Intracranial Interventions

Moderator: *Jim Zidar*
Panel Members: *Max Amor, John Anderson, Doug Cavaye, Michael Lawrence-Brown*

John Anderson: In the U.S. and in Australia, stroke is the third leading cause of death and the leading cause of disability. Yet despite this, there is an air of therapeutic nihilism about stroke. Patients who present to the emergency room with a stroke are often considered beyond help. Unfortunately, Nick is correct: Where neurologists are with stroke today is essentially where cardiologists were with acute coronary syndromes in 1980, and treatment is not progressing very quickly. General physicians today seem unaware of the fact that things can be done for stroke patients. Unfortunately in the case of stroke, unlike in cardiology, the window of opportunity is considerably smaller for intervention. Several stroke trials have been conducted using systemic fibrinolysis. One such trial conducted in Australia used streptokinase. The neurologists involved in the Australian trial were advised that streptokinase probably would not work and that it may cause more harm than good by precipitating intracranial hemorrhage. Systemic fibrinolysis does not work in the brain; it must be catheter-directed and often must be done all at the one time, requiring someone to actually stand by the patient with a small microcatheter to dissolve the clot by hand infusion or to pulse a thrombolytic agent directly into the lesion. Fortunately, some good quality catheters are available for this application from Target Therapeutics, and more recently from Cordis. However, the peripheral story does not end with occlusion, it includes hemorrhage as well. When basilar angioplasty is performed, particularly by an aggressive operator, perforators can actually be sheared off. In these cases, because the patients are anticoagulated, fatal subarachnoid hemorrhage frequently occurs. My personal experience is limited to the posterior circulation. It may be surprising, but the patients referred to me — a vascular surgeon — usually come from neurologists as opposed to radiologists, because the former are not very aggressive in stroke treatment.

I have avoided the use of stents in the intracranial circulation because the arteries are very difficult to get up into and trackability is a problem. When I perform a diagnostic study using the groin approach I sometimes change to the brachial approach in order to get up into the vertical and basilar arteries. It's often a matter of looking at the angles and choosing the best approach. Since I work in a cardiac catheterization lab, I tend to use cardiac balloons, all of which are Monorail — we don't use any coaxial cardiac balloons. These balloons have proven fairly effective, especially when combined with an appropriate guiding catheter. Maneuvering these devices, however, is difficult; sometimes you push a little more than necessary and the balloons tend to fly forward and jump around. This procedure is time-consuming and needs to be performed when the patient presents, but the results can be rewarding. Unlike cardiologists, we often don't have the same degree of evidence-based medicine to work with because we deal with a very fragmented group of physicians: neurologists, general physicians, emergency room physicians, radiologists, and others. Most interventional neuroradiology is probably still handled by radiologists in my country where very few, if any, facilities offer acute stroke services. I congratulate Nick for establishing such a service in Buffalo.

Nick Hopkins: I believe we have a terrific opportunity to make a dent in stroke treatment, but neurology cannot do this without cardiology's help. For one thing, cardiology has the manpower. I don't see how we can train enough neurosurgeons and neuroradiologists to make significant progress in the treatment of stroke. Many cardiologists have asked me to teach them how to perform neuro interventional procedures and current technology makes it fairly easy to do this. I think there is an opportunity for cardiology to expand its horizons — but I will probably be shot for saying it!

Gary Roubin: I had the opportunity to speak at the American Heart Association Stroke Conference two weeks ago in San Antonio where it was very clear that the neurology community is accepting of interventional cardiologists participating in the acute stroke interventional programs throughout the country. In fact, nearly all interventional cardiology meetings where a peripheral vascular component is included offer a segment on intracranial intervention, both acute and elective. I am encouraging the American College of Cardiology to accept a role in this field. We are now seeing a move toward cardiologists treating carotid bifurcations and some intracranial anatomy cases. Interventional cardiologists need to get on board if we are to meet the challenge of treating the 750,000 stroke cases we see each year. At our institution, the interventional cardiologists will be handling some of the stroke cases under the guidance of Jiri Vitek, an experienced and talented neuroradiologist who is with us here today. Other centers may want to have the neurosurgeon offering guidance to the cardiologists. I think this cooperative method between the disciplines is the best way to proceed.

