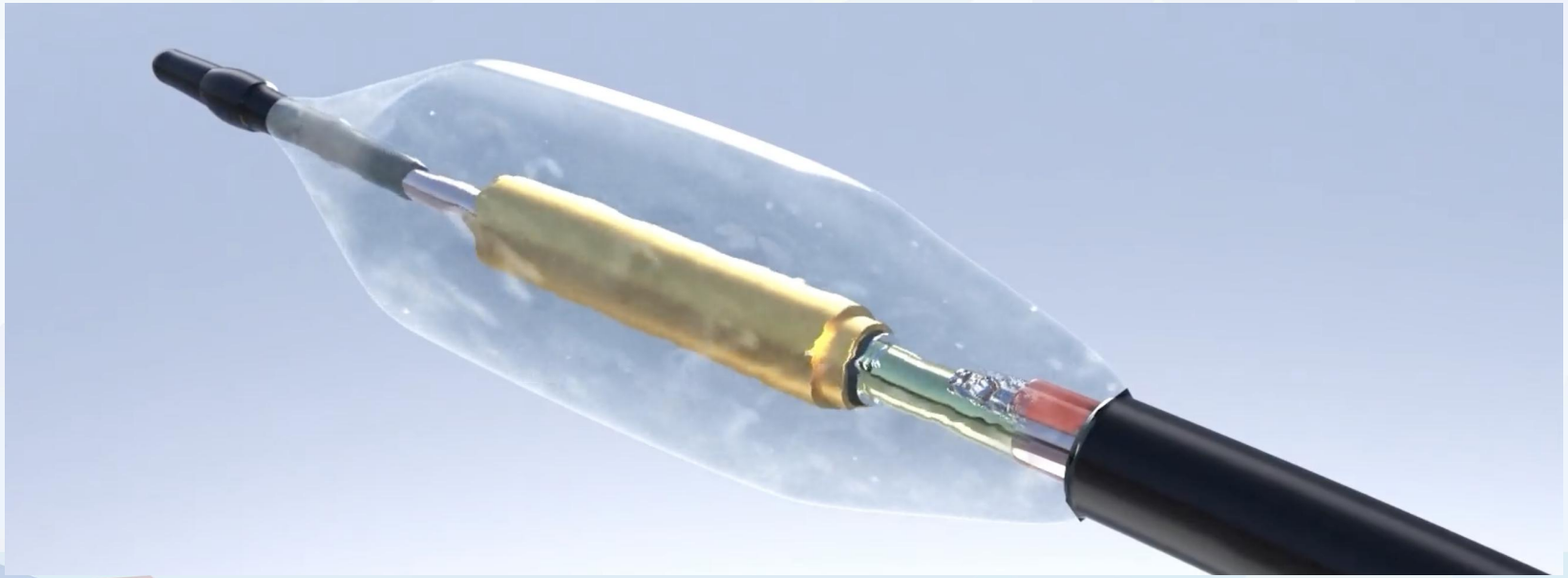
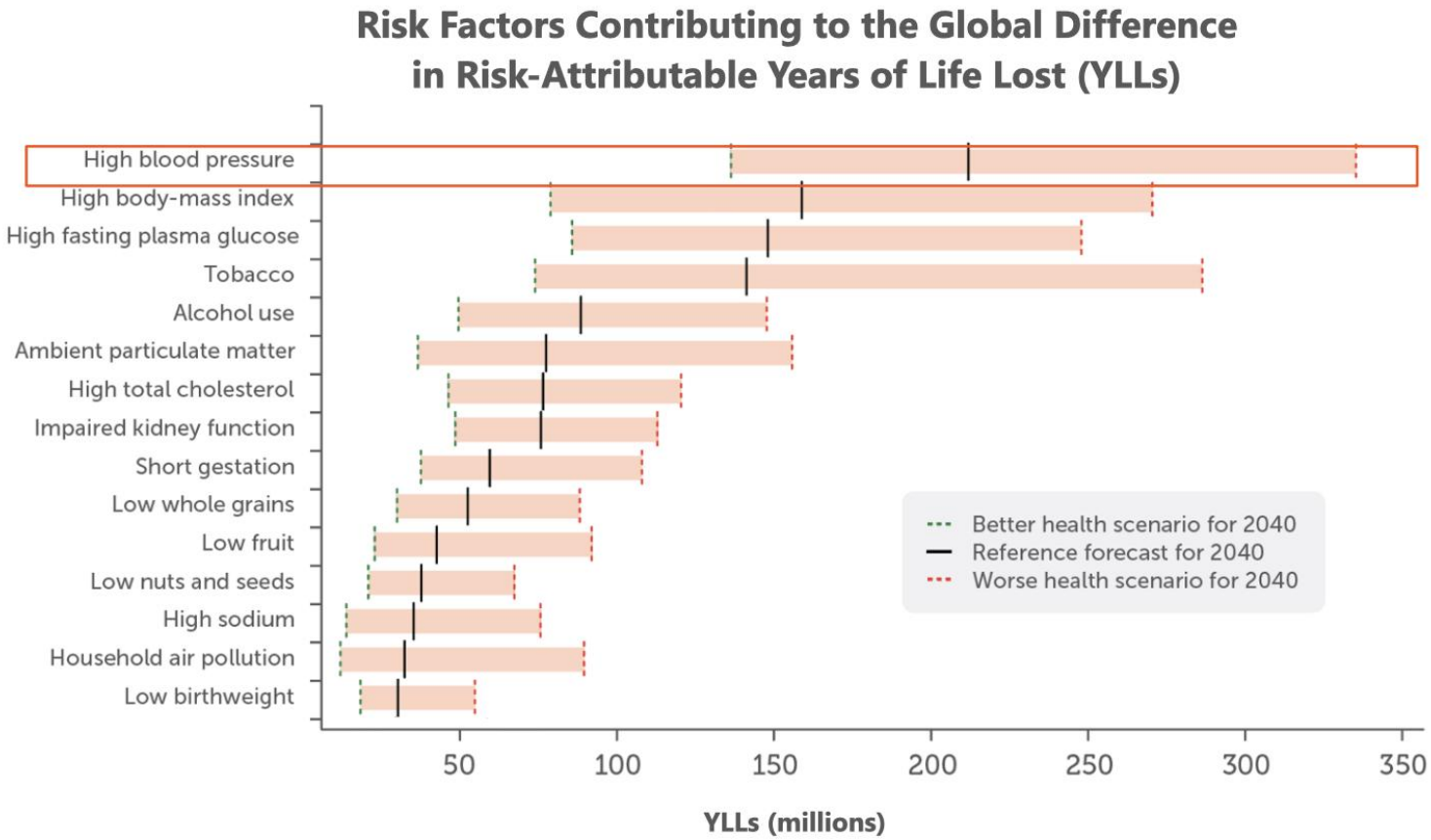
Nuevo sistema de denervación renal mediante ultrasonido PARADISE SYSTEM



