

# A Patient With a PFO and Cryptogenic Stroke Outside the Recommended Age Range: Is PFO Closure Appropriate?

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September 23, 2018*

**Tufts** Medical  
Center

# Disclosure Statement of Financial Interest

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

## Affiliation/Financial Relationship

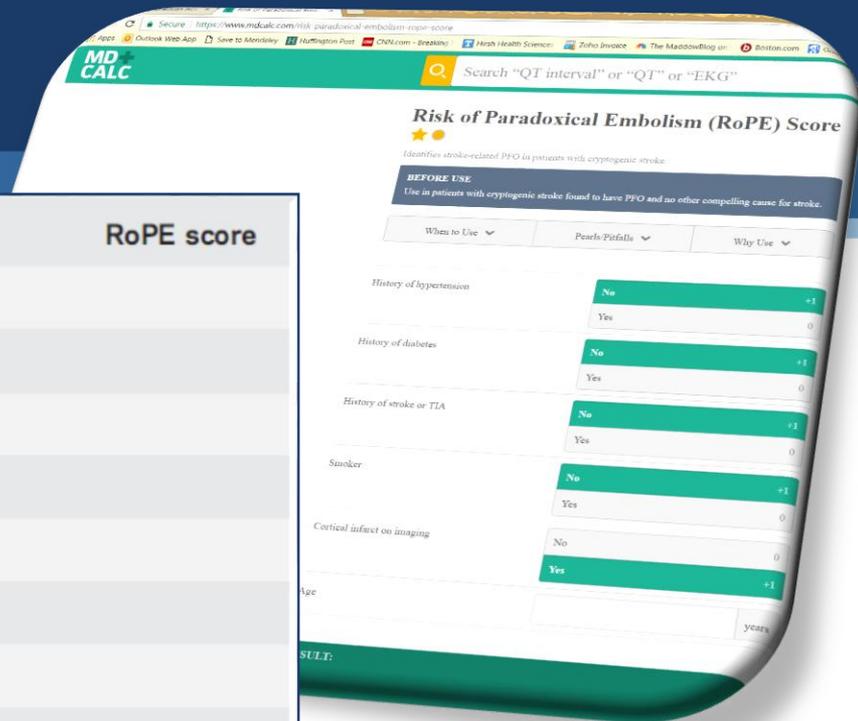
- Research Support for clinical trial
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- Consulting Fees for RESPECT/ACP/PFO Post-approval Study – Steering Committees
- Grant Support for RoPE Study

## Company

- WL Gore Associates
- Abbott (prev St. Jude Medical)
- Abbott (prev St. Jude Medical)
- NINDS (NIH)

