VAD Mechanical Circulatory Support in ACHD as a Bridge to Recovery/Transplant or Destination Therapy

David N. Campbell MD

Professor of Surgery, UC, Denver
and the Children's Hospital
Colorado

Surgical Management of End Stage Heart Failure

- Heart Transplantation is the Gold Standard.

BUT

There are many more people who require the surgical management of advanced heart failure than there are heart donors(<5000 worldwide per year), and each day this number continues to grow.

Do I look genetically engineered?

XENOTRANSPLANTATION

WHEN PIGS FLY!

LIFE

Can Women Cut It
in the Military?

September 1981/$2.00

THE ARTIFICIAL HEART IS HERE

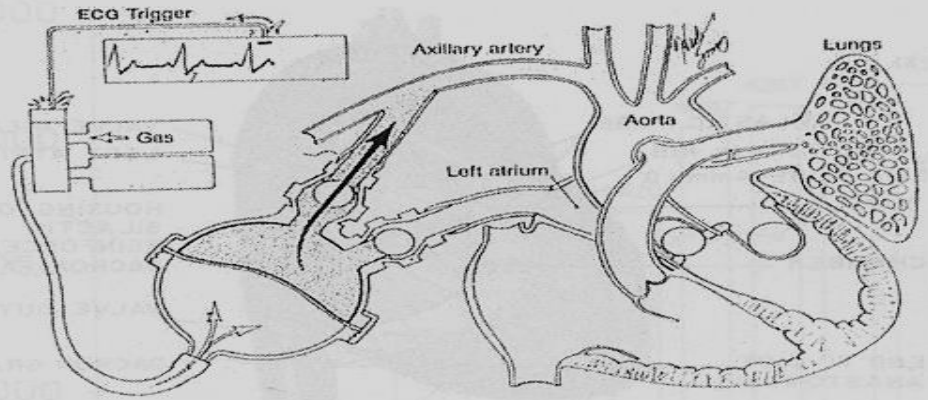
EXCLUSIVE PICTURES OF DR. COOLEY'S HISTORIC HEART SURGERY

TRAIL RIDGE ROAD ROCKY MOUNTAIN NATIONAL FOREST, COLORADO

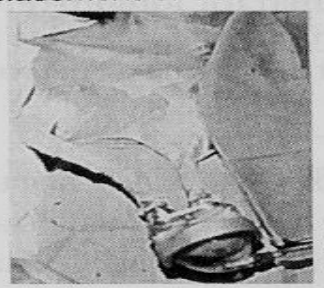
HIGHEST CONTINUOUSLY PAVED ROAD IN USA 12,183 FT

The Evolution of Mechanical Circulatory Support Systems

- **1966** First successful use of an LVAD for post-cardiotomy cardiogenic shock (De Bakey blood pump)



After extensive experimental work, the left ventricular bypass pump was employed in a 37 year old woman whose left ventricle was unable to resume adequate function following replacement of aortic and mitral valves.



After ten days of circulatory support her left ventricle recovered enough to resume function and the device was removed. She returned to normal activity for about six years until she was tragically killed in an automobile accident.

Spurred on by this initial success, a variety of devices, such as the intra-aortic balloon, has been created to provide hemodynamic stabilization for gravely ill patients.

A subsequent version of the DeBakey blood pump, the Baylor left ventricular assist device, was first used successfully for postcardiotomy heart failure in 1966.

(Reprinted with permission from Excerpta Medica.[5])

The Evolution of Mechanical Circulatory Support Systems

- **1967** Clinical application of the intraaortic balloon pump (IABP) (Kantrowitz)

- **1969** First successful use of a total artificial heart (TAH) as a bridge to transplant (Cooley)

- **1978** First successful use of an LVAD as a bridge to transplant (Frazier)

Dr. Willem Kolff (1911-2009)
FATHER OF ARTIFICIAL ORGANS

DEVELOPED INTEREST IN ARTIFICIAL HEART EARLY IN HIS CAREER

Became Head of the University of Utah's Division of Artificial Organs

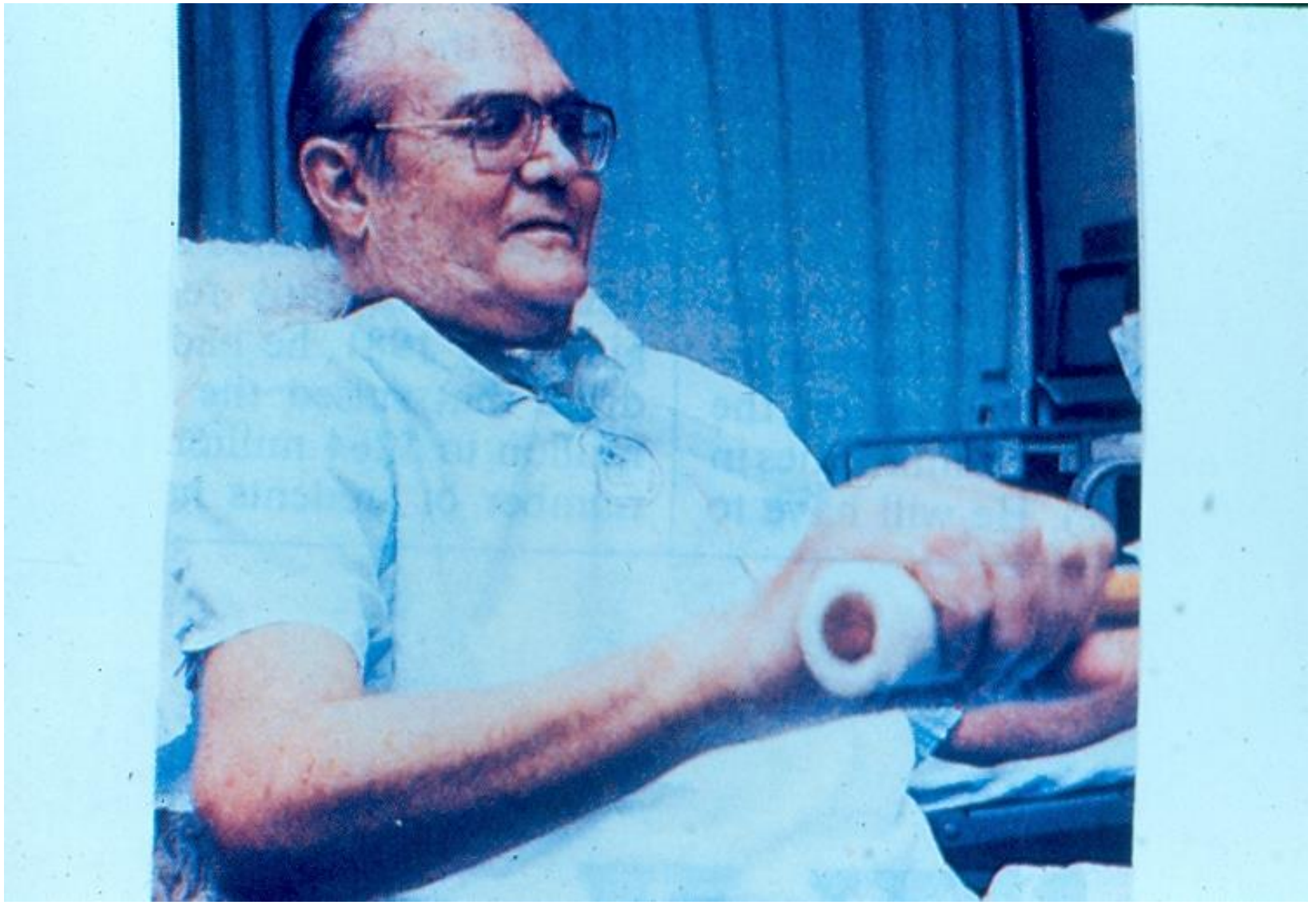
1967

DR. ROBERT JARVIK WORKED IN DR. KOLFF'S LAB AND WAS ASSIGNED TO DEVELOP AN ARTIFICIAL HEART

The Evolution of Mechanical Circulatory Support Systems

- **1982** First clinical use of The Jarvik 7 TAH as “permanent” device (De Vries)

Lived 112 days



Barney Clark and the Jarvik 7 at University of UTAH

The Evolution of Mechanical Circulatory Support Systems

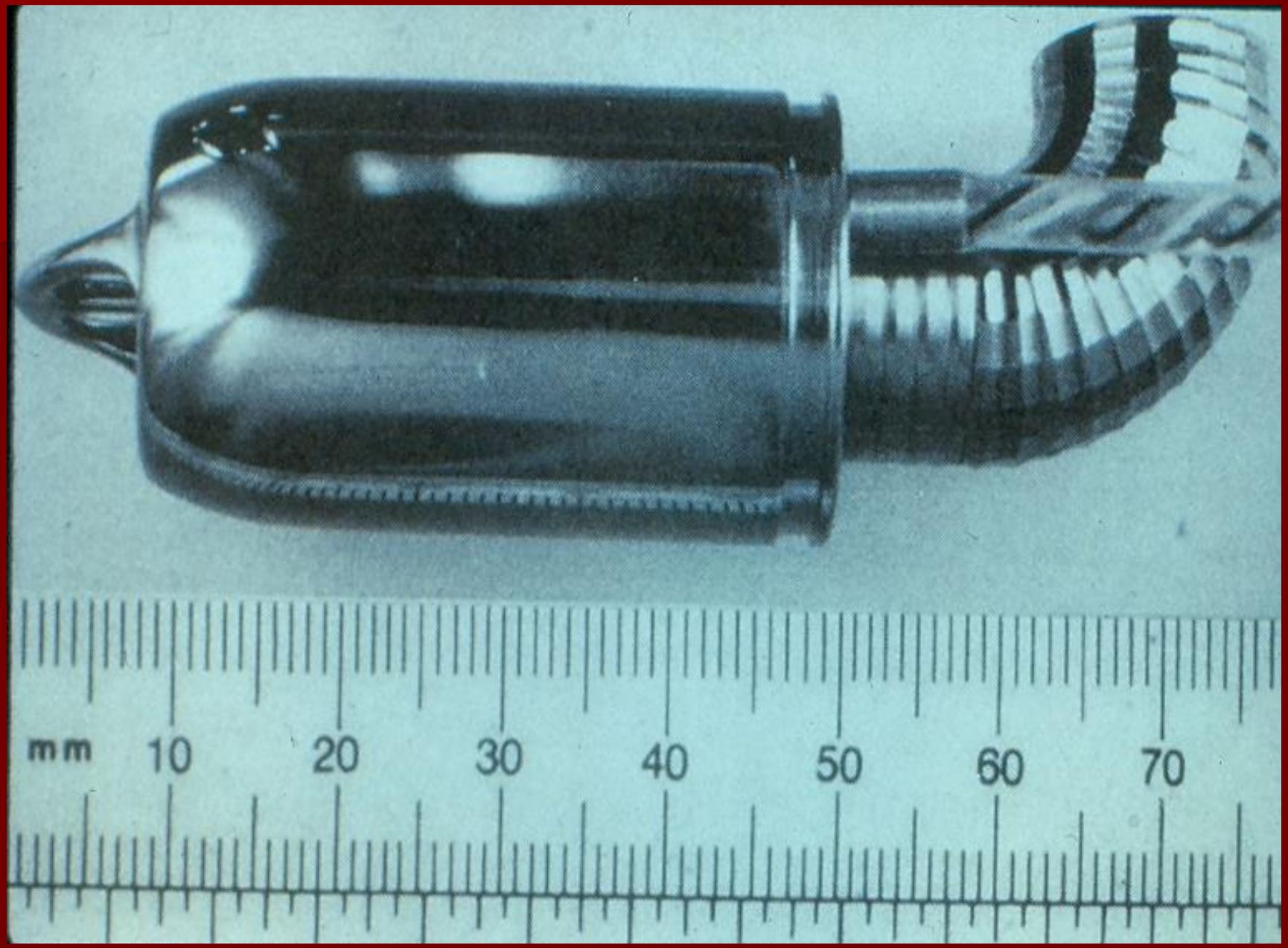
- **1995** First clinical use of LVAD as “permanent” device (Frazier)
- Catanese KA Outpatient LVAD Support a Destination rather than a Bridge Annals Thoracic Surg 1996

