Update in Left Atrial Appendage Occlusion: More Options

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Director, Structural Heart Disease Program
Director, Interventional Echocardiography
Director, Heart Valve Clinic
Non-Valvular Atrial Fibrillation: An EPIDEMIC

- Mayo Clinic data (assuming a continued increase in AF incidence)
- Mayo Clinic data (assuming further increase in AF incidence)
- ATRIA study data (50% >80 yo)

Patients with atrial fibrillation (millions)

Year


2050
15.9
15.2
14.3
13.1
11.7
11.1
11.7
12.1
5.61
5.42
5.16
4.78
4.34
3.8
4.33
3.33
2.94
2.66
2.44
2.26
2.08

1990
Prevalence of Atrial Fibrillation

The estimated number of US persons in 2005 with AF was 3.03 million

Naccarelli GV et al. *Am J Cardiol* 2009;104:1534–1539

The estimated prevalence of AF is 0.4% to 1% in the general population, increasing with age to 8% in those older than 80 yr.
Figure 25. Population aged 80 or over: world, 1950-2050

- 2050: 379.0
- 2025: 153.4
- 2000: 69.2
- 1975: 31.4
- 1950: 13.8

UN population study
AF is a Growing Problem Associated with Greater Morbidity and Mortality

AF = most common cardiac arrhythmia, and growing

AF increases risk of stroke

- Higher stroke risk for older patients and those with prior stroke or TIA
- 15-20% of all strokes are AF-related
- AF results in greater disability compared to non-AF-related stroke
- High mortality and stroke recurrence rate

\[ \text{~5 M people with AF in U.S., expected to more than double by 2050} \]

\[ \times 5 \text{ greater risk of stroke with AF} \]

Connection Between AF-Related Stroke and the Left Atrial Appendage

RESECTION OF THE LEFT AURICULAR APPENDIX
A Prophylaxis for Recurrent Arterial Emboli

JOHN L. MADDEN, M.D.
New York

A therapeutic problem which remains unsolved is the one pertaining to recurrent arterial emboli. Once a peripheral embolus has occurred there is a high incidence of recurrence. Unfortunately, all too frequently the recurrent embolus is fatal, commonly involving one of the cerebral arteries. As Jefferson so aptly stated: "In the nature of things a very high percentage of successes is unlikely ever to be attained, for emboli are apt to be multiple and further infarction will sometimes carry off the patient in whom a local success has been won."

Since a thrombus is the precursor of every arterial embolus, the ideal prophylaxis for recurrent arterial emboli should be the removal of the thrombus together with its site of origin. Rheumatic mitral stenosis is one of the commonest causes of a peripheral arterial embolus, an embolus occurring in approximately 45 per cent of the cases. In this disease the embolus originates as a mural thrombus within the left auricle or its appendix, more commonly the latter.

Examination disclosed an embolic occlusion of the left common iliac artery. The heart was not decompensated. Approximately twenty hours after the onset of symptoms a transperitoneal embolectomy was performed successfully.

The patient was admitted to the hospital for the second time on Jan. 11, 1948 (fifteen month interval), complaining of numbness and tingling in the right leg of two hours' duration. In the interval between admissions to the hospital manifestations of congestive heart failure occurred several times, but the symptoms abated after an increase in the maintenance dose of digitalis.

Examination showed an embolic occlusion of the right popliteal artery. About five hours after the onset of symptoms the embolus was removed successfully.

In view of the history of chronic rheumatic heart disease with mitral stenosis, auricular fibrillation and recurrent peripheral arterial emboli, a resection of the left auricular appendix was advised. On February 21, with intratracheal anesthesia (gas, oxygen and ether) a resection of the left auricular appendix was performed.

During the operation stoppage of the heart occurred. Immediate manual massage of the heart was begun concomitant with the maintenance of artificial respiration by a rhythmic compression of the breathing bag. The recovery of the patient was complete.

An examination immediately postoperative revealed a left hemiparesis, which was believed to be secondary to a right cerebral embolus. Subsequently, a decided personality change was observed, which persisted throughout the stay in the hospital.
Connection Between Non-Valvular AF-Related Stroke and the Left Atrial Appendage

AF Creates Environment for Thrombus Formation in Left Atrium

- Stasis-related LA thrombus is a predictor of TIA\(^1\) and ischemic stroke\(^2\).
- In non-valvular AF, >90% of stroke-causing clots that come from the left atrium are formed in the LAA\(^3\).

Warfarin

- 1933 – Ed Carlson (farmer)
- 1941 – dicumerol
- 1948 – patented
- Wisconsin Alumi Research Foundation
  - WARFarin
Wisconsin Alumni Research Foundation

Rat Control with warfarin

PROF. LINKS "WARFARIN-INS" TO PUT YOUR...
Use in Humans

- 1951 – failed suicide by a navy recruit tx w/ Vit K
- Clinical studies in humans
- 1955 – President Eisenhower after his MI
Adjusted Dose Warfarin Compared with Placebo

Hart et al
2014 AHA/ACC/HRS Treatment Guidelines to Prevent Thromboembolism in Patients with AF

• Assess stroke risk with CHA₂DS₂-VASc score
  – Score 1: Annual stroke risk 1%, oral anticoagulants or aspirin may be considered
  – Score ≥2: Annual stroke risk 2%-15%, oral anticoagulants are **recommended**

• Balance benefit vs. bleeding risk
• **Warfarin**
  
  – Effective treatment
  
  – Difficult to achieve therapeutic target
Use of OACs in AF Patients peaks at ~50%, use declines with increasing risk

