Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Population definitions

Intention-to-Treat (ITT)
The ITT population was defined as all randomized subjects analyzed according to their original randomization assignment.

There were 150 ultrasound renal denervation (uRDN) and 74 sham patients included in the ITT population.

Multiple imputation was employed for subjects with missing ambulatory BP data at 2 months (5 subjects randomized to uRDN and 1 subject randomized to sham). Subjects meeting escape criteria for initiation of anti-hypertensives (4 subjects randomized to uRDN and 6 subjects randomized to sham) were imputed using last observation carried forward.

As-Treated (AT)
The AT population was defined as all randomized subjects analyzed according to their original randomization assignment excluding subjects randomized to treatment who received no ablations.

One subject randomized to treatment received no ablations and is excluded from the AT population. A total of 149 uRDN and 734 sham patients were included in the AT population.

Complete Ambulatory Blood Pressure (CA)
The CA population was defined as all randomized subjects analyzed according to their original randomization assignment that had ambulatory BP values at both baseline and follow-up.

There were 5 uRDN subjects and 1 sham subject that were missing ambulatory BP values at 2 months. A total of 145 uRDN and 73 sham patients were included in the CA population.

modified Intention-to-Treat (mITT)
The mITT population was defined as all randomized subjects analyzed according to their original randomization assignment, except excluded subjects that met the protocol defined High BP Action criteria necessitating the re-start of anti-hypertensive medication prior to the 2-month primary endpoint.

There were 4 uRDN and 6 sham subjects that met protocol-defined High BP Action criteria that restarted medications that were excluded from the mITT analysis. A total of 146 uRDN and 68 sham patients were included in the mITT population.

Per-Protocol (PP)
The PP population was defined as all subjects who were randomized, had treatment delivered successfully and were free from major issues which may affect the assessment of the treatment:

- Baseline daytime ambulatory BP <135/85mmHg or failure to obtain baseline ambulatory BP recording
- Renal artery anatomical exclusion deviations
- Failure to obtain 2-month follow-up ambulatory BP recording
- Subjects restarting antihypertensive medication, for any reason, prior to the 2-month primary endpoint.

There were 19 subjects excluded from the PP analysis in the uRDN group: 5 missing the 2-month ambulatory BP, 4 started medications prior to 2-months who met the High BP Action criteria, 8 added medication prior to 2-months without meeting the High BP Action criteria, 2 with unsuccessful treatment.

There were 11 subjects excluded from the PP analysis in the Sham group: 1 missing the 2-month ambulatory BP, 6 started medications prior to 2 months who met the High BP Action criteria, 4 added medications prior to 2 months without meeting the High BP Action criteria.
A total of 131 uRDN and 63 sham patients were included in the PP population.

eTable 1. Angiographic and procedural characteristics in the ultrasound renal denervation group (uRDN) and in the sham group

Characteristic	uRDN (n = 150)	Sham (n = 74)
Procedure time (sheath removal – sheath insertion) (min)	76.7 (25.2)	43.9 (16.6)
Device time (catheter out - catheter in) (min)[a]	33.4 (18.7)	NA
Total Emission Time (seconds)[a]	38.9 (7.3)	NA
Sedation		
Conscious Sedation (e.g. midazolam, fentanyl, and/or morphine)	114 (76.0%)	57/73 (78.1%)
Monitored Anesthesia Care (e.g. propofol)	19 (12.7%)	10/73 (13.7%)
General Anesthesia (e.g. inhaled anesthetics, muscle relaxants or neuromuscular blocking agents, intubation, and/or ketamine)	17 (11.3%)	6/73 (8.2%)
Contrast volume[b] (cm^3)	135.7 (67.4)	64.6 (30.4)
Fluoroscopy time[c] (min)	15.9 (8.6)	4.2 (4.6)
Total Number of Emissions[a]	5.6 (1.0)	NA
Left [a]	2.7 (0.7)	
Right [a]	2.8 (0.7)	
Subjects with Treated Renal Accessory or Proximal Side Branch [a]	30 (20.0%)	NA
Treatment successfully delivered (minimum 2 emissions bilaterally)	148 (98.7%)	NA

Data displayed as either number of patients (%), or Mean (SD).
[a]There was one patient in the uRDN group incorrectly treated as sham (receiving no treatment) not included.
[b]There was one patient in the sham group missing contrast volume.
[c]There was one patient in the uRDN group and two patients in the sham group missing fluoroscopy time.

eTable 2. Bang and James blinding indices at hospital discharge and 2 months

	uRDN (n=150) (95% CI)	**Sham (n=74) (95% CI)**
Bang Blinding Index at Discharge	0.26 (0.17, 0.36)	-0.19 (-0.33, -0.05)
Bang Blinding Index at 2 Months	0.23 (0.09, 0.37)	0.25 (0.07, 0.42)

	All Randomised Patients (n=224) (95% CI)
James Blinding Index at Discharge	0.77 (0.72, 0.83)
James Blinding Index at 2 Months	0.53 (0.46, 0.59)

eTable 3. Patients with change in antihypertensive medications prior to the 2-month visit in the ultrasound renal denervation group (uRDN) and in the sham group (intention-to-treat population)

Circumstances and Timing of Antihypertensive Medication Restart	uRDN (n = 150)	Sham (n = 74)	P value[a]
Patients receiving additional antihypertensive medications at the 2-month ABPM	12 (8.0%)	10 (13.5%)	.19
Protocol defined (escape) criteria	4 (2.7%)	6 (8.1%)	.09
Physician decision or patient preference	8 (5.3%)	4 (5.4%)	>.99

