Lee R. Guterman, PhD, MD

A medical technology enthusiast and expert neurointerventionist discusses his interest in device development and what's needed to find the Holy Grail of intracranial aneurysm treatment.

How did you choose your specialty?

When I finished my PhD in chemistry, it was my intention to pursue a postdoctoral position in neurobiology with the thought of becoming faculty at a medical school. During graduate school, I worked summers at the Marine Biological in Woods Hole Laboratory in Massachusetts dissecting and mounting squid giant axons for optical nerve impulse transmission studies, under the direction of Lawrence Baruch Cohen, PhD. It was suggested to me that I would be a more productive medical school faculty member if I obtained an MD degree after my PhD. In my first year of medical school, I fell in love with neuroanatomy. My mentor, Harold Brody, PhD, MD, encouraged me to go into neurosurgery. At the time I started residency training in neurosurgery, I was able to incorporate catheter-based treatments for cerebrovascular disease into my training from day one, thanks to L. Nelson Hopkins, MD.

I now have a full-time clinical practice that includes endovascular and general neurosurgery. I am medical director of stroke at the Catholic health system of Buffalo. I see patients 1.5 days per week in the office and operate 3 days. I also do a good amount of stroke call in our five-hospital system.

What is the focus of your current research?

My current research involves development of devices for the treatment of hemorrhagic and ischemic stroke. I have designed a retrievable stent that would be placed adjacent to a cerebral aneurysm during coil occlusion. The stent enabled blood flow through the parent vessel while helping hold the coils in the aneurysm. This device has been used in patients outside of the United States. More recently, I have devised a system to evacuate deep intracranial hemorrhages from the brain using minimally invasive techniques. This series of devices is in development. Most recently, I have been working on a device to augment the exchange of cerebrospinal fluid between the cranial and spinal compartments. This series of devices would be useful for patients with Chiari malformation type 1.

When did you first become involved with venture capital? Are there technologies in their portfolio that have caught your attention?

I have been involved with Sapient Capital (Wilson, WY) since its inception in 2000. My role was to evaluate new medical technology in a wide range of medical disciplines. I have had the opportunity to participate in development of an endoscopic gastric bypass device, which has been used in preliminary human trials. Mitch Dann and I have authored a few patents that are owned by the minimally invasive gastric bypass company, ValenTx (Carpinteria, CA).

I have also been involved with Longitude Capital (Menlo Park, CA) along with Juliet Bakker and Jeff Gold. My role has been to evaluate new stroke and neuroscience technology before investments by Longitude Capital. Having the opportunity to speak with industry professionals, engineers, and inventors continues to provide access to multidisciplinary thought processes relative to stroke solutions.

I guess I am a medical technology junkie. I love to think about device solutions for disease management. It is remarkably stimulating intellectually, and it is also great fun.

What are the developments in robotic catheterization that have most interested you?

I recently had the opportunity to use a robotic catheter and wire advancement system in a research laboratory. The product was produced by Corindus Vascular Robotics (Natick, MA). Once the guide catheter was placed, the microwire, balloon, and eventually the stent were all guided and deployed by a remote robotic actuator. I sat in a booth, without a lead gown, situated at the foot of the angio table. It was remarkable. Less fatigue, less radiation, and a true one-to-one control of catheter and guidewire through joysticks. I believe this represents the future direction for neuroendovascular technology. I can also envision coils and glue material being delivered more precisely and with greater safety using technology such as Corindus.

(Continued on page 81)

(Continued from page 82)

How is the role of the neurovascular interventionist changing?

The role of interventional neurosurgeons is still evolving. It is clear that for the treatment of cerebral aneurysms and arteriovenous malformations (AVMs), there is an increasing role for the catheter-based skill set. Throughout the past decade, many practitioners have finished residency training in neurosurgery followed by additional fellowship training participating in both endovascular and open surgical fellowships for cerebrovascular disease; physicians such as Ricardo Hanel, MD, (Mayo Clinic Jacksonville) and Eric Sauvageau, MD, (Ohio State University) have completed this training path. Their training method has produced neurosurgeons who are comfortable in both treatment venues and may represent the ultimate cerebrovascular practitioner.

