# 20 years of TAVI

## *From the Idea of TAVI to Nowadays Reality: State of the Art*

*Alain Cribier, University of Rouen, France*


**TAVI First-in-Man - Rouen, April 16th 2002**

INTERNATIONAL SYMPOSIUM
CARDIOVASCULAR DISEASES
MC MEDICOR SLOVENIA

December 16th, 2022

# Statement of financial interest

**Alain Cribier:**

2005-2020: Consultant for Edwards Lifesciences
SAB: Cardiawave
SAB: Robocath

INTERNATIONAL SYMPOSIUM
CARDIOVASCULAR DISEASES
MC MEDICOR SLOVENIA

December 16th, 2022

# Celebration of the 20th Anniversary of TAVI

## Rouen, Chapelle du Lycée corneille

## May 21st, 2022

# Looking backwards on the past 20 years

## An indescribable amount of emotions

- Constant alternance of enthusiasm and disappointment
- Facing doubt, criticisms, skepticism, irony or even insults from the medical community at the early phase of development
- Immense satisfaction on the view of the first technical successes and extraordinary /durable improvement of patients
- Proudness to see TAVI now accepted worldwide and approved whatever the surgical risk

# Predisposing factors to the birth of TAVI in Rouen

## 1 - A personal journey

1976 USA
Fellowship

**Pr Brice Letac**
*Head of Department*

**Jeremy Swan**

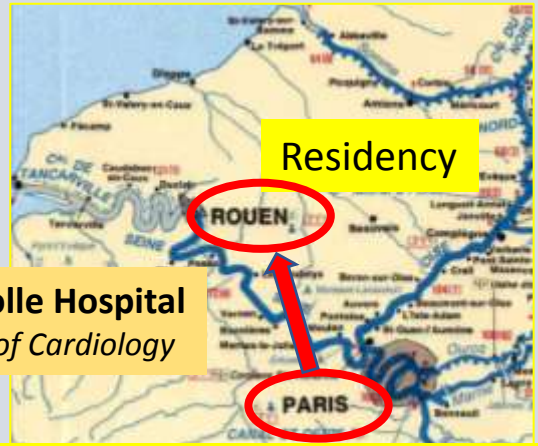
**Willy Ganz**






*Cedars Sinaï*
*Med Center*

1977, back to Rouen
**One leitmotiv:**
**Innovation**




**Charles Nicolle Hospital**
*Department of Cardiology*

From 1962: Medical Studies in Paris
*Early stays in world leading department of cardiology and cardiac surgery*

# Predisposing factors to the birth of TAVI in Rouen

## 2- A wonderful supportive “dream team”

### Since the 1990’s

A wonderful and rare partnership between interventional cardiologists and cardiac surgeons and an outstanding team of nurses and technicians

# Since 1985 in Rouen

## Development of two successive innovations for treating *acquired Aortic Stenosis*

**Rational: Attempt to solve a major unmet clinical need**

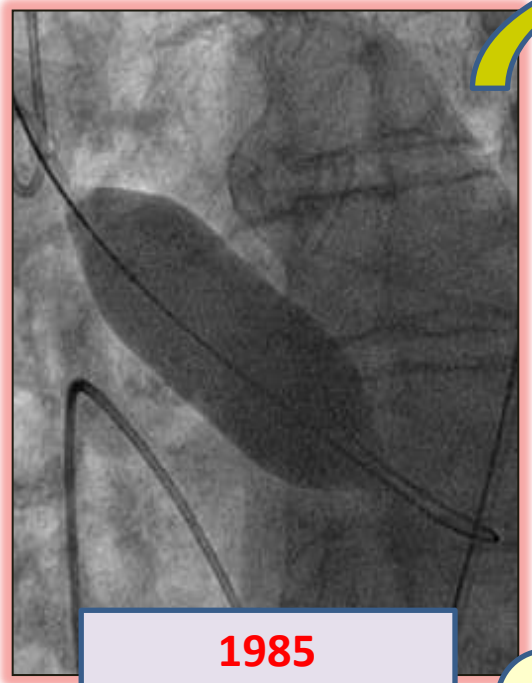
**BAV**
**FIM case**
**Rouen, Sept 1985**

- A bomb effect in the world of Cardiology
- Wide expansion worldwide
- > 1250 articles
- One limitation:

***Non lasting results***
***Recurrence: 80% at 1-y***

**What to do next ?**

**TAVI**

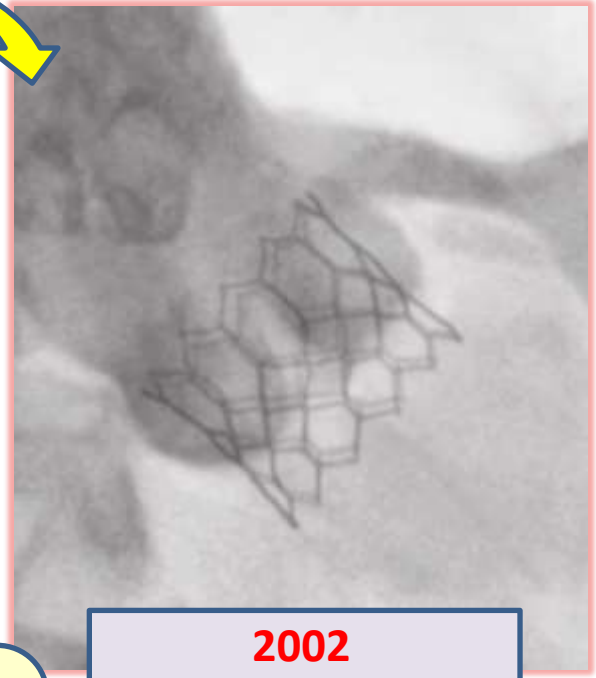


**1985**
Balloon Aortic Valvuloplasty
*F.I.M. Lancet, 1986*

**A single goal for these two linked innovations:**
To provide a live saving therapeutic option for patients with symptomatic AS and declined for surgical valve replacement

**In the 2000s**:
1/3 of symptomatic AS non operated on
**Mortality # 80% at 2-y**

**In the 1980s,**
**Age per-se > 70-y was an usual CI to SAVR**
***In Rouen, 95% of our SAVR pts were younger than 75-y***



