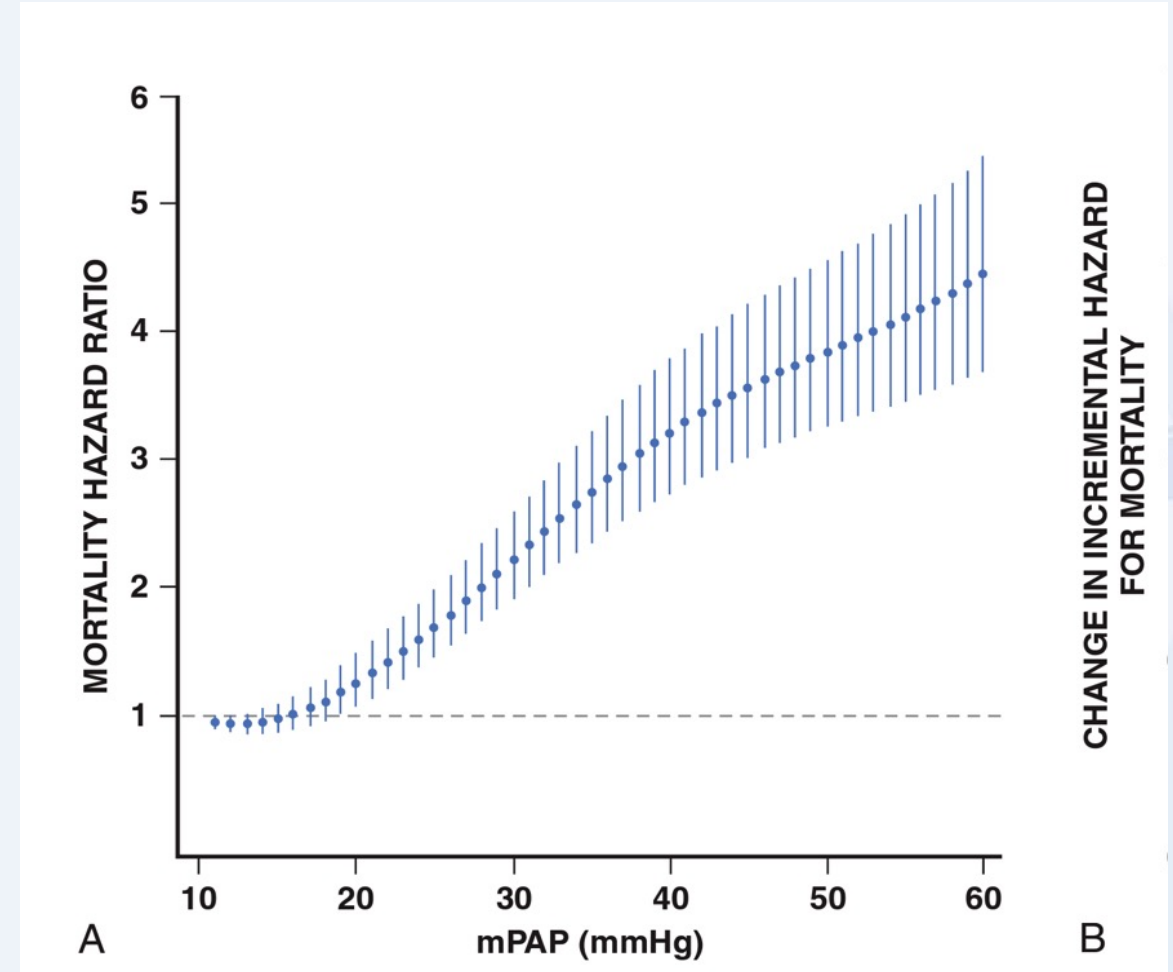