



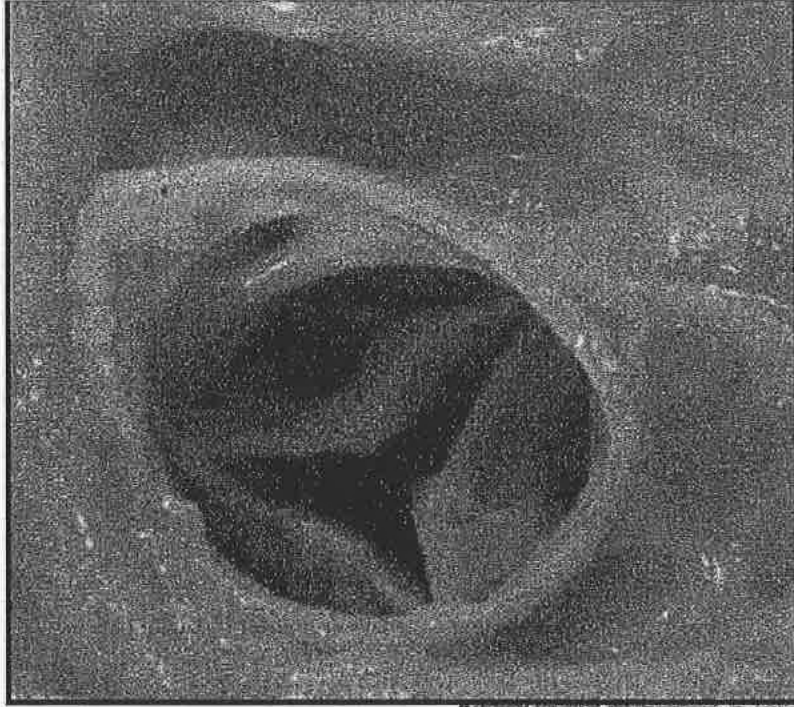
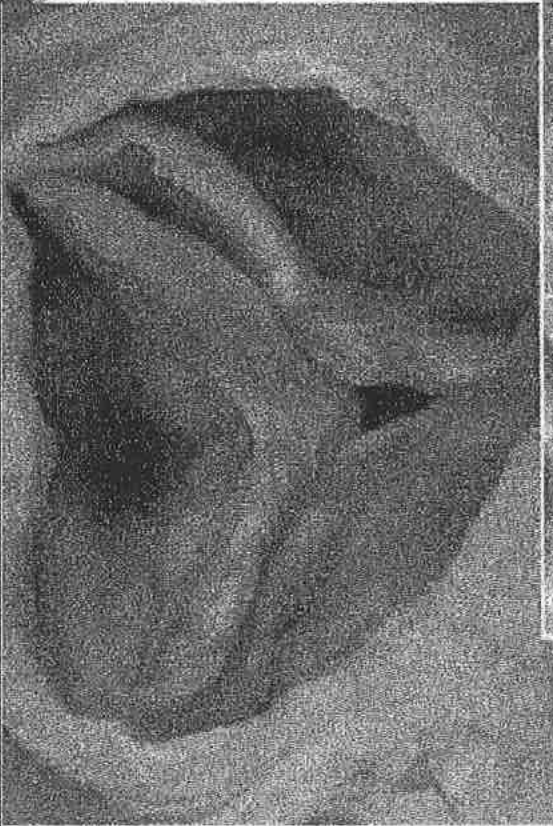
History of Sapien and the Future of THV

Stanton Rowe
Corporate Vice President
Chief Scientific Officer



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Aortic Stenosis



© Cornell University Medical College

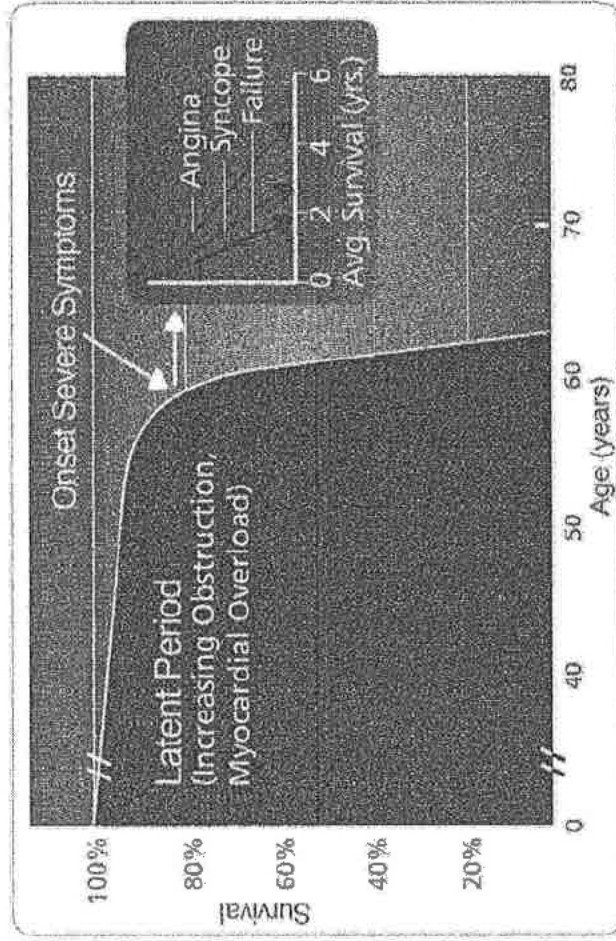
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EDWARDS 02433144

Aortic Stenosis is Life-threatening and Progresses Rapidly



Survival after onset of symptoms is 50% at two years and 20% at five years¹

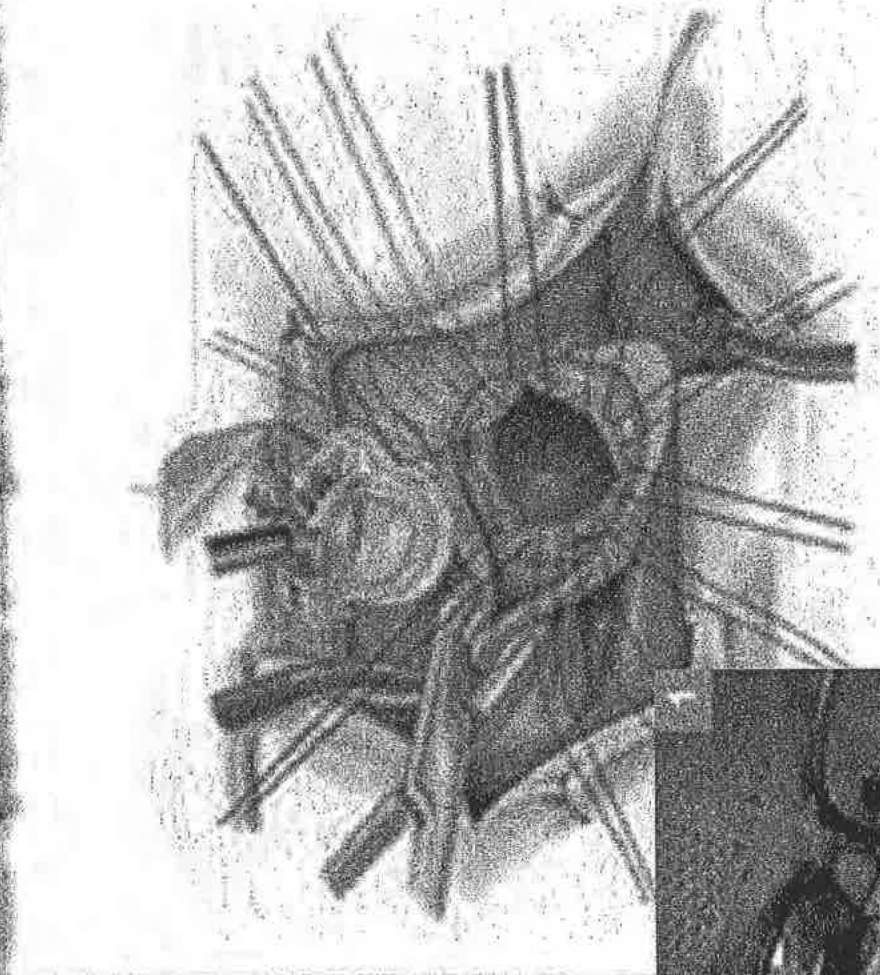
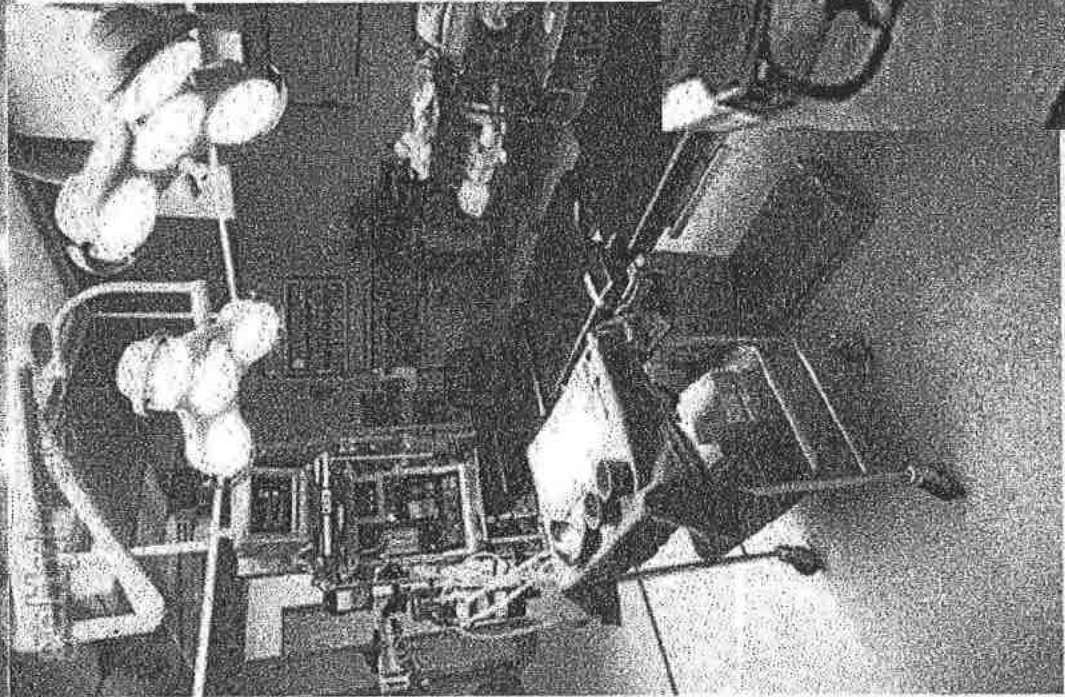
“Surgical intervention [for severe AS] should be performed promptly once even...minor symptoms occur”²