Data displayed as number of patients (%). ABPM: ambulatory blood pressure monitoring
[a] P value from Chi-square or Fishers exact test as appropriate.

eTable 4. Tipping point analysis for primary endpoint of daytime ambulatory systolic blood pressure

A tipping point analysis was conducted as a sensitivity analysis to evaluate the effect of missing endpoint data. The tipping point analysis evaluated single imputations for missing blood pressure based on the observed treatment group specific best-case (greatest reduction in blood pressure in the uRDN group and greatest increase in blood pressure in the sham group), worst-case (greatest increase in blood pressure in the uRDN group and greatest reduction in blood pressure in the sham group), and quartiles between these values. In this analysis, a tipping point between significant/non-significant results does not occur. Out of the 25 imputation scenarios, all 25 (100%) result in the primary endpoint of daytime ambulatory systolic blood pressure as lower in the uRDN arm.

		uRDN				
		0% (-41 mmHg)	**25%** (-15 mmHg)	**50%** (-9 mmHg)	**75%** (-1 mmHg)	**100%** (26 mmHg)
Sham Procedure	**0%** (-30 mmHg)	<.001 (<.001[a])	<.001 (<.001 [a])	<.001 (<.001[a])	<.001 (<.001[a])	0.006 (<.001[a]) (worst case)
	25% (-7 mmHg)	<.001 (<.001[a])	<.001 (<.001 [a])	<.001 (<.001[a])	<.001 (<.001[a])	0.003 (<.001[a])
	50% (-1 mmHg)	<.001 (<.001[a])	<.001 (<.001 [a])	<.001 (<.001[a])	<.001 (<.001[a])	0.003 (<.001[a])
	75% (5 mmHg)	<.001 (<.001[a])	<.001 (<.001 [a])	<.001 (<.001[a])	<.001 (<.001[a])	0.002 (<.001[a])
	100% (26 mmHg)	<.001 (<.001[a]) (best case)	<.001 (<.001[a])	<.001 (<.001[a])	<.001 (<.001[a])	0.002 (<.001[a])

P value from ANCOVA, adjusting for baseline value. The P value ([a]) from a baseline adjusted ANCOVA on the ranks is also provided.

eTable 5. Incidence of major adverse events adjudicated by the clinical events committee (primary safety endpoint)

	uRDN group (n=150)	Sham group (n=74)
Overall Composite MAE Rate	**0.0%**	**0.0%**
30-day events		
All-cause mortality	0	0
New onset end-stage renal disease (eGFR< 15 mL/min/m^2 or need for renal replacement therapy)	0	0
Significant embolic event resulting in end-organ damage	0	0
Renal artery perforation requiring an invasive intervention	0	0
Renal artery dissection requiring an invasive intervention	0	0
Major vascular complications requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion	0	0
Hospitalization for hypertensive or hypotensive crisis	0	0
Hospitalization for major cardiovascular- or hemodynamic- related events	0	0
New onset Stroke	0	0
New onset Myocardial Infarction	0	0
6-month events		
New onset renal artery stenosis of more than 70%, confirmed by CT or MR angiography	0	0

Data displayed as number of events unless otherwise noted.

As stated in the statistical section, with 150 patients in uRDN we had 95% power for the primary safety endpoint assuming an observed 3% major adverse event rate in the uRDN group compared with a 9.8% safety performance goal. Here, the upper limit of the 95% confidence interval of the overall composite MAE rate for uRDN was 2.4%.

eTable 6. Change in ambulatory, office, and home blood pressure at 2 months in the ultrasound renal denervation group (uRDN) and in the sham group in the modified-intention-to-treat population (n = 146 uRDN, n = 68 sham)