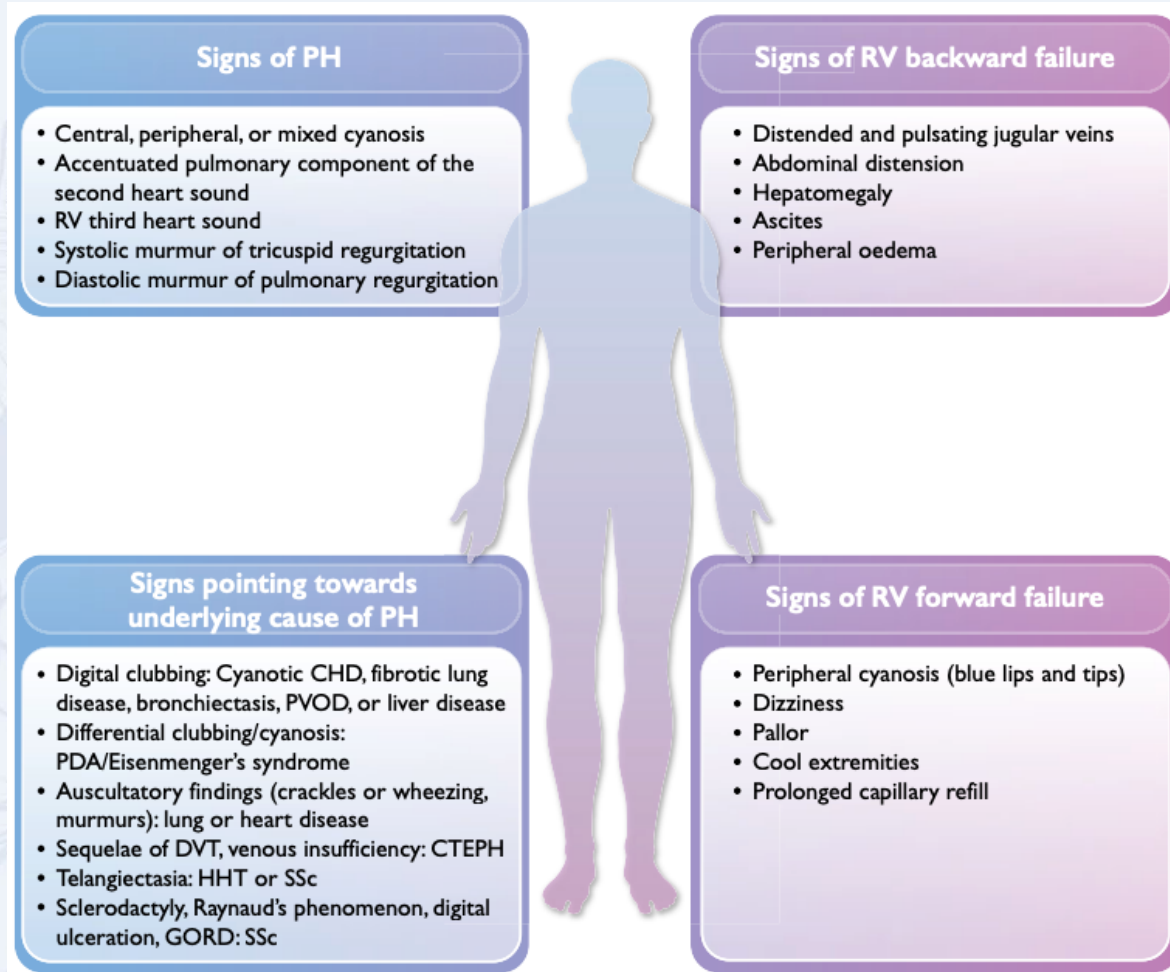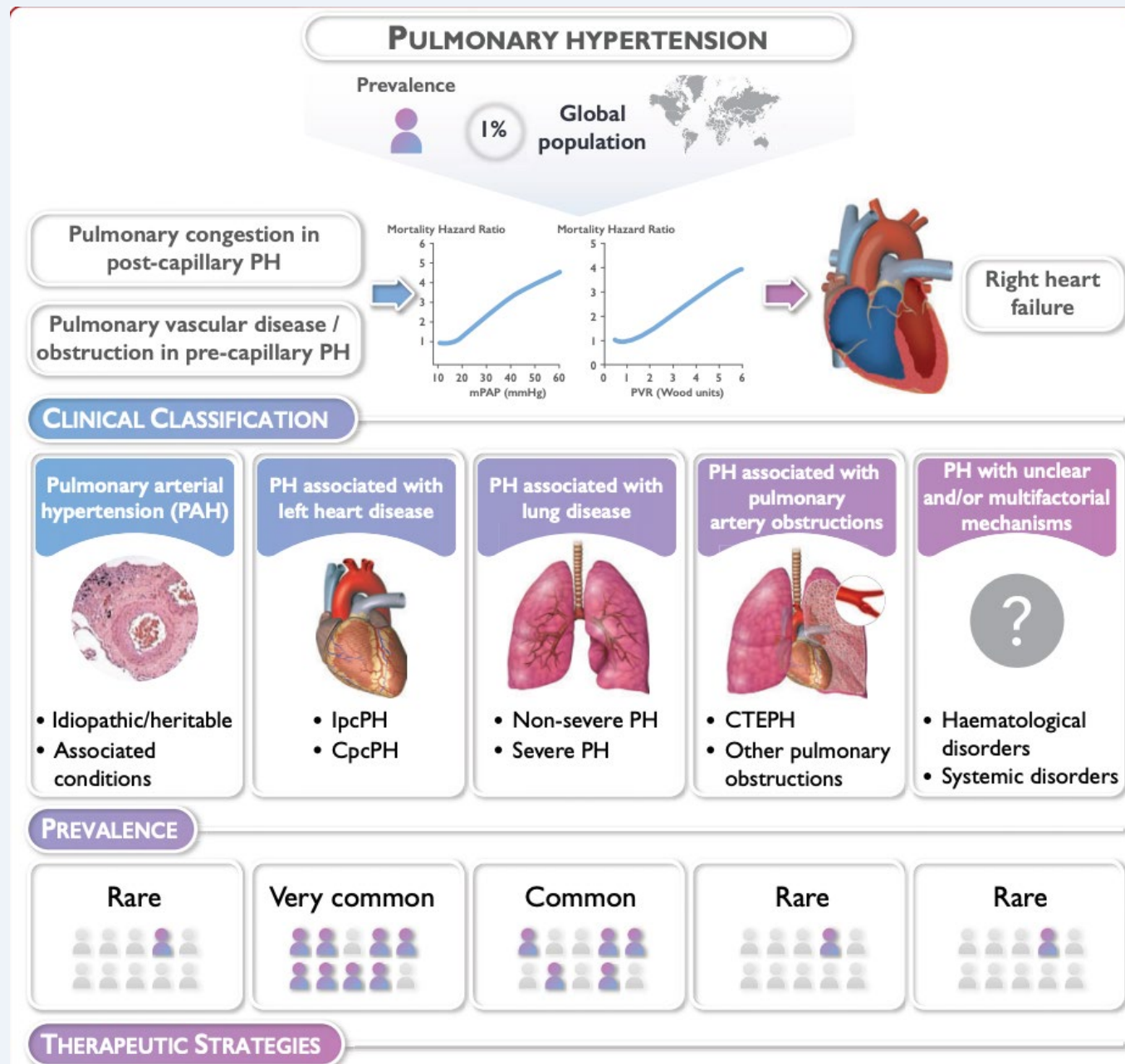# Radiofrequency Ablation of the Cardiac Plexus

