HTH Technology Matters. Return on experience
The Vessix technology

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Faculty disclosure

I disclose the following financial relationships:

I have no financial relationships to disclose.

Vessix Renal Denervation System

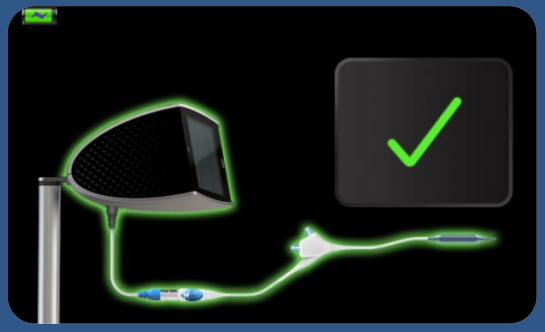
- **Balloon-based technology**
  - ***4 to 7 mm diameters***
  - ***Helical pattern of bipolar radiofrequency electrodes***
- **30 second treatment time**
- **All electrodes are activated simultaneously**

- **Bipolar energy delivery, ~1 Watt**
- **Temperature-controlled algorithm**
- **ensures energy delivery at 68°C**
- **One button operation**

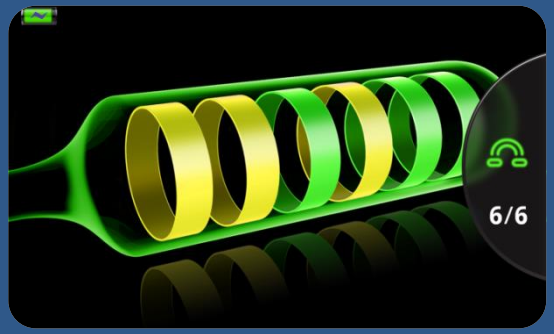
Vessix™ System: *Intuitive User interface*

Splash Screen

Image flashes prompting user to connect catheter

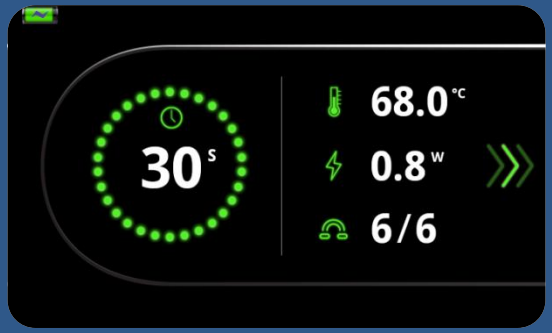


Confirms catheter is connected



Electrode pairs light up to confirm apposition inside renal artery

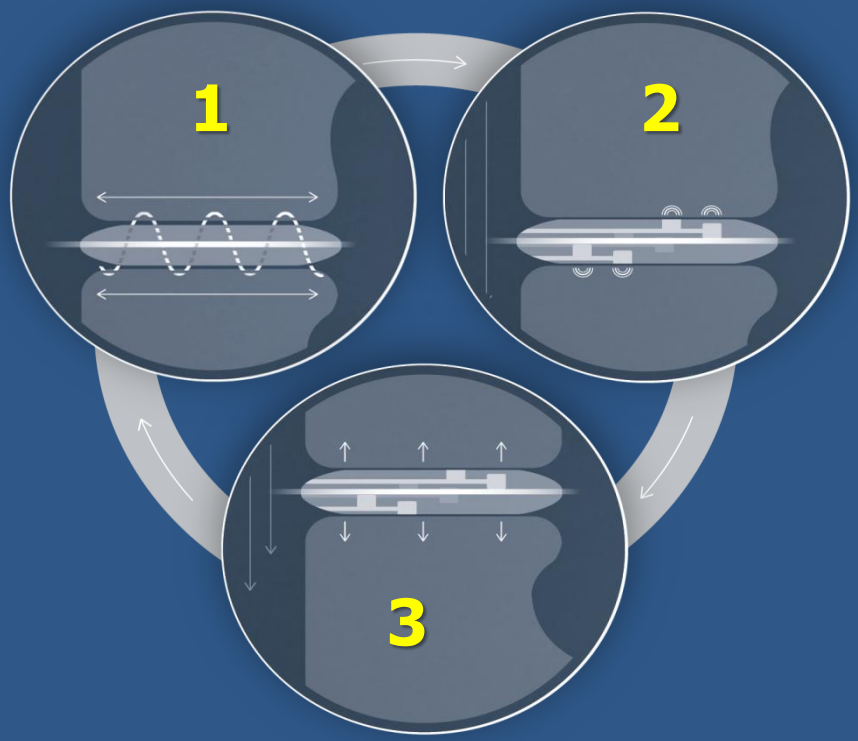
Treatment screen, indicates temperature, time, power, and # of electrodes treating



End of treatment screen, displaying average treatment temperature, time, power and # of electrodes activated

Vessix™ System Attributes

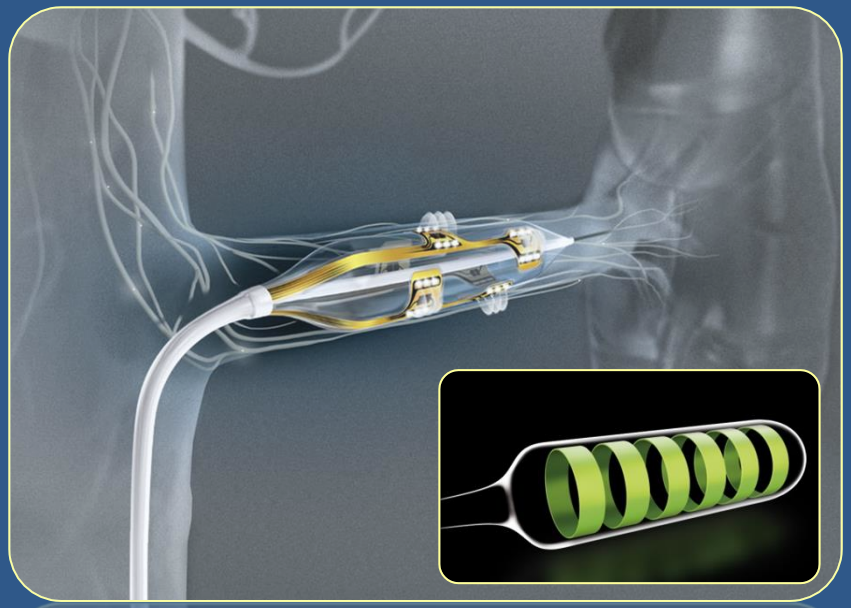
Fixed Pattern
Vessix System treats the full length of the artery in a fixed helical pattern

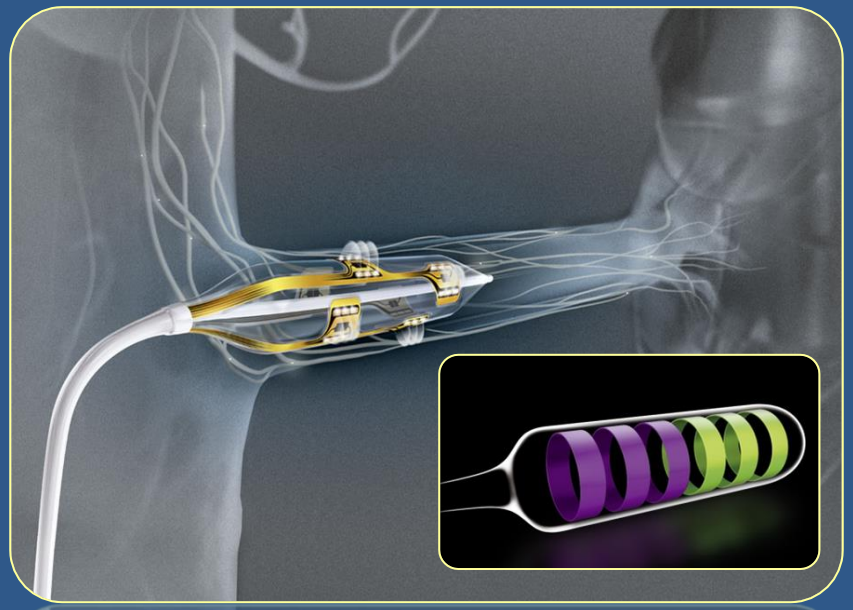


Bipolar
Bipolar electrodes on a balloon platform enable targeted, temperature controlled energy delivery

Balloon
Balloon provides firm vessel apposition of electrodes and occludes blood flow, for predictable treatment