Source:
¹S.J. Lester et al., "The Natural History and Rate of Progression of Aortic Stenosis," *Chest* 1998.
²C.M. Otto, "Valve Disease: Timing of Aortic Valve Surgery," *Heart* 2000; *Chest*: Ross J Jr, Braunwald E, Aortic Stenosis. *Circulation*. 1968;38(Suppl 1):61-7



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Current Therapy- Open Heart Surgery



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The Gold Standard: Aortic Valve Replacement (AVR)

STS Cardiac Surgical Database

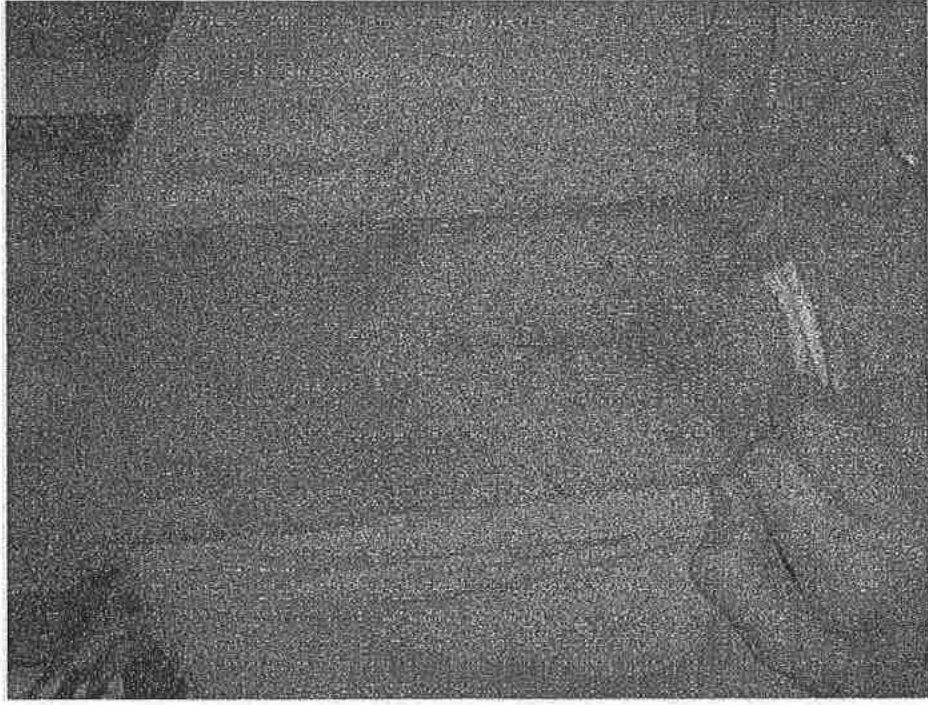
- 32,968 AVR Alone
 - Mortality 3.4%
 - Stroke 1.5%
- AVR+CABG
 - Mortality 4.6%

New York State 2002

- 19,057 Valve operations
 - 4943 Isolated AVR
 - Mortality 2.54%

Columbia Univ Med Center 2006

- 146 Isolated AVR
 - Mortality 0.7%
 - Stroke 1.4%
- 34 patients with EUROSORE >20
 - Mortality 0%
 - Stroke 0%



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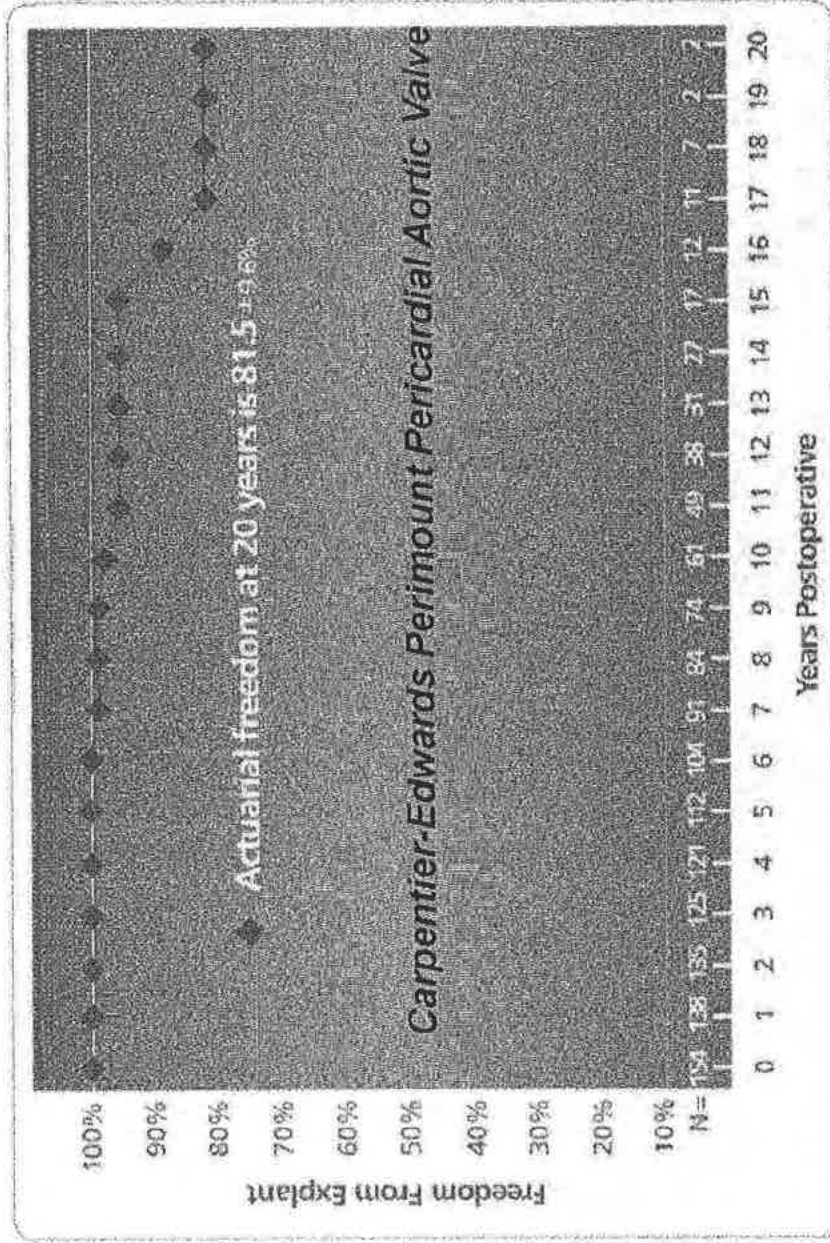
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PVT Design Considerations

Freedom from Explant Due to Structural Valve Deterioration
 Patients \geq 65 Years

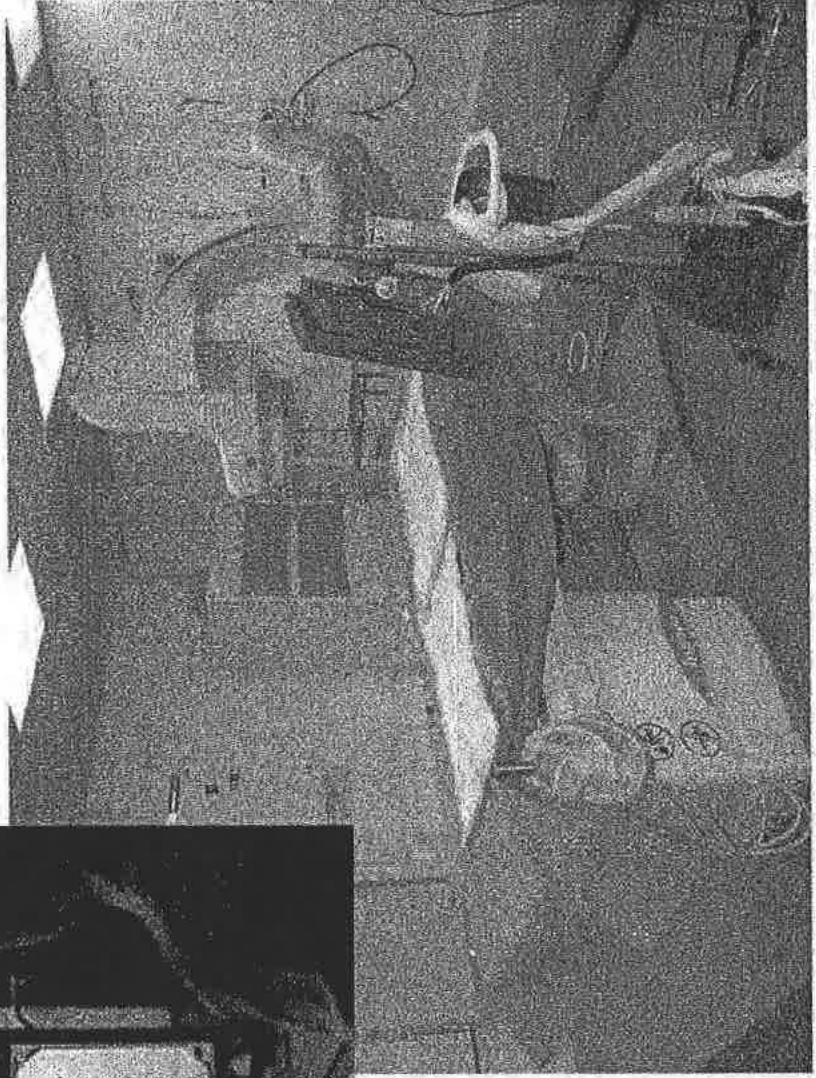


Data from Fig. 40, Edwards

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Cardiac Cath Procedure



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	SURGICAL	PERCUTANEOUS
Incision	Thoracotomy/less invasive	0.5" upper thigh
Anesthesia	General w/ post-surg intubation	Conscious sedation
Heart Status	Full cardiopulmonary bypass	Beating heart
Operation	Cardiothoracic surgical suite (CT surgeon)	Cardiac cath lab (Cardiologist)
Mortality/Stroke	2-9%, 0-3%	TBD
ICU Time	2-3 days	none
Length of Stay	6-8 days	2-4 days?
Re-operative risk	High	Low
Cost		

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Percutaneous Valve Concepts

Moulopoulos et al 1980 and Pavcnik et al (1992)