Nick Hopkins: Neuroradiologists are very concentrated in major urban centers, whereas cardiologists can be found everywhere. I also agree that it's crucial for cardiology to get involved. Every year we have a neuro-interventional complications conference attended by many neuro-interventionists from across the country. At this conference three years ago, I asked the question using the polling system: Should we train interventional cardiologists to perform these procedures? One-hundred percent of these physicians responded No! (laughter) The following year, however, two responded affirmatively, and last year, 15–20% were in favor, which is a significant shift in opinion.

Paul La Violette: From industry's perspective, stroke is an enormously important issue and a potentially huge market. Boston Scientific has the largest interventional neuroradiology business in the industry and does a significant amount of cardiology and interventional radiology business as well. I can say for certain that we will never make inroads into stroke intervention with the existing pool of interventional neuroradiologists. Boston Scientific is funding neurosurgery and interventional fellowships, but there are only one to eight fellows a year on average. As was mentioned earlier, the disparity between interventional cardiology programs and interventional neurology programs is 100 to 1. There really are no technology barriers, only technology needs, and we will meet those needs. The overlap between the interventional fields will undoubtedly create

These discussions took place in February 2002 during the 8th biennial meeting of the International Andreas Gruentzig Society.

those technologies, with neurology actually lending some technologies to the cardiology field. However, it makes no economic sense to invest in those technologies if only a handful of centers can ultimately utilize them. All of the $40 billion spent annually in the U.S. on stroke management goes toward patients who have already had a stroke. This is a total waste of money. We have a massive global budgeting problem, and I think stroke is probably one of the best examples of how not to spend money. We wait until it's too late, and then throw a bunch of money at the problem.

Nick Hopkins: I don't think you should underestimate the importance of your fellowship program because it's not so much that you are training neurosurgeons how to technically perform the work; what you are doing, rather, is planting a valuable "seed" in a major center with a major department of neurosurgery. Neurosurgeons and neuroradiologists, who have traditionally had a very negative or almost nihilistic approach to stroke, are suddenly beginning to see the light and are excited about it. Thus, one "enlightened" neurosurgeon in a department can have an enormous impact on the way the others in the department look at stroke. We are very grateful for your fellowship programs.

Jim Zidar: Over the past fifteen years at Duke we have developed a team approach to stroke management. Duke has three or four vascular surgeons who did all the carotid endarterectomy work but who were not very interested in the endovascular side of things. We began to make some progress when the interventional cardiology department teamed up with the interventional radiologists. Two of these interventional radiologists in particular have been involved; one has some previous neurology training, and the other is a neuroradiologist. Duke's program is similar to that of Lenox Hill with Jiri Vitek where a group of people from different specialties work toward one goal. The key to Duke's success involved situating a cardiology-based peripheral room exactly opposite the radiology suite, in the radiology department, so that we share a control room. Staff members from both disciplines talk to one another every day. When, for example, the radiology staff asked about new wires, we were able to say, "We have this new Whisper wire and the Choice PT — give them a try." We share ideas and new information on balloons, stents, and so forth. There seems to be considerable difficulty with tortuosity in the brain that requires even more challenging balloon/wire and stent/wire combinations. Duke's interventional radiologist, Tony Smith, will sometimes hear about a new device that the interventional cardiology department is using experimentally. He will then call the company to find out what he can do with the device up in the head and whether he can get a registry started. I think stroke treatment requires a group effort involving multiple specialties because each discipline has something valuable to offer. At Duke, Mike Alexander, a neurosurgeon with endovascular training, has made the biggest impact. Mike is a young, aggressive physician who came to Duke as the only neurosurgeon with radiology privileges. He performs carotid endarterectomies — which had always been vascular surgery's territory — as well as carotid stenting and intracranial work. Duke also now holds weekly conferences where we discuss complications with representatives from all of the different specialties. As a result, we will hopefully do well in CREST, ARCHER, and other trials.

