

Palma - 2017



**Avenues to innovation  
reimbursement:  
the innovator's (inventor's)  
perspective**



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# Disclosure Statement



Research Grants	Biosense Webster, Stereotaxis, Medtronic, Cardiofocus, Abbott
Consultant / Advisory Board	Abbott, Edwards, Stereotaxis, Valtech, Cardiofocus, Apama, SynapticMed,
Ownership Interests	Cardiac Implants (co-founder), Jena Valve, Khalila, Apama
Speaker's Bureau Honoraria	Biosense Webster, Medtronic, St. Jude, Abbott, Cardiofocus, Biotronik, Valtech
Fellowship Support	None
Other	None
Off-label drugs/devices	None

# Invention



- An invention is a new (or novel) concept or device that is derived from an individual's ideas or from scientific research.
- Invention implies “creativity” and can be either iterative (most commonly) or completely original (rarely).



## Thomas A. Edison

(iconic genius in his Menlo Park workshop)

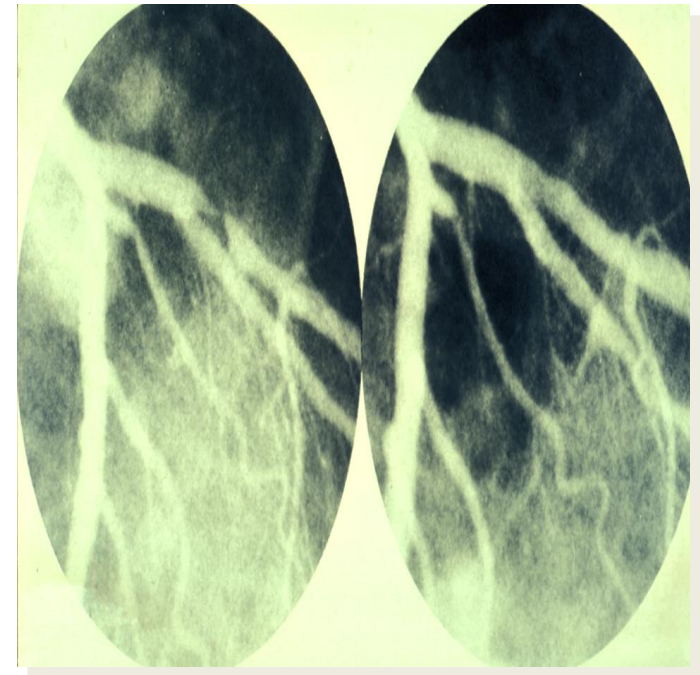
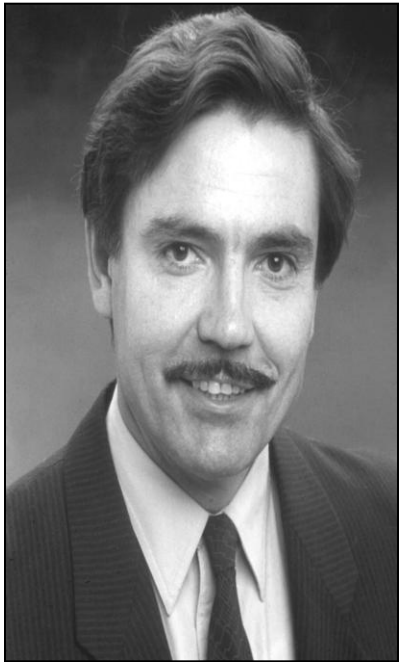
*“I have not failed. I've just found 10,000 ways that won't work.”*

*“Genius is one percent inspiration and ninety-nine percent perspiration.”*

# Invention



- The invention of balloon PTCA (Gruentzig's brainchild) was original and transformational, setting the stage for all future catheter-based therapies!

