Pioneering Insights: Why EVAR's History Must Guide Its Future

Aortic experts and enthusiasts convened at the 2016 VERVE Symposium in Sydney, Australia, to reflect on the first 25 years of EVAR, as well as how past lessons can streamline modern innovation.

This article summarizes personal recollections of the emergence of endovascular aneurysm repair (EVAR) shared by a group of vascular luminaries at the VERVE Symposium, with an eye toward how lessons from the past can help to shape EVAR advancements of the present and future. It is no doubt incomplete, with many pioneering names and foundational device concepts not mentioned, but includes the unique insights and colorful memories of key moments that heralded the present landscape.

In retrospect, the unfavorable forces encountered by EVAR and its early proponents could have easily eliminated any chance the procedure had for long-term success and widespread adoption.

A durable standard of care was available for most abdominal aortic aneurysm (AAA) patients. The new procedure required skill sets and equipment not yet possessed by most of its potential adopters—if in existence at all. Full understanding of the anatomic environment, disease progression, resultant forces, and predictive modeling were lacking. And, the initial reports of success were met with considerable doubt and detraction, technologic and regulatory hurdles, and the Iron Curtain.

And yet, as the panelists took the stage in Sydney, Australia, more than 2 decades after Juan C. Parodi, MD, and colleagues disseminated their initial EVAR experience, the procedure had evolved from an experimental approach for cases deemed too risky for open surgery to the standard, first-choice option for low- and moderate-risk patients in hospitals around the world, and back to the complex end of the spectrum again.

The panel assembled in Sydney included pioneers and early adopters, collaborators, and friends. Moderated by Hence J.M. Verhagen, MD, PhD, the session began with anecdotes from the earliest days of EVAR in the Western Hemisphere, focusing on the specifics of the first cases, device designs, and barriers its proponents quickly met. Although Dr. Parodi himself was not a participant in the panel, the perspectives of his colleagues provided unique windows into those transformative years.

There were many reasons the procedure almost never made it out of the experimental phase, but as the panelists eloquently described, a mix of ingenuity, serendipity, and hardheaded determination was as vital to its progress as the void it aimed to fill.

EVAR BEHIND THE IRON CURTAIN

Frank J. Criado, MD, an early EVAR champion and friend of Dr. Parodi, reminded the audience that the first EVAR cases were actually performed and reported by Ukrainian Nicholas Volodos, MD, and colleagues in the late 1980s. However, the cases were performed behind the Iron Curtain, which prevented news of the developments from widely spreading in the global medical community despite first being published in 1988, several years before Dr. Parodi's landmark article. It was not until years later that most surgeons in the West learned of Dr. Volodos' seminal work, which included abdominal and thoracic cases and the development of both bare and covered stents, said Dr. Criado.

However, the group from Instituto Cardiovascular de Buenos Aires in Argentina was able to share its developments with colleagues on several continents leading up to and soon after their initial successes, although not always to enthusiastic audiences.

"¡LO HICIMOS Y FUNCIONÓ BIEN!"

Practicing in the United States, Uruguayan-born Dr. Criado was interested in endoluminal applications of all kinds. He knew of Dr. Parodi's early work, including his efforts to modify and adapt the vascular stent designs of Julio Palmaz, MD, as Dr. Parodi had studied

and worked in the United States at the Cleveland Clinic and the University of Illinois.

In his presentation at VERVE, Dr. Criado recounted EVAR's version of Alexander Graham Bell's "Mr. Watson, come here" telephone call, in which the surgeon's phone rang at 2:30 AM on September 8, 1990, while at a conference in Yokohama, Japan. On the other end was Dr. Parodi in Argentina.

"We did it, and it worked," said Dr. Parodi.

