Take Heart Despite a Bad Heart: Advances in Restoring Clogged Coronaries without Bypass Surgery
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Objectives
- Review pathophysiology of coronary disease
- Brief history of coronary interventions
- Discuss new percutaneous options for revascularization of complex lesions
- Discuss advances in stent technology

Atherosclerosis Progression

"CAT" Scan

CT Angiography

Coronary Angiography – remains the Gold standard
Emergency Department Visits Annually in the U.S.

- 95 MM visits
- 8 MM for chest pain
- 6.1 MM Non-cardiac
- 0.6 MM for ST-segment Myocardial Infarction
- 0.4 MM for Non-ST-segment Myocardial Infarction
- 1.0 MM for Unstable Angina

ECG – Massive Anterior STEMI

Diagnostic Algorithm for Acute Coronary Syndrome Management

- ST segment elevation MI
- Non-ST elevation ACS
- Non-ST elevation MI

Therapeutic goal: rapidly break apart fibrin mesh to quickly restore blood flow

Consider fibrinolytic therapy, if indicated, or primary percutaneous coronary intervention (PCI)

Therapeutic goal: prevent progression to complete occlusion of coronary artery and resultant MI or death

Consider GP IIb-IIIa inhibitor + aspirin + heparin before early diagnostic catheterization

Acute Myocardial Infarction

Acute Coronary Syndrome with Unfavorable Outcomes

Plaque rupture with thrombosis

Sudden Death

Clinical Manifestations of Arterial Thrombosis

STEM:
- Occlusive thrombus (platelet-dominated)
- Intra-plaque thrombus (platelet-dominated)
- Plaque core

Handrail:
- Partially occlusive thrombus (primarily platelet)
Coronary Angiography – RCA thrombus

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 SF
- 1977 Andreas Gruentzig performs first cath lab PTCA on awake pt 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
  - 50% Restenosis - A new disease
    - Elastic recoil
    - Vascular negative remodeling
    - Neointimal hyperplasia
    - Abrupt and threatened closure

Coronary Stent - 1994

- Palmaz-Schatz Coronary Stent
  - Primary Stent implantation
- Why are we stenting?
  - Limitations of PTCA, atherectomy, laser
    - Restenosis, dissection, abrupt closure, suboptimal result
  - Stenting - Scaffolding
    - Predictable, quick, angiographically seductive

Coronary Stenting

- Restenosis reduced to 25%
- Prevents elastic recoil
- Prevents negative vascular remodeling
- Increase intimal hyperplasia – In-stent restenosis
**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

**Coronary Angiogram – Left Coronary Artery**

**Question of PCI or CABG?**

- Typical PCI patient
  - 1 or 2 vessel disease
- Typical referral for CABG
  - Severe Left Main disease
  - Severe multivessel CAD
  - Chronic total occlusions
  - Severe LV dysfunction and diabetes
  - Severe valvular disease

**Two Very Different Procedures…**

**Answer is not so clear anymore**

- Severe Left Main disease
  - Syntax LM Subset
- Severe multivessel CAD
  - Syntax Trial
  - EXCEL Trial
- Chronic total occlusions
  - New technologies and equipment
SYNTAX Trial Design

*De novo* disease (n=1800)

- **Limited Exclusion Criteria**
  - Previous interventions
  - Acute MI with CKP>2x
  - Concomitant cardiac surgery

- **Left Main Disease** (isolated, ≥1, ≥2 or ≥3 vessels)
- **3 Vessel Disease** (revasc all 3 vascular territories)