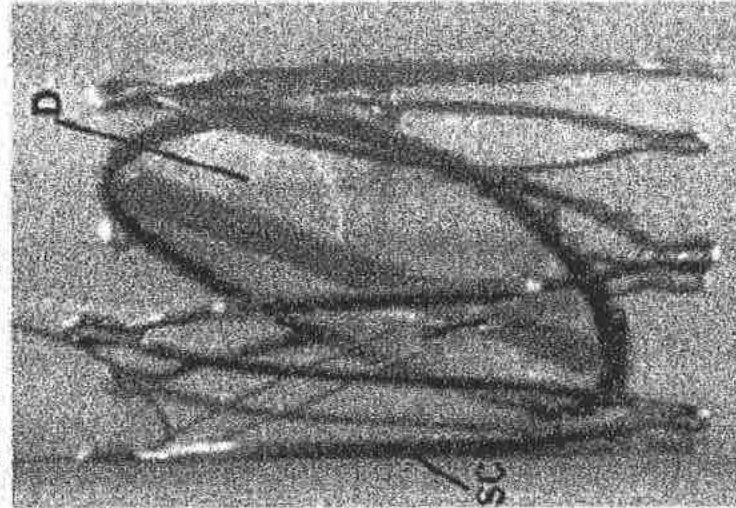
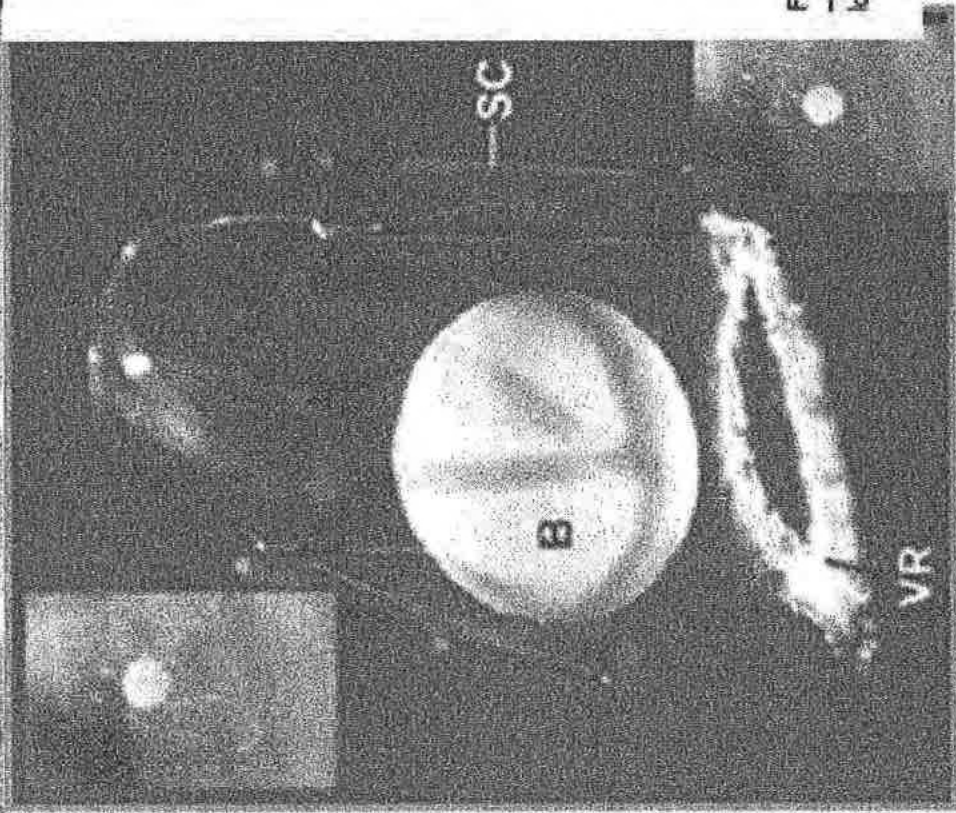
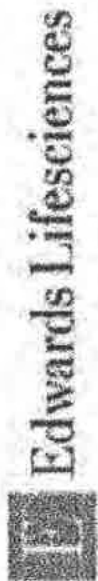


Fig. 2. Mechanical disc valve design for two-step deployment. SC - stent carrier (deployed in the first step); D - disc (deployed and locked in the second step)

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Balloon Aortic Valvuloplasty

The First Percutaneous Approach

- Balloon dilatation of the aortic valve
- Popularized in the 1980's and performed in many cath labs
- Good acute results with low complications
 - 0.6 cm^2 valve area to 1.0 cm^2
- Poor patency, 75% restenosis at one year



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SEVERE AORTIC STENOSIS

NON-SURGICAL
REFUSALS
MEDICAL THERAPY
ASYMPTOMATIC

BALLOON AORTIC VALVULOPLASTY

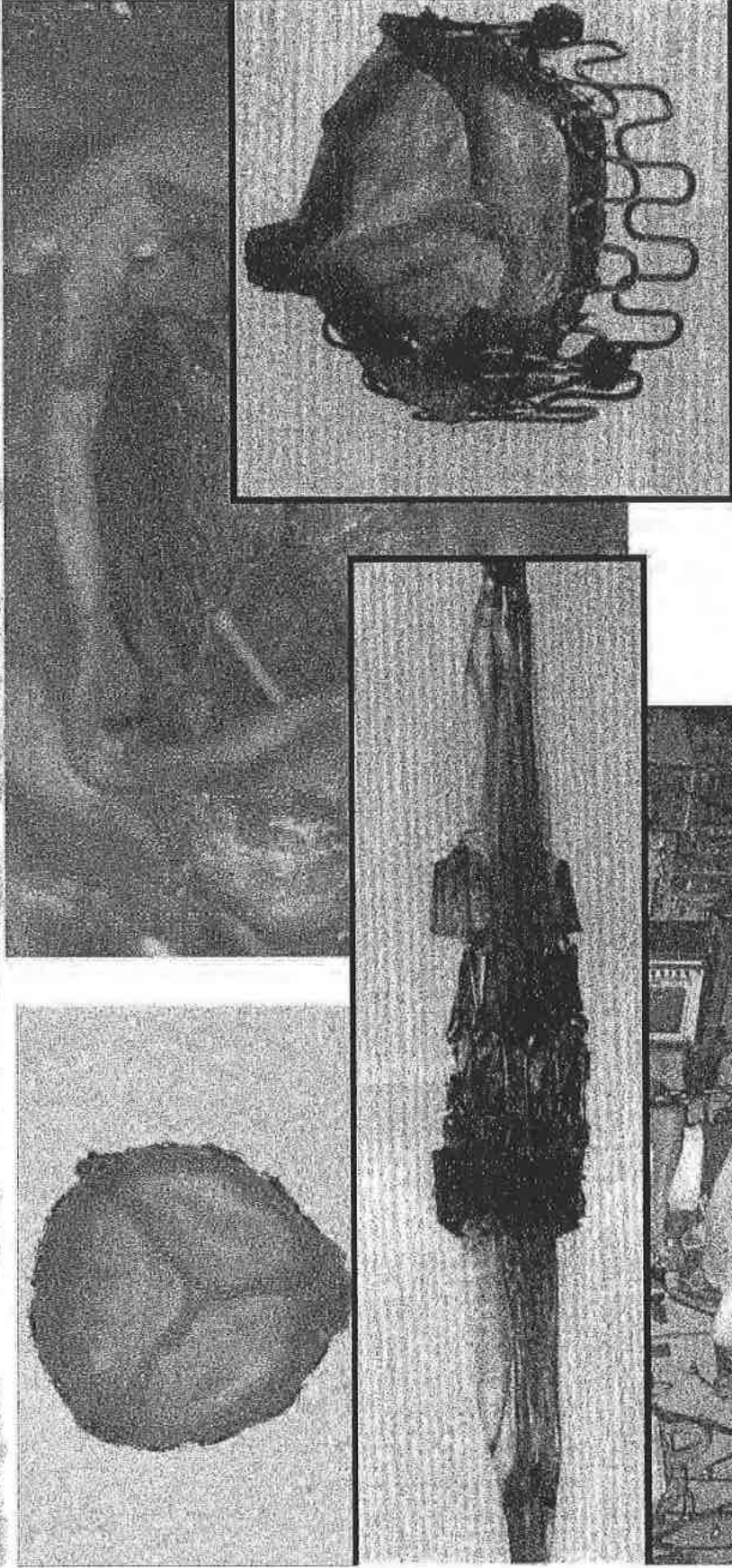
**AORTIC VALVE
REPLACEMENT SURGERY**



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Henning Rud Andersen 1992

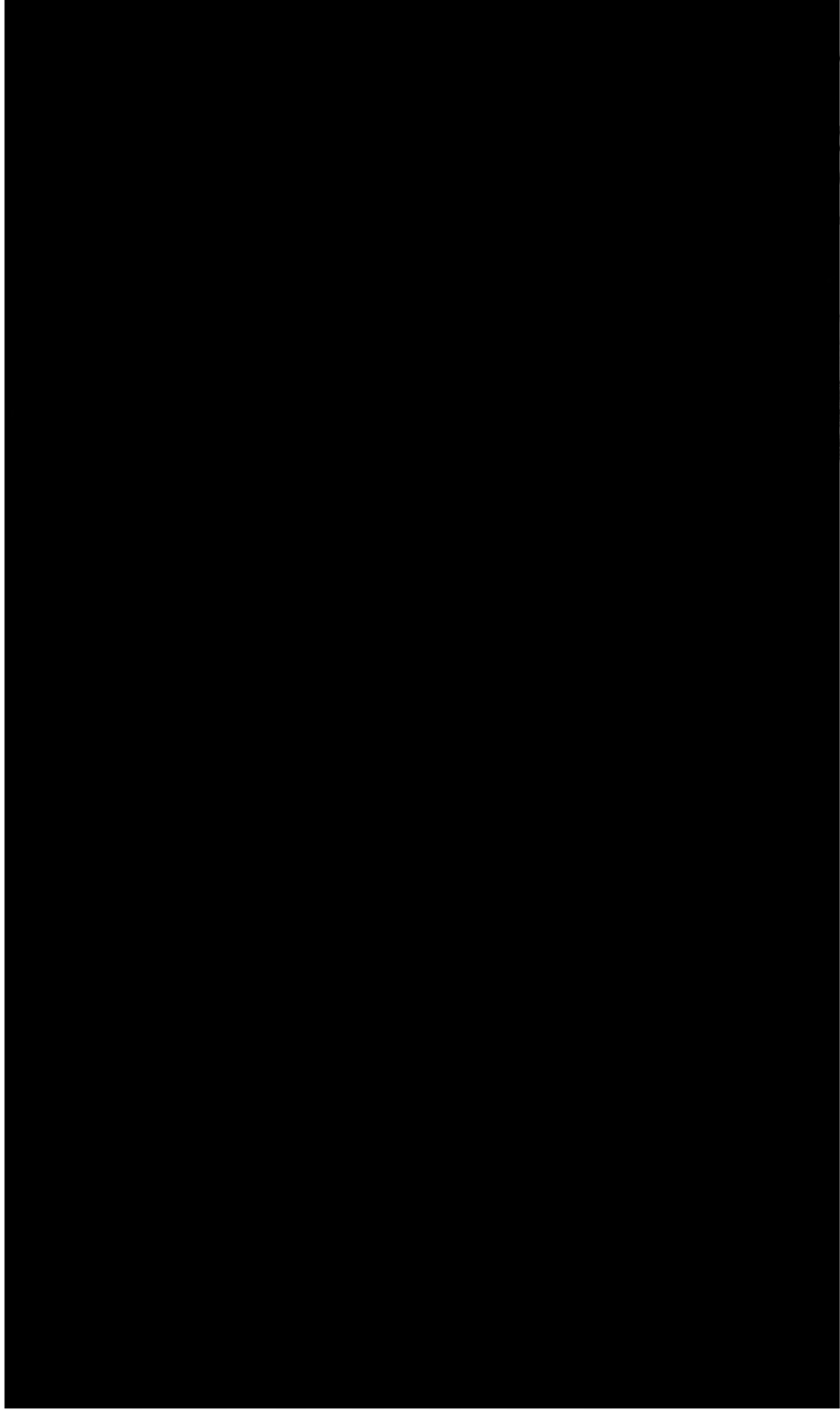


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Johnson & Johnson
INTERVENTIONAL SYSTEMS CO.

