PCI for Chronic Total Occlusion: Evolving Technology
Evolving Technology

- Excimer Laser
- Ultrasound
- Radiofrequency
- Microdissection
- Fibrinolysis
- MDCT
- IC NaviView
- Magnetic RF Wire
Evolving Technology
Ablative Tools

Excimer laser
Prima Laser wire 0.014”

- **Specifications**
  - Size = .014”
  - Fiber = 8 fibers (45 microns)
  - Coil = 30 cm radioopaque
  - Proximal shaft = 150 cm
    Nitinol hypotube Teflon coated
  - Exchange length = 180 cm
  - Active area = 0.127 mm²
  - % active area = just over 11%
  - Max energy = 1 – 1.2 mj
Superwise

- Next generation .014” laser guidewire
- Steering and handling characteristics similar to standard mechanical guidewires
- Laser ablation enhances CTO crossing ability (approximately 0.04 mm/pulse)
- 180 cm working length
Point 9 X-80 Catheter

- Two product configurations
  - Vitesse (Rx) 110-004
  - Extreme (OTW) 110-002
- 0.9 mm tip diameter
- .014 or smaller guidewire compatibility
- 6 French guide catheter compatibility
- 80 fluence, 80 hertz maximum laser parameters
- 10 second “on”, 5 second “off” lasing sequence
TOTAL: Total Occlusion Trial with Angioplasty by Using Laser Guide Wire

- 18 European Centers, 303 patients
- **1<sup>st</sup> Endpoint:** Reaching the True Lumen Within 30 Min of Fluoroscopic Time

<table>
<thead>
<tr>
<th>Category</th>
<th>Laser Wire (n=144)</th>
<th>Mechanical Wire (n=159)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint (%)</td>
<td>52.8</td>
<td>47.2</td>
<td>NS</td>
</tr>
<tr>
<td>Acute Adverse Events (%)</td>
<td>0</td>
<td>0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Restenosis Rate at 6 mo (%)</td>
<td>45.5</td>
<td>38.3</td>
<td>NS</td>
</tr>
<tr>
<td>Reocclusion Rate (%)</td>
<td>25.8</td>
<td>16.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

P. Serruys et al, *Eur Heart J* 2000:21;1797-1805
Debulking Prior To Stenting After Revascularization of Chronic Total Occlusions

176 CTO Lesions Treated With Excimer Laser, Directional or Rotational Atherectomy

<table>
<thead>
<tr>
<th></th>
<th>Stent Alone (n=126)</th>
<th>Debulking+Stent (n=50)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Angio.Success (%)</td>
<td>97.1</td>
<td>100</td>
<td>NS</td>
</tr>
<tr>
<td>Final MLD (mm)</td>
<td>2.62 ± 0.7</td>
<td>2.70 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Hospital MACE (%)</td>
<td>3.7</td>
<td>2.3</td>
<td>NS</td>
</tr>
<tr>
<td>MACE at FU (%)</td>
<td>19.6</td>
<td>25.6</td>
<td>NS</td>
</tr>
<tr>
<td>TLR (%)</td>
<td>14.4</td>
<td>16.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Gruberg et al, *JACC*, 2000
Evolving Technology
Ablative Tools

Ultrasound
Description of Procedure

- Generator provides an electrical signal to the reusable handpiece

- Handpiece converts the signal to acoustic energy

- Small diameter flexible guidewire vibrates at 20 kHz, ablating tissue via cavitation along distal 20 cm active length
OmniWave Technology

- OmniWave Technology is the first technology that delivers controlled acoustic energy along the active section of a flexible 0.004” – 0.025” wire.
First-Generation Ultrasonic Energy Delivery vs. OmniWave™ Technology

Previous tip-based energy delivery

OmniWave Technology energy delivery

Effective Diameter

Effective Diameter
Evolving Technology
Ablative Tools

Radiofrequency
OCR Waveform Displays

Simple Display Feature

Investigational Device, Not available for sale in the US.
CTO: Technical Challenges

OCR Monitor Signal

PLAQUE

ARTERY WALL
OCR SafeSteer System

- Forward looking guidance system, using OCR to determine tissue types (*plaque vs arterial wall*).
- Designed to navigate through total occlusion.
The Crosser™ System

- **Generator** converts line power into high frequency current
- **Transducer** converts electric current into mechanical vibration
- **The Crosser catheter**
The Crosser™ System

Clinical Experiences

54 pts with 56 CTO, Refractory to guidewire
Mean occlusion length 27 mm (8~46 mm)

• Average time spent 2:43 min
• MACE (2 NQMI) 3.6% (2/56)
• Clinical perforation 0%

High frequency mechanical recanalization is a promising technology.