ICD-10 Coordination and Maintenance Committee Update

March 2025

Signs of PH

- Central, peripheral, or mixed cyanosis
- Accentuated pulmonary component of the second heart sound
- RV third heart sound
- Systolic murmur of tricuspid regurgitation
- Diastolic murmur of pulmonary regurgitation

Signs of RV backward failure

- Distended and pulsating jugular veins
- Abdominal distension
- Hepatomegaly
- Ascites
- Peripheral oedema

Signs pointing towards underlying cause of PH

- Digital clubbing: Cyanotic CHD, fibrotic lung disease, bronchiectasis, PVOD, or liver disease
- Differential clubbing/cyanosis: PDA/Eisenmenger's syndrome
- Auscultatory findings (crackles or wheezing, murmurs): lung or heart disease
- Sequelae of DVT, venous insufficiency: CTEPH
- Telangiectasia: HHT or SSc
- Sclerodactyly, Raynaud's phenomenon, digital ulceration, GORD: SSc

Signs of RV forward failure

- Peripheral cyanosis (blue lips and tips)
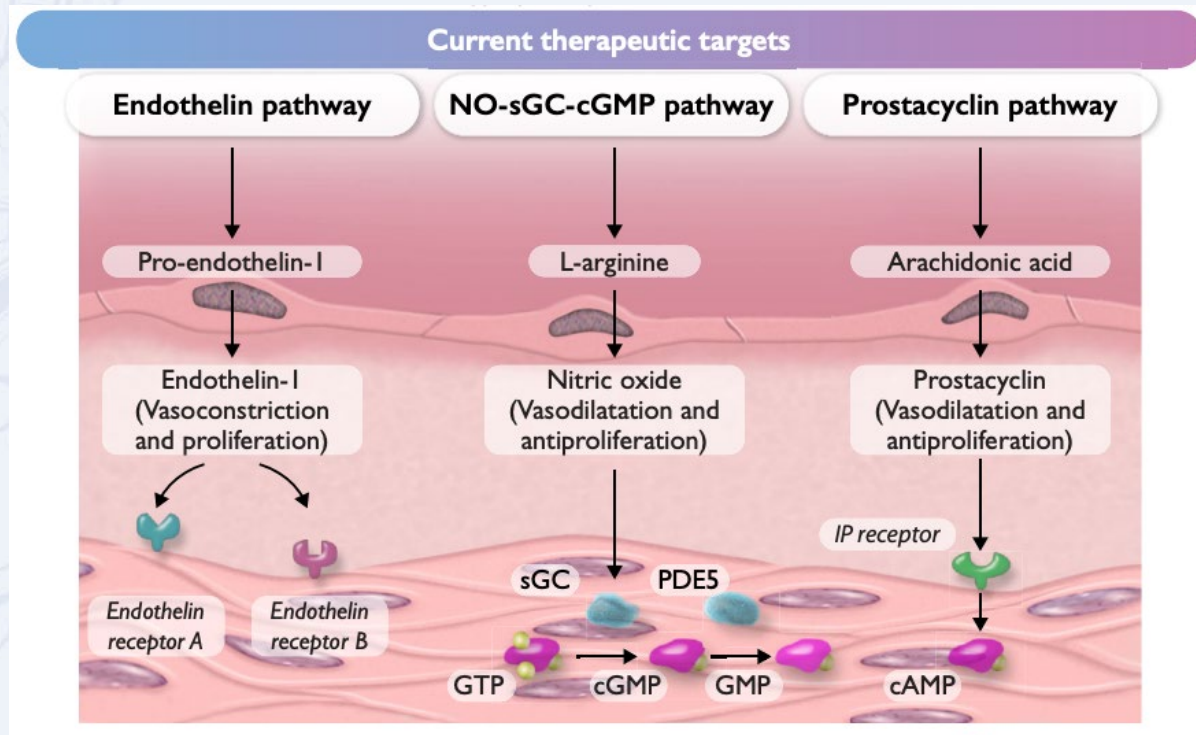- Dizziness
- Pallor
- Cool extremities
- Prolonged capillary refill

PULMONARY HYPERTENSION ETIOLOGY

PH – Group 1
(Pulmonary Arterial Hypertension)

Increased frequency diagnosed in aged > 65yr

Current therapeutic targets

- Difficult administration
- Multi-group often needed
- Limited efficacy
- Side effects
- Expensive

