ADVANCES IN CARDIAC ARRHYTHMIAS AND GREAT INNOVATIONS IN CARDIOLOGY XXVII GIORNATE CARDIOLOGICHE TORINESI



ActisDato RobertoBosio artificial heart





Malcolm Bell, Usa Martin Borggrefe, Germany Amir Lerman, Usa Jean François Leclercq, France Dipen Shah, Suisse

Organization Committee Carlo Budano, Italy Davide Castagno, Italy *Torino, 23-24 ottobre 2015*

TURIN

and

The

First Artificial heart

Sebastiano MARRA, FESC

Luca CHECCO, MD



ADVANCES IN CARDIAC ARRHYTHMIAS and GREAT INNOVATIONS

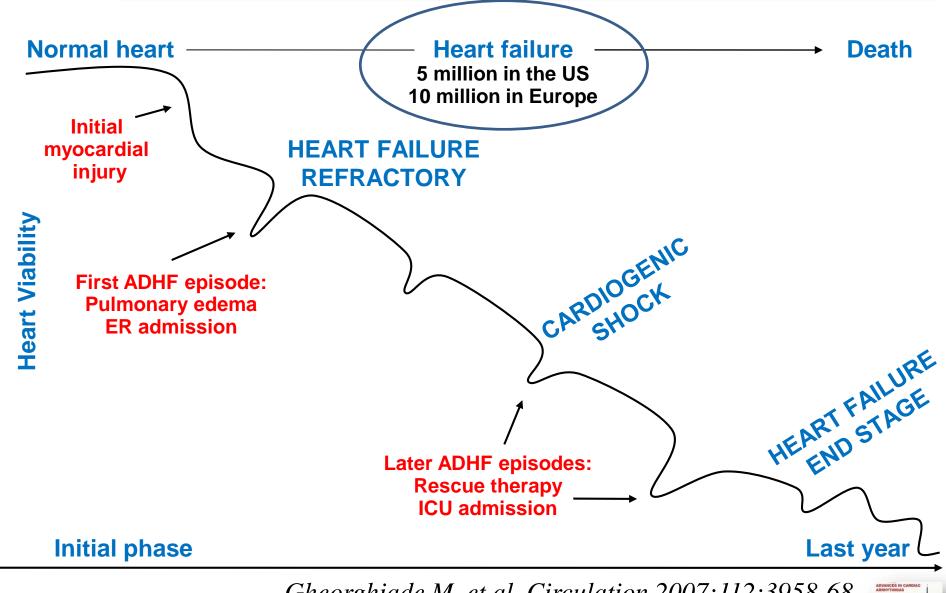
IN CARDIOLOGY

XXVII GIORNATE CARDIOLOGICHE TORINESI

Fiorenzo Gaita Sebastiano Marra

Turin October 23-24, 2015 Centro Congressi Unione Industriale di Torino

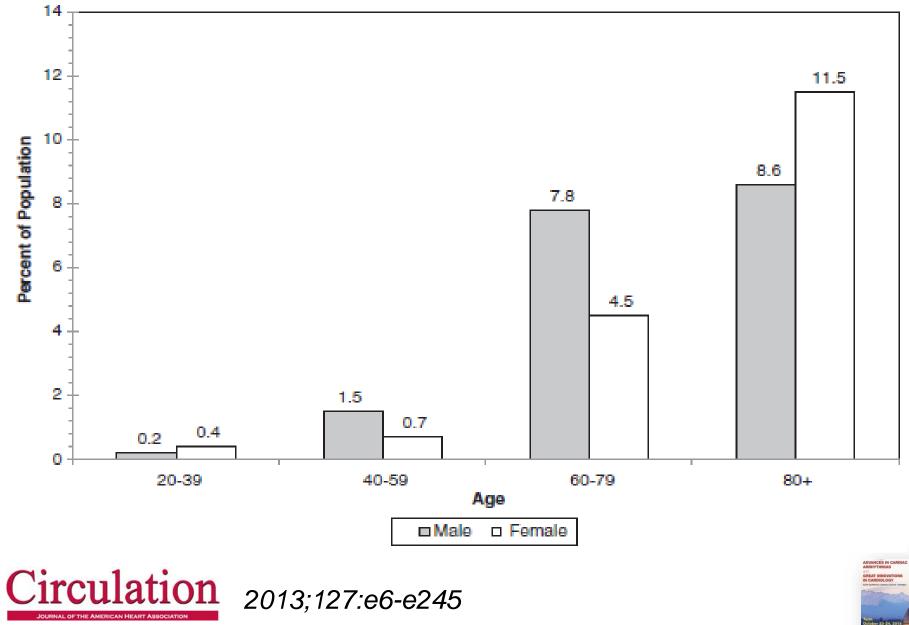
Heart Failure evolution



Gheorghiade M, et al. Circulation 2007;112:3958-68



Heart Failure population



Beyond the NYHA IV: INTERMACS risk profiles

INTERMACS Levels of Limitation at the Time of Implantation and the Time Frame of Need for Consideration of MCS

INTERMACS Profile Level	Status	Time Frame
1	Critical cardiogenic shock	Hours
2	Progressive decline	Days to week
3	Stable but inotrope dependent	Weeks
4	Recurrent advanced HF	Weeks to few months if baseline restored
5	Exertion intolerant	Weeks to months
6	Exertion limited	Months, if nutrition and activity maintained
7	Advanced NYHA class	

Stevenson et al.¹¹ Copyright © 2009, Elsevier.

