

1 blow up a balloon. The balloons are a size balloon
2 so that whether you are at 3 atmospheres or 10
3 atmospheres, the balloon is inflated to that size
4 unless you don't break the dog bone or the stenosis
5 itself and that was not an appropriate way to do
6 the procedure and that is not how the investigators
7 would have done the procedure. So, what you are
8 doing is you are deciding how many times do I go
9 after this blood vessel to get a good result. What
10 I think the data shows is that if you do not get a
11 pristine result from your first balloon inflation
12 or with minimal manipulation of the vessel with an
13 appropriate size balloon, the safest strategy for
14 the patient appears to be placement of the stent
15 early on in the procedure, not waiting until later
16 in the procedure. Certainly, I think that is what
17 the safety data showed us.

18 DR. ROSENFELD: It is a great question.
19 It is really central to any suboptimal indication
20 when you decide to bail out with whatever in any
21 clinical scenario. I mean, it is almost the same
22 question as when do you decide to do a procedure up
23 front in the first place. A lot of it is clinical
24 judgment.

25 By the way, the same decision point is

1 faced with those of us who are placing stents in
2 iliac arteries, and the indication for the iliac
3 approval, or the approval that was granted by the
4 FDA and you all for iliac is for a suboptimal
5 balloon angioplasty result. I have to say, I don't
6 know whether that is delineated in the approval for
7 the Palmaz stent and the WallStent. I know what
8 the approval was based on. It was the residual 5
9 mm mean gradient or residual 30 percent stenosis,
10 but there is no delineation of what you have to do
11 up front to make sure you have done the best you
12 can before you measure that gradient or before you
13 measure that residual stenosis. So, that is a
14 problem that is faced across the board.

15 You know, I can tell you that my own
16 impression, actually having looked at this data, is
17 that I would have a relatively low threshold. I
18 would probably start with balloon angioplasty alone
19 and see if I could try it a couple of times, but I
20 wouldn't be pushing that to the limit because of
21 this concern that we are pushing to the point, as
22 you said, where you broach the safety issues.

23 [Slide]

24 DR. LABOUNTY: On the screen here I put
25 down what is actually on the Palmaz P308 stent for

1 their indication. It says that the primary
2 dilation, what I view as the initial dilation, must
3 produce an inadequate and/or hemodynamic result.
4 So, the actual indication for that stent is after
5 the initial angioplasty. I was also involved in
6 the WallStent iliac study and I know it was based
7 upon just an initial dilation. They did not go
8 ahead and do multiple dilations and then have
9 suboptimal results and then enroll the patients in
10 the study.

11 How this was actually looked at, it was
12 probably more this way because the physicians did
13 not even realize that this was a suboptimal result
14 so they didn't really have to bias what their
15 initial reading was to enroll the patient. So,
16 what we are seeing on the case report forms I
17 believe are true values of what the physicians were
18 seeing at that time and it is really not a biased
19 result which you may see in some other iliac
20 studies or renal studies.

21 DR. TRACY: Just one final question, kind
22 of playing the devil's advocate here, was there
23 anything in the people who developed renal failure?
24 I didn't see baseline parameters for renal
25 function. I see that they were pretty closely

1 matched for diabetes, hypertension etc. Was there
2 anything that would have targeted these three as
3 being particularly at risk? What were there
4 baseline creatinines? Was there something
5 particularly bad about them?

6 DR. ROSENFELD: I am not a statistician
7 but I would say that I am unaware that there is a
8 difference between the two groups of patients, the
9 randomized groups, and it would seem to me that if
10 you have comparable -- that is the reason you
11 randomize actually, if you have comparable numbers
12 that end up being the same across all platforms,
13 and we showed pretty clearly that they are the same
14 across all platforms, there is going to be -- I
15 mean, from a statistical standpoint I am not sure
16 you could sort of separate out those three patients
17 and say is there something special about them
18 because there was probably something special about
19 the three patients in the other group.

20 DR. TRACY: That is fair enough. It is
21 just that I didn't see those baseline renal
22 function parameters listed anywhere.

23 DR. LABOUNTY: We don't have those.

24 DR. TRACY: Okay. I will pass along to
25 Dr. Laskey.

sgg

1 DR. LASKEY: It is hard not to dwell on
2 the small numbers because as an interventionalist I
3 certainly share your passion for the need for
4 something to bail you out of trouble. On the other
5 hand, sitting up here, there is an equal, if not
6 greater, need to do this in a rigorous fashion and,
7 certainly, backing into a retrospective post hoc
8 definition for suboptimal results is not the way
9 anybody really wants to do this.

10 My colleagues have spoken to this already
11 very eloquently, I have some questions about these
12 small numbers and, again, I don't understand why
13 these are hierarchical complications which you
14 describe in table 18 or combined. But, of the two
15 patients with abrupt closure -- let's do the in-
16 hospital stuff and then we can do the out of
17 hospital and combined complications. This is table
18 18, page 59 of the CDAC analysis. The two abrupt
19 closures just ring commensurately with the two
20 TLRs. So, what was going on there? You have in-
21 hospital TLR so obviously something happened in the
22 short term that wasn't good, that led you to go
23 back. Was the abrupt closure abrupt in lab or out
24 of lab? Are these the same two that were taken
25 back?

1 DR. LABOUNTY: If you add them up there
2 are 8 of them and there are 7 total in-hospital
3 complications. So, it must have been one of those
4 patients. I am not sure if it was the abrupt
5 closure --

6 DR. LASKEY: Well, the unit of analysis
7 needs to be consistent here and I need to
8 understand how we are comparing 15 to 2 because
9 that is what the whole basis of your safety claim
10 is. It is comparing 15 adverse events to 2. So,
11 are these events or patients?

12 DR. LABOUNTY: The total number of 7 is in
13 the hospital, 4 out of hospital, for 11 total.

14 DR. LASKEY: Right. I am sorry, 11.
15 Sorry, 11 versus 2. The total number of what?
16 Events?

17 DR. LABOUNTY: Total number of patients.

18 DR. LASKEY: Okay.

19 DR. LABOUNTY: Out to 30 days.

20 DR. LASKEY: Okay.

21 DR. ANSEL: Dr. Laskey, while we try to
22 figure that out with CDAC, why don't we move on to
23 another question and then we will address that one
24 after they give a coherent answer.

25 DR. LASKEY: Again, I sit over there as

1 well and we would like to have a device that gets
2 us out of trouble, but we also want to make sure
3 that it is of substantive benefit and, obviously,
4 the numbers here speak strongly to the absence of
5 substantive benefit clearly in the long term. So,
6 is it of any use to have something which is of
7 benefit in the short term if it isn't any good in
8 the long term? I guess we can get into the
9 difficulty of how to separate out the future of the
10 69 patients you have classified with the suboptimal
11 result because their in-hospital MACE is zero
12 percent. If I read table 1 right in the CDAC
13 subanalysis, it is hard to defend something bad is
14 happening is happening to the suboptimal definition
15 group. Again, we don't know the fate of the N
16 minus 10, the 69 or 70 minus 10, the ones that were
17 officially crossed over and clearly had a
18 disastrous complication happening. So, that is
19 what I am struggling with here and perhaps you
20 could help me with the numbers because, again, 11
21 versus 2 is difficult to sell.

22 DR. ROSENFELD: Can I just clarify? I
23 think the suboptimal group, the 70 patients or 69,
24 is in the stent arm. Those are patients that were
25 in the stent arm, not in the PTA arm. That does

sgg

1 not include the patients that crossed over.

2 DR. LASKEY: I understand that. But,
3 still, you have defined a group of patients with a
4 suboptimal result. Forgetting how you defined
5 that, it wasn't done up front. In my line of work,
6 and maybe Rick can address this, even patients that
7 had bail-out coronary stents still did worse in the
8 long term. Again, there may be a number problem
9 here but I am trying to extrapolate from my
10 experience in the coronary stent area and, to that
11 end, I can't help but be persuaded by our
12 experience with the one stent that was indicated
13 for a bail-out indication that did terribly in the
14 long term. The restenosis rates in the long term
15 were certainly not propitious. So, that is the
16 bias that I am trying to overcome here. Again, it
17 is difficult to feel strongly in defense of these
18 data when the long-term outcomes are, smack on,
19 really not different at all, with the proviso that
20 it is not statistically powered to show a
21 difference.

22 I would also wonder -- I think I know the
23 answer to this, but in looking at your acute MACE,
24 your in-hospital MACE, is there any virtue in doing
25 a multivariate analysis because there are so many

1 things that can go into it? For example, the three
2 folks that developed renal failure -- maybe they
3 were older; maybe two of them were diabetic. Is
4 there any way to get a handle on this where you can
5 show that the variable stent versus angioplasty
6 comes out looking statistically significant, or is
7 the event rate too small so you can do this
8 analysis?

9 DR. KUNTZ: With three outcomes it would
10 be a little bit too small. We would have to look
11 at that. But if you are trying to say basically
12 could you identify a prespecified group at risk
13 that would justify the use of the stent up front, I
14 think that is a good point. We had ten crossovers;
15 we had three with renal failure in the ensuing
16 three days. Three is certainly kind of small. The
17 data set would be fitted to the sample without a
18 whole lot of reference inferential capability. The
19 ten cases for predictors of which ones crossed over
20 would be an interesting outcome to look at. Maybe
21 there are some features of those. In our
22 experience with the coronary treatments, there tend
23 to be such predominant lesion characteristics that
24 lead to abrupt closures rather than patient
25 baseline characteristics that my guess is that

1 there are probably no identifiable prespecified
2 patient characteristics to determine which ones
3 would have a bad outcome from angioplasty up front.
4 So, I think those are probably good exercises for
5 one to go through and do, but I suspect potentially
6 the number of outcomes is too few to be meaningful.

7 DR. LASKEY: I wasn't suggesting an N of 3
8 but an N of 13 because there is a total of 13 major
9 complications in your table 18. So, that still may
10 be marginal.

11 Were the ten patients that then crossed
12 over from PTA to stent in the other third? You had
13 two-thirds who were in ideal lesion
14 characteristics. There is another third here that
15 are not so ideal. Can we get more of a handle on
16 these folks that crossed over?

17 DR. LABOUNTY: Are you talking about
18 lesion length?

19 DR. LASKEY: Yes, anything that put them
20 in the non-ideal lesion group that would make this
21 more palatable?

22 DR. ROSENFELD: That is a great question
23 that needs to be answered. That should be
24 answered. That is an excellent question.

25 DR. LASKEY: I am struggling here to work

sgg

1 with you. The femoral issue is one thing but the
2 popliteal issue is clearly another, and I wonder
3 whether we really need to break these out because
4 you have so few popliteal targets. I forget the
5 number off hand but it is clearly quite small and I
6 really wonder whether you can make any conclusions
7 based on so few patients who had a popliteal stent.

8 DR. ROSENFELD: I think 18 percent
9 lesions were in the popliteal.

10 DR. LASKEY: Sixteen patients.

11 DR. ROSENFELD: I guess 16 patients, 18
12 percent of the lesions. I think it is a legitimate
13 question. As a person who used this in the
14 popliteal in a number of my cases, I think the real
15 issue in the popliteal, in my mind, is, is there a
16 safety issue. That would be the thing that would
17 raise a red flag for me. I don't believe there are
18 any safety issues in the popliteal. Do you want to
19 address that?

20 [Slide]

21 DR. LABOUNTY: This is a tally from the
22 patient listing which we did with all the popliteal
23 lesions. You can see from the complication MACE,
24 the major complication at 30 days was zero percent
25 in the stent group. MACE out to 30 days was 7.1

1 percent in the PTA and 17.9 percent for major
2 complication rate for that group. If you look at
3 late TLR, which was defined as greater than 30 days
4 and less than or equal to 270 days, there were 4
5 events in the stent group and 7 events in the PTA
6 group, one requiring surgery.

7 DR. LASKEY: So, doing confidence
8 intervals, 0 out of 28, you still need to be fair
9 to the process; you still have very few patients.
10 It is very confusing trying to go back and forth
11 between patients and lesions and events. So, one
12 needs to be clear about the unit of analysis. But
13 my concern is still making a claim about a minority
14 of this data set.

15 DR. DEWEESE: I am sorry, were the
16 popliteal lesions well below the adductor canal,
17 and did any of them also involve the trifurcation
18 or the branching?

19 DR. ROSENFELD: The inclusion criteria
20 allowed stenting down to the tibial trifurcation,
21 down to the end of the popliteal artery. I know in
22 my case, I think there were three patients in my
23 institution who were actually stented down to that
24 level almost and those patients did well.

