Healthcare Dialogue with

M. STEPHEN HEILMAN

Founder of Medrad, Intec Systems, Lifecor and Vascor

M. Stephen Heilman

In the United States, sudden cardiac arrest is a leading cause of death among adults, as evidenced by the roughly 330,000 deaths recorded annually.[1] Unlike a heart attack, with sudden cardiac arrest there is often no prior indication of trouble, and, as such, the majority of victims die. However, the availability of a defibrillator, whether it be an automated external defibrillator, an implantable cardioverter defibrillator (ICD) or a wearable defibrillator i.e. the LifeVest®, [2] can drastically improve one's chances of survival.

In 1991, Brown Brothers Harriman Partner, Bill Whelan, initiated BBH's first credit relationship with a medical device company, ZOLL Medical Corporation (ZOLL). At the time, ZOLL was a single product manufacturer of defibrillators — devices that were already ubiquitous in hospitals — and was gaining market share. In 1995, ZOLL sought to diversify within the defibrillation market, and Rolf Stutz, CEO, agreed to make an early stage minority investment in Lifecor Inc., a company that was deep in the development of a wearable defibrillator. Rick Packer, ZOLL's President at the time, joined the board of Directors of Lifecor. While the strategic fit for ZOLL was obvious, creating a wearable defibrillator was no easy task. Steve "Doc" Heilman is the physician entrepreneur who had the vision, perseverance and charisma to create a truly innovative product that has saved thousands of lives.

After practicing overseas as a General Medical Officer with the U.S. Air Force, entrepreneur and inventor Doc Heilman returned to the U.S. in 1964 and founded Medrad Inc., a medical research and development company. Focused on more accurately diagnosing heart and blood vessel disease, Medrad became the leading worldwide supplier of angiographic injectors and syringes for various X-ray, computed tomographic (CT) and magnetic resonance (MR) medical imaging procedures. As a spin-out from Medrad, Intec Systems, in cooperation with Dr. Michel Mirowski, successfully undertook the development of the world's first ICD. After the sale of the ICD technology to Eli Lilly, Heilman founded Lifecor and Vascor. Lifecor created the world's first and only wearable defibrillator, the LifeVest® defibrillator. The LifeVest® defibrillator is provided worldwide by ZOLL. Vascor is developing a heart assist system designed to greatly reduce the complications experienced by patients with present day heart assist devices.

Dan Head, leader of BBH's Healthcare Lending practice, asked Rick Packer for an introduction to Doc Heilman, so that he could share his story with our readers.

BBH: Could you describe your background and how it led you to become a medical device inventor and serial entrepreneur?

Steve Heilman: I grew up in Western Pennsylvania, in a town 25 miles northeast of Pittsburgh. My forebearers were medical and business/management role models. On my father's side, my grandfather, father, uncle and aunt were physicians. Together, they provided a very strong medical influence. My mother's father was trained as an engineer and became the plant manager of the Pittsburgh Plate Glass Co. plant in Creighton, PA; he was my business influence.

I majored in chemistry at the University of Pennsylvania, where I received a Bachelor of Arts degree. I earned my M.D. in 1959 from the University of Pennsylvania School of Medicine. During medical school, two ideas came together for me. The first was that emerging technologies were likely to greatly impact medicine by improving both diagnostic and therapeutic capabilities for physicians. The second was that there might be an exciting opportunity in the private sector to play a significant role in making that happen. A successful private medical device company could, in theory, use its profits to develop not one, but a series of game-changing medical products. This was a highly risky concept, but because there was a physician shortage at the time, if the company failed, I could always make a living as a physician in one specialty or another.

BBH: Did you start your company immediately following medical school?

SH: To fulfill my in-school military service deferment obligation, I enlisted in the Air Force as a General Medical Officer in 1961. Stationed in the Netherlands at the Soesterberg Air Base, my unit was responsible for the first level of medical care for the country's 3,500 or so U.S. military troops and their dependents. I returned to the U.S. in 1963, settled near family in the Pittsburgh region, and made a living working in emergency rooms. In 1964, I founded Medrad.

Medrad's first product development venture was a flow-controlled angiographic injector that used disposable syringes. Heart attacks and strokes are both vessel-related diseases, therefore the nascent field of angiographic imaging

[1] *Source: Sudden Cardiac Arrest Foundation,*

[2] *ZOLL Medical Corporation, ZOLL LifeVest®, 2015*

"The injector design had two important components. First, it was flow-controlled, so a physician was able to deliver imaging fluid, contrast media or dye to a patient's vessels at a desired flow rate. Second, the imaging fluid was delivered through a disposable syringe able to withstand up to 1,000 PSI of pressure and prevent patient-to-patient disease transmission."

held great diagnostic promise. Before angiography, physicians were literally and figuratively in the dark with regard to the details of a patient's diseased heart or brain vessels.

