

1 percent of cancers were visible on mammography with
2 implants, and when implant displacement views were
3 included, again, very small numbers, but 72 percent of
4 those cancers were then visible on mammography.

5 That's lower than the expected
6 sensitivity, as I mentioned.

7 Next.

8 I think of greatest concern though, it's
9 difficult to make recommendations because the
10 performance of mammographic screening in women with
11 saline implants or any other implants, for that
12 matter, has really not been adequately evaluated,
13 particularly with high quality mammography and implant
14 displacement views.

15 We can suspect from the data that does
16 exist that there's at least a ten to 20 percent
17 decrease in mammographic sensitivity, and that alone,
18 even that relatively conservative number, has the
19 potential for delayed diagnosis of cancer in 20 to
20 40,000 women.

21 Are there other alternatives to
22 mammography? Very briefly, yes, there are, but they

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1 all have their limitations as well. Ultrasound is
2 being used more and more widely. It has a clear role
3 in evaluating palpable abnormalities in all patients,
4 including those with implants. We also use it when
5 there's a mammographic density that we're concerned
6 about.

7 It's easy to guide biopsy lesions as we
8 see under ultrasound, but the problem is screening
9 ultrasound is less sensitive to the very early
10 carcinomas, particularly ductile carcinoma in situ,
11 than is mammography.

12 Further, it's technically extremely
13 demanding. It requires a lot of expertise on the part
14 of the person doing the ultrasound, usually requires
15 a physician to perform the task, and at least in the
16 United States the costs of screening ultrasound are on
17 the order of \$300 per patient compared to
18 approximately \$75 for mammography.

19 Further, lesions behind the implant will
20 not be well seen even on ultrasound.

21 Next.

22 Just another slide that illustrates a

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1 cancer adjacent to the implant on ultrasound.

2 Next slide, please.

3 It has been suggested that MRI may be
4 appropriate in these patients. In fact, one recent
5 reference suggested it's the modality of choice for
6 detection of primary breast cancer in the augmented
7 breast.

8 Well, it's clearly a very sensitive test.
9 The implant does not obscure detection of lesions.
10 However, it does require injection of intravenous
11 contrast. It's extremely expensive. A billed cost is
12 about \$1,000 for a contrast enhanced MRI.

13 It's difficult to guide biopsy lesions
14 seen only on MRI. It's technically very demanding and
15 not widely available.

16 Next slide, please.

17 Just to illustrate though, it is very nice
18 to demonstrate cancers on MRI. We have here an
19 implant at the lower right-hand corner of the slide,
20 and you can see the area of enhancement just above it
21 is a spiculated mass with associated rim enhancing
22 lesion, and these were two adjacent cancers that were

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1 nonpalpable in a woman with implants.

2 Next slide, please.

3 MRI done improperly, however, still
4 doesn't help obviously and it can be very demanding.
5 This is a woman that we saw in our practice with a
6 saline implant, some periprosthetic fluid
7 inferiorally; several cysts in the breast, but no
8 contrast had been administered and, therefore, no
9 lesions were detected of significance, and she had a
10 breast cancer that went undetected for another year.

11 Next slide, please.

12 One other potential method for screening
13 would be nuclear medicine techniques, such as
14 Sestamibi or Miraluma, as it's more commonly known.
15 However, again, the sensitivity is not very good.
16 It's an expensive test, again, and in particular, I
17 call your attention to the statistic that nonpalpable
18 lesions under a centimeter, only 48 percent of these
19 were detected.

20 And so I don't think there are very many
21 good alternatives to mammography, in summary, but I
22 think we also have at least reason to consider that

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1 there may be some limitations of mammography in
2 patients with implants.

3 Thank you for your attention.

4 CHAIRMAN WHALEN: Do any of the panel have
5 questions for Dr. Berg?

6 DR. ROBINSON: I have a question.

7 CHAIRMAN WHALEN: Yes.

8 DR. ROBINSON: Just a question. How do
9 you think MRI will evolve as an imaging technique in
10 the evaluation of women with implants or one where you
11 really cannot get good imaging by your other --

12 DR. BERG: I think more and more we're
13 finding from data from international studies and grant
14 sponsored research trials now that it is an extremely
15 effective method at finding early cancer. I think the
16 problem is going to be who's going to foot the bill.

17 It's an extremely expensive test. It's
18 very demanding, and if insurance companies will foot
19 that bill, great, we can do the test. But I think
20 that as a society, we really can't afford to screen
21 women with breast MRI at this point. So we've got
22 that double edged sword.

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1 DR. ROBINSON: What numbers would be
2 involved if you weren't screening them per se, but
3 just doing women where you could not get good imaging
4 by another technique?

5 DR. BERG: Well, again, I think you're
6 looking at at least probably 30 percent of women with
7 implants where you've got significant limitations.
8 You've got women with dense breasts, women who are at
9 high risk. We're probably looking overall at the
10 population of maybe, again, probably 30 percent of the
11 overall population who has mammography routinely where
12 MRI would stand to benefit them.

13 It is routinely done in women who are at
14 high risk at some centers already, and it's being more
15 and more widely used.

16 DR. ROBINSON: Yeah, that's what my
17 impression was.

18 The last question. I'm sorry. For
19 lesions behind implant, is spherical CT or helical,
20 anything in that area going to have any implication?

21 DR. BERG: I thought about including CT.
22 The reason I did not is that it's got very high

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1 radiation dose to the patient, on the order of two to
2 three rads as opposed to mammography is on the order
3 of .2. You don't want to irradiate the breast with
4 tenfold as much radiation. You're going to be causing
5 a significant number of cancers.

6 So it also is not -- it's clearly not as
7 sensitive a test for certainly not in situ disease and
8 may pick up invasive cancers with the injection of
9 contrast, but, again, I don't think anybody wants to
10 advocate CT for that purpose.

11 Any other questions?

12 DR. BURKHARDT: I have a question. Most
13 of the studies that you quoted here are of necessity
14 a few years old.

15 DR. BERG: Right.

16 DR. BURKHARDT: In the last five years or
17 so, there's been a tremendous shift in the placement
18 of these implants in the plastic surgery community.
19 They're almost all put behind the muscle now --

20 DR. BERG: Right.

21 DR. BURKHARDT: -- in nonreconstructive
22 cases.

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1 DR. BERG: That's right.

2 DR. BURKHARDT: Do the ACR standards still
3 require double the radiation dose?

4 DR. BERG: Yes, they do. I think it's
5 very explicit. I looked in the most recent ACR
6 standards that I have, which is 1998, and it does
7 require the implant displacement views be obtained as
8 part of routine practice, and I think you'd be very
9 hard-pressed to defend if you missed a cancer as a
10 result.

11 It's very difficult. Even with
12 subpectoral implants it's very difficult to adequately
13 compress the entire tissue, depending how much tissue
14 the patient has.

15 DR. BURKHARDT: Do you have any sense of
16 what percentage of women in the eligible and in the
17 recommended cancer screening group actually have
18 mammograms according to the ACR standards?

19 DR. BERG: Good question. I was thinking
20 about discussing that. I don't really have good data
21 on that, but I can tell you that many women with
22 implants hesitate to have mammography even once they

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1 become of that age because it's a painful exam, and
2 it's more involved.

3 DR. BURKHARDT: How about women without
4 implants?

5 DR. BERG: Well, without implants, we know
6 it's about 60 to 70 percent who do under -- have had
7 a mammogram within the last two to three years.

8 DR. BURKHARDT: Thank you.

9 DR. BERG: Un-huh.

10 CHAIRMAN WHALEN: Ms. Brinkman.

11 MS. BRINKMAN: For routine screening
12 mammography, does insurance pay for the extra views
13 then for the displacement of the implant?

14 DR. BERG: As a rule, insurance does pay
15 the additional cost, although oftentimes a woman will
16 still have a deductible and still bear a greater cost
17 as a result of having to have a diagnostic mammogram
18 on a yearly basis for what amounts to screening.

19 CHAIRMAN WHALEN: Thank you, Dr. Berg.

20 We are now going to proceed to the review
21 of the first PMA, and that is going to be the one of
22 Mentor Corporation. So I would ask those who are

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1 going to be making that presentation to come forward.

2 I would like to remind all of the public
3 observers at this meeting that while this portion of
4 the meeting is open to your public observation, you as
5 public attendees may not participate unless there were
6 to be a specific request of the panel.

7 We now turn it over to Mentor Corporation
8 who, if necessary, can take upwards of a full hour for
9 their presentation.

10 I'm being outvoted by the mutiny here. I
11 was going to hold off on the break until afterwards,
12 but it seems that all of the panel has bladders the
13 size of walnuts --

14 (Laughter.)

15 CHAIRMAN WHALEN: -- we will take about a
16 seven minute break and then resume.

17 (Whereupon, the foregoing matter went off
18 the record at 2:43 p.m. and went back on
19 the record at 3:04 p.m.)

20 CHAIRMAN WHALEN: And, again, we are now
21 going with the sponsor's presentation. So we turn the
22 table over to Mentor Corporation.

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1 MR. GETTE: Thank you, Mr. Chairman and
2 distinguished members of the advisory panel.

3 I am Anthony Gette, President and CEO of
4 Mentor Corporation.

5 For more than 30 years, Mentor has been
6 dedicated to the research, development, and marketing
7 of innovative and effective medical devices that meet
8 the needs of patients and physicians. We sell
9 products in more than 60 countries around the world.
10 These products include devices used in plastic and
11 reconstructive surgery which we will present here;
12 products to treat urological disorders, such as for
13 prostate cancer, bladder cancer, erectile dysfunction,
14 and pelvic flora disorders; and a variety of
15 consumable products, primarily for the management of
16 urinary incontinence.

17 All of our products are designed to
18 improve the quality of life for patients who use them.
19 Today we focus with you on our saline filled breast
20 implant products. The heart of our presentation is
21 data that we believe confirms that our implants are
22 both safety and effective and warrant your

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1 recommendation of approval of our PMA to the FDA.

2 For breast implants, our goal is to
3 provide a safe and effective option so that women can
4 choose whether to restore the breast following cancer,
5 trauma, or correct a deformity, and also to choose a
6 more satisfying breast appearance through
7 augmentation.

8 Saline breast implants have been available
9 for more than 25 years. There is a large body of
10 information based on such a long history. Reports
11 from prestigious scientific organizations, such as the
12 Institute of Medicine and others, have provided
13 invaluable information with respect to the long term
14 safety of breast implants.

15 For a number of years we have worked
16 closely with the FDA to develop the preclinical and
17 clinical information contained in our PMA submission.
18 We will present some of the results of this
19 comprehensive effort this afternoon.

20 We believe that our PMA application
21 clearly demonstrates safety, defines the localized
22 risks of implant surgery, and for the first time

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1 quantifies the effectiveness and benefits of saline
2 filled breast implants.

3 Our commitment is that the implants we
4 manufacture are safe, effective, and are appropriately
5 supported by scientific studies. We are proud of our
6 pivotal trial, the saline prospective study, or SPS,
7 and believe it will significantly advance the clinical
8 knowledge about breast implants.

9 Our job does not end there. We are
10 committed to continuing research and to the
11 development of ever better products.