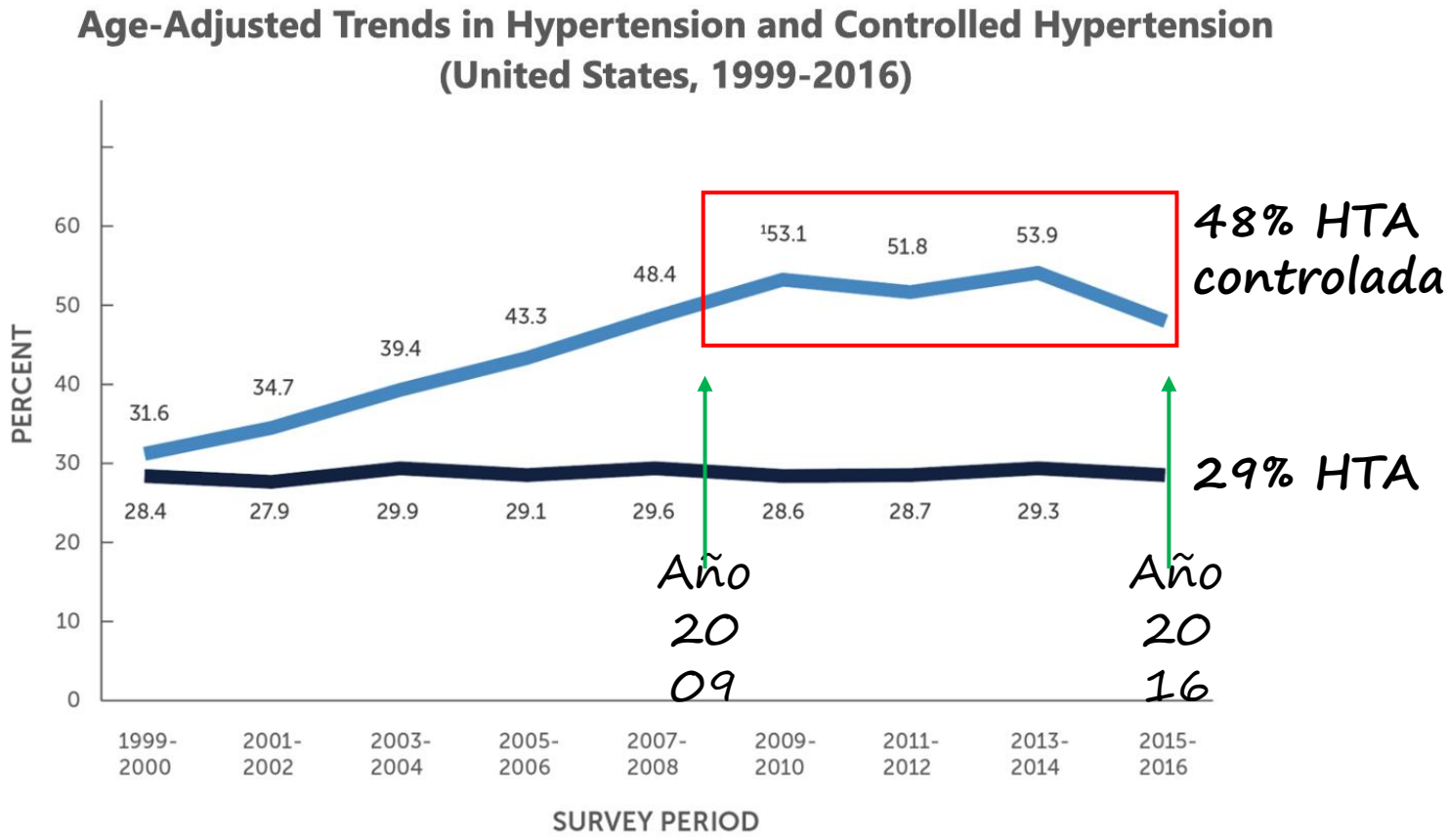
Hypertension is the #1 Cause of Global Disease Burden



HIGH BLOOD PRESSURE projected to remain the leading risk factor in 2040.

Foreman et al. Lancet 2018; 392: 2052-90

Hypertension Control Rates are No Longer Improving



No significant changes observed from 2009 – 2010 through 2015 – 2016

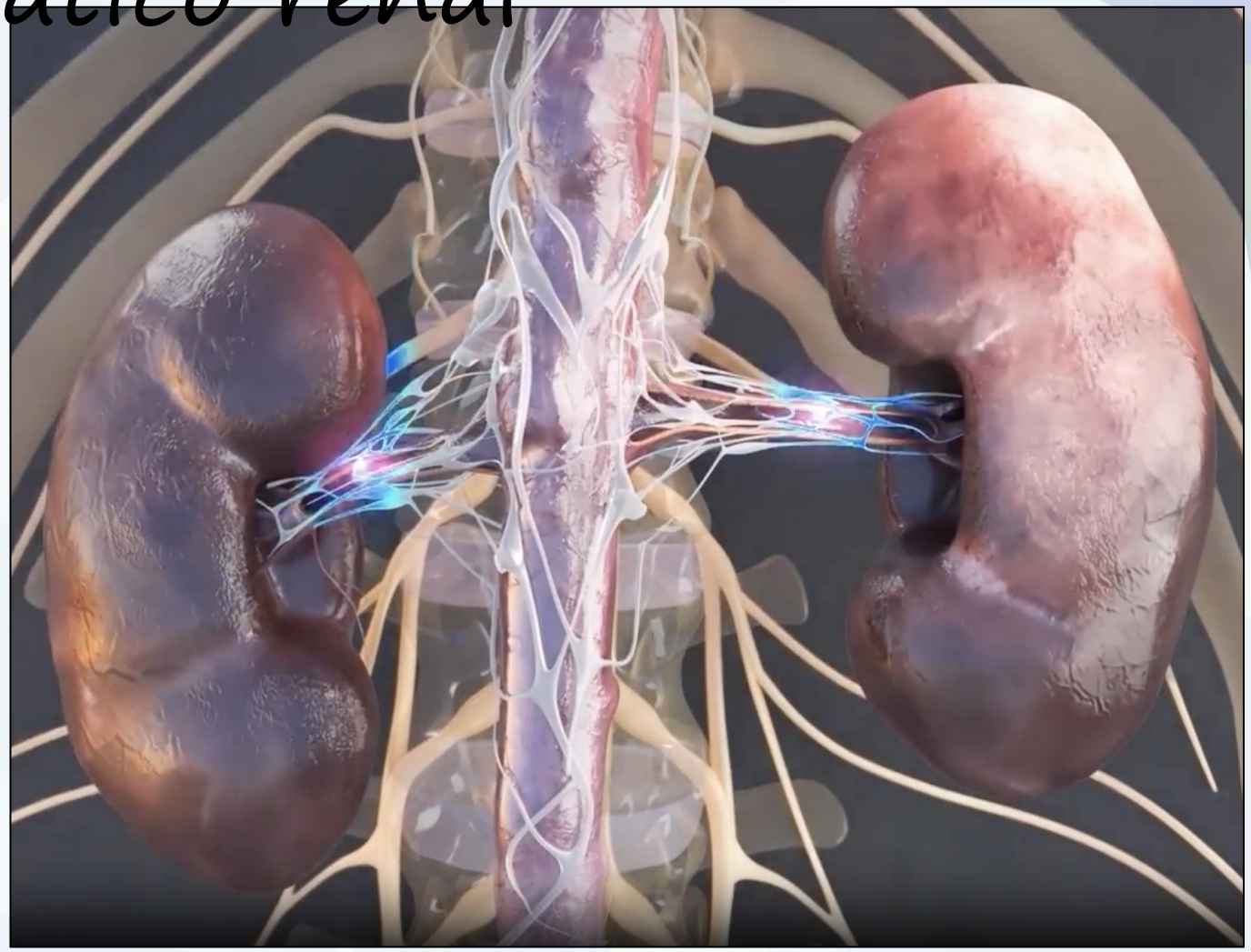
Fryar CD, NCHS Data Brief, No 289, October 2017, cdc.gov/nchs/data/databriefs/db289.pdg

