2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

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ROX Endovascular System for Hypertension: A Novel Concept

Global Impact of HTN

- HTN was the cause of about 10.3 million deaths and loss of 208 million disability-adjusted life years in 2013
- Cause of 50% of heart disease, stroke and heart failure
- Responsible for 19% of deaths overall
- Responsible for >40% of deaths in persons with diabetes
- Leading risk for
  - Fetal and maternal death in pregnancy
  - Dementia
  - Renal failure
- Public Health Epidemic
  - 4 in 10 adults >25 yo have HTN
  - Estimated 9 of 10 adults who live to 80 will develop HTN
- Impact on healthcare spending is immense
  - 10% of total healthcare spending is directly related to HTN and its complications

Global Burden of Disease Study, 2014

World Health Organization. A Global Brief on Hypertension: Silent Killer, Global Public Health Crisis. World Health Day 2013. Geneva, Switzerland: World Health Organization; 2013.

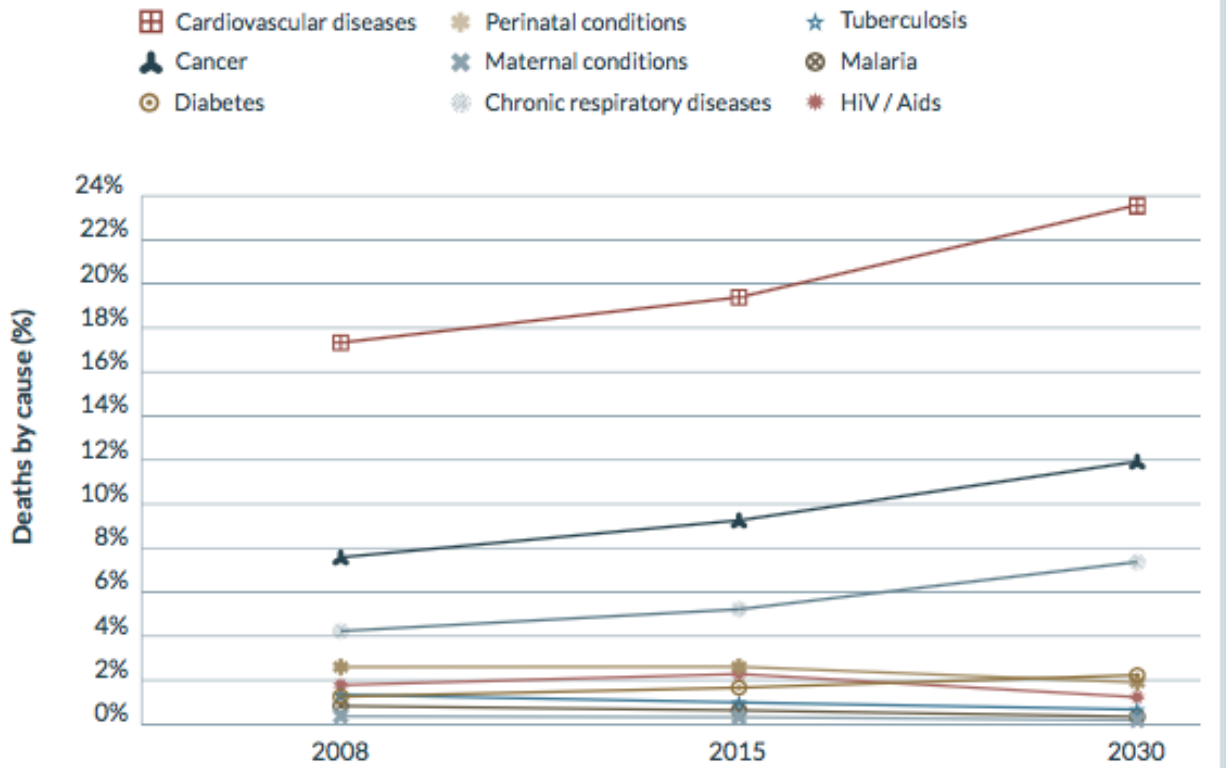


FIGURE 04

THE PROJECTED MORTALITY TREND FROM 2008 TO 2030 FOR MAJOR NONCOMMUNICABLE DISEASES AND COMMUNICABLE DISEASES

Source:

The Global Burden of Disease, 2004 update. Geneva, World Health Organization, 2008.

