

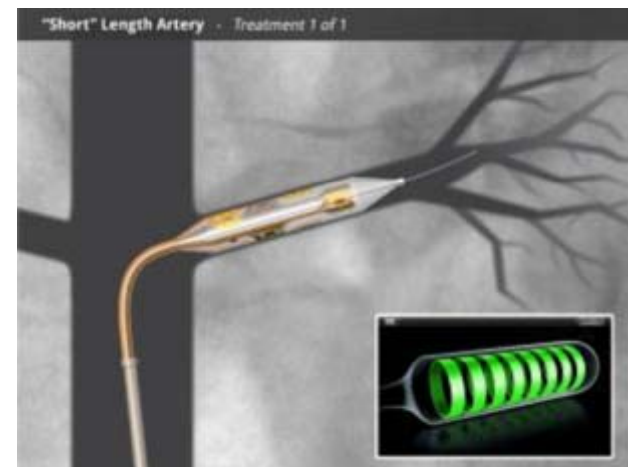
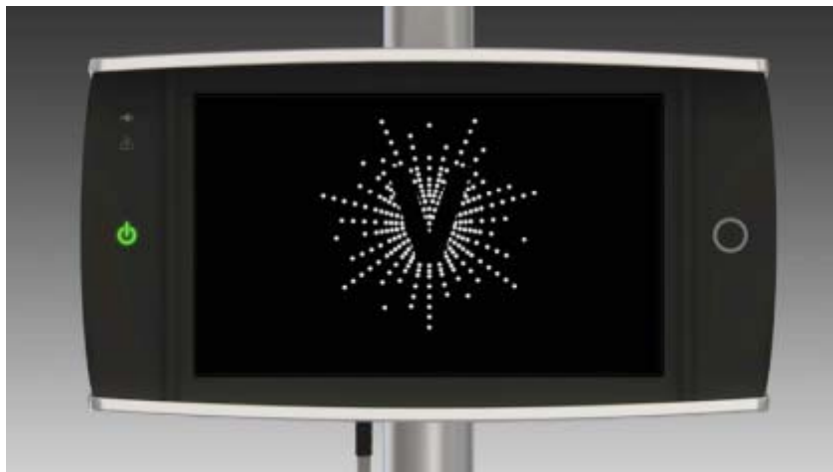


ANGIOPLASTY SUMMIT
TCTAP 2012

Vessix Vascular V2 Renal Denervation System *Achieving Safety and Efficacy in < 1 Minute*

James R. Margolis, MD

Jackson South Community Hospital, Miami, Florida USA





Disclosure

Consultant and stockholder Vessix Vascular



RF is Tricky/RF Experience Matters

- Bipolar RF is Vessix' domain, and for 8 years Vessix engineers have worked on nothing else.
- There are an unlimited number of variables and parameters involved in delivering ultra-safe and predictable RF — simply and quickly — nuances that can only be understood after years of study, trial and error.
- The treatment algorithm (temperature, time, impedance, apposition parameters) must align with the clinical application. Vessix has worked on a countless # of algorithms.
- Vessix has invested more than 128,000 engineering man-hours on RF and occluding balloon catheters with mounted electrodes.
- Vessix is currently on its 12th generation of RF generator, and its 60th version of RF balloon catheter.
- Vessix devices have been tested in hundreds of animals (including 128 renal denervation procedures), and in more than 100 human arteries.



Optimized RF Balloon Catheter for Renal Denervation

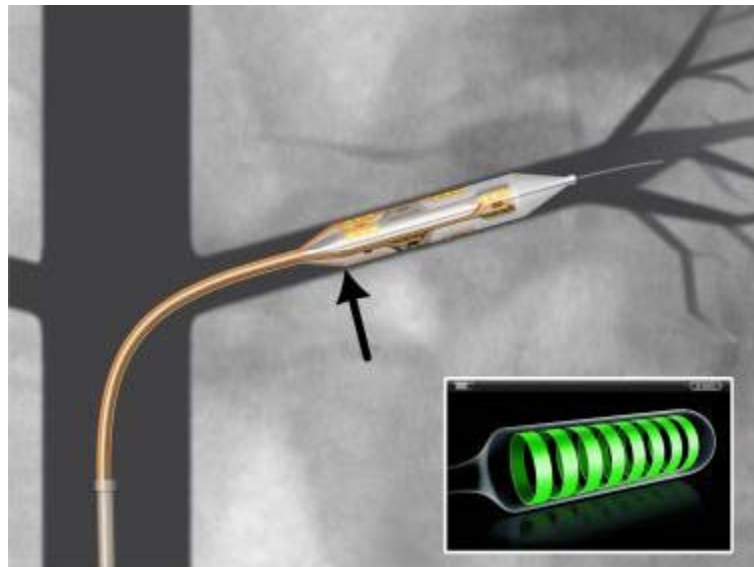
- Low pressure balloon (3 atm) eliminates possibility of barotrauma and facilitates good apposition
- Offset electrode pairs placed in helical pattern
- Solid gold electrodes for good thermal and electrical conductivity, radiopacity of each electrode on Angiogram
- Temperature precisely sensed and controlled at 68° C
- Optimized for delivery of thermal energy to adventitia (3-4 mm deep)



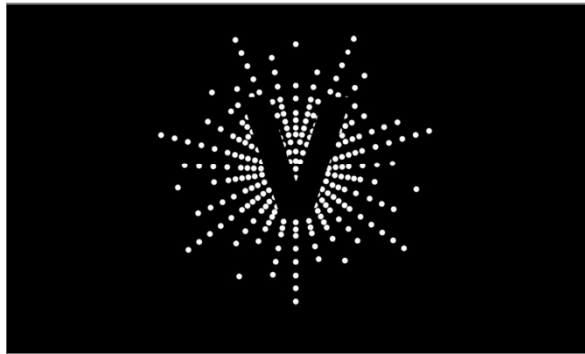
Vessix RF Balloon Catheter available
in 4, 5, 6, 7 mm diameter sizes



Vessix Bipolar RF Generator



- One button operation – no foot pedal
- Bipolar technology obviates the need for the grounding pad
- Battery operated (rechargeable)
- Algorithm controls temperature to achieve necessary depth of penetration for renal denervation in 30 seconds
- Graphical User Interface to confirm size of electrode, apposition of balloon catheter, display key parameters of treatment time and temperature
- Data storage – accessible via standard USB drive