EVAR IN THE USA

In New York, Frank J. Veith, MD, and Michael Marin, MD, were also aware of Dr. Parodi's work. Soon after learning of the first case, when trying to determine the best course for a patient with a large, symptomatic aneurysm who was unsuitable for open repair, they reached out to the team in Argentina to see if Dr. Parodi would teach them how to perform the procedure. Unable to successfully deliver the films to Buenos Aires, Dr. Marin soon brought the x-rays and scans to a conference Dr. Parodi was attending in Milwaukee. The two surgeons hit it off, and Dr. Parodi agreed to come to New York.

Before the case could be undertaken, however, a significant hurdle emerged—the device manufacturer did not want to jeopardize its existing goals for US Food and Drug Administration (FDA) approval. In his talk for the VERVE audience, Dr. Veith recalled that at the time, Johnson & Johnson was working toward FDA approval for the Palmaz-Schatz stent in a coronary application and was concerned about allowing use of a modified version, especially in an application for which it was not designed. The two surgeons eventually exhausted their company contacts into standing down from their understandable protest, and plans were initiated for the case.

Making the trip to the Bronx with Dr. Parodi were several of his colleagues, including interventional radiologist Claudio Schönholz, MD, and engineer Hector Barone, who first modified and upsized the Palmaz stents to better fit the aortic dimensions. The case was a success.

"When we saw this case, at least for me, it was a total epiphany," relayed Dr. Veith in his presentation to the VERVE audience. "I said, 'My God, if we don't embrace this technology, we're going to be out of a job. We're going to become an extinct specialty.'"

The group would soon embark on an endovascular program, custom-making devices using Palmaz stents and polytetrafluoroethylene tubular grafts to treat a wide variety of aneurysms and even traumatic lesions. Although there were early failures, the overall results they saw in inoperable patients had them feeling that this approach was making the impossible possible.

However, the skeptics turned out in greater number than the supporters when the early results were first presented to vascular congress audiences.

PLEASE, HOLD ALL TOMATOES UNTIL THE END OF THE SESSION

"Nobody wanted to listen to this," said Dr. Criado, who explained that EVAR could not get past the "wall" of the vascular surgery establishment, from the society to annual meeting and the journal. Then, after seeing Dr. Parodi present his work at a June 1991 meeting in Miami, John Bergan, MD, called his friend Ramon Berguer, MD, who was the editor of *The Annals of Vascular Surgery*, and emphasized the tremendous potential of this work and why it should be published as soon as possible. By November 1991, it was in print in the *Annals*.

Similarly, when Dr. Veith first presented his group's results, with Drs. Marin and Parodi in the audience, the group did not receive the warm embrace they expected.

"We thought we were going to be heroes, messiahs leading vascular surgery into the Promised Land," recalled Dr. Veith. "It didn't turn out that way at all. Everybody thought we were lying, coloring the truth, or crazy. There wasn't a single person in the audience of current and future leaders who thought we were bringing anything important to the table."

Deflated but not defeated, the group carried on, and innovative work was spreading in labs and operating rooms around the world. In 1996, addressing the Society of Vascular Surgery as its President, Dr. Veith would give a lecture on the experience entitled "Charles Darwin in Vascular Surgery," in which he emphasized vascular surgery's evolution-or-extinction crossroads and the importance of working with interventional colleagues in the years ahead.

BECAUSE YOU HAVE TO START SOMEWHERE

As groundbreaking as the first EVAR concepts were, they left considerable room for advancement. Dr. Parodi himself modified the device configuration multiple times in the early days, gaining new ideas from each previous design's shortcomings, a trend that continues through the present day. Fortunately, groups of inventive minds quickly embraced EVAR in centers around the world. Innovative development began taking place on multiple continents simultaneously, and EVAR-inclined surgeons were traveling to each other's centers to collaborate.

The VERVE panel pondered the rationale of the initial designs, especially that of a single tube that required an adequate distal seal zone—not entirely common in AAA patients—to even have a chance of working. The responses to this question essentially boiled down to: We didn't know what we didn't know yet, and we had to start somewhere.