25 Dr. Laskey, I think it is a problem across

1 the board with this trial in terms of numbers, but
2 I am also concerned about sort of throwing the baby
3 out with the bath water. I think the concern for
4 me, as a clinician, is whether there is a safety
5 issue with popliteal artery stenting with this
6 stent. You know, if there is not a safety issue,
7 then to have it available as a bail out or as
8 whatever, as a suboptimal result -- in fact, even
9 with small numbers it is fairly impressive data,
10 but it would suggest that the threshold should
11 probably be lower for stenting the popliteal
12 artery. But, to me, it would to be throw the baby
13 out with the bath water if we said, well, give this
14 a suboptimal approval; the results are valid for
15 the SFA but they are not for the popliteal. I
16 think it is the whole group together, but
17 acknowledging that there are problems with numbers.

18 DR. LASKEY: Well, just for my own
19 information, are the popliteal lesions likely to be
20 as long and have all the other adverse
21 characteristics that you defined for the femoral?
22 These long segments of occlusion, I mean, are they
23 likely to be bad actors?

24 DR. ANSEL: The actual lesions themselves
25 tend to be shorter. However, the resultant

1 complication of a severe dissection or flow-
2 limiting dissection abrupt closure would be at a
3 high clinical standpoint because of the lack of
4 collateral flow. Many patients will tolerate
5 especially a chronic occlusion of the SFA where the
6 popliteal is usually leading to much more
7 symptomatic state.

8 DR. LASKEY: Again, now we are mixing our
9 long-term outcomes with short-term outcomes. If
10 the safety issue is what we are here about, then I
11 think we really need to have a better understanding
12 about these lesions that fell apart. Certainly the
13 ten that crossed over, were they clearly doomed to
14 fail, or was there some other factor operating
15 here? So, it would be useful to have that
16 information.

17 On another point, someone had dwelled on
18 ankle-brachial index and how significant that was,
19 but of the four or five measures of the quality of
20 life over the time period of the study, it looks
21 like the two arms are dead on and that the only
22 thing that changes is over time, that things did
23 get better over time, which would suggest some
24 adjunctive or ancillary factor equally active in
25 both arms, but that there was no distinguishing

1 feature in quality. I guess claudication is
2 certainly one of those issues. Do I read that
3 right?

4 DR. ROSENFELD: Yes. I think, again,
5 that the numbers are relatively small so it is
6 difficult to say. As we said at the outset, I
7 think this trial really did not show a difference
8 between the stent and the PTA groups in terms of
9 that endpoint.

10 DR. LASKEY: But there was a lot of
11 emphasis given to ABI and on the other hand, to be
12 fair --

13 DR. ROSENFELD: First of all, the ABI was
14 accumulated in many more patients so it is much
15 more powered, and I think that many of the other
16 endpoints, whether it be walking distance or an
17 important endpoint -- quality of life certainly
18 probably would be the most important endpoint,
19 which may get to Dr. Freischlag's comments about
20 how do you change people's life style and risk
21 factor modification, and so on -- all those things
22 are very important but in terms of numbers, the one
23 thing that was really looking for objective data
24 and something you could hang your hat on, I think
25 the ABI was accumulated in more patients than any

1 of the other endpoints, if you will, and is the one
2 that showed the most statistically significant
3 difference actually. Notwithstanding the standard
4 error of the mean that is involved there, but the
5 fact is that it is a statistically significant
6 difference. I think it is a valid endpoint.

7 We have actually talked about that. Gary
8 and I have talked about that, why is that a
9 difference, and there has actually been some data
10 in coronary stenting to suggest that there may be a
11 hemodynamic benefit. You know, if you look at the
12 binary endpoint of restenosis, you can have a focal
13 stenosis that is 53 percent of 55 percent and, all
14 of a sudden that is a restenosis lesion. So, we
15 didn't analyze in what way these patients
16 restenosed. Did they restenose with focal lesions
17 or nice, smooth tapered lesions? A focal or
18 tapered lesion in a stent might be a much better
19 endpoint, if you will, or a better outcome, if you
20 will, than an irregular restenosis lesion in a
21 balloon angioplasty.

22 The ABI improvement, which is a valid
23 statistical endpoint, would suggest that the flow
24 characteristics within the stent are better in the
25 long term than in balloon angioplasty alone, but

1 that is all you could say about it. It is a
2 presumption.

3 DR. LASKEY: I don't want to hog the rest
4 of the panel's time but I have a final thought and
5 I would like you to just comment on it. It is more
6 of a sentiment. If we loosen up the definition of
7 acute and threatening closure which, in my book, is
8 a very stringent definition, to suboptimal result
9 are we leaving ourselves open to widespread
10 stenting of the fem/pop system which, by your data,
11 on average, in the long term, doesn't do any better
12 than angioplasty and, in fact, carries with it a
13 very dire consequence of in-stent restenosis which,
14 as you know, is a very difficult thing to treat?
15 So, my concern here is letting something out of the
16 bag which we may regret in the long term, that by
17 loosening up the entry criteria, which is critical
18 to your requirement for training, are you leading
19 to widespread stenting because people say, "oh
20 well, it's not working; let's put a stent in," and
21 there you are, to 80, 90 percent stenting of the
22 fempop system with a consequent downside in the
23 long term?

24 DR. ANSEL: From my perspective, first of
25 all, we have already done that in the iliac system.

1 We have accepted those results and that is an
2 acceptable way to treat these patients. The in-
3 stent restenosis, especially with this type of
4 stent, actually is not the same as in coronaries.
5 In the coronaries the matrix is very tough; it is
6 very hard to redilate and it is very prone to
7 recurrence. That does not occur. Secondary
8 dilation responds very well because of the very low
9 metal-to-luminal area that it has.

10 I think that it allows you to potentially
11 get a safer outpatient procedure for these
12 patients. And, I think that from a symptomatic
13 standpoint, again, we can't go back and say these
14 patients are doing okay. They have a terrible
15 mortality at five years because they are all
16 sedentary. They can't get out of their chairs.
17 They have a very terrible quality of life, and we
18 don't have any other answers for them. So, the
19 question is whether this therapy offers them the
20 safest, most effective way to do that and I think
21 that for suboptimal angioplasty the safest way to
22 treat these patients is with a femoral stent.

23 DR. ROSENFELD: I just want to make a
24 couple of comments about that. I think that is a
25 valid question to ask, are we opening this up to

1 widespread misuse, abuse, whatever? I would say to
2 that that these data show that there is no
3 difference between the balloon angioplasty -- it is
4 not worse. This stent is not worse than balloon
5 angioplasty.

6 Just to address that one step further, Dr.
7 Laskey, because you referred back to an earlier
8 stent that was approved in the coronary circulation
9 for a suboptimal result and I would say that this
10 stent is different than that stent. This is a
11 nitinol stent. This is not a stainless steel
12 stent. This is a self-expanding stent. There is
13 quite a bit difference I think in many, many
14 respects, aside from it being a peripheral vessel
15 versus a coronary artery.

16 So, this stent is not worse than balloon
17 angioplasty but it is better than balloon
18 angioplasty in terms of the safety results.
19 Listen, when I am treating patients what I care
20 about is getting the patient through the procedure
21 safely so that they can go home and do the things
22 that they want to do, as Gary is pointing out.

23 Do I think it is a disservice to put a
24 device in a patient that gets them through a
25 procedure more safely and with a nice at least

1 acute endpoint? Regardless of the 9-month
2 endpoint, as long as the 9-month endpoint isn't
3 worse I don't care. I want to get them through as
4 safely as possible. I think that is where we
5 should all be. This is about patient care. So,
6 that addresses my personal opinion about this.

7 DR. LASKEY: Well, it certainly addresses
8 your personal opinion and, other than the approach
9 of just stenting everybody, one clearly needs to
10 have an up front idea about who this stent is
11 appropriate for.

12 DR. SIMMONS: I guess I don't have a lot
13 of questions; maybe a couple of comments. During
14 the study I saw that a change was made to allow
15 ipsilateral dilatation of the iliac system on the
16 same side that the stent or the PTCA was going to
17 be done. How many of those patients actually got
18 done, and how many of them were in the stent group
19 versus the PTCA group?

20 DR. LABOUNTY: I do not know the answer to
21 that question.

22 DR. SIMMONS: That seems like an important
23 question, doesn't it? I mean, if you are a
24 stenting kind of guy and you are going to put
25 stents in the femoral and you decide to go ahead

1 and stent the iliac, isn't that going to affect
2 your ABI quite a bit? Isn't that going to affect
3 your acute occlusion and your chronic occlusion?
4 Isn't that going to affect a lot of issues?

5 DR. ANSEL: Yes, but it is randomized
6 between the two groups so that still holds true
7 with the angioplasty group as well. So, as long as
8 it is a randomized trial -- that is why that was
9 done.

10 DR. SIMMONS: I am not sure you can use
11 that definition. I mean, I would like to know what
12 the numbers were. If you got ten in one group and
13 zero in the other -- I mean that could easily
14 happen. Just because you randomize patients it
15 doesn't mean their iliacs got randomized.

16 DR. ANSEL: Wait, but the patient didn't
17 get randomized until you crossed the lesion with
18 the wire. So, you had no idea. If the patient had
19 an iliac lesion you couldn't say, well, now I am
20 going to stent the popliteal and I am going to
21 stent the iliac too. You couldn't do that because
22 you didn't know, going into the procedure, whether
23 you were going to do an angioplasty of the femoral
24 or a stent. So, how you treated the iliac actually
25 was randomized.

1 DR. ROSENFELD: Just to clarify the issue
2 of the iliacs, you are right, there was a change
3 made and it had to do with a lot of investigators
4 complaining that, "well, gee, this patient that I
5 want to randomize has an iliac stenosis." I am
6 thinking back, when that question came up, can you
7 correct an inflow lesion before randomizing the
8 patient, and the question came up is that going to
9 influence the results? We certainly didn't want it
10 to have an untoward effect on the results. I think
11 there was an assessment made at that time that
12 iliac angioplasty, and I think everybody here would
13 pretty much agree, is a pretty durable procedure
14 whether you stent or not. And, the feeling was
15 that that wouldn't influence the results one way or
16 the other. But, I think it should be examined as
17 to how many patients actually got treated in the
18 iliac. My sense is it was a very small number but
19 I don't know that for sure.

20 DR. SIMMONS: When the patients left the
21 lab or were sent home, were they aware of which of
22 the groups they were in? I assume they must have
23 got a card or a thing in their wallet that told
24 them that they had an implantable device. So, they
25 knew which group they got randomized to. Is that

1 correct?

2 DR. ROSENFELD: Yes. Yes, they knew
3 whether they got the stent or the non-stent.

4 DR. SIMMONS: And whether or not there is
5 some placebo effect here or not, certainly from the
6 vasovagal pacemaker trials and things like that it
7 was very clear that patients who get surgical
8 procedures want a good result, and they will do
9 just about anything to get it. In spite of that
10 your quality of life assessment is totally flat.
11 So, I don't know, and I just have the sense from
12 what you are telling me, and in fact you admitted
13 it yourself, your investigators were terribly
14 biased. Your whole set of investigators were
15 terribly biased people and had a very severe lack
16 of enthusiasm for the PTCA group.

17 You use all numbers, you keep using that
18 word, and you use the small numbers to explain that
19 the bad things weren't really bad but the small
20 numbers weren't hurting the fact that the good
21 numbers were really good. I guess it bothers me
22 quite a bit. I think there were only 16 patients
23 in your total group with popliteal dilatations in
24 the group with the poor result with the
25 angioplasty. So, I don't know.

1 One of the ways I look at this kind of
2 data is would this data get published in a major
3 journal? And, I am not convinced at this point in
4 time that this data could get published in a major
5 journal. I mean, you said you have a tone of these
6 patients hanging around. Why don't you do a bail-
7 out study, or why don't you do a study that just
8 shows that this thing really is of value? Why not
9 scrap this and start, if you really have a ton of
10 patients -- I certainly have a ton of patients with
11 diabetes, and smoking, and coronary-artery disease.
12 Why not design a study you want to prove?

13 It seems like there was this tremendous
14 lack of enthusiasm among the investigators from the
15 very beginning. You didn't do the Dopplers. You
16 didn't do the angiograms. You didn't do the
17 follow-ups. Then we stopped the study at half
18 point and now we are trying to find a way to get
19 this thing in because your clinical impression is
20 that this is so good.

21 DR. ROSENFELD: One thing that has been
22 an eye opener to me, and I will be very frank about
23 this, has to do with the difference, and I do
24 coronary trials and I do peripheral trials, so I
25 can tell you that being on both sides and wearing

1 the two hats, it is really interesting that there
2 is a difference between the two groups of patients
3 as much as anything else. I mean, I think this has
4 been alluded to some degree because it is really
5 true. It is a tough group of patients. I mean,
6 the smoking issues that I mentioned, these are
7 patients that come in and some of them tend to be
8 more non-compliant than the average patient in the
9 coronary trial -- coronary, electrophysiology
10 trial, or whatever. It is just a fact.