12 Our presentation today has four parts.
13 Mr. Bobby Purkait, Mentor's Senior Vice President for
14 Science and Technology, will describe our preclinical
15 testing program.

16 Ms. Pamela Powell, Manager of Mentor's
17 Clinical Programs Department, will describe the
18 clinical trials we have sponsored, including our
19 pivotal trial, the saline prospective study.

20 Dr. Bruce Cunningham of the University of
21 Minnesota will describe the results with regard to
22 clinical safety.

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1 Dr. Rebecca Anderson of the Medical
2 College of Wisconsin will then describe the
3 effectiveness and benefits of Mentor's saline filled
4 breast implants.

5 At the conclusion, Mr. Purkait will
6 summarize our presentation and lead our response to
7 your questions. He will also introduce our question
8 and answer response team at that time.

9 It is now my pleasure to introduce Mr.
10 Bobby Purkait. He is a polymer science engineer, and
11 for the past 15 years has led Mentor's research and
12 development efforts. He has been the primary
13 coordinator of Mentor's preclinical and clinical
14 submissions on the saline filled breast implant.

15 Mr. Purkait.

16 MR. PURKAIT: Thank you, Mr. Gette.

17 Good afternoon, Mr. Chairman and members
18 of the panel. I'll be presenting an overview of our
19 preclinical data today.

20 In that overview I'll be describing the
21 devices which are seeking approval today. I'll be
22 also describing the separate issues that we have

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1 considered in our evaluation, and in that evaluation
2 we have conducted various testings, such as
3 biological, chemical and mechanical and manufacturing.
4 I'll be describing some of those testings and the
5 findings from those test results, and finally I'll
6 summarize.

7 These pictures represent the Mentor's
8 family of saline filled mammary prosthesis. There are
9 two saline filled mammary prosthesis. The one on the
10 left-hand side is a fixed polymer prosthesis, which
11 has been filled at the time of implantation. The
12 right-hand side is an adjustable volume prosthesis.
13 It's filled intraoperatively or postoperatively.

14 These two devices come either in smooth or
15 textured surface and also can be found in round or
16 contoured shapes, and the sizes vary from 125 to 700
17 cc's. All the variations of these sizes and shapes
18 are denoted by styles number, which has been given in
19 our PMA.

20 These schematic diagrams furthermore
21 illustrate the design and the materials that we have
22 used in our devices. These two devices, one on the

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1 left-hand side, has elastomer silicone shell, and the
2 right-hand side the adjustable one also has silicone
3 elastomer shell.

4 These silicone materials are being used
5 commonly in many other medical devices, and a large
6 body of data exists both in Mentor data bank, as well
7 as in the open literature.

8 The left-hand side, the fixed volume one,
9 has a valve called diaphragm valve on the anterior
10 surface of the device, and the right-hand side, the
11 adjustable volume prosthesis called Spectrum has a
12 kink valve which is used to fill intraoperatively or
13 postoperatively.

14 All variations of these devices have same
15 materials, have been manufactured under similar
16 conditions, tested and released under same requirement
17 and specification.

18 In our preclinical safety issues we have
19 considered safety assessment by two different ways.
20 First, we concentrated on the toxicological safety
21 assessment by chemical characterizing our device and
22 materials, and also conducting some various biological

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1 battery of testings.

2 To assess the performance and durability
3 of these devices, we have done mechanical testing and
4 also developed information from manufacturing process
5 and quality of the products information.

6 In the toxicological safety assessment, we
7 have used the biomaterial toxicity risk assessment
8 paradigm. From that paradigm we have done a chemical
9 characterization of the device material and also we
10 have characterized the toxicity of those materials.
11 We also have developed information regarding exposure
12 to the constituent materials in the course of the
13 device.

14 Now I want to share with you some of the
15 chemical testing that we have conducted. This
16 particular slide shows a battery of testings, and
17 these testing demonstrate in case of biodegradation we
18 found a device or material, stable and
19 nonbiodegradable, under the exposures of harsh
20 conditions of enzyme, peroxides or lipids.

21 When we look into the surface, we found
22 the surface composition is made solely from

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1 polydimethosol siloxin (phonetic), and those surfaces
2 were examined by various different instrumentation
3 techniques, such as IRS, SIMs, SEM, to say some of
4 those instrumentation techniques.

5 When you look into the state of the cure
6 of our shell, we found it is fully polymerized, and
7 the cure is 100 percent cured there. PCBs are not
8 detectable in our devices. When we looked into the
9 metals and extractables, we found all levels are below
10 the toxicological concerned.

11 This shows the total battery of our
12 chemical calculation of a device and our materials.

13 Similarly we have done a significant
14 battery of biological safety testings, and this
15 particular site, we present those testings. The
16 results from those, we have not found any reproduction
17 or developmental toxicity problem, no pyrogenicity
18 with our materials or our devices, no genotoxicity.

19 The biostability of our device was found
20 to be excellent. No chronic toxicity and
21 carcinogenicity, and when we look into the
22 immunological response, no adverse reaction from those

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1 either. This represents the total battery of testings
2 for our device and materials.

3 As we move on and characterize these
4 materials under mechanical testings, these are the
5 test batteries that we have conducted on a device and
6 materials.

7 We recognize that this device would be
8 used in clinical settings, and in that use there will
9 be -- it will be subjected to mechanical load and
10 stresses in order to establish an evaluative behavior
11 of a device and materials under various mechanical
12 conditions. We subjected the device to the various
13 mechanical testings.

14 Now I will share some of the test results
15 with you now. As you look into the basic mechanical
16 properties of our material and device, we conduct ASTM
17 testing, such as tensile, ultimate elongation,
18 tear/break force, et cetera, and we found our device
19 and materials exceed ASTM specification.

20 When you look into the joint testings, we
21 also found it meets the ^{**}specification as defined by
22 ASTM. Active material, what we use in our device, has

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1 excellent abrasion properties. However, when it has
2 been upgraded (unintelligible), we found no silicone
3 materials were found on the surface.

4 When looking at the expanded devices, some
5 of the devices were implanted up to six years, but
6 when we test those, we found the mechanical properties
7 have not significantly changed.

8 Fold flaw was determined by the explanted
9 devices. When we examined those devices, we found the
10 fold failure was primarily due to the concentrative
11 force that was onto the fold.

12 The fatigue testing has been applied to
13 our devices. Through this testing we have established
14 the F and N curve (phonetic), and that has
15 demonstrated a large safety factor against rupture.

16 I'll share with you an example of our test
17 mechanism and test set-up where we used in a
18 laboratory. This particular device shows the
19 procedures or the set-up, what we use to understand
20 the mechanism of rupture failure. There's a device
21 sitting in the bottom of this cage. There's the foam.
22 This is the case. The whole thing has been emersed

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1 into 37 degree saline solution, and we have applied
2 the load conditions of 30 to 85 pounds and cycled
3 those many, many times.

4 Here is an example for ten million cycles,
5 no failure.

6 We looked into the static impact testing.
7 Our devices can withstand a significant amount of
8 energy on our device exceeding in excess of three
9 times that one might experience in a car accident for
10 35 miles an hour collision.

11 I'll show you an example of those test
12 mechanisms again. Here the prosthesis is sitting in
13 the bottom under the saline solution at 37 degrees,
14 and the weight has been dropped from 9.2 feet, with a
15 load factor of 35 pounds and then 45 pounds. Impact
16 energy generated on this device, about 444 to 570 and
17 no rupture was noted.

18 However, this device also cycled even
19 before this for ten million cycles, indicating a great
20 assistance to rupture of these devices.

21 This particular^{**} impact test has been shown
22 previously. Again 35 pounds, 45 pounds load were

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1 impacted on these devices and no failure was achieved
2 or seen.

3 Static rupture is also an important
4 phenomenon for our device to understand. When we can
5 place our devices to a load of 162 to 344 pounds of
6 weight, we can practically get this device into a
7 pancake shape without noting any particular rupture or
8 crack on the particular device.

9 Looking at the valve competence test, we
10 found this internal pressure of this valve exceeds in
11 excess of the in vivo use.

12 Looking into the radiolucency testing, we
13 found the radiolucency is significantly higher in
14 comparison to the silicone gel.

15 As we complete this battery of mechanical
16 testing, we conclude that our devices and materials
17 survive mechanical stress that exceeds the clinical
18 use conditions.

19 We looked into our manufacturing process
20 extensively. We have a rigorous manufacturing process
21 and a quality system. The process validation system
22 has been done extensively to understand our processes

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1 table, and we produce consistent quality product. We
2 have a significant amount of in process and other
3 testing throughout the operation. We do not release
4 any product without having any finished device
5 specification being met.

6 We believe that our manufacturing provides
7 a good, consistent, reliable product, and the
8 conclusion from our operation of the evaluations of
9 the results are devices are produced using a validated
10 process and equipment under GMP, which meet quality
11 standards. We have a well documented quality system
12 that insures that we have a safe, reliable, and
13 quality products.

14 I'd like to summarize our preclinical
15 testings by this way. We have done an extensive
16 preclinical testings which has been documented to
17 understand the behavior of our materials and device
18 by the state of the art methods.

19 We have characterized the potential
20 extractables, identified and quantified those which
21 are found to be below the toxicological concern. Our
22 device materials and devices are stable and

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1 nonbiodegradable. A total battery of biological
2 testing documented no toxicity testing issues, and
3 devices and materials survived mechanical stress
4 testing that exceeds clinical use conditions.

5 Now I would like to invite Ms. Pamela
6 Powell to describe our clinical studies. She will be
7 primarily talking about the design and the design
8 parameter of our studies.

9 Ms. Powell.

10 MS. POWELL: Thank you, Mr. Purkait.

11 Mr. Chairman, panelists, I will present
12 the clinical studies that Mentor has undertaken in
13 support of the saline PMA and focus primarily on the
14 three year saline prospective study.

15 Mentor is seeking approval for the
16 indications of cosmetic augmentation, breast
17 reconstruction following mastectomy or trauma,
18 asymmetry, ptosis, aplasia, hypoplasia, replacement or
19 revision of unsatisfactory implants, and combined
20 breast and chest wall deformities.

21 Mentor has funded or conducted five
22 clinical studies, two prospective and three

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1 retrospective. The prospective studies include
2 Mentor's three year saline study of 1,680 patients and
3 the large, simple trial, a one year study of 2,400 --
4 excuse me -- 2,347 patients.

5 The three retrospective studies include
6 Mentor's study of 822 patients with ten years of
7 follow-up, the SEER study with 1,159 patients with ten
8 years of follow-up, and the Cunningham study with a
9 minimum of ten years of follow-up on 450 patients.

10 These results will be presented by Dr.
11 Bruce Cunningham.

12 With the data of the prospective study
13 unavailable until its completion in 1998, FDA wanted
14 safety data on a large population in a short period of
15 time. The large, simple trial was designed to meet
16 those needs and consists of one year of follow-up on
17 2,347 augmentation, reconstruction, and revision
18 patients, with the safety objectives to assess
19 infection, deflation, and capsular contracture.

20 The patients were seen at baseline four to
21 six weeks, six months and ^{**}one year.

22 The saline prospective study or pivotal

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1 clinical trial is a comprehensive study designed to
2 look at both safety and effectiveness. The primary
3 safety objective was to assess short term
4 complications, such as infection, seroma, deflation,
5 capsular contracture, and nipple and breast
6 sensitivity.

