

A Catheter-Based Treatment for Hypertension: ARDIAN

*A/Prof. Robert J. Whitbourn,
MD, MBBS, FRACP
St. Vincent's Hospital
Melbourne, Australia*



Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

Grant/Research Support

Consulting Fees/Honoraria

Major Stock Shareholder/Equity

Royalty Income

Ownership/Founder

Intellectual Property Rights

Other Financial Benefit

Company

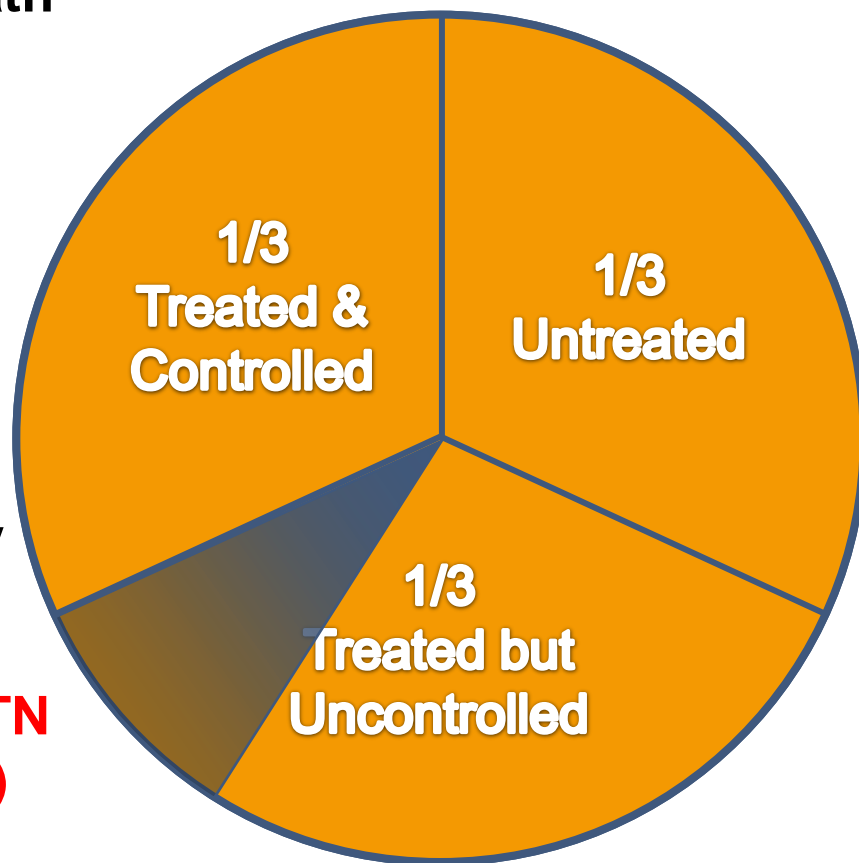
Boston Scientific, Medtronic, Abbott
Vascular, Cardiomind, Ardian.



Hypertension – the Numbers...

- Is the #1 attributable risk for death (49% for IHD) worldwide (WHO)
- 72M Americans (1 in 3 adults)
- 230M in US, EU5 & Japan
- 1B Worldwide
- 7.1M deaths/year
- A doubling of mortality for every 20mmHg increase