Denervación del sistema nervioso simpático renal

La DNR es un tratamiento adyuvante indicado para el manejo de la HTA resistente no controlada

Consiste en la ablación de los nervios simpáticos renales, consiguiendo:

- **Aferentes:** disminuir el tono vascular e incrementar natriuresis
- **Eferentes:** disminuir actividad del eje RAA; disminuir retención de sodio



La DNR ahora recomendada por las GPC

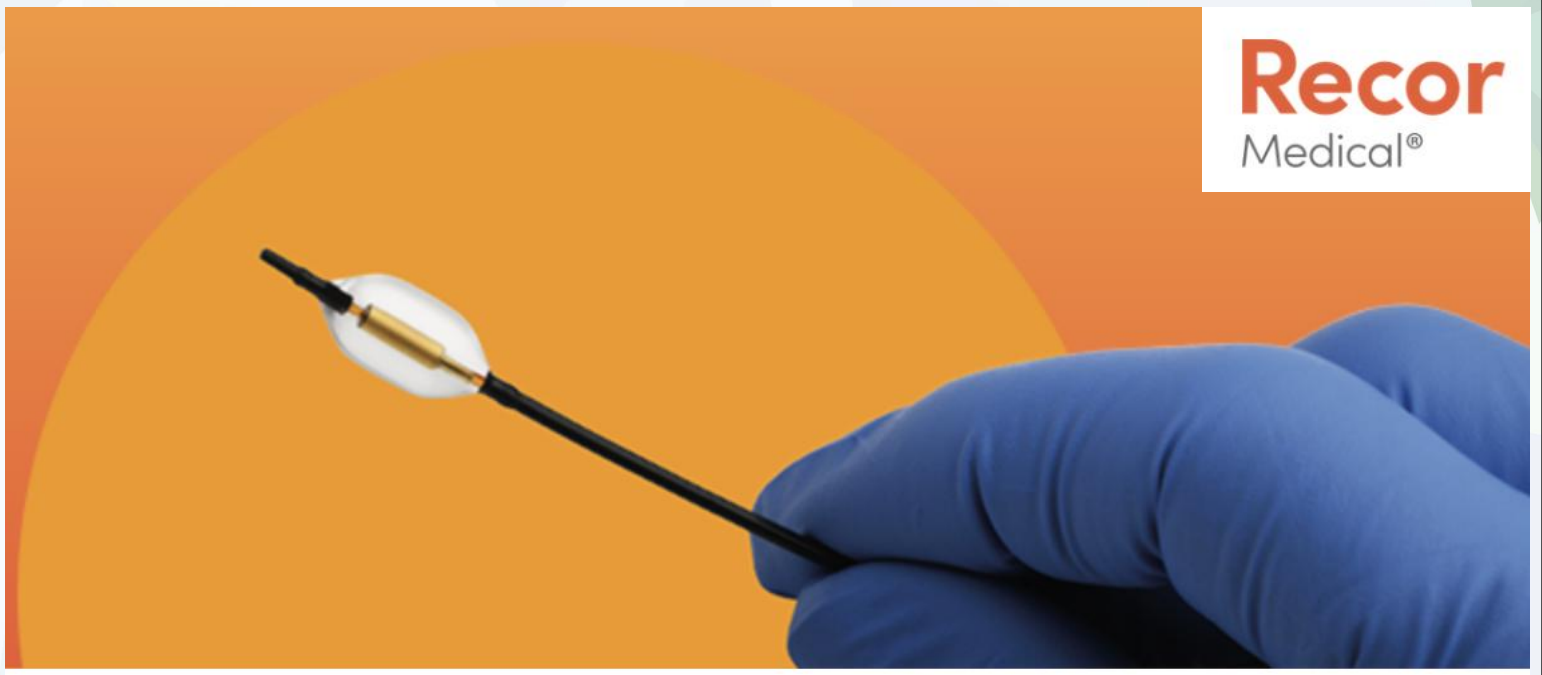
Recommendations in 2018 version	Class[a]	Level[b]	Recommendations in 2024 version	Class[a]	Level[b]
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	III	B	To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	B
			To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	A
			Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension.	III	C
			Renal denervation is not recommended for treating hypertension in patients with moderately to severely impaired renal function (eGFR <40 mL/min/1.73 m^2) or secondary causes of hypertension, until further evidence becomes available.	III	C

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

Denervación renal por ultrasonidos (sistema Paradise™)

Utiliza un sistema basado en catéter balón

Ablaciona térmicamente los nervios aferentes y eferentes del sistema simpático renal mediante la emisión circunferencial (360º) de ultrasonidos



Componentes del sistema Paradise™

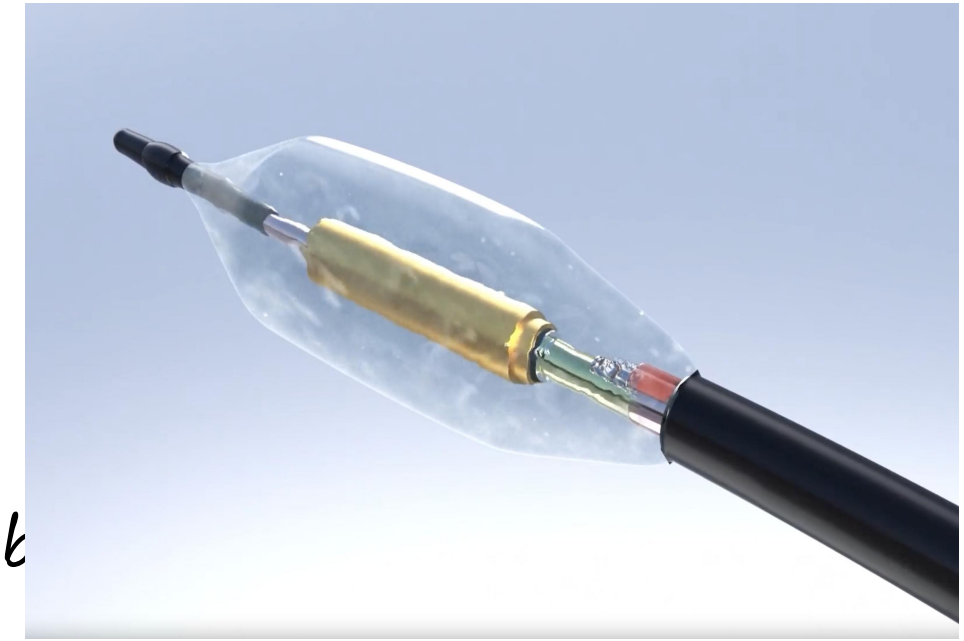
Paradise System (PRDS) Component	Sterile	Reusable
Paradise™ Catheter	Yes	No
Paradise™ Generator	No	Yes
Paradise™ Cartridge	Yes	No
Paradise™ Connection Cable	Yes	No
Paradise™ Remote	No	Yes