London man gets permanent electric heart

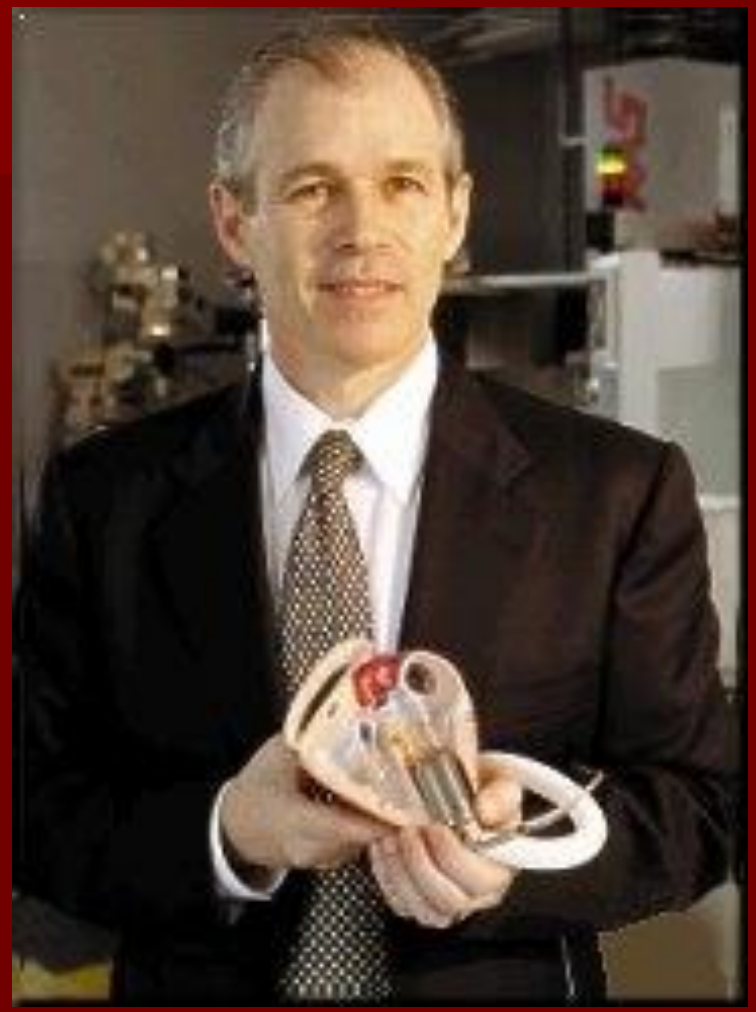
Deutsche Presse Agentur

June 2000

JARVIK 2000 Westaby and Jarvik



Jarvik 2000



ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

PERSPECTIVE

Mechanical circulatory support and heart transplantation in the Asia Pacific region

Cumaraswamy Sivathasan, MBBS, FRCS(Eng), FRCS(Edin), FAMS,[a] Choon Pin Lim, MBBS, MRCP,[a] Ka Lee Kerk, RN,[a] David K.L. Sim, MBBS, MRCP,[a] and Mandeep R. Mehra, MD[b]

From the [a]National Heart Centre Singapore, Singapore; and the [b]Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston, Massachusetts.

J Heart Lung Transplant 2017;36:13-18

Heart Transplantation and MCS remain low in the Asia Pacific region (including the ACHD population)

North America, which comprises 7.5% of the world population, accounted for 55.8% of the transplants in the 2012 ISHLT Registry, whereas Asia with 62.5 % of the world population, accounted for 5.7% of the Transplants

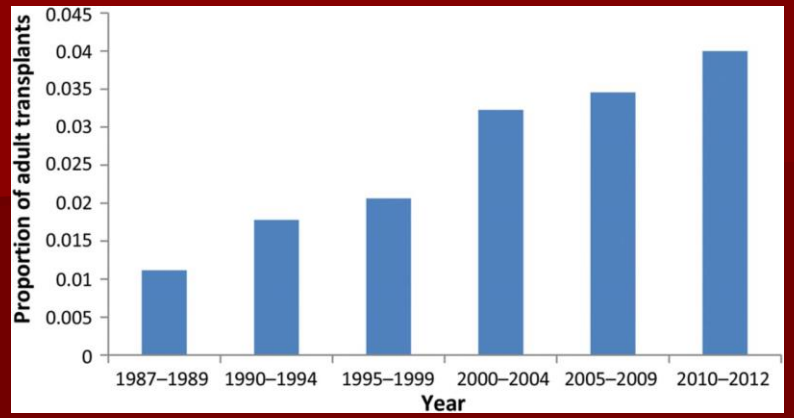
Cost
Wide variation in Health Care Infrastructures
Multi-cultural and racial factors
Religious beliefs
Diverse Traditions

Asia: most common MCS system implanted is the HeartMate II
Australia: most common MCS system implanted is the HeartWare HVAD

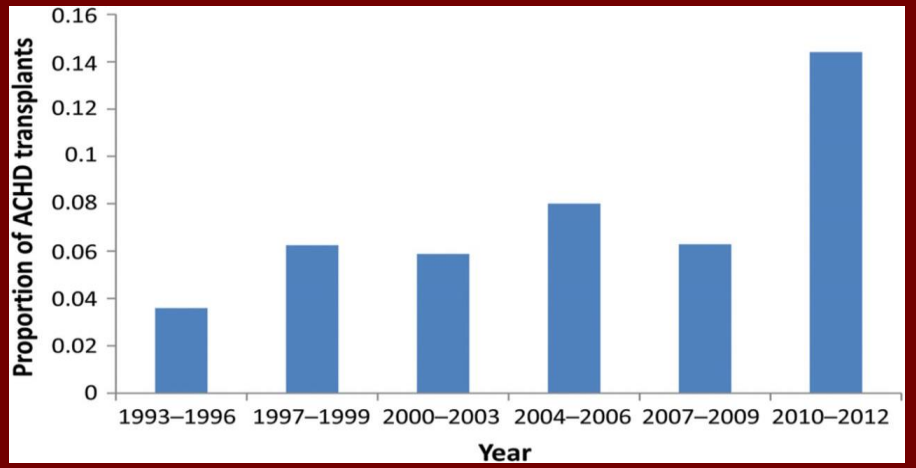
50% of the patients coming to transplant in Australia are on MCA

ACHD UNOS DATA

Proportion of ACHD transplants relative to all transplants



Proportion of ACHD transplants supported With MCS relative to all ACHD



Maxwell et al. European J of Cardio-thoracic Surg 2013

USE of MCS in Heart Failure for ACHD Patients

OPTN SRTR data from 1987-2012

- 47,160 adult transplant recipients, 1,213 (2.6%) had CHD
- Proportion of ACHD transplants recipients relative to all adult transplant increased yearly, with concomitant increase in MCS for ACHD yearly
- MCS used in 83 patients (6.8%) with CHD as compared to 8,625 (18.8%) patients without CHD
- No difference in 30 day mortality between MCS and non MCS patients with ACHD, but both had higher short term mortality than adults without CHD

Maxwell et al. European J of Cardio-thoracic Surg 2013

Darwin

GALAPAGOS ISLANDS

STUDY OF EVOLUTION

A DATA BASE LIKE INTERMACS

INTERAGENCY REGISTRY FOR MECHANICALLY ASSISTED CIRCULATORY SUPPORT(JUNE 2006)

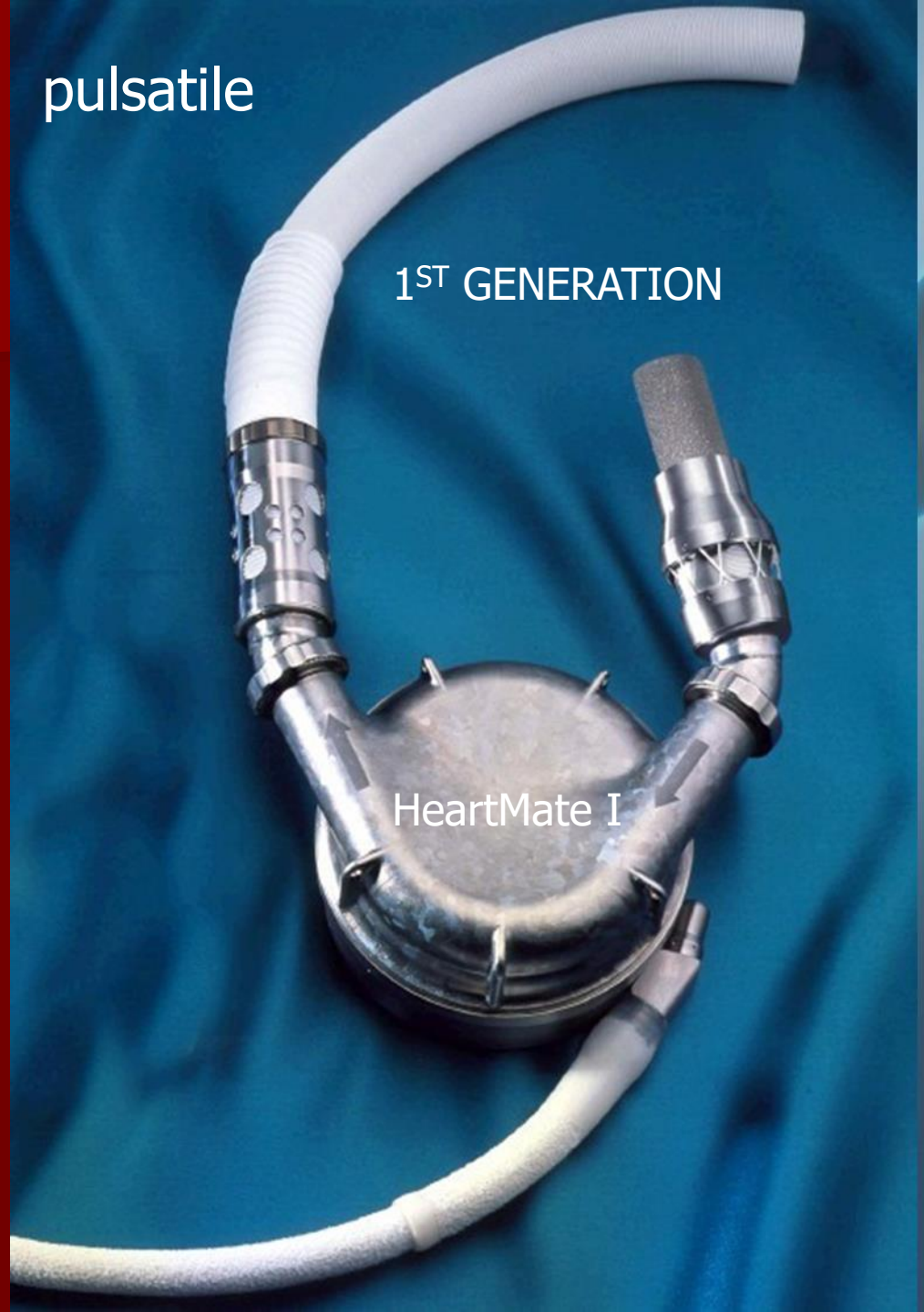
- IDEAL FOR STUDY OF THE EVOLVING LANDSCAPE OF MCS IN THE USA
- SPONSORED BY THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE IN PARTNERSHIP WITH CENTER FOR MEDICARE SERVICES AND THE FOOD AND DRUG ADMINISTRATION
- UNDER STEWARDSHIP OF JAMES KIRKLIN

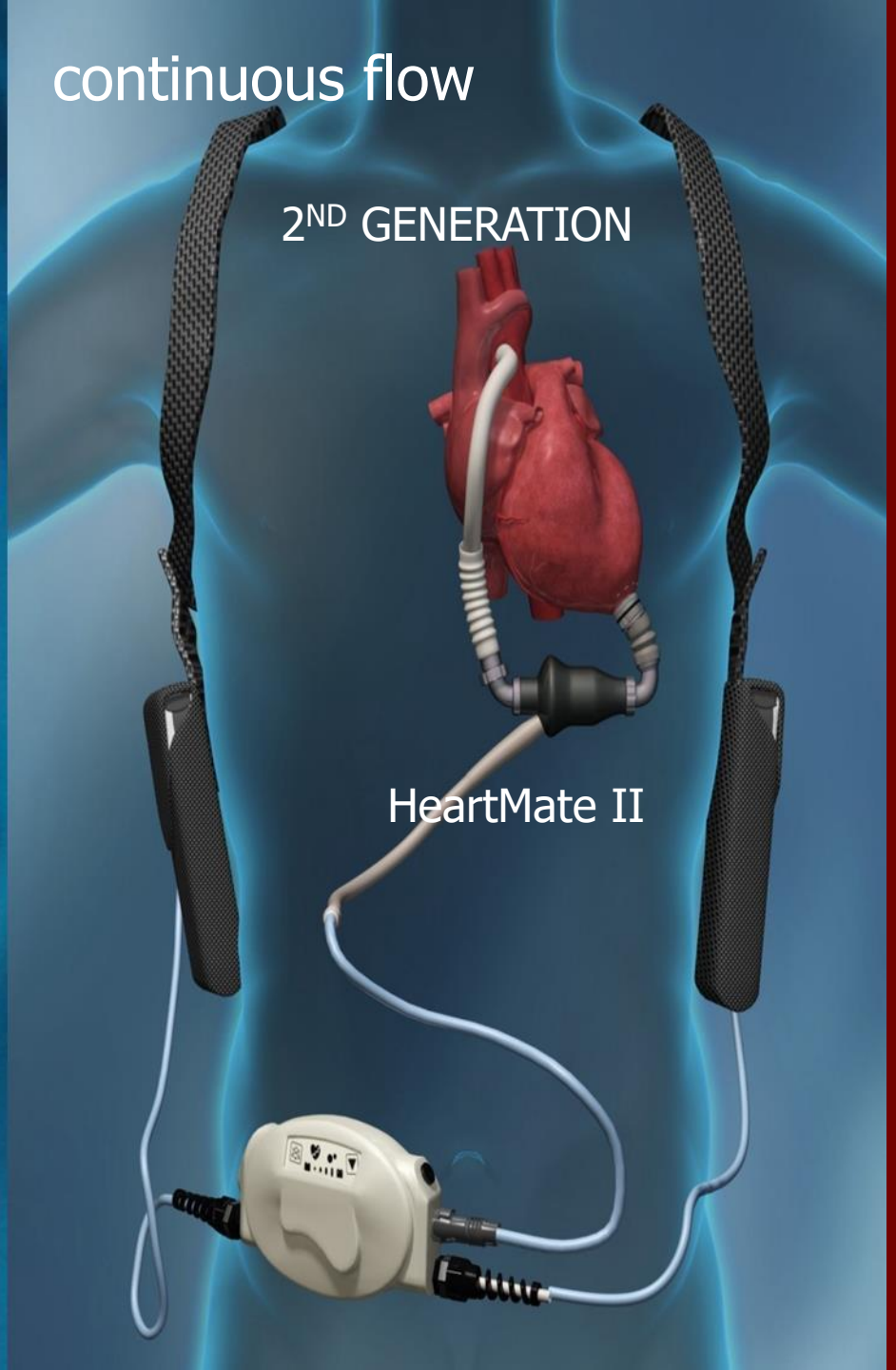
Other MACS registries, but newer and fewer patients