**Refractory HTN
~10% (7.2M)**



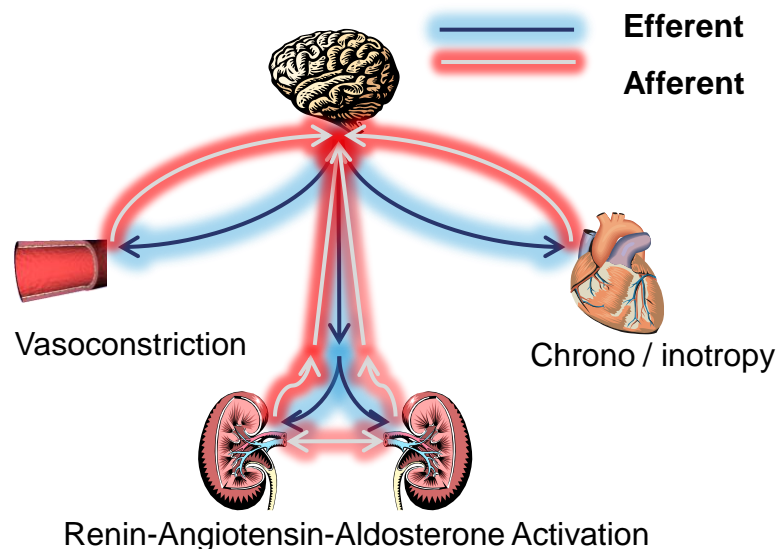
Chronic over-activation of the Sympathetic Nervous System

Renal Efferent Sympathetic Nerve Activity

- ↑ Renin release
- ↑ Na reabsorption
- ↓ Renal blood flow

Renal Afferent Sympathetic Nerve Activity

Systemic HTN
LVH
Arrhythmia
Insulin Resistance



Renal Sympathectomy: Physiology, Preclinical Data & Surgical Precedent

Surgical Nephrectomy or Surgical Sympathectomy
Comprehensive data dating to 1930s

THE EFFECT OF RENAL DENERVATION ON THE LEVEL OF
ARTERIAL BLOOD PRESSURE IN HYPERTENSIVE PATIENTS
Journal of Cardiovascular Pharmacology™
26(Suppl. 2):S24-S28 © 1995 Lippincott-Raven Publishers, Philadelphia

(From the I

VOL. 152, NO. 16

SPI

Sympathetic Nervous System: Contribution to Human
Hypertension and Progression of Organ Damage

Neural Control of the Kidney
Past, Present, and Future

Gerald F. DiBona

Abstract—This article provides a chronological perspective on the development of knowledge concerning the neural control of renal function and is divided into three parts: the past, the present, and the future. (*Hypertension*. 2003; 41[part 2]:621-624.)



Renal Sympathectomy: Physiology, Preclinical Data & Surgical Precedent

Surgical Nephrectomy or Surgical Sympathectomy

Comprehensive data dating to 1930s

Surgical renal denervation shown to:

- ↓ sympathetic activation of kidneys
- ↓ renin
- ↑ urine output
- Reduction of Central Adrenergic Drive

While maintaining electrolyte and volume homeostasis

Renal Denervation: Animal Studies

Multiple animal studies in different species

- Rodents, swine, canine & ovine

In summary, Renal Denervation in animal studies:

- ↓ BP in multiple animal HT models
- ↓ Ventricular filling pressures & ↑ LV function in MI models
- ↓ physiologic & anatomic Δ s of early diabetic nephropathy