Nick Hopkins: I agree that it is crucial to bring the different specialties together in order to broaden our perspective. In each institution, local politics will play a role, and every institution plays by different rules. Some institutions, for example, have radiology departments that don't want to cooperate. The bottom line is that if the different specialties will work cooperatively with one another and offer privileges, then we can begin to actually make some progress and the movement will snowball, as it has at Duke.

Max Amor: I have no magic bullet, but I think that politics are an extremely important component of this issue. In France in the past ten years, I have not seen any changes in the approach to treating stroke. There are still efforts to make advances in some centers, but I have realized that it is very difficult to convince neurologists to enter into that domain. It has also been difficult to convince neuroradiologists to involve cardiologists in stroke treatment. I would say that the situation has been quite stagnant in my country over the past four to five years. From my experience with carotid angioplasty and carotid stenting, I think it is extremely important to organize collaborative, multi-disciplinary studies on an international, European, and national basis. These types of studies show local practitioners how to treat stroke. Perhaps the IAGS could have a role in defining a multidisciplinary territory to convince local practitioners to work as a team. If we don't do this, we will continue holding meeting after meeting while the stroke situation remains unchanged. Likewise, industry will have no incentive to invest money in stroke research.

Gary Roubin: I called Richard Stack twelve years ago to ask how I could get our people organized at UAB to improve stroke treatment. Following Richard's advice, I got interventional radiology and neuroradiology involved. It is important for the group here to understand that it was actually at the IAGS meeting ten years ago, attended by Bob Ferguson and a few other interventional radiologists, where we had discussions like this one today regarding carotid stenting. That meeting ten years ago gave us the confidence to join with Jiri Vitek and get carotid stenting started. There has been a major change over the last decade in the way that carotid disease is treated, and it started with this group. This change is something we should be able to replicate in other areas as well. I would be interested to know what Fayaz Shawl, Howard Cohen, and perhaps some of our South American colleagues think about this.

Some of the practical issues we need to address involve finding ways to share information and ideas, overcoming some of the interdisciplinary barriers that we face, and getting major players such as Cordis, Boston Scientific, and Guidant more involved in bringing different disciplines together. For a number of years thought leaders such as yourself, Nick, have acknowledged that there will be no progress in stroke intervention without the help of interventional cardiology. The national bodies of neurology have just recently acknowledged that interventional cardiologists are far ahead in acute myocardial infarction intervention and now have many experienced operators available to help in acute stroke intervention. And yet, we are still struggling. We should perhaps turn this discussion over to those of you who come from some of the largest centers in the country — many of them very influential academic centers such as Mayo Clinic, Montreal Heart Institute, and Duke, which has the largest interventional laboratory in the country. As a society, the IAGS doesn't quite have the "muscle," but with companies like Cordis, Guidant, and Boston Scientific behind us, we can get organized.

Tom Linnemeier: Medical technology seems to be outpacing the medical subspecialties. There is nothing you showed us, Nick, that can't be fixed with the devices currently available from the major catheter companies. This is a good place to start, but I think that industry is hoping that medicine will move things forward. You can give example after example of failure for every successful Lenox Hill or Duke. One such example would be at my own institution, St. Vincent Hospital, where we thought we would solve the interventional radiology problem by hiring Don Schwarten. Within a two-week time period, the vascular surgeons hired their own interventional radiologist and Dan sat around for a long time with nothing to do. This is a very complex subject with complex dynamics. It

requires someone like Nick Hopkins to stand up and say that interventional cardiology and neurology ought to work together. I am glad to hear that the American Heart Association is encouraging interventional cardiologists to get involved with stroke intervention. Some of our own societies such as the AMA, the ACC, and the AHA have some relatively conservative views on how this ought to be handled. There certainly are some influential people in this room today — so let's work through the professional societies to help move this technology forward.