**2002**
Transcatheter Aortic Valve: **TAVI**
*F.I.M. Circulation, 2002*

**TAVI**
**FIM case**
**Rouen, April 2002**

**Moving from dream to reality**

The starting point of development of a breakthrough technology

# 1990: Birth of the idea of TAVI
# As a solution against early restenosis post-BAV

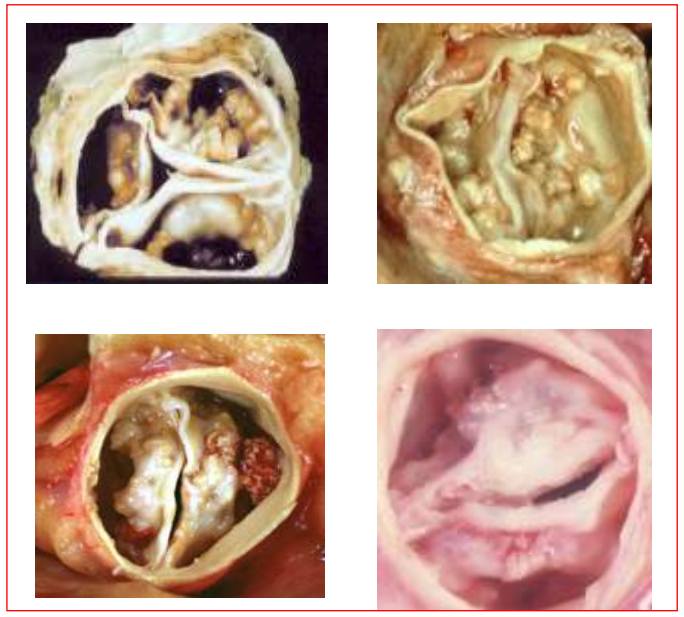
***The most challenging "crazy" concept***

> ***"Implanting a stented-valve prosthesis within the diseased calcific native valve, on the beating heart, using regular percutaneous catheter-based techniques and local anesthesia !..."*** ***A. Cribier, 1990***

## IMPOSSIBLE !

***Heavily calcified valves !***

***No chance of crossing the diseased valve with a prosthesis and deploy it***



## DANGEROUS !

***Surrounding structures !***

- ***Just above:***

***- Coronary ostia***

- ***Just below:***

***- Mitral valve***

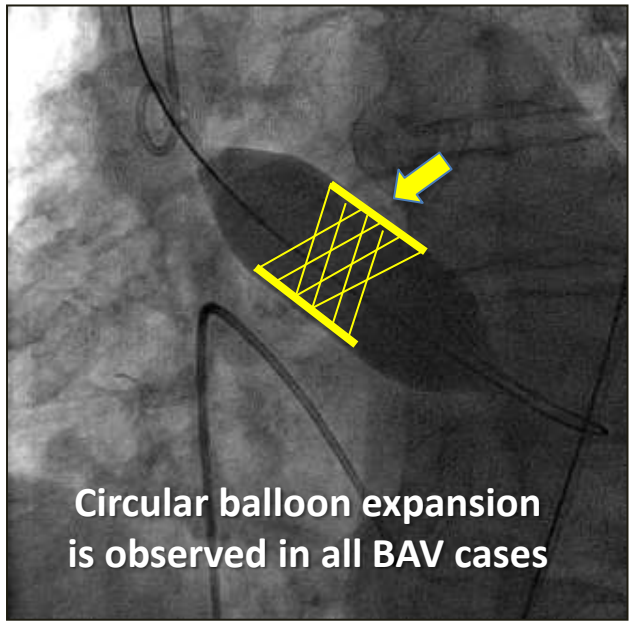
***- His bunddle***

# 1994 - Proof of concept – stenting an AS valve is possible

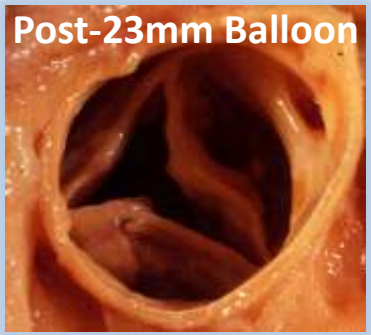
**A crucial landmark autopsy study**

**Rouen 1994**
**(16 fresh specimen of calcific AS)**
***With H. Eltchaninoff and R. Koning***

**Regular observation during BAV**



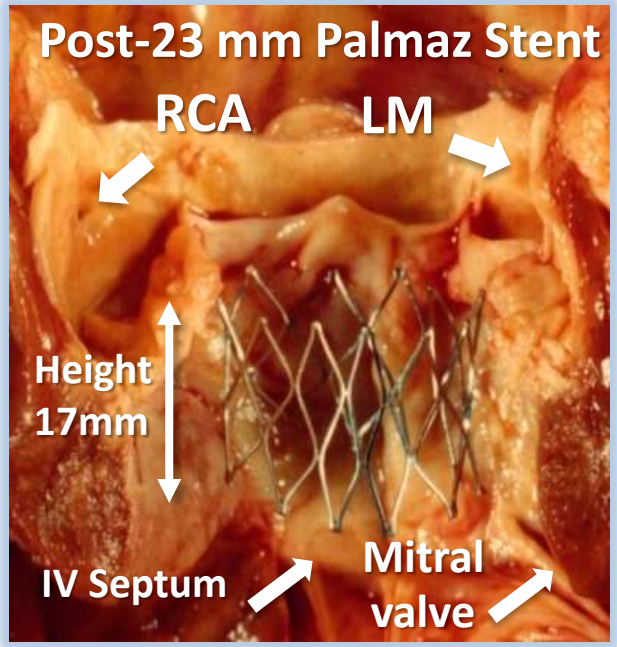

**Question:**
**Could a balloon expandable stent be used to maintain the valve open?**





**Circular stent opening in all**

**Renu Virmani, MD**
**Washington DC, 2002**
**Confirmative findings**




**Respect of adjoining structures**
- Forceps needed to remove the stent (traction force 2kg)

# 1994 - Figuring the stented valve and the procedure of TAVI

***EU Patent application***

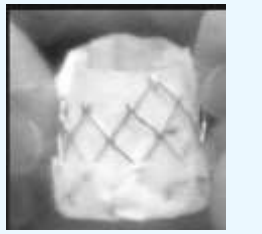
Systole

Diastole

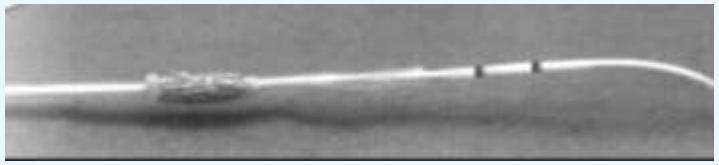
**- Valve structure: biologic or polymer?**

