Pierre Gobin, MD

A prominent neuroradiologist describes his experience with GDC coils and inventing the Merci Retriever device.

How did you become involved in the early work with Guglielmi Detachable Coil embolization? The technique was invented and developed by Guido Guglielmi, MD, a physician from Rome who went to UCLA to conduct his early work. The first patient was treated at UCLA in 1990. I was not involved with the very early development, but I performed the first case in France, where the company making the coil, Boston Scientific, decided to expand out of the US. We were a big center in Europe—I was working at the Hospital Lairiboisiere in Paris at the time—and we were the first ones to perform this procedure in France. Just after this patient, I did a few more, and I was recruited by UCLA at the end of 1992.

How did you come to invent the Concentric Merci Retriever for cerebral embolectomy in stroke patients? It was out of frustration with using intra-arterial lytics. Their effectiveness is somewhat limited, especially when there is a major artery occlusion due to high clot burden, which is the amount of clot that must be dissolved before the artery recanalizes. For example, when you have a large clot in the leg that you want to dissolve, you will place an infusion catheter and inject tPA for 24 or 48 hours. It will take all of that time for the drug to progressively dissolve the thrombus. However, in the brain, you don't have the luxury of that amount of time. You need to reopen the artery within 1 or 2 hours. The time window for stroke is very short, usually 6 to 8 hours. You must act quickly if you want the brain to still be alive after we reopen the artery.

It was this frustration with doing intra-arterial thrombolysis, limited effectiveness, and risk of hemorrhage that made me wonder what we could do to create a device that would allow us to pull the clot out instead of dissolving it with a drug.

The idea came out of a brainstorming session with one of our fellows at that time, J.P. Wensel, MD, and together we disclosed the idea to the UCLA patent office. I was a little unlucky in the beginning. The first company with whom I developed this device went bankrupt. I had filed a patent with UCLA, so after the bankruptcy, the patent went back to UCLA. I further worked on this project by myself and with an engineer, and then I went to meet with several incubators. An incubator is a company that starts other companies—they set up the infrastructure and the venture capital funding. This incubator helped me to start Concentric.

What are the competing devices and technologies? In terms of mechanical embolectomy, there is no competition as of yet. However, there are some other emerging treatments. First, the available lytics are improving. The only drug that is approved for brain recanalization is intravenous tPA, but abciximab might have a better safety profile than tPA. Still, there is an increased risk of bleeding with use of lytics. When you reinstate blood flow into tissue and capillaries that are damaged, there is a "shock of reperfusion." When brain arteries are reopened, we have to think not only about the neurons and the astrocytes, but also the capillaries forming the blood/brain barrier. It is from the leaking capillaries of the damaged blood/brain barrier that petechial hemorrhages will occur after reperfusion. However, if you add a lytic drug to this shock of reperfusion, then you have all of the conditions to create a large hematoma. The MERCI studies showed that when only mechanical embolectomy is used, although the shock of reperfusion still exists, there is a reduced incidence of large hemorrhage when no lytic was used.

The best way to control the shock of reperfusion is to keep the blood pressure low. Before the reperfusion, I prefer the patient to be hypertensive because it helps the collaterals. Hypertension forces flow through the collaterals, but as soon as the arteries are reopened, I then administer medication to lower the blood pressure.

In the heart, 90% of arterial occlusions are due to an atheromatous plaque. The plaque ruptures and blocks

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the artery. So, there is a small amount of thrombus and a lot of atheromatous plaque. That is why when you reopen a coronary artery with a balloon and a stent it works so well. It is completely different, however, in the brain. In stroke, the proportion of embolus to plaque is exactly the opposite—90% embolus and 10% plaque. The emboli have frequently migrated from the carotids or the heart and have lodged into a brain artery, but the artery itself is healthy.

Do you foresee other mechanical embolectomy devices entering the market in the future? In the same way that, 15 or 20 years ago, myocardial infarctions were treated with intravenous thrombolysis and we were giving intravenous urokinase or streptokinase, it took many years to prove that actual mechanical reperfusion was better than drug administration. I am sure that there will be competitors entering the field. There has also been improvement in helping the action of thrombolytic drugs by using laser or Doppler to shake and fragment the clot so that the lytic agent has more surface area with which to interact and to act more quickly.

What are your thoughts on intracranial stenting? There are really two applications for intracranial stenting. Intracranial stenting for aneurysms is doing very well right now, and I think it is helping us considerably in providing long-term solutions for aneurysms. We are now able to treat large-neck aneurysms, which before the availability of stents could only be treated with coils with a high rate of recanalization. The second application is for intracranial atherosclerosis. Intracranial atherosclerosis is not very prevalent, but it still affects a significant number of patients. Stents for intracranial stenosis is a significant need because the recent studies of warfarin versus aspirin in the treatment of intracranial atherosclerosis showed that aspirin was safer than warfarin. However, it also showed that the risk of stroke recurrence in the same territory that involved the first stroke was approximately 10% at 1 year. This means that, even with the best medical treatment, the risk of recurrence of symptomatic severe stenosis in the brain is 10%. We really can improve that number; it is a significant unaddressed need, and hopefully the use of stents will help to address it.

Drug-eluting stents for intracranial use are currently in development. Another very interesting area is self-expandable stents for intracranial use. The first data from Europe demonstrate safety, but we do not yet know about the efficacy.

Are you working on any new methods of treating stroke? Yes, I want to associate hypothermia with recanalization. I have invented an indwelling catheter device to induce hypothermia. It is a catheter that is placed into the inferior vena cava that exchanges heat with blood, which makes it much more powerful than external cooling. We know that hypothermia is beneficial in stroke (in any kind of neuronal injury). Hyperthermia is very detrimental, but we think that hypothermia might be beneficial. Mild hypothermia is enough to achieve benefit (approximately 35ºC). Of course, this is all based on animal models.

Are there differences between how interventional neuroradiology is practiced in the US as opposed to Europe and the rest of the world? Well, it is a bit frustrating in the US because of FDA restrictions. We always get the new toys 1 to 3 years after our colleagues in Europe and South America. Sometimes there are some unaddressed needs in which you would really like technology to be available earlier. The humanitarian device exemption does, however, make it easier for some exceptional indications. Because neuroradiology does not have the same number of patients as cardiology, the regular FDA process has been frustrating for companies that will have to go to a lot of expense to run a full-blown trial for a market that will stay small.

Neuroradiologists are finding themselves treating more and more cerebral ischemia. Previously, we have mostly been treating aneurysms and arteriovenous malformations, whereas now we are treating ischemic disease that is much more frequent (eg, stroke, intracranial stenting, carotid stenting), which is a very important evolution. Parallel to this evolution, we find ourselves also treating more mainstream diseases because there are a limited number of arteriovenous malformations and aneurysms, but there are many strokes and many carotid stenting cases.

We have all of these interventionists entering the arena from other specialties, such as from interventional radiology, vascular surgery, cardiology, etc. It is not only the neuroscientists who are now doing, or will soon do, endovascular work in the brain. I think it will open interesting doors because we have a very limited number of interventional neuroradiologists, and it takes a long time to train one. I don't know if the other specialists are going to want to go through the intense training that we have. On the other hand, for me, carotid stenting is the easiest procedure that I perform, but for someone who is doing peripheral work, it could be a most difficult endeavor, but that does not mean that he cannot do it well. ■