

1 MS. ABEL: No, no. What I'm saying is
2 let's just pretend that -- that developing a graft.
3 They did some testing, they found that it fractured.
4 They're not going to run up and say oh well we
5 started developing this graft and it fractured, so
6 we changed it. They're going to change it, they're
7 going to redo the testing. And you're going to hear
8 about the final designs --

9 DR. WHITE: Well, then let's ask the
10 question. Has anyone found ten year testing to be
11 predictive of failure that they've developed?

12 MR. SMITH: I would say in answer to
13 that you've got to look at a different way. What I
14 learned from our ten pulsatile fatigue test is that
15 we shouldn't have a lot of fractures, that the
16 instant rate should be very low, especially in the
17 attachment zones. And that is what has -- the
18 income is that clinically.

19 So predictive, that's a strange word but
20 you can say, okay, I've got -- what's my sample
21 size, what conditions did I run them under. Okay.
22 I didn't see any fractures. That says to me that if

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1 I do get a fracture rate, it's going to be real low
2 and it's going to be caused by something else
3 potentially that I hadn't put in this test. But the
4 test is predictive in that manner.

5 And in the case of the excluder device,
6 we do not have fractures in the attachment region,
7 and that is really what the test was all about. And
8 our clinical data is showing that our pulsatile
9 fatigue test was predictive of that performance;
10 that the incident rate should be extremely low.
11 It's almost impossible unless you test hundreds and
12 hundreds of devices to say that the incident will be
13 zero. So generally the phrases are, you know,
14 there'll be no fractures under normal clinical use
15 or something like that.

16 So to me that's predictive.

17 MS. ABEL: But also I mean just the
18 example that Mark gave. I mean, Mark, when you redid
19 your testing, I'm assuming that --

20 MR. DEHDASHTIAN: Yes, I was going to
21 say in the same context that the testing, the
22 parameter in which we ran our tests under was wrong.

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1 It wasn't the tests. You can set the parameters and
2 the conditions and get the results that you most
3 likely will see in clinical. They may not be -- I
4 think the parameters that you send may not be
5 correct. That means we don't know how to test.

6 MS. ABEL: Did you test your old design
7 with your new test?

8 MR. DEHDASHTIAN: Yes, we did. And it
9 duplicated the fracture.

10 MS. ABEL: Da-ah.

11 MR. SMITH: What's the new test? Is
12 that a ten year pulsatile test?

13 MR. DEHDASHTIAN: Yes. It's the same
14 test, it's just more compliance, we induced more
15 loads to the stent break.

16 MS. ABEL: But I think it's fair to say
17 that we should be looking at clinical failures more
18 closely and try to figure out if there are ways to
19 evaluate for those specific failures because the
20 current testing doesn't address them?

21 DR. CONTI: I agree. I think Dr. White's
22 point is a very good one. If you do a ten year test

1 and it doesn't predict what you see in the clinic,
2 then that test is a waste of time. And it's exactly
3 what we've addressed in the standards. And I think
4 it's important that we all understand that based
5 upon the testing recommendations that we're coming
6 up with now, a huge percentage of all the testing
7 that has been done has been flawed. And this is what
8 has motivated us to come up with the new protocols.
9 And not new instruments, but new protocols.

10 And so I agree, if a test doesn't
11 predict, you shouldn't do it. That's why the new
12 protocols have been developed.

13 And even to this day I think the
14 transfer over to the new approach to durability
15 testing is just in its infancy. So in my opinion a
16 huge percentage of all the durability testing done
17 on stents and stents grafts has been done
18 incorrectly. And that's why we're having a hard
19 time correlating clinical relevance of these tests.

20 MR. WANINGER: I guess I would say if
21 you're running this test and it's not predicting the
22 failures you see in clinical, that doesn't mean you

1 don't do the test. It means you improve your test
2 and you take the information from the clinic and
3 feed it back into your protocol design and your
4 apparatus design until you do get something that
5 predicts what you're seeing the clinic.

6 Because I would have corroborate what
7 both Mark and Lou are saying. We have found this
8 testing methodology to be predictive and also be
9 reflective of the rates.

10 MS. ABEL: Compliance. At the last
11 workshop I think we spent at least half a day
12 talking about compliance and we pretty much got
13 nowhere with it. So I don't want to go down the
14 route.

15 Can we all agree that there is
16 difficulty in trying to figure out the compliance
17 and the testing? And also to determine whether an
18 appropriate soon compliance is for the abdominal
19 aorta. Because the last workshop we talked about
20 the compliance of the aorta ad nauseam and how it
21 was different in the back versus the front, and up
22 and down in old people, in young people, in rats and

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1 mice and everything else. So can we just note that
2 that's still something that's of question or has
3 there been some great epiphany or whatever you call
4 since the last workshop that we now understand it
5 better?

6 DR. FILLINGER: I think it's still well
7 defined or well enough defined, but I think we know
8 a lot more about it than we did at the last
9 workshop. I mean, certainly some of the things that
10 you've seen like what Tim was showing with basically
11 the movement of the stent with sitting inside the
12 aorta, some of the work that Mark was describing
13 with changing the compliance in the FEM model and
14 reproducing the fractures in both the prediction and
15 the model and the actual testing and the things I
16 showed with taking the final model and reproducing
17 the motion that we see on dynamic imaging, I think
18 we're a lot closer to being able to tell you what
19 the compliance of the aorta is, again within a range
20 than we were two or three years ago.

21 MS. ABEL: Is there a range that you
22 would have in mind right now?

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1 DR. FILLINGER: I don't think I'm quite
2 there yet.

3 MS. ABEL: Okay.

4 DR. FILLINGER: But, you know, I'll bet
5 within the next six to 12 months that we'll have a
6 reasonable range. And I think, you know, we're
7 closed like with the stuff that Mark was talking
8 about. And actually I think we're closer now than
9 we were before. And we know it's probably, you
10 know, twice as high as we used to think it was. Or
11 at least we've designed for twice as high as we used
12 to think. Some people have -- but we don't care
13 about that.

14 MS. ABEL: Right.

15 DR. WHITE: Well, I think you could put
16 a number on it now, though, right? I mean, what is
17 it? I mean, you can define a diameter change with
18 pulsation, if that's your definition of -- and you
19 know what that is in the range.

20 DR. FILLINGER: Well, I think it's
21 probably in the order of 1½ percent, but what the
22 range should be, I don't know. I can't tell you yet

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1 what the range should be.

2 DR. WHITE: No, no. I mean but that's
3 the number. I mean, there is a number that we know.

4 DR. FILLINGER: I think that's a
5 reasonable number.

6 DR. WHITE: And that's a lot stiffer
7 than a young patient.

8 MS. ABEL: So 1½ percent in terms of --

9 DR. WHITE: Diameter change of the
10 pulsation. And that's an active sclerotic 80 year
11 old patient, and it's much different in a younger
12 patient. It's as much as 10 or 15 percent.

13 MS. ABEL: Well, like I say, we want to
14 test for the --

15 DR. FILLINGER: Yes, there's also a
16 range, though.

17 MS. ABEL: Right.

18 DR. FILLINGER: That's the question.
19 When you're testing for the worse case what should
20 you test for? And I don't know the answer to that,
21 yet.

22 DR. WHITE: But there's also a
time frame on that. And Tim showed you that

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1 earlier. Compliance a device goes over time.

2 MS. ABEL: And we're just talking about
3 the plane old aorta. We can't even start talking
4 about the --

5 DR. WHITE: Well, put the fatigue rates
6 and the length of the tests are relevant to that.

7 MS. ABEL: You incorporate a response up
8 to what the aorta compliances when you're trying to
9 determine the compliance then with your device and
10 figuring out the diametric displacement. So you
11 have to start with the basic information.

12 DR. WHITE: Sure.

13 MS. ABEL: And build on it. So we're
14 just talking about the basic --

15 DR. WHITE: Well, I'd say we know the
16 basic and it decreases to some end point within two
17 years.

18 MS. ABEL: So you know it but Mark
19 doesn't yet, and Tim's going to tell us what he
20 knows.

21 DR. CHUTER: We just jump over the
22 discussion of the compliance of the aorta, since

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1 we're talking about the implantation sites. What we
2 really care about is the compliance of the aorta
3 prosthesis composite. And that is, number one,
4 device specific the most extreme example being the
5 balloon expanded devices.

6 Number two is measurable. There are very
7 good methods to measure these things now. If you
8 want real numbers, you can go out and get them.

9 And number three, it changes with time.

10 MS. ABEL: Again, I think what you have
11 what the compliances of the aorta first because
12 you're imputing that information in order to
13 determine the compliance aorta with the graft in
14 place.

15 DR. CHUTER: See, I don't think you need
16 to determine it. I think you can observe it. I
17 don't think you need to calculate it.

18 MS. ABEL: How are you going to observe
19 it?

20 DR. CHUTER: I think you just -- you
21 measure the movement of the aorta in a patient.

22 MS. ABEL: So we're going to implant it

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1 in a patient before we do our preclinical testing --

2 DR. CHUTER: Well, as always, this is an
3 iterative process. You just heard the most
4 predicted tests are the ones that have been
5 calibrated to reflect clinical experience. And I
6 think there is a lot of clinical experience already
7 out there with which you can calibrate this
8 particular aspect of testing.

9 MS. ABEL: Although you said yourself
10 that it's dependent upon the device design.

11 DR. CHUTER: Well, absolutely. And you
12 need to go to the devices that are out there, every
13 manufacturer can find examples of their own devices
14 or comparable devices, devices that they think will
15 behave in the same way.

16 MS. ABEL: I mean it seems rational with
17 respect to if you're going to be modifying your own
18 device and you understood the modifications and how
19 they could effect the potential for the compliance.
20 But, you know, if someone were to come up to me and
21 say well, my device is kind of like their device and
22 so I'm going to use information from their device,

1 I'd have to say well okay show me the -- tell me
2 what the characteristics are that I need to compare
3 to demonstrate that it's comparable with respect to
4 its effect on compliance. Show me the data with the
5 control information to demonstrate that it is
6 comparable.

7 DR. CHUTER: And as always, you would be
8 asking the right questions. And I think those are
9 justifiable, and I think it's tough on people who
10 are coming into the arena with a completely novel
11 device because they will not have that. Then they
12 have to resort to comparisons with other things that
13 may be a bit more tenuous. But the people who have
14 been in this arena for a little while have a
15 baseline to go with. I'd go with it if it's
16 available.

17 MS. ABEL: You know, the reason I bring
18 it up is because it's very difficult to do the
19 comparisons so say that I'm just like that person.

20 DR. CHUTER: Oh, I agree.

21 MS. ABEL: Or just like that device.
22 You know, people can't even afford to buy the

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1 control devices to do the direct comparisons
2 themselves.

3 MR. YU: Yes, I would like to offer a
4 further to Mark's comment. You know, we're talking
5 about a range of compliance and in the case of
6 durability testing, obviously the obvious thing
7 would be to choose for the upper case, upper range
8 which puts you at the maximum load. And that was
9 probably also on the basis when in the early days of
10 the -- testing that the lower range was, you know a
11 lower number was chosen because all the published
12 data are based on those calcific disease or toxicity
13 specimen. So that kind of led us to on the
14 estimated, you know, the real live environment.
15 You're not only looking at those elder, but when you
16 get to some younger patient you have a greater
17 compliance.