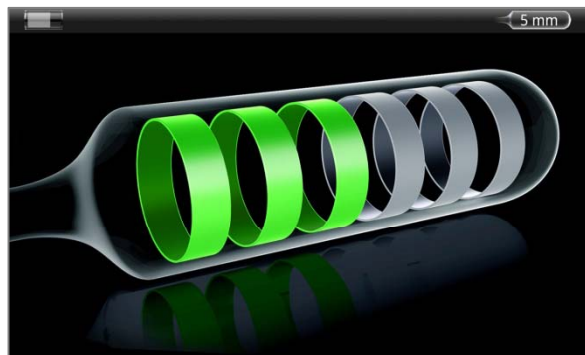
Splash Screen



Glow flashes prompting user to connect catheter



Confirms catheter size (diameter) and that catheter is connected



Electrode pairs light up green to confirm apposition inside renal artery



Once apposition achieved, asks user to begin treatment with x of y pairs



Active Treatment screen, indicates power, temp, time and # of electrodes active



End of Treatment screen, data captured and saved to memory includes power, temp, time and # of electrodes activated



Comparison vs. Ardian/Medtronic





Comparison vs. Medtronic

| FEATURES | VESSIX VASCULAR | ARDIAN/MEDTRONIC |
|-----------------------|--|--|
| Catheter Type | <u>Inflatable balloon</u> with balloon mounted RF electrodes; <u>requires only basic interventional skills</u> . | RF ablation type <u>catheter with 1mm hot tip</u> ; <u>requires special skills to manipulate</u> . |
| # RF Treatments | <u>30 sec inflations per renal artery</u> | 6-8 two minute (<u>12-16 min</u>) RF treatments <u>per renal artery</u> |
| Procedure Time | 30-60 seconds per artery; <u>10 minutes per procedure</u> | 25-30 minutes per artery; <u>50-60 minutes per procedure</u> |
| Catheter Placements | Balloon positioned as in <u>standard PTA</u> or stent <u>procedure</u> . | Random ablation points are selected along artery; <u>need to skillfully manipulate catheter to achieve complete coverage</u> . |
| RF Technology | Bipolar on balloon; allows for directed energy into adventitia. No grounding pad. <u>Requires < 2 watts power</u> . | Unipolar; requires grounding pad, <u>much higher power (8 watts)</u> |
| RF Generator Features | Small size; <u>battery operated</u> ; one button operation. | Larger size; <u>AC powered</u> ; requires foot pedal. |
| Patient Comfort | <u>Very short treatment times</u> for each artery. | <u>Severe pain during each of 6-8 two minute inflations</u> . |



Pre-Clinical Work



Renal Denervation Program

Pre-clinical Study Timeline

2010 - 2011

Development and iterative phase employing various designs of RF balloon catheter for renal denervation with new treatment algorithms

Verification testing of final V2 RDN System

Sep-Mar
Initial animal studies
confirming depth of
penetration

Apr - Jul
18 animals
with kidney NEPI
comparison
to establish efficacy at
7, 14, 28 days.
Angiograms and
histology to confirm
lack of flow limiting
stenosis in renal artery
at 28 days

Aug
20 animals
to confirm NEPI, histo
& angios with final
balloon catheter
design, and final
candidates for
temperature control
algorithm

Aug
32 animals
to confirm final dose
NEPI, histo & angios.
Compare unilateral to
bilateral treatments,
surgery, shams and
endogenous levels

