries a safety
5 implication, I have concerns.

6 CHAIRMAN MEHTA: Alicia, you were
7 indicating some concerns?

8 DR. TOLEDANO: Yes, I'm concerned. I
9 think we need sufficient data to establish high
10 sensitivity, so that we have a very little, tiny false
11 negative rate, and we need to establish, also, that
12 the recommendation for short-term interval followup is
13 an appropriate recommendation to preserve patient
14 safety.

15 CHAIRMAN MEHTA: Let's move to Question 3.

16 DR. PHILLIPS: Question 3 or do you want
17 to do (b) and (c)? It's repetitive of the earlier
18 one.

19 "(b) the additional data in Amendment 5
20 consists of 78 masses. Are these additional data by
21 themselves sufficient for the assessment and
22 determination of safety of the BCS 2100?"

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1 CHAIRMAN MEHTA: I think I can probably
2 speak for the Panel -- you can correct me if I'm wrong
3 -- that we have probably addressed (a), (b), and (c)
4 collectively in the discussion for Question 2. Unless
5 the Panel feels differently, we can skip to Question
6 3.

7 DR. PHILLIPS: Fine, we'll go to three.
8 No. 3: "Please discuss whether safety and
9 effectiveness has been established. As part of this,
10 please discuss the risk/benefit tradeoff whereby a
11 false negative results in a six-month delay of cancer
12 diagnosis and a true negative obviates a biopsy that
13 would otherwise turn out to be benign."

14 DR. HOOLEY: I think there's a high
15 risk/benefit tradeoff with the amount of false
16 positives. I think that the patients, about 80
17 percent of the patients with a false positive will be
18 subjected to another test, a little more emotional
19 turmoil during the time of their diagnosis. I think
20 that that is a concern. I think that that is fairly
21 high, and it is also going to add an expense.

22 CHAIRMAN MEHTA: One of the implicit

1 suggestions in this question is that a false negative
2 results in only a six-month delay in cancer diagnosis.
3 Do we have data to support this? And is the Panel
4 concerned about the fact that we haven't seen any data
5 to suggest that it's only six months and not longer?
6 Because we don't really know in clinical practice what
7 that is going to be. It may be six months for most
8 patients. We don't really know that.

9 MS. PETERS: Well, patients can tend to
10 fall between cracks in terms of doing their own
11 outreach for their health care. They can fall between
12 the cracks. So it could be longer, I would think.

13 CHAIRMAN MEHTA: Go ahead, Alicia.

14 DR. TOLEDANO: I also don't know the
15 natural history of DCIS to establish if a six-month
16 interval is appropriate. Not being a radiologist, I
17 asked some of my respected radiology colleagues, and
18 I was told, no, we don't really know the natural
19 history of DCIS. So I'm concerned about that.

20 I'm concerned about the recommendation for
21 six months in the first place, and then I'm concerned
22 about what happens with that recommendation in

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1 practice.

2 DR. HOOLEY: By convention, we usually use
3 a two-year followup in the mammography to determine
4 benignity of a suspected lesion. There's really no
5 clear data on ultrasound followup, but generally we
6 use about two, possibly three, years.

7 CHAIRMAN MEHTA: Prabhakar, as a physician
8 treating breast cancer patients, would you be
9 concerned about a six-month delay in diagnosis if,
10 indeed, that was the case for every patient?

11 DR. TRIPURANENI: I think if you look at
12 the bigger picture of all the breast cancer patients
13 that are diagnosed, I think there is quite a
14 variation. But in DCIS patients waiting for six
15 months is probably not deleterious, as opposed to
16 somebody who has a small infiltrating cancer that
17 actually could blossom out in the next six months.

18 I think that's a rather difficult
19 question, and I suspect if the device were to be
20 approved and used in the clinic routinely, you do
21 probably see a spectrum of the patients from one end
22 to the other end.

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1 CHAIRMAN MEHTA: So perhaps we can
2 summarize the answer to that question by stating that,
3 if, indeed, it were a DCIS, and if, indeed, the delay
4 were only six months, which we don't know a priori,
5 then we wouldn't be concerned. But if it were an
6 infiltrating ductal carcinoma or the delay were
7 significantly greater, which are real possibilities in
8 the clinical world, then we would be concerned.

9 Go to Question 4. I'm sorry, one more
10 point, Alicia.

11 DR. TOLEDANO: I did want to say that I
12 think that the data does suggest efficacy, and very
13 strongly suggest safety and suggest efficacy. So it
14 is not, in my mind, a complete wash. There is a
15 suggestion that the device is effective.

16 CHAIRMAN MEHTA: We can go to Question 4.

17 DR. PHILLIPS: "Is the proposed labeling
18 adequate to ensure safe and effective use of the BCS
19 2100? Please include in your discussion the following
20 specific items:

21 "(a) Given that only two of the 105
22 cancers were smaller than 5 millimeters, should the

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1 labeling specify a lower size limit for an eligible
2 mammographic mass? If so, what size limit?

3 "(b) Should the labeling address lesion
4 depth? If so, in what way?"

5 CHAIRMAN MEHTA: Let's take Question 4(a)
6 first. Who on the Panel would like to try and deal
7 with this question? Geoff, go ahead.

8 DR. IBBOTT: I will comment, but I'm sure
9 Alicia should comment as well here.

10 (Laughter.)

11 And it's the same answer as before. There
12 isn't enough data here to say anything about such
13 small lesions. So, no, I don't think -- or, rather,
14 I suppose the answer is, yes, it should specify a
15 lower limit that is somewhere above the point where
16 there are significant numbers of examinations.