**- High radial force balloon expandable stent**

**- External cuff**

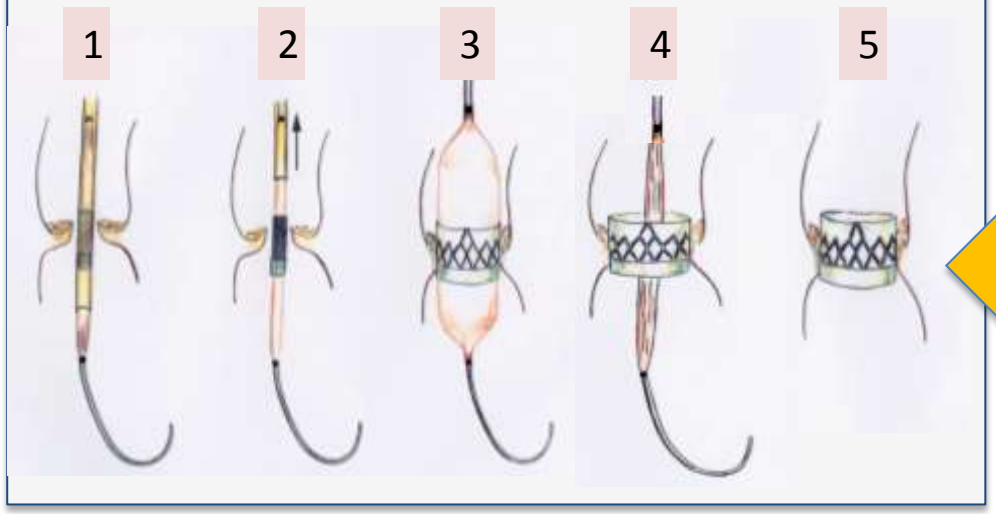


Rouen, Hand-made Model of THV
**(with Pr JP Bessou)**



Crimped diameter = 8mm

**Transfemoral approach conceivable**




***Let's make it !***

# 1994- 1999 Looking for a sponsor: 5 discouraging years

## *Comments from experts of all biomedical companies*

### *(Including Edwards, Medtronic, Boston Scientific)*

" Totally unrealistic, major technical issues "

" Definitely impossible to stent a calcific aortic valve "

"**Unavoidable life-threatening complications:**

*Stroke, myocardial infarction, annulus rupture, ventricular arrhythmias and conduction disturbances, endocarditis, THV embolization*

"Would never be approved by FDA"

"Surgery covers 100% of the need. No indication"

**"Most stupid project ever heard…" Just forget it !!!**

# 1994- 1999 Looking for a sponsor: 5 discouraging years

***It could have been the end of the story…***

When a distinguished scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong !

1972 Arthur C. Clarke

**One Key Word to Innovate in Medicine**
**PERSEVERANCE !...**

# 1999 - Project of TAVI still alive

**Creation of a start-up:**

**Percutaneous Valve Technologies Inc, NJ, USA**


**December 1999: Signed agreement with ARAN R&D, Caesarea, Israel: Investment, Development**

***I express my deepest gratitude to the team of ARAN, and to my friends' co-founders of PVT who brought my dreams to reality***

# 1999 *Highly challenging requests to Aran's engineers*

- A prosthesis made of a highly resistant frame
- Containing a uni-, bi-, or tri-leaflet valvular structure
- Able to be homogeneously compressed over a high pressure balloon, for its introduction into a sheath (femoral artery) of 7 to 9 mm in diameter
- Enlarged by balloon inflation to an external diameter of 23mm without damaging the frame and valvular structure

**And they made it!**

# 2000 *The PVT Heart Valve*

***Tri-leaflet valve***
***(polymer, then horse pericardium)***
***Stainless steel stent***
***Single diameter  23mm***
***24F crimped size***

# 2000-2002 The PVT Valve: *Preclinical evaluation*

## IN-LAB TESTING TESTiNG

### Valve Durability (5 years)


### Frame Tests

Radial force

Fatigue testing

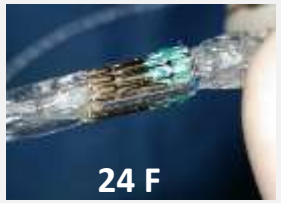
Frame geometry

### Hemodynamics

## CRIMPING

PHV Ø 23mm






## IN-VIVO TESTING,

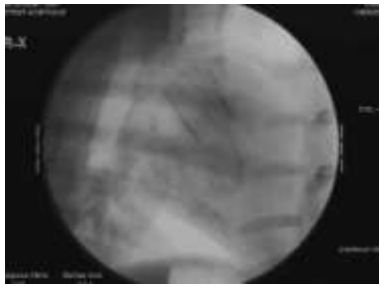
Sheep model, CERA, Paris

(A. Cribier, H. Eltchaninoff,)