	uRDN			Sham			Baseline Adjusted Observed		Baseline Adjusted with Multiple Imputations	
	Randomization	2 Months	Difference	Randomization	2 Months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[c]	Mean Between-Group Difference (95% CI)[a]	P value[c]
SBP Parameters (mmHg)										
Daytime Ambulatory[e]	150.1 (8.7)	142.0 (13.4)	-8.1 (11.7)	150.7 (8.6)	148.7 (10.9)	-2.0 (9.9)	-6.2 (-9.4, -3.0) -7.0 (-10.0, -4.0)[b]	<.001 <.001[d]	-6.2 (-9.4, -3.0) -7.0 (-10.0, -4.0)[b]	<.001 <.001[d]
24-hour Ambulatory[f]	143.1 (9.0)	135.2 (13.0)	-7.9 (10.8)	144.0 (9.6)	142.2 (10.4)	-1.8 (9.6)	-6.3 (-9.3, -3.3)	<.001	-6.3 (-9.2, -3.3)	<.001
Nighttime Ambulatory[f]	131.9 (12.5)	125.0 (14.8)	-6.8 (12.9)	133.5 (13.5)	132.0 (12.3)	-1.4 (11.8)	-6.0 (-9.4, -2.6)	<.001	-5.9 (-9.3, -2.5)	<.001
Home[g]	152.3 (9.5)	143.0 (12.2)	-9.3 (9.5)	148.4 (9.8)	147.1 (11.2)	-1.4 (8.0)	-7.2 (-9.9, -4.5)	<.001	-7.1 (-9.7, -4.4)	<.001
Office[h]	156.6 (13.4)	145.2 (15.8)	-11.4 (13.6)	155.5 (12.7)	149.5 (15.8)	-6.1 (12.6)	-5.0 (-8.8, -1.2) -6.5 (-10.5, -2.5)[b]	0.01 .003[d]	-4.9 (-8.6, -1.1) - 6.5 (-10.5, -2.5)[b]	<.001 .003[d]
DBP Parameters (mmHg)										
Daytime Ambulatory[e]	93.8 (5.2)	88.2 (7.5)	-5.6 (6.5)	92.9 (5.1)	91.4 (6.3)	-1.4 (6.0)	-3.8 (-5.6, -2.0)	<.001	-3.8 (-5.6, -2.0)	<.001
24-hour Ambulatory[f]	88.4 (5.9)	82.9 (7.7)	-5.4 (6.4)	87.9 (5.6)	86.6 (6.0)	-1.3 (5.6)	-4.1 (-5.8, -2.3)	<.001	-4.0 (-5.7, -2.3)	<.001
Nighttime Ambulatory[f]	79.8 (8.4)	74.9 (9.8)	-4.8 (8.2)	80.0 (8.2)	79.4 (7.6)	-0.6 (7.0)	-4.3 (-6.5, -2.2) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]	-4.3 (-6.4, -2.1) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]
Home[g]	97.7 (6.2)	92.5 (7.3)	-5.2 (6.0)	94.8 (7.0)	94.3 (7.1)	-0.5 (4.6)	-4.0 (-5.7, -2.4	<.001	-3.9 (-5.5, -2.3)	<.001
Office[h]	101.7 (7.7)	95.7 (10.1)	-6.1 (9.4)	101.0 (7.5)	97.0 (10.7)	-4.1 (8.9)	-1.8 (-4.4, 0.9)	0.195	-1.6 (-4.2, 1.0)	0.225

Data displayed as mean (SD) unless otherwise specified. DBP=diastolic blood pressure, SBP=systolic blood pressure

[a]Estimate of treatment difference, from baseline adjusted ANCOVA (observed or with multiple imputations).

[b]In the event that change from baseline in either cohort is non-normal, the Hodges-Lehmann estimator of location shift (median) and associated 95% confidence interval (using observed data) is also provided.

[c]P value from baseline adjusted ANCOVA (observed or with multiple imputations).

[d]In the event that change from baseline in either cohort is non-normal, the P value from a baseline adjusted ANCOVA on the ranks (using observed data) is also provided.

[e]There were 141 patients in the uRDN group and 67patients in the sham group with daytime ambulatory BP.

[f]There were 140 patients in the uRDN group and 67 patients in the sham group with 24h and nighttime ambulatory BP.

[g]There were 136 patients in the uRDN group and 63 patients in the sham group with home BP.

[h]There were 133 patients in the uRDN group and 65 patients in the sham group with office BP.

eTable 7. Change in ambulatory blood pressure at 2 months in the ultrasound renal denervation group (uRDN) and in the sham group in patients with complete ambulatory blood pressure data both at baseline and 2 months (n = 145 uRDN, n= 73 sham)

	uRDN			Sham Procedure			Baseline Adjusted Observed	
	Randomization	2 Months	Difference	Randomization	2 Months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[c]
SBP Parameters (mmHg)								
Daytime Ambulatory[e]	150.2 (8.6)	142.3 (13.4)	-7.9 (11.6)	151.3 (9.0)	149.5 (11.1)	-1.8 (9.5)	-6.3 (-9.4, -3.2) -7.0 (-9.0, -4.0)[b]	<.001 <.001[d]
24-hour Ambulatory[f]	143.2 (9.0)	135.6 (13.0)	-7.7 (10.7)	144.5 (9.7)	142.9 (10.5)	-1.7 (9.3)	-6.3 (-9.2, -3.4)	<.001
Nighttime Ambulatory[f]	132.1 (12.6)	125.5 (15.0)	-6.6 (12.8)	133.8 (13.3)	32.4 (12.2)	-1.3 (11.3)	-5.9 (-9.1, -2.6) -6.0 (-9.0, -3.0)[b]	<.001 <.001[d]
Home[g]	152.4 (9.5)	143.4 (12.3)	-9.0 (9.5)	149.7 (10.3)	148.8 (12.3)	-0.9 (7.9)	-7.8 (-10.4, -5.1)	<.001
Office[h]	156.8 (13.3)	145.8 (15.9)	-11.0 (13.5)	156.7 (12.9)	151.2 (16.4)	-5.5 (12.9)	-5.5 (-9.2, -1.8)	.004
DBP Parameters (mmHg)								
Daytime Ambulatory[e]	93.8 (5.2)	88.4 (7.4)	-5.4 (6.5)	93.2 (5.6)	91.8 (6.7)	-1.3 (5.7)	-3.9 (-5.6, -2.2)	<.001
24-hour Ambulatory[f]	88.4 (5.8)	83.1 (7.6)	-5.3 (6.4)	88.2 (5.8)	87.0 (6.3)	-1.2 (5.4)	-4.1 (-5.7, -2.4)	<.001
Nighttime Ambulatory[f]	79.8 (8.3)	75.1 (9.7)	-4.7 (8.2)	80.2 (8.0)	79.6 (7.5)	-0.5 (6.7)	-4.3 (-6.3, -2.2) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]
Home[g]	97.8 (6.3)	92.7 (7.4)	-5.1 (6.0)	95.7 (7.6)	95.5 (8.1)	-0.3 (4.5)	-4.4 (-6.0, -2.9)	<.001
Office[h]	101.9 (7.8)	96.0 (10.2)	-5.9 (9.4)	101.4 (7.5)	98.1 (11.2)	-3.3 (9.2)	-2.4 (-5.1, 0.2)	.07

Data displayed as mean (SD) unless otherwise noted. DBP=diastolic blood pressure, SBP=systolic blood pressure

[a]Estimate of treatment difference, from baseline adjusted ANCOVA (observed or with multiple imputations).

