Breakthrough Technologies Driving the Transformation of Cardiovascular Care

Hong Kong Hospital Authority Convention 2008

Eric K Louie, MD, FACC
Vice President, Sg2

6 May 2008

Agenda

The Transformation of Cardiovascular Care

Seeing Is Believing: Image-Guided Therapy

From Open to Endovascular Intervention

Repair, Replace and Regenerate

GRACE International Registry—Triumph for Evidence-Based Care in STEMI

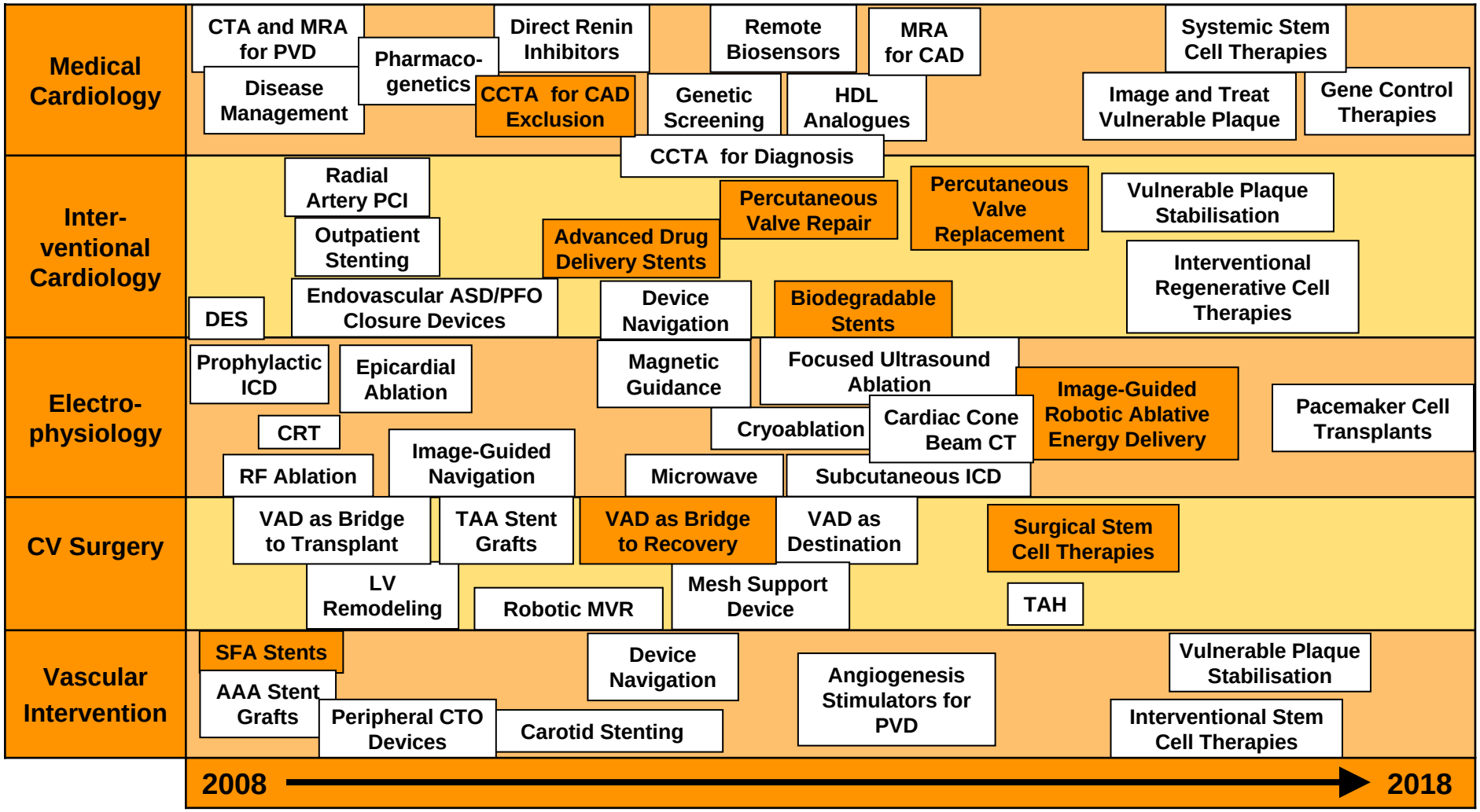
Trends in STEMI care over the period July 1999 to December 2005

Multinational real-world experience with enhanced patient management, guided by evidence-based care for STEMI, results in significant improvements in outcomes.

- Fibrinolytic therapy decreased 22%.
- Primary PCI increased 37%.
- CHF or pulmonary oedema decreased 9%.
- In-hospital mortality decreased 3.9%.

Sources: Fox KA et al. *JAMA* 2007;297:1892–1900; Sg2 Analysis, 2008.

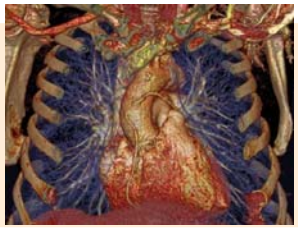
Breakthrough Technologies Driving the Transformation of Cardiovascular Care



Note: Timings reflect consensus adoption.
Source: Sg2 Analysis, 2008.

The Transformation of Cardiovascular Care

Exam and ECG



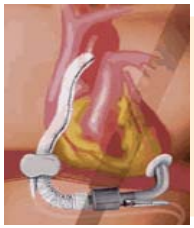
Functional and Anatomic Imaging

Seeing Is Believing: Image-Guided Therapy

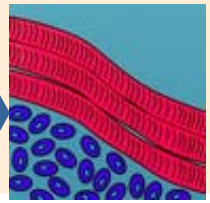
Open Heart Surgery

Endovascular Intervention

From Open to Endovascular Intervention



Repair, Replace and Transplant



Regenerate

Repair, Replace, Regenerate

Chest CT: Courtesy of Siemens and University Medical Center Grosshadem, Munchen, Germany; Stent: Image provided courtesy of Cordis Corporation; VAD: Courtey of NASA. Regenerate: The Promise of Stem Cell Research I National Institutes of Health, Department of Health and Human Services. http://stemcells.nih.gov/info/media/. Accessed 01/Feb/2008.