Nick Hopkins: One of the biggest problems is that we fail sometimes and we will continue to experience failures in some of our cases, with devastating outcomes. The neurology community is tightly focused on clinical research and outcomes, as well they should be. However, a very powerful force against the new technology crops up when a disaster occurs. We experienced a huge battle at our institution following a failed procedure that resulted in committee hearings. It was just awful. Neurology basically said, "You had a hemorrhage here; the patient died." I told the committee that the patient had an NIH stroke scale of 23 when we started, which is worse than death by almost anyone's definition. Yes, the patient died. He died because he had a hemorrhage. But frankly, if it were my stroke, I would hope you would intervene on me — I'll take my chances, thank you. Progress will come only when we train more neurologists who will then go back to their institutions and preach the gospel to their colleagues. As Gary Roubin said, the neurology meeting represented an enormous breakthrough this year because there was finally a recognition that they need the help of cardiology. Neurology still represents a major hurdle, however. They will hold our feet to the fire, as they should, but we must bring them along.

Tom Linnemeier: Generally speaking, one doesn't become a neurologist because one enjoys performing acute interventions. I've watched Gary Roubin get shot down so many times over the past fifteen years for performing carotid angioplasty, I don't know how he's still standing! The amount of grief Gary has taken is unbelievable. It takes people like Gary, Andreas Gruentzig, Richard Myler, and Eberhard Zeitler, to stand up and say: "Yes, we will have complications, but we need to move this technology forward." It takes courage, charisma, and perseverance. I guarantee you that Andreas Gruentzig did not back off when a patient died or when a patient had a complication. We simply wouldn't be gathered here today if not for the courage of these men.

Doug Cavaye: I am a vascular surgeon. My intervention work ends in the carotid artery. I have jotted down some comments which all happen to start with the letter "p." The first "p" represents the concept of a neurological penumbra — an area of ischemic or dying brain cells that are electrically negative and that may or may not be able to be rescued. Thus, the concept of a penumbra implies that time is very important. If a patient has a deficit that lasts for 60 minutes, my understanding of the literature is that he has about a one in four chance of rescue. If the deficit is present at two hours, the patient has a less than 10% chance of the event being a transient ischemic attack. In other words, a stroke is established in more than 90% of patients at two hours post-event. Thus, getting a patient to the hospital — which is the second "p" for protocol — is just as important as the penumbra. The third "p" is for perforators, which are deadly little arteries. You can't blow up a balloon 2 cm long in intracerebral vessels without getting a perforator, and it is difficult to predict the occlusion's locality. A perforator occlusion is dramatic and disastrous. The final "p" — for pharmacology — is something we have not yet discussed. Many of the cardiological improvements, or rescues of cardiac interventions, have relied on pharmacology — whether these are anticoagulants, lytic agents, or anti-spasmodics. What is the current situation with intracerebral or neurological pharmacologic rescue? From what I understand, very few agents are effective.

Nick Hopkins: You talked about the window of time, the first "p." In certain circumstances a stroke is indeed likely to be established within two hours. But everything depends on the substrate. For patients with no underlying collateral, there may not be very much penumbra. That's actually one of the big "bugaboos": we have difficulty determining which patients will do well and which ones will not. If you see a big infarct on the CT scan, you know the patient is cooked; there's nothing you can do. But if you don't see a big infarct on the CT scan, you don't really know the status of the penumbra. There is no test available yet to quickly assess a patient's condition. We have all seen patients — particularly cases involving the vertebral-basilar system — who were as long as 12, 14, even 24 hours out, were locked in neuroradiology, and who then made dramatic recoveries when their vessel was opened up. As for the pharmacological aspect, we are trying to inch our way along at our center with small numbers of patients. We've been reporting groups of 15 to 20 patients, with 15 patients in thrombolysis alone. There was a high rate of hemorrhage and a relatively low rate of reperfusion in these patients. If we used thrombolysis plus mechanical disruption of the clot, 85–90% were reperfused, but there was still a significant incidence of hemorrhage. Now with a much lower dose of thrombolytics and the addition of abciximab, we are achieving much better reperfusion and many fewer strokes. We still experience a good number of failures, however. We are now looking toward opening the window of time with techniques such as cooling, which a lot of previous work has shown to be the best brain protectant available. Thus, we are inching along with the same pharmacologic agents that are being used in cardiology, but it's a slow process and it's difficult to get patients into the centers. Neurology does control most of the strokes and we must keep working to convince them that we should be entering these patients in the experimental trials.

