CERTUS CRITICAL CARE INC.

# Certus Critical Care: Precision Blood Pressure Control Improves Outcomes

*Certus has developed an endovascular aortic balloon catheter that functions automatically to sense and adjust the balloon volume to enable second-to-second control of blood pressure. This precision control will be the key to improved outcomes after hemorrhage, cardiac arrest, and stroke.*

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Medical device start-up **Certus Critical Care Inc.** is much farther along than you'd expect for a company seeking their first round of external equity investment. Founded in 2017, the company's core hemorrhage control technology has been supported by almost $20 million in nondilutive funding from the Department of Defense to ensure that the company's catheter and suite of other critical care devices gets to the wounded warfighters who may need it. According to Lucas Neff, MD, US Air Force Veteran, surgeon, and co-founder of Certus, hemorrhage is the number one cause of potentially preventable death on the battlefield.

Now a pediatric surgeon, Neff and co-founder Timothy Williams, MD, a vascular surgeon, both practice at Atrium Health Wake Forest Baptist. Their reasons for making this company their mission were personal and stretch back almost a decade. They met while deployed to Afghanistan as surgeons in support of Operation Enduring Freedom. Neff notes that for day-to-day patient care, stateside surgeons who deal with trauma cases generally see horrible things. But in Afghanistan, the two grappled with the tragedy of US casualties dying en route to the hospital after firefights. Before the medical staff could apply the interventions that could save them, their comrades had already bled to death. "That was obviously very impactful," says Neff.

Once back in the US, the two teamed up with Certus co-founders Austin Johnson, MD, PhD, an emergency physician, and Jason Adams, MD, a pulmonary and critical care physician, at the University of California, Davis, to find ways to save patients experiencing hemorrhage. Beginning in 2014, the team began a hemorrhage and resuscitation program at Travis Air Force Base, California.

They began to focus on precision control of blood pressure, a key parameter influencing life or death for trauma patients. Working nights and weekends in Williams' garage, they developed the initial versions of an automated endovascular device that could provide minute-to-minute precision control of blood pressure to support patients long enough for surgeons to repair their injuries.

Along the way, the team realized that a device that achieves precision blood pressure control would be valuable for several applications besides hemorrhage, including cardiac arrest and stroke. Johnson's neuroscience background led the team to forge partnerships with stroke neurologists who understood that tight blood pressure control could help in stroke because extreme blood pressure fluctuations worsen outcomes. To address all the potential applications of their catheter, they founded Certus Critical Care in 2017 with an initial focus on two applications that represent a US market opportunity worth more than $1.5 billion, with a later market in stroke care that will be even larger. And the company didn't stop there—with four other products in the pipeline and a growing team in Salt Lake City and the Bay Area, what started as a

research project in a garage in California is now building the future of automated intensive care.

## A Dimmer, Not an On-Off Switch

Their lead product is an endovascular catheter designed to keep a patient's blood pressure steady following a traumatic event such as a gunshot, a cardiac arrest, or a stroke. The predicate for the Certus *EVAC* (endovascular variable aortic control) catheter is a simple balloon catheter used in a lifesaving hemorrhage control procedure called resuscitative endovascular balloon occlusion of the aorta (or REBOA). These catheters, inserted through the groin, track up into the aorta where the balloon is inflated to occlude the aorta and stop bleeding. Obviously, the lower half of the body also needs blood, and the aorta cannot be completely occluded for long periods of time without causing downstream tissue injury, so clinicians must manually inflate or deflate balloons in response to blood pressure readings to give downstream tissues the much-needed blood without creating more bleeding from the injury.

Although these are potentially lifesaving interventions, endovascular therapies like REBOA also risk causing as much harm as good. With respect to the management of an unstable patient's blood pressure, it's an all-or-nothing proposition that alternates between entirely stopping the blood flow with resulting tissue ischemia, and opening the flood gates of downstream flow, potentially causing significant electrolyte imbalances and profound drops in blood pressure to the vital organs. With current catheter technology, there is no way for physicians to manage blood flow and blood pressure in a precise manner for two reasons: the inaccuracy of blood pressure readings in these clinical settings, and the binary "on" or "off" nature of a simple balloon being manipulated by hand. As Neff notes, "It is difficult for clinicians to do this manual work when their attention is divided amongst all the other lifesaving interventions that are simultaneously occurring in a chaotic emergency scenario."

In their animal lab, using minute amounts of fluid to inflate balloons in tiny increments, Neff says it became clear to the Certus team that even the slightest change in balloon inflation has a much greater than expected impact on changes in blood pressure. "Within a couple of tenths of a milliliter of fluid, you go from a completely occluded aorta to a massive rush of downstream blood flow that was more robust than at baseline." It's not entirely predictable when the "floodgates" open, Neff notes, which occurs over a very small range of deflation volume. "With current balloon catheters, the clinician is flying blind with both hands tied behind her back," Neff says.

To achieve this delicate balance, Neff continues, "Instead of a light switch—on, off—we needed a dimmer switch. And we needed that dimmer switch to respond every second to what the patient's blood pressure is doing, with precision control that we can't achieve by hand with unstable patients in chaotic environments."

To create such a device, the team had to ensure that patient physiologic data was as robust as possible. They thus developed a more accurate way of obtaining blood pressure readings, since currently used devices on the wrist or the groin are highly susceptible to signal loss and aren't dependable when subjected to movement and electronic interference.

The Certus team developed thin solid-state blood pressure transduction sensors that mount onto the catheter to directly measure pressure inside the aorta, the best place in the body to do so. An external controller inflates the balloon in very small increments if there is an unwanted drop in pressure and deflates it when the signal says the pressure is too high.