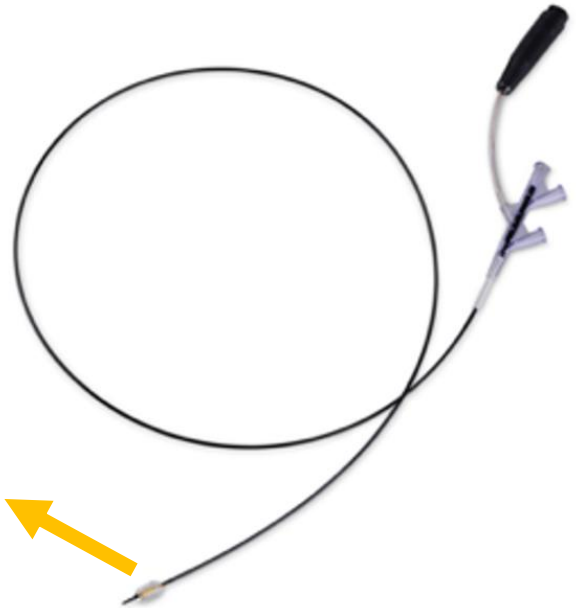
Características del catéter Paradise™

Multi-lumen

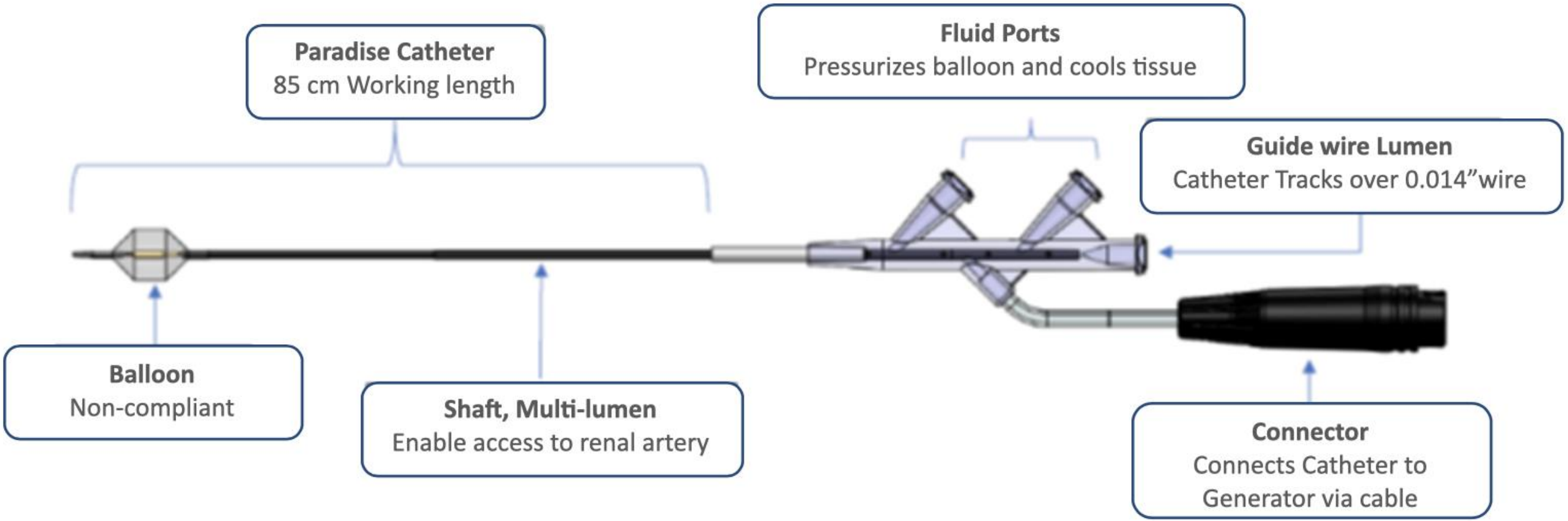
6Fr over the wire

Transductor cerámico piezoeléctrico cilíndrico dentro de un balón inflab





Diseño del catéter Paradise™



Características del generador Paradise™

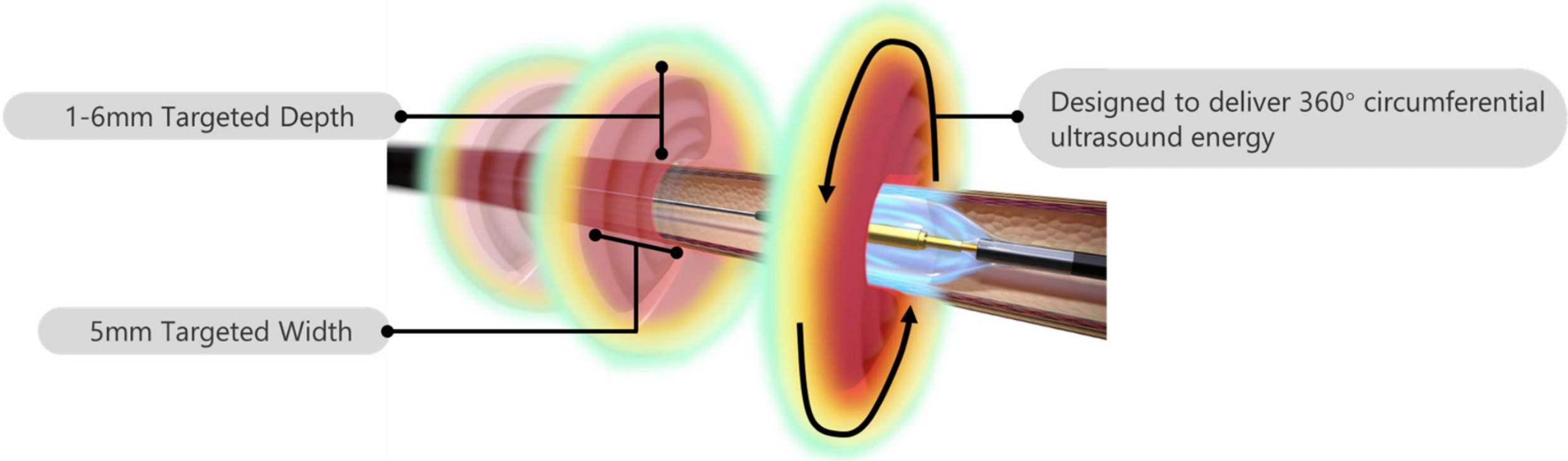
- Controla el suministro de energía y de líquidos
- Contiene los controles electrónicos mediante una pantalla táctil
- Detecta y emite automáticamente la dosis de energía según el tamaño del balón
- Suministra la energía eléctrica que convierte en energía ultrasónica en el transductor piezoeléctrico

Cartucho del sistema Paradise™

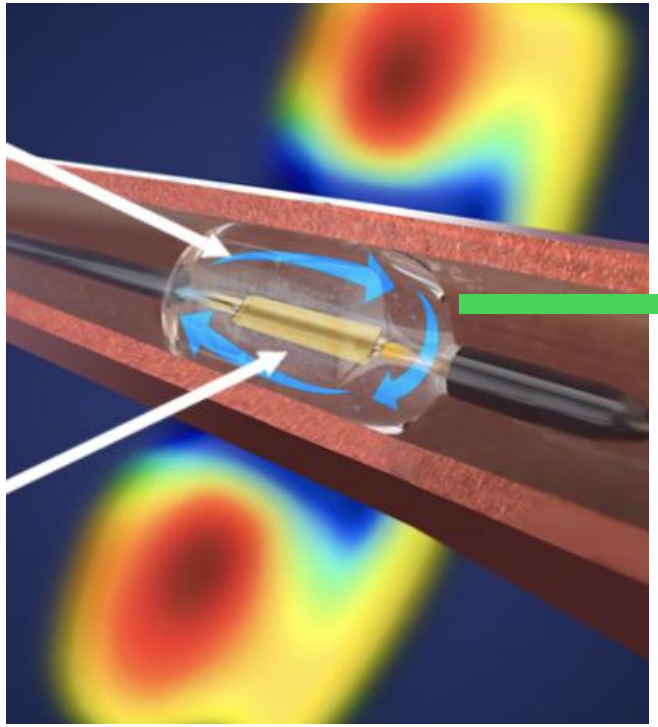
Controla el flujo de líquido dentro y fuera del catéter

