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EDITORIAL

Totally Implantable Artificial Heart: Still a Major Challenge

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The first mechanical heart was placed by Liotta and Cooley in 1969 in a dying patient at the Texas Heart Institute in Houston as a 2 ½-day bridge for a transplant, albeit the patient died 32 hours after transplantation.¹ Years later (1982) a totally implantable artificial heart (model Jarvik-7) was permanently implanted in a patient by DeVries et al at the University of Utah Medical Center in Salt Lake City, Utah, USA and the patient lived for 112 days.² Subsequent attempts of implantation of a total artificial heart (e.g. CardioWest/SynCardia models) have limited its use as a bridge to transplantation, like the left- or bi-ventricular assist devices (VADs).³⁻⁷ The SynCardia model (SynCardia Systems Inc., Tuscon, AZ) has been approved for compassionate use by the Food and Drug Administration (FDA) for patients with end-stage biventricular heart failure as a bridge to transplantation since 1985 and has had FDA approval since 2004.³⁻⁵ The SynCardia™ total artificial heart, weighing 180 g, providing a stroke volume of 70 cc, is a pneumatically driven, pulsatile system capable of flows of >9L/min. It is indicated for temporary use as a bridge to transplantation in patients with end-stage non-reversible bi-ventricular failure. Currently, the recipients of this device are hospital-

bound and attached to a large pneumatic driver. The bridge to transplantation rate has been ~80% in >1100 implants. In 2010, the FDA gave conditional approval for an Investigational Device Exemption clinical study of the portable Freedom driver (SynCardia) (www.syncardia.com).

Researchers and investigators are still exploring ways to develop a safe, effective mechanical replacement for the human heart. To date, total artificial hearts are still plagued with major problems, including thromboembolism, bleeding, infection and need for portable drivers.⁸⁻¹¹ In contrast, ventricular assist devices (VADs)—partial artificial hearts—have had a much more successful course and are currently in widespread use, despite similar drawbacks and limitations (Table 1).^{6,7,12-14} Thoratec's HeartMate II was the first continuous-flow left-VAD approved by the FDA for transplant-ineligible heart-failure patients (January 20, 2010) as a destination therapy. The FDA originally approved HeartMate II as a "bridge to transplant" in 2008; the device has been available in Europe for both indications since November 2005. Other miniaturized VADs approved as bridge to transplant include the HeartWare® (CE mark since 2009 and FDA approval since 20/11/2012), and CircuLite's SYNERGY® Micro-pump systems (CE mark since 5/9/2012).

Biventricular support can be achieved using paracorporeal biventricular assist devices (BiVADs), the total artificial heart (TAH), and implantable VADs.^{3-5,8,14,15} However, one needs to understand the difference among these various devices. The total artificial heart offers biventricular “replacement”, rather than “assistance”, as

the device is implanted orthotopically after excision and removal of the entire ventricular myocardium and all four native valves.^{3-5,8} In contrast to patients with Bi-VADs, patients with the total artificial hearts have no requirements for postoperative inotropic support, are not afflicted by arrhythmias and have no inflow/ outflow cannulae-related complications. The recent development of a portable drive may facilitate hospital discharge. Thus, the total artificial heart is an effective therapeutic option for the treatment of patients dying of heart failure who are not suitable candidates for left VADs and are in need of biventricular support. Patients who may have a chance for recovery should not be considered candidates for the artificial heart. Currently, the main difficulty in applying this device as a destination therapy is its lack of portability, limited durability and questionable safety.

Device implantation is not risk-free. Perioperative and postoperative bleeding, thromboembolic events and infections are still plaguing all devices.^{9,10} The continuous flow pumps, heralded as a major breakthrough, may increase the risk of gastrointestinal bleeding and have been shown to affect von Willebrand's factor.¹¹ Further limitations of the LVADs of the continuous flow pump type include the acute risk of right heart failure and the long-term morbidity of right heart dysfunction in a significant number of patients who receive LVADs. Thus, there has emerged a renewed interest in developing a continuous- (non-pulsatile) or axial-flow (which restores some pulsatility) biventricular support system and in the use of a total artificial pulsatile heart in order to address the morbidity associated with right heart failure.^{8,14,15}

The growing availability and hopefully a diminishing cost¹³ of mechanical circulatory support devices will allow for more widespread use than that offered by heart transplants with the limited supply of donor hearts and will allow for the implementation of clinical trials and technology improvements at a scale that cannot be attained by heart transplantation. Thus, we may see a proliferation of complex, more miniaturized implantable devices and more durable and sustainable with each generation.

