LVADs: Ready for Prime Time?

Bruce B Reid, MD  Surgical Director
Artificial Heart Program/Heart Transplantation
Embracing Progress

The Evolution of Communication

First Written Word

Movable Type

Mass Publication

Email

Twitter

140 Characters. What More Is There to Say?
Technology Adoption

"The Chasm"

Innovators
Early Adopters
Early Majority
Late Majority
Laggards

Technology Adoption Lifecycle

Area under the curve represents number of customers
Automobile
Automobile

- Ford Model T
- 1908 – 1927
- First affordable automobile
- Mass production
- Moving assembly line: every three minutes
- 20 horsepower 1.7 L 4 cylinder engine
- Top speed ~40 mph
Automobile

- Most influential car of the 20th Century
- Widespread adoption worldwide
- 50% of all cars in 1920
- 1909: 10,666 produced and sold for $825 ($21,650 in 2015)
- 1925: 1.9 million sold for $260 ($3,500 today)
Aviation
Adoption of Technology

CONSUMPTION SPREADS FASTER TODAY

Percent of U.S. Households

ELECTRICITY

CLOTHES WASHER

CLOTHES DRYER

DISHWASHER

MICROWAVE

VCR

INTERNET

TELEPHONE

REFRIGERATOR

STOVE

AUTO

RADIO

COLOR TV

COMPUTER

AIR-CONDITIONING

CELLPHONE

VCR

INTERMOUNTAIN
Heart Institute
Intermountain Medical Center
Three apples changed the world,
the first one tempted eve, the second inspired newton and
the third was for Steve Jobs

Rest in Peace....

1955 - 2011
“A surgeon who tries to suture heart wounds deserves to lose the esteem of his colleagues.”

Theodor Billroth
(1829 – 1894)
Closed Mitral Commissurotomy
Pioneer in the development of extracorporeal circulation
Massive Pulmonary Embolus
Early Heart Lung Machine
Thomas Jefferson University

First successful open heart surgery using cardiopulmonary bypass

May 16, 1953
Science Unveils Machine That Acts As Both Heart and Lungs of Humans

Philadelphia (AP) — A machine that functioned as both heart and lungs of a human being for the first time in medical history was unveiled yesterday by surgeons at Jefferson Medical College Hospital.

Invented by Dr. John H. Gibbon Jr., director of surgical research at the college, the machine was shown to newsmen yesterday with the announcement that it had performed the combined functions of both organs while surgeons closed an abnormal opening in the wall of a patient’s heart.

The operation was performed Wednesday on Miss Cecelia Bavo- lek, of Swoyersville, Pa., 18-year-old student at Wilkes College in Wilkes-Barre, Pa.

For years the girl had suffered large opening between the auricles causing the trouble. Dr. Gibbon said the opening “about the size of a half dollar” meant that a large portion of her blood was continuously being recirculated through her lungs. Only a small part of it was pumped through the remainder of her body, causing a condition known as circular septal defect which deprives the muscles and bones of the body of their normal nourishment.

Dr. Gibbon described the operation in this way:

The patient’s heart was opened and the abnormal opening closed. The surgeons placed tubes in the two big veins leading to the heart and another in the artery in the chest. The tubes were connected to pumps which drew the blood out and circulated it.
Heart Lung Machine
Mechanical Circulatory Support

Short Term / Emergency
- Time frame: hours to days
- Rapid MCS for cardiogenic shock, post cardiotomy failure, or during high-risk Cath Lab procedures

Bridge to Transplant (BTT)
- Time frame: months to years
- Temporary implanted MCS for patients waiting for a donor heart to become available

Destination Therapy (DT)
- Time frame: Permanent (years)
- Long-term implanted MCS for patients who are not eligible for a heart transplant
An increasing percentage of patients listed for cardiac transplantation require VAD support as a bridge.

