Left Ventricular Assist Devices (LVADs): Overview and Future Directions

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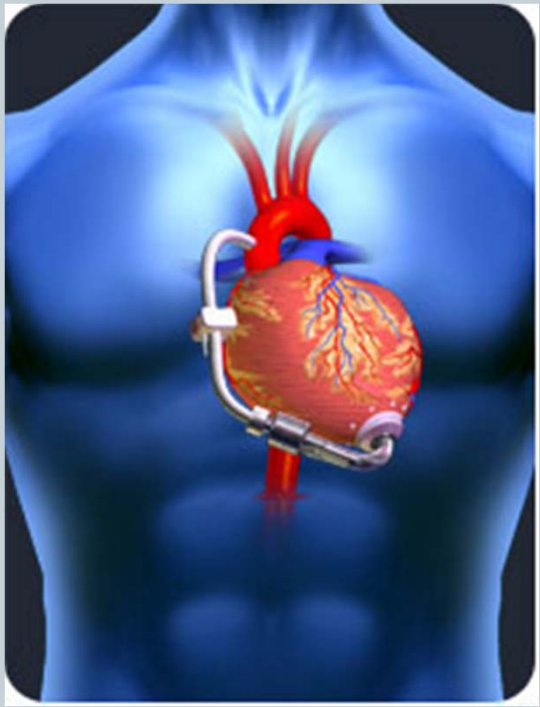

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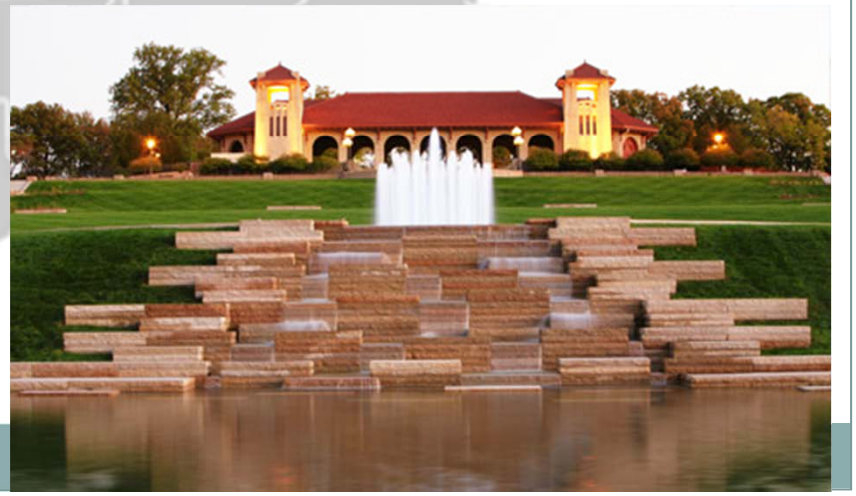

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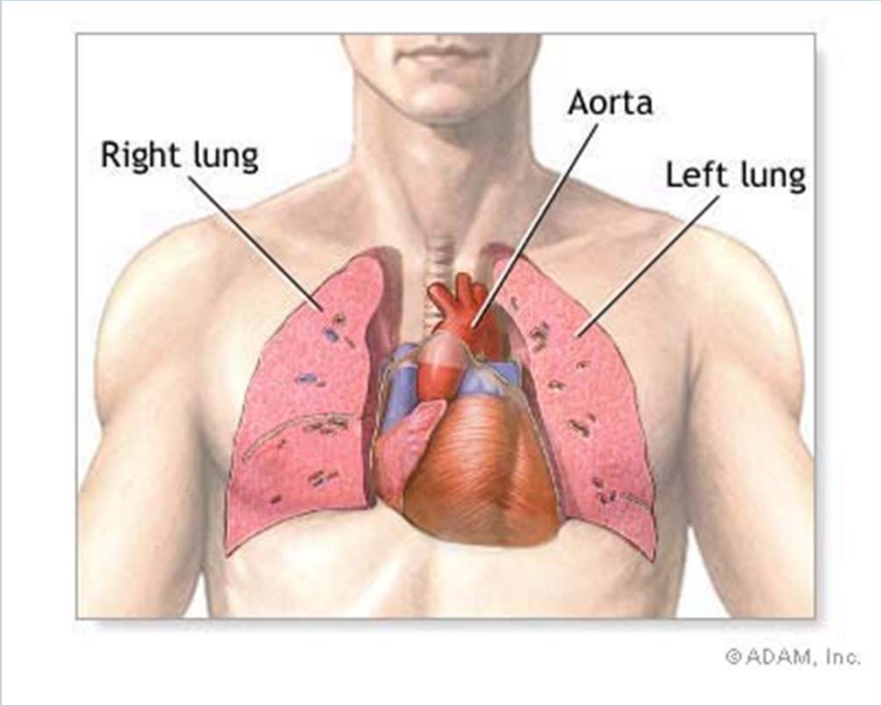
Medical Technology in the U.S.