- European heart Journal 2022; 43:3618
- Pulm Circ 2021;11: 2045894020977300 3

PH – Group 2
(Left Heart Disease)
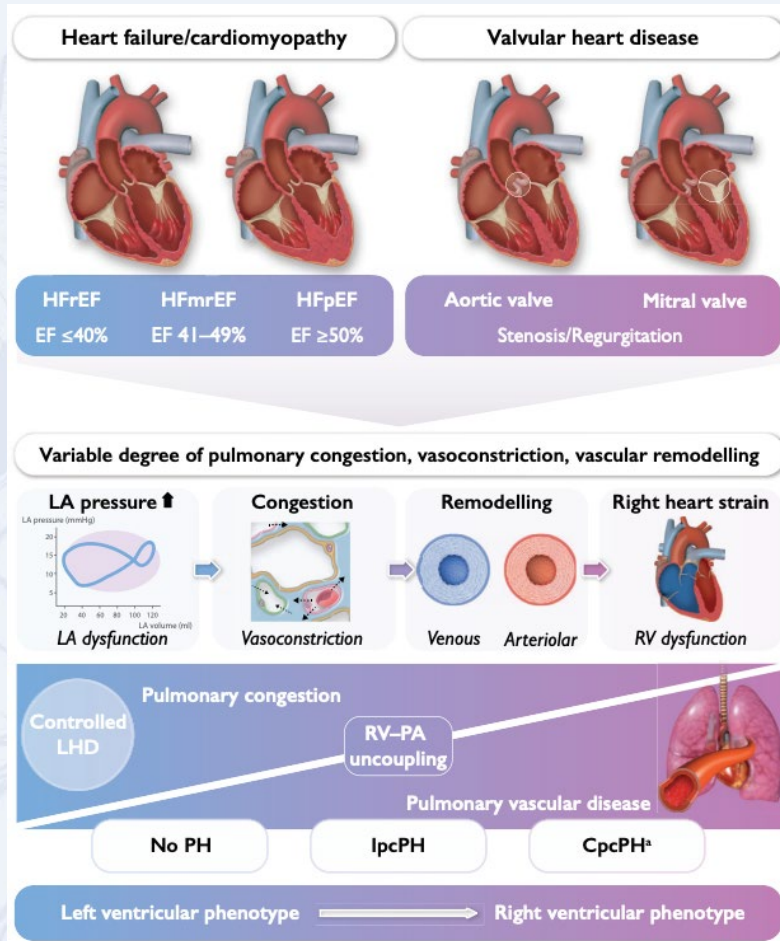
- 61.7 million patients with HF worldwide
- >80% are aged >65yr
- Incidence 20.5/100,000/year (US: 70,000/yr)
- Prevalence of PH increases with severity of left-heart disease

Recommendations	Class[a]	Level[b]
In patients with LHD, optimizing treatment of the underlying condition is recommended before considering assessment of suspected PH[27,28]	I	A
RHC is recommended for suspected PH in patients with LHD, if it aids management decisions	I	C
RHC is recommended in patients with severe tricuspid regurgitation with or without LHD prior to surgical or interventional valve repair	I	C
For patients with LHD and suspected PH with features of a severe pre-capillary component and/or markers of RV dysfunction, referral to a PH centre for a complete diagnostic work-up is recommended[29,47,142]	I	C
In patients with LHD and CpcPH with a severe pre-capillary component (e.g. PVR >5 WU), an individualized approach to treatment is recommended	I	C
When patients with PH and multiple risk factors for LHD, who have a normal PAWP at rest but an abnormal response to exercise or fluid challenge, are treated with PAH drugs, close monitoring is recommended	I	C
In patients with PH at RHC, a borderline PAWP (13–15 mmHg) and features of HFpEF, additional testing with exercise or fluid challenge may be considered to uncover post-capillary PH[133,143]	IIb	C
Drugs approved for PAH are not recommended in PH-LHD[c][631,678,683,684,701,706]	III	A

- European heart Journal 2022; 43:3618
- Lancet 2015;386:743–800
- J Am Coll Cardiol 2009;53:1119–1126
- Circ Cardiovasc Qual Outcome 2018;11:e003973

