The Advent of Stenting

Perhaps no type of device more aptly embodies the state of modern endovascular care than does the stent. With far more proponents than detractors in each of the specialties, stenting has dominated for more than a decade, and recent progress with many new developments indicates that it will be a mainstay for at least the near future. The early developmental days of the vascular stent saw work from several revolutionary physicians, each of whom had a unique concept regarding the most efficient design. One such design, initially conceived by Julio Palmaz, MD, was the balloon-expandable stent, which drew attention in the mid-1980s and came to be used successfully for years to come. The device's further successes can be seen in the technologies it has since inspired, such as the numerous adapted stent designs and the AAA stent graft. For these reasons, there is no better person than Dr. Palmaz to describe the early days of stent research and the subsequent developments that would not otherwise have been possible.

Endovascular Today: As the inventor of the balloon-expandable stent, you are in a unique position to share with us what the early days of stent development were like. Which physicians were involved, and what did each contribute?

Julio Palmaz: The first report of a stent ever published, to my knowledge, was by Charles Dotter, MD, in 1969, in a then little known journal called *Investigative Radiology*. His stent was actually a nonexpanding stent; it was a fixed-diameter metal coil tube that he had placed in the hind legs of dogs. Dr. Dotter reported sustained patency in two animals, but he didn't publish anything else until 1983. In 1983, I had already done work on balloon-expandable stents, and I was getting ready to send my results to the RSNA. At that time, three papers appeared almost simultaneously in the *Radiology* journal. One was by Dierk Maas on self-expanding spiral stents; the other two were by Dotter's and Amplatz's groups on self-expanding, thermal memory stents. Up to that point, I was still the only proponent of the balloon-expandable stent. I presented my material at the end of 1984 at the RSNA meeting—the same meeting during which Dr. Cesare Gianturco's group presented his zigzag self-expanding stent. So, by 1984 there were already four different stents being proposed: three self-expanding and one balloon-expandable.

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EVT: How did your invention of the balloon-expandable stent meet with the previous standard of care?

Dr. Palmaz: Well, those were confusing times. Everything was in a state of flux. The most prevalent thing at that time was obviously Andreas Gruentzig's balloon angioplasty, which he presented in the mid-1970s. I was fortunate enough to hear one of his earlier presentations in North America, and actually, his presentation inspired me to come up with the idea of the balloon-expandable stent. Percutaneous balloon angioplasty was an early project, and it was incredibly well received and embraced with great enthusiasm. However, everybody acknowledged that there was still a lot of work to do in terms of proving the principle. Although balloon angioplasty was very popular among cardiologists and radiologists, who loved the idea, there was great skepticism among surgeons.

Then, in the early 1980s, atherectomy and lasers appeared. These concepts were also embraced with great enthusiasm by the community, but they had to go through long, rigorous clinical trials before they could be proven as useful and safe. So, all of a sudden by 1984 to 1985, there was a scenario in which there were a lot of new opportunities in percutaneous therapy, but none of them had yet been properly appraised by clinical trials. My perception at the time was that percutaneous revascularization was a very crowded field. Stents probably had a chance, but they had to wait their turn. Obviously, people would much prefer to fix a vessel without the need to leave any prosthetic implant behind. Balloon angioplasty, atherectomy, and lasers were receiving much attention. In one of his presidential addresses, Ronald Reagan even mentioned laser angioplasty and its promise. There was a lot of expectation that any one of these options was going to be the way to go. Everybody at that time, particularly manufacturers deciding whether to get involved in implantable stents, was skeptical. A typical comment would be: "Yeah, stents sound interesting, but there are so many other promising things. Why get into putting metal in the arteries?" That was pretty much the scenario in the early '80s.

EVT: You mentioned that your inspiration for the stent had come from seeing Dr. Gruentzig's presentation. Can you discuss that further?

Dr. Palmaz: I was a second-year resident in radiology, and I went to my first cardiovascular meeting of the SCVIR in New Orleans in 1978. That year, my boss, Dr. Stewart Reuter, was the president of the society. Andreas Gruentzig, the keynote speaker of the meeting, gave the last talk of the program. The audience was no more than 50 people in a small room. Gruentzig was brilliant and enthusiastic, but I was particularly impressed by his honesty. He actually described in greater detail the limitations of angioplasty than he did its therapeutic potential. He showed specimens of what angioplasty could do in terms of producing dissection and disruption of the arterial wall, causing acute occlusions following angioplasty. The graphic detail of his talk elicited in my mind the idea of leaving a scaffold behind. I think anybody in the audience with a mechanical mind like mine could have actually thought of a stent.