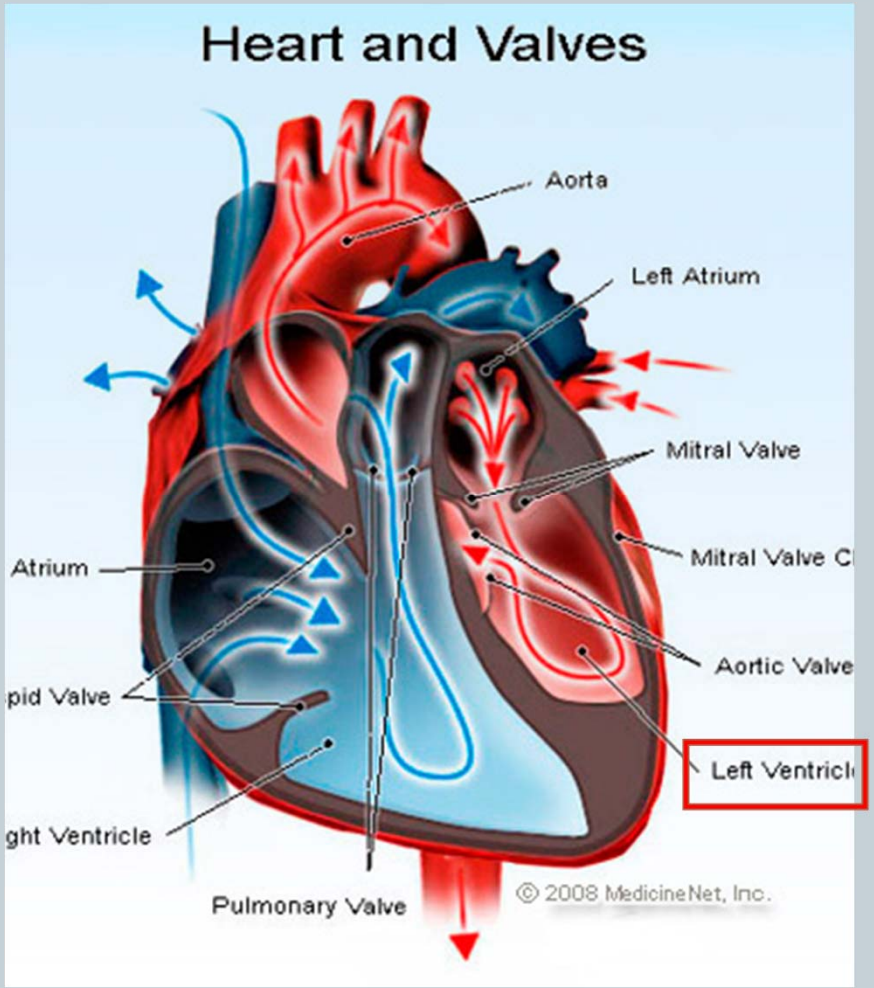
- Largest producer and consumer of medical technology worldwide: 40% of the global market
  - American healthcare is expensive: 17% of the GDP
- $100 billion market in 2010; $38 billion in exports
  - Electromedical (pacemakers, MRI, ultrasound)
  - Radiation (CT, diagnostic imaging)
  - Surgical supplies (orthopedic joints, stents)
- Investment in medical device R&D doubled in the 1990s
- Focus on: Medical Technology therapies in Heart Failure
  - Ventricular Assist Devices (VADs)

Definition and Epidemiology of Heart Failure

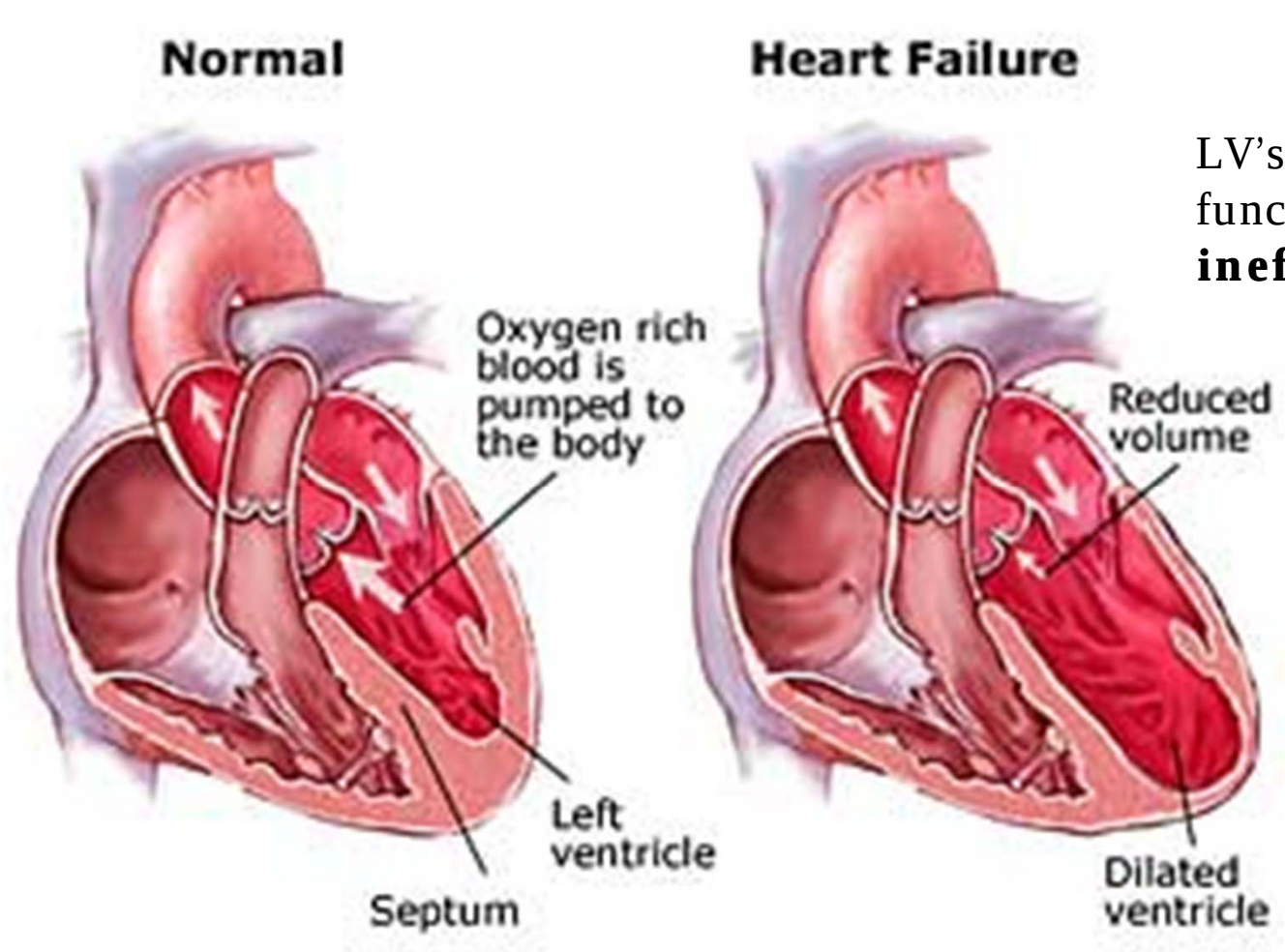
- Systemic perfusion inadequate to meet the body's metabolic demands due to **impaired cardiac function**
- Most common cause is **left ventricular (LV) dysfunction**
  - Coronary artery disease / Ischemic cardiomyopathy
  - Dilated cardiomyopathy
  - Valvular heart disease
  - Hypertensive heart disease
- 5.8 million Americans in 2006 (2% of the U.S. population)
  - 550,000 new cases diagnosed annually
  - 23 million individuals worldwide (est.)
- Over time → decreased quality of life and more frequent admissions
  - One million hospital admissions and $28 billion annually
- Cardiac transplant: well-accepted treatment for end-stage heart failure
  - Severe organ shortage

