LimFlow Procedure

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Disclosure

• **Workshop/Speaker Honourarium:**
  Medtronic, Abbott, Straub Medical, Boston Scientific, Bard, Biotronik

• **Consultancy:**
  MdStart/LimFlow, Acelity, Abbott, Boston Scientific, Vascuros Medical, Orbus Neich

• **Equity**
  LimFlow (patent)
We are facing a **Global** CLI Pandemic
Concept of Surgical Venous Arterialization

Deep Venous Bypass

Artery

Vein

Courtesy Pramook
Surgical DVA
Failed Intervention
+
No distal target for bypass
Distal anastomosis is difficult as vein is small and prone to twisting. Valves are not easily addressed.
Extreme calcification

Post DVA
Concept of Venous Arterialization

- Artery
- Vein
- Venous collateral
- Valves
- Capillary bed
Concept of LimFlow
Anatomy of a Valve

Leaflet

Annulus
Cutting Balloon Vs Valvulotome

Cadaveric Angioscope with Flow
Case Examples
Distal Foot Angioplasty Failed

Severe Calcium
Arterial Flow to Venous Arch achieved
Non healing for 6 months

Almost fully healed in 2.5 month
80 Male
Severe Rest Pain & Toe Gangrene
Diabetic
Hypertensive
85 yrs old Female
Severe Rest Pain & Toe Gangrene
Diabetic
Hypertensive
Poor Perfusion TcpO2 = 3mmHg

Day 150
Wound healed

LimFlow 4
LimFlow 10

85 yrs old Female
Severe Rest Pain & Toe Gangrene
Diabetic
Hypertensive
Poor Perfusion TcpO2 = 16 mmHg

Day 194
Wound healed
62 yrs old Female

*Heel Gangrene Failed Intervention to PT*

Diabetic
Hypertensive
Poor Perfusion TcpO2 = 29 mmHg

Day 114
Wound healed
72 yrs old Male
Severe Rest Pain & Toe Gangrene
Protein C/S Deficiency + Thrombocytosis
Multiple Interventions and Thrombolysis
Poor Perfusion TcpO2 = 4 mmHg
Cellutome Epidermal Graft

Day 190
Wound healed
Some of the European & US cases.
Antonius Ziekenhuis, Netherlands

Daniel Van den heuvel
Jean Paul DeVries

LimFlow

6.5 months
150mm Covered Stent
7F deliverable
now CE marked

27 July 2017
Peroneal feeds
Tarsal Branch
There is perfusion after the graft occludes...
Singapore
No. 3

28 July 2014

TCPO2 = 24

Symptom Free
Persistent AVF signal even with graft occlusion

7 months of primary patency
8 months for wound healing

7 Oct 2015

TCPO2 > 50
3 months of primary patency
8 months of secondary patency
5 months for wound healing

28 Aug 2014

22 Oct 2015

TCPO2 = 19

TCPO2 = 75

Symptom Free
Persistent AVF signal even with graft occlusion

Singapore No. 4
Leipzig No. 3

Before LimFlow

Control After LimFlow
Stent Occluded

Continued Perfusion despite Occlusion
Collaterals after Occluded Surgical DVA

TCPO2 = 8mmHg

4 months

TCPO2 = 65 mmHg

Courtesy Ferraresi
TCPO2 remains high despite no DVA post explantation of covered stent.
HYPOTHESIS

Pressurization of Venous Bed allows collaterals to reach CAPILLARY BED

Persistent collateral circulation after occlusion of PBDVA

Courtesy Pramook
DCB Assisted Patency

564 Days of Patency from procedure date

15/09/14 → 07/01/16
Pilot Study – 7 “No-Option” CLI patients


* Minor complications: two non-ST, non-procedure related elevated MIs; one patient developed spontaneous retroperitoneal bleeding 8 weeks’ post-procedure and was managed conservatively after cessation of anticoagulation.