The Vessix™ System: Treatment of the full length of artery





Automatic de-activation of unapposed electrodes

For longer length renal arteries, 1-2 treatments can be applied

Balloon inflated to a maximum of 3 Atm

Renal Denervation Technologies

	BSC Vessix	MDT Flex	MDT Spyral	STJ EnligHTN	JNJ RenLane
					
Catheter Design	**Balloon catheter, 4-8 electrodes**	**Single electrode**	**Pigtail Catheter, 4 electrodes**	**Basket, 4 electrodes**	**Pigtail Catheter, 5 electrodes, irrigated**
Balloon	✓	--	--	--	--
Guidewire	✓	--	✓	--	✓
Energy	**Bipolar RF**	**Monopolar RF**	**Monopolar RF**	**Monopolar RF**	**Monopolar RF**
Power	**~1W**	**~ 8W**	**6.5W**	**8W**	**Unknown**
Total Treatment Time	**1-2 min.**	**16-24 min.**	**2-4 min.**	**4 min.**	**Unknown**

Boston Scientific Renal Denervation Program

Vessix™ Global Clinical Program

> 1200 Patients planned worldwide

REDUCE-HTN Clinical Series

Studies evaluating the Vessix System technology in the currently defined hypertension space:

- **REDUCE-HTN FIM Study**
- **REDUCE-HTN Post Market Study**
- **REDUCE-HTN Global Pivotal Study**
- **REDUCE-HTN Regional Reg. Approval Studies**
- **REDUCE-HTN EU Post Market Trial**

RELIEVE Clinical Series

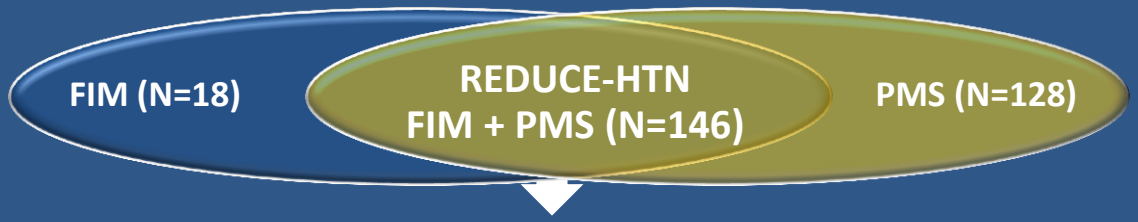
Includes pre-clinical, clinical and investigator initiated research evaluating the Vessix System technology in additional disease states:

- **RELIEVE - End Stage Renal Disease**
- **RELIEVE - Heart Failure**
- **RELIEVE - Atrial Fibrillation**
- **RELIEVE - Diabetes**

REDUCE-HTN Clinical Sites

Institution	Principal Investigator
Parcelsus Medical University	Prof. Dr. Uta C. Hoppe
Allgemein Affentliches Krankenhaus der Stad Linz	Prof. Dr. Clemens Steinwender
Onze-Lieve-Vrouwziekenhuis, (OLVZ)	Dr. Eric Wyffels
Monash Heart Southern Health	Prof. Dr. Ian Meredith
CardioVasculares Centrum (CVC) Frankfurt	Prof. Dr. med Horst Sievert
George Pompidou Hospital	Prof. Dr. Michel Azizi
The Prince Charles Hospital	Associate Prof. Darren Walters
Cardiology Center Geneva university Hospitals	Dr. Georg Ehret
Auckland City Hospital	Dr. Mark Webster
Flinders Medical Centre	Dr. Ajay Sinhal
Erasmus Medical Center	Dr. Joost Daemen
Vascular Center Berlin	Dr. Ralf Langhoff
Main Tanus Kliniken	Prof. Dr. med. Nicolaus Reifart
St. Vincent's	Dr. David Muller
Zentrum für Gefäßmedizin	Prof. Dierk Scheinert
Academic Medical Center	Prof. Robbert-Jan de Winter
Cliniques Universitaires Saint Luc	Prof. dr. Alexandre Persu
Clinique Pasteur	Prof. Jean Fajadet
German Heart Centre	Prof. Dr. med. Ilka Ott
Universitäres Herz- und Gefäßzentrum Hamburg	Prof. Dr. med. Joachim Schofer
Zentralklinik Bad Berka GmbH	Dr. med. Ahmed Farah
Royal Adelaide Hospital	Prof. Steven Worthley
Mercy Angiography - Auckland	Dr. John Ormiston

REDUCE-HTN FIM+PMS



Key Inclusion Criteria

- Office-based blood pressure (average of 3 readings):
  - First in Man (FIM): systolic blood pressure ≥ 160 mmHg
  - Post-Market Study (PMS): systolic/diastolic ≥ 160/90 mmHg
- ≥ 3 antihypertensive drugs at maximally tolerated doses with stable regimen for at least 2 weeks prior to enrollment
- Renal artery length:
  - FIM: ≥ 20 mm
  - PMS: ≥ 15 mm
- Renal artery without significant stenosis (i.e., baseline diameter stenosis <30%)
- Main renal artery diameter of ≥ 3.5 mm and ≤ 7.0 mm for each kidney:
  - FIM: Single renal artery
  - PMS: Subjects with accessory renal arteries were enrolled

Efficacy Measures

- Office blood pressure (through 18 months)
- 24-hour ambulatory blood pressure (6 and 12 months)

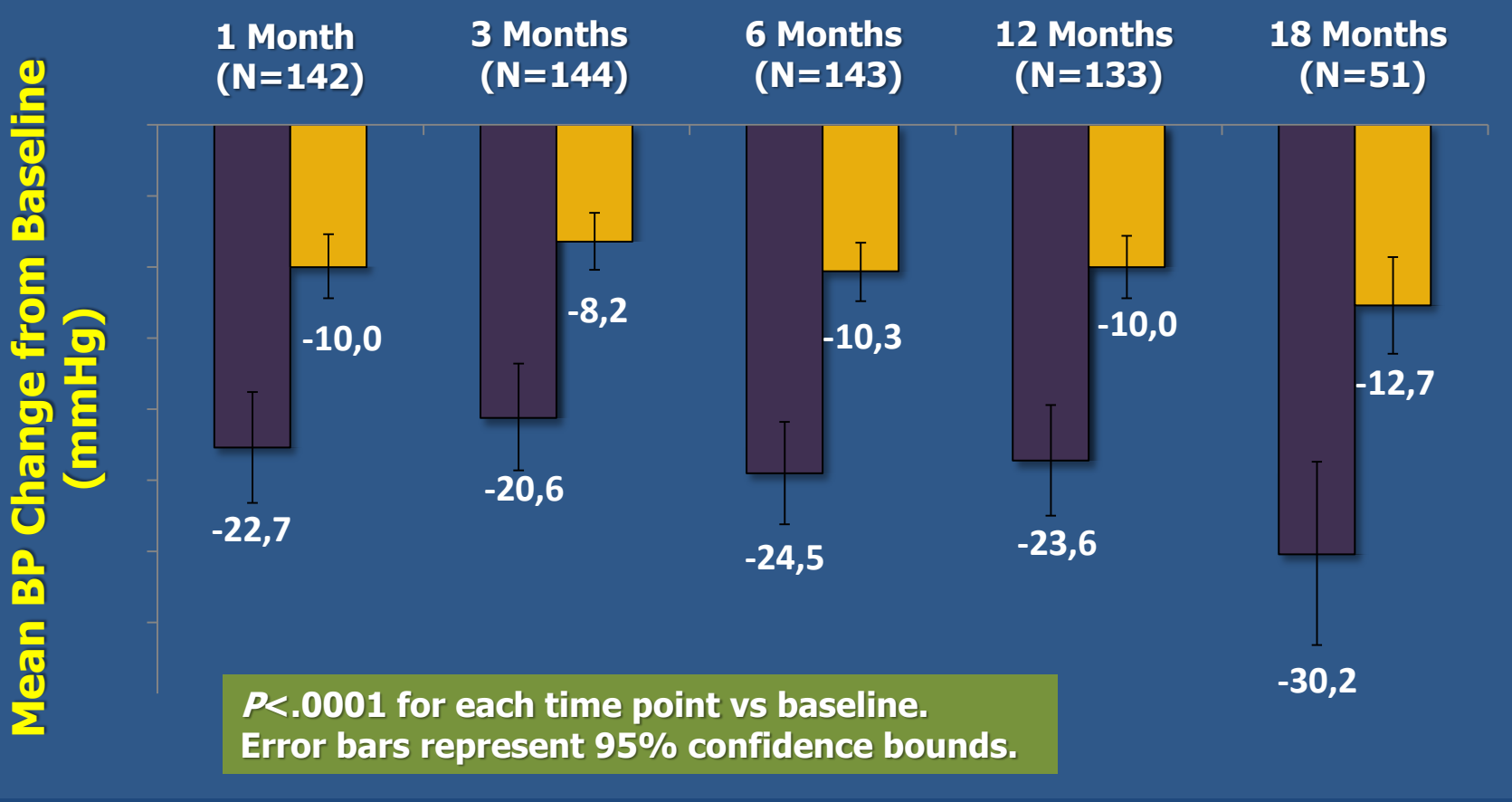
35% of patients (51/146) have completed 18 month follow-up to date