LW Stevenson, FD Pagani, JB Young et al.

INTERMACS profiles of advanced heart failure: the current practice, J Heart Lung Transpl. 2009;28:535-41



HOW Heart Failure population?

EUROPEAN SOCIETY OF CARDIOLOGY European Heart Journal (2006) 27, 1207-1215 doi:10.1093/eurheartj/ehi845 Clinical research Heart failure

Nationwide survey on acute heart failure in cardiology ward services in Italy

Luigi Tavazzi^{1*}, Aldo P. Maggioni², Donata Lucci², Giuseppe Cacciatore³, Gerardo Ansalone⁴, Fabrizio Oliva⁵, and Maurizio Porcu⁶ on behalf of the Italian survey on Acute Heart Failure Investigators

Nationwide, prospective, observational study setting 206 cardiology centres with intensive cardiac care units. During 3 months, 2807 patients were enrolled with de novo acute HF (44%) or worsening chronic HF (56%)

The HF profiles were classified by the investigators as:

Cardiogenic shock in

7.7% patients

•Acute pulmonary oedema in

49.6% patients

• Worsened NYHA functional class (III and IV) in 42.7% patients



INTN

- 100.000 European/years, suffering from severe CHF, need new hearts
- Only 2.000 patients/year receive heart transplant
 MANY PATIENTS DIE WAITING FOR A NEW HEART
- A suistable alternative to donor hearts could prolong thousands of lives



ESC 2014

The systems of mechanical assistance to the circle MCS - Mechanical Circulatory Support

implantable type like, begin to be developed from the '60s

TAH: Total Artificial Heart

assistance systems completely replacing orthotopic native heart

VAD: Ventricular Assist Device assistive devices only for the ventricles

 Paracorporeal Pneumatic Pulsatile Uni- or Biventricular 	 Implantable Electric Pulsatile Large Multiple moving parts 	 Implantable Electric Continuous flow Axial design Smaller Single moving part 	 Implantable Electric Continuous flow Centrifugal design Smaller Bearingless 	 Implantable Electric Continuous flow Axial design Smaller Partial support
1150 g	800 g	400 g	200 g	90 g

Henning LM, Mueller J, Spiegelsberger S et al, Long-term circulatory support as a bridge to transplantation, for recovery from cardiomyopathy, and for permanent replacement. Eur J Cardiothorac Surg 1997;11:S18-S24

MCS: why yes?

TAH or VAD are used

As

bridge the time

to a heart transplant

or

As

a life extending

device





Heart Failure population





2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Clyde W. Yancy, Mariell Jessup, Biykem Bozkurt, Javed Butler, Donald E. Casey, Jr, Mark H. Drazner, Gregg C. Fonarow, Stephen A. Geraci, Tamara Horwich, James L. Januzzi, Maryl R. Johnson, Edward K. Kasper, Wayne C. Levy, Frederick A. Masoudi, Patrick E. McBride, John J.V. McMurray, Judith E. Mitchell, Pamela N. Peterson, Barbara Riegel, Flora Sam, Lynne W. Stevenson, W.H. Wilson Tang, Emily J. Tsai and Bruce L. Wilkoff

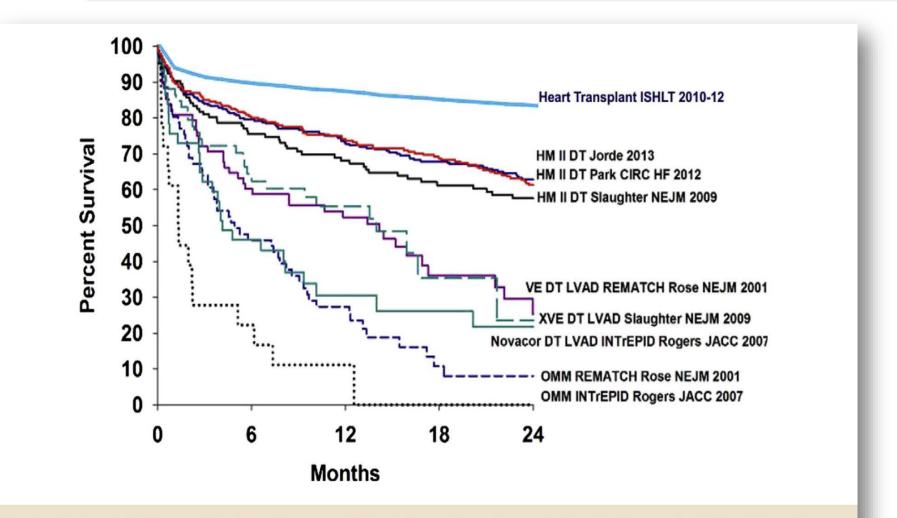
Circulation. 2013;128:e240-e327; originally published online June 5, 2013;

Best implanted MCS before

- Impairment of the clinical condition, according to the INTERMACS Classification
- Impairment of renal function
- Occurrence of pulmonary hypertension
- Impairment of RV function



MCS: why yes?



