

PFO Closure for Conditions Beyond Cryptogenic Stroke

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest, arrangement, or affiliation with the organization(s) listed below:

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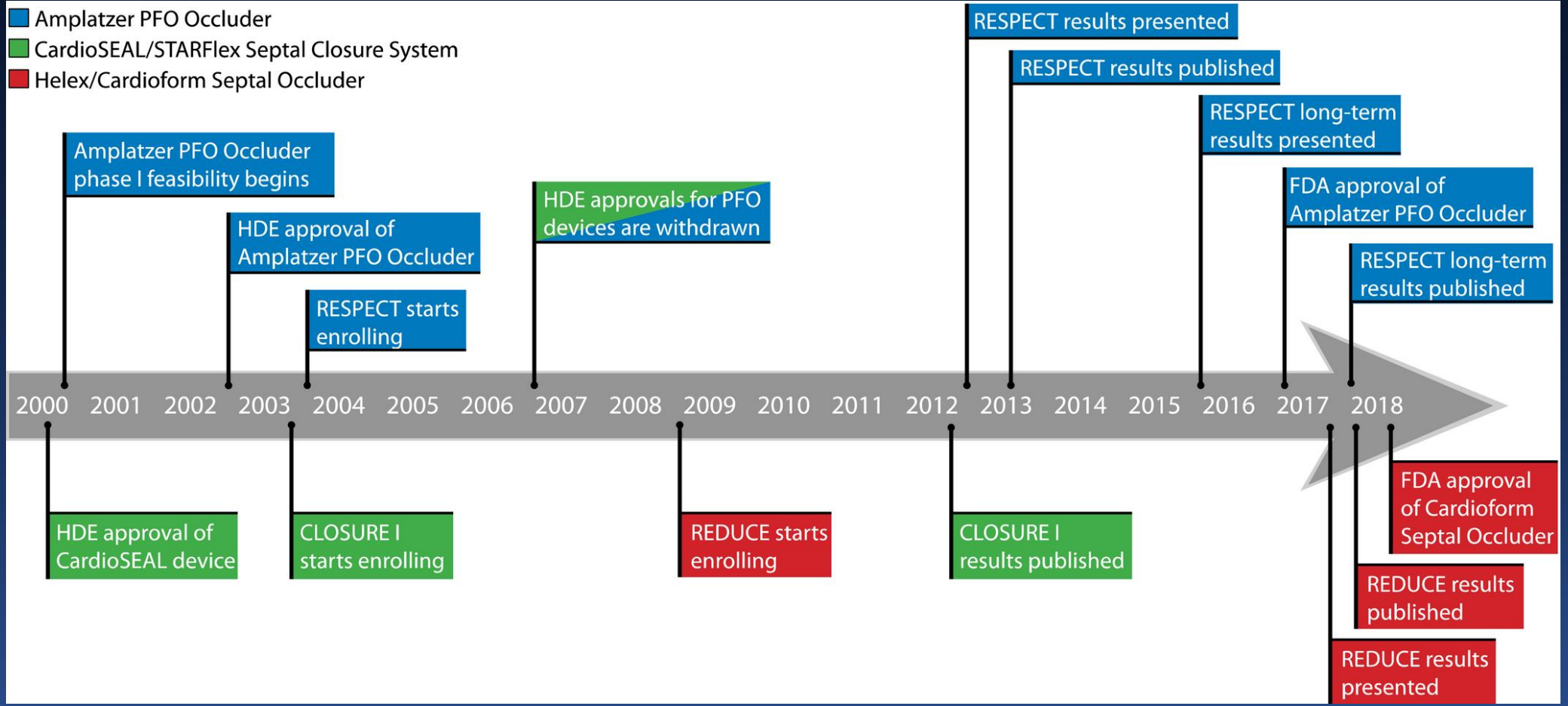
Company

Abbott, Edwards, Medtronic, W.L. Gore

Abbott, Medtronic, W.L. Gore

Purpose

- Explore other clinical manifestations of PFO with right to left intracardiac shunt
- Define anatomic and physiologic features that promote intracardiac right to left shunt
- Describe the current outcomes of treatment for non-stroke prevention indications
- Propose a “hole-istic” model of PFO pathology and treatment approach