Baseline Demographic and Clinical Characteristics

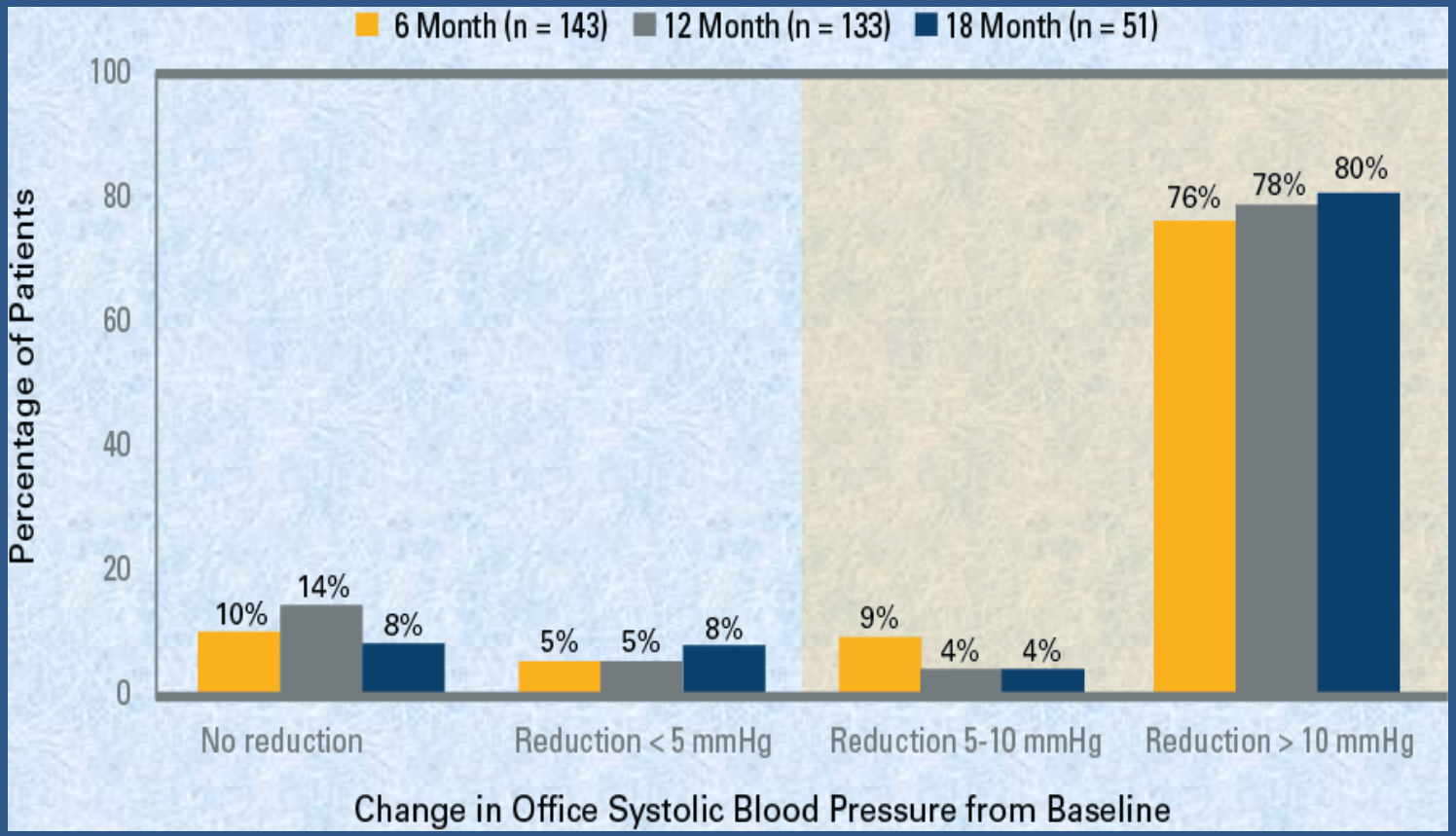
Vessix Global Clinical Program REDUCE FIM+Post-Market Study HTN

N=146	
Demographic Characteristics	
Age (years)	58.5±10.5
Gender (male)	61.0%
Ethnic origin (white)	92.5%
Comorbidities	
Type 2 diabetes	**28.1%**
Coronary artery disease	37.7%
Dyslipidemia	58.2%
Congestive heart failure	2.1%
Blood Pressure	
Systolic blood pressure (mmHg)	**182±18**
Diastolic blood pressure (mmHg)	**100±14**
Kidney Function	
eGFR (mL/min/1.73 m^2)	**82.7±22.5**
Serum creatinine (µmol/L)	82.0±20.0

18 month f/u results



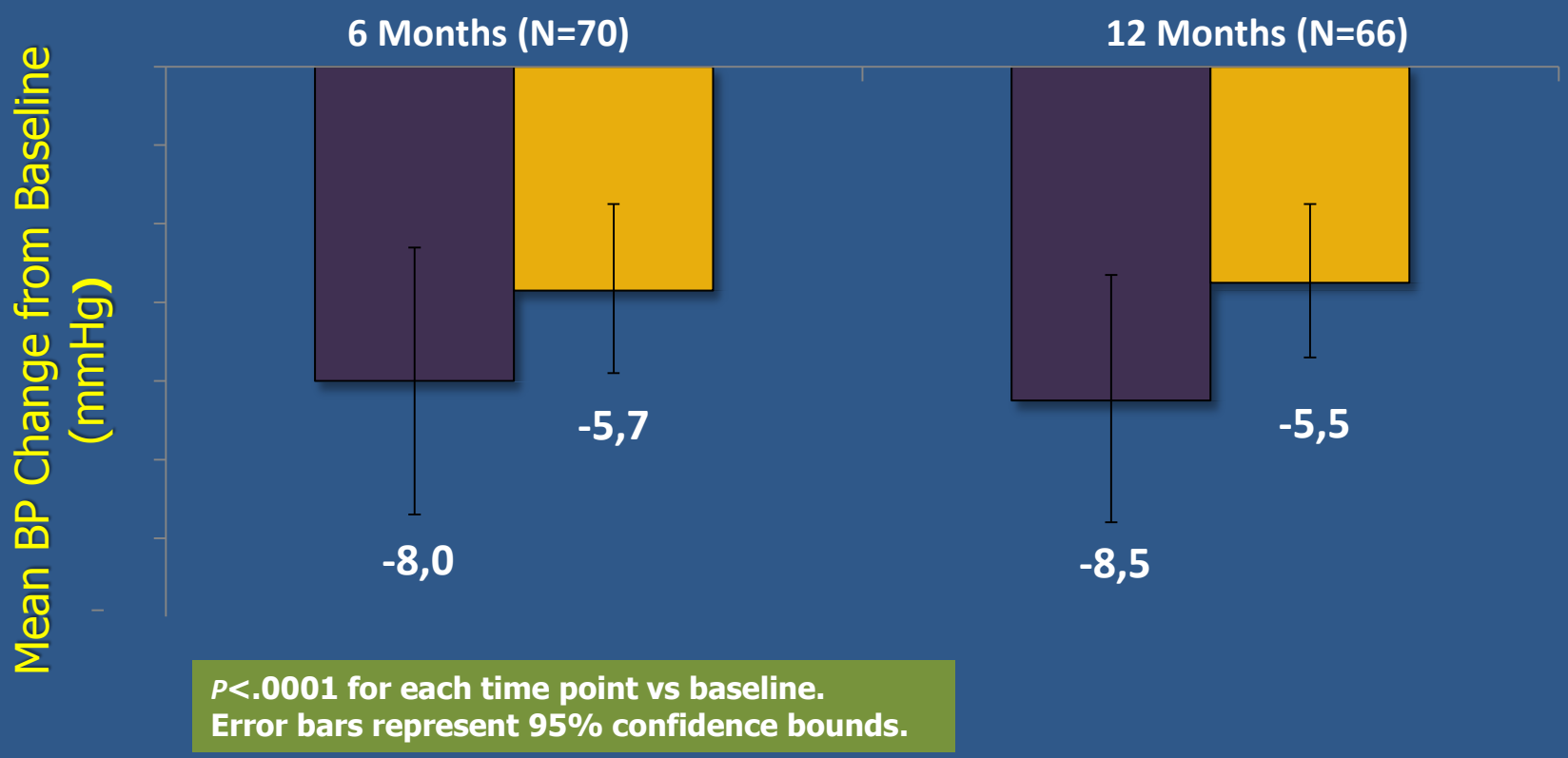
18 month f/u results
Rate of Responders



80% had a clinically meaningful response (ie, reduction >10 mmHg) based on office systolic blood pressure at 18 months