2013

J-MACS 2010

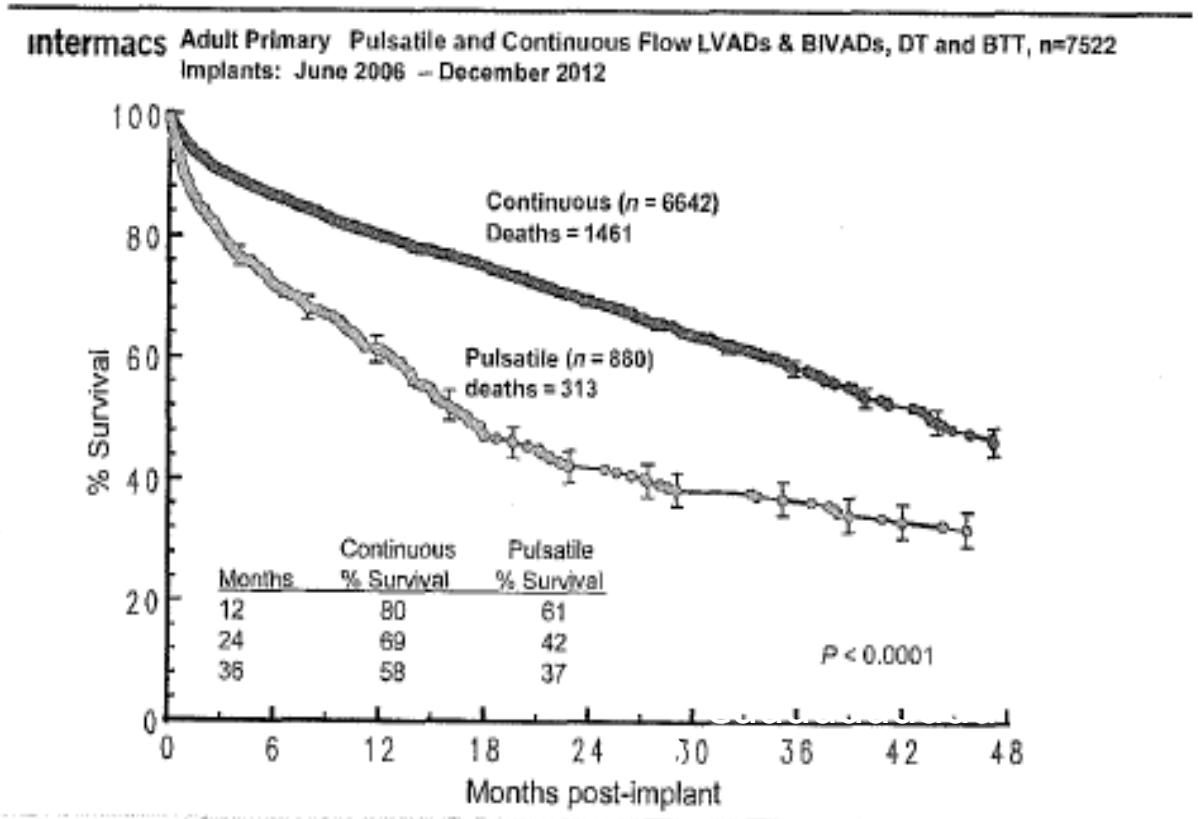
EUROMACS 2009


pulsatile
1ST GENERATION
HeartMate I

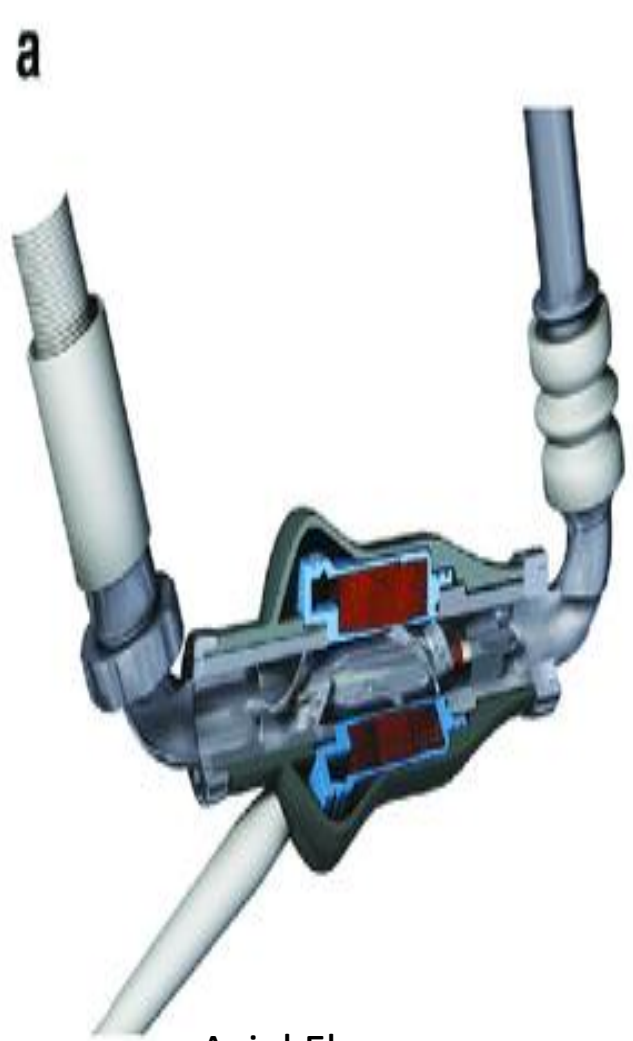

continuous flow
2ND GENERATION
HeartMate II

EDITORIAL AUGUST 2013

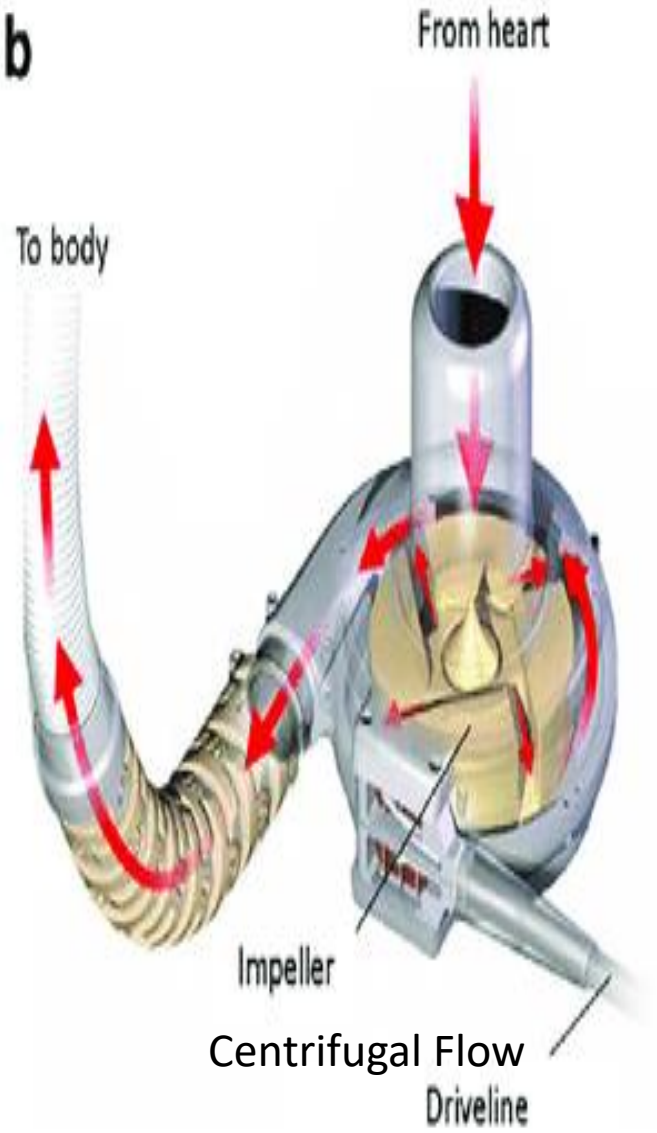
J.K. Kirklin / European Journal of Cardio-Thoracic Surgery



SINCE 2010, >99% of USA IMPLANTS = CONTINUOUS FLOW TECHNOLOGY



Axial Flow



Centrifugal Flow

2nd GENERATION

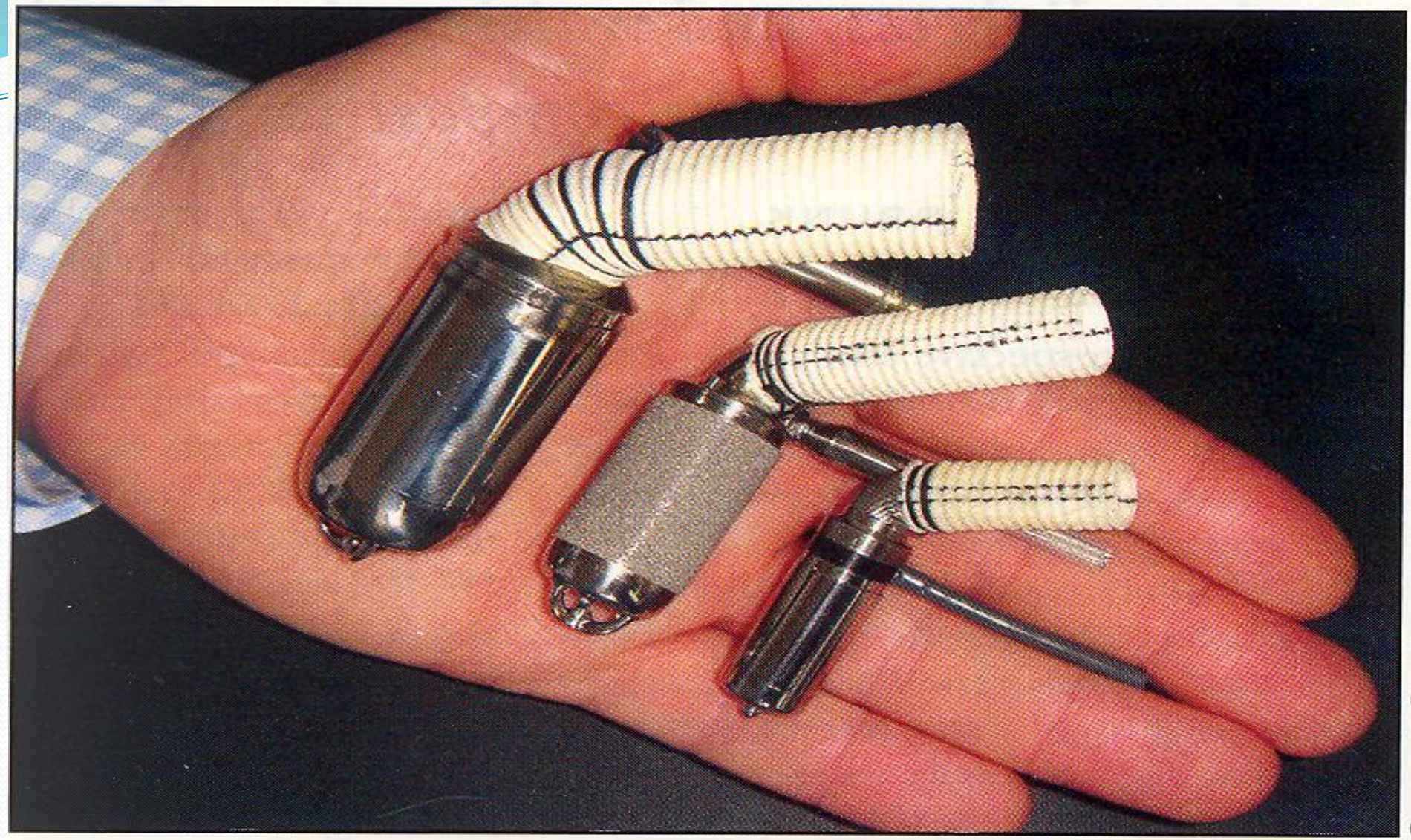
3RD GENERATION

Second Generation VADs

- The key mechanical element was the implementation of a valveless axial pump with a rotary motor as the only moving part in the system.
- More specifically, the design introduced an internal rotor in the axial path of flow that was suspended via blood-immersed bearings (i.e., the rotor is in direct contact). The theoretical benefit of this design was further reduction of prothrombotic sites and minimization of wear and tear associated with multiple moving parts.
- Efficiency was further enhanced with elimination of the reservoir chamber and inflow/outflow valves