**OUTCOMES AT OUR CENTER:**
HM II Survival to Transplant: 100%
Bridge to Transplantation (BTT)

Recent transition to HeartWare HVAD with excellent outcomes as bridge
Heart Transplants Reported per Year

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
Former Vice President Dick Cheney

- HeartMate II implant August 10, 2010 as BTT
- 1.5 years of support
- Successful bridge to transplant
- Age 70

“It’s brought me back from end-stage heart failure,” says Cheney, who has suffered five heart attacks, the first at age 37. “I was in bad shape 14 months ago. Now I’m back to leading a relatively normal life. I fish, hunt a little bit, write books, (am) able to travel.”
Lisa waits for a heart

50,000 Americans need new hearts. Most will never get one. Who lives? Who dies?

A special report
Hemodialysis

1: Blood coming from patient
2: Blood is drawn by pump
3: Pressure is sensed here
4: Blood pump speed
5: Pressure of blood flow
6: Blood then flows to the kidney where unwanted components are removed by diffusion. Excess fluid is removed by pressure.
7: Blood is diffused against the 'dialysate' fluid which is made up of an 'acid' and bicarbonate mixed to the correct strength with treated water.
8: The blood then leaves the kidney, treated, and returns to the patient.
9: Blood returning to patient

Display showing time left on treatment, fluid to be removed, and much more.

Bag of saline to wash blood back at the end of treatment.

The source of bicarbonate
The source of 'acid'
Artificial Kidney

- Early efforts began in 1913
- First artificial kidney in 1943 (Kolff)
- First patient regained consciousness after 11 hours of hemodialysis—lived for many years
- 1950s—Kolff’s dialyzer was only for ARF
- First outpatient dialysis facility opened in 1962 in Seattle
Chronic Kidney Disease

The Rotating-Drum Artificial Kidney
The first clinically effective artificial kidney
Year: 1946

Willem J. Kolff
ESRD Survival and Cost

- 735,000 deaths per year
- ~8 year survival in pts aged 40-45 (v. 30-40)
- ~4.5 year survival aged 60-65 (v. 17-22)
- 26% of population over 60 has stage 3 CKD
- Annual cost of HD: ~$82,000
- Annual expense transplant recipient: ~$30,000
Dialysis versus Kidney Transplant

Patient Survival Rates by Dialysis and Transplant

<table>
<thead>
<tr>
<th>Year</th>
<th>Dialysis Patients</th>
<th>Transplant Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>2 years</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>3 years</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>4 years</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>5 years</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

1 year (2008–2009)
2 years (2007–2009)
3 years (2006–2009)
4 years (2005–2009) No data available
5 years (2004–2009)

Intermountain Heart Institute
Intermountain Medical Center
Chronic Kidney Disease

Estimating Prognosis for Dialysis Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>years</th>
<th>Serum Albumin</th>
<th>3.8 g/dL</th>
</tr>
</thead>
</table>

Charlson Comorbidity Scoring System

One Point
- Myocardial infarction (history, not ECG changes only)
- Congestive heart failure
- Peripheral vascular disease (includes aortic aneurysm > 6 cm)
- Cerebrovascular disease: CVA with mild or no residua or TIA
- Dementia
- Chronic pulmonary disease
- Connective tissue disease
- Pepto ulcers disease
- Moderate or severe renal disease
- Diabetes with end-organ damage (retinopathy, nephropathy, neuropathy, or brittle diabetes)
- Mild liver disease (without portal hypertension, includes chronic hepatitis)
- Tumor without metastasis (exclude if > 5 y from diagnosis)
- Diabetes without end-organ damage (excludes diet-controlled alone)
- Leukemia (acute or chronic)

Two Points
- Moderate or severe liver disease
- AIDS (Not just HIV positive)