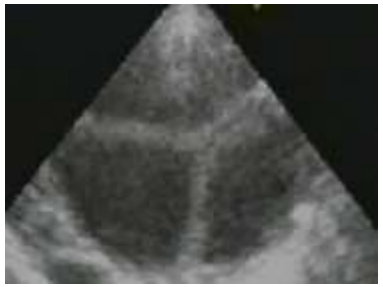
NuMed Balloon

Carotid approach

Acute in Ao V



5 Months in aorta



## Essential lessons

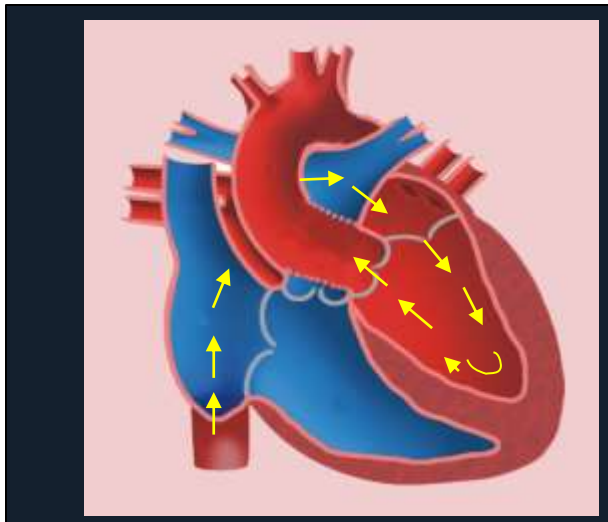
- Vascular access with large size sheath
- Delivery system
- Guidewires
- All procedural aspects of valve delivery
- **Rapid pacing**
- Anticoagulant regimen

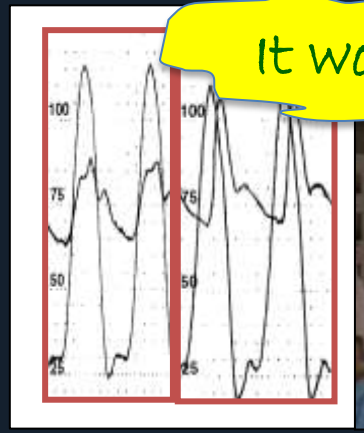
**But no valve calcification**
**Different anatomy**

**Moving to human ?**

# April 16th, 2002 - *The top milestone* : F.I.M –TAVI

## *Moving from concept to clinical execution*







# 2003-2005 - First Rouen series of TAVI

***One year spent before getting approval of the French Health Authority to start a prospective series of TAVI in Rouen***

**Drastic conditions**

1- Spontaneous life expectancy not exceeding 2 weeks

2- Transeptal approach requested as in the first case

**38 TAVI performed**

I-REVIVE / RECAST trials

Trans-septal approach in 31

Transfemoral approach in 7

**Procedural Success 85%**

***A. Cribier et al, JACC, 2004 & 2006***

- **TAVI (transeptal) takes its flight in the world:**
  ***USA, Canada, Italy, Holland***
- ***2005: a total number of 100 TAVI peformed***

**Lessons**

1- Feasibility of TAVI confirmed

2- Accuracy of valve placement

2- No THV embolization

3- No coronary occlusion

4- No MR

5- No AV - Block

6- Optimal valvular function

7- Excellent hemodynamics

8- *Paravalvular AR≥ 2 in 25%*
***(single size 23mm too small)***

# Rouen, 2002-2004 - First series *of critically ill patients*

## *Spectacular patient's improvement: a key element for the acceptance and future expansion of TAVI*

**Patient # 3**

- *83 y/o woman*
- *Multi comorbidities*
- *2 BAV procedures*
- *Cardiogenic shock*

**Transseptal TAVI as a last resort option**


***Invited guest at TCT, Washington, DC***

*Hemodynamic results unchanged since 2004*

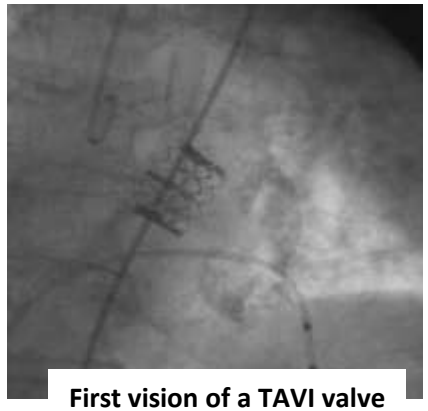
*6.5-Y post-TAVI (2010)*

**Patient # 10**

- **85 y/o Woman with severe AS**
- Massive pulmonary edema,
- Cardiogenic shock *Declined for SAVR*
- Transferred from Paris in pre-mortem state
- *Associated MS: no possible TS approach*