BBH: How did your angiographic injector work?

SH: The injector design had two important components. First, it was flow-controlled, so a physician was able to deliver imaging fluid, contrast media or dye to a patient's vessels at a desired flow rate. Second, the imaging fluid was delivered through a disposable syringe able to withstand up to 1,000 PSI of pressure and prevent patient-to-patient disease transmission. The imaging fluid contained iodine, a very dense element that makes the vessels visible on X-ray film. Dr. Mark Wholey, one of the first radiologists specifically trained in angiography, and Rudy Kranys, former Senior Vice President of Cordis Corporation, were both very helpful in the formation of Medrad and the design of the first injector.

Medrad's second injection system was much more polished than the first, and, as a result, helped the company raise angel capital to hire six direct U.S. sales representatives. In 1971, the business started growing rapidly and sales exceeded a million dollars.

Today, Medrad's angiographic product line, which is owned by Bayer Healthcare, is used in roughly 65 million procedures annually.

BBH: How did Medrad's angiography product line lead to defibrillators?

SH: At a cardiology convention in Singapore in 1972, while looking for dealers for Medrad's products in Asia, I met Dr. Michel Mirowski. Michel, a Holocaust survivor, trained at Johns Hopkins University and later settled in Israel as a practicing cardiologist. After his cardiology chief had an episode of ventricular tachycardia — an abnormal heart rhythm that is a precursor to sudden cardiac death (SCD) — he considered the possibility of taking a large external defibrillator, miniaturizing and automating it, and then implanting it to prevent SCD. In the event of a lethal heart arrhythmia, the implanted device would detect the arrhythmia and then deliver life-saving shock(s).

Believing at the time that only in America could such a product be developed, Michel moved his family to Baltimore and took a part time job as the director of a coronary care unit. He left half his time free to pursue his dream of developing the world's first ICD. Michel worked with Medtronic, a medical technology and services company, for a year or so on the ICD project. But when experts in the cardiology field cast doubt on the product's promise, Medtronic dropped the project.

BBH: How did the implantable defibrillator come to fruition?

SH: Within Medrad, I created a skunkworks of eight to ten people with various technical abilities. To limit liability, the ICD development effort was placed in a separate corporation called Intec Systems. Alois Langer was hired as the Chief Engineer on the ICD development project. Al had an electrical engineering degree from MIT and a PhD in bioengineering from Carnegie Mellon. His PhD thesis involved a complex analysis of the human electrocardiogram, which was important to the ICD development. Steve Kolenik, who had managed

research and development for a pacemaker company, was also hired. Steve brought substantial implant technology knowledge to the project.

The first human implant occurred at Johns Hopkins in 1980, and the ICD received FDA approval for marketing in 1985.

BBH: How was the project funded?