**How long is a piece of RoPE?**

# The RoPE Score Calculator



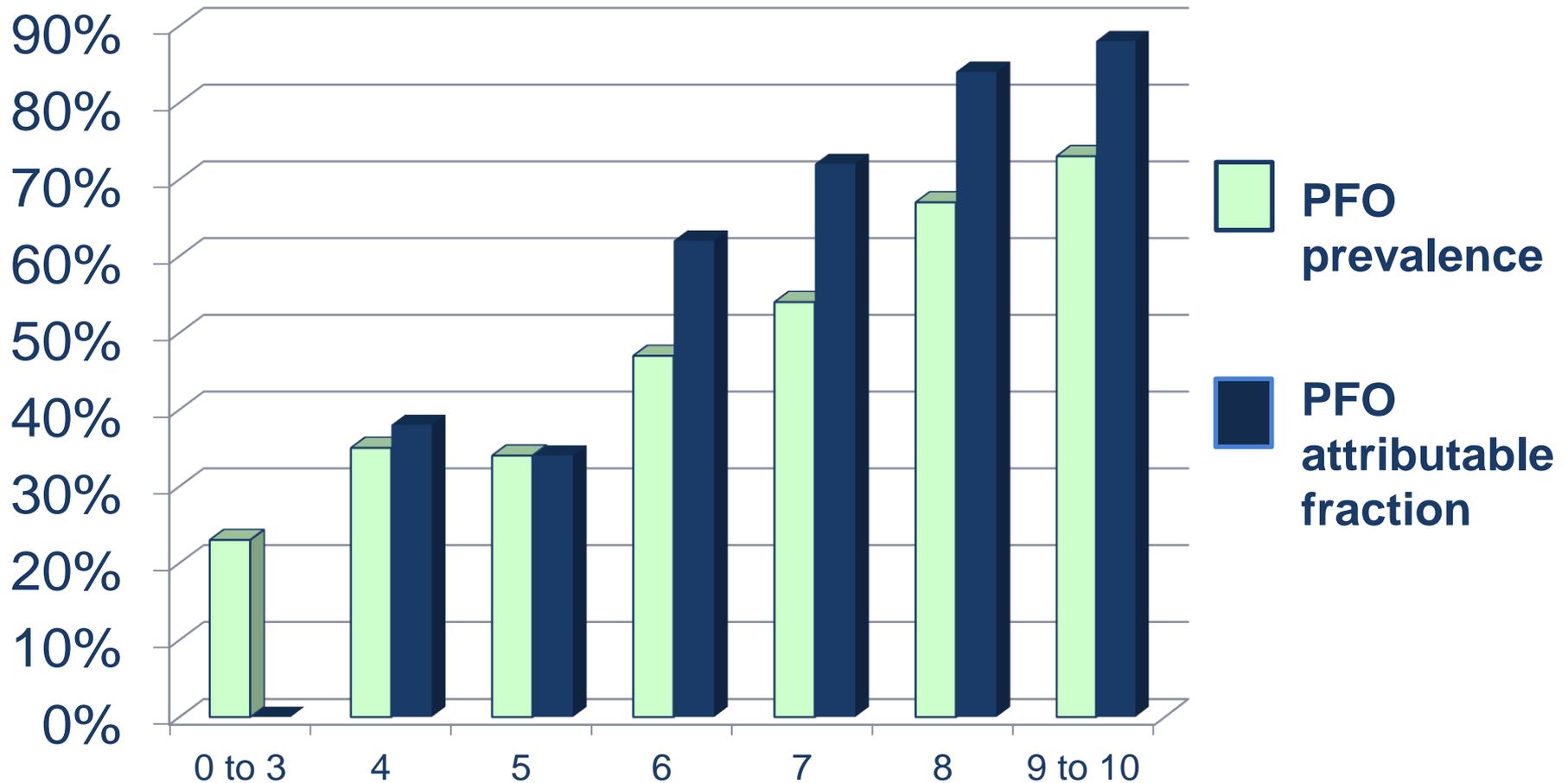
<https://www.mdcalc.com/risk-paradoxical-embolism-rope-score>

Characteristic	Points	RoPE score
No history of hypertension	1	
No history of diabetes	1	
No history of stroke or TIA	1	
Nonsmoker	1	
Cortical infarct on imaging	1	
Age, y		
18-29	5	
30-39	4	
40-49	3	
50-59	2	
60-69	1	
≥70	0	
<b>Total score (sum of individual points)</b>		
Maximum score (a patient <30 y with no hypertension, no diabetes, no history of stroke or TIA, nonsmoker, and cortical infarct)		10
Minimum score (a patient ≥70 y with hypertension, diabetes, prior stroke, current smoker, and no cortical infarct)		0