18 And the other issue in terms of knowing
19 the range, you know in terms of the actual native
20 arteries -- normally be looking at pulsatile
21 duplicated flow models, but you're also looking at
22 the possibility of producing those things from the

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1 FEA point of view. And a lot of FEA modeling, you
2 know, some of the nicer ones certainly you would
3 take that into consideration where you have combined
4 native -- the stent structure calculation in
5 combination. So I think some of those numbers are
6 still quite valuable you know assisting this part of
7 testing.

8 DR. CHUTER: I just want to make a point
9 of making sure, you know, clinical -- data of the
10 aorta, we tried to do that based on a -- it turns
11 out the measuring error is of the order of about 10
12 percent. We're trying to estimate, you know,
13 compliances of 3 to 4 percent. So the problem is you
14 could probably determine relatively accurately the
15 mean, you know, compliance. But, of course, for the
16 testing you're looking at the extremes and it turns
17 the standard deviation and the errors are so huge
18 you would have to pick compliances of 20 or 30 based
19 on your data, which is unrealistic.

20 So, clinical data may not help you in
21 establishing worse case conditions. You may have to
22 go back and look at some type of other data, you

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1 know, do some testing of the actual tissue to get
2 those values.

3 DR. CHUTER: MRI may not be the highest
4 resolution test that you can apply to this, though.

5 DR. GREENBERG: Well, I think there's a
6 lot of tests that should give you accuracy in terms
7 of both diameter and -- measurements in the realm of
8 about .1 millimeters.

9 MS. ABEL: Could you put your microphone
10 closer to your face and say that again, please.

11 DR. GREENBERG: I think that there's a
12 lot of imaging studies that should be able to give
13 you diameter in are area measurements in the realm
14 of .1 millimeters. And with the technology that's
15 out now in terms of gated studies, you can calculate
16 using a gated study the systolic and diastolic
17 diameters of devices.

18 DR. WHITE: I think in the clinical
19 scenario you've done a lot of these measurements
20 with any device, I don't care what it is -- or
21 expanded, that compliance is not more than 5 percent
22 and it's less in most cases. One or two percent and

1 it goes away over time. And where the pulsatility
2 remains is where Tim showed you today, at points
3 where it goes from a fixation site into an aneurysm
4 where there is no support of the device. And the
5 rest is none compliant.

6 I mean if everybody here on an
7 engineering basis is willing to throw out anything
8 under 2 percent, it's not an issue and we've done
9 that since Robert covered the whole wall yesterday
10 with that big formula.

11 DR. GREENBERG: But don't you think
12 compliance is a little bit more complicated than
13 that because there is a compliance that's
14 compromising the device or comprising the aorta and
15 there's cyclical compliance in that manner, but
16 there's also a longitudinal but we're not measuring
17 it because we don't how.

18 DR. WHITE: Well, that's right. We're
19 talking diameter now. We're not talking --

20 DR. GREENBERG: But they're both related
21 and important.

22 DR. WHITE: They're not related at all

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1 and the translational force that Tim talked about is
2 a different issue.

3 DR. CHUTER: It's more a fabric and
4 suture issue.

5 DR. WHITE: Yes, that's a different
6 issue

7 DR. CHUTER: And the diameter I think is
8 more of a stent issue.

9 DR. WHITE: Yes.

10 DR. GREENBERG: But I think it's all
11 related to the stiffness of the device, the overall
12 device.

13 DR. WHITE: In this area, though, a
14 stent aorta combination is essentially noncompliant.

15 DR. MATSUMURA: You've said this twice
16 today, but I just want to echo that and emphasize it
17 that the importance is testing of that boundary
18 between the next and the aneurysm. And that's where
19 we're clinical in certain failures.

20 And when you guys had the discussion of
21 is the test the issue. Well, it's because that's
22 one of the factors that have not been incorporated

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1 in models that result in clinical prediction where
2 you heard that not estimating the forces is another,
3 and not testing in angles. But I think not testing
4 that transition point is the --

5 DR. WHITE: Well, and that's a different
6 issue. But it's not the device in the graft. It is
7 the transition or the angle.

8 MR. DEHDASHTIAN: I think one of the
9 shortcomings of the testing is inability to test all
10 the parameters. We primarily test on a uniform
11 relating on the anchoring zone area, or that's what
12 we're looking for. But the truth is in the clinical
13 environment there are nonuniform loads due to
14 torsion, bending, calcification and essentially not
15 uniform loads that we can't really duplicate it in
16 the bench. And that's where the test is -- the
17 shortcomings of the testing that we do.

18 MR. GREENAN: I'd also like to comment
19 on the location of failures I think is very device
20 specific. So I wouldn't want to say that, you know,
21 at this particular transition is where we see
22 failures. I mean, each device is going to have

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1 failures in different areas depending on its
2 particular design.

3 MS. ABEL: That's one potential area for
4 having a failure, I guess, is the point.

5 MR. SMITH: So I look at the table that
6 we have on page 7 of this section and it says ISO
7 assumed compliance of the abdominal aorta is five to
8 seven percent. All the numbers that I've heard in
9 terms in calcification and disease and whatever are
10 lower than that. Obviously a very healthy aorta
11 could be higher than that.

12 I guess I'd like to weigh in on the 5 to
13 7 percent we put in the ISO standard. Is that
14 something that people would consider, you know, a
15 worse case compliance for these devices?

16 PARTICIPANT (Medtronic): Actually, I
17 have a question. When we say five to seven percent,
18 do we mean compliance or are we doing that diametric
19 deflection? I'm still confused.

20 MS. ABEL: Compliance.

21 DR. CHUTER: Compliance. It means a
22 change -- all interchange of pressure -- change of

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1 diameter --

2 MR. SMITH: As defined in the other ISO
3 719--

4 DR. WHITE: It's diameter for pulsatile
5 pressure. And pulsatile pressure is critical.

6 MR. SMITH: The definition of compliance
7 in the ISO is related to vascular graft ISO.

8 DR. WHITE: Right.

9 MR. SMITH: Which is basically per 100
10 millimeters of mercury.

11 PARTICIPANT (Medtronic): I think then
12 we should correct the units and say per millimeters
13 of mercury then.

14 MR. SMITH: It's already defined as
15 that.

16 MR. GREENAN: Wait. But I think that
17 the discussions that we're having now, we're talking
18 about diametric displacement and not to confuse the
19 5 to 7 percent which is over a pressure range as
20 opposed to an absolute diametric displacement. And I
21 think when you do the calculations you come much
22 closer to some of the values that some of the

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1 physicians have been mentioning.

2 DR. WHITE: Well, and a vascular graft
3 standard is not an aortic measurement. It is a
4 peripheral vessel measurement that goes back to
5 what --

6 MS. ABEL: We'll we're talking about the
7 definition.

8 DR. WHITE: These are vascular graft
9 standards that came out of small vessel testing.

10 MS. ABEL: No, no, no. We're just
11 talking about the definition of compliance in --

12 DR. WHITE: Right. That's where that
13 definition came from. It's not a aortic definition.
14 It's a perpherial vessel.

15 DR. CHUTER: Can I just comment on that
16 definition? Because in real life the compliance of
17 that aorta is going to vary enormously depending on
18 the pressure wave range in which you're testing it.
19 Because you got from elastic to collagen. And
20 they're different.

21 DR. FILLINGER: So, Tim, what you're
22 saying and what David is over here sitting here

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1 talking about, too, is that basically we should just
2 define the per 100 millimeters -- but what the mean
3 pressure is for that compliance measure as well?

4 DR. WHITE: It's the pulsatile pressure.
5 Because if you take --

6 DR. FILLINGER: So I'm asked to define
7 the pulse pressure and the mean pressure though that
8 that testing --

9 DR. WHITE: That's right. And then
10 there is no compliance -- the compliance is zero
11 once it's fully distended.

12 DR. GREENBERG: Well, and I think the
13 worse case issue becomes a pretty controversial
14 issue because a lot of aneurysms are caused by
15 dissections. And if you the compliance in a
16 dissected aorta, it's much worse than the compliance
17 in a nondissected aorta.

18 MS. ABEL: In a -- aneurysm, a lot are
19 caused by dissection.

20 DR. CHUTER: At the implantation side, I
21 think not. I don't see a lot of dissected
22 implantation sides in the abdominally aorta cases.

1 DR. GREENBERG: When you're talking
2 about doing this there's -- if you're talking about
3 a worse case scenario and you want to know what the
4 limits of compliance are going to be, we can specify
5 it and say in the absence of the dissection or in
6 the presence of an aneurysm or something like that.
7 But if you want to do a worse case scenario,
8 dissections are a worse case scenario.

9 DR. FILLINGER: But how often are you
10 implanting the graft at the attachment, having a
11 dissection at the attachment site in the abdominal
12 aorta? I mean, that's a very uncommon -- I mean a
13 thoracic and thoracic sections, that's a whole --
14 that's a whole different story --

15 DR. GREENBERG: I have the feeling that
16 these definitions and things will transcend
17 abdominal and thoracic and they may not be separate
18 standards for each of them, and that's why I bring
19 it up.

20 DR. WHITE: Most of the dissection
21 patients, they are extremely hypertensive. And the
22 compliance of the aorta then is almost zero. It's

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1 very hyperdynamic.

2 DR. GREENBERG: I only bring up what is
3 the worse case scenario.

4 DR. WHITE: Well it's fully distended
5 there so the compliance is low. It's actually a
6 normal tensive young patient that has the greatest
7 compliance because then the variation is great --
8 the pulse pressure is real wide. It goes from
9 minimum distally to maximum systole and as it
10 stiffens or the pressure gets higher, the compliance
11 goes away.

12 DR. GREENBERG: Now within a dissection
13 you're going to exceed any young patient because the
14 diameter change and the area change in the -- which
15 is where the graft would probably sit, is huge.
16 It's much greater than any young patient will
17 generally have.

18 So I think we can eliminate dissections
19 and just say in a worse case scenario excluding
20 dissections. But if we try to transcend these
21 standards to thoracic grafts, this is going to be
22 very important. And when we want to look at these in

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1 abdominal grafts, then you just have to make some
2 caveats.

3 DR. WHITE: Does that compliance hold
4 after you've placed the stent graft and close the
5 dissection?

6 DR. GREENBERG: It depends how you treat
7 the dissection. You can eliminate some of the
8 compliance by equalizing the pressure. Say, for
9 example, you put a stent graft and you see a
10 tremendous amount of compliance and then you
11 fenestrate it distally so you're making big holes to
12 equalize things, you drop the compliance of the
13 whole situation which probably would make the stent
14 graft more durable, which is what people hypothesize
15 doing. But in the circumstance it's becoming a very
16 critical issue. And in terms of thoracic design, I
17 think it's important.