The HeartMate II
2nd generation device

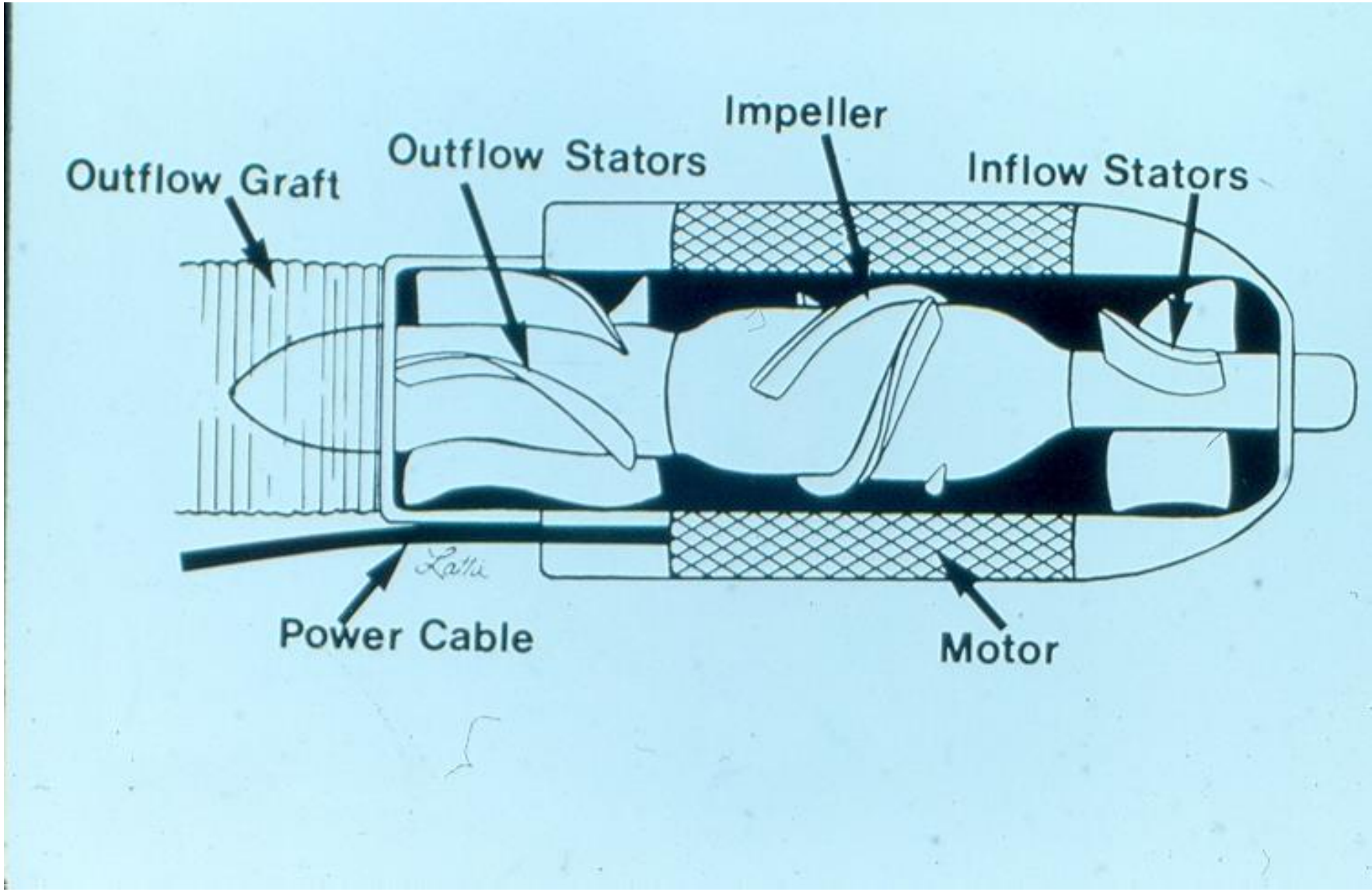
FDA APPROVED FOR BRIDGE TO TRANSPLANT 2008



COURTESY DR. ROBERT JARVIK

The pump used in the Jarvik 2000 booster VAD for adults (left) is being developed for children (center) and infants (right).

FDA APPROVED FOR CLINICAL TRIAL AS BTT and DESTINATION(2012)

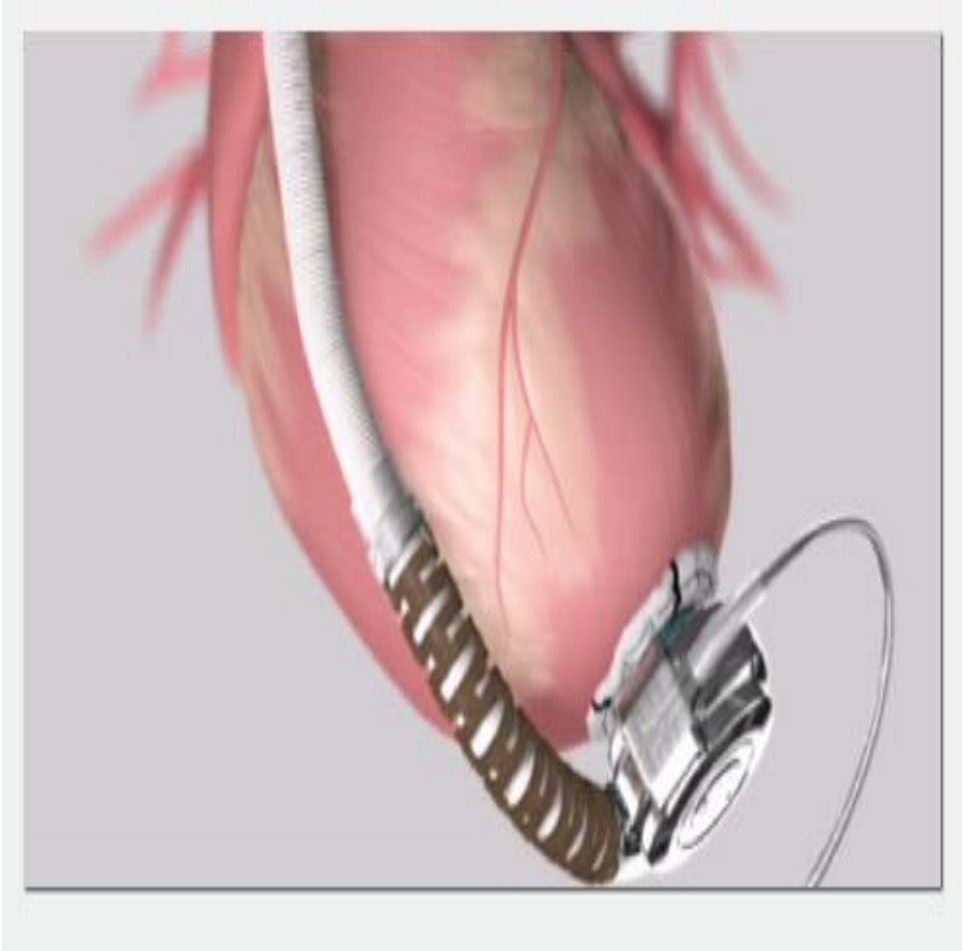

Impeller
Outflow Stators
Outflow Graft
Inflow Stators
Power Cable
Motor

Third Generation VADs

- The critical distinguishing factor between the second- and third-generation LVADs is the employment of contact versus noncontact bearings, respectively.
- The latter employs the technology known as magnetic levitation (MAGLEV), which allows for rotation without friction or wear.
- The goal of this design is to further minimize prothrombotic sites while enhancing efficiency and durability