11 It is also a difference because when you
12 talk about peripheral vascular disease there are a
13 lot of different management modalities and it is
14 all over the map as far as how people think that
15 these patients should be managed. Should they all
16 be managed conservatively? Should they all be
17 intervened? It is not nearly as standardized as in
18 coronary-artery disease. So, it is much more
19 difficult to conduct a trial looking at an isolated
20 segment of the peripheral vasculature.

21 This is one of the first trials that has
22 really done that in a randomized, controlled
23 fashion. Mind you, the iliac stent trials that
24 were done before that gained approval for those
25 devices were not randomized, controlled trials.

1 They were registries that then --

2 DR. ROBERTS: The WallStent was
3 randomized.

4 DR. ROSENFELD: WallStent was randomized
5 -- no, that is not true --

6 DR. LABOUNTY: No, it was a registry using
7 the Palmaz data as a control.

8 DR. ROSENFELD: I was a registry; it was
9 not a randomized, controlled between balloon
10 angioplasty alone versus stenting, in the same mode
11 that this was. Regardless of that, the point is
12 that it is difficult -- it became clear how
13 difficult it was to enroll. Yes, during the
14 conduct of the trial there was an evolving
15 investigator bias. I think that happens when you
16 do a balloon on a long SFA lesion that is 10 cm
17 long and you dilate, and you dilate, and you dilate
18 and you get this recoil and you say, well, you
19 know, my next patient -- and it is two hours on the
20 table and you say my next patient, I am not sure I
21 want to randomize this patient now that we have
22 available a number of off protocol stents, not
23 approved but, you know, they work. Instead of
24 going through this process, I am not sure I want to
25 randomize next time. That is just a natural

1 selection. We all want to do the best for our
2 patients. I don't think it is so much bias as
3 wanting to do as well as we can for our patients
4 and maybe, yes, we are biased in that making an
5 artery look good at the end of the day is a better
6 thing for our patients, at least acutely.

7 I think the important point about this
8 trial is to go back and say, well, at the end of
9 the day you made the artery look good. And, was it
10 a disservice to the patient in the long run? No, I
11 don't think it was a disservice. The restenosis
12 rate wasn't higher. It didn't show that there was
13 a clear-cut differential. Who knows? Maybe had we
14 accumulated the full complement of patients there
15 might have been a separation. We know that there
16 is a lot of bias in the angiographic result because
17 patients tend to only come back if they have
18 restenosis. So, I am not even sure how to
19 interpret the primary endpoint, which is the
20 angiographic restenosis at 9 months. I acknowledge
21 all the limitations of the trial. There are a lot
22 of them. That is very evident.

23 DR. WITTES: Well, I am not going to have
24 much to add because obviously we are all struggling
25 with two of the same questions. One is, how do we

1 interpret the data for the suboptimal group? Two
2 is, is the 30-day safety that we see real, and is
3 it worth it in the light of the lack of difference
4 at 270 days?

5 But let me ask you a couple of questions.
6 The other thing I want to stress is we have to look
7 at the data, not what might have happened in
8 another study or if the trial were larger or if
9 different people were entered. These are the data
10 we have and this is what we need to look at.

11 I must say, I guess we are also switching
12 over not only to the primary group that we are
13 looking at, which is no longer the total group but
14 this suboptimal group, but also we have to look at
15 a new endpoint because for the angiographic
16 endpoint at 9 months we only have a really a very
17 small percentage of people back.

18 So, my questions are a series of questions
19 related to numbers, of course, and then also a more
20 global question about why there wasn't more what I
21 call aggressive analysis of the suboptimal group,
22 and let me get back to that in a minute.

23 But let me ask some questions first about
24 numbers. I too had a lot of trouble about what
25 analysis is per patient and what analysis is per

1 lesion. Sometimes when the denominators are very
2 small in relation to the total number of people or
3 lesions you can't even tell which is which. So,
4 question number one is in the analysis per lesion,
5 did you adjust for the correlation within lesion
6 within a person or did you just take each lesion as
7 an independent observation?

8 DR. KUNTZ: The lesions were treated
9 independently based on multiple previous data
10 showing independence of lesions within patients.

11 DR. WITTES: And, can I presume in any
12 given table if there are two denominators that the
13 larger of the denominators is lesions and the
14 smaller is people, or is that not always true?

15 DR. KUNTZ: I think the tables should
16 actually say lesions or patients in them. If there
17 is something that is questionable we can look at
18 the tables.

19 DR. WITTES: I am sorry about this but on
20 table 8, table 8 of the subanalysis where there
21 seems to be a third denominator which seems to be
22 number of stents. Am I reading this right, that
23 the average number of stents in the suboptimal
24 group was more than two? Is that how I should read
25 this table? This is page 19.

1 DR. LABOUNTY: Yes.

2 DR. WITTES: So, the denominator 172 --
3 tell me what that denominator means, and tell me
4 what 60 means, and tell me what 80 means.

5 DR. LABOUNTY: So, for post-procedure
6 hospital length of stay, that is based upon
7 patients. Diameter of stents implanted, which is
8 from the stent tracking form, was based upon
9 lesions. Now, there was a difference in the number
10 of lesions the QA reported versus what the sites
11 reported. Also, for the dissection after the
12 initial PTA, the 60 is lesions. Post-procedure
13 dissection, the 80 is lesions. Post-procedure
14 thrombus is lesion, and number of stents in lesion
15 is lesion.

16 DR. WITTES: So, the 172 means in the 87
17 lesions there were 172 stents? Is that right?

18 DR. LABOUNTY: Which part is that from?

19 DR. WITTES: In the diameter stent
20 implanted section.

21 DR. LABOUNTY: Yes, that must be in there.
22 Hang on, no, that is based upon number of stents
23 implanted. So, there are 172 total stents
24 implanted --

25 DR. WITTES: In these 87 lesions?

1 DR. LABOUNTY: Yes.

2 DR. WITTES: Again, I understand why
3 people didn't come back for their 9-month
4 angiogram, but I don't understand why they didn't
5 come back for the 9-month clinical visit or other
6 measurements. For example, let me give you the
7 numbers that I calculated and see if this is right.
8 The ABI, which we all agree is the most
9 statistically significant result, but as I look at
10 the data, one third of the suboptimal group is
11 missing. One half of the total group is missing,
12 the total stented group is missing, and 60 percent
13 of the PTA is missing.

14 So, the question is why was there such a
15 low rate of measurement at 9 months and why the
16 differential? And, the reason I am asking about
17 the differential follow-up is that it actually has
18 implications to the interpretation of these
19 differences. And, we see similar kinds of
20 differences in other endpoints. I am just pulling
21 that one out because that is the one that is the
22 most significant one.

23 DR. LABOUNTY: Part of this data right
24 here that you are looking at is the 7/28/00 report.
25 It is older data, and it was updated with

1 additional information. The summary tables were
2 updated and did include some additional 9-month
3 follow-up that was received.

4 DR. WITTES: So, can you give us a sense
5 of what those numbers are?

6 DR. LABOUNTY: Yes, I can do that. For
7 the suboptimal group we don't have the ABI in this
8 table.

9 DR. ROBERTS: Sorry, can I interrupt?
10 Where are you looking so that maybe we can all
11 follow along?

12 DR. LABOUNTY: The additional information
13 tab, table 2, page 5. You have to see updated
14 summary tables, so table 2, on 11/10/00, updated
15 data.

16 DR. WITTES: You also have to look at
17 table 1. Is that right?

18 DR. LABOUNTY: Table 1 is for the whole
19 group.

20 DR. WITTES: So, it is 83 over 135.

21 DR. LABOUNTY: So, it is still low, and
22 there was a little bit of an issue in the study
23 when half way through the study the previous
24 sponsor, prior to IntraTherapeutics, the treadmill
25 testing was halted at baseline so it was not a

1 requirement in the study anymore, and there were
2 several sites that took that as meaning that
3 resting ABI was also not necessary at that time.
4 So, there is actually some missing baseline ABI
5 data, randomly distributed between the two groups,
6 for a portion of the study.

7 DR. WITTES: I am just calculating in my
8 head so I could be wrong but I am still getting a
9 differential follow-up in the three groups, 83 over
10 135 versus 48 over 70 versus 64 over 135 and that,
11 quickly, looks to me like a considerable
12 differential. So, again, the question is, and I
13 think it is related to the enthusiasm -- who know
14 what it is related to, but why the differential?
15 That is the question.

16 DR. LABOUNTY: I think that is partially
17 because some of the baseline ABI was not gathered
18 at several of these centers because they had sent a
19 letter out to the investigators saying basically
20 the baseline treadmill testing was not required
21 anymore as inclusion criteria for allowing the
22 patient to be in the study. So, in that regard
23 several centers at that time interpreted that as
24 also that the resting ABI was not required. So,
25 that was not performed over a certain period of

1 time.

2 DR. WITTES: I don't want to persevere on
3 this, but the question is not only why others are
4 missing but why is there a differential.

5 There was one other thing I wanted to
6 raise. Obviously, we all know that the problem
7 with retrospective analyses, and there are lots of
8 problems with retrospective analyses -- there is
9 the problem of how do we, as a panel, know this is
10 the only one you did; how do we know that the
11 criteria that you used to define suboptimal is the
12 only criterion that you used, and all that.

13 And, now I want to get to my aggressive
14 analysis piece. It seems to me that the argument
15 that you are using is because the outcomes for the
16 suboptimal group are comparable to the outcomes of
17 the PTA group in general, it must mean that the
18 stent is good because you would expect a priori
19 that this group would be worse. But it seems to me
20 that in order to make that argument you need to
21 show us that these were not people that were
22 differentially older, or differentially younger, or
23 differentially in one center and so forth. So, I
24 guess I am asking also for some kind of analysis to
25 give us assurance, reasonable assurance -- we will

1 never have full assurance because it is
2 retrospective and so forth and so on, but more
3 assurance that we are not seeing some kind of an
4 artifact.

5 DR. LABOUNTY: On the 7/28 report of the
6 CDAC analysis, and I think there is also a portion
7 in the CDAC subanalysis, there is a univariate
8 predictor of target lesion revascularization at 270
9 days, on table 30, page 89.

10 DR. WITTES: Tell me what this means.

11 [Slide]

12 DR. LABOUNTY: this summarizes the
13 statistically significant covariates in the
14 univariate analysis. The lower your ABI was, the
15 higher your TLR rate. Men have a higher TLR rate
16 than women. If you had a previous MI you have a
17 higher TLR rate. If you have a lower reference
18 vessel diameter, you have a higher TLR rate, and
19 the longer your lesion the higher your TLR rate.

20 DR. KUNTZ: I don't know if this answers
21 your question but let me just address it straight
22 on. There is always a tension between a parsimony
23 of doing a retrospective analysis and a full-
24 fledged aggressive one, as you know. And, in this
25 situation, in order to minimize a multiple

1 comparison and multiplicity, we elected to use
2 conventional definitions. So, the 30-day endpoint
3 definition is a conventional definition used in
4 previous peripheral studies. Similarly, the
5 criteria to define suboptimal was a standard
6 definition used in other FDA approved trials. So,
7 in order to reduce multiplicity, those are the only
8 two analyses that we did in order to evaluate the
9 suboptimal group. Further aggressive analyses
10 might have led to the potential for multiplicity.
11 On the other hand, in order to make sure that they
12 are balanced, the suboptimal analysis did
13 artificially associate with higher numbers of
14 individuals that predicted outcome. These were
15 compared and there were no statistical differences
16 among the groups versus the optimal versus the
17 group its group that was drawn from and so on.

18 From my perspective of looking at these
19 data and trying to be as objective as possible
20 because I have absolutely no gain for this to be
21 approved or not approved, what happened was that
22 this study was negative in terms of its primary
23 endpoint. If you show that everything is equal,
24 and nobody would ever elect to approve a stent when
25 something as simple as balloon angioplasty could be

1 easily substituted because why would you put an
2 implantable device in the body, and why would you
3 sell something that is going to cost money. So,
4 the question is was there any other utility of this
5 stent that was somewhat less than the primary
6 endpoint but better than absolute equivalence among
7 both sides? That is what the company sought to
8 look at.

9 One was that using the conventional
10 definition of 30-day MACE endpoints, there was a
11 statistically different reduction. Some of them
12 are not counted at the 9-month endpoint; some are.
13 For example, if you have abrupt closure
14 necessitating the use of this stent in a crossover,
15 we didn't count that at the 9-month endpoint. So,
16 some of the issues about the measured endpoints at
17 30 days were mitigated because of the availability
18 of the stent for crossover that would mask its
19 event at the 9-month measure.