7 The secondary objective was the detection
8 of calcification surrounding the implant.

9 The primary effectiveness objective was
10 change in breast size. The secondary objectives were
11 patient satisfaction and quality of life.

12 Dr. Rebecca Anderson will be presenting
13 these results.

14 At the baseline visit, study parameters,
15 benefits and risks of the implants and procedure
16 itself were discussed with patients. A history and
17 physical and rheumatology assessment was done by the
18 plastic surgeon, and the patient completed the quality
19 of life questionnaires.

20 Complication information or adverse
21 reactions occurring or ^{**}reported at scheduled or
22 unscheduled visits were also reported to Mentor.

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1 The saline prospective study was conduct
2 at 153 centers throughout the United States, providing
3 a broad geographic and demographic diversity of
4 clinical sites. Sixteen hundred and 80 patients were
5 enrolled in the study; 1,264, or 75 percent,
6 augmentation and 416, or 25 percent, reconstruction,
7 with over 80 percent of the patients returning for
8 their two year visit.

9 The augmentation patients were between the
10 ages of 20 and 40, with about one half married and 30
11 percent single. The educational level of the patient
12 population was representative of women throughout the
13 United States.

14 The majority of the reconstruction
15 patients were between the ages of 30 and 60, 63
16 percent marries and 15 percent single. Most had some
17 college.

18 Based on the demographic data and other
19 characteristics presented here, we believe that the
20 saline prospective trial population was a
21 representative cross-section of women who were seeking
22 breast implants for augmentation, reconstruction, and

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1 revision.

2 Now I am pleased to turn the presentation
3 over to Dr. Bruce Cunningham, the Medical Director of
4 the three year saline study, professor and chair of
5 plastic surgery at the University of Minnesota. Dr.
6 Cunningham is also former chair of Silicone Implant
7 Research for the Plastic Surgery Educational
8 Foundation for the American Society of Plastic
9 Surgeons.

10 Dr. Cunningham.

11 DR. CUNNINGHAM: Thank you, Ms. Powell.

12 Mr. Chairman, panelists, my name is Dr.
13 Bruce Cunningham. I'm a professor of surgery at the
14 University of Minnesota and also conduct a busy
15 clinical practice. I'm the paid Medical Director for
16 the study that Mentor is presenting today, and in
17 addition, have been contracted to do research for
18 Mentor and the McGhan Corporation, which will be
19 presented by McGhan.

20 I want to address some of the issues of
21 clinical safety. The goals of my presentation are to
22 characterize and quantify the clinical risks defined

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1 by the large, prospective study and other clinical
2 data to demonstrate the method and extent of physician
3 and patient information and education, to place the
4 clinical risks in perspective with the medical
5 literature for similar devices and indications, and
6 then to summarize.

7 There are four types of major safety
8 concerns which have been raised with respect to saline
9 filled breast implants. The first of these, and most
10 important, is systemic disease, and this has been
11 addressed by the Institute of Medicine and other
12 scientific panel reports.

13 Local complications are a special area,
14 highlighted by the Institute of Medicine, and will be
15 addressed by the large simple trial and the saline
16 prospective study.

17 Durability or the survivability of the
18 devices in vivo will be addressed by the Cunningham
19 ten year, multi-center, retrospective outcome study,
20 as well as the prospective study.

21 And then cancer detection and treatment
22 issues are very important, and Dr. Lenore Iverson, our

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1 breast radiologist, can address those during the
2 question and answer session.

3 The recent reports of the multi-specialty
4 review panels have drawn some major conclusions.
5 Three scientific review panels, two in America and one
6 in the United Kingdom, have concluded that there's no
7 evidence for systemic disease associated with these
8 devices. We believe this is not an issue of major
9 concern at this time.

10 These panels have also concluded that
11 breast feeding is safe and beneficial for the child,
12 and that there are no second generation effects on
13 children of women with breast implants.

14 The large, simple trial goals have been
15 addressed. The data provided the FDA with assurance
16 that during the short term, while the long term three
17 year data is being collected, that there were no major
18 serious risks and complications of the procedure.

19 I want to move now to the saline
20 prospective study, the goals of which were recounted,
21 and this is the signal study that's being presented by
22 the Mentor Corporation today.

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1 There were a number of statistical methods
2 which were applied to this data set. Most of them are
3 survival analyses which are statistical methods to
4 examine the time to occurrence of various
5 complications. We felt that the best way to represent
6 this was with the Kaplan-Meier analysis, which is used
7 to provide the estimate of cumulative incidence for
8 each complication by indication.

9 In some incidences we performed other
10 analyses, such as a Cox proportional hazards model to
11 examine for risk factors of individual complications
12 and a logistic regression analysis to examine the risk
13 factors for breast and nipple sensitivity.

14 The prospective study includes two
15 distinct clinical populations with different
16 objectives and different complication rates. So we
17 will present them separately.

18 First, the augmentation patients. The
19 devices that were placed are shown here. The majority
20 of them are the textured SILTEX devices or the
21 textured adjustable volume SPECTRUM device. The
22 remaining third of them are smooth devices.

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1 The location of placement is three
2 quarters in the submuscular position, which is
3 beneficial for mammography, and also gives a better
4 shape and feel to the device. Only 28 percent were
5 placed in the subglandular position.

6 I want to spend a moment on this slide
7 because it will serve as a template for the data slide
8 which follow. This is the standard Kaplan-Meier
9 analysis, and in this case for infection. To make it
10 easier to depict, the curve always shows one minus the
11 survival curve, and the scale is pretty consistent at
12 40.

13 The graph typically shows the incidence,
14 cumulative incidence at 36 months, banded by the 95
15 percent confidence interval, and in the upper right-
16 hand corner in this book, we will cite the relevant
17 statistics from the medical literature.

18 So in this case, the cumulative incidence
19 in the augmentation patients who are receiving
20 elective, noncomplicated surgery is 1.7 percent for
21 infection, which is a cumulative over three years, and
22 in a situation where the curve is flat or the graph is

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1 flat, this does not mean that this is the incidence
2 which is continuing to occur each year, but a flat
3 graph rather means that there are no new occurrences
4 of the complication.

5 Every time we generated a number or a
6 complication from the data, we wanted to make sure
7 that it was reflected in the patient and physician
8 information. Here's the citation of the data
9 reflected in the product information data sheet which
10 is given to physicians, and here it is in the product
11 information sheet which was given to patients, citing
12 the data right out of the study.

13 I won't continue to show these, but for
14 every data point we've reflected it in the product
15 information.

16 Here's the Kaplan-Meier analysis for a
17 significant concern, which is Baker II and IV capsular
18 contracture. A Baker I classification contracture is
19 essentially a normal breast. So we wouldn't report
20 that. The Baker II classification is a firmness which
21 is basically detectable by the patient, and it's only
22 when you get into the III and IV level complications,

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1 grades of capsular contracture that the presence of
2 the implant might be detected by someone else.

3 This is the Level III, Baker III
4 classification, 6.9 percent, and the Baker IV at .6.
5 We feel that the Baker III is not a significant
6 clinical problem and rarely results in reoperation,
7 but we wanted to check that out.

8 So our statistics show that of patients in
9 this classification of three and four capsular
10 contracture, only 23.5 chose to have surgical release
11 of this scar tissue contracture.

12 We also had a group of patients who had
13 capsular contractures which are classified as unknown.
14 In order to show the most adverse possible analysis,
15 we included these patients as though they all had
16 Baker III and IV grade classification, and that
17 results in a classification for augmentation patients
18 of nine percent.

19 Let's look at deflation among this
20 augmentation group. The incidence, cumulative
21 incidence at three years of deflation of the implants
22 is 3.3 percent. We did, however, want to know whether

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1 this is a trend that continues or what the long term
2 deflation rate is, and to address that, the Cunningham
3 study was commissioned.

4 This is a multi-center, retrospective
5 cohort outcome study. The study design was consistent
6 with the recommendations made by the FDA epidemiology
7 panel. The study included 450 patients and 882
8 devices, with a minimum of ten year follow-up.
9 Ninety-four percent of these patients were
10 augmentation. So it seems appropriate to include this
11 at this point in the presentation.

12 Well, I'm going to deal with the Mentor
13 devices in a moment. The deflation rate for devices
14 made by the current manufacturers, which are McGhan
15 and Mentor, was 5.8 percent. This is 5.8 percent
16 cumulative incidence at three years. It does not mean
17 that it is an annual incidence of 5.8 percent. It's
18 a cumulative incidence.

19 With respect to the Mentor devices, 86
20 percent of the devices in the study were Mentor
21 devices, and we could isolate them as we look back at
22 the data.

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1 The incidence of deflation per device for
2 Mentor or Heyer-Schulte Model 16 devices was 3.7
3 percent cumulative incidence at ten years. For
4 comparison, the saline prospective study, when looked
5 at on a per device incidence, is 1.9 percent.

6 Other significant findings from this long
7 term, ten year retrospective study include an overall
8 patient complication rate of 27.6 percent and an
9 overall patient reoperation rate of 25.8 percent.

10 However, despite these two complications
11 and the number of reoperations, 93 percent of patients
12 were satisfied or very satisfied with their implants.

13 The Kaplan-Meier analysis for augmentation
14 patients undergoing reoperation is shown here. The
15 incidence is 13.2 percent. We wanted to look behind
16 this number a bit and see what were the causes for
17 this, and here are the causes for reoperation.

18 These are a good assortment of causes and
19 indications which we would expect to see in a group of
20 patients having elective surgery, and I'll address
21 this other classification in a moment.

22 There were a number of patients in this

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1 augmentation group who had their devices removed, 8.1
2 percent, in fact. And again, we wanted to know why
3 was this occurring. Was there a clinical reason for
4 it?

5 And when we look at that, we find that
6 there are the usual things that we are citing as
7 complications, but also in terms of this number,
8 patient request alone, and this indicates for most
9 patients that they're choosing to change the volume of
10 their implant, and in fact, the critical finding is
11 that 72 of the 88 patient implants that were removed
12 were replaced again at the same surgery, indicating
13 that this was an elective procedure, perhaps a size
14 change that the patient chose.

15 Other complications are shown. One of the
16 goals of the study was to reflect the incidence of
17 calcifications in this patient, which is extremely
18 low, less than one percent.

19 Cancer detection is a significant issue,
20 as Dr. Berg pointed out. The clinical issues are: do
21 breast implants interfere with mammography? Is cancer
22 detection delayed? And is clinical outcome

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1 compromised by the presence of the devices?

2 The data to be presented can be drawn from
3 the SPS study results. However, it's important to
4 realize that this was not a study design goal, and
5 this data is anecdotal.

6 The population based research conclusions
7 we feel are very important and will be drawn from
8 papers that were included in the PMA submission.
9 First, let's look at the data from the study.

10 There were two breast cancers detected by
11 mammography among this augmentation cohort. The first
12 patient had treatment which was effective for a small
13 lesion with a very favorable outcome.