17 CHAIRMAN MEHTA: Other opinions on this?

18 DR. CONANT: Not getting into size and
19 depth so much, but more sort of general use of it, I
20 hate to keep harping on ultrasound, but I would
21 specify that this would be to be considered after
22 completion of conventional imaging, which in this day

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1 and age means mammography and ultrasound.

2 There were too many cases excluded and too
3 many cases imaged that didn't seem to get ultrasound
4 until the fact, and I think that's a very confusing
5 part of this data. So that I think that needs to be
6 incorporated, that a mass is a mass, and it's
7 determined solid by ultrasound. It's not an
8 asymmetric density. It's not seen by ultrasound, but
9 it, indeed, is there.

10 CHAIRMAN MEHTA: Can we get a statistical
11 answer on two out of 105, Alicia?

12 DR. TOLEDANO: I think Geoff already gave
13 us the statistical answer on two out of 105.

14 CHAIRMAN MEHTA: Okay. Let's talk about
15 lesion depth then. Are there concerns? If so, in
16 what way?

17 DR. HOOLEY: I have concerns about lesion
18 depth. First of all, I think in a very large woman
19 with pendulous breasts, I think imaging the patient in
20 the prone positioning and imaging on the CTI table and
21 imaging her upright with mammography would produce a
22 large degree of discrepancy and introduce a lot of

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1 variability. So I think that needs to be addressed.

2 I am also surprised that depth was not
3 thought to be a considerable factor, based on the
4 design of the table. I know with my experience with
5 stereotactic biopsy that lesions that are very far
6 posterior or in the axillary tail cannot be imaged,
7 and I would imagine that these would be excluded by
8 the thermal imaging.

9 Also, women with very, very small breasts,
10 there's just not enough tissue going through the
11 aperture of the table to be imaged.

12 DR. CONANT: Have you found that an issue,
13 the small breasts away from the detector, or does that
14 make a difference at all? Because the distance of the
15 pad is fairly substantial. I think distance to --

16 DR. CALLAHAN: Is this a question?

17 CHAIRMAN MEHTA: Yes, it's a question.

18 DR. CONANT: Yes.

19 (Laughter.)

20 CHAIRMAN MEHTA: Please, if you could
21 answer it?

22 DR. CALLAHAN: We did look originally at

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1 depth, and that was assessed mammographically in our
2 first, original study. We had the mammographers
3 quantify depth as superficial, intermediate, or deep,
4 and didn't see a degradation in performance.

5 We have subsequently looked at -- we've
6 done a study of normals, not patients with going to
7 biopsy, but looking at issues of physiological changes
8 based on breast size and age, and we have not found
9 that small-breasted or large-breasted women, that
10 those pose particular difficulties with just the basic
11 imaging process.

12 DR. PARISKY: Do you want me to comment on
13 depth?

14 CHAIRMAN MEHTA: Yes, please, go ahead.

15 DR. PARISKY: Because of the references
16 you made to stereotactic and lesion location, let me
17 remind you we're not measuring the lesion directly.
18 Let me remind you that the anatomy of the breast is
19 likely looking at venous drainage, which in the breast
20 goes to the surface.

21 So you are looking at lesions that, if
22 malignant, their environment is affected by, in all

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1 likelihood, increased capillary flow, and that
2 relatively coming to the surface. So we're not in
3 terms of depth, while we did look at depth and found
4 no degradation based on depth, what we really are
5 looking at is warmer blood or greater volume of warmer
6 blood in a cancer milieu coming to the surface.

7 I apologize for not saying that upfront
8 during the comments about angiogenesis and such. I
9 thought that that was fairly common knowledge.

10 DR. CONANT: But I would think that a very
11 large, pendulous breast with a small posterior central
12 chest-wall lesion would not bring blood flow so much
13 to the surface?

14 DR. PARISKY: That would be speculative
15 because we did not encounter a false negative invasive
16 cancer in the hundred-and-some-odd that we looked at,
17 of all the distributions, and I apologize.

18 DR. CONANT: No, that's the way they came.

19 DR. PARISKY: That's the way they came,
20 and we got them all.

21 DR. CONANT: We have a lot of big-breasted
22 women in our practice actually. Do you find that

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1 where you all are at the sites?

2 (Laughter.)

3 I mean, but it's a big issue. So I'm just
4 wondering, are there women who can't fit in there?

5 DR. PARISKY: We had no exclusion, at
6 least in my center we had no exclusion, and I had both
7 the County Hospital with a large Latino population --
8 I'm not making any references, but I would think that
9 in some instances -- we had a large Latino; we had a
10 relatively large African-American and Caucasian
11 population distributed along Los Angeles County, and
12 we did not have any of those patients rejected because
13 of breast size.

14 DR. CONANT: Great.

15 CHAIRMAN MEHTA: So I think the consensus
16 Panel answer for 4(a) would be that we feel there
17 aren't enough data and, therefore, we are concerned
18 about making categorical recommendations for all
19 sizes, and that we simply don't know enough about
20 lesion depth to give an appropriate or an erudite
21 answer to that question.

22 So we can move on to Question 5.

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1 DR. PHILLIPS: No. 5: "Should the
2 labeling be revised to address any potential
3 psychological impact of a positive mammogram followed
4 by a positive BCS 2100 result on a woman who does not,
5 in fact, have cancer; i.e., false positive?"