20 So, if we look at the initial 30-day
21 endpoint in and of itself and there was a
22 statistical difference in the standard definition
23 of MACE, which isn't as powerful as the primary
24 endpoint but it is something that we should
25 evaluate. The other thing is that there were 10

1 cases that required crossover. We will never know
2 exactly whether those patients would have done
3 better without the stent or not, but we do know
4 that with those 10 patients crossing over the
5 overall outcomes of the PTA group were the best
6 ever seen in the history of PTA. That is, there
7 are no data to this point that show results as good
8 as this trial, not to mention the fact that this is
9 the first attempt to do a randomized trial in the
10 superficial femoral artery. So, many of the kinks
11 along the way of not being able to get duplex and
12 not being able to get good angiographic follow-up
13 are basically because of pioneering territory
14 during a randomized trial the first time in
15 peripheral vessels.

16 So, I think in a way the company should
17 actually be congratulated for making an attempt to
18 do a very, very good, powerful, controlled
19 randomized trial in an area where other products
20 have been approved without randomized trials before
21 in the past. And, what they found were major
22 stumbling blocks that were associated with
23 peripheral studies that some investigators had
24 identified early on.

25 So, you are right that there is no

1 difference in the endpoint. You are right that the
2 suboptimal analysis is in and of itself suboptimal.
3 We elected to do not a whole lot of aggressive
4 analyses to avoid multiplicity by picking some
5 standard endpoints up front. But, there are a few
6 shining stars that pop up every once in a while,
7 like the availability of the stent for crossovers;
8 a conventional definition of MACE at 30 days which
9 was statistically different; and a difference in
10 the ABIs in the end.

11 The real question is are those enough to
12 push it over to be approved in some limited fashion
13 for availability for patients, given the outcome in
14 both arms is the best ever seen in the history of
15 treatment for this area, and one questions whether
16 the PTA group would have actually been worse if
17 they didn't have the availability of the stent,
18 both because the operators were more aggressive
19 because they had the confidence of having the stent
20 for a backup and the use of those stents in a
21 smaller number of patients, 8 percent.

22 So, I just wanted to make those kind of
23 general statements about our approach to analyze
24 this otherwise negative study to see if there was
25 any value in this overall, given the very, very

1 good outcomes of both arms on both sides. So, the
2 suboptimal analysis group -- I think we could stand
3 to do some covariate adjustment to make sure that
4 we still show no statistical difference, as you are
5 stating, among those. But there was minimal, if
6 any, data dredging in this analysis. There was
7 essentially use of very conventional definitions of
8 MACE and of the selection criteria for the
9 suboptimal group to go forward.

10 DR. WITTES: Let me ask one more question.
11 The 69 or 70 in the suboptimal group, how were they
12 distributed over the centers? The reason I am
13 asking that is that there has to be some
14 subjectivity in operator difference.

15 DR. KUNTZ: Right. Maybe if I could
16 restate your question, the use of stents obviously
17 might be subjective to the sites because that is an
18 arbitrary call by the site. The actual decision
19 about who gets into the suboptimal analysis was
20 done from a dispassionate clinical events committee
21 and core laboratory based on data.

22 Now, some of that is influenced by case
23 report data so there might be some slight influence
24 at that level. Others was influenced by core
25 laboratory data which are slightly more objective

1 to some degree. But I will let the company answer
2 if they have seen any clustering among the sites.
3 As far as I can tell, it I think it seemed to be
4 somewhat evenly distributed but we certainly can
5 check to see if there was clustering to one side.
6 But, my guess is that because of the way the
7 definitions for entry into the suboptimal group
8 were defined, in an objective way, it would be
9 surprising to me if there were clustering in one
10 side or another because much of the decision-making
11 was from a dispassionate group rather than the site
12 itself.

13 DR. WITTES: But there is no operator
14 difference in the likelihood of becoming
15 suboptimal?

16 DR. KUNTZ: Right, it is very hard to look
17 at the differences in operators in any of these
18 trials because operator performance is so
19 arbitrarily defined, number one, and the frequency
20 of complications is low enough that with 20 sites
21 and 250 patients there just isn't enough power.

22 DR. WITTES: No, I am not asking to look
23 at that; I am just saying that if there were some
24 way that you could measure, it could reflect itself
25 in differential.

sgg

1 DR. KUNTZ: Right, I acknowledge that.
2 Sure.

3 DR. TRACY: Dr. Aziz?

4 DR. AZIZ: Obviously, a lot of questions
5 have been asked about the small numbers. I am
6 going to ask a very few questions. Did you use
7 this stent in a number of patients with calcified
8 lesions, and how easy was it to deploy in those
9 patients?

10 DR. ANSEL: The deployment was very
11 simple. The only time that there was ever any
12 difficulty wasn't the stent; it was the antegrade
13 access with a short delivery device early on. But
14 after that, I mean it goes very easily. It is
15 really not difficult to deliver.

16 DR. AZIZ: In terms of restenosis, was
17 there a difference in the number of patients with
18 renal failure or renal dysfunction between the two
19 groups, or were they excluded?

20 DR. ANSEL: We are looking that up.

21 DR. ROSENFELD: In answer to your first
22 question, on page 36 there is a table from the core
23 lab identifying the calcification. That was judged
24 from the core lab, looking mostly at cut film
25 angiograms and trying to determine whether there

1 was any calcification, and if it was evident then
2 it was checked off. I think there is none, mild,
3 moderate and severe and maybe a little over a third
4 of the patients had calcification that was evident
5 on angiography.

6 DR. CRITTENDEN: I want to say I admire
7 you guys for standing the onslaught from the panel.
8 I have been a little afraid that some of these
9 stones were going to bounce over here but,
10 fortunately, they haven't.

11 I must say that I think all of the
12 questions so far have been right on point. This is
13 a little troubling and, just from my time on the
14 panel, it has been rare for me to have so much
15 agreement with what everybody else has said. I
16 have kind of felt differently at times and have
17 decided to stay silent at times and other times to
18 say a lot. But I think everybody has really been
19 on point.

20 I want to ask a question, in your initial
21 presentation for a secondary endpoint you stated
22 that the major complication rate at 30 days was
23 better for the total stent group versus the PTA
24 group, but if you are asking for a suboptimal
25 indication, which I think is perhaps your best

1 chance versus primary stenting, isn't it better to
2 use the suboptimal group versus the PTA group?
3 Again, if you do that there doesn't seem to be a
4 statistically significant difference. If you look
5 at table number 2, which is the most recent data
6 you submitted in the additional information, it
7 seems to me that for the major complication at 30
8 days the confidence interval crosses zero. So, if
9 I understand statistics correctly, that would be
10 not significant statistically.

11 DR. KUNTZ: You are right, it does cross
12 zero but we are looking at 2.9 versus 8.4, about
13 the same magnitude as in the overall study. It is
14 just that with the smaller sample size there is
15 less power to show the difference.

16 DR. CRITTENDEN: Right.

17 DR. KUNTZ: So, I think -- what was the
18 initial number?

19 DR. CRITTENDEN: It was 8.4 to 1.5 --

20 DR. KUNTZ: And, this is 8.4 versus 2.9.
21 So, the difference narrows a little and the sample
22 size goes down substantially in the stent group to
23 reduce the power to show that difference. So, you
24 are right, the statistical difference isn't there.
25 I think that probably a large part is explained by

1 the smaller sample size, and some of it is
2 explained by the increase in rate on the stent
3 side.

4 DR. CRITTENDEN: Then, to reiterate the
5 point about the ABI, we are missing a whole bunch
6 of folks in the suboptimal group. There are 22
7 patients missing. So, that would have to influence
8 the results, you would think. I am sorry, 9-month
9 follow-up in lesion minimal lumen diameter, change
10 in ABI -- both of those have missing data and I
11 understand the reasons why but, again, that was
12 touted as an advantage of the stent.

13 DR. KUNTZ: Right, in the analysis of the
14 overall groups there was a higher ascertainment in
15 the stent group than the PTA group. In the
16 suboptimal analysis actually it is a float. There
17 is higher ascertainment in the PTA group compared
18 to the overall suboptimal group.

19 One could envision that higher
20 ascertainment might actually bring in patients with
21 fewer systems to have a better ABI. They kind of
22 flip-flop both ways. There is no question that as
23 you start to reduce the number of follow-up and
24 incomplete ascertainment plays a bigger role, the
25 inferential ability of the data is reduced to some

1 degree, but this is the data we have and even with
2 those limitations there is a significant
3 difference.

4 So, you are right. I think that what we
5 can say is that the mean differences are definitely
6 there. The validity is reduced with incomplete
7 ascertainment, there is no question, but that is
8 the best data that we have at this point.

9 DR. CRITTENDEN: Finally, I am no longer a
10 vascular surgeon but I do remember that the
11 popliteal artery is different than the femoral.
12 Why did you guys decide to use the femoropopliteal
13 segment as a single segment versus segregating the
14 two? Finally, do you have a subgroup analysis of
15 the popliteal versus PTA?

16 DR. ROSENFELD: I think that even in the
17 TASC document actually the femoropopliteal -- in
18 many publications and in many analyses the two
19 vessels are combined. I think that, you know,
20 there was initially discussion about how we can
21 stratify these patients up front in this
22 randomized, controlled trial and the more you
23 stratify the more numbers of patients you need in
24 order to power the study. So, what we ended up
25 doing was lumping more than splitting. We

1 stratified based on diabetes versus non-diabetes.
2 But to stratify any further would have probably
3 doubled or tripled the number of patients that
4 would have been required to power the trial. I am
5 not a statistician.

6 The reason that we wanted to include the
7 popliteal artery in this trial, and I was a part of
8 that original femoral stenting trial using the
9 balloon expandable Palmaz stent, the one I
10 described earlier where we showed this compression
11 problem. In fact, I was the one that wrote an
12 article that described this and it probably led to
13 the termination of that trial. So, I should say up
14 front here I seem like I am coming across like a
15 major proponent of stenting and I just want to say
16 that I consider myself one of the more conservative
17 people when it comes to stenting where it is not
18 proven to be either safe or efficacious, or some
19 reason to stent over just balloon angioplasty
20 alone.

21 But the reason to include the popliteal
22 artery in this trial is that this stent has certain
23 unique properties which allow it to be placed on a
24 bend, and offer advantages over other stent
25 technologies which can't be flexed and bent to the

1 same degree. So, it is an opportunity to, again,
2 enhance a result or prevent an untoward outcome in
3 what can be a tricky vessel.

4 DR. CRITTENDEN: We don't have any long-
5 term information about popliteal stents, do we?

6 DR. ROSENFELD: Only what is in this
7 trial, and Michelle Henry's data does not extend to
8 the popliteal artery. Well, he does have data from
9 the popliteal artery but I don't think it is
10 separate out in his analyses. It is pretty well
11 acknowledged that balloon expandable stents are not
12 a good idea for the femoral artery. I think
13 everybody on the panel would probably agree with
14 that.

15 DR. CRITTENDEN: In this particular slide
16 that you have up, that is from the entire group of
17 patients who had stents or those people who were in
18 the suboptimal group?

19 DR. LABOUNTY: This is randomized
20 popliteal. So, not the roll-in but just the
21 randomized. All the patients, not the suboptimal
22 group.

23 DR. CRITTENDEN: You don't have that
24 sorted out?

25 DR. LABOUNTY: No, we don't.

1 DR. CRITTENDEN: That is all I have.

2 DR. TRACY: Dr. Najarian?

3 DR. NAJARIAN: I have a long list of
4 questions but they have all been answered as we
5 have come down the line. So, that is it.

6 DR. TRACY: Do any of the panel members
7 have additional questions?

8 DR. ROBERTS: Actually, I have one, and
9 that is that I notice that there is very, very
10 little data on the run-off on patients before the
11 procedure, in other words, what the run-off looked
12 like. I forget exactly -- I calculated it out, but
13 it is a very small percentage, much less than half
14 I think, at least in terms of the core laboratory.
15 There is very little data in terms of the run-off
16 and I can't find anywhere that anyone looked at the
17 run-off after the procedure in terms of emboli. We
18 can discuss why that might be very important, but
19 even asymptomatic -- I mean, if you don't look you
20 are not going to find, and they may have an embolus
21 that is asymptomatic and the patient doesn't
22 complain of it because it is down one of the
23 trifurcation vessels but it may impact the ABIs
24 down the line or may, in fact, impact their walking
25 and everything else that goes along with that. Can

1 you explain that for me?