Current Awareness of PFO as a Risk

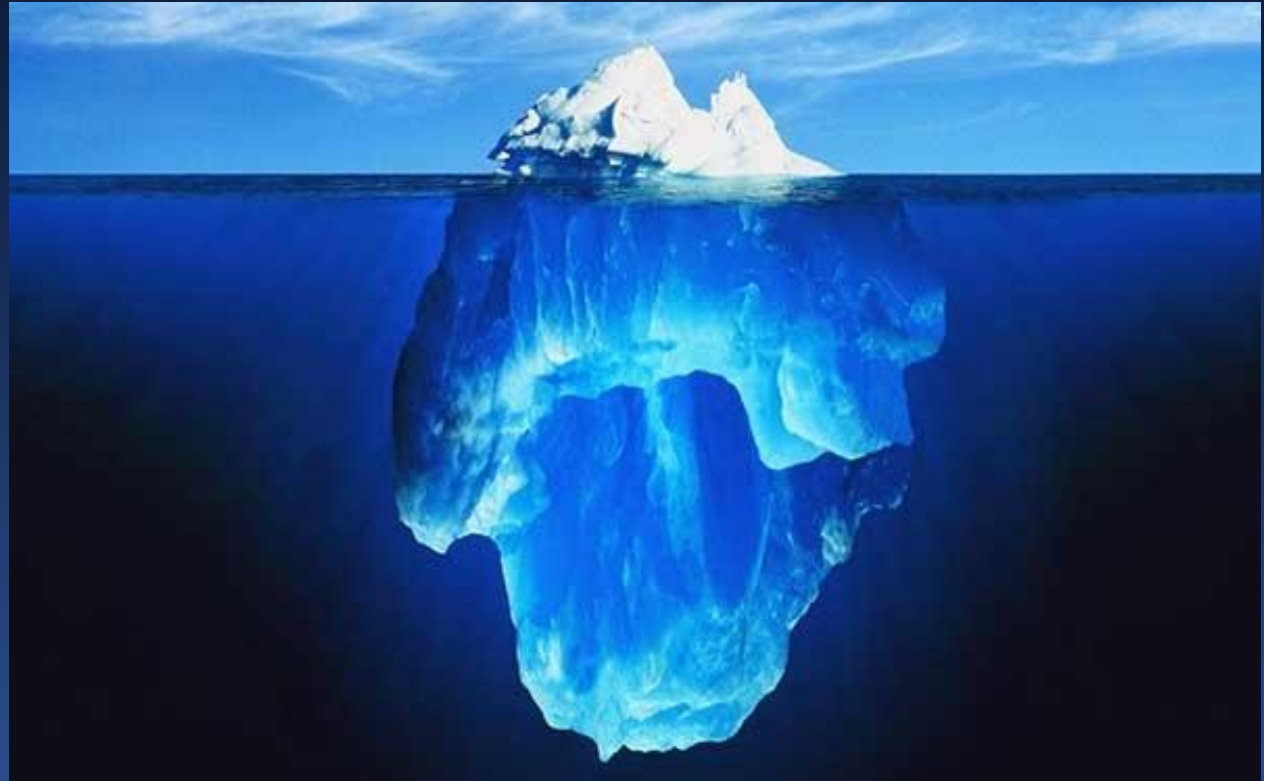
What we see: recurrent stroke prevention

What we don't see:

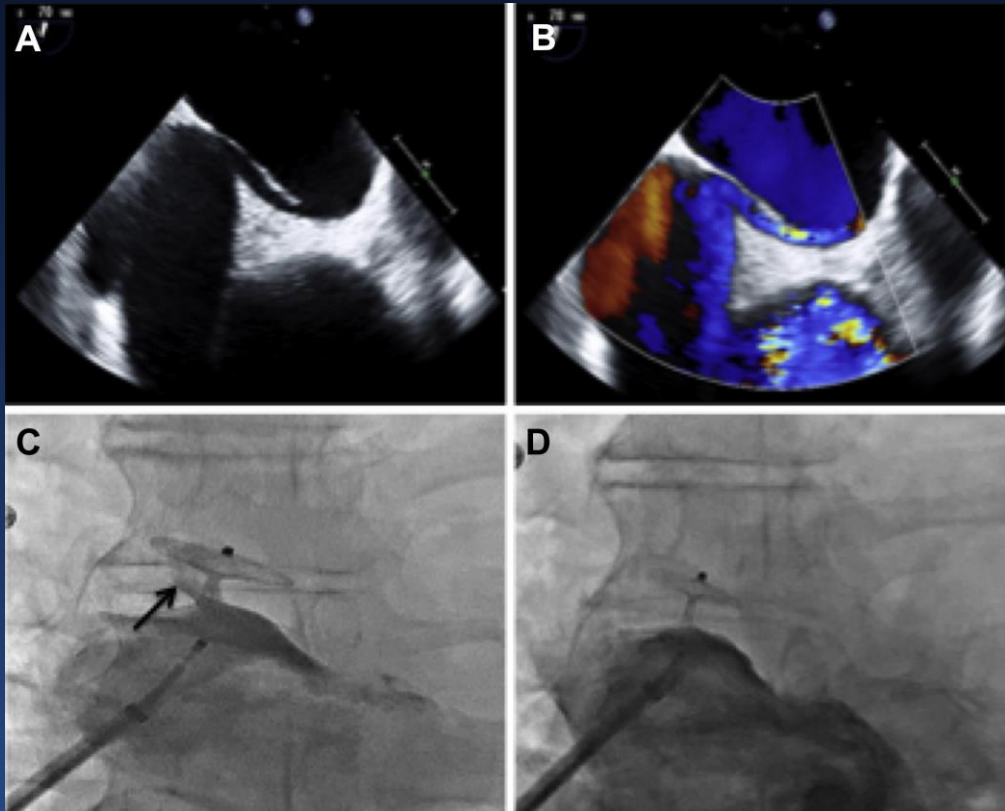
Migraine

Hypoxemia

Systemic emboli

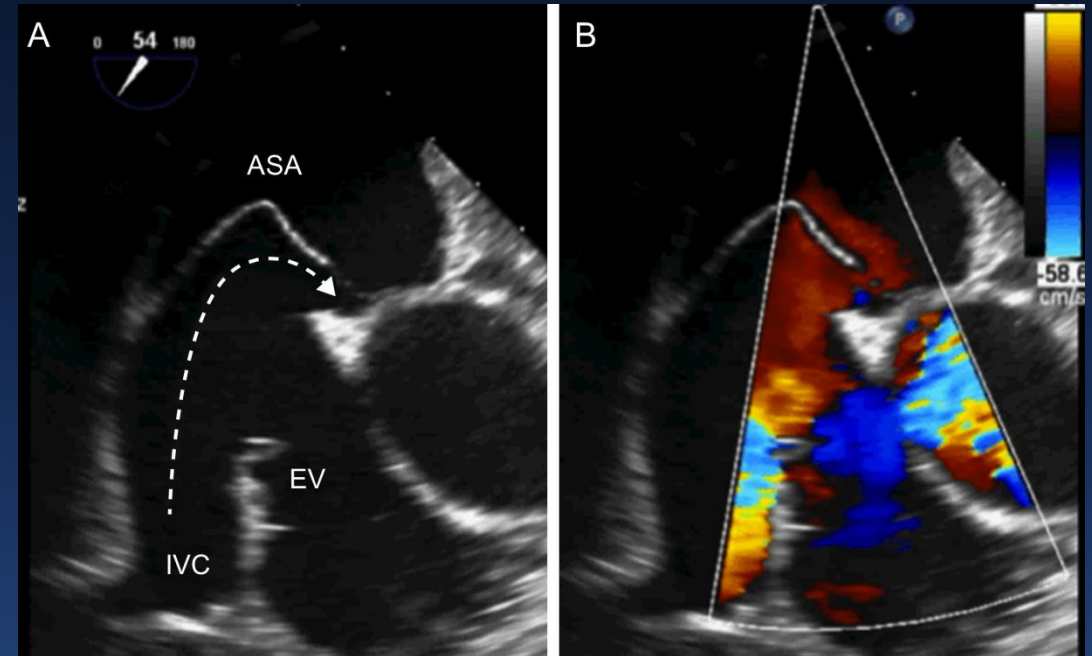


Anatomic Features Predispose R->L Shunt



IVC-Atrial Septal Angulation

Shah, Horlick, et al. JACC Cardiovasc Interv. 2016

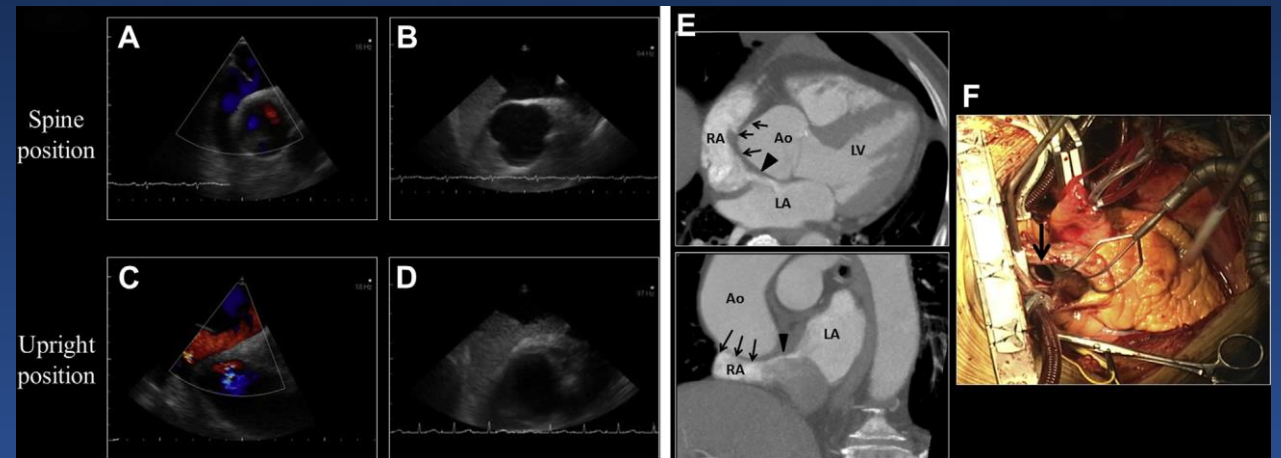


Prominent Eustachian Valve

Hernández-Enríquez, et al. Rev Esp Cardiol. 2014

Physiologic Features Predispose R->L Shunt

- Decline in RV compliance compared to LV
- Majority of atrial level shunting in diastole
- Factors leading to reduced RV compliance:
 - Reduced PA capacitance
 - RV hypertrophy/fibrosis
 - PHT
 - RVOT obstruction
 - RV scar
 - Tricuspid valve pathology



Yoshida S, MD et al. JACC 2013

PFO (with R->L shunt) and Migraine

- Numerous observational studies have established a link between migraine (especially with aura) and stroke*
- 712 patients with stroke**
 - 127 (18%) were “cryptogenic”
 - 68/127 had an adequate PFO evaluation
 - 59% of cryptogenic stroke had PFO
 - 79% of stroke + migraine had PFO
 - 93% of stroke + migraine with aura had PFO

*Wilmhurst P, et al. Am J Cardiol 2006

**West BH, et al. StrokeAHA 2018

PREMIUM Trial*

(Prospective, Randomized Investigation to Evaluate Incidence of Headache Reduction in Subjects with Migraine and PFO Using the AMPLATZER PFO Occluder to Medical Management)

- Double blind, sham controlled trial
- Subjects had 6-14 days of migraine/month, failed at least 3 preventative medications & PFO with significant R->L shunt
- Randomized to closure vs sham cath procedure
- Primary endpoint: 50% reduction in migraine attacks/month
- Secondary endpoints: reduction in migraine days and efficacy in patients with and without aura

*Tobis, JM, et al. JACC 2017

PREMIUM Trial

