Renal Sympathetic Denervation for HTN

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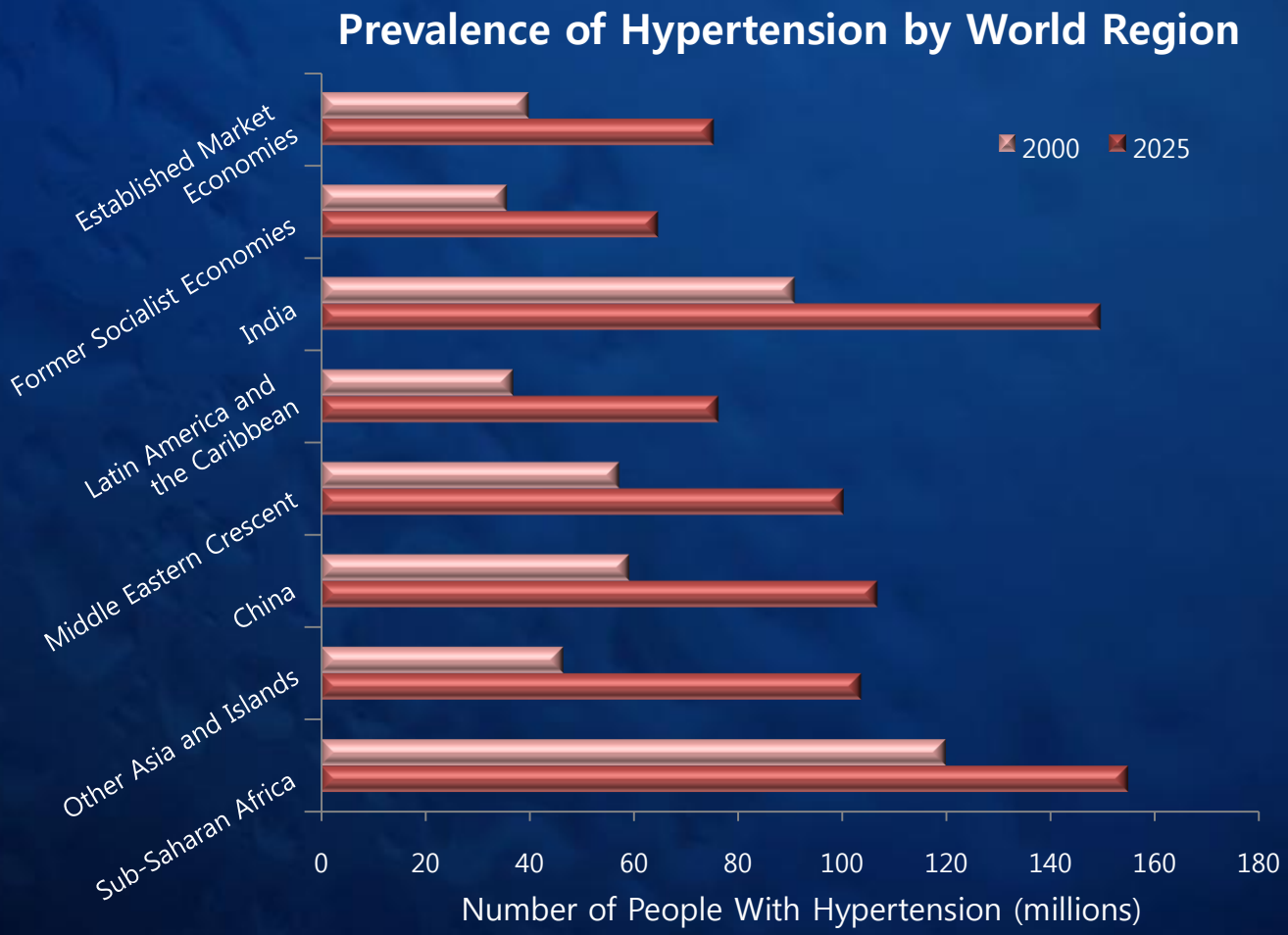
Worldwide Prevalence of Hypertension Is Increasing

- In 2000, 972 million (26%), of the adult population had hypertension
- By year 2025, 1.56 billion (29%) are projected to have hypertension
- Most of the expected increase will be in economically developing regions



Kearney PM, et al. *Lancet.* 2005;365:217-223.

JNC 7 Classification of Blood Pressure Levels

BP Classification	Systolic (mm Hg)		Diastolic (mm Hg)
Normal	<120	and	<80
Pre-hypertension	120 – 139	or	80 – 89
Stage 1 Hypertension	***140*** – 159	or	90 – 99
Stage 2 Hypertension	≥160	or	≥100

JNC 7 = The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP.
Chobanian AV, et al. *Hypertension*. 2003;42:1206-1252.

2007 ESH-ESC Classification of BP Levels

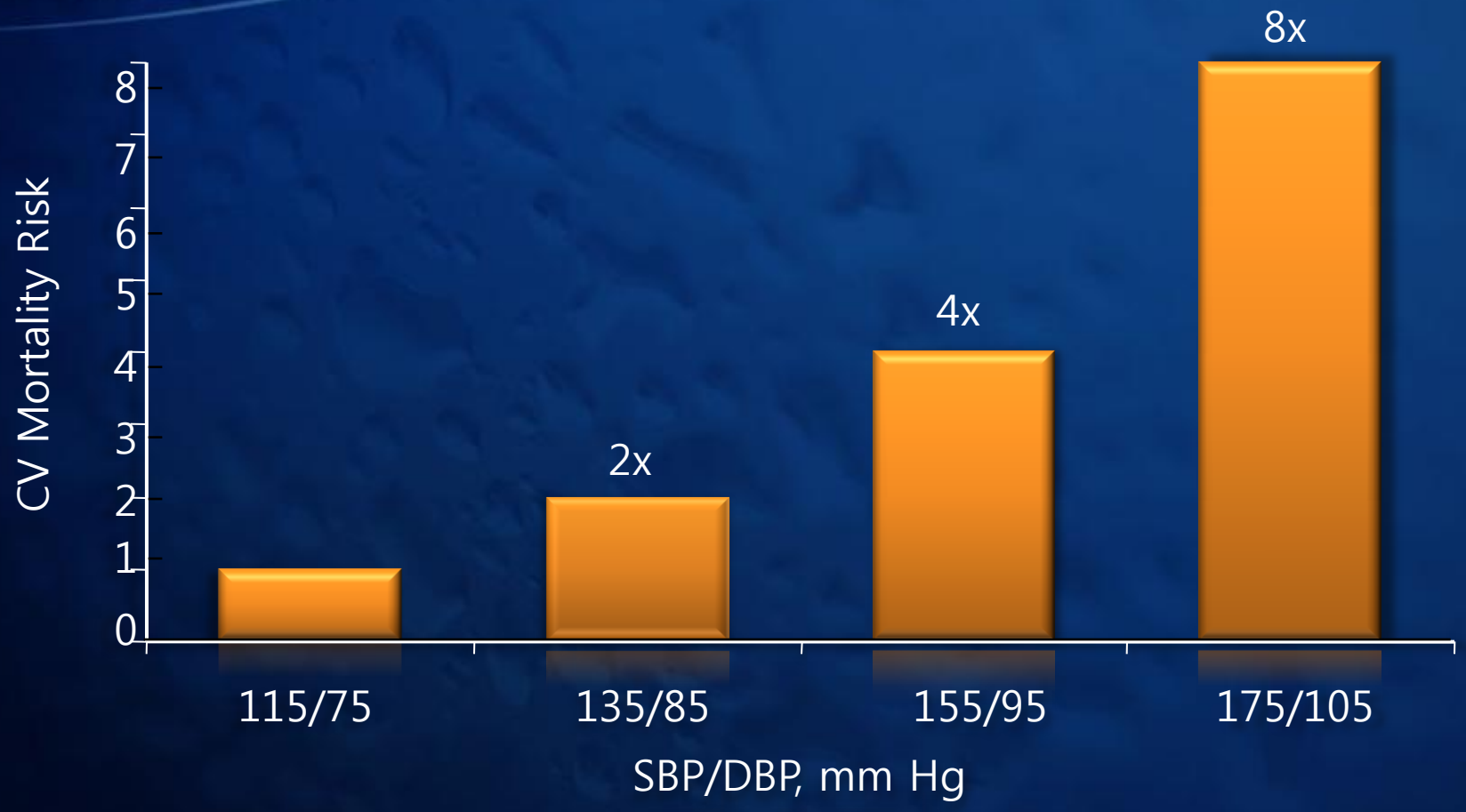
BP Classification	Systolic (mm Hg)		Diastolic (mm Hg)
Optimal	<120	and	<80
Normal	120 – 129	and/or	80 – 84
High Normal	130 – 139	and/or	85 – 89
Grade 1 Hypertension	***140*** – 159	and/or	90 – 99
Grade 2 Hypertension	160 – 179	and/or	100 – 109
Grade 3 Hypertension	≥180	and/or	≥110

2007 ESH-ESC = 2007 Hypertension Practice Guidelines of the European Society of Hypertension (ESH) and European Society of Cardiology (ESC).
Mancia G, et al. *Eur Heart J*. 2007;28:1462-1536.

Even Small Reductions in BP Reduce Risk of CV Mortality

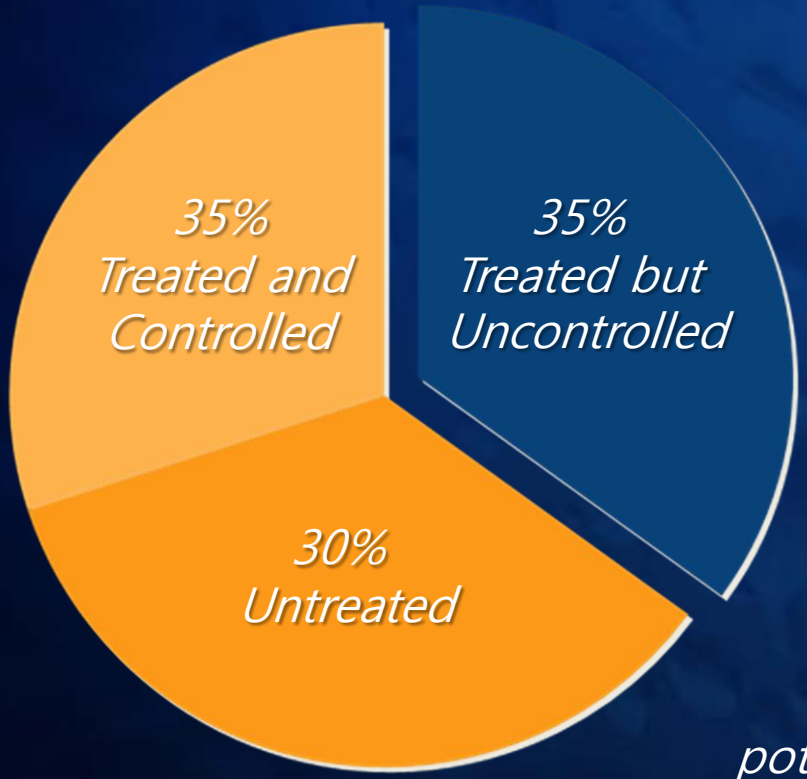
SBP = systolic blood pressure.
Lewington S, et al. *Lancet.* 2002;360:1903-1913.