18 MR. CARDELLA: Is the issue that you're
19 trying to get to not so much of the compliance of
20 the tissue, but you're trying to talk about the
21 excursion of aortic wall between systole and
22 diastole? I mean why couldn't you define -- what I

1 think you guys are talking about, I think what you
2 want is diameter of the aorta at systole, minus
3 diameter of the aorta at diastole divided by the
4 diameter of the aorta at diastole times a 100
5 percent. Is that what you're talking about? How
6 much it moves or are you talking about the intrinsic
7 characteristics of the tissue, how much that tissue
8 can distend and tolerate with pressure changes?
9 Which are you after?

10 DR. CONTI: Both. Both.

11 DR. WHITE: Well, the definition you
12 describe is the definition of compliance. The only
13 variable you didn't mention is the pulse pressure.
14 And if you add that in and you know what the mean
15 pressure is, then you can calculate the compliance.
16 Otherwise, it makes -- there is no way to calculate
17 the variable.

18 MR. CARDELLA: See, I think what you
19 ought to be concerned about is how far the aortic
20 wall moves between systole and diastole so that your
21 landing zone remains in apposition with the graft.
22 That's what you're worried about. I don't think it

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1 matters about the pulse pressure. Certainly the
2 compliance number or the excursion number will be
3 bigger with the high pulse pressure because if you
4 water hammer against the aorta with, let's say, a
5 pressure of 180 over 40, that's going to make more
6 excursion. But the compliance of that tissue I
7 don't think changes. The compliance of aortic wall
8 tissue, the stretchability or the elasticity of it
9 is the same. I'm not sure --

10 MR. YU: No. The aorta stay constant
11 here or consist of collagen and elastin and that
12 changes over the pressure load.

13 DR. FILLINGER: The mean pressure is
14 important because of what Tim -- both just
15 mentioned. The amount of loading on the fibers
16 changes depending on the mean pressure. So the mean
17 pressure and the pulse pressure are both important.
18 And this is all within the context of the T testing
19 and trying to determine what that excursion is.

20 So, I mean, you're right. What we're
21 trying to get at is what is the excursion that we
22 want to test during the T testing to get the stress

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1 ring -- you know, the stress on the device. But that
2 requires us to know or at least it would be helpful
3 to know the compliance of the aorta in order to
4 figure that out or the compliance of the combination
5 of the aorta and the device.

6 DR. WHITE: The worse case scenario is
7 when the fixation length compliance is zero, there's
8 no movement and then there is a transition to an
9 aneurysm where there's lots of movement. So the
10 greatest stress is in a zero compliance fixation
11 site.

12 MR. SMITH: Well, I mean to a degree.
13 You have the greatest compression, meaning maybe the
14 greatest mean stresses. But if you don't deflection,
15 then you don't have alternating stresses. And if
16 you don't have alternating stresses, you won't have
17 a fracture in that region. So it is about the
18 transition. It is about movement. And it is about
19 the combination of mean and alternating stresses.

20 DR. WHITE: And I will then take your
21 point one step further. You're exactly right. Where
22 there is no alternating stress, which is the ten

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1 year straight model, there is no relevance. It is
2 the transition zone from zero compliance to a larger
3 compliance is where they occur in everybody's
4 device.

5 Now, there are other methods of failure,
6 but that is the stent fractured model for failure.

7 MR. SMITH: So what we try to reproduce
8 in the test is a means stress condition and an
9 alternating stress condition. A combination of
10 those two and compare that to where we would expect
11 the material to lax. So, I mean, you could do that
12 in many ways. You could do it with -- you could do
13 it with whole devices, but it is the combination.
14 And so these pulsatile fatigue tests have a mean and
15 alternating stress component with them, which the
16 slides for FEA I showed said okay use a technique
17 like FEA to determine what they may be in their
18 pulsatile T test.

19 The other thing I'd like to comment is
20 arteries are vesical-elastic materials combined with
21 whatever you want to call it, elastin and collagen.
22 So they do behave differently under different

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1 stresses.

2 MS. ABEL: Mark, I just wanted to ask
3 you to tell David that he can use the microphone,
4 too, so he doesn't have to just whisper to you. He
5 can share with the rest of the group.

6 DR. FILLINGER: He just wanted to blame
7 me if anything came out bad.

8 MS. ABEL: Okay. So we've had plenty of
9 compliance discussion. That wasn't nearly as bad as
10 last time.

11 DR. CHUTER: I thought you were going to
12 tell us about what would happen if we were
13 noncompliant.

14 MS. ABEL: You know about that. Do you
15 want to tell the rest of the group.

16 PARTICIPANT: Nobody else is sharing
17 here.

18 MS. ABEL: Dan, are you just exercising
19 or do you have something else to say?

20 PARTICIPANT: No, I'm just exercising.

21 MS. ABEL: Okay. Just checking.

22 All right. I think a lot of the other

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1 parameters that we've mentioned, you know, are based
2 on the compliance discussion. So I don't know that
3 we really need to go into them unless I -- if people
4 disagreeing there's other information that we need
5 to have. I think we talked about displacement, and
6 it may be possible to actually measure displacement
7 clinically and then you get away from the compliance
8 issue.

9 Test frequency, we've already discussed
10 the fact that you should justify your test frequency
11 based on the physiologic conditions as opposed to
12 just cranking up as fast as you can, and make sure
13 that you monitor and that your device continues to
14 go through any excursions that you expect it to, and
15 that it stays in contact with the mock artery.

16 The length of junction or overlap
17 clearly needs to be per the IFU. But there are a
18 lot of people that at the time that they did their
19 testing didn't have overlaps. Cycles don't have
20 modular devices and then it's justified.

21 Will had said earlier that it's
22 difficult to test all the components, but can we at

1 least agree that if you've got a modular bifurcated
2 device for the most part, unless you're testing some
3 different conditions, you should be using you know
4 the modular bifurcated device. So hold the device
5 to T testing basically.

6 PARTICIPANT (Medtronic): I have a
7 comment on modular devices. One of the problems
8 that I see is if you're doing a pulsatile 400
9 million T test with modular components, if you put
10 in modular components that pretty much reduces your
11 compliance, composite compliance. So if you think
12 about the ultimate in strengths, they're going to be
13 lower than they would be if you're not using modular
14 components. So you're pretty much under testing your
15 samples.

16 As far as the other things are
17 concerned, wear of the graft material and threading
18 and contact -- metal to metal contact, we're not
19 looking at that in this test anyway. So what's the
20 value of modular in this test?

21 MR. GREENAN: Well, I think you have a
22 difference here between modular meaning, you know,

1 extinctions on either end as opposed to, you know, a
2 -- limb. So I think, you know, we definitely test
3 with a -- limb in place in a bifurcated device. The
4 question comes in if you -- I mean you can make a
5 much stiffer device if you put an approximal cuff in
6 it. So that's where we run into maybe some typical
7 challenges on how to interpret the results of those
8 tests.

9 MS. ABEL: Yes. That's why I was saying,
10 you know, just the bifurcated device, not with any
11 additional extenders or cuffs.

12 DR. WHITE: I don't think there's any
13 value at all. We're back to a clinical scenario --

14 MS. ABEL: You don't think there's any
15 value in this testing at all --

16 DR. WHITE: No, no. I do. But with the
17 modular clinical failure model is in angles. It is
18 not, again, in pulsatile stress testing. And we
19 know, we got -- I hate to confuse it with clinical
20 data. But we have data.

21 MS. ABEL: But again, you're not trying
22 to test for all the failure modes in this one little

1 test. You're looking at this diametric excursions
2 that theoretically you're duplicating --

3 DR. WHITE: Then there's no new
4 information. It's not worth it. You've got other
5 things to waste your money on.

6 MS. ABEL: That's fine. You don't like
7 the test anyway, so --

8 DR. WHITE: Yes, okay.

9 DR. CHUTER: the angles are a problem,
10 but a pulsatile model that's particularly -- the
11 combination of a pulse and an angle is a bad one.
12 And I think that that's why Rod is picking up
13 fractures and whatever else at angles or at places
14 where a constrained and unconstrained graft meet.
15 It's because that's where the movement happens.

16 DR. WHITE: That's it.

17 MR. BIGGERSTAFF: Excuse me. Can I just
18 confirm whether the displacements are in the native
19 vessel or at the point where the graft is inside the
20 vessel? Anyone have a point that you want to make?

21 MS. ABEL: I'm sorry, could you repeat
22 it?

1 MR. BIGGERSTAFF: Yes. Are the
2 displacements that you put on this slide there are
3 they of the native vessel or is that the vessel with
4 the device in?

5 MS. ABEL: With the device in.

6 See, I can answer a question. Come on,
7 guys.

8 DR. MARIN: Dorothy, I was going to
9 suggest thanks to Mark's new and improved number of
10 1.5 percent, do we need to adjust that range that
11 we've got at that point in that chart?

12 DR. FILLINGER: Let me answer that
13 question. No, don't adjust it. It's new and
14 improved, but it's still too new and necessarily
15 improved enough. It's just not enough patients. We
16 need more testing, more patients. You know, there's
17 a lot more work to do to say what -- and I think the
18 current outer boundary is still a good outer
19 boundary.

20 MS. ABEL: And that gets back to again
21 just the whole compliance issue. This is actually
22 the reported values. This is what people did use in

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1 their testing. And so we aren't going to change
2 what they did use to what we think they should use.

3 Some people did try this with their --
4 extenders, and I think we've heard enough about that
5 we could probably could note separate testing is
6 necessary to evaluate the interaction of the --
7 extenders with the main device.

8 Sample selection, most used FEA or
9 something along those lines to come up with the
10 conditions.

11 Oversizing, according to the IFU -- for
12 maximum. Sorry.

13 Any thoughts with respect to oversizing,
14 would it make sense to have a maximum oversizing or
15 a minimum oversizing to most challenge the device
16 or--

17 PARTICIPANT (Cook, Inc.): I would just
18 ask a question. Because we have a size 10 to 23
19 percent or whatever, and that's in the -- and the
20 graft is supplied by the manufacturer. But my
21 understanding is that that diameter is measured as
22 the inner part of the crimp. When you unpressurize

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1 a graft, what happens when you supply it uncrimped?

2 MR. YU: I think the other issue with
3 oversizing that's -- you know, as we try to relate
4 to the clinical activity is that, you know, what do
5 we mean by oversize in a clinical situation that's--
6 probably most of you know, I mean there is a
7 situation where there are different unit modality it
8 provides different kind of answers, as well as
9 people who use the internal -- and apply to
10 oversizing.

11 So I think from where I sit and when
12 you're testing on bench, that the measurements are
13 very specific. And once you translate the clinical
14 that range suddenly opens way out. And I think
15 that's something that should be considered.

16 MS. ABEL: It's according to the IFU, so
17 it is considered. I mean, if you -- when you make
18 your measurements for the test, you do it for the
19 external --

20 MR. YU: Right. But at the same time,
21 you know, as we know there is still a discrepancy
22 between what one can measure for an internal

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1 diameter of an artery versus one that's the actual
2 sample. If you take a specimen out and you measure
3 it physically, but the right measurement there is
4 actually a discrepancy there also. So what I am
5 saying is that for your actual testing you may test
6 for a range, but in the real life situation that
7 range is much bigger than you would think.