6 CHAIRMAN MEHTA: Maybe we can have Ms.
7 Peters get us started on this question first.

8 MS. PETERS: Well, this is always a scary
9 thing for women. Having something that's going to or
10 having a person having the time to reassure the
11 patient that this does not necessarily mean that they
12 do have cancer, but a lot of times time is precious
13 and that isn't taken, so that patients can feel a lot
14 of anxiety in the waiting and the not knowing, and
15 their own assumptions, especially if they aren't into
16 asking questions of health care providers about what
17 is going on and they just take the word of the
18 provider at face value and go home with their fears
19 and anxiety.

20 I don't know how labeling that could help,
21 except that the person who is using the instrument or
22 making the decisions needs to have the time to give

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1 adequate information to their client patient.

2 CHAIRMAN MEHTA: Further comments from the
3 Panel? Prabhakar?

4 DR. TRIPURANENI: No test is perfect.
5 Every test has some false positives and false
6 negatives. I think in this particular group of
7 patients that a positive mammogram, presumably
8 ultrasound is such that today they probably would have
9 gone for a biopsy anyway, but for this test, and
10 presumably the test will save some patients going to
11 biopsy.

12 So I'm not too concerned about this
13 question. I think that is the fact of life and
14 medicine is such that there are going to be patients
15 that will require biopsy, as statistics have shown
16 over and over again. We do lots of biopsies to
17 absolutely exclude the cancer.

18 It's the cancer that you miss, the
19 importance that could have on the life is more
20 worrisome than this.

21 CHAIRMAN MEHTA: Does anyone else have
22 further comments on this?

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1 (No response.)

2 I do have a point I would like the Panel
3 to think about a little bit. One of the things that
4 we have heard is that in this study and in real-life
5 practice there are many women that have abnormalities
6 that are identified and are thought not to be highly
7 suspicious, and a recommendation is actually made
8 based on available published information not to biopsy
9 these.

10 Yet, a significant proportion of these
11 women demand biopsies. As we heard in the context of
12 this study, these biopsies get done primarily to
13 alleviate anxiety and potentially because of the
14 litigious medical climate that some of us live in.

15 As a consequence, this device, too, may
16 face that same scenario, that this device might
17 identify women who could potentially be saved a
18 biopsy; yet, because of a considerable level of
19 anxiety amongst these women, they may decide not to
20 follow that advice and go on to biopsy and, therefore,
21 reduce potentially the proportion of women who did not
22 actually go on to biopsy.

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1 So there is some potential psychological
2 impact. Is it enough to require labeling information?
3 Is it enough to actually do a study on what are the
4 psychological consequences of this?

5 Go ahead, Alicia.

6 DR. TOLEDANO: No.

7 CHAIRMAN MEHTA: Does anyone else feel
8 different?

9 (No response.)

10 Okay, then we have the answer to that
11 question.

12 We'll move on to No. 6.

13 DR. PHILLIPS: No. 6: "Do the above or
14 any other issues (a) require resolution before
15 approval of the PMA; (b) suggest the need for a post-
16 marketing study?"

17 CHAIRMAN MEHTA: Well, this is a good
18 opportunity for the Panel to think about other issues
19 that need resolution. So, as we have been thinking
20 through this and discussing this, we have brought up
21 many, many issues. Are there other issues? For
22 example, there were some questions about

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1 reproducibility. There were issues about phantom
2 studies. Do you wish to bring these up as issues that
3 should be resolved prior to the approval of the PMA?

4 DR. GENANT: Well, I think that we
5 certainly raised a number of really critical issues
6 that need to be addressed and resolved. It is not
7 clear that they can be resolved within the context of
8 the clinical data that currently exists, but I think
9 we need some answers to those issues before
10 recommendation for approval.

11 CHAIRMAN MEHTA: Well, if you could at
12 least even highlight some of those areas, that would
13 be useful for the FDA, I think. So maybe we can give
14 them a list of the concerns and areas that we think
15 should probably be considered for resolution.

16 DR. GENANT: Well, two of the areas that
17 I had raised before deal with reproducibility. I
18 think we need information about the readers and their
19 capability to reproduce the results, and we need
20 information about, and some feeling of security about,
21 the stability of the instrument and ways to assess its
22 stability. I think we also need information along

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1 this line with regard to repeat measurements on the
2 same individual.

3 CHAIRMAN MEHTA: Geoff, any QA issues?

4 DR. IBBOTT: Yes, I would repeat my
5 request that there be some sort of quantitative QA
6 procedures to ensure that, as has just been mentioned,
7 the instrument does work reproducibly one day to the
8 next, one patient to the next.

9 Oh, and I'm still concerned about the
10 equilibration. Not every clinic is going to maintain
11 the room temperature between 67 and 73. I think there
12 should be some data to see what effect there might be
13 of equilibrating the patient at 75 or 77 or some other
14 temperature.

15 And my third comment would be the
16 establishment of the threshold for the IOS. I think
17 that is a serious concern.

18 CHAIRMAN MEHTA: Dr. Hooley, you had IOS
19 special concerns as well. Do you want to expand on
20 that a little?

21 DR. HOOLEY: Well, I think that we would
22 benefit by having a direct comparison of a control of

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1 masses and determining the IOS threshold based on just
2 masses, since that's what we want to target the use of
3 the CTI for, just masses. So that the threshold
4 should be focused on just masses, not a wide variety
5 of lesions.

6 CHAIRMAN MEHTA: Go ahead, Alicia.

7 DR. TOLEDANO: I would like to see
8 effectiveness established in a target population that
9 is directly relevant to the proposed indications for
10 use, taking into account clinical flow of the
11 patients.