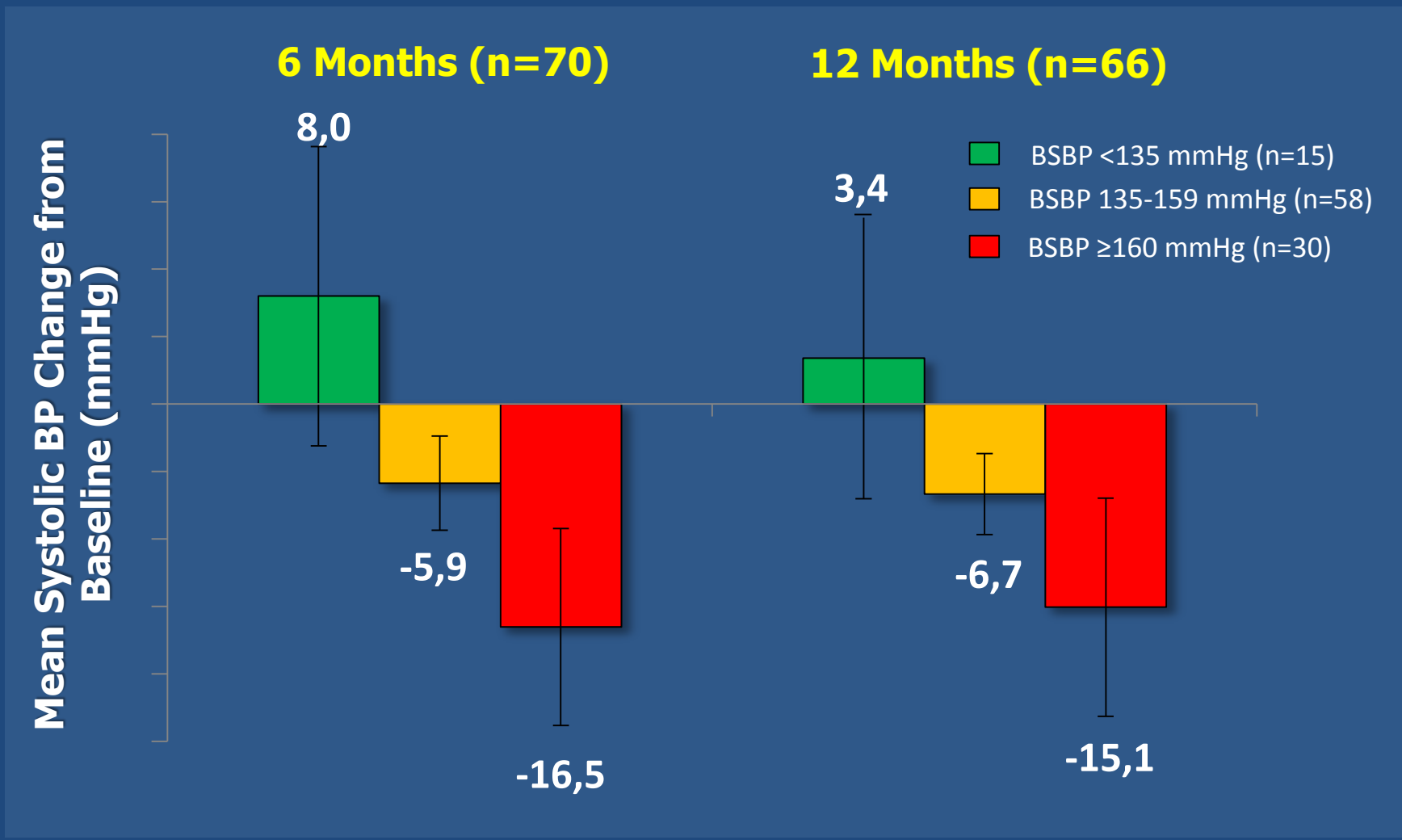
Schofer J, MD. REDUCE-HTN Clinical Study Interim 12- and 18-Month Data. Presented at EuroPCR; May 2014.

18 month f/u results
24H ABPM



153/88 mmHg (N=103)

18 month f/u results
24H ABPM



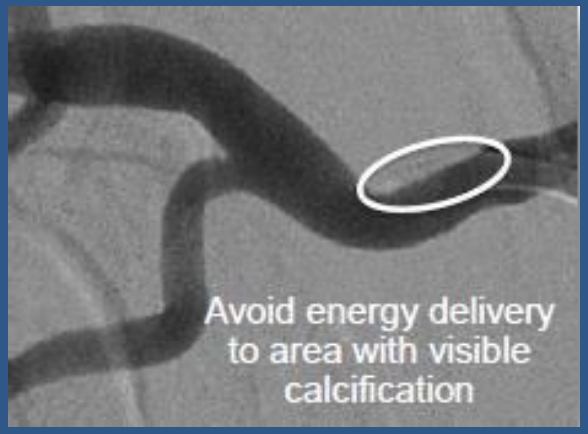
REDUCE-HTN Study
Anatomic Consideration

- Flow limiting stenosis
- Artery Diameter
  - Standard is ≥4mm
  - **Vessix is ≥3mm**
- Artery Length
  - Standard is ≥20mm
  - **Vessix is ≥15mm**
- Absence of Stent(s)

REDUCE-HTN Study

Anatomic Consideration: areas to avoid

Avoid treating areas of visible disease



Mahfoud, F. ESC 2012.

REDUCE-HTN Study

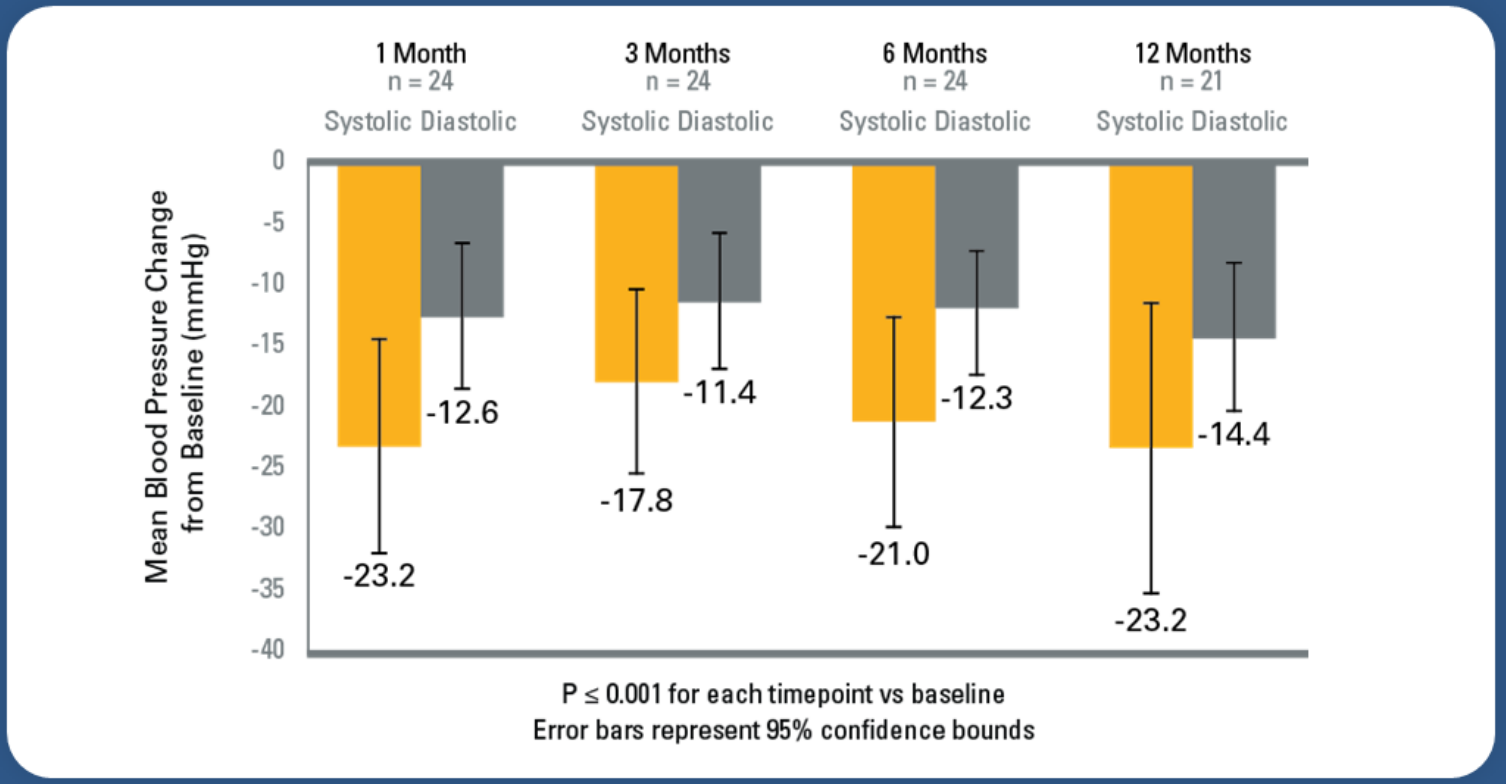
Anatomic Consideration: RA size

Recommended Catheter Sizing Table				
Artery Size	**3.0 – 4.0mm**	**3.8 – 5.0mm**	**4.7 – 6.0mm**	**5.6 – 7.0mm**
4mm balloon	**Yes**	X	X	X
5mm balloon	X	**Yes**	X	X
6mm balloon	X	X	**Yes**	X
7mm balloon	X	X	X	**Yes**