2 DR. ROSENFELD: Those are great points.
3 Let me just speak to the issue of the core lab and
4 the analysis of run-off. It wasn't a requirement
5 of the trial that the run-off films be all sent in.
6 I mean, this would be an overwhelming amount of
7 angiographic material that would have to be
8 reviewed, and I am not even sure there is a
9 precedent for that in any other trial looking at
10 balloon angioplasty. In fact, to the sponsor's
11 credit, they identified the fact that there would
12 be a core lab with automated quantitative analysis
13 which, to my knowledge, actually is the first time
14 that that has been done also in a peripheral trial
15 of this kind of magnitude.

16 So, that assessment of run-off was
17 supposed to have been done at the site by the
18 investigator and reported in. It is a huge, huge
19 undertaking to look at run-off vessels in all of
20 these patients before and after and compare them,
21 especially when you are getting all these different
22 types of modalities of film from all the different
23 kind of sources. One of the other problems is that
24 if you require a complete run-off before and a
25 complete run-off after the amount of contrast you

1 are talking about could be that much greater. The
2 point was to try to make this trial doable, and I
3 am not sure that that requirement wouldn't make it
4 that much less able to be accomplished.

5 DR. ROBERTS: Well, I would agree with
6 that but I think that one of the things that is
7 really concerning is that you are really hanging
8 your hat on the clinical outcome and, yet, you
9 really don't know what the status of those
10 trifurcation vessels is and, I agree with you, it
11 is an enormous job to look at but when you are
12 looking at ABI and you are looking at people being
13 able to walk, and you don't know what their distal
14 run-off is looking like I would, quite frankly,
15 submit to you that a vascular surgeon who is going
16 to have to bail out the bail outs or bail out the
17 stents or bail out anything is going to be quite
18 unhappy, I would think, probably if they don't know
19 where they are going to have to go to, and to not
20 have gotten that information ahead of time I find,
21 quite frankly, not appropriate.

22 DR. ROSENFELD: I am saying the wrong
23 thing then because I think the point is that run-
24 off was to have been obtained at every single one
25 of these vessels --

1 DR. ROBERTS: Okay, but it is not
2 reported.

3 DR. ROSENFELD: It was to have been
4 reported by the investigator but not analyzed by
5 the core laboratory.

6 DR. ROBERTS: I see, and what about the
7 follow-up in terms of looking for emboli in these
8 vessels? What happened with that?

9 DR. ROSENFELD: Post-procedure?

10 DR. ROBERTS: Yes. Is that reported
11 anywhere? I couldn't find it.

12 DR. ROSENFELD: The embolization rate is
13 reported. The investigator was to have looked for
14 embolization and reported it if it was identified,
15 and I think there was a trivial number of cases.

16 DR. ROBERTS: That is what concerns me.
17 It may be because they are very short lesions and
18 it wasn't a problem.

19 DR. ROSENFELD: I mean, recognizable
20 embolization at a trifurcation is a relatively low
21 incidence event, and one would presume if there is
22 large embolization to the trifurcation, if it is
23 sitting at the distal trifurcation, of course, that
24 is going to lead to an untoward event which would
25 be recorded as an adverse event. But, my

1 impression was that the incidence of embolization
2 during the course of this trial is relatively
3 small. Now, we are not talking about
4 microembolization, which is almost impossible to
5 record.

6 DR. ROBERTS: No, I am not asking for
7 microembolization; I am just looking for distal
8 trifurcation -- I mean beyond the trifurcation but
9 down in the anterior tibial or down in posterior
10 tibial or down in the peroneal where you might not
11 otherwise know that you have a problem. But if you
12 have a problem with those trifurcation vessels to
13 begin with and now you have lost some more of your
14 trifurcation, what is going to happen is your ABIs
15 are now no longer perhaps going to give you the
16 information that you thought they were giving you,
17 and since we are hanging our hats so much on these
18 clinical outcomes as opposed to angiographic or
19 duplex data, that becomes more important.

20 DR. ROSENFELD: Interestingly, you don't
21 go all the way down with the duplex data. So, if
22 we had hung our hat on the duplex data we wouldn't
23 show evidence of distal embolization one way or the
24 other.

25 DR. ROBERTS: The point is not the duplex

1 data in terms of looking at embolization but, in
2 fact, the duplex data in terms of giving a better
3 way of looking at the lesion afterwards because now
4 what we are doing is we are saying we don't have
5 something quantitative --

6 DR. ROSENFELD: I understand, although
7 the fact that there is actually a significant
8 difference in the ABI between the two groups is a
9 suggestion that there certainly wasn't any more
10 distal embolization in the stent group, if that is
11 the concern. I mean, I think the issue here is
12 what is the difference between the two groups. Is
13 there more distal embolization with stenting than
14 there is with routine conventional balloon
15 angioplasty? With this stent and with this device
16 and with this trial, I don't believe the answer to
17 that is yes. I think it is no.

18 DR. ANSEL: Dr. Roberts, if you go under
19 additional information, page number 1, table 1,
20 second to the last line, distal embolization was
21 reported and looked at. I know at our center there
22 was 100 percent of that. There was zero percent
23 distal embolization in the IntraCoil group in the
24 randomized patients and there was 1.8 percent in
25 the angioplasty group. But I totally agree with

1 everything you said. It is imperative even on
2 routine procedures. We do that as a routine
3 because it is so important.

4 DR. NAJARIAN: Was it done on every
5 patient? I guess that is the question.

6 DR. ANSEL: Yes, the N is 135 on both of
7 those.

8 DR. NAJARIAN: So, the run-off was looked
9 at on all of the patients, pre and post?

10 DR. ANSEL: That was part of the protocol.

11 DR. ROSENFELD: It was part of the
12 protocol. That was a requirement of the protocol,
13 a run-off before and after. In fact, you could not
14 enroll a patient unless they had adequate run-off
15 to support the stent.

16 DR. NAJARIAN: But you just said that you
17 didn't look at run-off sometimes because of the
18 increased contrast.

19 DR. ROSENFELD: No, no. I think that
20 what I am saying is that in order to record this
21 information for a core laboratory and to get
22 adequate pictures to have a core laboratory do an
23 appropriate analysis of run-off, I think it would
24 require an exorbitant amount of contrast to achieve
25 that in every case, either that or you send a stack

1 of films like this. When I look at contrast at
2 run-off I don't necessarily flood the leg with an
3 overwhelming amount of contrast and get one picture
4 that shows the whole thing. You might give a bolus
5 of contrast and follow it down. So, then you have
6 to film at multiple locations down the leg. You
7 know, run-off is as much a dynamic thing -- it is
8 more a dynamic thing than it is a static thing. I
9 don't know if I have answered your question.

10 DR. NAJARIAN: Well, let me just ask you,
11 in your study was there a form that said, you know,
12 the number of run-off vessels visualized?

13 DR. ROSENFELD: Yes.

14 DR. NAJARIAN: Before and after?

15 DR. ROSENFELD: Yes.

16 DR. NAJARIAN: Did you look at the petal
17 arch?

18 DR. ANSEL: No, it went down to the level
19 of the ankle.

20 DR. TRACY: Dr. Wittes, do you have a
21 question?

22 DR. WITTES: Yes, I have a question again
23 about the possibility of an equal kind of return at
24 9 months. Let me read you some numbers. These
25 come off table 1 and table 2 in the additional

1 information. If you look at the ratio of lesions
2 to people in the overall group, the suboptimal
3 group and the PTA group at baseline, it is
4 basically 1.3. It is 1.3 or 1.4. On table 9 you
5 see 89 to 70, 180 to 131. Then, in table 1 you see
6 181 to 135. If, however, you look at those who
7 returned at 9 months and you look at the ratio of
8 lesions to people, you see in the PTA group that it
9 stays the same, at 1.4. In the overall group, the
10 overall stent group, it is 97 to 83, which is 1.2.
11 But if you look at the suboptimal group, which is
12 the one we are focusing on, it is 1. It is 48 to
13 46, suggesting that there is something -- I mean, I
14 would assume the fewer lesions that you have,
15 somehow the less sick you are and that somehow
16 those who came back in the suboptimal group had, on
17 average, fewer lesions than they did when they
18 started and fewer lesions than the other group.
19 Can you comment? Do you know who these were? What
20 was the mechanism for coming back?

21 DR. KUNTZ: I don't do peripheral
22 angioplasty but it seems to me that usually in a
23 patient would have a suboptimal result you might
24 not elect to do a second lesion. So, it is not
25 surprising to me that the patients who were

1 identified as the suboptimal group would be the
2 ones who would have one lesion per patient.

3 DR. WITTES: But they don't have that at
4 the beginning.

5 DR. KUNTZ: For the suboptimal?

6 DR. WITTES: For the suboptimal in the
7 beginning. No, I would have understood that. It
8 is 89 to 70 at baseline but then when they come
9 back, the group that comes back, it is 48 to 46.
10 Do you see where I am getting these numbers? If
11 you look at page 5 in the suboptimal group, up at
12 the top, there are 70 patients who have 89 lesions,
13 which is a ratio of 1.3 lesions per patient. But
14 if you go back down to the 9-month follow-up, you
15 see that there are, I think, 48 patients -- that is
16 the change of the ABI denominator unless I am
17 reading these denominators wrong -- 48 patients who
18 have 46 lesions.

19 DR. KUNTZ: Okay, there is not one to one
20 mapping. The ABIs in that group, many of them
21 didn't get an angiogram. So, it isn't the same
22 patients that had the lesion. So, what we are
23 saying is that there is a little bit of variance
24 here on follow-up, but if we have 70 patients in
25 the suboptimal group and 131 in the PTA group, in

1 that group of 70 patients 48 were available
2 clinically for measurement of ABI; 46 lesions were
3 available probably in 35 patients for angiographic
4 follow-up. So, patients that had angiography
5 weren't one to one mapped to the people who had ABI
6 measurements.

7 DR. WITTES: So, is there any way of
8 knowing how many patients these lesions correspond
9 to at follow-up?

10 DR. KUNTZ: Sure, we can do that analysis.
11 That is an interesting analysis you are doing
12 because of the indirect aspect with respect to how
13 you are relating patients to follow-up, but what
14 you are doing is you are assuming that the people
15 that came back for an ABI measurement, which is one
16 measurement per patient outcome, is the same
17 patients that you do your potential 2 to 1
18 measurements or 3 to 1 measurements of lesions to
19 patients in the angiographic follow-up group but
20 actually they are two separate cohorts. In the ven
21 diagram there is a fair amount of overlap. I don't
22 know that we have the answer for any of those
23 analyses actually on these tables alone. So, we
24 would have to go back and look at that to see what
25 the mapping was.

1 DR. WITTES: Thank you.

2 DR. ROBERTS: Could I ask another
3 question, and that is that this trial started in
4 1997 or thereabouts. Obviously, at least some of
5 these patients are out a number of years, and we
6 know from looking at the other randomized studies
7 that have been done of the SFA, and I actually have
8 papers right here on three of them, mostly from
9 Europe.

10 DR. ROSENFELD: Recent?

11 DR. ROBERTS: Yes, one published this
12 year, from Europe, from Vienna; one from the
13 Netherlands but, nonetheless, we know that there is
14 a decrement in terms of the success rate over time.
15 My understand from looking at the protocol was that
16 these patients were to be followed on a yearly
17 basis until the PMA was approved. I am wondering
18 if you have any of the data on those patients, on
19 the ones that are longer out.

20 DR. LABOUNTY: We do have data on case
21 report forms but this whole PMA submission was just
22 based upon 9-month follow-up.

23 DR. KUNTZ: That data is available on two-
24 , three- and five-year follow-up. So, that can be
25 summarized. I am not quite sure what the density

1 now of the two-year follow-up is to make meaningful
2 inference. But the second node of follow-up is the
3 two-year point which we should be getting into
4 clinically for the majority of cases overall. That
5 has not been processed yet, and it is a good point.

6 DR. DEWEESE: Do you have any data on what
7 the recurrences are of the stenosis? I want to
8 know specifically is it higher at the level of the
9 adductor? Do you have that information or not?

10 DR. KUNTZ: The vast majority of lesions
11 in the restenosis analysis was target lesion
12 revascularization. That is, it was the initial
13 lesion to begin with. So, the distribution of the
14 baseline lesions that were treated the target
15 lesions, was also distribution of the follow-up
16 lesions. I don't know if we have this analysis or
17 not but we generally do a target vessel
18 revascularization analysis where we look at
19 analysis of the entire vessel, and the difference
20 between the two are non-target lesion analysis to
21 look at the development of new lesions that weren't
22 the initial target lesions. But in eye-balling
23 this, it looks like the vast majority, like in
24 coronary trials, lesions that did come back were,
25 in fact, initial target lesions.