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Repair, Replace and Regenerate

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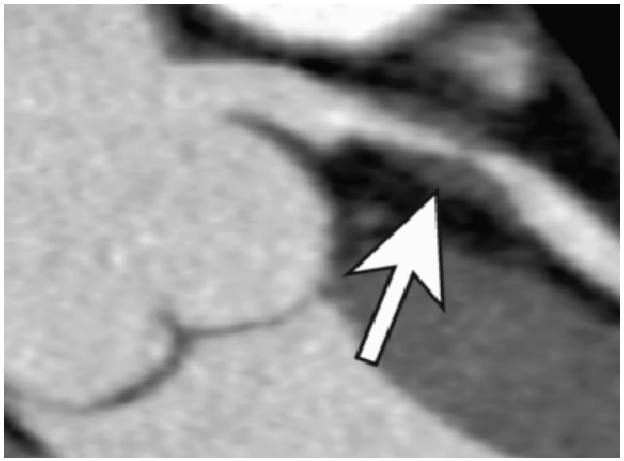
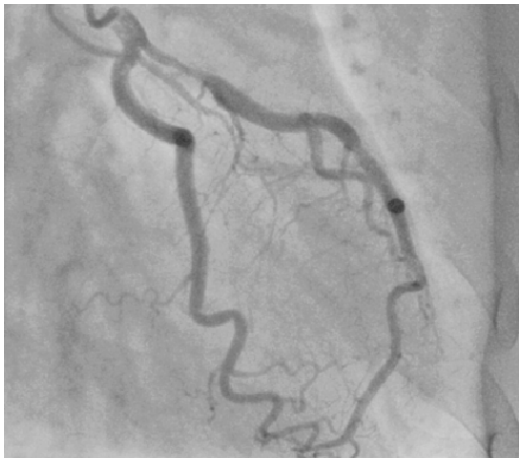
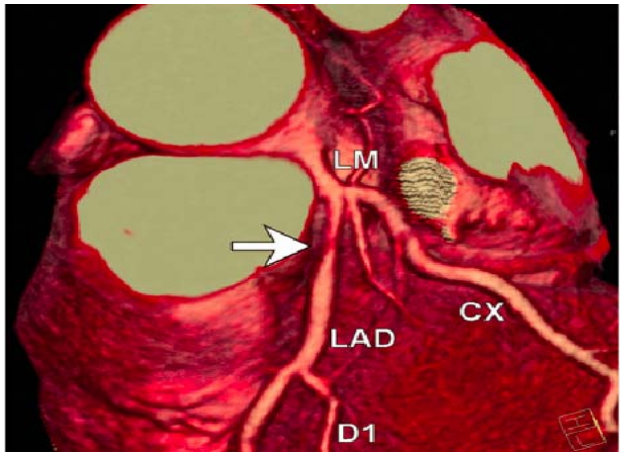
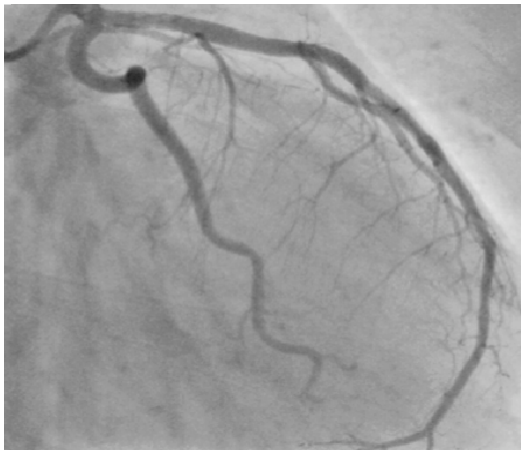
CT Angiography Identifies Coronary Obstruction as a Cause for Chest Pain









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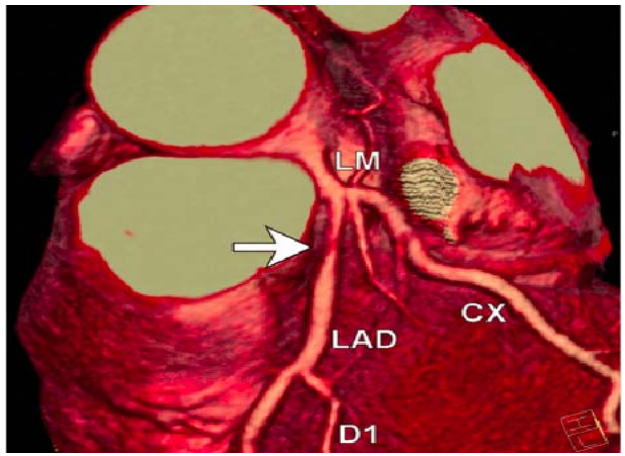
Source: Sg2 Analysis, 2008.

CORE 64: Multicentre International Trial AHA, 2007, Orlando, FL

Coronary CTA with 64 MSCT (in patients with Agatston calcium scores <600) compared to QCA for the detection of 50% stenoses

- Per patient analysis
  - Sensitivity 83%
  - Specificity 91%
  - Positive predictive value 92%
  - Negative predictive value 81%
- Per vessel analysis
  - Positive predictive value 82%
  - Negative predictive value 89%
- 25% of enrolled patients were excluded from analysis and vessels <1.5 mm in diameter were excluded from analysis

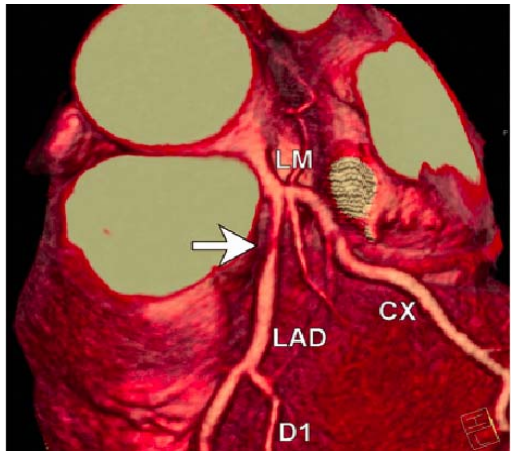


Printed with permission of Siemens.