Are we close to a first-line treatment for wide-necked intracranial aneurysms?

For sidewall aneurysms, those not located at a vessel bifurcation, we have device solutions: Pipeline (Covidien, Mansfield, MA; US Food and Drug Administration premarket approval) and Surpass (Surpass Medical Ltd., Israel; not available for sale in the United States). When the aneurysm grows at a bifurcation, such as the middle cerebral artery, the endovascular task is more difficult. We still lack a technology that will reconstruct the neck of the bifurcation enabling coil or liquid embolic agent delivery. This is mainly because any of the arteries involved in the bifurcation can become part of the aneurysm body. An intracranial construct that can be used in a multitude of aneurysm shapes is not yet available. A device specifically for bifurcation stenting in the cerebral circulation is not yet available.

Using a stent or a removable balloon to keep the coils or liquid embolic in the aneurysm after delivery can still be challenging. The nitinol self-expanding stents and the delivery catheters have improved orders of magnitude in the past 10 years. Stent-assisted and balloon-assisted aneurysm cases have successfully enabled the treatment of many bifurcation aneurysms, but the Holy Grail, wide-necked bifurcation aneurysms, represents an elusive challenge that has not yet been solved. Once a stent has been placed intracranially, antiplatelet therapy must be used to prevent subacute stent thrombosis. This can be problematic in patients with intracranial hemorrhage.

What has your experience been with the use of liquid embolic agents for AVM treatment?

During the past 2 decades, I have used various acrylates as polymerization agents for treating cerebral AVM and dural AV fistulas. With acrylates (eg, nBCA), polymerization occurs once the monomer comes in contact with ionic solution, namely blood. Along with Ajay Wakhloo, MD, PhD, we tried to adjust the polymerization rate by adding lipiodol and even concentrated glacial acetic acid to the monomer acrylate before injection.

Although this worked well, injections could be stressful for the operator. Waro Taki, MD, invented a better polymer for occlusion of these lesions. His formula used a polymer dissolved in a polar organic solvent, DMSO. During injection, the DMSO dispersed when it came in contact with blood. As a result, the polymer precipitated because it was not soluble in blood. This lent more control to the embolization process resulting in delivery of larger polymer volumes into the malformation. Onyx was formulated and sold by Micro Therapeutics, Inc. (formerly of ev3; now acquired by Covidien). I tend to use this product exclusively for these lesions.

What are your thoughts on the halting of the SAMMPRIS trial?

It appears that intracranial stent placement using the Wingspan stent (Boston Scientific Corporation, Natick, MA) was associated with perioperative complication rates > 10%. I believe strongly that intracranial revascularization has a role for symptomatic intracranial stenosis. Operator skill and patient selection can affect clinical trial outcomes immensely. I will continue to use the Wingspan stent in appropriate cases. There is another trial in progress using balloon-mounted alloy stents for intracranial atherosclerotic disease. This study, VISSIT, which has Mike Marks, MD, as the principal investigator, may have different results than SAMMPRIS. Time will tell.

What can be done to improve the timeliness of tPA administration in acute ischemic stroke intervention?

Public awareness of stroke signs and symptoms will facilitate early presentation to emergency departments. This in turn could enable early tPA administration. Alternatively, the time window for tPA administration can be extended through the use of adjunctive therapy such as systemic hypothermia and/or neuroprotective drugs. Perfusion MR and CT imaging can be used to differentiate between infarcted and salvageable brain tissue. These imaging studies can open the time window. ■

Lee R. Guterman, PhD, MD, is Medical Director of Stroke, Catholic Health System, and is with the Buffalo Neurosurgery Group in Buffalo, New York. He has disclosed that he has patent ownership in ValenTx and is a shareholder in Sapient Capital and Longitude Capital. Dr. Guterman may be reached at lguterman@buffaloneuro2.com.