Interventions in Congenital & Structural Heart Disease:

Who Drives New Techniques and Devices?

Lee Benson MD  
Professor Pediatrics (Cardiology)  
Director, Cardiac Diagnostic & Interventional Unit  
The Hospital for Sick Children  
Toronto, Canada
Millions of patients depend on a widening array of medical devices to support the diagnosis of disease and management.

In the US the medical device industry has

>$200 billion in annual revenue,

~9% growth rate during the past few years.
Who controls the development and application of medical devices?

The physician-investigator?
   i.e. a need is seen in a clinical area

The market place?
   i.e. potential investors see a profit?

The hospital or institution?
   i.e. publish or perish

The regulatory agency
   i.e. the process by which a device gains access to the market place

Existing devices in use?
   i.e. is there a unique or improvement in existing technology?
Innovation in medical technologies happens at a public/private interface

Idea

Concept development

Design

Regulatory approval and clearance

Post-market activities

Process is a complex interplay of each component
One way to assess medical device innovation is through an analysis of patents related to the development of a given product. Such reviews provide data on the timing and nature of an individual's contribution to a given field.
The example of bare metal stents for treatment of CAD, a transformative device that spawned the modern era of interventional cardiology can be illustrative of what drives innovation.

(Circ Cardiovasc Qual Outcomes. 2012;5:743-749)
## Timeline of Major Preclinical, Clinical and Regulatory Events in the Early Development of Coronary Artery Stents

<table>
<thead>
<tr>
<th>Event</th>
<th>Event Type</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>Preclinical</td>
<td>Earliest description of balloon angioplasty for use in the coronary arteries by Gruentzig</td>
</tr>
<tr>
<td>1978</td>
<td>Clinical</td>
<td>Gruentzig presents his angioplasty technique at the 1978 Society of Interventional Radiology Meeting in New Orleans, and concern about restenosis. Palmaz is in attendance</td>
</tr>
<tr>
<td>1985</td>
<td>Preclinical</td>
<td>Gruentzig initiates a collaboration with Gianturco to develop a stent to reduce restenosis</td>
</tr>
<tr>
<td>1985</td>
<td>Clinical</td>
<td>Palmaz and Schatz describe the use of balloon-mounted slotted-tube stent in the peripheral arteries</td>
</tr>
<tr>
<td>Mar 1987</td>
<td>Preclinical</td>
<td>First experimental coronary stent implantation in human patients by Sigwart using WallStent design</td>
</tr>
<tr>
<td>Event</td>
<td>Event Type</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>-----------------------------</td>
<td></td>
</tr>
<tr>
<td>May 1987</td>
<td>Strecker describes a new flexible intravascular stent at the Cardiovascular and Interventional Radiological Society of Europe and the Society of Cardiovascular and Interventional Radiology</td>
<td>Preclinical</td>
</tr>
<tr>
<td>Feb 1991</td>
<td>FDA approval of Palmaz-Schatz balloon-expandable stent (Expandable Grafts Partnership, Johnson &amp; Johnson) for the biliary system</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1992</td>
<td>Studies report efficacy and use of Gianturco-Roubin (Cook Inc) stent to prevent emergency bypass surgery after angioplasty</td>
<td>Clinical</td>
</tr>
<tr>
<td>May 1993</td>
<td>FDA approval of Gianturco-Roubin stent for coronary procedures, specifically emergency management of coronary closures during angiography</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1994</td>
<td>BENESTENT study demonstrating efficacy of Palmaz-Schatz stent in patients with new coronary lesions in the main coronary arteries (n=520) published</td>
<td>Clinical</td>
</tr>
<tr>
<td>Event</td>
<td>Event Type</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>-------------------------------------</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>STRESS study demonstrating efficacy of Palmaz-Schatz stent (n=410) published</td>
<td>Clinical</td>
</tr>
<tr>
<td>Aug 1994</td>
<td>FDA approval of Palmaz-Schatz stent for elective coronary artery stenting</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1997</td>
<td>Stent use found in 69% of angioplasty procedures</td>
<td>Clinical</td>
</tr>
<tr>
<td>1998</td>
<td>Restenosis Stent Study Group reported a major benefit of stenting for patients who experienced restenosis of a coronary vessel after balloon angioplasty</td>
<td>Clinical</td>
</tr>
</tbody>
</table>
There were 245 patents relating to coronary artery stents between 1984 & 1994

Private companies held the most patents (110, 44.9%)
Public companies (77, 31.4%)
Individual inventors (44, 18.0%)
Non-profit entities (14, 5.7%)

The most highly-cited patents, which contributed to coronary artery stent development belonged to privately-held companies

- privately-held companies contributed 31 (51%)
- publicly-traded companies 16 (26%)
- individuals contributed 12 (20%)
- nonprofit entities 2 (3%)

The top 10 cited patents all came from privately held companies
Starting in 1984, the total # of stent-related patents/year increased.

Privately-held companies dominated patenting early contributing the majority of patents in every year through 1989.

Publicly-traded companies did not control a majority of patents until the final 2 years (1993 and 1994).
This assessment suggests that physician-innovators and their small private companies were instrumental in the discovery and early stages of development. Larger public companies made their contributions to this innovation at a relatively late stage, after significant product development & testing had already occurred.

New policies aimed at encouraging transformative innovation should focus on providing the necessary tools and support to physician-innovators. And this in part answer the question of ‘who drives’ innovation.
Concept of percutaneous valve implantation


The valve of choice for percutaneous implantation is a valve which:

- easily available at variable sizes
- biocompatible
- has excellent intrinsic properties
- has a low profile
- can be sutured into an expandable stent
- does not lose its property after crimping and re-expansion

After testing different types of valves opted for a bovine jugular venous valve
Key points for a marketable medical device

You need an elegant *technological solution to a real* clinical problem or unmet need

- A *substantial addressable market of* customers who will pay for the solution

- A *well designed product that meets* customer needs in their environment

- Cogent strategy for *regulatory clearance* and market launch
Cảm ơn
Thank you