A Treatment Challenge

- < 50% of patients achieve optimum BP control and maintain long-term adherence
- Medication non-compliance
- Need for polypharmacy compounds complexity of treatment

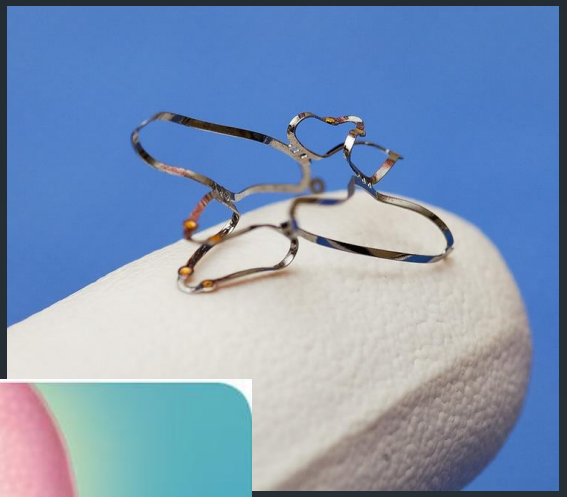
- Small increments in BP increase are clinically significant
  - ↑ 2mm Hg SBP leads to
    - 7% increase in risk of dying from CAD
    - 10% increased risk for CVA

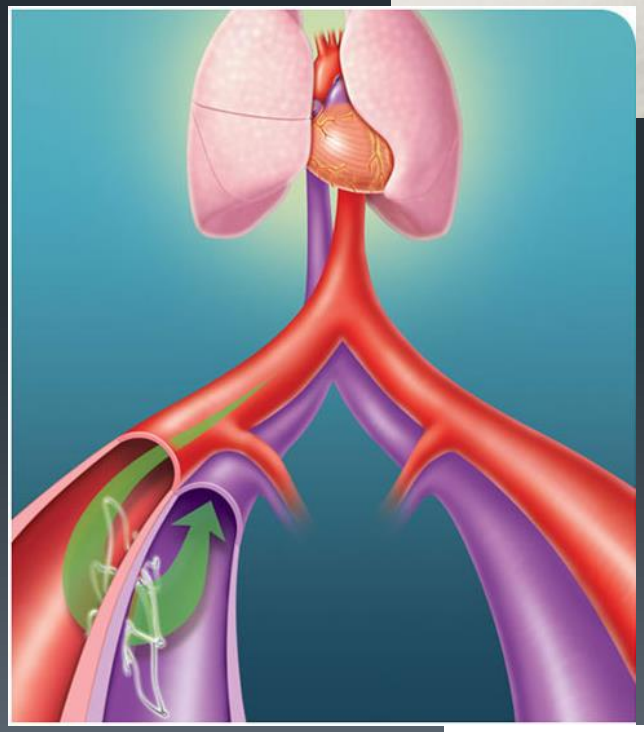
- Safe, acceptable and effective treatment strategies required
  - Polypharmacy often not conducive to adherence
  - Drug-resistant HTN

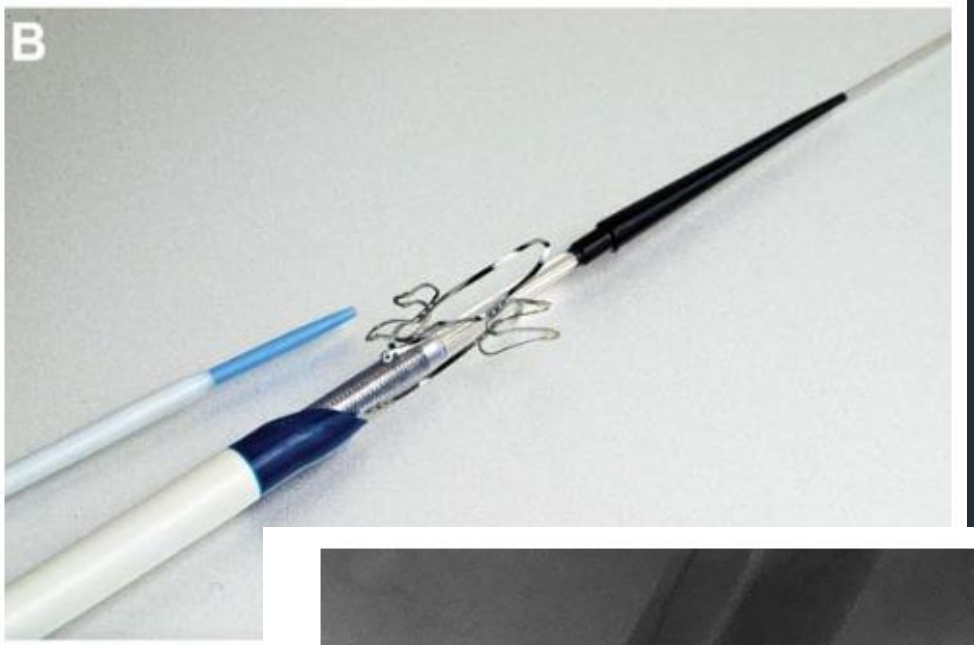
A safe and effective medical device capable of lowering BP would address these concerns