Sep
18 animals
GLP Safety Study
28, 60, 90 days with
angiograms and
histology

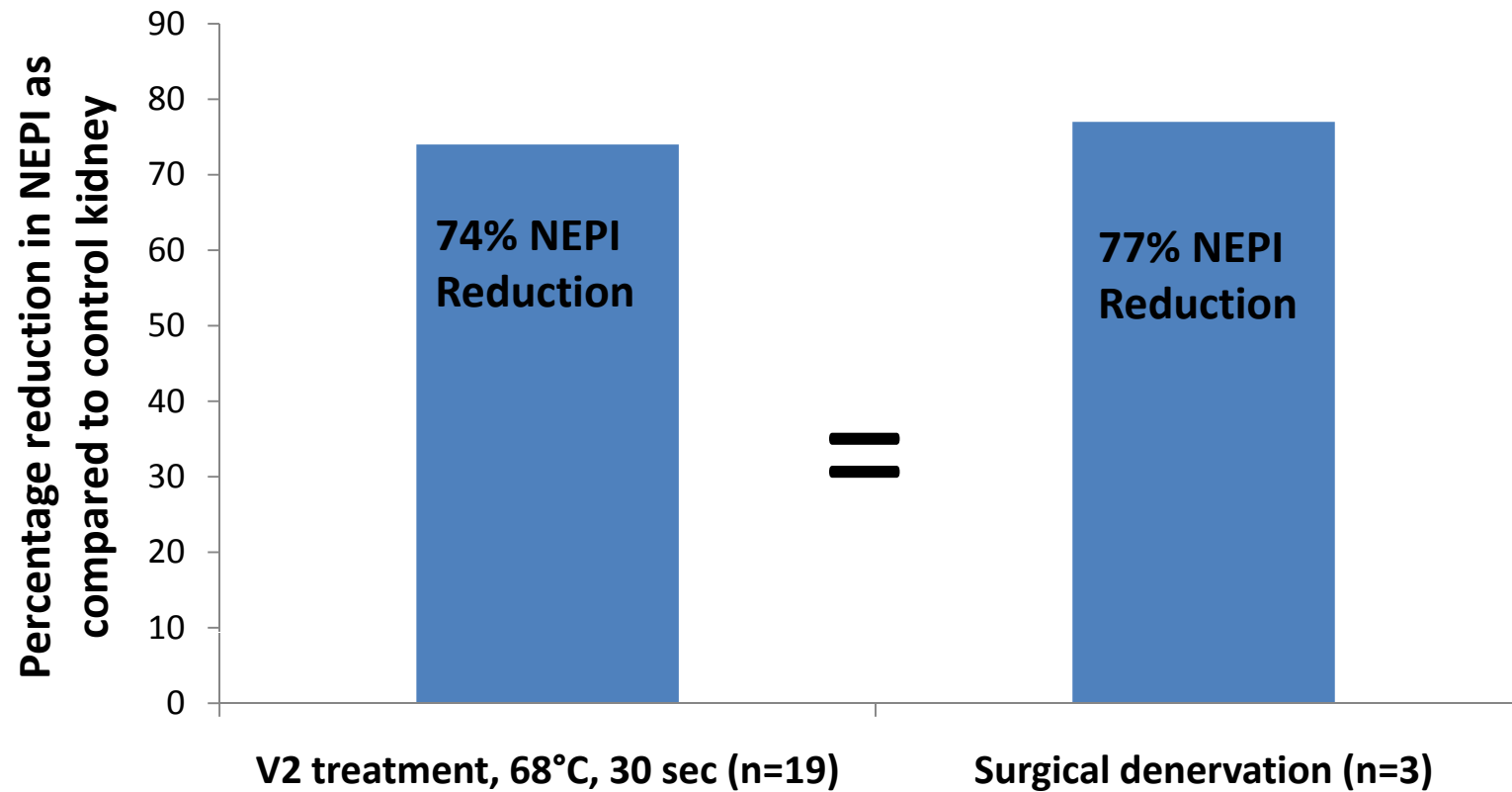
Oct
18 animals
Final Confirmatory
Study

Dec 11, Feb 12
22 animals
180 day GLP Safety

128 animals
studied

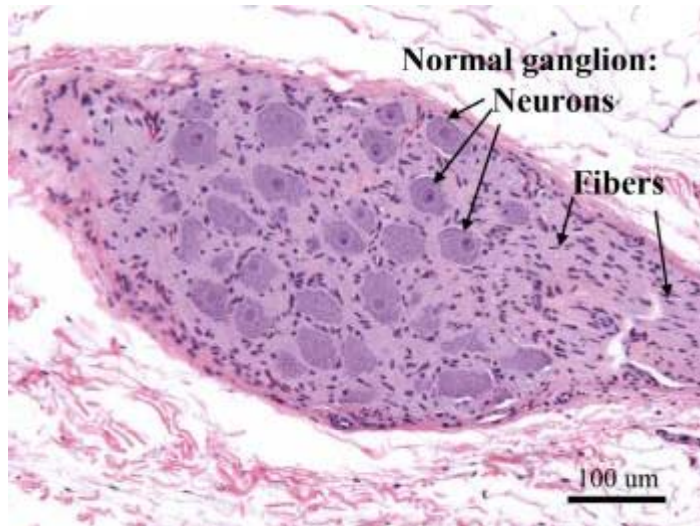


Reduction of Kidney Norepinephrine (NEPI) Content

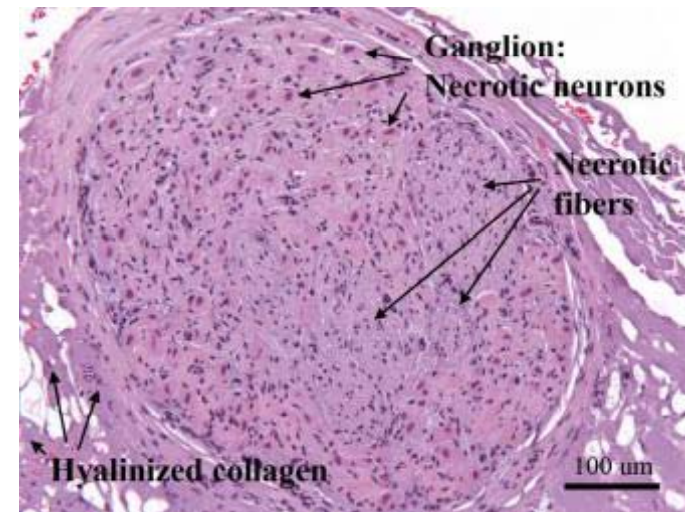




