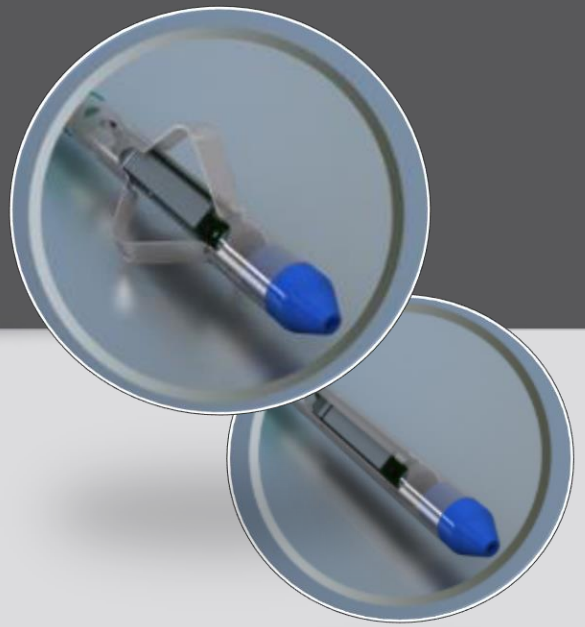
Company Presentation



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Technology to Treat Pulmonary Hypertension

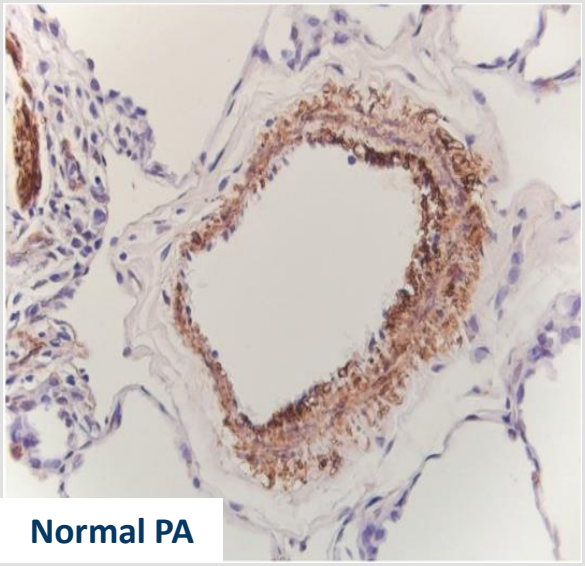
SoniVie

- Established: Q4/2014
- 10 Employees
- In clinical stage

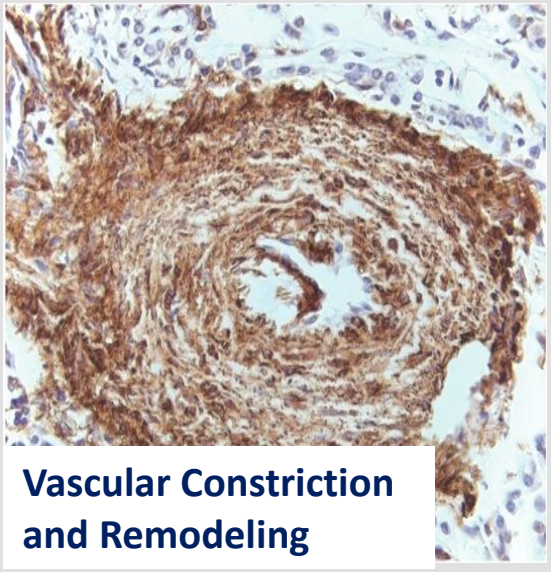
- Experienced management and top-notch SAB
- ISO13485 certified

Pulmonary Hypertension

A progressive disorder characterized by high blood pressure (hypertension) in the arteries of the lungs (mPAP) ≥25 mmHg)



Normal PA



Vascular Constriction and Remodeling

PH is divided into 5 main groups according to similar clinical presentation, pathological findings, haemodynamic characteristics and treatment strategy. Sub populations of all groups (Ex. Group 4) present similar histopathological manifestation of pulmonary arteries remodeling.