Survival Rates in Trials and Registry Reports of Heart Transplantation and Chronic Mechanical Circulatory Support Lifetime Therapy (DT)



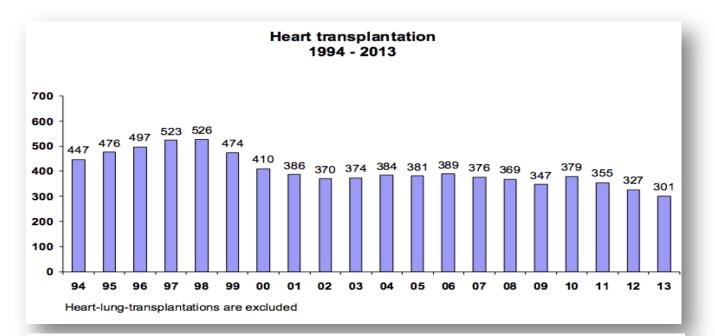
SG. Drakos et al, JACC 2014; 63 (17): 1758-62

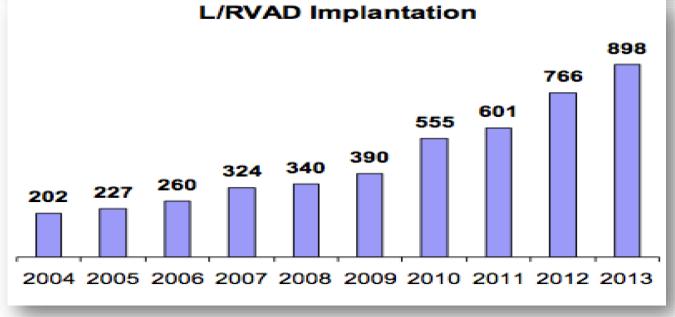
- Post MCS: 75% patients are able to walk and about 60% are able to walk 100ft long after two weeks following the implantation.
- The estimated amount ranges from a low \$100,000 to a high \$300,000 instead of \$500,000 for medical cost of CHF



JACC 2013

Heart Failure population









Hermann Reichenspurner president ISHLT, 2014-15

AATS Annual Meeting Toronto (CAN) 26-30/04/14





JACC JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Volume 65, Issue 23, June 2015 >

The Present And Future: State-of-the-Art Review | June 2015

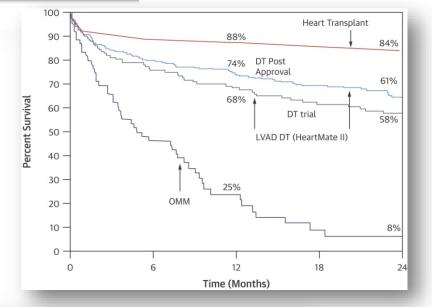
Left Ventricular Assist Devices

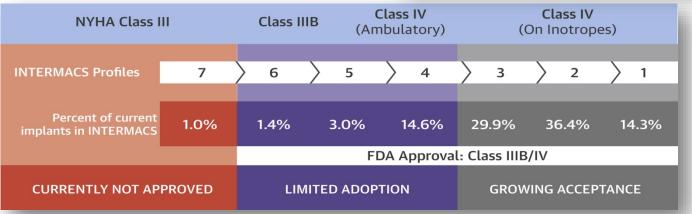
A Rapidly Evolving Alternative to Transplant

Commentary by Dr. Valentin Fuster

Donna Mancini, MD; Paolo C. Colombo, MD

J Am Coll Cardiol. 2015;65(23):2542-2555. doi:10.1016/j.jacc.2015.04.039







Piemonte CHF population



Programma Nazionale Esiti – PNE

Edizione 2014

Piemonte population	4,424 milions
Prevalence of CHF	2.54%
Potential CHF patients INTERMACS 7 -> 1	111.264
Real CHF patients: INTERMACS 6 -> 1	11.880
Hospitalizations	14.369
Potential advance INTERMACS 3 -> 1	700 ?
INTERMACS 2 -> 1	60-70 ?

Piemonte Heart Transplant Program

Waiting List patients	58
Active list	38
Work-up list	20
mean years/waiting heart transplant:	
Piemonte MCS implanted	

Piemonte Hearts tranplant			
2010	total 26	adult 22	pediat 4
2011	28	26	2
2012	10	9	1
2013	19	16	1
2014	27	22	5
2015	12	9	3



1800: the beginning of cardiac artificial heart

EXPÉRIENCES

SUR

LE PRINCIPE DE LA VIE,

NOTAMMENT

SUR CELUI DES MOUVEMENS DU COEUR,

ET SUR LE SIÈGE DE CE PRINCIPE ;

SUIVIES du RAPPORT fait à la première classe de l'Institut sur celles relatives aux mouvemens du cœur.

PAR M. LE GALLOIS,

Docteur en médecine <u>de la Faculté de Paris</u>, membre adjoint de la société des professeurs de cette Faculté, membre de la société Philomatique, médecin du Bureau de bienfaisance de la division du Panthéon.

