

1 important, again talking about distortion. Here you
2 have a conical or reverse taper neck and I can
3 guarantee you that the effective fixation and sealing
4 length is not the 15 millimeters that you see here.
5 You can see the device is tapering along with the neck
6 and so the effective fixation and sealing is not what
7 was the instructions for use, 15 millimeters for this
8 particular device. Yet again, we spend very little
9 time in preclinical testing figuring out how these
10 sort of variations, the degree of oversize period.
11 Let's just say it's a uniform diameter neck, how does
12 the degree of oversize affect fixation and sealing?
13 Some of you know that to some degree, but I would
14 wager that we don't know enough about this and we
15 certainly don't know enough about conical necks,
16 funnel shape necks, barrels, hour glass, all those
17 sorts of things. If you limit the length of the neck
18 to a 10 percent diameter change that helps a lot in
19 sort of keeping this problem to a minimum, but it
20 doesn't eliminate the problem and for one stent graft,
21 it may be much more of a problem than for another
22 stent graft. There's a lot of variability in how well

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1 the individual stent grafts handle this type of a
2 situation as pretty much all the clinicians know.
3 We'll pick different devices for different situations.

4 Things like again, the preoperative device
5 sizing is a big deal. In this case, there's a short
6 neck. They thought it was longer than this, but the
7 diameter measurement was wrong, so the device was too
8 small. You can see it doesn't even go out all the way
9 to the wall. This is a nice uniform -- it's not that
10 this is compressed, not getting full position to the
11 wall, but basically the device was undersized, the
12 neck was too short and even so, even then, there was
13 enough column strength in the device in sort of an
14 ancillary means of fixation that it lasted for more
15 than a year in an adequate position and actually did
16 its intended function.

17 Unfortunately, the sort of an unintended
18 consequences sort of a thing, because there was very
19 little fixation in the iliac, eventually the very
20 little fixation there allowed enough instability that
21 the column strength was overcome and the device
22 buckled, now overcoming this very sort of poor sort of

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1 fixation in the top in allowing the device to migrate
2 substantially.

3 Even after all of this, notice, however,
4 that the good part of the neck still looks like a
5 fairly good part of the neck. And so being able to
6 quantitate that ahead of time, knowing which device to
7 put in, sizing it properly, probably would have made
8 a big difference, I wager, in this particular patient
9 or maybe doing an open repair for the aorta.

10 Along those same lines, it's all sort of
11 a continuum in how we treat the patient. It's not
12 just preoperative patient selection, preoperative
13 device sizing. It's also what we do intra-operatively
14 to the device. So again, sort of things that get
15 beyond control, if you're the manufacturer. You can't
16 always, even with education and training, you can't
17 convince people -- I was speaking to somebody not too
18 long ago where they were saying they were having a
19 great deal of difficulty convincing their clinicians
20 that when you have an angulated neck, if you look at
21 this with a straight AP view, you can see that you'll
22 deploy the device here, thinking you're right below

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1 the renal, when in fact, you're a long way away from
2 the renal.

3 And they had a hard time convincing many
4 clinicians of this, many just say well, it will be
5 fine. Don't worry about it. It's okay. Here's a
6 good example of that. It looks like the device was
7 deployed right below the renal artery, when in fact,
8 it was 12 millimeters below in a fairly short neck.
9 That can't be good. So you start out with anatomy
10 that is sort of on the margins, but the device would
11 work much better if you used all of the good real
12 estate that was there. So you also have to build in
13 again sort of this tolerance to misadventures.

14 Getting down toward the end here,
15 dynamics. I sort of -- in order to keep the D theme
16 going here -- dynamics is sort of biomechanics and
17 changes over time.

18 Acute and chronic issues. There's vessel
19 compliance and elasticity, variations due to disease
20 like patient characteristics like hypertension, vessel
21 calcification, medications like steroids, possibly
22 doxycycline. Device placement itself affects the

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1 compliance of the vessel, of course.

2 The strength of the vessel is affected by
3 smoking and steroids. We know that when the device is
4 not in place in patients looking at the natural
5 history of aneurisms. So it stands to reason that
6 these would also affect the strength of the device,
7 sorry, the strength of the aorta with the device in
8 place.

9 Tissue remodeling, due to the device
10 itself, we've talked about a little bit already.
11 Diameter increases, wall thickening, the aneurism sac
12 atrophying when you take the pressure off of it.
13 Tissue ingrowth and its relationship to the degree of
14 oversize and outward radial force. We know almost
15 nothing about these things.

16 Sorry, injecting just a small amount of
17 science into the nonscience part, but hopefully most
18 of you know about the things that we're doing with
19 finite element analysis and vessel biomechanics,
20 looking at stress on the aneurism wall. That same
21 sort of technology we're actually working on right
22 now, looking at -- using our finite element model to

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1 look at vessel motion and comparing this to dynamic MR
2 and vessel motion which this actually mimics pretty
3 well. And what you can see, this is actually not the
4 dynamic MR. This is the finite element model itself,
5 but you can see there's not just outward radial
6 motion. There's also, if you look at this blue spot,
7 there's some radial, there's some rotational motion of
8 the aneurism. There's also, not in this patient very
9 much, but there's also some longitudinal movement in
10 here and this is all complex and in three dimensions.
11 And we pretty much ignore all that too when we're
12 designing and testing devices.

13 This I'm going to skip over, but talks a
14 little again -- again, it's too much science, but
15 talks about the effective compliance and device
16 design.

17 And lastly, durability which we're going
18 to talk about later, but that includes not just device
19 durability which we sort of think about a lot in terms
20 of metal fatigue and fabric wear and very little talk
21 about the unknown effects of cuffs or adjunct devices
22 that are placed in there, but also attachment site

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1 durability, degeneration, necrosis or erosion we
2 talked about earlier with a lot of outward radial
3 force, inflammation, diameter changes due to the
4 stent, Fibrosis remodeling. All those sorts of things
5 go on over time and again we have very little
6 information about what happens in patients and how it
7 affects those forces on the graft that we're trying to
8 design for the design life of the stent graft.
9 Hopefully, some of these things like dynamic MR, that
10 sort of thing, will help give us an idea of how these
11 -- how the tissue characteristics are changing over
12 time, but I can tell you, yes, they change with a
13 device in place and yes, patients vary quite a bit
14 from one to another.

15 So that again, design tolerances, I think
16 is an important concept. How in the world can you
17 test for all of this? Well, you can't, basically.

18 What can you test for? And we can just
19 very quickly, you can pull out force, we talked about
20 a lot, varying the amount of oversizing, attachment
21 length, device diameter and angulation. The outward
22 radial force and resistance to compression and

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1 bending. Compliance -- these are more research topics
2 for the academics rather than the manufacturers, but
3 compliance of normal and diseased aorta we know little
4 about. Degree of force that require to damage, normal
5 and diseased aorta. There was a nice study from the
6 Sydney group a while back that looked at this with
7 balloon expandable devices and like as far as I know
8 almost nothing since then from anybody.

9 Flow models, computational fluid dynamics,
10 bench work, finite element models for the stent and
11 the stent aorta combination, fabric porosity,
12 thrombogenicity and fatigue. And fatigue, not just in
13 a simple straight configuration, but something with
14 bending and compression in these complex three-
15 dimensional movements that we're talking about that
16 are much more stringent and much more likely to damage
17 a graft than a simple animal model. We need something
18 that's much tougher in terms of the bench testing than
19 what we can possibly create in an animal model.

20 So that's my opinion. Thanks.

21 (Applause.)

22 MS. ABEL: Robert, are you ready to share

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1 some opinions?

2 DR. WHIRLEY: Well, thank you. I
3 appreciate everybody's attention and attendance right
4 after lunch. This talk is entitled "Fixation and
5 Sealing, a Scientific Perspective". Dorothy asked me
6 to speak to a fixation and sealing, but I think we'll
7 go a little light on the science right after lunch,
8 just so we keep the people from going to sleep.

9 But nevertheless, I think there's some
10 important complements to Dr. Fillinger's talk that we
11 can see and make some observations.

12 When we first deploy an endovascular graft
13 its very first job is to get a grip and hang in there.
14 That migration prevention is a serious aspect of
15 device performance and it starts just within a second
16 after the device is initially deployed. That fixation
17 is critical to device performance. Migration, if we
18 think about migration as the event we're really trying
19 to predict or trying to prevent, migration happens
20 when load exceeds fixation, so we really can't talk
21 about fixation without talking about load and getting
22 to understand what the loads are that we're trying to

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1 anchor.

2 And studies, numerous clinical studies
3 suggest that migration may be a powerful predictor of
4 late problems in endovascular grafts.

5 So let's spend just a minute to talk about
6 forces on an endovascular graft. The forces can be
7 found from the momentum equation here in integral
8 form. If you just create a control volume here. This
9 is a big, long, complex equation. I certainly won't
10 take us through all the math to turn that into an
11 equation for forces, but essentially it says the time
12 or rate of change of momentum in that control volume
13 plus the change net flux into and out of that control
14 volume is the applied force or just forces, the time
15 rate of change of momentum.

16 Before we really bang on that a little
17 bit, we can do some dimensional analysis to see what
18 terms might be most important. And one of the
19 dimensional numbers include mechanics that's important
20 is the Reynolds number and that is very simply a ratio
21 of inertial forces to viscous forces. And we can
22 evaluate the Reynolds number based on just the

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1 density, the flow velocity, the diameter of the graft
2 and the viscosity and if we can consider the
3 evaluation of the Reynolds number at peak systolic
4 conditions, for example, we can see that the Reynolds
5 number in the graft is relatively low in both the
6 aorta and the iliac and that allows us to make a
7 couple of quick engineering conclusions.

8 Now if there are any fluid machinations
9 out there you could say but this is transient, dynamic
10 flow. It's not steady state. We're making some
11 assumptions here and I'll give you all those up front.

12 You can make this problem arbitrarily
13 complex, but I think as you looked at those, you find
14 that those changes are a few percent of the answer and
15 that some very simple considerations will lead you to
16 a very good estimate of the forces on the ground.

17 To evaluate the Reynolds number, we'll see
18 it's low. What that tells us is that viscous forces
19 dominate inertial forces. It doesn't tell us how big
20 either of them is, it just tells us that that's the
21 ratio. It also tells us that laminar flow may be a
22 reasonably good assumption. It's not an ideal

1 assumption because you do have transient effects from
2 the cardiac pulsatility, but it's a reasonable
3 assumption.

4 And with those two statements, you can
5 estimate the pressure gradient through the graft from
6 this well-known engineering formula that just says the
7 pressure gradient is related to the velocity, the flow
8 velocity through the graft, the viscosity, the length
9 of the graft and is very sensitive in that it has a
10 diameter squared in the denominator. So as the lumen
11 of the graft gets big, the pressure drop goes down
12 very quickly which is something that makes intuitive
13 sense to everyone.

14 So when you substitute in realistic values
15 for these parameters, you find that under most
16 conditions the total pressure drop in an endovascular
17 graft under peak systolic flow conditions is less than
18 5 millimeters of mercury and that's not much
19 longitudinal force on the graft.

20 And so if you take that momentum equation
21 and do a lot of manipulations, you can turn that into
22 a fairly simple equation that gives you an engineering

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1 estimate of the longitudinal forces acting on the
2 graft and I think it's illustrative to kind of look at
3 the various terms.

4 If you look at this one, this is the flow
5 velocity in the aorta squared times the density in
6 that area. That's essentially the momentum term
7 coming in. If we evaluate that here for in this chart
8 at 160 millimeters of blood pressure, these various
9 numbers represent the contribution to the migration
10 force on the device in pounds. You see that's
11 3/100ths of a pound. That's not a major player here.