Cordis
a Johnson & Johnson company



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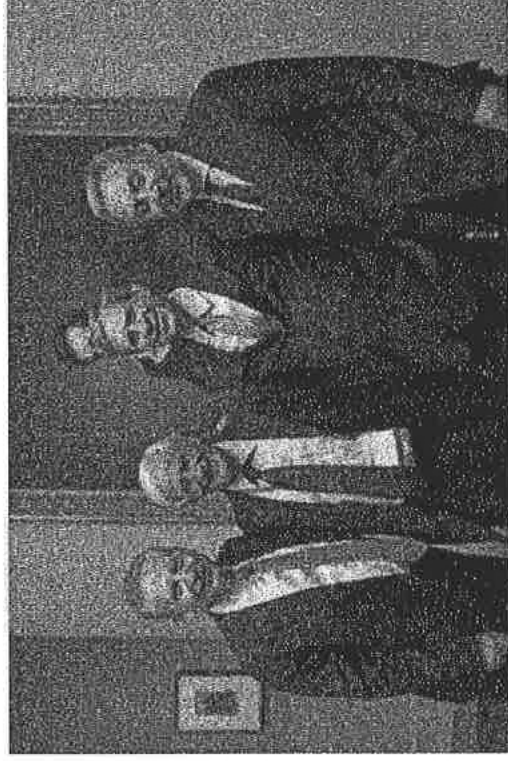
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PVT Background

PVT

Percutaneous Valve Technologies

- PVT was “born” in 1998 and formally founded in late 1999
- Founders:
 - Stanton Rowe
 - Stanley Rabinovich
 - Dr. Alain Cribier
 - Dr. Marty Leon
- Development Partner:
ARAN Research & Development Ltd



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Percutaneous Valve Technologies, Inc. (PVT)

➤ **1999 Incorporated- Founding Partners**

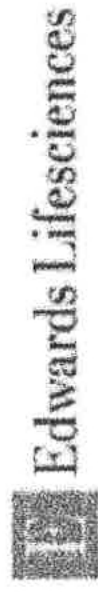
• **Dr. Alain Cribier**

• **Dr. Martin Leon**

• **Stanley Rabinovich**

• **Stanton Rowe**

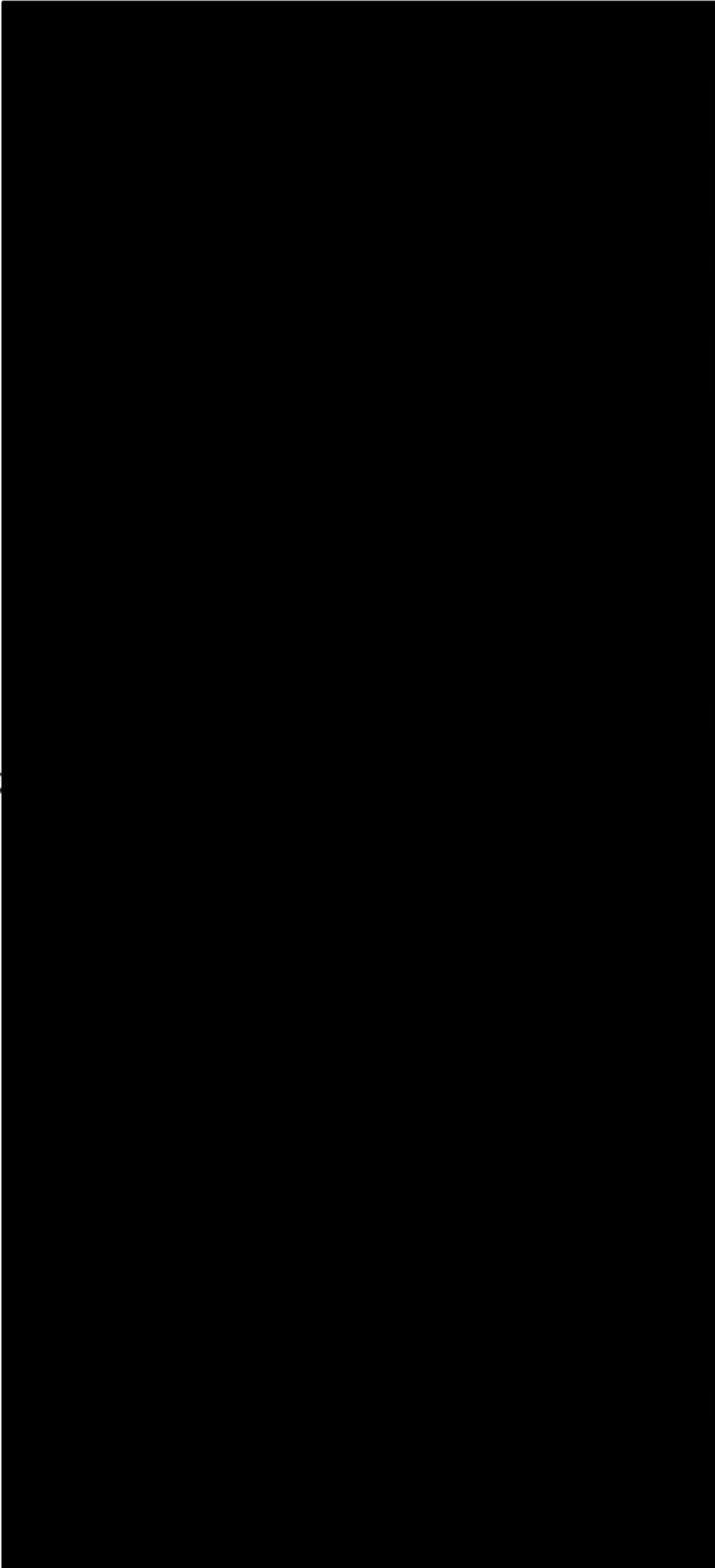
➤ **May-2000**



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Alain Cribier; Rouen: first sketches

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Cribier Drawings

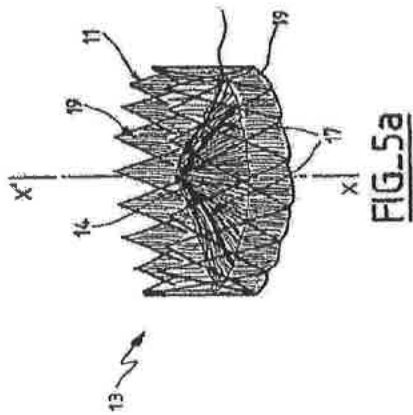


FIG. 5a

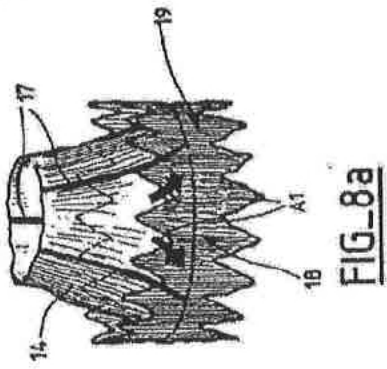


FIG. 8a

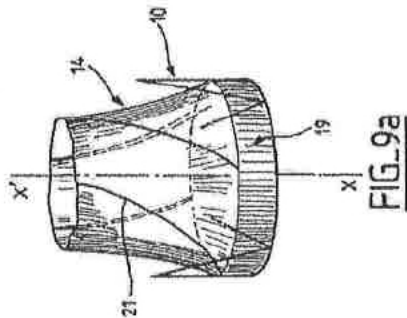


FIG. 9a

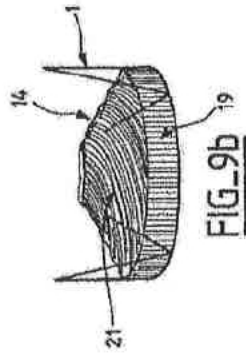


FIG. 9b

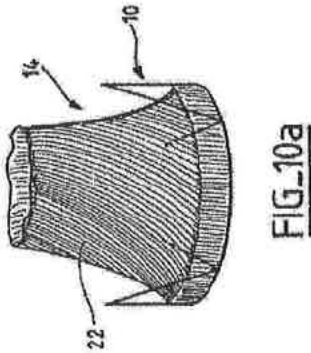


FIG. 10a

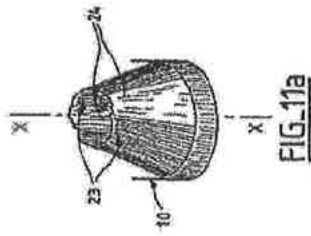


FIG. 11a

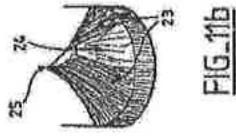


FIG. 11b

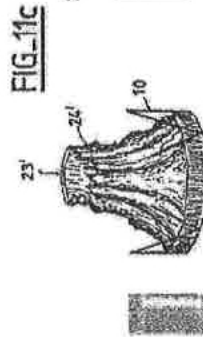


FIG. 11c

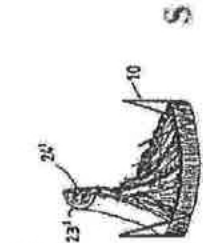


FIG. 11d

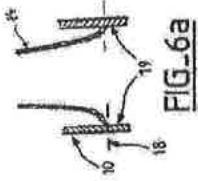


FIG. 6a

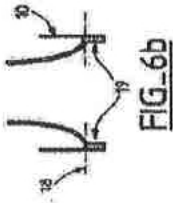


FIG. 6b

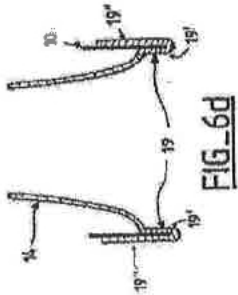


FIG. 6d

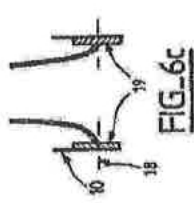


FIG. 6c

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Patents and Development Efforts

