History
of
Interventional Cardiology

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Disclosures

- Boston Scientific - Consultant
- Abbott Vascular - Consultant
- Medtronic - Consultant
- Direct Flow Medical - Consultant
History of Interventional Cardiology

- 3000 BC - Egyptians perform bladder catheterization using metal pipes

- 400 BC - Catheters fashioned from hollow reeds and pipes are used in cadavers to study the function of cardiac valves

- 1711 - Hale conducts first cardiac catheterization of a horse using brass pipes, glass tube and trachea of a goose

- 1844 - French physiologist, Bernard coins the term “Cardiac Catheterization” and uses catheters to measure intracardiac pressures in animals
History of Interventional Cardiology

- 1895 - Discovery of X-ray
  Wilhelm Conrad Roentgen

- 1896 - Invention of Fluoroscopy
  Enrico Salvioni

- 1913 - Improved X-ray tubes
  William Coolidge
History of Interventional Cardiology

• 1929 - First documented human cardiac catheterization is performed by Dr. Werner Forssmann on himself in Eberswald, Germany - Immediately fired from his position

• 1941 - Cournand and Richards employ cardiac catheterization as a diagnostic tool for the first time utilizing catheter techniques to measure cardiac output

• 1956 - Forssmann, Cournand and Richards share the Nobel Prize - Cournand states in acceptance speech “the cardiac catheter was the ....key in the lock”
History of Interventional Cardiology

- **1958** - The diagnostic coronary angiogram - The key to selective imaging of the heart is discovered by Dr. Mason Sones - Open cut-down - brachial

- **1964** - Transluminal Angioplasty, the concept of “remodeling” an artery is introduced by Dr. Charles T. Dotter (Dottering)

- **1967** - Introduction of the Judkins Technique of Coronary Angiography

- **1967** - First SVG bypass surgery Dr. Rene Favaloro
History of Interventional Cardiology

- 1974 - Andreas Gruentzig performs first peripheral human balloon angioplasty

- 1976 - Gruentzig presents results of animal studies of coronary angioplasty at American Heart Association

- 1977 - First human coronary balloon angioplasty performed intra-operatively by Gruentzig, Myler and Hanna in San Francisco

- 1977 - Andreas Gruentzig performs first cath lab PTCA on awake patient in Zurich
Interventional Cardiology - 1977

- A new specialty is born
- PTCA - Percutaneous Transluminal Coronary Angioplasty
  - Plaque compression
  - Stretching of medial wall
  - Controlled injury
PTCA - 1977

- Percutaneous Transluminal Coronary Angioplasty
- Non-compliant balloon Angioplasty

- 50% Restenosis - A new disease
  - Elastic recoil
  - Vascular negative remodeling
  - Neointimal hyperplasia
- Abrupt and threatened closure
PTCA - 1978

- First PTCA in USA
  - Simon Stertzer - Lenox Hill Hospital New York City
  - Richard Myler - St. Marys Hospital San Francisco

- Andreas Gruentzig -
  - First live case demonstration course in Zurich, Switzerland
  - 1980 - Last of five live case demonstration course
    - Sones, Judkins, & Dotter in attendance
  - 1982 - Steerable wires and Over-the-wire balloon catheters
  - 1985 - Gruentzig, Dotter, Sones, Judkins - all pass away within 9 months of each other
Directional Coronary Atherectomy - 1984

- DCA
  - Plaque compression
  - Plaque removal by excision (debulking)
  - 10 French Guide
  - Restenosis similar to PTCA
  - Technically challenging
Rotational Atherectomy -1988

- Percutaneous Transluminal Coronary Rotational Atherectomy
- PTCRA - Rotablator
  - Diamond burr - 1.25 mm - 2.5 mm
  - Plaque ablation
PTCRA

- Effective for calcified plaque
- Debulking
- Technically difficult to use
- Restenosis similar to PTCA
Intra-Vascular UltraSound - IVUS
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Coronary Stent - 1994

- Gianturco-Roubin Stent - 1993
  - Abrupt and threatened closure
    - GR II
- Palmaz-Schatz Coronary Stent
  - Primary Stent implantation
Coronary Stent

- Coronary Stent

- Restenosis reduce to 25%
- Prevents elastic recoil
- Prevents negative vascular remodeling
- Increase intimal hyperplasia
Coronary Stent

- Why are we stenting?
  - Limitation of PTCA, DCA, Rotablator, Laser
    - Restenosis, Dissection, Abrupt Closure, Suboptimal result
  - Stenting - Scaffolding
    - Predicatable, quick, angiographically seductive
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Coronary Stent