Sources: AHA, 2007; *Cardiology News* 2007; *Cardiology Today* 2007; Miller JM et al. *Circulation* 2007;116:2630.

ACCURACY: US Trial RSNA, 2007, Chicago, IL

- **Coronary CTA with 64 MSCT** (in 232 patients with typical or atypical chest pain compared to QCA for the detection of 50% stenoses at 16 US centers



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Per patient analysis	**Sensitivity**	93%
	Specificity	82%
Per vessel analysis	**Positive predictive value**	51%
	Negative predictive value	97%

  - Radiation dose reduction algorithm using EKG modulation resulted in an exposure of ~10-15 mSv

Sources: RSNAA, 2007 Dr. Min, NY-Presbyterian *Cardiology News, January 2008;6:11*

ROMICAT: CTA Exclusion of Stenosis and Plaque Has 100% NPV for ACS Exclusion

103 Patients: >5-minute chest pain, no ischaemic ECG changes, normal biomarkers

64 × 0.6 mm MSCT

330 ms rotation, 78 ml contrast, 6 to 11 mSv

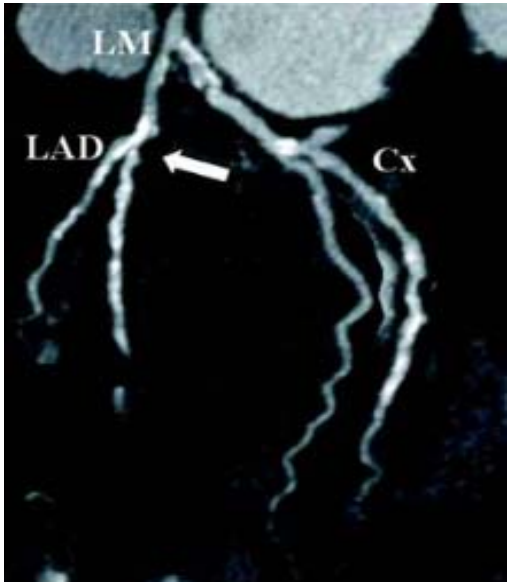
Exam time: 12 min; scan time: 14 sec; read time: 10 min

Presence of Plaque			
Sens	**Spec**	**PPV**	**NPV**
100%	46%	23%	100%

Presence of >50% Stenosis			
Sens	**Spec**	**PPV**	**NPV**
100%	82%	47%	100%

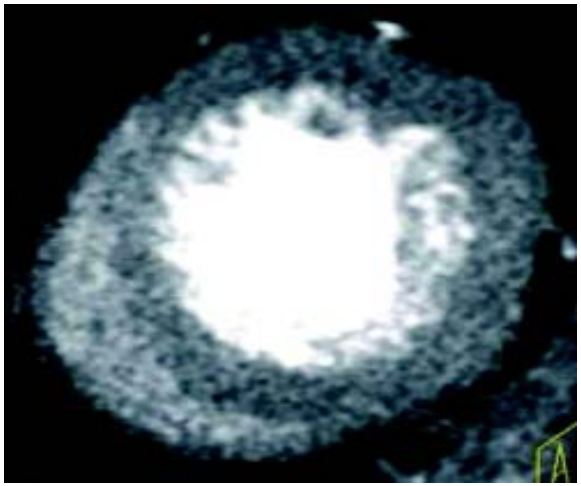
Sources: Hoffmann U et al. *Circulation* 2006;114:2251–2260; Sg2 Analysis, 2008.

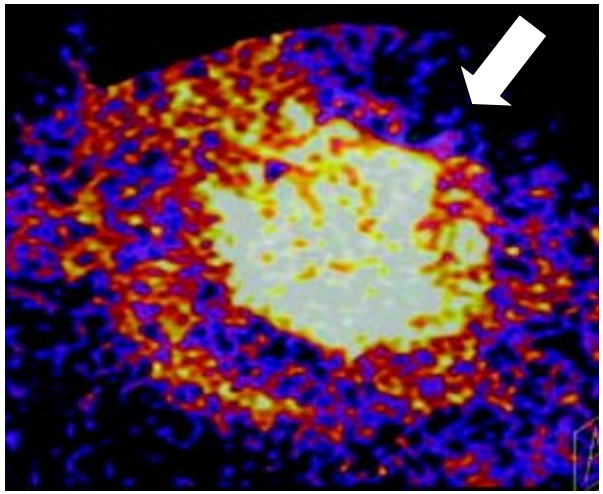
Dual Energy MSCT Provides a Noninvasive Angiogram …

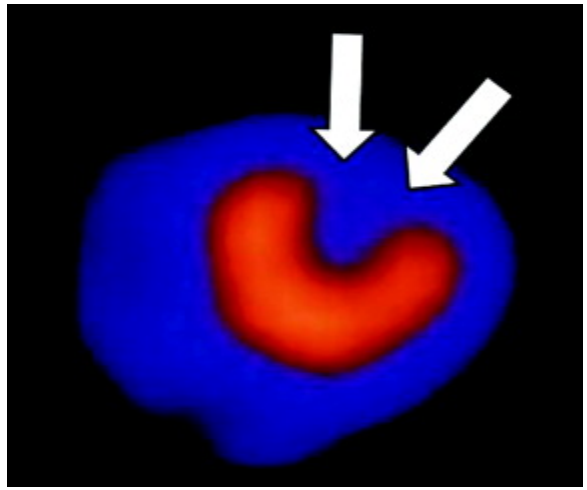


Sources: Circ 2008;117:1244 [Dual-energy CT reconstruction merging 70% of 140-kV spectrum and 30% of 80-kV spectrum shown as 3-D and curved multiplanar reformations along side coronary angiogram]; Sg2 analysis 2008

