Newer Methods To Achieve Renal Denervation: Can Catheter Based Ultrasound (Surround Sound) Be Effective And Safe For Lowering BP, For Treating Heart Failure (The RETREAT Trial): What About Catheter Chemical Denervation With Alcohol And DW 2013: How Are They Delivered

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CardioVascular Center Frankfurt - CVC, Frankfurt, Germany

Devices for Renal Denervation

- Radiofrequency catheters
  - Spiral - Medtronic
  - St. Jude Medical
  - Cordis
  - Angiocare – Terumo
  - Verve
- Radiofrequency balloons
  - Vessix – Boston
- Microwave
- DenervXCooled

Medtronic’s Multi-Electrode Spyral

- 4 electrodes
- 60 second per artery
- Guaranties circumferential ablation and sufficient number of ablations

SPYRAL FIM (n=40)

1 month (n=40)

182.4/95.1 mm Hg to 166.4/88.0
P < 0.001

Whitbourn ESC 2013

Randomized Sham-Controlled Trial of Renal Sympathetic Denervation in Mild Resistant Hypertension

Intention to treat

Per protocol

24 hour ABPM, 6 months

S. Desch, TCT 2014
SJM: EnligHTN
Renal Artery Ablation Catheter

- Basket with 4 electrodes
  - Two basket sizes:
    - 16 mm length; 6 mm
    - 18 mm length; 8 mm
  - Good for arteries 4-8mm
- 8F guide compatible
- Ablation time 90 sec
- CE mark

EnligHTN-1
Office BP reduction from baseline

Cordis ThermoCool

- Spiral radiofrequency catheter
- Multiple electrodes
- Irrigation for cooling
- Potential advantages
  - Lower temperature at electrode-tissue contact
    - Less thrombus formation
    - Less endothelial damage
    - Less char formation
  - Higher degree of tissue penetration

Verve
Transurethral denervation

- Radiofrequency

- Animal results:
  - Tissue norepinephrine levels dropped 70%

Verve FIM – 1 month results
Transurethral denervation

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- Drugs
  - Mercator
  - Northwind
  - Ablative Solutions
  - Kiroprakton Hospital, Athens
- Radiation
  - Best Medical Int.
  - CyberHeart (CyberKnife)
- Ultrasound
  - Recor Medical
  - CardioSonic
  - Kona

R. Heusser, TRENDS 2013
R. Heusser, TCT 2014
R. Heusser, TCT 2013
Vessix Vascular - Boston
V2 Renal Denervation System

- Balloon catheter with gold bipolar RF electrodes
- 3-7 mm renal arteries
- Low pressure (<3 atm)
- Simultaneous energy delivery to all electrodes
- Temperature sensors at each electrode: independent titration of power
  - 68°C fixed
  - 30 seconds
  - < ½ to 1 watt

CE mark

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Cooled Microwave Catheter Prototype

- Microwave transducer inside of a balloon
- Cooling
- Ablation zone controllable; 1 to 5mm from intima
- Treatment time 30 – 60 sec

Microwave Heating Plus Conductive Cooling: Net Thermal Effect

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Northwind Approach

- Local administration of a neurotropic agent
  - NW2013: Specifically destroying nerves, leaving other tissue unaffected
- Catheter-based delivery using micro-needles
  - 0.014 guide wire-based,
  - 6-8F delivery system

Northwind Ambulatory BP over 3 Months

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Month</th>
<th>3 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMRA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Std.</td>
<td>14.7</td>
<td>22.8</td>
<td>18.0</td>
</tr>
<tr>
<td>SEM</td>
<td>6.6</td>
<td>10.2</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Ablative Solutions

PeriVascular Renal Denervation (PVRD)

- Renal nerves
- Micro-needles
- Renal artery cross-section
- Ethanol or other agents

Comparison of Alcohol at 2 Volumes to RF

(Values Are ± SD)*

<table>
<thead>
<tr>
<th>Ablation Depth</th>
<th>Norepinephrine Reduction</th>
<th>Ablation Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol 0.3 mL</td>
<td>66%</td>
<td>9%</td>
</tr>
<tr>
<td>Ethanol 0.6 mL</td>
<td>77%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Both volumes of alcohol show increased efficacy, with both showing significance.

Drugs
- Mercator
- Northwind
- Ablative Solutions
- Kiprokrak Hospital, Athens

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  - Kona
Radiation: Best Medical Int.

- Radiation selectively destroys nerves
- Device is based on the Novoste system for brachytherapy
- Clinical trial ongoing

CyberHeart - CyberKnife

- Percutaneous radiation therapy
- Ready for clinical trial

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Potential Advantages of Ultrasound

- Ultrasound energy passes through the fluids and generates frictional heating inside of the tissue
- Unlike RF, no direct tissue contact required

Ultrasound: Recor Medical

- Ultrasound transducer mounted inside of a low pressure balloon
- Cooled water in the balloon protects the endothelium against heat
- 30 seconds of circumferential heating

REDUCE:
Office Systolic Blood Pressure (93% Responder Rate)

- Source: Company Data
Kona Medical Surround Sound™ System

- Fully non-invasive system utilizing ultrasound for targeting / tracking
- Wave I, II and III trials: BP reduction 25mmHg after 6 months

Conclusions

- Technical issues had been a major reason why HTN-3 failed
- There are many new devices already approved OUS or under development
- These devices have different advantages
  - Guaranteed circumferential ablation
  - Guaranteed number of ablation points
  - Some use other energy sources or chemicals with increased penetration depth
- Initial results with non-invasive denervation are promising