Three Points

Six Points

Charlson Comorbidity Index (CCI) 8

<table>
<thead>
<tr>
<th>Survival based on CCI</th>
<th>1 year</th>
<th>2 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival based on Serum Albumin</td>
<td>64 ± 10.8 %</td>
<td>35 ± 10.8 %</td>
</tr>
<tr>
<td>Survival based upon both serum alb and CCI*</td>
<td>86 ± 5.9 %</td>
<td>76 ± 7.1 %</td>
</tr>
<tr>
<td>Survival based upon both serum alb and CCI*</td>
<td>75 ± 5 %</td>
<td>52 ± 6 %</td>
</tr>
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</table>

Prognosis for ESRD patients can be estimated using the Charlson Comorbidity Index (CCI), shown in Table 1 and below, and the serum albumin. Based on the medical literature referenced below, the CCI is as good as or better than other prognostic tools for ESRD patients, and is easier to use in the non-research setting than the Index of Coexistent Diseases. CCI scores were calculated in 1761 individuals who participated in a comorbidity assessment project conducted between 1988-2001 in 41 dialysis units from Dialysis Clinic Inc. (DCI), a non-profit dialysis provider. All were hemodialysis patients with similar demographic characteristics as contemporary USRDS populations: the mean age was 62 (SD 15); 28% were African American; 52% were male; and 44% had diabetes as the cause of ESRD. Forty-eight percent were incident to dialysis, meaning that they had started dialysis less than a year prior to the time of the comorbidity assessment. The prognostic calculator (see Table 2) is based on observation of this study population and provides estimates of one- and two-year survival probabilities across subgroups defined by CCI Level and serum albumin. The 95% confidence intervals have been included to aid in interpretation of the data.

In the systematic literature review conducted by the RPA-ASN workgroup that developed the second clinical practice guideline (CPG), Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis, it was found that the CCI is an important tool in estimating prognosis for ESRD patients.

Intermountain Heart Institute
Intermountain Medical Center
Willem Kolff

PIONEER OF ARTIFICIAL ORGANS

“THE exciting thing is to see somebody who is doomed to die, live and be happy.”

Inducted: 1971
Economic Impact of CHF

- Annual cost of $30 billion in U.S.
- Most costly diagnosis in the Medicare population
- More costly than all forms of cancer combined
- 11 million office visits; 3.5 million hospitalizations
- Average total annual cost in Utah of $46 million dollars (79% paid for by the government)*
- $19,843 per hospitalization in Utah*

*Utah Department of Health
Heart Failure: The Final Cardiovascular Disease

Enhanced survival in other CV diseases leads to expansion of HF Population

Coronary deaths are down by half

But heart failure has almost tripled

Source: National Hospital Discharge Survey data. Centers for Disease Control and Prevention/National Center for Health Statistics and National Heart, Lung, and Blood Institute.
1969 - first artificial heart to be implanted into a human (Dr. Denton Cooley).

The patient was sustained by the device for 3 days, but only lived for 36 hours post transplantation.

The patient’s widow accused Cooley of making her husband the “unfortunate victim of human experimentation.”
1982 – Barney Clarke with Mrs. Clarke after his initial recovery.
Jarvik, DeVries and Kolff examine Clarke’s artificial heart after autopsy.
Total Artificial Heart
REMATCH Summary

- NEJM November 2001
- LVAD vs. optimal medical management
- LDS Hospital - largest enrollment in the country
- Landmark trial leading to FDA approval
- 129 patients with NYHA Class IV CHF ineligible for transplant
- 48% risk reduction of death with LVAD
- 52% vs. 25% survival at 1 year
- 24% vs. 8% survival at 2 years
- Improved quality of life (LVAD patients felt better, less depressed, more mobile and active)
HeartMate II – FDA approved for DT

TRIAL SUMMARY:

• Total of 200 patients
• Median age of 62 years (range 26 to 81)
• Mean LVEF of 17%
• 77% of patients receiving IV inotropes
• 2:1 Randomization HM II vs. HM XVE (stopped at mid-study point due to favorable results)
• All 200 patients were followed for at least 2 years or until death, transplantation or device explantation
• QOL improvement to NYHA Class I - II