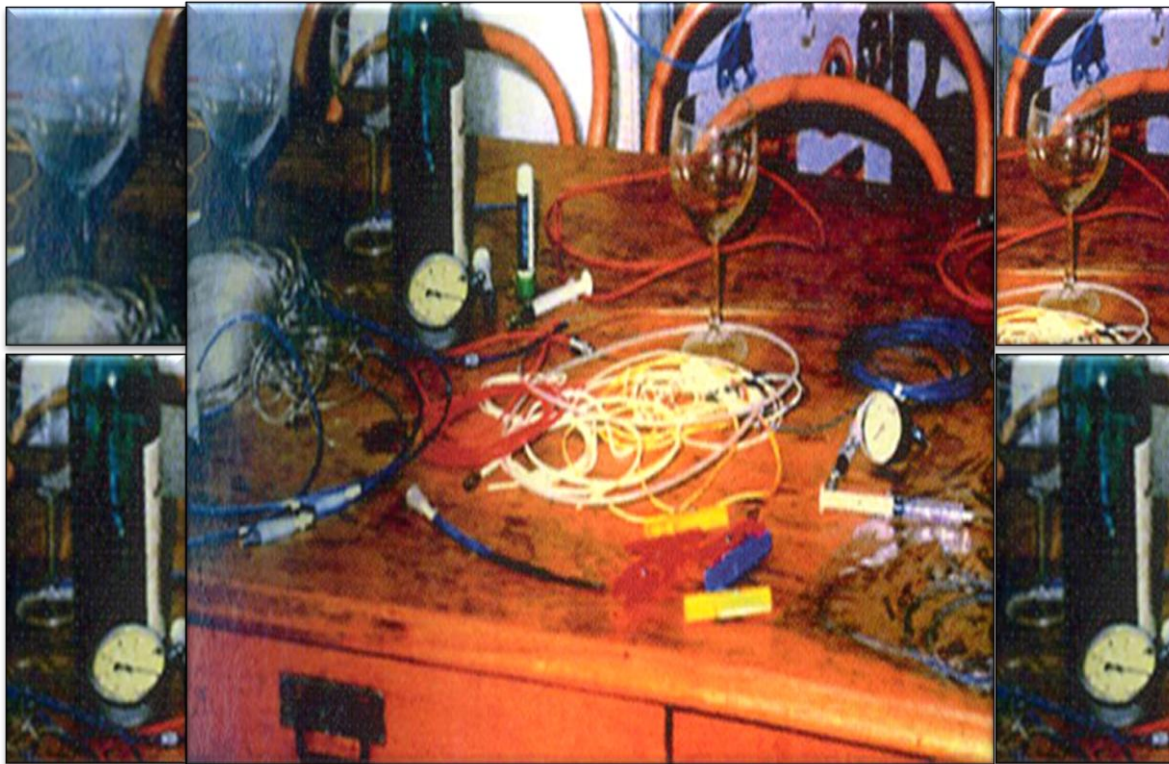


Sept 16, 1977

# Invention



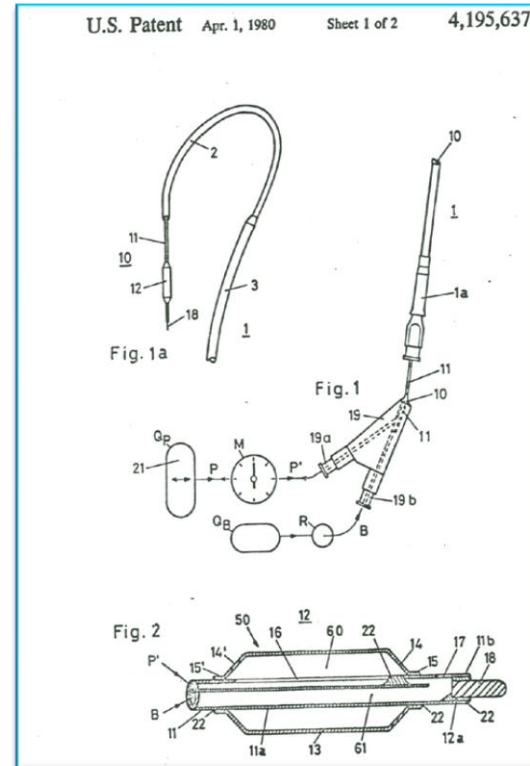
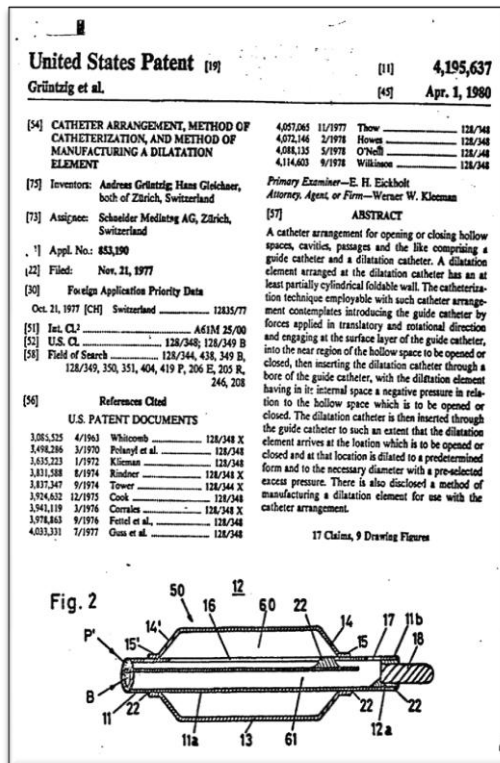
**Gruentzig's famous kitchen table,  
where the 1<sup>st</sup> balloon catheters were fabricated**