The Vessix catheter can treat arteries as small as 3mm

REDUCE-HTN Study

Anatomic Consideration: Treated accessory RAs



Preliminary Ambulatory BP 12 month data in 12 patients with treated accessory renal arteries show a mean reduction of 5.7/4.0 mmHg

REDUCE-HTN Study
Conclusion-1

Office-based blood pressure measurements over long-term follow-up in the REDUCE-HTN study continue to show significant reductions

- ***Preliminary 18-month results (N=51) show a mean office blood pressure reduction of 30.2/12.7 mmHg***
- ***Preliminary 12-month data for the subgroup of patients with treated accessory renal arteries (N=21) show a mean reduction of 23.2/14.4 mmHg***

REDUCE-HTN Study
Conclusion-2

24-hour ambulatory blood pressure measurements through 12 months in the REDUCE-HTN study support sustained efficacy of the Vessix System in treating resistant hypertension

- ***Preliminary 1-year results (N=66) show a mean pressure reduction of 8.5/5.5 mmHg***
- ***Preliminary 12-month data for the subgroup of patients with treated accessory renal arteries show a mean reduction of 5.7/4.0 mmHg***

Case # 1

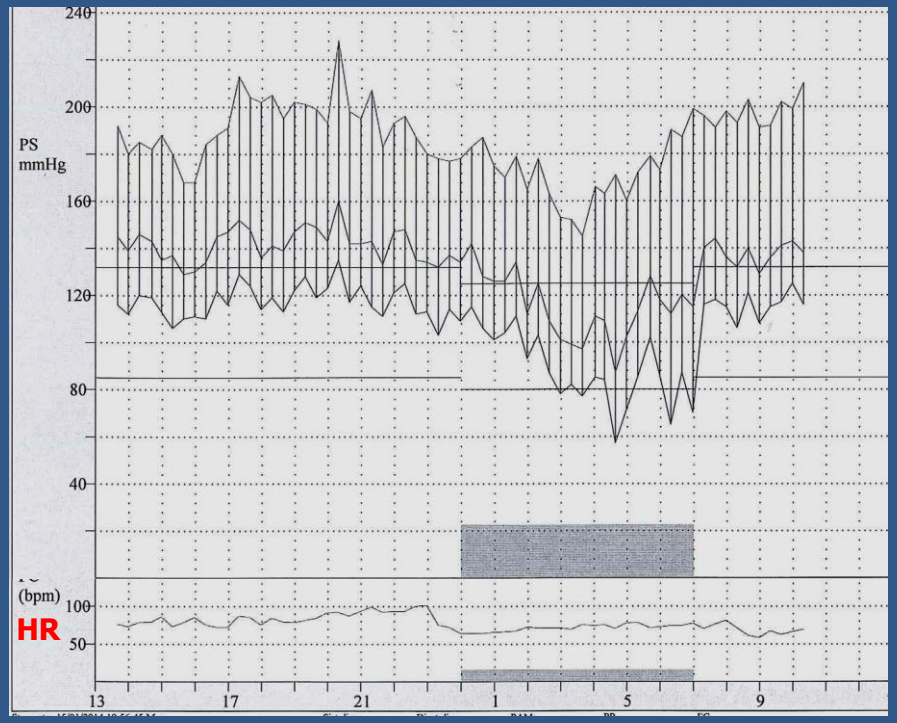
- 57 yom
- Family history of HTN and premature CAD
- HTN, HyperCh, previous smoker, obesity
- Type 2, NIDDM
- 2001 Hemispheric TIA → first detection of severe HTN
- 2007 AAA (<4 cm) in f/u with ultrasound
- 2013 Normal renal anatomy and ultrasound Doppler assessment
- Refractory HTN despite: metoprolol 100 mg x 2, Amlodipine 10 mg x 2, Telmisartan/hydroclorotiazide 80/12.5 x 2, Spironolattone 50 mg/day

- 175 cm x 108 Kg, BMI >35
- BP on admission: 160/100 mmHg
- Blood chemistry: glucose 135 mg%, renal 35/0.86/3.88/94 ml/', cholesterol 169/41/91, Trygliceride 186, TSH 2.5
- Rest ECG: aspecific ST-T abnormality.
- Echocardiogram: mild LVH. LA dilation (51/24). Normal EF: 62% Absence of diastolic dysfunction

Ambulatory BP monitoring data

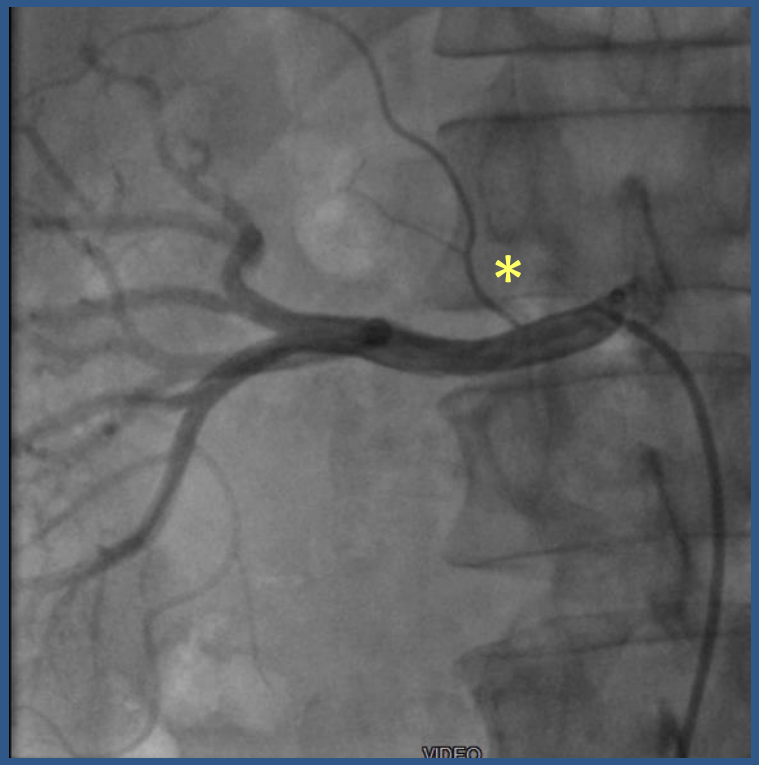
Office BP:
200/120 mmHg (S)
180/120 mmHg (U)

