Interventions in Congenital & Structural Heart Disease:

Who Drives New Techniques and Devices?

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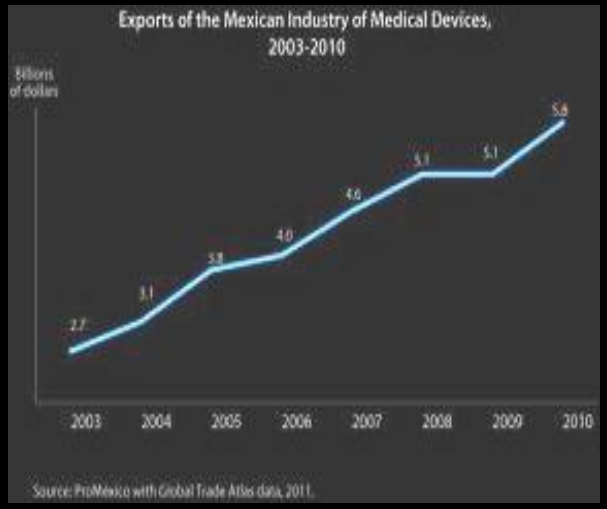
Millions of patients depend on a widening array of medical devices to support the diagnosis of disease and management

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

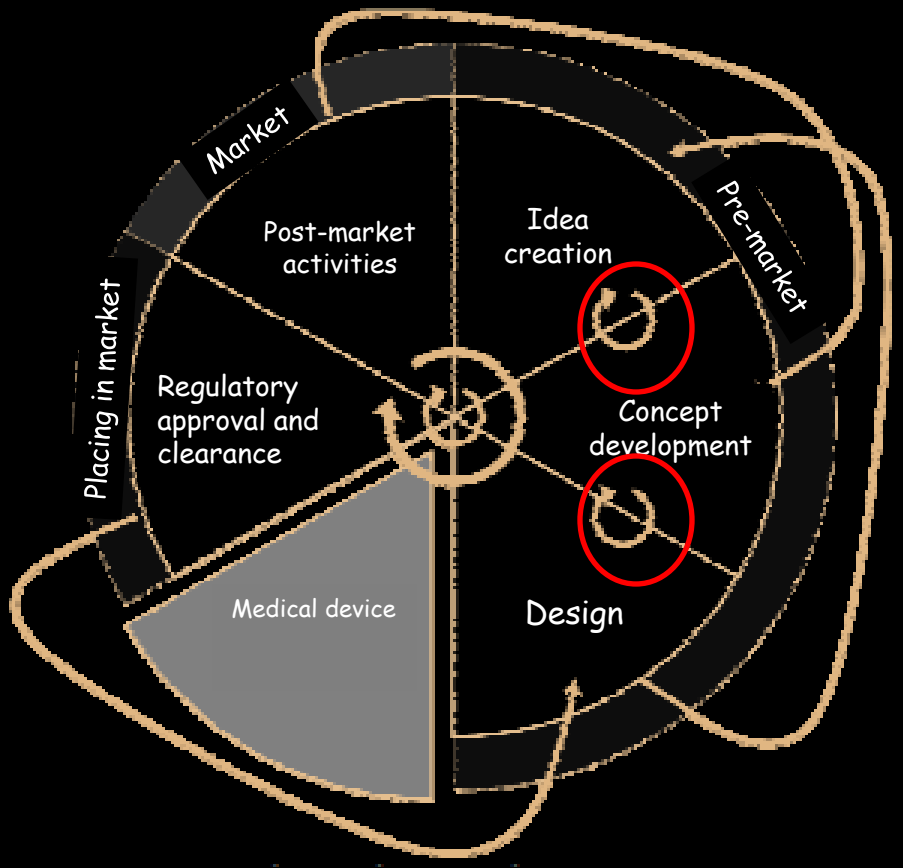
Idea

Concept development

Design

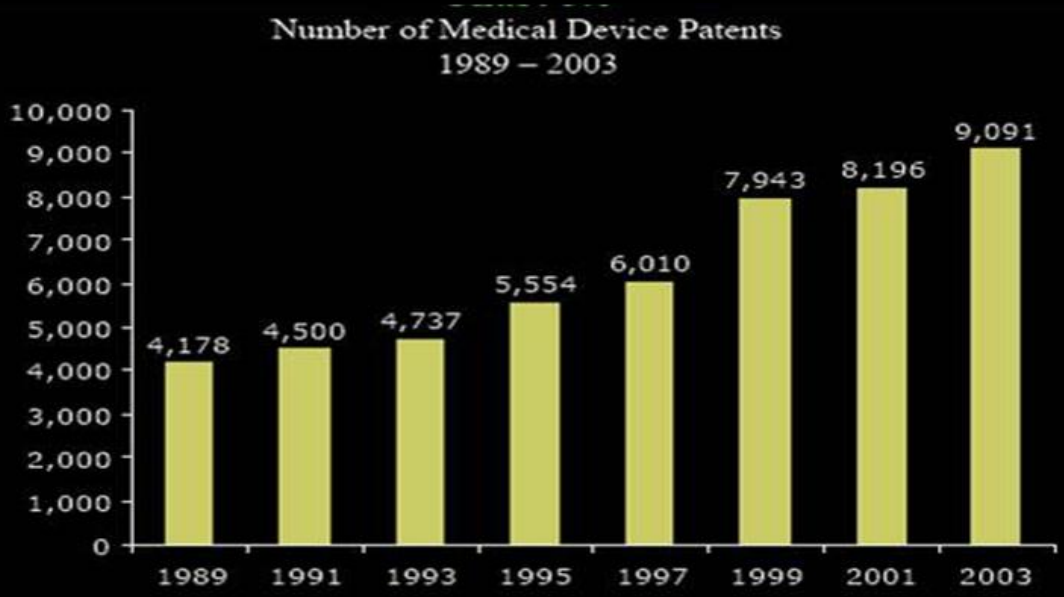
Regulatory approval and clearance

Post-market activities



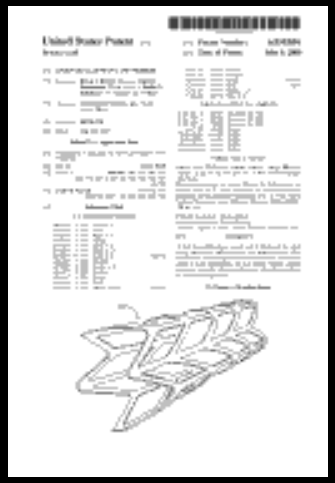
Process is a complex interplay of each component

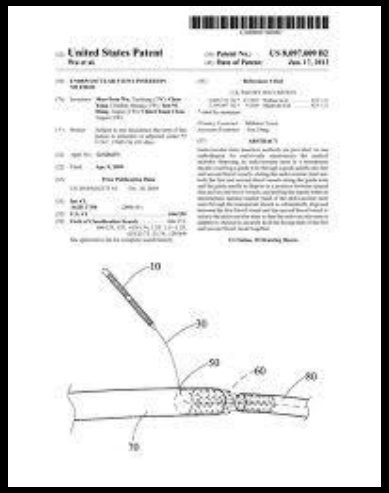
One way to assess medical device innovation is through an analysis of patents related to the development of a given product



Such reviews provide data of the timing and nature of an individuals 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 droves innovation.....





Origins of Medical Innovation

The Case of Coronary Artery Stents

Shuai Xu, MSc; Jerry Avorn, MD; Aaron S. Kesselheim, MD, JD, MPH

(*Circ Cardiovasc Qual Outcomes. 2012;5:743-749)*

Timeline of Major Preclinical, Clinical and Regulatory Events in the Early Development of Coronary Artery Stents

	Event	Event Type
1976	Earliest description of balloon angioplasty for use in the coronary arteries by Gruentzig	Preclinical
1978	Gruentzig presents his angioplasty technique at the 1978 Society of Interventional Radiology Meeting in New Orleans, and concern about restenosis. Palmaz is in attendance	Clinical