G. Sutsch et al, JIM 2004
The prospective Guided Radiofrequency Energy Ablation of Total Occlusions (GREAT) trial

116 Lesions 21 Centers with CTO “Failure to Cross”
GREAT Trial

116 pts 21 Centers

• Device Success 54.3%

• Complications
  - Clinical Perforations 2.6% (3)
  • Device related 0.9% (1)
  - MACE (6 NQMI) 5.2%
  - MACE + Clinical Perforations 6.0% (7)

Baim DS et al. Am J Cardiol 2004;94:853-858
Evolving Technology
Mechanical Tools

Blunt Microdissection
LuMend Frontrunner® X39 CTO Catheter
with Micro Guide Catheter

Coronary & Peripheral CTO’s
Frontrunner™ CTO Catheter

- Indicated for Chronic Total Occlusions
- Controlled Blunt Micro Dissection Technique
- Multiple distal tip openings
- 4.0 & 4.5 French catheter platforms
- No external energy source
FrontRunner Catheter

Controlled Blunt Micro-Dissection

• Blunt controlled passage through occlusion
• Uses elastic properties of adventitia vs. inelastic fibrocalcific plaque
25° Distal Tip Angle 36° Distal Tip Angle
Frontrunner™ CTO Catheter

**Controlled Blunt Micro-Dissection Technique**

- Gently separates atherosclerotic plaque in various tissue planes, creating a passage through the CTO.
- Uses elastic properties of adventitia versus inelastic properties of fibrocalcific plaque to create fracture planes.
LuMend Frontrunner®
X39 CTO Catheter

- .039” (2.8F) distal tip size
- 2.3mm opening
- 55% reduction in catheter surface area
  vs. original Frontrunner
- Shortened distal rigid segment
  (improves tip shape and steerability)
- Guide wire like handling/size

X39 compared to .035” guide wire

X39 compared with the original
Frontrunner
LuMend Frontrunner® Micro Guide Catheter

- Support/Transitional catheter used with Frontrunner X39
  - *PTCA baloon/guide wire concept*
- Tapered tip
- 4.5 French/127cm working length
- Torqueable braided shaft
- 7 French guide cath recommended
- Easy transition of ancillary devices to and from occlusion site
  - *Wires, balloons, etc.*
Frontrunner Technique

Actuation, Retraction, and Torque

1. Firm engagement before actuation
2. Feel for resistance, and look for slow opening
3. Retract after every actuation and confirm jaw closure
4. Torque back into position before next actuation
   - Assures closure
   - Improves engagement
Equipment Selection

Guiding Catheters
1. 6F vs 8F
2. Left Coronary
   - JL4 vs XB vs AL
3. Right Coronary
   - JR4 vs HS vs AL (.75 vs 1)

Frontrunners
1. Curved vs Straight jaws
2. Curved 25 degree vs 36 degree
3. Small vs Large jaws
4. New devices
   - Bottlenose, FR 4.0, FR 2.8
Frontrunner™ CTO Catheter

Clinical Trial

- Prospective, controlled multi-center trial
- 107 patients enrolled
- CTO patients refractory to a ten minute (fluoroscopy time) guide wire attempt
- Success defined as placement of guide wire beyond CTO in the true vessel lumen
- Mean Lesion Length: 22mm
- Range of Lesion Length: 2-53mm
# FrontrunnerTM CTO Catheter Clinical Trial

*Results (Lesion length=23mm)*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number (n=107)</th>
<th>Rate (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful delivery to CTO</td>
<td>96</td>
<td>89.7%</td>
</tr>
<tr>
<td>Advanced distal to CTO</td>
<td>66</td>
<td>61.7%</td>
</tr>
<tr>
<td>Wire placed distal to CTO in true vessel lumen</td>
<td>60</td>
<td>56.1%</td>
</tr>
</tbody>
</table>
Frontrunner™ CTO Catheter Clinical Trial

Complications (Potentially Device Related)

- **Perforation**
  - With tamponade or hemopericardium: 0
  - Without tamponade or hemopericardium: 2 (1.9%)

- **AMI**
  - Q-Wave: 0
  - Non Q-Wave CK>3x: 2 (1.9%)