Normal Anatomy Review





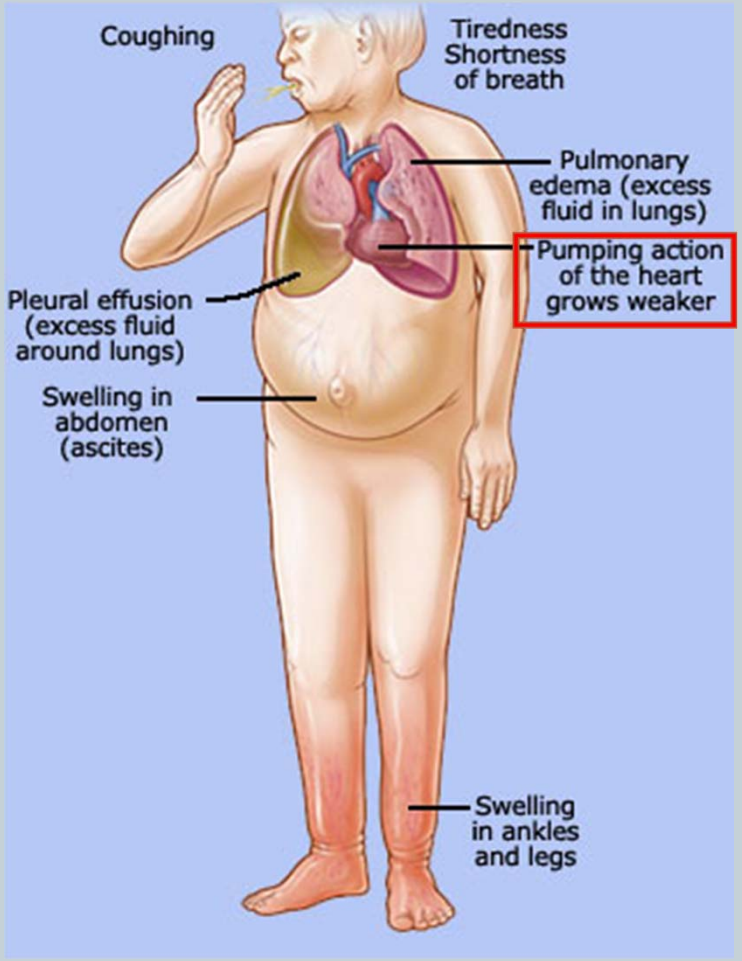
Pathophysiology of Heart Failure



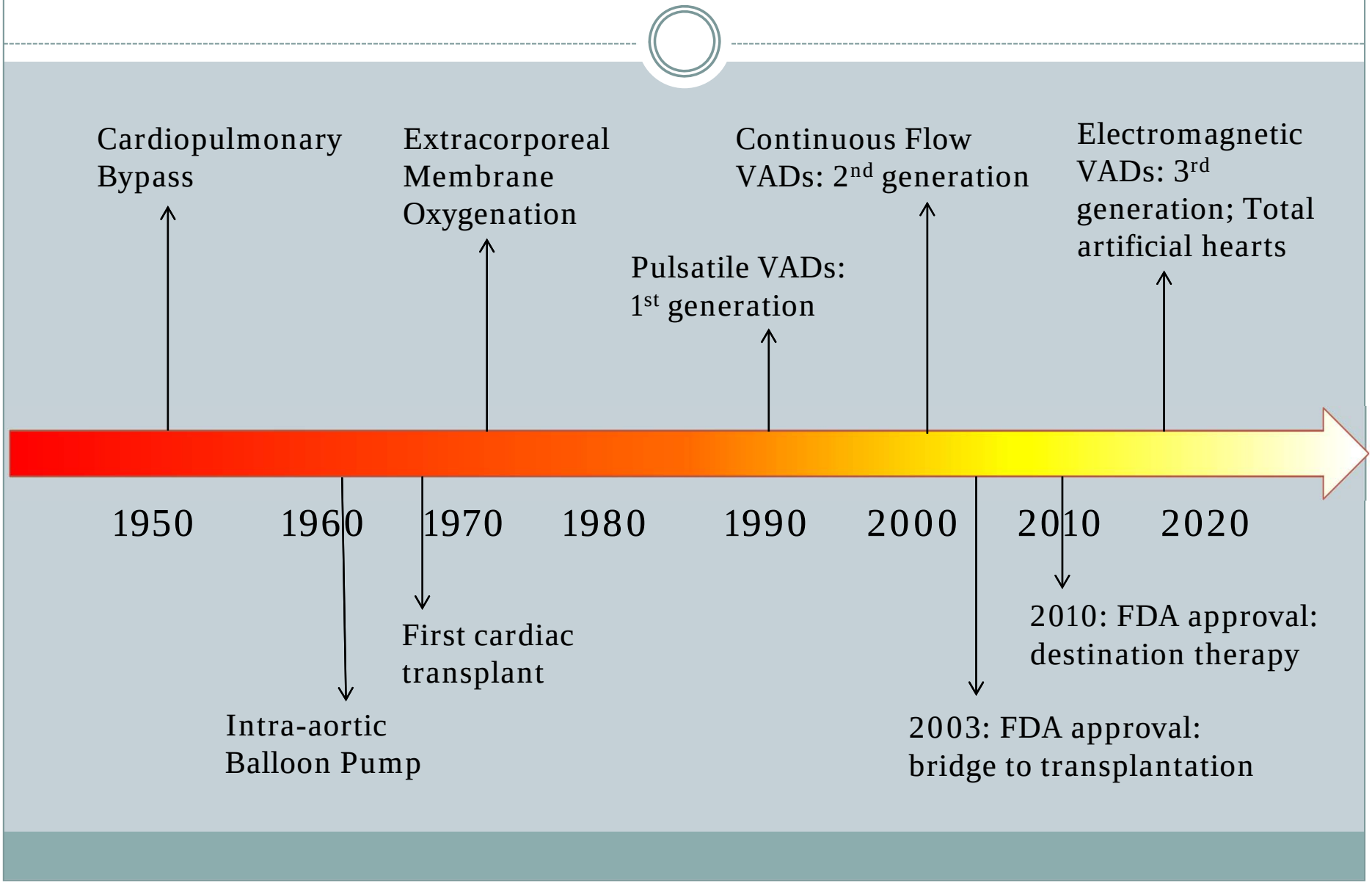
LV's pumping function is **ineffective**