- Andersen, 1995 5,441,552
- Stevens, 1996
- Andersen, 1998 5,840,081
- Cribier filed PCT, 1996-1999
- Andersen, 2001 6,168,614
- Heartport attempted this project in 1993-4 and filed patents on **REMOVING** the old valve with a catheter designed to cut out the valve.
- **What can you do other than cut out the stenotic valve, the same way as CT surgeons?**



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Engineering questions

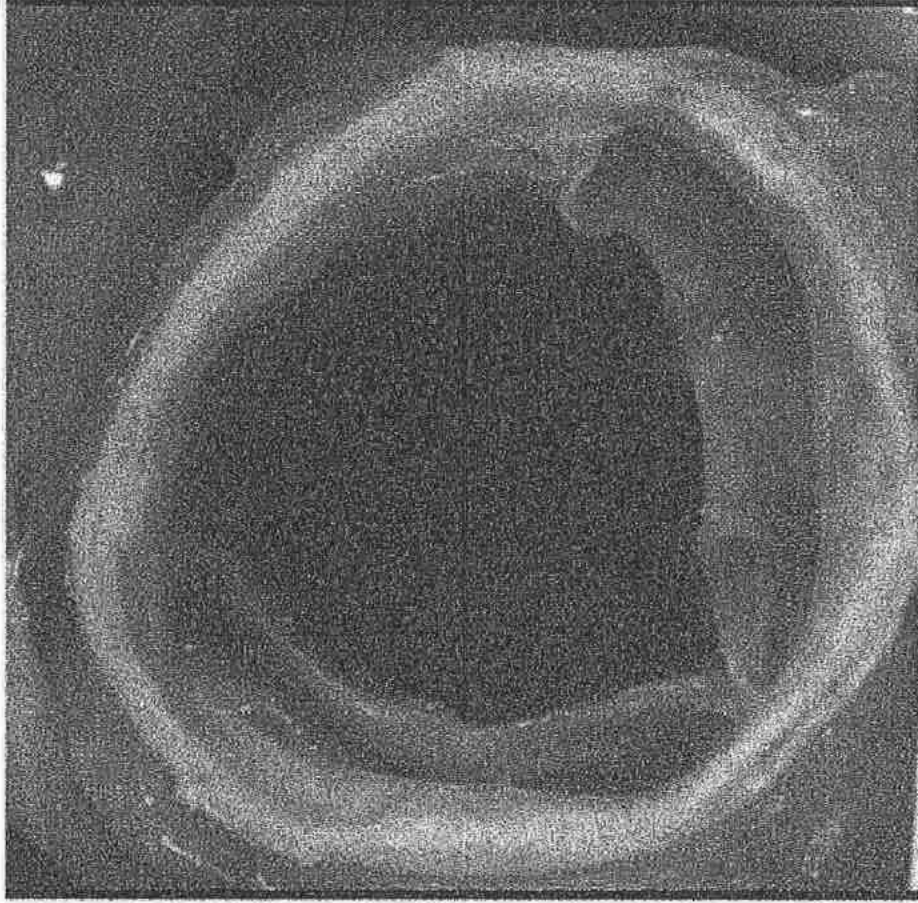
- What compressive forces must the frame (stent) resist?
- How strong must we make the frame to form a circular valve?
- How can we manufacture a frame that large; no tubing that large?
- What material is preferred for the frame?
- How do we attach a fixed diameter valve to an expandable and collapsible frame?
- How do you make the attachment durable?
- How can we seal around the valve and prevent PVL? Without increasing profile?
- What is the optimal valve design for hemodynamics/profile/tissue damage? Unicuspid, bicuspid, tricuspid or quadricuspid?
- What is the optimal valve material? Polymers, co-polymers, tissue?



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Human Cadaver Stented Valve



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EDWARDS 02433162

What surgeons said about THVs... (to VC's)

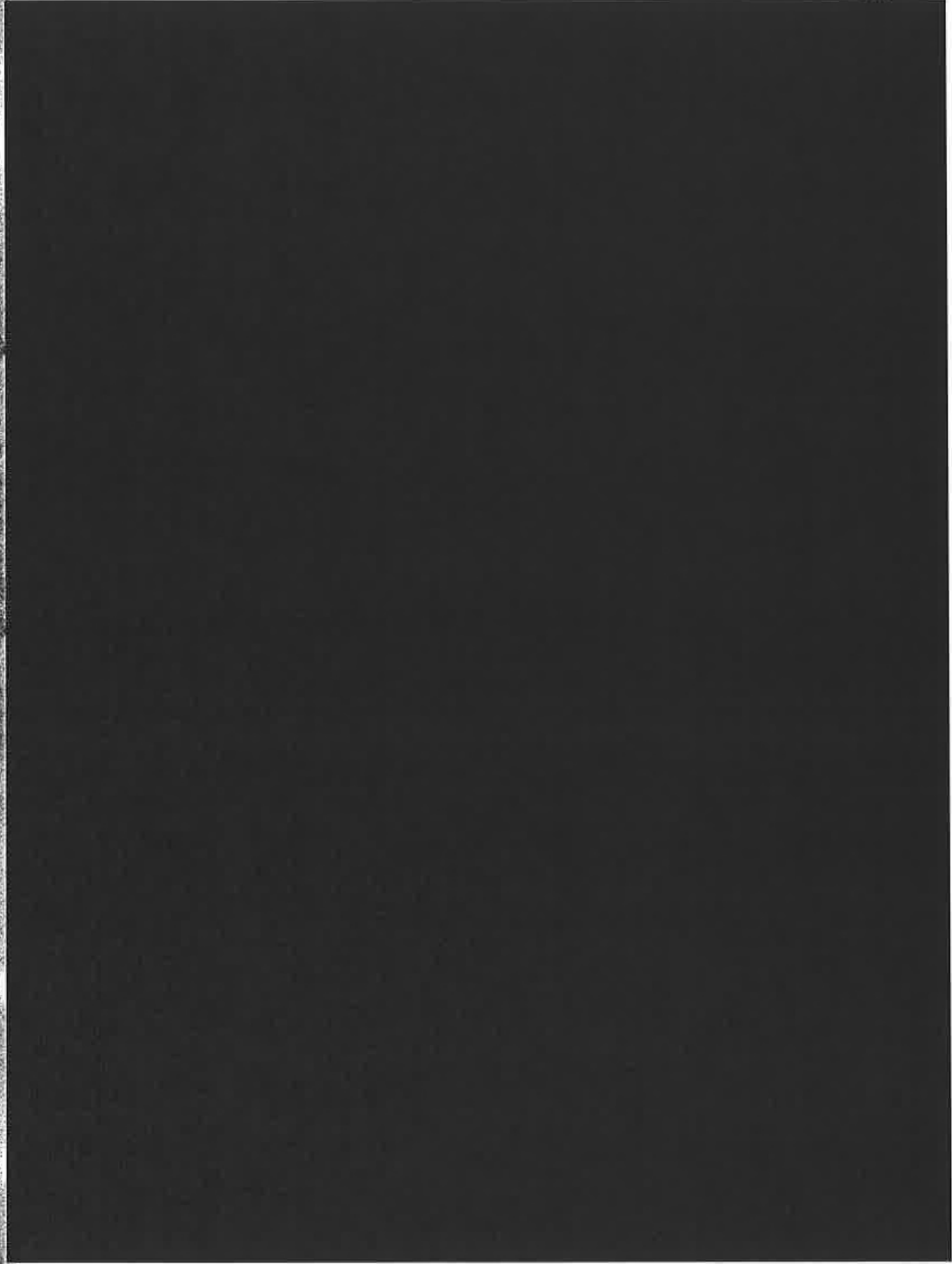
- Don't touch the pericardial tissue, it's fragile and cannot withstand crimping to a smaller profile
- The native calcified aortic valve cannot be stented open
- If you tried to stent open the calcified native valve, you will cause strokes by embolizing the calcium and debris
- The THV cannot/will not be retained and will embolize itself
- THVs will have smaller valve areas and therefore be inferior to surgical valves in performance
- The THV cannot be made durable
- The THV will have perivalvular leaks which will cause endocarditis
- Cardiologists know nothing about Aortic Stenosis and should not treat these patients



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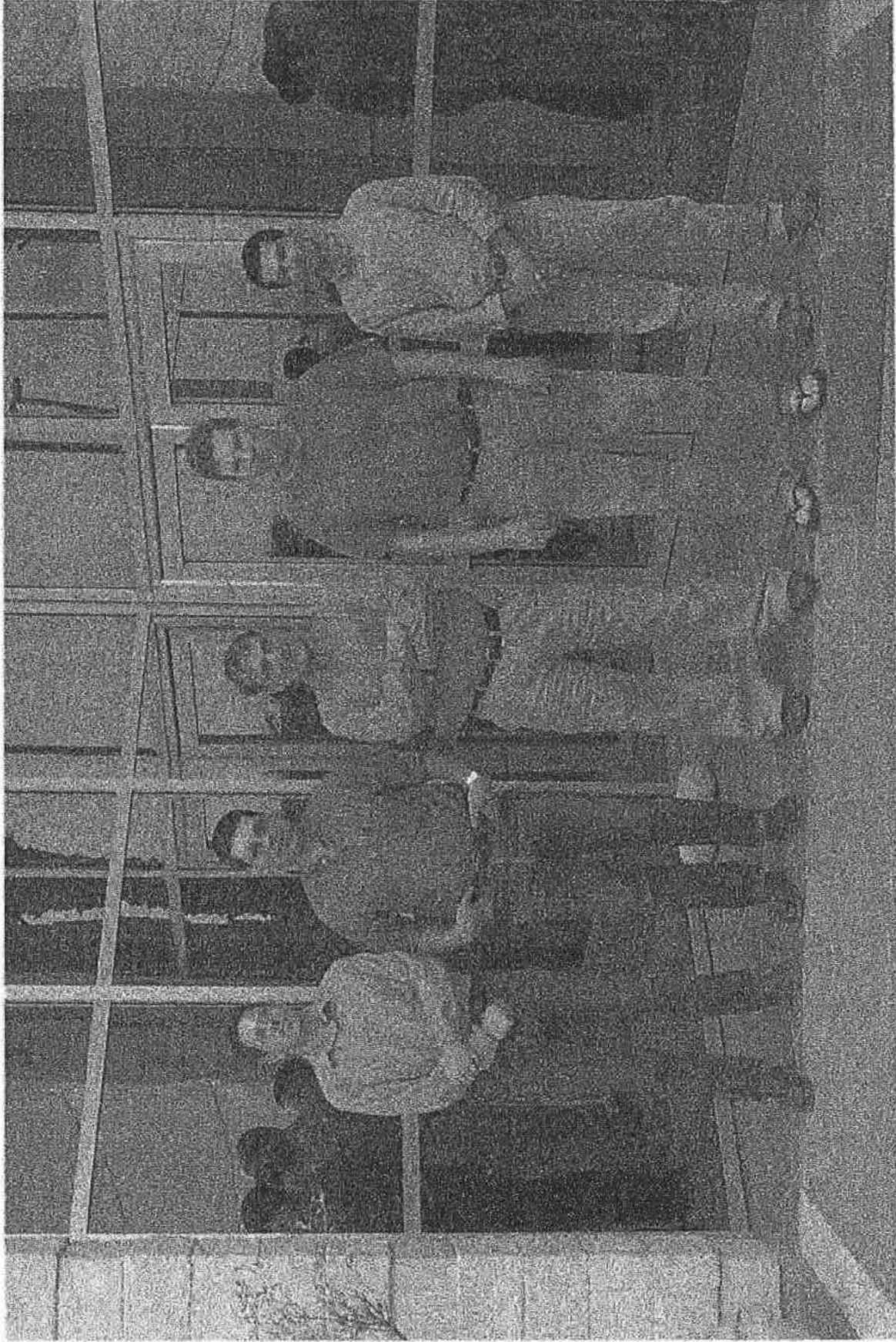
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Don't Judge



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Percutaneous Valve Technologies



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Would you have invested?