## A Platform with Multiple Use Cases

With a working prototype of its single-use disposable, battery-operated, 7-French *EVAC* catheter, Neff says, "We then realized that this catheter and controller were really good at modulating blood pressure. So *EVAC* isn't only for controlling bleeding, it is controlling blood pressure itself." When the team realized the power of such a "resistor" in the aorta, other large clinical applications opened up, including cardiac arrest and hemorrhagic stroke, which have few adequate therapies.

Many patients in cardiac arrest are treated every day in every emergency room across the country, Neff says, yet the care algorithms for advanced cardiac life support haven't really changed in the last several decades; cardiac arrest resuscitation is in need of an "innovation reset." The current standard of care revolves around cardiopulmonary resuscitation (CPR) and administering adrenalin. "Placing the *EVAC* catheter in the aorta gives you more bang for the buck during every compression of CPR because you have something to push against. The ability to restart the heart and fill those coronary arteries with blood is so much greater when you have a balloon in the aorta that is inflated.

The patient isn't necessarily out of the woods though once the heart is restarted, Neff points out. With a restarted heart, the next problem emerges. "A very sick heart must now pump against the high pressure from that occluded aorta. So, the provider just deflates the balloon, right? Not so fast! If you aren't using precision deflation, then when downstream flow suddenly comes roaring back, the

upstream pressure bottoms out and the heart will rearrest." Instead, the *EVAC* sits in the aorta and automatically modulates changes in balloon volume based on the patient's blood pressure. "With the high-fidelity inputs from the on-board sensors, the precision movements of the controller allow it to make small changes second by second with a degree of fidelity no human can achieve." In an animal study, the company found that *EVAC* reduced rearrests by 60%.

With such an intervention, notes Neff, more patients could achieve return of a purposeful heart rhythm during cardiac arrest and have a "bridge to survival" from the emergency room to the cardiac cath lab where there are more options for advanced therapies. The company's estimate of the potential of the cardiac arrest market is 260,000 in-hospital patients, and 70,000 out-of-hospital arrest patients, for a total addressable market of approximately $1.2 billion.

Finally, in both ischemic and hemorrhagic stroke, emerging literature suggests that clinical outcomes are linked to the degree of blood pressure fluctuation that patients experience in the neuro ICU. In ischemic stroke, a version of *EVAC* designed for prolonged use would be placed in the neurointerventional cath lab following a thrombectomy procedure and remain with the patients for ongoing blood pressure support. For the larger percentage of ischemic stroke patients that don't get thrombectomy, and for hemorrhagic stroke patients, *EVAC* could help limit the wide swings in high and low blood pressure that further damage a brain that has little ability to compensate for these pressure changes itself.

Stroke is the company's largest potential market—it estimates its addressable patient population for ischemic stroke at 500,000 (the approximate number of patients who receive thrombolytic drugs and/or thrombectomy), plus half of the remaining population. It aims to reach approximately 100,000 hemorrhagic stroke patients (one-third of the entire patient population).

Because stroke is a more involved regulatory pathway, Certus has positioned it as its third market thrust. While prioritizing the hemorrhage and cardiac arrest markets, the company continues to develop its future products, some of which could be useful in the stroke application, where drugs also play a role.

Certus Critical Care expects to enter the market in hemorrhage control in 2023 with a design freeze in the first quarter of the coming year, and then verification and validation for the remainder of 2022. After meeting with the FDA, the company anticipates a 510(k) regulatory pathway based on predicate devices.

While hemorrhage might not be the largest of the company's potential applications—adding up applications in trauma and obstetrics, the estimated treatment population is 366,000, for a $350 million addressable market—this strategy allows the company to position the *EVAC* catheter sales in the emergency department, the operating room, labor and delivery, and interventional radiology settings where its competitive advantages will be seen, and where reimbursement pathways already exist. *EVAC* can increase the duration of therapy (as compared with other aortic occlusion balloons on the market) threefold. "Others can provide therapy for 30 minutes, which isn't a lot of time," says Neff. "Ninety minutes for *EVAC* is a game changer." And for two members of the founding team, hemorrhage control for obstetric complications hits close to home as their wives experienced postpartum hemorrhage.

Certus is fundraising for a $10 million Series A round, to get the first product to commercialization, and to make progress on the pipeline of other non-trauma indications for the catheter. To potential investors, Neff touts the diversified and relevant skill sets of the team. CEO Johnson is a neuroscientist and an emergency physician who stays clinically sharp by still taking the occasional shift in the ER when not running the company. Vascular surgeon Williams, the company's chief technology officer, whom Neff describes as a "polymath," brings not only endovascular skills but also expertise in robotics, adaptive algorithms, and smart endovascular devices. In addition to his work as a pediatric surgeon, Neff is also an expert on large animal models of complex diseases and helps run a translational research lab in North Carolina. Kobi Iki, director of development, brings medical device expertise, having worked at Gravitas, BARONova, Leptos Biomedical, Vascular Architects, and Oratec Interventions. Director of Engineering David Poisner spent the first 35 years of his career as an electrical engineer at Intel.

About the founding team, Neff also points out, "We are physicians. We are scientists. We are adept at writing and applying for grants. We have leveraged those skills to bring almost $20 million into the development of these technologies and we intend to keep doing so."

Finally, as physicians that still actively care for patients, Neff notes, "This is deeply personal to all of us. Every couple of months I take care of a teenager who has been shot or otherwise seriously injured. It is the worst thing in the world to have to tell a parent that their child is not coming home. If we can come up with something that saves a soldier, a child, a new mother, a grandparent...that defines success for us. We live the mission every day. We are working to build the devices we ourselves need at the bedside to save our patients." MTS

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