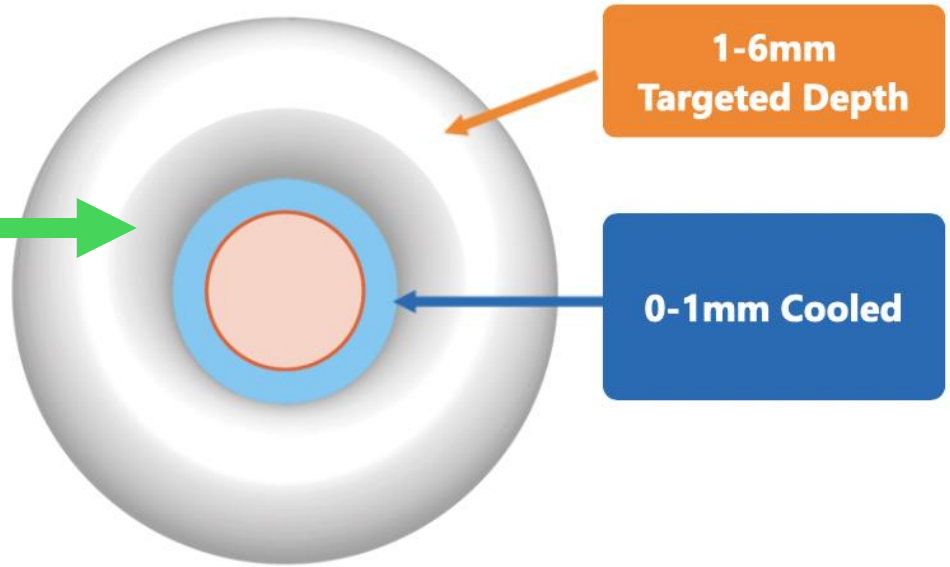
Monitorea la presión del balón del catéter para mantener una presión precisa del balón en cada fase de uso

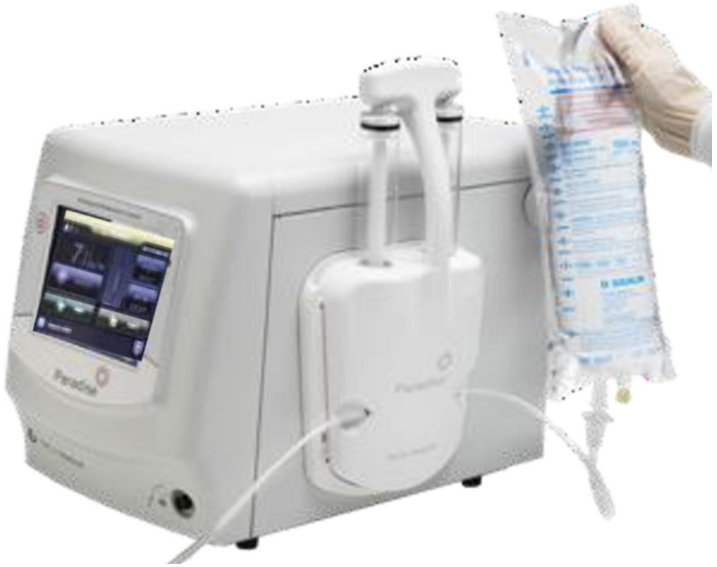
Denervación 360° con el sistema Paradise™



Paradise incorpora un sistema HydroCooling™ para proteger la pared del vaso

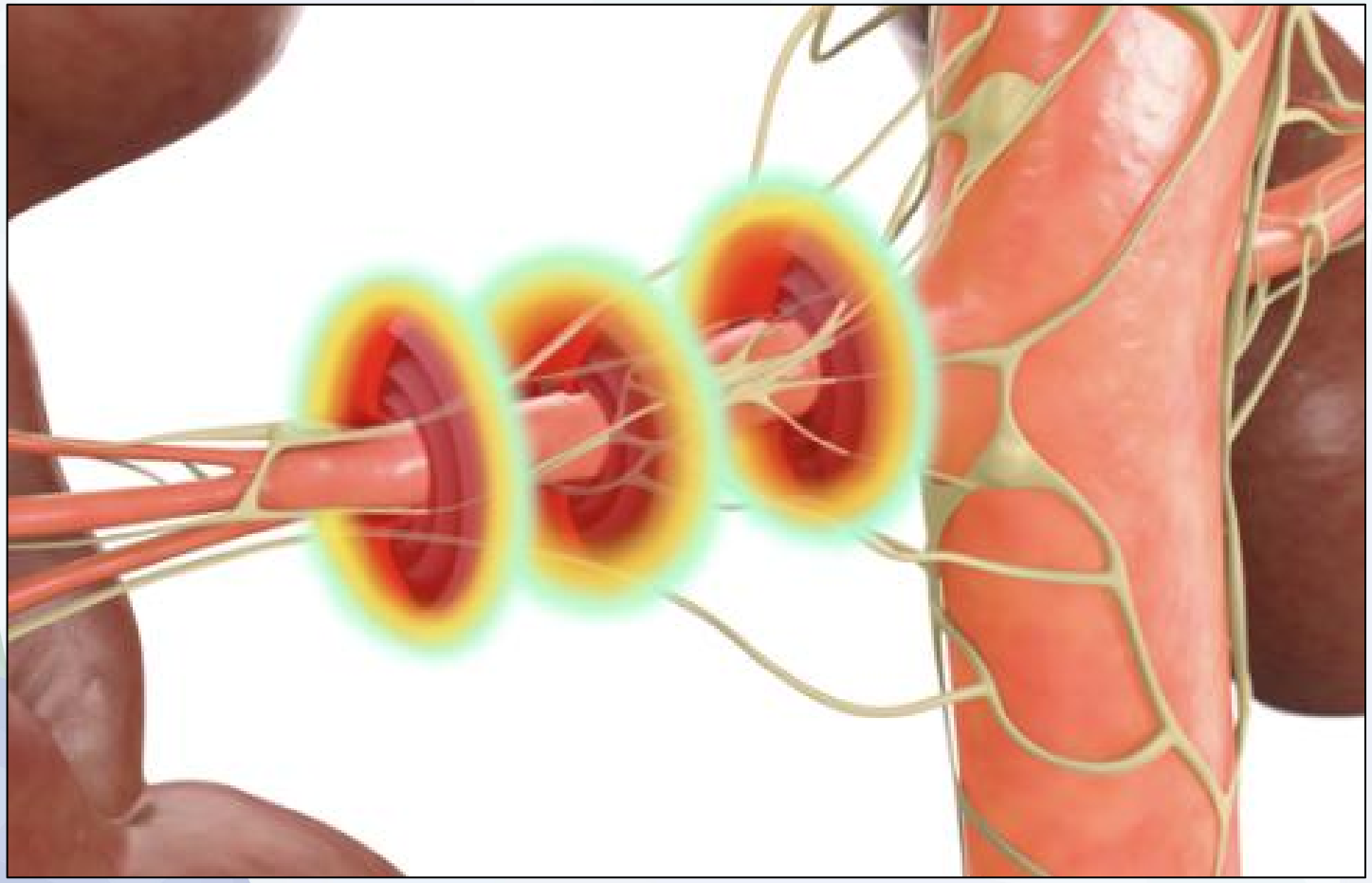






The HydroCooling™ system circulates sterile water in the catheter balloon to help protect the arterial wall during renal denervation

