

The CARMAT total artificial heart

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HISTORICAL PERSPECTIVES

Research into the subject of total artificial heart (TAH) began in the USA in 1963 under the impetus of the American Congress; however, it soon hit the snags of haemocompatibility, autoadjustment of operation to the patient's physiological needs, miniaturization, portable energy and reliability in the long run.

Michael DeBakey was the first to use an external heart pump successfully in a patient as a left ventricular bypass pump in 1966. The first TAH, called Liotta-Heart, was implanted by Denton Cooley in 1969 in Houston, TX, USA. The 47-year old male recipient was bridged for 65 h until heart transplantation was possible. This first TAH was developed by the Argentinian surgeon Domingo Liotta who was hired at Baylor College of Medicine in Houston, Texas as Director of the Artificial Heart Program by Michael DeBakey in 1961 and returned to his homeland later. Finally it remained unclear how many Liotta-TAHs were implanted.

The next TAH, called Jarvik-7, was implanted in 1982 to a retired dentist. The patient survived 112 days. The Jarvik-7 heart led to a remarkable reaction in the media. Meanwhile the original Jarvik-7 heart was further developed, named CardioWest and finally placed on the market under the name Syncardia TAH. The Syncardia TAH has two pneumatically driven ventricles, separated from each other and with two mechanical valves each. It was originally implanted mainly in Europe (France and then Germany). In 2004, the device was approved by the FDA as a bridge to transplant, allowing several US centres to implant the device. Owing to the introduction of portable drivers in 2010, patients could now be discharged home and the utilization of the Syncardia TAH increased. Over 30 years, more than 1300 were implanted. The company received a humanitarian device exemption to test its TAH for destination therapy in 2012, but has not yet begun clinical trials for this indication. The patient who lived the longest time on the Syncardia TAH was successfully bridged to heart transplantation after 4 years of support. The Syncardia TAH has ventricles of 70 ml, which does not fit in smaller women and adolescent patients. Meanwhile, Syncardia started to develop a smaller version with 50 ml ventricles.

The AbioCor[®] TAH was developed by the company AbioMed. It was the world's first fully implantable and completely self-contained artificial heart. The internal battery is charged by a transcutaneous energy transfer (TET) system. A 71-year old man survived for 17

months with the AbioCor TAH. A feasibility study in fourteen patients and the end-point of 60-day survival led to an initial rejection by the FDA circulatory system devices advisory panel. In 2006, the FDA approved the AbioCor TAH as a humanitarian use device because of its limited market for patients ineligible for transplantation. The device has since been implanted according to our knowledge in one case (2009).

THE CARMAT TAH

Development of the CARMAT TAH began in 1993 in Paris by a medical team led by Alain Carpentier in collaboration with an engineering team from Matra Defense, a subsidiary of Airbus Group (then EADS). In 2008, a company (CARMAT SAS) was founded to accelerate development and manufacturing of the prosthesis, with funding from venture capital, the French Innovation Agency and from an Initial Public Offering in 2010 (CARMAT SA).

The CARMAT TAH contains two chambers, each of which are separated by a membrane into a blood compartment and a fluid compartment (www.carmatsa.com). This viscous fluid, put in motion by two electro-hydraulic pumps, actuates the membranes, producing pulsatile flow. Pressure sensors and electronics that drive the system and adapt to the patient's needs are embedded in the prosthesis. Biological valves are placed at the inlets and outlets of the ventricles. The TAH is connected to the atria with bioprosthetic suture flanges; Dacron outlet conduits are sutured onto the aorta and pulmonary artery. The device is partially covered by a flexible compliance bag that contains the actuating fluid (Fig. 1). A percutaneous driveline provides power to the TAH and retrieves information on device performance. In the current configuration, the driveline is connected to a hospital console.

What distinguishes the CARMAT TAH from the existing artificial hearts and what are the challenges?

The blood-contacting surface of the membrane is bioprosthetic material—processed bovine pericardial tissue—similar to the biological valves developed by Carpentier in the early 1980s [1, 2].