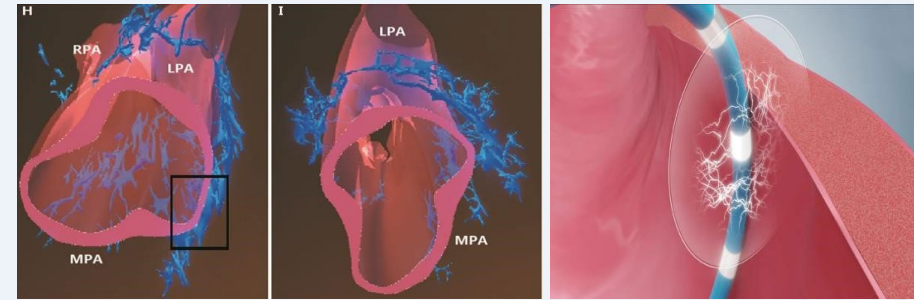# Pulmonary Artery DeNervation (PADN)
TECHNOLOGY OVERVIEW

PHD 360 Multi-pole Pulmonary Artery RF Ablation Generator (PHD 360 RF Generator)

Enhancor™ Multi-pole Pulmonary Artery RF Ablation Catheter (Enhancor™ RF Catheter)

Mechanism Of Actions

PADN A novel therapy to inhibit sympathetic nerve overactivation

| Radiofrequency energy to the sympathetic nerves located in the adventitia of the pulmonary artery | disappearance of the myelin sheath and the fusion of axons | **Inhibiting sympathetic nerve activity** | Increasing cardiac output, reducing pulmonary artery, improving patient exercise tolerance |

1. Vaillancourt M, Chia P, Sarji S, et al. Respir Res. 2017;18(1):201.
2. Ogo T. Arterioscler Thromb Vasc Biol. 2019;39(6):979-981.

IDENTIFICATION of PADN TARGET SITE

Pulmonary artery innervation is predominantly **sympathetic**, with fibers concentrated in the **adventitia** and at the **adventitia-media junction**. Near the **pulmonary hilum**, a **perivascular nerve network** branches extensively. The main sympathetic trunk lies in the **left nerve groove of the main pulmonary artery**, branching into left and right nerves at the **bifurcation**. In humans, proximal pulmonary artery nerves produce **catecholamines** and **neuropeptide Y**, confirming their sympathetic origin.
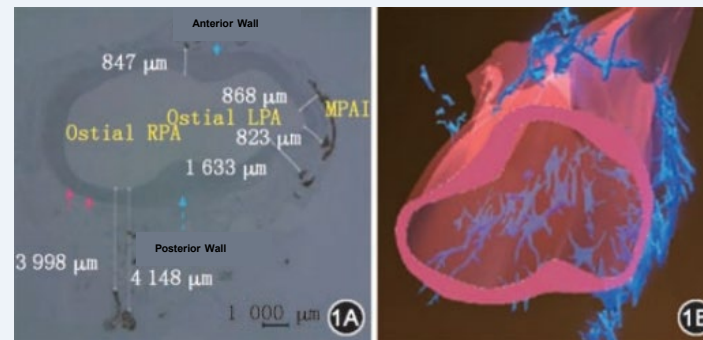
1. Chinese expert advisory on percutaneous pulmonary artery denervation for the treatment of pulmonary hypertension
2. Verity MA, Bevan JA. Fine structural study of the terminal effecror plexus, neuromuscular and intermuscular relationships in the pulmonary artery[J]. J Anat, 1968, 103(Pt 1):49-63.
3. Haberberger R, Schemann M, Sann H, et al. Innervation pattern of guinea pig pulmonary vasculature depends on vascular diameter[J]. J Appl Physiol (1985), 1997, 82(2):426-434. DOI: 10.1152/jappl.1997.82.2.426.
4. Martling CR, Matran R, Alving K, et al. Innervation of lower airways and neuropeptide effects on bronchial and vascular tone in the pig[J]. Cell Tissue Res, 1990, 260(2):223-233. DOI: 10.1007/BF00318626.2. Haberberger R, Schemann M, Sann H, et al. Innervation pattern of guinea pig pulmonary vasculature depends on vascular diameter[J]. J Appl Physiol (1985), 1997, 82(2):426-434. DOI: 10.1152/jappl.1997.82.2.426.
5. Allen KM, Wharton J, Polak JM, et al. A study of nerves containing peptides in the pulmonary vasculature of healthy infants and children and of those with pulmonary hypertension[J]. Br Heart J, 1989, 62(5): 353-360. DOI: 10.1136/hrt.62.5.353.
6. Hung KS, Hertweck MS, Hardy JD, et al. Innervation of pulmonary alveoli of the mouse lung: an electron microscopic study[J]. Am J Anat, 1972, 135(4): 477-495.DOI: 10.1002/aja.1001350404.