8 MS. ABEL: Michael's question didn't get
9 answered. Can anyone help out with respect to that?

10 PARTICIPANT (Cook, Inc.): I might have
11 put it very well, but the 20 percent may be very
12 different according to where you start. So if you
13 start on that measurement, you're actually
14 oversizing maybe 30 percent because the graft is
15 different when it's pressurized to the measurement
16 that you're given. And maybe that's taken into
17 account by the IFU. But we don't standardize what
18 the diameter of the graft material is in this.

19 DR. MATSUMURA: So to follow up on that,
20 there's lots of reasons for oversizing. There can
21 be the nominal diameter versus the actual when under
22 pressure, which we know -- stand. Then there's the

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1 manufacturing tolerances that they're allowed when
2 they say it's nominal. And then there's the
3 measurement error. And then there's what we intend.
4 So it really could really tremendous if you get a
5 confluence of those four factors.

6 PARTICIPANT (Cook, Inc.): I think for
7 the performance for this particular test we're
8 looking at that stent. So, you know, that whole
9 diameter of the graft probably has less of an
10 influence than the nominal standards being tested in
11 a appropriate condition.

12 DR. MATSUMURA: With that device, but
13 not with the others necessarily.

14 PARTICIPANT (Medtronic): I think one of
15 the things we have to be careful when we do this
16 test is that when we actually try to simulate the
17 same oversizing, we have to put in the stent graft
18 into the tube that has the intended diameter at the
19 mean testing pressure, not when it's deflated. And
20 that's what some people fail to understand. But you
21 have to think of what diameter too will take at the
22 mean testing pressure.

1 MR. RODGER: Yes. Just a comment. One
2 of the things you have to take into account here is
3 that it's designed specific because, for example,
4 you can have a graft and the diameter of that is
5 constrained by the stent. So your graft material
6 may not be fully expanded but it's limited by the
7 size of the stent, the attachment system. So there's
8 two separate things there.

9 DR. FILLINGER: And vice versa.

10 MR. RODGER: Yes, absolutely.

11 DR. FILLINGER: And that's why, you
12 know, yesterday we talked a lot about further design
13 tolerance and characterizing the device over a
14 range, not just limited to the IFU. And I think
15 that's sort of the stent sizes that we can --

16 MS. ABEL: Well, on this test it would
17 be difficult to do that sort of thing, you know,
18 where you're going to do multiple oversizing
19 conditions -- cheers.

20 We don't incorporate that into this test
21 as far as the oversizing. And people have a
22 tendency -- I mean, I guess people did -- yes. Some

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1 folks had a range -- well. I'm trying to remember
2 with our compiled information if people used 10
3 percent or if they said we used a range between 10
4 and 23 percent. I can't remember.

5 But, I mean, does it make sense to only
6 use the maximum or does anyone care as far as
7 oversizing?

8 PARTICIPANT: You know, I think it
9 depends on the stent. If you think of Nitinol stent
10 structure, the oversizing can shift your mean and
11 alternating components very significantly and the
12 failure envelop for those will differ. So you've
13 got to analyze in a design by design basis.

14 DR. WHITE: This one actually is not
15 hard for me to figure out how to do because these
16 are in the bench, these aren't in the patients. So
17 the variables where sizing we're about occurs,
18 there's bad imagining and you don't know if the
19 variability was -- when you're putting in a tube
20 that's a fix diameter, you can calculate it. The
21 sizing is actually the most accurate scenario.

22 MS. ABEL: Yes. But what size do you

1 use is all I'm asking in terms of --

2 DR. WHITE: Whatever that device will
3 tolerate. If it won't tolerate any, you don't do
4 any. And that is a manufacturer --

5 MS. ABEL: Most people have range of
6 oversizing indicated in their IFU.

7 DR. WHITE: Well, it may be zero or it
8 may 50 percent.

9 MS. ABEL: But it's a range. What if
10 the range is zero to 50 percent?

11 DR. WHITE: It's okay if it makes sense
12 for that device and they test --

13 MS. ABEL: What do you test at?

14 DR. WHITE: All of them, zero to 50.

15 MS. ABEL: What would be worse case?

16 DR. WHITE: Anything that doesn't fit.
17 I mean, and it would make sense for that device.

18 MR. SMITH: See, worse case can vary
19 depending on what you're trying to find out. If
20 you're trying to create the maximum stresses in the
21 stent, wire framed, then you want to have as much
22 mean and alternating strain as possible. If you're

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1 trying to figure out how components are going to
2 separate, then you're probably going to want to go
3 with the least amount of oversizing to see between--

4 MS. ABEL: Well, remember which test
5 we're talking about.

6 MR. SMITH: Right. I know. So, you
7 know, that's why multiple tests and multiple
8 scenarios. In our IFU we don't ask the physician to
9 calculate the percent oversizing. We give him a
10 table.

11 DR. WHIRLEY: I would echo that I think
12 the right place the test varies is whatever's worse
13 case for the device. And you may have to go to an
14 FEA to know that, but it's usually not difficult to
15 figure out.

16 MS. ABEL: Worse case oversizing you --

17 DR. WHIRLEY: That's right. Which could
18 be an either and depending on the device design, the
19 materials, etcetera.

20 PARTICIPANT (Medtronic): I think I'd
21 like to make a comment. I will just try to relate
22 to Lou's point that in this testing it is all by the

1 combination, the mean strain and alternating strain.
2 And if we're really talk about -- talk to some
3 people from developed industries like airline
4 industry, they would ask us okay so what are the
5 real service conditions. Because if we only use the
6 maximum oversizing in clinical studying we would
7 have less ultimate extreme. If you go at the
8 minimum oversizing you have more ultimate extreme.

9 And the only really way to figure out
10 which the worse there is to test both scenarios.

11 But we're so far from these developed
12 industries, and then I guess what we do is just we
13 consider let's do the worse case scenario based on
14 the assumption that the more oversizing is the worse
15 case. But that may not be true.

16 MR. PELTON: Let me comment on that and
17 follow up with a couple of comments that were made
18 earlier.

19 MS. ABEL: Could you please tell people
20 who you are?

21 MR. PELTON: I'm sorry.

22 MS. ABEL: I know you're famous, but not

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1 everyone knows.

2 MR. PELTON: My name is Alan Pelton.
3 I'm with Nitinol Device System Components. So as
4 the name of our company implies, I'm not a Nitinol
5 metallurgist. And so I know that a lot of the stent
6 grafts used do have skeletons made out of nitinol.
7 And one of the topics that I haven't heard discussed
8 here is, you know, how do we determine not
9 necessarily what are the right physiological
10 conditions because I know that's under a lot of
11 debate, but what's appropriate for the nitinol
12 skeleton. And if we're using this pulsatile fatigue
13 test solely or mainly to determine what's the
14 fatigue behavior of the nitinol, then we really need
15 to know what's the fundamental behavior of nitinol.

16 So, for example, we do not rely on a
17 straight pulsatile fatigue test whether it's
18 bifurcated or not to determine the fatigue behavior.
19 We consider that to be an FDA test. What we'd
20 rather do is do a lot of side testing which looks
21 specifically the fatigue behavior where we changed
22 the mean and the alternating strains to determine

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1 how that compares through an FDA analysis to the
2 conditions that we've chosen through our IFU.

3 In the case specifically if we're going
4 to test at one extreme or the other, the most
5 important thing to remember about nitinol fatigue
6 behavior is that everything is controlled through
7 the alternating strain. It's not like stainless
8 steel that you can draw a straight line boardman
9 analysis.

10 The mean strain is relatively of little
11 importance. In fact --

12 PARTICIPANT: I would argue that. I
13 would say the mean strain can be important and it's
14 able to shift the function or behavior of the
15 alternating component. It's been shown.

16 MR. PELTON: No.

17 MS. ABEL: Could you please talk into
18 your microphone?

19 PARTICIPANT: Sure. I think the mean
20 strain does have an effect. It's able to shift.

21 MR. PELTON: If you talk to -- Brian
22 Byrd, you know, he would argue that in fact as you

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1 increase the mean strain you actually get better
2 fatigue --

3 PARTICIPANT: Well, he describes a sweet
4 spot. So if you know where you are within the
5 spectrum, if you acted -- around .1 percent versus
6 over one percent. So you need to know where you are
7 within there.

8 MR. PELTON: More complete data sets
9 that we have shown have shown actually that above
10 about 1½ percent mean strain you can actually get
11 like almost an order of magnitude increase in
12 fatigue behavior for the same alternating strain.

13 PARTICIPANT: Correct.

14 MR. PELTON: So the important thing is
15 is to make sure that when you are doing your testing
16 for the worse case scenario for nitinol is that you
17 do take into account that the important factors are
18 the alternating strain. So that will be design
19 specific. But again, the alternating strain rules.

20 MR. YU: I would just add two point.
21 One is again going to the IFU. I think when you
22 define IFU oversizing we really should define both

1 what imagining modality we're using because
2 different imagining modality does give different
3 responses.

4 And secondly, it's a case where, you
5 know, depending on the example -- I mean, again it's
6 a device specific on number internal that range.
7 For instance your -- if you go to a minimum
8 oversizing which case invariably the Y structure
9 will be up to open up to its maximum size and then
10 even though the stress and strain is very evenly
11 distributed right across that wire form, but you
12 also -- that's put a high mean stress in the system.
13 But whereas, in a case where if you have greatly
14 oversized, then you actually -- it becomes a
15 nonuniform distribution of the stresses within that
16 wire form. So, yes, so the two numbers are quite
17 relevant in terms of the testing requirement.

18 MR. DEHDASHTIAN: I think Lou explained
19 as well, in order to find out which one is worse,
20 you have to test both of them. Both mean and
21 alternating. So there is -- until you don't know the
22 value, you don't know which one's worse. The design

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1 contemplates how much oversizing come to be a
2 factor.

3 MS. ABEL: I didn't follow that. You
4 mean in alternating with respect to determine the
5 mean of the worse case oversizing?

6 MR. DEHDASHTIAN: Right. Yes. The
7 question was is worse case scenario is when you do
8 minimum oversizing or when you do maximum
9 oversizing. And I think you don't know the answer -
10 - first of all, it's design dependent, material
11 dependent. But you have to understand or have to
12 calculate for both mean or/and alternating and then
13 compare the two or combination of the two.

14 MS. ABEL: Yes, Tom?

15 DR. FOGARTY: There's a whole bunch of
16 people that can get NIH grants in this room.

17 MS. ABEL: Thank you, Tom.

18 DR. FOGARTY: Yes. Thank you.

19 MS. ABEL: I'm glad I talked to you
20 about it.

21 As far as pressure, I don't know that we
22 need to talk about because that's going to be driven

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1 by the other parameters or tests, right? I mean,
2 it's not like you need to pick an appropriate
3 pressure. You have to pick the pressure that goes
4 along with what you're trying to -- okay. We don't
5 have to talk about that.

6 And while we, again, talked about in
7 detail with respect to the impact of -- it's
8 insignificant, so we don't have to spend time on
9 that.

10 So the other parts of this section I
11 think we'll probably go through fairly quickly in an
12 effort to actually to have lunch.