**First planned retrograde approach**

***Local anesthesia*** ***Procedure duration: 60 min***



**First vision of a TAVI valve implanted retrogradely**

*Hemodynamic results unchanged since 2004*


***A good vision of the future of TAVI***

# 2004 - A war between companies to acquire PVT

## Edwards Lifesciences is the winner

***New valve, New delivery systems, New approaches***

**Cribier-Edwards**
23mm

**Edwards SAPIEN**
23mm, **26mm**

**Treated tri-leaflet bovine pericardial valve**
**Stainless steel stent - External cuff**
**(50% of frame's height)**

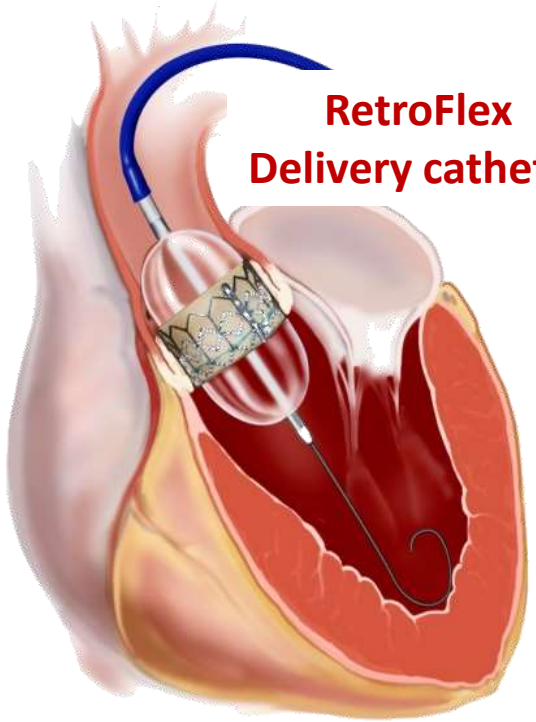
**TF: RetroFlex 3 delivery system**

*Sheath size: 22F (23mm), 24F (26mm)*

- **SOURCE EU** Registry
- **PARTNER 1**

**Transfemoral**

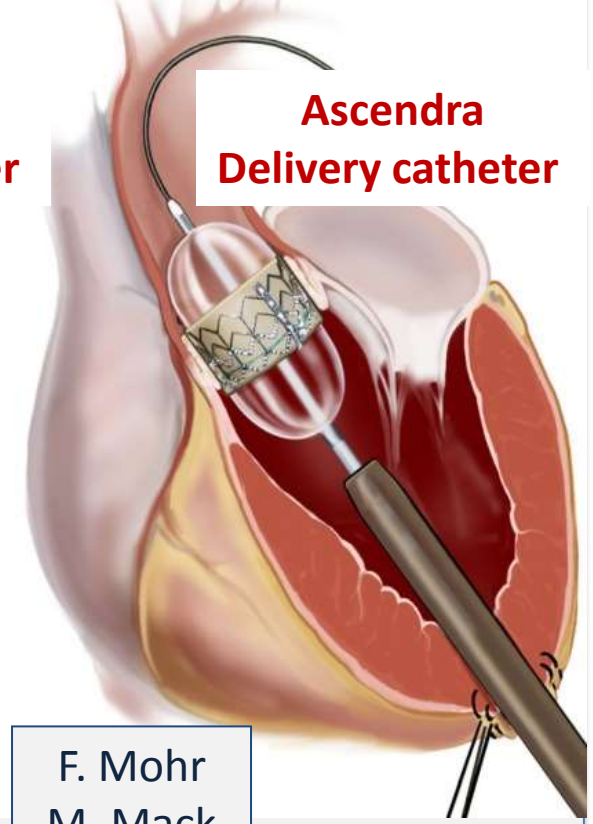
**RetroFlex Delivery catheter**



J. Webb

**Transapical**

**Ascendra Delivery catheter**



F. Mohr
M. Mack
T. Walther

# 2005: An alternative approach

## *Transapical access*

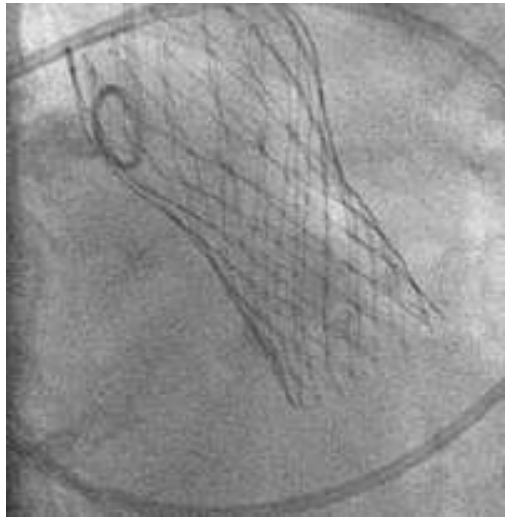
## *Surgeons start being involved with TAVI*


2005 First Transapical TAVI in Leipzig

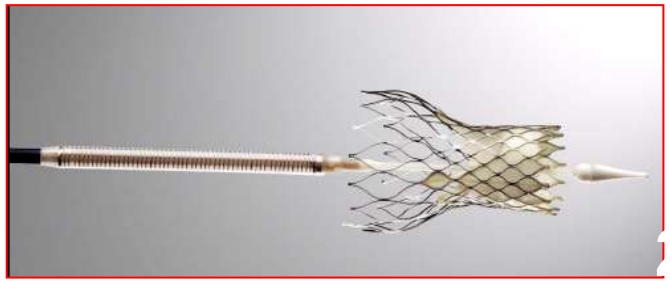
***The devil enter the OR !***

**With TF and TA, almost all TAVI candidates can be treated**

# 2004 - Launch of a concurrent device *The self expanding CoreValve later acquired by Medtronic*



**Jacques Seguin** **Eberhard Grübe** **J.C. Laborde**



*Start of a fair and ongoing competition between the two devices*

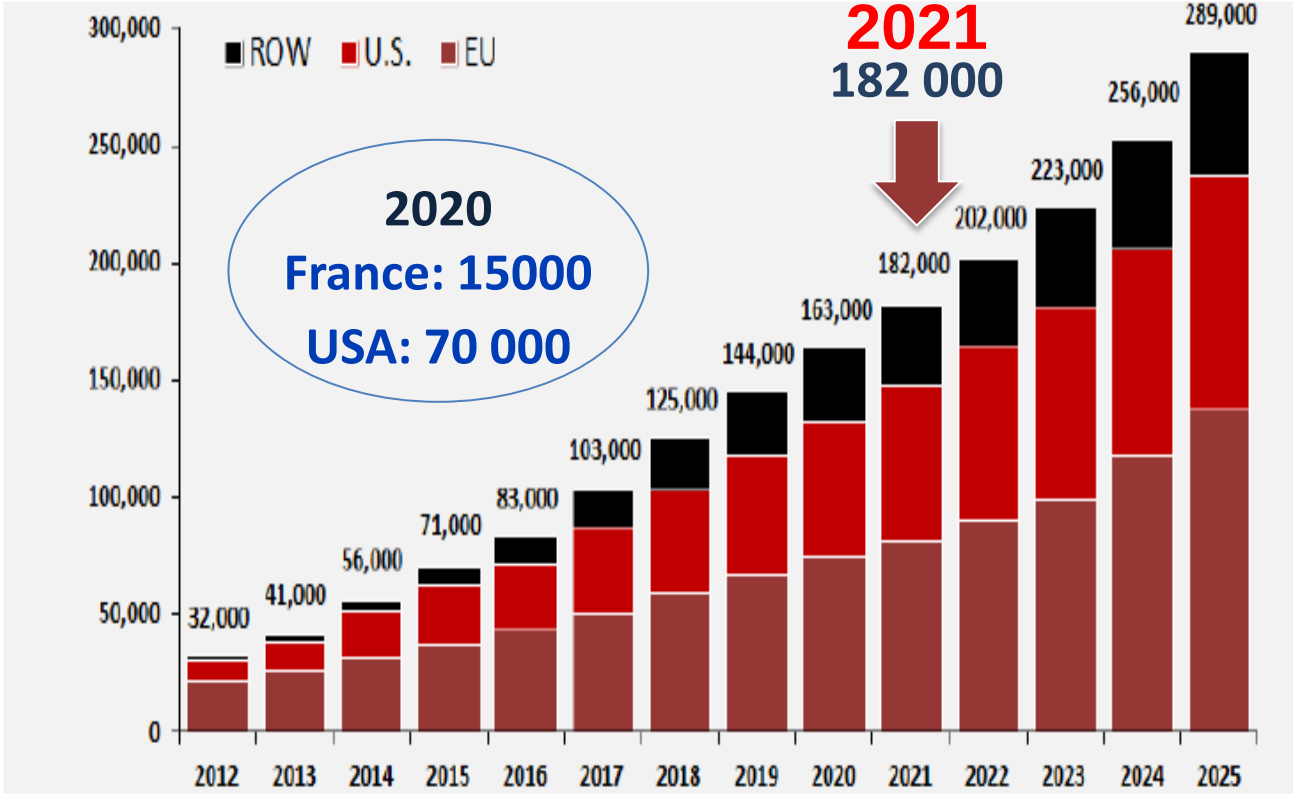
**Smaller 21F sheath size:**
***A convincing feature for many operators***