Cardiovascular Mortality Risk Doubles With Each 20/10 mm Hg Increase in BP*



CV = cardiovascular.
SBP = systolic blood pressure.
DBP = diastolic blood pressure.
*In individuals aged 40 to 69 years (10-year study period), starting at BP 115/75 mm Hg.
Lewington S, et al. *Lancet.* 2002;360:1903-1913.

Drugs Work, But Not as Well as You May Think



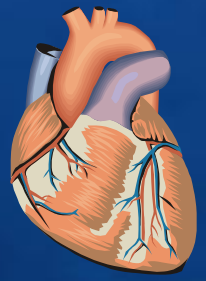
Current approach failing:

- Physician inertia
- Patient compliance
- Resistant HTN

Renal denervation (RDN) =
potentially a compliance-independent therapy

Renal Sympathetic Nerve Activity: Kidney as Origin & Recipient of Central Sympathetic Drive

- Vasoconstriction
- Atherosclerosis



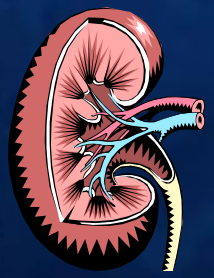
- ↑ Contractility
- ↑ Heart rate

Efferent Nerves

Afferent Nerves

-- Renal Denervation (RDN)--

Blood Pressure



- ↑ Renin Release → RAAS activation
- ↑ Sodium Retention
- ↓ Renal Blood Flow
- ↓ Kidney function

Renal Denervation: A New Therapeutic Approach

- Recently, renal denervation using a novel approach (percutaneous, catheter-based radiofrequency ablation) was shown to significantly reduce BP in patients with resistant hypertension[1-3]

- The procedure was found to be simple and safe with minimal procedure-related adverse events[2,3]

- Catheter-based renal denervation could represent a significant advance in the management of resistant hypertension

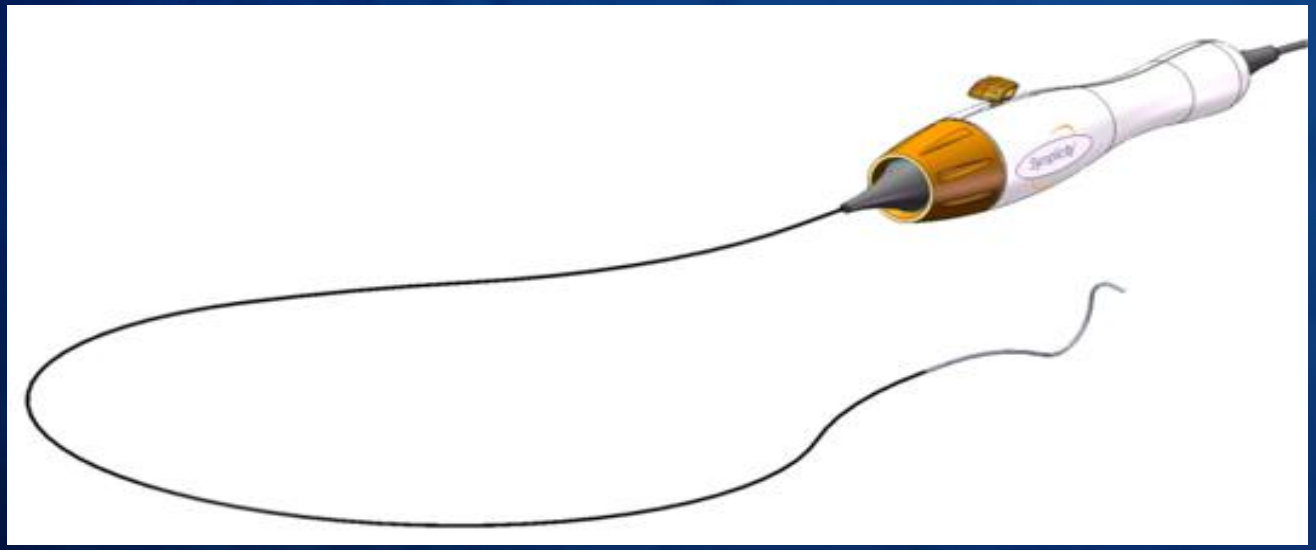
1. Schlaich MP, et al. *Hypertension.* 2009;54:1195-2001.
2. Symplicity HTN-2 Investigators. *Lancet.* 2010;376:1903-1909.
3. Symplicity HTN-1 Investigators. *Hypertension.* 2011;57:911-917.

Equipment

- Symplicity™ catheter and generator
  - Dispersive electrode (ground pad) – sent with Symplicity catheter
- 6 French sheath
- 6 French renal guide catheter
  (45-55 cm, RDN-D1/RDC-1, or IMA/LIMA)

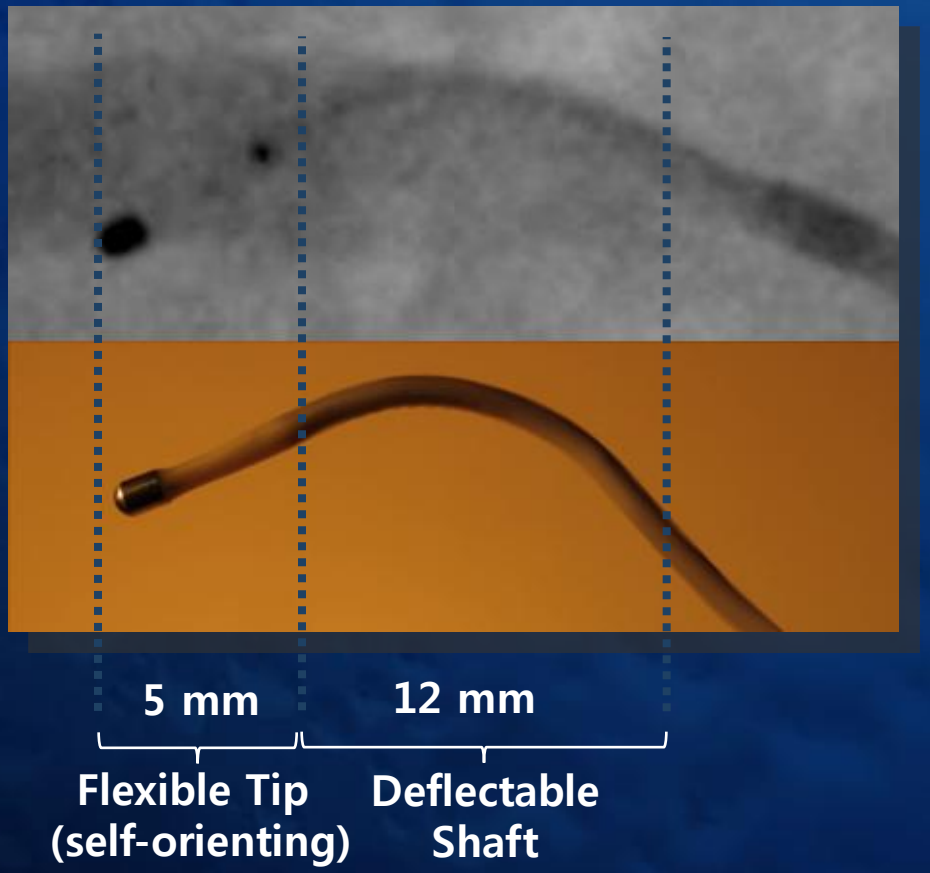
- Guidewire (0.014", non-hydrophilic)
- Tuohy (RHV)
- Non-ionic contrast (dilute to 50:50)
- Heparinized saline flush bag (pressurized)
- Radiopaque ruler

Symplicity™ Catheter



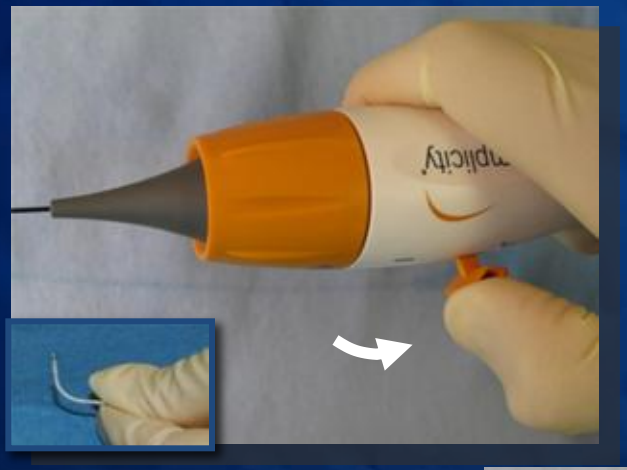
- Symplicity™ catheter 길이 108Cm
- 두께 1.3mm(0.051 inch)
- Tip ~ Deflectable Shaft 길이 17mm