13 And can someone wake up the projector,
14 please. That discussion took so long using the
15 projector.

16 So we're moving on to stress screen,
17 which we'll move to stress. Everyone used FEA for
18 their stress screen analyses. The main difference
19 between what people reported was the way that they
20 determined the boundary conditions. And some did it
21 in an examination of the clinical environment and
22 the manufacturing. The worse case conditions for

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1 the IFU nonlinear model, physical and thermal
2 stresses, compliant tube, enforcing aorta; all these
3 things were essentially used in determining the
4 boundary conditions.

5 People conformed to the ISO standard.

6 And I think we can go on.

7 So we mentioned that people are using
8 different methods to establish their boundary
9 conditions. Should displacement be considered? I
10 think, obviously yes.

11 And I think we've talked enough about
12 displacement and compliance and that sort of thing
13 with respect to the T testing. All that could apply
14 here.

15 Degree of angulation, is this something
16 that's incorporated within the FDA's current -- does
17 it need to be? Yes, it is already or yes it needs
18 to be done? So the answers just yes. Is there any
19 additional information we need in order to improve
20 that input? Because, again, people have done FEA
21 analysis intending to determine whether their
22 product is going to break or at least have

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1 information to go back to look at. You know, and it
2 hasn't been predictive because devices have broken.
3 So, maybe there have been some things input in the
4 boundary conditions that weren't 100 percent
5 accurate.

6 We know enough about angulation?

7 Physiologic pressures. Is this
8 something that's part of a FEA? I don't do FEA.

9 DR. WHIRLEY: Physiologic pressures
10 probably don't influence radial dilatation analysis,
11 but the FEA should include consideration of axial
12 loads that resist migration and physiologic
13 pressures certainly as we saw yesterday and in the
14 presentations today have a significant and maybe
15 dominant role in the definition of those axial
16 loads.

17 DR. FILLINGER: Yes. Physiologic
18 pressures in, again, sort of the worse case scenario
19 not just the typical physiologic pressures, but the
20 worse case.

21 DR. WHIRLEY: Well, how do you define
22 that pressure?

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1 DR. FILLINGER: Well, I think that
2 that's something that people just have to make a
3 logical -- I don't think we should necessarily
4 create a standard for what the worse case scenario
5 is, but when someone creates a model they should
6 justify what they used for the pressures basically.

7 MS. ABEL: That was Mark Fillinger in
8 case you're trying to figure out.

9 Vessel diameter, obviously, is part of -
10 - flow? We don't care about flow? I'm just looking
11 at Robert because he's looking at me.

12 All right. Let's go to the other table.

13 PARTICIPANT (Medtronic): I think
14 there's one more. I don't know if that should be
15 incorporated here, but also manufacturing process.
16 In everything that spring goes through.

17 MS. ABEL: Yes, that's part of the ISO
18 testing.

19 PARTICIPANT (Medtronic): So we know how
20 much plasticity there is.

21 MS. ABEL: Right. I mean that's
22 certainly part of it.

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1 MR. WOODS: I have a question on that
2 table before you leave it. Is the purpose of the
3 discussion to seek recommendations? Why wouldn't we
4 specify and define what physiologic pressure is?

5 MS. ABEL: But the question is, I'm
6 sorry -- unfortunately, you've got a cheap seat back
7 there. But if you look in your little handy dandy
8 binder, you can look at table 3.2.1. And the
9 question is what additional information regarding
10 the specific parameter would be needed to improve
11 this analysis?

12 So we agree that something like pressure
13 is important and then we've had a little discussion
14 to say that worse case pressure may be what we
15 really need. We beginning to find out or learn or
16 how do we figure out what case pressure is. Because
17 I don't think we have agreement in the room of what
18 worse case pressure is. So that's all we're trying
19 to do is identify areas that we need to get some
20 additional information, possibly do some additional
21 study, do some research, do whatever in order to
22 have that information available to input into these

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1 tests.

2 DR. FILLINGER: Basically some things
3 come up over and over again like the degree of
4 angulation. We can't define it and say okay what is
5 the absolute degree and yet it may vary from device
6 to device depending on your IFU. And it may be --
7 you may have benefit of some clinical information of
8 seeing what the device does after it's implanted.
9 But that's why some of this is sort of necessarily
10 vague because basically it's identifying where we
11 need to do more study, but we can't say this is the
12 pressure and this is the angle because we don't have
13 enough information yet to say that. It's just we
14 know we need to do more study about it, whether it's
15 the people getting the NIH grants or whether it's
16 the manufacturer. But somebody needs to study it
17 more.

18 MR. WOODS: See, the problem that I see
19 is if you develop a standard, and I mean I've been
20 involved in writing some standards for SIR, maybe
21 different than these types of standards, and I've
22 been involved in an IEC and SIR standards, not ISO

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1 or not FDA. But sometimes it may be a value as a
2 starting point to say we should test the degree of
3 angulation at 45 degrees. And we should say
4 physiologic pressure is 120 over 80 or 150 over 70.

5 If you leave it to individual
6 manufacturers and vendors to say, well, our device
7 is a little bit unique so for us the worse case
8 scenario is 120 over 80, somebody else says well for
9 us the worse case is 220 over 150; you lose
10 comparability of results. That's my only point.

11 MS. ABEL: And I think where -- I'm
12 sorry. Just going to respond and then you can, Tom.

13 The ISO standard is intended to capture
14 standardized testing methodology. So it only
15 captures what has already been agreed upon to be the
16 standardized testing. And we can't just make things
17 up and put in an ISO standard. That's not what it's
18 intended to do.

19 What we can do in a forum like this is
20 talk about things that have not yet been
21 standardized and try to figure out how to get to
22 that point and try to get some definitions.

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1 I think we have to be very careful about
2 saying that we should apply the same stuff to all
3 manufacturers because although we want to have
4 standardized testing as much as possible and it's
5 useful for comparison purposes and all sorts of
6 other things, we also have the potential of
7 squashing progress with respect to development of
8 tests. And so if we force the next guy that comes
9 along, you know what if these guys sitting next to
10 those guys had to do the same tests that they did
11 ten years ago, that doesn't make any sense.

12 It's a dynamic process. We need to
13 continually improve upon it. We need to encourage
14 individual manufacturers to take the initiative to
15 step outside of the box, if you will, to come up
16 with what makes real sense. And until we can all sit
17 here and agree, for example, of the worse case
18 conditions, even the people in the room can't agree,
19 you know does it make sense to say well that's what
20 it should be. And I think that's potentially very
21 limited.

22 Michael?

1 PARTICIPANT (Cook, Inc.): These are
2 vascular patients and most of them are hypertensive.
3 So it may be misleading to say physiological
4 question. Maybe you should just say systolic
5 pressure or pathological pressure because it's not
6 uncommon for them to go to 200. And when these
7 people exercise, their pressure always goes up
8 because the capacity of the aorta is down. They
9 don't have it. So these people are walking around
10 with a blood pressure that will often go to 200, and
11 that's what you need to test for because that's what
12 will dislodge the graft.

13 MS. ABEL: Tom?

14 DR. FOGARTY: Tom Fogarty.

15 This can be simplified. I don't think
16 anybody would take anybody in the operating room or
17 a cath lab or a radiology suite if their blood was
18 220 over 180.

19 MS. ABEL: Okay. But after you let them
20 out of the suite, you have very little control over
21 them.

22 DR. FOGARTY: Well, you do, actually.

1 You have medication, you have IV drips. Now, they
2 may not be used properly, but --

3 MS. ABEL: But that's the point. I
4 mean, patient compliance with medication --

5 DR. FOGARTY: Well, no. That's nurse
6 compliance in that setting.

7 MS. ABEL: But eventually they are
8 leaving.

9 DR. FOGARTY: Well, they are leaving but
10 I think --

11 MS. ABEL: Unless the patients don't
12 make it out of the hospital.

13 DR. FOGARTY: Well, some may make it
14 somewhere either to a funeral home or you know,
15 someplace. But the fact is I don't think any
16 patient that gets in a hospital and the nurse comes
17 around and measures a blood pressure and it's 220
18 over 80, they're not going to have a procedure done
19 until the blood pressure is under control.

20 MS. ABEL: We're talking more long term.
21 And, you know, hopefully the blood pressure will be
22 somewhat controlled, but I don't think it's

1 realistic to assume that it will always be.

2 DR. FOGARTY: I believe that also. But
3 you can only do so much.

4 MS. ABEL: Yes. And you want to test
5 for reality to the extent --

6 DR. FOGARTY: Well, I think the reality
7 is there is very few people going around with a
8 systolic pressure over 220. Am I right or wrong?

9 MS. ABEL: You said 200.

10 DR. FOGARTY: No, I said 220.

11 MS. ABEL: You said 200.

12 PARTICIPANT (Cook, Inc.): I think
13 that's probably right if you measure their blood
14 pressure at rest. But you don't know what it is
15 when they go upstairs or when they put me on an
16 exercise machine my blood pressure went up to 200.

17 DR. FOGARTY: Well, you had to be on
18 antihypertensives.

19 PARTICIPANT (Cook, Inc.): Well, it's
20 not 200 at rest. It's only 200 when they're running
21 you on the exercise --

22 DR. FOGARTY: Look, you're talking about

1 something none of us know because we can't measure
2 arterial blood pressure continuously beat by beat.

3 PARTICIPANT (Cook, Inc.): No. But we
4 have to make a device that is able to withstand the
5 blood pressure at its maximum, which may be 200 in
6 many patients of this group.

7 DR. FOGARTY: Well, why don't you make
8 it 240?

9 PARTICIPANT (Cook, Inc.): Okay. Then
10 make it 240.

11 MS. ABEL: Do I hear 300?

12 MR. SMITH: I'd like to interject. I
13 just wanted to make a comment. Pressure in FEA
14 doesn't mean anything without compliance. So I
15 think you have to add compliance. You don't have to
16 say mean anything up there.

17 MS. ABEL: Yes, we can say that.

18 MR. SMITH: Well, you could say
19 pressures in combination with the compliance.
20 Because what the FEA wants to know is how far it's
21 moving. And so pressure and compliance go hand-in-
22 hand.

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1 MS. ABEL: I think we just didn't want
2 to go there. I don't know why compliance isn't on
3 the chart and then we don't want to talk about it
4 anymore.

5 PARTICIPANT: Because the table says
6 boundary conditions. Otherwise we would have gone
7 there.

8 DR. FOGARTY: But compliance is a
9 boundary condition.

10 PARTICIPANT: Yes, you're right.

11 DR. FOGARTY: Are we talking about
12 patient compliance?

13 MS. ABEL: We've moved on. You missed
14 that comment.

15 Now we go into corrode. The respondents
16 indicated evaluated pitting, about half of them
17 evaluated crevice and the other half, or possibly
18 part of that same half evaluated galvanic corrosion.

19 The acceptance criteria varied widely
20 and depending upon the method used. And the
21 characteristics not addressed had to deal with the
22 differences between test solutions and blood.

1 So we've got the various types of
2 corrosion listed here. And we -- it was kind of
3 difficult to pull all this information together, so
4 I'm not even going to bother to go into it too much.
5 But, obviously, everyone didn't test all the various
6 types of corrosion and certainly as far as it has
7 been seen in clinical use.

