The ROX Coupler: Status and Data Supporting an Endovascular Iliac A-V Fistula for Resistant Hypertension

David H. Deaton, MD FACS
Vascular Surgery, University of South Carolina / Columbia, SC
Chief Medical Officer, Syntactx / New York, NY

Placement between Iliac Artery & Vein

CLOSED
182 mmHg

CLOSED
180 mmHg

OPEN
158 mmHg

Disclosures
- Clinical Practice: Palmetto Health / University of South Carolina / Columbia, SC
- Chief Medical Officer: Syntactx, New York, NY (CRO)
- Consultant: LimFlow / Medtronic

As We Age, Hypertension is Increasingly Mechanical


2001

Isolated Systolic HTN
Subset of 'Mechanical Hypertension'

85% of uncontrolled patients are over 50y

The ROX Technology & Procedure
- The ROX procedure creates a precise 4mm anastomosis within the iliac circulation
- This ROX Coupler is inserted through a catheter based system percutaneously
- The ROX procedure is performed in an angiography suite, under local anesthesia
- The procedure takes about one hour
- Typically requires an overnight stay in the hospital

Immediate Results: Recent Experience in Europe

Recent patient treated in Toulouse, France:
- Immediate 70+ mmHg reduction in systolic blood pressure
- 32 mmHg reduction in systolic ABP

Data from Europe in 54 patients treated has shown:
- A mean drop of 28mmHg systolic blood pressure on the day of the procedure
- ALL Patients had a Reduction in BP on Day 0 and/or Day 1

* Data presented at the European Society of Hypertension, June 2018

205/119
134/69

Day 0:
Immediate Reduction On the Table:

Day 1:
Reduction in ABP

Data from Europe in 54 patients treated has shown:
- A mean drop of 28mmHg systolic blood pressure on the day of the procedure
- ALL Patients had a Reduction in BP on Day 0 and/or Day 1

The Lancet (6 Months) and Hypertension (12 Months)

Central Iliac Arteriovenous Anastomosis
for Uncontrolled Hypertension:
12 Month Follow Up Results of the ROX Control HTN Randomized Controlled Study

The ROX procedure creates a precise 4mm anastomosis within the iliac circulation.

This ROX Coupler is inserted through a catheter based system percutaneously.

The ROX procedure is performed in an angiography suite, under local anesthesia.

The procedure takes about one hour.

Typically requires an overnight stay in the hospital.

Immediate Results: Recent Experience in Europe

Recent patient treated in Toulouse, France:
- Immediate 70+ mmHg reduction in systolic blood pressure
- 32 mmHg reduction in systolic ABP

Data from Europe in 54 patients treated has shown:
- A mean drop of 28mmHg systolic blood pressure on the day of the procedure
- ALL Patients had a Reduction in BP on Day 0 and/or Day 1

* Data presented at the European Society of Hypertension, June 2018

205/119
134/69

Day 0:
Immediate Reduction On the Table:

Day 1:
Reduction in ABP

Data from Europe in 54 patients treated has shown:
- A mean drop of 28mmHg systolic blood pressure on the day of the procedure
- ALL Patients had a Reduction in BP on Day 0 and/or Day 1

* Data presented at the European Society of Hypertension, June 2018

205/119
134/69
Study Design:
- Prospective, randomized 1:1, controlled
- Enrolled 83 patients randomized (44 treatment / 39 control) in 16 European centers
- Targeted patient population
  - Adults (18-80 years of age)
  - Stable on 3 meds of different classes including a diuretic
  - Office Systolic BP >140mmHg and 24hr ABPM >135/85 mmHg
- Arms:  Control: continued medications vs ROX Coupler + continued medications

Exclusion criteria:
- Secondary hypertension (other than sleep apnea)
- Type 1 diabetes
- Renal denervation (RDN) within the previous six months
- Pulmonary arterial hypertension (mean pulmonary artery pressure > 25 mmHg)
- Elevated pulmonary capillary wedge pressure (>25 mmHg)
- Significant known cardiac, vascular, or cerebrovascular disease or stroke within past year
- Severe chronic kidney disease (eGFR < 30 mL/min/1.73 m^2, MDRD calculation)