• Next Generation Stents - 1997
• One million Percutaneous Coronary Interventions in 1997

• Stent Thrombosis - Another new disease
  • Aspirin, Persantine, Heparin, Dextran 40, Coumadin
• Columbo - IVUS
  • Aspirin, Ticlid - No Coumadin
Coronary Revascularization

- PCI Procedures
- BMS
- DES
- CABG

Year:
- 1994: 17%
- 1995: 25%
- 1996: 35%
- 1997: 45%
- 1998: 65%
- 1999: 73%
- 2000: 77%
- 2001: 80%
- 2002: 85%
- 2003: 25%
- 2004: 19%
- 2005: 13%

Device:
- P-S Stent
- Stress & Benestent
- Colombo
- MultiLink GFX
- NIR
- Cypher SIRIUS
- Taxus TAXUS IV
Nomenclature

- Binary restenosis - >50% narrowing at time of restudy
- In-Stent Restenosis
- In-Segment Restenosis
- Target lesion revascularization - TLR
- Target vessel revascularization - TVR
- Target Vessel Failure - Cardiac Death, MI, TVR - TVF
- MACE - Death, MI, TVR

MLD<sub>post-procedure</sub> + MLD<sub>follow-up</sub> = Late Loss 1.0mm
Brachytherapy

- In-Stent Restenosis - ISR
- Achilles heel of Percutaneous Coronary Intervention
- Occurs by 6 - 12 months
- Recurs > 70% with standard therapy
- Brachytherapy - Local radiation
  - Gamma - Very penetrating - Iridium\(^{192}\)
  - Beta - Limited penetration - Strontium\(^{90}\)
Drug Eluting Stents - 2003

- Restenosis rate with Bare Metal Stents ~ 25%
- Pathophysiology of restenosis defined
- Drugs identified
  - Inhibit smooth muscle cell migration
  - Inhibit smooth muscle cell proliferation
  - Inhibit extracellular matrix formation
- Sirolimus - Rapamycin
- Paclitaxel - Taxol
- Polymer coating to bind drug, control release, vascular biocompatible
Radiation

Actinomycin D (DNA)

Cell Division

Growth Factors / Cytokines

FKBP

S

G_2

M

cell cycle

p27, Cyclins/Cdk

↑

G_0 → G_1 → S → M

Cell Division

Smooth muscle cell

Arterial Injury

Thrombus (platelets)

Inflammation (macrophage)

Growth Factors / Cytokines

Dexamethasone

Batimistat

Sirolimus

• Activation

• Signal Transduction

TOR

FKBP

Radiation

Actinomycin D (DNA)

Paclitaxel (microtubules)

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Drug Eluting Stents

XIENCE™ V
Cypher® Select
Endeavor™
Taxus® Liberté
SIRIUS: 8 Month Angiographic Follow-up Restenosis Rates

In-stent Restenosis

- Sirolimus Stent: 3%
- Bare Stent: 35%

91% reduction
p<0.001

In-segment Restenosis

- Sirolimus Stent: 9%
- Bare Stent: 36%

75% reduction
p<0.001
Restenosis

Control (n=267)

TAXUS (n=292)

RR=0.23 [0.13, 0.38]  P<0.0001

RR=0.30 [0.19, 0.46]  P<0.0001

In-stent

Analysis segment

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SIRIUS: Clinical Events Through 9 Months

MACE

Sirolimus Stent: 7.1%
Bare Stent: 18.9%
p<0.001

Target Vessel Failure*

Sirolimus Stent: 8.6%
Bare Stent: 21.0%
p<0.001

*Primary clinical endpoint; defined as cardiac death, MI, TVR

Thursday, May 19, 2011
Do drug-eluting stents increase deaths?

Two separate, independent meta-analyses, presented in Hot Line session 1, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year’s meeting.

“Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown,” said Yusuf. “Yet a feeling the data we’re seeing today is only the tip of the iceberg. We need to encourage more public access to the data.”

Presenter, Edoardo Camerini (Geneva, Switzerland), said recent case reports had flagged up the problem of in-stent thrombosis resulting from DES. “The BASKET-LATE data obtained this data from the manufacturer,” said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

Yusuf widened the debate to include percutaneous coronary intervention (PCI). “The essence of PCI is an indispensable change in the culture of cardiology that needs to be reversed,” he said. The use of PCI was established in MI, high-risk unstable angina and cardiogenic shock. However, its use in stable disease was a totally different question.