Chris Cates: I want to revert back to what we were discussing earlier. I have done carotid work since 1994 after training under Gary Roubin. I am constantly amazed at the visceral response that carotid stenting by cardiologists evokes in colleagues who are on the multi-disciplinary team. It seems that at the early, vestigial phase, there is a lot of camaraderie. However, as soon as success and notoriety come along, a visceral reaction — subtle nastiness —takes over. The quality assurance process is used in every way possible to stifle the program. Given that, I would like to address what Paul and Tom have said about industry's influence. Paul said that because not many physicians are involved in stroke intervention, it is difficult for industry to justify expenditures in that area. On the other hand, you (Paul) and others have done a lot to try to be politically correct and develop the protocols for the very small group that you were just complaining about. One way to "enlarge the pie" would be to start involving cardiology more in those protocols. In fact, instead of putting the stroke protocol with the typically anti-intervention neurology group, give it to the group you want it to grow with, which is cardiology. Let the others either join in or not. This would be a way to justify from the company's and the FDA's point of view that the physicians you involve in this protocol are in fact eligible to perform the procedures it calls for. I think this type of strategy will have a much greater impact on the marketplace than you think.

Richard Myler: I have always believed that you don't read history, you repeat it. You may never have heard about Richard Schneider who was the chief of Werner Forsmann in Germany. In 1929, a 24-year-old man who worked with Schneider had the idea to catheterize himself. Richard Schneider recognized the genius of this young — and perhaps crazy — man's idea. Schneider stood behind him and

interventional cardiology was born. Don Effler stood behind a young man from Argentina who didn't even have a license to practice medicine in the U.S. Then René Capalero performed his first interventional cases. And so things progressed. Andreas Gruentzig had a failed early case — about his seventh, I believe — and had to send the patient to surgery. There were a lot of sharks in the water at that time, young cardiac surgeons who wanted Gruentzig to fail so bad, they could taste it! Andreas was broken emotionally oftentimes as a result of this animosity. The head of surgery at the time, Dr. Sening, asked his young men: "What was the plan for this patient if Andreas hadn't done the procedure?" They replied that the plan was to perform bypass surgery. Dr. Sening said, "He had his bypass operation; he had to go emergently. The patient did very well." Sometimes it's not a bad idea to enlist the support of some gray-haired people in your department, or even someone from outside your department. It's wonderful to have the support of another physician who has a high regard for the imagination and courage of those who are trying new things, especially in neuroradiology since it is such an emotional area. I remember when Gary first taught, we were all thrilled about it, but we didn't have quite the "umph" needed. It sure would have been terrific to have someone like a neurosurgeon at the time.

Eberhard Zeitler: In the past, approximately 90% of all neurology procedures were diagnostic. This will hopefully change with the arrival of new diagnostic imaging methods, especially in the area of early stroke treatment for which accurate and rapid diagnostic methods are needed. I have several questions for our young neuroradiologists: Can CT scans be done for most strokes instead of MRIs? What is the decision-making process today? How do we decide which patients should go to the interventional lab and which should receive active, conservative treatment?