> Unde anima atque anime constet natura videndum. LUCRRT. lib. I, v. 152.

Ornées d'une planche gravée en taille-douce.

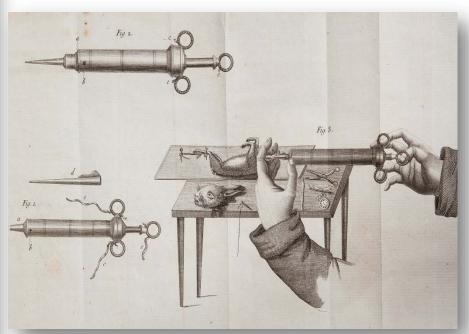
A PARIS,

Chez D'HAUTEL, libraire, rue de la Harpe, nº 80, près le collége de Justice.

1812.

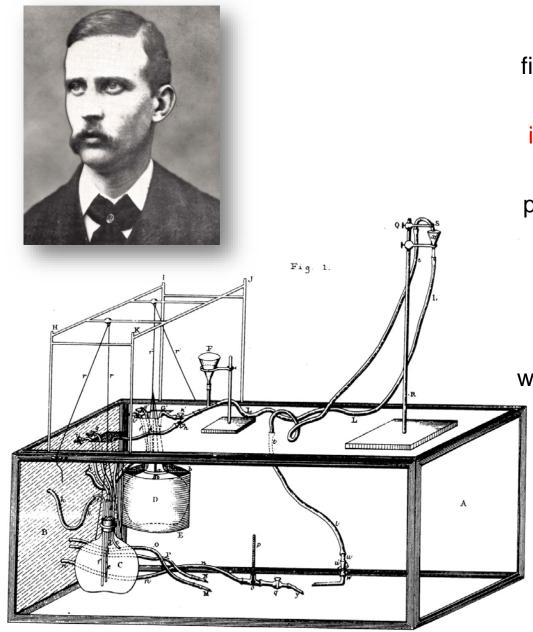
In 1812 Julien-Jean Cesar Le Gallois (1770-1814) said that

"... if we could replace the heart with a kind of injection of arterial blood, it would be possible to keep alive indefinitely any part of the body..."





1800: the beginning of cardiac artificial heart



In 1880, **Henry Martin** (1848-1896), first british professorship of physiology at John's Hopkins University (USA), introduced its own system of isolated perfusion of the heart and lungs, principles of which are still used today with the CEC (heart-lung machine).

He developed the first isolated mammalian heart lung preparation which Starling later used to great effect

Martin's own scientific career was curtailed around 1893



1900's: the new era

In 1928 **HH Dale** and **EHJ Schuster** in England planned their first diaphragm pump.

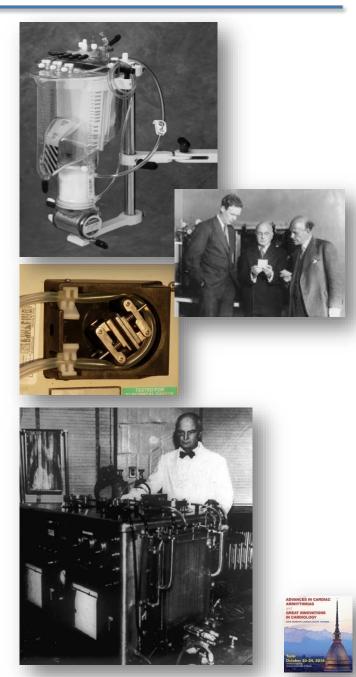
It had been studied in order to replace the function of the both cavity of the natural heart and to provide a complete circulation in an experimental animal.

In 1927 **C Lindbergh**, along with **A Carrel** developed a pump oxygenator.

In 1934 **M DeBakey** invented a rotary pump or "roller" yet still used in all heart-lung machines.

In 1935 **A Carrel** developed a pump oxygenator ; the pump for perfusion attracted the attention of journalists who called it " robots heart" or "heart of glass ".

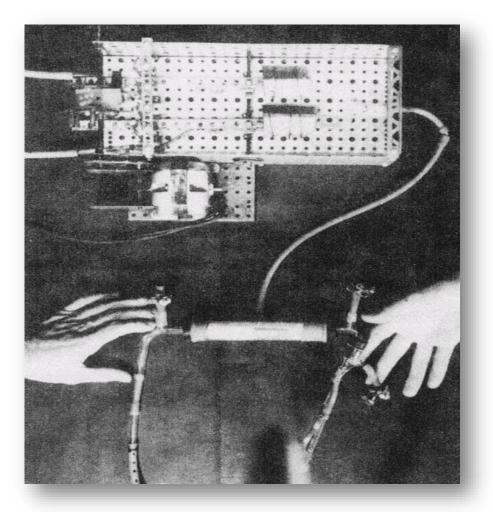
In 1937 **J Gibbon** began working on his heart-lung machine that was introduced into clinical practice in 1953.



1940's: other projects became to go

In 1949, a precursor to the modern artificial heart pump was built by doctors **W Sewell** and **W Glenn** of the Yale School of Medicine using an Erector Set, assorted odds and ends, and <u>dime-store toys</u>.

The external pump successfully bypassed the heart of a dog for more than an hour.