14 The second patient unfortunately had a
15 very aggressive cancer. This was detected in the
16 first six months following implantation with her
17 device, and unfortunately the patient expired five
18 years later. She expired outside of the terms of the
19 study time frame, but we felt it was important to
20 present her data nonetheless.

21 There are two major studies that I would
22 like to address. First is the Birdsell study from

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1 Alberta, Canada. This is a population based study
2 design which we feel is much more significant and
3 powerful study design than the case study reports
4 which have been cited.

5 The study group was 41 women with cosmetic
6 breast implants who had developed breast cancer. The
7 control group was 13,000 women with breast cancer, but
8 who did not have breast implants.

9 In terms of the findings, the women with
10 implants were diagnosed at a younger age than
11 controls. The study population tumors were smaller.
12 Lymph node and distant metastases occurred equally
13 frequently in the two groups, and the distribution of
14 tumor histological types was not significantly
15 different.

16 Of greatest importance, however, is the
17 fact that the five and ten year Kaplan-Meier survival
18 rates did not differ between the implanted and the
19 control groups.

20 Another significant study was reported by
21 Dr. Deapen in 1997. This is another population based
22 study using the cancer registry from Los Angeles

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1 County. It looked at women who were implanted between
2 1953 and 1980. The study group consisted of 31 breast
3 cancer patients in 3,182 women with breast implants.

4 The control group was the Los Angeles
5 County cancer surveillance program, and the patients
6 were demographically matched as closely as possible to
7 the women without implants.

8 The median follow-up was 14.4 years. The
9 findings showed that the stage at diagnosis did not
10 differ between the implanted and the control groups.
11 In fact, there was a lower than expected incidence of
12 breast cancer with 31 observed cases against an
13 expected rate of 49.2.

14 This data has been further elaborated on
15 by a recent study that Dr. Deapen published this
16 month. In that study, he points out that cancer
17 detection was not delayed in the group of implanted
18 patients and treatment was not compromised.

19 Let's look now at the reconstruction
20 cohort. Reconstruction patients are a special
21 population. They have more extensive initial surgery.
22 In that case breast tissue and skin is removed, and

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1 flaps or skin grafts may be required just to close the
2 wound.

3 Additional procedures and interventions
4 are frequent, and the general health of the patient
5 may be severely affected by adjunctive treatment, such
6 as chemotherapy or bone marrow transplantation.

7 A special clinical problem exists for
8 plastic surgeons treating patients for breast
9 reconstruction. Symmetry is much more difficult to
10 achieve than a simple enlargement of the breast.
11 Complications have to be compared to the chief
12 alternative to implants, and not to the augmentation
13 group that we've just discussed.

14 The major alternative to breast implant
15 reconstruction are major flaps and major surgery, and
16 when flaps fail, they have a significant morbidity and
17 impact on the patient's life.

18 The reconstruction patients were implanted
19 by and large, a significant majority, with textured,
20 contoured, textured devices, the SILTEX. The SPECTRUM
21 device was used in 44 percent of patients, and this is
22 a unique device which is specifically applied and of

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1 great use to plastic surgeons in reconstruction
2 because it can serve as a soft tissue expander and as
3 a permanent implant, allowing many patients to have
4 the reconstruction in one stage.

5 Most of the devices were placed in a
6 submuscular position. Some were subglandular, perhaps
7 in patients who were having lumpectomy and radiation.

8 The Kaplan-Meier analysis for infection
9 shows an incidence of 9.1 percent cumulative at 36
10 months, which is three times the amount in
11 augmentation patients. This is in a group of
12 complication prone individuals who are receiving
13 adjunctive treatments and much more significant
14 surgery.

15 The Baker Grade III and IV capsular
16 contracture is significantly higher, 24.1 percent
17 capsular Grade III and 6.7 percent capsular Grade IV.
18 Again, the question arises: how significant is this
19 and what kind of impact does it make on the patient's
20 life?

21 And of note, only 27.8 percent of patients
22 chose to have the capsule released with surgery.

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1 Deflation is a significant problem in this
2 group of patients, again, almost three times as
3 frequent as in the augmentation group. However, this
4 is a group of patients who are having subsequent
5 treatment, biopsies, needle aspirations, radiation,
6 chemotherapy to treat their primary underlying
7 disease, and this can easily account for this
8 increased complication of deflation among this group.

9 We looked at the reoperation rate, which
10 is higher than the ten year retrospective study and is
11 at 40.2 percent. We want to look behind the number.
12 What are the causes for this, and it's important to
13 note that many of the causes for this operation in
14 this group have to do with the underlying tumor
15 problem, lymphadenopathy, breast cancer or mass,
16 necrosis, which is probably related to the flaps at
17 the time of the mastectomy, or delayed wound healing,
18 again, related to healing at the time of the
19 mastectomy.

20 There are a lot of patients who are
21 undergoing operations as a part of their
22 reconstruction, either a staged reconstruction or a

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1 nipple/areolar complex or some other part of the
2 breast mound is being built or for asymmetry many of
3 these patients were recorded, although they had
4 surgery on the contralateral breast, such as a
5 reduction or a mastopexy.

6 So there are a number of good clinical
7 reasons not related to the implant for these
8 subsequent operations.

9 The Kaplan-Meier analysis of explantation
10 shows that 26.8 percent of patients have their
11 implants removed, but a lot of them were elective and
12 were being done to release scar capsular contracture
13 or infection or, again, to deal with the problems
14 related to their breast cancer.

15 Of this group, 60 of the 97 percent of
16 implants were replaced at the same time that they were
17 removed, indicating that this was not a group of
18 patients, by and large, who gave up or abandoned their
19 reconstruction, but rather were a group of patients
20 who were electively trying to fine tune or complete
21 their reconstruction.

22 The revision after explantation, which is

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1 the revision group that the sponsor is seeking
2 approval for, the data is shown here. It's a
3 difficult group to categorize because it includes both
4 augmentation and reconstruction patients, and the
5 variance, statistically significant variance, from the
6 previous initial operation is shown with the
7 augmentation cohort and the reconstruction cohort and
8 the difference in the variant.

9 This is a summary slide of the short term
10 risks and complications similar to what was presented
11 in the large simple trial for augmentation and
12 reconstruction. This is presented on a per patient
13 basis. The revision was always presented on a per
14 implant basis. So we can only give you a qualitative
15 assessment with respect to incidence.

16 Additional statistical analyses were done,
17 and this is one of the major benefits of the study
18 because it will provide significantly important
19 clinical information for plastic surgeons and for the
20 patients. Cox proportional hazard models were used on
21 factors contributing to deflation to understand them,
22 and logistic regression analysis was done to determine

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1 factors affecting breast and nipple sensitivity.

2 Here are all of the risks factors that
3 were identified and reported in this large group of
4 patients, and the ones which had clinical statistical
5 significance are noted on the right. Let's take a
6 closer look.

7 In the group of patients who had -- this
8 is an analysis with respect to deflation, and when the
9 augmentation is used as the reference, immediate
10 reconstruction patients had a significantly higher
11 rate of deflation which, again, would go with the fact
12 that they are having subsequent interventions,
13 biopsies, aspirations and things to treat their
14 underlying problem, and the delayed reconstruction
15 patients who have by and large completed that process
16 have a lower rate of deflation.

17 The unilateral versus bilateral simply
18 reflects the statistical chance of having two implants
19 versus one, and this is a clinical interest. The
20 average incision size is the reference, and incision
21 size below reference of three sonometers results in a
22 two times risk factor for deflation of the device,

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1 indicating that surgical choices and surgical
2 technique have a definite impact on the outcome of the
3 durability of the device.

4 Of great significance is the effect of
5 Betadine, a common antibiotic irrigant which is used
6 by many plastic surgeons, despite the fact that the
7 product labeling specifically interdicts such use, to
8 attempt to prevent an infection. Patients who have
9 their devices bathed or irrigated with Betadine had a
10 3.5 times risk factor for deflation of the device.
11 This is clearly information that needs to be in the
12 hand of every plastic surgeon so that this practice is
13 abandoned.

14 We wanted to look at breast and nipple
15 sensitivity. Above the yellow line show patients who
16 had increased sensitivity. Below the line are
17 patients who had less sensation carried out to 36
18 months. We wanted to know if there were any factors
19 that impacted clinically on this incidence of change
20 in sensation.

21 When we look at the inframammary incision
22 as the reference site and compare it to periareolar or

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1 transaxillary incision sites, there are statistically
2 significant findings. Periareolar patients had a
3 significantly greater risk of diminished or changed
4 sensation than the inframammary site patients, and
5 this would follow from an intervention that occurs
6 close to the insertion of the nerves in the end
7 sensory organs.

8 The transaxillary patients had a
9 significantly lower risk of change in sensation,
10 obviously being operated on from a more remote site.
11 This is good information that will allow plastic
12 surgeons and their patients to make better informed
13 choices.

14 So what does this all mean? What's the
15 impact of this amount of data?

16 First, the clinical risks and local
17 complications have been effectively defined and
18 quantified by the data presented today. Physicians
19 and patients are fully informed about the risks and
20 complications, and that's based on the study data
21 directly.

22 The risks are consistent with those

1 reported in the medical literature for similar devices
2 and indications. Augmentation patients have a lower
3 risk consistent with their elective surgery.

4 Reconstruction patients have a higher
5 risk, but they also have greater potential emotional
6 and physical benefits from the implants.

7 Revision patients experience similar or
8 somewhat higher complication risks than that of their
9 primary indication, and population based studies have
10 shown that breast implants do not delay detection or
11 compromise treatment of breast cancer in implanted
12 women.

13 It's now a pleasure to turn the podium
14 over to Dr. Rebecca Anderson. She's a full-time Ph.D.
15 clinical psychologist in the Department of Plastic
16 Surgery at the Medical College of Wisconsin in
17 Milwaukee. She actively counsels patients undergoing
18 plastic surgery, and many of those are patients having
19 implants.

20 She also occupies a unique role within
21 plastic surgery as being one of the key players in the
22 outcomes movement within plastic surgery, which is

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1 funded by the Educational Foundation.

2 Dr. Anderson.

3 DR. ANDERSON: Thank you, Dr. Cunningham.

4 Members of the panel, guests, I'm Rebecca
5 Anderson, and I'm here today as a paid consultant for
6 Mentor Corporation. I have no other financial
7 interest in the company.

8 As a psychologist in an academic plastic
9 and reconstructive surgery practice in a university
10 setting, I have the opportunity to speak with
11 thousands of women who have undergone or who plan to
12 undergo breast surgery. I see both augmentation and
13 reconstruction patients in my clinical practice.

14 Women report seeking implants to restore
15 the breast following cancer, trauma, or deformity, or
16 to achieving a satisfying breast appearance through
17 augmentation.

18 When I see breast reconstruction patients,
19 I generally see them at least once prior to their
20 surgery in an effort to discuss their adjustment to
21 the diagnosis of cancer. I often see these patients
22 during their hospitalization and again for follow-up

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1 as long as the situation dictates.

2 When I see augmentation patients, I
3 generally see them prior to their surgery to discuss
4 body image issues and expectations of the surgery. I
5 also try to see these patients at least once following
6 their surgery to discuss their level of satisfaction.