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Pulmonary Hypertension – Groups

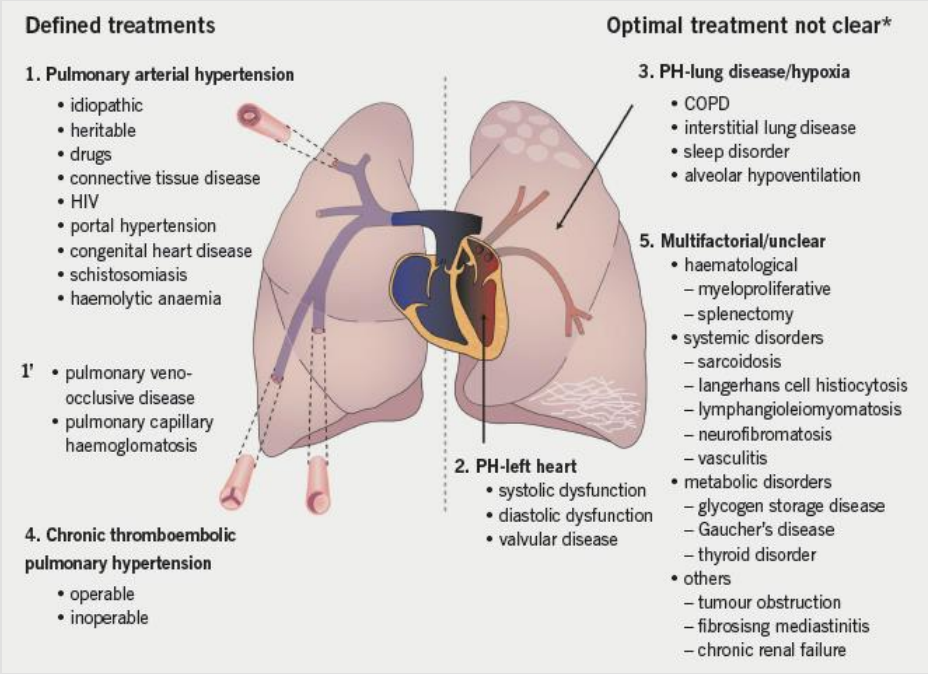
Group 1 (PAH) - (PCWP) ≤15 mmHg) Pulmonary Arterial Hypertension in the absence of other causes of PH

Group 2 (LHD) – (PCWP >15 mmHg) PH due to Left Heart Disease (LHD). The left heart dysfunction creates a backward hydrostatic pulmonary venous pressure ("Passive" PH stage). The disease may progress to an increase in the Pulmonary Vascular Resistance (PVR) and elevation of pre-capillary pressure, ("Mixed" PH stage).

Group 3 (COPD) - (PCWP ≤15 mmHg) PH due to lung disease. The PA reacts to long term hypoxia and inflammatory processes with remodeling of the PA vasculature that results in increased PVR and elevated pressure.

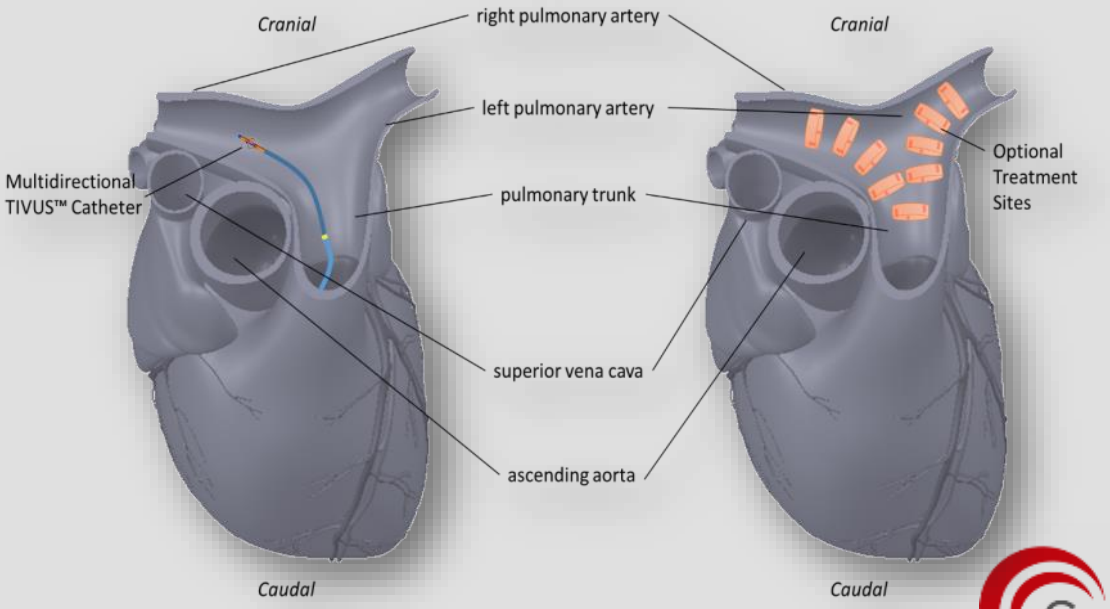
Group 4 (CTEPH) - (PCWP ≤15 mmHg) PH due to thromboembolic occlusion of the proximal or distal pulmonary vasculature.