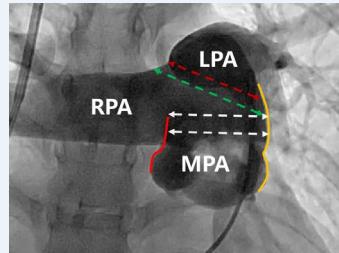# PADN: PROCEDURE STEPS

Preparation

Diagnosis and Consent

- **Echocardiography**
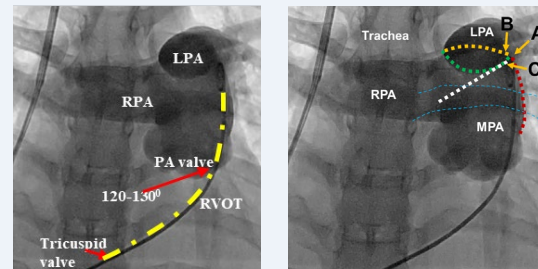- **RHC**
- **Pulmonary Angiogram**

Vascular Access

- **Right Femoral Vein**
- **Inferior Vena**
- **Right Atrium**
- **Right Ventricle**
- **Main Pulmonary Artery**

Operating Procedure

① Pulmonary Arteriography and diameter of PA measurement

② Establish Catheter Delivery Pathway and select ablation targets

- **Red line** indicates the **lateral** wall of the MPA
- **Green line** and **Yellow line** respectively indicate the **anterior** and **posterior** wall of the ostium of LPA
- *Point A* is defined as the intersection point of those lines
- *Point B* and *Point C* respectively locate on the **Yellow line** and **Green line** with 2 mm next to *Point A*
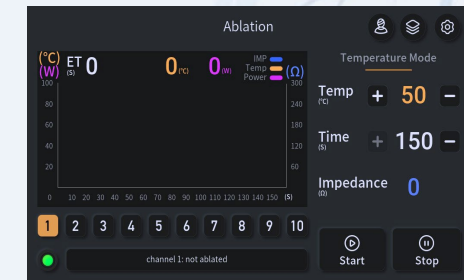- The White Line indicates the position of the RF segment

MPA: Main pulmonary artery; RPA: Right pulmonary artery; LPA: Left pulmonary artery

③ Positioning the RF ablation catheter to the right site

any three of the electrodes align with the target ablation points A, B, and C

④ Setup the RF generator and conduct 'point-to-point' ablation

ADDITIONAL CONSIDERATIONS for PADN

• The PADN procedure consists of the following : Percutaneous transcatheter thermal ablation of nerves innervating the pulmonary arteries, including right heart catheterization, pulmonary artery angiography, and all imaging guidance.

• One PADN device is commonly used per procedure. It is single use and disposable.

• The PADN procedure is performed on 3 sites of the pulmonary artery (PA) – the main trunk of the PA, along with the left and right PAs.

• PADN is performed either on an inpatient or outpatient basis depending upon the condition of the patient

http://www.pulnovomed.com

PUBLISHED CLINICAL EXPERIENCES

WHO group	Study design and follow up	Outcomes	PADN
WHO group 1: pulmonary artery hypertension (PAH)	RCT PADN + meds vs, sham + meds; 6 months (N=128)	No statistically significance in clinical worsening 1.5% PADN vs. 13.8% sham (HR = 0.11)	BETTER
WHO group 1: pulmonary artery hypertension (PAH)	RCT PADN+meds vs, sham+meds; 12 months; (N=128)	Clinical worsening 4.8% PADN vs. 23.1% sham (P=0.006)	BETTER
WHO group 1 pulmonary artery hypertension (PAH)	RCT PADN+meds vs, sham+meds; median 4.8 year; N=120)	PADN resulted in significant improvements in function (6MWD) at long-term follow-up vs. sham in FC 3-4 (P=0.037)	BETTER
WHO group 2: PH + LHD	RCT PADN+meds vs. sham+meds; 6 mths (N=98)	Clinical worsening 16.7% PADN vs..40% sham (P=0.014)	BETTER
WHO group 2: PH + LHD	RCT PADN+meds vs. sham+meds; 12 mths (N=98)	Clinical worsening 37.5% PADN vs..62% sham (P=0.011)	BETTER
WHO group 4: PH + CTEP	RCT PADN+meds vs. sham+meds; 12 mths (N=50)	6-min walk test distance significantly increased in the PADN group vs. sham (P=0.03)	BETTER