Baseline 11/6/2013



SAP: 187±15 mmHg
DAP: 107±17 mmHg
HR: 77±9 bpm

Renal arteries angiography

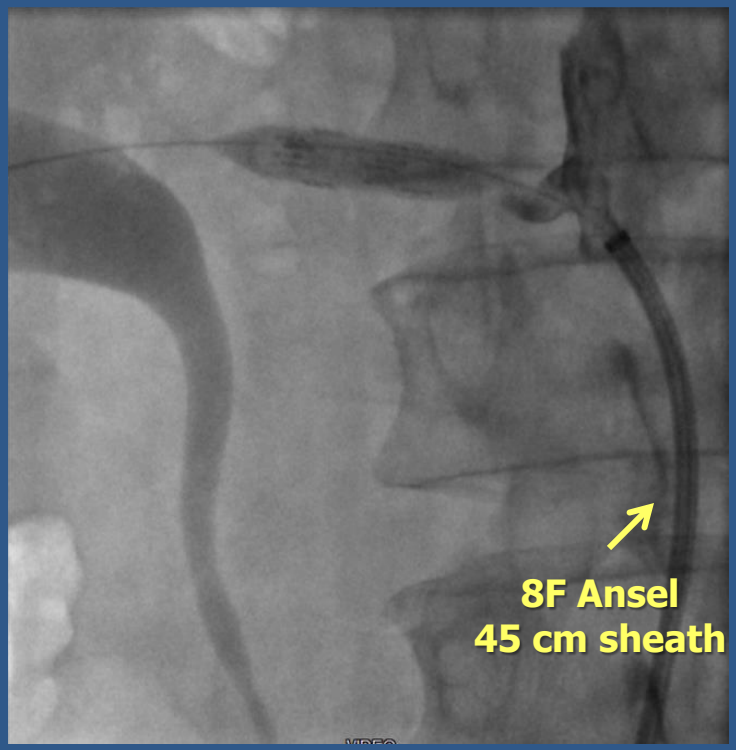


Right renal artery

Left renal artery

* ISA: inferior suprarenal artery

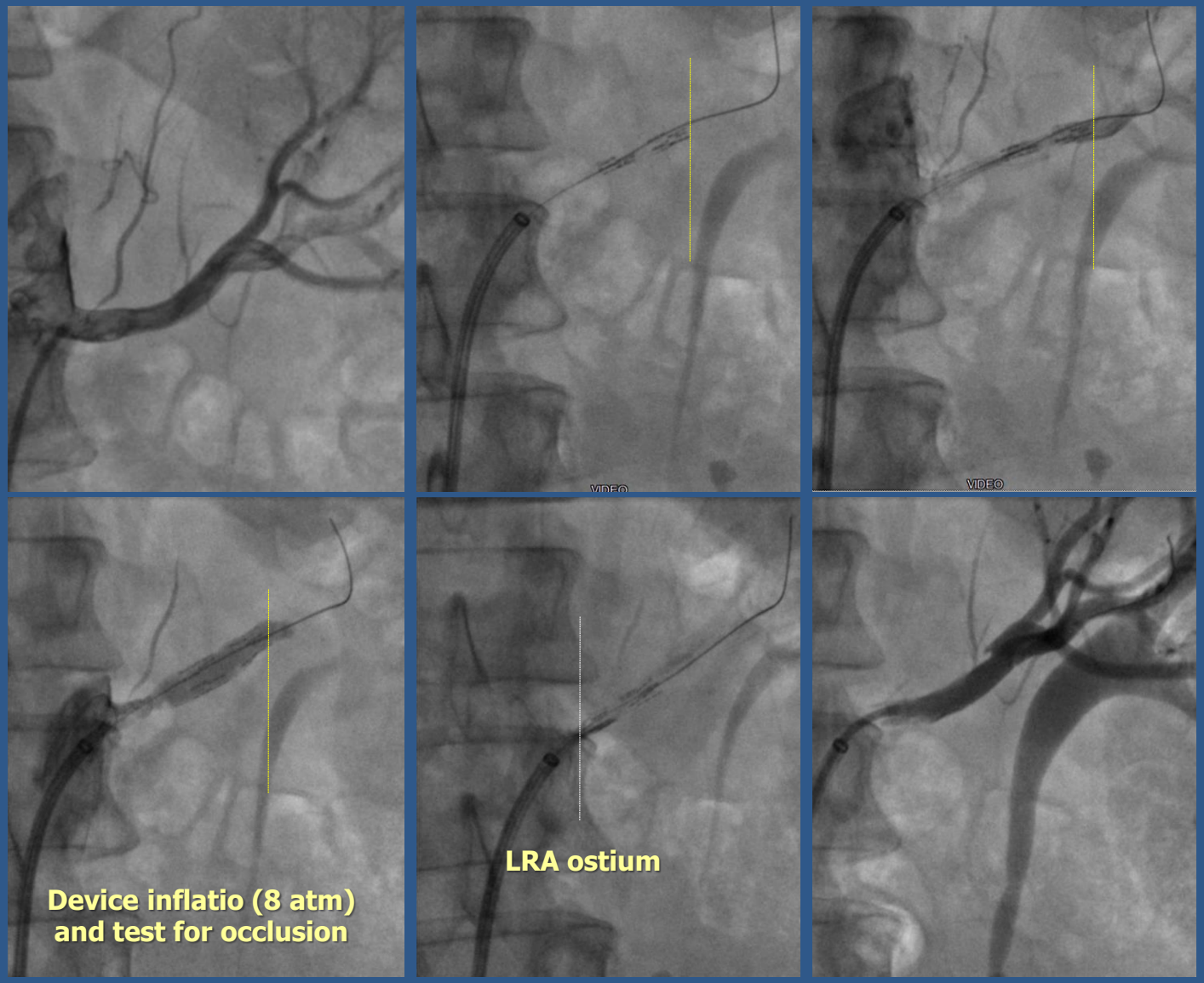
Renal artery denervation procedure



Right RDN, 3 amt inflation.
(Test for occlusion)

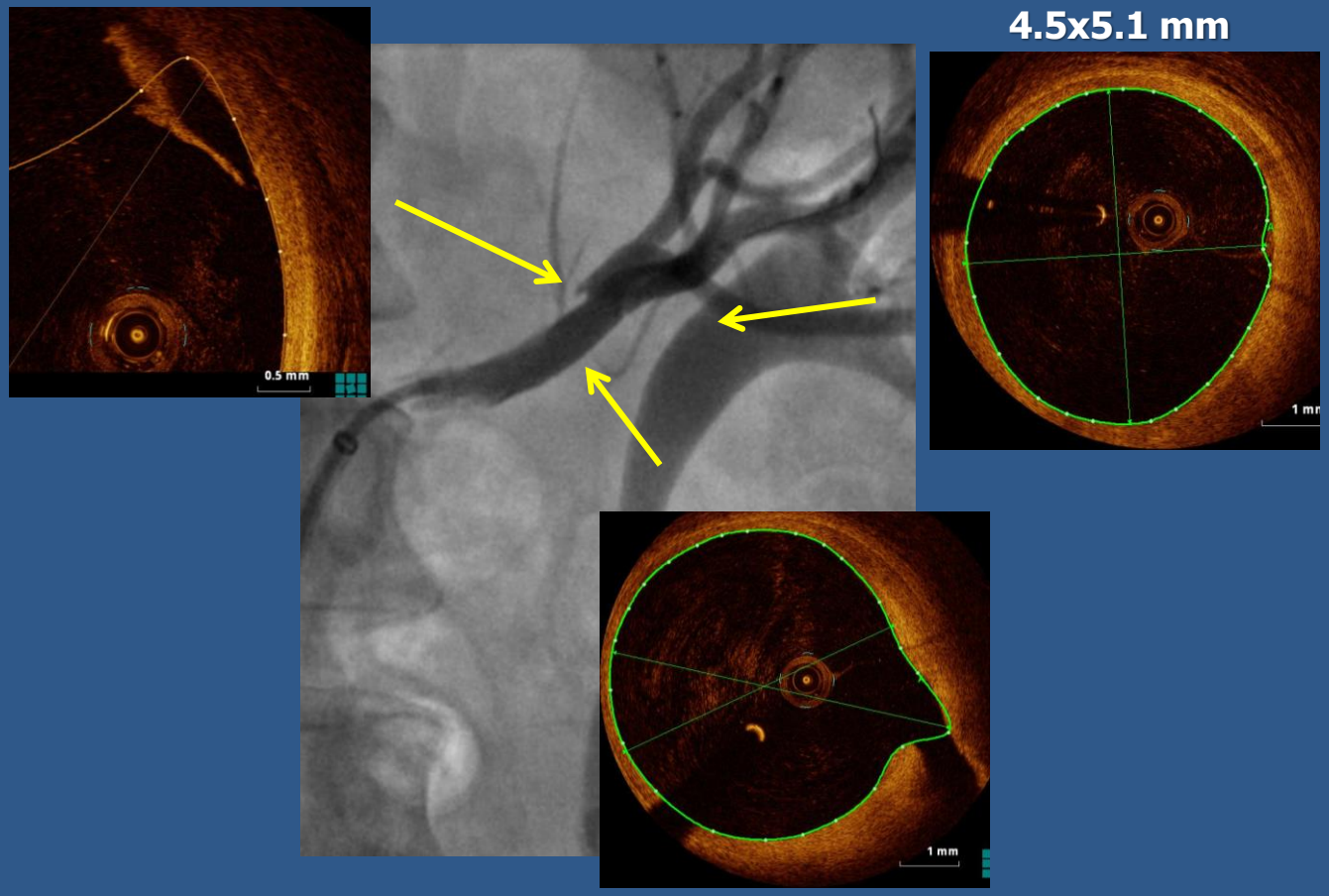
Post-RDN
(x2 inflations)