HeartWare HVAD

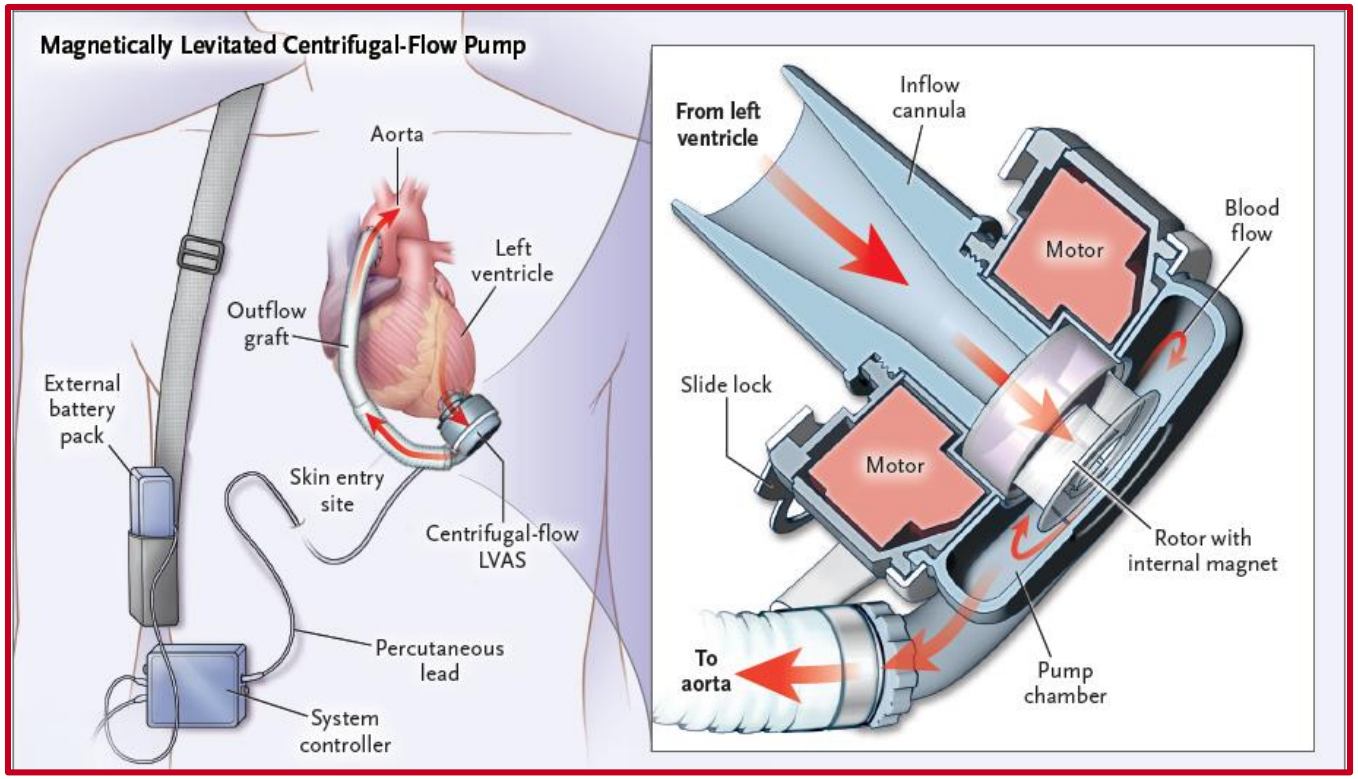
3RD GENERATION DEVICE



FDA APPROVED BRIDGE TO TRANSPLANT NOV 20, 2012

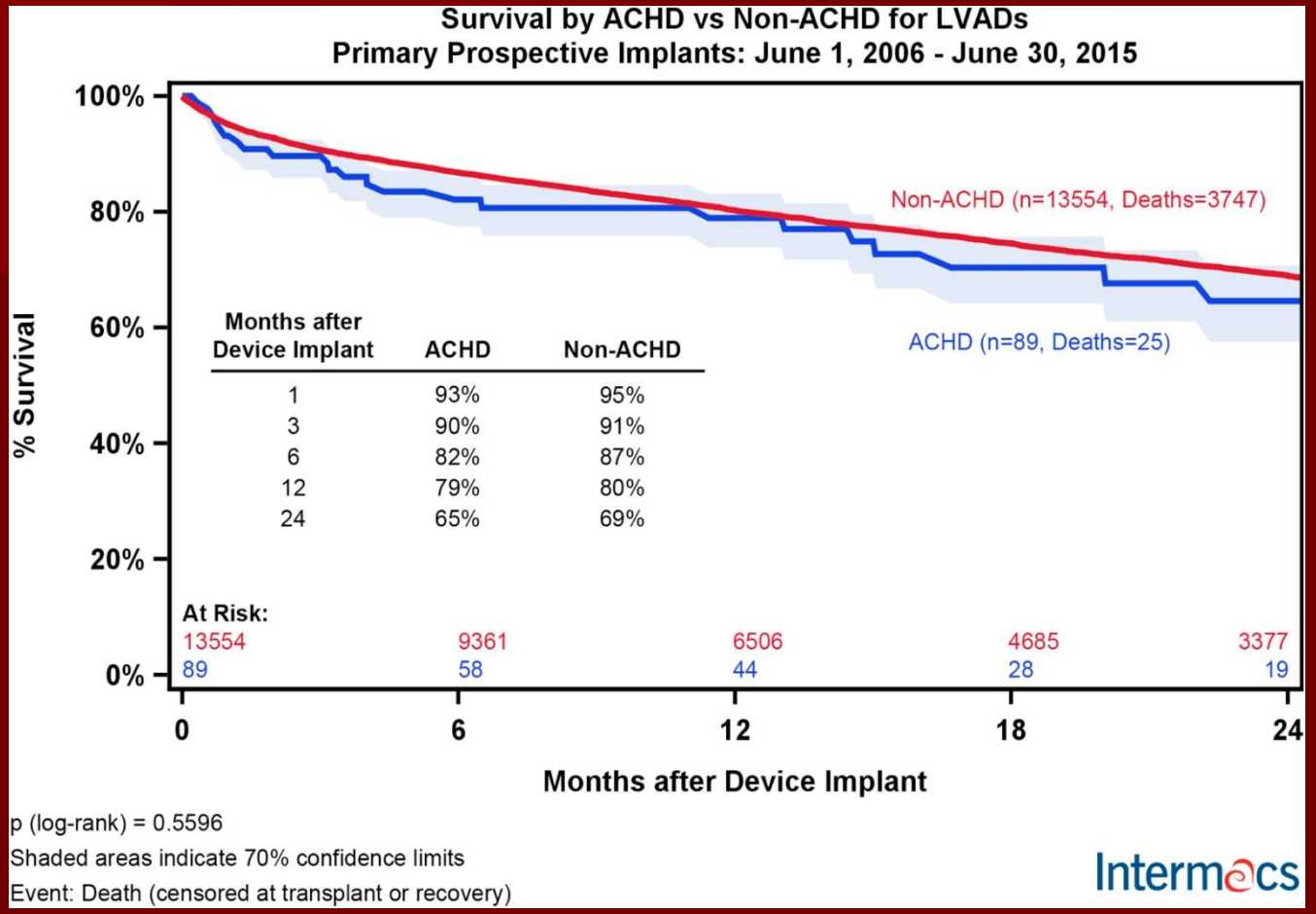
HeartMate III

3rd generation



FDA APPROVED FOR BRIDGE TO TRANSPLANT AUG 28, 2017

HOW DO ADULTS WITH CHD and LVADs COMPARE WITH THOSE ADULTS ON LVAD SUPPORT WITHOUT CHD?

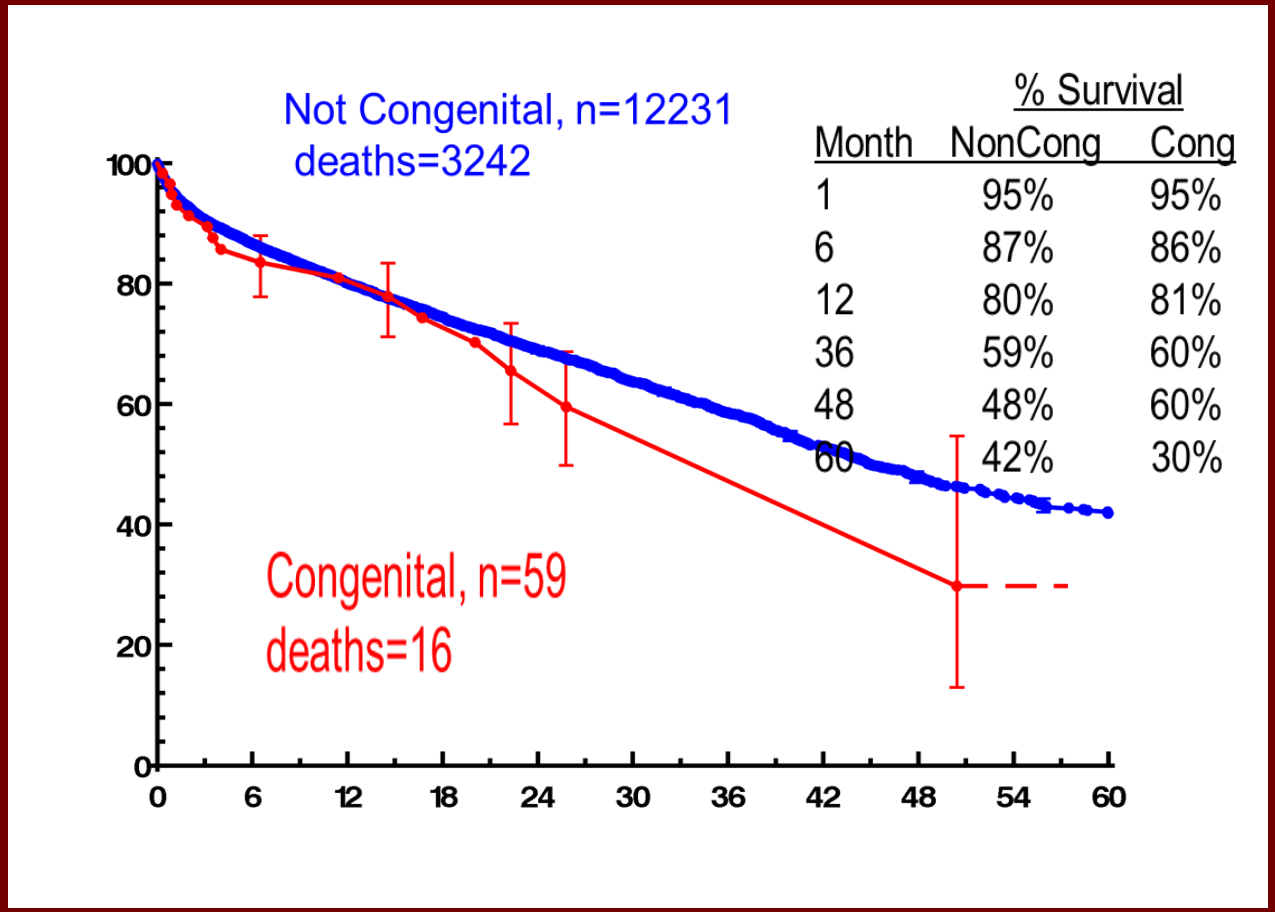


Utilization and Outcomes of Ventricular Assist Device Support in Adult Congenital Heart Disease: An Analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)

C.J. VanderPluym, P. Eghtesady, B.G. Maxwell, J.M. Gelow, L.J. Burchill, S. Maltais, R.S. Cantor, E.D. Blume

The Journal of Heart and Lung Transplantation
Volume 35, Issue 4, Pages S151-S152 (April 2016)
DOI: 10.1016/j.healun.2016.01.420

Survival of adults with and without CHD on Continuous Flow device



% Survival

Month	NonCong	Cong
1	95%	95%
6	87%	86%
12	80%	81%
36	59%	60%
48	48%	60%
60	42%	30%

INTERMACS DATA VanderPluym et al

VANDERPLUYM et al

CONCLUSION

While VAD utilization is much less common in ACHD, the survival outcomes are similar to non-ACHD patients even in the setting of complex congenital disease.

1 year survival for ACHD VAD: 72%

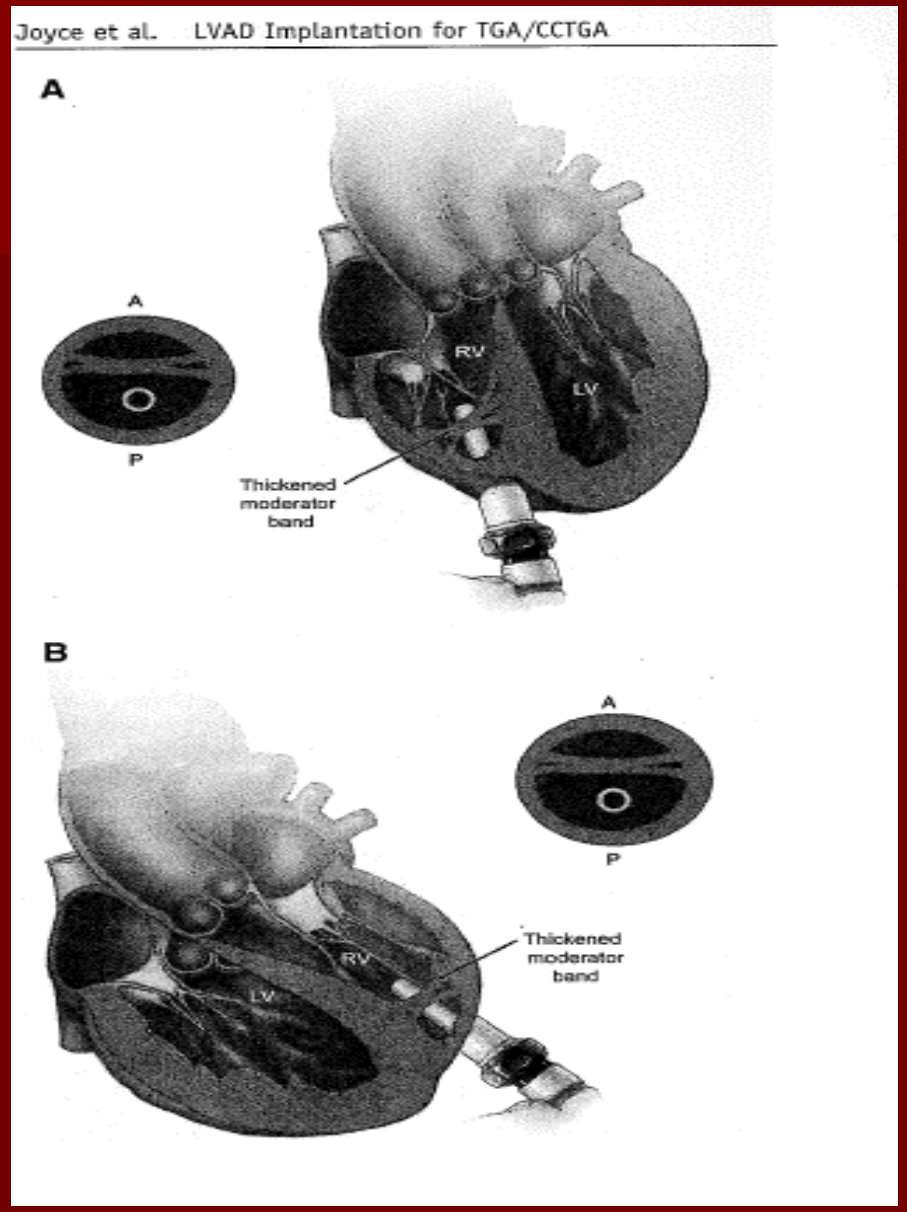
A Bit of Good News

Almost half (44%) of the high complexity lesions were D-TGA following the Atrial Switch operation: easy implant?

25% were palliated Single Ventricle circulation: more difficult but good results!