7 Today I will discuss motivations and
8 expectations of women seeking implants. I will review
9 the results of the primary and secondary objectives of
10 the saline prospective study, and I will present a
11 summary of the clinical findings.

12 The effectiveness objectives of the saline
13 prospective study included a primary objective, which
14 was to evaluate a change in breast size. The
15 secondary objective was to evaluate patient
16 satisfaction and quality of life outcomes.

17 As Dr. Cunningham mentioned, the breast
18 augmentation and reconstruction patient are really two
19 distinct patient populations, and for that reason I
20 will also discuss the results separately for these two
21 population groups.

22 Women report seeking augmentation

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1 mammoplasty to improve body image and self-confidence;
2 to enlarge the size of the breast; to make the breast
3 more proportionate with the rest of the body; to
4 regain size and shape following pregnancy and
5 lactation; or to correct severe asymmetry.

6 In the saline prospective study, in an
7 effort to address the effectiveness in the
8 augmentation mammoplasty patients, the following
9 assessments were provided. Breast size was assessed
10 by looking at a change in bra cup size, a change in
11 chest circumference, and the use of a breast
12 dimensional analysis measurement.

13 Quality of life outcomes were assessed by
14 use of the breast evaluation questionnaire, which was
15 specifically designed and validated for use in this
16 study. Additionally, the multi-dimensional body self-
17 relations questionnaire and the Tennessee self-concept
18 scale were used.

19 With respect to breast size, a bra cup
20 size change was demonstrated in the augmentation
21 patients with 96 percent of the patients experiencing
22 at least a one cup size bra cup increase.

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1 Breast size was also demonstrated when we
2 looked at chest circumference. From the preoperative
3 to the postoperative assessment, there was a
4 statistically significant increase in chest
5 circumference of 7.2 centimeters for the augmentation
6 patients.

7 Based upon these size measurements, it is
8 clear that breast size was increased by use of the
9 implants in the augmentation patients.

10 Quality of life issues were assessed in
11 the augmentation patients. The breast evaluation
12 questionnaire, which was developed for this study,
13 assessed satisfaction with a number of aspects of
14 breast size, shape, firmness, and general appearance.
15 The breast evaluation questionnaire utilized a five
16 point scale. Patients were asked to respond rating
17 their satisfaction from very dissatisfied to very
18 satisfied.

19 And as you can see, preoperatively the
20 majority of the patients reported being somewhat or
21 very dissatisfied with the general appearance of their
22 breast. However, postoperatively the majority of the

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1 patients reported being somewhat or very satisfied
2 with the general appearance of their breast.

3 The BEQ looked at size, shape, and
4 firmness of the breast and patient satisfaction with
5 these attributes across three settings: intimate,
6 social, and professional. And as you can see, with
7 respect to breast size, preoperatively patients
8 reported low levels of satisfaction, whereas
9 postoperatively there was a statistically significant
10 improvement in satisfaction with breast size, with
11 well over 80 percent of the patients reported being
12 satisfied or very satisfied with breast size.

13 The same was true with patient
14 satisfaction regarding breast shape. Preoperatively,
15 low levels of satisfaction were reported, and again,
16 postoperatively at the 36 month follow-up there was a
17 statistically significant improvement with, again,
18 over 80 percent of the patients reported being
19 satisfied or very satisfied with breast shape.

20 The trend also continued when we looked at
21 breast firmness with the patients reporting a
22 statistically significant improvement in their

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1 satisfaction with breast firmness. Again, over 80
2 percent of the patients were satisfied or very
3 satisfied.

4 This is not only statistically
5 significant. It's clinically relevant to the patient
6 with respect to their satisfaction of attributes of
7 their breast.

8 The multidimensional body self-relations
9 questionnaire was also used with the augmentation
10 patients. The MBSRQ is a frequently used body image
11 assessment. When taking the MBSRQ, the patient is
12 asked to record their agreement with statements on a
13 five point Likert (phonetic) scale.

14 And as you can see, from the preoperative
15 to the 36 month follow-up there was a statistically
16 significant increase in satisfaction with general
17 appearance on the scale of the MBSRQ which assess
18 satisfaction with general appearance.

19 We looked at a statement on the MBSRQ, "I
20 like the way I look without my clothes," and again,
21 you can see that there was a statistically significant
22 improvement in agreement with that statement from the

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1 preop. into the 12 month follow-up, and that
2 improvement was maintained through 36 months.

3 With respect to the statement, "I like the
4 way my clothes fit me," there was also a statistically
5 significant improvement in agreement with that
6 statement from the preop. to the 12 month follow-up,
7 and again, that was maintained at 36 months.

8 Based upon the results of the MBSTQ, we
9 see that there is a clinically significant increase in
10 satisfaction with body image, which is statistically
11 significant and clinically relevant to the patient.

12 In summary, regarding effectiveness for
13 the augmentation patients, we see that there was an
14 increase in breast size. This was demonstrated by an
15 increase in bra cup size and an increase in breast
16 circumference.

17 Patient satisfaction and quality of life
18 outcomes were also demonstrated. Satisfaction with
19 breast attributes increased, and comfort and
20 satisfaction with appearance also increased among
21 these patients.

22 The breast reconstruction patient faces a

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1 number of emotional and physical challenges. Today
2 one in eight to ten women faces a lifetime risk of
3 developing breast cancer.

4 Once diagnosed with breast cancer, the
5 patient will have a number of decisions to make, and
6 her life will be changed. For women who face
7 mastectomy, implants may provide the only
8 reconstruction option.

9 Women report the following motivations and
10 expectations of reconstruction: to feel whole again
11 after breast removal; to avoid the need of an external
12 prosthesis; to improve body image and self-confidence;
13 to put the cancer behind them; to wear more clothing
14 styles; to regain a sense of femininity; and to
15 correct deformity.

16 In the saline prospective study, breast
17 size and quality of life measures were also assessed
18 with regard to effectiveness. Regarding breast size,
19 a change in chest circumference was used as a
20 measurement, as was the breast dimensional analysis
21 measurement.

22 Regarding the secondary objective, which

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1 was to look at quality of life outcomes, the
2 multidimensional body self-relations questionnaire,
3 the Tennessee self-concept scale, the functional
4 living index of cancer, and the Beck depression
5 inventory were used.

6 An increase in chest size was
7 demonstrated in the delayed reconstruction patients.
8 There was a statistically significant increase in
9 breast size from the preoperative to the 36 month
10 follow-up of 3.8 centimeters. This is indicative of
11 restoration of the breast mound in these patients.

12 There was no need to assess change in
13 breast size among the immediate reconstruction
14 patients because the breast mound was created at the
15 time of the mastectomy.

16 The functional living index of cancer is
17 a widely used assessment which evaluates patient
18 adjustment following the diagnosis of cancer. Higher
19 scores reflect improved physical and psychological
20 adjustment, and as you can see on the functional
21 living index of cancer, the immediate and delayed
22 reconstruction patients both experienced a

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1 statistically significant improvement in physical and
2 psychological functioning.

3 The Beck depression inventory is a widely
4 used outcome measure for assessing symptoms associated
5 with depression. Lower scores reflect lower symptoms
6 associated with depression. The immediate
7 reconstruction patients experienced a statistically
8 significant decrease in symptoms associated with
9 depression. There was a decrease in symptoms
10 associated with depression among the delayed
11 reconstruction patients. It was not statistically
12 significant. However, it does represent a trend in
13 the desired direction.

14 The Beck depression inventory evaluates
15 various levels of clinical depression. For example,
16 a score of ten or greater represents a low level of
17 clinical depression, with scores from ten to 16
18 indicating mild depression. Higher scores indicate
19 moderate to severe depression.

20 We looked at 196 patients for whom we had
21 data, both preoperatively and at 36 month follow-up on
22 the Beck depression inventory, and as you can see, at

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1 the preoperative assessment, 43 patients reported
2 scores of ten or greater on the Beck depression
3 inventory, whereas at the postop 36 month follow-up,
4 only 26 patients reported scores of ten or higher on
5 the Beck depression inventory, which is indicative of
6 a statistically significant decrease in symptoms
7 associated with depression in this population.

8 In summary, with respect to the
9 effectiveness for the reconstruction patients, an
10 increase in breast size was demonstrated. Chest
11 circumference increased in the delayed reconstruction
12 patients, which was indicative of restoration of the
13 breast mound on these patients.

14 Patient satisfaction and quality of life
15 outcomes were also demonstrated. Physical and
16 psychological adjustment in cancer patients increased,
17 and symptoms associated with depression decreased.

18 So what does this all mean? The Mentor
19 saline filled mammary prostheses are effective and
20 beneficial. In the augmentation patients, an increase
21 in breast size was demonstrated. In the
22 reconstruction patients, the breast mound was

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1 restored.

2 The saline prospective study and the
3 professional literature demonstrate that the risk and
4 benefits are well defined and documented, and these
5 results are consistent with the quality of life
6 benefits reported in the professional literature.

7 Despite possible complications, patients
8 report high levels of satisfaction and improved
9 quality of life.

10 And finally, many women facing
11 reconstruction or desiring augmentation have a wealth
12 of information available to them as they make their
13 decisions, and they continue to choose implants.

14 Mr. Purkait will return for concluding
15 remarks.

16 MR. PURKAIT: Thank you, Dr. Anderson.
17 Thank you, Dr. Cunningham, and thank you, Ms. Pamela
18 Powell.

19 I'd like to summarize our presentation
20 today. First, we have shared with you the preclinical
21 findings. We have submitted our scientific study data
22 in our PMA to show the safety and effectiveness of our

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1 product.

2 In the toxicological safety assessment, we
3 have shown that our materials and devices are
4 extractables below the toxicological concern.

5 In our durability and performance
6 assessment, we have shown that our devices can
7 withstand excessive forces equal to the interval used.

8 As you look through our clinical findings,
9 we have established risk and complications, and we
10 have shown that the long term durability of our
11 implant through the retrospective study to be over ten
12 years.

13 In our studies we also have well
14 characterized risks. We have shown that our product
15 improved the quality of patients and this information
16 and education materials will be provided to both
17 patients and physicians for their decision.

18 Thus, we believe that we provide a safe
19 and effective option for women who want to restore the
20 breast following cancer, trauma, or deformity, or to
21 achieve a satisfying breast appearance through
22 augmentation.

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1 Finally, we recognize that there are no
2 objective measures or standards by which the relative
3 risks and benefits of these devices can be weighed
4 against each other. On the patient and individual can
5 make the decision and will be the judge, and this
6 decision is different from each person.

7 Mentor provides the necessary information
8 to the patient and their physician so that a patient
9 can make a truly informed decision.

10 We thank you for your attention.

11 CHAIRMAN WHALEN: Thank you fry much.

12 For those members of the panel who now may
13 have any questions of the sponsor. Dr. Blumenstein.

14 DR. BLUMENSTEIN: When you compute the
15 Kaplan-Meier estimates of risk, how did you handle the
16 explantation event for the computation of the Kaplan-
17 Meier curve for something like infection or
18 contractures, and so forth? Were these for patients
19 who had an explantation censored in those curves?

20 MR. PURKAIT: You know, I have not had a
21 chance to share with you our Q&A team, but in order to
22 address that, I'd like to invite our biostatistician,

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1 Dr. Gene Poggio to explain our Kaplan-Meier analysis
2 on those.