… And Fuses Form with Function

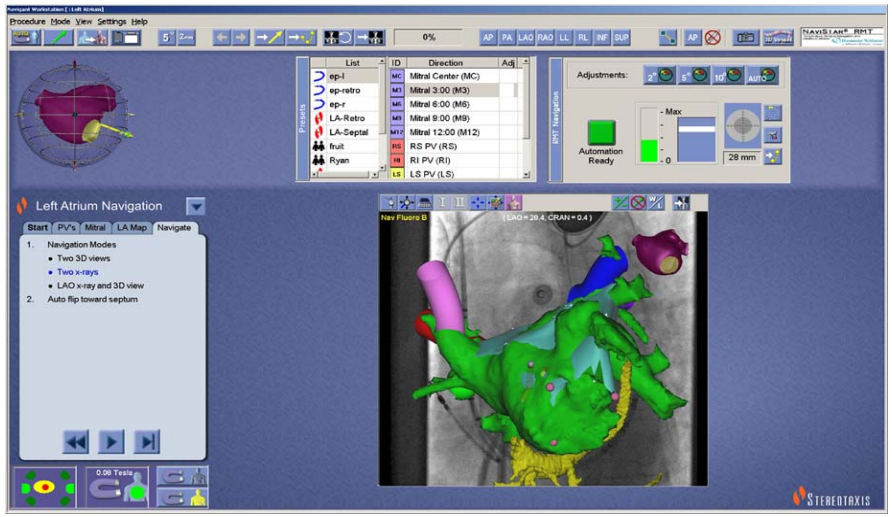


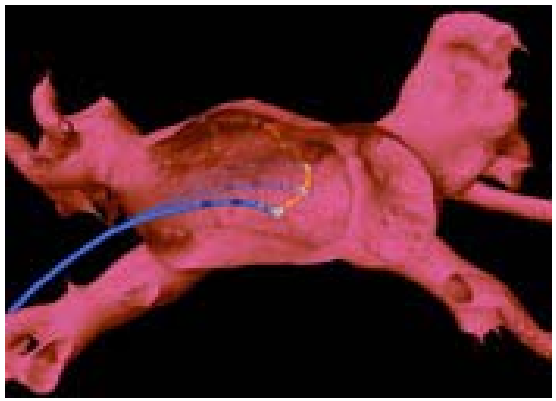




Sources: Circ 2008;117:1244 [Multiplanar reformation in short-axis view of dual-energy CT scan reconstructions based on 140-kV spectrum next to dual energy CT “iodine map” of myocardial blood pool compared to SPECT thallium perfusion image]; Sg2 analysis 2008

Image Fusion with Magnetic Guidance of AF Ablation—Milan 2006





Printed with permission of Stereotaxis Inc.
Source: Sg2 Analysis, 2008.

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Real World Registry Data Reaffirms the Role of CABG—a Surgeon's Viewpoint

	Low Risk ~1VD	Intermediate Risk ~2VD	High Risk ~3VD
1986–1990 PTCA Era	CABG = PCI	CABG = PCI	Survival favors CABG
1991–1995 Early BMS Era	CABG = PCI	CABG = PCI	Survival favors CABG
1995–2000 Mature BMS Era	CABG = PCI	CABG = PCI	Survival favors CABG

Duke and Miriam Hospital Registry
Peter Smith, MD
Scientific Sessions of The Society of Thoracic Surgeons, 2006

PTCA = percutaneous transluminal coronary angioplasty.
Sources: *Cardiology News* 2006; Sg2 Analysis, 2008.

Do Drug Eluting Stents Change the Equation? Broad Application of SES in CAD

1 Y Hierarchical	ARTS II—SES	ARTS I—CABG	SES:CABG RR
Mortality	1.0%	2.7%	**0.37 [0.15–0.94]**
CVA	0.8%	1.8%	0.45 [0.16–10.29]
MI Q-wave	0.8%	3.5%	0.24 [0.09–0.62]
Death CVA MI	3.0%	8.0%	0.37 [0.22–0.63]
Re CABG	2.0%	0.7%	**2.98 [0.97–9.17]**
Re PCI	5.4%	3.0%	**1.82 [1.04–3.19]**
MACE	10.4%	11.6%	0.89 [0.65–1.23]

CVA = cerebrovascular accident.
Sources: *EuroIntervention* 2005;1:147; Sg2 Analysis, 2008.

NY State Registry Data Supports CABG Over PCI for MVD in the DES Era: 2003-2004

1 Y Hierarchical	CABG	DES	CABG:DES HR
3 Vessel Disease			
18 Mo Adj Mortality	6.0%	7.3%*	**0.80 [0.65–0.97]**
18 Mo Adj Mortality or MI	7.9%	10.3%**	**0.75 [0.63–0.89]**
2 Vessel Disease			
18 Mo Adj Mortality	4.0%	5.4%***	**0.71 [0.57–0.89]**
18 Mo Adj Mortality or MI	5.5%	7.5%**	**0.71 [0.59–0.97]**