12 DR. CONANT: That's my biggest concern, is
13 to really be very strict about the inclusion criteria
14 and where imaging fits in with ultrasound, and, also,
15 that for inclusion the BIRADS categories should really
16 be limited to those recommending biopsy. Now I know
17 that others go, but I don't think those are the ones
18 that should be included in this prospective trial.
19 They should really be 4s and 5s.

20 DR. TOLEDANO: I'm going to argue a little
21 bit against Dr. Conant. Sorry, Emily.

22 Because we know that recommendation for

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1 biopsy does occur in women who are not BIRADS 4 and 5,
2 I think we need to say, if the indication for use is
3 recommended for biopsy, then you include recommended
4 for biopsy. If the indications for use were BIRADS 4
5 or 5, then that's what you would include. But since
6 the indication for use is recommended for biopsy, I'm
7 fine with any BIRADS category as long as they have
8 been recommended for biopsy.

9 DR. CONANT: So then you will be including
10 patients with palpable lesions that have areas
11 possibly not seen on mammography, that it has to be
12 clarified that the lesion has to be localized by
13 ultrasound and then labeled by whomever, so that the
14 readers can go forward with that.

15 DR. TOLEDANO: Right. The current
16 indication is mammographically-something mass. It's
17 seen mammographically, or whatever it is. So it is in
18 the indication for use.

19 DR. CONANT: Well, then that has to be
20 clarified, whether it is just mammographic masses or
21 things going to biopsy, which include palpable lesions
22 as well. So just a clarification of that.

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1 DR. TOLEDANO: I agree.

2 CHAIRMAN MEHTA: Any other issues that the
3 Panel feels require resolution?

4 (No response.)

5 Six (b). Sorry, go ahead. I didn't mean
6 to cut you off.

7 DR. TOLEDANO: So now that we have
8 discussed what issues might require resolution, could
9 I note that it might be possible to resolve some of
10 those issues without additional formal clinical trial
11 data? So we should be looking very carefully at which
12 issues can be resolved without additional clinical
13 trial data and which issues require additional
14 clinical trial data. That is just a recommendation.

15 CHAIRMAN MEHTA: Thank you.

16 Six (b) "Do the above or any other issues
17 suggest the need for a post-market study?"

18 DR. TOLEDANO: Yes.

19 CHAIRMAN MEHTA: Any other thoughts?

20 MS. BROGDON: Could I ask Dr. Toledano to
21 clarify her answer?

22 (Laughter.)

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1 DR. TOLEDANO: I guess I should clarify
2 that, if it turns out that this company has to go back
3 and do a whole other clinical trial for their pre-
4 market approval, then no. But if it turns out that we
5 are able to use what we know from the existing
6 clinical data and from physics and from experience to
7 posit answers that are good enough to allow approval,
8 then we do need to see the actual empirical data, the
9 clinical data, that bears that out in a post-market
10 sense.

11 So does that help?

12 MS. BROGDON: Thank you.

13 CHAIRMAN MEHTA: Alicia, I'm going to ask
14 you to keep on talking a little bit. So you've
15 obviously made two suggestions. One is, assuming that
16 there is a PMA approval, that you would suggest a
17 post-market study, and that if there isn't a PMA
18 approval, then obviously the post-market study
19 question is a moot question because the idea would be
20 that the study would be repeated.

21 Assuming that there is the need for a
22 post-market study, do you have a suggestion what that

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1 should be?

2 DR. TOLEDANO: This is like "Study Design
3 in 30 Seconds," right? Great.

4 Well, you start out looking at your
5 indications for use, and perhaps before you design
6 your post-market study or before you -- actually, it's
7 post-market would come after approval, right?

8 CHAIRMAN MEHTA: Correct.

9 DR. TOLEDANO: Okay, so that's it. You're
10 stuck with the indications for use. You can't change
11 them. You have to use the ones that exist.

12 You look at the indications for use. You
13 define a target population. You enroll that
14 population.

15 You determine, what are you trying to
16 establish for the effectiveness and safety? We have
17 discussed safety means an incredibly high sensitivity.
18 We've discussed effectiveness means a non-zero
19 specificity, because all these women have already been
20 recommended for biopsy.

21 You design up a study that is either based
22 on the local reads, the real-time reads, like what Dr.

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1 Hughes is doing in practice, possibly supplemented by
2 a secondary reader study that would allow you to look
3 at inter-reader variability, possibly supplemented by
4 studies that would allow you to look at intra-reader
5 variability.

6 Use acceptable methods to design that
7 study. Give it adequate power. Analyze them with
8 methods for multiple-reader, multiple-modality,
9 diagnostic accuracy data, and prove the indications,
10 so much easier said than done.

11 I'll entertain a question.

12 DR. PARISKY: Would you be interested in
13 us providing invasive and non-invasive malignancy
14 because the results --

15 CHAIRMAN MEHTA: Please come up to the
16 microphone.

17 DR. PARISKY: I appreciate all your
18 comments.

19 How about also dividing, subsetting the
20 masses we're going to look at into pathologically
21 invasive and non-invasive? Because I think it has
22 clinical implications.

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1 DR. TOLEDANO: I think it depends on what
2 you would like to say in the labeling. If you would
3 like --

4 DR. PARISKY: Yes, because you can't
5 predict --

6 DR. TOLEDANO: Okay, so you know?

7 DR. PARISKY: Yes.

8 DR. TOLEDANO: Right, you can't predict
9 it.

10 DR. CONANT: You don't know that upfront.

11 DR. PARISKY: Huh?

12 DR. CONANT: You don't know that
13 upfront --

14 DR. PARISKY: You don't know that upfront,
15 but --

16 DR. CONANT: -- when you're scanning the
17 patient.

18 DR. PARISKY: You don't know that upfront,
19 but, I mean, I think the numbers here would have shown
20 if we had divided them upfront between invasive and
21 non-invasive. There would have been a much stronger
22 argument.