Heart Failure Signs and Symptoms

- As the stage of heart failure progresses (I →IV), mortality increases
- Treatment options for end-stage heart failure are limited
- The significant morbidity and mortality of heart failure led to exploration of **mechanical cardiac support devices** for end-stage heart failure



History of Mechanical Cardiac Support



Ventricular Assist Devices (VADs)

- A **mechanical** circulatory device used to partially or completely **replace cardiac function**
- Mechanical support and ventricular unloading enables:
  - Hemodynamic stabilization
  - Organ recovery (reverse remodeling, normalization of chamber geometry)
  - Improved contractile performance
- May replace the right, left, or both ventricles
  - Left ventricular assist device (**LVAD**) most common
- Most commonly used in **end-stage heart failure**
- More than 4000 **HeartMate II** implanted since 2008
  - 1700 devices per year in the U.S.
  - 430 per year in Europe

Heart Mate II

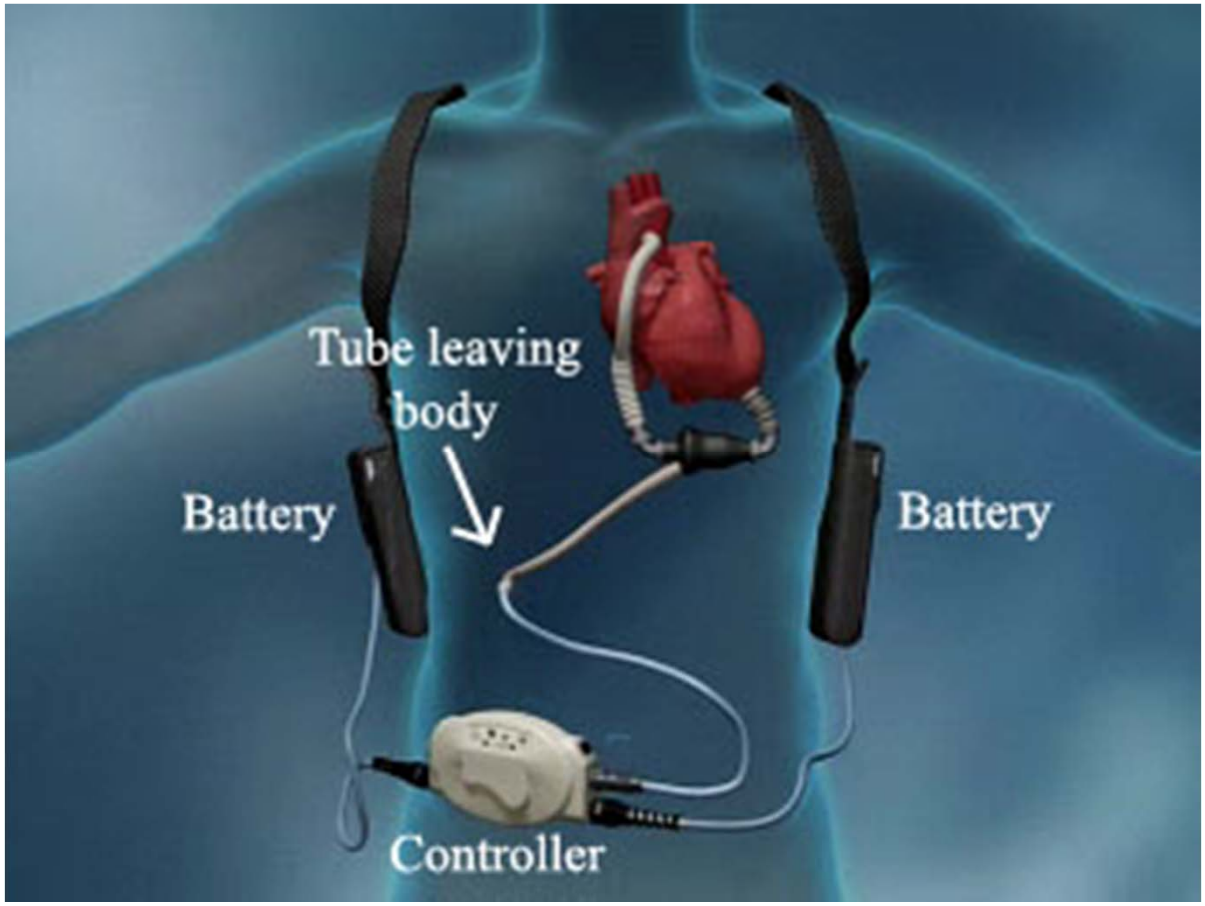
B

Figure 1

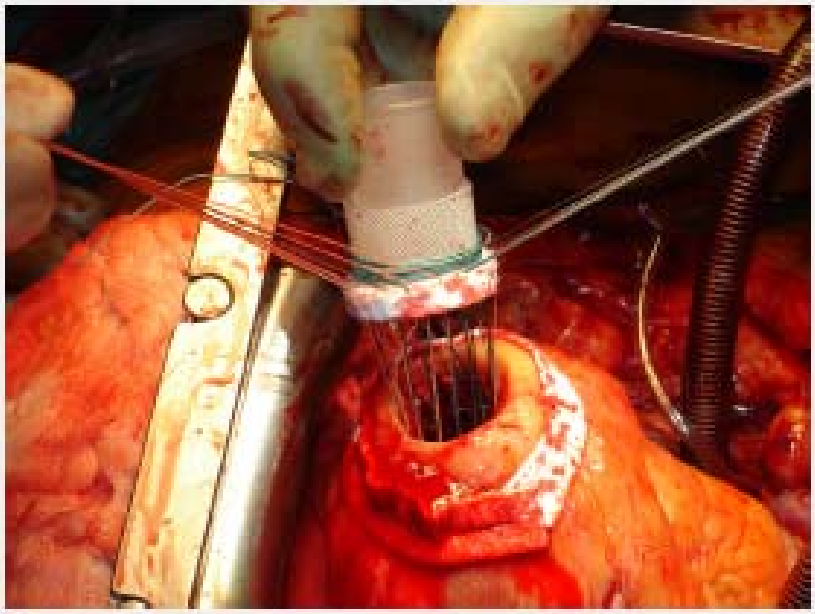
The Heart Mate II left ventricular assist device (reprinted with permission from Thoratec corporation). **A**: Housing with vascular prothesis to the ascending aorta. **B**: The impeller which is located within the housing. (© With courtesy by Thoratec Corporation).

LVAD Function

- Inflow cannula connected to LV apex
- Outflow cannula connected to aorta
- Intracorporeal pump with continuous axial flow rests below diaphragm
- Device mechanically pumps blood
- Up to 15,000 rotations/min = 8-10L/min blood flow



Surgical Implantation



A

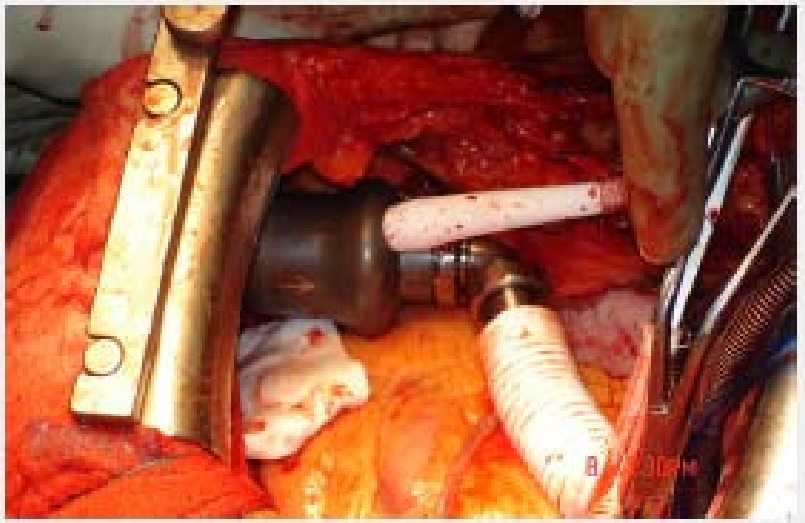


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Figure 2:

A: Fixation of the sewing ring for further insertion of the device wihtin the left ventricular apex. B: Device in situ (intrapericardial).