12 This term that I shaded, the pressure in
13 the aorta times the cross sectional area, that gives
14 us two and a half pounds. That's clearly the dominant
15 player here. If we look at the weight of the graft
16 and this particular size was a little over a tenth of
17 a pound, keeping in mind that includes the fluid
18 that's involved. And then there's some iliac flux
19 terms that actually subtract off of this load. The
20 iliac momentum, 4/1000ths of a pound. That's trivial.
21 That's of no real interest.

22 However, the iliac pressure term is about

1 a third of a pound here and that comes from the
2 pressure times the area and this angle, theta, is a
3 half angle of the iliac splay. So what this really
4 says is that if you were trapped on a desert island
5 with one stickie note and you needed to calculate the
6 force on an endovascular graft, if you simply took the
7 pressure in the aorta times its cross sectional area,
8 you'd be within a good 20 percent estimate of what it
9 might be. And you can go and do a lot of additional
10 corrections to that and other considerations, but
11 that's going to get you pretty close.

12 A couple of things you can also surmise
13 from this, this pressure is the net pressure
14 difference between the aorta and the sac pressure. So
15 you can see the influence of sac pressure. These
16 numbers assume the sac pressure was zero. The sac
17 pressure systemic then, this total force load number
18 over here gets very small. So sac pressure means
19 something.

20 Also, transient hypertension may be
21 relevant because this equation applies essentially
22 instantaneously over time.

1 So with the loads now in mind, we can take
2 a little closer look at migration resistance. The ISO
3 standard 25539 has a specific test for migration
4 resistance. In that test, the stated purpose is to
5 determine the force required to displace the
6 prosthesis in a mock artery, that is, to determine the
7 resistance to migration. Well, the test method is
8 kind of simple, deploy the device in a mock artery,
9 measure the pull out force. Doesn't say anything
10 about disease, angulation, some of these other
11 effects. Certainly those are considerations that one
12 needs to apply in determining this test. You can look
13 -- this is an example of a human cadaveric aortic
14 that's got some moderate disease. There's some focal
15 calcium nodules in there. The surface is very
16 irregular. It's got a lot of diffused plaque.
17 Clearly, the pullout behavior in this kind of
18 environment is going to be very different than pulling
19 out from a solastic tube and that's a consideration
20 that needs to be accounted for.

21 Distal limb migration also happened. I'm
22 talking about the proximal and the same forces in many

1 ways apply on the distal end. I found this image.
2 I'm not even sure what device it was. I found it on
3 the web and it shows on the contralateral iliac limb
4 here you can see that it's migrated approximately from
5 the seal zone here up into this area. So proximal
6 migration of the distal limb can happen.

7 One of the other topics Dorothy asked me
8 to think about was conjunctive devices and any special
9 considerations there might be. Typically, they're
10 tubular rather than bifurcated. The good news is the
11 load analysis methodology we just looked at still
12 works. The longitudinal load on an adjunctive device
13 depends a lot on the configuration. A straight
14 configuration like this we can all see and intuitively
15 relate there's very, very little longitudinal load on
16 this.

17 On the other hand, if it's strongly bent,
18 there can be substantial longitudinal displacement
19 forces, depending on how much vessel support you get
20 from down in this area.

21 However, the previous analysis still works
22 and it suggests that a very simple estimate of that

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1 load is the pressure times the cross sectional area.

2 So let me switch and speak for just a
3 couple of seconds about sealing. If we back up and
4 look at the clinical objective of our endovascular
5 graft, it's to prevent aneurism-related death, but as
6 an engineer, we need to turn that clinical objective
7 into a design objective and so that design objective
8 is to exclude the aneurism from hemodynamic pressure
9 and presumptively thereby prevent rupture.

10 However, if we look back at the ISO
11 standard for sealing, we find there's a number of
12 relevant tests, three in particular. There's
13 conformability to the vessel wall, simulated use,
14 radial force and then quite a number of other indirect
15 tests. What characteristic is not mentioned is a
16 sealing test. Why? Testing for sealing is a lot more
17 complicated and involves a lot more complex
18 considerations than testing for migration resistance
19 where it's a simple pullout. So there's no obvious
20 one test one could envision that addresses all the
21 aspects of sealing. Sealing has clearly got design
22 issues, device design issues and a number of other

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1 aspects, so there's no simple way to come at that.

2 One observation that the FDA made from the
3 various work assignments was that most respondents
4 considered the simulated use test to be a delivery
5 system performance test rather than an implant test
6 and angulation was generally absent. So what that
7 does say is that most people aren't looking at
8 simulated use as a way to evaluate sealing.

9 I think the best we can do now is take a
10 look at what are some of the considerations one might
11 need to think about in defining a good sealing test
12 and actually Dr. Fillinger and I did not collaborate
13 at all on what we're showing. There's probably a
14 message in the fact that we independently came up with
15 many of the same kinds of slides. A big part of
16 sealing is what the seal surface looks like. This is
17 a hostile territory. In this case, you've got a lot
18 of mural thrombus here. You've got some focal calcium
19 and a very irregular lumen here, almost a triangular
20 lumen over here. The walls may be hard calcium, may
21 be compliant tissue, might be thrombus. That thrombus
22 might be fresh or might be quite well organized. And

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1 it's hard to know ahead of time what you're getting
2 into. And the testing at the very least, whatever
3 test one would develop pre-clinically for sealing
4 should recognize that this is the real world and
5 that's the kind of area in which the device is going
6 to be deployed.

7 A final comment about sealing, let's look
8 at the thoracic aorta. We've all been thinking about
9 abdominal aortas, but we're supposed to be thinking in
10 the broad context of endovascular grafts. If you
11 think of deploying a device up around this aneurism
12 adjacent to the arch, the device might take a contour
13 like this, depending on its stiffness and the plane of
14 the end of the device here may not be aligned
15 perpendicular to the vessel wall which may give a
16 region of deficient apposition here on the lesser
17 curve. The end switch could be potential sites for
18 loss of seal.

19 So these are some of the anatomical
20 factors that clearly should figure into any kind of
21 sealing test for such a device.

22 So just to summarize, I think I'd like to

1 leave you with the idea that loads really drives
2 fixation requirements. You can't talk about fixation
3 without talking about loads. Testing for seal is
4 challenging. You've got to keep in mind where the
5 device is going to be used and come up with a test
6 that's appropriate to a particular design.
7 Conformance to the wall may not equal seal in all
8 cases and the most important aspect I think is that
9 realistic anatomy should drive the consideration of
10 test conditions.

11 Thank you.

12 (Applause.)

13 MS. ABEL: I think you guys pretty much
14 covered everything, so we can probably just break for
15 the day.

16 (Laughter.)

17 That would make it easy on the rest of us.

18 I just wanted to touch on a few other
19 things from the work assignment, just to set the stage
20 again for the discussion and I wanted to mention some
21 of the information that we captured from the clinical
22 summaries from individuals with respect to sealing

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1 fixation effectiveness. We haven't broken down in
2 less than 30 day and the longer term and some people
3 put their 30-day information in longer term, some
4 probably included it in less than 30 days. So the
5 first thing to tell you is that none of this
6 information truly can be * (2:47:01). We put it
7 together here just to kind of give a general idea of
8 some things that we can realize, for example, not
9 technical success is always 100 percent. It is for
10 everyone in the room right now that currently has
11 advice on the market, I'm sure.

12 Conversion, and I should mention like the
13 percentages we have here, we're not pretending that
14 truly is representative of the percentage for that
15 parameter for endovascular grafts, in general. It
16 just gives you an idea if you take this number over
17 this number, what kind of percent you get and it's
18 more useful when you're looking at the range. So you
19 can see if there isn't very much variability because
20 in some of them there is a much greater range in terms
21 of the individual recorded percentages that people
22 gave us.

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1 So from this side, I mean the main point,
2 obviously, is just that endoleaks do happen. Type 1
3 endoleaks happen. Everyone acknowledged that they had
4 some Type 1 endoleaks and as far as Type 3 endoleaks,
5 we separated out those who did have some Type 3
6 endoleaks and those who didn't and actually, there was
7 only one person that had that.

8 So all of this information is in your
9 packets or will be available on the side. So I just
10 wanted to show you what we were thinking with respect
11 to the information that was provided to us.

12 Endoleaks for the follow-up observations
13 was a little more difficult to pull together because
14 people gave it to us in different formats, so what we
15 ended up doing was tallied all the patients in
16 individual intervals and tallied all of the endoleaks,
17 came up with an average on this one and then the
18 range.

19 So again, just looking at the variability
20 for the various devices. And we have the total
21 endoleaks, the Type 1 and the Type 3.

22 Adverse events due to excessive radial

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1 force. I know you can't guess who that was that
2 actually did -- one respondent reported that they had
3 that sort of a problem and it manifests in migration
4 requiring secondary intervention.

5 Others, we have two respondents that said
6 they didn't see any migration and then we had four
7 that did see migration. Again, a big range in terms
8 of what people observed. So we have a lot of
9 variability in terms of what people have seen, but the
10 bottom line is we are observing all these types of
11 failures in the clinical studies.

12 Probably nothing terribly critical with
13 respect to the other follow-up information. We just
14 put it on the slide so it would be complete and again,
15 it will be on the website.

16 So we're ready to start talking about the
17 individual testing. Migration resistance is the first
18 test we'll talk about and the respondents indicated
19 that they did a wide variety of tests. Some of them
20 were tensile tests. Some of them were perforized
21 fluid flow models. And then there were some people
22 that used animals or cadaver testing. Only three

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1 respondents incorporated any type of angulation in
2 their testing.

3 The acceptance criteria varied greatly and
4 so that's something we wanted to touch upon in terms
5 of what is the appropriate type of testing, but then
6 also how do you establish reasonable acceptance
7 criteria?

8 Characteristics that were identified as
9 not being addressed were changes in morphology,
10 tortuosity, atherosclerotic disease vessels, neck
11 angulation and effects of pressure.

12 Now it's interesting because everyone
13 pointed these out, but they haven't been incorporated
14 in the test either.

15 So now we're going to go to Angie's
16 tables.

17 MS. SMITH: I think the first thing we
18 wanted to start looking at and both of our speakers
19 did a good job of illustrating this in their talks was
20 that there's a big difference between a device used in
21 a clinical study where there are inclusion/exclusion
22 criteria and an IFU that is followed as opposed to

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1 when they're used in clinical practice where the -- I
2 guess the practice is a little more open, so the
3 question is do we want to have testing -- is it
4 appropriate to test to the IFU or to how you know what
5 will be used in clinical practice. And in addition,
6 based on that answer, are there changes to the
7 labeling that should be made that would help address
8 those issues.

9 MS. ABEL: I think Mark has already said
10 that it make sense to test outside. You have to show
11 kind of a -- what do you call it?

12 DR. FILLINGER: Tolerances.

13 MS. ABEL: And I don't know that that's
14 really what people have done overall. Actually,
15 during the last workshop, there was a discussion that
16 unanimously people said there was no reason why we
17 should have to test beyond what we're telling people
18 to do. And I think what we've seen here is that may
19 not have played out very well in the clinical setting.

20 I'm sorry, before we get into the
21 discussion, I just realized, of course, we're in a new
22 session, so there are new faces.

