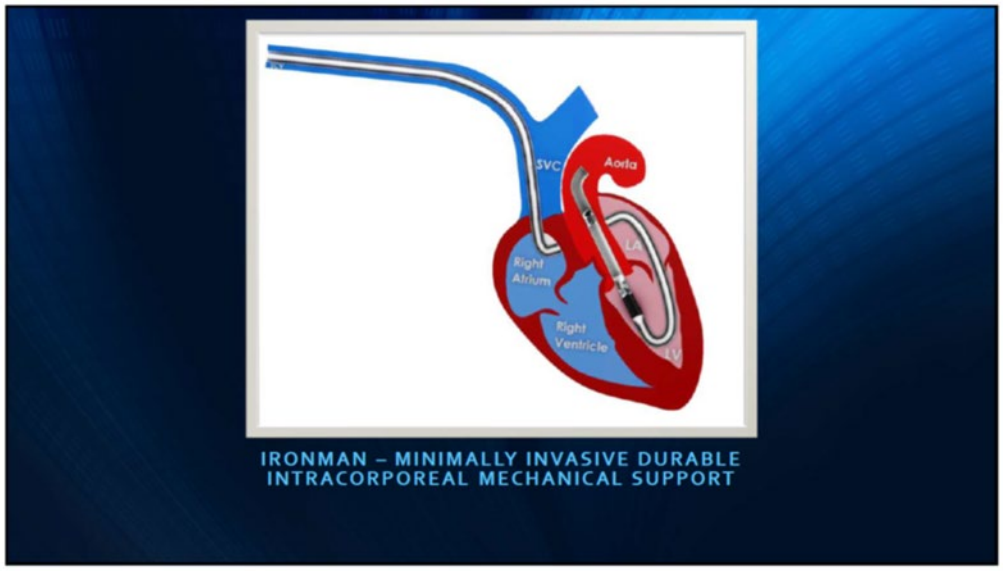
IRONMAN - Intermediate-term Restoration Of Normal Myocardial Activity in NYHA IV

The technology is an endovascular non-arterial left ventricular assistance device to provide up to 10L/min of flow for intermediate and long-term use. The proposed IRONMAN device addresses these needs with a 30F self-centering transaortic catheter featuring an axial flow impeller capable of delivering up to 10 L/min. The device is powered by a subcutaneous generator in the right chest with wireless charging. The patent is licensed from Washington University in St. Louis and the Veteran's Administration. There is an International Patent Application No. PCT/US2024/021079 titled "Mechanical Cardiac Support Device and Methods of Using Same" filed March 22, 2024 with priority to US Patent Application No. 63/491,585 filed March 22, 2023. There is a U.S. Patent Application No. 63/698,917 titled "Mechanical Cardiac Support Device and Methods of Using Same" filed September 25, 2024



The implantation involves transseptal puncture and advancement of the device via the mitral and aortic valves, guided by imaging. This design leverages venous access to accommodate large-caliber catheters, reducing pump speed and shear stress, thereby enhancing durability and minimizing hemolysis. The intracorporeal approach eliminates the need for sternotomy and supports patient mobility. Initial prototypes developed using CFTurbo and modeled with Simerics CAD software required high speeds (30,000–50,000 rpm) to achieve target flow, prompting ongoing refinements to optimize hemodynamics and reduce shear.

The IronMan device has already undergone initial design trials. It was initially tested for 10 L/min flow with a 21 Fr Caliber (7 mm size) design (Fig 1). This was tested in Newtonian and non-Newtonian fluid models. At physiologic pressures, very high RPMs were necessary to drive blood like fluids (30k-40k rpm). At these RPMs, significant shear stresses were noted, mimicking performance of similar smaller caliber devices. However, at these high RPMs, we anticipate significant hemolysis (blood breakdown) and thrombosis (clot formation), in addition to substantial wear and tear in the moving parts which may limit their tolerance in human subjects as well as durability.

