The Price of Innovation
The Frenzy, the Finances, and the Fun

Albert Starr, M.D.

93rd AATS Luncheon Keynote
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Minneapolis, MN

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Outline

1. The frenzy: how things happen

2. The finances: the price of innovation
   A. Money
   B. Brain Power
   C. Collaboration

3. The fun: you had to be there
The First Portable Pacemaker

1957

C. Walton Lillehei

Earl Bakken
Dr. Walton Lillehei and young patient with portable, battery-powered pacemaker invented by Medtronic's Earl Bakken
Medtronic

Employees: 45,000 worldwide

THEN

NOW
How things happen

1958

Edwards
1940, World War II
Boeing’s B-17 fuel pump malfunctioned at altitudes of over 20,000 feet because fuel vaporized and bubbles blocked the fuel lines.
1941, Edwards invented a centrifugal fuel pump that solved this problem.

This valuable patent was owned by M Lowell Edwards AND financed the heart valve.
By the end of WWII, 75% of US military aircraft had Edward’s fuel pump.

1945; P 51 Mustang
Our collaboration started in 1958...
The Problem

All but one thrombosed by 1 month
The Sole Long-Term Survivor
Problem solved!
“Go to Man” (1960)

Dr. Griswold
Chief of Cardiology

Blackie licks his hand
Animal to Man: Challenges

• Regulatory
  — No FDA or IRB
  — No informed consent
  — No ethical guidelines

• Technical
  — No surgical technique yet developed
  — No ICU

• Business
  — Name for the valve?
  — Manufacturing company?
BIG question: Which valve to use in Man?

Simple or Complex
First Successful Mitral Valve Replacement

September 21, 1960
First Production Model (1960)

Outflow Struts: Too thick

Inflow Face: A danger zone for thrombus
Crucial for SUCCESSFUL innovation

• Rapid fine tuning
• Occupying the space
Fine Tuning

Evolution from Model 6000 to 6120
Operative Mortality by Implant Year for Mitral Valve

Operative Mortality (%)

Year of Implant

1960: 50%
1961: 36%
1962: 29%
1963: 25%
1964: 14%
1965: 8%
Occupy the Space

Added Aortic Valve

Mitral 1964

Aortic 1966

Final ball valves in use until 2004
Occupying the Space: Continuing to Innovate

Attempted improvements
• Disc valves
• Beaded metal valve
• Carbon impregnated sewing ring
• Cloth-covered valves
New Space to Occupy: Tissue Valves

Bioprosthesis, 1965:

- Biological valve
- Prosthetic sewing ring

Alain Carpentier
Chamonix Ski Resort, 1967
Glutaraldehyde Preservation
Edwards Acquires the Space (1969)
Carpentier-Edwards Bioprosthesis

Porcine  Pericardial
More Space…

TAVR

Rapid Deployment

Edwards Sapien

Edwards Intuity
Edwards

Employees: 7,800 world wide

THEN

NOW
THE MULTIVERSE THEORY
Looking Back: An alternate universe?

The Almost St Jude Valve

The FIRST Bi-leaflet Valve made and inserted into a dog in 1958.

The Bi-leaflet St Jude Valve was introduced in 1980.
Looking Back: An alternate universe?

The Almost Heart

Edwards’ fuel pump
(1941)

HeartWare HVAD® pump
(2009)
Global Financial Impact of the Industries Created by Medtronic and Edwards with Physician Collaboration

Pacemaker Market
Forecast to reach **$5.1 billion** by 2018

Heart Valve Market
Forecast to reach **$1.7 billion** by 2015

http://www.transparencymarketresearch.com/
Summary
Types of Innovation

• Disruptive: game changer
  ▪ Greater long-term return in value and growth

• Sustaining: small improvements
  ▪ Faster short-term return
Economic Value of Innovation

“... innovation drives long-run economic growth, creating jobs and improving living standards in the process.”

NIH-funded Research generated $69 billion in new economic activity and ~500,000 new jobs in the U.S. in 2010.
Important Drivers of Innovation

- Money
- Brain Power
- Collaboration
Important Drivers of Innovation

• Money

• Brain Power

• Collaboration
R&D represents a very small percentage of the total cost

Source: Research! American analysis
U.S. Health Research Investment by Source

*Universities; State and local Gov; Research Institutes; Philanthropic foundations; Voluntary Health Assns

Source: Research!America analysis

- Total
- Industry
- Federal Gov.
- Other*

*Universities; State and local Gov; Research Institutes; Philanthropic foundations; Voluntary Health Assns
U.S. Health Research Investment by Source
Venture Capital (VC) Investment

VC still represents a relatively small percentage of total research funding

Early Stage Funding Methods

- **Seed Grant** to try innovative ideas that cannot be funded from other sources.
- **Proof-of-Concept Fund** to advance technologies from the idea-to-marketable IP, and to attract additional funding.
- **Philanthropic Venture Fund** to accelerate the commercialization of university technologies already in a start-up.
New Industrial Entities to Bridge the Gap & Enhance Capital Access for Universities

Discovery

Entry

Exit

Ready for human trial

BioPontis Fund 1, L.P.