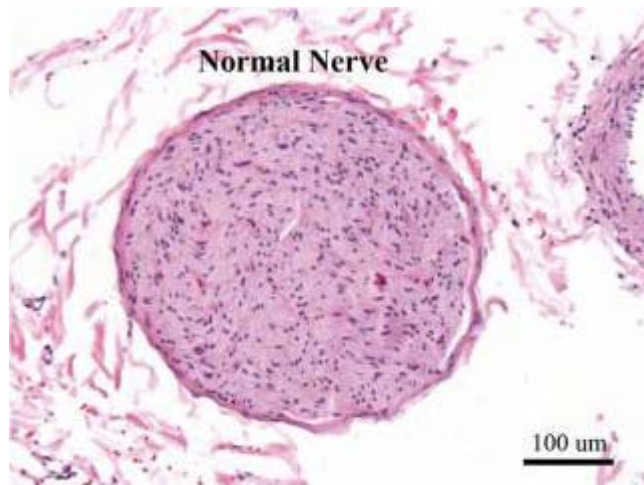
Histology Confirms Denervation



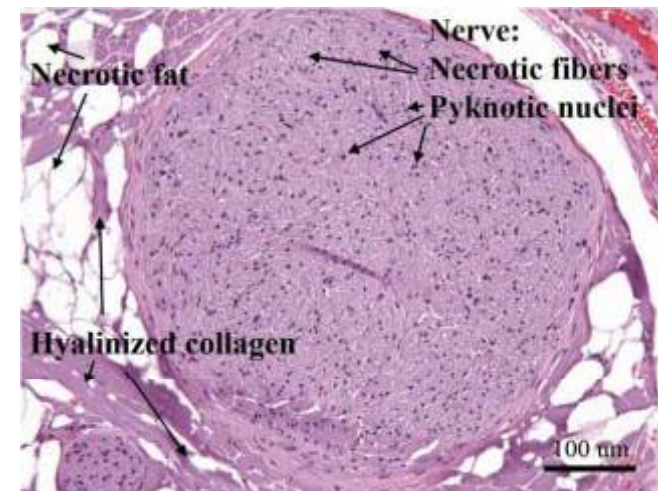
Normal Renal Nerve Ganglion pre-Tx



Post RF treatment Necrotic Renal Nerve Ganglion



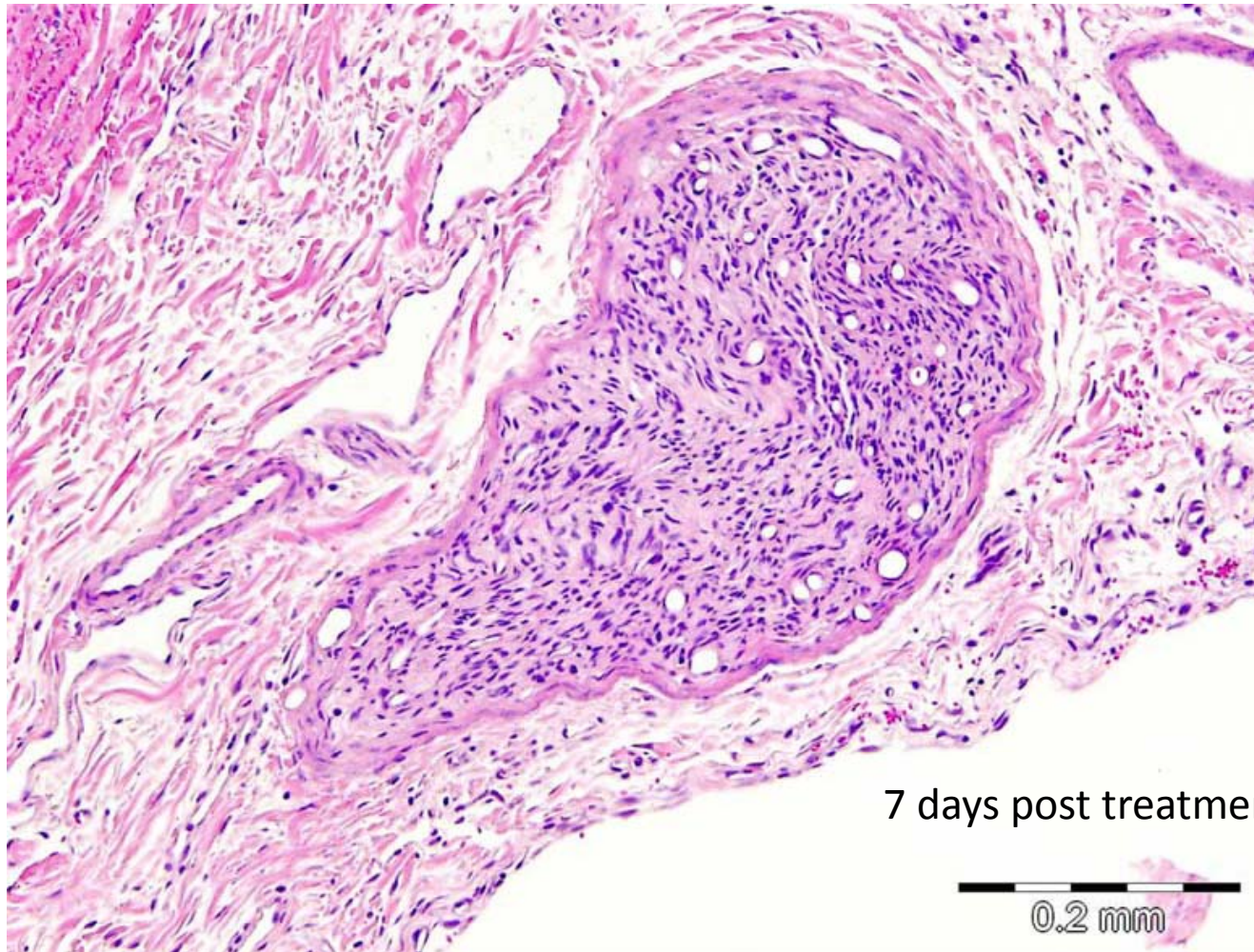
Normal Renal Nerve pre-Tx



Normal Renal Nerve post-Tx



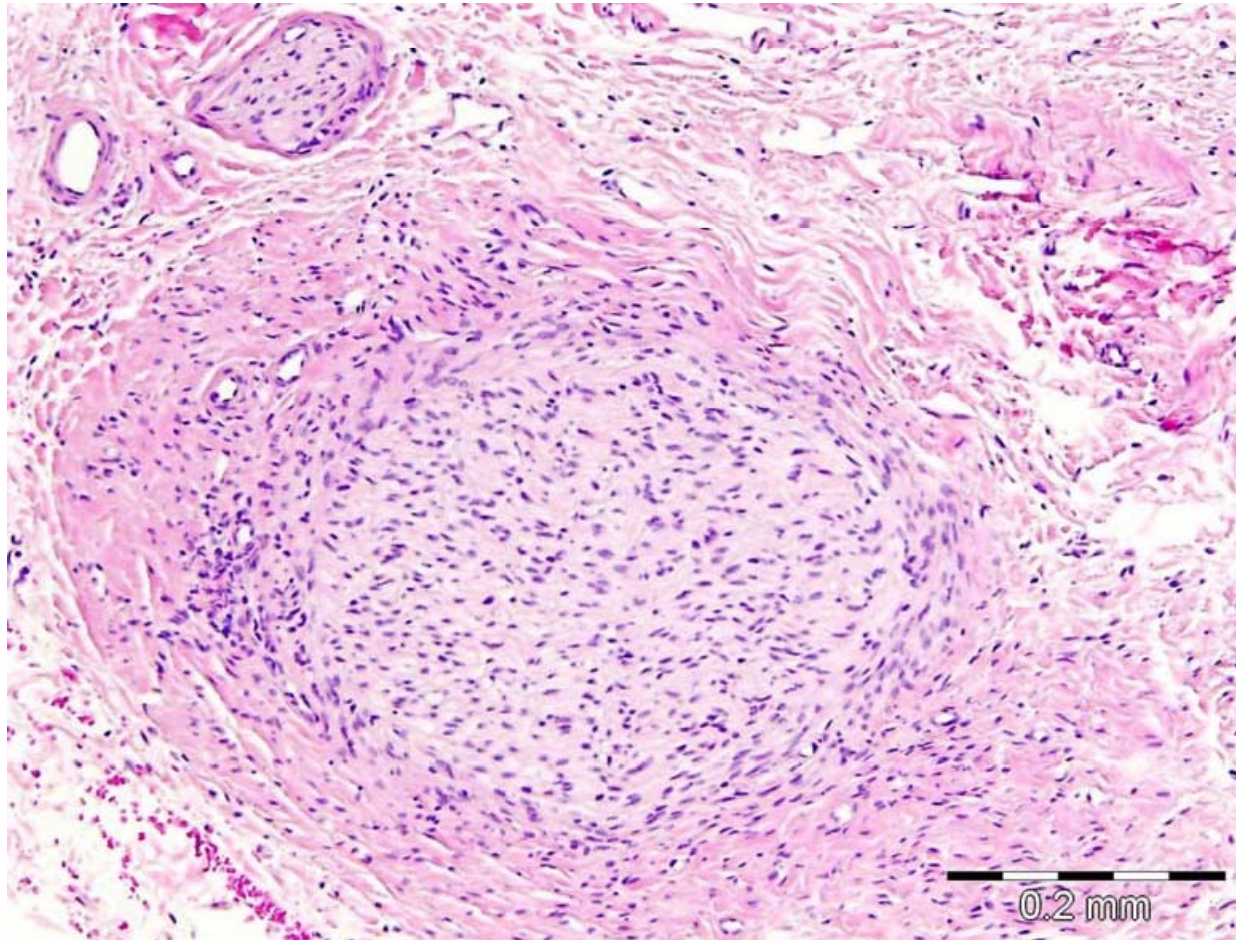
Histology Confirms Acute Denervation at 7 Days