ROX Coupler

- Investigational device
  - Approved for use in Europe
- Developed by ROX Medical
- Percutaneously inserted to create AVF between distal external iliac vein and artery
  - 4mm anastomosis
  - ~ 800ml/min blood flow
- Initially studied in COPD patients with hypoxemia and its effect on exercise capacity
  - Noted significant drop in BP in hypertensive participants in the study
- International CONTROL-HTN trial to study effect on BP has been completed







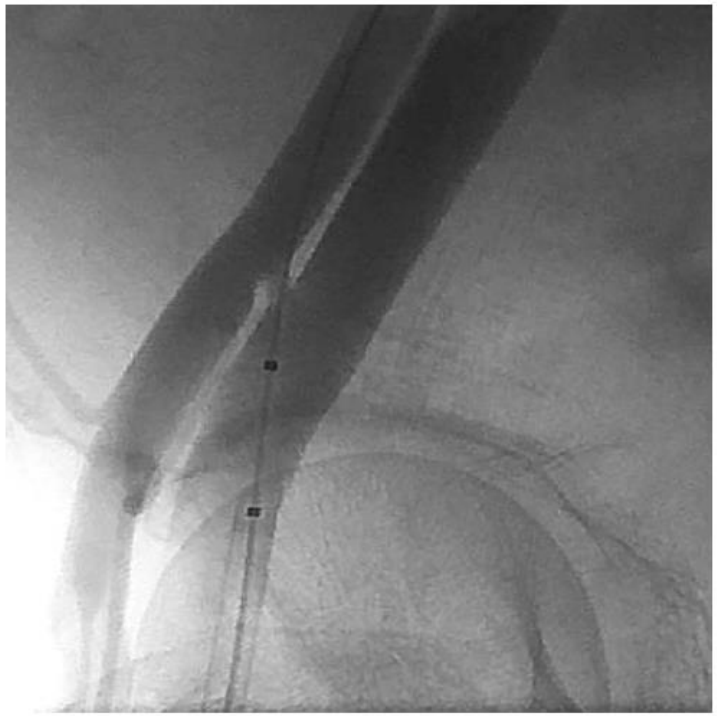


Fig. 3. Radiograph of the coupler in proper position, between the distal external iliac vein and artery, following balloon dilation.