20 YEARS OF
INNOVATION
TCT2008

A Catheter-Based Treatment: Renal Denervation



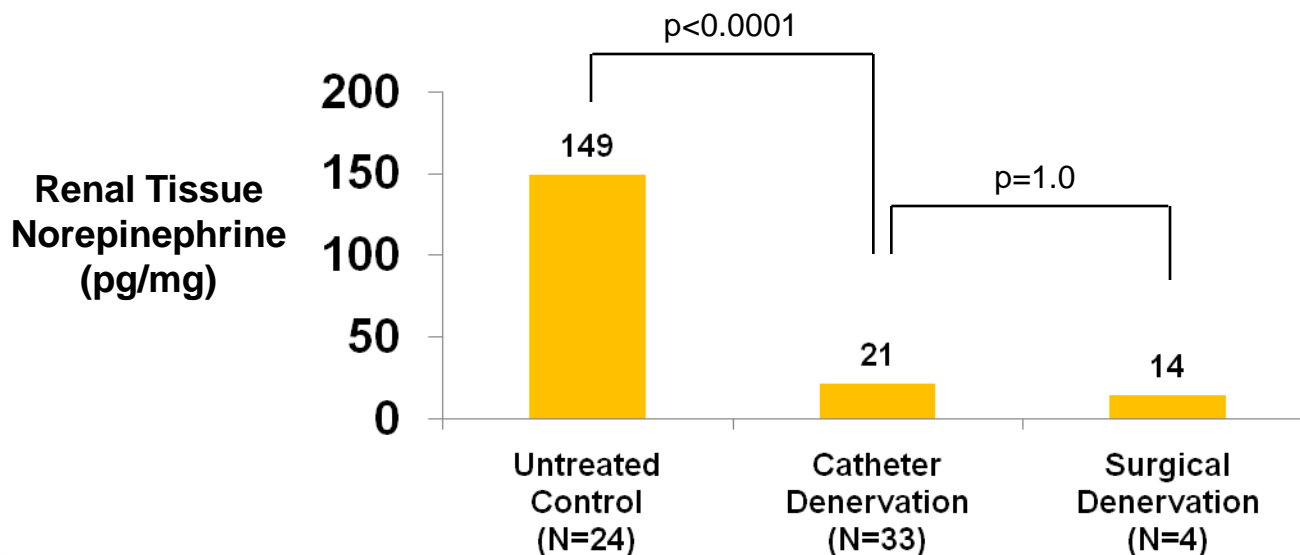
ARDIAN



CARDIOVASCULAR RESEARCH
FOUNDATION

Renal Sympathectomy: Large Animal Data

- **Safety:**
 - Swine model with angiography, gross pathology, histopathology & clinical pathology at 7, 30, 60 & 180 days
 - Intact endothelium by 7 days
 - Vascular architecture & integrity preserved at all follow-up points
 - No renal artery stenosis out to 180 days
- **Effectiveness:**



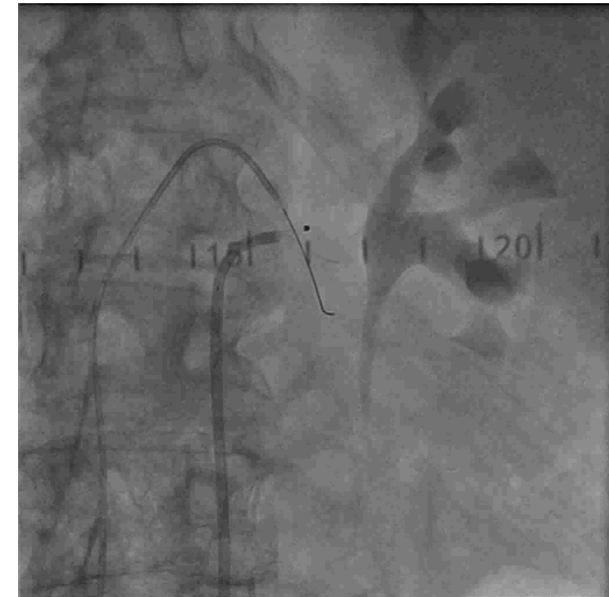
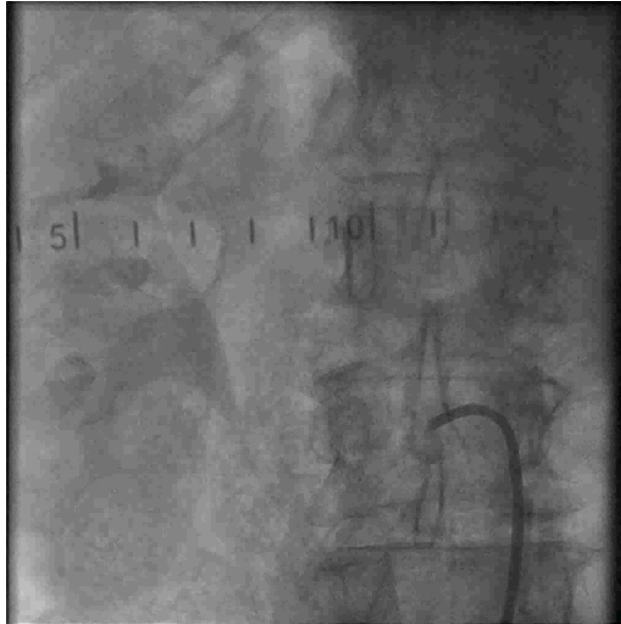
Human Feasibility Trials: Catheter Based Renal Denervation