1 Can people who are different, who haven't
2 introduced themselves, go ahead and do so.

3 MR. ELLER: Allen Eller with Cook,
4 Incorporated, Senior Engineer.

5 MS. ABEL: Anyone else?

6 MR. GREEN: Trevor Green, Metronic
7 Engineering.

8 MR. * (2:52:32) Dan *, Metronic.

9 MR. HANEY: David Haney, Cordes,
10 Mechanical Engineer.

11 MS. ABEL: Everybody else is pretty much
12 the same here or no? Okay, now you know each other.

13 So now we can start arguing. So how do
14 you figure out, you know, what the extreme is if you
15 do tests beyond your IF field. Does anyone have any
16 thoughts on that?

17 DR. FILLINGER: I think the reason that
18 you have to test beyond your IFU is because of the
19 problem of knowing the dimensions precisely. And the
20 problem is that people may think they're following the
21 instructions for use, but they may not be and I don't
22 think you need to get crazy with that and say well,

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1 you know, we say that you need a 15 millimeter long
2 neck and therefore we're going to test in 5 millimeter
3 necks. That's ridiculous, but I think if you have
4 some at least idea of what happens to the pull out
5 force as the neck goes from 15 to 10 or some -- at
6 least justify your testing as to why you're testing
7 the limits, you know that there's going to be some
8 variance. And if you tell people to over size the
9 device by 10 to 15 percent, you know that some people
10 are going to over size by 5 or 20 percent. And so
11 knowing what that does to the radial force, the
12 pullout force, the effectiveness of apposition to the
13 wall, I think if you know what happens, you can be --
14 you can at least guide people in your education as to
15 how critical those points are.

16 You may find that 20 percent actually is
17 okay and it's not a big deal, but 5 percent is
18 horrible. And so it may give people some guidance
19 when you're educating the clinicians.

20 MS. ABEL: So some of that may have to
21 deal with testing things as a function of length or as
22 a function of oversizing or something along those

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1 lines to have, instead of just saying the radial
2 forces, this value to look at it over a range and
3 relate it to the various parameters. Is that
4 accurate?

5 John?

6 DR. MATSUMURA: I had one unrelated
7 comment and then one related to your question. I
8 think when you showed the homework assignments
9 compiled, the way you calculate the rates certainly is
10 probably the lowest estimate because mainly those are
11 timed in a time-dependent phenomena and we divide it
12 by the denominator of those initially enrolled, so
13 many of those things may be more frequent.

14 I think there's a difference between
15 having design tolerances to accommodate imprecise
16 measurements which I agree with Mark is important
17 because they are precise. Even with open surgical
18 grafts, I think very few of us size the order with
19 electronic calipers before we select a graft. And so
20 design tolerances help to give better clinical results
21 and the difference between that and saying a
22 manufacturer should test the device to what is outside

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1 the label, say a 35 millimeter proximal neck with the
2 current devices.

3 So I'm an advocate of the first. I'm not
4 sure the second is useful.

5 MS. ABEL: I think in terms of being
6 useful, I agree that you have to stay within the realm
7 of something rationale, but doesn't it seem like it
8 would still be appropriate to just look at things as
9 a function of whatever it is that could be affected by
10 it. So whether it's oversizing or neck length, you
11 know, if you say that my migration resistance is X
12 pounds, shouldn't you say that if I have a one and a
13 half centimeter length and let me just tell you, if it
14 goes down to one centimeter, it's out the window. I
15 don't have that any more. Or it could be for a lot of
16 manufacturers, you know, because of their design, with
17 active fixation, there won't be any difference and
18 that would be important to communicate also.

19 DR. MATSUMURA: I guess the number of
20 hypotheticals that you test with short back more
21 angulation and sizing would be very great and the
22 answer to your question is yes, it's useful if we have

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1 it. But I suppose there's some intermediate zone
2 where you could say this is a situation that may arise
3 clinically, very frequently.

4 The question is how do you make that cut
5 off, I suppose.

6 MS. ABEL: Yes.

7 comprehensive plan

8 DR. GREENBERG: I actually think that
9 we're trying to define a success criteria. In
10 reality, what we really want to know are what the
11 limits of the device are. So test it to failure. And
12 tell us when it fails. Does it fail at 45 degrees?
13 Does it fail at 10 millimeters? Does it fail at 15
14 millimeters?

15 We all know that if you have 15
16 millimeters in your IFU for a preoperative assessment
17 that no one is going to be able to place the device 15
18 millimeters exactly. Is the average error 2
19 millimeters or is the average error 7 millimeters? We
20 don't really know that, so it's very hard to look at
21 it and say make sure your device is okay for this
22 minimum amount of neck. Instead, tell us where it's

1 not okay. And then it's up to the physician to say am
2 I going to be accurate enough to put it in this amount
3 of neck?

4 MS. ABEL: I think -- I mean that's one
5 thing to say you can't ask the manufacturers to do
6 that, but that's certainly the only thing they're
7 doing now. Right now, they're giving a number.

8 DR. GREENBERG: I agree, but that's
9 because the impetus is on testing to success and I
10 think that effort needs to be testing to failure.

11 MS. ABEL: See, I don't. I would disagree
12 with that. I think that that number has been selected
13 because of whatever reasons. I don't think it has
14 anything to do with the testing to be quite honest.

15 DR. GREENBERG: Well, how many
16 manufacturers here tested their device to failure to
17 come up with a minimum neck length? Most of them
18 relied on either kind of hearsay or gut instinct or
19 failures of clinical data to modify their IFU.

20 MS. ABEL: Right.

21 DR. GREENBERG: So the message I would
22 want to give to manufacturers is to tell us when the

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1 device is going to fail.

2 And then as clinicians, we would know when
3 it's going to fail.

4 MS. ABEL: Robert?

5 DR. WHIRLEY: Just a brief thought on
6 that. I can certainly understand the clinical utility
7 of that, but in light of some of the factors that I
8 pointed out, that's a very difficult -- it would be a
9 very difficult kind of thing to quantify because the
10 answer would, of course, be it depends and it depends
11 on so many variables that trying to give a specific
12 number where a device ceases to perform in a
13 particular parameter like fixation of sealing I think
14 would be a very difficult, ill-defined process.

15 MS. ABEL: I mean we don't even know
16 exactly what the force is that we need to be able to
17 withstand and so it would be very difficult to draw
18 that line anywhere.

19 But I think certainly looking at it as a
20 function of that parameter you could lay it out and
21 you can say this is how we label it. I mean most
22 people are at the point where they've already decided

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1 what the limitations are going to be, but just to show
2 how things vary within those limitations or at the
3 extremes or beyond the limitations.

4 MR. SMITH: I guess my thought is that
5 what ends up in the instructions for use is exactly
6 what we're talking about in the end. It's where
7 outside of that you can consider there to be greater
8 risk for failure, no matter what part we're talking
9 about. If you go outside the IFU, that means there's
10 a higher probability that you may get an endoleak or
11 you'll get migration or you'll get a fracture,
12 whatever.

13 And so the IFU itself is that line. Now
14 how they came up with it, whether you've done a bunch
15 of development testing and decided hey, we were
16 shooting for a 10 millimeter neck length, but we found
17 in R&D testing that really we're at 15 or greater is
18 still the ideal. That's what ends up in the IFU. I
19 think there can be some assumption that manufacturers
20 decided outside these limits in the IFU we can't tell
21 you exactly what's going to happen and you have a less
22 of a probability of success.

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1 I mean everything else is great. Like I
2 agree with Robert. It could be an iterative process.
3 It could take as long as the development of the graph
4 itself.

5 DR. GREENBERG: I agree with that. The
6 difference is that inside the IFU you still can't tell
7 us because you don't know where that device is going
8 to be placed. You're testing it to a 15 millimeter
9 neck. That means if your preoperative imaging shows
10 a 15 millimeter neck, you're getting 12 millimeters of
11 coverage on a good day. How does the device behave in
12 that region? I mean I agree with Mark that you have
13 to test these devices outside of the IFU. But the
14 reason is is that inside the IFU you've come up with
15 your boundary conditions. You've told us this device
16 is okay. So where did those boundary conditions fail?
17 I mean you have to justify that these are the boundary
18 conditions we're applying to these testing because it
19 logically makes sense. I mean if you take Robert's
20 equation for pressure in area, then it's very simple
21 to do that. Now I don't at all want to say that this
22 is an easy test because it's a very complicated

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1 analysis to look at migration and fixation and I
2 completely separate it from seal because once we try
3 to combine them, you've got grafts that fixate in one
4 part and seal in another part and they're totally
5 separate issues.

6 But I'm just trying to say that the
7 impetus here can't be to tell us where the device is
8 okay. It has to be to tell us where the device will
9 not be okay.

10 MR. SMITH: I can understand that. I'm
11 not trying to disagree with that. I think you go into
12 either a clinical study, an evaluation of some sort
13 and that is a validation of your instructions for use.
14 Okay, I instructed the clinicians to go 15 millimeters
15 of neck and sure, so therefore I come up with a
16 number, anywhere from 12 to 18 or whatever. And does
17 the clinical study show acceptable results? That's
18 the ultimate validation.

19 DR. GREENBERG: But you can take it a step
20 further because you can say let's take your device and
21 use a 28 millimeter proximal neck that ends in 216
22 millimeter iliac diameters and compare that to the

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1 same proximal neck that ends in 212 millimeter iliac
2 diameters. You've got a different failure in terms of
3 the displacement force for those two grafts.

4 You've got different force.

5 MR. SMITH: You don't have any failure.

6 DR. GREENBERG: Well, but there's probably
7 a different minimum neck length.

8 DR. MARIN: I would think you would want
9 to include certainly the tolerance in the indication.
10 If you're specifying 15 millimeter neck length that
11 should have a built in, typical or some error in
12 placement because that is clearly going to be device
13 dependent, much like the maximum pressure rating on
14 your car tire. They're assuming a certain error in
15 the measurement when you're inflating it and if you
16 exceed it by small amounts it's not going to rupture,
17 but I think the manufacturer should accumulate data
18 that suggests with that system how close are they
19 going to get to their target and then build in that
20 error into the indication as opposed to letting people
21 build experience over time and understanding how much
22 they're going to miss it by and then only then

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1 deciding whether or not to take that adequate margin.

2 I think then there's also the clinical
3 aspect in terms of -- you know, you talk about what
4 the various angulations and stuff. So the
5 manufacturers are saying 15 millimeters and a certain
6 amount of angulation, so when you've got a device I
7 understand that each device is going to behave
8 differently, but when you combine all those various
9 angles and factors that you don't get at sitting in
10 there the way that Mark demonstrated on the side where
11 you've got it at an angle, you know, what kind of a
12 seal zone are you really getting or attachment zone or
13 whatever you want to call it in those situations?
14 What are the common anatomies that you run into in the
15 issues? I don't know that every manufacturer can
16 specify that on an individual basis.

17 MR. LU: Number one, just to follow on to
18 Roy's question, testing to failure. I mean should we
19 also put a time point in that. I mean you can have
20 attachment at a time of implant, but it's going to
21 fall out, that might be only 5 millimeter, but to the
22 24-hour later, it's going to fall out where there's a

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1 bit more aortic movement. Are we talking about that
2 or are we talking about, we're looking for even
3 greater durability.

4 And the second issue, just to follow up,
5 Mark's -- the point Mark made in relation to
6 tolerance, an example, given what's most accurate in
7 terms of length measurement, approximately neck length
8 measurement, angulate the neck. And people provide
9 one single number and typically say if you use a
10 preview software, you're talking about center line
11 measurement. And if you have a 60-degree angulated
12 neck, the actual attachment zone is invariably with
13 the 30 or 40 percent reduction, so you're talking
14 about potential. The actual attachment zone, the unit
15 curvature could potentially go down to 9 millimeter.
16 And so the question you come down to is what is the
17 definition of neck length? Should we talk about
18 center line neck length or should we really be talking
19 about what is the minimum, the lesser curvature
20 attachment length? I mean maybe that's a better
21 definition to all practical effect. And what
22 obviously the greater curvatures are will provide you

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1 with longer contact length. So that might be an issue
2 to consider.