# three procedure unrelated deaths within 12 months: 2 patients died of pneumonia at 6 and 8 months, respectively; 1 patient had a fatal MI at 7 months following above-the-knee amputation.
Pilot Study – 12 months Endpoints

Median time to wound healing = 145 days

Complete Wound Healing
- 6 Months: 57%
- 12 months: 71%

Limb Salvage
- 6 Months: 71%
- 12 months: 86%

Perfusion - TcPO2
- @ Baseline: 8
- @ Wound Healing: 59

p = 0.080
Summary of Experience – Objective Measurement of Perfusion with TCPO2
• 43 “No option” patients

• Mean age 68 y.o. (range 36-94 y.o.)

• Majority of male patients (61% male, 39% female)

• 81% of the patients were diabetic

• As of today 22% of patients were on dialysis
Clinical Summary – all patients to date

First 43 LimFlow Patients
Survival and Amputation Free
Kaplan-Meier

71% patients alive and amputation free 6 months after pDVA
AFS were 86 ± 2%, 81 ± 2%, 77 ± 3%, and 74 ± 3% at 3, 6, 9, and 12 months, respectively.

Independent predictors for AFS

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;18.5</td>
<td>2.22(1.23-4.01)</td>
<td>0.008</td>
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<tr>
<td>Statin administration</td>
<td>0.59(0.30-1.13)</td>
<td>0.11</td>
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<tr>
<td>Anemia</td>
<td>1.80(0.97-3.32)</td>
<td>0.06</td>
</tr>
<tr>
<td>Heat failure</td>
<td>1.73(1.02-2.91)</td>
<td>0.04</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1.89(1.07-3.32)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Secondary Endpoint:
Time to wound healing

Median time requiring complete wound healing was 97 ± 10 days.
The proportion of not-healed patients was 54 ± 3%, 29 ± 3%, 18 ± 3%, and 14 ± 3% at 3, 6, 9, and 12 months, respectively.

Factors predicting failure to achieve healing after 97 days

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;18.5</td>
<td>0.54 (0.31-0.96)</td>
<td>0.03</td>
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<tr>
<td>Hemodialysis</td>
<td>0.79 (0.58-1.09)</td>
<td>0.15</td>
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<tr>
<td>Wound infection</td>
<td>0.60 (0.36-0.98)</td>
<td>0.04</td>
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<table>
<thead>
<tr>
<th></th>
<th>Pilot</th>
<th>Pre and Post CE Mark</th>
<th>U.S. Feasibility</th>
<th>OUS Post-Market</th>
<th>U.S. Pivotal</th>
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<tbody>
<tr>
<td><strong># Patients</strong></td>
<td>7</td>
<td>36</td>
<td>10 ➔ 25</td>
<td>50</td>
<td>60 – 120</td>
</tr>
<tr>
<td><strong># Centers</strong></td>
<td>1</td>
<td>9</td>
<td>3 ➔ 6</td>
<td>10</td>
<td>20</td>
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<tr>
<td><strong>Protocol</strong></td>
<td>Single-center, prospective, open label</td>
<td>Multi-center, prospective, open label</td>
<td>Multi-center, prospective, single-arm</td>
<td>Multi-center, prospective, single-arm</td>
<td>Multi-center, prospective, efficacy and safety study</td>
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<td><strong>Countries</strong></td>
<td>Singapore</td>
<td>France, Germany, Italy, Netherlands, Singapore</td>
<td>U.S.</td>
<td>EU, Singapore</td>
<td>U.S.</td>
</tr>
</tbody>
</table>
Hello doctor Kum,

Thank you for the successful Limflow operation on January 19th, 2017 in Alkmaar. Everything is going well now and I’m working full time as a moving agent. We just enjoyed our honeymoon to New York. Thanks for everything!

Kind Regards,
Michel & Elvira Gruizinga from Holland
Summary

• Safe, effective but there is a learning curve

• A **viable solution** to treat patients with “No Option CLI” eg Desert Foots, Renal Failure, Severe calcification

• In Combination with a **Dedicated Wound Care Service**, can yield acceptable **Limb Salvage** and **Wound Healing** in a complex group of patients

• Potentially **applicable to any angiosome** that cannot be opened via conventional techniques

• **Sustained Perfusion** after graft occlusion is surprising and has potential benefits

• FDA granted Expedited Access Pathway Oct 2017. Site selection on going focussing on ability to deliver quality wound care.
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