**No doubt that this device plaid an important role in the worldwide expansion of TAVI**

# At this stage, no one could have predicted the incredible success and world expansion of TAVI

## *Where are we today, 20 years later?*

- About 2.000.000 procedures in > 80 countries
- TAVI market exceed SAVR market in many countries including USA
- Expected growth of >10% per year



# *The reasons of success*

## 1) Improved devices technology and skill

- **Better patients screening and launch of accessory devices**

  ***Thanks to the constant support of the industry***

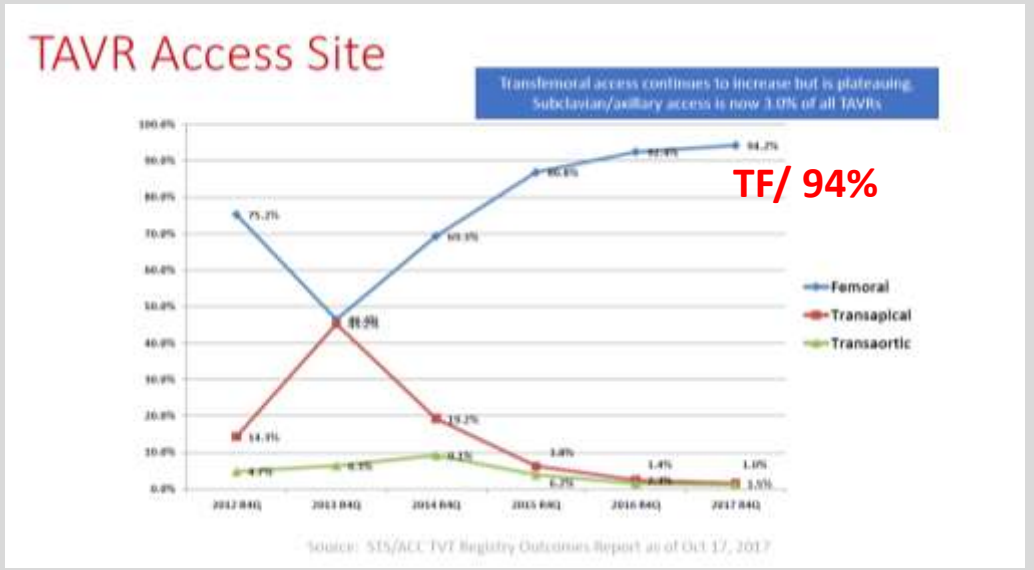
- **Continuous improvement of valves and delivery systems**

  ***« Démocratization » of TAVI: Procedures easier, faster and safer***

**USA**: Initially fiercely opposed to TAVI under local anesthesia / sedation.

**Later convinced:**

***STS/ACC TVT Registry,***




**Minimalist TF Approach in 90%**

# *The reasons of success*

## 2) large body of scientific evidences

- **Multiple TAVI registries**
  - Initially in High Risk patients
- **Matched registries vs SAVR**
  - Intermediate Risk patients
- **Evidence based trials**
  - Inoperable and High Risk, Intermediate Risk, Low Risk patients

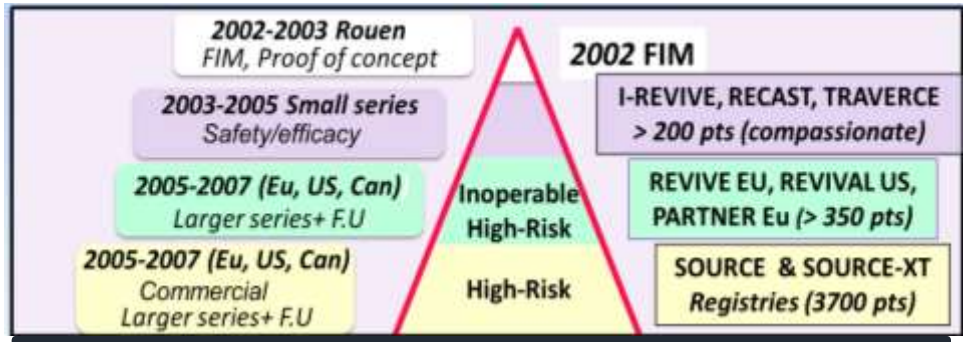
***Few other medical technologies were subjected to such great and challenging scientific evaluation !***

**Evaluating the benefit of a beakthrough technology, first on critically ill patients then step by step on lower risk patients**