ECHOCARDIOGRAPHY

- It’s indispensable for optimum pump placement
- Both TEE and Epicardial ECHO together are additive in usefulness
- Optimal cannula placement occurs when the inflow cannula is directed towards the AV valve
- Liberal resection of the moderator band, RV trabeculae, and the papillary muscles is necessary to ensure unobstructed flow when placed in the right ventricle


A
A
P
RV
LV
Thickened
moderator
band
B
A
P
RV
LV
Thickened
moderator
band

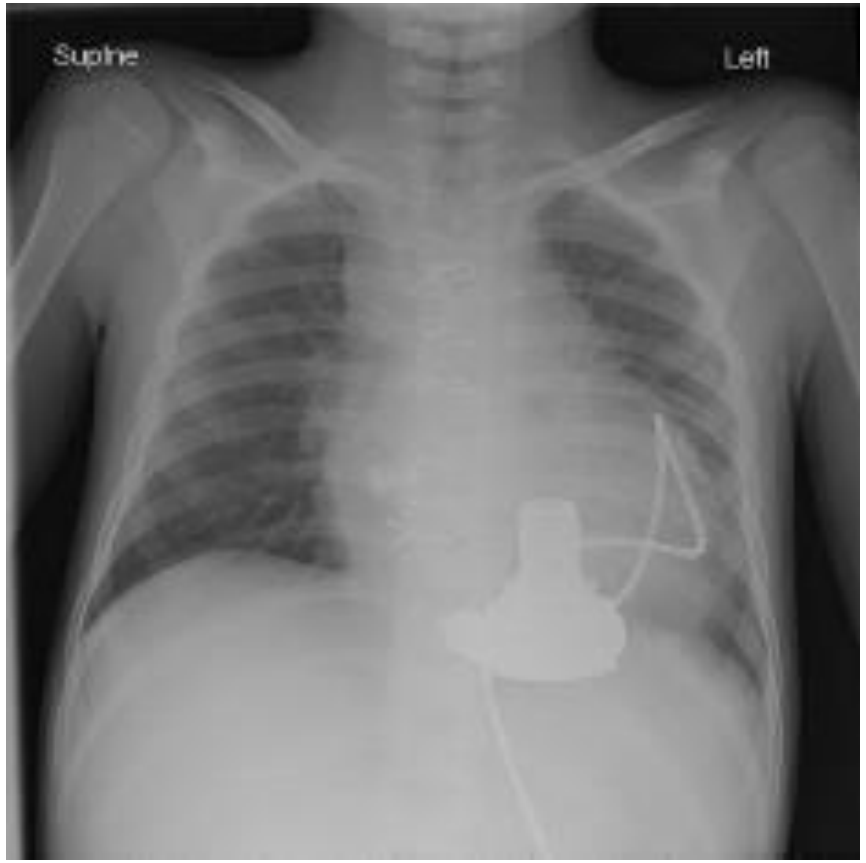
A BIT OF BAD NEWS ADVERSE EVENTS

- STROKE
- DRIVELINE, PUMP, POCKET INFECTION
- GASTROINTESTIONAL BLEEDING

- PUMP THROMBOSIS RARE

- ADVERSE EVENT RATES DECLINING WITH NEWER GENERATION DEVICES

LVAD For Failing Single Ventricle



3RD GENERATION EASIER TO IMPLANT

Use of a HeartWare Ventricular Assist Device in a Patient With Failed Fontan Circulation

Robert A. Niebler, MD, Nancy S. Ghanayem, MD, Tejas K. Shah, MD, Andrea De La Rosa Bobke, CPNP, Steven Zangwill, MD, Cheryl Brosig, PhD, Michelle A. Frommelt, MD, Michael E. Mitchell, MD, James S. Tweddell, MD, and Ronald K. Woods, MD

Herma Heart Center, Children's Hospital of Wisconsin; Department of Pediatrics, Section of Critical Care, Medical College of Wisconsin; Department of Pediatrics, Section of Cardiology, Medical College of Wisconsin; and Department of Cardiothoracic Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin

We present a successful case of the use of a HeartWare ventricular assist device as a bridge to transplantation in an 11-year-old with a hypoplastic left heart and failed Fontan circulation.

(Ann Thorac Surg 2014;97:e115–6)

Heart Transplantation for ACHD : The Destination ?

The artificial heart is very effective as a bridge to transplant, but the number of people that can be saved with human hearts is limited. A perfect artificial heart could save many more patients.

Robert Jarvik

The New England
Journal of Medicine

VOLUME 345 NOVEMBER 15, 2001 NUMBER 20

LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE FOR END-STAGE HEART FAILURE

ERIC A. ROSE, M.D., ANNETINE C. GELIJNS, PH.D., ALAN J. MOSKOWITZ, M.D., DANIEL F. HEITJAN, PH.D., LYNNE W. STEVENSON, M.D., WALTER DEMBITSKY, M.D., JAMES W. LONG, M.D., PH.D., DEBORAH D. ASCHEIM, M.D., ANITA R. TIERNEY, M.P.H., RONALD G. LEVITAN, M.SC., JOHN T. WATSON, PH.D., AND PAUL MEIER, PH.D., FOR THE RANDOMIZED EVALUATION OF MECHANICAL ASSISTANCE FOR THE TREATMENT OF CONGESTIVE HEART FAILURE (REMATCH) STUDY GROUP*

Durable Mechanical Circulatory Support gained acceptance as long term "Destination Therapy" in the USA

129 patients in NYHA class 4 CHF and who were ineligible for heart transplant

68 received MCS

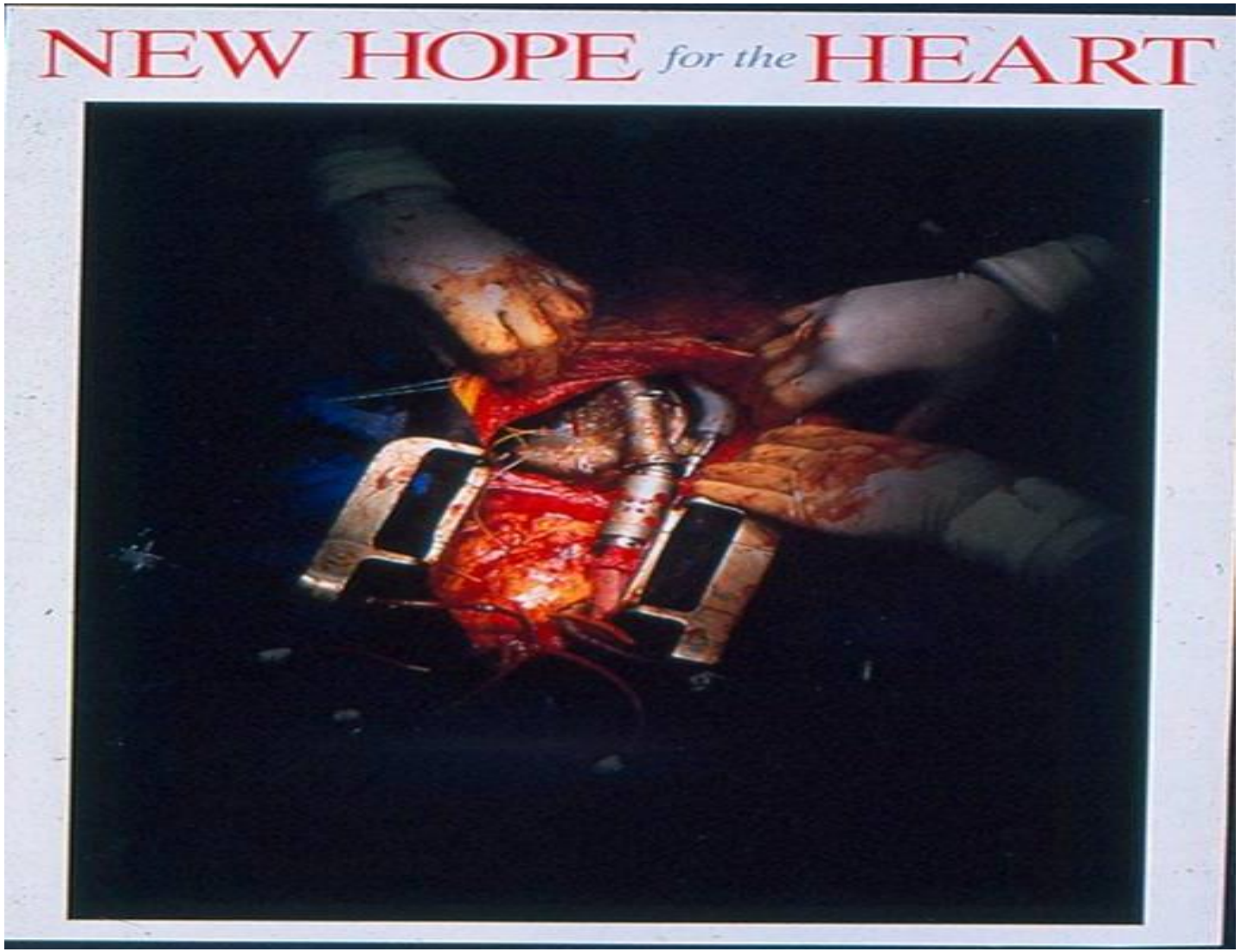
61 received medical therapy

LVAD "Destination" Therapy REMATCH Trial

Results
48% reduction in the risk of death from any cause in the group that received LVAD vs medical therapy(MT)