[b]In the event that change from baseline in either cohort is non-normal, the Hodges-Lehmann estimator of location shift (median) and associated 95% confidence interval (using observed data) is also provided.

[c]P value from baseline adjusted ANCOVA (observed or with multiple imputations).

[d]In the event that change from baseline in either cohort is non-normal, the P value from a baseline adjusted ANCOVA on the ranks (using observed data) is also provided.

[e]There were 145 patients in the uRDN group and 73 patients in the sham group with daytime ambulatory BP.

[f]There were 144 patients in the uRDN group and 72 patients in the sham group with 24-hour and nighttime ambulatory BP.

[g]There were 140 patients in the uRDN group and 69 patients in the sham group with home BP.

[h]There were 137 patients in the uRDN group and 71 patients in the sham group with office BP.

eTable 8. Change in ambulatory, office, and home blood pressure at 2 months in the ultrasound renal denervation group (uRDN) and in the sham group in the per-protocol population (n = 131 uRDN, n = 63 sham)

	uRDN			Sham			Baseline Adjusted Observed	
	Randomization	2 months	Difference	Randomization	2 months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[c]
SBP Parameters (mmHg)								
Daytime Ambulatory[e]	149.8 (8.5)	141.9(13.4)	-7.9 (11.7)	150.0 (8.3)	149.0 (10.8)	-1.0 (9.0)	-6.9 (-10.2, -3.6) -7.0 (-10.0, -4.0)[b]	<.001 <.001[d]
24-hour Ambulatory[f]	142.6 (8.6)	135.0 (13.0)	-7.6 (10.8)	143.3 (9.3)	142.4 (10.4)	-0.8 (8.7)	-6.9 (-9.9, -3.8)	<.001
Nighttime Ambulatory[f]	130.9 (11.9)	124.6 (14.7)	-6.3 (12.9)	132.8 (13.3)	132.2 (12.5)	-0.6 (11.0)	-6.3 (-9.8, -2.8)	<.001
Home[g]	151.5 (9.2)	142.6 (12.3)	-8.9 (9.0)	148.0 (10.0)	147.2 (11.6)	-0.9 (8.1)	-7.7 (-10.4, -4.9)	<.001
Office[h]	155.9 (13.5)	145.1 (16.0)	-10.9 (13.3)	155.4 (12.9)	150.1 (16.1)	-5.4 (12.3)	-5.4 (-9.3, -1.5) -6.5 (-10.5, -2.5 [b]	.007 .002[d]
DBP Parameters (mmHg)								
Daytime Ambulatory[e]	93.8 (5.1)	88.5 (7.4)	-5.3 (6.4)	92.4 (4.9)	91.6 (6.3)	-0.9 (5.6)	-4.1 (-5.9, -2.2)	<.001
24-hour Ambulatory[f]	88.3 (5.8)	83.0 (7.7)	-5.2 (6.4)	87.4 (5.4)	86.7 (6.1)	-0.7 (5.2)	-4.3 (-6.1, -2.5)	<.001
Nighttime Ambulatory[f]	79.5 (8.3)	74.9 (9.9)	-4.6 (8.4)	79.5 (7.9)	79.3 (7.7)	-0.1 (6.4)	-4.5 (-6.7, -2.2) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]
Home[g]	97.6 (6.1)	92.6 (7.4)	-5.0 (5.6)	94.7 (7.1)	94.3 (7.3)	-0.4 (4.7)	-4.1 (-5.8, -2.4)	<.001
Office[h]	101.5 (7.4)	95.7 (10.1)	-5.8 (9.2)	100.8 (7.6	97.4 (10.8)	-3.3 (8.6)	-2.2 (-5.0, 0.5)	.12

Data displayed as mean (SD) unless otherwise noted. DBP=diastolic blood pressure, SBP=systolic blood pressure

[a]Estimate of treatment difference, from baseline adjusted ANCOVA (observed or with multiple imputations).

[b] In the event that change from baseline in either cohort is non-normal, the Hodges-Lehmann estimator of location shift (median) and associated 95% confidence interval (using observed data) is also provided.

[c]P-value from baseline adjusted ANCOVA (observed or with multiple imputations).

[d]In the event that change from baseline in either cohort is non-normal, the P value from a baseline adjusted ANCOVA on the ranks (using observed data) is also provided.

[e]There were 131 patients in RDN group and 63 patients in the sham group with daytime ambulatory BP.

[f]There were 130 patients in RDN group and 63 patients in the sham group with 24-hour ambulatory and nighttime ambulatory BP.

[g]There were 125 patients in RDN group and 58 patients in the sham group with home BP.