James May, MD, elaborated on specific challenges related to the technology available at the time EVAR emerged, which included delivery catheters that were thick and stiff, requiring immersion in boiling water to achieve sufficient pliability. Additionally, balloons were

not readily available, and the only Dacron on hand was the material used for open procedures, which was also quite thick. The largest hemostatic valve available in the early days was 14 F, requiring on-the-table improvisation to get all of the components on the patient side of the valve to ensure delivery without losing too much blood prior to the development of larger valves.

"To add to the magnitude of the issue," commented Alan B. Lumsden, MD, "there was no previous experience, the worst imaging systems, and these were the most complex endovascular procedures ever invented. It is shocking that it ever worked."

"The extent of our ignorance regarding the biology of the aneurysm and what was going to happen when you put in a stent graft was amazing," agreed Timothy Chuter, MD. "We had absolutely no idea, which is still true to some extent. We based this whole field on several fairly astounding assumptions regarding vascular biology, and none of them could undergo meaningful animal testing in the absence of realistic models of the aortic aneurysm in the elderly atherosclerotic arterial tree. Australia was ground zero for a lot of the endovascular revolution, particularly the complex endovascular reconstruction of the aorta, due to a high level of on-the-fly ingenuity and a willingness to push the boundaries."

THE AUSTRALIAN EXPERIENCE

Prof. May and David Hartley, FIR, represented the esteemed history of Australian adopters and adapters on the VERVE panel. Mr. Hartley captivatingly provided the Perth perspective on the evolutionary steps that took an initial single tube design and incrementally advanced it as physicians representing many countries and continents collaborated to move the technology forward:

In 1991, the Royal Perth Hospital Endovascular Unit was formed as a collaboration between Michael Lawrence-Brown, a vascular surgeon, and Peter Kelsey, MD, an interventional radiologist. At the time, Geoff White, MD, and Dr. May, among others were becoming engaged in EVAR concepts in Sydney after visits to Buenos Aires, as well as by Dr. Parodi's presentations at the International Endovascular Symposium (IES)—an influential and invaluable Sydney-based forum for emerging AAA education and idea exchange. Mr. Hartley commented that upon seeing Dr. Parodi's presentation at IES in 1992, the Perth group came home very excited about EVAR's prospects and were converts to the cause, which would shape their storied careers over the next several decades.

They worked quickly on developing the Perth aortic tube graft based in part on design elements described by Cesare Gianturco, MD, but after performing several cases, the group concluded that a bifurcated graft was needed. One possible solution came at a subsequent IES, when Timothy Chuter, MD, of San Francisco, presented clinical experience with the first bifurcated endograft, recalled Mr. Hartley.

The Perth team then set a goal of designing a flow model to test new graft concepts. They evaluated unibody developments under x-ray control until Dr. Lawrence-Brown suggested attempting a modular design that could be delivered in multiple pieces. John Anderson, MD, of Adelaide, collaborated with the group and suggested that the introducer must be improved.

Among the major developments to come out of Australia in the late 1990s and early 2000s were fenestrated designs aimed at abdominal aneurysms with short necks, as well as fenestrated thoracic grafts and branched devices (Cook Medical). Mr. Hartley also described the contributions of Roy K. Greenberg, MD. Collaborating for years with his colleagues at the Cleveland Clinic, those from Australia, and others such as Krassi Ivancev, MD, from Sweden; Stephán Haulon, MD, from France; and Cherrie Abraham, MD, from Toronto, Dr. Greenberg performed hundreds of complex fenestrated and branched cases with excellent results. After naming more than a dozen pioneers, Mr. Hartley lamented not being able to credit so many more who were instrumental.

"It's the dedication of these and many other clinicians I haven't had time to recognize that has made possible the range of devices to treat the aorta from the sinotubular cusp to the external iliac artery. It has been my pleasure to have been a part of it," he concluded.

Recognizing the humility of his friends from Australia, Dr. Chuter made his thoughts on their contributions clear: "Basically, all of complex endovascular treatment can be traced back to these two characters—Michael Lawrence-Brown, and David Hartley."