1 DR. DEWEESE: Well, were the original
2 target lesions more frequent at the adductor tendon
3 level?

4 DR. ROSENFELD: I don't think we have
5 that information, but it is probably retrievable
6 because the vessel was divided into four sections,
7 popliteal, distal one third of the femoral, mid one
8 third and proximal one third, and I don't think
9 that subdivision has been done. I am not sure the
10 numbers are large enough.

11 DR. DEWEESE: In studies of this lesion
12 through the past, 80 percent start at the adductor
13 tendon level. Now, how about in your former study
14 when the Palmaz stents were compressed, where were
15 they compressed?

16 DR. ROSENFELD: The adductor canal more
17 often than not. The proximal SFA had reasonable
18 results. It was the adductor canal where you saw
19 this.

20 DR. DEWEESE: So, it would be interesting
21 to find out with your new stent if this is still
22 true.

23 DR. ROSENFELD: Absolutely.

24 DR. DEWEESE: In addition, you say the
25 stent is not compressible. Is this by squeezing

sgg

1 it?

2 DR. ROSENFELD: Even if you do compress
3 it outside the body, it springs back. It opens up
4 again immediately. Within the body I think a
5 different thing happens. I think it becomes
6 incorporated as part of the vessel and becomes, you
7 know, cast like the vessel but it is not
8 compressible like a balloon expandable stent.

9 DR. DEWEESE: It would be interesting to
10 know whether you still have adductor tendon
11 compression which will initiate the lesion at that
12 level as it can experimentally.

13 DR. ROSENFELD: I can't speak from the
14 standpoint of data, but I think I can speak from
15 the standpoint of seeing these lesions. I think
16 the restenosis that occurred was not on the basis
17 of compression; it was on the basis of neointimal
18 hyperplasia within the stent. I think where they
19 did restenose, they did restenose on the basis of
20 neointimal growth.

21 DR. DEWEESE: So, we can expect in time
22 that there is going to be more and more hyperplasia
23 over the stents.

24 DR. ROSENFELD: You may want to speak to
25 that. I think the experience in other stent trials

1 has not been that case. It has been that there is
2 a time course during which the acute phase of
3 scarring and reaction occurs and the lesion is
4 pretty much stabilized. At what point do they
5 stabilize, at what point is it a new plaque that is
6 forming on top of old plaque versus neointimal
7 growth, I am not sure we know the answer to that
8 question.

9 DR. DEWEESE: How about kinking? Do you
10 see kinking if you do bend the knee when you put
11 them in the popliteal level?

12 DR. ROSENFELD: I think Gary Ansel's
13 slide is as good as any to show --

14 DR. DEWEESE: It did not show flexion.

15 DR. ROSENFELD: It does not kink. It
16 bends; it flexes.

17 DR. DEWEESE: That is kinking.

18 DR. ROSENFELD: Well, kinking to me means
19 does it actually crimp; does it create a slit-like
20 lumen? No, and that is one of the positive things
21 about this stent. We have done angiography with
22 patients flexing the knee and you maintain the
23 curvature and the circular configuration of the
24 stent.

25 DR. DEWEESE: Good. Thank you very much.

sgg

1 DR. TRACY: Any additional questions from
2 the panel members for the sponsor? If not, we will
3 take a break until two o'clock and return at that
4 point to begin our review of the FDA questions.
5 The second open public hearing will be a little bit
6 delayed. So, we will see everybody back here at
7 two o'clock.

8 [Whereupon, at 1:00 p.m., the proceedings
9 were recessed until 2:00 p.m.]

1 AFTERNOON PROCEEDINGS

2 DR. TRACY: Good afternoon. I think
3 enough of us are back so that we will resume this
4 meeting of the Circulatory Devices Panel meeting.

5 Before we move on to the FDA questions,
6 there is a point of clarification that we would
7 like to ask Mr. Dillard. In the panel packets that
8 we received there is a good deal of information
9 pertaining to a study performed in the U.K., and we
10 have been told by the sponsor that they can't
11 discuss that. We want to have some guidance as to
12 how to deal with this information that we have
13 already had an opportunity to review.

14 MR. DILLARD: Yes, I think at this point,
15 if Dr. Roberts and others would like to actually
16 question the sponsor, we do have the opportunity
17 that we could close the panel session for a period
18 of time and then reopen it. We can do that in
19 order to present some confidential information at
20 least at this point. I think what you all need to
21 do is just decide how important that is at this
22 point for your deliberation. If it is something
23 that you think is important enough, we can do that.
24 We can clear the room. We can have a short
25 discussion of the closed material and then bring

1 everybody back for the questions and the open final
2 discussion and the vote.

3 DR. TRACY: My impression is that it would
4 be difficult to make a decision about the entire
5 packet without doing that.

6 MR. DILLARD: Then, I think what we need
7 to do at this point is take about three minutes and
8 clear the room. The sponsor needs to make sure
9 that the only people that are in the room are
10 people associated with their particular company,
11 and we will make sure that the remaining are the
12 FDA staff. Then, what we will do at this point --
13 maybe I will just ask the panel, do you think it is
14 going to be an extensive discussion or a short
15 discussion?

16 DR. TRACY: I don't think it will be
17 terribly extensive but I am guessing twenty
18 minutes.

19 MR. DILLARD: Then, why don't we have
20 people assemble back here at 2:25?

21 [Whereupon, the proceedings were recessed
22 for a closed session, to be resumed in
23 open session]

1 [Whereupon, the proceedings resumed in
2 open session.]

3 DR. TRACY: Thank you, everybody. Sorry
4 for the interruption there. We are about to resume
5 the open public hearing and I am going to ask Mr.
6 Dillard to make some comments.

7 MR. DILLARD: Thank you, Dr. Tracy. A
8 couple of things that I just wanted to make some
9 points on. We went ahead and we closed the session
10 in order to clarify the situation associated with
11 the data. I believe the company is going to make a
12 statement in a minute.

13 For the record, I would just like to state
14 that during this closed session there was no
15 discussion about any of the data that might be
16 referred to from the sponsor, and that during this
17 particular meeting this data will not be considered
18 in deliberation over this PMA. So, anything that
19 the panel members might have seen cannot be used in
20 order to otherwise affect any recommendation that
21 they might have today on this particular PMA.

22 During this closed period of time there
23 was no discussion about any other data that was
24 otherwise discussed this morning, nor was there any
25 discussion about anything substantive associated

1 with this particular PMA. The time was merely
2 spent to try to clarify from people who are
3 associated and know much more than I do in terms of
4 panel deliberations and the process about how to
5 most appropriately handle this particular
6 situation. So, I guess that would be the end of my
7 statement at this point and I think the company is
8 going to make a statement also.

9 MS. BRITTLE: The company, based on
10 further input from the agency and what the rules of
11 order were at the public presentation forum has
12 decided not to discuss and basically pulls the U.K.
13 data out of the presentation.

14 DR. TRACY: Thank you, and again we
15 apologize for the interruption of the proceedings.
16 We will move on then to the FDA questions and, as
17 they are putting them up there I will just read the
18 background again.

19 The U.S. clinical trial of the IntraCoil
20 Stent System was based on primary stenting versus
21 PTA in the treatment of atherosclerotic disease of
22 the superficial femoral and/or femoropopliteal
23 artery. The sponsor has described why this primary
24 stent study could not be completed. They have also
25 described why they believe a re-analysis of the

1 data supports the use of the IntraCoil stent study
2 could not be completed. They have also described
3 why they believe a re-analysis of the data supports
4 the use of the IntraCoil stent when the PTA results
5 are suboptimal. Central to their justification is
6 the suboptimal classification of 69 patients who
7 had greater than or equal to 50 percent stenosis or
8 a greater than or equal Grade C dissection
9 following the pre-dilatation step, prior to
10 receiving the IntraCoil stent as the primary
11 treatment method.

12 Question 1a, please discuss the use of the
13 suboptimal pre-dilatation classification as a
14 surrogate for system results with PTA.

15 I will start by saying I think there is a
16 sense in the panel that the suboptimal pre-
17 dilatation classification may not be clinically
18 equivalent to a suboptimal result of PTA. I will
19 ask if anybody else in the panel has other comments
20 to make on that. No?

21 We will move on to question 1b. Please
22 discuss any expected differences in terms of
23 clinical outcomes between patients with suboptimal
24 pre-dilatation and patients with suboptimal results
25 from PTA.

1 Again, I will take a stab at this. The
2 comments from this morning seemed to indicate the
3 panel feels that these results may not be
4 equivalent, the clinical outcomes may not be
5 equivalent because of sort of the severity of
6 disease or the point at which the transition was
7 made to the stent in a clinical bail out versus in
8 this surrogate endpoint. Any other comments from
9 the panel?

10 DR. LASKEY: Some of the language does
11 need to be cleaned up I think. It is not clear
12 what pre-dilatation is. If you just go by the
13 strict grammar here, pre-dilatation is before you
14 even touch anything. So, we ought to be clear
15 about what pre-dilatation is and how that is
16 defined, although I agree with you, we will come
17 back to thinking it is not equivalent to
18 suboptimal, but what is suboptimal pre-dilatation?
19 Is that dilatation pre-stenting? We need to define
20 these terms.

21 DR. ROBERTS: Yes, my understanding is
22 that what is meant by that is that it is pre-
23 dilatation of the lesion in preparation for
24 stenting, and that was the subgroup that was pulled
25 out and looked at in terms of whether or not that

1 would be equivalent to a suboptimal PTA, which
2 would be a PTA that was designed for that part of
3 the trial.

4 DR. CRITTENDEN: So, this is more than
5 just high risk pre-dilatation morphology. You do
6 an angiogram, you look at it and say, oh, this is
7 high risk. This is not what you mean?

8 DR. ROBERTS: Yes. This, I think, was
9 defined as a PTA that was done in preparation for
10 putting in the stent and it met the criteria for
11 having a greater than 50 percent stenosis and/or a
12 grade 4 or higher dissection.

13 DR. TRACY: So, pre-dilatation meant pre-
14 placement, the dilatation that as done before the
15 stent was placed. Any other points on that?

16 [No response]

17 Then, the agreement is that --

18 DR. LASKEY: They need to change the
19 words.

20 DR. TRACY: They need to change the words
21 in the question but they are not equivalent. The
22 clinical outcomes might be different.

23 So, we will move to question 1c, which is
24 a little bit different in our paper. We have here,
25 given the IntraCoil stent data shows improvement in

1 the acute safety, and no difference in safety and
2 effectiveness at nine months, please discuss
3 whether there is adequate data for a primary stent
4 indication. If not, please discuss what additional
5 information would be necessary to support a primary
6 stent indication in the femoral and/or
7 femoropopliteal arteries.

8 I have the sense that the panel has
9 commented that there is a difference in the acute
10 safety that has been seen but that the differences
11 significantly were mitigated by the 9-month follow-
12 up period. I think that the safety data alone, in
13 my opinion, would not be adequate for a primary
14 stent indication for this device, given the other
15 data that follow, the 9-month data that follow.
16 So, my impression would be that there would
17 certainly need to be additional data, additional
18 patients included to gain a primary indication.
19 Any other comments from the panel? Any other
20 points on that particular question?

21 DR. ROBERTS: Well, I think we discussed a
22 fair amount this morning, although I think we were
23 focusing on the suboptimal pre-dilatation group and
24 this is really asking for whether or not, with the
25 study as it was originally designed, they have met

1 the safety and effectiveness. My feeling is that
2 given the paucity of data that we have, looking at
3 this in terms of the safety and efficacy between
4 the stent and the PTA group, and the fact that
5 there was no difference that we could find in terms
6 of the outcomes, they certainly haven't met the
7 criteria that they set up. Now, whether or not it
8 is safe and efficacious I think is not clear given
9 the lack of data.

10 One of the questions was whether there was
11 additional information that could be obtained, and
12 one of those things, as we talked about this
13 morning, was perhaps getting some duplex ultrasound
14 to look at these lesions. The other thing would
15 be, since we know there are a number of studies
16 that show that there is a fall-off in good outcomes
17 as you go up to about 24 months, and since many of
18 these patients have been in this study for at least
19 that period of time, perhaps some of that
20 information could be obtained to show that, in
21 fact, it does have some long-term beneficial
22 outcome. I think that would probably go a long way
23 to making people feel more comfortable with the
24 fact that there is some chance that this may, in
25 fact, benefit some patients.

1 DR. TRACY: Any additional comments from
2 the panel?

3 DR. AZIZ: I think the company mentioned
4 they do have the data for some of these long-term
5 patients but they haven't analyzed it, or at least
6 they don't have it available for us to see. Can I
7 ask them a question or not?

