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

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

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

Sources: Fox KA et al. JAMA 2007;297:1892–1900; Sg2 Analysis, 2008.
Breakthrough Technologies Driving the Transformation of Cardiovascular Care

**Medical Cardiology**
- CTA and MRA for PVD Disease Management
- Pharmacogenetics
- CCTA for CAD Exclusion
- Genetic Screening
- HDL Analogues
- MRA for CAD
- Image and Treat Vulnerable Plaque
- Gene Control Therapies

**Interventional Cardiology**
- Radial Artery PCI
- Outpatient Stenting
- Advanced Drug Delivery Stents
- Device Navigation
- Biodegradable Stents
- Vulnerable Plaque Stabilisation
- Interventional Regenerative Cell Therapies

**Electrophysiology**
- Prophylactic ICD
- Epicardial Ablation
- Magnetic Guidance
- Focused Ultrasound Ablation
- Cardiac Cone Beam CT
- Image-Guided Robotic Ablative Energy Delivery
- Pacemaker Cell Transplants

**CV Surgery**
- VAD as Bridge to Transplant
- TAA Stent Grafts
- VAD as Bridge to Recovery
- VAD as Destination
- Surgical Stem Cell Therapies
- TAH

**Vascular Intervention**
- SFA Stents
- AAA Stent Grafts
- Peripheral CTO Devices
- Device Navigation
- Angiogenesis Stimulators for PVD
- Interventional Stem Cell Therapies

**2008**

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

Cultured Pluripotent Stem Cells

Regenerate

Repair, Replace, Regenerate

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The Transformation of Cardiovascular Care

Seeing Is Believing: Image-Guided Therapy

From Open to Endovascular Intervention

Repair, Replace and Regenerate
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

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)

<table>
<thead>
<tr>
<th>Per patient analysis</th>
<th>Sensitivity</th>
<th>93%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Specificity</td>
<td>82%</td>
</tr>
<tr>
<td>Per vessel analysis</td>
<td>Positive predictive value</td>
<td>51%</td>
</tr>
<tr>
<td></td>
<td>Negative predictive value</td>
<td>97%</td>
</tr>
</tbody>
</table>

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

Sources: RSNA, 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

<table>
<thead>
<tr>
<th>Presence of Plaque</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens</td>
<td>100%</td>
<td>46%</td>
<td>23%</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Presence of &gt;50% Stenosis</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens</td>
<td>100%</td>
<td>82%</td>
<td>47%</td>
<td>100%</td>
</tr>
</tbody>
</table>

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
Agenda

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

<table>
<thead>
<tr>
<th></th>
<th>Low Risk ~1VD</th>
<th>Intermediate Risk ~2VD</th>
<th>High Risk ~3VD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1986–1990</strong></td>
<td>CABG = PCI</td>
<td>CABG = PCI</td>
<td>Survival favors CABG</td>
</tr>
<tr>
<td><strong>PTCA Era</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1991–1995</strong></td>
<td>CABG = PCI</td>
<td>CABG = PCI</td>
<td>Survival favors CABG</td>
</tr>
<tr>
<td><strong>Early BMS Era</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1995–2000</strong></td>
<td>CABG = PCI</td>
<td>CABG = PCI</td>
<td>Survival favors CABG</td>
</tr>
<tr>
<td><strong>Mature BMS Era</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Duke and Miriam Hospital Registry
Peter Smith, MD
Scientific Sessions of The Society of Thoracic Surgeons, 2006
Do Drug Eluting Stents Change the Equation? Broad Application of SES in CAD

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

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

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

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.
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

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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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Seeing Is Believing: Image-Guided Therapy
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Repair, Replace and Regenerate
Cardiovascular Injury and Repair—Shifting Interventions

Technological advancements will promote a paradigm shift from remediation and repair of cardiac injury to myocardial regeneration.
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 (α-myosin heavy-chain promoter driving expression of nuclear targeted β-galactosidase [LacZ]) by transplanted marrow cells calls into question the concept of “transdifferentiation.”— Murry CE et al. J Am Coll Cardiol 2006;47:1777–1785.

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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

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

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

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

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

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