INNOVATION: CREATING A WAVE AND SURFING IT

Echoing the sentiments shared earlier by Drs. Veith and Criado, Dr. Chuter pointed out that innovation often involves the elimination of a previous standard, which can upset those who have a vested stake in the status quo, who are often quite powerful. Although the early devices did not actually work that well, they announced the arrival of a new era. "Vascular surgeons suddenly woke up to find that their sacred cow was about to be butchered," he said.

Dr. Chuter described innovation as often coming in one of two forms—the disruptive and the iterative. Disruptive innovation could be visualized as the formation of a wave, and iterative innovation is the surfing of that wave. Continuing the metaphor, nobody can surf the back of the wave, saying, "Today, I would not recommend anyone try to design a new bifurcated stent graft for a regular infrarenal aneurysm unless it's something really special."

Innovation, continued Dr. Chuter, does not occur spontaneously or in isolation, even if it may appear to; there are always antecedents, as well as a considerable amount of

failure. "The real information comes from experimentation," he said. "And if we're truly honest, it comes from the failures of experimentation—you have to be honest enough and open-minded enough to learn from your mistakes."

As for the iterative process, the panel agreed that there is no substitute for clinical experience. Preclinical testing has its limits, and while short-term issues can sometimes be predicted, long-term issues often cannot be seen without long-term experience and data. One of the challenges inherent in innovation is protecting patients from risk, which is complicated when the associated risks are not well understood. For this reason, innovation often begins in patient populations for which there is no alternative—in the case of EVAR, the very ill and those with large aneurysms.

One further caution voiced by Dr. Chuter was the need to learn the lessons of experience. "There were lots of ideas long ago discarded that are now being polished up and presented as new by new entrants to the field," he observed.

COMBINING EMERGING APPROACHES

In a presentation that highlighted a relatively new endovascular approach to complex cases currently under evaluation, Jean-Paul de Vries, MD, described ChEVAS—augmenting the Nellix polymer-filled endobag system (Endologix, Inc.) to better support parallel grafting techniques. "One-third of AAA patients have visceral segment involvement, and 50% of those have short necks," he began. These patients largely fall outside of current instructions for use, and hostile necks are likely to lead to early failures and the need for secondary procedures, as well as long-term failures and higher aneurysm-related mortality.

Combining the Nellix technology with a variety of branch graft configurations, investigators in the ASCEND registry aim to completely seal the aneurysm sac while preserving branch patency in complex anatomies. Dr. de Vries presented promising 1-year follow-up data showing a low rate of all endoleaks, including type IA, as well as high patency rates for the celiac trunk, superior mesenteric artery, and both renal arteries. Freedom from aneurysm-related and all-cause mortality was similarly high.

FOUR-DIMENSIONAL ADAPTIVE INFRASTRUCTURE

Frans Moll, MD, PhD, detailed some of EVAR's "one step forward, two steps back" iterations before segueing into what the next true innovations in this space must include. As Dr. Chuter indicated, it would seem that every idea and its opposite has been put forth and tested in standard bifurcated stent grafts. Endoskeletons and exoskeletons, fixation above and below the renals—most devices appear designed to correct the failures of previous iterations, while Prof. Moll suggested that what is most needed is a concept that addresses the disease itself.

Through the failures of devices designed in the late 1990s and throughout the 2000s, "We discovered that you have to deal with the dynamics of the aorta," said Prof. Moll. Using imaging platforms with electrocardiogram triggering, surgeons were better able to understand the dynamic forces and movement of the aorta during the cardiac cycle. However, due to these forces and the natural progression of aneurysmal disease, he believes any solution involving a device alone is destined to fail. "It's like chemotherapy versus immunotherapy—you do not cure."