3 MS. ABEL: I think that's what I was
4 trying to sort of babble about and wasn't doing a very
5 good job of it. But I don't know if every individual
6 manufacturer can come up with those lengths as opposed
7 to clinically there should be -- I understand that
8 devices will function differently, but I don't know
9 how you can label for a clinician to have a certain
10 length of seal zone or whatever you call it.

11 MR. LU: Well, maybe that's the whole
12 issue of providing a margin of safety of say 30
13 percent. You know you can label 15, but if you tested
14 successfully at 30 percent, shortening that length to
15 10 millimeter, then you know that might be -- I think
16 that's what Mark was trying to get to in terms of
17 building a safety factor in there.

18 MS. ABEL: Right. I mean that makes sense
19 to me. I understand that. What I'm thinking of is
20 I'm trying to envision in the IFU telling the
21 clinician that they have to have a particular length
22 of seal zone or whatever, as opposed to a neck length.

1 I mean I think we can count on the clinicians to mess
2 up the neck line. If we're getting more complicated
3 than that, we're in real trouble.

4 MR. LU: Yes, right. It depends on the
5 imaging technology available, yes.

6 MS. ABEL: I'm sorry, David?

7 VASUTEK: I was just going to say to me,
8 it relates back to this testing for worst case. We
9 assume our worst case in the lab and say right, we'll
10 test 230 degrees or 10 percent over sizing or 30
11 percent oversizing and we get one figure, one result
12 which goes into the submission, that sort of figure.
13 And it doesn't characterize the performance of the
14 device over the range and I think what Roy's coming at
15 is if the surgeon has some indication of how the
16 device performs over a range, then he can see when
17 he's getting into the danger zone.

18 The problem is that you've got
19 multifactorial tests. You've got sealing
20 effectiveness, over sizing, migration resistance, all
21 acting together, angulation, tortuosity. So you have
22 to test them all individually, really, but at least

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1 you could look at characterization of anchor force
2 against angle and come up with * (3:08:34) as 25
3 percent angulation what we find there up to 45 we may
4 be in trouble and then beyond that you can see that
5 you're going to have migrations. You're giving the
6 user some kind of range of safety. He can visibly see
7 where he's going to be in trouble or where the safe
8 zone is.

9 MS. ABEL: Well, at the very least, maybe
10 you'll understand and even if you don't tell the
11 Commission what you've learned.

12 MR. QUIGLEY: A lot of our testing has
13 evolved over the last three or four years and we're
14 now understanding better the forces, the
15 displacements. And I think we're defining the
16 envelopes better and perhaps three or four years ago
17 or even longer we understood the clinical performance
18 and then used that to define what the working envelope
19 is. I think nowadays we ascribe factors of safety.
20 It gets more and more complex as we try and describe
21 the failure envelope first.

22 Some of the tests we're considering are

1 really static tests. What about long-term testing?
2 So if you think about that simple pull out test,
3 that's a test that's not repetitive. It's not under
4 varying conditions of cellular or conformance as it
5 changes with tortuosity and remodeling over time. I
6 really don't understand how you can test those short
7 term and get some outcome to predict long term.

8 DR. CHUTER: You know, we're hoping a big
9 much from our pre-clinical testing. If we think that
10 we can predict in absolute terms how a device is going
11 to behave clinically, based upon how it behaves in
12 these very artificial models, certainly we can
13 calibrate our artificial tests by reference to
14 clinical results, but I think we're more likely to be
15 able to say that if a device performs in a certain
16 test better or worse than another device performs in
17 the same test, then perhaps it will perform better or
18 worse in a clinical thing. So try to do it in a
19 relative rather than an absolute way. And I think
20 that that would argue in favor of Roy's point, testing
21 to failure because then you actually do have a
22 parameter that you can compare one to the other.

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1 MS. ABEL: Define failure. Let's say it's
2 migration resistance. Define failure.

3 DR. CHUTER: Of course, any of these tests
4 have to have failure to define whether you're going to
5 test for success or not, but let us say we were
6 testing for pull out, I think a certain degree of
7 migration could be a criterion. I'm not arguing to
8 the validity of the detailed pattern of testing, no.
9 What I'm saying is testing to failure will give you a
10 result. Whatever those criteria are, obviously, they
11 have to be validated somewhere and they have to be
12 calibrated by reference to clinical circumstances.
13 But you need to have a number. You can't just have
14 zero, zero, zero, zero and expect that to help guide
15 you in terms of the clinical consequences of changes
16 that you make.

17 MR. QUIGLEY: Can we use clinical
18 knowledge, if we can reproduce known demonstrated
19 failures and use that as a control or a baseline and
20 test your design against that?

21 DR. CHUTER: You can. I think you
22 certainly need to calibrate these against what you see

1 in the clinic.

2 MR. QUIGLEY: So that's a way of
3 approaching this?

4 DR. CHUTER: That is a way of approaching
5 it. It's just that I think even with that calibration
6 I think you're more likely to be able to just say one
7 is better or worse than another. And I think that
8 there are standards out there in terms of clinical
9 performance that we can shoot for.

10 MS. ABEL: I guess what I'm thinking of
11 for example, if you keep making a more extreme neck,
12 at what point in time is the amount of force that
13 you're taking to pull it out too low? How do you come
14 up with that number?

15 MR. SMITH: I can say that that is an
16 interactive answer. It has to be interactively
17 figured out between that and some sort of flow model,
18 whether it's in a clinical trial, where there is flow
19 and angulation or a tensile test where there's just
20 angulation and no flow. So for me, they're very
21 interactive with the types of forces that Robert
22 described and how they're distributed along the length

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1 of the graft during angulation.

2 So I'm very -- a tensile test for me
3 doesn't really mean anything.

4 DR. GREENBERG: I mean really when we look
5 at testing for failure, you have a design standard and
6 you have to meet your design standard and how you come
7 up with your design standard is up to each individual
8 company and that has to be justified in a certain
9 manner, but I would just reiterate that it would seem
10 to make a lot more sense to have in the instructions
11 for use that your minimum cover of neck length is 15
12 millimeters and your minimum preoperative neck length
13 is 15 millimeters.

14 MR. CARDELLA: I'd like to speak on behalf
15 of the clinician types that have to work with these
16 devices.

17 MS. ABEL: I'm sorry, I just wanted to
18 point out that was Roy Greenberg, clinician, that
19 works with those devices.

20 MR. CARDELLA: It's very beneficial to
21 understand that individuals who use devices like thee,
22 whether it's a simple angioplastic balloon or whether

1 it's a complex endograph device, are often working at
2 the fringe of what is indicated in the instructions
3 for use. And it's very beneficial for me as an
4 inserted of these devices to know something like this.
5 This is what the manufacturer recommends for this
6 device. Let's say very simply it's an angioplasty,
7 but we recommend you run this angioplastic balloon at
8 10 atmospheres. At 15 atmospheres, 50 percent of
9 these balloons fail and at 20 atmospheres, 95 percent
10 of these balloons fail in a test environment. That's
11 very important information for me to know. Now if you
12 use it for these grafts, you know, you could say a 15
13 millimeter landing zone is recommended. At 12
14 millimeters a 50 percent fail or migrate and at 5
15 millimeter landing zone, 95 percent of them fail.
16 That's important information if it can be gotten.

17 MS. ABEL: If it can be correlated to
18 actual clinical. I mean what you do with the clinical
19 evaluation is you set your limits and maybe it should
20 be set at 15 millimeters or actual coverage as opposed
21 to a neck length, whatever. But the bottom line is
22 the device has only been tested within the parameters

1 of the labeling and so you know the other information
2 that you would get would just be able to show you the
3 more angulated the neck, the quicker the force goes
4 down or the shorter the length, the quicker the force
5 that's purely force. It's not going to be anything
6 directly clinically correlated.

7 MR. CARDELLA: I was speaking in support
8 of the notion that you test the device to failure.
9 Then you know a recommended level that's chosen
10 perhaps by the manufacturer's engineering department
11 to say -- it's like building bridges. This is a 50
12 percent safety factor on this device based on our
13 testing to failure. Then you back it up. Then you
14 have the data which will enable you to say 50 percent
15 of them failed here and 95 percent of them failed
16 here.

17 That is important information for a user
18 of these types of devices.

19 MS. ABEL: Let's hear from another user
20 for a minute.

21 DR. WHITE: I understand the principle,
22 but I think the only thing that you can do is sort of,

1 as you suggested, in angles and with varying
2 diameters, quantitate the pull out strength for
3 something in that in vitro setting, but the failure
4 mode actually we have a clinical demonstration of the
5 testing failing for that. What we've done is 10-year
6 cycling which predicted failure. And where the
7 devices have failed for stent fractures have been at
8 angles, not at 10-year cycles, but early in increasing
9 at angulation. So that the failure has been short-
10 term angulation testing, rather than the long-term
11 durability and the failure testing hasn't been
12 predictive of anything.

13 DR. WHIRLEY: Because it wasn't in the
14 angulated neck.

15 DR. WHITE: That's it, so it's an angle
16 test acutely for pullout and fatigue. It is not the
17 straight model that we're all saying is an animal or
18 an in vitro test that's currently there.

19 MS. ABEL: Yes?

20 MEDTRONIC: I just had a question whether
21 there's present for any device to label failure modes
22 or incident rates outside of the IFUs. Are we just

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1 going in an uncharted territory here?

2 MS. ABEL: I agree. That's what I'm
3 saying, the clinical study within the IFU and that
4 that benchtop information may be of interest, but it
5 certainly, it would imply by putting it in there that
6 you know, you would be expanding your indications to
7 include values outside of the label and that --

8 DR. CRIADO: Dorothy, I would suggest that
9 what was suggested which theoretically is a good one
10 about the PT balloons is absolutely unachievable and
11 unrealistic in this scenario. It's just impossible to
12 predict with that kind of precision and quantitatively
13 like that when a graft is going to fail, particularly
14 from a clinical perspective. It's just not
15 achievable.

16 MS. ABEL: I think testing to failure
17 though for various parameters would be a possibility.
18 It's just what you do with that information.

19 DR. CRIADO: But you can't really
20 translate that necessarily into a clinical outcome.

21 DR. GREENBERG: This is something that
22 we've tried to teach computers for a long time and we

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1 call it artificial intelligence. It's just iterative
2 incorporation of that and the states. Now hopefully,
3 since we're mostly human, we'll just call it
4 intelligence and use our data, all of it, together in
5 terms of our hypothetical situations in the beginning
6 and our clinical data to give us some recommendations
7 as to when this is not a good idea. That's all I was
8 saying.

9 MS. ABEL: Tom, did you want to say
10 something? I keep ignoring you.

11 DR. FOGARTY: Me? Roy, you're a friend of
12 mine? Are you a friend? Do you mind if I insult you?
13 You're full of shit as a Christmas turkey and it ain't
14 even Christmas.

15 (Laughter.)

16 Okay, there are so many things we cannot
17 measure right now and to design a test to things you
18 can't measure is testing an invalid test. We know
19 nothing about compliance. We know nothing about
20 displacement of the artery as you pass a catheter. We
21 don't know which arteries will displace and not
22 displace. It's looney-tuney, truly.

