Occlusion Perfusion Catheter (OPC)

Next Generation Treatment for Restenosis

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Regardless of the interventional treatment utilized to maintain vessel patency in vascular disease, there will potentially always be restenosis and/or occlusions.

The only way we are going to optimally control the development of this neointimal hyperplasia is to treat it at the cellular level.

This can be accomplished by treating the “controlled injury” at the cellular level utilizing biologic, live cells or pharmaceuticals.
There are drug eluting stents and balloons in the market today which demonstrate some degree of success; however, there are significant limitations to these approaches.

- 1) There is a **single** agent tied to a **single** device
- 2) Only limited amount of an agent can be incorporated into either a balloon or stent.
- 3) At best, only 18% of a stent is in contact with the vessel wall. This leaves 82% of the wall untreated with the agent.
- 4) Stents potentially burn bridges.
- 5) Treating long and/or multiple lesions and lesions below the knee.
- 6) **COST**
What is required to address these limitations?

A universal agent delivery system:

- One that will accommodate any form of agent that is presently in the market, or those which will be developed in the future.

- One that will not be limited by long and/or multiple lesions and lesions below the knee, and will not require a stent to be placed.

- And most importantly, one that will deliver the agent(s) into the media and adventitia of the entire area of injury, circumferentially, and longitudinally.

- It is to be used following other therapies such as angioplasty, stenting or atherectomy.
Controlled, Local Delivery of Desired Agent

- Fiber Optic Pressure Sensor
- Inflow Lumen
- Inflation Lumen for Space Occupying Balloon
- Outflow Lumen
- Guide Wire Lumen
- Inflation Lumen for Occlusion Balloons
The OPC is a five lumen catheter designed with proximal and distal occlusion balloons, a center space occupying balloon, an inflow (infusion) port, an outflow port and a guide wire lumen compatible with standard 0.014” sizes.

A fiber optic pressure sensor is incorporated into the inflow lumen to monitor pressure within the treatment region.

The two compliant occlusion balloons define the treatment region.

The non-compliant center space occupying balloon reduces the total volume of the treatment region, reducing the amount of therapeutic agent used during the procedure.

The center space occupying balloon may also be used to manipulate the agent in the treatment region.

The center space occupying balloon is sized so that it does not touch the interior of the vasculature.
OPC Procedural Technique

The OPC is placed over a guidewire and the distal end of the catheter is positioned at the desired targeted treatment area of the blood vessel. The proximal and distal occlusion balloons are inflated simultaneously to control blood flow and create a treatment chamber. In addition, they serve to prevent systemic distribution of the therapeutic agent. The fourth and fifth lumens are for inflow and outflow ports located within the established treatment chamber. The trapped blood is removed from the treatment chamber by flushing with saline. The space occupying balloon can be inflated to minimize the amount of therapeutic agent necessary to treat the area(s). The space occupying balloon can also be used to control the amount of pressure required to allow the therapeutic agent to optimize penetration to the treatment area including the media of the vessel wall.

Once the treatment chamber has been evacuated, therapeutic agents are delivered through the inflow port and lumen. A sensor is incorporated into the treatment chamber at the site of the inflow port to monitor, control and optimize pressure within the chamber. Any unused portion of the therapeutic agent can be retrieved through the outflow port and lumen by again flushing with saline once the area has been treated.

The Occlusion Perfusion Catheters will be available in various sizes (length and diameter) depending on the vessel size and length of the area and disease being treated. The OPC is a single use device. Additional options for future development include the possibility of the delivery of live cells and biologics, repositioning within the same patient, incorporating a visualization device and extending use to the coronary vasculature.
# OPC Key Features Competitive Matrix

## Optimal Universal Local Drug Delivery

<table>
<thead>
<tr>
<th>Key Features</th>
<th>ACT OPC</th>
<th>Acrostat Genie</th>
<th>Atrium ClearWay RX</th>
<th>Lutonix</th>
<th>TAPAS</th>
<th>Mercator</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Places agents circumferentially into media of vessel wall</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Coats vessel wall circumferentially</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>3. Accommodates multiple therapeutic agents</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>4. Ability to flush treatment chamber</td>
<td>✓</td>
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<tr>
<td>5. Evacuates blood from treatment chamber prior to treatment</td>
<td>✓</td>
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<tr>
<td>6. Evacuates residual agent from treatment chamber</td>
<td>✓</td>
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<tr>
<td>7. Measures pressure applied inside treatment chamber</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>8. Not limited by lesion length</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>9. Not limited by multiple lesions</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>10. Treats all vascular beds (arterial and venous)</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>11. Not limited to a specific agent volume</td>
<td>✓</td>
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<tr>
<td>12. Atraumatic to vessel wall</td>
<td>✓</td>
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<tr>
<td>13. Minimizes stent usage</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Potential for angioplasty balloon to be incorporated into device</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>14. Potential for stent to be incorporated into device</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>15. No adverse affects from polymers or coatings</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>16. Does not require long term expensive anti-platelet therapy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>17. Does not require long term expensive anti-platelet therapy</td>
<td>✓</td>
<td>✓</td>
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OPC Pre-clinical Studies - Purpose

**Phase 1**
Purpose:
To assess the efficacy to deliver Paclitaxel via the OPC and to determine it’s distribution and retention within the arterial wall of a rabbit ilio-femoral artery.