8 Now I don't know that we want to go to
9 the next column at this point in time at this time
10 today. But I think we could go to should this
11 failure mode be evaluated for all EVG. So should
12 everyone look at crevice, galvanic, pitting
13 corrosion?

14 Go ahead, Dan.

15 MR. CHWIRUT: Well, I think all of them
16 need to be addressed depending on design of the
17 device, fretting or you know, galvanic may not be
18 appropriate so you can dismiss it.

19 MS. ABEL: Can you start over in front
20 of the microphone.

21 MR. CHWIRUT: Right. I think all of
22 those different types of corrisions need to be

1 addressed at some point, but depending on the device
2 design if there are not any articulating
3 subcomponents that would lead to fretting, you can
4 justify not testing fretting. If it's all a single
5 metal, you can justify not doing galvanic. However,
6 if your device gets into one of those categories
7 where there are possibilities, then yes that
8 particular mode of corrosion ought to be addressed
9 probably for all devices pitting and -- excuse me.
10 Pitting and crevice ought to be addressed.

11 MS. ABEL: So it should be addressed,
12 but that may not necessarily involve additional
13 testing. It's just, you know, you have to look at --

14 MR. CHWIRUT: Well, I guess you know
15 your acceptance criteria and how high a confidence
16 factor you want. Obviously, there's a lot of
17 experience both bench and clinical with the
18 materials that have been used and are being used.
19 And do we want to identify grandfathered or
20 clinically successful materials for which additional
21 testing may not be necessary. You know, we will
22 accept history as an appropriate demonstration of

1 corrosion resistance. I mean, that's certainly a
2 legitimate question. And, you know, you can get
3 into long discussions about the effects of
4 processing and how much of a change in surface
5 characteristics processing can impart and change the
6 corrosion resistance.

7 MS. ABEL: Roy?

8 MR. SMITH: I have a question on what
9 the standards actually say in terms of testing with
10 potential mating components. For example, a Nitinol
11 stent graft that may end up with a balloon
12 expandable stainless steel stent and a proximal neck
13 or a stainless steel stent graft that may end up
14 with a Nitinol self-expanding stent in an iliac.

15 MS. ABEL: I think it's something to the
16 effect that if there are dissimilar metals that
17 would be in contact, you should consider galvanic
18 erosion, but I don't remember exactly what it says.
19 But that's by way of that last column on our little
20 table here.

21 I think it's one thing to say this is
22 how we've designed the devices and this is how, you

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1 know, our materials are all cool with each other.
2 But it's another thing again to deal with reality
3 that clinicians do put various devices in together.
4 So I guess it's somewhat related. You know, should
5 you be required to look at galvanic corrosion for
6 all intervascular grafts because people could easily
7 be sticking in other devices that aren't your own?
8 You know, should you look at that interaction?
9 Should everyone have to do that? Why not?

10 DR. FOGARTY: If physicians are doing
11 it, which they are, we have to know the results of
12 it under some circumstances. That's not a big
13 challenge I don't think.

14 MS. ABEL: Dan, what did you want to
15 say?

16 MR. CHWIRUT: Well, I think it's an
17 undue burden on manufacturers to anticipate what's
18 going to come in the future. Right now, you know,
19 there's really three metals being used for metallic
20 components for these devices but what's going to
21 come in tomorrow --

22 MS. ABEL: But even those three metals

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1 should you be testing?

2 DR. FOGARTY: The physicians are using
3 those three metals in the same patient in contact
4 with one another or only separated by fabric.

5 MS. ABEL: Sometimes. They're not even
6 separated by fabric sometimes.

7 DR. FOGARTY: Yes, that's correct.

8 MS. ABEL: So it's reality? This is
9 happening currently that people take different
10 pieces of different devices and throw in stents from
11 somewhere else and --

12 MR. SMITH: Is there evidence that that
13 causes corrosion activity in vivo right now?

14 MR. DEHDASHTIAN: It will happen, it is
15 just matter of time. I don't think it happens short
16 time. It happens long term.

17 DR. MARIN: And we've observed this type
18 of corrosion through the years of our retrieval
19 program that we've been working on. So it has been
20 observed.

21 MS. ABEL: So you've seen it with the
22 combination or with an individual device?

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1 DR. MARIN: Sorry. A combination with
2 an individual device. For example, with a nitinol
3 wire and a platinum or palladium --

4 MS. ABEL: So you've seen it with the
5 individual manufacturers, what they've put together.
6 Have you seen anything with respect to someone
7 putting a polymer stent into a device with a nitinol
8 structure?

9 DR. MARIN: I don't recall.

10 MR. SMITH: Martin, are these currently
11 marketed devices? See, I think that makes a big
12 difference. I think we've learned a lot about how
13 to process nitinol, for instance. We've learned a
14 lot about how to process other metals and used them
15 in combination to avoid these situations.

16 So, I'm wondering with currently
17 marketed devices worldwide is this an issue or not?

18 DR. CHUTER: You know, the complications
19 from this seem to be extraordinarily rare. I haven't
20 seen any reported cases. And you have how many
21 explants were reported in this series?

22 MS. ABEL: Almost 300 I think.

1 DR. CHUTER: Almost 300. And I'd be
2 very interested to know how many of those explants
3 had exotic stents in them. Because if the number is
4 small, then you can forget about it. If the number
5 is big, then you can evaluate it.

6 MS. ABEL: Unfortunately, asked very few
7 questions of the manufacturers with respect to
8 adjunctive devices and the use of in every aspect,
9 and we got no information back. So I think there's
10 just a complete lack of information, although we all
11 know that it's out there and they're being used.
12 And so is there a lack of information because no one
13 wants to tell me what's really happening or is
14 nothing happening?

15 MR. YU: This is really the
16 responsibility of the industry, I mean, you know the
17 fact that they are having interaction between the
18 mentioned three metals, I mean they have already
19 been studies through various academic research and
20 so forth. I mean, it is a risk. But at the same
21 time from a clinical consideration invariably the
22 time when you actually want to use those situations

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1 where you want to combine one device to the other,
2 there is obviously some clinical indication, you
3 know, that you don't have any alternative. So, you
4 know, the cost benefit ratio it's obviously
5 perceived to be the overriding factor.

6 MS. ABEL: See, I will disagree from the
7 standpoint of I think there are a lot of clinicians
8 that would say oh I've got this patient who needs an
9 adjunctive device or else they would need to be
10 converted. And I am not aware of any problem with
11 using these different devices all thrown together.
12 I don't believe that there's any problem with that.
13 Therefore, I believe that it's appropriate to go
14 ahead and stick in whatever. It could be standard
15 risk patient. They just don't -- clinicians aren't
16 always savvy about the need for evaluating systems
17 together. And I mean, people will take different
18 pieces from different devices. They'll put one
19 manufacturer's limb in with another manufacturer's
20 body. I mean, and there's no way that that's been
21 evaluated.

22 MR. RODGER: There's no way that could

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1 be evaluated.

2 MS. ABEL: Oh, I know. I'm just saying
3 the clinician will do that in absence of having the
4 knowledge that there is information to show that
5 that should work.

6 MR. RODGER: I think there's a huge
7 number of tests that -- the information that are
8 actually impractical to do. The one that's a good
9 example is using different manufacturers components
10 and putting together.

11 But I think one of the things of this
12 particular question here is if it's in your IFUs,
13 then you have to test it. If it's something that
14 you don't supply that some physician using is
15 completely with the industry's control, and I think
16 it's much more important to mandate or even suggest
17 that that should be tested.

18 MS. ABEL: So, I don't have any
19 difficulty whatsoever because, again you know that
20 your device out there and it could have a -- stuck
21 in the top of it, for example. You know that that's
22 the case. And I think it's one thing to, you know,

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1 think you're going to have to test to all the
2 extreme things that clinicians could possibly do.
3 This really isn't that extreme and this is fairly
4 common as far as my understanding. So there's a
5 difference.

6 MR. YU: Even -- institute smoking,
7 tobacco, warning on cigarette packets. You know,
8 it's a fact that it should be made more aware, you
9 know users should be aware if you're doing this, you
10 know there is a potential risk. But at the same
11 time, you know, the specific risk it's not very
12 clearly defined dependent again defined on your
13 perception and your point of view.

14 MS. ABEL: So maybe what would be useful
15 to have done is just some basic testing and some
16 additional information on corrosion in general, not
17 necessarily all very, very specific to see is this
18 truly a problem or maybe we can get some information
19 on these devices in the clinical setting.

20 DR. FOGARTY: Yes. Tom Fogarty.

21 I'd like to ask the engineers is this a
22 difficult test? Does this place a real burden?

1 MR. SMITH: I think it can if you're
2 trying to acquire another company's devices to see
3 how they're going to interact.

4 DR. FOGARTY: Look, I'll get all the
5 devices you want as long as you pay me for them,
6 okay.

7 PARTICIPANT: You know you just have to
8 ask Taco. He's got tons of everybody's devices

9 DR. GREENBERG: But the bottom line,
10 isn't it just a case of the interaction between the
11 two specific materials? I mean, does it have to be,
12 you know, endolink graft endolink graft can't it
13 just be, say, an wire placed an -- wire. I mean,
14 that's what you're looking at, isn't it?

15 MR. SMITH: Well, really it should be
16 done in the context of which the devices are used.
17 So you deploy your stent graft and you blow up a
18 balloon expandable stent in the neck. And I
19 understand the imputes of the question, but I would
20 say that -- as to how difficult it is, but I would
21 say that the majority of these tests that are
22 required for stent graft analysis are probably

1 difficult.

2 MR. YU: Right.

3 DR. GREENBERG: The majority of the
4 tests that are being required by the standards are
5 probably difficult. I brought this up, really, to
6 see, you know, it's a concern and it's a theoretic
7 concern and it would be nice to know that there is
8 some validity to this concern.

9 MR. YU: Right. Maybe there should be
10 a rating system, say, you know 9 mil versus
11 stainless steel there's a hard rate of corrosion
12 versus a stainless steel in contact with nitinol, or
13 something like that maybe that's more useful.

14 DR. GREENBERG: But I was just saying
15 that that has to be done in the context of its being
16 used because you can only imagine blowing up a
17 stainless steel balloon expandable stent inside a
18 nitinol stent and, you know, creating a fracture or
19 part of a defect on the electropolishing. Then all
20 of a sudden you're in a different ball game with
21 respect to the corrosion analysis.

22 MR. YU: Yes, right.

1 MR. GREENAN: And where do you put the
2 limit on this type of testing? Because, you know,
3 the next thing is and maybe an even more important
4 concern is putting this into a device in an
5 angulation and the potential of fabric wear. I
6 mean, you know, I think you start going on this path
7 that puts a fairly large burden on the industry for
8 testing outside of the IFUs. And I think, you know,
9 and different devices have different incidents of
10 using adjunctive components.

11 MR. WANINGER: I would just wonder -- I
12 would agree with that. I just want to say that's
13 important. Well, I'm wondering how you would use
14 that information? I mean, if you run a test where
15 you're looking at a piece of -- wire and nitinol
16 wire and you get some sort of corrosion data, are
17 you actually going to change the labeling for your
18 device, put some kind of precaution or warning? I
19 mean, how would that information be used.