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1 DR. TOLEDANO: Right. So you can't say
2 that in terms of designing up a trial, but what you
3 can say is that you would be going for the possibility
4 of putting something in the labeling that says:
5 Having a false negative result is associated, was
6 associated with non-invasive cancer in our study.

7 DR. PARISKY: That's what I'm getting at.
8 Thank you.

9 DR. TOLEDANO: Okay.

10 CHAIRMAN MEHTA: So you could have a false
11 negative for invasive malignancy. You could have a
12 rate for false malignancy when there's a malignancy
13 which would be a special rate that you don't want to
14 exceed.

15 Go ahead.

16 DR. GENANT: I think that we have raised
17 enough serious issues with regard to the validity of
18 the data in the various cuts that have been taken at
19 the data, such that I don't think that it is
20 appropriate to recommend a post-approval study at this
21 point, because I believe that it will require actually
22 new data to be obtained.

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1 Basically, we saw that the equipment was
2 changed to some extent during the study. We also had
3 various amendments that impacted the validity of the
4 analyses. We have considerable concerns about the
5 manner in which the data were analyzed relative to
6 clinical practice and whether it is really relevant,
7 and problems with the matter of the imaging
8 interpretation.

9 I think that, in sum, that we simply don't
10 enough have a sufficiently high level of comfort with
11 the documentation of the efficacy and safety to be
12 making recommendations with regard to a post-approval
13 study.

14 CHAIRMAN MEHTA: Okay. Alicia?

15 DR. TOLEDANO: I think that whether the
16 study should be pre-market approval or post-market
17 approval depends in large part on the extent to which
18 we expect results from such a study to differ from the
19 current results.

20 CHAIRMAN MEHTA: Okay. Seeing no further
21 comments, I think we are coming to the end of the
22 Panel discussion questions.

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1 We have time for a short break to let
2 people use the bathrooms and things of that sort.
3 Please know that we are still in open Committee, so
4 don't discuss things outside this room.

5 Let's plan on meeting back, say, in ten
6 minutes, and then we will begin the open public
7 hearing at that time.

8 (Whereupon, the foregoing matter went off
9 the record at 2:56 p.m. and went back on the record at
10 3:08 p.m.)

11 CHAIRMAN MEHTA: Are there any open public
12 members, speakers, who want to address the Panel?

13 (No response.)

14 Seeing none, before we move to the Panel
15 recommendations and vote, is there anything additional
16 the FDA would like to address?

17 DR. PHILLIPS: Yes. Somebody asked me on
18 the way out how long it would take to get a cab here
19 when you're over with.

20 (Laughter.)

21 I spoke to the desk. They said it could
22 take as long as 30 minutes. If you talk to Tom, who

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1 is the gentleman in the white shirt behind the desk,
2 he will help you get something expeditiously.

3 CHAIRMAN MEHTA: A very important piece of
4 information. Thank you.

5 Is there anything else the sponsor would
6 like to address to the Panel at this point?

7 DR. PARISKY: As an academic and
8 practicing radiologist who is quite familiar with
9 adjunctive testing in breast cancer issues, I would
10 like to remind you that the thresholds that you set
11 today for safety in terms of false negative cannot be
12 met by any single existing modality, nor do I believe
13 it can ever be met by any future modality, because the
14 standard you have set is so high.

15 For example, PET scan, meta-analysis shows
16 5 to 6 percent false negative rate. MRI, if it's
17 DCIS, it's upwards of 30-40 percent false negative
18 rate. If it's invasive cancer, it's 10-15 percent
19 false negative rate.

20 Let's take another. Let's take
21 ultrasound, which we have talked about. You know the
22 false negative rate for that. It is well below the

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1 so-called safety standard which you have set today.

2 So in your consideration, another aside,
3 in terms of exclusion of data, the ATL presentation of
4 their ultrasound PMA started with 1,200 subjects, then
5 excluded cysts. They went to 400. Mr. Monahan will
6 verify that. I believe those were the numbers. There
7 did not seem to be an issue about exclusion.

8 You've taken it upon yourselves to set a
9 standard today that will only allow the existing
10 technologies, because they've already met approval, to
11 persist and may very well have pulled the rug out for
12 any other innovative technologies by setting that high
13 a standard for false negative.

14 Nevertheless, I thank you for your time.
15 I thank you for the exchanges and the ideas and the
16 comments you have made. For myself, for a learning
17 experience, and for my fellow investigators, thank
18 you.

19 MR. BRENNAN: Just a couple of comments
20 myself, as the president of this company. We have
21 worked very closely over the past couple of years with
22 FDA. There was quite a bit of discussion and

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1 agreement along the way regarding all the amendments,
2 the confirmatory studies, the confirmatory plan.

3 I am a little confused today, and you need
4 to know that. You are looking at a product that is
5 non-invasive, painless, safe. It is adjunctive. It
6 is categorized as a product that will be under control
7 of the radiologist as an adjunctive device.

8 It shows extreme promise with the
9 sensitivity results. This gentleman is concerned
10 about missing cancers. We can prove that our
11 databases show at about 99.3 percent sensitivity and
12 about a 19.2 percent increase in specificity over
13 current biopsy methods.

14 Now I agree with Dr. Parisky that you need
15 to consider the decision you are making today. This
16 is new, innovative technology that has only one place
17 to go over the next five-to-ten-year period.