Symplicity™ Catheter Tip Features

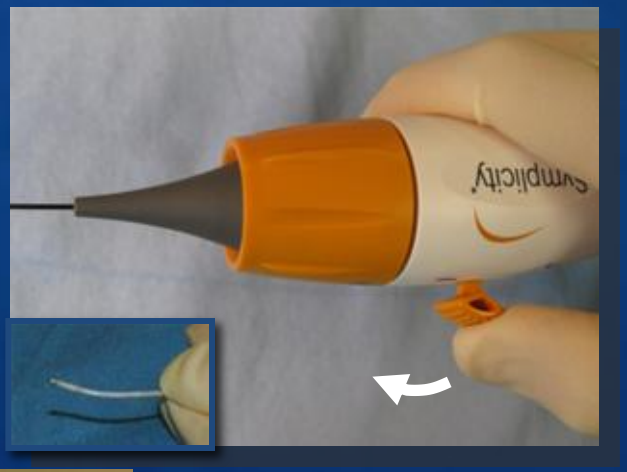


Symplicity™ Catheter Handle Features

Deflect tip by pulling lever towards back of handle

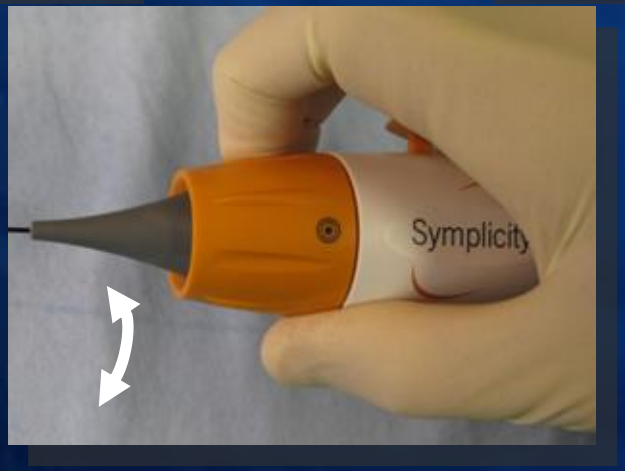


Straighten tip by pushing lever towards front of handle



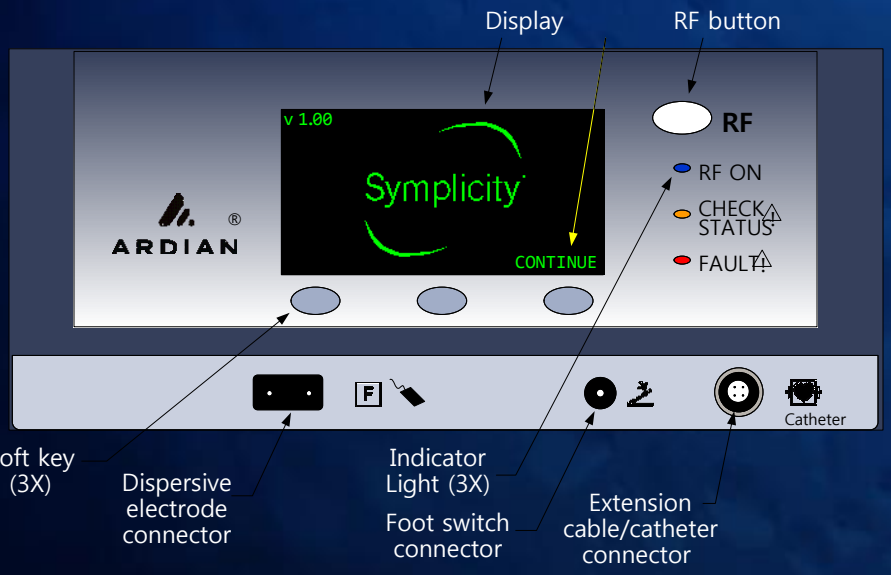
Shaft and electrode can rotate independently from handle body

- Handle rotator has tactile "click" every 45 degrees
- Dot on rotator gives relative rotational reference



Generator

Front Panel



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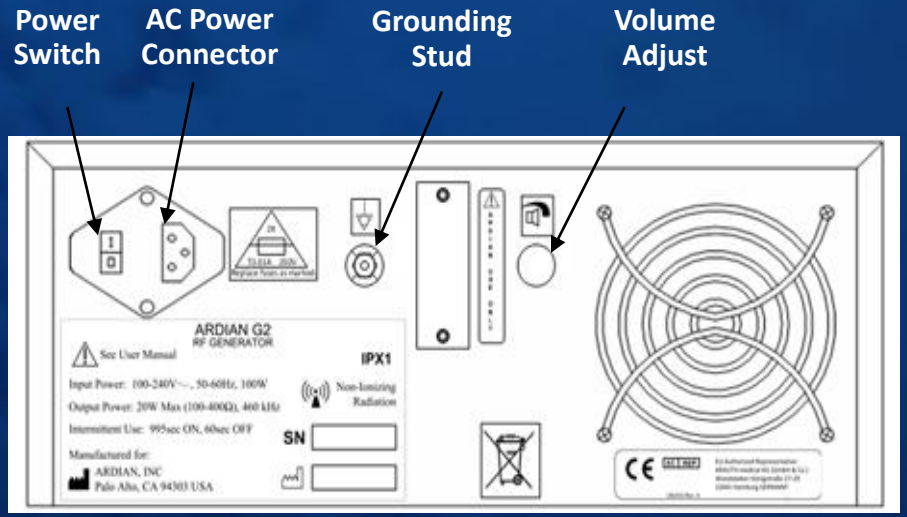
Back Panel



Model G2

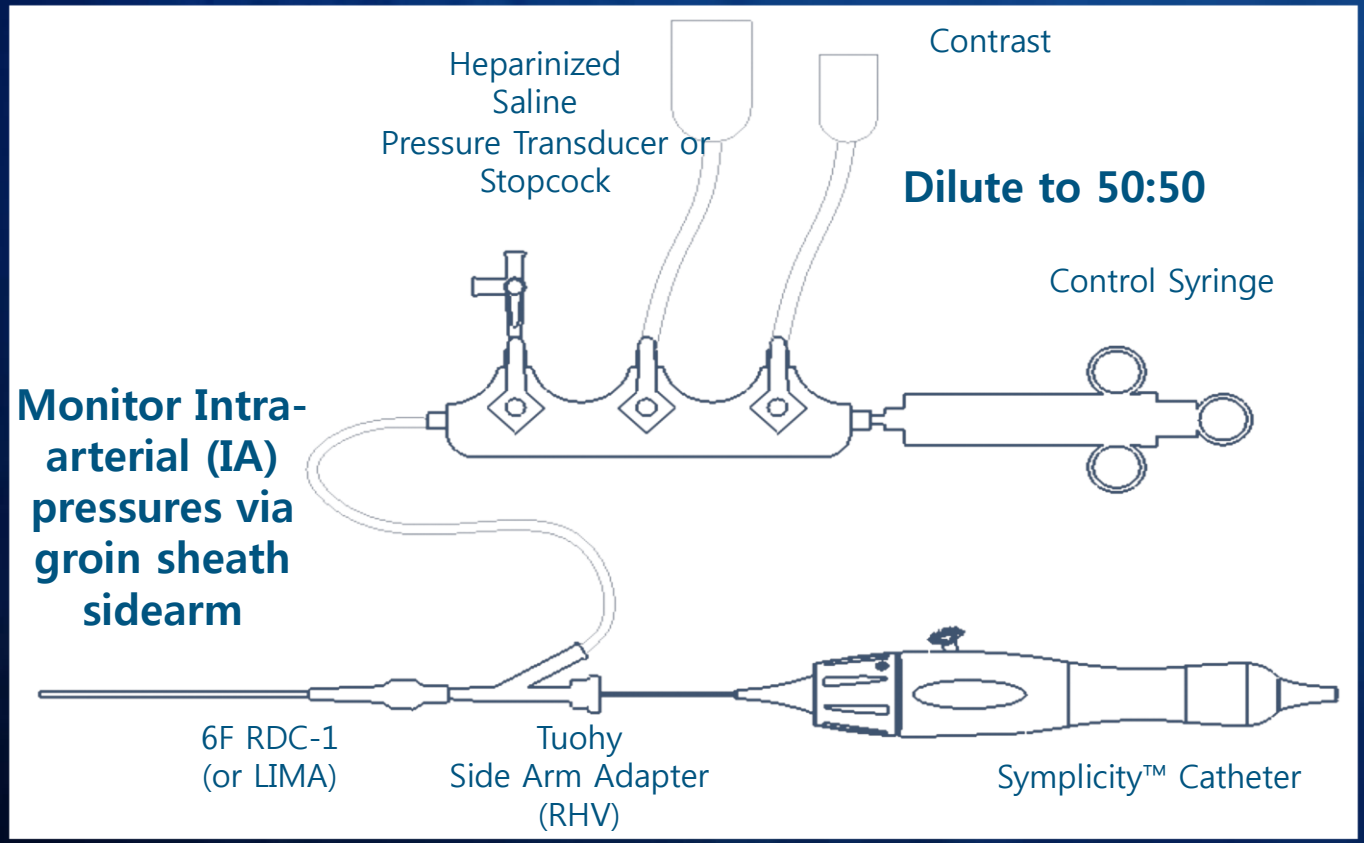
Guiding Catheter

- Key Guide Selection Criteria
  - Takeoff angle of renal arteries
  - Engagement at ostium to prevent deep seating of guide catheter
  - Soft tip at engagement with both active and balanced support
  - 6fr, 45~55Cm