20 MS. ABEL: I would.

21 MR. WANINGER: Would you?

22 DR. FOGARTY: Yes. You know, there's a

1 whole bunch of ways. It may protect you in a company
2 with a competing stent that's put on top of yours
3 from getting sued. And it's really true.

4 MR. PELTON: First let me say is that
5 there is a body of data out there that has been
6 published with respect to, for example, galvanic
7 corrosion effects with a whole host of materials
8 primarily, as Stan said, you know there's three
9 primary stent materials that are out there. And so
10 those have been tested as well as all the noble
11 materials that are used as markers. And what the
12 data show very conclusively is that stainless steel
13 in combination with elgiloy or in combination with
14 nitinol is not a major risk factor for galvanic
15 corrosion alone. It could be for other reasons with,
16 you know, fretting or wear or something like that.
17 But there is a major problem if you have unprotected
18 gold, platinum, platinum meridian, etcetera in
19 combination with any of those more active materials,
20 the engineering materials. So, you know, the data
21 have been published and, you know, I think people
22 are starting to add to that database to understand

1 the full effects.

2 MS. ABEL: That's very helpful.

3 DR. MATSUMURA: You know I just -- to
4 follow up on both those comments, yes, are we going
5 to ask them to test for intercomponent migration
6 stability? You know, obviously we're not. But my
7 understanding is it's not a corrosion issue it's a
8 nickel leaching issue. Maybe this nitinol expert
9 can help with that.

10 MR. PELTON: It isn't a nickel leaching
11 issue whenever there's something that can promote
12 that part of the corrosive activity and especially
13 if you have not properly prepared your surface with
14 either a chemical polish or an electropolishing
15 technique, you can have rapid raps of nickel
16 dissolution into the material, as rapid as stainless
17 steel under similarly poor prepared surface. So
18 that's what we believe is going on.

19 DR. FOGARTY: Did you say just don't use
20 metals of different properties?

21 MS. ABEL: No. He said it's not a
22 problem.

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1 MR. SMITH: In most cases, and there's
2 been data published for some time especially in the
3 electrophysiology area of pacing the industry where
4 they're conducting electricity through several
5 dissimilar metals all the way down to the electrode
6 and back and these devices have to last 20, 25
7 years. So there is a lot of information to find out
8 whether you're at any corrosive risk, especially
9 galvanic. That's already published for biomaterials
10 that are being used. And more than just the three
11 he spoke of.

12 MR. CHWIRUT: I just wanted to echo
13 something that was alluded to by Trevor and maybe a
14 couple of others, and that is there are various
15 interactions when one uses manufacturer A's
16 accessory component with manufacturer's B -- B's
17 basic device. And corrosion may not be the biggest
18 problem.

19 MS. ABEL: I'm sure it's not the biggest
20 problem.

21 MR. CHWIRUT: Potentially metal on metal
22 wear, you know, with a nitinol exoskeleton inside an

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1 elgiloy endoskeleton or something like that. I'd be
2 concerned more about that. And once you go down
3 this path of putting a burden on somebody to
4 demonstrated that his device will be compatible with
5 any accessory that anybody can possibly put in and
6 then use with, that's a whole Pandora's box of
7 issues that we can't address.

8 MS. ABEL: And then we're talking about
9 testing every potential interaction and issue. I
10 mean, the biggest problem isn't even those potential
11 failure modes. The biggest problem is someone's
12 trying to provide a new attachment system probably
13 using something that's never been evaluated for an
14 attachment system. I mean, I think there's a huge
15 problem with this whole situation.

16 I agree that galvanic corrosion isn't
17 the biggest problem, it's just one that's relatively
18 straightforward that theoretically could be
19 addressed. But I think knowing that there's already
20 data out there, that's the answer. Data already
21 exists. Between that and not having the reports of
22 there truly being an issue from the clinic, there's

1 no reason to do it.

2 So our final test for this morning is
3 the strength of the stent or attachment system to
4 the graft. All of the tests reported involved
5 tensile testing. Some people tested just components
6 versus completed devices. And the acceptance
7 criteria varied, which you would expect.

8 I think what the problem is with this
9 particular test is that, again, we assume some
10 devices that have a lot of suture breaks and
11 abrasion. We've certainly seen stent separation from
12 the graft material. We've seen graft tears and
13 abrasion. So, you know, are these things that can
14 be evaluated in this test and can this test be
15 improved for other different tests that need to be
16 developed to address these failure modes?

17 MR. YU: I think there's one additional
18 area that's worth considering, it is the
19 irregularity of loading across the circumference of
20 attachment for a basic stent structure to the graft
21 and because of angulation and also various forces
22 sometimes there can be uneven distribution into a

1 particular area, you know, apex of that structure,
2 you know, which is much greater whereas in general
3 as I state that most people will just assume kind of
4 an averaging of the load. That might be an area
5 worth looking into.

6 MS. ABEL: And I would say certainly
7 that would apply to establishing your acceptance
8 criteria. I don't know if you would modify the test
9 necessarily to look at that. Does that make sense?

10 So suture breaks and abrasion certainly
11 it's something that you should be looking for in
12 this test, right? And so we have -- like I said, a
13 lot of devices out there that have seen a lot of
14 suture breaks. Fortunately, they aren't associated
15 with a lot of events. They have on occasion been
16 associated with problems, though. So do we need to
17 look at this differently? And maybe -- you know do
18 we just need to better define the forces and come up
19 with better acceptance criteria? Or do we need to
20 test it differently?

21 DR. FILLINGER: Do, Dorothy, were you
22 saying that all the tests that are being done

1 currently are just simple tensile tests?

2 MS. ABEL: That's what people reported
3 for this particular test. And I think, like you
4 say, there is probably additional testing to look at
5 interaction of components that's not standardized
6 testing.

7 DR. FILLINGER: But shouldn't there be
8 some sort of cyclical testing to look for a --

9 MR. WANINGER: Actually, I was going to
10 speak to that. This is an area where we have done
11 some additional testing basically learning to echo
12 some of Lou's comment and some of the forces that
13 Tim showed us on his video earlier to look at
14 cyclical longitudinal forces, not just the straight
15 pool test. But we've actually gone to looking at
16 longitudinal fatigue testing of attachment systems
17 out to 400 million cycles.

18 DR. DEATON: Can you do that testing
19 with eccentric forces on the -- I mean every neck is
20 angulated to some degree or is it just a straight
21 pull.

22 MR. WANINGER: This was just a straight

1 pull for this test. This is basically a place where
2 -- well, for example we were talking about some of
3 the barb separations that have been seen. And that
4 was not predicted by the pulsatile fatigue testing.
5 However, we did see a low rate of barb separations
6 clinically, and so we went back and took a look at
7 the testing and looked at the other forces and the
8 other modes of forces being applied to the graft and
9 came up with a longitudinal fatigue test where we
10 were actually able to mimic the clinically failures.

11 And for us that was a big advantage in
12 terms of then once we had a test that we could
13 duplicate that failure looking at design
14 improvements being able to compare between designs.

15 So it's one of the things that we feel
16 like we've improved in.

17 MR. SMITH: And I would echo what Matt
18 said. What we did with our device was a separate
19 anchor fatigue test that would evaluate whether the
20 anchors would fracture as well as whether that part
21 of the stent would detach from the graft material in
22 a longitudinal cycle of manner seeing what matches.

1 MR. WANINGER: Yes, we looked at
2 detachment in the graft material as well.

3 DR. WHIRLEY: And I'd like to echo what
4 they said, that although we haven't seen clinical
5 failures, we identified longitudinal fatigue as
6 being an area that merited a special test.

7 MR. KING: On a separate issue I would
8 suggest that abrasion resistant is an issue that we
9 have contributed to failures that's been seen in the
10 reports, and that that test needs to be a separate
11 issue addressed where you control both the two
12 surfaces that are rubbing and the frequency and
13 pressure at that interface. Because clearly the
14 stent and the graft material do undergo abrasion
15 when there micromotion. And that one needs to
16 reproduce that in a more appropriate way than we
17 have with this pulsatile test. Particularly I think
18 we're aware at angulations so that there needs to be
19 some component of controlling a bent configuration
20 when you do this type of test.

21 There are fabric abrasion tests out
22 there that have been designed for car upholstery and

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1 car pits and a whole range of textiles that do not
2 apply here. And it's clear that we need to be more
3 specific in controlling both the way we present the
4 abrillant to the surface and we control the pressure
5 and the frequency of the conditions so that we can
6 get a more reproducible prediction of this
7 phenomenon.

8 MS. ABEL: Was that comparable to what
9 you were talking about or separate?

10 MR. SMITH: This has nothing to do with
11 longitudinal, this fatigue.

12 MS. ABEL: I just wanted to make sure
13 that I was understanding --

14 MR. SMITH: Yes. Martin's talking about
15 --

16 MS. ABEL: You're talking angles, you're
17 talking straight. You're angled.

18 MR. SMITH: Right. I think what Martin
19 is saying is, you know, one thing that keeps coming
20 up is fabric wear and we don't actually specify like
21 anywhere in the standard or really it's only an
22 adjunctive observation in several of these tests

1 instead of something that's directly tested for.
2 And I think Martin's suggesting that we may want to
3 consider some sort of direct test.

4 MS. ABEL: Right.

5 MR. CARDELLA: Comment from the cheap
6 seats.

7 I had just a question. In terms of the
8 pull test, is that just a straight longitudinal
9 force? Because if you're trying to analyze suture
10 breaks, you know, you might use the analogy of a
11 piece of copper wire. If you just pull on a piece
12 of copper wire, it has what appears to be pretty
13 good durability. But if you start working it back
14 and forth in a complex motion, you can quickly break
15 that copper wire.

16 So I would think an improvement in this
17 test if you're trying to interrogate suture material
18 in the environment that it's in, it should be a bit
19 of a complex motion rather than just trying to pull
20 it. And I don't know enough about the test to know
21 if that's what the test is or not, but I don't think
22 simply pulling on a piece of suture replicates what

1 it's being subjected to in an endograph.

2 MS. ABEL: So I think that's why we've
3 had the suggestion of adding additional testing to
4 look at longitudinal forces, to look at wear and
5 interaction between components. This particular
6 test doesn't do it, so we need additional tests.

7 PARTICIPANT: Or perhaps even consider
8 getting rid of this test.

9 MS. ABEL: I don't think I would agree
10 that we need to get rid of this test. You know,
11 maybe eventually if we get some standardized testing
12 that is more useful, if we decide whether or not
13 it's something to deal with.

14 Okay. We're going to quit 10 minutes
15 earlier. So you get ten extra minutes for lunch.
16 See you back at 2:00.

17 (Whereupon, at 12:49 p.m. the meeting
18 was adjourned, to reconvene at 2:00 p.m.

19
20
21
22

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2:13 p.m.

1
2
3 MS. ABEL: Roy, don't expect me to get
4 up and introduce you.