**Primary endpoint** = death/MI/stroke/repeat revasc at 1 year

N=705

N=1095

Serruys PW et al. NEJM 2009;360:961-72

**SYNTAX: MACCE to 5 Years**

**Left Main Subset**

- **CABG (N=348)**
- **TAXUS (N=357)**

Month 0-1

- **P=0.12**

Month 1-2 years

- **P=0.22**

Month 2-3 years

- **P=0.78**

Month 3-4 years

- **P=0.35**

Month 4-5 years

- **P=0.82**


**MACCE to 5 Years by SYNTAX Score**

*Low to Intermediate Scores (0-32)*

- **CABG (N=196)**
- **TAXUS (N=221)**

**CABG**

- Death 15.1%
- CVA 3.9%
- MI 3.8%
- Death, CVA or MI 19.8%
- Revasc. 18.6%

**PCI**

- Death 7.9%
- CVA 1.4%
- MI 6.1%
- Death, CVA or MI 14.8%
- Revasc. 22.6%

**P-value**

- 0.02
- 0.11
- 0.33
- 0.16
- 0.36


**MACCE to 5 Years by SYNTAX Score**

*High Scores ≥33*

- **CABG (N=149)**
- **TAXUS (N=133)**

**CABG**

- Death 14.1%
- CVA 4.9%
- MI 6.1%
- Death, CVA or MI 22.1%
- Revasc. 11.6%

**PCI**

- Death 20.9%
- CVA 1.6%
- MI 11.7%
- Death, CVA or MI 26.1%
- Revasc. 24.1%

**P-value**

- 0.11
- 0.13
- 0.13
- 0.40
- <0.001


**Answer is not so clear anymore**

- **Severe Left Main disease**
  - Syntax LM Subset
- **Severe multivessel CAD**
  - Syntax Trial
  - EXCEL Trial
- **Chronic total occlusions**
  - New technologies and equipment

**SYNTAX Trial Patient Distribution**

- **Surgery For LM Still gold standard 66%**
- **PCI LM Legitimate 34%**

*Results of the SYNTAX Trial suggest that 1/3 of all patients with Left Main lesions are best treated with PCI. Excellent alternative to surgery... at least up to five years.*
Answer is not so clear anymore

- Severe Left Main disease
  - Syntax LM Subset
- Severe multivessel CAD
  - Syntax Trial
  - EXCEL Trial – Ongoing enrollment
- Chronic total occlusions
  - New techniques and equipment

Chronic Total Occlusions

- Recanalization of a CTO – The Final Frontier
- Technically the most challenging coronary interventions
- Difficult to Treat
  - Time intensive
  - Significant contrast load
  - Significant radiation exposure
  - Complications
  - Previous success rate ~ 50%
  - Success rates now 80 – 90%

Rationale for CTO Revascularization

- Improvement of symptoms
  - Improve coronary blood flow - O₂ Supply
- Reduction in ischemic burden
- Enable completeness of revascularization
- Improvement in LV function
- Increase long-term survival
- Improve electrical stability of myocardium - reduce predisposition for arrhythmic event
- Avoidance of surgical bypass procedures
- Reduced medications
Predictors of Success

- Predictors of lower success
  - Increasing age of lesion - chronicity
  - Longer length of occlusion
  - Non-tapered stump
  - Origin of side branch at occlusion
  - Bridging collaterals

Guidewires

- Intermediate coils: Maintain 0.014” diameter for smooth device delivery
- BMW
- Universal
- Pilot/Whisper
- Miracabr 3

Newer Specialty CTO Asahi Wires

- BMW
- Universal
- Pilot/Whisper
- Miracabr 3

Guidewire Techniques – Support catheters

- Crossing
  - Balloon - OTW otherwise 1.5 mm Monorail
  - Support - Finecross, Transit, Minnie, Quickcross
  - Torus
  - Gopher

CTO – Newer Device Technology

- Blunt Microdissection (Frontrunner - Cordis)
- Radiofrequency (SafeCross - Kensey Nash)
- Vibrational (Crosser - FlowCardia)
- Dissection/Reentry (Cross Boss - Boston Sci)

“Definition of insanity is doing the same thing over and over again and expecting the same result.”
Frontrunner - Blunt microdissection

Adventitia
Fibro-calcific CTO

The CROSSER™ System
High Frequency Mechanical Recanalization Technology

The Electronics
- Generator provides high frequency current – 20 kHz
- Transducer converts high frequency current → vibrational energy

Excimer Laser Coronary Atherectomy

Cross Boss CTO Catheter
- Bi-directional rotation of the torque device with the FAST SPIN Technique
- 1 mm atraumatic rounded tip
- Intended to cross directly through the CTO or bypass the obstruction via a subintimal path

Stingray CTO Re-Entry System
- Reentry Device
  - Guidewire in false lumen beyond CTO
  - Combined CTO and adventitia

CTO of the RCA
- Contralateral injection of the L → R collaterals
CrossBoss Catheter

Angioplasty and Stenting

Final Angiography

Retrograde Technique
- Collateral Channel
  - Bypass graft
  - Epicardial collateral
  - Septal perforator
- Technique
  - Retrograde wire crossing
  - Kissing wire technique
  - CART technique

Collateral Pathways After RCA Occlusion

Corsair Catheter
Collateral Crossing and Support Catheter

Flexible tapered tip of ASAHI Corsair contributes excellent channel tracking and also effectively works for super-selective tip injection
CTO of the RCA – Retrograde Approach