# Increasing RoPE score

→ Increasing PFO prevalence, and

→ Increasing PFO attributable fraction

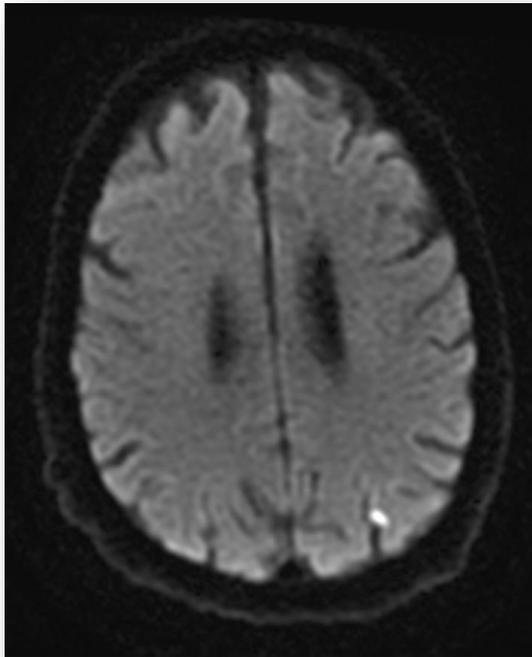


## Mr FW: How long is a piece or RoPE?

- 70 y/o M with recurrent R-HP and stroke
  - Mar 2016: ASA → rivaroxaban
  - May 2016: Rivaroxaban + ASA (81mg)
  - Jul 2016: Rivaroxaban + ASA (325mg)
  - Nov 2016 Dabigatran + clopidogrel
- Emphysema, no HTN/DM, remote smoking
- No h/o DVT/PE in him, sibs (x2), or kids (x2)
  - Mother had “clots in her legs”

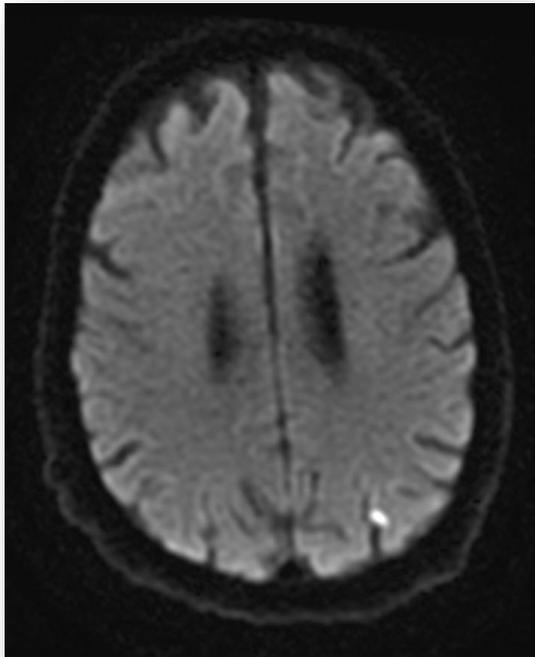
## Mr FW: How long is a piece or RoPE?

- MRI – L hemisphere DWI lesions
- CTA – mild calcifications at ICA origins
- Hypercoag testing nl
- ILR *in situ*



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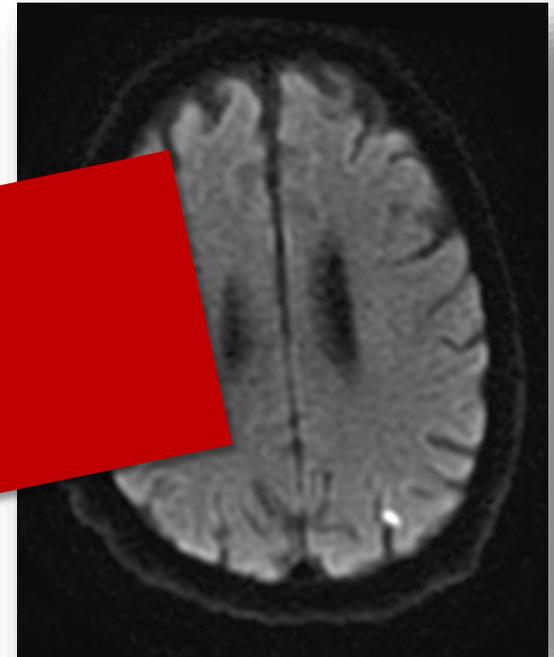
- Transthoracic echo:
  - mild diastolic dysfunction
  - R-L shunting “moderately positive with Valsalva”
  - “mobile atrial septum”
  - “prominent Chiari network”