18 If I go back 20 years ago and I look at a
19 CT scanner from 1982, and I look at a CT scanner today
20 in 2002, I say it has changed quite a bit, and there
21 was dissension back then.

22 But that type of technology was allowed to

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1 enter into the radiology community. Through the
2 product maturation process controlled by radiology,
3 you brought it to where it is today.

4 I am just very concerned, and I share the
5 same sentiment that Dr. Parisky did, and I thank you.

6 CHAIRMAN MEHTA: Any further comments from
7 the sponsor? It is an opportunity to tell us anything
8 additional that you might want to at this time.

9 (No response.)

10 Mr. Doyle will address the Panel.

11 DR. PHILLIPS: We will now move to the
12 Panel's recommendations concerning PMA P010035.

13 The medical device amendments to the
14 Federal Food, Drug, and Cosmetic Act, referred to as
15 "the Act," as amended by the Safe Medical Devices Act
16 of 1990, allows the Food and Drug Administration to
17 obtain a recommendation from an expert advisory panel
18 on designated medical device pre-market approval
19 applications, PMAs as they're often called, that are
20 filed with the agency.

21 The PMA must stand on its own merits, and
22 your recommendation must be supported by safety and

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1 effectiveness data in the application or by applicable
2 publicly-available information.

3 Safety is defined in this case, in the
4 Act, as reasonable assurance based on valid scientific
5 evidence that the probable benefits to health under
6 conditions of intended use outweigh any probable
7 risks.

8 And effectiveness is defined as reasonable
9 assurance that in a significant portion of the
10 population the use of the device for its intended uses
11 and conditions of use, when labeled, will provide
12 clinically-significant results.

13 Now your recommendation options for the
14 vote are as follows, and there are three of these:

15 Approvable. That's straight approval if
16 there are no conditions attached.

17 Then approvable with conditions. This
18 Panel may recommend that the PMA may be found
19 approvable subject to specified conditions, and these
20 include physician or patient education, labeling
21 changes, or further analysis of existing data. Prior
22 to voting, all of the conditions should be discussed

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1 by the Panel.

2 And the third, not approvable. The Panel
3 may recommend that the PMA is not approvable if the
4 data do not provide a reasonable assurance that the
5 device is safe or if a reasonable assurance has not
6 been given that the device is effective under the
7 conditions of use prescribed, recommended, or
8 suggested in the proposed labeling.

9 If you should vote for non-approvable, the
10 Panel will have to indicate what steps the sponsor may
11 take to make the device approvable.

12 CHAIRMAN MEHTA: Would anyone on the Panel
13 like to make a motion?

14 DR. TOLEDANO: I'll do it. I move for
15 approvable subject to specified conditions. Do you
16 want the conditions?

17 CHAIRMAN MEHTA: Is there a second?

18 (Motion seconded.)

19 CHAIRMAN MEHTA: Is there discussion of
20 the main motion?

21 DR. CONANT: I'm still concerned that, not
22 that there hasn't been some wonderful data and

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1 suggestions that this, indeed, will be helpful to some
2 women, but I'm not sure that I'm at the point with the
3 data presented that I can establish that.

4 I think there have been too many
5 exclusions, too narrow a group, too many cases that I
6 feel didn't follow a regular clinical flow. So that
7 the amount of data I have right now, small number of
8 cancers and very limited patients, I'm not yet
9 comfortable with in terms of the effectiveness.

10 DR. GENANT: I would like to echo that.
11 I also share some of the concerns with regard to the
12 data that we have to analyze and feel that there is
13 insufficient information and support for effectiveness
14 to approve, to vote for approval.

15 CHAIRMAN MEHTA: Alicia?

16 DR. TOLEDANO: So I would subset that out
17 because it is not straight approval, and we have been
18 told that the specified conditions include further
19 analysis of existing data. We have been told that our
20 recommendation can take into account applicable
21 publicly-available information in order to show
22 effectiveness.

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1 My opinion is, my very thoughtfully-
2 considered opinion is that, with reanalysis of the
3 current data in an exploratory manner, and with
4 knowledge that already exists, we can establish a high
5 probability of effectiveness for this device.

6 So that's why I make the recommendation of
7 approval subject to conditions.

8 CHAIRMAN MEHTA: Is there any other
9 discussion on the main motion?

10 (No response.)

11 If not, let's proceed to vote on the main
12 motion, which was approvable with conditions.

13 All those members in favor of the motion
14 for approval with conditions raise your hands, please.

15 (Show of hands.)

16 MR. DOYLE: Three.

17 CHAIRMAN MEHTA: For the record, we count
18 three.

19 DR. CONANT: Can we try that again after
20 we talk about the conditions?

21 MR. DOYLE: No.

22 DR. CONANT: Okay. I just thought I would

1 ask.

2 DR. TOLEDANO: May I ask you a question of
3 clarification?

4 CHAIRMAN MEHTA: Yes.

5 DR. TOLEDANO: Okay. In previous meetings
6 when we have recommended approval subject to specified
7 conditions, those specified conditions have reflected
8 only changes in the labeling.

9 My understanding from what Mr. Doyle has
10 just stated is that the conditions can include further
11 analysis of existing data, and I just wanted to
12 confirm that.

13 MR. DOYLE: That's correct.

14 CHAIRMAN MEHTA: I think that finishes the
15 vote.

16 So is there anybody else who wants to make
17 a different motion?

18 I was assuming that those who didn't raise
19 their hands were against, but we need to clarify that
20 that's really the case.

21 So all those members who are not in favor
22 of the motion please raise your hands.

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1 (Show of hands.)