1985	Gruentzig initiates a collaboration with Gianturco to develop a stent to reduce restenosis	Preclinical
1985	Palmaz and Schatz describe the use of balloon-mounted slotted-tube stent in the peripheral arteries	Clinical
Mar 1987	First experimental coronary stent implantation in human patients by Sigwart using WallStent design	Preclinical

Timeline of Major Preclinical, Clinical, and Regulatory Events in the Early Development of Coronary Artery Stents

	Event	Event Type
May 1987	Strecker describes a new flexible intravascular stent at the Cardiovascular and Interventional Radiological Society of Europe and the Society of Cardiovascular and Interventional Radiology	Preclinical
Feb 1991	FDA approval of Palmaz-Schatz balloon-expandable stent (Expandable Grafts Partnership, Johnson & Johnson) for the biliary system	Regulatory
1992	Studies report efficacy and use of Gianturco-Roubin (Cook Inc) stent to prevent emergency bypass surgery after angioplasty	Clinical
May 1993	FDA approval of Gianturco-Roubin stent for coronary procedures, specifically emergency management of coronary closures during angiography	Regulatory
1994	BENESTENT study demonstrating efficacy of Palmaz-Schatz stent in patients with new coronary lesions in the main coronary arteries (n=520) published	Clinical

Timeline of Major Preclinical, Clinical, and Regulatory Events in the Early Development of Coronary Artery Stents