Group 5 - (PCWP ≤15 mmHg) — Pulmonary hypertension with unclear multifactorial mechanisms.



Pulmonary Arterial Denervation (PDN) Rationale

- Muscle sympathetic nerve activity (MSNA)[2] and circulating Catacholamines[1] are increased in patients with PAH
- Pre-clinical studies show early promise[3,4]
- Recent pilot clinical study (using RF technology) provides substantial POC[5,6]



1 - Nootens M., et al. J Am Coll Cardiol. 1995;26:1581–1585.
2 - Velez-Roa S., et al. Circulation. 2004;110:13081312.
3 - Rothman et at,. Circ Cardiovasc Interv. 2015
4 - Chen S-L., et al. EuroIntervention. 2013;9:269–276.
5 - Chen S-L., et al. J Am Coll Cardiol. 2013;62:1092–1100.
6 – Chen, S-L., et al. Circ Cardiovasc Interv. 2015; 8.

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Pulmonary Artery Denervation to Treat Pulmonary Arterial Hypertension

The Single-Center, Prospective, First-in-Man PADN-1 Study (First-in-Man Pulmonary Artery Denervation for Treatment of Pulmonary Artery Hypertension)

Shao-Liang Chen, MD,*† Feng-Fu Zhang, MD,* Jing Xu, MD,* Du-Jiang Xie, MD,* Ling Zhou, MD,* Thach Nguyen, MD,‡ Gregg W. Stone, MD§

Nanjing, China; Hobart, Indiana; and New York, New York

Objectives This study was designed to test the safety and efficacy of pulmonary artery (PA) denervation (PADN) for patients with idiopathic PA hypertension (IPAH) not responding optimally to medical therapy.

Background Baroreceptors and sympathetic nerve fibers are localized in or near the bifurcation area of the main PA. We previously demonstrated that PADN completely abolished the experimentally elevated PA pressure responses to occlusion of the left interlobar PA.

Methods Of a total of 21 patients with IPAH, 13 patients received the PADN procedure, and the other 8 patients who refused the PADN procedure were assigned to the control group. PADN was performed at the bifurcation of the main PA, and at the ostial right and left PA. Serial echocardiography, right heart catheterization, and a 6-min walk test (6MWT) were performed. The primary endpoints were the change of PA pressure (PAP), tricuspid excursion (Tei) index, and 6MWT at 3 months follow-up.

Results Compared with the control group, at 3 months follow-up, the patients who underwent the PADN procedure showed significant reduction of mean PAP (from 55 ± 5 mm Hg to 36 ± 5 mm Hg, $p < 0.01$), and significant improvement of the 6MWT (from 324 ± 21 m to 491 ± 38 m, $p < 0.006$) and of the Tei index (from 0.7 ± 0.04 to 0.50 ± 0.04, $p < 0.001$).

Conclusions We report for the first time the effect of PADN on functional capacity and hemodynamics in patients with IPAH not responding optimally to medical therapy. Further randomized study is required to confirm the efficacy of PADN. (First-in-Man Pulmonary Artery Denervation for Treatment of Pulmonary Artery Hypertension [PADN-1] study; chiCTR-ONC-12002085) (J Am Coll Cardiol 2013;62:1092–100) © 2013 by the American College of Cardiology Foundation

Pulmonary Hypertension – A True Clinical & Economic Unmet Need

SoniVie is initially targeting the following two groups of :

Group 1 (PAH)

Survival is less than **50%** at **5** years[1]; only definitive cure is transplantation

$30,000 - **$200,000** annual cost of medical treatment per patient

Group 2 (LHD) subgroup of "Mixed" disease that doesn't response to vasodilation treatment ("Fixed" stage)

No available treatment. Initial studies with PAH specific drugs demonstrate promising results

1 - Hurdman, J. et al., 2012. European Respiratory Journal, 39(4),945–955.

2 – Hoeper, M. et al., 2004. European Respiratory Journal, 24(6),1007–1010.

3 - Butler, J., D.B. et al . J Am Coll Cardiol, 1999. 34(6): p. 1802-6.

4 - Aronson, D., et al., Circ Heart Fail, 2011. 4(5): p. 644-50.