# Invention



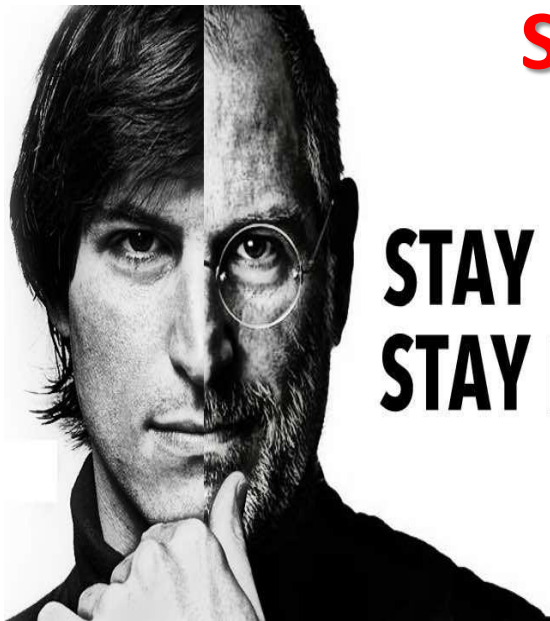
## Gruentzig's PTCA Patent (US); filed Nov 21, 1977 and issued April 1, 1980



# Innovation

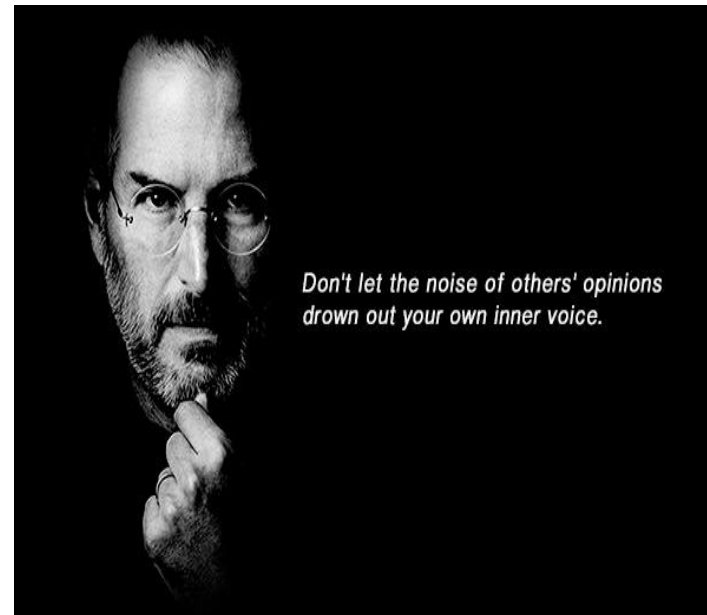


- Innovation is the commercialization of the invention itself; the process of developing an invention which may address a clinical need and create “value” (clinical and financial)