[h]There were 121 patients in RDN group and 61 patients in the sham group with office BP.

eTable 9. Change in ambulatory blood pressure at 2 months in the ultrasound renal denervation group (uRDN) and in the sham group in the as-treated population (n = 149 uRDN, n = 74 sham)

	uRDN			Sham			Baseline Adjusted Observed		Baseline Adjusted with Multiple Imputations	
	Randomization	2 months	Difference	Randomization	2 months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[c]	Mean Between-Group Difference (95% CI)[a]	P value[c]
SBP Parameters (mmHg)										
Daytime Ambulatory[e]	150.2 (8.6)	142.2 (13.4)	-8.0 (11.6)	151.3 (9.0)	149.5 (11.1)	-1.8 (9.5)	-6.4 (-9.4, -3.3) -7.0 (-9.0, -4.0)[b]	<.001 <.001[d]	-6.4 (-9.4, -3.3) -7.0 (-9.0, -4.0)[b]	<.001 <.001[d]
24-hour Ambulatory[f]	143.2 (9.0)	135.5 (13.1)	-7.7 (10.7)	144.5 (9.7)	142.9 (10.5)	-1.7 (9.3)	-6.3 (-9.2, -3.5)	<.001	-6.3 (-9.1, -3.4)	<.001
Nighttime Ambulatory[f]	132.0 (12.7)	125.4 (15.0)	-6.6 (12.8)	133.8 (13.3)	132.4 (12.2)	-1.3 (11.3)	-5.9 (-9.2, -2.6) -6.0 (-9.0, -2.0)[b]	<.001 <.001[d]	-5.8 (-9.1, -2.6) -6.0 (-9.0, -2.0)[b]	<.001 <.001[d]
Home[g]	152.3 (9.5)	143.3 (12.3)	-9.0 (9.5)	149.7 (10.3)	148.8 (12.3)	-0.9 (7.9)	-7.8 (-10.4, -5.2)	<.001	-7.6 (-10.2, -5.0)	<.001
Office[h]	156.8 (13.3)	145.6 (15.9)	-11.2 (13.4)	156.7 (12.9)	151.2 (16.4)	-5.5 (12.9)	-5.7 (-9.4, -2.0)	0.0025	-5.6 (-9.2, -2.0)	0.002
DBP Parameters (mmHg)										
Daytime Ambulatory[e]	93.7 (5.2)	88.3 (7.5)	-5.4 (6.5)	93.2 (5.6)	91.8 (6.7)	-1.3 (5.7)	-3.9 (-5.6, -2.2)	<.001	-3.9 (-5.6, -2.2)	<.001
24-hour Ambulatory[f]	88.3 (5.8)	83.1 (7.7)	-5.3 (6.4)	88.2 (5.8)	87.0 (6.3)	-1.2 (5.4)	-4.1 (-5.7, -2.4)	<.001	-4.1 (-5.7, -2.4)	<.001
Nighttime Ambulatory[f]	79.9 (8.3)	75.2 (9.8)	-4.7 (8.2)	80.2 (8.0)	79.6 (7.5)	-0.5 (6.7)	-4.2 (-6.3, -2.2) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]	-4.2 (-6.3, -2.2) -5.0 (-7.0, -3.0)[b]	<.001 <.001[d]
Home[g]	97.8 (6.3)	92.6 (7.4)	-5.1 (6.0)	95.7 (7.6)	95.5 (8.1)	-0.3 (4.5)	-4.5 (-6.1, -2.9)	<.0001	-4.4 (-5.9, -2.8)	<.001
Office[h]	101.9 (7.8)	95.9 (10.1)	-6.0 (9.3)	101.4 (7.5)	98.1 (11.2)	-3.3 (9.2)	-2.6 (-5.2, 0.0)	.05	-2.4 (-5.0, 0.1)	.06

Data displayed as mean (SD) unless otherwise noted. DBP=diastolic blood pressure, SBP=systolic blood pressure

[a]Estimate of treatment difference, from baseline adjusted ANCOVA (observed or with multiple imputations).

[b] In the event that change from baseline in either cohort is non-normal, the Hodges-Lehmann estimator of location shift (median) and associated 95% confidence interval (using observed data) is also provided.

[c]P value from baseline adjusted ANCOVA (observed or with multiple imputations).

[d]In the event that change from baseline in either cohort is non-normal, the P value from a baseline adjusted ANCOVA on the ranks (using observed data) is also provided.

[e]There were 144 patients in RDN group and 73 patients in the sham group with daytime ambulatory BP.

[f]There were 143 patients in RDN group and 72 patients in the sham group with 24-hour and nighttime ambulatory BP.

[g]There were 139 patients in RDN group and 69 patients in the sham group with home BP.

[h]There were 136 patients in RDN group and 71 patients in the sham group with office BP.

eTable 10. Number and percentage of patients with a decrease in daytime ambulatory blood pressure at 2 months ≥ 5 mmHg, ≥ 10 mmHg, and ≥ 15 mmHg in the ultrasound renal denervation group (uRDN) and in the sham group among patients with ambulatory blood pressure measurements at 2 months (n = 145 uRDN, n = 73 sham)

Definition	uRDN (n=145)	Sham (n=73)	P value
Daytime ambulatory systolic blood pressure reduction ≥5 mmHg	93 (64.1%)	25 (34.2%)	<.001
Daytime ambulatory systolic blood pressure reduction ≥10 mmHg	69 (47.6%)	12 (16.4%)	<.001
Daytime ambulatory systolic blood pressure reduction ≥15 mmHg	37 (25.5%)	7 (9.6%)	.006

Data displayed as number of patients (%).