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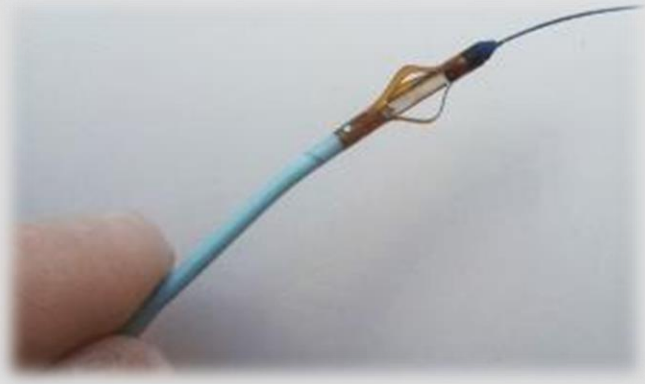
SoniVie Technology - TIVUS™ System

Non Focused Ultrasound for intra-vascular denervation



The system and the catheter obtained CE mark for renal denervation indication and was used in dozens of procedures.

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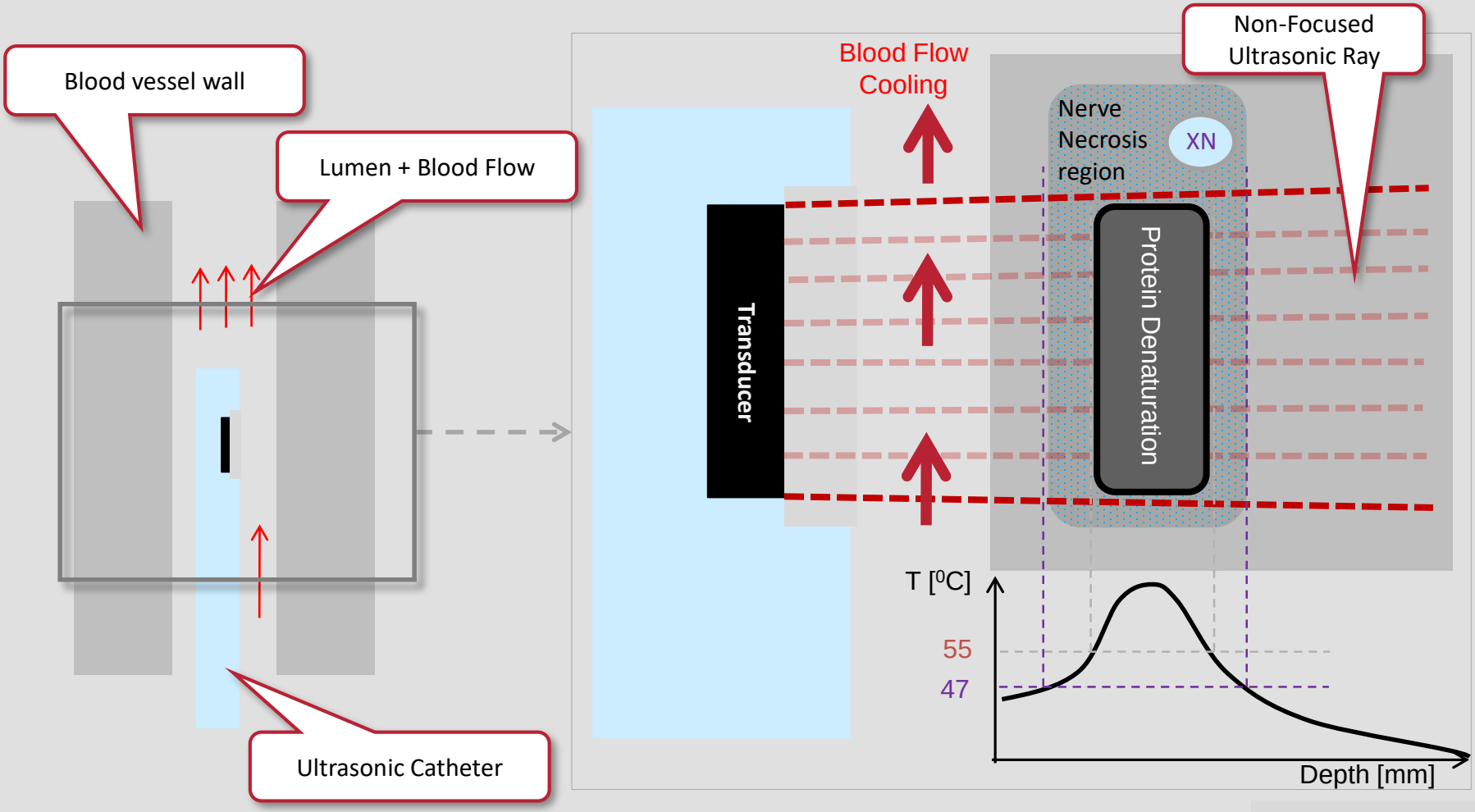
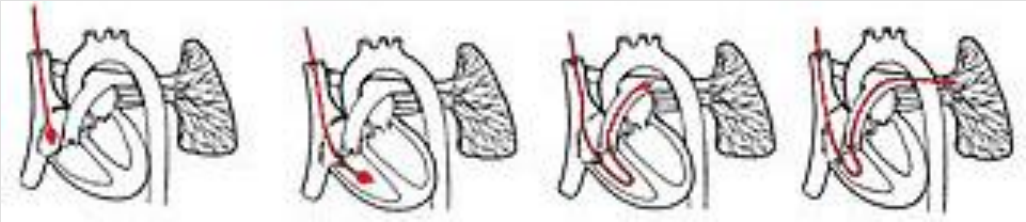
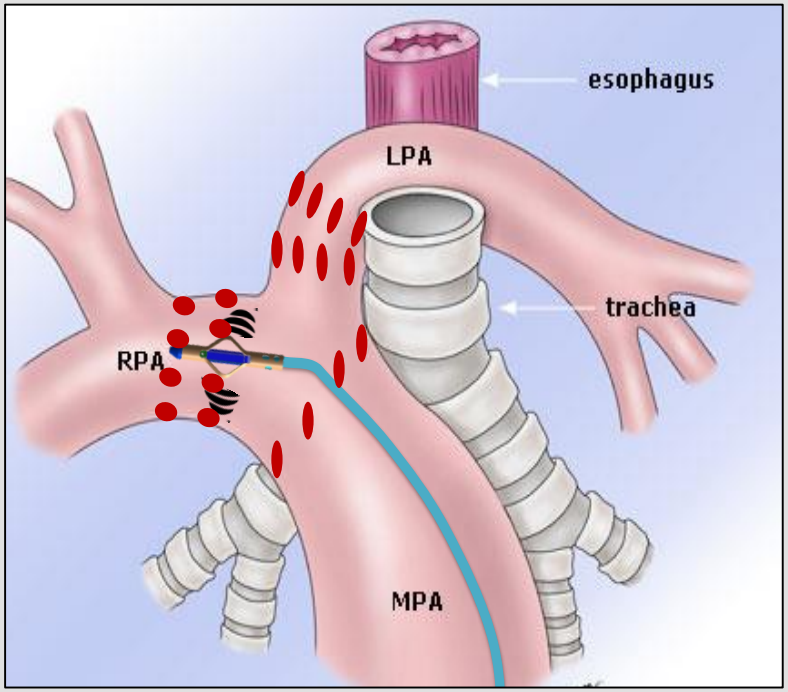
Core Technology: Non-Focused, High Intensity Ultrasonic Catheter