Left artery denervation procedure



Left renal artery denervation

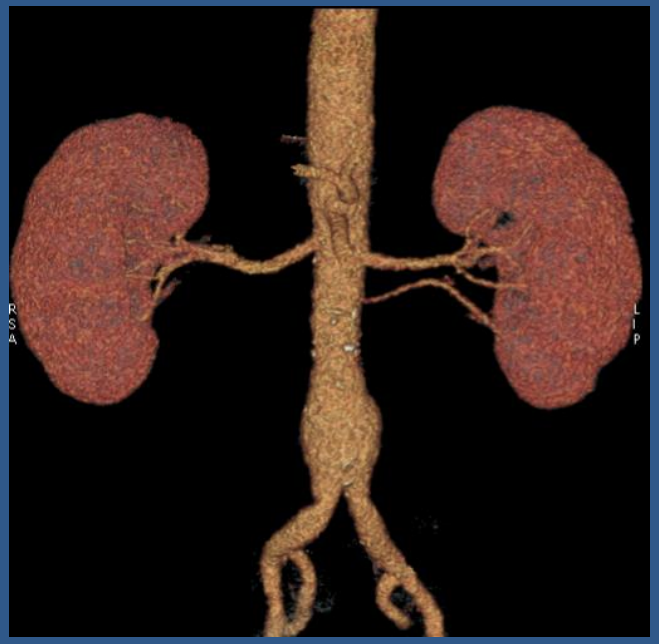
Angiographic and OCT findings

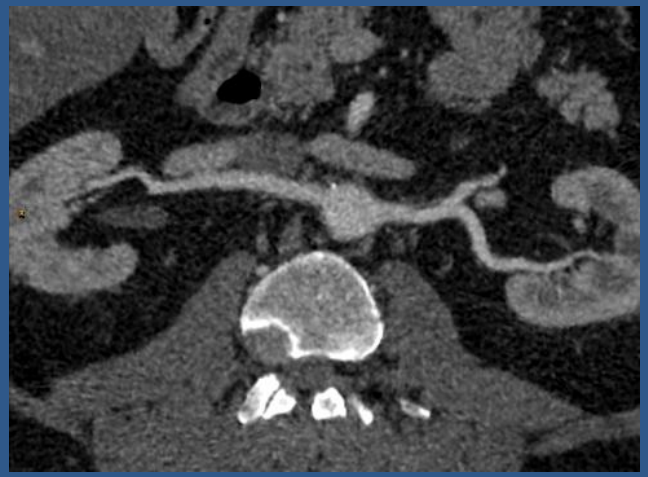


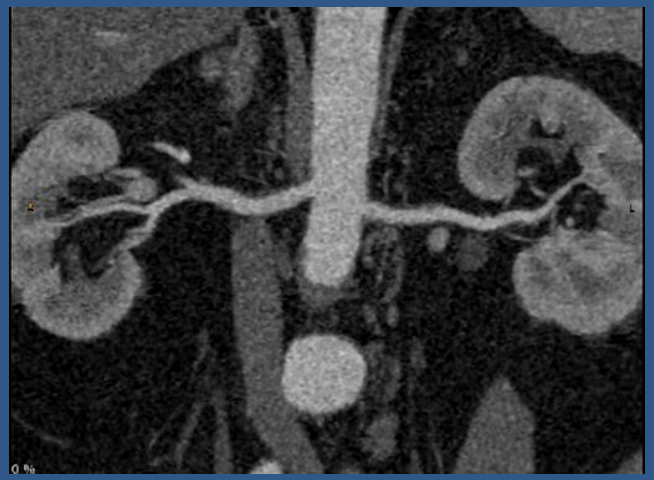
OCT catheter: C7 Dragonfly™ LightLab Imaging Inc., Westford, MA, USA

Follow-up CT-Angiography

1/23/2014

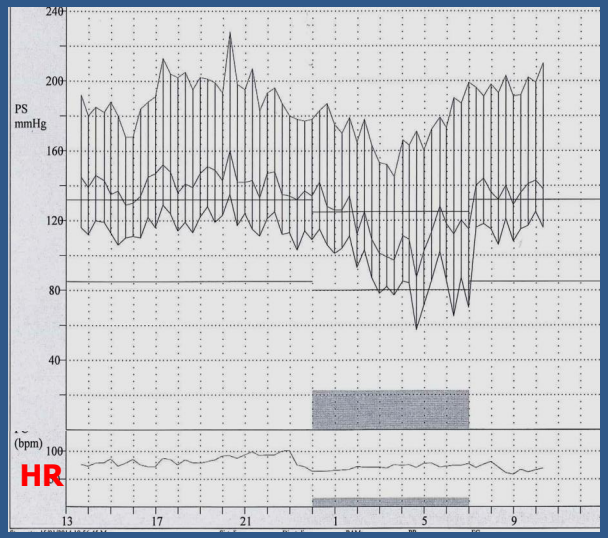






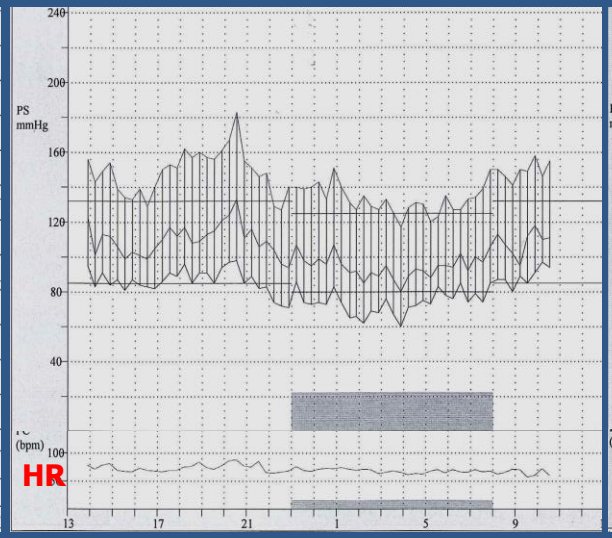
Office & Ambulatory BP monitoring data in the F/u

Baseline
Office BP: 210/120 mmHg



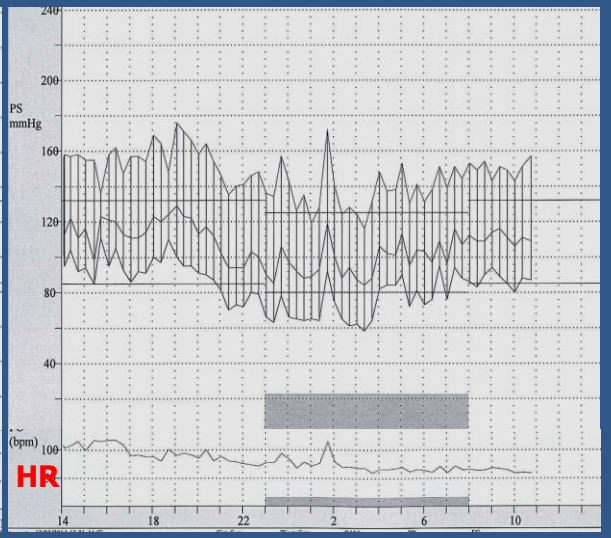
SAP: 187±15 mmHg
DAP: 107±17 mmHg
HR: 77±9 bpm

30 days post-RDN
Office BP: 140/85 mmHg



SAP: 142±13 mmHg
DAP: 81±9.1 mmHg
HR: 70±6 bpm

90 days post-RDN
Office BP: 130/85 mmHg



SAP: 147±13 mmHg
DAP: 84±13 mmHg
HR: 80±17 bpm

Medical treatment unchanged

Case # 2
Moderate Resistant Hypertension

Definition: Office BP >140/90 mmHg and <160/100 mmHg
ABPM ≥ 130/80 mmHg (Ott C et al. *JACC* 2013)

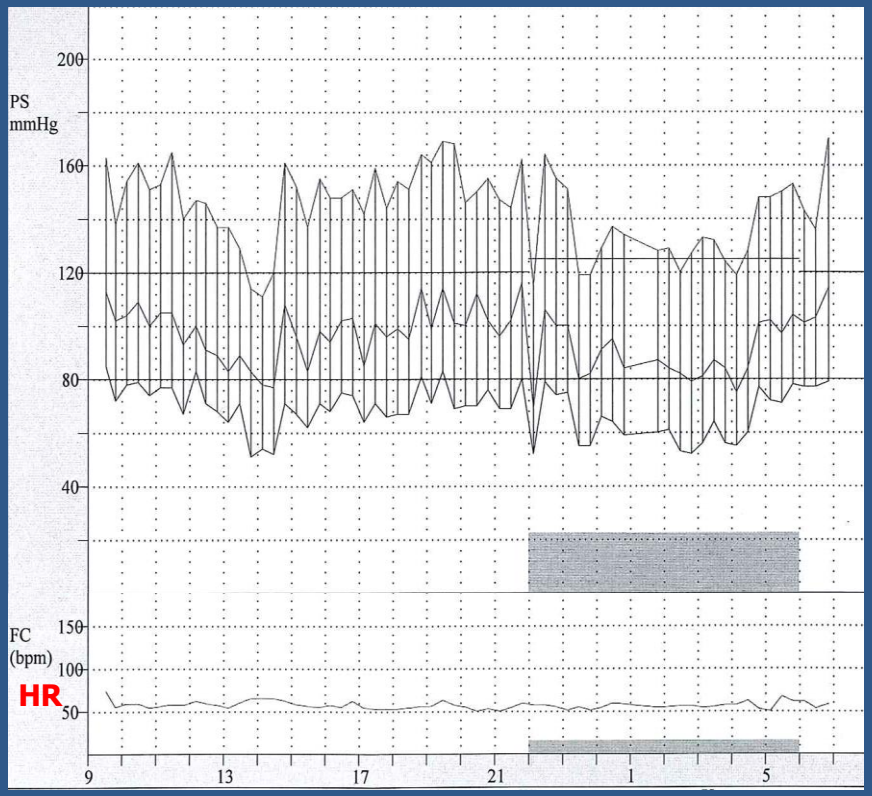
- 69 yom
- Family history of HTN and diabetes
- HyperCh, previous smoker, obesity
- Type 2, NIDDM
- 2011Hypertension
- Refractory HTN despite: olmesartan 40 mg/day, Amlodipina 10 mg/day, Atenolol 100 mg/day, Amiloride+Triamterene ½ cp , Metformin 500 mg x 2