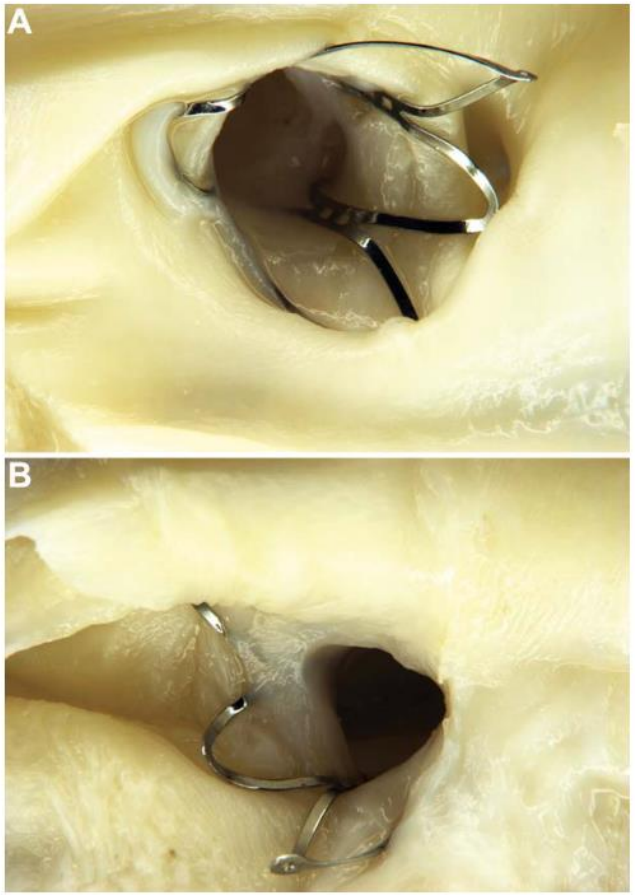


Fig. 1. Anastomosis created by arteriovenous coupler in sheep aorta at 6 months. The lumen of the anastomosis does not demonstrate overgrowth or obstruction, and the circular entry and exit faces are preserved. A, Artery; B, Vein. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Central arteriovenous anastomosis for the treatment of patients with uncontrolled hypertension (the ROX CONTROL HTN study): a randomised controlled trial

*Melvin D Lobo, Paul A Sobotka, Alice Stanton, John R Cockcroft, Neil Sulke, Eamon Dolan, Markus van der Giet, Joachim Hoyer, Stephen S Furniss, John P Foran, Adam Witkowski, Andrzej Januszewicz, Danny Schoors, Konstantinos Tsioufis, Benno J Rensing, Benjamin Scott, G André Ng, Christian Ott, Roland E Schmieder, for the ROX CONTROL HTN Investigators**

Lancet 2015; 385: 1634–41

- Open-label, multicenter, prospective RCT
- 83 patients, drug-resistant
- 2 treatment arms
  - Implantation of coupler device + current pharmaceutical treatment (42)
  - Current treatment alone (35)
- Primary Endpoint – 6 months
  - Mean change from baseline and 24h SBP
- Intention-to-treat analysis

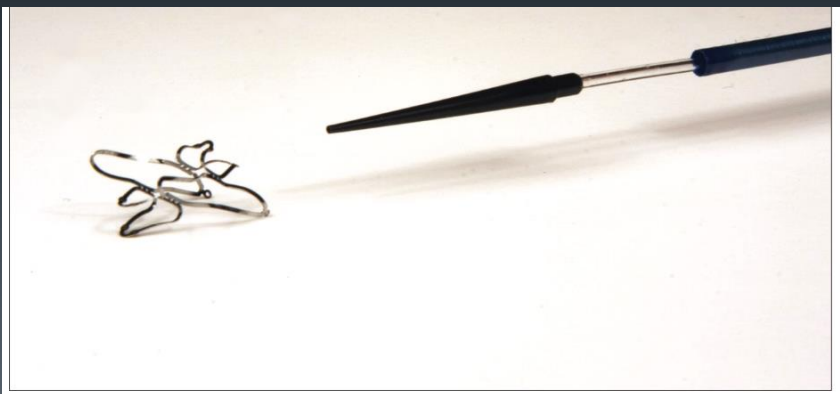


Figure 1: **Arteriovenous ROX Coupler and deployment catheter**
Reproduced by permission of ROX Medical, San Clemente, CA, USA.

Results

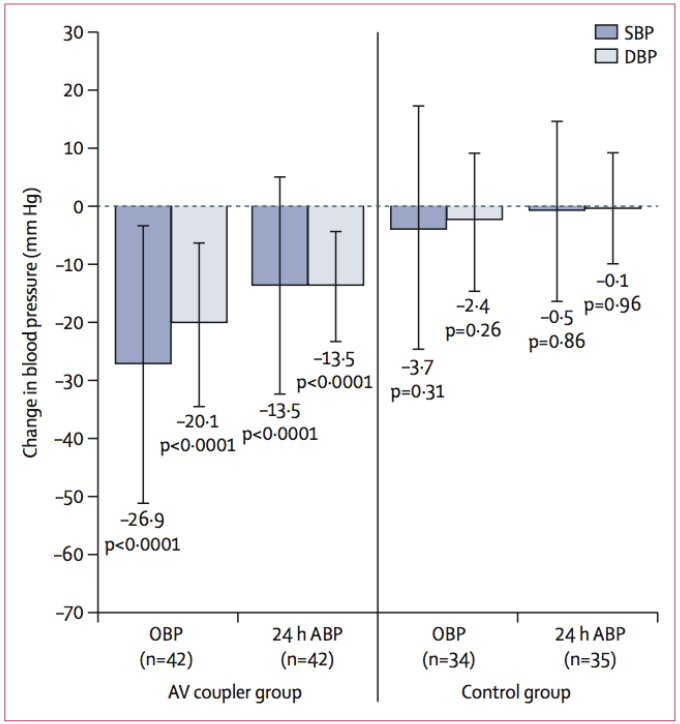


Figure 3: **Change from baseline in blood pressure at 6 months**
Data are mean (SD). SBP=systolic blood pressure. DBP=diastolic blood pressure. OBP=office blood pressure. ABP=ambulatory blood pressure. AV=arteriovenous.