The assembled pump attached to the cam-lever unit driven by a small Erector[™] set motor which opens the suction and pressure lines alternately, for the purpose of forcing blood through and out of the pumping chambers. The hand on the right supports the outflow end of the pump and attached pulmonary cannula while the hand on the left supports the inflow end of the pump and the single atrial cannula. In other experiments, the right atrium was isolated by removing the systemic venous return

with a single venae cavae cannula.



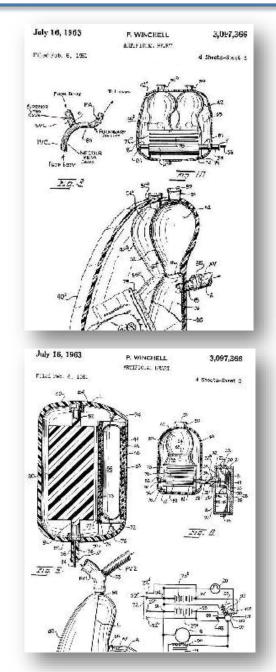
1940's: other projects became to go

P Winchell invented an artificial heart with the assistance of **H Heimlich** (the inventor of the Heimlich maneuver) and held the first patent for such a device.

The University of Utah developed a similar apparatus around the same time, but when they tried to patent it, Winchell's heart was cited as prior art.

The university requested that Winchell donate the heart to the University of Utah, which he did. There is some debate as to how much of Winchell's design **R Jarvik** used in creating Jarvik's artificial heart.

The basic principle used in Winchell's heart and Jarvik's heart is exactly the same." Jarvik denies that any of Winchell's design elements were incorporated into the device he fabricated for humans which was successfully implanted.

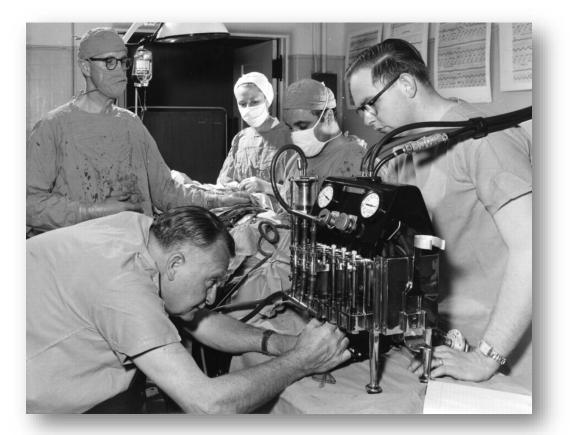




1950's: come the Dodrill–General Motor machine

The Dodrill–GMR machine was the first operational mechanical heart successfully used while performing open heart surgery.

It was developed by **F.D. Dodrill**, a surgeon at Harper University Hospital in Detroit, and General Motors Research.



On July 3 1952,

Dodrill used the machine to bypass Henry Opitek's left ventricle, a man 41yo suffering from shortness of breath at Harper University Hospital in Michigan, for 50 min. while he opened the patient's left atrium and worked to repair the mitral valve.

The Dodrill–GMR heart machine, considered by some to be the first operational mechanical heart was successfully used while performing heart surgery.

The machine performs the functions of the heart, allowing doctors to detour blood and stop the heart of a patient during an operation.

The machine is external of the body and is only used during an operation.



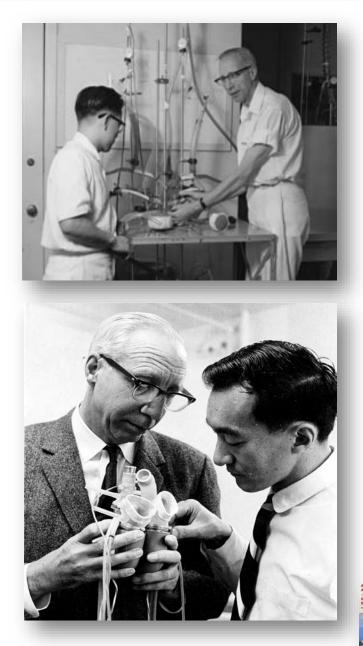
1950's: come the first experimental artifical heart

In 1957 **T Akutsu** (1922-2007) and **W Kolff** (1911-2009) at Cleveland Clinic, proposed for the first time a project of totally artificial heart by placing two compact pumps in the chest of a dog instead of the heart.

In the first experiment the artificial heart was made of polyvinyl chloride and was driven by an extracorporeal source of compressed air.

The dog survived for about 90 min.

In 1967 Kolff left Cleveland to Salt Lake City, founded the Division of Artificial Organs at the Utah University, where he was able to combine medical research to engineering disciplines .



Pioneer experience

Pioneering experiments conducted in the 60's by Liotta, DeBakey, Cooley and Hall lead to the emergence in the 70's to a line of medical research of systems for mechanical assistance into the general circulation, to support to the work of the native heart .