CTO of the RCA - Retrograde

Identify an appropriate septal collateral

CTO of the RCA - Retrograde

Septal channel wiring – In real time

CTO of the RCA - Retrograde

Successive Balloon Angioplasty

CTO of the RCA - Retrograde
Multiple drug-eluting stents placed

Final Angiography

Approaching CTO’s

Success not guaranteed

Improved techniques & technologies

More complex interventions
Still no guarantees

Drug Eluting Stents for CTO

Drug-Eluting Stents: 1st Generation

Sirolimus-Eluting Stent: 7 year F/U

Target Lesion Revascularization at 5 Years

1st Gen Drug-Eluting Stents

The good, the bad, and the ugly!
Definite/Probable ARC Stent Thrombosis to 5 Yrs (Per Patient)

Acute ≤1d
Subacute 2-30d
Late 31-365d
Very Late 366-730d
Total 5 Year

Serruya PW et al. TCT 2012

European Society of Cardiology 2006

Drug-Eluting Stents: 2nd Generation

Promus Element

Xience V

Everolimus

Polymer

Drug

VDF + HFP copolymer

Stent

SPIRIT II, III, IV and COMPARE trials

MACE (Cardiac Death, MI, ID-TLR)

Pooled database analysis (n=6,789)

EES (n=4,247)

PES (n=2,542)

Cardiac Death, MI, Ischemic TLR (%) P<0.001

HR: 0.64 [0.54, 0.75]

EES (n=4,247)

PES (n=2,542)

Number at risk

XIENCE

TAXUS

Cardiac Death, MI, Ischemic TLR (%)

Time in Months

SPIRIT II, III, IV and COMPARE trials

Stent thrombosis (ARC definite/probable)

Pooled database analysis (n=6,789)

EES (n=4,247)

PES (n=2,542)

Stent thrombosis

ARC def or prob (%)

Time in Months


'Saged' (Stented) Vessel

Etiology of DES events beyond 1 year

Delayed Healing: Stent Thrombosis?

Benign NIH

Neo-Atheroma

Stent Thrombosis?

In-Stent Restenosis

Late Acquired Malapposition

Stent Thrombosis?
**Potential of a Fully Bioresorbable Vascular Scaffold**

Since struts disappear, issues related to very late persistent strut malapposition and chronically uncovered struts become irrelevant.

**Rationale:** Vessel scaffolding is only needed transiently.

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**Polylactide Degradation & Lactate Metabolism**

Lactate shuttle: Lactate serves as a carbohydrate fuel source for multiple metabolic pathways.

- Intracellular Mitochondria
- TCA (Krebs) Cycle


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**Krebs Citric Acid Cycle**

- Complete strut apposition
- Late acquired incomplete strut apposition with tissue bridges between fractured struts
- Smooth endoluminal lining
- Struts largely disappeared although remnant just visible (arrow)

**ABSORB Trial (BVS cohort A): OCT Results**

**Abbott Vascular Everolimus-Eluting Bioresorbable Vascular Scaffold Components**

<table>
<thead>
<tr>
<th>Bioresorbable Scaffold</th>
<th>Bioresorbable Coating</th>
<th>Everolimus</th>
<th>XIENCE V Delivery System</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLLA (eluting everolimus)</td>
<td>Poly (L-lactide) (PLL)</td>
<td>Poly (D,L-lactide) (PDL) coating</td>
<td>PLLA (w/PDLA coat eluting sirolimus)</td>
</tr>
<tr>
<td>Abbott Absorb</td>
<td>Naturally resorbed, fully metabolized</td>
<td>Naturally resorbed, fully metabolized</td>
<td>Magnesium (eluting paclitaxel)</td>
</tr>
<tr>
<td>Reva ReSolve</td>
<td>PLLA (w/PDLLA coat eluting everolimus)</td>
<td>PLLA (w/PDLLA coat eluting sirolimus)</td>
<td></td>
</tr>
<tr>
<td>Abbott Vascular Everolimus</td>
<td>PLLA (w/PDLLA coat eluting everolimus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elixir DESolve</td>
<td>PLLA (w/PDLLA coat eluting everolimus)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Bioresorbable Vascular Scaffolds (BVS)**

- PLLA
- PLLA (w/PDLLA coat eluting everolimus)
- Iodinated tyrosine-derivative (eluting sirolimus)
- PPLLA (eluting myolimus)
- Magnesium (eluting paclitaxel)
Extensive Publications
More than 120 Absorb Publications by CE Launch

Overview of ABSORB Studies

Bioresorbable scaffolds have been called “The Fourth Revolution” in PCI

Summary
- Significant advances have been made in the field of Interventional Cardiology
- Previous bypass surgery patients are being successfully treated with PCI and stenting
- Stent technologies are constantly evolving
- BVS technology is promising and may improve upon some of the known drawbacks of metallic stents
- Ongoing studies and future studies will be necessary to demonstrate their long-term efficacy and safety in a broad range of patients

Thank You