- Coupler group has significantly greater decrease in baseline BP than control group
- Reduction in antihypertensive meds
  - 19% in coupler group
  - none in control group
- hospital admissions for hypertensive crises
  - None in coupler group
  - 8% in control

Procedural and Device Complications

	Number (%) of adverse events (n=42)
Procedural complication	
Arterial deployment*	3 (7·1%)
Intimal dissection iliac artery	1 (2·4%)
Transient bradycardia	1 (2·4%)
Contrast reaction	1 (2·4%)
Urinary retention	1 (2·4%)
Anaemia	1 (2·4%)
Transient or localised pain	2 (4·8%)
Nausea or lethargy	1 (2·4%)
Deep venous thrombosis	1 (2·4%)
Lower limb pain	1 (2·4%)
Device-related event	
Venous stenosis	12 (28·6%) ★

*Coupler retrieved via arterial sheath and second coupler successfully deployed.

Table 3: **Adverse events related to arteriovenous coupler placement or device**

★ symptomatic

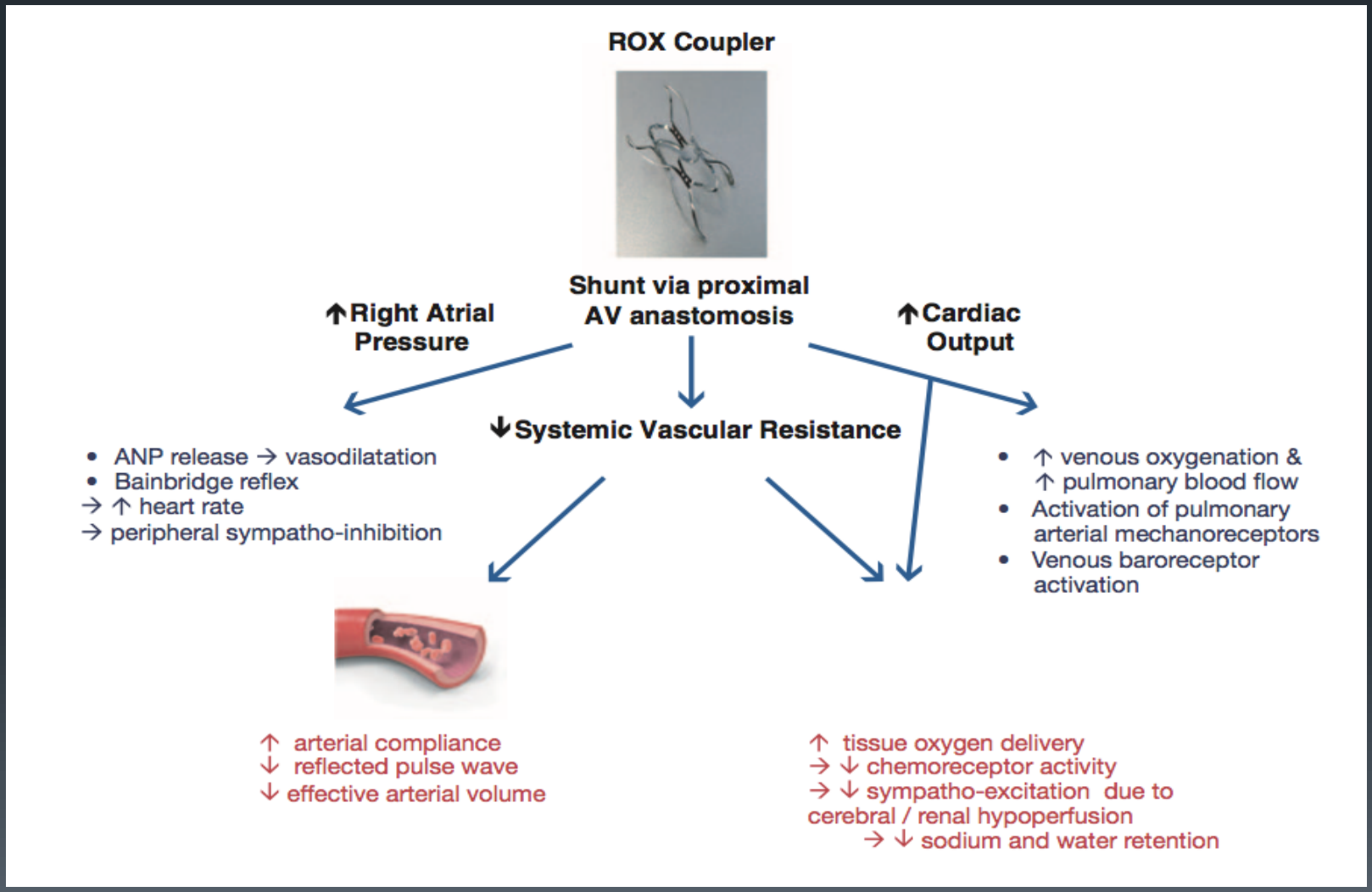
ROX Coupler Trials

Rox Medical Coupler trials				
Phase	Study name	Description	Enrolment	Trial ID
Phase II	RH-01	European pilot study in resistant hypertension	8	NCT01682057
Phase III	RH-02	European pivotal study in resistant hypertension	100	NCT01642498
Phase III	RH-03	European post-approval registry in hypertension	100	NCT01885390
Phase III	US HTN-01	US pivotal study in resistant hypertension	500	NCT02895386

Current ROX Coupler Trials - US

Rank	Status	Study
1	Not yet recruiting	AF Ablation With or Without ROX Coupler Study **Conditions:** Atrial Fibrillation; Hypertension **Interventions:** Procedure: Atrial fibrillation ablation; Procedure: ROX Coupler insertion **Phase:** Phase 4
2	Recruiting	Registry to Evaluate the ROX COUPLER in Patients With Resistant or Uncontrolled Hypertension **Conditions:** Hypertension; Blood Pressure, High; Blood Pressure, Resistant; Blood Pressure, Uncontrolled **Intervention:** Device: ROX COUPLER **Phase:** Phase 3
3	Not yet recruiting	A Multicenter Study to Evaluate the ROX Coupler in Subjects With Hypertension **Conditions:** Hypertension; Blood Pressure **Interventions:** Device: ROX Coupler; Other: Sham procedure **Phase:** Phase 3