# The reasons of success

## 2) large body of scientific evidences

**2003-2007 REGISTRIES**




- **Multiple TAVI registries**
  - Initially in High Risk patients




H. Eltchaninoff

**FRANCE registry**



M. Gilard

**FRANCE 2 registry**

**+ 27 ancillary studies**
**Followed by « FRANCE TAVI »**
**and « FAST-TAVI »**

# *The reasons of success*

## 2) large body of scientific evidences

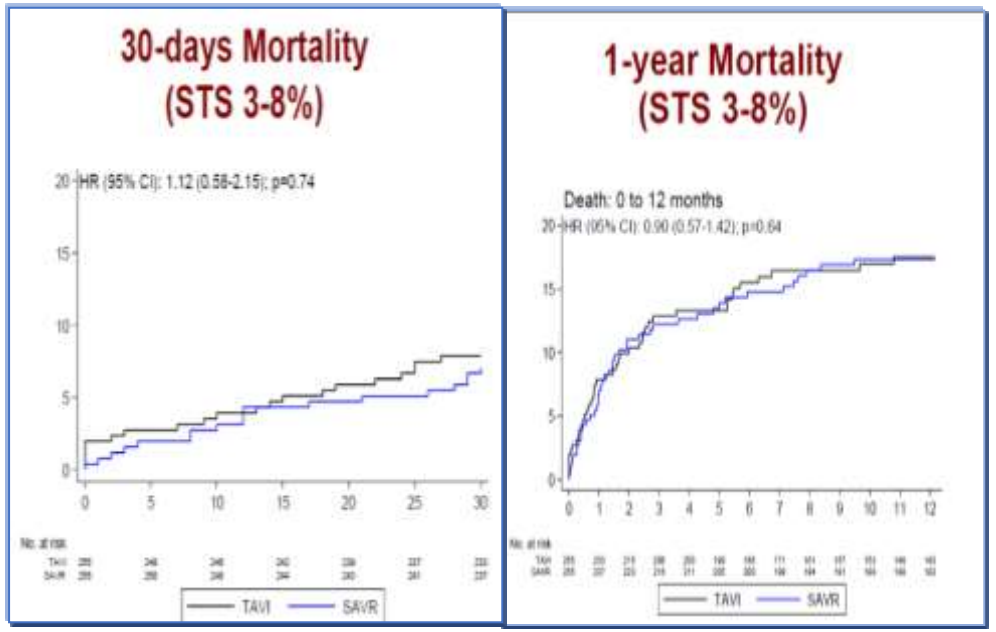
- **Multiple TAVI registries**
  - Initially in High Risk patients
- **Matched registries vs SAVR**
  - Intermediate Risk patients

***BERMUDA Triangle study***

From 3666 patients enrolled (TAVI 782, SAVR, 2884)

**754 matched patients, 255 in each group**

**at Intermediate risk: STS >3% - < 6%**




N Piazza, ESC 2012

# The reasons of success

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  - Intermediate Risk patients
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  - Inoperable and High Risk, Intermediate Risk, Low Risk patients

Edwards

**PARTNER 1**
*N=1240*
Inoperable
High-risk
2012 FDA

Edwards-Sapien

**PARTNER 2**
*N=2032*
Intermediate Risk
2016 FDA

Sapien XT

**PARTNER 3**
*N=1000*
Low Risk
(>75y/o)
2019 FDA

Sapien 3

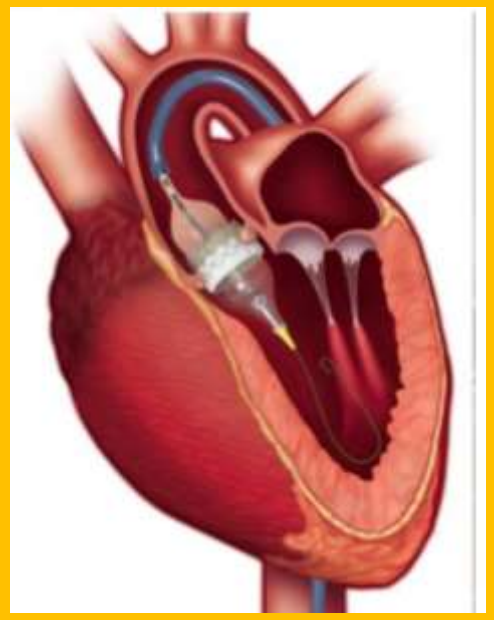
**NON-INFERIORITY OR SUPERIORITY of TAVI on main end-points (mortality, stroke, QOL, rehospitalization)**

**Comparable scientific pathway and results with CoreValve**

# 2019 - *Last milestone*: the apotheosis of TAVI

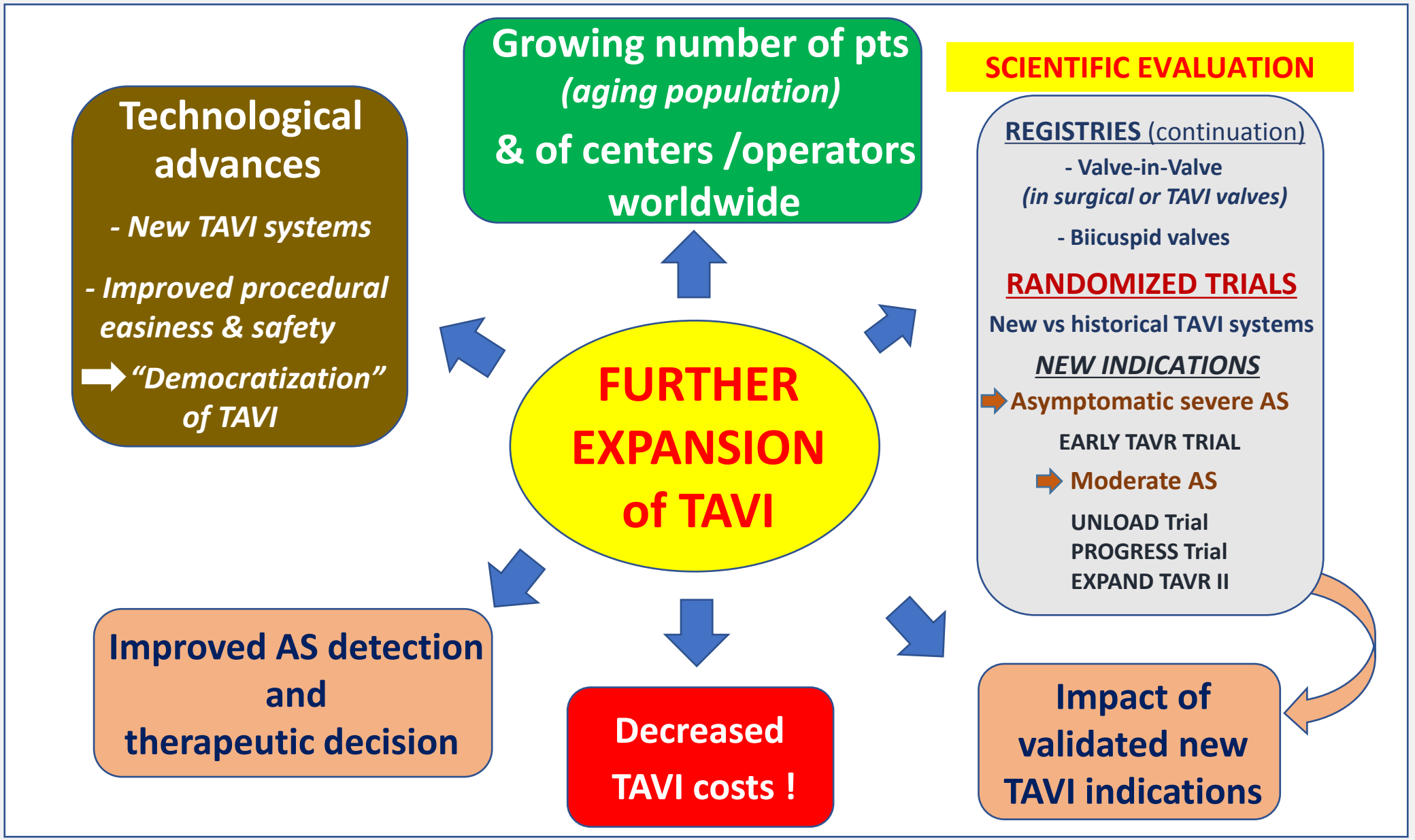
## *FDA Approved TAVI for LOW-RISK Patients > 65 years*