**Steve Jobs**

**STAY HUNGRY  
STAY FOOLISH**

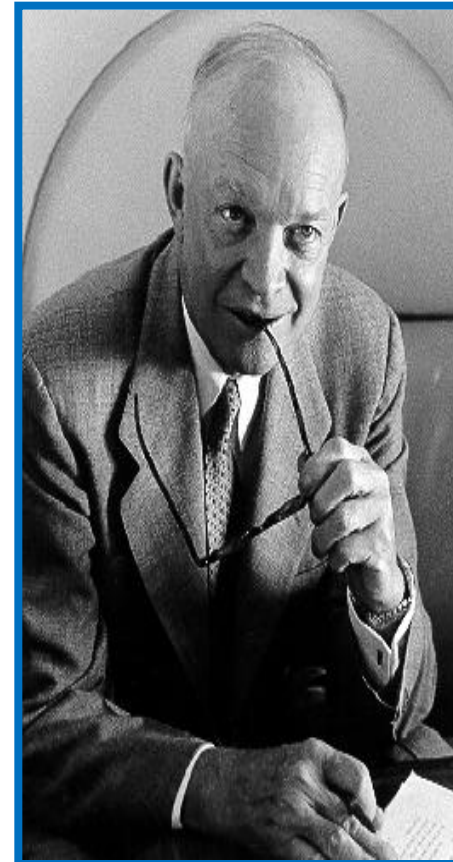


*Don't let the noise of others' opinions  
drown out your own inner voice.*

# Innovation - AMI Therapy



**1955**

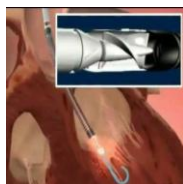
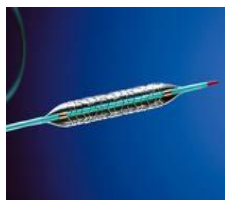