(Prospective, Randomized Investigation to Evaluate Incidence of Headache Reduction in Subjects with Migraine and PFO Using the AMPLATZER PFO Occluder to Medical Management)

- 7 year study!
- 1,653 subjects consented, 230 enrolled, 123 closed, 107 sham
- One device related AE: transient AF
- Primary endpoint not achieved
- Reduction in HA days was significant
- Complete remission of HA (aura): 10.8% closure, 1.5% of sham ($p = .02$)

	PFO Closure	Sham Procedure	p Value
% Responders	38%	32%	.3
Mean HA days/mo	2.0	3.4	.03

The Blind Leading the Blinded*

“There’s something happening here. What it is ain’t exactly clear.”**

- Refractory episodic migraine population was difficult to recruit
- Limited enrollment led an underpowered study
- HA days, not HA episodes more common endpoint in drug trials of less responsive populations
- Safety of PFO closure confirmed
- Not a failure of the PFO-migraine hypothesis but of the selected episodic medication refractory population in which it was studied

*Whisenant, B., Reisman, M. JACC 2017

**Steven Stills “For What It’s Worth” 1966

Platypnea-Orthodeoxia Syndrome (exertional hypoxemia syndrome)

- Frequently described as rare or uncommon
- It is neither
- The closer you look at the 'PFO + symptoms' population, the more you find evidence of exertional breathlessness and exercise intolerance
- Provocative exercise testing with pulse oximetry
- At risk populations: PFO plus: aortic dilation, COPD, OSA, pneumonectomy, LVAD, RV infarct, CHD

PFO closure for POS

The Toronto Experience*

- Used strict definition of postural desaturation
- 52 patients/18 years
- Systemic sats: 81 -> 95%
- Standard approach to obtain PV sats to exclude intrapulmonary shunt
- 25% had septal aneurysms/large defects, ASD occluders
- Shorter primum septum overlap and greater septal angulation with midline