**SAPIEN 3** **Medtronic Evolut**

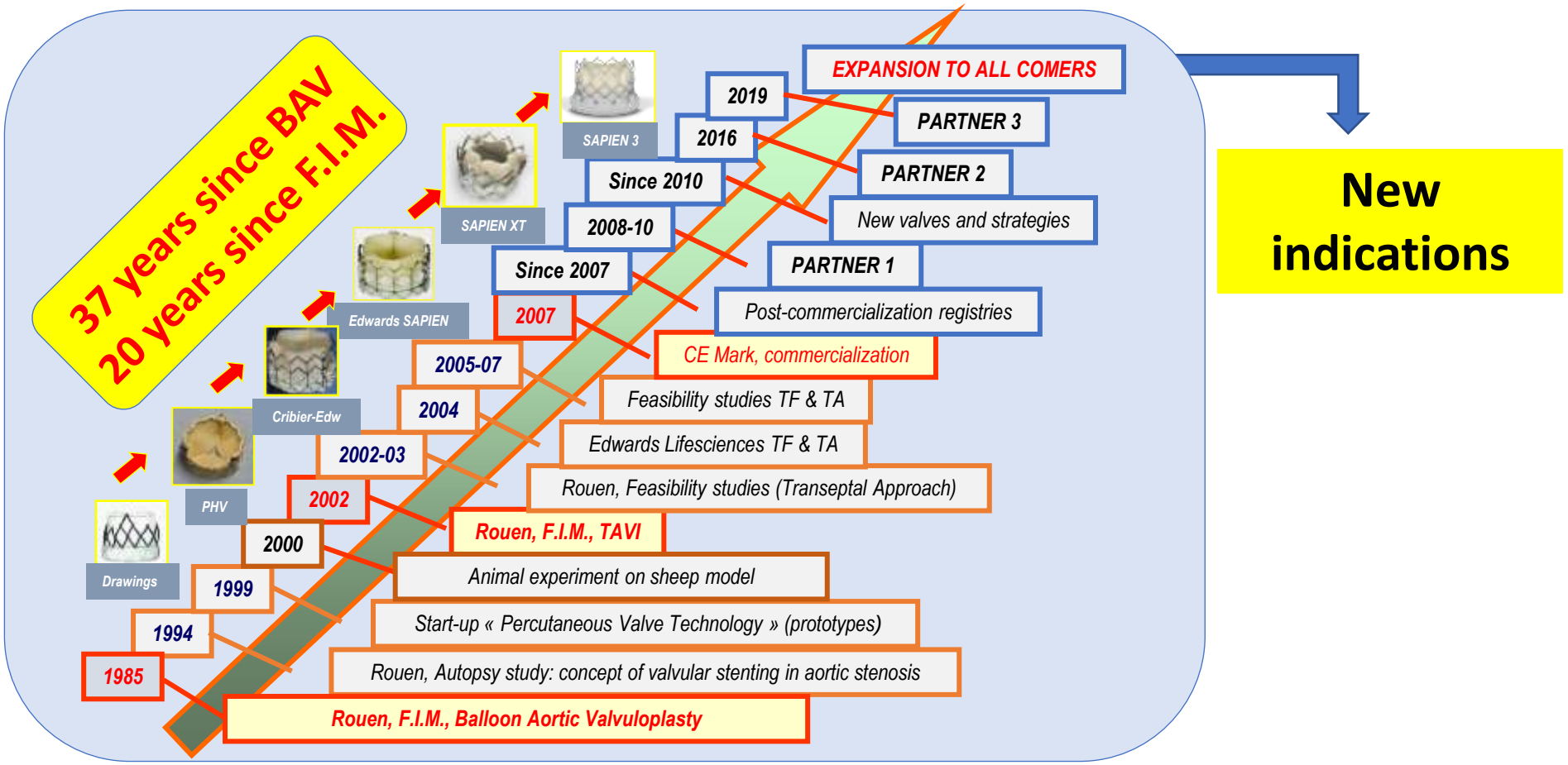


**2021 - European recommendations in Low-Risk patients: all patients > 75 year of age**

# 2022 - How can we predict the future of TAVI?



# Developing TAVI: A long bulky road




**New indications**

**Of note that this breakthrough technology has open a new world in cardiology by stimulating the transcatheter treatment of many other valvular (mitral, tricuspid) and structural heart diseases**

# Conclusions

- In 20 years, TAVI, this disruptive technology, initially considered impossible and « insane », has known a considerable expansion based on continuous advanced technologies leading to procedural facilitation and safety together with an outstanding scientific evaluation.
- The invaluable partnership with the industry has played a major rôle.
- Many investigations are ongoing to answer the remaining questions. This should lead to a further accelerated expansion of this breakthrough technology in the near future

**A bright future for TAVI !!!**


Thank you
Very much
Transcatheter
Aortic
Valve
Implantation
20 YEARS!