Liotta D, Crawford ES, Cooley DA, DeBakey ME, De Urquia M, Feldman L. Prolonged partial left ventricular bypass by means of an intrathoracic pump implanted in the left chest. Trans Am Soc Artif Intern Organs 1962; 8: 90-99

Liotta D, Hall CW, Henly WS, Beall AC, Cooley DA, DeBakey ME. Prolonged assisted circulation during or after cardiac and aortic surgery 1-Prolonged Left ventricular bypass by means of an intrathoracic circulatory pump. Il-Diastolic pulsation of the descending thoracic aorta. Trans Am Soc Intern Organs ,1963; 9 :182-185.

Liotta D, Hall CW, Henly WS, Cooley DA, Crawford ES, DeBakey ME. Prolonged assisted circulation during and after cardiac or aortic surgery. Prolonged partial left ventricular bypass by means of intracorporeal circulation. Am J Cardiol, 1963; 12: 399-405.

Liotta D, Hall CW, Cooley DA, DeBakey ME. Prolonged ventricular bypass with intrathoracic pump. Trans Am Soc Intern Organs, 1964; 10: 154.

Liotta D, Maness JH, Bourland H, Podwell D, Hall CW, DeBakey ME. Recent modification in the implantable left ventricular bypass. Trans Am Soc Intern Organs, 1965; 11: 284.

DeBakey ME, Liotta D, Hall CW. Prospects for implications of the artificial heart and assistive devices. J Rehab;1966,32:106

Liotta D, Hall CW, Villanueva A, O'Neal RM, DeBakey ME. A pseudoendocardium for implantable blood pumps. Trans Am Soc Intern Organs, 1966;12: 129.



1960's: first clinical application

First clinical application of an intrathoracic pump

On July 19 1963, **E S Crawford** and **D Liotta** implanted the first clinical Left Ventricular Assist Device (LVAD) at The Methodist Hospital in Houston, Texas, in a patient who had a cardiac arrest after surgery. The patient survived for 4 days under mechanical support but did not recover from the complications of the cardiac arrest; finally the pump was discontinued and the patient died

First clinical application of a paracorporeal pump

On April 21 1966, **M DeBakey** and **D Liotta** implanted the first clinical LVAD in a paracorporeal position (where the external pump rests at the side of the patient) at The Methodist Hospital in Houston, in a patient experiencing cardiogenic shock after heart surgery. The patient developed neurological and pulmonary complications and died after few days of LVAD mechanical support.

On October 10 1966, **DeBakey** and **Liotta** implanted the paracorporeal Liotta-DeBakey LVAD in a new patient who recovered well and was discharged from the hospital after 10 days of mechanical support, thus constituting the first successful use of an VAD for postcardiotomy shock





1969: the First uman implant

In 1969 **D Cooley** with a patient who was unable to wean from CEC after cardiac surgery, was forced to remove the patient's heart and to implant a full prosthesis of cardiac ventricles, operated by a pneumatic system.

This heart prosthesis, inserted it orthotopic, was designed and built by **D Liotta** and kept the patient alive for 64 hours, after which underwent a heart transplant.

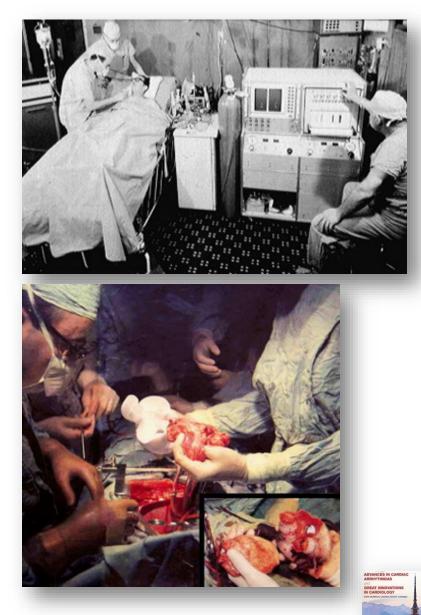


1969: the first uman implant

The artificial heart worked for 64 hours, before being replaced by a natural heart, but unfortunately patient died shortly after receiving the heart and Cooley was banned by the Food and Drug Administration (FDA) because his experiment was not previously authorized.

Among those opposed to the intervention of Cooley, there was also **C. Barnard** who put it this way:

"I do not believe in artificial heart, a successful transplant is always better than an artificial device. The mechanical devices fail and will never guarantee a good quality of life for the patient, who should remain the main objective of any medical intervention."

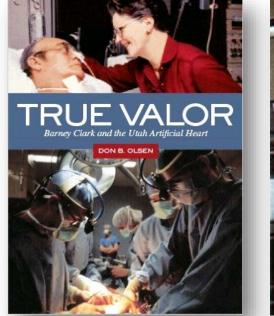


In 1981, **W DeVries** submitted a request to the FDA for permission to implant the Jarvik 7 into a human being.

On December 2, 1982, Kolff implanted the Jarvik 7 artificial heart into **B Clark**, a dentist from Seattle who was suffering from severe congestive heart failure.