Renal nerve with degenerative changes e.g., fibrosis, hypercellularity, axonal drop-out₁₅



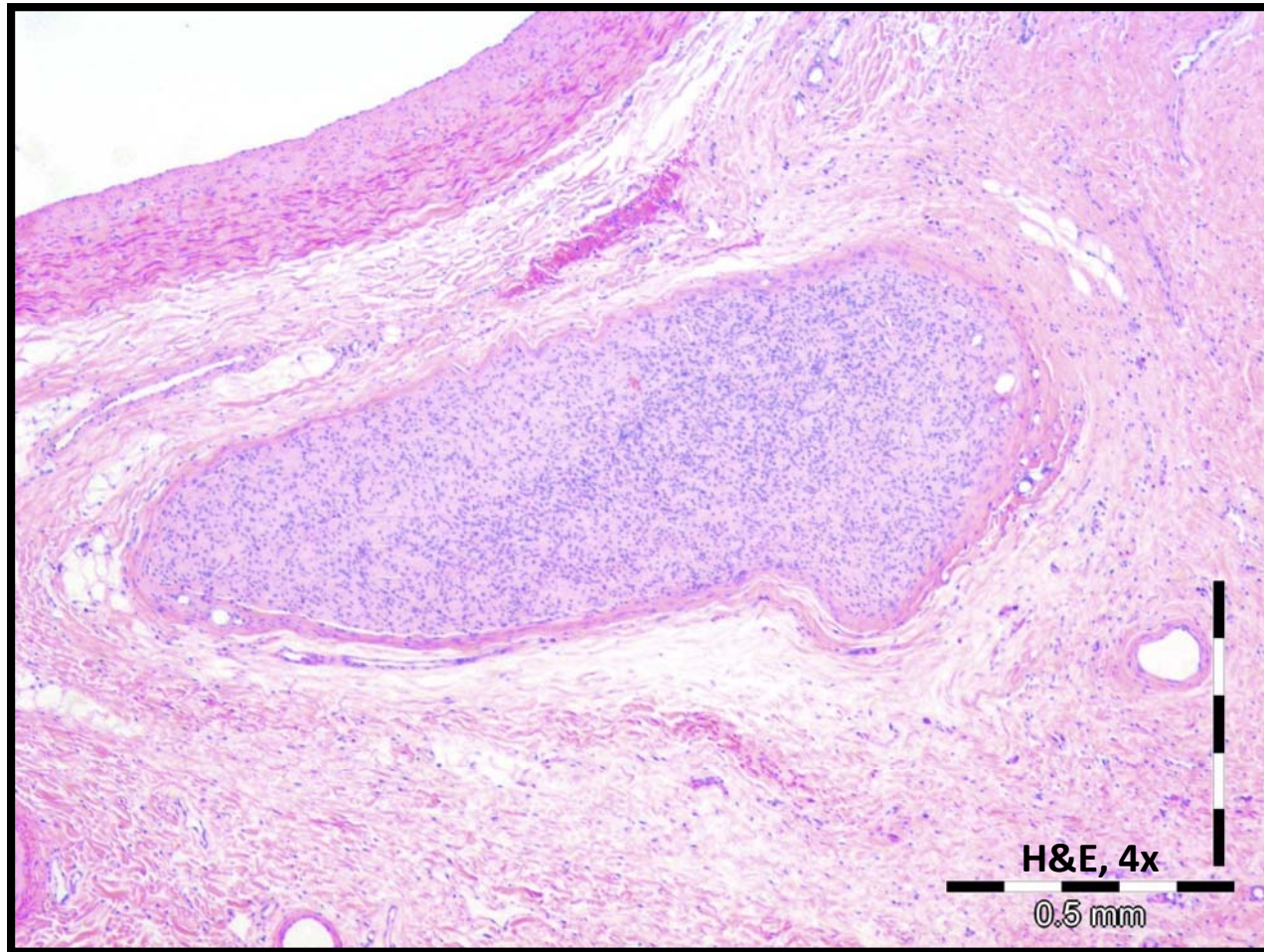
Histology Confirms Chronic Denervation at 28 days



Renal nerve with chronic degenerative changes at 28 days post treatment



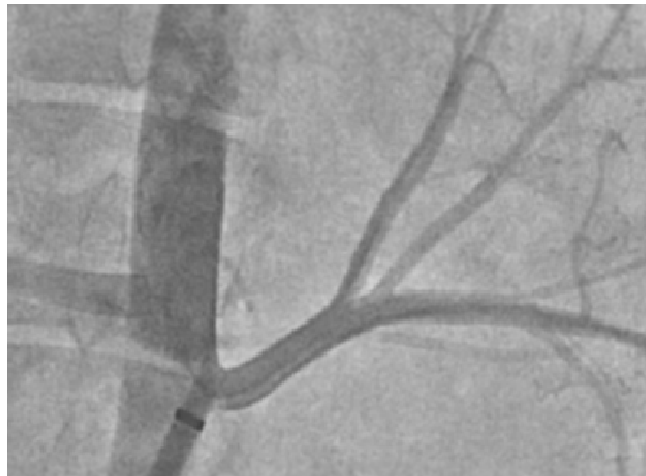
Histology Confirms Chronic Denervation at 90 days



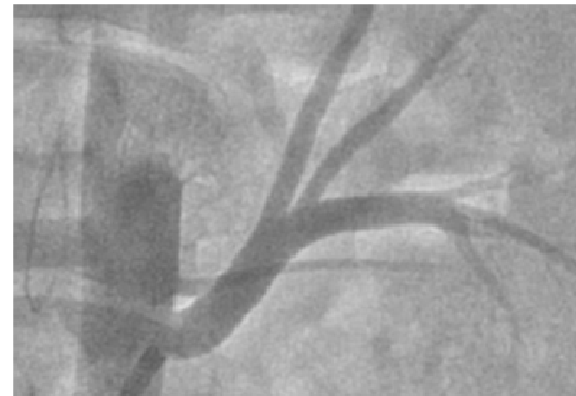
Nerve with chronic degenerative changes at 90 days post treatment