Survival
1 year LVAD 52% MT 25%
2 year LVAD 23% MT 8%

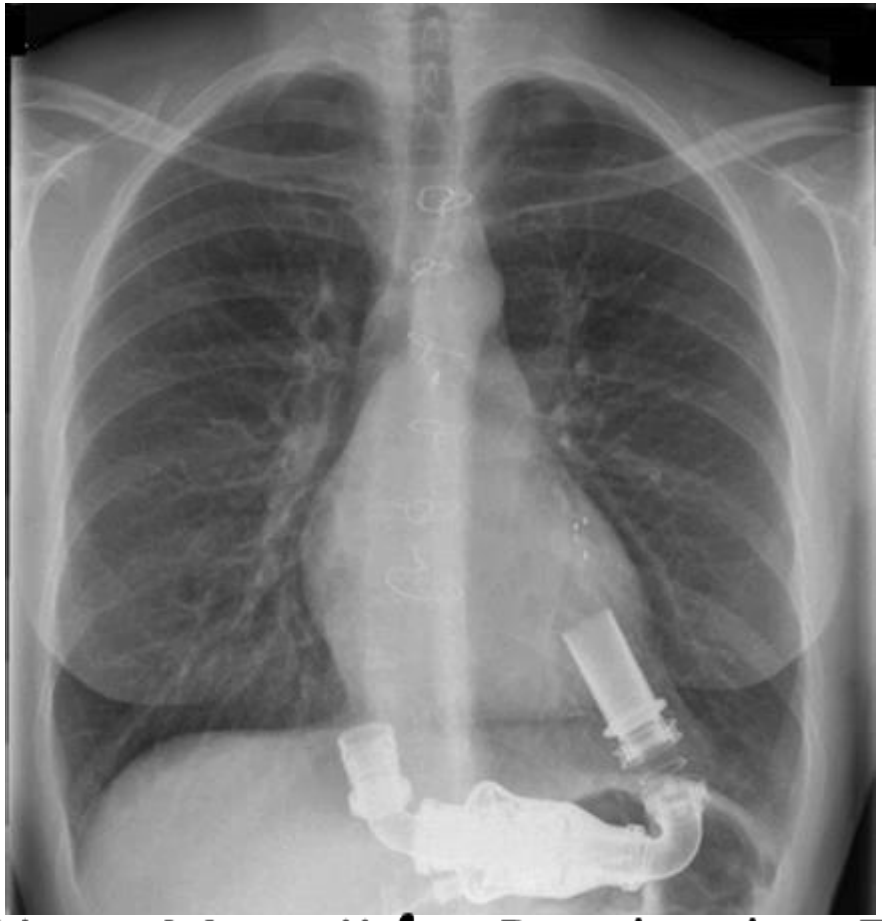
XVE HeartMate I Device 1st generation



BULKY, PRONE TO INFECTION and PUMP FAILURE

BUT

IN THE USA

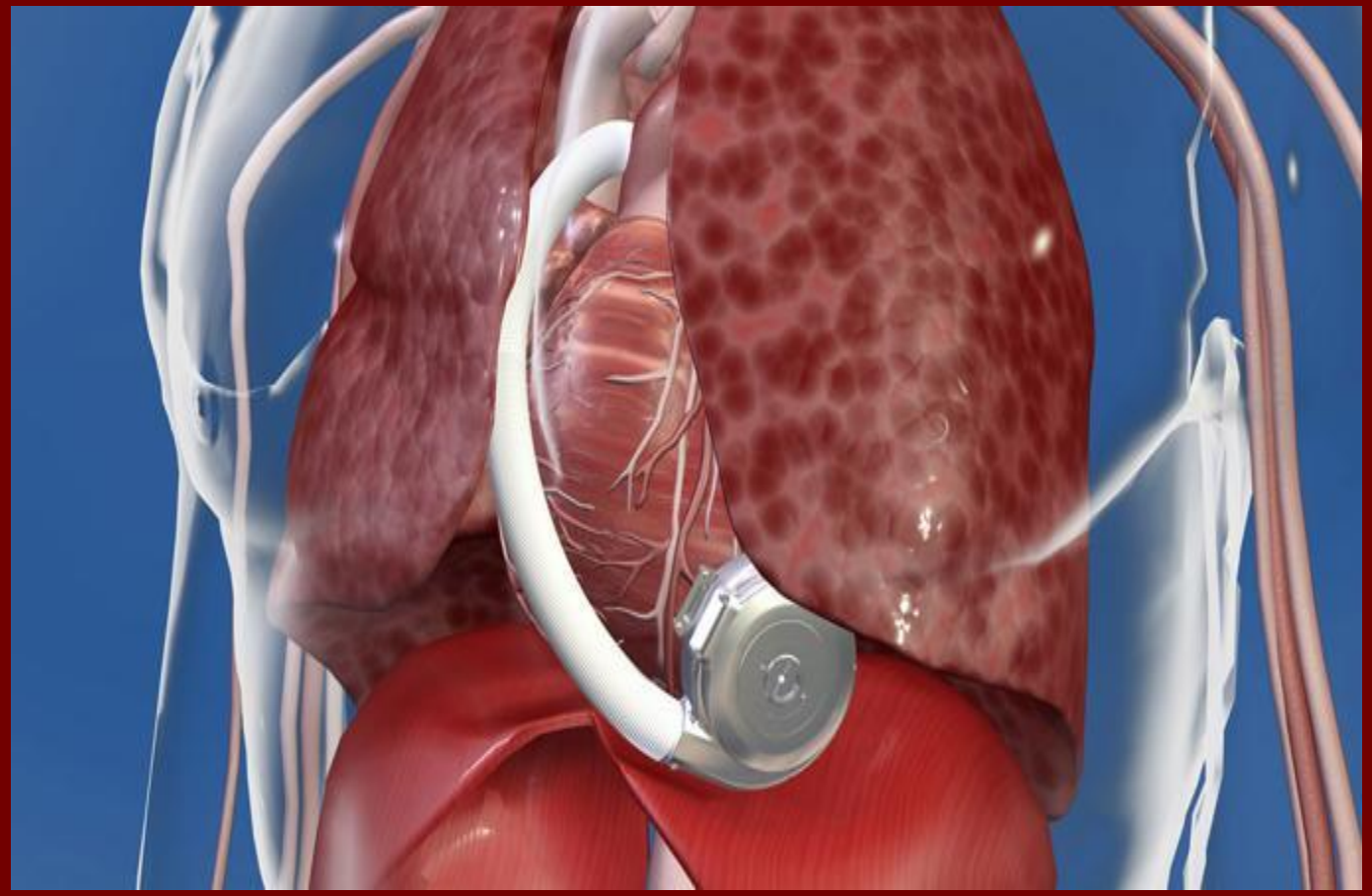


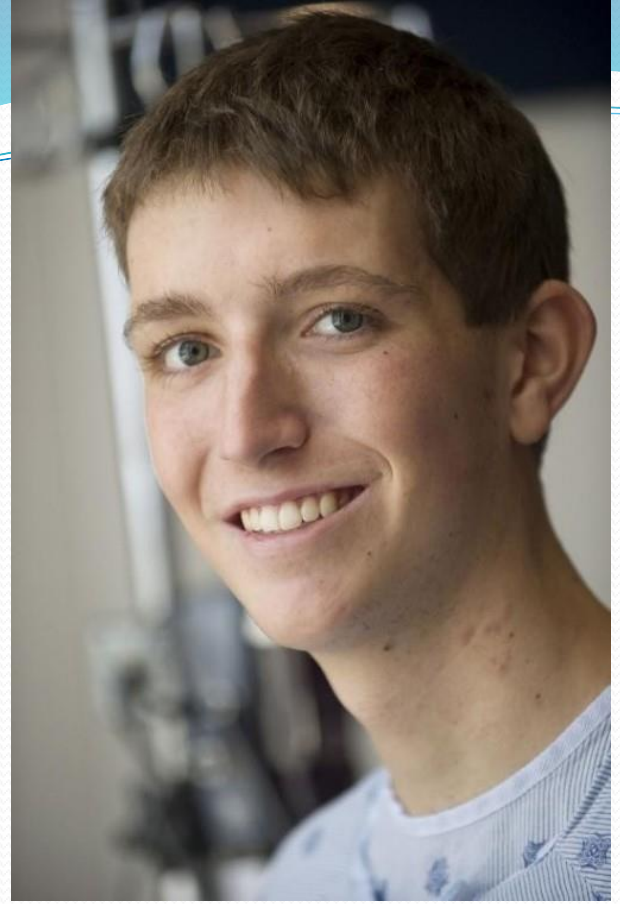
Approval of the HeartMate II for Destination Therapy in 2010 by FDA, opened the door for increased surgical impact on heart failure over heart transplantation alone

October 4, 2017

Medtronic HeartWare HVAD System APPROVED for Destination Therapy

FDA clears HVAD for patients with End Stage Heart Failure





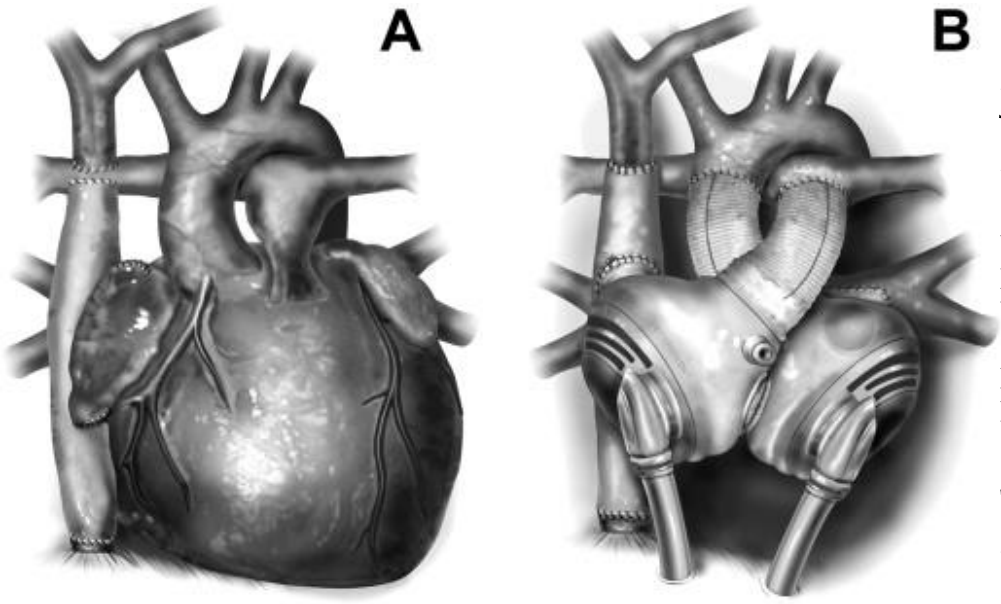
SynCardia TAH implant May 22, 2011,
Texas Children's Hospital

17 y/o Jordan Merecka

Complex CCTGA, Biventricular failure
Bridge to successful Transplant

FDA approved 2004 BTT

Total Artificial Heart for Failed Fontan



Successful Use of the Total Artificial Heart in the Failing Fontan Circulation

Joseph W. Rossano, MD, David J. Goldberg, MD, Stephanie Fuller, MD, Chitra Ravishankar, MD, Lisa M. Montenegro, MD, and J. William Gaynor, MD

Division of Cardiology, Department of Pediatrics, Division of Pediatric Cardiac Surgery, Department of Surgery, and Department of Anesthesia and Critical Care Medicine, The Cardiac Center, The Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania

Typical left ventricular assist devices are often ineffective for the failing Fontan circulation. We report the first successful use of a total artificial heart as a bridge to transplant in a patient who had previously undergone a Fontan operation.

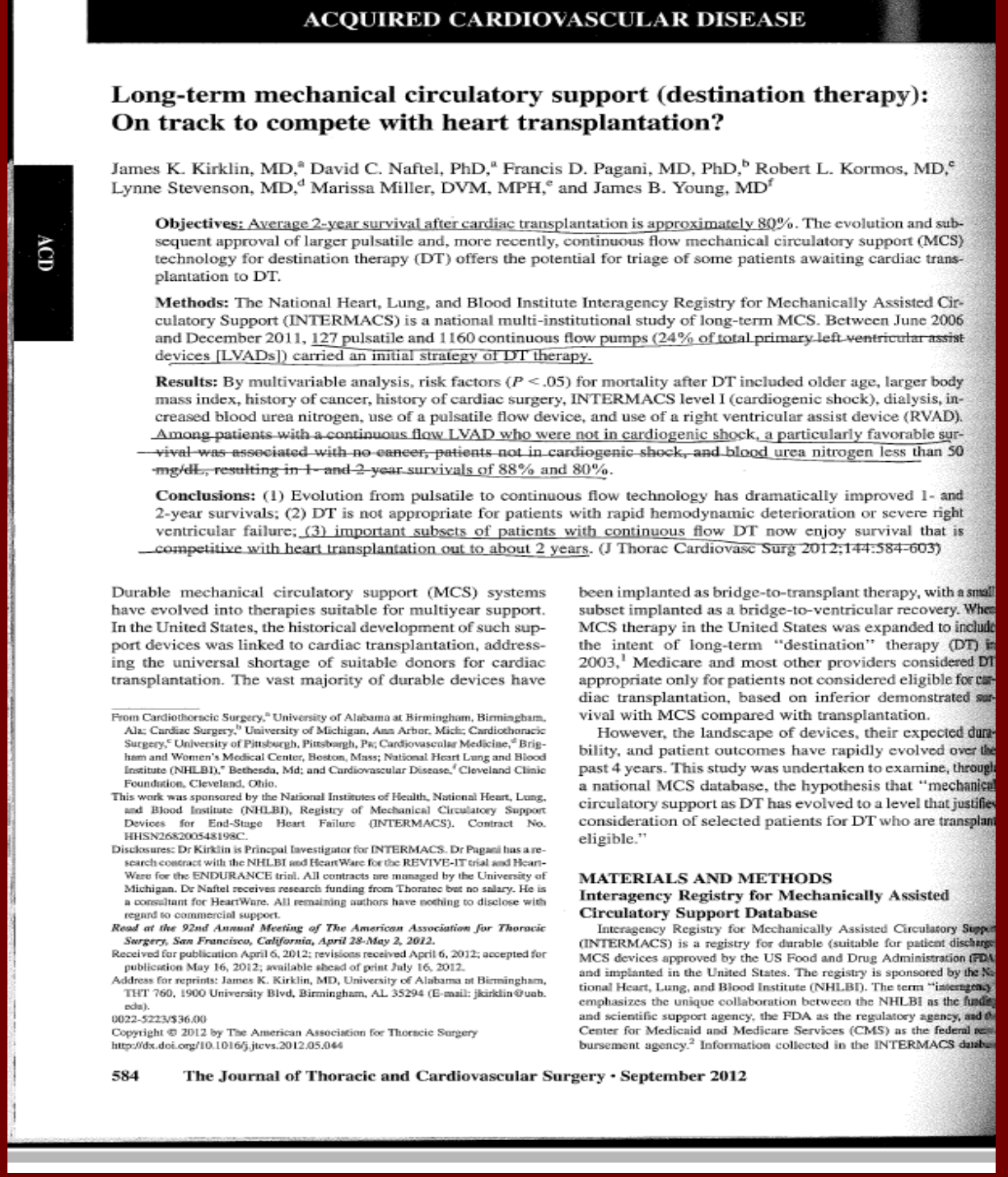
(Ann Thorac Surg 2014;97:1438–40)

September 2012

"Important subsets of patients with continuous flow DT now enjoy survival competitive with heart transplant out to 2 years"

No cancer
No cardiogenic shock at implant
No dialysis
BUN < 50 mg/dL
No severe right heart failure

1 year survival 88%
2 year survival 80%
Heart Transplantion
80%/2years



Long-term mechanical circulatory support (destination therapy): On track to compete with heart transplantation?

James K. Kirklin, MD,[a] David C. Naftel, PhD,[a] Francis D. Pagani, MD, PhD,[b] Robert L. Kormos, MD,[c] Lynne Stevenson, MD,[d] Marissa Miller, DVM, MPH,[e] and James B. Young, MD[f]

Objectives: Average 2-year survival after cardiac transplantation is approximately 80%. The evolution and subsequent approval of larger pulsatile and, more recently, continuous flow mechanical circulatory support (MCS) technology for destination therapy (DT) offers the potential for triage of some patients awaiting cardiac transplantation to DT.

Methods: The National Heart, Lung, and Blood Institute Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a national multi-institutional study of long-term MCS. Between June 2006 and December 2011, 127 pulsatile and 1160 continuous flow pumps (24% of total primary left ventricular assist devices [LVADs]) carried an initial strategy of DT therapy.

Results: By multivariable analysis, risk factors ($P < .05$) for mortality after DT included older age, larger body mass index, history of cancer, history of cardiac surgery, INTERMACS level 1 (cardiogenic shock), dialysis, increased blood urea nitrogen, use of a pulsatile flow device, and use of a right ventricular assist device (RVAD). Among patients with a continuous flow LVAD who were not in cardiogenic shock, a particularly favorable survival was associated with no cancer, patients not in cardiogenic shock, and blood urea nitrogen less than 50 mg/dL, resulting in 1- and 2-year survivals of 88% and 80%.