	Event	Event Type
1994	STRESS study demonstrating efficacy of Palmaz-Schatz stent (n=410) published	Clinical
Aug 1994	FDA approval of Palmaz-Schatz stent for elective coronary artery stenting	Regulatory
1997	Stent use found in 69% of angioplasty procedures	Clinical
1998	Restenosis Stent Study Group reported a major benefit of stenting for patients who experienced restenosis of a coronary vessel after balloon angioplasty	Clinical

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%)

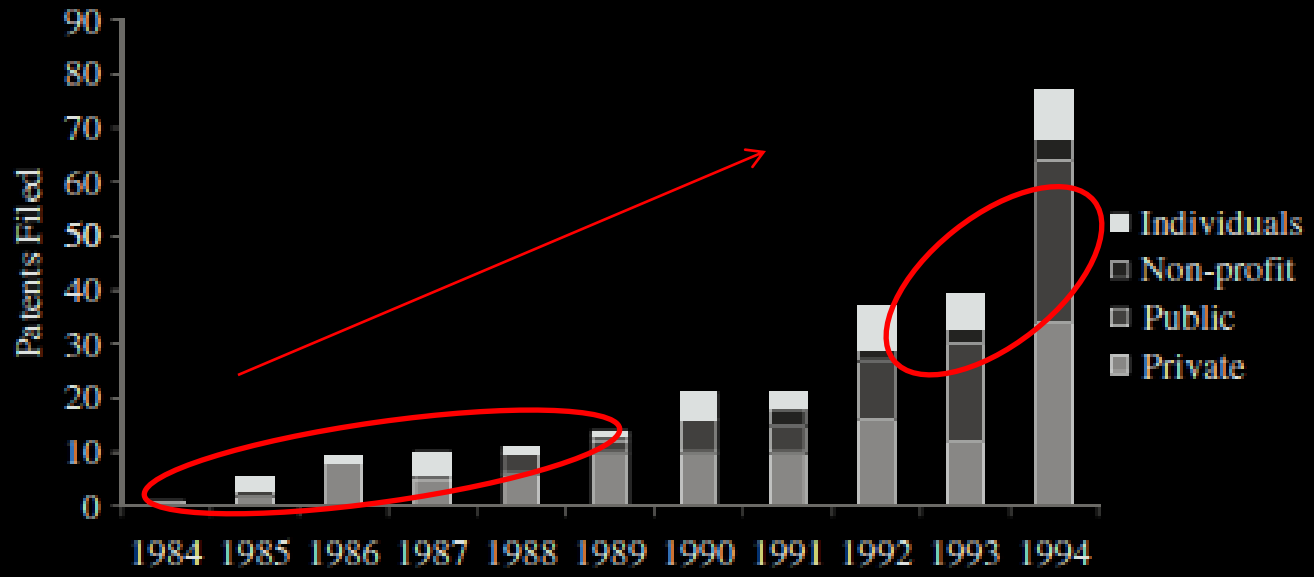
Non-profit entities (14, 5.7%)

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

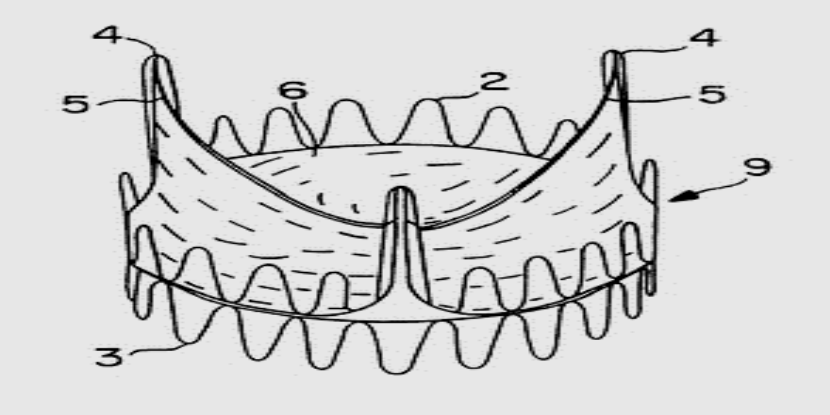
New policies aimed at encouraging transformative innovation should focus on providing the necessary tools and support to physician-innovators

And this in part answer the question of 'who drives' innovation

Concept of percutaneous valve implantation

Andersen HR, Knudnen LL, Hasenkam JM: Transluminal implantation of artificial heart valves. Description of a new expandable aortic valve and initial results with implantation by catheter technique in closed chest pigs. Eur Heart J. 1992 May;13(5):704-8. Department of Cardiology, Skejby University Hospital, Aarhus, Denmark.

Knudsen LL, Andersen HR, Hasenkam JM: Catheter-implanted prosthetic heart valves. Transluminal catheter implantation of a new expandable artificial heart valve in the descending thoracic aorta in isolated vessels and closed chest pigs. Int J Artif Organs. 1993 May;16(5):253-62.



Boudjemline & Bonhoeffer

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

Cám ơn

Thank you