Background: The PARADISE system (ReCor Medical, Menlo Park, CA) is a unique therapeutic non-focused ultrasound system designed to perform renal denervation while preventing circumferential damage to the renal artery for resistant hypertension. The system allows for targeted delivery of ultrasound energy with thermal injury at depths beyond 0.5 mm while cooling and preserving tissue in its immediate vicinity. A preclinical porcine animal study was conducted to evaluate the safety and effectiveness of this technology.
Methods: Renal denervation was performed bilaterally using the PARADISE system in healthy Yorkshire cross swine (n=9). Animals were either survived for 7 days, or sacrificed acutely. For the acute study, a standard denervation protocol was used distally within each renal artery, and for comparison, the same treatment without cooling was delivered proximally. The arteries were removed, flushed, and stained with triphenyltetrazolium chloride (TTC) to assess for medial damage. At 7 days, whole kidney norepinephrine levels were obtained (HPLC-MS) to assess damage to sympathetic nerves, and histopathologic assessment (H&E) of the renal arteries was performed to evaluate the integrity of the endothelium, media, and adventitia and nerve damage was assessed in the perirenal space.
Results: TTC staining of the renal arteries demonstrated non-viable tissue in the locations where energy was applied without cooling, while standard denervation treatment with cooling demonstrated preservation of the media. H&E staining demonstrated minimal to no injury to the endothelium and media at 7 days. Extensive periadventitial damage was observed with up to 80% nerves damaged within susceptible zones. Kidney norepinephrine levels were significantly reduced in all animals and correlated with the degree of nerve damage.
Conclusions: The Paradise ultrasound system effectively ablated the sympathetic nerves surrounding the renal arteries while preserving the media thus demonstrating the importance of cooling.

TCT-498

Safety and performance of the next generation EnligHTN™ Renal Denervation System in patients with drug-resistant, uncontrolled hypertension: a first-in-human multicentre study

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Background: Catheter-based renal artery denervation therapy has become established as a therapeutic option in patients with resistant hypertension. We have previously presented safety and efficacy using the first generation multi-electrode renal denervation system with the EnligHTN™ catheter (St. Jude Medical). The next generation system utilises a novel algorithm for the delivery of 1 minute of radiofrequency energy, optimised for simultaneous delivery of therapy through all electrodes, with an interactive generator interface. This study will evaluate the safety and performance of the next generation EnligHTN™ Renal Denervation System in patients with drug-resistant, uncontrolled hypertension.
Methods: Inclusion criteria include patients 18-80 years of age with a systolic BP ≥160 mmHg and an average daytime systolic ambulatory BP ≥135 mmHg on three or more antihypertensive agents (including a diuretic). The primary end-points are 1) to characterize the rate of serious procedural and device related adverse events through 6 months and 2) the change in office BP at 6 months. The secondary end-points include the changes in 24 hour ABP and the characterization of renovascular safety and renal function change over time. The multi-electrode RF catheter will be introduced in a renal artery, and RF energy will be delivered simultaneously for 60 seconds across all 4 electrodes. Next, the catheter will be withdrawn slightly and rotated, and the denervation sequence will be repeated. This process will then be repeated on the contralateral renal artery. A minimum of 30 patients will be included in the trial.
Results: To date 10 patients from three sites (63.4 ± 6.4 years, 7M/3F) have been included. Baseline BP 178.5±15.2/97.3±14.0 mmHg, ABPM 159.4±20.1/87.3±9.6. Eight denervations were successfully performed in each artery for all patients. Median ablation procedure time was 19 min. No vascular or renal artery complications were observed.
Conclusions: Accumulated results from all sites will be presented at the meeting. Initial experience suggests that the SJM next generation EnligHTN™ System may shorten procedure times while still delivering a safe, predictable and reproducible denervation pattern.