**Close or  
No close?**

RoPE Score = 4 (PFO af = 38%)

# Mr FW: How long is a piece or RoPE?



**Close or  
No close?**

- 1<sup>st</sup> stroke in 1982 (age 35)
- 1982 RoPE Score = 8 (PFO-af = 84%)



Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Center - W066-G609  
Silver Spring, MD 20993-0002

October 28, 2016

St. Jude Medical, Inc.  
Rashmi Bhushan, PhD  
Manager, Regulatory Affairs  
5050 Nathan Lane North  
Plymouth, Minnesota 55442

Re: P120021

Trade/Device Name: AMPLATZER PFO Occluder

Filed: November 30, 2012

Amended: August 12, 2013, September 9, 2013, February 26, 2014, April 28, 2014, July 1,  
2014, February 27, 2015, September 17, 2015, October 8, 2015

Product Code: MLV

The AMPLATZER™ PFO Occluder is indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke.

See important safety information referenced within.

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**Incidence  $\neq$  Prevalence**

# Analysis of 1008 Consecutive Patients Aged 15 to 49 With First-Ever Ischemic Stroke

## The Helsinki Young Stroke Registry

Jukka Putaala, MD; Antti J. Metso, MD, PhD; Tiina M. Metso, MD; Nina Konkola, MD;  
Yvonn Kraemer, MD; Elena Haapaniemi, MD, PhD;  
Markku Kaste, MD, PhD; Turgut Tatlisumak, MD, PhD

**Background and Purpose**—To analyze trends in occurrence, risk factors, etiology, and neuroimaging features of ischemic stroke in young adults in a large cohort.

**Methods**—We evaluated all 1008 consecutive ischemic stroke patients aged 15 to 49 admitted to Helsinki University Central Hospital, 1994 to 2007. Etiology was classified by Trial of Org 10172 in Acute Stroke Treatment criteria. Comparisons were done between groups stratified by gender and age.

**Results**—Estimated annual occurrence was 10.8/100 000 (range 8.4 to 13.0), increasing exponentially with aging. Of our 628 male and 380 female (ratio 1.7:1) patients, females were preponderant among those <30, whereas male dominance rapidly increased around age of 44. The most frequent risk factors were dyslipidemia (60%), smoking (44%), and hypertension (39%). Males and patients >44 clearly had more risk factors. Cardioembolism (20%) and cervicocerebral artery dissection (15%) were the most frequent etiologic subgroups. Proportions of large-artery atherosclerosis (8%) and small-vessel disease (14%) began to enlarge at age 35, whereas frequency of undetermined etiology (33%) decreased along aging. Posterior circulation infarcts were more common among patients <45 years of age. Left hemisphere infarcts were more frequent in general. There were 235 (23%) patients with multiple and 126 (13%) with silent infarcts, and 55 (5%) patients had leukoaraiosis.

**Conclusions**—The frequency of ischemic stroke increases sharply at age 40. Etiology and risk factors start resembling those seen in the elderly in early midlife but causes defined in younger patients still are frequent in those aged 45 to 49. Subclinical infarcts were surprisingly common in the young. (*Stroke*. 2009;40:1195-1203.)