1 DR. CHUTER: Could I speak in Roy's
2 defense?

3 (Laughter.)

4 DR. FOGARTY: No. I know how upset he is.

5 (Laughter.)

6 DR. CHUTER: But you know what, let us
7 say, if you in the clinical circumstance you observe
8 something that breaks and then you design a test and
9 you make it break and then you change it, and you do
10 another test and it breaks again, but it breaks after
11 five times the duration of testing, you can be pretty
12 sure that you have improved the situation and then you
13 have evidence that this testing may be of some value.
14 You can go forward with those changes. That's all I'm
15 saying in terms of testing, but it really works best
16 if you test to failure.

17 DR. FOGARTY: That may or may not be the
18 case, but the problem is you can't replicate all the
19 circumstances in a benchtest.

20 DR. CHUTER: That's exactly right, so you
21 can't necessarily translate from the bench to the
22 clinic, but you can translate from the bench to the

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1 bench and the clinic to the clinic. You have some
2 idea of when you make something stronger it will
3 perform better. You can test then.

4 DR. FOGARTY: That's wrong.

5 MS. ABEL: Remember the beginning, sorry
6 I asked, by the way, Tom.

7 DR. FOGARTY: I knew you would.

8 (Laughter.)

9 MS. ABEL: But you know at the beginning
10 of the day we talked about their various uses of pre-
11 clinical testing. I think what I would caution is the
12 sort of things we're talking about here. I don't know
13 that it translates directly to the clinician. I think
14 it's characterizing the device and you know, hopefully
15 as we learn more and we can make correlations like you
16 suggest, it will translate to the clinicians, but for
17 now at the very least I would think it would be a good
18 idea for the manufacturers to have an understanding of
19 how their device will function differently with the
20 different things that everyone has identified as
21 potentially affecting sealing and migration or sealing
22 and fixation. So you know, we should be looking at

1 angulation and I think looking at the force in
2 relationship to the amount of angulation in the model
3 makes some sense and test it to failure, I just have
4 a hard time figuring out because I don't know what
5 failure is, but because you're membering a force and
6 a lot of that is purely for characterization and I'm
7 not sure exactly what it will tell you other than just
8 keep testing it and find out what some extremes are
9 and know, like you say, when you modify how you've
10 affected that parameter.

11 DR. CHUTER: Can I just make one more
12 comment? One of the things you put up, Dorothy, early
13 on is a list of who tested with angulation -- or not
14 who, but how many of your respondents tested with
15 angulation. I would just emphasize that angulation is
16 one of the most challenging things for fixation
17 mechanisms to deal with because it can throw all of
18 the forces on to one tiny little part of the fixation
19 mechanism which then becomes very much a risk for
20 breakage. So if that fixation mechanism is not tested
21 with angulation, it's not being tested period.

22 MR. LU: Or the other way to look at it on

1 that point is to deploy a test graft in an angulated
2 model and then see what is the contact length. I mean
3 that's what your viewpoint was.

4 MS. ABEL: Right, so you correlate --

5 MR. LU: Right, if you have it highly
6 angulated, you can have a big, sort of long high-
7 pitched stent and then you're really talking about a
8 tiny contact around that bend and maybe that's a good
9 reference point in terms of a pre-clinical test data.

10 MS. ABEL: Right, so you could correlate
11 the amount of contact and the --

12 MR. LU: And the pullout force and then
13 you can potentially predict in terms of your abilities
14 to seal as to the clinical durability.

15 DR. CHUTER: I can give you a test for
16 sealing. If people are looking for test of sealing
17 you have an aneurism model with a neck in it. You
18 implant the device into that, a profuse aneurism
19 model. Then you take that aneurism out and you turn
20 it upside down and if the water falls immediately
21 after the aneurism on to the floor, you can assume
22 that there isn't much of a seal. If it dribbles very

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1 slowly you can feel hopeful.

2 MS. ABEL: That's going to be a good one.

3 DR. FOGARTY: I like that.

4 (Laughter.)

5 MEDTRONIC: I think one way of -- you want
6 to standardize some of these methods of looking what
7 happens outside the IFUs, kind of at what point does
8 your device degredate a certain percent. I think
9 that's a very easy test to do. Whatever arbitrary
10 value you determine is your pass/fail criterias for
11 let's say migration or seal and you can determine at
12 what point -- let's say a 25 percent degradation, I
13 think that's a much easier way of kind of
14 standardizing a lot of these issues.

15 MS. ABEL: That's a good suggestion. This
16 was supposed to be just a kind of a general
17 conversation with respect to -- it applies to most
18 testing, I would say, for endovascular grafts. Just
19 do you test to your IFU or do you need to do a little
20 bit beyond that and we already got into incorporating
21 the various parameters for different tests at the same
22 time, so we kind of -- we're crossing over into later

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1 discussions which is okay, but I just want to make
2 sure that we document, as far as test IFU or how you
3 know it will be used, is there agreement that possibly
4 you need to go a bit beyond just the IFU at this point
5 in time.

6 DR. WHIRLEY: One idea that might be
7 another approach to the particular question as posed
8 is that of quantitative assessment of design safety
9 margin with respect to the IFU parameters, rather than
10 mapping out what where it fails, but -- and I think
11 many manufacturers do this today is assessing not just
12 if it would pass, but some sense of how much margin
13 you have in the various parameters. And that margin
14 is what gives you confidence that if there's a little
15 bit of measurement error or a little bit of
16 misplacement or something that the device is still
17 going to perform as intended.

18 MR. CARDELLA: And beyond doing that
19 testing, I would make it available to the users. I
20 wouldn't keep that locked up as a secret in the
21 corporate vault. I think that's important information
22 for people that have tried to push the edge with those

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1 devices and they need to know how far it is safe to
2 push without getting into ridiculous trouble, so I
3 would publish it.

4 DR. FILLINGER: But you have to be
5 careful. Getting back to the point that Tom made is
6 that while you can characterize the device and how its
7 performance degenerates as you start to increase the
8 angle or change the amount of oversizing and that sort
9 of thing, translating that into clinical use and what
10 happens when you push the margins may be very
11 different, especially when you're pushing the margins
12 and like when I'm giving, I've given these training
13 courses when new devices have been released and I'll
14 say well look, you can push on the margins of
15 diameter. You can push on the margins of angle or you
16 can push on the margins of disease, but if you start
17 pushing on two of the three, it's trouble and if you
18 push on all three, it will fail.

19 And putting, translating that into a
20 quantified, 20 percent are going to fail if you do
21 this, is very, very hard to do. I think
22 characterizing the device and certainly that

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1 information needs to go to the FDA and I think
2 certainly that information can be used in the training
3 of the clinicians, but it's -- you really won't know
4 what's going to happen clinically until it gets
5 released and is used clinically and you do the outcome
6 studies and you'll get some of that from the clinical
7 trials, as long as you characterize that and that's
8 why I think it's so important to do it in pre-clinical
9 testing because then you can start to make -- refine
10 your tests and make them better because you have your
11 test data. Then you get your clinical data and then
12 you can refine it and make it better. You can compare
13 it to other grafts that you know have failed or not
14 failed at certain angles and those sorts of things,
15 but giving that exact, giving that raw data that
16 clinicians may be problematic.

17 MS. ABEL: I agree and I think it
18 encourages pushing the limits as opposed to providing
19 additional limits. I mean if there are limits, you
20 need to specify them. You need to have it in your
21 label and that's the way it is and I'm sorry, but
22 it's enter at your own risk beyond those limits. I

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1 don't see how you can ethically include information
2 that can't be directly correlated to clinical in the
3 first place.

4 DR. GREENBERG: Well, I thought this whole
5 workshop was a pre-clinical testing workshop. And in
6 that sort of context we all know the early
7 endovascular grafts were evaluated with erroneous
8 boundary conditions. And I'm not saying that we have
9 perfect boundary conditions now, but early on, most of
10 the people we're talking about, four to six Newtons of
11 displacement cause due to hemodynamic issues. And
12 now I would be surprised if there's companies that are
13 looking at less than 10 to 12 Newtons of displacement
14 force.

15 And so we certainly learn from these
16 things and I mean there are companies where they've
17 changed their IFU because of observed failures and had
18 they had that information, retrospectively, perhaps
19 that mistake never would have been made. And these
20 are issues that I think are important so that we
21 define our boundary conditions and we evolve as we
22 learn more about them and we apply the devices and we

1 have an understanding of how the devices are
2 combatting those displacement forces. And the
3 combatants to those displacement forces have to remain
4 durable over the course of time. So this has to be
5 linked to the integrity test because if you're
6 applying radial force and your stent fractures at 10
7 years, then your whole displacement force at 10 years
8 is in question.

9 And so they are iterative and it is a
10 learning process, but I do think it's important to
11 define limits and it's not appropriate, I think, just
12 to say here's a cut off that we've magically pulled
13 out of the air.

14 MR. SMITH: I hear what you're saying, but
15 most of the time that stuff that's in the IFU
16 incorporates without having all the detail in there,
17 that very thick, 15 millimeters of healthy neck,
18 knowing that the device can be deployed with up to a
19 5 millimeter inaccuracy and so on the one end you
20 don't want to cover renal and on the other end you
21 don't want migration. And then you start linking all
22 these other things. Sure, tensile pullout forces may

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1 be a little lower, but how does a clinician know it's
2 not going to migrate in the future. Maybe if there
3 was also a flow test that showed okay, for three or
4 four minutes under certain pressure and flow
5 conditions, this much and that, it doesn't move. Then
6 that gives the manufacturer more information to be
7 able to relate, but that doesn't mean he's going to
8 put it all in the IFU. See what I'm saying? The IFU
9 itself is okay, I know the device may be accurate to
10 a few millimeters and I know I need at least so much
11 of a healthy neck to be able to feel confident in the
12 outcome. The combination of those things is what's in
13 the IFU. So you see a 15 millimeter neck, you can
14 assume that the manufacturer understands that there's
15 going to be inaccuracy and has tested the sum of that.
16 So I'm all good with all of that. I come back to
17 agreeing with Dorothy. How do you put all that in an
18 IFU when you're trying to tell someone these are the
19 boundaries of use that we can stand by?

20 MS. ABEL: And also that view reflects the
21 clinical study.

22 MR. SMITH: It's kind of an iterative

1 thing.

2 DR. GREENBERG: I guess I'm looking, I'm
3 surprised to hear someone speaking on behalf of an
4 industry rep to talk about it like that.

5 As a clinician I would have thought the
6 IFU, you would be much more comfortable saying you as
7 a clinician need to have 15 millimeters of coverage
8 rather than you as a clinician need to have a 15
9 millimeter pre-operative neck length because you can't
10 predict how much error I'm going to have in placing a
11 device.

12 And so it would seem to make more sense
13 from a manufacturer's standpoint to say well, we're
14 assuming that you're going to cover this much neck.
15 If that means you need a 5 centimeter neck, so be it.
16 But if it means you're very accurate with this device
17 and you can place it in the 15 millimeter neck and get
18 15 millimeters of coverage, more power to you.

19 MR. SMITH: I hear you, but for me it's
20 fabricated. I want to give you instructions on how to
21 use the device. Where should you say yes, I'm going
22 to use such and such a device? Well, you haven't

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1 deployed it yet, so you don't know how much of a
2 landing zone you're going to get, so you're still
3 going to go in there and you're going to deploy it.
4 So if you didn't get the landing zone, what do you do?
5 Take it out?

6 It's all about preoperative decision
7 making.

8 MS. ABEL: Michael?

9 DR. MARIN: I think that what you have to
10 do as a manufacturer is say you need 15 millimeters of
11 wall contact and angulation would affect the length of
12 wall contact.