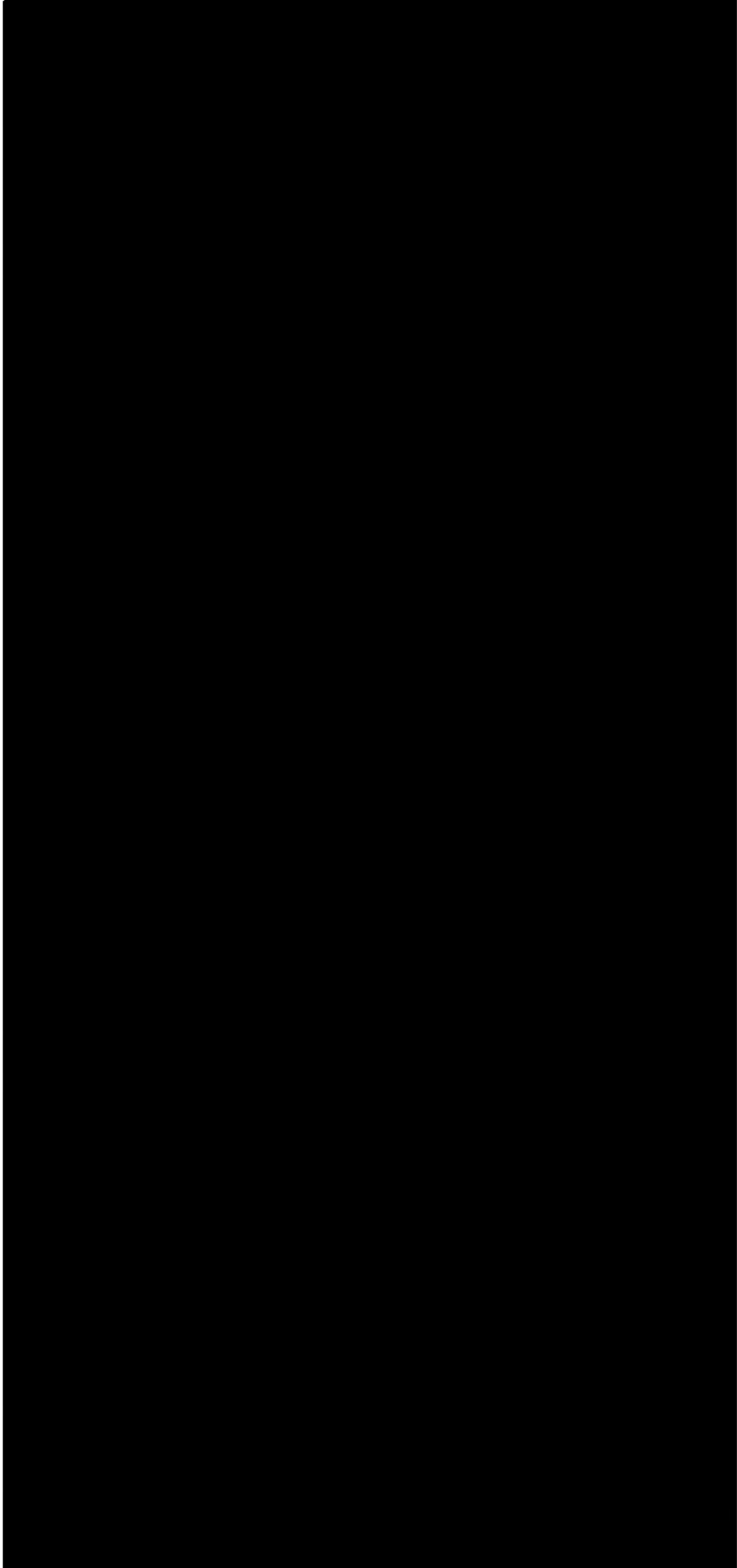
Microsoft Corporation, 1978

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EDWARDS 02433167

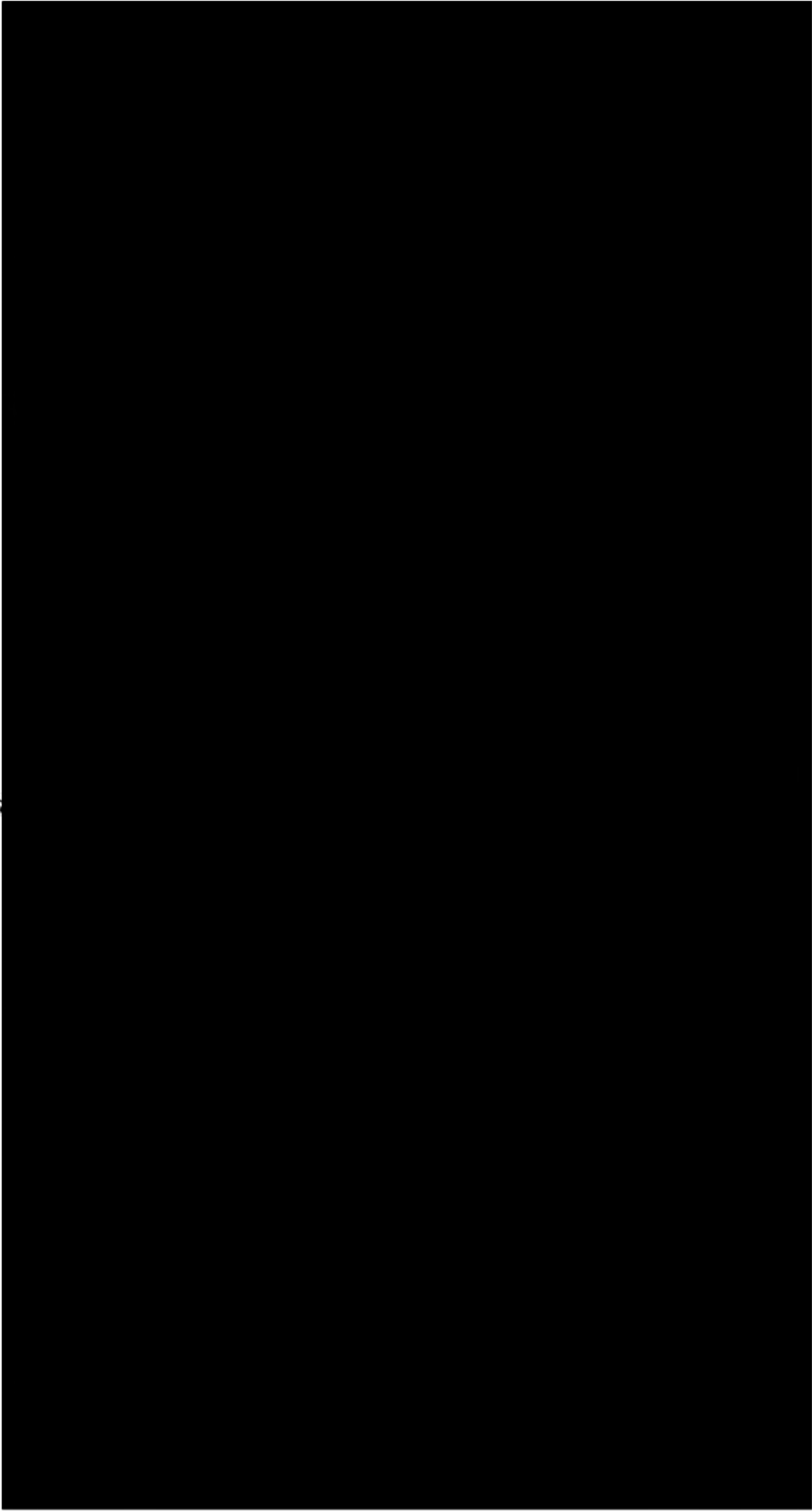
Scientific Advisory Board



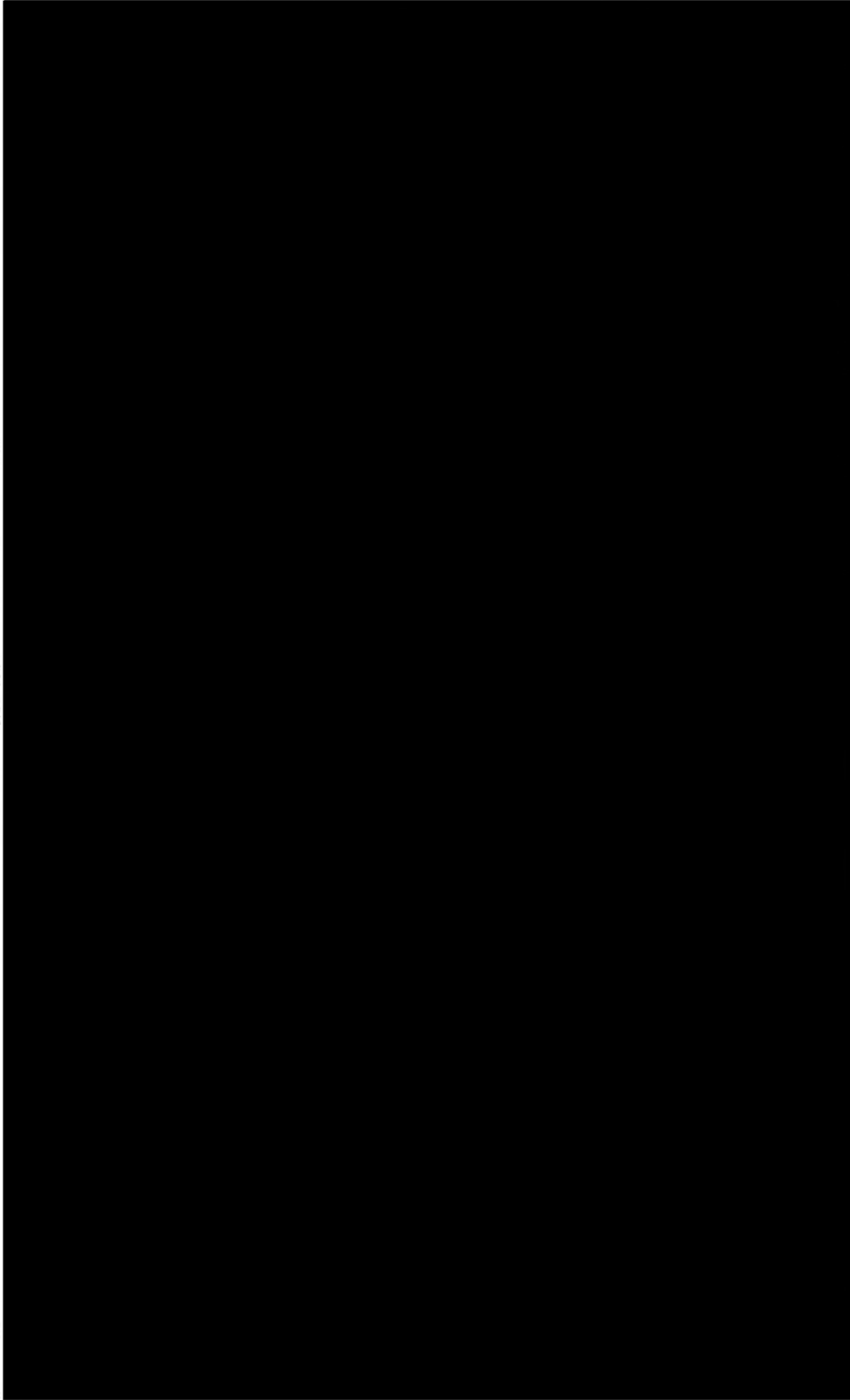
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Stent Design

- Stent engineer designed a proprietary stent for attachment and delivery of aortic heart valve.



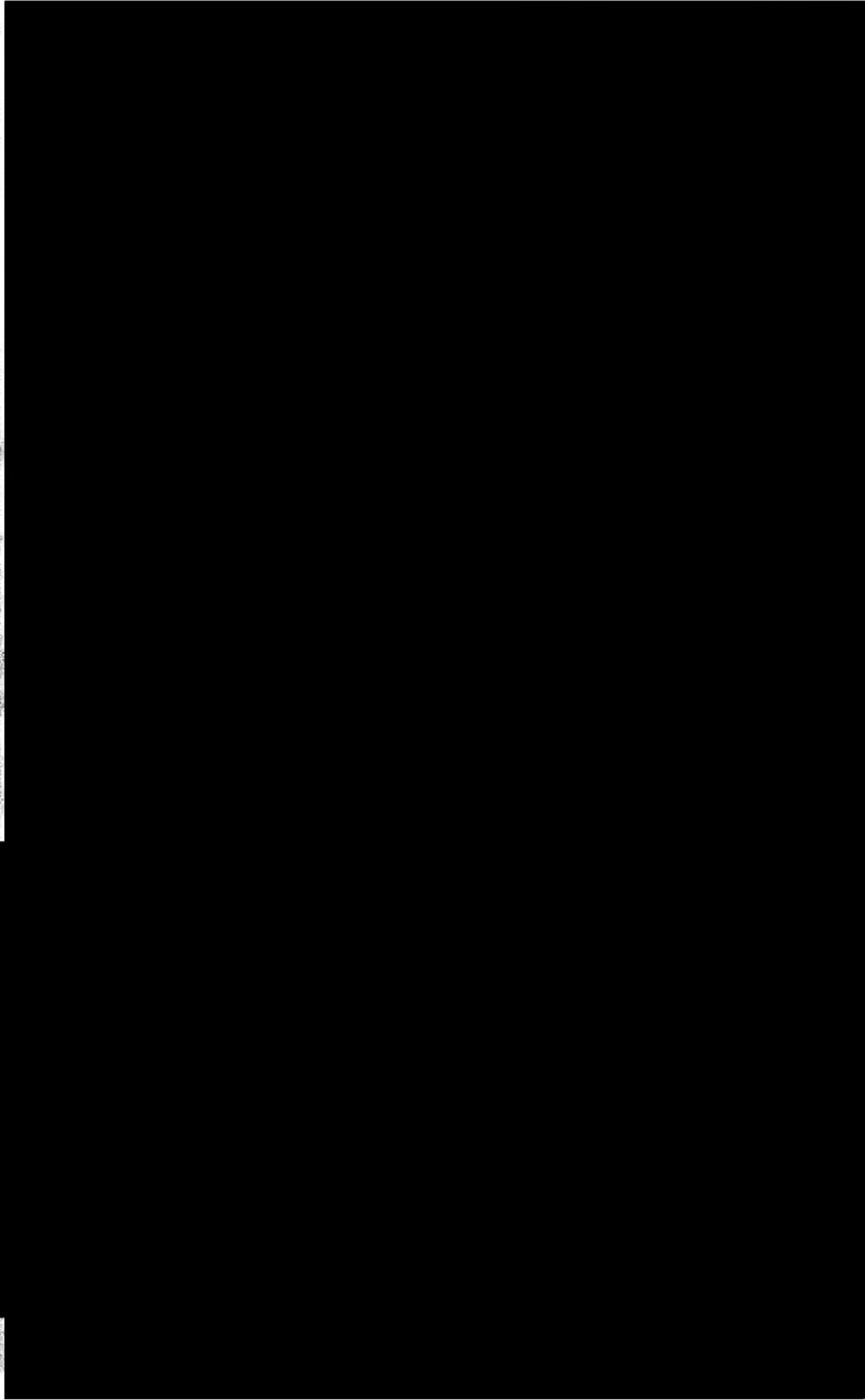
As a start up, PVT also



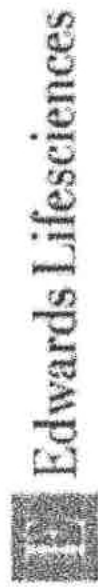