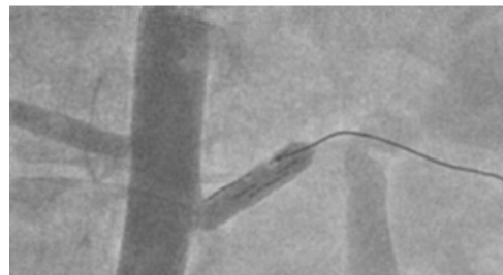
GLP Safety Study – Confirms No Stenosis at 90 days



Pre-Treatment



90 Days Post Treatment

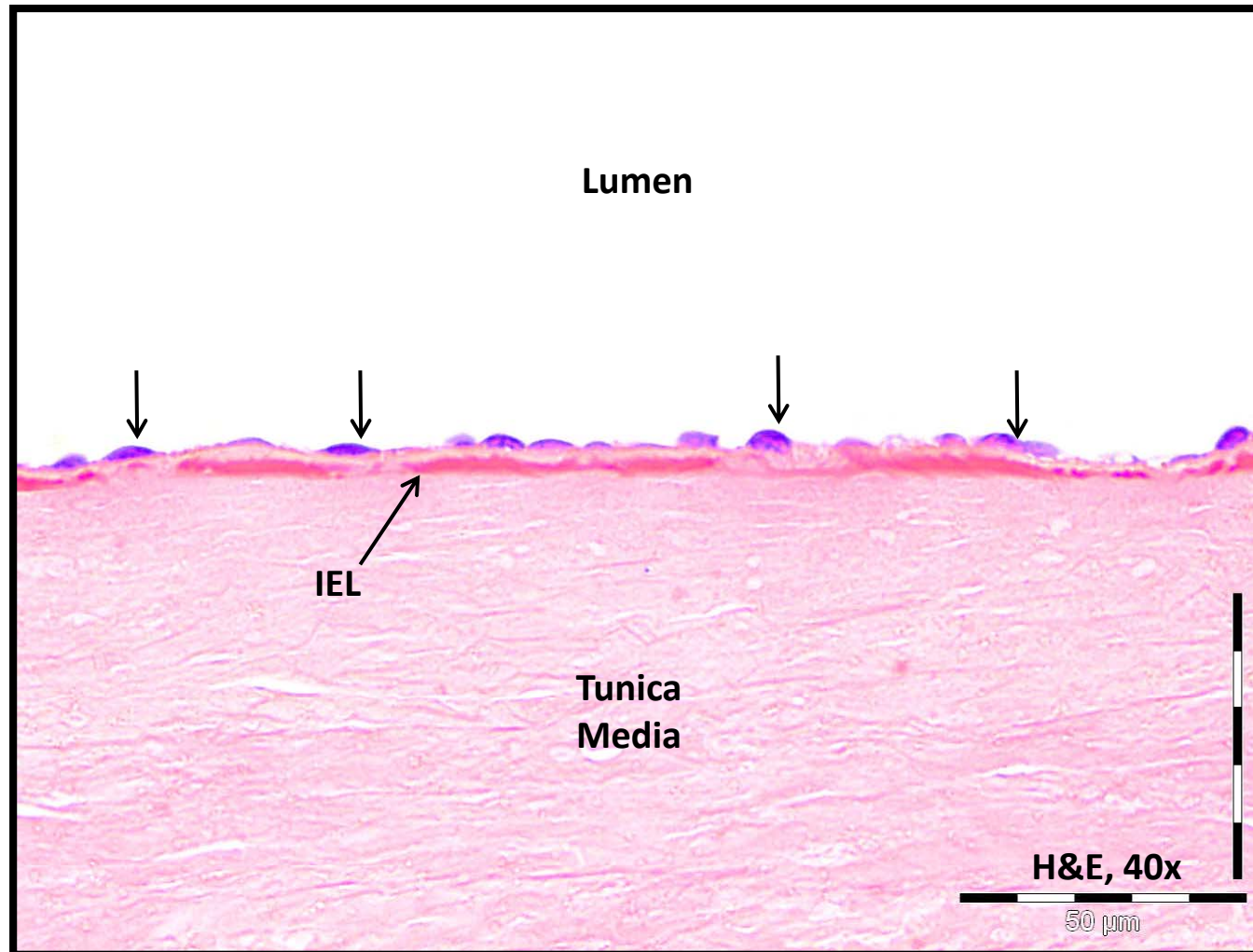


Balloon Location

Representative angiography images of a renal artery pre-treatment and
90 days following treatment