TCT-499

NT-proBNP reduction correlates with systolic blood pressure decrease in patients with therapy resistant hypertension undergoing renal denervation (RDN)

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Background: In arterial hypertension risk factor evaluation, including LV mass measurements and risk stratification using risk different charts and scores is usual practice. In chronic heart failure NT-proBNP has been shown to be a marker of wall stress and prognosis. Renal denervation (RDN) is a therapeutic strategy for patients with resistant arterial hypertension. The changes of NT-proBNP in patients undergoing RDN have never been described.
Methods: We investigated 33 patients with resistant hypertension (18 male, 15 female). Inclusion criteria at baseline were a systolic BP ≥160 mmHg (≥150 mmHg in diabetics), treated with ≥3 antihypertensive drugs, an estimated glomerular filtration rate ≥45 mL/min/1.73m2 and suitable renovascular anatomy. Medication was unchanged during the follow-up period. All patients underwent bilateral RDN. Systolic (SBP) and diastolic blood (DBP) pressures were measured at baseline and at the 6 months follow-up with an automated OMRON device. Plasma at baseline and after 6 months was analyzed for NT-proBNP using the commercially available Elecsys proBNP sandwich immunoassay on an Elecsys 2010 (Roche Diagnostics, Mannheim).
Results: (all results are given in mean±SEM). Mean age was 63 ± 6 years. Office SBP and DBP were reduced by −20.2 ± 2.5 and −5.8± 1.6 mmHg ($p<0.01$) after 6 months. Mean NT-proBNP was reduced from 173.4 pg/ml at baseline to 163.4 pg/ml after 6 months (p 0.25) Decrease of systolic blood pressure (SBP) significantly correlates with reduction of NT-proBNP (p 0.01). There was no significant correlation between diastolic blood pressure decrease and NT-proBNP reduction.
Conclusions: (i) Six months after RDN patients with resistant hypertension experienced a substantial reduction in SBP and DBP. (ii) Systolic blood pressure decrease correlates with NT-pro-BNP reduction as suggestive marker of reduced LV stress after successful RDN and significant SBP reduction.

TCT-500

Effect of Renal Denervation (RDN) in "Real World" Patients with trHTN Compared to Simplicity HTN-2 Trial. First Results of the Luebeck RDN Registry

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Background: Resistant hypertension is associated with substantially increased risk for cardiovascular events and mortality. The growing prevalence of hypertension worldwide (1.6 billion predicted by 2025) combined with an aging population highlights the need for effective blood pressure (BP) lowering therapies for patients of all ages. First data from randomized clinical studies suggest a marked reduction in systolic (SBP) and diastolic (DBP) 6 month after the procedure. However, there are limited data out side from clinical trials.
Methods: Data from "real world" patients enrolled in a local RDN program (inclusion criteria according to Symplicity HTN-2) who completed 12 months follow-up are compared to data of a controlled clinical trial. All patients had resistant hypertension defined as a systolic BP (SBP) ≥160 mm Hg (>150 mmHg in diabetics) while on ≥3 antihypertensive medications including a diuretic. Demographic data and change from baseline BP and HR was assessed for each subset at 6 and 12 month.
Results: Table 1

Parameter	Symplicity HTN 2 RDN group (n=52)	Luebeck RDN Registry (N =79)
Age in years	58 + 12	63 + 11
Body Mass Index	31+5	29 + 6
Diabetes (%)	40	33
No. of antihypertensive drugs	5.2 + 1.5	5.5 + 1.6
SBP @ baseline in mmHg	178 + 18	174 + 24
DBP @ Baseline in mmHg	97 + 16	92 + 15
HR @ baseline in 1/min	74	69 + 11
SBP @ 6 mths F/U in mmHg	- 32 + 7	- 23 + 9
DBP @ 6 mths F/U in mmHg	- 12 +3	-9 + 4
HR @ 6 mth F/U in 1/min	69	64 + 10
SBP @ 12 mths F/U in mmHg	- 28 + 7	- 20 + 8
DBP @ 12 mths F/U in mmHg	-10 + 4	-9 + 5
HR @ 12 mths F/U in 1/min	68	62 + 11

Conclusions: The results suggest that RDN performed in a clinical setting has equal blood pressure lowering effects as when performed in RCT. Furthermore, reduction of office BP and office heart rate after renal denervation is consistent under real world conditions.

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