“There’s no beneficial influence on mortality – PCI does nothing to prevent heart attack. All we are doing is providing short-term relief of chest pain. It’s not re-directs that kills but the thousands of lesions you can’t see. Stable angina can be controlled with full medical management.” Yusuf said vested interests included pharmaceutical companies, who have
DES Pendulum
DES Pendulum

2005 Perceptions →
• DES solves restenosis
• Pivotal data look good
• Maybe they are good for all lesion types

>80% penetration
DES Pendulum

~60 (40-75%) penetration

2006 Perceptions
• Increased LST (protocol def)
• Increased DES mortality (Camezind meta and SCAAR)
• Maybe the use of DES should be restricted dramatically

2005 Perceptions
• DES solves restenosis
• Pivotal data look good
• Maybe they are good for all lesions types

>80% penetration

Thursday, May 19, 2011
Cypher and Taxus compared to BMS - small increase in stent thrombosis that emerges 1 year after implant

Not associated with increase in death and MI (possibly owing to insufficient numbers or offset by reduction in events from prevention of restenosis and additional revascularization procedures)

Concerns about stent thrombosis do not outweigh benefits when implanted for approved indications
Everolimus-Eluting Stents

Everolimus concentration: 100 μg/cm²
Polymer: PBMA & PVDF-HFP (7 μm thickness)

XIENCE V / PROMUS (CoCr-EES)

PROMUS Element (PtCr-EES)

PBMA=poly (n-butyl methacrylate) (primer layer); PVDF-HFP=poly (vinylidene fluoride-co-hexafluoropropylene) (drug matrix layer)
Patient Flow

All Patients Randomized (N=1530)

CoCr-EES (N=762)
- No 12M f/u (N=27)
  - Withdrew consent: 6
  - Missed 12M visit: 21
- 12 Mo Follow-up 96.5% (735/762)

PtCr-EES (N=768)
- No 12M f/u (N=23)
  - Withdrew consent: 1
  - Missed 12M visit: 21
  - Other: 1
- 12 Mo Follow-up 97.0% (745/768)
Target Lesion Failure
Time-to-event analysis

Per Protocol
- CoCr-EES (N=747)
- PtCr-EES (N=756)

HR [95% CI] = 1.17 [0.66, 2.09]
$P = 0.59$

Intention-to-Treat
- CoCr-EES (N=762)
- PtCr-EES (N=768)

HR [95% CI] = 1.12 [0.64, 1.95]
$P = 0.70$

Target Lesion Failure (%)

CoCr
PtCr

No. at risk

CoCr-EES 747 735 731 723 707
PtCr-EES 756 745 740 734 719

Per Protocol

Intention-to-Treat

No. at risk

CoCr-EES (N=762) 762 747 743 735 718
PtCr-EES (N=768) 768 756 751 745 730

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<table>
<thead>
<tr>
<th></th>
<th>CoCr-EES (N=762)</th>
<th>PtCr-EES (N=768)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TVR</td>
<td>2.9%</td>
<td>2.7%</td>
<td>0.83</td>
</tr>
<tr>
<td>TLR</td>
<td>1.9%</td>
<td>1.9%</td>
<td>0.96</td>
</tr>
<tr>
<td>TLR, PCI</td>
<td>1.6%</td>
<td>1.3%</td>
<td>0.64</td>
</tr>
<tr>
<td>TLR, CABG</td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.69</td>
</tr>
<tr>
<td>TVR non-TLR</td>
<td>1.1%</td>
<td>0.9%</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Stent Thrombosis – ARC Def/Prob

12 Months – Intent-to-Treat

<table>
<thead>
<tr>
<th>Months</th>
<th>CoCr-EES (N=762)</th>
<th>PtCr-EES (N=768)</th>
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<tbody>
<tr>
<td>0</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>3</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>6</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>9</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>12</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

No. at risk

- CoCr-EES: 762, 755, 752, 745, 728
- PtCr-EES: 768, 761, 758, 752, 741

HR [95% CI] = 0.99 [0.20, 4.91]

P = 0.99

* All were definite ST
Bifurcation LAD

• 61 y.o. Male Physician
  • Wife & Daughter Physicians
  • Son - Medical Student
  • Hypertension and Hyperlipidemia
  • Self treated with Diovan/Hct 80/12.5
  • Chest Pain with exercise
  • Markedly positive nuclear myocardial perfusion scan
    • Anterior and anterolateral distribution
  • Coronary Angiography
Baseline - RAO Caudal
Baseline - LAO Cranial
Baseline - LAO Caudal
Baseline - RAO Cranial
Kissing Balloon
Diagonal Stent
Diagonal Stented
LAD Wired
LAD Balloon
LAD Stented
Kissing Balloon
Final RAO Cranial
Final RAO Caudal
Final LAO Caudal
Final LAO Cranial
Chronic Total Occlusions