3 If I could just request one thing and show
4 you our Q&A team so that all the questions that will
5 be coming to us, we'll be able to tell you exactly
6 who's answering what.

7 We have Dr. Wally Grant in our hand to
8 address or answer questions about material testings.

9 We have Dr. Gene Poggio who will be
10 addressing primarily the biostatistics related
11 questions.

12 We have Ms. Pamela Powell who will be
13 talking about the clinical protocol designs or
14 implementations.

15 We have Dr. Noel Rose at hand to answer
16 any questions on the immunology.

17 Mr. Clark Scherff from the manufacturing.

18 And Phil Yang for the preclinical data.

19 We also have Dr. Mark Allen for any
20 particular testings, long term testings.

21 Radiology, Dr. Leonard Everson.

22 And Dr. Roger Wixtrom on the safety

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1 assessment.

2 Thanks for your attention, and we'll be
3 addressing your question now.

4 DR. POGGIO: Mr. Chairman, Panelists, my
5 name is Gene Poggio. I'm a biostatistician. For the
6 last 15 years, I've directed the biostatistics group
7 at Apt Associates.

8 Apt Associates has contracts with Mentor
9 Corporation to do analysis, data management reporting
10 of clinical studies. Apt has no other financial
11 connection with Mentor, and I personally have no
12 financial connection with Mentor.

13 To address your question, as laid out in
14 the original analysis plan for the study, we did
15 censor patients, with one exception which I'll mention
16 in a moment. We censored patients at the time of
17 explantation. We thought it was very important to do
18 so because -- for two reasons.

19 The patients who are not reimplemented, we
20 felt that we've used a conservative strategy because
21 to keep patients in the denominator for incidence
22 estimates when they no longer have an implant we would

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1 think would bias the estimates.

2 And then for patients getting new
3 implants, complications that might occur. It could be
4 a different device, a different manufacturer's device,
5 and we wouldn't be able to attribute it to a given
6 device.

7 So we thought the cleanest approach was to
8 censor them at the moment immediately after the
9 explantation, if you will.

10 The one exception I mentioned is we did do
11 some analysis to look at the issue of revision
12 patients, and for those that was, if you will, the
13 baseline for revision patients. But aside from the
14 exception or aside from revision patients, they were
15 censored at the moment immediately after the
16 explantation.

17 DR. BLUMENSTEIN: One more question. Did
18 you do analyses in an attempt to try to characterize
19 the patients who did not have follow-up at various
20 time points following the original, following
21 baseline?

22 DR. POGGIO: I mean we basically have a

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1 quite high response rate. I believe it's off the top
2 of my head about 80 percent at two years. We could
3 pull those numbers up if you want.

4 We didn't specifically compare the ones
5 who did drop out to the ones who did not.

6 CHAIRMAN WHALEN: Dr. Bandeen-Roche.

7 DR. BANDEEN-ROCHE: Yes. I have a related
8 question to Dr. Blumenstein's. It may also go to you.

9 This involves the quality of life and
10 effectiveness analyses. At the three year visit, my
11 understanding is that those analyses, any summary
12 statistics excluded individuals who were lost to
13 follow-up up to that point, and that that loss to
14 follow-up included a relatively substantial number of
15 explantations; is that correct?

16 DR. POGGIO: It is true in the analyses
17 when we looked at simply the 36 month value, they
18 would have been excluded, but we did have summary
19 measures looking at the average change across all
20 visits.

21 There is generally a very consistent
22 pattern of one level at baseline and a very different

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1 level, especially for the primary efficacy measures or
2 primary effectiveness measures, the one level at
3 baseline and a quite different level consistently for
4 all the visits after it.

5 DR. BANDEEN-ROCHE: But to summarize, the
6 people at that different level would comprise people
7 who had not had explanations, correct?

8 DR. POGGIO: Yes, for all analyses. Yes,
9 for all analyses after explantation, patients were
10 excluded from those analyses aside from the revision
11 patients that I mentioned for separate analyses.

12 DR. BANDEEN-ROCHE: Thank you.

13 CHAIRMAN WHALEN: Dr. Li.

14 DR. LI: Yes, I'm not sure who can take
15 this question.

16 My question is when you were doing your
17 either retrospective study or your prospective study,
18 how you counted deflations. Perhaps you can correct
19 me if I'm wrong, but am I reading patients were scored
20 as having deflation as a reason for explantation when
21 that was the primary identified cause for the
22 revision, but if you went in to revise somebody for

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1 contracture and found the device deflated, it was not
2 counted as a deflation; is that correct?

3 DR. CUNNINGHAM: The saline devices,
4 unlike the gel devices, are readily apparent when they
5 deflate. The saline comes out. Either in the study
6 that I did, the retrospective study, the majority of
7 patients noticed a significant loss in volume over a
8 period of days or perhaps one week. Some of them
9 noted it over a longer period of time, but mostly it's
10 a short term, dramatic event.

11 So I think that going to some other
12 intervention and then finding an incidental deflation
13 is not anything that was reported in our study, and
14 I'm not aware of it being reported in the saline
15 prospective study.

16 The reason for reoperation would be to
17 correct, replace a deflated implant. It wouldn't be
18 something that would be discovered incidentally at
19 another operation.

20 DR. LI: Thank you.

21 Just a follow-up question, if I could.

22 There was a difference in deflation rates between

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1 those patients where the surgery was done for
2 augmentation versus reconstruction. You outlined
3 perhaps several maybe interventionally related reasons
4 why there was that difference in deflation rate.

5 However, can you discount the fact that in
6 the reconstruction group there was four time as many
7 SPECTRUM devices as there were SILTEX, and
8 coincidentally the incidence of deflation was on that
9 order?

10 So I guess my question is: how sure are
11 you that it's completely interventional and not device
12 related?

13 MR. PURKAIT: Perhaps if you could just
14 repeat that question for me so I can truly understand.
15 Are you asking that --

16 DR. LI: Let me simplify it for you.

17 MR. PURKAIT: -- if the SILTEX has higher
18 deflation rate than the non-SILTEX or the smooth? Is
19 that the question?

20 DR. LI: I'll take that. I'll start with
21 that one. Go ahead.

22 DR. CHANG: Could I rephrase that

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1 question? Would you be asking the same question I was
2 going to ask? Was there stratification in terms of
3 deflation rate for either augmentation or
4 reconstruction? Could you tell if it was a valve leak
5 or puncture or failure of the shell?

6 Was that stratified as an explanation of
7 deflation?

8 MR. PURKAIT: Yes, we have that
9 information we will share with you. Dr. Gene Poggio
10 will show you that information.

11 DR. POGGIO: I think the Cox proportional
12 hazards model we used perhaps might be the best answer
13 that we have to the question you're raising. We
14 looked at deflation rate. Probably most of the
15 panelists know this, but in case anyone doesn't, just
16 the Cox proportional hazard model is the most standard
17 way to look at time to occurrence of an event, in this
18 case a complication where you have varying lengths of
19 follow-up and you want to look at various risk
20 factors, either to adjust for confounding factors or
21 to evaluate the various risk factors.

22 So the factors we have on the left are the

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1 various factors we took into account in the model.
2 You'll notice indication reconstruction versus
3 augmentation or specifically immediate and delayed
4 reconstruction, augmentation, and so forth.

5 And so the only factors that were found to
6 be significant are the four shown there, indication
7 whether it was unilateral or bilateral, incision size,
8 and Betadine use, and so you'll see that we also have
9 valve type and surface type and implant shape there,
10 and none of those were significant in that model, and
11 it's adjusting for the other variables in the model.

12 DR. LI: I don't see in there a split
13 though between SPECTRUM and not SPECTRUM, for
14 instance.

15 DR. POGGIO: Well, this is characterized
16 by device characteristics, and the SPECTRUM is
17 characterized principally by the surface type of a
18 texture. You're correct, but it's characterized by a
19 textured surface and a specific valve.

20 So if SPECTRUM was different, you would
21 expect to see the difference in the valve type or the
22 surface type, and/or the surface type.

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1 DR. CUNNINGHAM: There are only two valve
2 types, the diaphragm valve and the kink valve, and the
3 kink valve only exists in the SPECTRUM device. So the
4 valve is a marker in effect for the product with
5 respect to this analysis.

6 DR. LI: Right, but then the whole
7 argument would hold only if the valve was the source
8 of the leak?

9 DR. CUNNINGHAM: Perhaps I can address
10 that more fully. Two, two, 16 would be the slide I
11 would like. Go ahead.

12 This is a breakdown of the occurrence of
13 deflation that the manufacturer can actually analyze.
14 There were 74 devices that deflated, and 37 of them
15 were returned to Mentor, and here are the breakdown
16 after physical examination of the devices based on
17 what the final concluding reason was for failure.

18 There were three valve leaks or tears.
19 There were 18 or there are, rather, eight iatrogenic
20 failures which in most cases were needle biopsy or
21 nicking with a suture or hitting with a scalpel.

22 There were 18 shell tears, which are very

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1 difficult to evaluate. It almost certainly is a
2 surgical event related to surgical technique, perhaps
3 as it was being removed or explanted.

4 And then there were six in which no
5 abnormalities were found. So to answer Dr. Chang's
6 question, the valve does not seem to be, at least in
7 the group of devices that could be examined, the major
8 cause for deflation.

9 CHAIRMAN WHALEN: Does that answer your
10 question, Dr. Li?

11 DR. LI: I'm not sure. Let me work on it
12 for a second. I'll come back.

13 CHAIRMAN WHALEN: Dr. Burkhardt.

14 DR. BURKHARDT: I have two questions. The
15 first is for Dr. Cunningham.

16 A reoperation rate of 25 percent -- and I
17 tried to follow this when you were presenting it -- is
18 that 25 percent of patients or 25 percent of implants?

19 DR. CUNNINGHAM: That is a per patient
20 analysis.

21 DR. BURKHARDT: So 25 percent of patients
22 who had implants had to go back for surgery. On the

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1 face of it, that would seem to be extraordinarily
2 high, and I couldn't quite understand the breakdown.
3 You said 72 of 88 were removed and replaced. Were the
4 88 all -- did that represent all of the patients who
5 were reoperated?

6 DR. CUNNINGHAM: That represented the
7 patients who were explanted. So what I was using was
8 the -- if we could go back to that slide.

9 DR. BURKHARDT: I'm just concerned. One
10 out of four patients is an awful lot to go back for a
11 second surgery.

12 DR. CUNNINGHAM: So there are two
13 different analyses that we showed. One was the
14 reoperation rate, which you're referring to. The
15 other was the explantation rate, and the patients that
16 were replaced, that statistic was on patients who had
17 an explantation and a replacement at the same time.

18 So in effect, one of the main causes for
19 reoperation in this group was an elective desire to
20 change the size of the device because a large
21 proportion, almost three quarters of them, had the
22 device replaced at the same time that they had the

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1 previous one removed.

2 Sometimes that may have been removing the
3 device to treat for an infection or capsular
4 contracture and then replacing it with a new device,
5 but many of them in the augmentations were to perhaps
6 change the size of the device.