# Innovation - AMI Therapy



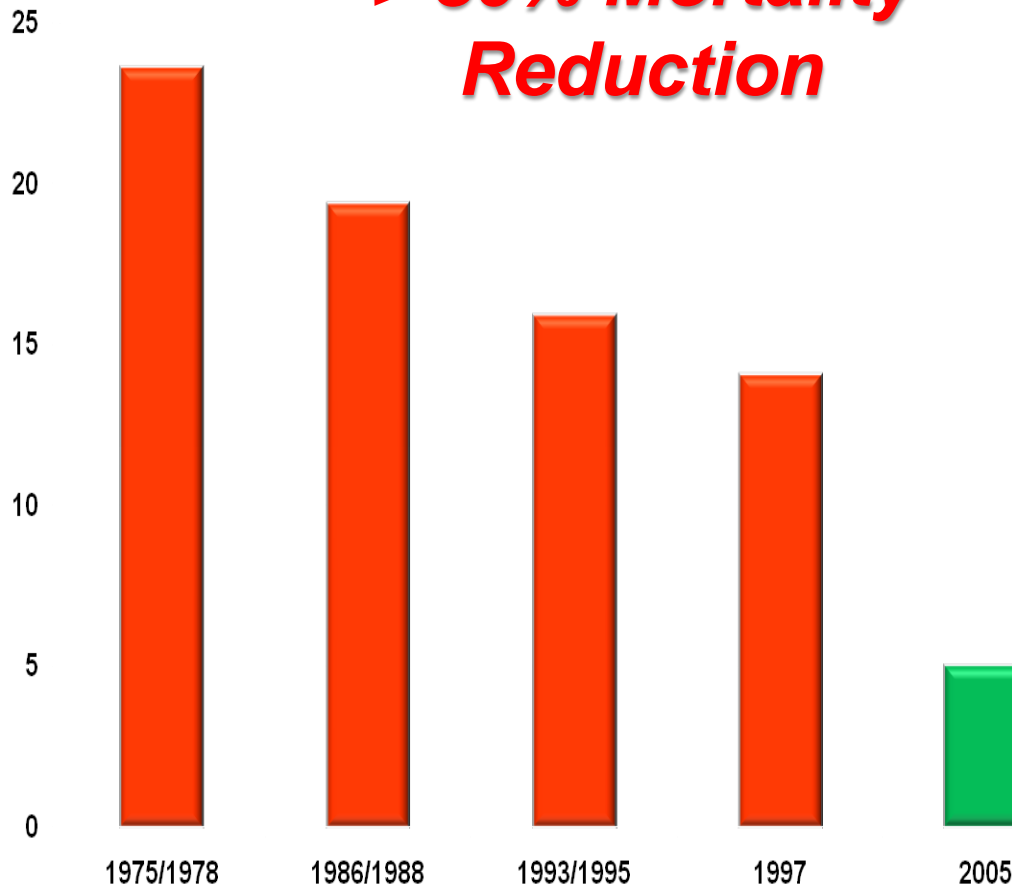
**2017**



# Innovation - AMI Therapy



**> 80% Mortality Reduction**



## *Reasons*

- Pharmacotherapy evolution
- Interventional device and procedural development
- Evidence-based medicine clinical research
- Environmental and logistic factors
- Society guidelines and outcome initiatives

Dauerman et al. Am J Cardiol 2002: The Worcester Heart Attack Study

# Innovation



***Progress in technology usually results less from individual genius and more from collective effort AND social, political and economic forces that come together to create an ecosystem which fosters innovation.***

# Innovation



- Innovation is a process requiring multiple individuals with different skill sets (multi-disciplinary) spanning the cycle from device refinement (engineering), to pre-clinical testing (often large animals), to human clinical translation (first-human-use and feasibility studies), to definitive clinical trial validation (evidence-based medicine), to regulatory approval (e.g. CE mark or FDA), to physician training (generalizability), and finally, to market development.
- Successful and sustainable innovation in CV disease requires that an invention is transformed (by the aforementioned process) into a meaningful clinical therapy.

# Innovation



- The path from the idea to a meaningful clinical product is a long process
- From the invention to selling the start up company usually takes ten years and ten percent of the companies will make it
- This journey costs on average 75 million USD (up to 150 million USD)
- After CE mark has been obtained, the reimbursement process starts

# Start-Up Costs Associated with Medical Devices



- Patent Costs: \$25,000-\$75,000 (Basic foundational patents)
- Incorporation and Organizational Costs \$10,000-\$25,000
- Facility/Equipment Costs Varied
- Employees/technical specialists Varied
- Device Development Costs: Varied
- Pre-Clinical Testing (Animal labs) Each study is approx. \$6,000-\$20,000  
(usually many studies required to get to clinic)

# Average Monthly Burn of Sample Medical Tech Company



## EXAMPLE

### Transcatheter Heart Valve Repair Device

PHASE	TYPICAL MONTHLY BURN
Early R&D	\$ 20,000
Proof of Concept	\$ 50,000
Early Feasibility (Pre-Clinical)	\$150,000
First in Man (Early Clinical)	\$450,000
EU CE Mark Trial	\$700,000
Pivotal Trial in US	\$1,000,000