Intervención relativamente sencilla y corta



7 segundos por terapia

2-3 terapias por arteria renal principal

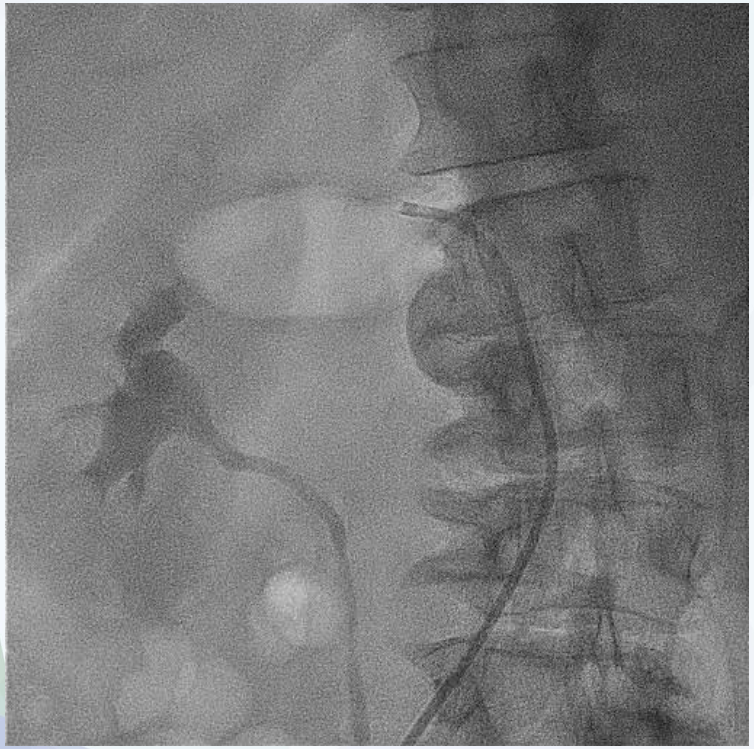
1 terapia en ramas accesorias

Selección del balón tras angiografía / TC

- Realizar angiografías renales selectivas bilaterales (incluidos los vasos accesorios)
- Determinar longitud y diámetro de cada arteria renal en las ubicaciones distal, media y proximal

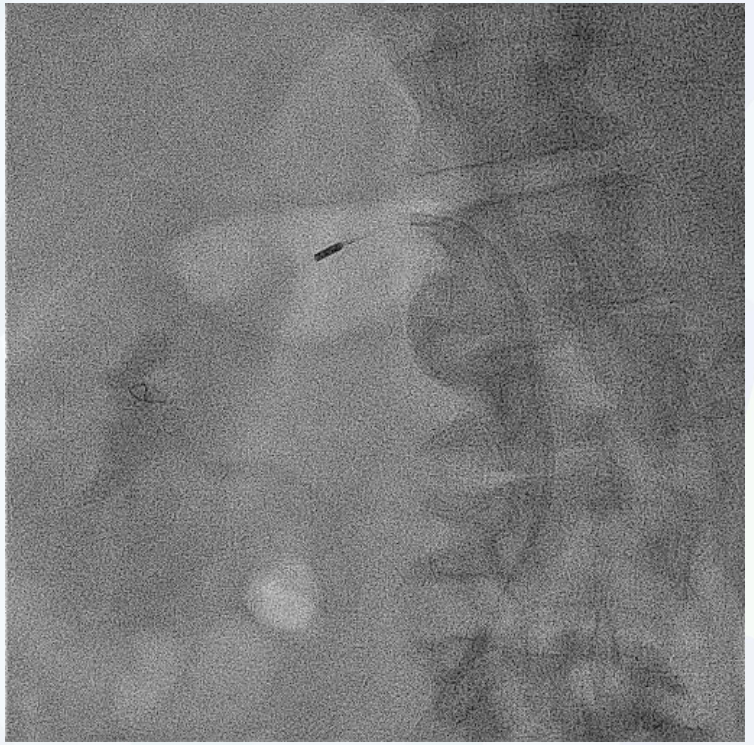
Artery Diameter Range	Balloon diameter
3 to < 3.5mm	3.5mm
3.5 to < 4.2mm	4.2mm
4.2 to < 5mm	5mm
5 to < 6mm	6mm
6 to < 7mm	7mm
7 to ≤ 8mm	8mm

Angiografía selectiva
Selección del tamaño del balón



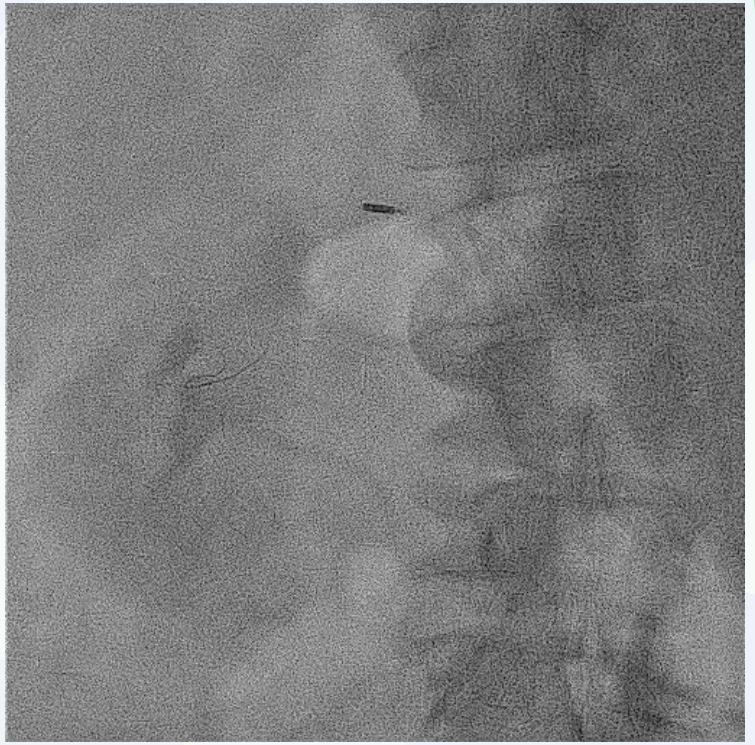
1

Comprobación de aposición del balón en posición 1



2

Comprobación de aposición del balón en posición 2



3

Evidencia clínica: estudios RADIANCE

3 ensayos clínicos de diseño ciego, aleatorizado, con brazo control tipo sham

RADIANCE-HTN SOLO[1]
(Off Meds → Med Titration)
Mild to Moderate HTN
(N = 146)

RADIANCE II Pivotal[2]
(Off Meds → Med Titration)
Mild to Moderate HTN
(N = 224)

RADIANCE-HTN TRIO[3]
(On-Meds, Single triple pill)
Resistant HTN
(N = 136)

1. Azizi et al. Lancet. 2018; 391(10137): 2335-2345

2. Azizi et al. JAMA. 2023; 329(8): 651-661

3. Azizi et al. Lancet 2021; 26: 2476-2486

	Mild to moderate hypertension		Resistant hypertension
	SOLO[1]	**RADIANCE II**[2]	**TRIO**[3]
Screening BP, Age, med and eGFR criteria	• Age ≥ 18 and ≤ 75 • Office BP ≥140/90 on 0-2 anti-HTN meds or controlled on 1-2 meds • eGFR ≥ 40 mL/min/1.72m^2	• Age ≥ 18 and ≤ 75 • Office BP ≥140/90 on 0-2 anti-HTN meds • eGFR ≥ 40 mL/min/1.72m^2	• Age ≥ 18 and ≤ 75 • Office BP ≥140/90 on 3+ anti-HTN meds • eGFR ≥ 40 mL/min/1.72m^2
4-week medicine washout/ standardization	Anti-HTN medication washout	Anti-HTN medication washout	Fixed dose, 3-drug combination pill stabilization
ABPM criteria at baseline	Daytime ABP ≥135/85 & <170/105 mmHg	Daytime ABP ≥135/85 & <170/105 mmHg	Daytime ABP ≥135/85 mmHg

