Going to the Source: A Disruptive Approach to Renal Denervation with the Non-vascular Verve System

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Presenter Disclosure Information

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• Medtronic, Abbott, AngioScore, Speaker;
• Acist Medical Systems Grant; and
• Verve Medical, Inc., Major Stockholder

**Patents**  -- RF, Snares, Wires, Balloon Catheters, Covered Stents, Devices for Arterial Venous Connection, Devices for LV and RV Closure
• RDN via the renal arteries results in a response rate of 50%-85%
Catheter-Based Renal Denervation Is No Simple Matter Lessons To Be Learned From Our Anatomy?

In humans, there is a greater abundance of efferent compared with afferent nerve fibers and the proportion of afferent nerve fibers is not different between the proximal, middle and distal segments...the efferent fibers are far greater than afferent fibers.
However, the results of pre-clinical studies should be interpreted with caution, as the influence of underlying atherosclerosis in human arteries as well as the depth of the nerve distribution may be different and cannot be assessed in healthy animals models.

The Bench-to-Bedside Transition

Limited destruction of renal nerves after catheter-based renal denervation: results of a human case study

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Symplicity Treatment

• 36 year old female died 12 days following treatment
• Multiple ICU admits for hypertensive crises
• Post mortem revealed a ruptured dissection of the ascending aorta
• Not related to RDN
Symplicity Treatment

• There was no interruption of the nerve bundles

• “If this pattern occurs in other cases as well, it might explain at least in part the great variability in blood pressure lowering effect”
Innervation of the kidneys is not exclusively via tracts parallel to the renal arteries.
Neuroanatomy

• We are not getting the correct nerves...if we were, why don’t we get an immediate BP drop?

“In contrast to the widespread distribution of EFFERENT Sympathetic nerve fibers in the kidney, the majority of the AFFERENT Renal Sensory nerves are located in the renal pelvic area”

Kopp UC, University of Iowa. Neural Control of Renal Function 2011
Intrarenal and Extrarenal Autonomic Nervous System Redefined


The nerves are in close proximity to the renal collecting system.
The Structure of the Kidney

Why Not Treat the Source?
Pre Nephrectomy Safety Study

• 3 Patients
• 4 Kidneys
• Verve treatment 1 week prior to nephrectomy
• Harvested kidneys sent to pathology
NephroBlate™ Catheter – Fluoroscopic View

Wings extended
Pelvis Wall - Distal to Ablation Zone (Control)

- Transitional epithelium
- Lamina propria
- Smooth muscle
- BV
- Renal Pelvic Space
- Serosa
Transitional epithelium
Lamina propria
Smooth muscle
Adipose tissue
Renal Pelvic Space

1.75 mm

< 1.00 mm

Treatment Depth
Does it work?
STUDY OBJECTIVES

In subjects with resistant hypertension:

- Assess that renal denervation via the collecting system is safe
- Assess the safety of the delivery device
- Assess the effectiveness of the treatment
Unlike other RDN devices, the blood pressure dropped immediately.
Reduction in Blood Pressure

1 Month Results

- 4 drug resistant patients on ≥ 2 drugs

All patients normotensive at 3 months
Is it Easy to Use?

It is a standard urologic procedure.
26 million Americans have chronic kidney disease
VERVE (Unique Applications)

- Existing disease or anatomic anomalies
- Patients who have failed arterial approaches
- Any degree of renal insufficiency
- **No systemic contrast utilized**
Reduction in Porcine Norepinephrine (Helical Electrode Design)

- 14 Day, n=8
- 90 Day, n=9

Mean Reduction: -68%
2 week histopathology
What is a Truly Innovative Product?

• Unmet Clinical Need
• Out of the Box Concept
• IP Position/Viability
• Biological Proof of Concept
• Regulatory Pathway
• Commercialization Potential
Out of the Box Concept

• All the other RDN devices treat the peri-arterial nerves
• This is not where the nerves are
Treatment Depth

- Transitional epithelium
- Lamina propria
- Smooth muscle
- Adipose tissue

Renal Pelvic Space

1.75 mm

< 1.00 mm
In the renal pelvis, all the nerves are within 1.75mm of the pelvic lumen
We believe we are the only company that possesses the renal pelvic RDN intellectual property...this will allow us to practice this technique.
We are the only company that has described RDN pathophysiology in a human clinical nephrectomy model.
There is a predicate device and application in urology which we feel will make a 510K approval possible in the niche application for patients with resistant hypertension and chronic renal disease.
75% of resistant hypertensive patients are managed by nephrologists...only 12% by cardiologists
In the Doctor’s Office
Commercialization Potential

• Only RDN that actually heats the afferent nerves
• Only RDN that can be done potentially in the doctor’s office
• This may be a more cost effective therapy in the third world
Verve Medical
Competitive Landscape

• We know of no other competitors addressing the nephrology/urology market for controlling hypertension.
Conclusion

More patients enrolled pre-nephrectomy

- Safety of the new probe
- Efficacy in treating hypertension
- Histopathologic analysis
Renal Denervation

A New Approach to Treatment of Resistant Hypertension
Cardiovascular Disease Management:
A Case-Based Approach

Richard R. Heuser, MD, FACC
Program Director

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