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So, we went straight from Gruentzig's talk to the street to grab a cab, and I had a ride with my chairman. I was enthusiastic about the talk and told him my idea. He said, "Sounds terrific. Write it up as a project and then send it to me." It took me a while, but I eventually reviewed the literature, read some of the material published on percutaneous angioplasty, and finally wrote a report and sent it to him. That initial report actually proved to be a very, very important document later on for me because the balloon-expandable stent eventually got patented in 1985, but that written report documented an earlier date of conception. It was a very lucky strike.

EVT: After putting your idea on paper, how did the design and development process unfold?

Dr. Palmaz: From the moment I had the idea of the stent it became my pet project. I decided at that point that this project was worth my best effort. I really didn't have any hopes that it was going to be a breakthrough or anything like that. I simply thought it was going to be a very interesting project because I like mechanical things, and it had the pizzazz of being potential therapy for the coronary arteries; it really had a lot of components that were just right for me. That passion for the project stayed with me forever. During my residency years, I spent a lot of my free time on it. I contacted companies, I talked to other doctors, and I went to see people to discuss the possibilities for manufacturing.

Eventually, I started to feel frustrated because I could-

n't get the project off the ground, to bring it to the level of a working prototype. That frustration led me to move from California to Texas. I did so at the counsel of my boss, Dr. Reuter, who at that time had already moved to Texas himself. He was always telling me, "If you want to bring this project to fruition, you will have to move to a place where you have adequate research facilities and time. You don't have them where you are, so it's time for you to move." I was resistant to that idea, but shortly after one of my advisors in California passed away, I decided to move to Texas.

EVT: How did your move to Texas facilitate the development process?

Dr. Palmaz: It was a very slow process. All of these events I'm describing in a few words actually took years. Since the day of first conception in 1978 to the time I moved to San Antonio to start doing serious research and work on the stent was almost 5 years. Things started moving very quickly when I got to Texas though. I had time allocated to do the research, and I was given some limited funding. I had a technician and facilities, and we started making some progress. In 1984, I presented my first paper with some animal experiment results. In 1985, I applied for a patent, met Richard Schatz, and shortly after met Phillip Romano, an investor who brought the project to the next level.

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With a significant research grant, I devoted a larger amount of my time to research. By 1985 to 1986, I had enough experimental evidence to show the great promise of the stent. I was able to get Johnson & Johnson interested, and eventually we licensed the stent to them. Then, life totally changed for me. From late 1986 onward, I didn't work in the research lab as much as I used to because we started clinical trials. Those were the years when I traveled a lot in the US and abroad to visit and train new clinical investigators. I took responsibility to be principal investigator in the US iliac stent trial, and we eventually finished it, published the results, and presented them to the FDA. The FDA approved the stent for iliac artery disease in 1991. It was the first vascular stent ever to be approved by the FDA.

EVT: When and where did the first human implantations take place?

Dr. Palmaz: Our first iliac stent placement took place in Germany in 1987, and in 1988, we did our first coronary stent placement in Brazil. Things were going really fast at that time. The coronary stent got approved in 1994.

EVT: What devices or concepts did your work directly inspire in the next few years?

Dr. Palmaz: Immediately after the time when we first had in our hands an advanced balloon-expandable stent prototype, we had a long list of projects waiting to be started. We began playing with things like porto-caval shunts and covered stents. Everyone was coming up with new ideas about using stents in various applications, so it was a very fertile field at that time. After first being exposed to the device, lots of people had ideas about how it could be used in different aspects of cardiovascular disease.

One example of how the stent actually spurred imagination was at the very first TCT meeting in Washington, DC. At the end of my presentation, Dr. Juan Parodi, whom I had not met before, approached me and said, "Your stent could be attached to a piece of bypass graft and used to bypass aortic aneurysms. If you are interested, we could work together on a project." So we did. We applied for and obtained a patent on the idea of using stents to fix a piece of bypass graft to the aorta, and we did a series of animal studies at my facility in Texas. Then, we performed the first procedure on a patient together in Argentina. Later, Parodi brought the procedure to the level of routine use.

EVT: How would you compare your experiences bringing your concept to market to the process that must be gone through today?

Dr. Palmaz: Today, it is definitely much harder, and rightfully so because we know so much more than we did in those early days. When I was presenting data to the FDA panel on the first iliac stent we were plowing completely new territory. Neither we nor the FDA had guidelines on how to measure and qualify the patient's response to the stent because it was the very first in its class. Afterward, the FDA started requesting standard guidelines from manufacturers and clinical investigators to have appropriate elements of measure of device performance. The FDA collaborated with the ASTM to create the manufacturing guidelines and standards of measurement, which made things both easier and more complex for manufacturers to go through the regulatory hurdles. I definitely knew that the field was going to become more regulated, and that it would be for the best. ■