- **Trials underway in Australia, Europe, & U.S. in patients with refractory hypertension**
 - **Objectives:**
 - **Safety – confirm preclinical experience**
 - **Evidence of denervation**
 - **Blood pressure control**
 - **SBP > 160 mmHg despite at least 3 anti-hypertensive meds**
 - **Enrolling Sites:**
 - **St. Vincent's Hospital, Melbourne, Australia**
 - **The Alfred Hospital, Melbourne, Australia**
 - **John Hunter Hospital, Newcastle, Australia**
 - **Jagiellonian University, Krakow, Poland**
 - **CardioVascular Center Frankfurt, Frankfurt, Germany**
 - **Hennepin County Medical Center, Minneapolis, Minnesota, USA**



Clinical cases:

- RF ablation
- Renal Artery & Venous
Blood sampling
At baseline, post, 30 & 45 days

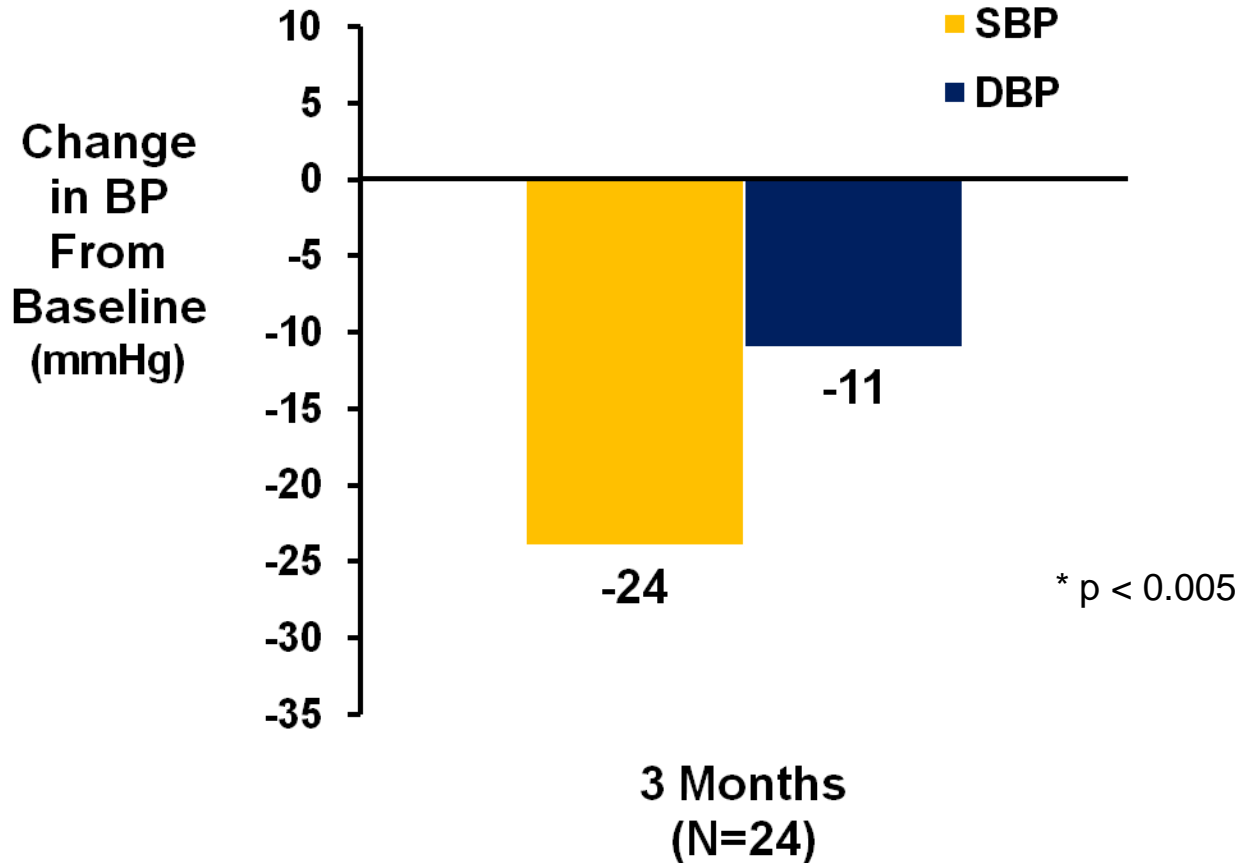


Catheter Based Renal Denervation Preliminary Results: Safety

- **No adverse renal events**
 - **No change in sCr or eGFR at any point in follow-up**
- **No electrolyte disturbances at any point in follow up**