Based on these issues, Ironman devices were redesigned to 30 Fr size (increase in diameter from 7mm to 10 mm). It was designed to be implanted via the subclavian vein, which is a large caliber vein in the body. This design was intended to deliver flows up to 10 L/min at 10, 000 rpm. Achieves predicted a flow of up to 10L/min at 11000 rpm and a 30-50 mmHg pressure head with blood in simulations. This design showed significantly reduced shear in simulation testing. The flow performance was similar to what was similar to what is seen with Heartmate 2 left ventricular assist device at similar rpm (Fig 2). This will favorably impact motor longevity and hemodynamic performance. This holds significant promise as an alternative support device to improve survival in current Stage D heart failure patients who are not candidate for heart transplant or surgical implantation of a LVAD. The Ironman device is intended to be a durable (yet reversible) support device that can be delivered via a catheter-based delivery, thus more tolerable in sicker patients. The device can be a destination therapy or a bridge to other advanced therapies allowing recovery / improvement in functional status of patients with advanced heart failure, which could allow them to become candidates for other advanced therapies including transplantation. This is currently an unmet need worldwide which the IronMan device can fill.

Heart failure is a clinical syndrome characterized by inadequate cardiac output to meet the metabolic demands of vital organs. Patients often progress through various stages, with Stage C representing symptomatic heart failure and Stage D denoting end-stage disease. At Stage D of heart failure, symptoms significantly impair daily life and lead to recurrent hospitalizations despite optimal medical therapy (Heidenreich et al., 2022). The prognosis for patients with Stage D heart failure is poor, with a median survival of less than two years. However, advanced therapies such as heart transplantation can extend survival to over 12 years. Durable mechanical circulatory support (MCS) devices like left ventricular assist devices (LVADs) serve as either destination therapy or a bridge to transplant. Unfortunately, many patients are ineligible for these interventions due to factors such as multiorgan failure, frailty, cardiac cachexia, or prior thoracic surgeries (Morris et al., 2021).

In the United States, approximately 6.2 million adults live with congestive heart failure (CHF), a number projected to exceed 8 million by 2030. CHF accounts for around 1.2 million hospitalizations annually, with 378,000 death certificates listing heart failure and 80,480 deaths directly attributed to it. Among Medicare beneficiaries, the incidence is about 30 cases per 1,000. Each year, nearly 40,000 to 50,000 patients experience acute cardiogenic shock, with in-hospital mortality rates around 30% and 50% of survivors dying within a year. Between 1987 and 2012, 26,943 heart transplants were performed for 40,253 patients in need, while over 25,000 patients received LVADs between 2006 and 2017. Despite these interventions, approximately 200,000 patients annually are classified as having refractory Stage D CHF, with 80,000 deaths per year. Of the estimated 50,000 patients with cardiogenic shock annually, only about 15,000 receive either a transplant or LVAD, leaving at least 25,000 patients at high risk of death without viable options.

Heart transplantation remains limited by donor availability, with only about 4,000 transplants performed annually and an average wait time of three months. Thirty percent of transplant recipients are already on MCS. Eligibility for advanced therapies is restricted by factors such as age, frailty, peripheral arterial disease (PAD), and multiorgan dysfunction. Similarly, LVAD candidacy is constrained by comorbidities like advanced pulmonary disease and prior thoracic surgeries. Temporary MCS options

such as intra-aortic balloon pumps (IABP), TandemHeart, and Impella devices are used in select cases but are not suitable for long-term ambulatory use. IABPs offer modest flow augmentation (1–1.5 L/min) and are limited by declining efficacy over time. TandemHeart provides up to 5–7 L/min of flow via transseptal access but requires large-bore cannulation and is associated with risks of arterial ischemia. The Impella 5.5, an intracorporeal axial flow pump, delivers up to 5 L/min but poses challenges related to arterial access, hemolysis, and high-speed operation (30,000–50,000 rpm), with no randomized controlled trials demonstrating mortality benefit.

Veterans are particularly affected due to older age at presentation, higher prevalence of tobacco-related diseases, and limited access to transplant centers and cardiothoracic surgery within the VA system. Social barriers that hinder civilian care may be mitigated by federal support, but therapeutic options remain limited. These include inotropic therapy, palliative LVAD implantation, and hospice care.

Next Steps

1. Stage 1: Fabrication of a working model and ex-vivo testing
2. Stage 2: In-vivo testing in pig model
3. Stage 3: In-human trials for palliation in current Stage D heart failure patients too sick for current advanced therapies
4. Stage 4: Head-to-head trials comparing performance against currently available durable LVADs such as Heart Mate III

Stage 1: The next stage of development includes starting catheter fabrication for in vitro testing with liquid and blood testing. The intention is to address design improvements for better in vivo performance. The catheter is intended to be implanted via subclavian access and then to be advanced across the interatrial septum into the left atrium, then to the left ventricle with the outlet in the aorta. This will require an interatrial septum and aortic anchor to keep the device centers. These are intended to be balloon controlled so the device can be explanted as needed. Stage will test designs axial flow pump controller and power plans. Stage 1 will also test flow (CF/PF) dynamics and impact on motor longevity and hemodynamic performance.