Definitive conclusions await ongoing clinical trials …

SYNTAX—PES vs CABG for unprotected LM and 3 VD

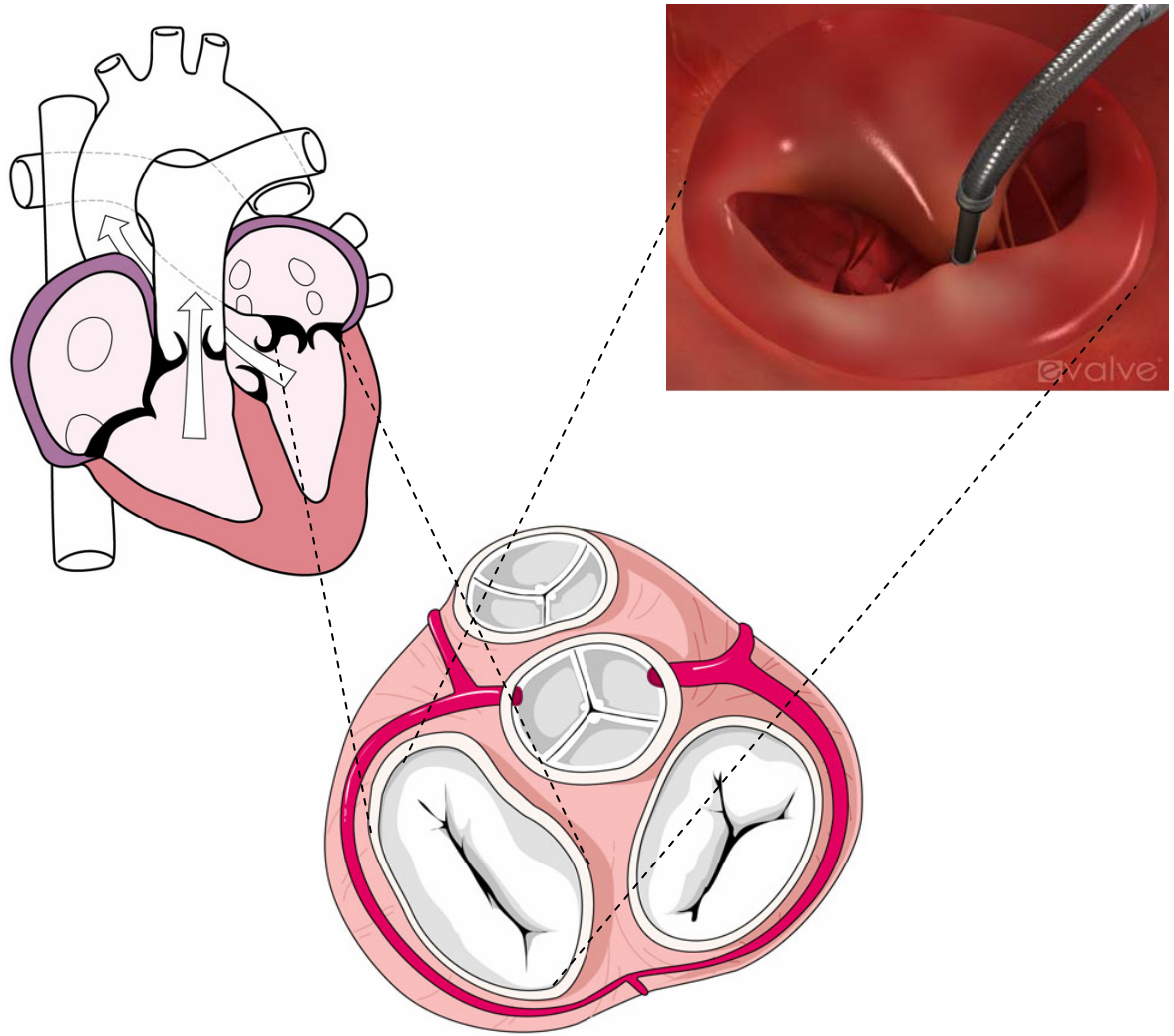
FREEDOM—SES or PES vs CABG for MVD in diabetics

Sources: Hannan EL et al. *NEJM* 2008;358:331; Sg2 Analysis, 2008.

* p<.03, ** p<.001, ***p<.003

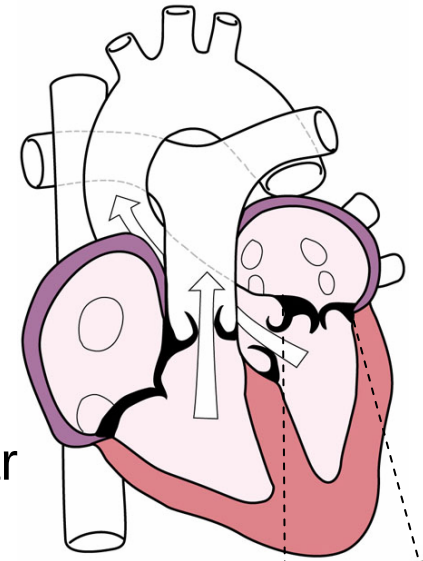
Evalve MitraClip™—Endovascular Mitral Repair for Mitral Regurgitation

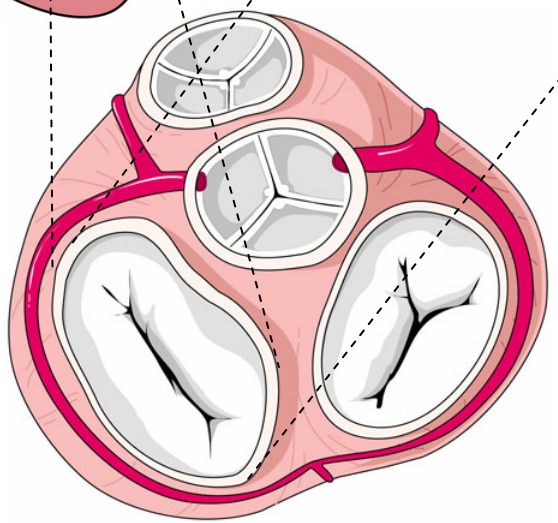
- Endovascular approximation of open Alfieri edge-to-edge leaflet apposition using a V-shaped fabric covered clip
  - Preserves conventional surgical options
  - Repositionable
- **EVEREST I** clinical trial complete
- **EVEREST II** clinical trial ongoing
- US market launch expected 2011

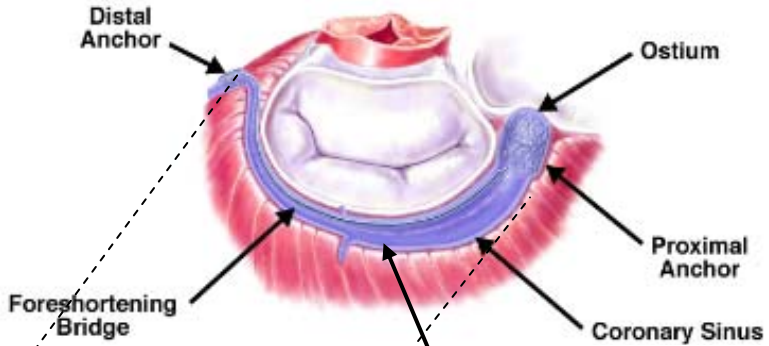


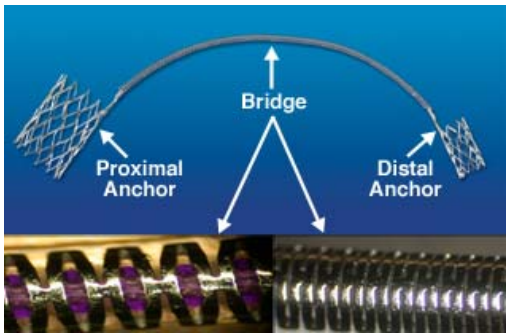
Edwards MONARC—Endovascular Resizing of Mitral Annulus for Mitral Regurgitation