NEJM, Nov. 2009
FDA approved Jan. 20, 2010
## HM II DT – Trial Data

<table>
<thead>
<tr>
<th></th>
<th>HM II</th>
<th>HM XVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival @ 2 years</td>
<td>58%</td>
<td>24%</td>
</tr>
<tr>
<td>Median duration of support</td>
<td>1.7 years</td>
<td>0.6 years</td>
</tr>
<tr>
<td>Relative Risk (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device repair or replacement</td>
<td>0.06</td>
<td>0.51</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.13</td>
<td>0.22</td>
</tr>
<tr>
<td>LVAD-related infection</td>
<td>0.48</td>
<td>0.90</td>
</tr>
<tr>
<td>Bleeding requiring surgery</td>
<td>0.23</td>
<td>0.29</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>2.64</td>
<td>4.25</td>
</tr>
</tbody>
</table>
HeartMate II Left Ventricular Device

- Continuous flow pump.
- Small and silent
- Requires warfarin (INR: 2.0 – 2.5)
- Available at Intermountain Medical Center as Bridge to Transplant (BTT) or Destination Therapy (DT)
- Durability: 6+ years
- Over 15,000 implanted world-wide
- UAHP: 103 implants to date
HeartWare HVAD™

• Centrifugal pump
• One moving part
• Short integrated inflow cannula
• 10mm outflow graft
• Dual motor stators
• Thin, flexible driveline
• Sewing ring

HVAD™ Pump

Sewing Ring

Strain Relief
HeartWare HVAD

- Inflow cannula integrated with device
- Small pump housing: 2 inch outside diameter, displaced volume of 50 cc
- Magnetically suspended impeller, only moving part (increased durability potential)
- Intrapericardial – no pump pocket
- Requires warfarin (INR: 2.0 - 2.5)
- Approved for use in Europe
- Destination Therapy clinical trial in U.S. (ENDURANCE)
- UAHP: 43 implants to date
Unique Features

- No abdominal surgery or pump pocket
- Fits in the pericardial space
- Anatomically fits smaller patients
- Less surgery; potentially minimizes blood transfusions
- Novel impeller design enables excellent hemodynamics
- Accurate flow estimation
- Log files enable flow and power waveform analysis
Interior of pump shown after 427 days of support in human patient

**IMPELLER**

- Impeller only moving part
- Completely suspended by a combination of passive magnets and hydrodynamic thrust bearings
- Never touches pump housing

**PUMP HOUSING**
HVAD™ Pump Implantation
HeartWare HVAD Survival

Consistent Survival with HVAD® System vs. Projected Survival

Observed Survival (%)

Years

0 0.5 1 1.5 2

HVAD ADVANCE (N=140)
SHFM Medical Therapy#
HVAD – CAP (N=242)
HVAD BTT – Europe (N=50)

# SHFM performed against the ADVANCE population

CAUTION: Federal Law (USA) restricts this device to sale by or on the order of a physician. Refer to the “Instructions For Use” for complete indications for use, Contraindications, Warnings, Precautions, Adverse Events and Instructions prior to using this device.

Intermountain Medical Center
Who and When?

NYHA CLASS

Adapted from Bristow, MR Management of Heart Failure, Heart Disease: A Textbook of Cardiovascular Medicine, 6th edition, ed. Braunwald et al.
Consider an evaluation when three of the following indications are present:

- Class III – IV heart failure symptoms
- Inability to walk < 1 block without dyspnea
- Sodium < 136 mEq/L
- BUN > 40 mg or Cr > 1.8 mg/dL
- ACE/ ARB/ BB intolerance
- Diuretic dose > 1.5 mg/kg/d
- 1 HF admit in the past 6 months
- No clinical improvement with CRT
Medicare Criteria for DT

- Medicare approved reimbursement for DT in 2003 for FDA-approved LVADs (HeartMate II).

- Medicare will also reimburse for LVADs in clinical trial, such as the HeartWare HVAD ENDURANCE Clinical Trial (DT).