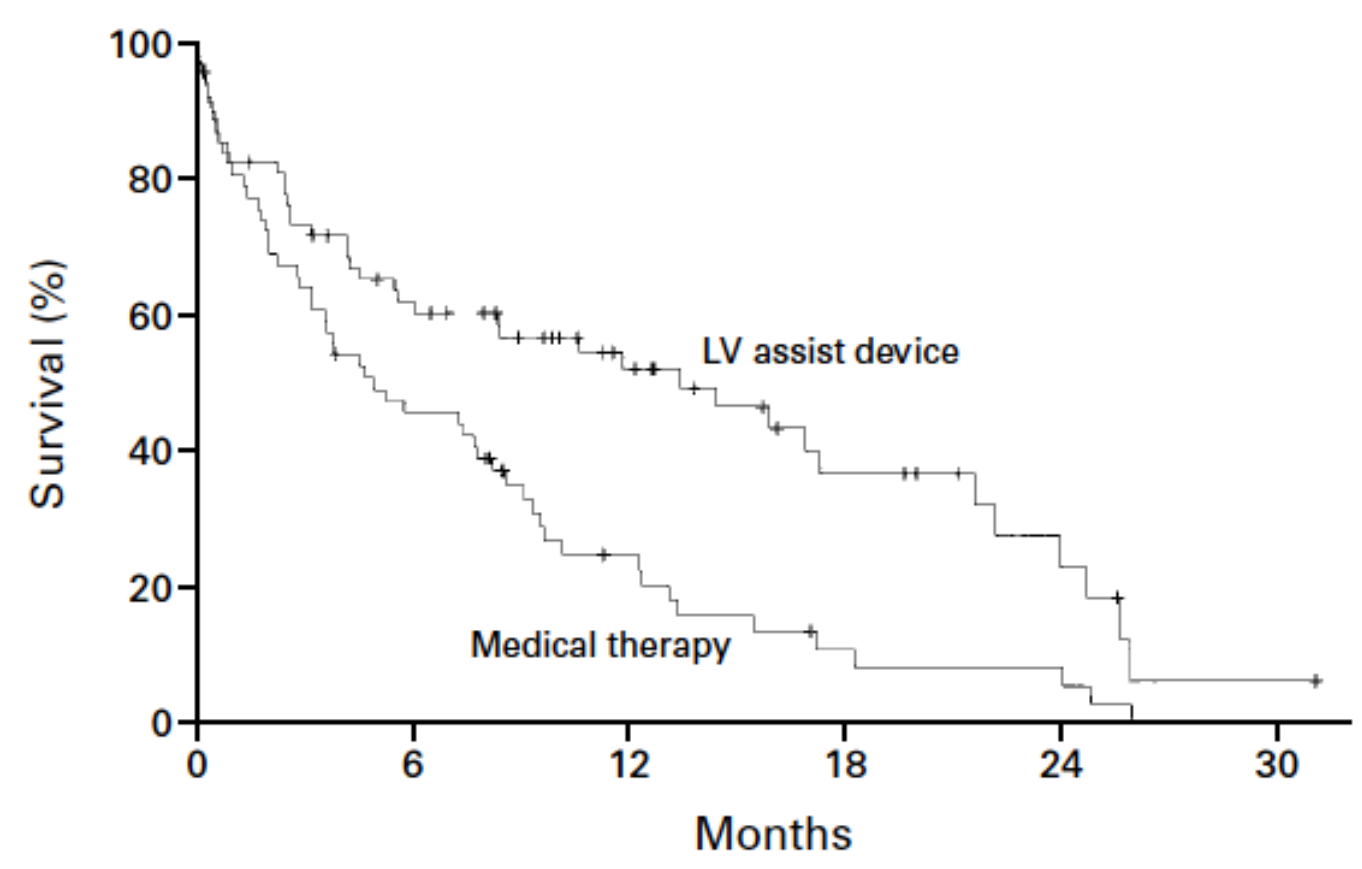
Patient Selection

- Bridge to **cardiac transplant**
  - Most frequent indication worldwide
- Bridge to **recovery**
  - Mechanical support during reverse remodeling
  - Acute MI, graft failure, postpartum cardiomyopathy
- **Destination therapy**
  - Not a transplant candidate (age, comorbidities, noncompliance)
  - USA, Canada, Germany, Austria
- Bridge to **decision** (short-term LVAD)
  - Emergency cardiogenic shock (Acute MI, fulminant myocarditis)
  - Immediate stabilization for days-weeks during further evaluation
- Candidates must:
  - Be on **maximal inotropic support** +/- intraortic balloon pump (**IABP**) AND
  - Systolic BP < 80 AND Cardiac index < 2.0 OR PCWP > 20
  - No irreversible secondary end-organ damage

Complications

- **Infection**: 28% at 3 mo
  - Especially of driveline and pocket; Fatal sepsis in 25%
- **Bleeding**: 42% at 6 mo
  - Perioperative
  - Postoperative anticoagulation: target INR 2.5-3.5