# Innovations in the DRG System



Introduction of new method

Expense not (yet) appropriately reflected in DRG system

Expense already appropriately reflected in DRG system

NUB process

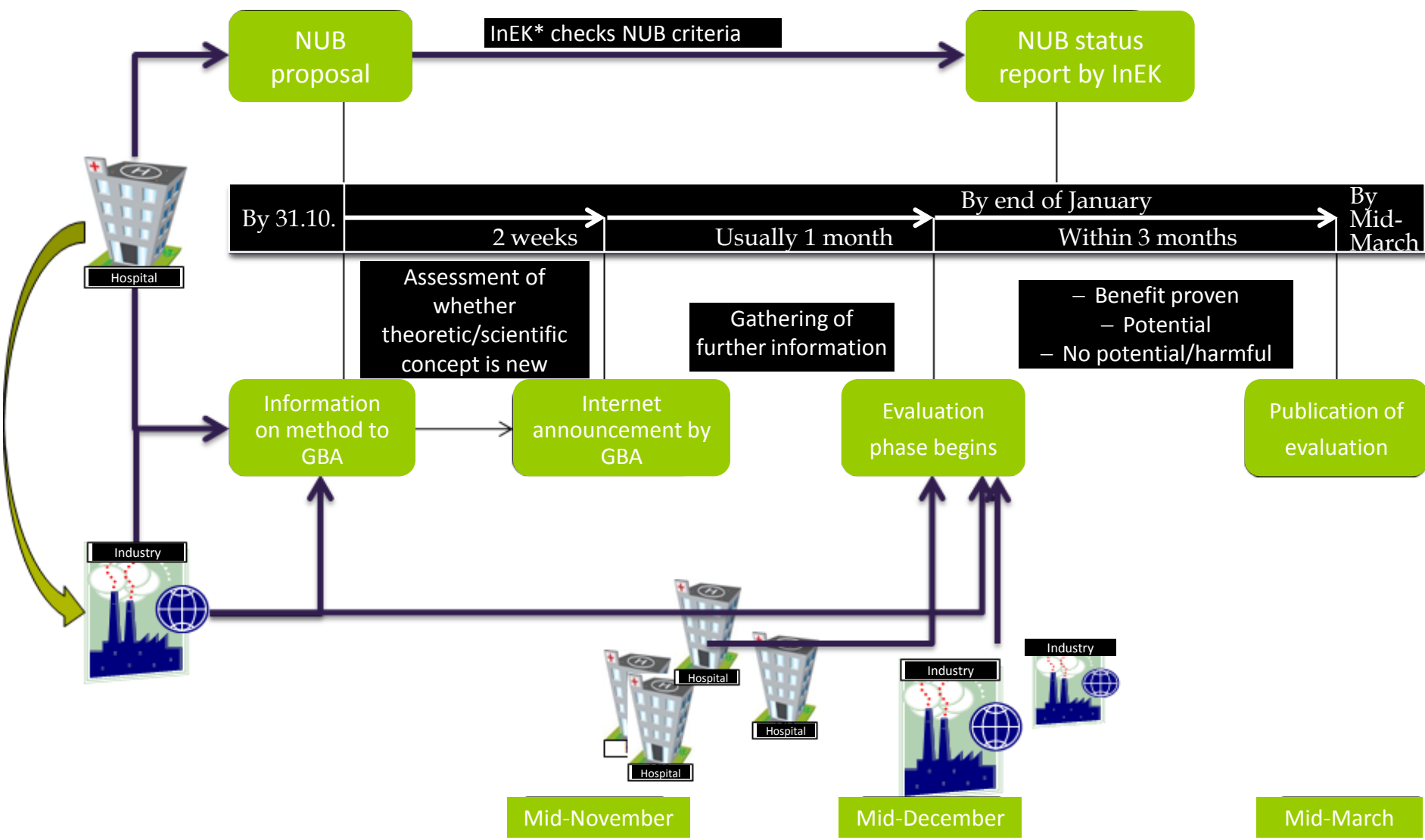
DRG and/or extra compensation

DRG and/or extra compensation

NUB = Neue Untersuchungs- und Behandlungsmethoden  
(New methods of examination and treatment)



# The expanded NUB process with §137h



\*Institut für das Entgeltsystem im Krankenhaus (Institute for the Remuneration System in Hospitals)

The benefit is not sufficiently documented, however the method offers the potential for a treatment alternative



- G-BA (Joint Federal Committee) shall decide within six months according to § 137e SGB V.
- Hospitals who wish to provide the method using the medical device at the expense of health insurance funds are obliged to participate in a trial according to § 137e SGB V.
- The trial shall be completed within two years, unless a longer trial period is necessary, even if the procedure decides within three months is tightened in individual cases. After completion of the trial G-BA decides within three months according to § 137c.

# Crisis in Cardiovascular Innovation



COMMENTARY

INNOVATION

## The Fiber of Modern Society

Elazer R. Edelman<sup>1,2,3\*</sup> and Martin B. Leon<sup>4</sup>

A powerful perception that innovation has stagnated persists in the biomedical research community. In a series of Commentaries—three in this issue and more in future issues—diverse professionals engage in a critical dialogue on innovation that explores whether novel ideas continue to emerge and whether their implementation continues to create value. The authors also discuss ways to resuscitate innovation through new risk-benefit analyses, correction of funding follies, monitoring conflicts of interest, defining the roles of public and private institutions, and the teaching of innovation.

