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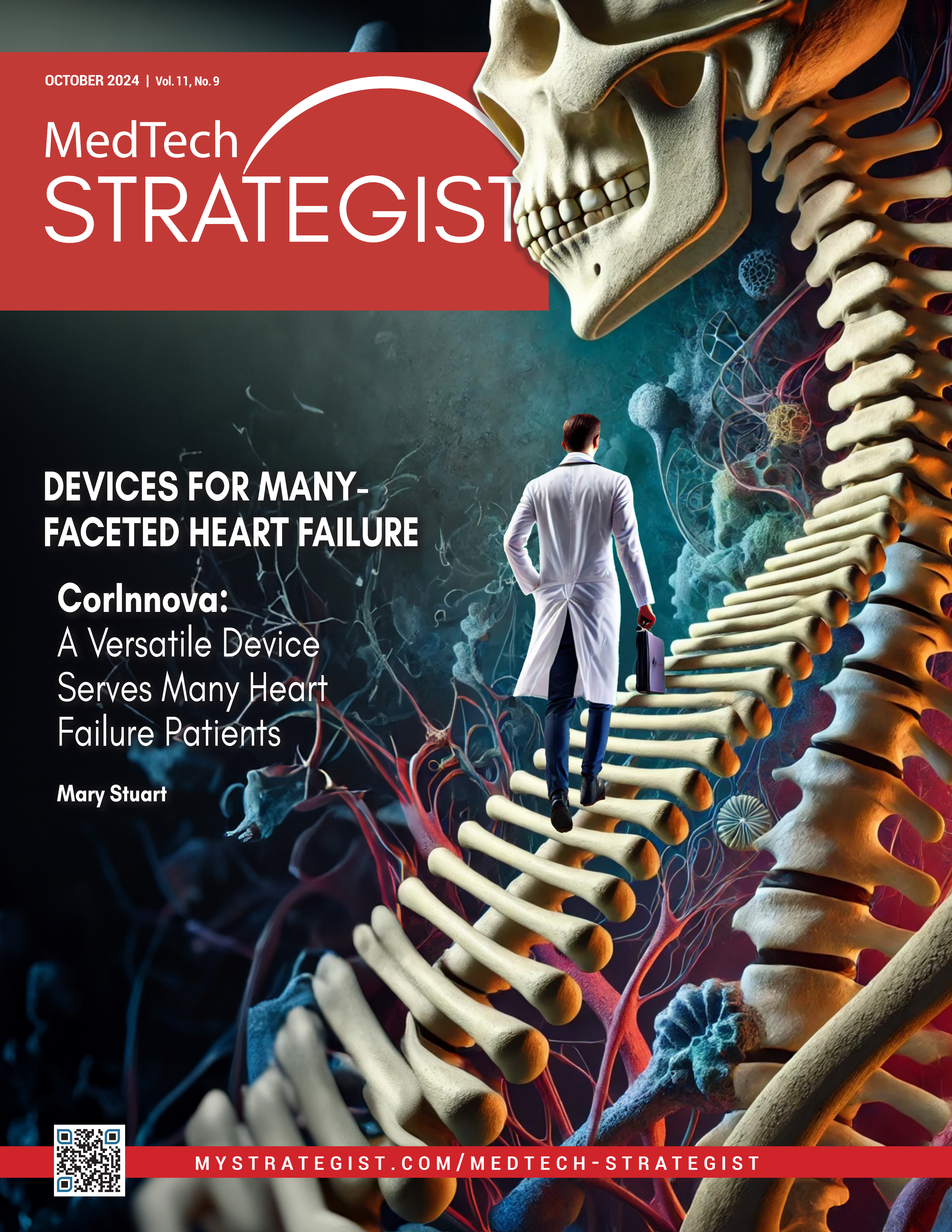

DEVICES FOR MANY-FACETED HEART FAILURE

CorInnova: A Versatile Device Serves Many Heart Failure Patients

Mary Stuart

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decompensation is a common late-stage feature of all types of heart failure when it isn't under control, we now know that depending on the patient's disease, there are many more potential pathophysiological points of intervention, which device companies are now targeting.

There are programs addressing heart failure from a structural angle by repairing mitral or other damaged heart valves that exacerbate the problem, and others that attempt to reshape and/or remodel enlarged ventricles. Many companies are working to electrically modify pathways relevant to disease, at the level of cardiac cells, for example, to increase contractility, or by stimulating the autonomic nervous system or the respiratory system. Others are creating new heart pressure monitoring systems (Endotronix, for example) to signal worsening trends of heart failure to allow timely intervention, and, ultimately, a greater understanding of disease processes. (*see Figures 1-3*).

In addition, work is being done by companies on the front end of the problem, to diagnose and characterize heart failure patients, an unmet need that makes therapy development all the more challenging.