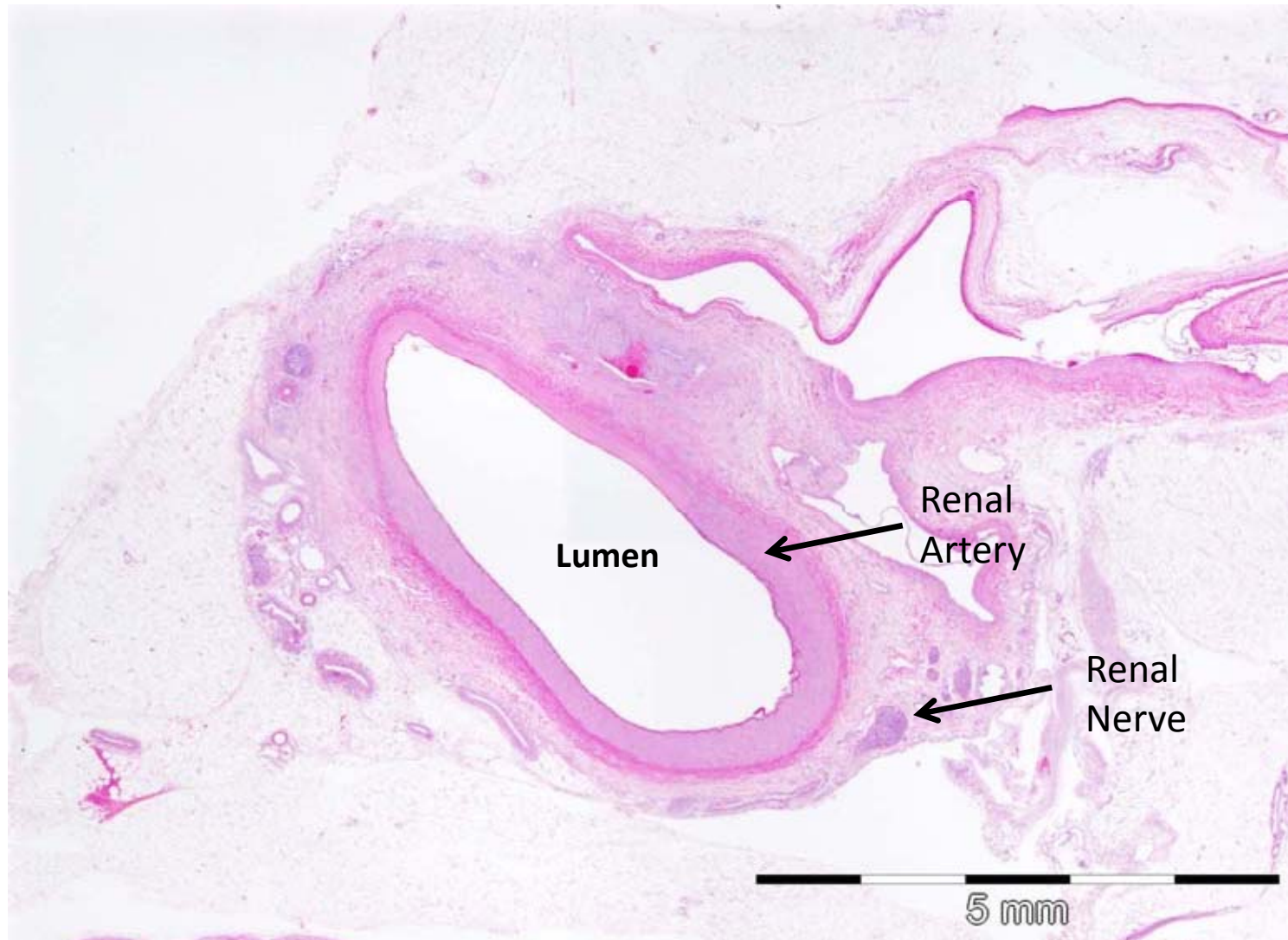


V² Treatment, Day 7 - No Endothelial Damage



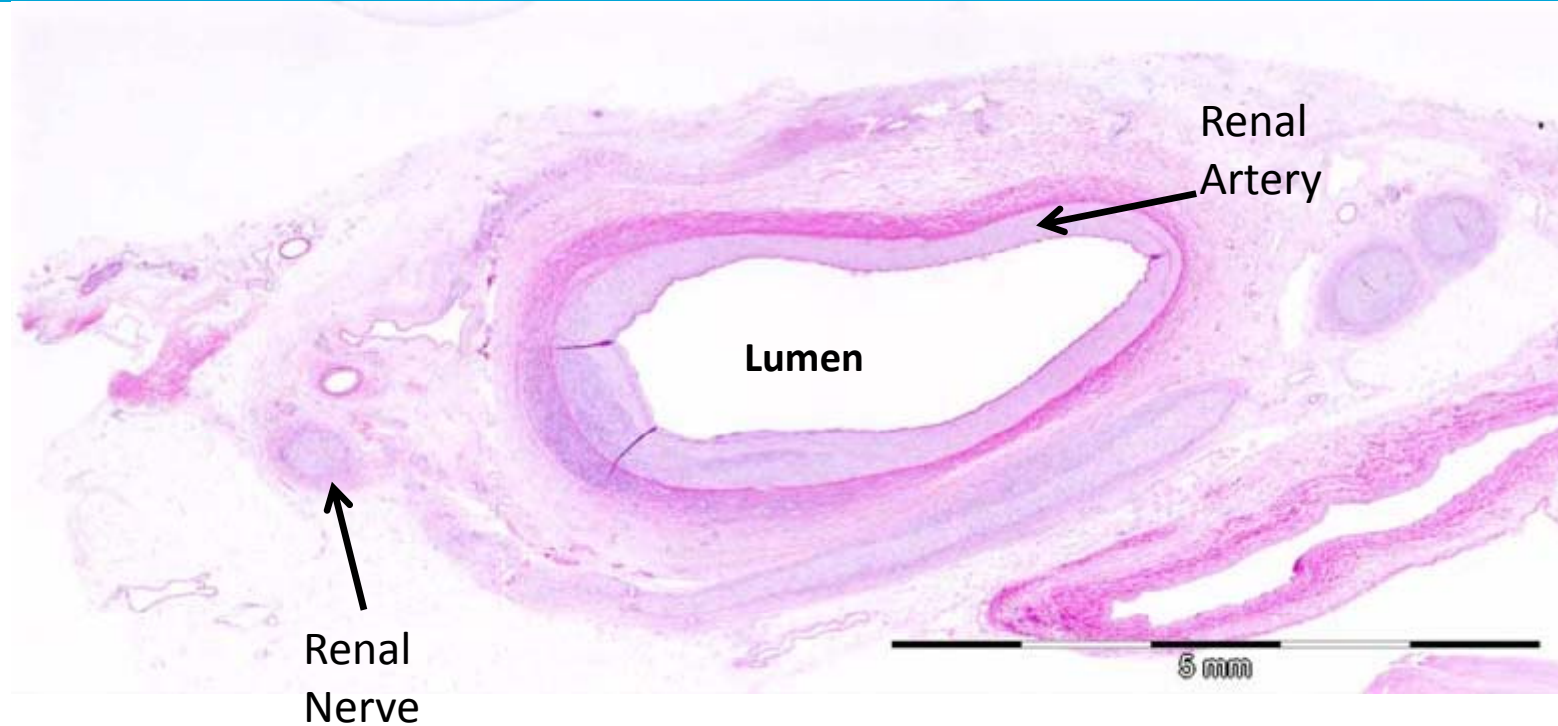


Histology Confirms Healing Response at 7 days





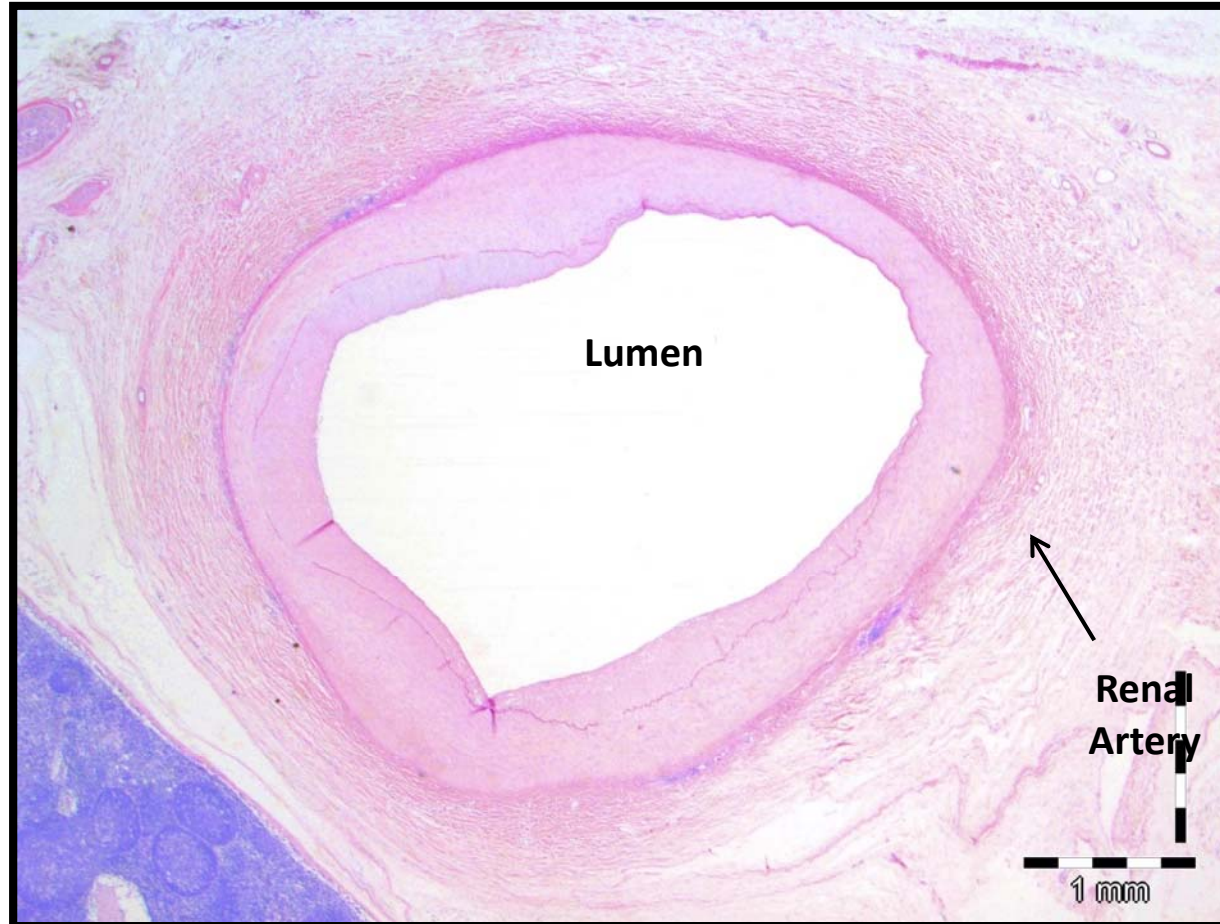
Histology Confirms Open Arteries at 28 days



Day 28 post treatment - Representative Microphotographs



Histology Confirms Open Arteries at 90 days



Day 90 post treatment Representative Microphotographs



REDUCE-HTN Clinical Study Overview

- **DESIGN** - Non-randomized, international, multi-center, prospective, single cohort study for the percutaneous therapeutic treatment of medication-resistant hypertension.
- **SAMPLE SIZE** - 64 subjects
- **STUDY SITES** - 10 international sites
- **STUDY OBJECTIVE** - To assess the safety, efficacy, and feasibility of the Vessix V2 System for the treatment of medication resistant hypertension
- **GENERAL INCLUSION CRITERIA** - Adults with SBP ≥ 160 mm Hg based on an average of three (3) office-based blood pressure readings. On ≥ 3 anti-hypertensive drugs (one must be a diuretic) at maximally tolerated doses and has had no changes to the medication regimen two (2) weeks prior to enrollment;
- **PRIMARY SAFETY ENDPOINT** - Acute safety of the renal denervation procedure. Absence of flow limiting stenosis in the renal artery at one (1) and six (6) months follow-up.
- **PRIMARY EFFICACY ENDPOINT** - Reduction of systolic blood pressure and diastolic blood pressure at six (6) months as measured by office-based blood pressure assessment (seated) and ABPM following therapeutic renal denervation compared to baseline.