8 DR. TRACY: Yes.

9 DR. AZIZ: How long would it take you to
10 get that information? I don't mean to get it today
11 but would it be in the next few weeks, a month?

12 DR. LABOUNTY: About a month.

13 DR. AZIZ: That might satisfy the question
14 that you are asking, which would be very important.
15 Particularly if it is beneficial later, it would be
16 very helpful.

17 DR. DEWEESE: Might it be also better if
18 they had some increased follow-up -- ABIs? It is
19 not only additional follow-up but improved follow-
20 up.

21 DR. TRACY: I think that is fair. Then,
22 the things that we think would be useful would be
23 more complete follow-up, if that can be gained on
24 the original cohort. Data such as ABI and duplex
25 ultrasound would be very helpful. I think the

sgg

1 other problem that we are having is the way this
2 application was set up. We were asked to take
3 something and take a subset out of it. Now we are
4 being asked to put it back together again and go
5 back to the original premise of the protocol. I
6 think that just makes it a little hard for us to
7 interpret. I would encourage you to rewrite it in
8 such a way that this is the first question that is
9 asked, if that is the approach that would be taken.

10 MR. DILLARD: Let me clarify. Because the
11 sponsor did actually come in with an application
12 for the subset indication that is certainly the
13 application that we wanted to bring before you and
14 wanted to concentrate your attention on. But after
15 we thought about it a little bit also, and
16 understanding that the sponsor did really try to do
17 an appropriate study with the right kind of control
18 group and ran into similar kind of difficulties
19 that I think we have encountered in other, not only
20 cardiovascular studies, but many studies where you
21 talk about randomized, concurrently controlled
22 clinical trials where the clinical community may
23 have a change of heart during the course of the
24 clinical trial; the patient population may change;
25 all the difficulties of doing clinical trials, we

sgg

1 felt like it probably would be unfair to assemble
2 you all here and not at least pose that broad
3 question that, you know, based on the data here and
4 the likelihood that we may never be able to do a
5 complete clinical trial in order to answer these
6 questions could it be considered enough to say that
7 the data exists to where we should at least
8 contemplate the broader indication for use?

9 So, I felt like we did kind of throw that
10 in at the end, but I didn't want to lose that
11 opportunity to at least pose it to you that way,
12 and the reason we did that was because the sponsor
13 asked for the other indication first. So, just as
14 a point of clarification.

15 DR. TRACY: If there are no other comments
16 on question one, we will move on to question two,
17 and I will briefly read the intro here. The
18 current laboratory indicates the use of the
19 IntraCoil stent for the treatment of superficial
20 femoral and/or femoropopliteal artery occlusions or
21 stenotic lesions in patients with suboptimal
22 results following PTA. Stents placed in the
23 popliteal artery location are subjected to
24 significant deformations due to flexing of the
25 knee. Bench testing demonstrated adequate kink

1 resistance of the IntraCoil stent. Based on the
2 qualitative analysis of 149 lesions in the
3 randomized study and 107 lesions in the roll-in
4 patients, IntraCoil stents were placed in 48
5 popliteal arteries, of which 16 were placed in the
6 suboptimal group.

7 Question two, please discuss with the
8 clinical data are adequate to determine the safety
9 and effectiveness of the IntraCoil stent
10 introduction the popliteal artery.

11 Again, I think that my instincts are that
12 they probably have demonstrated to an equal level
13 the safety and effectiveness in the popliteal
14 versus another location, but our reservations about
15 our data would make it difficult to be more
16 definitive in answering this question.

17 DR. ROBERTS: You know, I have to say that
18 I am even more concerned about the popliteal area
19 because I think, and I am sure the vascular
20 surgeons will comment on this as well, that the
21 popliteal artery has really sort of three different
22 areas, the above knee area which is relatively
23 protected, relatively straight, not perhaps under
24 the same constraints as the popliteal artery behind
25 the knee joint and its flexing all the time, and

sgg

1 perhaps not the same as the distal popliteal which
2 is getting ready to trifurcate into the run-off
3 vessels, and given the really small number of
4 popliteal stents that were placed and the lack of
5 understanding as to where exactly these popliteal
6 stents were placed in relationship to those three
7 different parts of the popliteal artery, and even
8 if we knew, I think the numbers then would be so
9 small that I honestly don't think that we can
10 really comment on the safety and effectiveness in
11 the popliteal area, less so even than the SFA.

12 DR. TRACY: Can I ask a question? Is
13 there anything that could be done to improve the
14 data on the popliteal? I mean, it seems like that
15 might just inherently be a very difficult thing to
16 get information on. Is there something that would
17 make it more reasonable to look at these data?

18 DR. ROBERTS: I suppose it would help just
19 to break it down into the three sections of the
20 above knee popliteal, the part at the knee joint
21 and then the distal popliteal and see whether or
22 not there is anything that is different about those
23 areas. I don't know.

24 DR. CRITTENDEN: I like that idea but I
25 think it really suffers from lack of numbers. They

1 just need to get more numbers. If you segregate
2 it, they have to get even more numbers. That would
3 give you meaningful information because I think you
4 are right about segregating the areas but that is
5 going to make the N that much more difficult to
6 attain. But I think you have to do it though. I
7 think it is relevant information.

8 DR. WITTES: Can I ask a question just in
9 terms of the bench studies? Is that not
10 convincing?

11 DR. ROBERTS: Not to me, no.

12 DR. FREISCHLAG: I think you have to take
13 in the fact of the atherosclerosis of the run-off
14 vessels. The popliteal is so dangerous that if you
15 make a mistake or something happens in an
16 atherosclerotic artery it is a whole different
17 thing. So, I don't think so. Again, I think
18 follow-up -- I am not sure what you can say at nine
19 months with popliteal lesions, and if you are using
20 more than two or three stents, they may have
21 covered all three areas of the popliteal artery so
22 it may come out that they are all just the same
23 because they have more than one stent.

24 DR. TRACY: So, it sounds like in general
25 more detail and more numbers would be needed to

1 make that a yes. If there are no other comments,
2 we will move on to question three, dealing with
3 product labeling.

4 One aspect of the premarket evaluation of
5 a new product is the review of its labeling. The
6 labeling must indicate which patients are
7 appropriate for treatment, identify potential
8 adverse events with the use of the device, and
9 explain how the product should be used to maximize
10 benefits and minimize adverse effects. Please
11 address the following questions regarding the
12 product labeling, section 2.

13 3a, please comment on the indications for
14 use section as to whether it identifies the
15 appropriate patient population for treatment with
16 this device.

17 The indications for use deal with the
18 suboptimal result group, and essentially are
19 superficial femoral or popliteal artery occlusions
20 less than 12 cm or stenotic lesions less than 15
21 cm, and a suboptimal PTA is defined as a
22 technically successful dilatation but suboptimal
23 optimal because of greater than 50 percent stenosis
24 or grade C or greater dissection.

25 This is going to be hard to answer but the

1 indication as is stated here would be appropriate
2 for the application that was filed. Since we have
3 questions about the results, I think we can't say
4 that this would be the only appropriate indication
5 and that would have to be evaluated if there was
6 additional information that came forth. Any other
7 comments?

8 DR. LASKEY: I know this is semantics, but
9 it is important nevertheless, can you consider
10 anything with a residual of greater than 50
11 technically successful? The way it reads they are
12 mutually exclusive. Technically successful can
13 include a residual of greater than 50. Does it
14 just mean that the vessel is open? How are you
15 defining technically successful dilatation?

16 DR. LABOUNTY: Technically successful
17 dilatation would be just one where you are able to
18 get the balloon there and perform the dilatation
19 without any perforation or thrombus at the site.

20 DR. LASKEY: In other words, you can have
21 a technically successful irrespective of the,
22 quote, residual stenosis. I personally think you
23 need to clean that up. It will make it less
24 confusing.

25 DR. LABOUNTY: That, again, is fairly

1 similar to what is in the iliac artery stents right
2 now.

3 DR. LASKEY: I guess that just betrays my
4 ignorance of the iliac but, again, it makes it grey
5 as to when you can use this thing.

6 DR. TRACY: Question 3b, please comment on
7 the contraindications section as to whether there
8 are contraindications under which the device should
9 not be used because the risk of use clearly
10 outweighs any possible benefit.

11 I think we can't answer that until we have
12 additional information regarding results.

13 DR. ROBERTS: I am sorry, I must be a
14 little slow after lunch. Just in terms of the
15 indications for use, one of the things in the
16 indications for use is that it suggests that it be
17 in occlusions less than or equal to 12 cm or
18 stenotic lesions less than or equal to 15 cm. I am
19 not really clear from the data that we have any
20 understanding of that because the way that I saw
21 the data is that it was broken down into lesions
22 that were greater than 7 cm. I mean, should we
23 have it 7 cm instead of 12 cm or 15 cm? I am not
24 quite sure where that number came from since, as
25 far as I can tell, it is not supported in the

1 information that came back.

2 DR. LABOUNTY: That was really in the
3 study design and those were the type of lesions
4 that were to be included in the study.

5 DR. ROBERTS: But is it fair to say that
6 in the data that you present in the panel pack you
7 only talk about lesions that are, you know, like
8 greater than 7? I mean, I don't know whether it is
9 7, 10 or 15.

10 DR. ROSENFELD: Actually, the original
11 trial, as it was written, was to have stratified
12 people based on these different lengths. So, when
13 it was clear that statistically it wouldn't work we
14 said, well okay, we will just lump them all. Yes,
15 in the data set that we discussed this morning we
16 pointed out that the vast majority, 60-odd percent,
17 were in this relatively simple category but the
18 other 40 percent had more complex or long lesions
19 or occlusions. So, we didn't really stratify them
20 out because the study wasn't powered to do that.

21 I just want to make a comment. I think it
22 would be, again, probably a disservice -- if it is
23 going to be approved for a suboptimal indication,
24 it would be awful to approve it for a suboptimal
25 result after dilating a 5 cm stenosis and not be

1 able to put it in a 10 cm one that might really
2 need it.

3 DR. ROBERTS: Yes, I am not saying that.
4 It is just that when I look at this the only group
5 that you talk about that is greater than 7, I don't
6 know if there is --

7 DR. ROSENFELD: Is that true?

8 DR. ROBERTS: I believe so. That is why I
9 went through here when I looked for the breakdown.
10 That is the last bottom one, greater than 7.

11 DR. ROSENFELD: Yes, I guess so. I am
12 even confused by all the data, but under the
13 additional information --

14 DR. ROBERTS: For example, on table 10 in
15 the CDAC analysis it says lesion length, and the
16 longest is lesion length greater than 7 cm, but it
17 doesn't really give you a flavor as to where there
18 any that were 15? Were there any that were 12?
19 That might be something to think about.

20 DR. LABOUNTY: Yes, we can break that
21 down.

22 DR. ROSENFELD: Absolutely, great
23 question.

24 DR. TRACY: Question 3c, please comment on
25 the warnings/precautions section as to whether it

1 identifies all potential hazards regarding use of
2 this device.

3 The warnings essentially state that the
4 stent is intended for use by physicians who have
5 received appropriate training in interventional
6 techniques and placement of intravascular stents in
7 patients in whom antiplatelet and/or
8 anticoagulation therapy is contraindicated would be
9 treated with caution.

10 The precautions are the stent system is
11 provided sterile for one use only. Carefully
12 inspect the package. Stent placement precaution,
13 if resistance is encountered do not force.
14 Resistance may cause damage to the stent or vessel.
15 System not intended for repositioning or
16 recapturing. Caution to be used when crossing a
17 deployed stent with any adjunct device.

18 Those are the warnings and precautions
19 that are in the labeling. I noted that somewhere
20 later under specific patient populations in which
21 this has not been shown to be safe and effective
22 are patients allergic to nickel, which I found to
23 be sort of a fascinating idea. I didn't know what
24 would happen to those patients, but I don't know if
25 that is something that should be put as a warning

1 or a precaution rather than saying that it wasn't
2 tested there. Then, I don't know exactly how
3 somebody would figure out necessarily everybody who
4 was allergic to nickel. So, I think that is just a
5 clinical indication. That was the only specific
6 comment I had.

7 DR. ROBERTS: Just a couple of things to
8 at least think about, that is that I saw, in
9 looking through the descriptions of the procedure,
10 that there were a number of patients in which there
11 was apparently stent movement, or they described it
12 as a jumping forward of the stent which required
13 other stents to be placed. I don't know whether
14 that is something that could be put in the warnings
15 that, you know, one needs to be careful of that.

16 There was also at least one case where the
17 stent was undersized and so it migrated, and that
18 required other stents to be placed. So, it might
19 be necessary to make sure that that information in
20 terms of a proper sizing and if there is anything
21 that can be done in terms of teaching people how to
22 put it in so that you don't end up putting in two
23 stents where one would have been enough.