A recent EVAR credo became that we must accept the aneurysm but prevent it from rupturing, said Prof. Moll. He recalled that the concept of filling the aneurysm sac with a polymer was first posited by a Dutch group that included Hans Brom, MD, PhD, and Alexander de Vries, MD, PhD; and was then advanced by Nellix at his suggestion to involve containing the polymer, ultimately in the platform's endobags. However, Prof. Moll believes that filling the aneurysm sac cannot match the flexion and extension of the aorta, and long-term outcomes may not support this approach. "The next credo is, 'Accept the aneurysm, but prepare the arterial wall and make it rupture-proof,'" predicted Prof. Moll.

What might this involve? Prof. Moll described a mesh-based concept involving four-dimensional printing, declaring three-dimensional (3D) printed devices suitable for anatomies that are fixed, but inadequate for dynamic and changing environments such as the aneurysmal aorta. He is currently working with Ferdinando Auricchio, MD, in Pavia, Italy, on a concept he calls adaptive infrastructure, which involves combining plastics with smart materials. Other ideas include shape-memory polymer filters. These structures could be combined with preparing the medial layer of the wall with glycated cross-links, a concept explored by Moll and colleagues in a 2016 publication in the *Journal of Vascular Surgery*.

THE TRAP OF INNOVATION FOR THE SAKE OF INNOVATION

Dovetailing with the presentations of Dr. Chuter and Prof. Moll, Prof. Verhagen detailed failure modes associated with popular stent grafts from each postmarket generation. "They were completely unpredicted," he said. "All, in retrospect, were due to mechanical and biological unknowns. The solution for all these problems has always been the same—just improve the design and fix that particular problem."

The crux of Prof. Verhagen's lecture was the quest for lower-profile platforms, which constitutes a considerable amount of the recent effort in improving the current generations of stent grafts. However, he wondered if low-profile EVAR might represent iterative innovation for the sake of innovation. This goal was more vital when delivery diameters were much larger, but Prof. Verhagen asserted that lower

profiles than are currently available would expand the pool of potential EVAR candidates by a relatively small fraction.

And, to date, many such efforts have been unsuccessful. Prof. Verhagen described industry efforts to bring truly low-profile EVAR to the market with limited success, and in some cases, considerable failures. "Methods of reducing profile include using thinner graft material to make them more packable, three-piece instead of two-piece construction, fewer markers, and different materials," said Prof. Verhagen. However, suboptimal results observed to date include fabric issues, stent fractures, component detachment/separations, thromboembolic complications, and little if any favorable effects on outcomes compared to previous generations. "What we're doing with low profile is turning the clock back," he continued. "We're seeing problems we haven't seen in 10 to 15 years."

With recently presented data from DREAM and EVAR 1 showing that approximately half of all patients are still alive after 10 years, durability is far more important than profile in the next generation of devices, concluded Prof. Verhagen.

EVAR: A GATEWAY TO INNOVATION

Houston-based Dr. Lumsden concluded the session with a lecture that connected many of those that preceded it, while predicting a bright road ahead.

"I was taught that before you drink from the well, first honor the people who dug it," he began, a nod to the pioneers who gave EVAR its start, "some of whom are sitting on this stage."

"As a fellow, the most complex catheter-based intervention I did was push a Fogarty catheter blindly up the aorta, blow up a balloon, and pull it out—no angiograms, you passed it four or five times and hoped you got inflow."

Presenting some complex aortic cases recently performed at his center, Dr. Lumsden illustrated just how far the field has come. Rather than focusing on the specifics of the implantable device in each case, he described optimized preprocedural planning that involves printing and practicing on a 3D-printed model aneurysm that directly matches the patient's own (as verified by "back-fusing" the 3D printing against the source image). Particularly in complex cases for which off-the-shelf options do not exist, this enables a safe environment to construct and practice possible solutions that can then be brought into the operating room.

The advent of stent grafting drove surgeons to learn about imaging and gain access to it; to learn about wires, catheters, and stents; and to collaborate with other specialties. These efforts transformed the specialty. The innovation that has surrounded EVAR—both technologically and culturally—will endure long beyond the procedure itself. ■