Randomized Lancet Study RH-02

Office BP Changes

Results - Effectiveness

Prior Renal Denervation Subset

Venous Stenosis Occurrence - RH-02 HTN Randomized Trial

100% Resolution

All Successfully treated with iliac venous stent with no recurrence
Randomized Lancet Study RH-02

Non-Responders

- 2 of 39 patients in primary 12-mo analysis did not have ≥ 5mmHg OSBP or ABP drop
- 1 of 2 had pre-existing Afib that resolved at 12-mo; patient then had >25mmHg drop at 24 mo's

ROX CONTROL HTN-2 FDA Pivotal Trial: Study Design

Prospective, Randomized, Adaptive, Double-Blind, Sham-Controlled, Multicenter Study

- Study Objective: To evaluate the safety and effectiveness of the ROX Coupler used to create an arteriovenous anastomosis in the iliac region (between the iliac artery and vein) in subjects with hypertension
- Study Enrollment: Up to 500 subjects (First Bayesian evaluation at 250 patients)
- Follow-up Visits: Days 1, Week 4, and Months 1, 3, 6, 9 and 12
- Withdrawal Visit: Subjects who voluntarily withdraw from the study prior to completion
- Primary Endpoint
  - Change in 24-hour ABPM mean systolic blood pressure at Month 6 as compared to baseline
- Secondary Endpoint
  - Change in mean office systolic blood pressure at Month 6 as compared to baseline
- Safety Outcomes
  - Incidence of complications directly associated with the ROX or sham procedure
  - Incidence of adverse events

ROX CONTROL HTN-2 Key Inclusion & Exclusion Criteria

Inclusion
- Individuals taking 3 or more blood pressure medications:
  - A diuretic drug AND
  - Two additional antihypertensive drugs from two different classes OR
  - Have a documented intolerance to at least 3 of the 4 major classes of hypertensive medications and still have systolic blood pressure greater than 155 mmHg
- Subjects must meet the blood pressure inclusion criteria and be euvolemic on a stable drug regimen for 3 months prior to screening
  - This drug regimen should be maintained throughout the screening and for 6 months post-randomization
  - Individuals must be on stable regimen of diet, exercise and medications and still demonstrate an elevated blood pressure over the first 3 office visit screenings

Key Exclusions
- Significant peripheral arterial or venous disease
- Unstable heart disease or heart failure
- Severe chronic kidney disease
- Body Mass Index greater than 40 kg/m²

ROX Iliac AVF vs. Denervation

- Denervation
  - No procedural endpoint (no immediate BP effect)
  - Smaller and inconsistent BP effect
  - Autonomic nerves regenerate
  - Dependent on renal artery anatomy
  - Risk of renal artery injury
- AVF
  - Immediate and significant BP effect
  - Scalable and reversible
  - Independent of renal artery anatomy
  - Effective in patients with prior renal denervation
  - DURABLE

Thank you
YES.... But

- How many patients affected by Type II
  - Roughly 15-20%
- How many of those with Type II persist and need treatment
  - Roughly 20% of those with Type II
- So 20% of 20% is 4% of all patients treated
- What are the implications??

### CONTROL-HTN Study: Durable Benefits

**12 Month Outcomes (Hypertension, 2017)**

<table>
<thead>
<tr>
<th></th>
<th>ROX® 6 Months (N=42)</th>
<th>ROX® 12 Months (N=36)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in Systolic In-Office BP vs. baseline</td>
<td>-26.9</td>
<td>-25.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean change in Diastolic In-Office BP vs. baseline</td>
<td>-20.1</td>
<td>-20.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean change in Systolic ABP vs. baseline</td>
<td>-13.5</td>
<td>-12.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean change in Diastolic ABP vs. baseline</td>
<td>-13.5</td>
<td>-15.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Significant BP reductions sustained at 12 months