However, despite advances in device technology, the dream will remain alive for a totally implantable, self-contained and energy-sufficient device, which currently still remains a major challenge. Recently (December 18, 2013), a glimpse of real hope was offered by French Dr Alain Carpentier whose team implanted a new fully implantable artificial heart manufactured by Carmat, in a 75-year old patient at the Georges Pompidou European Hospital in Paris (<http://www.carmatsa.com/>). The device comprises two chambers, each divided by a membrane that holds hydraulic fluid on one side (http://en.wikipedia.org/wiki/Artificial_heart). A motorized

pump moves hydraulic fluid in and out of the chambers, and that fluid causes the membrane to move; blood flows through the other side of each membrane. The blood-facing side of the membrane is made of tissue obtained from a sac that surrounds a cow's heart, to make the device more biocompatible. The Carmat device also uses valves made from cow heart tissue and has sensors to detect increased pressure within the device. That information is sent to an internal control system that can adjust the flow rate in response to increased demand, such as when a patient is exercising. This distinguishes it from previous designs that maintain a constant flow rate. The device weighs 900 grams; it requires the patient to carry around an additional Li-Ion battery. The device will be used as destination therapy; its projected lifetime is estimated around 5 years (230 million beats).

CONCLUSION

A fully implantable autonomous artificial heart without any external components remains a major challenge. Apart from other major technical demands, it is dependent on the capacity of the implanted battery, which should be charged transcutaneously.^{16,17} However, this technology is still in the beginning; MIT scientists have founded a company, WiTricity (Watertown, MA), which has partnered with Thoratec Corp. (Pleasanton, CA) to develop a fully implanted left-VAD (www.mddionline.com/article/wireless-power-medical-devices). For now, the availability of the Freedom® portable driver that powers the SynCardia temporary Total Artificial Heart will allow stable patients to live life at home, while smaller devices are going to be available (e.g. the 50cc version in addition to the 70cc SynCardia temporary Total Artificial Heart) to fit women and younger and smaller stature patients. Finally, the first-in-man implantation of Carmat's bioprosthetic artificial heart is most encouraging (<http://www.carmatsa.com/>).

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Table 1. Currently Used Ventricular Assist Devices (VADs) & Totally Implantable Artificial Heart Devices

Device (Company)	Configuration/ Function	Flow Type	Weight	CO	Use	Placement/ Direction	Flow	Longevity
Berlin Heart Excor® VAD (Berlin Heart)	LVAD/RVAD/ BiVAD	Pulsatile	?	SV 10- 60 ml *	BTT	Extracorporeal		~3y
Berlin Heart Incor® VAD (Berlin Heart)	LVAD	Continuous flow	200 g	→6 L/min	BTT / DT	Intracorporeal		→6y
Jarvik 2000 (Jarvik Heart)	LVAD	Continuous flow	85 g	6 L/min	BTT	Intracorporeal / LV → Desc or Asc Ao		→8y
HeartMate II (Thoratec)	LVAD	Continuous flow	375 g	→10 L/min	BTT/ DT	Intracorporeal/ LVA →AscAo		2-8y
DuraHeart (Terumo)	LVAD	Continuous flow	540 g	2-9 L/min	BTT/ DT	Intracorporeal/ LVA →AscAo		≥4y
HeartAssist 5/** DeBaKey (MicroMed/ ReliantHeart)	LVAD	Continuous flow	92 g	→10 L/min	BTT/ DT	Intracorporeal/ LVA →AscAo		→6y
HeartWare HVAD (HeartWare)	LVAD	Continuous flow	160 g	→10 L/min	BTT/ DT	Intracorporeal/ LVA →AscAo		→7y
Synergy (CircuLite)	LVAD	Continuous flow	< 25 g	2-4 L/min	BTT/ DT	Intracorporeal/ LA →Subclavian artery		→2y
MiFlow (WorldHeart / HeartWare)	LVAD	Continuous flow	< 30 g	→ 6 L/min	BTT/ DT	Intracorporeal / LVA →DescAo		?
SynCardia TAH-t (Syncardia) ***	TAH	Pulsatile	180 g	≥ 9 L/min	BTT	Intracorporeal/ orthotopic		~4 y
Carmat (Carmat)	TAH	Pulsatile	900 g	3-9 L/min	BTT / DT	Intracorporeal / orthotopic		~ 5 y
AbioCor I / II **** (AbioMed)	TAH	Pulsatile	1090g (I) /700g (II)	≥ 9 L/min	BTT	Intracorporeal/ orthotopic		1-2y (model I)/ ~ 5y (II)

AscAo = ascending aorta; BTT = bridge-to-transplant; CO = cardiac output; DT = destination therapy; HTx = heart transplant; LA = left atrium; LVA = left ventricular apex; LVAD/RVAD = left/right VAD; SV = stroke volume; TAH = total artificial heart

* pediatric versions available

** remote monitoring capabilities

*** an evolution of the Jarvik 7 model, renamed CardioWest and then SynCardia (since 2010)

**** battery is charged through the skin with a special magnetic charger. Energy from the external charger reaches the internal battery through an energy transfer device called transcutaneous energy transmission, or TET. An implanted TET device is connected to the implanted battery. An external TET coil is connected to the external charger.

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