eTable 11. Number and percentage of patients with controlled blood pressure according to ambulatory and office blood pressure measurements in the ultrasound renal denervation group (uRDN) and in the sham group

Definition	uRDN	Sham	P value
Intention-to-Treat Population	(n=150)	(n=74)	
Daytime ambulatory blood pressure less than 135/85 mmHg	27/145 (18.6%)	4/73 (5.5%)	.009
24-hour ambulatory blood pressure less than 130/80 mmHg	33/144 (22.9%)	4/72 (5.6%)	.001
Office blood pressure less than 140/90 mmHg	31/137 (22.6%)	14/71 (19.7%)	.63
Patients Achieving Controlled Blood Pressure in the Absence of Antihypertensive Medication[a]	(n=138)	(n=64)	
Daytime ambulatory blood pressure less than 135/85 mmHg	25/133 (18.8%)	3/63 (4.8%)	.009
24-hour ambulatory blood pressure less than 130/80 mmHg	31/132 (23.5%)	3/63 (4.8%)	.001
Office blood pressure less than 140/90 mmHg	29/125 (23.2%)	13/61 (21.3%)	.77
Per-Protocol Population	(n=131)	(n=63)	
Daytime ambulatory blood pressure less than 135/85 mmHg	24 (18.3%)	3 (4.8%)	.01
24-hour ambulatory blood pressure less than 130/80 mmHg	30/130 (23.1%)	3 (4.8%)	.002
Office blood pressure less than 140/90 mmHg	28/121 (23.1%)	13/61 (21.3%)	.78

Data displayed as number of patients (%).
[a]Excludes 12 patients in the uRDN group and 10 patients in the sham group who restarted medications prior to the 2-month ambulatory BP measurement evaluation.

eTable 12. Changes in ambulatory heart rate at 2 months in the ultrasound renal denervation group (uRDN) and in the sham group in the intention-to-treat population

	uRDN			Sham			Baseline Adjusted Observed	
	Randomization	2 months	Difference	Randomization	2 months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[b]
Daytime HR[c] (bpm)	77.7 (10.6)	77.6 (10.1)	-0.1 (6.6)	75.9 (9.8)	75.1 (10.2)	-0.9 (7.3)	1.2 (-0.6, 3.0)	.19
24-hour HR[d](bpm)	73.7 (9.8)	73.8 (9.3)	0.1 (5.8)	71.9 (9.1)	71.2 (9.6)	-0.7 (6.4)	1.2 (-0.5, 2.8)	.16
Nighttime HR[d](bpm)	67.9 (10.2)	68.3 (9.8)	0.5 (6.6)	65.5 (9.3)	65.7 (9.8)	0.2 (6.3)	0.8 (-0.9, 2.6)	.34

Data displayed as Mean (SD) unless otherwise noted; bpm: beats per minute, HR: heart rate
[a]Estimate of treatment difference, from baseline adjusted ANCOVA.
[b]P value from baseline adjusted ANCOVA.
[c]There were 145 patients in RDN group and 73 patients in the sham group with daytime day time heart rate measurements.
[d]There were 144 patients in RDN group and 72 patients in the sham group with 24-hr and nighttime heart rate measurements.

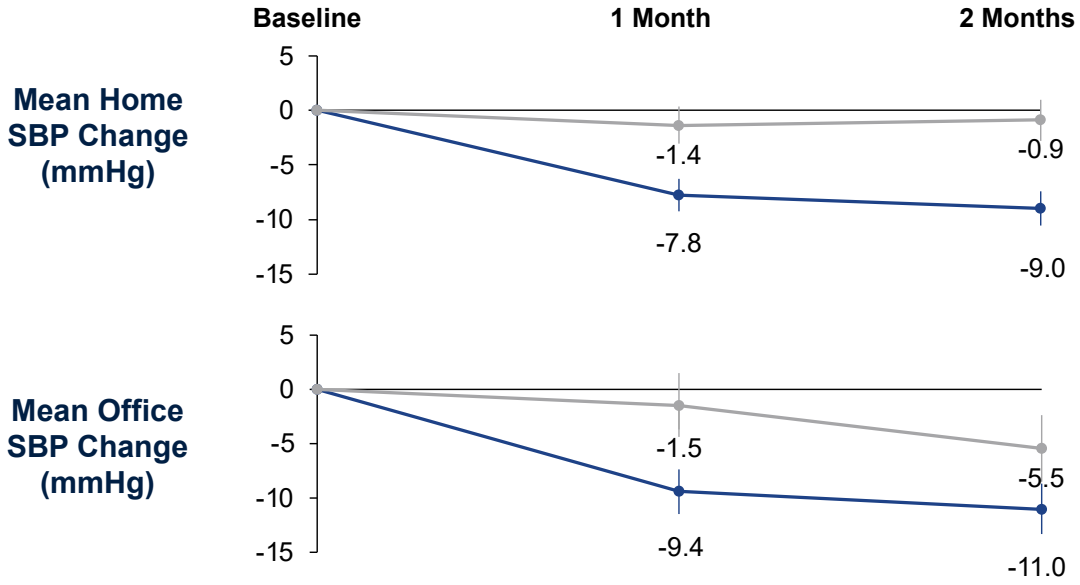
eTable 13. Estimated glomerular filtration rate (eGFR) and serum creatinine at baseline and 2 months in the ultrasound renal denervation group (uRDN) and in the sham group for subjects with data at both timepoints (n = 136, uRDN; n = 72, sham)

	uRDN			Sham			Baseline Adjusted Observed	
	Randomization	2 months	Difference	Randomization	2 months	Difference	Mean Between-Group Difference (95% CI)[a]	P value[b]
eGFR[c] (mL/min/1.73m^2)	81.4 (14.6)	82.5 (14.9)	1.1 (8.2)	81.8 (14.6)	81.7 (15.1)	-0.1 (8.0)	1.1 (-1.1, 3.4)	.33
Serum Creatinine (mg/dL)	0.9 (0.2)	0.9 (0.2)	-0.0 (0.1)	1.0 (0.2)	1.0 (0.2)	0.0 (0.1)	-0.0 (-0.0, 0.0)	.22