- **Stroke and peripheral thromboembolism**
  - Incidence lower with newer devices
- **RV failure**
  - RV function must be optimized prior to implantation
  - May require postoperative vasopressors
- **Arrhythmia**
  - Monomorphic VT
- **Hemolysis**
  - Acquired von Willebrand syndrome
- **Device failure**: 0 at 1 yr; 35% at 2 yr
- Complications limit the ability of the technology to provide indefinite support

REMATCH Trial: NEJM 2001



- 129 patients assigned to LVAD vs optimal medical therapy
- Survival 52 vs 25% at 1 yr; 23 vs 8% at 2 yr = 48% reduction in mortality
- Significantly improved quality of life at one year

HeartMate II: Bridge to Therapy

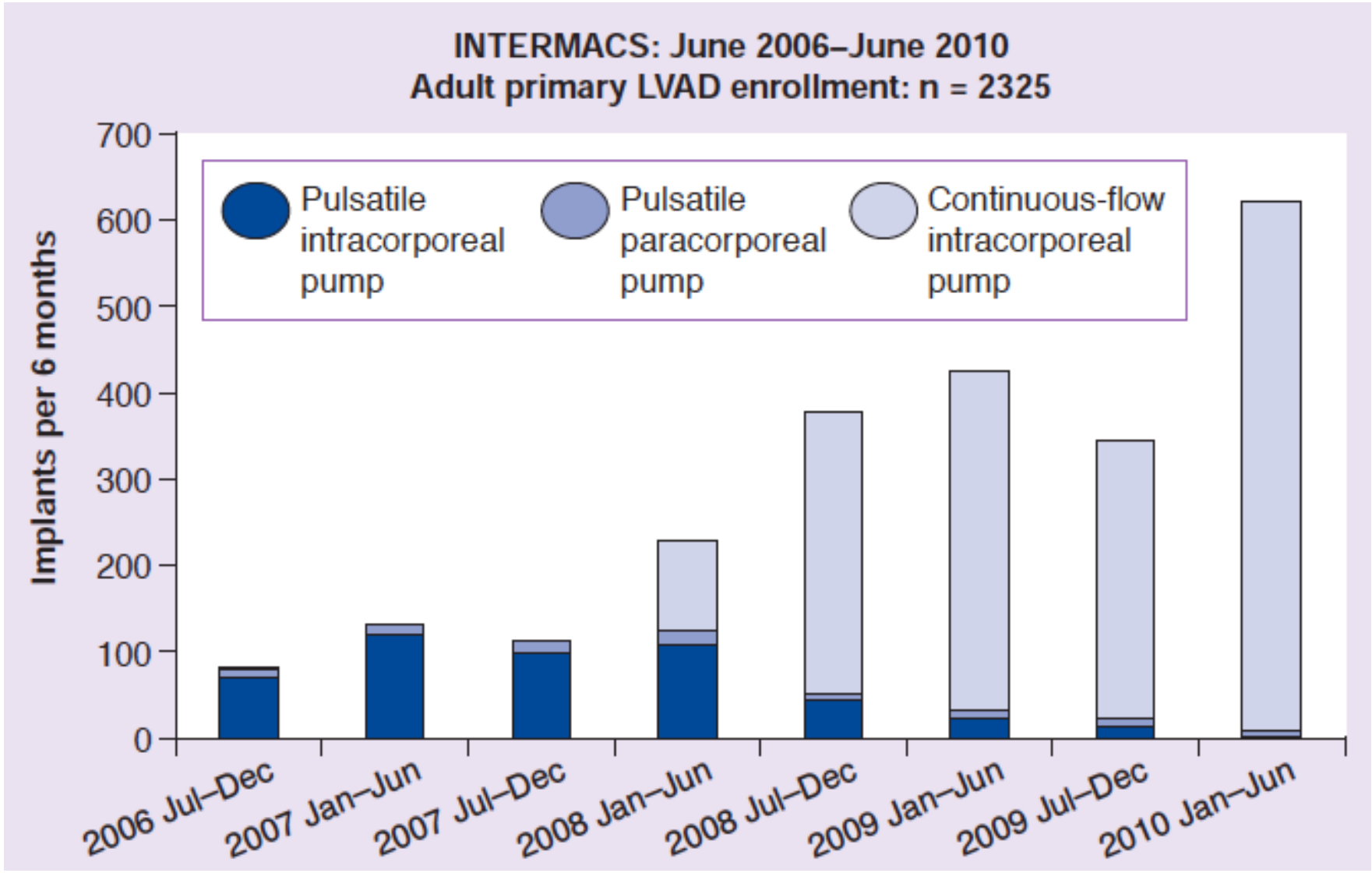
- One study of 133 patients receiving HeartMate II demonstrated:
  - Primary outcome of cardiac recovery, cardiac transplant, or survival occurred in 75%
  - 68% survival at one year
  - Significant improvements in NYHA functional class, 6 minute walk, and quality of life at 3 mo