Conclusions: (1) Evolution from pulsatile to continuous flow technology has dramatically improved 1- and 2-year survivals; (2) DT is not appropriate for patients with rapid hemodynamic deterioration or severe right ventricular failure; (3) important subsets of patients with continuous flow DT now enjoy survival that is competitive with heart transplantation out to about 2 years. (J Thorac Cardiovasc Surg 2012;144:584-603)

Durable mechanical circulatory support (MCS) systems have evolved into therapies suitable for multiyear support. In the United States, the historical development of such support devices was linked to cardiac transplantation, addressing the universal shortage of suitable donors for cardiac transplantation. The vast majority of durable devices have been implanted as bridge-to-transplant therapy, with a small subset implanted as a bridge-to-ventricular recovery. When MCS therapy in the United States was expanded to include the intent of long-term "destination" therapy (DT) in 2003,[1] Medicare and most other providers considered DT appropriate only for patients not considered eligible for cardiac transplantation, based on inferior demonstrated survival with MCS compared with transplantation.

However, the landscape of devices, their expected durability, and patient outcomes have rapidly evolved over the past 4 years. This study was undertaken to examine, through a national MCS database, the hypothesis that "mechanical circulatory support as DT has evolved to a level that justifies consideration of selected patients for DT who are transplant eligible."

From Cardiothoracic Surgery,[a] University of Alabama at Birmingham, Birmingham, Ala; Cardiac Surgery,[b] University of Michigan, Ann Arbor, Mich; Cardiothoracic Surgery,[c] University of Pittsburgh, Pittsburgh, Pa; Cardiovascular Medicine,[d] Brigham and Women's Medical Center, Boston, Mass; National Heart Lung and Blood Institute (NHLBI),[e] Bethesda, Md; and Cardiovascular Disease,[f] Cleveland Clinic Foundation, Cleveland, Ohio.

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MATERIALS AND METHODS

Interagency Registry for Mechanically Assisted Circulatory Support Database

Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a registry for durable (suitable for patient discharge) MCS devices approved by the US Food and Drug Administration (FDA) and implanted in the United States. The registry is sponsored by the National Heart, Lung, and Blood Institute (NHLBI). The term "interagency" emphasizes the unique collaboration between the NHLBI as the funding and scientific support agency, the FDA as the regulatory agency, and the Center for Medicaid and Medicare Services (CMS) as the federal reimbursement agency.[2] Information collected in the INTERMACS database

PROVOCATIVE EDITORIAL

How do we care for the potential > 80,000 patients/per year in USA and Europe alone in need of surgical management of heart failure?

Continuous flow blood pumps: the new gold standard for advanced heart failure?

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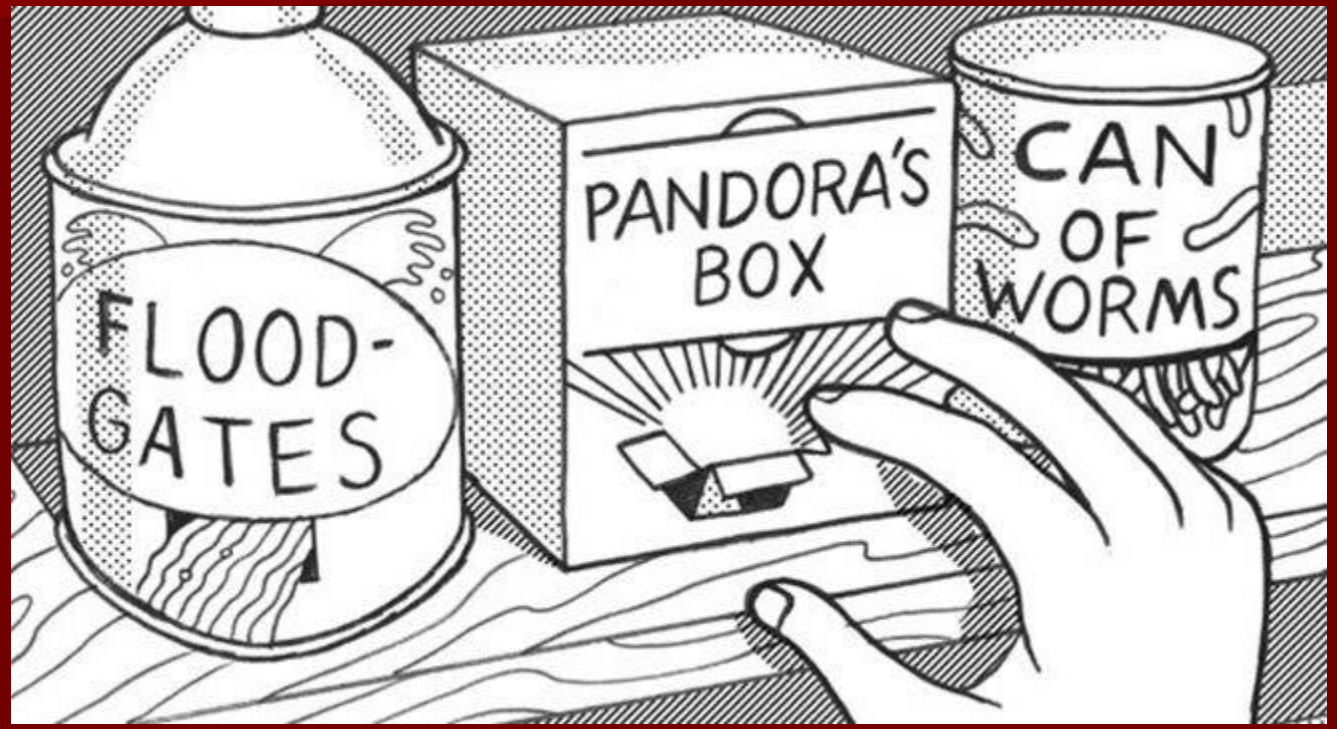
Keywords: Heart transplantation • Mechanical circulatory support • Heart failure • Continuous flow pump

Consider the familiar phrase ‘cardiac transplantation sets the gold standard for the treatment of severe heart failure’. Does this still ring true? For the advanced heart failure (AdHF) patient, the primary objective is to provide symptomatic relief from intolerable breathlessness, lethargy and fatigue [1]. The secondary aim, conditional upon the primary objective being met, is to extend life. Neither is accomplished easily in refractory Stage D heart failure (New York Heart Association (NYHA) IV). Conventionally, at this stage, only cardiac transplantation or palliative care options remain

TRANSPLANTATION REMAINS A RARE COMMODITY THAT BENEFITS A SMALL SELECTIVE GROUP OF YOUNGER PATIENTS

ACHD patients might not be best candidates for "Destination Therapy"

- Criteria for Destination Therapy continue to evolve as devices continue to improve
- ACHD patients who are highly sensitized or have elevated PVR should be considered for a destination VAD then reconsidered for transplant when criteria met
- Initial mortality following heart transplant is higher for ACHD, but long term outcomes are better
- Multiple previous operations, complex anatomy, single ventricle, and Failed Fontan physiology, ie., Protein Losing Enteropathy, plastic bronchitis, favor heart transplant over a VAD
- Should ACHD candidates receive preference for heart transplant donors? I believe so.


FLOOD-
GATES
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WORMS

“Fighting for peace is like screwing for virginity.” – George Carlin.

Distribution of Device Strategy for ACHD and non CHD patients: INTERMACS 2008-2014

Device Strategy (Pre-implant)	Primary Diagnosis	
	Congenital Heart Disease	Not Congenital Heart Disease
	N (%)	N (%)
BTT Listed	39 (51%)	3786 (29%)
BTT Likely	17 (22)	2819 (21%)
BTT Moderate	6 (8%)	1271 (10%)
BTT Unlikely	3 (4%)	411 (3%)
Destination Therapy	10 (13%)	4737 (36%)
BTR	1 (1%)	100 (1%)
Rescue Therapy	0 (0%)	76 (1%)
Other	0 (0%)	12 (0.1%)
Totals	76 (100%)	13,212 (100%)

INTERMACS database 2006-2015

VAD recipients with ACHD were more likely to have a Bridge to Transplant strategy (45 vs 28%, $p<0.001$) than non-ACHD, and destination therapy was less frequent in ACHD patients compared to non-ACHD patients(16 vs 37%, $p<0.001$)

What Does The Future Hold?

HEART HEALTH

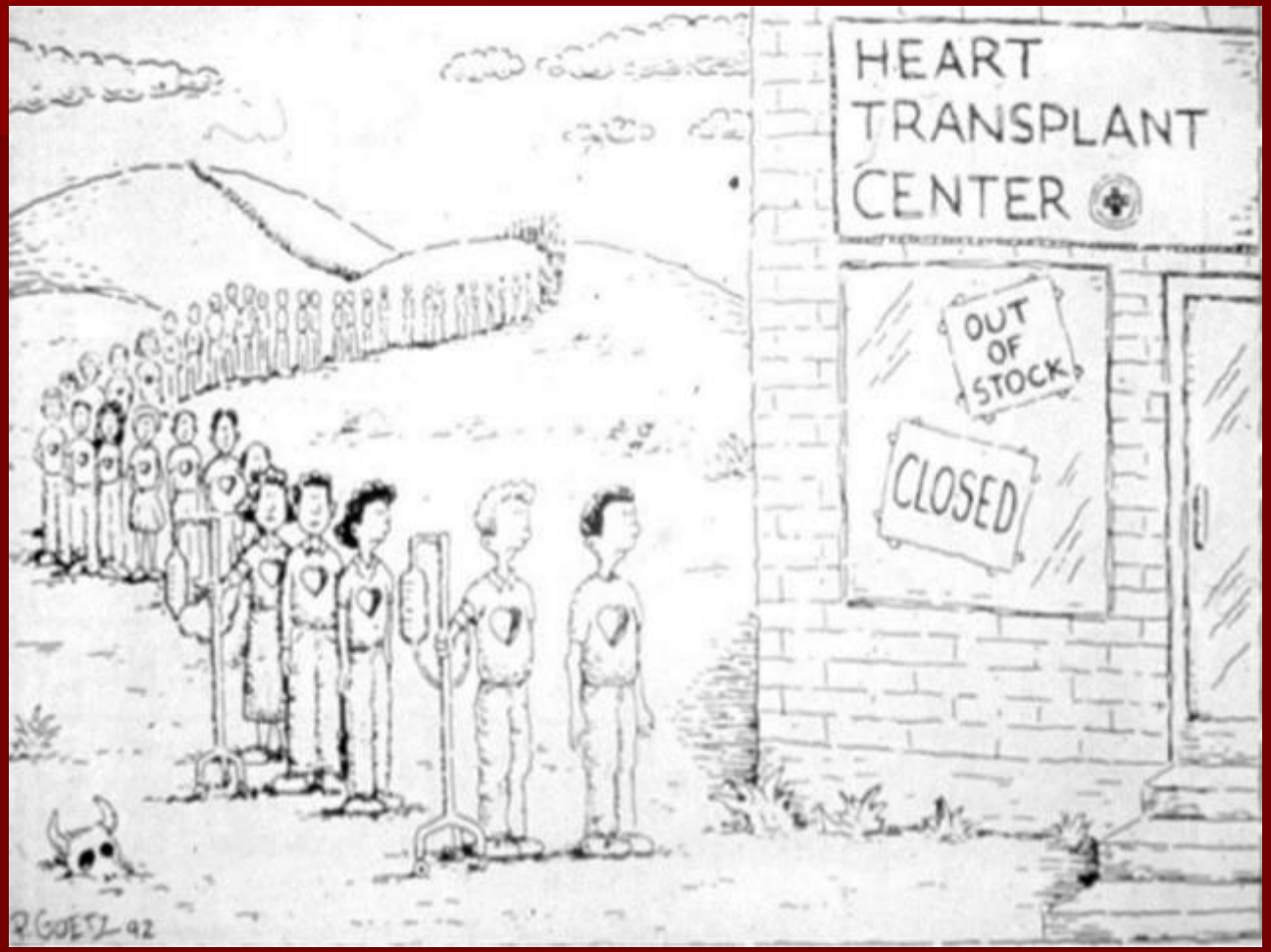
Permanent artificial heart could eliminate the need for transplants

By Melinda Carstensen

Published March 24, 2016

Fox News

Costs must decrease, patient selection has to be refined, and technology has to advance to point where external driveline is avoided(transcutaneous energy transfer system)


HEART
TRANSPLANT
CENTER
OUT
OF
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CLOSED
R GOETZ 92

PARADIGM SHIFT

In the future, patients will be given a VAD when it is clinically needed; most patients will stay on the device, and those who experience device complications will undergo transplantation along with patients who are not suitable for device implantation in the first place…
i.e. ACHD patients

In that way, good candidates can be listed for transplantation after full evaluation, and the limited organ supply can be allocated most appropriately.

Texas Heart Inst J 2011 A Changing Trend Toward Destination Therapy

COST IS STILL A HUGH ISSUE!

DESTINATION THERAPY NOT APPROVED

Quality Adjusted Life Year(QALY) still above 100,000 USD

By 2015, 50% of MCA devices implanted in the USA were implanted for “Destination” Therapy

2017 INTERMACS REPORT

ONLY TIME WILL TELL


Royal Mecca clock, Mecca, S.A.
World's largest clock tower
AP

THANK YOU!