**Phase 2**
Purpose:
To determine and optimize the delivery and retention of Paclitaxel using the OPC.

Study objectives:
1) To develop and validate an in vitro (bench top) vascular bioreactor system utilizing a pig carotid artery under physiological pulsatile and flow conditions to determine Paclitaxel retention using the OPC.
2) To optimize a set of criteria (pressure, concentration, excipient and dwell time) during delivery to maximize retention of Paclitaxel delivered by the OPC.
3) Test the optimal parameters identified in objective 2 in a rabbit ilio-femoral artery.
4) To evaluate the histopathologic response and drug retention of the optimal parameters long term (28 days)
The Results: Pre-Clinical 1

OPC performance in rabbit model study

- Confocal analysis demonstrated
  - Successful delivery of fluorescent paclitaxel
  - Uniformly within media and adventitial layer
  - Circumferentially and longitudinally
  - 7x increase in PK over our predicate device
The Results: Pre-Clinical 2

Deliver parameters: 2 ATM for 2 minutes
Drug: Flutax-1
Excipient: None (diluted in saline)
The Results: Pre-Clinical 2

Deliver parameters: 2 ATM for 2 minutes
Drug: Flutax-1 (Molecular Weight: 1 kDa)
Excipient: ‘X’, Molecular Weight: 30-40 kDa
Paclitaxel-induced growth inhibition of haSMCs.

A

- cell counting
- BrdU-ELISA
- MTT-test

percent control

0.0001 0.001 0.01 0.1 1.0 10.0

μmol/l paclitaxel

B

- 8 days
- 24 hours
- 20 min

percent control

0.0001 0.001 0.01 0.1 1.0 10.0

μmol/l paclitaxel

The Results: Pre-Clinical – PK Analysis

Cytotoxic range of paclitaxel\(^1\)

Effective range of paclitaxel\(^1\)
(0.085-0.85mcg/ml)
90-99% inhibition of human arterial SMC.

The Results: Pre-Clinical – 7 Day SEM
OPC equal to or better than DEB

OPC w excipient 7-day SEM
Myofibers demonstrating Paclitaxel delayed healing effect.

IN.PACT DEB 7-day SEM
Myofibers demonstrating Paclitaxel delayed healing effect.
The Results: Pre-Clinical – 28 Day Histology
OPC equal to or better than DEB

South Alabama Data
Normal Endothelium

28-day OPC (paclitaxel with excipient)

Published Data
28-day IN.PACT DEB

www.leizlip-interventional-course.com
Presented by: Robert J. Melder, Senior Director R&D, Medtronic Cardiovascular, 2012
Live Cell Testing (Not Cleared by FDA)

Assessing Endothelial Cell Viability Following Delivery via the Occlusion Perfusion Catheter Device

Conclusions

The goal of these experiments was to determine if any mechanical damage occurs during cell delivery using the OPC catheter. For this purpose, we selected a vascular cell, endothelial cells, cultured from rat aorta. Two delivery pressure parameters, 1.0-1.5 ATM (low) and 4.0 - 5.0 ATM (high), were chosen for these experiments. The results demonstrated that 80.88% of ECs displayed no damage to their cell membrane following perfusion through the 1.4 m length of the OPC catheter at the low pressure parameter. For the high pressure, 70.41% of ECs showed no cell membrane damage. Taken together, these results suggest that OPC can deliver cells with minimal mechanical damage at a wide range of pressure.
COPPER A and B TRIAL
Summary of Pre-Clinical Results

These pre-clinical studies demonstrate the OPC is as effective as the IN.PACT DEB, while providing additional advantages.

Added advantages of the OPC:
- has the ability to deliver an agent circumferentially and longitudinally into the vessel wall even with larger molecular weight agents/excipients.
- utilizing controlled pressure monitoring, it has the ability to deliver the effective range of Paclitaxel for 90-99% inhibition of human arterial SMC utilizing an excipient, while maintaining normal intimal endothelial function by non-coating.
- is not restricted to a single agent
- it can be used multiple times in the same patient
- has the ability to deliver live cells with minimal mechanical damage to the cell membrane over a wide range of pressures
- controlled pressure within the chamber negates the requirement for accurate balloon to wall measurements
- has the ability to flush the chamber, resulting in no blood/agent admixture
- minimizes systemic effect by evacuating residual agent via flushing
- decreases cost
THANK YOU!!