LVAD: Long-Term Outcomes

- Medicare database analysis of 1476 LVAD recipients
- 55% were discharged alive
- Of these,
  - 56% readmitted within 6 months
  - 21% underwent heart transplant at one year
- Overall one-year survival 52%
- Mean Medicare payment $ 178,714 for one year
- INTERMACS study showed survival 56% at one year

The Growing LVAD Market

- In the US, 50-60,000 patients annually could benefit from heart transplant
  - 1,897 transplants performed in 2003
  - LVADs designed to fill the gap
- Market analysis estimates 54,000 annual LVAD candidates in the developed world
  - US: 20,000 destination therapy, 1500 bridge to transplant
  - Similar rates estimated in Europe
- Rates expected to increase as more patients are placed on transplant list and eligibility criteria increase in flexibility


INTERMACS: June 2006–June 2010
Adult primary LVAD enrollment: n = 2325
Implants per 6 months
700
600
500
400
300
200
100
0
Pulsatile intracorporeal pump
Pulsatile paracorporeal pump
Continuous-flow intracorporeal pump
2006 Jul–Dec
2007 Jan–Jun
2007 Jul–Dec
2008 Jan–Jun
2008 Jul–Dec
2009 Jan–Jun
2009 Jul–Dec
2010 Jan–Jun

LVAD in Japan

- 113 patients underwent cardiac transplant 1999-2011
  - Longest waiting period of all available countries, > 2. 5 years
  - Law change regarding brain death in 2010; 30 transplants in 2010
- 90% of transplant candidates require LVAD
  - Mean wait time 877 days
  - Internationally, 27% require LVAD with 50 day wait time
- Japan Social Reimbursement System approved Nipro LVAD (1^{st} gen)
  - In 2011, approved Evaheart and Duraheart (2^{nd} gen.)
  - More common LVADs anticipated approval soon

Financial Considerations

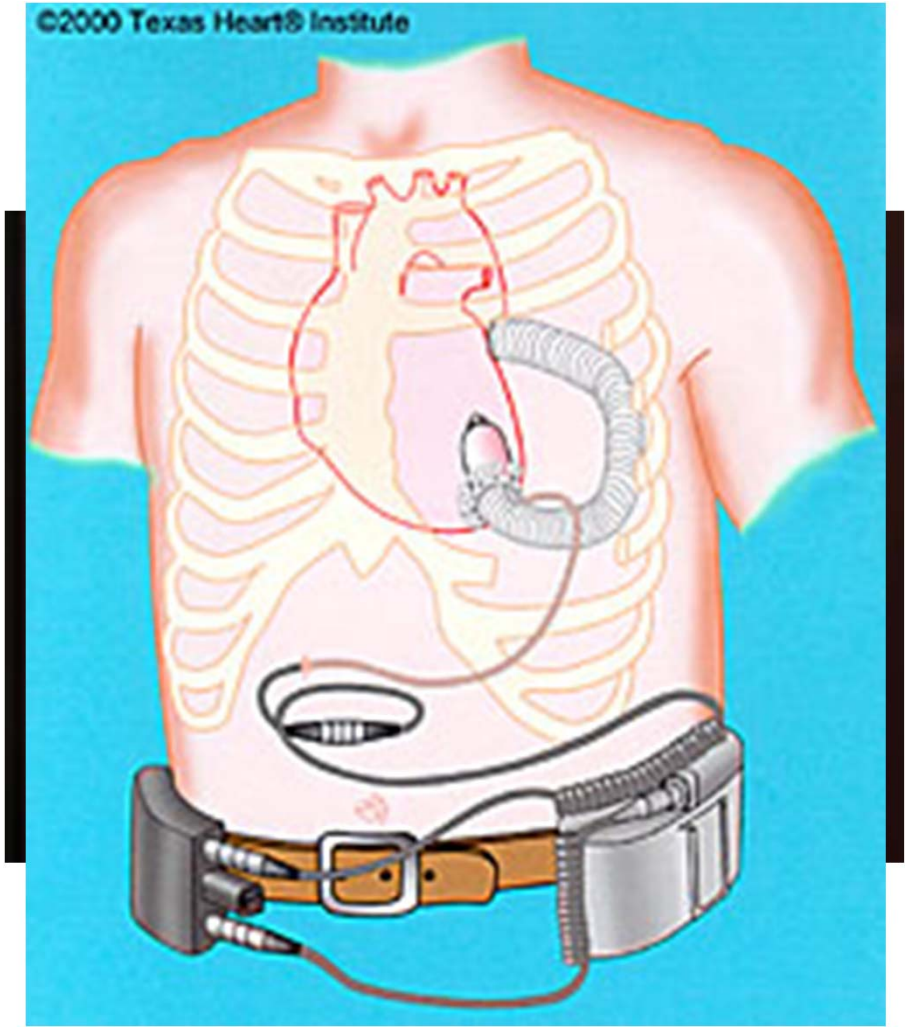
- Extensive debate regarding high LVAD costs versus potential benefits in US healthcare politics
- Cost estimates vary
  - Initial hospitalization costs $200,000
  - Fully functional HeartMate XVE costs $100,000
  - Outpatient costs after discharge $13,200
- Quality-adjusted life year (QALY)
  - Initial estimates $800,000 per QALY
  - More recent analyses estimate $100,000-150,000 per QALY
- Assumption that costs will fall over time as technology becomes more widespread