*Shah AH, Horlick E, et al. JACC Cardio Interv 2016

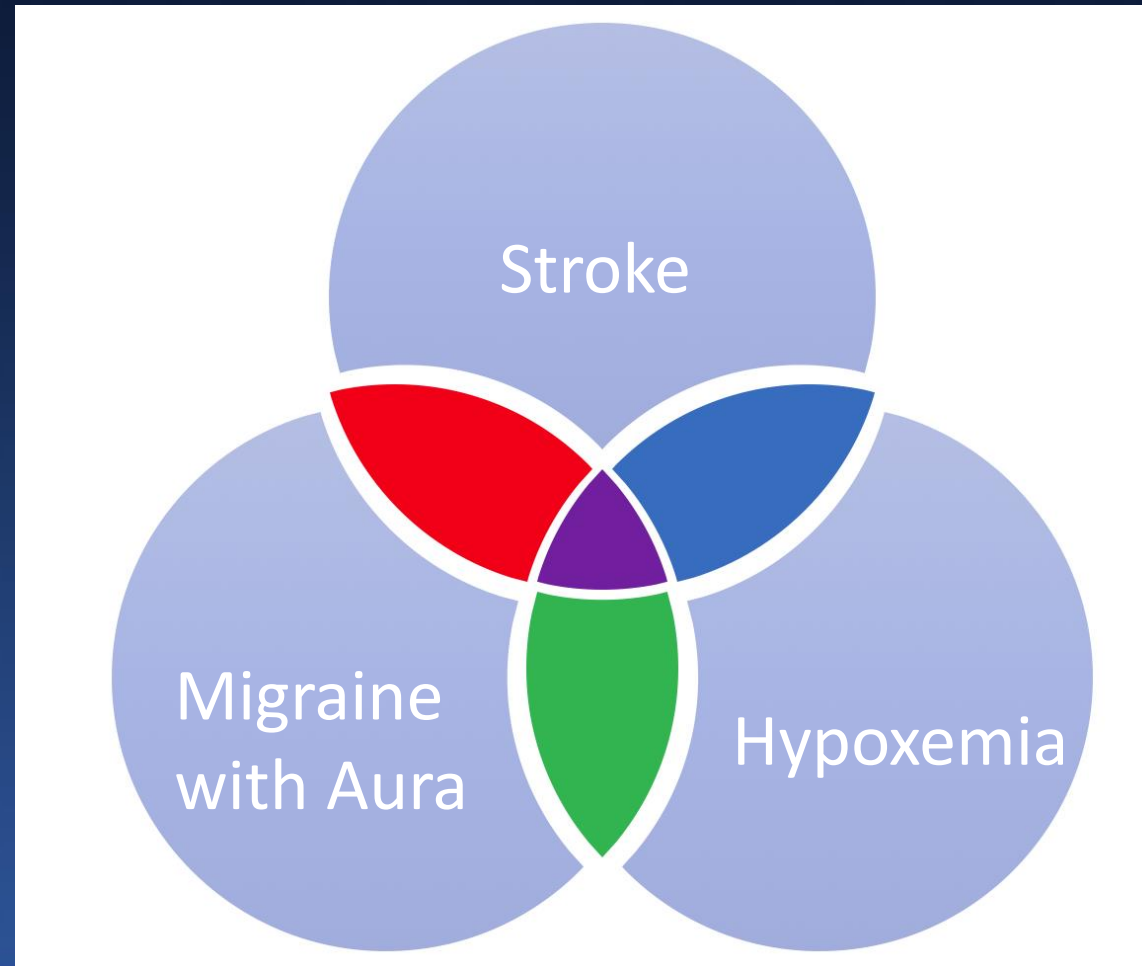
Predictors of NYHA Class Improvement After PFO Closure in COPD

- Increased work of breathing increases right to left shunt
- PFO closure in selected COPD population with large PFO shunt led to significant improvement in NYHA class and oxygen requirement

	OR (95% CI)	P Value
Pulmonary Comorbidities	0.18 (0.053-0.60)	0.005
Male Gender	0.30 (0.111-0.807)	0.017
Moderate to Severe Shunt	4.67 (1.23-17.7)	0.024
Age (Per Decile Increase)	1.84 (1.26-2.70)	0.0017
NYHA Class at Referral	2.9 (1.30-6.08)	0.0087

Fenster BE, Carroll J. *Am J Cardiol.* 2013

Current Model of PFO Pathology



“Hole-istic” Model of PFO Pathology