5 DR. GREENBERG: I just didn't know what
6 time you were going to start.

7 Well, I guess I'm going to kick off the
8 first session or the only session of the afternoon,
9 the last session. And Dorothy gave me a topic that
10 was quite a hodgepodge, so I took a little bit of
11 poetic license here and, hopefully, we're going to
12 come back to earth from your concepts of testing and
13 evaluating devices.

14 Whenever I come to these workshops and
15 meetings I tend to leave more confused than when I
16 came. So she asked me to talk on the clinician's
17 perspective of endovascular grafts; what's happen in
18 the past, what's happened in the future, where we
19 are today and how we deal with it. And I can tell
20 you how I deal with it, which is knowing the
21 Serenity Prayer because there are things that we
22 know and there are things that we don't know and

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1 there are things that we will never know. And we
2 just have to know where to draw the line. And I
3 can't tell you where those lines are.

4 It's nice to establish a wish list for
5 everything we want to know, but ultimately when push
6 comes to shove, no intended pun in terms of
7 endovascular grafting, we're going to have to make
8 some judgments. And that's up to the clinician, and
9 this where we need your help as manufacturers and
10 industry and regulators.

11 If we look back in time at the year
12 2000. And I apologize this is a little bit cutoff.
13 I didn't want to drop the resolution because then
14 the x-rays won't be so apparent.

15 But if we look back at the year 2000
16 when the AneurX and the Ancure graft were kind of
17 intermittently available in the United States, the
18 Gore clinical trial was well underway. The Zenith
19 trial had just started. The Vanguard hadn't actually
20 died quite yet, at least formally. It was still in
21 a European phase 3 phase. There had been a few
22 fenestrated devices that were placed and thoracic

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1 grafts had been done and were certainly being talked
2 about a lot, but they weren't a commonplace reality.

3 Well, this is really kind of a
4 perspective, and I took three different perspectives
5 for this talk. One is what I would think a
6 regulatory perspective would be. What I would think
7 an industry perspective be. And a clinician a
8 perspective.

9 So this is the regulatory perspective.
10 Got a bunch of animals walking around. They are
11 quite content, there's lots of things to do but they
12 see a storm coming.

13 This is, of course, is the industry's
14 perspective. Again, lots of food, lots of things
15 going on. We've got some defense here.

16 And this is the clinician perspective.
17 We don't really know what's going on. We're kind of
18 new in this world and we're going to make the best
19 of it.

20 These will become clear as we move later
21 on, go later on here.

22 I'm actually thinking I might have to

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1 change the resolution of this, otherwise we'll miss
2 some of the things.

3 Okay. So what were the popular
4 conversations in the year 2000? Well, the frequent
5 debates that were going on is whether endovascular
6 grafting was even a viable option for anyone. And I
7 think that question today is answered. Limb
8 thrombosis was, again, a very popular topic of
9 discussion, yet at least in this meeting we breezed
10 over it pretty quickly because it's not a real
11 problem now. Endoleak shouldn't be treating them.
12 What are the treatment options? What do we need for
13 fixation? The thoracic order we all thought, or
14 some people thought was easier because it's straight
15 and branch vessel were somewhat like gene therapy:
16 They were going to happen but they were always
17 around the corner. You never quite knew when.

18 In this interval between 2000 and 2004
19 we've seen several things happen. We've had
20 problems with devices. We've all seen FDA warning
21 letters, device mortality. And by that I don't mean
22 patient mortalities, I mean devices that have left

1 the scene. And we've seen problems with
2 commercialization; what happens when we put these
3 devices in the hands of non-IDE institutions. How
4 do we train physicians? And then after we train
5 physicians and release devices, how do we track
6 these patients?

7 We realized there's problems with all
8 the devices. There's migration across the board
9 whether it's the Ancure, the AneuRX, the Zenith, the
10 Gore they all have problems. And I choose two
11 devices, and I didn't chose these devices for any
12 purpose other than to illustrate that there are
13 differences between the devices. And one was the
14 Gore device and the other is the Zenith device. And
15 so papers by John Matsumura and myself in terms of
16 the phase II U.S. trial results.

17 And the reason that these devices can be
18 put on the same graft is because they were analyzed
19 with the same definition at the same aneurysm
20 diameter, at the same endoleak diameter, with the
21 same core lab etcetera. And so from the published
22 data you can see here's the data from one device and

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1 here's the data from another device and you can see
2 the overall endoleak incident rate is quite
3 different between these two devices. And when you
4 put them on a chart, it looks at them in a
5 comparison fashion at the same time point across the
6 board, there's drastic differences.

7 The mistake comes in when we start
8 looking at registry data because these devices are
9 drastically different. And when we look at registry
10 data, and this was data published from the Eurostar
11 registry, you saw the strongest predictor of
12 mortality was aneurysm growth. Can we then
13 retrospectively apply this to the patients with two
14 different types of devices? And my answer would be
15 no, it doesn't make any sense. It really doesn't
16 help us with our analysis of what's going on in
17 terms of these devices in the absence of a very
18 device specific evaluation.

19 But there are some new things that have
20 come along. The devices are limited by the proximal
21 neck and the hyogastriacs. And today I think you'll
22 agree that these things are being developed. There's

1 hypogastric branches done by several companies. We
2 can go Super Reno, there are a number of companies
3 that are looking at branches and fenestrated devices
4 and thoracic aorta, etcetera. And so this is a much
5 more complicated field, and as we sit today and talk
6 about endovascular grafts and standards we need to
7 be thinking of the broad picture and how will these
8 same definitions and applications be applied in a
9 more broad fashion.

10 In the year 2000 approved and trial
11 devices really had a lot of problems. And those
12 devices have undergone several modifications so that
13 there's improved device designs of the same devices
14 that were approved in 1999 where the fabrics have
15 been altered, the stents have been altered, the
16 attachment systems are different and the delivery
17 system has improved.

18 And in the year 2000 the importance of
19 tortuosity and neck length were really under
20 estimated. And today the patient in device
21 selections are really paramount to success aneurysm
22 repair.

1 So we think we have this greater
2 knowledge. We have an improved understanding. We
3 realize migration is a problem and it occurs. We
4 realize the sac behavior is different and it's
5 different among different devices and has to be
6 looked at in a device specific manner, and so are
7 endoleaks. And, you know, the bottom line is that
8 each clinical piece of information has to be taken
9 in the context of its device. And conglomerate data
10 that's reported is not really helpful with these
11 specific areas. But we're missing certain things,
12 and I think the biggest thing that we're missing is
13 the ability to train physicians to think. And this
14 is something that comes back here. We all struggle
15 with how to make constructions for use, but
16 ultimately we have to rely on physicians to make the
17 judgment as to whether this device will succeed.

18 We have to have appropriate selection,
19 and appropriate selection relates to both selection
20 of the device, selection of the patient and the
21 selection of the physician.

22 And really there's all sorts of issues

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1 in terms of imagining and analysis and the
2 assessment of which patients we should be treating
3 and how we should be treating them. And this is
4 something I'm going to go into more details.

5 But we need to look at these issues in
6 the context of where technology is going. And these
7 are cases where you can see extremely torturous
8 iliac arteries with internal and common iliac
9 aneurysms or extreme tortuosity here of, you know,
10 several leaks of external iliac where they're both
11 successfully treated with branch devices into the
12 internal iliac artery.

13 Similarly these devices won't just be
14 used for aneurysms. They will be used for other
15 conditions as in this aortic coarctation where you
16 then have a stent graft here with ballooning of the
17 coarctation to alleviate these sorts of problems.

18 And finally, they're going to be
19 extended into more proximal regions of the aorta
20 like the abdominal grafts here where you've got
21 branches into both the renals, the -- and celiac are
22 accounted for here or in this thoracic graft extends

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1 down below the celiac and the SMA in a fenestrated
2 type design.

3 And how is this technology evaluated?
4 Well, we sit here and we talk about fatigue testing
5 looking at stent fractures and whatnot, but you have
6 to realize the gold standard isn't what we see in
7 the clinics. Because this is a chest x-ray of a
8 patient with a device fracture. Where is the device
9 fracture? Well, we can't see it on the chest x-ray
10 and we never could see it on the chest x-ray. And
11 this is not a gold standard that we need to compare
12 our fatigue testing to.

13 We do have certain advantages in terms
14 of imagining. This is that same patient where we've
15 done some special manipulation with the CT data to
16 reproduce things where we're just looking at the
17 stent. And so by doing that, what we've done is take
18 the raw data and using special reconstruction
19 algorithms that are specifically designed to look at
20 nitinol in this particular case, reconstruct the
21 image and we can take this image and look at it in
22 any dimension we want to look at. And here you can

1 see this stent fracture right here as this bar comes
2 apart.

3 Similarly, you can see this particular
4 example where you've got graft in the place and this
5 is an Anaconda graft and you can see even the hooks
6 and the barbs that are coming around this corner,
7 all of the nitinol are readily apparent. And in this
8 particular case when we're looking at Zenith grafts,
9 we've even gone so far as to image the barbs on the
10 Zenith grafts or the renal stents that are placed in
11 a fenestrated device.

12 The resolution of this imagining is in
13 the realm of .1 millimeters and in actuality can be
14 looked at not just in the one dimension, but in
15 three dimensions. And as we rotate these devices
16 around and get a picture of these devices and how
17 they'll all sitting in terms of the relationship
18 between the components, we're going to all of a
19 sudden detect more fractures. Does that mean the
20 devices are worse than they were before? No,
21 they're the same devices but our gold standard has
22 changed, which is now we're going to clinically be

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1 able to see these fractures and have to come up with
2 some sort of solution to them.

3 So these are, I think, real issues that
4 we're going to have to confront in the short term,
5 not the long term.

6 And in conclusion, I think we've come a
7 long way. The devices that we're using today are
8 better than the devices that we used in 2000 or in
9 1999. The patient selection is better. The bar for
10 a new device coming into the market is certainly
11 higher. We're closer to establishing realistic
12 boundary conditions. We still have a long way to
13 go.

14 The future? I think we're going to see
15 moderate improvements in the current device and
16 delivery system design. I think we're a bit away
17 from any sort of huge technologic leap. We're going
18 to have a better understanding of displacement
19 forces and fatigue issues and this will incite some
20 changes in the devices.

21 We've got better modeling for pre-
22 implant analysis and post-implant failure as far as

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1 imagining goes. But the environment's changed. And
2 if we go back to our previous perceptions of what
3 the environment was like, I would say this would be
4 the regulatory perception of the environment,
5 perhaps from the reviewer's perspective.

6 MS. ABEL: Especially today.

7 DR. GREENBERG: What's that?

8 MS. ABEL: Especially today.

9 DR. GREENBERG: Especially today.

10 This may be the clinician's perspective
11 of what the environment's changed into. Because now
12 with HIPA laws and the new regulatory compliance
13 issue clinicians have to think twice before they
14 agree to embark on a study and now compliant they're
15 going to be able to be with this.

16 And I think this is the industry
17 perspective. It's getting hot out there and we've
18 got to be careful as to what's going on because,
19 really, it's a different world than it was in 2000
20 with respect to the consequences of studies that are
21 not properly done.

22 That's all I have. Thanks.

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