- 100 cm x 163 Kg, BMI >35
- Office BP: 170/90 mmHg
- Blood chemistry: glucose 148 mg%/7.8% HbA1c, renal 63/1.09/>60 GFR, cholesterol 215/48/101, Trygliceride 332
- Rest ECG: within normal limits.
- Echocardiogram: Mild LVH (17/12 mm). LA dilation. EF: 73%

Ambulatory BP monitoring data

Office BP:
185/90 mmHg (S)
180/80 mmHg (U)

Baseline, 10/23/2013

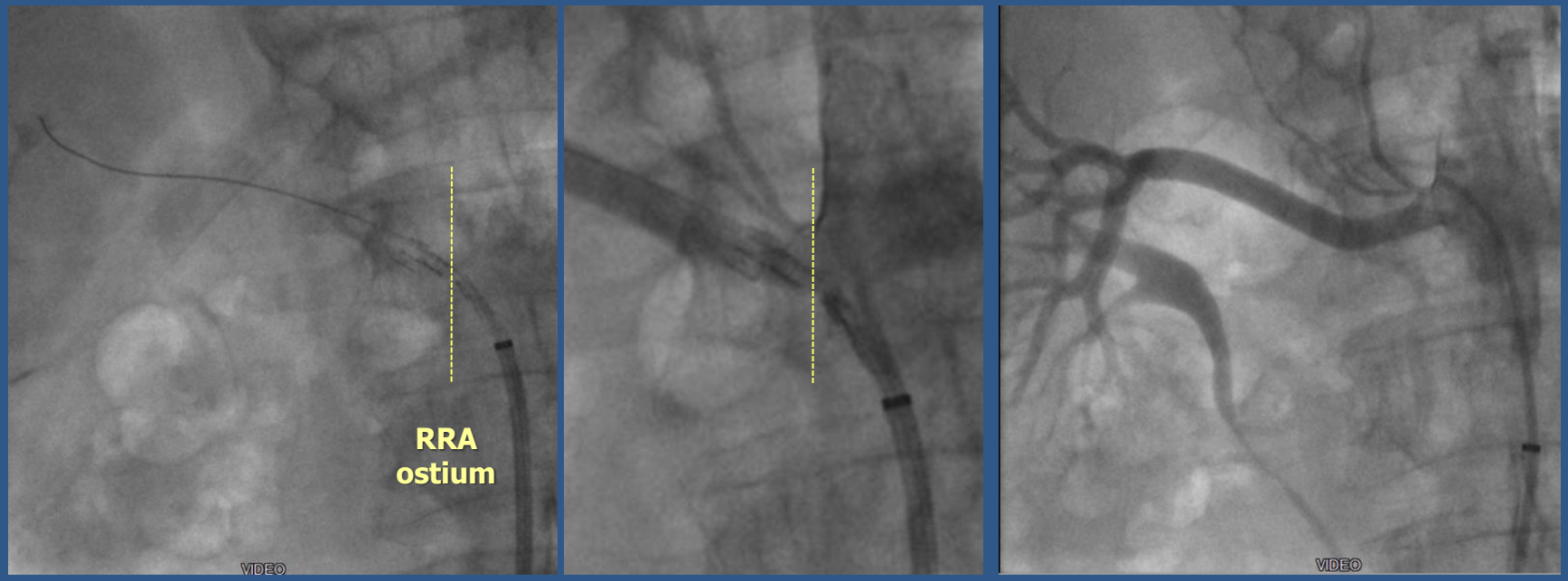


SAP: 144±15 mmHg
DAP: 68±9 mmHg
HR: 57±4 bpm

RDN Procedure: Right renal artery

RDN Procedure: Left renal artery

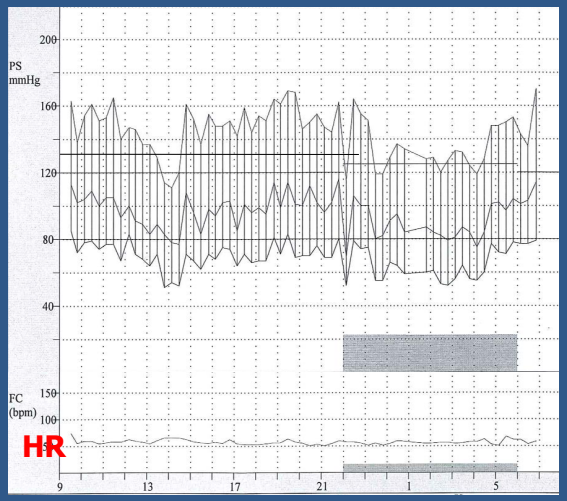
RDN Procedure: Right renal artery



RDN at the right renal artery ostium (second site of energy erogation)

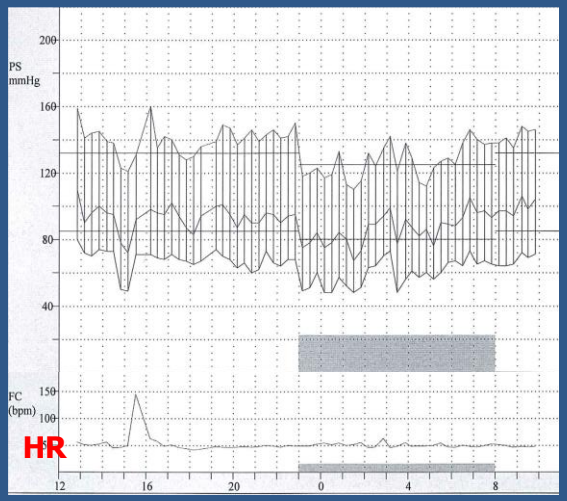
Office & Ambulatory BP monitoring data in the F/u

Baseline
OBP:170/90



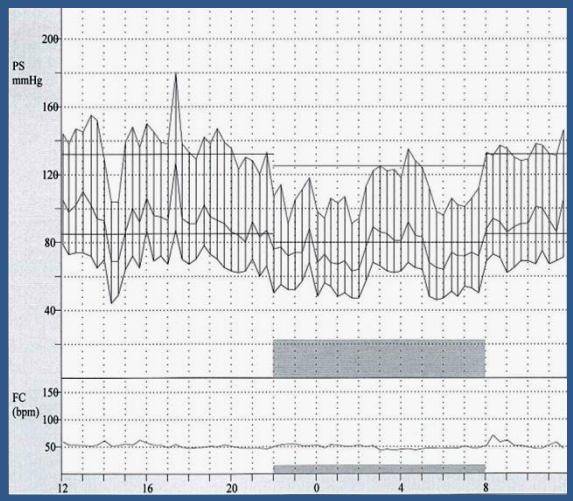
SAP: 144±15 mmHg
DAP: 68±9 mmHg
HR: 57±4 bpm

30 days post-RDN
OBP: 140/80



SAP: 134±11 mmHg
DAP: 64±8 mmHg
HR: 51±12 bpm

90 days post-RDN
OBP: 135/80



SAP: 125±18 mmHg
DAP: 63±10 mmHg
HR: 51±5 bpm

Medical treatment unchanged

Take home messages

- Both patients with true resistant hypertension & moderate resistant hypertension may be candidates for RDN
- The Vessix technology appears to be safe and effective. Non-flow limiting dissections of renal arteries may be found, likely due to balloon inflation distal to major artery bifurcation.
  Spontaneous sealing of this dissections occurrs as shown in the CTA after 1 month w/o clinical complications.
- Sustained BP reduction was observed up to 3 month-F/U