Asset Source

University Alliance Partners

BioPontis Alliance LLC R&D and Scientific Development Network

Market Demand

Pharmaceutical Partners

Pfizer

J&J

MERCK

Celgene
Transforming relationships. Unleashing innovation.

**Alliance University Partners**
- Columbia University
- New York University
- Memorial Sloan Kettering Cancer Center
- University of Pennsylvania
- Thomas Jefferson University
- University of Virginia
- University of North Carolina (Chapel Hill)
- University of Florida
- University of Kansas
- Oregon Health & Science University

**Translational Development Partners**
- Albany Molecular Research, Inc.
- Covance, Inc.
- Taconic Farms, Inc.
- Rosa & Co.
- Provid Pharmaceuticals
- DOCRO, Inc.
Another New Concept
Healthcare Accelerators/Incubators

Bring together:

1. Startups who need support
2. Mentors who have experience
3. Investors who want access to early stage startups
Healthcare Accelerators: Examples
Important Drivers of Innovation

• Money
• Brain Power
• Collaboration
“... National Research Council noted ... an overall shortage of medical researchers and inadequate funding for scientists working in the United States ... <which> may well encourage medical researchers to seek employment elsewhere.”
Increasing Government support for Medical Research in Asian Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Increase from Previous Year</th>
</tr>
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<tbody>
<tr>
<td>China</td>
<td>2010</td>
<td>67%</td>
</tr>
<tr>
<td>India</td>
<td>2010</td>
<td>15%</td>
</tr>
<tr>
<td>South Korea</td>
<td>2009</td>
<td>24%</td>
</tr>
<tr>
<td>Taiwan</td>
<td>2009</td>
<td>4%</td>
</tr>
<tr>
<td>Singapore</td>
<td>2010</td>
<td>13%</td>
</tr>
</tbody>
</table>
Current U.S. Immigration Policy Too Restrictive

• Discourages retention of U.S trained foreign graduates

• Discourages skilled immigrants
Immigration Reform

STEM: Science, Technology, Engineering, and Math

Brookings Recommendations

• Automatic green cards for foreign science and tech graduates
• H1-B visas should go back to 195K/year and permanent resident status simplified
• O-1 “genius” visa now 45K/year should be increased
• EB-5 visa program for foreign individuals investing in the U.S. should be expanded
Immigration Reforms Needed

To Convert

Brain Drain  Brain Gain
Important Drivers of Innovation

• Money

• Brain Power

• Collaboration
The Translational Gap
By Degree of NIH Principal Investigator

The Translational Gap
- Collaboration Opportunity!

Public-Private Partnership

The newly launched (2012 Dec)

http://www.deviceconsortium.org/

• Industry
• Academia
• CDRH (FDA Center for Devices and Radiological Health)

http://www.deviceconsortium.org/
A Model For Industry Collaboration
Key Strategies & Synergies

Get state matching money for SBIR and other grants

Create pathway for research and collaborations

Co-host an annual business/academic research symposium

Postdoctoral training in entrepreneurship

Jointly recruit for research and business
Using these innovative models, we innovate innovation itself, and achieve:

Innovation$^2$
Behind the scenes in innovation:
Importance of Networking (The Fun!)
Mechanical vs. Tissue valves

Donald Ross
Valve replacement/Heart Transplantation

Shumway
The French Connection -- Early

Henry Bahnson
Charles Dubost
Prof. d'Allaines
The French connection – 30 years later

Dubost

Carpentier
First lung and first heart transplant
DeBakey & Cooley: Reconciliation, Paris 2000
First heart transplant talking to first mechanical heart
Innovation can be fun, too

Christian Barnard
The pianist

Carpentier
To innovate, it helps to be …

Oregon Cattle Ranch

Donald Ross
… a bit of a cowboy …

Alain Carpentier
... and have a taste for new things

Oregon Cattle Ranch Branding

Rocky Mountain Oyster

Charlie Hahn