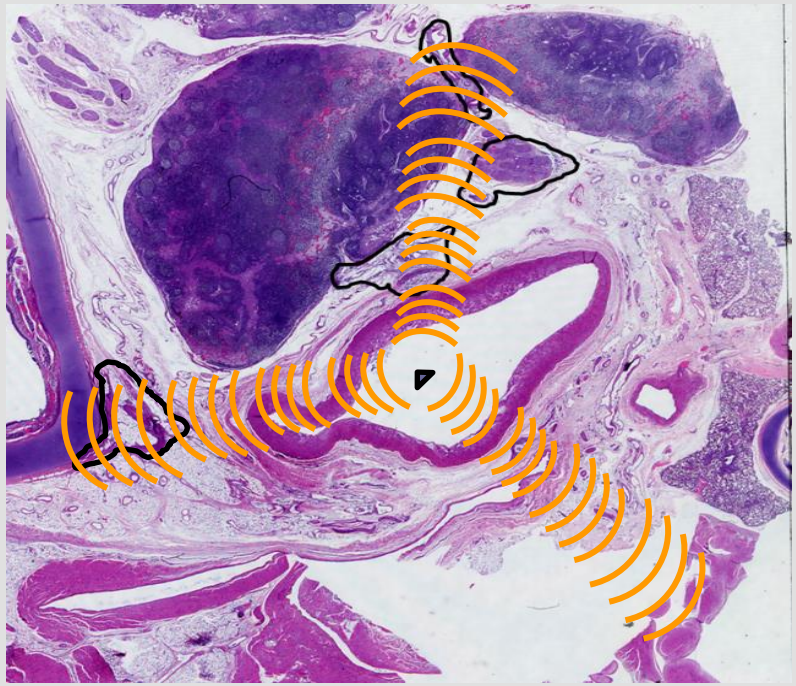
Tivus™ Procedure



Right Hear catheterization



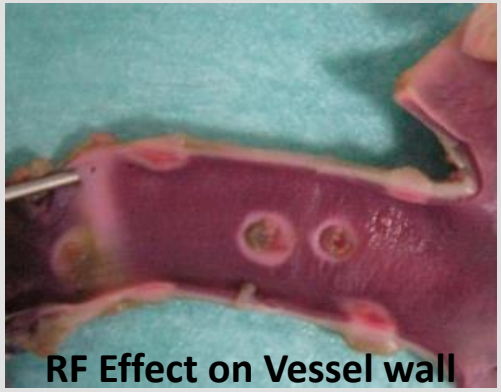
Denervation Sites

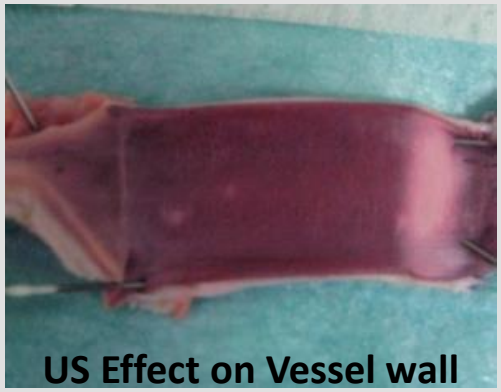


Partial Circumferential denervation effect

TIVUS™ Advantages

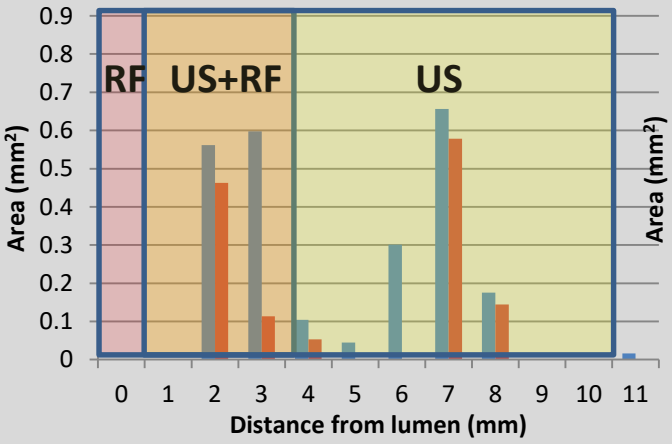
	TIVUS (Ultrasound)	RF
Energy effect on artery wall		
Energy Penetration		
Device Usability		
Patient Comfort		
Other		


RF Effect on Vessel wall

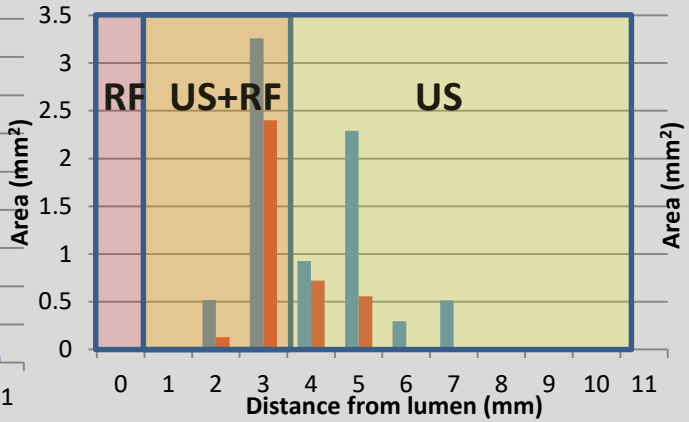

US Effect on Vessel wall

TIVUS™ Advantages

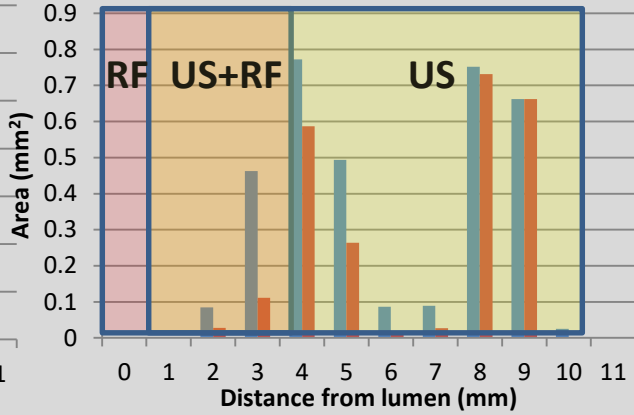
- The effective treatment range (RF and TIVUS) Considering the nerve distribution in PA of healthy human subject[1]
- PA in advanced PAH is thicker (media hypertrophy[2])