Nick Hopkins: Based on the available evidence which, as you know, is very limited, we know that if a patient has a very low NIH stroke scale — that is, less than 10 — and the patient is within three hours of onset, then the patient may benefit from intravenous t-PA. It is very difficult to get any neurologists to agree to treat those types patients aggressively. At our institution, we asked the question: How about the patient who we know will do poorly with intravenous t-PA? The odds ratio of a patient doing poorly when his NIH stroke scale is over 10 rises, I believe, to > 75% — a huge number. For every increase in the stroke scale number, the odds of that patient recovering are correspondingly lower. Thus, we established an arbitrary cut-off point at 15. If a patient's NIH stroke scale is over 15, we don't care how fresh he is, if he is one minute post-stroke, we will treat him aggressively by taking the patient directly to the angio suite. If, however, a patient's stroke scale is 10 or less, we treat him with intravenous t-PA. We have been tweaking this method as we go along based on what we've learned from cardiology as well as from our own mistakes in order to come up with a protocol that makes sense. We are starting a new protocol now, in fact. Thus, we are making progress with each step along the way, but we are learning the hard way because we don't have the numbers that cardiology does. This is a real problem for us — not having the numbers. The floodgates will open when more neurologists and neurosurgeons get trained in this area and enter the fray.

Howard Cohen: We have a very active stroke program at the University of Pittsburgh under the guidance of Gary Roubin who encouraged our cardiologists to get involved in stroke treatment in cooperation with the neurointerventionists, neurosurgeons and vascular surgeons. We undertook this form of collegial teamwork with carotid stenting as well. Some of my colleagues are on the bandwagon while others are not. Every institution seems to have its own local politics: some people want to work together, while others are rather territorial about their work. In my view, we need significant involvement from cardiology, particularly in the areas of intracranial and stroke interventions, and it will require an incredible commitment. An interventional cardiologist simply cannot expect to get an occasional call from the neurointerventionist at his institution inviting him to help treat a stroke patient. Obviously, the head is a different discipline with many challenges; the circulation and the way it responds are different. It's not something a cardiologist can just dabble in occasionally; there must be a commitment like that shown by Gary Roubin. Interventional cardiologists have experience with urgent acute interventions to offer the huge population of patients who require acute stroke or intracranial intervention. As was pointed out earlier, things are a little different in the cerebral circulation and there are times when intervention is appropriate and other times when it is not. Neurologists, from my perspective, tend to be more conservative in treating their patients, while cardiologists tend to be more aggressive. The two disciplines need to join forces to strategize and develop new techniques because as Paul mentioned, we are spending a significant amount of money in the wrong place. We need some new ideas which would come more readily if we worked together. Cooling, for example, is a very exciting area, not only in intracardiac applications, but in the area of intracerebral intervention as well.

Nick Hopkins: I think you are absolutely correct. In reality, our differences are not as great as we think. What we do in the head is not terribly different from what you do in the heart. Working in the head is little more delicate, thus we need industry to continue providing the tools that will enable us to work effectively in the brain. I can guarantee you that the catheter skills you interventional cardiologists have today in the area of intracranial stroke management, including the treatment of atherosclerotic disease in the head, are far greater than the skills of most neuroradiologists. I will probably get shot for saying that, but it's true! You aren't going to publish that comment, are you?

Gary Roubin: I would like to encourage interventional cardiology groups to identify a young, aggressive member of their practice who would focus on the array of procedures related to the cerebrovascular bed and stroke, starting with vertebral intervention, which is like ostial intervention, saphenous vein grafts in the right coronary, subclavian intervention, and carotid bifurcation intervention. More than 10% of the 750,000 strokes annually are due to patent foramen ovale — a lesion that cardiologists are most qualified to treat. We treat these lesions in our invasive cardiology group. Cardiologists know a lot more than neurologists, vascular surgeons, and neuro-radiologists about the pharmacology, disease management, adjusting the ACT with Angiomax — which most outside of cardiology have never heard of, but which cardiologists are very familiar with — using IIb/IIIa agents, dosing of aspirin and Plavix, and so on. Cardiology truly has so much to offer. I was invited to the neurologists' annual meeting to talk about what we do in the cardiac cath lab. The neurology community wants us to approach their department chairs and determine how we can help them. As one of the speakers said two weeks ago at this meeting, "All we have to assess our patients who present with stroke is a clinical NIH stroke scale. We don't even have electrocardiograms. We can't assess how much injury is occurring at the time." Imagine if we had no EKG, let alone the ischemic penumbra! The neurology community has no idea about the vascular anatomy. Everything depends on the collateral supply to the affected area. Over the past ten years or so, Jiri Vitek has taught me how to assess these stroke patient. And yet, there is no way to assess collateral supply in the case of acute stroke.