Data displayed as mean (SD) unless otherwise noted.
[a]Estimate of treatment difference, from baseline adjusted ANCOVA
[b]P value from ANCOVA, adjusting for baseline value.
[C]Calculated using MDRD formula

eFigure 1. Time course evolution of home (top) and office (bottom) systolic blood pressure (SBP) changes between baseline, 1, and 2 months in the ultrasound renal denervation group (uRDN, blue line) and in the sham (grey line) group (intention-to-treat population)

Data are mean values and 95% CI



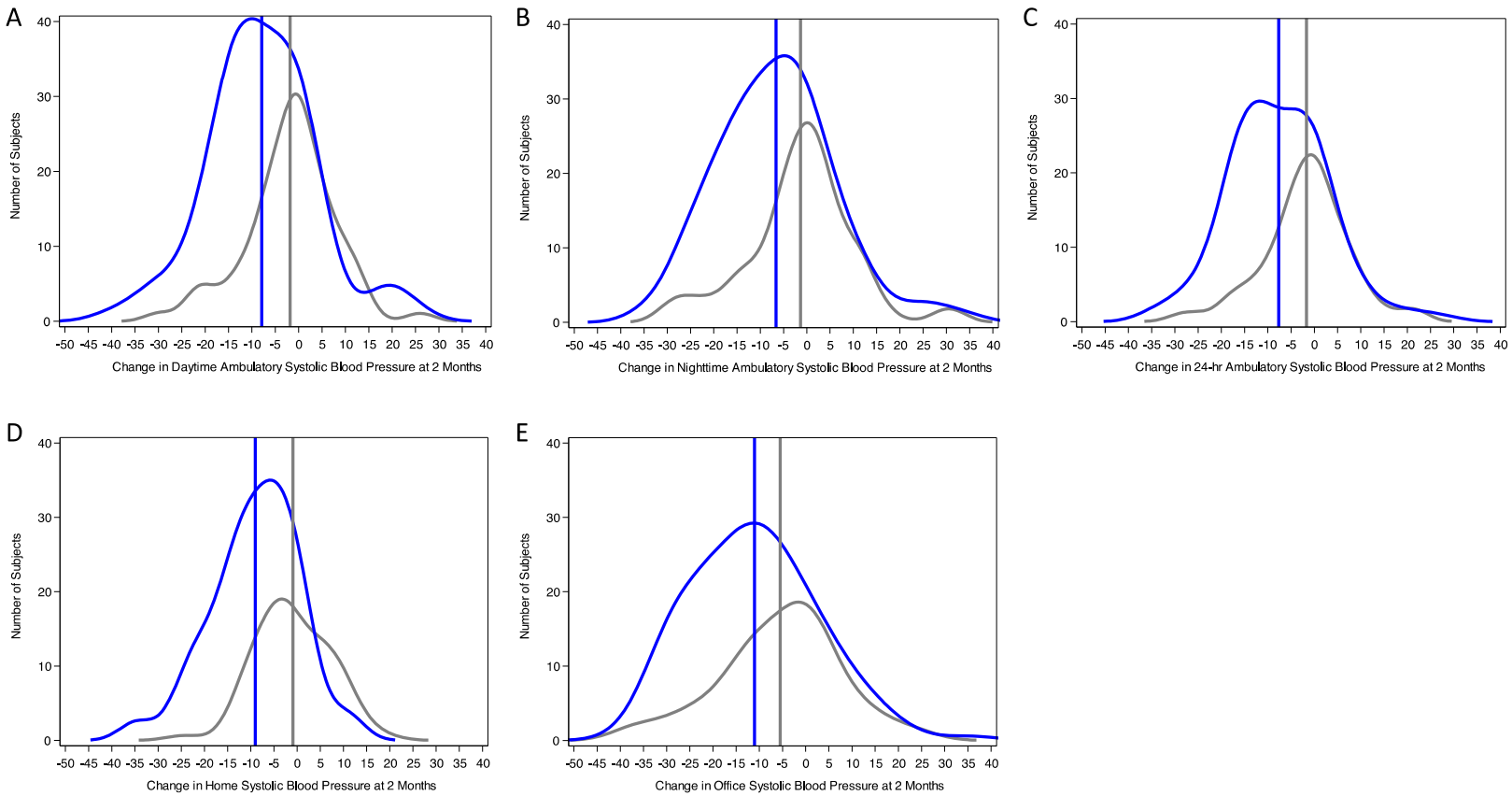
Mean Home SBP difference (95% CI)* (mmHg)	P-value
-6.8 (-9.0, -4.6)	<0.001