- Endovascular approximation of open mitral annular plication
- **MONARC** system has 2 stent-like anchors with interconnecting biodegradable spring bridge





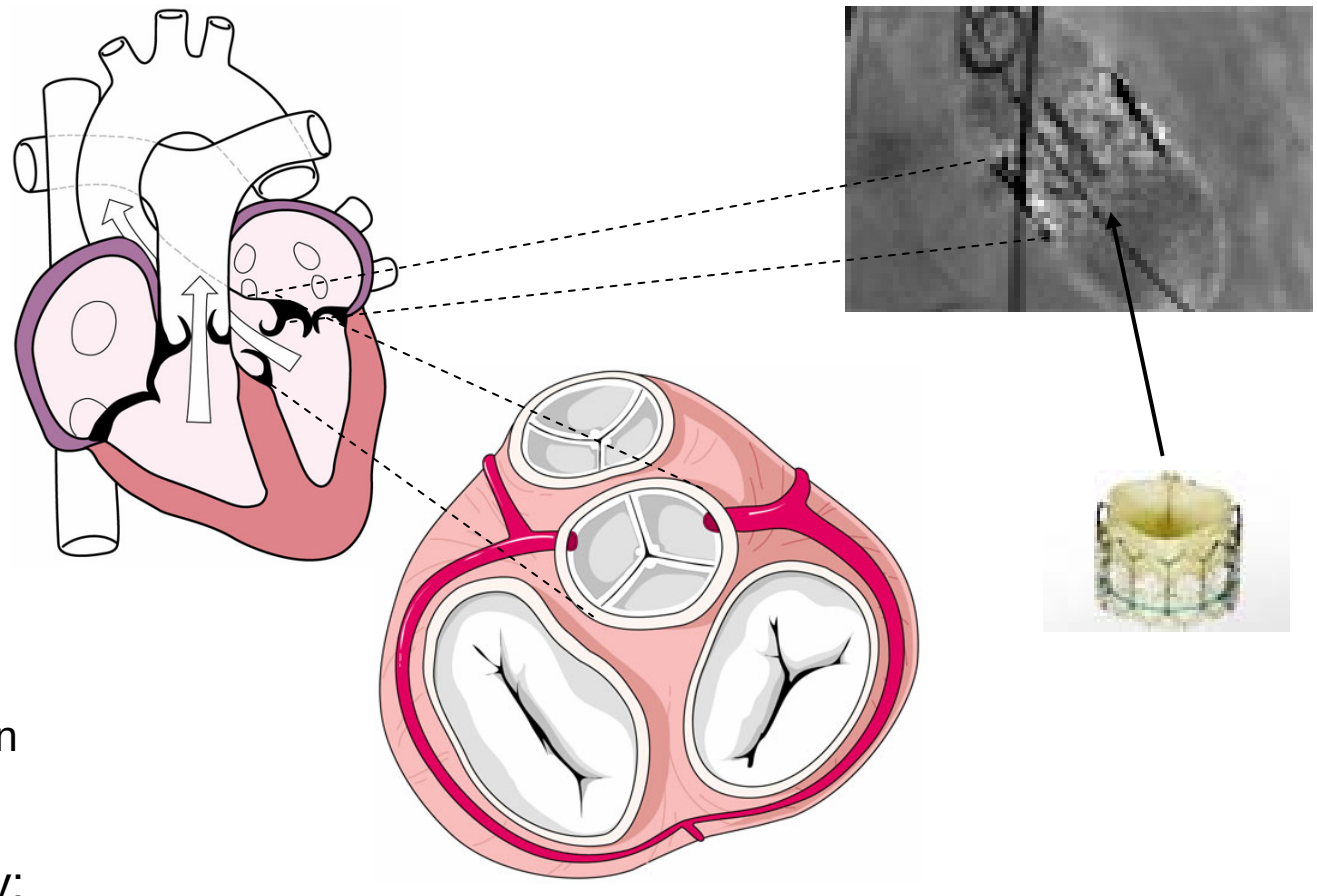




Edwards SAPIEN—Endovascular Aortic Stent Valve for Aortic Stenosis

Balloon expandable equine pericardial valve with fabric sealing cuff and stainless steel stent

- CE Mark approved
- **Edwards SAPIEN feasibility study**
- **PARTNER trial**
  - Anticipated completion late 2008
- Projected market entry: 2011+



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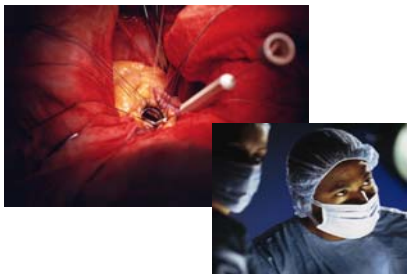
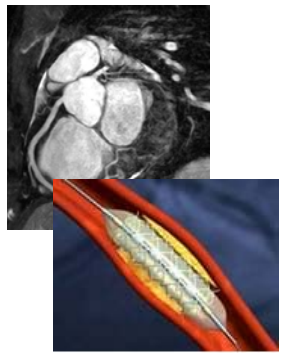
Cardiovascular Injury and Repair—Shifting Interventions

Technological advancements will promote a paradigm shift from remediation and repair of cardiac injury to myocardial regeneration.