In the typical case, a CT scan is performed, an NIH stroke score is determined, and then the patient is put to bed. It's absurd compared to what we are doing in interventional cardiology! Imagine if we could take the acute stroke patient to the cath lab for an imaging study which would show the status of the collateral supply to the brain and help us determine how to rescue the patient.

Nick Hopkins: I understand that neuroradiology spends 90% of its time dealing with aneurysms, arteriovenous malformations, arteriovenous fistulae, and other assorted malformations of the brain. Up until a few years ago, neurologists never performed intracranial angioplasty procedures. Never. It's all brand new to them. Angioplasty is something cardiologists obviously have been doing for years now. That is why I say that interventional cardiologists are probably better suited to the treatment of acute stroke and intracranial atherosclerotic vascular disease than most neuroradiologists.

Jeff Werner: Our institution recently implemented a teamwork strategy to launch a brachytherapy program. It was mandated that the team be comprised of a radiation oncologist, a radiation physicist, and a cardiologist. From the very start, the team members accepted the fact that each person contributed a particular set of skills and expertise. The radiation oncologists, once we got to know them, were very happy to be working as a team and were very interested in this program. It seems to me that this teamwork approach involving one or two successful therapies or a couple of types of clinical situations, is an effective way to move things forward.

Nick Hopkins: The team concept is certainly the best approach.

Raoul Bonan: I agree with what Paul and Jeff said. Even the neuroradiologists and radiology oncologists at certain institutions will not be in the lab anymore; they will delegate someone else to do the procedures. Through specifically focused studies, such as the one involving 50 sites in the U.S., we have been able to spread the notion in the U.S. and Canada that these radiation therapy programs represent a new approach to therapy.

Reginald Low: Why don't we form a committee whose task would be to establish a core curriculum for cardiologists to train in neurointervention work? If industry would help support this effort, we could have the first world course on the core curriculum for cardiology training in neuroradiology and neurointerventions. I have been involved in some animal pre-clinical testing with wires, balloons, and stents for neurointerventions. I find it interesting that companies in the industry have not developed cooperative working relationships between their neurology and cardiology units. There are numerous wires, balloons, and stents available for neuroradiology applications that industry has not fully explored in terms of possible cardiology applications. I have used stents that are so much more trackable than anything we have presently in cardiology and that could be very important niche products for certain cases.

Michael Lawrence-Brown: Politics aside, I find this a fascinating subject. I have seen a patient recover four hours after total loss of consciousness. The patient underwent carotid endarterectomy with total occlusion on the other side and two hours post-procedure, he lost consciousness. The ultrasound showed complete occlusion. I placed a sheath in the carotid artery and infused with heparin, then took the patient down to the angio suite where I diagnosed a dissection which extended right up beyond the siphon. I successfully got around the siphon and then placed a Wallstent all the way down, completing the patch at the bottom. The patient then regained consciousness. He did experience some deficit, but it was very interesting because it involved the collateral circulation and the situation we've discussed here regarding acute coronary syndromes. We may have more time than we think to recover these patients when their artery occludes.