Clark lived for 112 days tethered to an external pneumatic compressor, a device weighing some 400 pounds (180 kg)

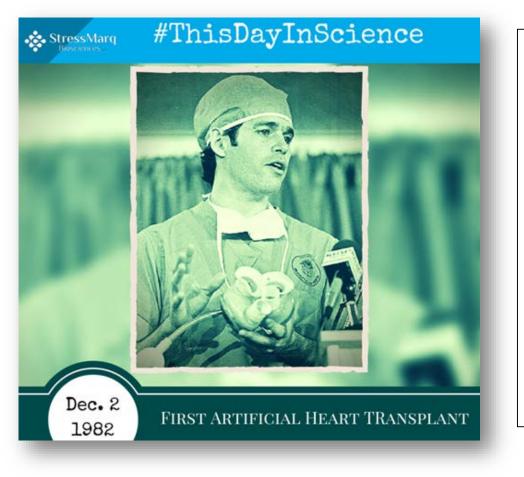
B Schroeder became the second recipient and lived for a record 620 days.







1982: first time in a man



Jarvik-7 was designed by R Jarvik as a temporary replacement device for patients awaiting heart transplants.

It was used as a permanent heart transplant for only four other patients, but was used by many people temporarily as they waited for heart transplants.

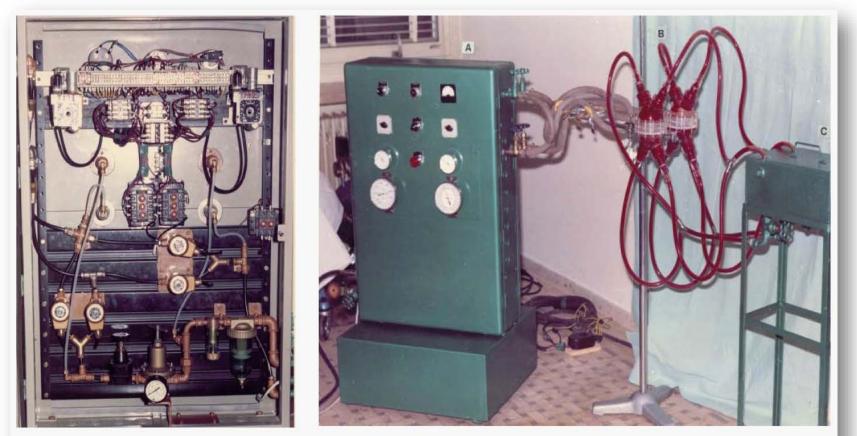
BEGINS MCS's ERA



IL PROGETTO ITALIANO di ROBERTO BOSIO

The italian project

In a context of extreme international scientific research, also in Italy were studied systems not only to repair the heart muscle but also to replace it.



Schema di comando e regolazione elettromeccanica.

Ventricoli artificiali in funzione al banco di prova.



In Turin, Cavalier Guido Bosio, owner of a mechanical industry, had 2 sons both worked as engineers in the industry family : Felice and Roberto.

Roberto Bosio was born in Turin in 1933 and graduated on 1960 at the Turin Polytechnic in industrial and electrical engineering.

Since early 60's, his work focused on the implementation of bioengineering equipment for the treatment of cardiovascular diseases, becoming at the time one of the top experts in biomechanics and cardiovascular bioengineering.

This passion will accompany him throughout his life, bringing it to teaching a nascent discipline at the Polytechnic of Turin: bio and molecular engineering.





1963 : the engineer Roberto Bosio meet A Actis Dato a young heart surgeon.

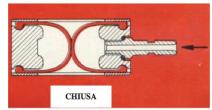
The meeting between a heart surgeon who had very clear concepts of pathophysiology circulatory and an engineer on the other hand had experience and expertise in hydraulics and fluid mechanics allowed to start a fascinating journey of design and testing, even with the use of technical solutions absolutely innovative and original as fluidic valves to reduce turbulence and hemolysis during operation of the ventricles tires



I due ventricoli del cuore artificiale esterno.







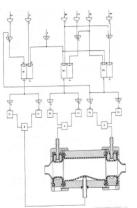
Sezione schematica del ventricolo artificiale in polimetilmetacrilato ed elastomero di silicone.Valvole fluidiche (R. Bosio).



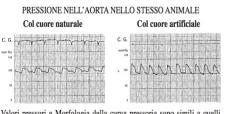
courtesy of Actis Dato family



Prof Angelo Actis Dato e il perfusionista Gino Lavista durante un impianto su animale



Schema dell'apparato di fluistori che comandano e coordinano il funzionamento del ventricolo artificiale (studio di ingegneria fluidifica di R. Bosio).



Valori pressori e Morfologia della curva pressoria sono simili a quelli precedenti del cuore naturale



Primo prototipo di cuore artificiale a campana con i due ventricoli contrapposti

That device caused the immediate attention of prof. A Senning, director of Clinical Surgery in Zurich Cantonal Hospital, and introduced A Actis Dato e F Bosio in the international medicalscientific board.