Mean Office SBP difference (95% CI)* (mmHg)	P-value
-6.7 (-9.6, -3.8)	<0.001

*By Linear Mixed Models Adjusting for Baseline BP

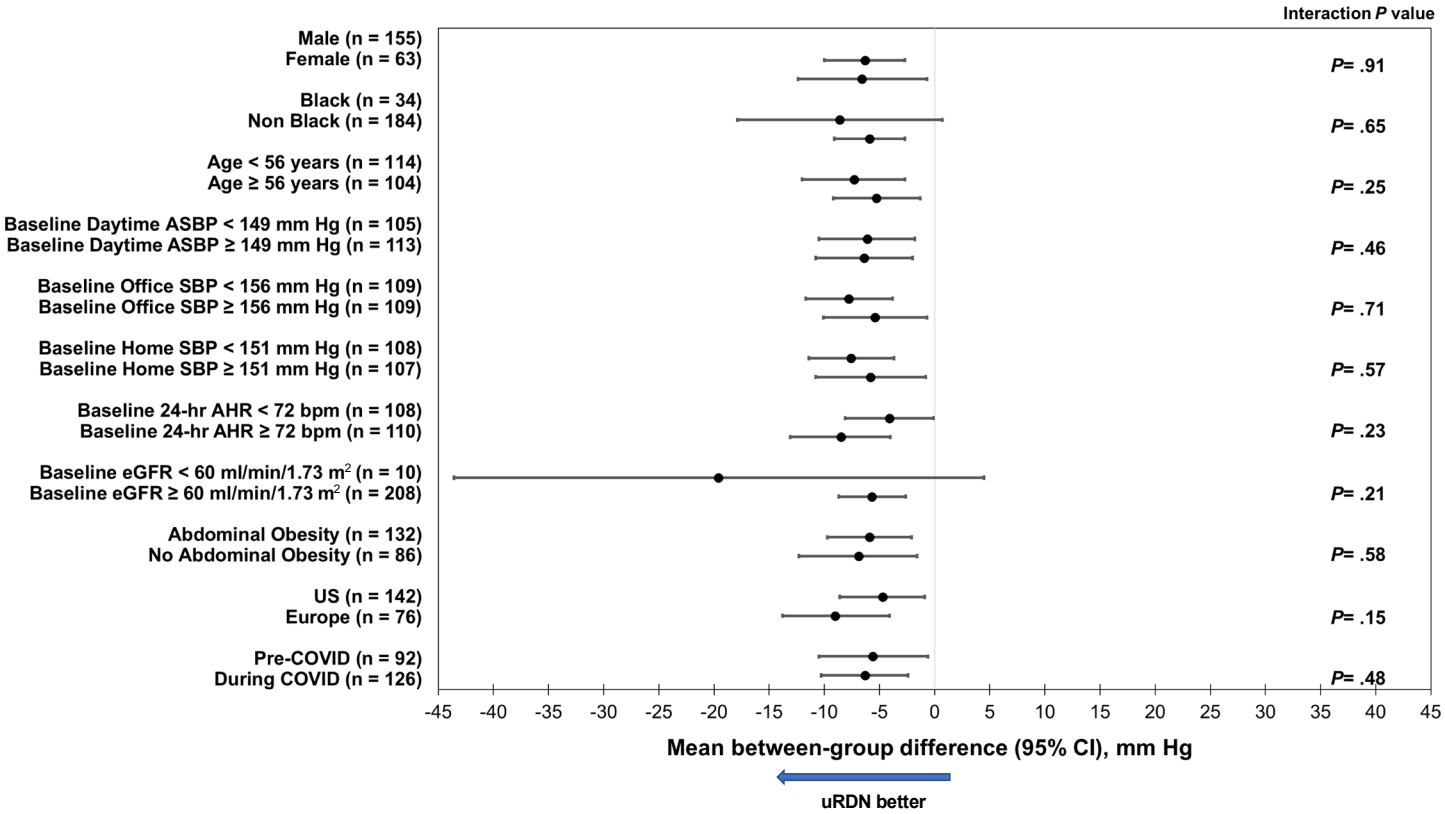
eFigure 2. Frequency distribution plots of daytime (A), nighttime (B), 24h (C), home (D) and office (E) systolic blood pressure (SBP) changes from baseline to 2 months in the ultrasound renal denervation group (uRDN, blue line) and in the sham (grey line) group

The vertical lines represent the mean value



eFigure 3. Forest plot of between-group differences (95%CI) in daytime ambulatory systolic blood pressure changes across pre-specified sub-groups in favor of ultrasound renal denervation group (uRDN) vs sham

Mean between group difference (shown for each specific subgroup as mean and 95% CI) is from a linear regression model with change in daytime ambulatory SBP at 2 months as the dependent variable and baseline daytime SBP and treatment group included as independent variables. P-value is for the treatment by subgroup interaction term from a linear regression model with change in daytime ambulatory SBP at 2 months as the dependent variable and baseline daytime SBP, treatment group, subgroup, and treatment by subgroup interaction term included as independent variables. No heterogeneity by site was noted (P= .73).



ASBP: ambulatory systolic blood pressure; SBP: systolic blood pressure; AHR: ambulatory heart rate; eGFR, estimated glomerular filtration rate; Median age (years), baseline ASBP (mmHg), home and office SBP (mmHg), HR (bpm) and eGFR (ml/min/1.73 m^2) are selected as cut-off points. Abdominal obesity was defined as a waist circumference greater than 102 cm for men and greater than 88 cm for women.