- **No renal artery stenosis at 1, 3, 6, or 9 M post-procedure**
- **No adverse acute or chronic hemodynamic events**

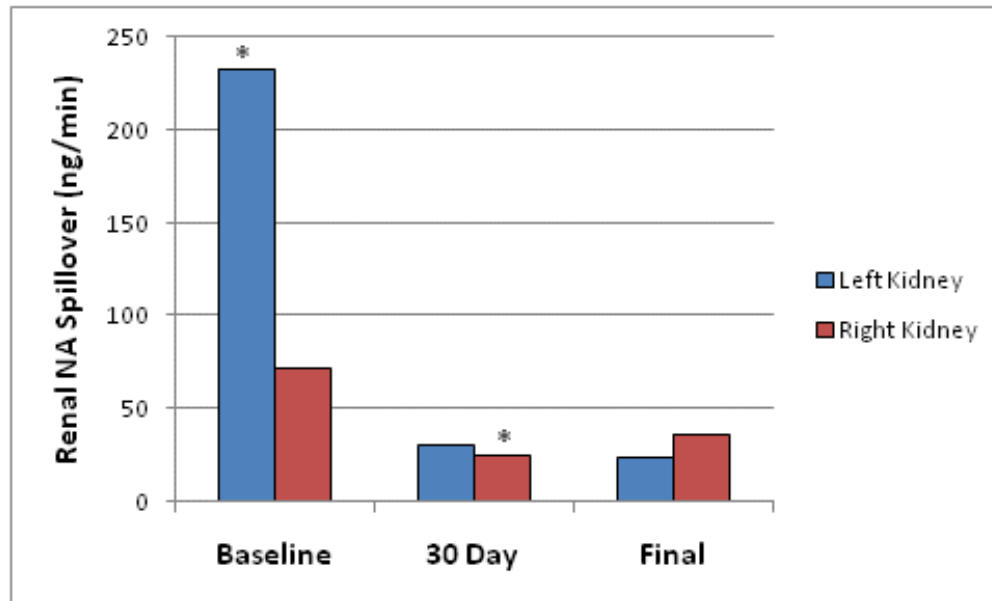


Catheter Based Renal Denervation: Preliminary Results: Reduces Blood Pressure



Evidence of Renal Denervation

- Renal Catecholamine Spillover measured



Evidence of Renal Denervation

- **Muscle sympathetic nerve activity measures**
 - **Documented reduction in bursts/min**
(neural impulse freq)
 - **Demonstrates a significant reduction in central adrenergic drive**



Therapeutic Renal Denervation: Conclusions

- **Safety – feasible, well tolerated with no adverse events**
- **Blood pressure control** a substantial reduction in Blood Pressure in refractory patients
- **A novel catheter-based procedure has successfully denervated the human kidney (afferent & efferent)**

Catheter-Based Treatment for Hypertension: ARDIAN

This treatment is in trial for:

- BP reduction in Hypertension
- LVH regression in Heart failure
- Nephroprotection in Chronic Kidney Disease