13 Now who makes the decision as to whether
14 you can get the 15 millimeters of wall contact is a
15 clinician's decision. So all you have to say is the
16 device needs 15 millimeters and the patients who are
17 actually in the commission will say I can get 15
18 millimeters and I'll deploy it to 15 millimeters. If
19 they don't, it's not a manufacturer's problem. It's
20 a clinician problem.

21 MS. ABEL: But you don't know for
22 individual devices how much the angulation is going to

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1 affect that contact length?

2 DR. MARIN: I think you have to assume
3 that it's going to fall at right angles to the access,
4 especially in the infrarenal aorta. So if you assume
5 that it's going to fall at 15 millimeters, it's going
6 to fall at right angles to the access of the artery,
7 then you can work out the wall contact.

8 MS. ABEL: But I don't know if you can
9 make that assumption for all the device designs.
10 That's all I'm saying.

11 Some are more flexible in the neck region
12 than others and can accommodate angulation better than
13 others. Some are very stiff. And so it's not going
14 to be able to take the angle the same way. You're
15 going to have more of that.

16 DR. MARIN: Or you can say in that context
17 this is the stiffness and it will take this angle and
18 you can measure that pre-clinically.

19 You can say this much angle will give you
20 this much loss in wall contact.

21 DR. WHITE: I was looking for the answers
22 to the questions you had about the IFU in that handout

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1 before and as I remember some of that was have you
2 ever gone outside the IFU? Do you ever read it? Do
3 you ever do that sort of stuff? And my assumptions or
4 I'll tell you what my answers were and I'd like to
5 poll you on that, but I've read them at the time of an
6 approval or prior to and never during a procedure.
7 And the IFU does give me the limits of what is, in
8 fact, the tolerance and that gives me some suspicion
9 of when it's going to be under or over, but I would
10 assume everybody uses outside of the IFU. I'd be
11 surprised if they don't. So we all get a feeling from
12 the IFU now as to what -- but I guess the question is
13 who -- what percentage, when you poll that, used
14 outside the IFU?

15 Maybe nobody else answered the question.

16 MR. LU: But isn't it also true that at
17 the neck length --

18 MS. ABEL: Excuse me, on the one clinician
19 admitted to never reading an IFU for an endovascular
20 graft, most clinicians had read an IFU in the past
21 three years. There are those that only read IFUs
22 during training, while others take a look

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1 intermittently.

2 DR. FOGARTY: But how many clinicians have
3 used the device out of an IFU in this audience?

4 MS. ABEL: How many clinicians are in the
5 audience is what Tom wants to know.

6 (Laughter.)

7 DR. FOGARTY: No.

8 (Laughter and applause.)

9 MS. ABEL: Okay, well this horse is
10 probably pretty dead.

11 (Laughter.)

12 DR. FOGARTY: Can't I just kick it one
13 more time?

14 MS. ABEL: Can you just link up with that
15 slide one more time? Okay, so as far as the IFU, is
16 there anything that we could do for the labeling and
17 I think we pretty much agree that we should consider
18 whether there are different ways to present the
19 information with respect to length of fixation or
20 length of contact versus neck length and other than
21 that, I don't know that we have to say a lot more
22 about changes in the label. Is that -- yes?

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1 AUDIENCE MEMBER: If the IFU is giving you
2 a limit as to where the device is likely to perform
3 well, and if Mark's original concern was that you
4 can't measure all that accurately and you give in an
5 IFU a tolerance, what is there to prevent people from
6 just moving the margin to the edge? It's a new edge.
7 You still have the same margin of error and you are
8 just in a worst position than you were because instead
9 of it being beyond this boundary there be dragons, is
10 a we suggest you kind of use it like this, but it's
11 okay if you slide. If people are not paying attention
12 to the boundaries all that seriously, any attempt to
13 make that boundary softer I think puts everybody in a
14 more dangerous position.

15 MS. ABEL: I think the only other thing I
16 have to say about that is it's written for all
17 clinicians, not just for you, Roy. You might know
18 exactly how well you can do the job, but it's written
19 for all clinicians. So you have to take that into
20 consideration.

21 DR. FILLINGER: That's why I was saying
22 that's why you do the testing, but you don't

1 necessarily put that information in the IFU. You do
2 that testing to help create the IFU, given the known
3 problems with people not being able to deploy the
4 device appropriately, etcetera, etcetera. But you
5 don't necessarily say oh yeah, you can cheat. You
6 know they're going to do that anyway, so you do the
7 testing to create the IFU.

8 MR. LU: And I'd like to make two more
9 points. Why is that given that is true for the
10 recommended neck length, it's very much market driven.
11 You don't know if you're going to get a company to
12 come out and say look, everyone should use -- have 20
13 millimeter neck, even though 20 millimeter will give
14 you a fantastic result compared with everybody else,
15 but from a user standpoint of view, oh, you require 20
16 millimeter neck. Does that mean your device has a
17 lower level of performance? So it seems that
18 everybody is locked on to this 15. If you don't reach
19 15, you're not competitive. So it's not really driven
20 by size. It's driven by the market perception.

21 And the second, the attachment length in
22 terms of the pullout force is that should we be

1 considering a test in terms of conformity tests.

2 MS. ABEL: The specific testing.

3 MR. LU: Right, okay.

4 MS. ABEL: Thank you. As far as whether
5 it's because of marketing or because that's the
6 limitations of these devices, I think certainly as Roy
7 mentioned there are people who had changed their
8 recommended numbers based on what they saw in clinical
9 results and I think it is a -- the 15 is something
10 that most people have used in studies and have found
11 to be -- there's still some problems here and there,
12 but in terms of risk benefit analysis, seems like a
13 rational number and I don't see people going longer
14 than that and not necessarily from a marketing reason,
15 but because then you're excluding more patients. Why
16 would you want to develop a device that you wouldn't
17 be able to use in as many patients. That's just me
18 speaking as an FDA'er as opposed to industry person.

19 Pull test for modular components. Never
20 mind, sorry, we have to go back up. I forgot about
21 these other little slides we have. I got distracted.

22 MS. SMITH: I think what we wanted to look

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1 at here was which testing methodology should be used
2 to evaluate migration resistance. And I know that Lou
3 had said earlier, for example, that a tensile test
4 didn't mean much and so how -- what additional
5 methodologies should be used to evaluate this failure
6 mode?

7 MS. ABEL: So that people are using
8 different methods, the ISO standard I think specifies
9 tensile. Does it make sense the fluid full model
10 should also be used?

11 Robert?

12 DR. WHIRLEY: I think you pointed out a
13 good question there. And I think the right answer, it
14 would seem to me is the one that's appropriate for a
15 particular device design to capture whatever its
16 method of fixation is going to be clinically. And
17 there may be new designs that are different than the
18 ones we're all thinking about that wouldn't be
19 appropriate for one or other of these particular
20 tests.

21 MS. ABEL: But if you're talking about the
22 old designs where the majority of the fixation is

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1 either with some sort of an active fixation with hooks
2 or barbs or whatever and radial force, you know, is it
3 reasonable to just yank it out of a tube or should you
4 try to stick it under a flow, whether it be for a few
5 minutes or hours or whatever you said or longer term?
6 Are there any thoughts with respect to that?

7 DR. WHIRLEY: It seems to me you'd
8 probably learn more from an appropriate tensile test.

9 MR. SMITH: The only reason I favor
10 considering fluid flow is because the device is
11 deployed in something that's compliant. When you just
12 do a tensile test, you're basically loading the whole
13 thing in actually, so you don't have any change in the
14 material in a circumferential direction. So that's
15 one thing to get a number, so you end up with a
16 number, 10 pounds, whatever it is.

17 But how well is that number going to
18 prevent migration? This comes back to what's the
19 appropriate acceptance criteria. Okay? So you get a
20 tensile number, but you have no idea whether that
21 means in a biaxially loaded condition which is what
22 the aorta is, it's not going to move or not. So you

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1 go ahead and test in a pressure flow model with a
2 compliant host vessel and look for migration. To me,
3 they're very interactive, so that's the only reason I
4 would support that. It doesn't mean it has to happen
5 that way. The other option is go to the clinical
6 trial and cross your fingers.

7 DR. WHIRLEY: So Lou, if I understand, you
8 talked about pressure, but not necessarily flow.

9 MR. SMITH: It says pressurized fluid
10 flow.

11 DR. WHIRLEY: So does flow play a role or
12 is it just pressure? So it's pressurized to get that
13 biaxial --

14 MR. SMITH: I think your equation showed
15 the overriding thing is the pressure, but that's to
16 get the forces. Without the flow, if you're in a
17 system that doesn't have any flow, you're probably not
18 going to get any migration.

19 DR. WHIRLEY: Can we even cloud it more?

20 MR. SMITH: Think about it. If you put it
21 in a pressurized cylinder where there's no flow, it's
22 statistically pressurized, how is it going to move

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1 anywhere?

2 LOMBARD MEDICAL: Lou, do you mean
3 pressure?

4 MR. SMITH: I'm talking about just whether
5 it moves or not, right?

6 I assume you're talking about pulistile
7 flow, is that right?

8 MEDTRONIC: My name is Dan and I'm from
9 Medtronic. Actually, I spent some time on modeling
10 the blood flow and I'm definitely in favor of
11 pressurized fluid flow model that has physiological
12 pressure and physiological flow as well. However, the
13 other problem I find doing the test is how do you
14 actually prevent the leakage running through the graft
15 because if you allow water to leak through the graft
16 material, then you don't have the pressure
17 differential.

18 So I'd like to hear some suggestions.

19 COOK, INC.: I can make a point there.
20 You still get the pressure difference, even though
21 you've got fluid flow going through the model. You
22 still have the pressure difference there. And you can

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1 seal out the graft as well. We do that. We have a
2 pressure model and we just seal it up with silicon so
3 you can get that. One problem with the pressure fluid
4 flow model is what are you going to put it in? Are
5 you going to put it in an acrylic tube? Are you going
6 to put it in a pig aorta? You've got to have it in
7 something that's semi-realistic and you get the right
8 frictional sticking properties and then you have to
9 view it. At least with the pullout test, you can just
10 put in a pig aorta and just pull it and then it comes
11 on out. It's a bit more difficult with a fluid flow
12 model. You've got to observe it.

13 DR. GREENBERG: Sir, could I ask you a
14 question there? You know, some of the assumptions
15 that you make are the description of failure that we
16 were trying to get earlier, when does something fail.
17 And if you have kind of assumptions as to when a
18 device is going to fail and you have a loading cell
19 that's measuring the force on certain component of the
20 graft, can't you not look at a device in terms of
21 failure, but look at a device in terms of when the
22 load exceeds a certain boundary condition?

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1 COOK, INC.: You can but then you have to
2 secure the light cell to the ground, right? So it's
3 a little more -- you can do it in principle. You just
4 have to think about how you're going to put it on and
5 how the fluid is going to keep it and how you're going
6 to seal the fluid in, that sort of stuff. In
7 principle, it can be done.

8 DR. CHUTER: I understand you can control
9 the pressure outside the graft, but the question is
10 what do you set that pressure to be? because nobody
11 knows what that is.

12 DR. FILLINGER: We have some idea what the
13 pressure is. There have been some studies now where
14 people have done translumbar punctures, so we know the
15 range of the pressure outside the graft and that it's
16 quite variable. So if you have in your model your
17 bench model, if your aneurism sac has lumbar arteries
18 and you adjust the outflow from those arteries then
19 you can adjust the pressure in the sac as well, if you
20 really need to, but basically if you just test over a
21 range that accomplishes the replicating the clinical
22 scenario, you should be okay.