4	Active, not recruiting	A Multicenter Study to Evaluate the ROX Arteriovenous Coupler in Patients With Treatment-Resistant Hypertension **Condition:** Hypertension **Intervention:** Device: ROX COUPLER **Phase:** Phase 3
5	Unknown †	The Iliac Arterio-venous Fistula for Treatment of Neurally Mediated Syncope Study **Condition:** Neurally Mediated Syncope **Interventions:** Device: ROX COUPLER; Procedure: Right heart catheterisation and routine care **Phase:**
6	Completed	A Multicenter Study to Evaluate the ROX Anastomotic Coupler System (ACS) In Patients With Severe Hypertension **Condition:** Hypertension **Interventions:** Device: ROX ANASTOMOTIC COUPLER SYSTEM (ACS); Device: ROX Anastomotic Coupler System (ACS) **Phase:** Phase 2
7	Completed	A Pilot Study to Evaluate the ROX Anastomotic Coupler System in Patients With Chronic Obstructive Pulmonary Disease **Condition:** Chronic Obstructive Pulmonary Disease **Intervention:** Device: ROX Anastomotic Coupler System (ACS) **Phase:** Phase 2
8	Completed	Study of the Effect of the ROX AC1 on Exercise Capacity and Quality of Life in Chronic Obstructive Pulmonary Disease (COPD) Patients **Condition:** Chronic Obstructive Pulmonary Disease **Intervention:** Device: Arteriovenous Fistula (ROX AC1) **Phase:** Phase 4

Proposed Mechanism of Action



Conclusions

- Drug-resistant hypertension, and hypertension in general, is a growing global health epidemic with significant morbidity and mortality.
- Tremendous financial impact in terms of lost productivity as well as health care delivery costs
- Current medical therapies fail in ~ 50% of patients
- ROX coupler may present a novel approach to the treatment of hypertension
  - Relatively safe, quick and minimally invasive procedure
  - Has shown some efficacy

- BUT
  - Cardiovascular consequences remain unknown, especially long term
    - increased risk of high-output cardiac failure?
  - 30% venous stenosis rate with possibility of significant morbidity
  - Currently not approved for use in the US

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Thank you for your attention