- Medicare criteria for reimbursement is generally followed by private insurance companies:
  - NYHA Class IV Symptoms for at least 45 of the last 60 days despite optimal medical management.
  - LVEF must be < 25%
  - Peak Oxygen Consumption (VO2) < 14 mL/kg/min or <50% of patient’s predicted consumption, or patient requires intravenous inotropic therapy
  - Ineligible for cardiac transplantation
HVAD and MVAD Side-by-Side Comparison

- MVAD® Pump is approximately half the size of HVAD® Pump
- Similar hydrodynamic and magnetic impeller technology to HVAD Pump

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HVAD</th>
<th>MVAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump Type</td>
<td>Centrifugal</td>
<td>Axial</td>
</tr>
<tr>
<td>Weight</td>
<td>160 g</td>
<td>58 g</td>
</tr>
<tr>
<td>Pericardial Volume</td>
<td>50 cc</td>
<td>15 cc</td>
</tr>
<tr>
<td>Priming Volume</td>
<td>15 cc</td>
<td>5 cc</td>
</tr>
<tr>
<td>Inflow OD</td>
<td>Same</td>
<td>Same</td>
</tr>
</tbody>
</table>

CAUTION – IN DEVELOPMENT. NOT AVAILABLE FOR CLINICAL USE
• MVAD® Pump is a next-generation platform designed to enable:
  - Support for a wider range of patients
  - Left and right ventricular support (LVAD, RVAD)
  - Partial and full flow (turn-down capability)
  - Less invasive implant technique (e.g. thoracotomy)
HeartMate III*

Ultra-Compact, Fully Mag-Lev VAD
(Finalizing Design)

- Full magnetic levitation optimized for efficiency
  - Low power consumption - Longer battery runtime
  - Designed to generate a near physiologic pulse which may have meaningful clinical benefits\(^1\)
  - Easily adaptable to Fully Implantable LVAS

- Enhanced hemocompatibility / minimal thrombogenicity
  - Large blood path passages (10X greater than hydrodynamic devices) with centrifugal flow and Full Magnetic Levitation (FML)
  - Proven HeartMate textured blood contacting surfaces – low/no anticoagulation therapy
  - Facilitates low speed operation without an increased risk of thrombus formation\(^1\)

- Less invasive Implantation
  - Intra-thoracic placement
  - Designed to reduce tunneling path size (20% reduction)

- Ultra-long life
  - Non-contacting FML rotor
  - Modular percutaneous lead (driveline)

* In development and not available for clinical use

\(^1\) To be determined in clinical trial
SYNERGY Surgical System

- Pump in subcutaneous pacemaker pocket
- Right sided mini-thoracotomy
- Extubation in OR possible
- Off-pump procedure
- Currently upgrading cannula and pump, prior to re-launch 2H 2014

Fully Implantable System

Advanced Technology

- Based on Transcutaneous Energy Transfer ("TET") technology
- Periodically recharged using inductive coupling across the skin
- Fully implantable controller & battery optimized for long term support and patient mobility
- Wireless monitoring and management of VAD parameters

Patient Benefits

- Designed for both HVAD® Pump and MVAD® Pump
- No exit site care or risk of trauma to exit site
- Patient physical freedom from external components
- Discreet physical appearance

Intermountain Heart Institute
Intermountain Medical Center
Ready for Prime Time?

"The Chasm"

Innovators

Early Adopters

Early Majority

Late Majority

Laggards

Technology Adoption Lifecycle

Area under the curve represents number of customers
Steps to

- Viable tool for management of CHF
- Improve patient selection and perioperative management
- Fewer complications and shorter length of stay
- Smaller, less expensive, more durable devices
- 100% success as a bridge to transplantation
- 5 - 10 year DT survival equal to transplantation
- Enhance patient length and quality of life
Contact Information

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24 Hour Hotline: 801-507-LVAD
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Increasing the LENGTH and QUALITY of life for patients with heart failure...