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1 I think the pressure fluid flow model is
2 easier to replicate angulation of the neck and that
3 sort of thing. It's hard to put, to get a good load
4 sell on an angulated when you put the graft in an
5 angulated neck. So you may have to do both.

6 Certainly, one is very simple, so at least
7 it gives you a starting point.

8 DR. FOGARTY: I think what we should
9 really be looking at is pulse pressure. We should be
10 looking at pulse pressure, not systolic and diastolic.
11 The difference between the two is really more related
12 to displacement forces.

13 Is that guy right, engineers?

14 LOMBARD MEDICAL: That is true.

15 DR. FOGARTY: Oh, it is true. No, no, I'm
16 talking about flow and forces and if you've got a wide
17 pulse pressure of 100, there's more displacement force
18 than a systolic of 120 and a diastolic of 80.

19 I'm not talking about sac pressure at all.
20 Just assume -- do we ever know what sac pressure is
21 constantly as a constant over 24 hour period of time?
22 You don't know or you do know or what's the answer?

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1 DR. MARIN: We don't really know. We just
2 go to zero and that's the steady state condition.

3 MS. ABEL: Could you use a microphone or
4 take it out to the hallway.

5 (Laughter.)

6 DR. MARIN: Clearly, the sac pressure has
7 a lot to do with the delta P. The delta P is what
8 determines the loads and that's the pressure inside
9 minus the pressure outside. We don't' really know
10 what the sac pressure is per your comment and so we
11 assume it just goes to zero. It might only go to 10
12 or 20 or 30 millimeters, but if you assume it's zero
13 that's conservative, but at least that's the direction
14 you want to err.

15 There may be certain situations where it
16 never drops, but there are times when it gets very,
17 very low and so if we just assume zero, it can't get
18 lower than that.

19 DR. FOGARTY: You can get minus 2 degrees
20 can't you?

21 MR. CARDELLA: I think Dr. Fogerty is
22 correct. I don't think it's related at all to what

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1 the pressure is in the sac outside the graft. If
2 you're looking for mobility forces. It's the pulse
3 pressure that slams against the graft from the inside
4 that's going to move it. And that's what also moves
5 the aorta as well. If you've got a pressure of 120
6 over 20 with a pulse pressure of 100, that's a real
7 jack hammer water pick against that graft. I don't
8 think it matters what pressure in the sac outside the
9 graft is.

10 DR. MARIN: And instantaneously, the
11 pressure drag on the device is just the surface
12 integral of the pressure difference everywhere along
13 the interior surface. So when you're at the 120 and
14 if you're at 20 outside, you have an instantaneous 100
15 difference. You integrate that over the entire area
16 and now calculate an instantaneous downward
17 displacement force or actually the vector will be
18 whichever way the net integral tells you it is.

19 DR. FOGARTY: You're making the assumption
20 the viscosity is constant and related to a constant
21 level over the level of what hematocrit?

22 DR. MARIN: I'm not making any

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1 assumptions.

2 DR. FOGARTY: Somebody made the assumption
3 that viscosity was involved and was relatively
4 constant. Isn't that what you said?

5 DR. MARIN: No, the assumption was whether
6 the Reynolds numbers were such that we could ignore
7 certain terms in the momentum equation and just
8 basically calculating drag due to pressure differences
9 is very accurate.

10 DR. FOGARTY: With a regular pulse, not
11 atrial fib, not volume overload. You didn't assume
12 that.

13 Stroke volume is always the same.
14 Peripheral resistance zone is the same.

15 Stroke volume varies constantly. Most
16 people that have this operation have afib. So the
17 stroke volume varies related to that. I think
18 engineering assumptions often deviate from the real
19 world pathology.

20 DR. MARIN: Clearly, we're making
21 simplifications like just assuming the sac pressure is
22 always zero deviates from the real world, but it

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1 deviates in the direction which gives you a greater
2 force than reality. So that's the better way to
3 assume your boundary conditions to be.

4 DR. FOGARTY: I don't even know if the sac
5 pressure is high, low or varies from day to day,
6 whether or not you have an endoleak type 1 or type 2.
7 I think there's too many variables to make assumptions
8 that make it more variable.

9 DR. MARIN: Assuming it to be zero,
10 whenever it's higher the forces are lower, so if I
11 test, assuming it's zero, I'm safe. I may be over
12 designing the fixation, but I won't have a problem
13 with migration if I just assume the forces are as big
14 as they could ever be and just all the other times
15 when they're lower I've got extra margin.

16 DR. FOGARTY: Jon Matsumura, why don't you
17 give us your impression from a clinical standpoint?

18 He knows something about sac pressures.

19 DR. MATSUMURA: I think you guys started
20 off with a little difference in your understanding.
21 What they're talking about is the downward drag
22 calculated is related to the difference between the

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1 pressure inside and outside the graft and so they're
2 assuming zero so that they have it designed to the
3 greatest possible force it could be.

4 What you're talking about, I think is the
5 pulse pressure wave or the systolic and diastolic
6 which in my understanding when we do our fluid
7 mechanics model, relates to the tangential force in
8 the graft that's angulated in a curvature. When the
9 pressure is higher, than tangential pressure, that
10 vector is higher which makes the vector pull out
11 forces either pulling out of the iliac which we see
12 clinically or pulling down from the inferenal neck
13 greater. So I think you guys are in agreement, but
14 what they're saying is for the forces they calculate,
15 they figured out what is the highest amount of force
16 they have to account for or tension I guess.

17 I think both of you are right, there are
18 pressure matters too. If you have a very angulated
19 graft with a high opitious hypertensive or maybe
20 variably becomes more hypertensive than other times,
21 the forces are going to be different. I think you're
22 right that it's very difficult to simulate all these

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1 variables, but what the engineers are saying let's
2 assume the worse case scenario, the perfect storm and
3 try to design for that.

4 I guess one of the things, just to follow
5 up on Roy's initial comment after mine, I think I
6 agree with it, what he was saying designing for
7 failure and a lot of times when we use a balloon
8 catheter, we get these things. We get burst pressure.
9 We get radial force on a stent. We can get that.
10 Maybe we ought to be asking the manufacturers not so
11 much to know what Roy was asking but to give us some
12 standardized measure how their device performs in
13 terms of displacement or burst pressure and parameters
14 that could be defined uniformly that might allow
15 comparison between them. And then clinically we could
16 decide when do we need an accurate -- like I think the
17 one Roy was talking about was what is the 95 percent
18 chance that the device will deploy in a 45 percent
19 angled neck within 3 millimeters of where you want it?
20 Or what is the probability of that? And that would
21 allow us to know when to use the device for a short
22 neck and not.

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1 MS. ABEL: The amount of variability among
2 users and everything else, I just -- it's just not
3 possible. I think we can count on your guys to be
4 able to push the syringe or crank the thing or do
5 whatever you've got to do to blow up a balloon fairly
6 consistently. But when you're talking about your
7 ability to accurately deploy, I think it's very
8 different and then you get into the variability of the
9 patient anatomy. It might be relatively easy to
10 deploy in one patient because didn't he have to go
11 through some horrendous iliac anatomy to get there.
12 I mean I can't imagine being able to come up with that
13 precise of recommendation.

14 DR. GREENBERG: I have one just one
15 comment back to this topic here on a tensile test
16 versus a pressurized fluid flow model. I think that
17 they're both important and the reason that they're
18 both important is because not all of the fixation is
19 applied in the proximate neck. There's a certain
20 degree of columnar support. There's a certain degree
21 of cross sectional area reduction that will affect the
22 pullout and all of these other things that come into

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1 play.

2 And the only way those things can be
3 tested is in a pressurized flow model. However, we
4 don't have the perfect pressurized flow model, nor do
5 we know the exact criteria. So I would say that
6 they're both very important and we need to invest some
7 efforts to developing the pressurized fluid flow model
8 that will help us detect things. And I would
9 recommend that the efforts not try to look for
10 migration, but to simply define the forces that the
11 grafts are experiencing because it's too difficult to
12 reproduce migration, but it is not too difficult to
13 define the forces.

14 MS. ABEL: It sounds hard.

15 DR. FOGARTY: It is - you say it is or
16 isn't hard? I don't care what you say, the
17 significance of those numbers relative clinical
18 performance may or may not be appropriate.

19 MS. ABEL: But if you think back some
20 testing is purely for characterization, you know? So
21 --

22 DR. FOGARTY: Leave it for the FDA.

1 MS. ABEL: Dorothy says. Dan?

2 AUDIENCE MEMBER: I think there's a larger
3 question that we haven't really discussed in enough
4 length that was brought up by the gentleman from Bard
5 earlier and that is do we need to do a pulsatile or a
6 cyclic test as opposed to a static or quasi-static
7 test. I think the comment was made earlier for the
8 pressurized flow model, you don't get migration
9 without flow which I guess I would agree with. The
10 minutes up there say without pulsatile flow you don't
11 get migration. You can get migration with steady
12 state flow and the question I'm posing to the group
13 for discussion is is a steady flow or a static tensile
14 test the appropriate way of testing migration
15 resistance or do we need to go to a cyclic test,
16 whether it's a mechanical pull or a pulsatile flow
17 test?

18 MEDTRONIC: I think all of these dynamic
19 tests assume that we have the appropriate modeling of
20 fixation of the wall which I don't think we have with
21 any of these tests. So I think you use the dynamic
22 test to characterize the device and you can translate

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1 that into a tensile test which you can actually
2 measure values and compare between devices. But to
3 put it in a pressurized model and say whether it moves
4 or not is probably not relevant because you have very
5 different engagement with whatever conduit you've
6 designed.

7 DR. FILLINGER: But that's part of the
8 reason of trying to do the test is to -- I mean the
9 first go around is probably not going to come up with
10 some test that correlates extremely well into the
11 clinical outcomes, but if we don't try any of this.
12 If we continue to not test angulated devices, for
13 instance, and then wait until they get out in the
14 clinical, the clinical trials and then say oops, we've
15 got to go, we've got to take the angle of the neck
16 back because everything over this many degrees fails,
17 then that's not a good way to do it.

18 And early on, these tests are probably not
19 going to be -- they're certainly not going to be
20 perfect, but I think some of the comments like Tim and
21 others have made earlier that we can at least test
22 against existing devices, test pullout forces, test

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1 them in a model, you're right. The anchoring is not
2 going to be perfect, none of this is going to be
3 ideal, but it will at least allow us to approach
4 something that's better than what we've got now which
5 in some cases is no testing of angulation.

6 COOK, INC.: I think they're better suited
7 for design development and characterization.

8 MS. ABEL: Yes. I think characterization
9 seems perfectly rational. I'm so tired of this slide.
10 We're going to go to the next one.

11 (Laughter.)

12 Which gets into a lot of things that we've
13 already talked about.

14 (Pause.)

15 So we're going to assume that we're doing
16 both the tensile and a fluid flow model and that would
17 be pulsatile flow? Are we guessing? Perforized.
18 Thank you.

19 I want to quickly go through, rather than
20 do it for both types of tests. We assume -- well,
21 they may be one or the other, so if you can just
22 quickly, are there things that you can incorporate

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1 into either of those tests that would better reflect
2 atherosclerotic disease vessels, you know, do you need
3 to throw in some fake calcification? Is there
4 anything that is possible to do to make it a more
5 realistic test?

6 You can just yell out no, if you don't
7 think so.

8 (Nos.)

9 (Yes.)

10 MS. ABEL: Okay.

11 (Laughter.)