- **Other**: 4 (3.7%)
  - Includes one death

Adverse events evaluated by independent adjudication CEC/DSMB.
Clinical Outcomes of FrontRunner Catheter

- **N = 909**
  - Pre-approval phase: 119 (using the largest device),
  - Post-approval phase: 197 (using a smaller, more flexible catheter),
  - Current design: 593 (using X-39 Frontrunner)
- **Lesion length**: >30mm in 21%
- **Success rate**
  - Pre-approval phase: 56%
  - Post-approval phase: 59%
  - Current design: 61%
- **Perforation**: 0.9%

FrontRunner Catheter
Milan Experiences

50 pts with 50 CTO, Refractory to guidewire
Mean occlusion length 38.3 ± 22 mm

• Overall Device Success 50 % (25)
• Coronary perforation 17.3 % (9)
• Adverse events @ 30 days 15.7 % (8)
  7 non-Q wave MI, 1 sudden death

Relatively high risk of perforation!

A Colombo et al, ACC 2004
FrontRunner Catheter

**Advantages**
- Torqueable
- Guide support
- Directable/Steerable
- Hydrophilic coating
- Blunt tip to avoid perforation
- Avoids side branches

**Disadvantages**
- Difficult anatomy: tortuosity, small vessel, heavy calcium
- Expensive
- 8 Fr guiding for curved jaw
- Failure Modes
Evolving Technology
Mechanical Tools

Fibrinolysis
IntraCoronary Lytic Infusion for Failed PCI of CTO

- 85 patients with CTO ≥ 3 months, failed PCI
- 8 hour infusion (Guide + IC Catheter)
- 61 tPA 0.25 mg/hr (weight adjusted)
- 24 TNK 0.5 mg/hr
- IV Heparin, ACT 200-250 seconds
- Hematoma 8%; Transfusion 3.5%

IC Lytic Infusion for CTO

- Lytic Infusion did not directly recanalize the CTO – but did “facilitate wire crossing” – ?
Mechanism – clot lysis or activation of other proteolytic enzymes (Matrix metalloproteinases)
Matrix Metalloproteinase

- Zinc and calcium-dependent enzymes that catalyze the breakdown of protein
- MMP-1, MMP-2, MMP-9, MMP-3
- Degrade all extracellular matrix components
- 3 broad categories:
  - Collagenases, gelatinase, and stromelysins

Guide-Wire Crossing at 72 hours

Success
Collagenase 450 ug

Failure
Placebo

Description of Procedure

A: Chronic Total Occlusion

B: Failure to Cross with Guide Wire (Choice PT, Wizdom)

C: Infusion of Collagenase through Wire Port

D: Collagenase Diffusion Through Occlusion

E: Successful Guide Wire Crossing
Chronic Total Occlusion Revascularization

Alternative Technologies

• FlowCardia CROSSER System
  - High frequency mechanical revascularization
  - Monorail, and OTW
  - 0.014” wire and 6 Fr guide compatible
  - Straight and angled tip configurations

Investigational Product Only. Not Available for Sale in the U.S.
Chronic Total Occlusion
Evolving Technology and Strategy

New Generation

- MSCT
- IC NaviView
- Magnetic RF Wire
Multislice CT Coronary Angiography

- Quantification of the length of the occlusion
- Definition of plaque composition
- Identification of calcification
- Evaluation of distal vessel
- Definition of the intra-occlusion angle
CT angiography is able to provide complementary data to that of the conventional angiography that may be relevant to the success of the CTO recanalization.

May provide a more precise lesion length, accurate data on plaque composition and calcium extent and location and intraplaque angle.
Multislice CT Coronary Angiography
Predictors of success/failure

- Length <15 mm (+)
- Severe calcification (-)
  - Blunt stump
  - Occlusion length >15 mm
  - Severe calcification

Identify Point on CT Data
AXIOM Artis dFC Magnetic Navigation

- Magnets outside the body control the catheter, which is equipped with a specially magnetized tip.
IC NaviView* – From the Touch Screen

- Simply touch the vessel location to align the guidewire

* Powered by Paieon Inc., 3-D Reconstruction Software
Prototype Magnetic RF Wire* Steering and Ablation

Test in Agar Lesion Phantom

Methodology: Magnetic directional enhancement of .014” / .018” RF guidewire

Clinical Advantages: Provides distal tip steerability and flexibility (for optimized magnetic tip deflection) - while providing ablative energy at tip

* Developed in collaboration with Baylis Medical