The second important factor was that we reduced our shunt rate from 12% to 2% by allowing the brain to control the blood pressure (under a local anesthetic). Thus, there is more coming out of the brain than we know, as far as I can determine. We frequently see changes in hypertensive medication and difficulty controlling blood pressure for hypotension following carotid endarterectomy. Thus, there is a pharmacology of the brain that is not yet fully understood, but it has implications for all of us because if you treat patients with strong hypotensive agents to control the strain on the heart, you may actually be reducing cerebral perfusion if the patient has a carotid stenosis or an occlusion — and this could lead to stroke. Carotid disease therefore becomes very important in that context. But the process is even more interesting in that we can really look at the whole of atherosclerosis by looking at the carotid bifurcation which features a mobile section and central forces on the curve, as well as a fixed area. Another fixed area appears at the base of the skull where traumatic dissections commonly occur. Interestingly, those traumatic dissections of hematomas do heal. No artery bifurcation in the body better demonstrates the sheer forces that occur in the wall and the rotational forces that occur at a bifurcation better than the carotid bifurcation because there is a high-resistance vessel in the external carotid artery and a low-resistance vessel in the internal carotid artery. This means that every time it pulses, it rotates and is thus a perfect setting for fatigue fractures. Yesterday we touched on the idea that there is more than just the intima associated with the generation of atherosclerosis. Why is it that carotid occlusions are such isolated lesions? We know in most cases, except in some diabetics, that we are going to get to the end of the lesion. There is something mysterious about the bifurcation that we have yet to understand.

In 1993 we looked into materials to use in stents for stent grafts in the aorta and found much of our technology in the field of dentistry. Before Andreas Gruentzig, there was Dodder, and before Dodder, there was Stent. This is accelerated testing — one hour = one year. An ideal metal, with electron potentials and current, will give a nice line straight up and then when it goes beyond the electron potential, it will deform. A good metal will come back to the same point. The stainless steel material is shown on this slide in red. This slide shows a titanium alloy, a wonderful metal that comes from dentistry. Here are examples of nitinol, nickel, and titanium metals. Stainless steel is a little better, but when it deforms it does so completely, and once it deforms, it does not return to its initial shape. Nitinol, on the other hand, is a memory metal, so when it deforms it returns to its original point. Nitinol's slope is not straight, however, which means that every time it deforms, its crystallized structure is slightly changed. Thus, over time, nitinol changes its memory so that it becomes brittle and fractures. When we study stents, we take plain x-rays. If a nitinol stent is going to be placed in a carotid bifurcation, plain x-rays will routinely need to be taken to check for stent fractures. This slide demonstrates how we thought that if we gold-plated the stent, it might give better protection, but gold-plating makes it worse. The memory might be slightly better, but the slope means that it will corrode very quickly — a phenomenon which I believe has been observed in the heart as well.

Finally, if bare-metal stents are placed across orifices, there is no accretion; it will not substantially interfere with flow, especially if the artery orifice is > 3 mm. I can't take you down to 1 mm because the technology we had did not offer sufficient accuracy. The blood helps because it is a sheer, thinning fluid with vortex shedding. But at the edges, if intimal hyperplasia occurs, it may grow to cross the lattice, which might be seen with the Wallstent. This is a weld or a solder: there is greater corrosion there and some eluting may be occurring, but it is not eluting a substance that decreases intimal

hyperplasia. Instead, it increases intimal hyperplasia. Therefore, what we use — especially in the final frontier of the brain, the intracerebral circulation, and the carotid arteries — is very important. Perhaps the drug-eluting stent will be the answer, but it needs to be a self-expanding one because it will have to be able to negotiate around the curves in many instances. You saw the image Nick showed of the stenosis that was right on the apex of the curve. We obviously have a lot to learn yet and we must work together to arrive at a better understanding of vascular disease.

John Anderson: What I've heard today is excellent, but that's not where we are. There is not even a perception in the general medical community or in the general public that a treatment for stroke exists. We need to start with education and refer back to the excellent work that has been done in the past and that will hopefully continue in the future. We have trained paramedics to use defibrillators, but for most people, stroke is not an emergency; rather, it's often considered "a done deal." People don't tend to rush stroke patients to the hospital because they are not aware that there still might remain a therapeutic window of time during which the patient could be salvaged. Education of the public and the medical community is thus where we should start. Until we take that step, we will continue to see a large number of patients who are simply not retrievable no matter what innovative techniques we try on them.