7 DR. BURKHARDT: For those patients who had
8 an elective change of the device for size purposes
9 only, can you tell us how many wanted to go larger and
10 how many wanted to go smaller?

11 DR. CUNNINGHAM: We would have to find
12 that data for you. I don't have any --

13 DR. BURKHARDT: Do you have any
14 impression?

15 DR. CUNNINGHAM: I do not.

16 DR. BURKHARDT: Thank you.

17 DR. CUNNINGHAM: One of our statisticians
18 says that the majority of them were to increase size.

19 DR. BURKHARDT: Is this an appropriate
20 time to ask about the information that's provided with
21 the implant or do you want to wait until Wednesday?

22 CHAIRMAN WHALEN: You mean in terms of

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1 labeling? This is an appropriate time to ask any
2 questions of the sponsor that you feel is
3 appropriately answered by the sponsor.

4 DR. BURKHARDT: Mr. Purkait, I have a
5 question about the brochure that is provided with the
6 implants by Mentor. When you go to implant shape, you
7 have a rather carefully constructed sentence that
8 says, "Round implants are thought to give a fuller
9 shape to the breast, while contoured implants are
10 designed to offer a more anatomical shape."

11 And I'm sure that's correct, and then when
12 I look at the pictures that you have, if they weren't
13 labeled, I couldn't tell the difference between the
14 round and the anatomical shaped implant. Do you have
15 any basis for believing that the use of one implant
16 variety over the other implant variety makes a
17 difference that can be detected by a blinded observer?

18 MR. PURKAIT: I would like to see Dr.
19 Cunningham. Could you please address from your
20 experience on the anatomical versus the level implant
21 with the difference in cosmetic application?

22 DR. CUNNINGHAM: I don't believe that we

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1 broke down or at least I have not seen a breakdown of
2 the data that Dr. Anderson presented, namely the chest
3 circumference measurements by shape, and if we do have
4 it, perhaps we can get it put up.

5 But my personal clinical feeling is that
6 contour devices particularly in reconstructed patients
7 do not confer a significant difference in total
8 outcome of shape than do round devices.

9 DR. BURKHARDT: How about in augmentation
10 patients?

11 DR. CUNNINGHAM: Again, my personal
12 clinical belief is that when these devices are placed
13 in the submammary position in a thinner woman with a
14 lot of extra skin, it's possible that the shape of the
15 device could be conferred to the overlying breast
16 parenchyma and the skin envelope.

17 However, the majority of these devices are
18 placed underneath the muscle, and my personal feeling
19 and clinical observation is that underneath the muscle
20 they all become essentially round, and any shape that
21 might be conferred by the implant design is overridden
22 by the forces of the muscle.

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1 DR. BURKHARDT: Thank you.

2 CHAIRMAN WHALEN: Dr. Li?

3 DR. LI: Yeah, I thought about it. I
4 think I need a simpler answer to this.

5 Could you just simply tell me out of those
6 devices that were deflated how many of them were
7 SPECTRUM? That's the answer I'm looking -- that's the
8 question I would like to have answered.

9 MR. PURKAIT: Sure. I think we have the
10 data. Can I just come back to you while I was just
11 getting those information?

12 DR. LI: Sure, and I have a separate
13 question. Dr. Cunningham alluded to it and some of
14 your literature alluded to the fact that depending on
15 the shape of the device and where you place it or
16 maybe even the size of the incision, that that affects
17 the outcome of the device.

18 So my question is that seems to imply that
19 seems to imply that there's some kind of extra stress
20 or extra loading or extra some kind of kinematic
21 application to the device that somehow is not
22 advantageous to the device if you don't put it in in

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1 the appropriate fashion.

2 My question is: do you have any
3 biomechanical data that would suggest, for instance,
4 if you make the incision two centimeters smaller what
5 that increase in stress actually is, or if you use the
6 wrong profile and put it in the wrong place and the
7 stress is too high, do you have any biomechanical
8 information, again, that tells you exactly what that
9 increase in stress is, or is it stress or is it sheer
10 or is it something else?

11 MR. PURKAIT: We have some information
12 that shows that when you do apply load, regardless of
13 what incision site and where you're placing, if you
14 take an implant and if you apply certain types of
15 load, we have measurement that shows that what type of
16 internal pressure you can generate.

17 Now, do we have information between the
18 subglandular or some muscular? At this point in time
19 I couldn't tell you, but we have a general information
20 if we have a certain amount of load or if certain
21 types of women sleeping on the chest, what sort of
22 stress would be -- internal stress would be developed?

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1 We have that information.

2 DR. LI: I've read that information. I
3 guess what I'm looking for is the link between the
4 laboratory data for those calculations of pressure
5 under those different conditions to your instruction
6 to the surgeon that says, "Put it in this way or the
7 stresses will be too high."

8 So my question is versus your laboratory
9 data under different conditions where you generate
10 different internal pressures, compare that to your
11 instruction to surgeons that say don't do this or the
12 stress will be too high. What's the comparison,
13 numerical comparison, between those laboratory stress
14 data and then the stresses you think are being
15 generated in the patient at least to the level where
16 you're concerned enough that you're instructing the
17 surgeon to watch out for it?

18 DR. BOYKIN: I'd like to follow that
19 before you answer with a similar question because your
20 mechanical data indicates when you have looked at the
21 environment of the implant that a, as you define it,
22 stiffer tissue surrounding the implant significantly

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1 lowers the pressure per square inch. I believe it
2 goes below two pounds per square inch in this model.

3 It makes me wonder if that could be
4 translated into some instructions for the surgeon
5 who's trying to optimize the length of the implant.
6 I think that's what he's getting at because you have
7 data about this pressure on the implant in the
8 environment that it's in. How does that translate to
9 what we can do to improve the lifetime of it while
10 it's there?

11 The other question I'd like to pose is was
12 there any investigation of the possible presence of
13 clinical capsular contracture before implant
14 deflation. I didn't see that listed as a cause, but
15 did you go back to find out was there a capsule before
16 it inflated, or it might be subjective data, but did
17 anybody try to look at that possible correlation?

18 DR. CUNNINGHAM: Could I have Slide 109
19 while I answer the first question?

20 The first question really has -- if I
21 understand it correctly, you're asking is there a
22 good, effective way to model in the preclinical

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1 testing the kinds of forces and effects that would
2 result not from the daily use and activity of the
3 device when it's in the woman's body, but rather that
4 mimics the condition of actually placing the device.

5 DR. LI: Yes, that would be the global
6 question, yes.

7 DR. CUNNINGHAM: Right. Perhaps one of
8 the materials people can answer that, but let me say
9 that from a clinical point of view, the devices are
10 placed in deflated so that they are, you know, in a
11 very small volume when they're placed through the
12 incision.

13 So that it would be hard to model that
14 accurately, except for tear or sheer characteristics,
15 which of course have been recorded.

16 Surgeons vary so widely in their
17 techniques. Some surgeons fill the implant partially
18 so that they can then aspirate the air bubble and then
19 put it in partially inflated. Other surgeons put it
20 in completely empty. Some surgeons place it in
21 through a remote incision site, such as the axilla.
22 There are some surgeons who wad it up and place it

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1 through a long tube through the umbilicus.

2 You know, certainly these different
3 techniques would have different stresses and different
4 strains applied to the device. I think it would be
5 very hard to model.

6 With respect to the question of the
7 associations of risks with the deflation event, this
8 is the series of potential things that we felt could
9 affect the -- these are the factors that we looked at
10 that could affect deflation, and capsular contracture
11 is not one of them.

12 And these are the things that were found
13 to be statistically significant.

14 DR. BOYKIN: Well, I understand that, but
15 I guess what I'm asking is that obviously when it's
16 deflated, it's deflated, but could you -- did anyone
17 ask the patient or the physician if there was any
18 indication that a contracture may have been present or
19 developing at that time?

20 I mean that's just kind of a retrospective
21 analysis.

22 DR. CUNNINGHAM: I think from my personal

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1 clinical observation of how these devices function,
2 it's clear that we had a higher deflation rate in
3 reconstructive patients. Reconstructive patients also
4 had a significantly higher Baker Grade III, Baker IV
5 capsular contracture rate. In many cases personally
6 I believe that this is reported as a capsular
7 contracture rate when, in fact, what is actually going
8 on is that there is tissue inadequacy. There has been
9 tissue that's been removed.

10 So if I understand your question, it's
11 dealing with does a tight, confining space in somehow
12 or in some way predispose an implant to fail, and I
13 think the data would indirectly bear that out because
14 the higher degree of capsular contracture reported in
15 the reconstructions parallels a greater deflation
16 rate, and you could understand that that is a more
17 adverse environment. The implant is going to be more
18 likely to be folded on itself, and so it's not as --
19 it's a more adverse environment than underneath an
20 unoperated pectoralis muscle.

21 DR. BOYKIN: ^{**} Right. This is really
22 conjecture, but the reason I was curious about the

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1 data, the PSI and the firm environment is because what
2 you might be describing is a situation in, which the
3 submuscular pocket which by virtue of the nature of
4 the tissue is a stiffer environment, is probably
5 causing this lower load on the surface of the implant.
6 If it is significantly lower, does this correlate with
7 the decreased contracture rate? Does this correlate
8 with an increased lifetime, life span of the implant?

9 And if this information is variable, it
10 could be correlated to some pressure reading through
11 a remote valve that we could do clinically and perhaps
12 look at some U curve with the bottom being the optimum
13 side. When we get past that point we need to make
14 some changes.

15 So I'm just talking about the information
16 you've got and how we can use that clinically.

17 MR. PURKAIT: Dr. Li, we're still getting
18 your data. We'll come back to you.

19 CHAIRMAN WHALEN: While we're still
20 getting that, Dr. Morykwas.

21 DR. MORYKWAS: ^{**} Yeah, I just had a couple
22 of things, and one is actually related.

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1 MR. PURKAIT: Dr. Li, sorry. I'd like to
2 answer if I could, please, and show these data. The
3 deflation of SPECTRUM versus SILTEX versus the smooth
4 and the SPECTRUM versus the smooth.

5 Gene.

6 DR. POGGIO: I have a very specific
7 answer. I hope this -- you asked how many SPECTRUM.
8 There were 21 SPECTRUM had deflation out of 472
9 devices.

10 DR. LI: So that's 21 out of the 74 that
11 Dr. Cunningham alluded to?

12 DR. POGGIO: It is devices. So 21 devices
13 out of 472.

14 DR. LI: So then would that translate, Dr.
15 Cunningham, to 21 out of your 74? Oh, that was 37
16 that he had. He had 74 deflations, 37 of which they
17 analyzed.

18 MR. PURKAIT: That's right. The 57, I
19 suppose, are total deflations. That's what we've
20 seen. We received the 37 to examine that was what the
21 cause for the deflation. **

22 DR. LI: Right, but is the 21 out of the

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1 74 total or is the 21 out of the 37 that you analyzed?