2 MR. DOYLE: It's three to three. So you
3 can see there's a tie vote, so the Chair can now vote.

4 (The Chair votes no.)

5 MR. DOYLE: Now I guess we need another
6 motion.

7 CHAIRMAN MEHTA: We need a second motion
8 at this point. Does anybody want to make a second
9 motion?

10 DR. HOOLEY: I motion that the PMA is not
11 approved because there are significant questions on
12 the efficacy of the study and how it was performed and
13 omissions in the clinical reality of how we work up
14 breast masses.

15 CHAIRMAN MEHTA: Is there a second?

16 DR. CONANT: I second.

17 CHAIRMAN MEHTA: Is there discussion on
18 this main motion? Go ahead, Alicia.

19 DR. TOLEDANO: May I discuss? One of the
20 most difficult things that I have learned over three
21 years being on this Panel, and previous experience
22 with the Panel, is the difficulty of separating out

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1 the effectiveness of a device from what happens once
2 the device is released into market.

3 I think that, as we make our motions and
4 as we make our votes, we need to be considering the
5 device itself.

6 CHAIRMAN MEHTA: Any further discussion of
7 the main motion?

8 (No response.)

9 If not, let's proceed to vote on the main
10 motion.

11 All those members in favor of the motion,
12 which is for disapproval raise your hands.

13 (Show of hands.)

14 That's three.

15 All those members against the motion for
16 disapproval please raise your hands.

17 (Show of hands.)

18 That's three.

19 I guess I get to cast the vote for
20 disapproval.

21 What we are going to do at this point is
22 we're going to poll all the voting members for the

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1 reasons for their recommendations, and we will also
2 ask the industry and consumer representatives for
3 their comments on the recommendations.

4 As part of your comments, specific
5 statements regarding what it would take to obtain
6 approval would be very useful at this point,
7 specifically for the FDA and the company.

8 So perhaps we can just start at one end of
9 the table and go around. Prabhakar, we can start at
10 your end.

11 DR. TRIPURANENI: The reason I was in
12 favor of approving with conditions is it is a
13 relatively non-invasive machine, hardly any
14 invasiveness. The patient comes in for ten minutes
15 and then gone.

16 I think it does have its utility, and I
17 think we have probably seen the first wave of these
18 things. I think as the data gets finetuned a little
19 more, as the clinicians get more experienced on the
20 machine, the company gains more experience, I think
21 they can finetune the data a little bit more. Perhaps
22 presumably in the real clinic at this point somebody

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1 will get a mammogram followed by ultrasound, and
2 probably this IR imaging at this point in time.

3 So, for all those reasons, even though the
4 data is not as clean as I would like to see, but, once
5 again, with all the vagaries of doing a clinical
6 trial, being a clinician, I was in favor of doing
7 this.

8 Now that officially the Panel has
9 recommended, once again I abide by the Panel's
10 majority disposition at this point in time that this
11 is not approvable, but I think my own bias is that the
12 second clinical trial, if there is going to be one --
13 I presume there will be one -- will be take the real-
14 life situation such as a mass, perhaps followed by
15 ultrasound and followed by this machine in some shape
16 or form, basically, directly going right to what to do
17 to get the final approval to be done.

18 Thank you.

19 CHAIRMAN MEHTA: Mr. Stern, do you have
20 comments?

21 MR. STERN: Had I been able to vote, I
22 would have voted with the doctor (referring to Dr.

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1 Tripuraneni). I believe that if some tens of
2 thousands of women in America can be spared the
3 psychological trauma, thanks to a negative reading
4 with the BCS 2100, I'm for the PMA.

5 CHAIRMAN MEHTA: Geoff?

6 DR. IBBOTT: Well, I voted in favor of the
7 first motion, but, like Dr. Tripuraneni, I'm quite
8 comfortable with the approval of the second motion.

9 I have concerns, as you know, about this
10 device. I am not concerned that any significant
11 number of women will be injured or hurt by this
12 device, but I do have the concerns that have been
13 mentioned about the psychological effects of the
14 results, but I also have the concerns that not very
15 many women will be positively impacted by the use of
16 the device. It is only a small number of women whose
17 course of therapy appears likely to be changed, based
18 on the data that have been presented.

19 As you know, I have concerns about the
20 physics of the device, the reproducibility from a
21 physics and engineering point of view, and quality
22 assurance issues, and the concern about the procedure

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1 that was used to set the threshold for the IOS. I
2 think that can be done better, perhaps with the
3 existing data, perhaps not, but it does need to be
4 done.

5 DR. HOOLEY: I think that a future study
6 should be a prospective study which better
7 characterizes the definition of mass, whether the mass
8 is just clinically detected by only mammography or
9 seen with ultrasound. I think the omission of
10 ultrasound in the characterization of masses is
11 significant, and I think that that should be addressed
12 in the future.

13 DR. CONANT: I certainly look forward to
14 this because I think it is a promising device, and I
15 certainly do want to cut down unnecessary biopsies.
16 However, I am concerned that a real-life population is
17 women with masses felt on exam, not seen
18 mammographically. I think in the case of the data
19 presented this was an artificial exclusion.

20 I think that the power with a prospective
21 study will be very convincing, and I look forward to
22 that data. So I am very optimistic, but I am

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1 concerned about implementation in real life, and if
2 this was to go out now, what it could be used for,
3 masses, and that that is not as defined as it could be
4 and I think should be, what a mass is.

5 I am also very interested in refining
6 threshold for the IOS based on masses alone for this
7 indication, rather than on all different lesion types,
8 and moving forward to test that as a hypothesis.