Medtronic
Sherpa RDN-D1

Medtronic
Sherpa IMA

Manifold Set-up and Contrast Management



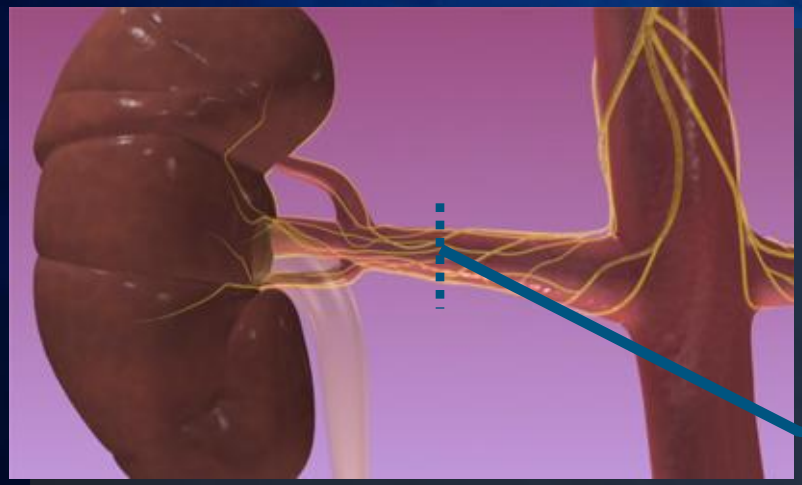
Medications

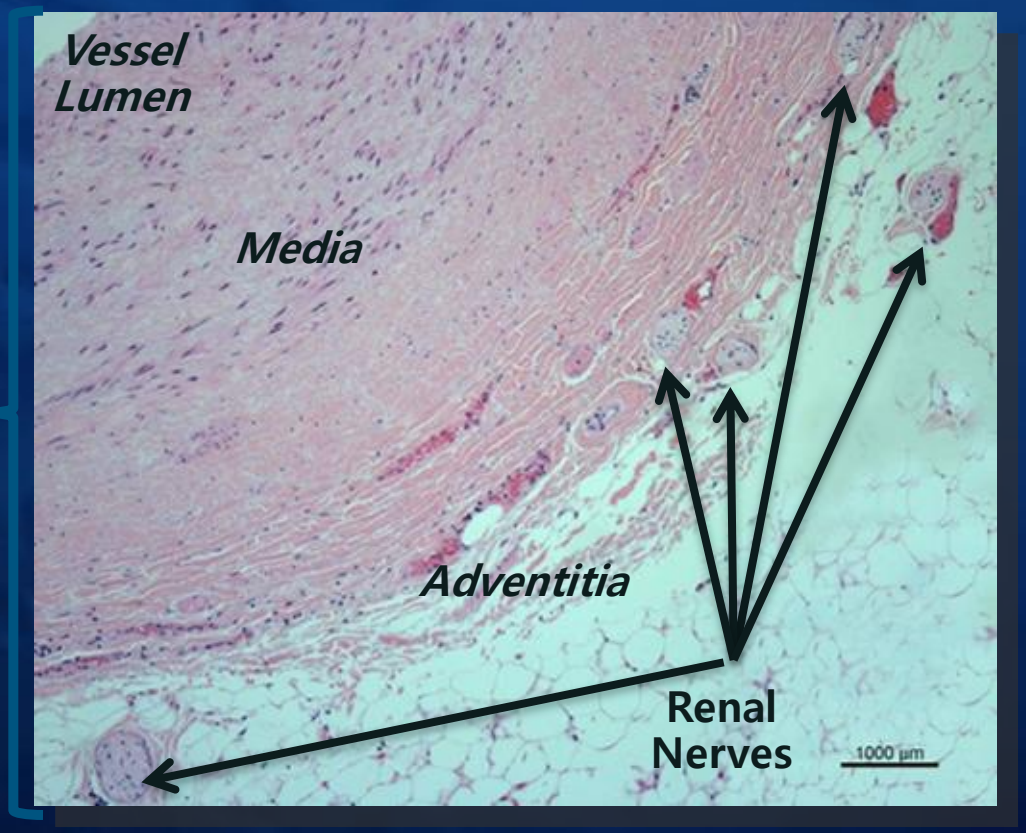
- Common medications to have available for procedure
  - Heparin
  - Midazolam (eg, dormicum, Versed) or similar
  - Fentanyl/morphine or similar
  - Nitroglycerine
  - Atropine

Renal Angiogram

- Absence of flow-limiting obstructions
- Diameter ≥4 mm in targeted area
- Absence of prior renal angioplasty, indwelling renal stents, or aortic graphs

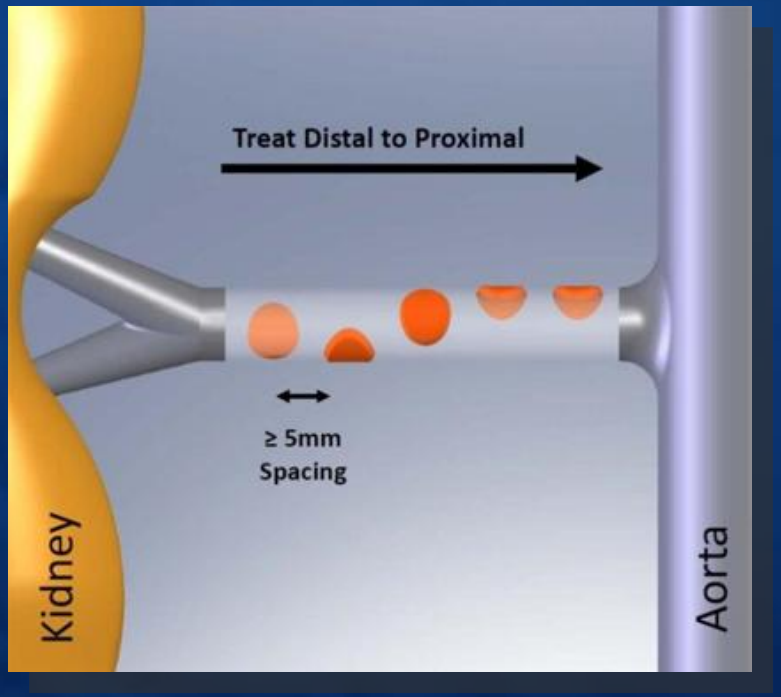
Targeting Renal Nerves





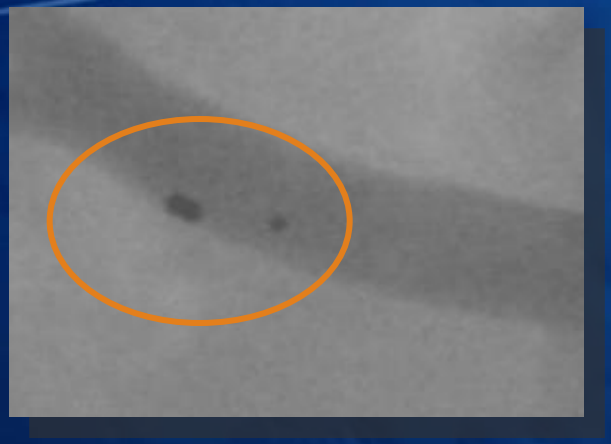
Targeting Renal Nerves

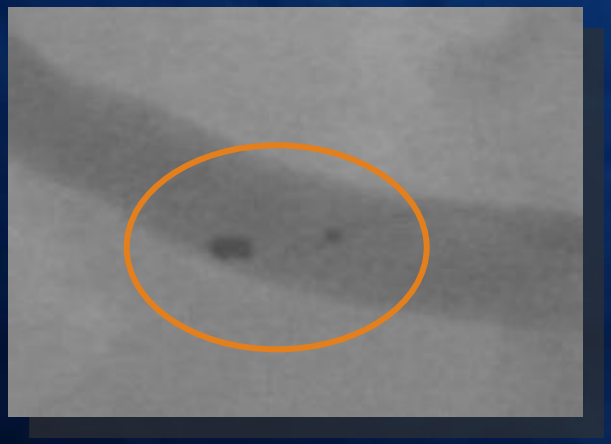
- Always treat distal to proximal
  - Do not re-cross previously treated site
- 4-6 focal treatments
  - 120 seconds per treatment
  - ≥ 5 mm between locations
  - Stable, unique locations
  - Circumferential coverage
- Common strategy (dependent on renal anatomy):
  - Distal: Inferior and inferolateral locations
  - Proximal: Superior and superolateral locations
  - If positioning is unstable, avoid purely lateral treatments (possible electrode movement with respiration)
  - Favor stable wall contact over circumferential treatment
- PULL, ROTATE, ASSESS new location and prior treatment site with cine *just prior to* each treatment



Optimizing Wall Contact

Sufficient Wall Contact



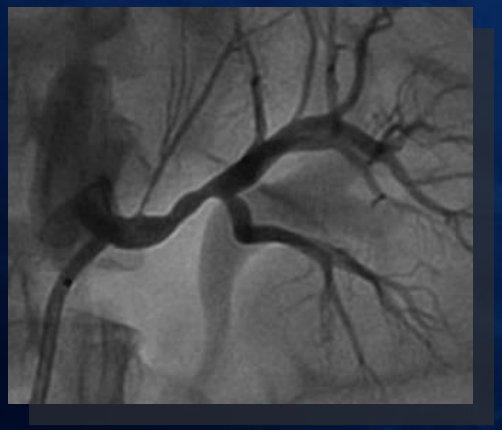


Excessive Wall Contact
(avoid distending vessel wall with electrode)

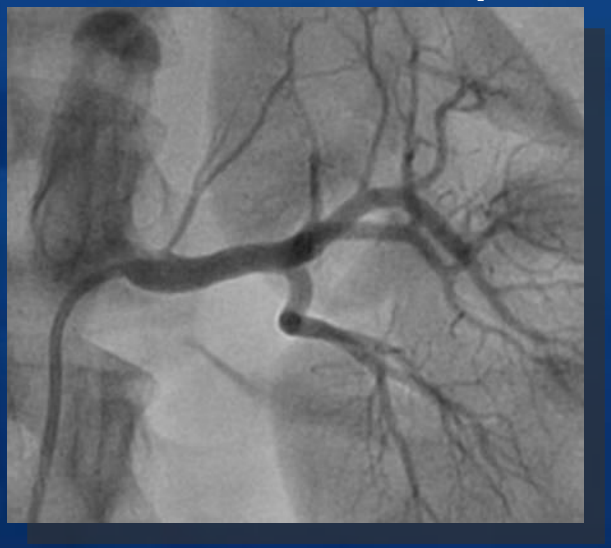
Angiographic Appearance – Less Common

Pre-Procedure

Acute Post-Procedure



1 Month Follow-Up



- Increased vessel reactivity, such as spasm, may be encountered when treating in areas with reduced blood flow, such as dual renal arteries or beyond significant renal artery branch points

Basic and Advanced Settings

- Per the Generator User Manual, using softkeys, it is possible to toggle between Basic and Advanced displays
- During RF ON, in addition to time and temperature, the advanced display also displays Power and % Impedance drop
- Generally, bigger impedance drops indicate better delivery of energy

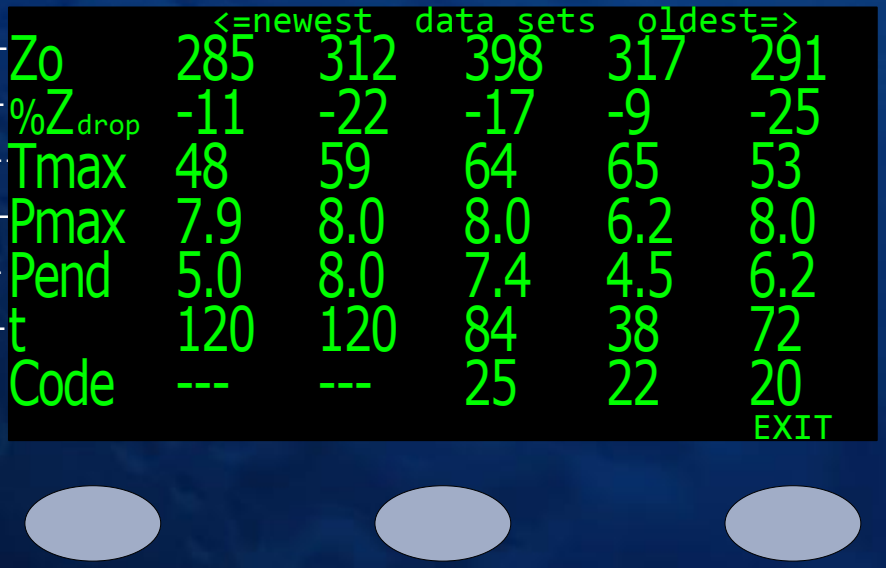
Basic Setting

Advanced Setting

Summary Screen

- Using a softkey, it is possible to view a summary of the last 5 treatments performed:

- Starting Impedance ----------
- % Impedance Drop ----------
- Max Temp (°C) ----------
- Max Power (Watts) ----------
- End Power (Watts) ----------
- Time (Sec) ----------
- Check Status Messages ------



End of Treatment Messaging

"Energy successfully delivered" message will automatically clear after 5 seconds

Strive for improved electrode contact on subsequent treatments (electrode in firm contact with and stable against vessel wall)