- Recanalization of a Chronic Total Occlusion - The Final Frontier
- Technically the most challenging coronary intervention
- Difficult to Treat
  - Time intensive
  - Significant contrast load
  - Significant radiation exposure
- Complications
  - Dissection, Perforation, Guide injury, Embolization, Myocardial Infarction, Death
- Usual Success rate ~ 50%
- Commitment to CTO’s - Success rates now 60 - 90%
  - Systematic approach
- New technical advances
Rationale for CTO Revascularization

- Improve symptoms
  - Improve coronary blood flow - $O_2$ Supply
- Increase long-term survival
- Improve left ventricular function
- Improve electrical stability of myocardium - reduce predisposition for arrhythmic event
- Increase tolerance of progressive coronary artery disease - provide collaterals
Anatomy and Histopathology

- Thrombotic occlusion, thrombus organization & tissue aging
- Histologically one-half of CTOs are <99% stenotic
- No relationship between severity of histopathic lumen stenosis and plaque composition or lesion age
- Atherosclerotic plaque of CTO
  - Intra and extracellular lipid
  - Smooth muscle cells
  - Extracellular matrix (predominate type I and III) in fibrous stroma
  - Calcium
  - Dense concentration of collagen rich fibrous tissue at proximal and distal ends - columnlike lesion of calcified fibrous tissue

Large - 59% of all CTO
Small - 41% of all CTO
Guidewire Technique

- Wire selection
  - Hydrophilic (slippery) wire tip has difficulty engaging entry point dimple
  - Low lubricity (spring coil) wire tip can more easily engage entry point dimple

- Tip curve should be just larger than lumen diameter

- CTO lumen diameter is 0 mm - Wire tip curve should be near 0

Penetrating in CTO fibrous cap
Reentry into true lumen
Ostial LAD CTO

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Ostial LAD CTO
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Ostial LAD CTO
Ostial LAD CTO
Ostial LAD CTO
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
CTO Retrograde
Summary

• Successful PCI of Chronic Total Occlusion may
  • Relieve symptoms
  • Improve LV function
  • Improve survival
  • Improve electrical stability
  • Enhance tolerance for progressive CAD

• Assess Risk / Benefit for each patient
  • Consider clinical, angiographic and technical factors

• Essentials of a CTO program
  • Knowledge of histopathology
  • Equipment knowledge and selection
  • Techniques - Guidewire, parallel wire, side branch, retrograde, STAR etc.
  • Specialty devices - Tornus, Frontrunner, Safe-cross, Crosser etc.
  • High resolution imaging, contra-lateral injection, orthogonal views
  • Operator, patient, staff, scheduling commitment to CTO program
Aortic Stenosis

• Etiology
  • Calcific degenerative
    • Degenerative process with proliferative & inflammatory changes, lipid accumulation, up regulation ACE, infiltration with macrophages & T lymphocytes → Bone formation (vascular calcification
  • Congenital - Bicuspid
    • Turbulent flow - traumatizes leaflet → fibrosis, rigidity, calcification & narrowed orifice
  • Rheumatic
    • Adhesion & fusion of commissures & cusps → retraction & stiffening cusps borders.
    • Calcific nodules both surfaces - small round or triangular opening
I-REVIVE  Patient 1

Aorta
Left Atrium
Left Ventricle
IVC
Femoral Vein
Femoral Artery
Cribier-Edwards

Retrograde Implant

Post Implant Aortogram
Cribier-Edwards

Retrograde Implant

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Cribier-Edwards

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Cribier-Edwards

Retrograde Implant

Post Implant Aortogram
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Retrograde Implant

Post Implant Aortogram
Mitral Regurgitation
Mitral Regurgitation
Mitral Regurgitation
Surgical Repair
Edge-to-Edge Surgical Repair Targets Patients with Degenerative MR

- Focused on repair of diseased, non-coapting leaflets
- Developed in Milan, Italy by Professor Alfieri and used in over 1,000 open heart surgical repair cases
- Addresses the inability of the leaflets to properly close and form a seal
- Five year freedom from re-operation ranges from 70% to 95%
Endovascular CVRS for E2E Mitral Repair
Cardiovascular Valve Repair System
Off-pump Edge-to-Edge Mitral Valve Technique Using a Mechanical Clip in a Chronic Model

Clip repair in porcine heart (6 months post repair)

Fann et al: Circulation 110:988-993, 2004

Suture repair in human heart (4 years post repair)

Privatera et al: Circulation. 2002;106:e173
Summary

It’s been an amazing ride
1977 - 2011

Car Accessory for Cardiac Surgeon