9 The talk about sensitivity again confuses
10 me because the sensitivity is 100 because our
11 population is incoming with mammographic masses.
12 Again, that is not reality. It goes back to the
13 definition of a mass, and a mass on an exam, a
14 physical exam, and I think that is a very important
15 population to address. So the sensitivity part, I'm
16 really looking forward to the improvement in your
17 specificity that I think you may show us in the
18 future.

19 Oh, the reproducibility of the exam which
20 would be shown, hopefully, by inter- and intra-reader
21 studies, I look forward to that data.

22 CHAIRMAN MEHTA: I think the sponsor has

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1 done an excellent job of building what looks like an
2 exciting device. I think they mounted a clinical
3 trial that was very broad, which in its original
4 design had very limited quantitative analysis built
5 in, which I suspect in hindsight was a statistical
6 error.

7 It had a variety of concerns in terms of
8 trial design, such as, for example, the inclusion of
9 600 patients, and then somehow 2,400 showed up, and
10 then we were told maybe there was supposed to be
11 3,000, but, sorry, there's only 2,400, but, oh, by the
12 way, it's not 600 per institution.

13 Then not all data were analyzed. There
14 were many, many exclusion criteria, and eventually a
15 subgroup was identified where it appears that there
16 may, in fact, be up to a 15 to 20 percent benefit in
17 terms of potentially delaying or avoiding biopsies, or
18 at least allowing these patients to be screened
19 closely.

20 This appears to be a finding in a subset
21 of patients. In fact, if, indeed, this device is
22 going to benefit this group of women, then a properly-

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1 designed clinical trial in this subset of women should
2 be conducted to verify that this was not artificial
3 finding as a consequence of this broad study, but a
4 real benefit in these women.

5 After all, we are talking about a target
6 population of half a million women. Before we allow
7 a half million women to be subjected to this, let's be
8 absolutely sure that this benefit is real. And that's
9 the reason I voted for disapproval.

10 DR. TOLEDANO: So it's my turn now. I
11 made a motion to approve subject to conditions, and
12 those conditions, as I brought up in my request for
13 clarification, I greatly wish I could have stated
14 those conditions before we took the vote.
15 Unfortunately, that's not allowed.

16 I did bring up something in the
17 clarification, that the conditions could be different
18 from the usual things that we see approval with
19 conditions, change the labeling.

20 And I appreciate all the issues that have
21 been brought up about clinical practice and I value
22 everybody's opinions and their experience. But when

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1 I look at this, what I see is somebody who has a
2 product that could work, and I see data that shows
3 that it probably does work, and the data may not have
4 been gathered in the optimal way, and it may not have
5 been analyzed in the optimal way, but I, honest to
6 goodness, believe that if you go out and collect new
7 data in the optimal way and analyze it in the optimal
8 way, you're going to come up with the same answer.

9 To me, that doesn't mean sending somebody
10 back to the drawing board. To me, that means saying
11 I think we're going to come up with the same answer,
12 approvable subject to conditions.

13 Look at your data the right way. Go
14 through the literature. Go through your physics.
15 Tell me what you think is going to happen. And if you
16 can prove to me that your device is going to be
17 effective, get your approval and do a post-market
18 study.

19 So that was the reason for my motion.
20 Unlike my esteemed colleagues, who I have really come
21 to enjoy, I am not comfortable with the recommendation
22 to disapprove.

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1 DR. GENANT: I basically agree with the
2 comments made by our Chairman. I thought that he
3 captured my own feelings about this issue very, very
4 well.

5 Perhaps, in addition, maybe I would just
6 comment. To the sponsors, I think that you have a
7 very exciting technology, and there are definitely
8 great possibilities.

9 I think it represents a refinement and a
10 substantial advance over earlier work that was done
11 with thermography and that has kind of lingered under
12 a cloud for some many years. I think you have the
13 opportunity now in designing prospectively a study
14 that will address the various issues that we have
15 raised and will bring to the larger community
16 somewhere down the road, hopefully, not too far down
17 the road, a technology that will, in fact, bring
18 benefit to women in this particular setting.

19 MS. PETERS: If I was able to vote, I
20 would have voted for the PMA with conditions, approval
21 of the PMA with conditions.

22 It is an adjunct therapy. It is not used

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1 as screening, which would make it what I think some of
2 that would really be necessary for. But I think with
3 its being non-invasive, that with education and some
4 of the additional changes in looking at the data, it
5 would make it very good.

6 MR. DOYLE: Before we adjourn for the day,
7 I would like to remind the Panel members that they are
8 required to return all materials they were sent
9 pertaining to the PMA itself. Of course, the list of
10 Panel members and agendas, and so forth, you're
11 welcome to keep.

12 Any materials you have with you may be
13 left at your table. Any others that you may not have
14 brought, you can send back to me at the FDA as soon as
15 possible. Thank you.

16 CHAIRMAN MEHTA: At this point I would
17 like to thank the speakers and the members of the
18 Panel for their preparation and participation in this
19 meeting.

20 I would also like to thank the sponsors
21 for being here to present the data to us, and to all
22 the members for attending.

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1 Since there is no further business, I
2 would like to adjourn this meeting of the Radiological
3 Devices Panel. Thank you.

4 (Whereupon, the Committee was adjourned at
5 3:35 p.m.)

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CERTIFICATE

This is to certify that the foregoing transcript in the
matter of: Radiological Devices Panel

Before: DHHS/PHS/FDA/CDRH

Date: December 10, 2002

Place: Gaithersburg, MD

represents the full and complete proceedings of the
aforementioned matter, as reported and reduced to
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