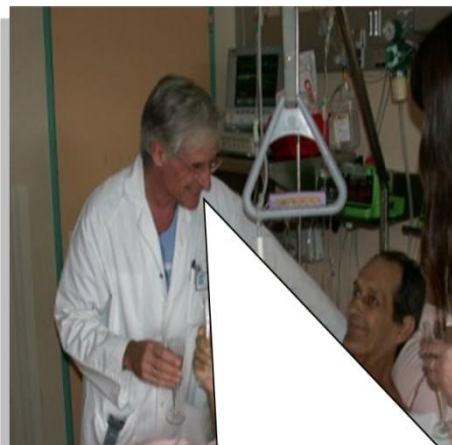
Science Translational Medicine; June 29, 2011

- Erratic global economies
- Stagnant growth in traditional cardiovascular markets
- Cost-sensitive reimbursement everywhere
- Reduced investment capital
- Declining patents
- Problematic regulatory environment
- Intense media and governmental scrutiny
- Physician conflict-of-interest constraints



# TAVR: A Breakthrough Technology?

## Dr. Alain Cribier *First-in-Man PIONEER*



**Circulation** American Heart Association  
Learn and Live.  
JOURNAL OF THE AMERICAN HEART ASSOCIATION

### Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis

#### First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD

*Conclusions* – “Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.”

**April 16, 2002**

Circulation 2002; AHA Abstract Presentation

- Addresses a compelling clinical need
- Multidisciplinary heart team concept
- Technology innovation and rapid iteration
- Impressive evidence-based medicine portfolio (PARTNER)
- Procedural improvements and generalizability (e.g. minimalist)
- Improved clinical outcomes over time (reduced complications)

# TAVR: A Breakthrough Technology?



## PARTNER THV Evolution



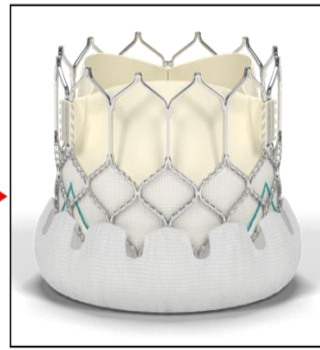
PI - 2007

Edwards SAPIEN™ THV  
23 mm and 26 mm



PII - 2010

Edwards SAPIEN XT™ THV  
23 mm, 26 mm, and 29mm



PII S3 - 2013

Edwards SAPIEN 3™ THV  
20 mm, 23 mm, 26 mm, and 29mm

**PARTNER enrolled 8,494 patients in FDA studies  
(including 4 RCTs) with 3 generations of  
TAVI systems in ~ 7 years!**

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# TAVR: A Breakthrough Technology?



## PARTNER Manuscripts in NEJM (October, 2010 – May, 2012)



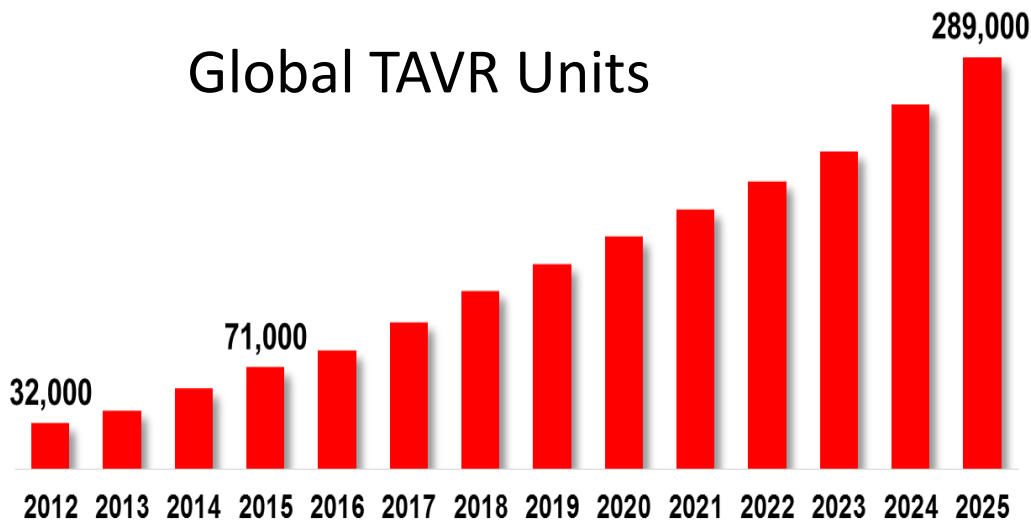
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# TAVR: A Breakthrough Technology?