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1 5 LUG. 1968

1968: after years of study and design with use of innovative and original technical solutions as the fluidic valves to reduce turbulence and hemolysis during the contractile activity of the artificial ventricles, there has been recording in the Patent Office of the first artificial heart Italian: Actis Dato-Bosio fluidic pump control for artificial circulation

TUDIO TECNICO JACOBACCI-CASE TA BREVETTI - WARCHI Via Alliati, 17 Italia " Pospa atta a realiszare una dircolazione, scc." 820372 Privation t6 Ottobre 1967 Depositialia 15 Inglio 1965 Rilascista 16 Ottobre 19 15 lanni stal. Durals Pratica o.m1 3 aninia datare dalla precedente Prioriti Marcalura articoli brevettati facoltati W Abdustments / Siffuto dil, per abbustimus, suotes delle da fare per montenens in validità della Strectora. Tailanty a dechan qualance separatelying and on optimal molece, if Ghanta non sizewate on inte prote



courtesy of Actis Dato family

The first experimental installation took place in Zurich University Hospital in Switzerland, by M Turina M and C Scherf of a german shepherd female dog of 8 years and 30 kg weight called Bless.

From the newspapers of the time:

"...after an operation that lasted about 4 hours, under the personal control of the engineer Bosio, the artificial heart has finally begun to beat. The emodinamic parameters was perfect..."

At 48 hours following implantation the animal was suppressed because the experiment was scheduled to last a number of hours.

M Turina said : "The artificial heart of R Bosio can be considered perfect . We can keep alive an animal what we want and until now we know that 24 hours of a dog corresponding to 5 days of a man. Today we can put an artificial heart in a patient suffered a heart attack and we can keep him alive at least ten days waiting for a transplant. We are on a wonderful road." Device consisting in 2 artificial ventricles each comprising a hollow body with one-way valves of inlet and outlet whose inner cavity was divided into 2 compartments by a membrane of elastically deformable material

The weight and size were very low



For reasons of lack of validation and authorization by the italian ministry of Health, this device was never implanted in Italy



1977 Switzerland experience

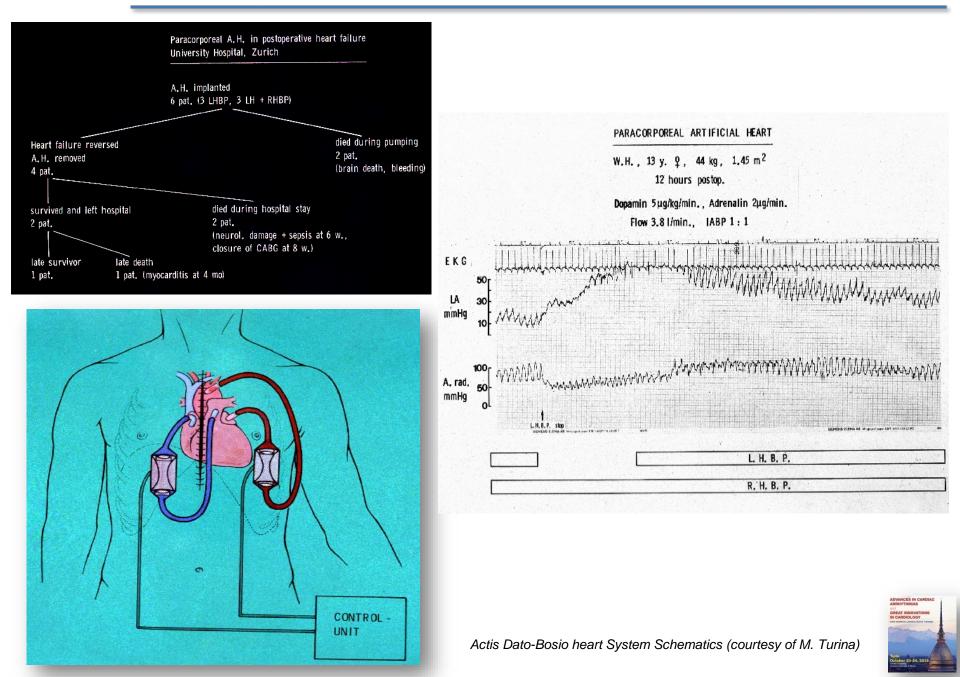
from 1977 as "bridge to recovery" in Zurich University Hospital implanted in 6 patients not wean by CEC after cardiac surgery.



A team of surgeons who saved the life of a heart attack victim, at the Zurich University Hospital in Switzerland, using an artificial heart, 20th December 1977.

from left to right, croatian cardiac surgeon Marko Turina, swedish cardiac surgeon Ake Senning and italian engineer Roberto Bosio, who developed the technology.

Switzerland experience







VAD in Italy

In Italy it took another 20 years to get permission from the Ministry of Health for the implanting of VAD in a man.

The first implant took place almost simultaneously in Pavia and Bergamo between late 1987 and early 1988.

On the night of december 24 1987, **M Viganò** in Pavia planted the first VAD in a patient, which a week after was transplanted an heart.

Simultaneously in january 4 1988, L Parenzan in Bergamo put in L-VAD a young man of 17 years suffering from dilated cardiomyopathy . The patient was subjected after 45 days to cardiac transplant with a donor of Turin.







VAD in Italy

The first bi-VAD support was implanted in Italy march 13 1988, to Niguarda by A Pellegrini on a patient of 41 years with a biventricular paracorporeal Pierce-Donachy as a bridge to transplant.

The patient was transplanted 31 days after bi-VAD implantation.



Il Prof Pellegrini - Il VAD impiantato a Milano nel 1988



Conclusion

MCS: sunrise of new era?