Check Status Messages

- The proprietary generator algorithm will occasionally stop RF delivery if certain temperature and/or impedance thresholds are crossed
- In these cases, some messaging will be displayed to guide users on how to proceed
- Check status messages can be cleared by pressing the foot switch twice within 3 seconds or by pressing the “continue” softkey on the generator

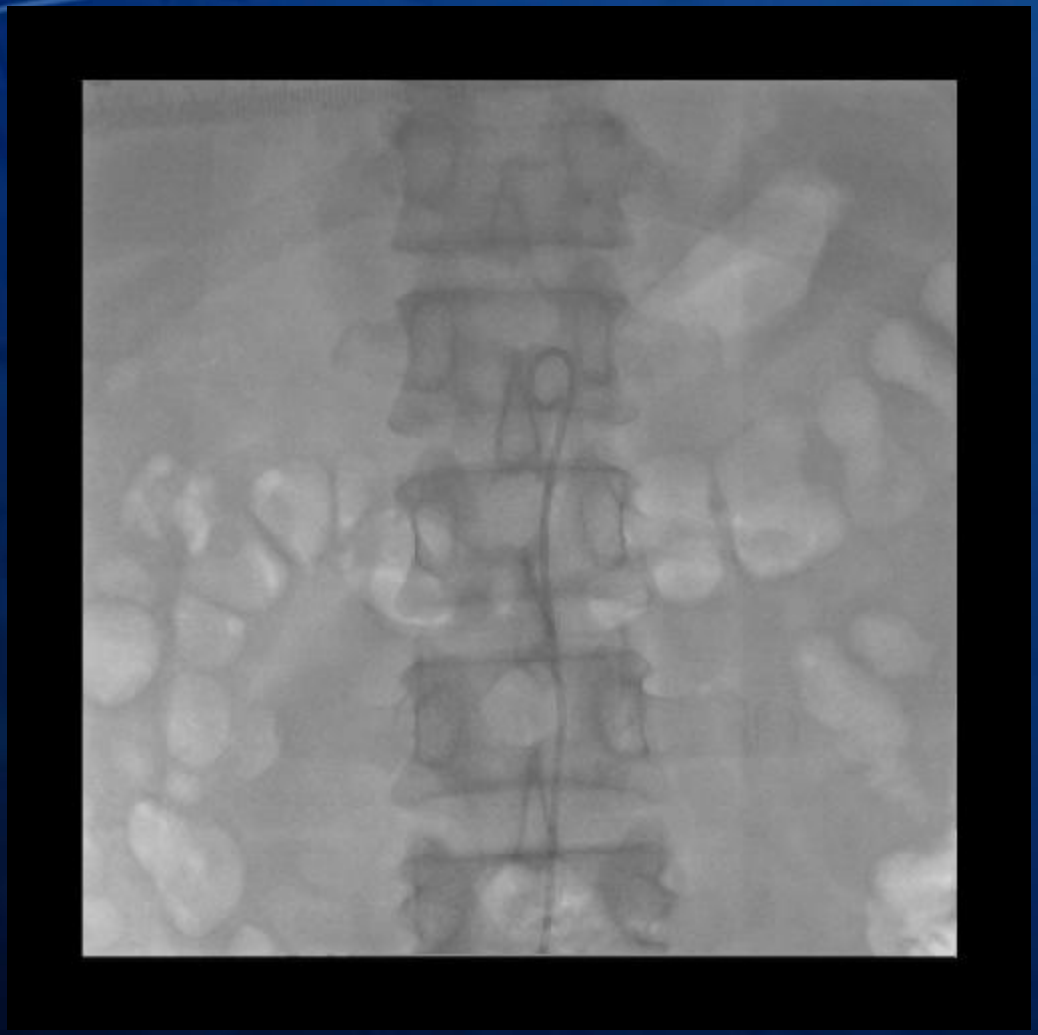
Status Messages – Commonly Encountered

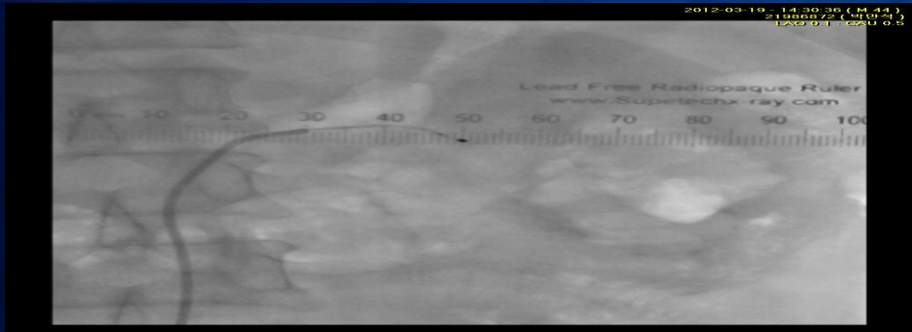
Generator messages commonly encountered and related action steps

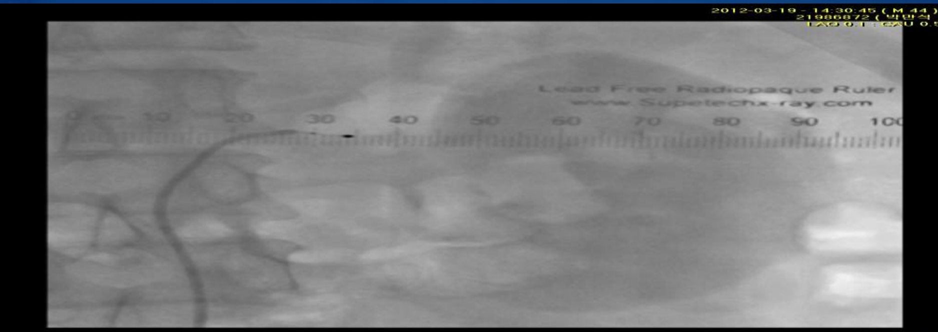
Message	Action	Check Status Code #
Image treatment site	Wait approximately one minute and image prior treatment site as increased vessel reactivity, such as spasm, may be encountered	22a, 22b, 24a
Electrode may have moved	When imaging vessel, be aware electrode may have moved during treatment	22b, 24b
Ensure proper electrode contact	Strive for improved electrode contact on subsequent treatments ▪ Electrode in firm contact with and stable against vessel wall	23, 24c
Ensure proper electrode contact for next treatment	Treatment was completed; strive for improved electrode contact on subsequent treatments ▪ Electrode in firm contact with and stable against vessel wall	50
High Impedance - check catheter position and/or connections	Ensure no excessive tissue/catheter electrode contact (ie, vessel distension) Ensure catheter is not positioned in guide, a branch, or small artery Reposition catheter electrode, if necessary, and attempt to restart treatment Check catheter and dispersive electrode connections ▪ Replace catheter and/or dispersive electrode as needed	20, 26

Additional detail sometimes provided but these portions of the message drive action.
(For more detail and other check status messages, consult Generator User Manual)