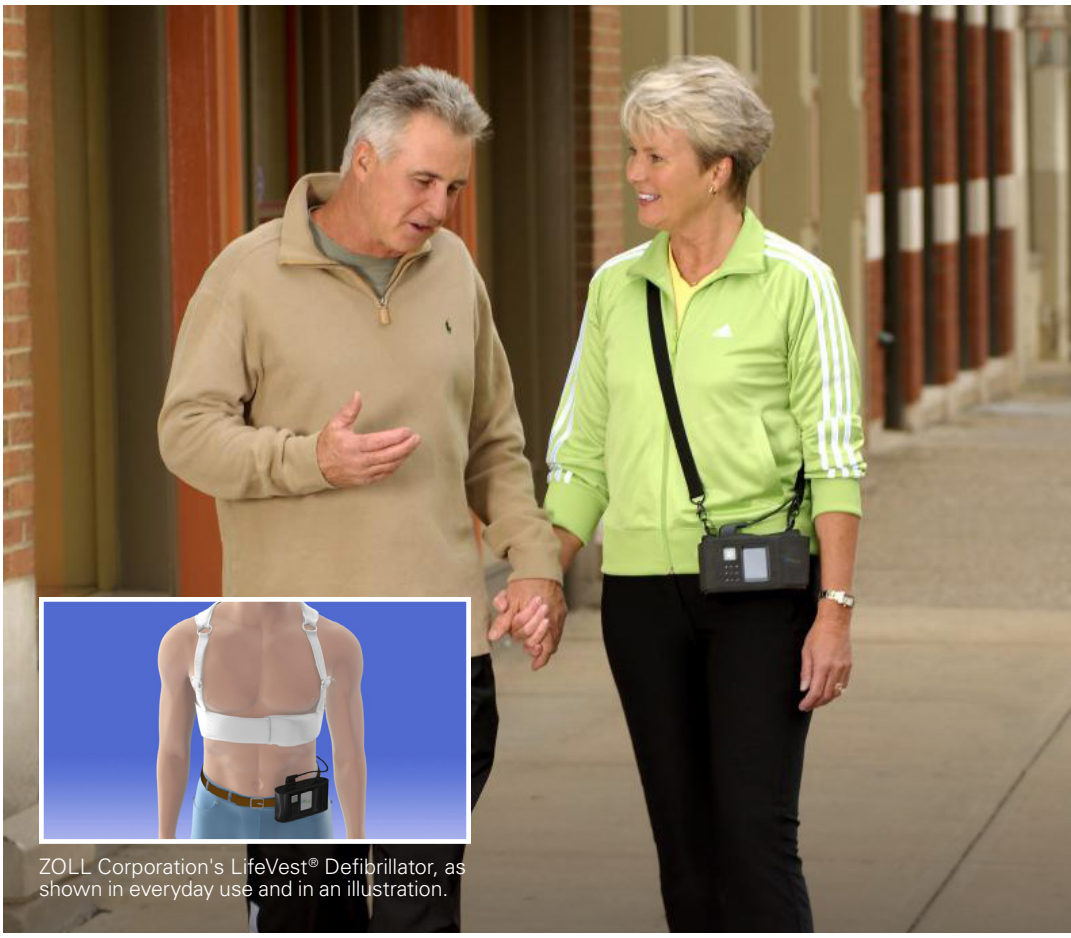
SH: The development of the first ICD required approximately $28 million. About $8 million came from Medrad's earnings, and $20 million came from venture capital sources. One of our key VC investors had a connection with Eli Lilly, the company that owned Cardiac Pacemakers Incorporated (CPI). CPI was a pacemaker supplier with a limited product line, and Lilly recognized the potential to increase CPI's value by acquiring the ICD technology.

In 1986, Medrad accepted an offer from Lilly to purchase its ICD technology for $45 million. The deal included an earnout formula that yielded another $50 million over five years, which satisfied our VC investors.

Today, ICD sales are roughly 250,000 units per year, representing a $6+ billion industry.

BBH: Has cardiac research advanced to the point where there are now less invasive procedures or drugs that can treat arrhythmia and other heart conditions?

SH: Many types of heart conditions have yielded to minimally invasive treatment. The most notable is stenting — opening coronary artery blockages — to minimize or prevent subsequent myocardial infarction heart attacks. Stenting has changed the nature of heart disease by substantially reducing the amount of infarcted or dead heart muscle in patients. In many instances, the treatment incision is so miniscule that stiches aren't required to close it.



ZOLL Corporation's LifeVest® Defibrillator, as shown in everyday use and in an illustration.

There is another potential minimally invasive procedure that would enable a cardiologist to use a special catheter to block off the left atrial appendage. In theory, this procedure would prevent strokes from floating blood clots in atrial fibrillation patients, and allow those patients to avoid anticoagulation therapy.

With regard to arrhythmia-caused SCD, many drugs used to minimize dangerous arrhythmias in the past have since been proven to be useless and, in some instances, even increase arrhythmia risk. Nonetheless, some drugs, such as beta blockers and amiodarone, are helpful in reducing arrhythmias. Yet the gold standard for SCD prevention remains the ICD. Where SCD risk is transient or uncertain, the LifeVest® wearable defibrillator is becoming the gold standard.

BBH: What was the process to obtain FDA approval and reimbursement from CMS (Centers for Medicare & Medicaid Services)?

SH: In the late 1960s, when Medrad was formed, the FDA had no authority over medical devices. Medrad's customers were hospitals and our constraints were those of an ordinary business — i.e., supplying a competitive product and reaching the customer base. To market the ICD, the FDA required a five-year clinical trial with successful outcomes. After the trial, we were fortunate to receive CMS reimbursement.

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To produce a new medical device today, both FDA marketing approval and CMS reimbursement approval are needed in series. Medicare CMS has a pilot program, wherein the reimbursement approval process runs parallel to the FDA approval process. If adopted, the policy would substantially speed up the new medical device reimbursement approval process.