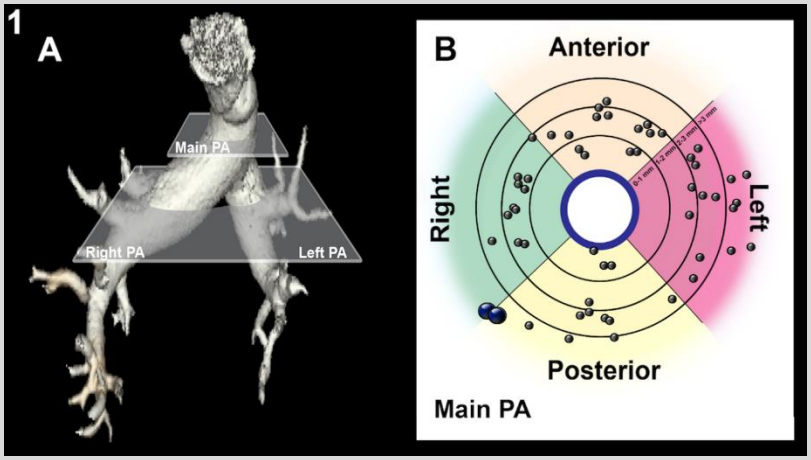
Left branch



Main trunk



Right branch



Total nerves area

Sympathetic nerves area

1 - Un published data, CBSET 2015

2 – Heath et al. J. Path. Bact., 1959

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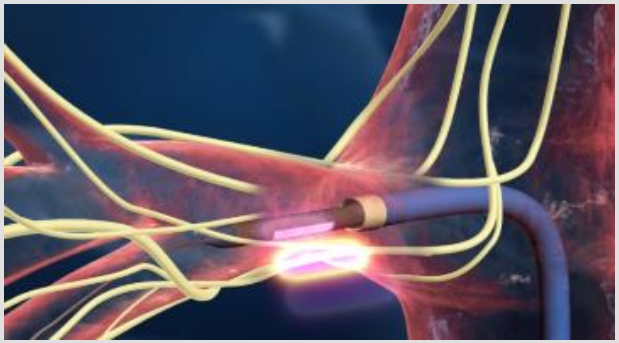
IP

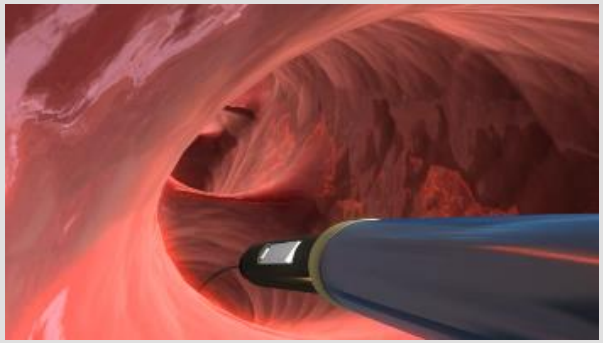
Licensed IP from Cardiosonic (Renal denervation)

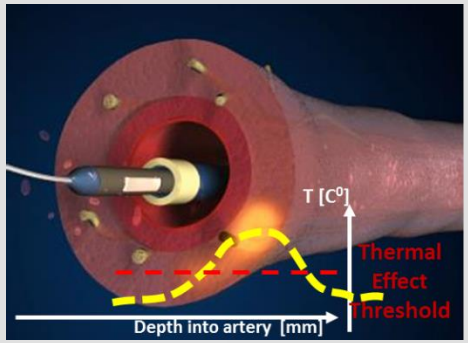
- Six families of patents, some are granted in US, EU, Japan and China

Vast Knowhow

- Design and manufacturing of intravascular ultrasound catheter and System







First in Human study - TROPHY I
EU &US

Study Objective

- To assess the safety, performance and initial effectiveness of the TIVUS™ System when used for pulmonary artery denervation in patients with PAH

Study Design

- Prospective, multicenter, non-randomized, open-label clinical design

Study Population

- Patients with idiopathic, connective tissue disease PAH, drug induced PAH or Heritable PAH, functional class III, with stable PAH on a stable drug regimen (2 PAH medications other than parenteral prostanoids)
  - Up to 15 subjects at up to 4 centers
  - Roll in Phase – First 3 enrolled patients

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TROPHY I - Study Main Endpoints

@ 1 month - Primary Outcome Measure - Safety

- Procedural related Adverse Events: PA dissection/perforation, acute thrombus formation, PA aneurysm, vascular stenosis, hemoptysis, death

@ 4 months - Secondary Effectiveness Measures

- Hemodynamic changes from baseline: mPAP, PVR, RAP, CI
- Change in exercise tolerance: 6MWD
- Change in quality of life: emPHasis quality of life questionnaires

@ 12 months - Secondary Safety Measures

- All adverse events and serious adverse events

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TROPHY I - Study status

- As of Sep 2016 - 5 patients
- One month F/U completed
- IDE approval received, local IRBs are in submission in 4 sites:

  US (San-Diego)

  Colum

  University

  UT

Company Team

Management

Experience team with track records

Assaf Bernstein – CEO

Dr. n – Medical director

Or – VP of R&D

Dr. hat – VP Clinical and Reg.