Courtesy of Matthias Stuber, PhD, Johns Hopkins University, 2004.

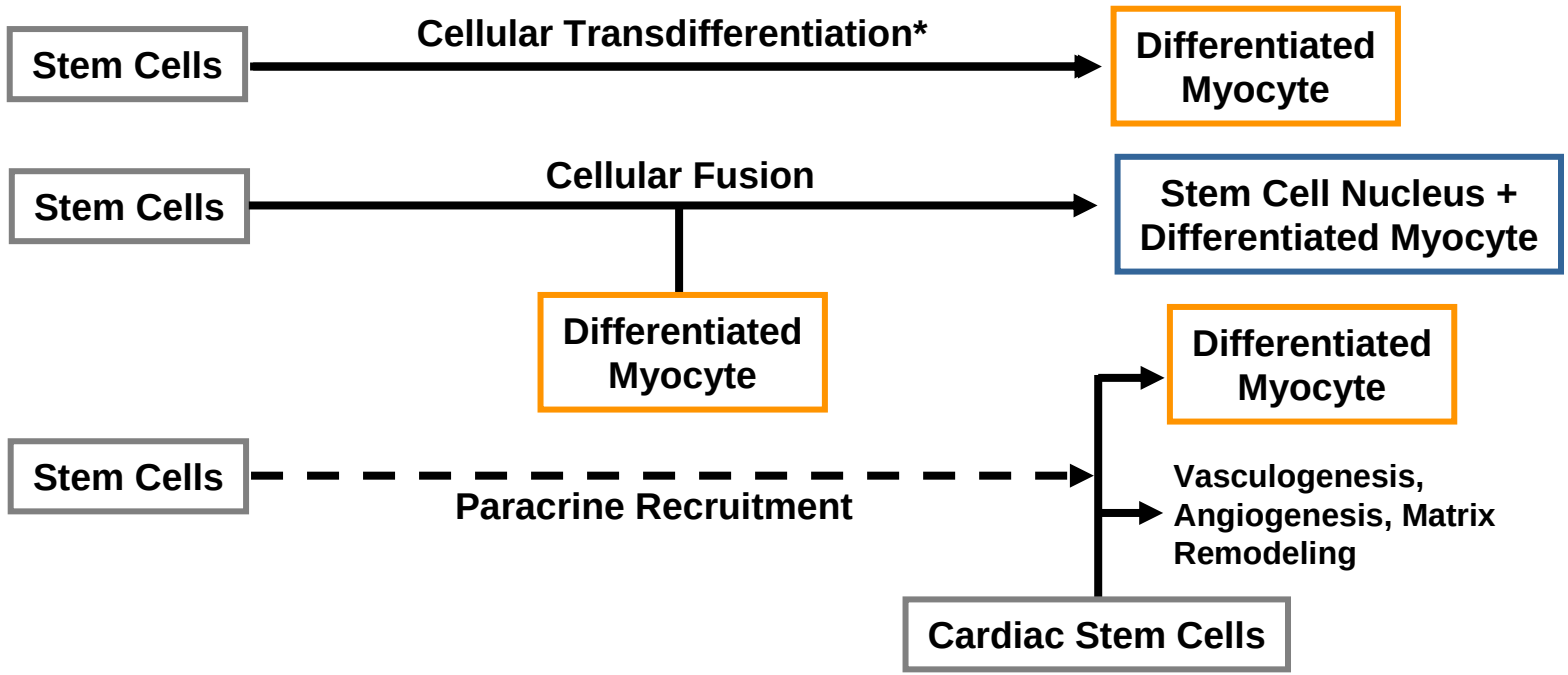
Mechanical Era
Cardiac surgery

Minimally Invasive Era
Endovascular approaches

Biological Era
Regenerative therapies

“Yesterday” **“Today”** **“Tomorrow”**

Apparent "Regeneration" May Involve Transdifferentiation, Fusion, Paracrine Effects