BBH: What project did you focus on after the success of the implantable defibrillator?

SH: In 1986, a colleague of mine, Larry Bowling, and I concluded that a wearable defibrillator could protect many patients at risk of SCD. The treatment logic was one of triage: during the wearable defibrillator SCD protection period, the risk would be evaluated, and then, based on the risk assessment, the patient would either receive an ICD or be sent home.

BBH: How did the wearable defibrillator become a reality?

SH: Larry and I created Lifecor Inc. to develop a safe and effective wearable defibrillator, but such a device involved overcoming a number of technological hurdles. To begin with, the product had to be miniaturized so that it could be worn comfortably. Additionally, the device needed comfortable and reliable sensing and treatment electrodes. Traditional electrocardiograph (ECG) sensing electrodes and defibrillation electrodes are attached to the skin with an adhesive that can become uncomfortable with time, cause allergic skin reactions and be painful to remove. We resolved these issues by developing dry electrocardiographic sensing electrodes that simply sit on the skin without causing irritation or pain.

To ensure the reliability of the device, we also developed a horizontal electrocardiographic vectogram sensing scheme using four ECG sensing electrodes that encircle a patient's chest. This scheme proved to be highly effective in detecting the onset of dangerous ventricular rhythms. Another key element was the creation of gel-filled treatment electrodes, which allow the defibrillation shock to have low electrical resistance through the patient's skin and chest.

A major difference between the ICD and the wearable defibrillator is the decision structure for shock treatment. The ICD treatment decision is automatic, based on sensing an abnormal ECG. When the wearable defibrillator senses an abnormal ECG, it first triggers a series of patient alarms, and then only delivers a treatment shock if the patient is unresponsive as evidenced by failing to push a response button.

A patient's chances of surviving sudden cardiac arrest on the street are about 7%; in the hospital, the chances increase to only about 17%. Because survival is largely dependent on the availability of a defibrillator, a patient wearing a defibrillator today has a 98% chance of survival.

BBH: How long did the product modifications and approvals take?

SH: The FDA deemed Lifecor's wearable defibrillator, trademarked as the LifeVest® defibrillator, as new technology, mostly because of the gel deploying electrodes. Because of that, we were required to obtain clinical proof of safety and effectiveness. We designed a clinical trial to prove that the wearable defibrillator significantly increased the chances of patient survival. The trial was lengthy, requiring many months of patient defibrillator wear time. After it was successfully completed, the challenge was to obtain reimbursement.

CMS determined the LifeVest® defibrillator to be "durable medical equipment"

(DME), and DME reimbursement is controlled by four physician administrators, each responsible for one of the four durable medical equipment regional centers (DMERCs) in the U.S. A LifeVest® was provided to each patient free of charge until we had serious physician proponents willing to convince the DMERC administrators that the product should be reimbursed. The business model was to rent the LifeVest® to high-SCD-risk patients for between $2,000 and $2,500 per month. A typical rental period is 2 to 3 months.

It took 10 years to fully develop the LifeVest® through three successive generations, three years to clinically test the product and obtain FDA marketing approval, and an additional four years to achieve increasing levels of reimbursement. By then, $65 million had been invested and we were running out of cash. But we were fortunate to have ZOLL as a strategic partner.

BBH: Was ZOLL already a partner when you were running low on capital?

SH: Yes. At that point, Rick Packer had already joined Lifecor's Board, and ZOLL had already invested $2 million in the venture after meetings in Pittsburgh with Rolf Stutz. In 2004, when Lifecor was tight on capital, ZOLL acquired Lifecor and financed the business to profitability.

Today, more than 100,000 patients have been treated with the LifeVest® defibrillator, and thousands of lives have been saved.

BBH: In 1986, you and several colleagues also formed Vascor. Tell us about what the company is up to today.

SH: The most significant form of heart disease that's not being safely and effectively addressed today is severe heart failure. It's a very difficult problem. Two companies, Thoratec and Heartware, share a $700MM market consisting of ventricular assist devices (VADs). Both companies have FDA-approved VADs that can be described as rotary pumps — small devices with spinning blades that propel blood. The good news is that patients receiving these VADs live significantly longer than they would without the devices. The bad news is that serious complications and adverse events are associated with their use. Vascor has spent years working toward a safer and more effective VAD than the rotary VAD, and we will soon begin animal testing with a VAD product that we believe meets safety and effectiveness goals.

BBH: We look forward to learning more about Vascor's product in the near future. Thank you for your time and your extraordinary contributions to medicine! ■

The BBH Healthcare Team

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