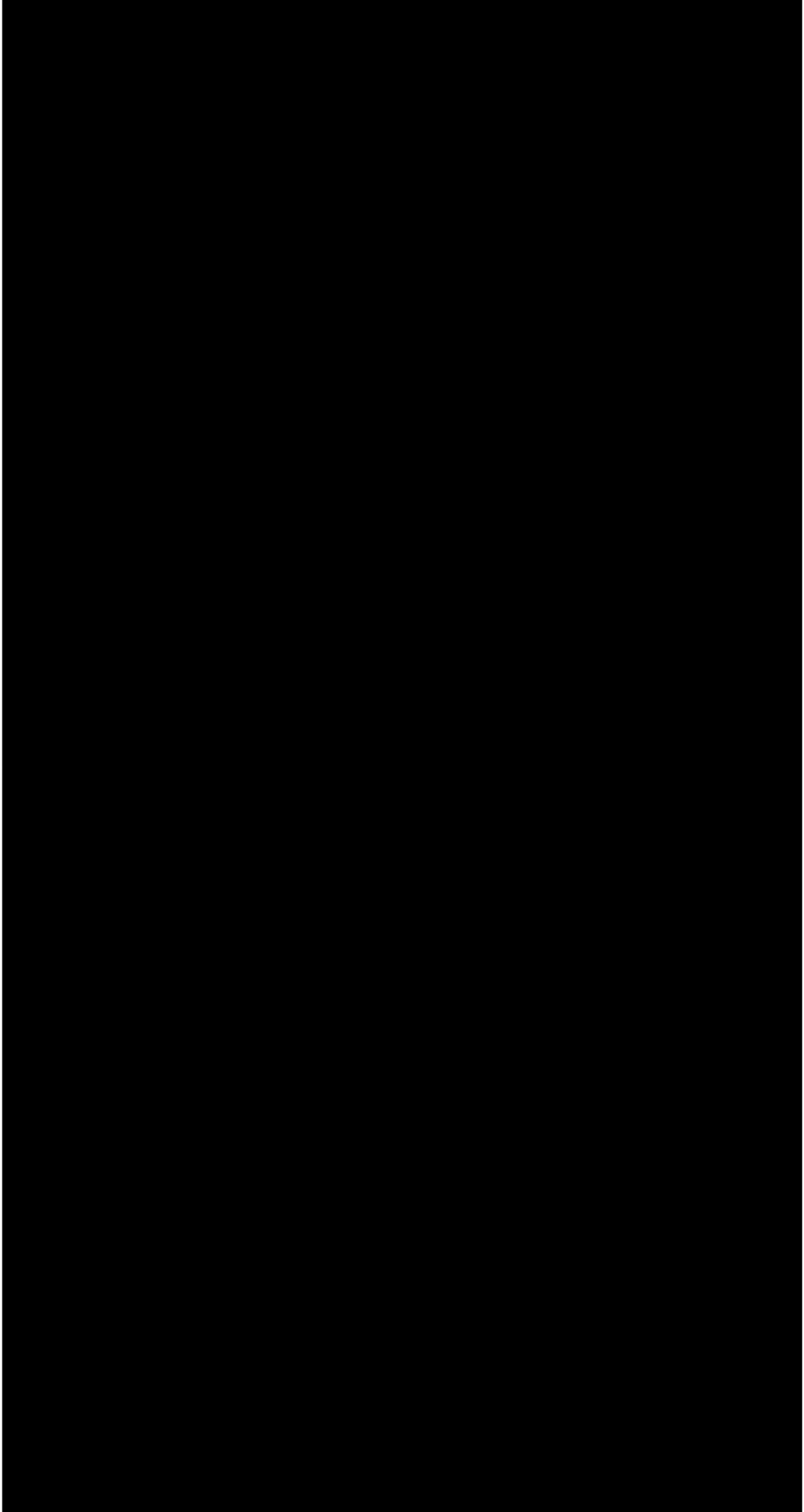
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Team also



Valve Materials



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Early PVT Prototypes

Valve design concepts



United States Patent
Spenser et al.

(16) Patent No.: US 8,632,586 B2
(45) Date of Patent: Jan. 21, 2014

(54) IMPLANTABLE PROSTHETIC VALVE

(73) Inventors: Benjamin Spenser, D.N., Hof East Jordan (U.); Nersis Bebekian, D.N., Hof East Jordan (U.); Assaf Bash, Barysaino, Great Ales (U.); Abraham Zakai, Zichron-Yisroel (U.)