**Key Words:** cerebral infarct ■ imaging ■ risk factors ■ stroke in young adults ■ young, stroke in

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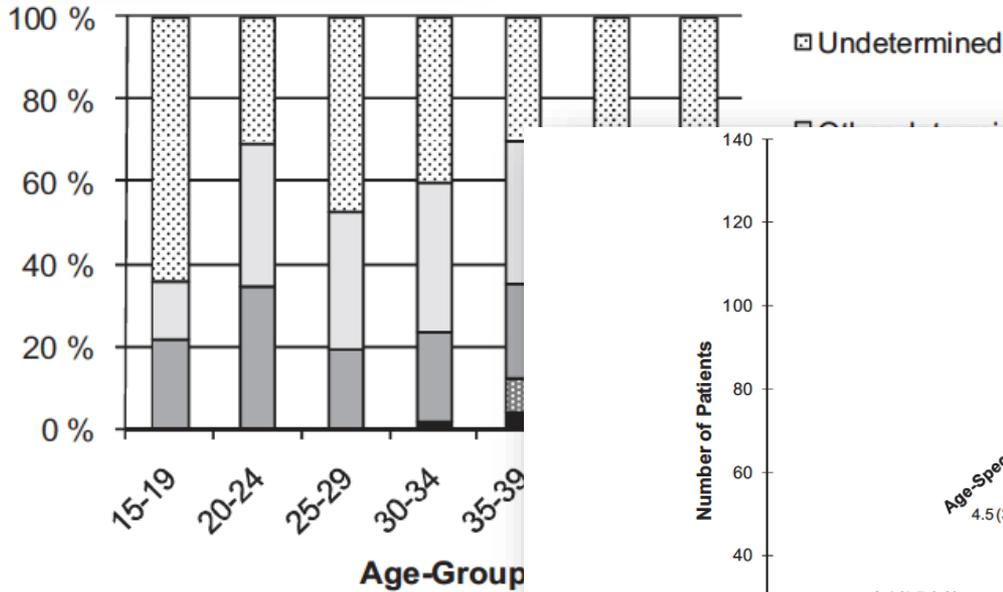
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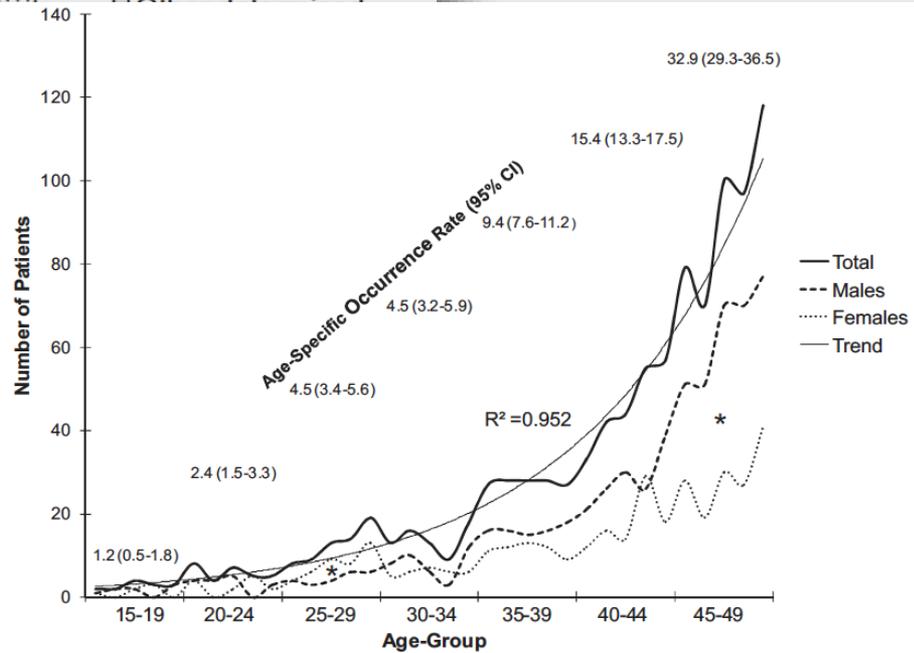
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**Figure 2.** Relative proportions age-groups.



**Figure 1.** Number of patients according to age and age-specific occurrence rates per 100 000. R indicates correlation coefficient of the trend line illustrating the exponential increase in occurrence as a function of age. \* $P < 0.001$  in comparison of age-specific proportions between genders by Chi-Sq test.

## Reasons that PFO related stroke may INCREASE in incidence with age

- Increased prevalence of DVT (thrombus source)
- Increased prevalence of PE (R-L shunting)
- Increased prevalence of cancer and hypercoagulability
- Increased peri-operative periods
- Increased sessility

**Like the RoPE Score, the FDA wording is a guide**

**Do not let either replace clinical judgment**



Thank you.