Procedure




Lead Free Radiopaque Ruler
www.Supetechx-ray.com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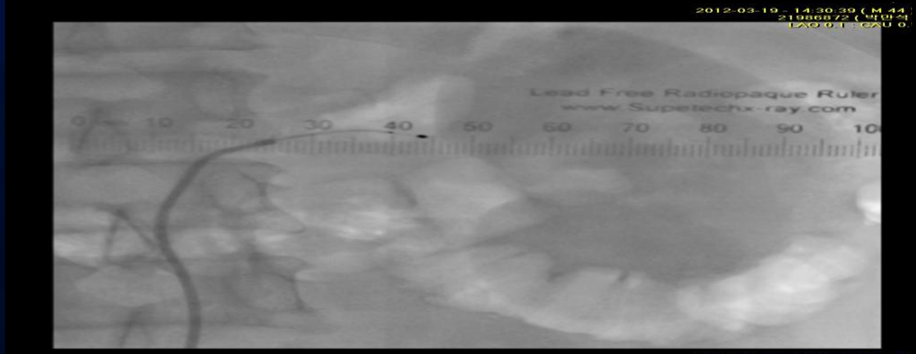
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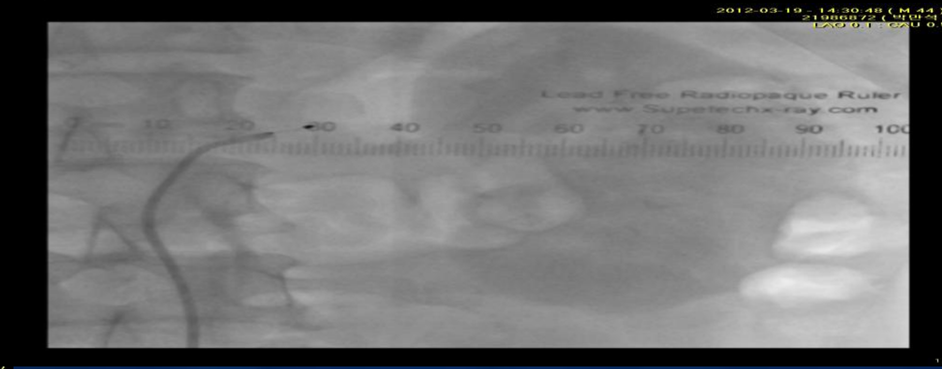
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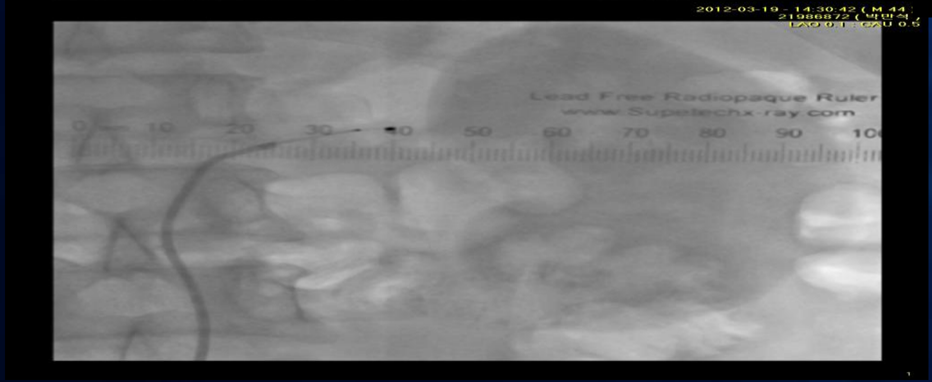
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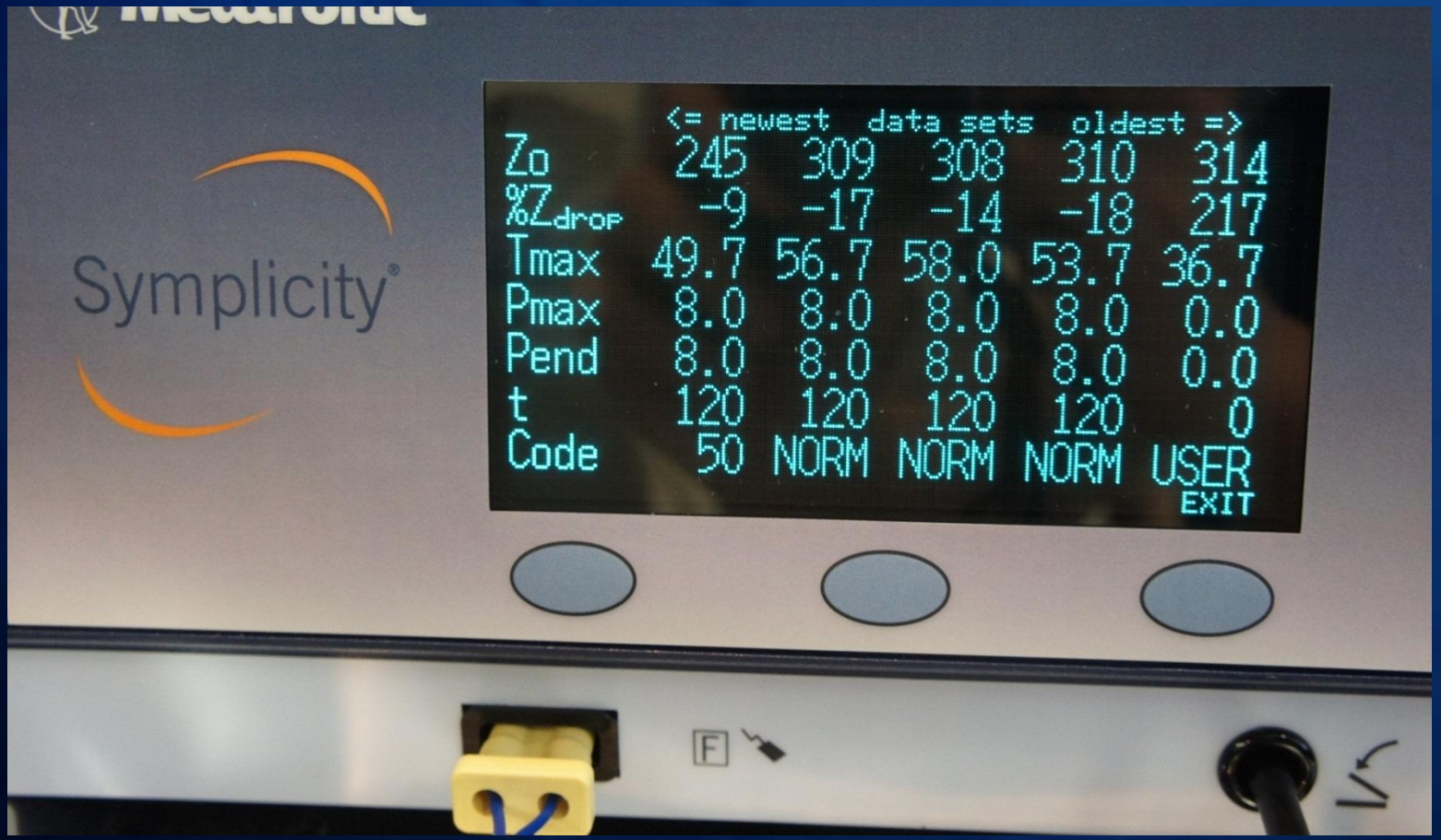
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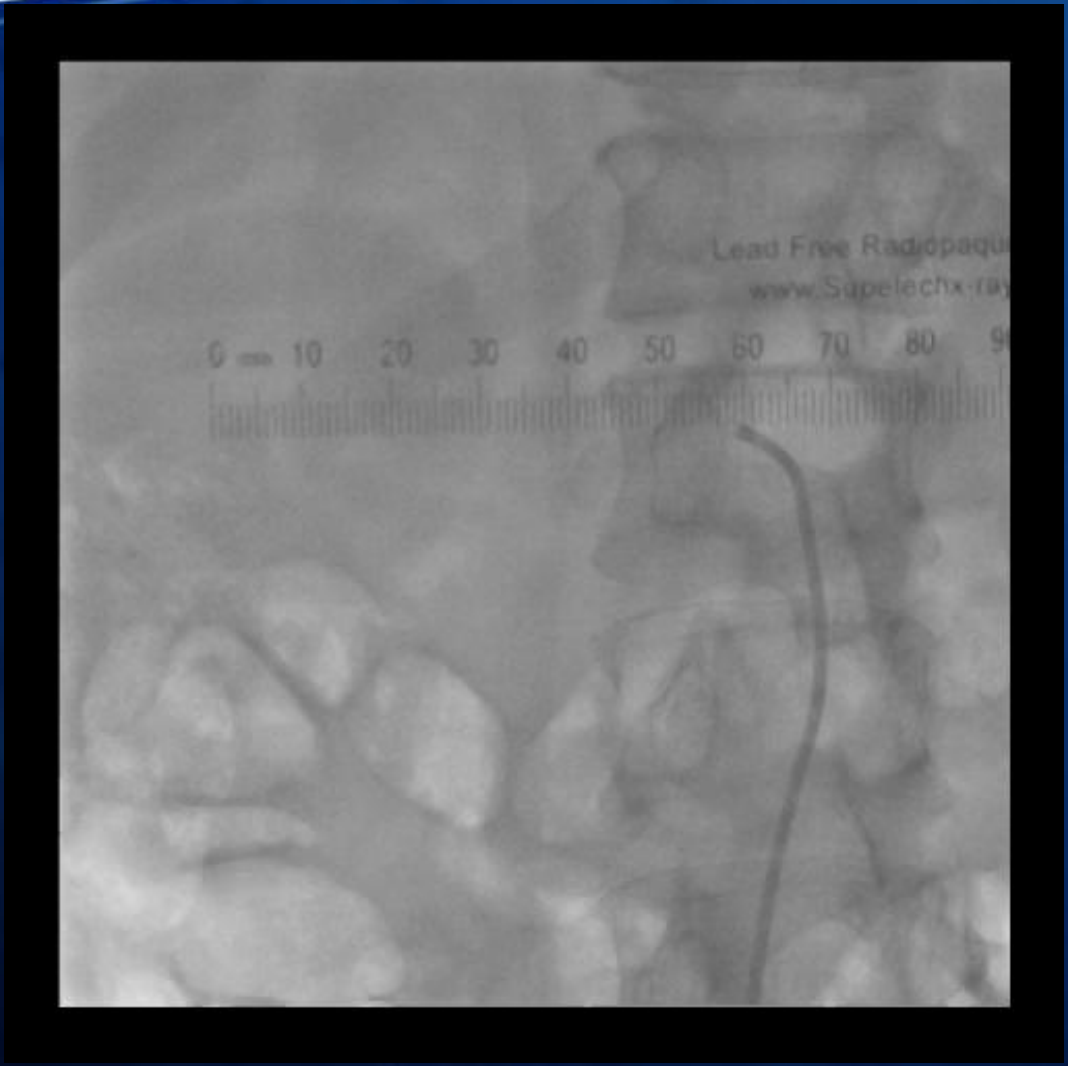
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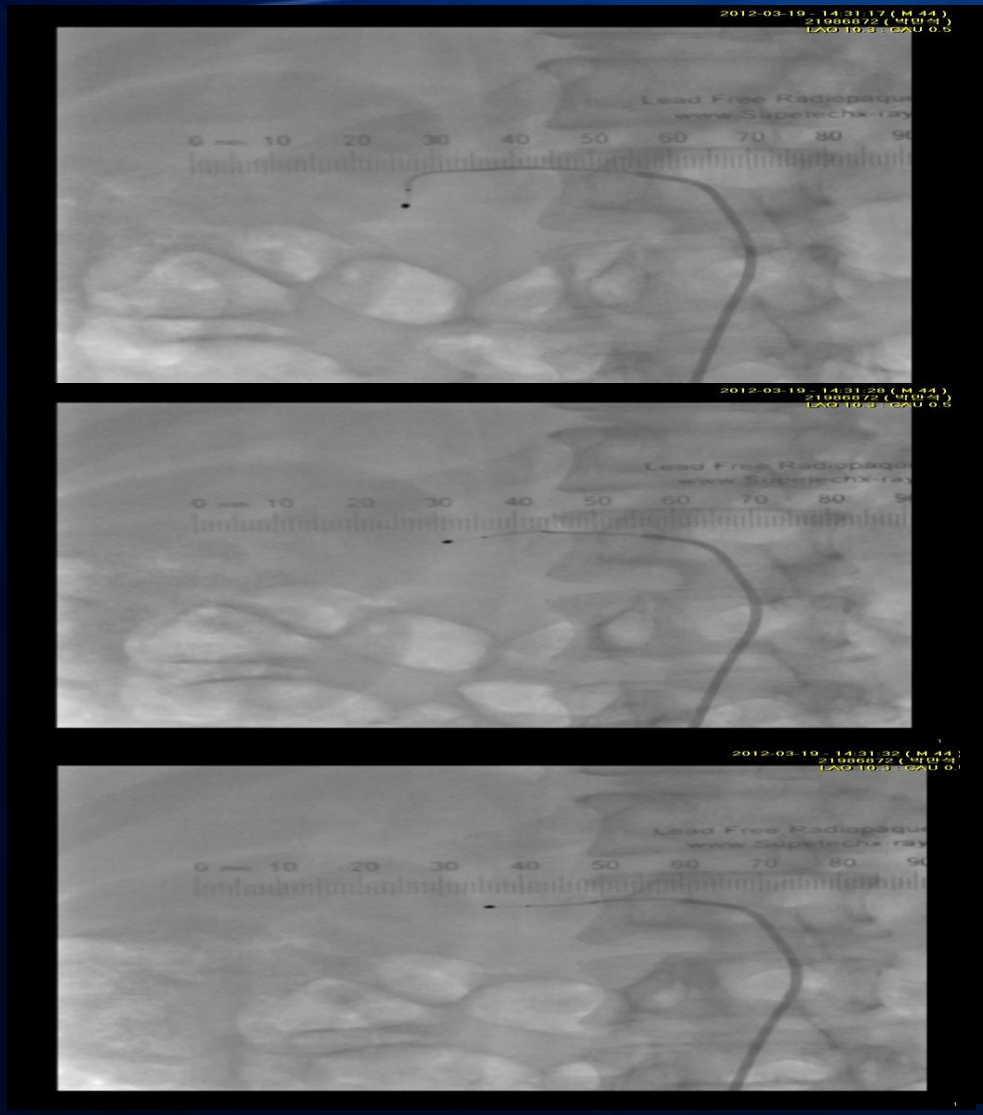
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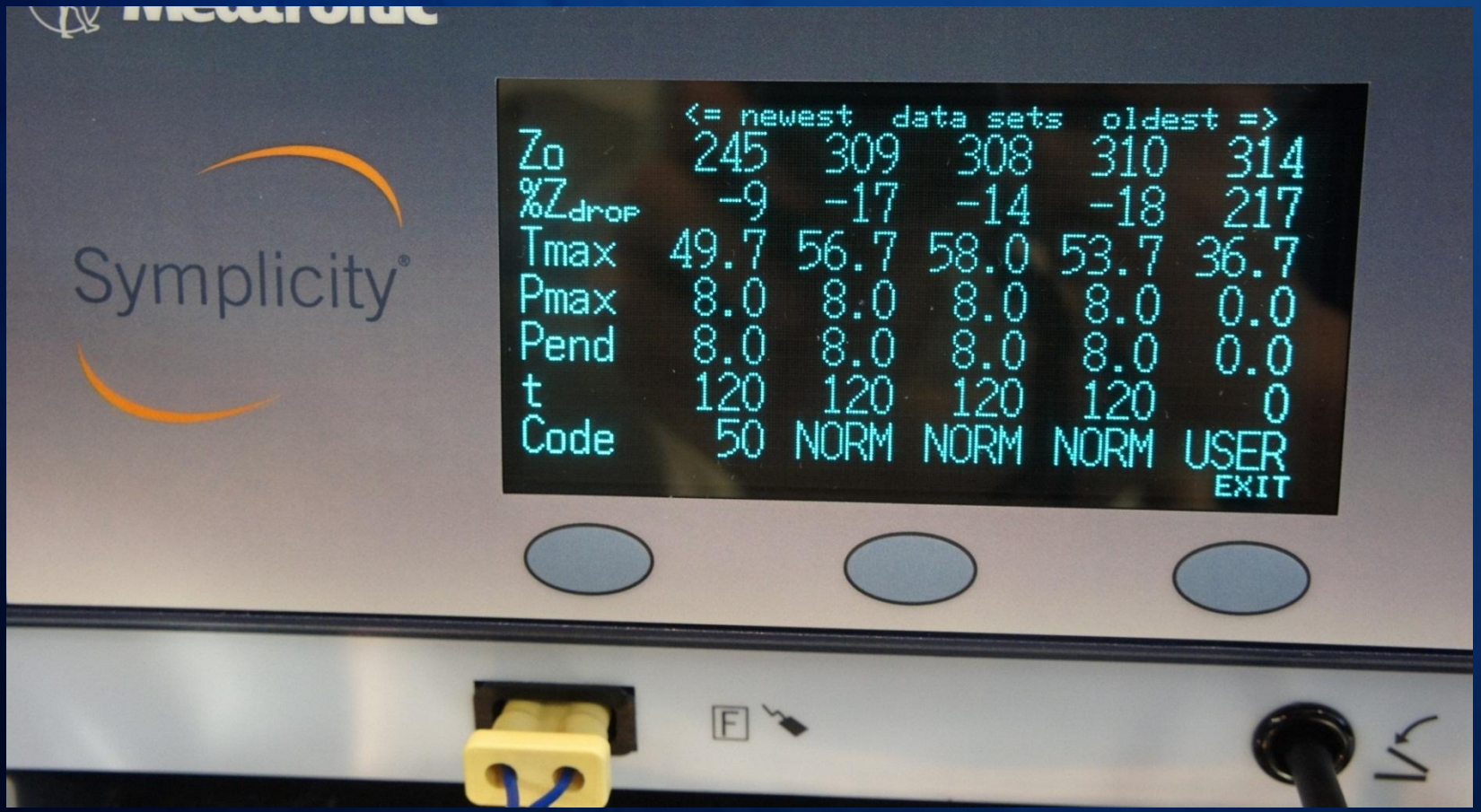
Symplicity
<= newest data sets oldest =>
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%Zdrop -9 -17 -14 -18 217
Tmax 49.7 56.7 58.0 53.7 36.7
Pmax 8.0 8.0 8.0 8.0 0.0
Pend 8.0 8.0 8.0 8.0 0.0
t 120 120 120 120 0
Code 50 NORM NORM NORM USER
EXIT