2 MR. PURKAIT: I believe it's the total, 24
3 out of the total 37 or 57, 57 or 74.

4 DR. LI: Seventy-four.

5 MR. PURKAIT: Right.

6 DR. LI: Okay. So most of them then were
7 the prefilled, not SPECTRUM devices; is that right?

8 MR. PURKAIT: I couldn't tell you exactly.
9 Most like from the data, it looks like that, yes.

10 DR. CUNNINGHAM: And there are no
11 prefilled devices. They're all filled at the time of
12 surgery.

13 DR. LI: So sorry. Thank you.

14 DR. MORYKVAS: Well, I guess I had a
15 couple of questions, and one is related to the
16 implantation. Since a lot of surgeons now do for
17 augmentation -- not a lot, but some do the
18 perienvolicol (phonetic) insertion. Since you have
19 presented data that shows that the length of the
20 incision appears to be related, are you going to
21 discourage surgeons from using the perienvolicol or
22 would that be something you would consider?

1 DR. CUNNINGHAM: Well, I personally -- and
2 I'll let someone else speak to the product labeling as
3 it exists -- but I personally feel that that is a very
4 strenuous and risky thing to do to an implant, and I
5 would not feel comfortable doing that in a patient of
6 mine. I don't think that the benefits outweigh the
7 risks of the device deflating, and I would feel
8 strongly that it should certainly be an interdicted
9 use of the device.

10 MR. PURKAIT: Yeah, to answer your
11 question, this information as we have found in our
12 study we have submitted to the agency. As these
13 things are approved and discussion occurs, we will put
14 in the patient information as well as the physician
15 information, yes.

16 DR. MORYKWAS: then I had a question about
17 your infections and how that was related. You also
18 had a delayed wound healing.

19 Now, the infections that you reported,
20 were they later infections? Did the incision had
21 healed and the breast had just swelled or developed a
22 draining tract or was it also just a nonhealing

1 incision that pus was coming out of at the time of
2 surgery?

3 DR. CUNNINGHAM: There could be several
4 events reported at the same time, such as delayed
5 healing and infection at the same time, but the
6 infections were all reported either with a positive
7 culture or with a positive clinical assessment.

8 There are times where the implant is in
9 place. A patient might have some symptoms of redness
10 or malaise, and there are times when you can treat
11 that effectively by intravenous or oral antibiotics.
12 So those are situations where you would not be able to
13 get an actual tissue culture positive, but it's
14 certainly your clinical impression that that's what it
15 is.

16 If you're able to treat it successfully,
17 the patient is not encumbered with an operation, and
18 it would be dangerous to try to needle aspirate it
19 simply to get a culture. So there are certainly cases
20 where it's clinically strong indication, but not
21 culture document.

22 DR. MORYKWAS: Sure, and then there are

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1 also indications where the patient might have been
2 double reported as nonhealing or delayed healing plus
3 infection.

4 And then the last thing is you had a very
5 small number of patients that were other. Are those
6 the combined smooth and textured implants?

7 DR. CUNNINGHAM: You're talking about the
8 pie chart of types of devices?

9 DR. MORYKWAS: Yes. In one it was .2
10 percent, and in another pie chart it was a one percent
11 and it just said "other."

12 DR. POGGIO: Just in rare instances there
13 were different devices in the two breasts, and it
14 reflects the mixture of one device in one breast and
15 one in another.

16 CHAIRMAN WHALEN: Ms. Dubler.

17 MS. DUBLER: I'd like to pursue a little
18 further the relationship between your findings and
19 your communication with physicians and with patients.
20 The findings on the Betadine washing are quite
21 startling, and when did you make those findings, and
22 what's happened to that information since it developed

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1 in your database?

2 MR. PURKAIT: The Betadine findings
3 approximately we came to know about this about a year,
4 a year and a half ago. As soon as we came to know
5 about this, we immediately contacted the agency with
6 that information to correct the patient information,
7 as well as the physician information.

8 So that was being done even long before
9 the clinical study results came to us.

10 MS. DUBLER: And do you state your
11 findings in a similar fashion in your patient
12 information and your physician information
13 communications?

14 MR. PURKAIT: I believe definitely I
15 recall that we do that in a physician's information on
16 this. I would have to check and get back to you about
17 the patient and so on.

18 DR. CUNNINGHAM: There would probably not
19 be a reason to inform the patient about this. It's
20 something that occurs while the patient is asleep. I
21 suppose in a best case circumstance the patient might
22 ask the doctor, "Do you do this?" but it may be more

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1 information than they can clinically use.

2 They're bombarded with a lot of
3 information as they try to make this decision.

4 MS. DUBLER: I agree, but there are some
5 very interesting examples of instances in which giving
6 patients information brought change in practice and
7 giving physicians information didn't. So that's the
8 background of my question.

9 DR. CUNNINGHAM: Certainly the reference
10 to the hand washing and patients being aware of that
11 and encouraging their physicians to do that is very
12 good, and hopefully this is something that will come
13 up on Wednesday when we discuss or on Friday, rather,
14 when we discuss this more fully.

15 CHAIRMAN WHALEN: Dr. Robinson.

16 DR. ROBINSON: A couple of question. Mr.
17 Purkait, in your fatigue impact studies, just to give
18 me a better perspective, what does that -- I know it
19 may be impossible to translate into real time, and
20 that's unfortunate, but can you give me an estimate of
21 what you think that translates to in real time? Is
22 that falling off a ten foot wall? Is that an air bag

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1 inflation? What do those maximum values tell you
2 about your device?

3 MR. PURKAIT: Yeah, sure. I'd like to
4 share with you some test data and show that to give
5 you a better understanding what it really means, and
6 I'll take about two minutes of your time. I'd like to
7 invite Mr. Phil Yang and Dr. Mark Allen to show you
8 some of the data and the test.

9 MR. YANG: I'm Phil Yang. I'm Vice
10 President of Technical Studies and Submissions for
11 Mentor Corporation.

12 The fatigue data is really comparing to
13 fatigue activities that you normally see in someone's
14 body. We've modeled this as someone walking. A
15 breast implant would go up and down. So we're
16 comparing it to those types of small, relatively small
17 effects that continually happen to a person in a
18 cyclic manner. So those are what we're comparing to.

19 In order to understand how we do the
20 testing very quickly and what it means in terms of
21 numbers, I'd like Dr. Mark Allen to come and explain
22 it.

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1 DR. ALLEN: I'm Dr. Mark Allen, Mentor
2 Corporation, Science and Technology Laboratory
3 Manager.

4 I would like to provide a very brief
5 overview of the fatigue testing that Mentor conducts
6 for an estimation of the in vivo lifetime prediction
7 or, more appropriately, an assessment of long term
8 durability of the implant.

9 To do this, as indicated on the slide, the
10 in vivo fatigue testing methodology, both
11 consideration of the fixture and experimentation,
12 include an assessment of the in vivo environment, the
13 stress magnitude and distribution on the implant, and
14 the physical activity associated with typical daily
15 routine.

16 This then can be used to develop safety
17 factor and lifetime prediction for an endurance limit,
18 safety factor calculation, Basquin relation or the
19 Gerber relation.

20 This slide indicates that the device, when
21 implanted, the posterior region is adjacent to the
22 chest wall, and accordingly is subject to minimal

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1 stress, whereas the annular and anterior region of the
2 device is probably that which is exposed to load
3 distribution.

4 When considering the activity of an
5 individual and the loads that might be imposed upon
6 the device, one can consider the at rest condition or
7 the motion condition. If this is done at rest,
8 typically one assigns the mass of the device as the
9 stress induced on the mammary and the regions
10 indicated. In motion, one would consider jogging
11 perhaps and equations can be shown which will allow
12 derivation of a magnitude of load of approximately two
13 times the mass of the device.

14 With these considerations then, in vitro
15 testing can be conducted, and this illustrates the
16 schematic of the test fixture. I believe Bobby showed
17 this earlier.

18 This design includes a hemispherical ram
19 which is used to load the device. The device is held
20 or supported within a steel spring cage. The steel
21 spring cage actually allows for the anterior region of
22 the device to protrude between the springs so that

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1 during this test under compression loading, both the
2 annular region and the anterior region are subjected
3 to loading for us, which is consistent with the in
4 vivo environment.

5 The testing that's typically conducted for
6 this kind of experiment, some of the conditions are
7 listed here, and as I mentioned previously, a typical
8 load that might be experienced by a device in vivo is
9 on the order of three pounds. The loads that are used
10 here for two different types of experiments range
11 anywhere from 40 to 80 pounds, which is extremely
12 excessive relative to the in vivo condition that's
13 typically encountered.

14 The failure analysis is then used to
15 construct the S-N curve. On the other hand, endurance
16 analysis is used to determine the load in which
17 failure will not occur.

18 A typical S-N curve is shown here. This
19 is derived from the data which results in failure, not
20 endurance. However, if one were to construct a
21 horizontal line along a stress amplitude consistent
22 with that measured for the endurance limit, that would

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1 define an elbow region of the curve.

2 DR. LI: Excuse me. Could I just
3 interject one?

4 DR. ALLEN: Yes.

5 DR. LI: Could you define for us what the
6 failure point is? At what point do you decide the
7 implant has failed?

8 DR. ALLEN: Catastrophic rupture defines
9 the failure for the data which is presented here, and
10 with that catastrophic failure, the failure mode is
11 measured and recorded, including the location,
12 dimensions, and thickness of the shell at the site of
13 failure.

14 DR. LI: Thank you.

15 DR. ALLEN: So all of these are
16 catastrophic failures that are incurred. They're
17 induced intentionally to develop the S-N curve data.

18 From these types of experiments then, one
19 can derive a safety factor. One of the most
20 straightforward approaches is the endurance limit
21 safety factor which uses, again, that stress amplitude
22 that I mentioned, which does not result in a failure

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1 of the device, a catastrophic device from this
2 cycling. That occurs at ten to the seventh cycles or
3 ten million cycles.

4 And then that can be compared to the in
5 vivo stress amplitude, which I identified previously,
6 approximately three pounds for a 325 cc mammary. This
7 allows for the construction of a safety factor, and
8 that yields in this case for a 325 value of about
9 eight.

10 Unfortunately, this only assesses the
11 safety factor of the device without failure. An
12 alternative approach to develop a safety factor relies
13 upon an equation based upon the Basquin relation, and
14 this allows incorporation of a time even, as indicated
15 below, the time event which would be consistent with
16 activity, daily routines such as jogging and walking.

17 An this case five hours of activity a day
18 were considered with one cycle per second for events,
19 and typically this would calculate to be about seven
20 million cycles per year.

21 If one assigns a ten year life then and
22 incorporates this value into the Basquin equation, a

1 stress amplitude results which is about 28 psi. This
2 then can be used with the in vivo stress amplitude and
3 yields a safety factor of about 8.6, which is very
4 consistent with the endurance limit safety factor and
5 would offer then a reasonable lifetime, if you will,
6 or long term durability of the implant under these
7 conditions.

8 One additional relationship that can be
9 used relies upon the Gerber equation, and that allows
10 also for the incorporation of ultimate tensile
11 strength of the shell to be included in the
12 calculation, and as you can see, a similar safety
13 factor is developed from that.

14 DR. ROBINSON: Could I try it a different
15 way? The real time part is missing.

16 What would be your conjecture if a woman
17 was sitting in the passenger side and an air bag
18 inflated?

19 DR. ALLEN: If I recall correctly -- maybe
20 I'm not the person that should be answering this
21 question -- but the impact testing resulted in a value
22 which is approximately three times that of a car

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