We are planning an NIH FastTrack proposal for these two stages for a January submision.

Fig 1. Initial designs for Ironman device for mechanical circulatory support in refractory Stage D heart failure.

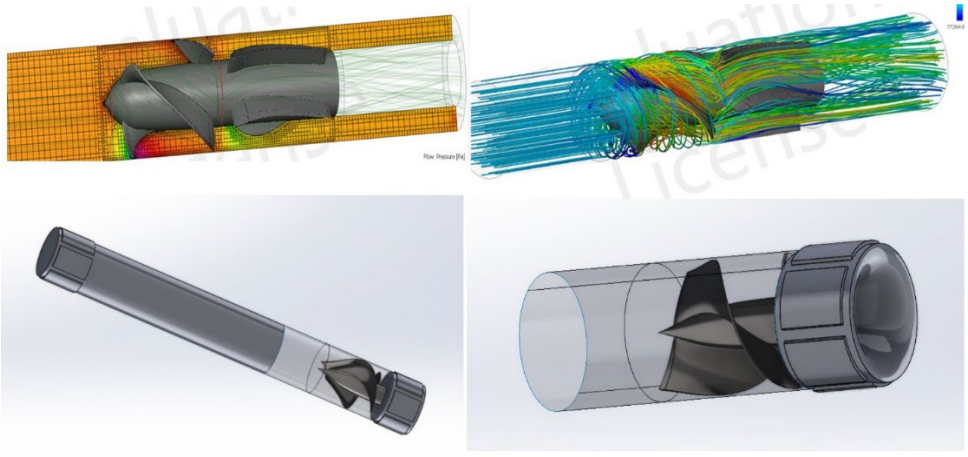
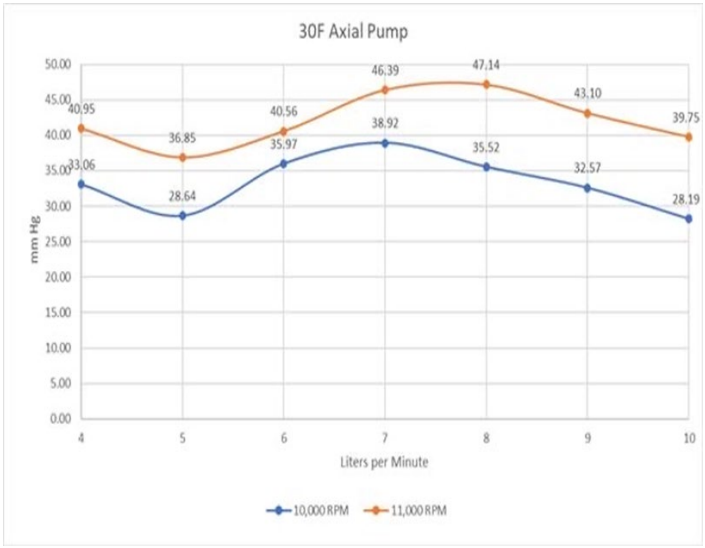
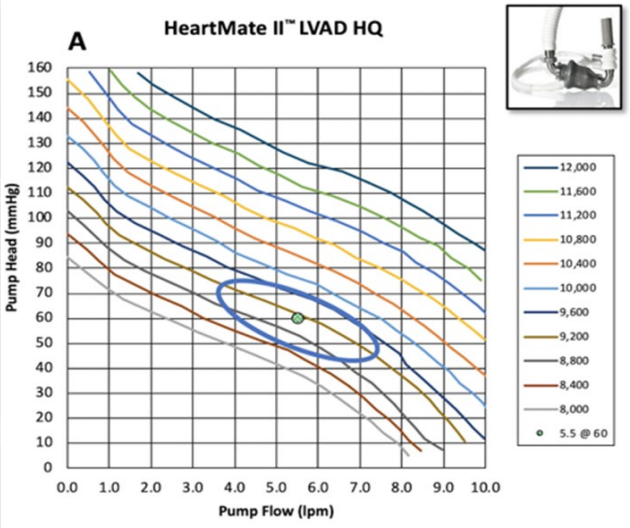


Fig 2. Flow dynamics of Ironman 30 Fr caliber device in simulations, compared to HeartMate II left ventricular assist device.





We are seeking license and collaboration opportunities with industry players and Angel / VC groups.

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