Lead Free Radiopaque
www.Supetechx-ray
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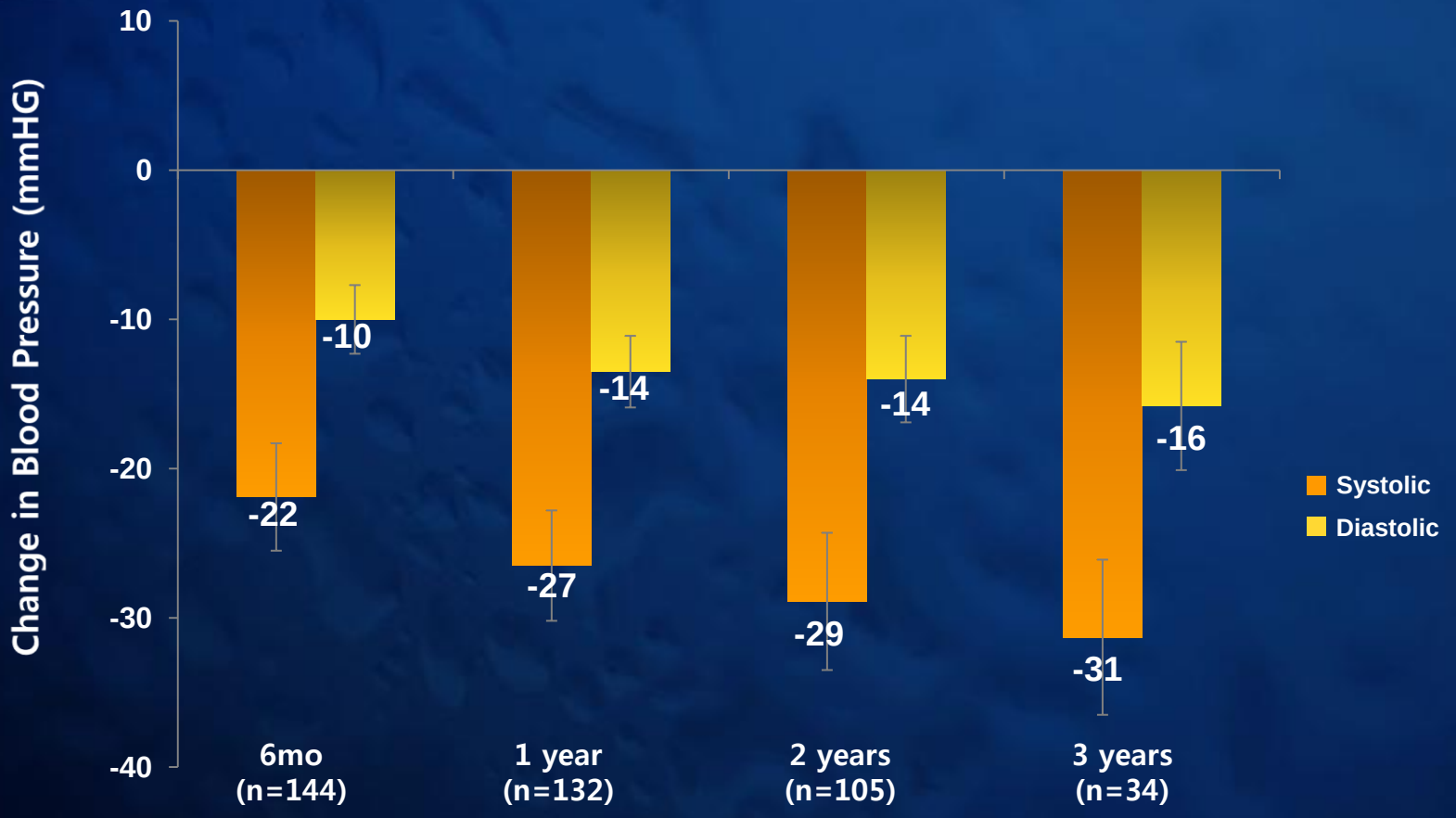
300
350
Workplace
1440 x 1440
Overlay 42%


Medtronic
Symplicity
READY
TIME
120 s
TEMP
37°C
POWER
0.0 W
IMPEDANCE
279 Ω
BASIC
SUMMARY