(72) Assignee: Edwards Lifesciences PVT, Inc., Irvine, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No. 13/629,909

(22) Filed: Jun. 11, 2012

(65) Prior Publication Data
US 2013/027786 A1 Nov. 1, 2012

Related U.S. Applications Data

(60) Continuations of application No. 13/168,046, filed on Jun. 24, 2011, now abandoned, which is a continuation of application No. 11/092,889, filed on Mar. 20, 2007, now abandoned, which is a continuation of application No. 10/637,882, filed on Aug. 8, 2003, now Pat. No. 7,510,573, which is a division of application No. 10/270,252, filed on Oct. 11, 2002, now Pat. No. 6,780,118, which is a continuation-in-part of application No. 08/975,768, filed on Oct. 11, 2001, now Pat. No. 6,898,468.

(51) Int. Cl. A61F 2/24

(52) U.S. Cl. 6232.19

USPC 6232.19

(58) Field of Classification Search

USPC 6232.19, 1.15, 1.24, 1.26, 2.1-2.15, 6232.18, 2.16, 2.17, 2.19
See application file for complete search history.

(56) References Cited

U.S. PATENT DOCUMENTS
6,982,609 A * 11/2003 Bumpass et al. 623.2.18
6,454,293 B1 * 9/2002 Schock 623.2.18
2001/0021872 A1 * 9/2001 Holtzer et al. 623.2.18
* cited by examiner

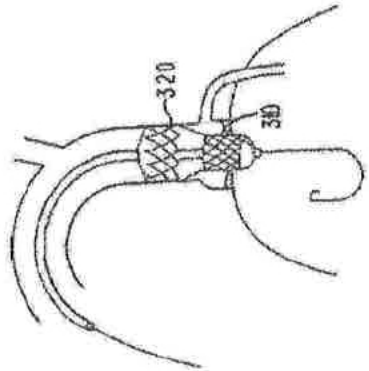
Foreign Examiner - William B. Manberne

(74) Attorney, Agent, or Firm - David L. Hauser, Paul Yong & Co.

(57) ABSTRACT

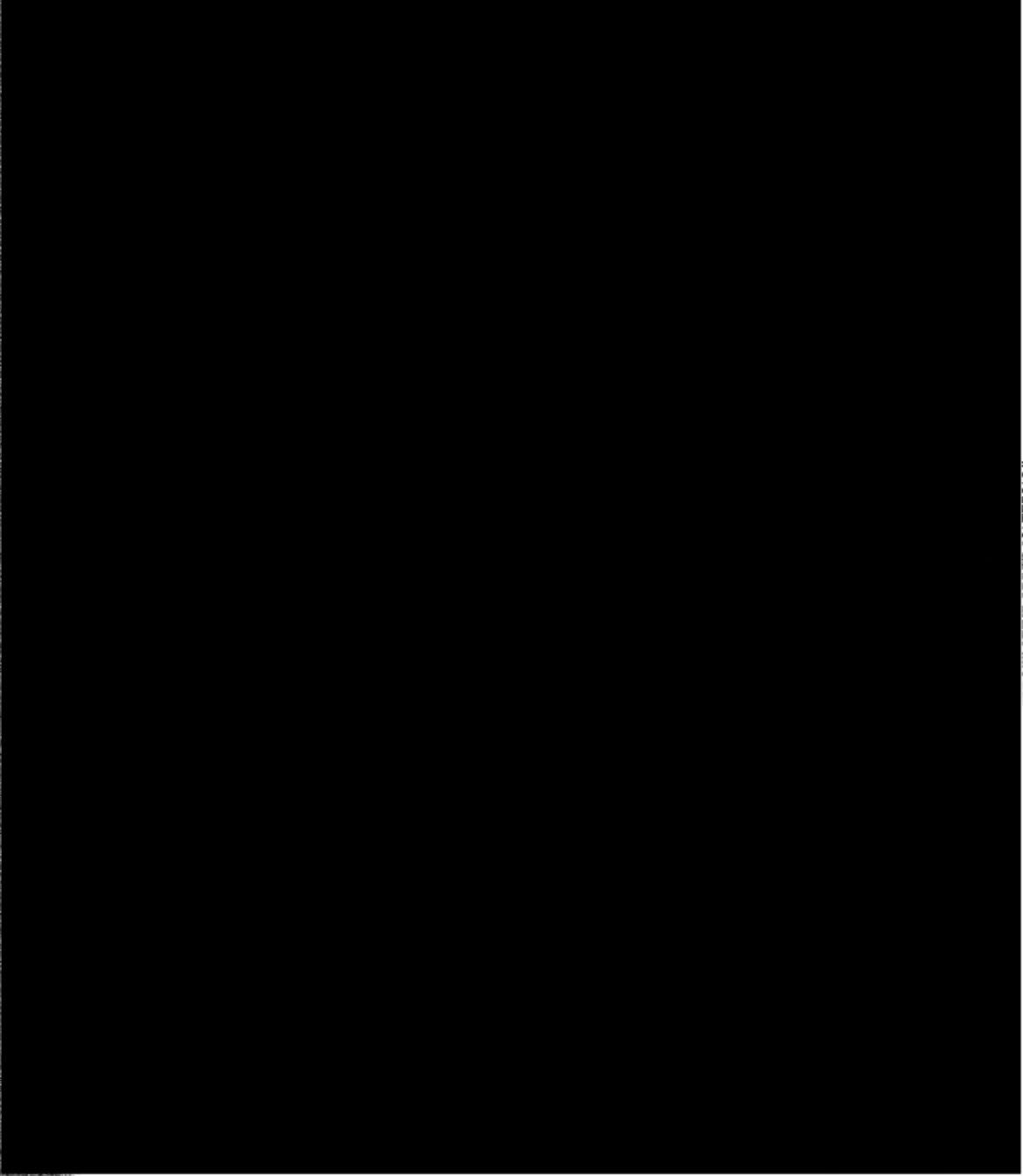
A method of replacing a deficient mitral/aortic valve with a self-expandable prosthetic valve is disclosed. The method involves advancing a self-expandable prosthetic valve through a tapered tube for crimping the prosthetic valve into a crimped sheath. The prosthetic valve is then advanced into a restriction tube for maintaining the prosthetic valve in its crimped diameter. The prosthetic valve is then advanced into a body and is positioned within the deficient mitral/aortic valve. The prosthetic valve is then released from the restriction tube such that the prosthetic valve self-expands to an expanded diameter for anchoring within the deficient mitral/aortic valve. The prosthetic valve comprises an expandable tubular support frame and a valve assembly positioned within the support frame. The valve assembly is formed with pericardial tissue and has three leaflets for providing flow to a reverse flow of blood.

H Claims, 53 Drawing Sheets



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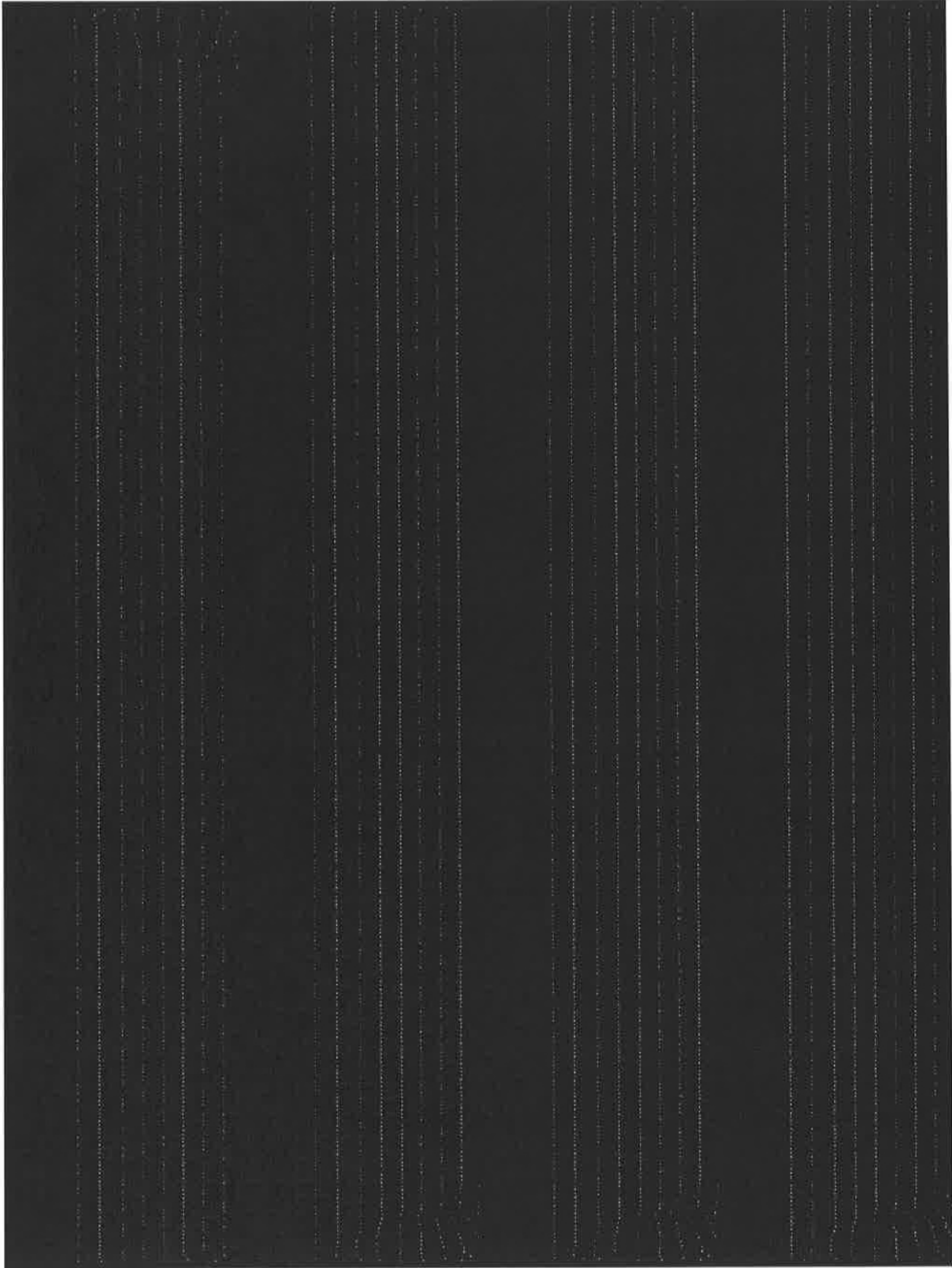
Cadaver Heart Studies



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