CTA / MRA, Renal Duplex, Renal Angiography

Ultrasound RDN (N=293)

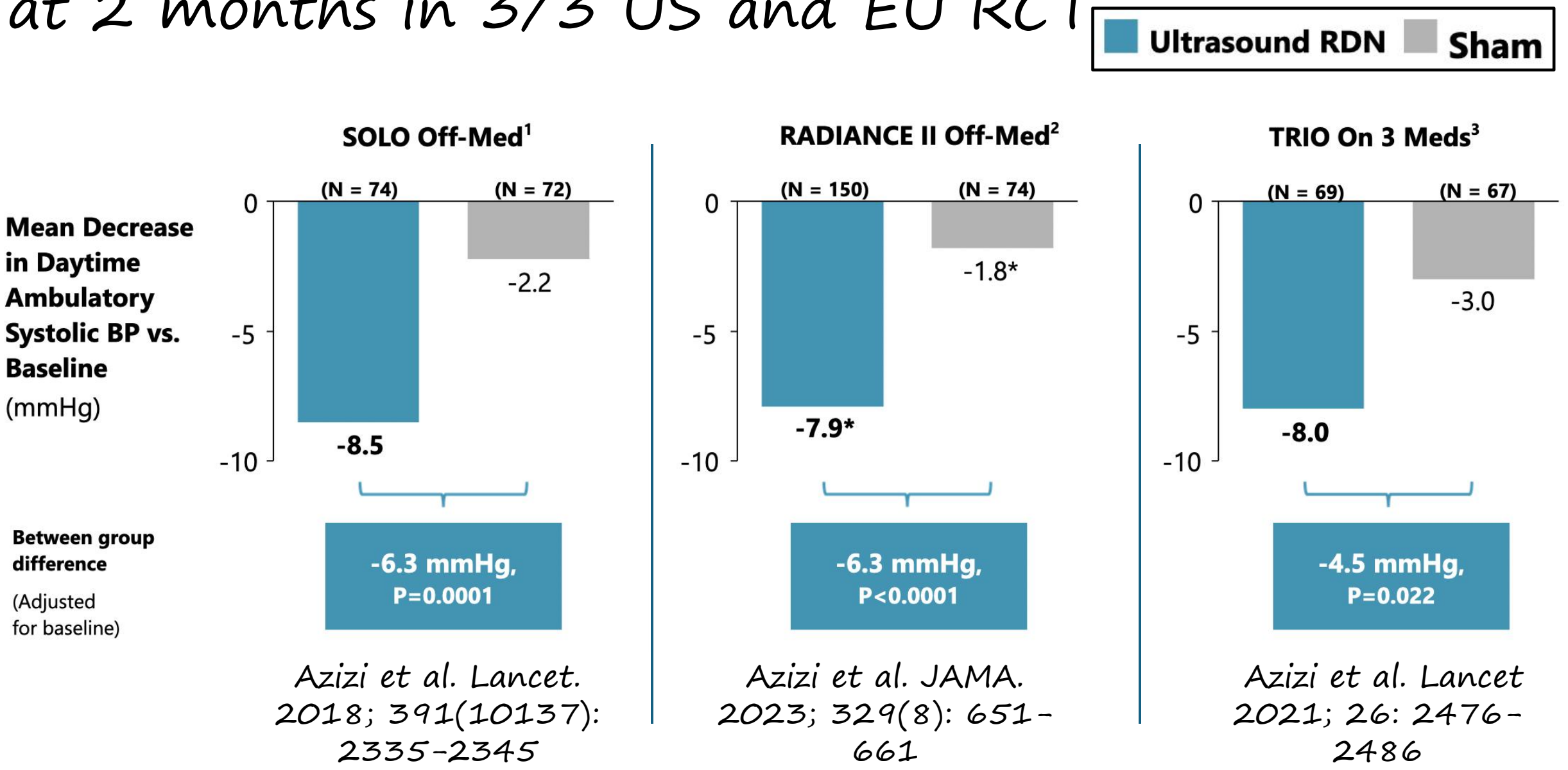
SOLO (N=74) | RADIANCE II (N=150) TRIO (N=69) |

Sham (N=213)

SOLO (N=72) | RADIANCE II (N=74) | TRIO (N=67)

Primary efficacy endpoint @ 2 Months
Δ Daytime ambulatory systolic BP

Ultrasound RDN met its primary efficacy endpoint at 2 months in 3/3 US and EU RCT