- **STUDY DURATION** – 24 months

Clinical Sites/Investigators REDUCE-HTN clinical study

Principal Investigator – Prof. med. Horst Sievert

10 Patients enrolled to date

| Institution | Clinical Investigator | Enrollment to Date |
|---|--|--------------------|
| Paracelsus-SALK Medical Center - Salzburg | Prof. Dr. Uta Hoppe | 7 |
| Monash Heart/Southern Health | Prof. Dr. Ian Meredith | |
| General and Academic Teaching Hospital | Prof. Dr. Franz Leisch, Dr. Thomas Lambert | |
| OLV - Aalst | Prof. Dr. B. de Bruyne, Dr. Eric Wyffels | 2 |
| UniversitatSpital Zurich | Prof. Dr. Thomas Luscher | |
| Georges Pompidou Hospital | Prof. Dr. Michel Azizi, Marc Sapoval | 1 |
| Hospital Erasme | Prof. Dr. P. Van de Borne | |
| U. of Amsterdam | Prof. Dr. R. de Winter | |
| Frankfurt Cardiovascular Center | Prof. Dr. Horst Sievert | |



Faster Easier Approach to Renal Denervation

- Can be used by anyone with standard angioplasty skills.
 - Interventional cardiologists
 - Interventional Radiologists
 - Vascular surgeons with endovascular skills
- Training time < 30 minutes
- Learning curve – none
- Fast user friendly procedure
 - Balloon catheter – prep time < 1min
 - Radiopaque solid gold electrodes allow precise positioning – time < 1 min
 - One button pre-programmed generator – treatment time 30 secs
- Patient friendly
 - Short procedure time
 - Less pain due to bipolar vs unipolar RF and short treatment times