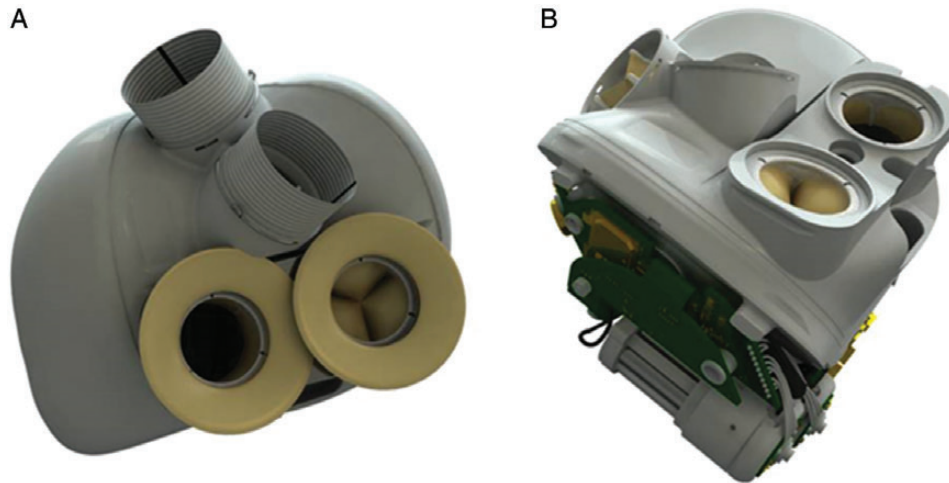


Figure 1: CARMAT TAH. (A) Compliance bag surrounding the prosthesis; atrial suture flanges and ejection conduits. (B) Partially open view of embedded electronics and motor-pump units.

The intended benefit of these bioprosthetic materials is improved haemocompatibility, potentially reducing the risk of bleeding/thrombosis and the need for prolonged anticoagulation [3]. The challenge is the long-term durability of the membranes and valves in this application.

The internal electro-hydraulic actuation of the membranes eliminates the need for an external actuator (such as Syncardia's pneumatic drivers) and, important from a quality-of-life perspective, produces no audible noise.

The device uses a control algorithm that responds to changes in preload and afterload, measured by the pressure sensors in the ventricles. The resulting blood flow ranges from 2–9 l/min, depending on the patient's needs. This is also a potential improvement in the quality of life.

The sensors, electronics and microprocessor that regulate the system are embedded inside the prosthesis. While this might reduce the risk of user-interface errors, failing components cannot be replaced without explanting the device.

The prosthesis has been designed to mimic the shape of the natural heart. With the volume of the ventricles (65 ml each), the actuating liquid and the embedded components, the displacement volume is at least 750 ml. The company provides a virtual anatomical fit tool to assist in selecting patients who have enough space in the thoracic cavity. Retrospective studies of 115 thoracic CT scans from patients with cardiac pathologies demonstrated a virtual fit in 86% of male patients but only 14% of females (data presented at the Annual Conference of the French Society of

Cardiovascular and Thoracic Surgery, Lyon, 2011). For a wider use of this TAH, a miniaturized version would be needed [4].

Based on preclinical verification and validation studies, the French National Agency for Medicines and Health Products Safety (ANSM) authorized a feasibility study on 4 patients in 2013. The first implantation took place in December 2013, in a 76-year old man ineligible for heart transplant. The first experience in man with this bioprosthetic TAH will be communicated after completion of the clinical trial.

Conflict of interest: Paul Mohacsi is a member of the scientific advisory board of CARMAT SA. He does not receive a salary or any financial support. Pascal Leprince is a member of the adverse event committee of CARMAT's feasibility study.

REFERENCES

- [1] Ménard J. Keys to the success of the CARMAT project? *Med Sci (Paris)* 2014;30:204–5. [Article in French]
- [2] Carpentier A. Lasker Clinical Research Award. The surprising rise of non-thrombogenic valvular surgery. *Nat Med* 2007;13:1165–8.
- [3] Jansen P, van Oeveren W, Capel A, Carpentier A. In vitro haemocompatibility of a novel bioprosthetic total artificial heart. *Eur J Cardiothorac Surg* 2012;41:e166–72. .
- [4] Leprince P, Bonnet N, Varnous S, Rama A, Léger P, Ouattara A *et al.* Patients with a body surface area less than 1.7 m² have a good outcome with the CardioWest Total Artificial Heart. *J Heart Lung Transplant* 2005;24:1501–5.