Future Directions

- **Jarvik 2000**: axial flow, continuous flow impeller pump
- Transcutaneous Energy Transfer System **(TETS)**
  - Avoid driveline infections
- Electromagnetic (centrifugal) continuous flow pump
  - 3rd generation LVAD
  - Magnetically levitated, more efficient, long lifespan
- **Total artificial heart**
  - Abiomed TAH currently undergoing clinical trials

Jarvik 2000

- Totally implantable, silent, unobtrusive
- Encapsulated within myocardium
- Decreased risk of infection and hemolysis
- Power cable to RUQ or base of skull
- Trial underway to compare to medical therapy



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CASE REPORT

The first clinical case in Japan of destination therapy using the Jarvik 2000 left ventricular assist device

Sokichi Kamata · Taichi Sakaguchi · Shigeru Miyagawa · Yasushi Yoshikawa · Takashi Yamauchi · Koji Takeda · Shunsuke Saito · Takayoshi Ueno · Toru Kuratani · Yoshiki Sawa

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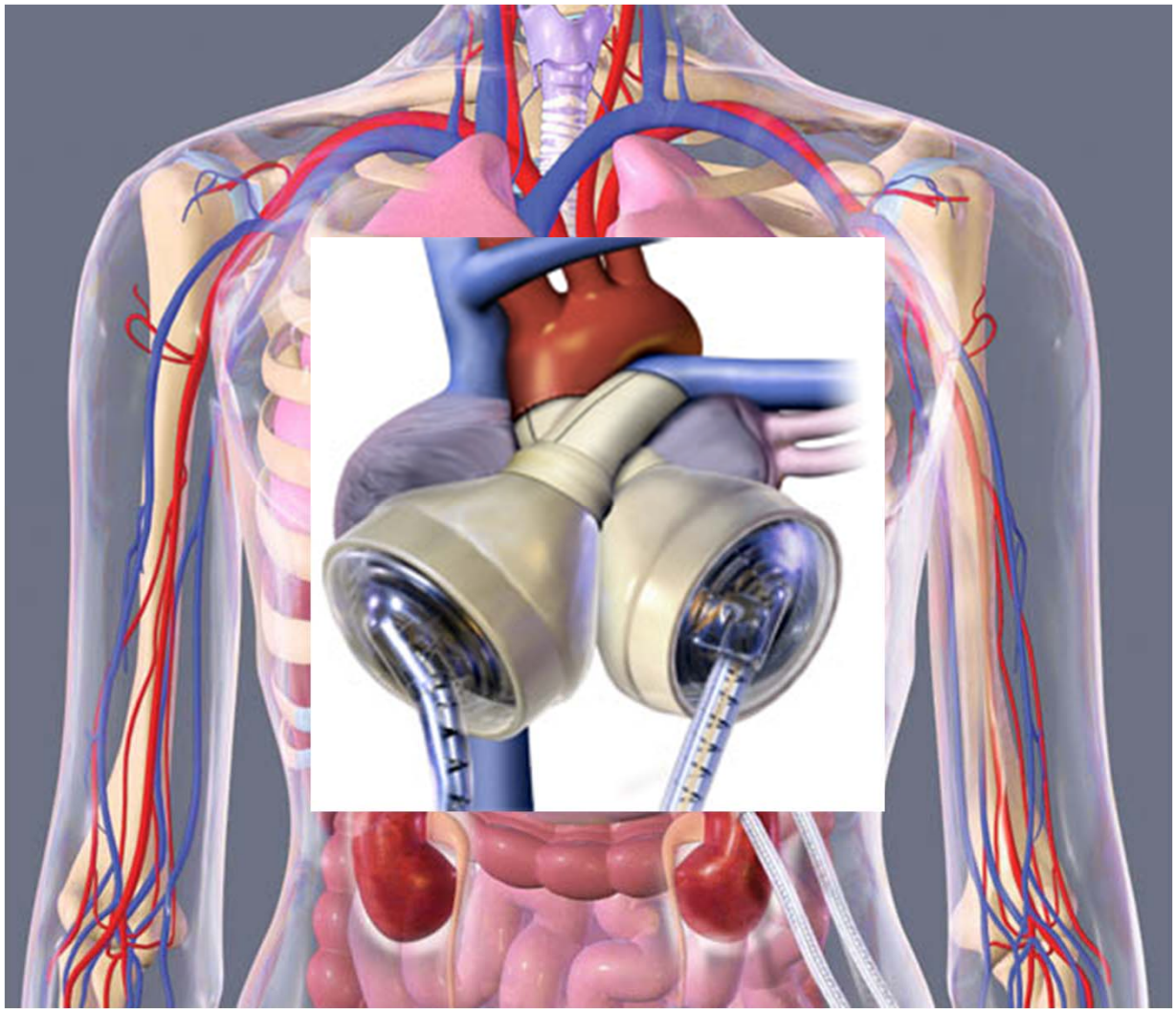
Abiomed Total Artificial Heart

- Patient's heart totally excised
- RV + LV replacement
- Device entirely within mediastinum
- Energy from low viscosity oil
- Wire in abdomen provides connection for transcutaneous energy transfer
- Currently under clinical trials



Questions?

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