For example, while HFrEF, which is a dysfunction of the heart's pumping action, is easily diagnosed by the ejection fraction or how much blood is pumped out with each heart contraction, HFpEF, which represents at least half of all heart failure, is difficult to diagnose. HFpEF patients have a normal ejection fraction, but a dysfunction in the filling cycle of the heart. The current criteria for diagnosing HFpEF, in patients having shortness of breath during exertion and other signs of heart failure, include a normal left ventricular ejection

Figure 2

Selected Physiological Therapeutic Devices for Heart Failure

Physiological Approach	Selected Company Examples
Interatrial shunts	Adona Medical, Alleviant (*Alleviant System*), Corvia (*Corvia* Atrial Shunt), Edwards (*APTURE*), InterShunt Medical (*PAS-C Catheter*), NoYA MedTech (*NoYA*), Occlutech (*Atrial Flow Regulator*), V-Wave (*Ventura*)
Heart valves	Devices for the repair or replacement of heart valves, SAVR, and TAVR: Abbott (*Navitor*), Edwards (*Sapien S3*), Medtronic (*Evolut FX*) Transcatheter valves in development for aortic regurgitation: Edwards (JC Medical and JenaValve) Transcatheter edge-to-edge mitral valve repair: Abbott (*MitraClip*), Edwards (*PASCAL*) Tricuspid valve repair or replacement: Abbott (*TriClip*), Edwards (*EVOQUE*)
Neuromodulation, various	Baroflex activation: CVRx (*Barostim Neo*) Vagus nerve stimulation: LivaNova (*VITARIA*) Splanchnic nerve ablation: Axon Therapies (for HFpEF) Immunomodulation: Humanitas Research (*HF-ImMod*)
Electrophysiology modulation	Cardiac resynchronization therapy: Abbott, Biotronik, Boston Scientific, Medtronic. Cardiac contractility modulators: Berlin Heals (*C-MIC*), Impulse Dynamics *(IMPULSE Optimizer*)
Respiratory modulation	Phrenic nerve stimulation: Respicardia
Fluid volume management	Reprieve Cardiovascular
Reduction of pulmonary hypertension	Aria CV
Ventricular reshaping	Ancora Heart (*AccuCinch*); BioVentrix (*Revivent TC*), Cardiac Success (*VSling*)

Source: "HFSA Scientific Statement: Update on Device Therapies in Heart Failure," *Journal of Cardiac Failure*, September 10, 2024; *MedTech Strategist*

the pressure. Both companies ran well-powered, high-quality randomized clinical trials, and both failed to prove their primary endpoints (of a reduction in heart failure events).

First, Corvia enrolled 626 patients in REDUCE-LAP HF II and randomized patients to either the *Corvia* Atrial Shunt, or a sham procedure. At two years, there was no difference in primary outcomes between the two groups. However, certain subsets of patients responded well to the therapy. Hence, Corvia is now running a second double-blinded, randomized, sham-controlled trial, RESPONDER-HF, and will study another 260 patients for two years, this time recruiting only certain patients with HFpEF (with an ejection fraction ≥ 40% and further qualified by their hemodynamics during exercise) and HFmrEF (heart failure with mid-range ejection fraction), to try to determine which heart failure patients benefit from shunting.

Likewise, V-Wave enrolled 508 patients in its pivotal trial RELIEVE-HF. Heart failure patients with any ejection fraction were admitted, but randomization was stratified across patients with either reduced or preserved ejection fraction. As noted, the trial failed to achieve primary endpoints around the reduction of heart failure events, but demonstrated a 45% reduction in adverse cardiovascular events for HFreF patients, and a higher rate of harm to those with HFpEF.

The clinical community remains positive about the potential for these devices, although not enough patients have been studied yet to make pronouncements. Both **Occlutech** (with its *Atrial Flow Regulator*) and **Alleviant** (which creates a shunt without leaving a device behind) are currently enrolling for equally large and robust clinical trials, so we can expect some clarification within the next five years or so.

While incumbents are focused on determining which kinds of heart failure patients respond to interatrial shunting, Brian Fahey, PhD, the co-founder, president, and CEO of interatrial shunt newcomer **Adona Medical**, believes that's not the only challenge, and that today's "one-size-fits-all" approach to interatrial shunts isn't likely to be broadly effective for such a heterogenous patient population. Further, current developers are challenged by the lack of a window into what, precisely, is happening with cardiac filling pressures as patients go about their lives. Adona Medical, profiled below, has designed its platform to address both shortcomings.

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Addressing late-stage heart failure and cardiogenic shock, **CorInnova** hopes to disrupt the space with a novel, physiological, and non-blood contacting device. The start-up faces the rigorous PMA pathway for a first-of-its-kind device, but its CEO believes that the patient population it is initially targeting is well defined and large, with more to follow. We interview CorInnova below.

Figure 3

Selected Heart Failure Monitoring Companies

Category	Selected Company Examples
Invasive monitoring of surrogates for cardiac pressure (predicting congestion)	Two FDA-cleared stand-alone products: Abbott (*CardioMEMS*), Edwards (*Cordella*) Diagnostic companions to implanted CRT or ICD devices: Medtronic (*TriageHF*), Boston Scientific (*HeartLogic*), Biotronik (*HeartInsight*) In development: Fire1, Vectorious
Noninvasive surrogates for cardiac pressure monitoring	Acorai (*SAVE* sensor), Analog Devices (*Sensinel*), Bodyport, Cardiosense (*Cardiotag*), Zoll (*Heart Failure Management System*)

Source: "HFSA Scientific Statement: Update on Device Therapies in Heart Failure," *Journal of Cardiac Failure*, September 10, 2024; *MedTech Strategist*