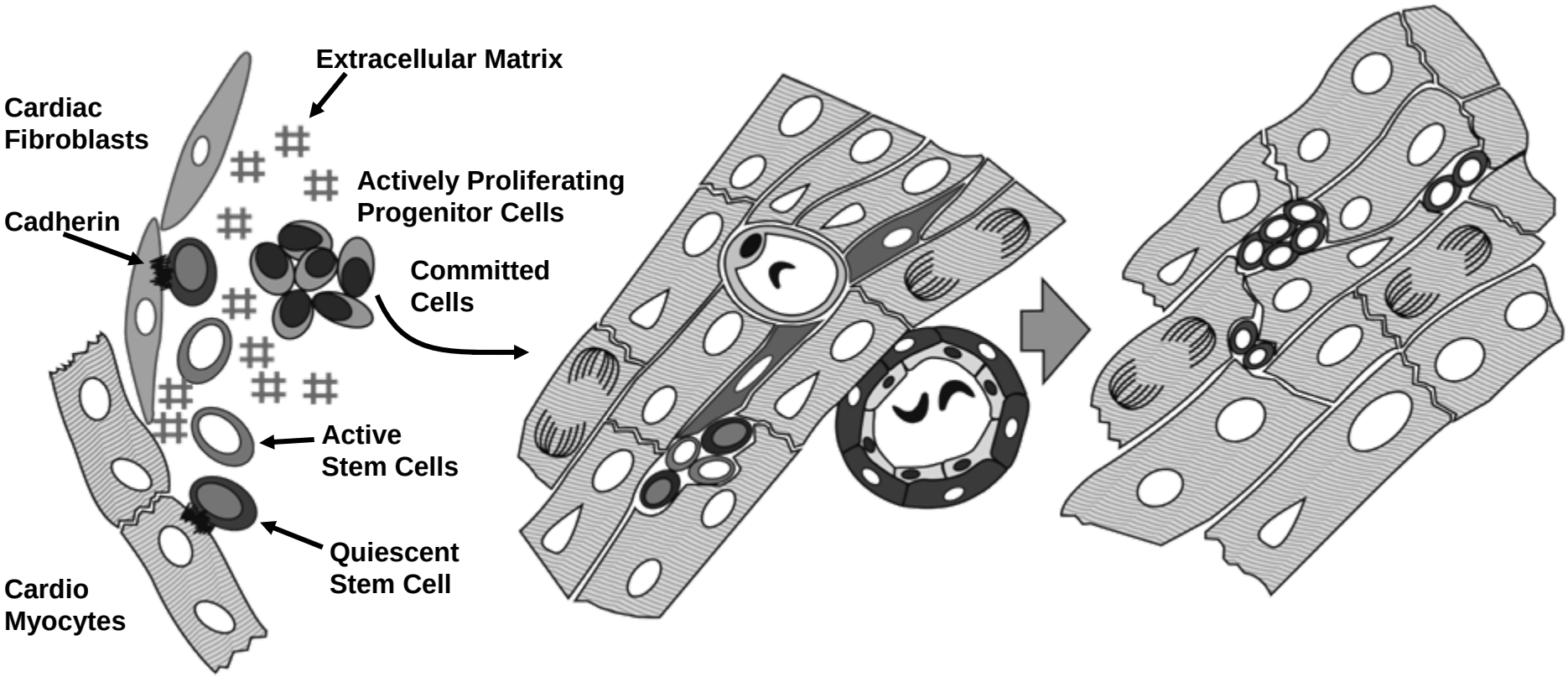


Sources for stem cells (self-renewing, clonogenic, multipotent)

- Embryonic stem cells, fetal cardiomyocytes, bone marrow cells, endothelial progenitor cells, skeletal myoblasts, fibroblasts, smooth muscle cells, resident cardiac stem cells

*Failure to demonstrate activation of a cardiac specific transgene (a-myosin heavy-chain promoter driving expression of nuclear targeted b-galctosidase [LacZ]) by transplanted marrow cells calls into question the concept of "transdifferentiation."— Murry CE et al. *J Am Coll Cardiol* 2006:47:1777–1785.
Sources: Anversa P et al. *J Am Coll Cardiol* 2006;47:1769–1776; Sg2 Analysis, 2008.

Cells Must Organize in Complex Patterns on an Ordered Substrate



Multipotent cardiac stem cells continuously repopulate the myocardium, replacing parenchymal cells and vascular smooth muscle cells and endothelial cells that die by apoptosis and necrosis.

Sources: Figure adapted from Anversa P et al. *Circulation* 2006;113:1451–1463; Sg2 Analysis, 2008.

Using Whole Organ Extracellular Matrix to Reconstitute a Rat Heart

nature medicine

Perfusion-decellularized matrix: using nature's platform to engineer a bioartificial heart

Ott HC et al. Published online January 13, 2008; doi:10.1038/nm1684

Methods

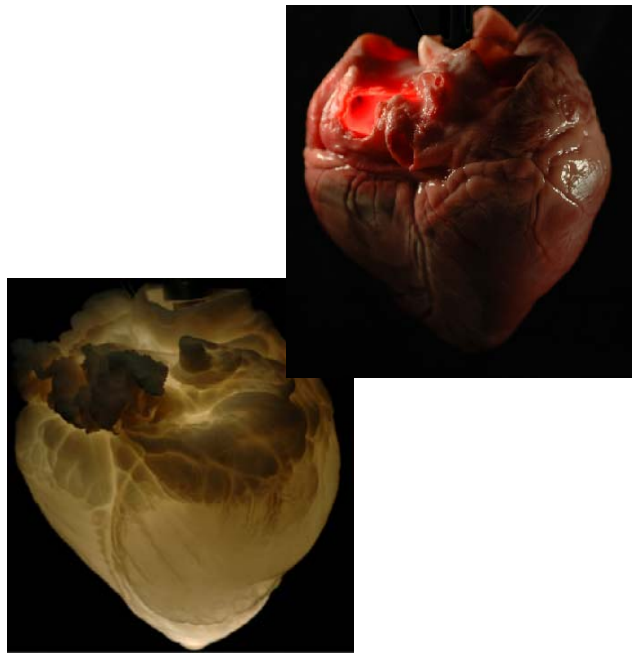
- Biocompatible cardiac ECM scaffold
- De-cellularized heart reseeded with neonatal cardiac cells and perfused with endothelial cells

Results

- Recellularized heart capable of contracting at 8 days of culture

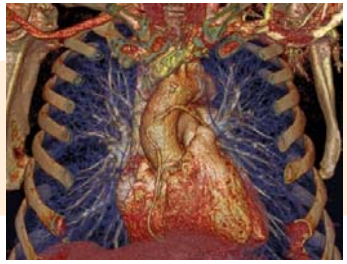
Implications

- Bioartificial hearts for transplantation
- Auto-repopulation of scaffolds
- Synthetic **organ** regeneration



ECM = extracellular matrix.

Implications for the Transformation of Cardiovascular Care

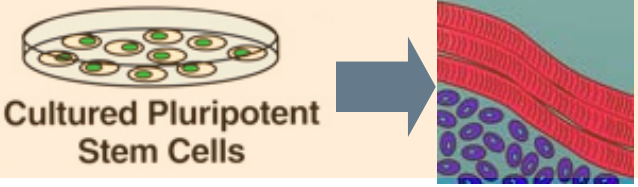


Functional and Anatomic Imaging

- Real-Time 3D Functional/Anatomic Fusion
- Increased Precision and Reduced Delay in Dx
- Image-Guided Robotic Intervention

Endovascular Intervention

- Expanded Interventional Indications
- Reduced Morbidity and LOS
- Hybrid Interventional Theatres
- Retraining of Cardiothoracic Surgeons



Regenerate

- Focus on Cellular and Molecular Therapies
- Potential Migration to Outpatient Sites of Care
- Translational Research

Chest CT: Courtesy of Siemens and University Medical Center Grosshadem, Munchen, Germany; Stent: Image provided courtesy of Cordis Corporation; VAD: Courtey of NASA. Regenerate: The Promise of Stem Cell Research I National Institutes of Health, Department of Health and Human Services. http://stemcells.nih.gov/info/media/. Accessed 01/Feb/2008.

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