Azizi et al. Lancet. 2018; 391(10137): 2335-2345

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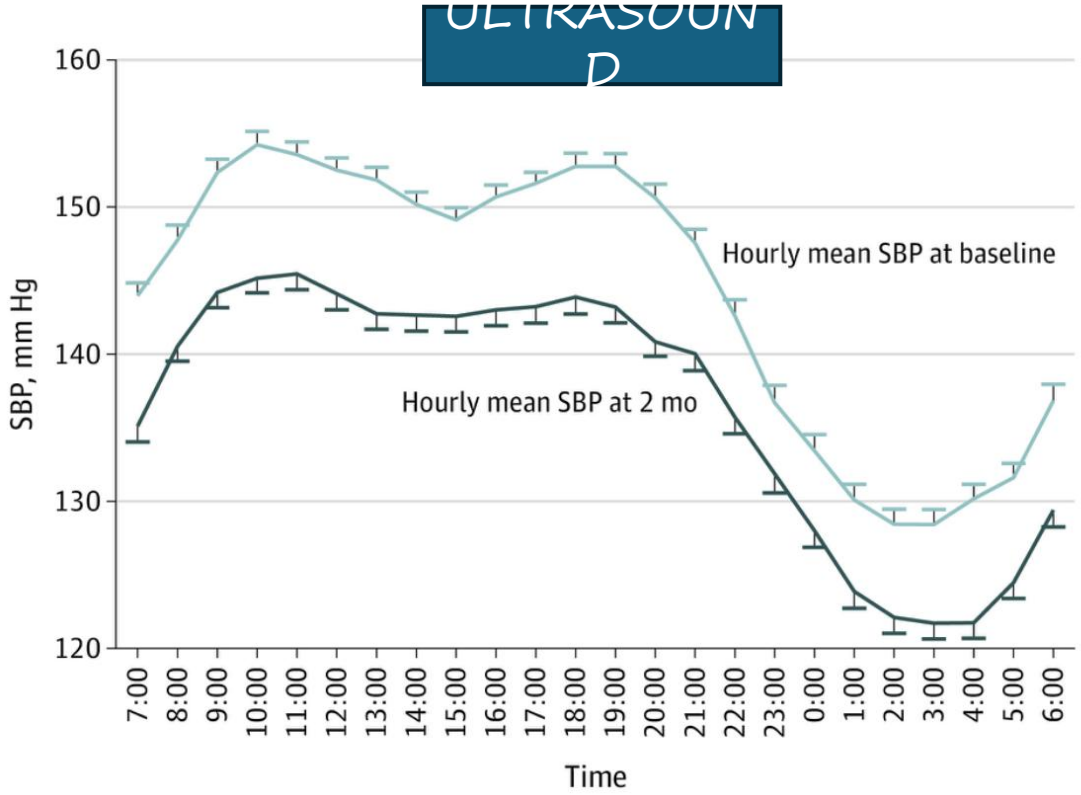
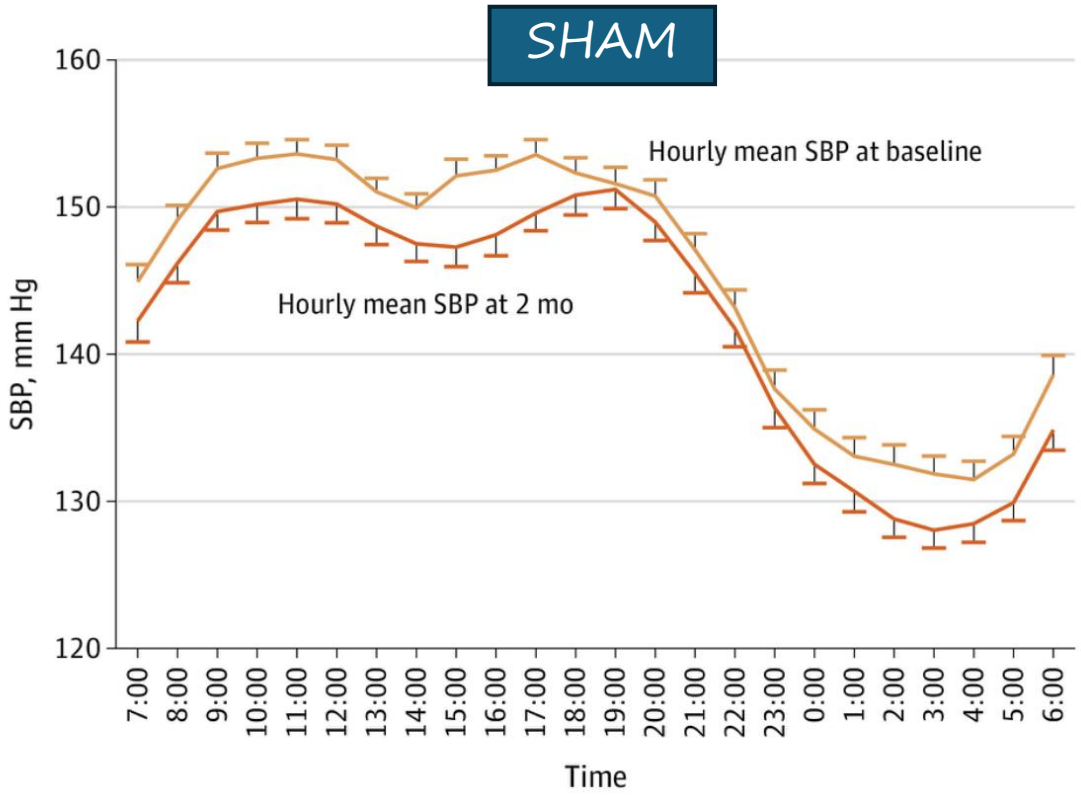
Azizi et al. Lancet 2021; 26: 2476-2486

Pooled Analysis of RADIANCE Trials: Lower Ambulatory BP throughout 24-hr Period

24-h Ambulatory SBP (mean change from baseline)	Nighttime ambulatory SBP (mean change from baseline)
uRDN = -7.9 mm Hg	uRDN = -6.7 mm Hg
Sham = -3.1 mm Hg	Sham = -3.0 mm Hg
Between-group = -5.3 mm Hg	Between-group = -4.7 mm Hg
(95% CI, -7.4 to -3.3)	(95% CI, -7.0 to -2.4)
P <.001	*P* <.001





JAMA Cardiol. 2023 May 1;8(5):464-473.

RADIANCE pooled major adverse event rates

	uRDN (N=293)	Sham (N=213)
30-day events		
All-cause mortality*	1 (0.3%)	0 (0.0%)
New onset ESRD (eGFR<15 mL/min/m^2 or need for renal replacement therapy)	0 (0.0%)	0 (0.0%)
Significant embolic event resulting in end-organ damage	0 (0.0%)	0 (0.0%)
Renal artery perforation or dissection requiring an invasive intervention	0 (0.0%)	0 (0.0%)
Major vascular complication requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion	1 (0.3%)	0 (0.0%)
Hospitalization for hypertensive or hypotensive crisis	1 (0.3%)	0 (0.0%)
Hospitalization for major cardiovascular or hemodynamic related events	1 (0.3%)	0 (0.0%)
New onset stroke	0 (0.0%)	0 (0.0%)
New onset myocardial infarction	0 (0.0%)	0 (0.0%)
6-month events		
New onset renal artery stenosis >70%	0 (0.0%)	0 (0.0%)

5 Major Adverse Events occurred in 3/293 patients (1.0%) in the uRDN arm. Multiple events occurred in a single patient: 2 vascular complications and a hospitalization for hypotension

* Death was unrelated to the procedure

JAMA Cardiol. 2023 May 1;8(5):464-473.

Experiencia local con DNR por ultrasonido

Hospital Clínico San Carlos

Características de la población

	Edad	Sexo	HTA	DM	DL	Fumador	Obesidad	Cardiopatía isquémica	Arritmias	Insuf Renal
Paciente 1	75	V	Sí	No	Sí	No	Sí	No	FA	No
Paciente 2	55	M	Sí	Sí	Sí	No	Sí	No	No	Sí
Paciente 3	77	M	Sí	No	Sí	No	Sí	No	No	No
Paciente 4	64	V	Sí	Sí	Sí	No	Sí	No	FA	Sí
Paciente 5	60	M	Sí	No	Sí	No	Sí	No	No	No
Paciente	79	V	Sí	Sí	Sí	No	No	Sí	FA	No

Características del procedimiento

	TA pre DNR	Ø renal derecha	Ø renal izquierda	No. balones renal derecha	No. balones renal izquierda	No. terapias renal derecha	No. terapias renal izquierda
Paciente 1	115/65	7 mm	7 mm	2	1	2	2
Paciente 2	220/100	6 mm	6 mm	1	1	3	2
Paciente 3	200/90	5 mm	5 mm	1	1	2	1
Paciente 4	180/100	8 mm	8 mm	1	1	2	2
Paciente 5	140/90	6 mm	6 mm	1	1	3	1
Paciente	220/80	6 mm	7 mm	1	1	3	3

Características del procedimiento

	Acceso	French	Hemostasia	Contraste	Tiempo de escopia	Tiempo total	Éxito de la DNR	Complicaciones
Paciente 1	FD	7	Proglide	148 ml	15 min	90 min	Sí	No
Paciente 2	FD	7	Angioseal	129 ml	12 min	60 min	Sí	No
Paciente 3	FD	7	Proglide	88 ml	12 min	90 min	Sí	No
Paciente 4	FD	7	Compresión	122 ml	12 min	60 min	Sí	No
Paciente 5	FD	7	Proglide	129 ml	10 min	90 min	Sí	No
Paciente	FD	7	Proglide	150 ml	10 min	50 min	Sí	No

Conclusiones

- La DNR por ultrasonido (Paradise™) ha demostrado ser eficaz y segura para el tratamiento adyuvante de la HTA resistente

- La DNR por ultrasonido (Paradise™) está recomendada por las GPC para el tratamiento de:
  - HTA resistente no controlada con ≥3 fármacos anti-HTA (IIB b)
  - HTA no controlada con <3 fármacos anti-HTA en pacientes con riesgo CV elevado (IIB a).