12 DR. FILLINGER: You can made the lumen
13 eccentric. Yes, it's not perfect. It's not the same
14 as an atheromatous plaque or a calcified plaque, but
15 if you make an eccentric lumen instead of a perfectly
16 circular cross sectional lumen, that at least
17 simulates, yes, it's not perfect, but at least creates
18 something that's more realistic than a perfectly
19 circular tube. So it's not atherosclerosis, but it's
20 at least closer to the real world.

21 DR. FOGARTY: That's reasonable.

22 MS. ABEL: Wait a minute, what?

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1 (Laughter.)

2 MS. ABEL: Can you say that in the
3 microphone?

4 DR. FOGARTY: I said that's reasonable.

5 MS. ABEL: That's what I thought.

6 DR. MATSUMURA: I think along with that
7 suggestion is not having a parallel neck, but going
8 for conical or barrel shaped is -- longitudinal as
9 well as cross sectional.

10 DR. FOGARTY: I don't think anybody
11 understands what you mean. Can you draw it?

12 DR. MATSUMURA: What I'm thinking about is
13 if you test everything in a completely cylindrical
14 neck, it's kind of ideal for some systems, but if you
15 have something that has a big bump in the 10
16 millimeters below the renal, but 10 millimeters above
17 is conical, then that's going to require the device
18 may perform differently in that type of anatomy.

19 DR. FOGARTY: The eccentricity doesn't
20 exist over a short length. Usually the plaque is
21 posterior and extends pretty far.

22 Is that what you're saying?

1 DR. MATSUMURA: Yes, that's what I'm
2 saying. It's not usually conical, same diameter at
3 the top and at the bottom. It's usually a different
4 one.

5 LOMBARD MEDICAL: What test vessel are we
6 imagining in this test? Are we thinking of cadaveric
7 aorta or are we thinking of silicon tube that's nice
8 and sticky and helps a lot or are we using Teflon
9 because it's slippery? Those things matter a hell of
10 a lot more than whether it's conical or sclerotic or
11 anything else.

12 DR. FOGARTY: You don't think it makes any
13 difference?

14 LOMBARD MEDICAL: Oh no, that makes a lot
15 of difference, but I mean if we're using it completely
16 on representative test tube, then I think we need to
17 decide what test you were talking about here. What
18 are we imagining? Are we talking about cadaveric
19 aorta?

20 MS. ABEL: No, I don't think we're getting
21 into the specifics of the mock artery material at this
22 point in time. I think it's a valid point that you

1 have to have a reasonable mock artery and you have to
2 figure out what the best thing is. I don't know that
3 we can get that done, since we're already running
4 behind today.

5 Neck angulation. We've already talked
6 about that. It should be incorporated and is that
7 something for the tensile test or both the tensile and
8 the flow, pressurized flow.

9 LOMBARD MEDICAL: Both.

10 MS. ABEL: Both. All right, changes in
11 morphology. Is there anything that you can do to
12 mimic the changes?

13 I think testing the ranges is somewhat
14 capturing the changes, I would suppose.

15 DR. CHUTER: You can assume that there's
16 going to be some neck dilatation and you can test at
17 a range of degrees of oversizing.

18 MS. ABEL: Ten degrees of oversizing.
19 That makes sense.

20 What about changes in forces due to
21 changes in morphology? Is there anything that you can
22 do in these tests? It seems a bit extreme to pretend

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1 that you can do anything like that? Maybe it's
2 something that should be considered with respect to
3 your severance criteria, but I don't know how you can
4 actually test.

5 MR. QUIGLEY: We can calculate what
6 maximum forces are and based on the angulation and use
7 that as an input so you can establish worse case
8 conditions.

9 MS. ABEL: We can't really incorporate the
10 changes. You can certainly come up with worse case
11 conditions.

12 MR. QUIGLEY: Correct, but you think it
13 represents all the changes.

14 MS. ABEL: Okay. Forces due to curvature.
15 I don't think it's really angles. I think angle is
16 more of * (4:05:13) as opposed to the curvature.

17 DR. FOGARTY: It depends on what view you
18 get, Dorothy. Curvature can end up as an angle taken
19 in another view. You can miss a kink which is an
20 angel.

21 MS. ABEL: I guess I'm differentiating
22 from the standpoint of what John was talking about

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1 earlier. If you've got it in there and it can pull
2 out from either end, is that something that you can
3 incorporate in the testing or is it something that you
4 again just look at with respect to acceptance
5 criteria.

6 DR. FOGARTY: You can incorporate it. I'm
7 not sure what it means. Depending upon the type of
8 graft, an exoskeleton or endoskeleton perform very
9 differently.

10 COOK, INC.: You could certainly put it in
11 a physical model. It's not a problem. And you could
12 certain work out what the forces are.

13 DR. MATSUMURA: I think that's the point
14 though. If the devices perform differently we want to
15 -- and maybe have clinical repercussions, then that's
16 what we should be testing for. You have a lot of list
17 things here. I just want to reemphasize, I think neck
18 angulation and curvature in the aneurism, of all of
19 the things in terms of expense relative to clinical
20 utility, to me, that's the one -- the most important
21 thing that we add to preclinical testing is that we
22 look at not just the things in this session, but when

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1 we get to fatigue, we look at performance and
2 angulated or curved anatomy which I think we have not
3 done, relative to the potential clinical benefits. I
4 think that's the most important addition.

5 MS. ABEL: All right. What about flow?
6 We already talked about it a little bit. If someone
7 could just summarize, so Angie can type it in.

8 MR. SMITH: Forces due to flow could be
9 neglected according to Robert's presentation.

10 DR. WHIRLEY: I think the forces due to
11 pressure are substantially larger than the forces that
12 are just due to flow.

13 MS. ABEL: Okay, we talked about the
14 differential pressures and so we assume that the
15 pressure of zero on the aneurism side, is that the
16 bottom line?

17 DR. WHIRLEY: I think that comment would
18 hold for any assumption of pressure in the aneurism
19 sac. I think the point that was made that we don't
20 what the pressure in the aneurism sac is is a very
21 valid one. I think we're pretty sure it's not less
22 than zero, so if you need a conservative assumption,

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1 there is one.

2 It's bigger than zero. But we don't know
3 what it is so we can assume whatever seems
4 conservative based on the data that's available.

5 Is that a non-answer for you?

6 MS. ABEL: We were just saying we assume
7 that it's zero. That's it.

8 COOK, INC.: With the worse case scenario.

9 DR. WHIRLEY: With pulse pressure and
10 flow, different outflow vessels may have different
11 resistance. Say you're adding a torsion factor,
12 because it will twist every time it pulses with
13 asymmetric anatomy and differential flow in the two
14 outflows.

15 Dorothy, can you go back to that former
16 slide? I don't think we're done with that yet.

17 MS. ABEL: This is a bigger version of the
18 next three slides.

19 DR. WHIRLEY: I see.

20 MS. SMITH: Is this what you want to look
21 at?

22 COOK, INC.: I just wanted to make the

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1 comment that if we're calculating forces due to
2 pressure, we should calculate them for the full range
3 of graft sizes because the graft size is a big factor
4 in that.

5 MR. DEHDASHTIAN: Add cross section area
6 reduction.

7 COOK, INC.: Yes, relative to limb size.

8 MR. DEHDASHTIAN: Or you can measure the
9 worse case of all.

10 DR. BIANCO: For that particular graft.

11 DR. WINN: So we're talking about forces
12 due to curvature and flow and asymmetry. So you're
13 talking about concluding that the momentum becomes
14 important when you're talking about a nonstraight
15 tube, those things aren't entirely negligible in those
16 sorts of situations.

17 Is that what you were saying earlier,
18 Michael, about the graft twisting?

19 COOK, INC.: They have a pulse pressure
20 and then the out flow through one artery may be
21 different to the out flow in the others. So you've
22 got different out flow resistance on each side. And

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1 because of the shape of the morphology, you're already
2 got some spiraling and then if you've got differential
3 out flow or differential resistance and each time it
4 pulses it also twists which is a force.

5 DR. WHIRLEY: You would also get that
6 torsional force if you simply add an asymmetric iliac,
7 you always will clinically. The simple analysis that
8 I showed in my presentation was for a highly idealized
9 situation that only looked at longitudinal forces. If
10 you look at forces in the other direction, the iliacs
11 are never symmetric, so every time you get a pressure
12 pulse, there is a moment that wants to cause periodic
13 twisting and that's not traditionally associated with
14 migration, but it may play a very important role in
15 durability for certain device designs. It's design
16 dependent how important it is, but that's a great
17 point that it's something to consider.

18 DR. FOGARTY: The atherosclerotic arteries
19 perform quite differently than CTs or MR on normal
20 arteries. In terms of torsion and in terms of
21 displacement --

22 DR. WHIRLEY: In terms of being less

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1 compliant?

2 DR. FOGARTY: No, in terms of less
3 compliant, all three of those aren't the same to me.
4 Yes, there's spiral motion to a normal artery and
5 sometimes you have or do not have that relative to an
6 atherosclerotic artery, particularly if you've got a
7 fixed point. There usually isn't torsional motion or
8 movement.

9 DR. WHIRLEY: Certainly, that kind of
10 thing could vary a lot depending on the disease state,
11 much like we were talking about sac pressure from an
12 engineering standpoint. We would look for what's the
13 worse case relative to the device design. What's the
14 most challenging situation and that would be the
15 situation that produces the largest force.

16 DR. FOGARTY: And that may be in a normal
17 artery on torsional force.

18 DR. WHIRLEY: It would probably be a less
19 diseased artery.

20 DR. FOGARTY: Well, we try not to usually
21 operate on normal arteries. I mean most of us do.
22 Sometimes we do it.

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1 MS. ABEL: Hurry up, switch slides while
2 they're not looking.

3 (Laughter.)

4 All right, if we get through this quickly,
5 you can have a break. I had mentioned that the
6 acceptance criteria were kind of all over the place
7 with respect to this testing and so I think we've
8 already hit on a lot of this during our discussions.
9 We probably don't even need to talk about it a lot
10 more. It's just in terms of is it rational or
11 migration, migration resistance to have an absolute
12 number for the tensile test, for example? I mean for
13 an individual manufacturer, not for us to specify.

14 DR. GREENBERG: I do want an absolute
15 number specifically for a tensile test. Why don't you
16 have an absolute number for displacement force?

17 MS. ABEL: I'm just asking. I'm not
18 saying that.

19 DR. GREENBERG: I'd be interested to hear
20 what each of the companies are using as essentially an
21 absolute number for displacement force.

22 DR. WHIRLEY: And that number would, of

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1 course, be sized dependent, depending on the aortic
2 and iliac size of a particular graft.

3 DR. GREENBERG: Are you willing to share,
4 Robert? What do you guys use for minimum or design
5 standard for displacement course?

6 DR. WHIRLEY: For?

7 DR. GREENBERG: For migration fixation.

8 DR. WHIRLEY: We actually drive them from,
9 more from various blood pressures.

10 (Laughter.)

11 Is that non-answer number two?

12 MR. SMITH: I don't work with him, but to
13 recalculate it if your blood pressure was systolic
14 120, I think it was about 5 or 6 Newtons, but if you
15 went up to blood pressure 180 it went up, but also the
16 angulation was a huge difference, Roy.

17 DR. GREENBERG: I'm not talking about what
18 we're expecting to see. I'm talking about what your
19 minimum design standards should be.

20 DR. WHIRLEY: So I would say I'd like to
21 a design standard up in the 8 to 10 millimeter range.
22 You did the Canterbury studies, right?

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