Clinical worsening defined as worsening PAH or atrial septostomy or listing for lung transplantation or all-cause death. PH – pulmonary hypertension; LHF – left heart failure; PADN – pulmonary artery denervation; 6MWD – 6 minute walk distance; FC – functional class; HR – hazard ratio

CONDITIONS COMMON TO PH PATIENT GROUP

- Heart diseases (heart failure, heart attacks, congenital heart disease, ventricular fibrillation)

- Lung diseases (infections, pulmonary embolism)

- Liver diseases (cirrhosis)

- Metabolic diseases (diabetes mellitus)

- Infectious diseases (parasitic worms, immunodeficiency diseases, hepatitis)

- Kidney diseases (nephritis, nephrotic syndrome, acute and chronic renal insufficiency)

PULMONARY HYPERTENSION (PH)
Unmet Clinical Need

- PH results in increased morbidity and mortality

- Increasing incidence and prevalence of left-heart-disease and severity resulting in PH

- Limited pharmacological therapy for Group 1 PAH

- No pharmacological therapy for Group 2 PH

- The sympathetic pulmonary artery hyperactivity has not been addressed yet

PULMONARY HYPERTENSION
Unmet Need for PADN

- Breakthrough Device Designation granted by FDA for PADN Group 1, 2 and 4 PH
- 2022 ESC/ERS Guidelines for diagnosis treatment of PH mention PADN
- Group 1 PAH: Humanitarian Use Device (HUD) granted by FDA
- Group 2: Submit IDE 2025Q1 anticipated study initiation in 2025Q4
- NTAP application planned for FY 2027 submission
- Performed in the hospital inpatient and outpatient settings.

The above supports the need for distinct identification of the PADN procedure, by a unique ICD-10 PCS code

- PA – pulmonary artery
- PH – pulmonary hypertension
- PAH – pulmonary arterial hypertension
- RF ablation – radiofrequency (thermal) ablation
- PADN – pulmonary artery denervation

Documentation of the PADN procedure is found in the operative report.

Reported complications from end of procedure to 6 month follow up from published randomized controlled clinical trials (PADN treatment vs. sham procedure)

Study	WHO group	Number enrolled	Clinical worsening (N)	Rehospitalization (N)	Worsening HF (N)	All cause death (N)
JACC CVI 2019	2 (PH w/LHF)	98	Treatment (8); Sham (20); P=0.014	Treatment (6); Sham (14); P=0.052	Treatment (7); Sham (18); P=0.016	Treatment (2); Sham (5); P=0.436
JACC CVI 2022	1 (PAH)	128	Treatment (1); Sham (9) HR = 0.11; 95% CI (0.01-0.87)	Treatment (0); Sham (5)	N/A	Treatment (0); Sham (0).

Clinical worsening was defined as any occurrence of the following: 1) worsening of symptoms defined as either failure to improve (persistent symptoms and signs of acute HF during treatment) or recurrent symptoms and signs of acute HF, pulmonary edema, or cardiogenic shock after initial stabilization since randomization, either of which requiring increased use of diuretics (as outpatient or inpatient), addition of a new intravenous therapy (diuretics, inotrope, or vasodilator) or mechanical support; 2) rehospitalization due to worsening HF requiring intravenous pharmacological agents (inotrope or vasodilator), mechanical ventilation, mechanical support or ultrafiltration, hemofiltration, or dialysis; 3) referral for heart/lung transplantation (rapidly progressive disease despite maximal medical therapy); and 4) all-cause death.