Scientific Advisory Board

Dr. Ori

Dr. Michael

Dr. Gregory

Dr. Alex

Dr. Lewis

Board of Directors

Chairperson: Dr. Iri

Dr. Ur, Mike n, Mo, Dr. Gi

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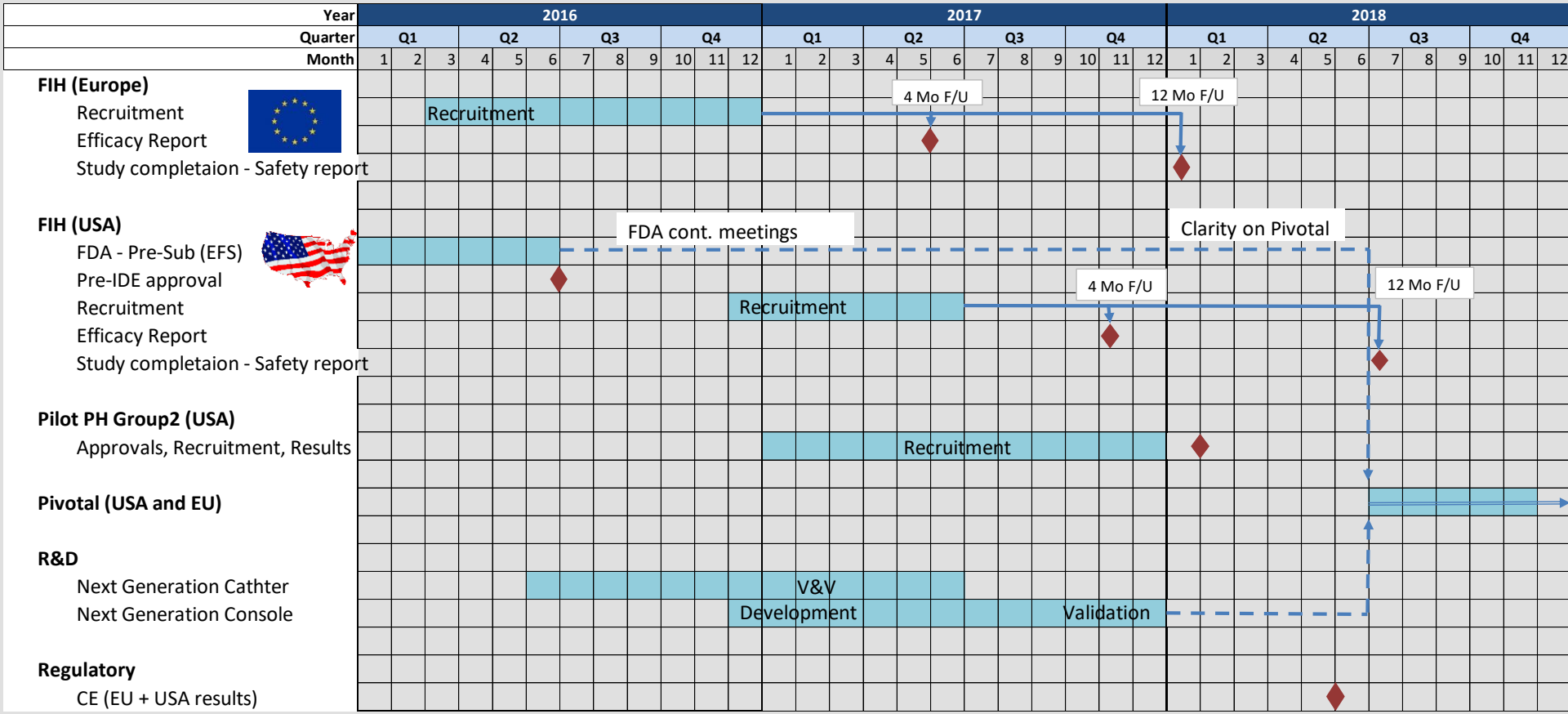
Road Map (2016-2018)



Thank You