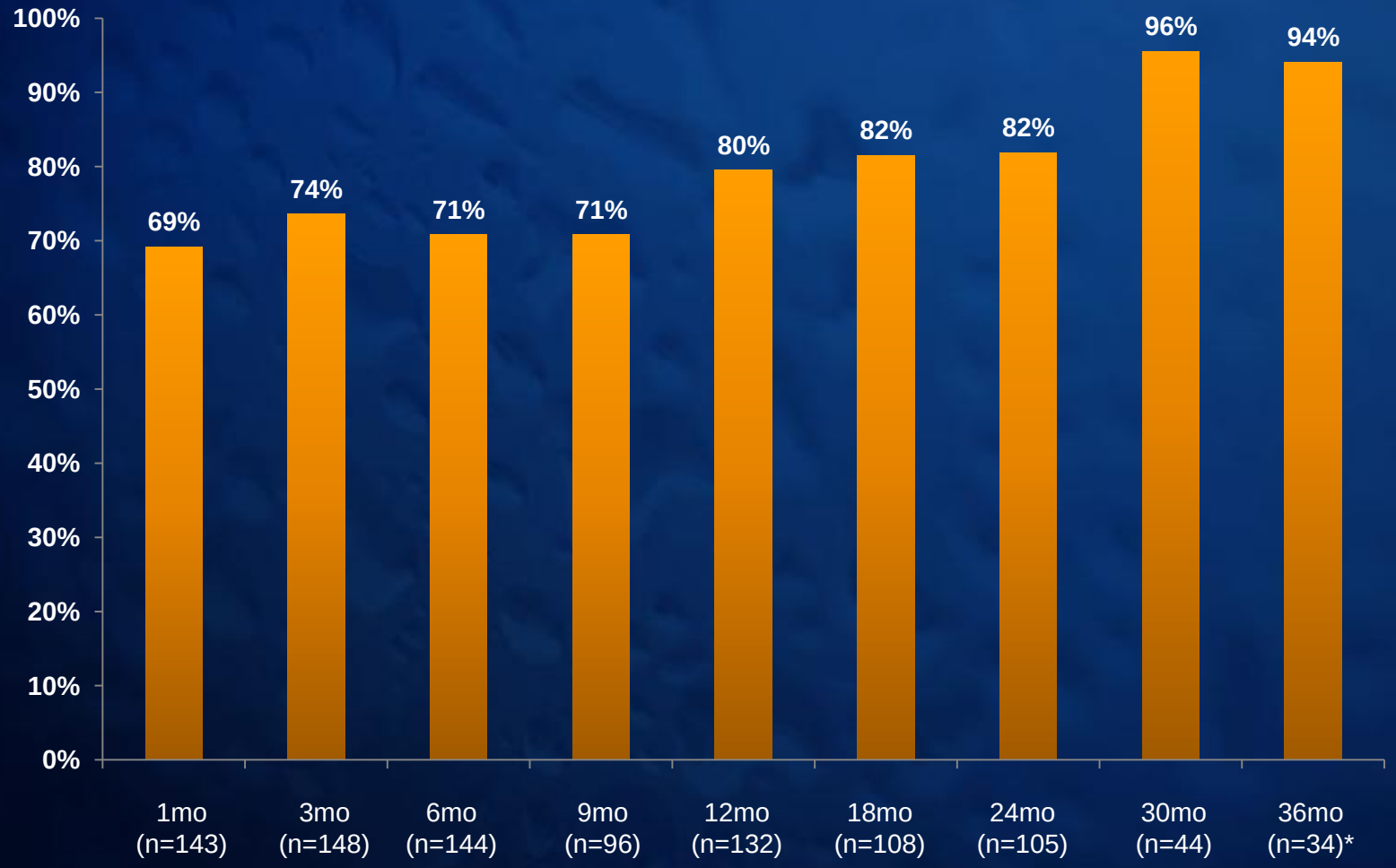
Symplicity HTN-1 Trial – Overview

- Design
  - Multicenter (19 sites in Europe, Australia, and the United States), nonrandomized, open-label, proof-of-concept study
- Population
  - 153 patients with treatment-resistant hypertension
- Treatment
  - Endovascular catheter-based renal denervation using the Symplicity™ renal denervation system plus baseline antihypertensive medications
- Duration
  - 36 months (assessments at 1, 3, 6, 12, 18, 24, and 36 months)
- Outcome Measures
  - Primary efficacy measure: change in office blood pressure (BP)
  - Primary safety measures: based on physical examination, basic blood chemistries, and anatomic assessment of renal vasculature

Symplicity HTN-1: Significant, Sustained Blood Pressure Reductions to at Least 3 Years



Symplicity HTN-1: This Clinical Benefit of RDN is Sustained



Responder was defined as an office SBP reduction ≥10 mmHg

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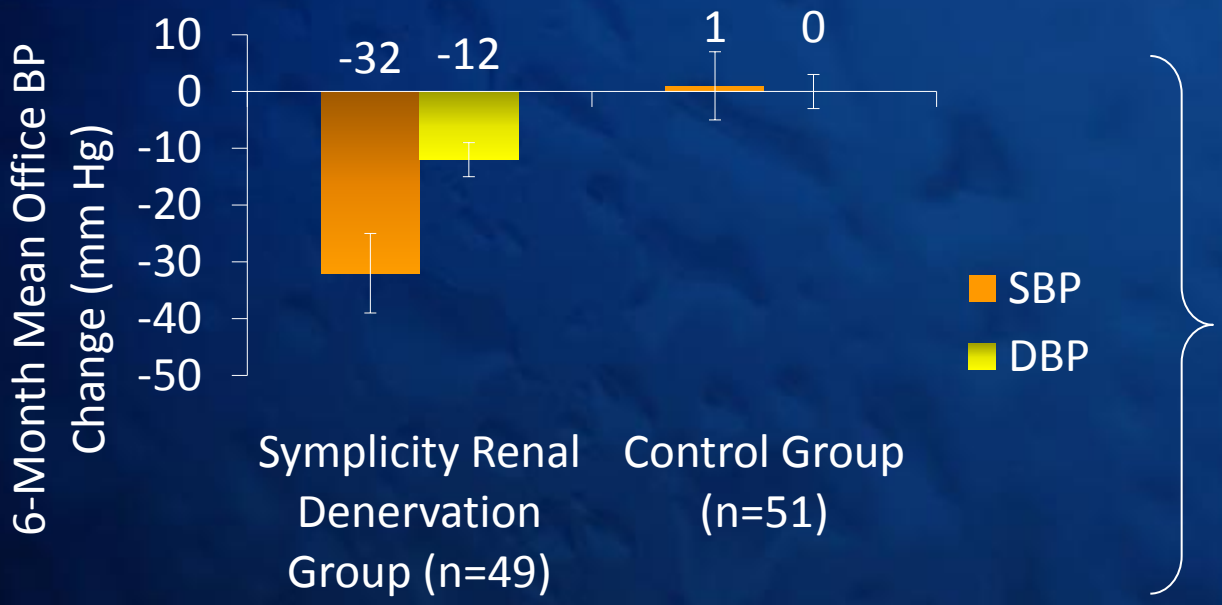
Symplicity HTN-2 Trial – Overview

- Design
  - Multicenter (24 sites in Europe, Australia, and New Zealand), prospective, randomized, controlled study
- Population
  - 106 patients with treatment-resistant hypertension
- Treatment
  - Intervention group (endovascular catheter-based renal denervation with the Symplicity™ renal denervation system plus baseline antihypertensive medications)
  - Control group (baseline antihypertensive medications alone)
- Duration
  - 6 months (for the primary endpoint) with follow-up to 3 years
- Outcome Measures
  - Primary endpoint: between-group changes in average office SBP from baseline to 6 months
  - Secondary endpoints: acute and chronic procedural safety, a composite cardiovascular endpoint, occurrence of ≥10 mm Hg SBP reductions, achievement of target SBP, change in 24-hour ambulatory BP, and change in home BP

Symplicity HTN-2 Investigators. *Lancet*. 2010;376:1903-1909

Symplicity HTN-2 Trial – 6-Month Office BP* (Primary Endpoint)



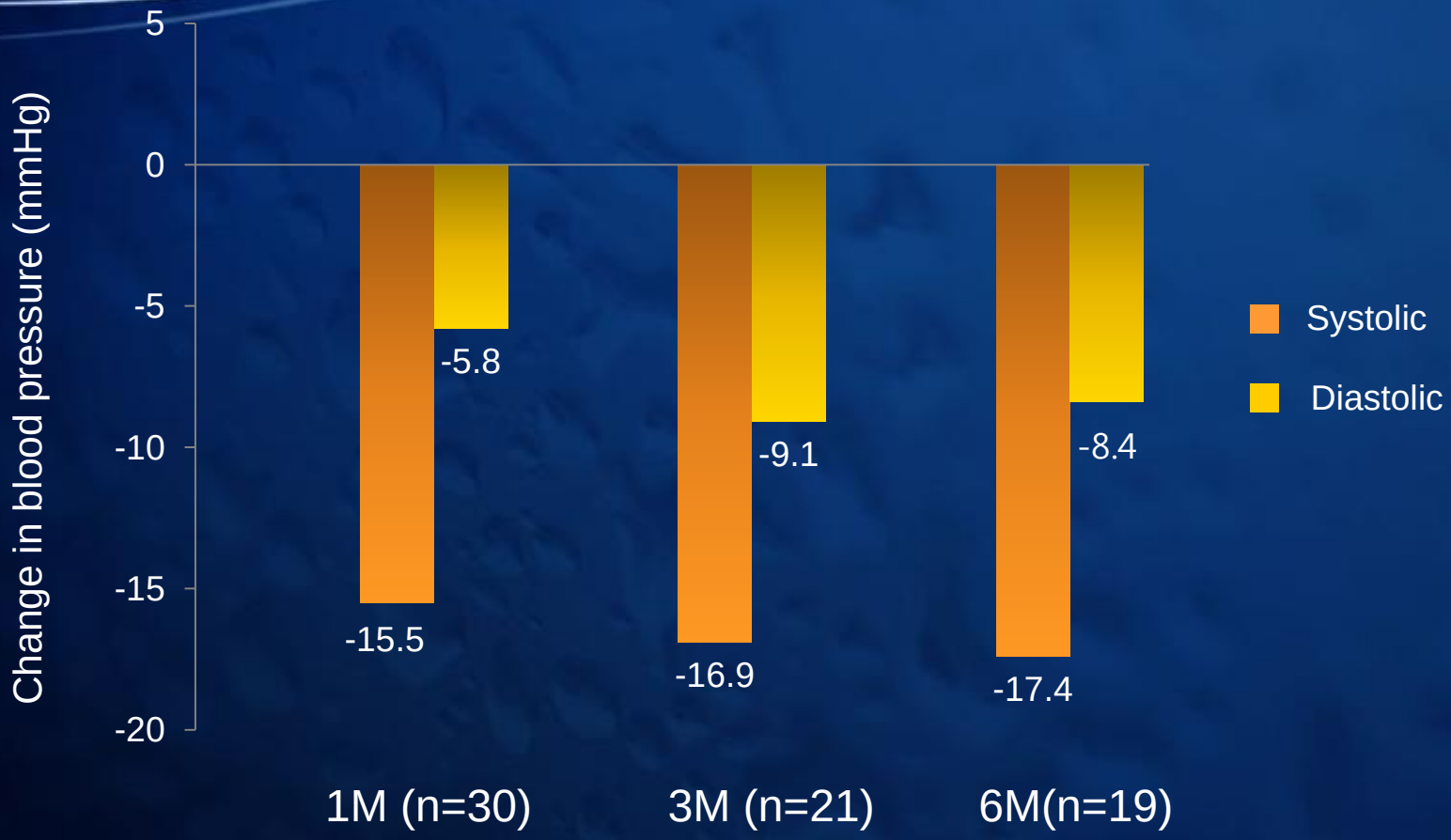
33/11 mm Hg difference between Symplicity renal denervation and control groups (P<0.0001 for SBP and DBP)

- 84% of patients in the renal denervation group had ≥10 mm Hg reduction in SBP
- 10% of patients in the renal denervation group had no reduction in SBP

SMC Result (n=35)

Demographics	Mean age ± SD (years)	52.6 ± 13
	Gender (% female)	20%
Comorbidities	diabetes mellitus (%)	25.7%
	Coronary artery disease (%)	19.2%
	Hyperlipidemia (%)	54.3%
	Mean eGFR ± SD (mL/min/1.73m^2)	78.1 ± 16.7%
BP	Mean baseline BP ± SD (mm Hg)	164/101 ± 19/19
	Mean number of antihypertensive medications ± SD	4.0 ± 1.3
	Diuretic (%)	77.1%
	ACE/ARB (%)	94.3%
	Beta-blocker (%)	74.3%
	Calcium channel blocker (%)	77.1%
	Spironolactone (%)	14.3%

SMC data (n=35)



1 Month Non-responder : 8/30(26.6%)
: defined as a SBP reduction of < 10mmHg

Summary

- Renal denervation is significantly reduce BP in patients with resistant hypertension
- The procedure was found to be simple and safe with minimal procedure-related adverse events
- Office BP reduced by 17.4/8.4 mmHg at 6 month follow up (In SMC)