**Estimated 4X TAVR  
Procedure Growth in 10  
Years**

Global TAVR Units



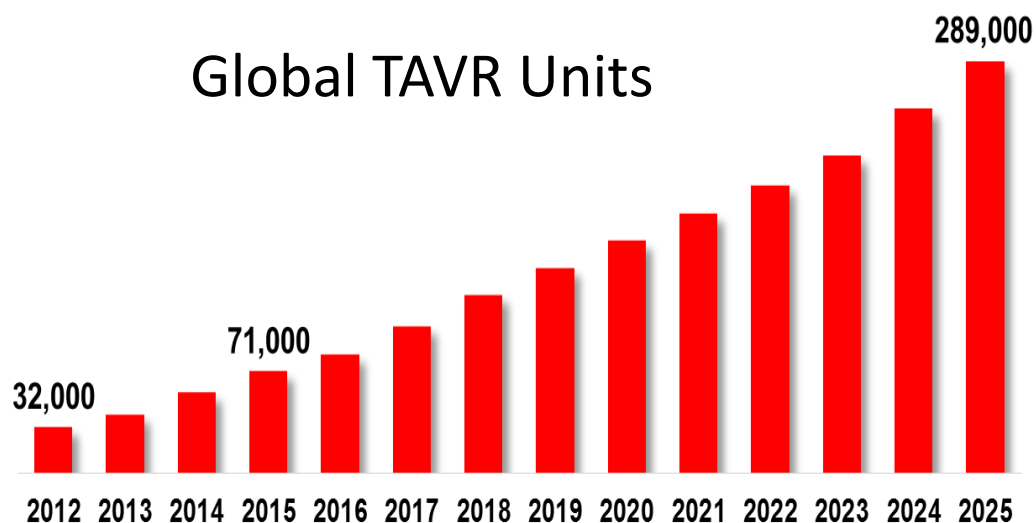
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# TAVR: A Breakthrough Technology?



## Estimated 4X TAVR Procedure Growth in 10 Years

### Global TAVR Units



## Expanding Clinical Indications

- Bioprosthetic valve failure (aortic and mitral)
- Moderate/ low risk AS patients
- Bicuspid aortic valve disease
- AS with concomitant CAD or MR
- Low flow - low gradient AS
- Asymptomatic severe AS
- Moderate AS with CHF



# Interventional Innovation

## *Lessons Learned*



- Must address a “clinical need” - a specific and well defined patient care clinical imperative!
- Ideally, should “invade” new large clinical markets with unsatisfactory current therapies - the big breakthroughs
- Must recapitulate the “ less invasive, catheter-based” treatment “mantra”
- Can be advanced technology, but must be simple to explain and easy to use (generalization)
- Avoid “science fair projects” or platform technologies - too risky and long-term

# Interventional Innovation

## *Lessons Learned*



- Must have a clear regulatory approval pathway - the demise of many otherwise worthy projects
- Evidence-based clinical data “reigns supreme” in 2017 - forget classical marketing concepts
- Must have a global strategy from the outset - consider all options for device development and commercial introduction
- Must be cost sensitive and respect problematic economic milieus during uncertain financial times and reimbursement challenges!

# Medical Innovation that produces COMMERCIAL SUCCESS



***Only few nations currently have all crucial elements of the innovation ecosystem; cultures of entrepreneurialism and commercialization, coherent reimbursement systems, IP protection, trained management, and a comprehensive network of reliable suppliers and distributors.***