24 DR. TRACY: Any other comments?

25 [No response]

1 Then, question 3d may actually be the
2 place to put these specific comments. Please
3 comment on the operator's instructions as to
4 whether it adequately describes how the device
5 should be used to maximize benefits and minimize
6 adverse events. That may be an appropriate place
7 to include that information. Any other comments on
8 3d?

9 DR. ROBERTS: There were some problems
10 that were described with stent deployment, breakage
11 of the wire. I guess that may not be a problem but
12 at least if there is any possibility of that, there
13 maybe should be something in terms of how to
14 resolve that problem.

15 There was at least one case where the
16 device was, quote, broken due to a bend in the
17 puncture site. So, maybe it is important also to
18 reemphasize the point that if you have a sharp bend
19 it may cause it to malfunction and not deploy
20 appropriately.

21 There was indication that there were 24
22 cases of delivery system release difficulty. Now,
23 I don't know exactly what was meant by that, but if
24 there are specific problems that can be identified
25 and that there can be either recommendations on how

1 to avoid that problem, or at least on how to
2 resolve that problem if it should occur, I think
3 that ought to be in the operating instructions.

4 DR. LASKEY: I have one question about the
5 nitinol. With these self-expanding properties, is
6 there a possibility of continued expansion over
7 time? The sub-question there is, is there a
8 possibility of aneurism formation with these over
9 the long term?

10 DR. DESAULNIERS: Dan Desaulniers,
11 employee of Sulzer IntraTherapeutics. The question
12 concerning will the stent continue to expand, no,
13 the stent will go to the diameter which it was
14 formed at.

15 DR. TRACY: Any other questions or
16 comments on 3d? No? Question 3e, do you have any
17 other recommendations regarding the labeling of
18 this device? I do not have any additional comments
19 here. Anybody else?

20 [No response]

21 Question 4, training program, please
22 identify and discuss the items that you believe
23 should be contained in a physician's training
24 program for this device.

25 Very simply, I think basically we should

1 follow the same types of recommendations that we
2 might make with any other similar device, that
3 there should be adequate training to ensure the
4 knowledge and technical skills of the operator
5 before they are approved for solo deployment of
6 this device. It is already indicated in here that
7 this should be reserved to somebody who is trained
8 in these types of interventional techniques in the
9 first place.

10 DR. DEWEESE: I think it important that we
11 find out what they would intend to do and what they
12 do, and that we know what it is, and that they be
13 required to send information regarding that when it
14 is sold to people.

15 DR. TRACY: I think that would be fair, to
16 ask for some type of protocol that would be
17 followed. Something on the order of sponsoring
18 training for operators would be appropriate, and
19 then some type of certification that the person has
20 shown competency or has completed successfully the
21 training that is in place for this device.

22 MR. DILLARD: Could I ask for one
23 clarification on that? That is a slippery slope,
24 of course, in terms of certification. So, I just
25 want to make sure that I am clear about what that

1 recommendation might be. Are you saying basically
2 that the company needs to ensure that the
3 physicians have had the training, or are you
4 advocating a broader certification by a
5 professional society or an overseeing body?

6 DR. TRACY: I think that all the company
7 can be held responsible for is certifying that the
8 physician has taken the course.

9 DR. DEWEESE: Yes, I think the first part
10 is important, that whoever is using it has been
11 approved by either the cardiology society or
12 vascular society radiology societies. I don't
13 think they all have to be the same requirements for
14 catheter training. If they can all three work
15 together and come up with that, it would be good
16 but, if not, I think that they be certified by some
17 appropriate group and that they be followed; that
18 they have not only sessions where they teach them
19 variations of this activity but also that they are
20 responsible for watching them do a few of them once
21 they get out there if they haven't had experience
22 before.

23 MR. DILLARD: Let me just try to clarify.
24 It is very common for us to work with a sponsor to
25 make sure they develop the right kind of training

1 program, which I think is really what this
2 particular question is focused on. Just to make
3 sure the panel understands, the FDA generally does
4 not enforce and/or make the company work with a
5 professional society in order for the professional
6 society to certify that somebody can use the
7 device. I think we will leave that up to the
8 professional societies.

9 DR. DEWEESE: No, I was just saying that
10 someone should have catheter skills before they use
11 it, and that is self-understood. That is the
12 important part. The more important part is that
13 they be responsible for the people doing it
14 correctly or they are going to get the bad name,
15 not us.

16 DR. TRACY: Dr. Crittenden?

17 DR. CRITTENDEN: I may have a little bit
18 of postprandial stupor as well, but I just wonder,
19 and maybe this is irrelevant, but is there anything
20 in the specifications here that would keep someone
21 from doing a carotid coronary, iliac and a femoral
22 all at the same sitting? Is that something that we
23 feel comfortable with, or is this out of what we
24 have been asked and what we can put in the
25 instructions?

1 DR. ROBERTS: I think that is probably out
2 of our purview in terms of indicating what medical
3 practice would be. Certainly, one would hope that
4 wouldn't happen but I think the most important
5 thing in terms of training is to make sure that
6 there be some kind of a training program developed.
7 Like I say, there are indications in the submission
8 that there are certain things that can happen in
9 deploying these stents where they move; they are
10 not quite where you expect them to be; they
11 migrate. I think it would be very important for
12 the company to try in working with the
13 investigators, as best as possible, to identify
14 what are the sources of those problems and to
15 structure a training program that would address
16 what those issues are. I am sure that the
17 investigators have a lot of experience and are
18 aware where those problems occur and how to best
19 teach people to avoid them.

20 DR. LASKEY: There are two levels to the
21 training though. The first level, the conservative
22 level, is just the technical manipulative skills
23 themselves in the placement of the instrument in
24 all-comers. But the indications for use are
25 limited to those in whom there is a suboptimal or

1 threatened closure. So, it may well be that during
2 the process of the acquisition of the manipulative
3 component the user is not subject to such a
4 complication and then he has to figure this out
5 after the sponsor has gone. So, this gets very
6 difficult when the indication is a very limited
7 indication in what otherwise would be a fairly
8 straightforward training program, which is just how
9 to pull what and when and where, and how to be sure
10 it is placed. So, do we have any help for them in
11 terms of guiding them, or doesn't it matter at all?

12 Really, the use is limited to a very,
13 hopefully, small subset but, as I expressed this
14 morning, it may well be the vast majority of all
15 interventions, which is my fear. But if the use is
16 limited to the small subset of technically
17 suboptimal results, then how do you train people
18 for that?

19 DR. TRACY: I think that is obviously a
20 difficult question but I think however the training
21 program is organized, it has to be organized around
22 the results that would allow this device to be
23 approved. It will have to simply state clearly
24 what the indications for approval would be at the
25 point of approval, and then use that as the basis

1 of the training program. No more can we regulate
2 the clinical competence through professional
3 societies, nor can we regulate clinical judgment,
4 but certainly indicating how the thing was
5 evaluated and approved would be an appropriate part
6 of the education process for physicians using the
7 device.

8 That is the last question. I would like
9 to ask the sponsor if they have any additional
10 comments or questions to make at this time. No?
11 Any additional comments or questions from the FDA?

12 MR. DILLARD: No, not at this time.

13 MS. MOYNAHAN: I guess we are getting
14 ready for the vote. I am going to read the voting
15 options that you have available today. The PMA
16 must stand on its own merits and your
17 recommendation must be supported by safety and
18 effectiveness data in the application or by
19 applicable publicly available information.

20 Safety is defined in the Act as reasonable
21 assurance, based on valid scientific evidence that
22 the probable benefits to health under conditions of
23 intended use outweigh any probable risks.

24 Effectiveness is defined as reasonable
25 assurance that in a significant portion of the

1 population the use of the device for its intended
2 use and conditions of use, when labeled, will
3 provide clinically significant results.

4 Your recommendation options for the vote
5 are as follows: One, approval if there are no
6 conditions attached.

7 Two, approvable with conditions. The
8 panel may recommend that the PMA be found
9 approvable subject to specified conditions, such as
10 physician or patient education, labeling changes or
11 further analysis of existing data. Prior to voting
12 all of the conditions should be discussed by the
13 panel.

14 Three, not approvable. The panel may
15 recommend that the PMA is not approvable if the
16 data do not provide a reasonable assurance that the
17 device is safe, or if a reasonable assurance has
18 not been given that the device is effective under
19 the conditions of use prescribed, recommended or
20 suggested in the proposed labeling.

21 Following the voting, the chair will ask
22 each panel member to present a brief statement
23 outlining the reasons for their vote.

24 DR. TRACY: At this point, I would like to
25 ask for a motion regarding this application. Just

1 to reiterate again, if the motion were to approve
2 with conditions, then we will discuss separately
3 each of the conditions before we will take the
4 final vote.

5 Dr. Roberts, since you were the lead
6 reviewer I will give you the option of being the
7 one who puts forth the motion, if you so choose.

8 DR. ROBERTS: I have a really tough time
9 with this submission, and that is that I know and I
10 am delighted that some of my cardiology colleagues
11 have found out how difficult these trials are to
12 do. They are really, really tough. So, knowing
13 how tough they are and knowing that we need devices
14 out there, I always tend to be more inclined to
15 give the benefit of the doubt but I honestly just
16 can't in this case.

17 So, I am going to recommend that we not
18 approve this. I think that there are some things
19 that the sponsor could do to improve their data,
20 and I think with some of that information it might
21 be approvable. But my own personal feeling is that
22 there is not the data to indicate that this is
23 really effective in terms of the small number of
24 study that there is, in terms of the small number
25 of patients. We were constantly going back and

1 forth in terms of whether or not the small number
2 of patients is that something bad, bad or something
3 good, good and I think we just don't have the data
4 to indicate that.

5 DR. CRITTENDEN: Second.

6 DR. TRACY: The motion which has been put
7 forth and seconded is that this device is not
8 approvable in with current application. I will
9 ask first for us to just vote by hand, and then I
10 will ask each individual to state their reason for
11 voting. So, all of those who agree that this is
12 not approvable, please raise your hand.

13 [Show of hands]

14 MS. MOYNAHAN: That is nine voting not
15 approvable.

16 DR. TRACY: So, that is unanimous. I will
17 ask each panel member to indicate what their vote
18 was and why they voted in that fashion, starting
19 with Dr. Najarian.

20 DR. NAJARIAN: As a clinician who deals
21 with this problem every day, I share the
22 investigators' wish to have a device available.
23 Suboptimal PTA in the SFA is a real problem.
24 However, I think the onus is on this committee
25 because this would be the first approved device for

1 the SFA, that the data be more -- I don't doubt the
2 data that you have but I think perhaps a design of
3 a different study that would look at this problem
4 prospectively and answer many of the questions that
5 we brought up today. So, again, I wish we could
6 approve it personally because I would love to use
7 this stent for that indication but I vote not to
8 approve.

9 DR. TRACY: You have done it but I will
10 ask all the panel members to just indicate how the
11 application could receive a favorable vote if it
12 were resubmitted, how to make it approvable.

13 DR. CRITTENDEN: I also voted to
14 disapprove the PMA, and I did it because the
15 strength of their application was based on a
16 retrospective analysis of data, with poor follow-
17 up, small numbers, and I think the numbers of the
18 popliteal cohort were terribly small. So, I could
19 not vote for it in good conscience.

20 I think a reanalysis of the data and
21 longer follow-up, and perhaps a segregation or
22 looking at the popliteal vessels in a little more
23 complex way may enhance the application.

24 DR. AZIZ: I would second that. I think
25 that probably within a month's time, as the company

1 indicated, if they could give us some longer term
2 follow-up -- personally, I think it is an excellent
3 device but I would just like to see the data better
4 presented.

5 DR. WITTES: I also found the data on
6 efficacy not convincing, and I also was concerned
7 about the retrospective nature of the analysis.
8 Most important to me was the lack of follow-up and
9 the small sample size, but mostly the lack of
10 follow-up. I do want to applaud you for running a
11 randomized trial. I recognize how hard it is, and
12 I wish the follow-up had been better.

13 DR. SIMMONS: I guess in spite of my
14 comments I was impressed by the passion of the
15 people who put these devices in. I don't do this.
16 But the data just doesn't substantiate either
17 safety or efficacy as far as I could tell. It is
18 unfortunate in that it seems like the study was
19 designed to address one particular group of
20 patients and, unfortunately, a second group of
21 patients was studied. I am not at all convinced
22 that this data will ever substantiate, the way it
23 is designed, an indication. I suspect that really
24 to get this approved you are going to have to look
25 at those patients that really need the device,