1. Hsu, J et al. *JAMA Cardiol.* Published online March 16, 2016. doi:10.1001/jamacardio.2015.0374
# Stroke Treatment Option: Novel Oral Anticoagulants

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran(^1)</th>
<th>Rivaroxaban(^2)</th>
<th>Apixaban(^3)</th>
<th>Edoxaban(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparator</td>
<td>Warfarin</td>
<td>Warfarin</td>
<td>Warfarin</td>
<td>Warfarin</td>
</tr>
<tr>
<td>Total Enrolled Subjects</td>
<td>18,113</td>
<td>14,264</td>
<td>18,201</td>
<td>21,105</td>
</tr>
<tr>
<td>Trial Design</td>
<td>Randomized, controlled, non-inferiority (doses of dabigatran were blinded)</td>
<td>Randomized, controlled, double-blind, non-inferiority</td>
<td>Randomized, controlled, double-blind, non-inferiority</td>
<td>randomized, controlled, double-blind, non-inferiority</td>
</tr>
<tr>
<td>Median Duration of Follow up</td>
<td>2 years</td>
<td>1.94 years</td>
<td>1.8 years</td>
<td>2.8 years</td>
</tr>
<tr>
<td>Average CHADS(_2) Score</td>
<td>2.1</td>
<td>3.5</td>
<td>2.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Results (primary outcome = stroke or systemic embolism)</td>
<td>Reduction in primary outcome compared to warfarin</td>
<td>Reduction in primary outcome compared to warfarin</td>
<td>Reduction in primary outcome compared to warfarin</td>
<td>Reduction in primary outcome compared to warfarin</td>
</tr>
</tbody>
</table>

1 Connelly SJ et al, *NEJM* 2009; 361:1139-51
3 Granger, J MD. *NEJM* 2012;365:981-92
4 Giugliano, R. *NEJM* 2013; 369(22): 2093-2104 – 2.8 yrs follow-up
Adherence to NOACs

• A retrospective study of 64,661 patients found that only 47.5% of patients on NOACs had >80% adherence during a median follow-up period of 1.1 years
  – Apixaban: 52.1%
  – Rivaroxaban: 47.6%
  – Dabigatran: 45.9%

• NOAC adherence was higher than warfarin
  – Warfarin: 38.7%
Despite Increasing NOAC Adoption, Overall Rate of Anticoagulation in High Risk NVAF Patients has Not Improved

Anticoagulant Use in Patients with NVAF and CHADS$_2$ ≥ 2

Results from the NCDR PINNACLE Registry$^1$

Anticoagulant Therapy Carries Risk of Intracerebral Hemorrhage or Death

Spontaneous intra-parenchymal bleed

Hemorrhagic transformation
# Stroke Treatment Option: Novel Oral Anticoagulants

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study Drug Discontinuation Rate</th>
<th>Major Bleeding (rate/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban(^1)</td>
<td>24%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Apixaban(^2)</td>
<td>25%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Dabigatran(^3)</td>
<td>21%</td>
<td>3.3%</td>
</tr>
<tr>
<td>(150 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edoxaban(^4)</td>
<td>33% / 34%</td>
<td>2.8% / 1.6%</td>
</tr>
<tr>
<td>(60 mg / 30 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin(^1-4)</td>
<td>17 – 28%</td>
<td>3.1 – 3.6%</td>
</tr>
</tbody>
</table>

There is an unmet need of stroke risk reduction for patients with AF who are seeking an alternative to long-term OACs.

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LAA and Stroke?

Clinically recognized as the primary source of cardioembolic thrombi

Exclusion has been shown to reduce risk of stroke in some patient populations

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Stroke Treatment Option: LAA Ligation

- Surgical approaches to thromboembolic prophylaxis have been explored since the 1940s

- LAA closure or obliteration has most often been considered as an adjunct to other cardiac procedures such as mitral valvotomy or cardiac bypass surgery

- A review of the literature on LAA closure prior to 2010 found surgical closure rates of 17%-89.7%\(^1\)

- Studies on patients undergoing LAA closure have shown a trend toward reduction in embolic events

A need exists for a less invasive approach that can consistently close the LAA

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2 Kanderian et al. *JACC* 2008, 52:924–9
Stroke Treatment Options: LAA Ligation, LAA Clips and LAA Closure

**LAA Closure (LAAC) Devices**

<table>
<thead>
<tr>
<th>PLAATO</th>
<th>WATCHMAN™ Device</th>
<th>ACP</th>
</tr>
</thead>
<tbody>
<tr>
<td>• First LAAC device</td>
<td>• Only LAAC device with 2 Randomized</td>
<td>• US Trial halted in 2013</td>
</tr>
<tr>
<td>(2001)</td>
<td>Controlled Trials</td>
<td></td>
</tr>
<tr>
<td>• Device no longer</td>
<td>• FDA approved with specific</td>
<td></td>
</tr>
<tr>
<td>available</td>
<td>indication to reduce the risk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>of thromboembolism</td>
<td></td>
</tr>
</tbody>
</table>

**LAA Clip**

**EXCLUDE Trial (completed)**
- AtriClip Device was FDA approved in 2010 for LAA closure
  - No specific indication for Stroke Reduction

**Surgical Ligation**

“Safety and Efficacy of Left Atrial Appendage Occlusion Devices”
Observational Study (retrospective)
- To compare LARIAT® vs. WATCHMAN™
- LARIAT currently does not have a specific indication for LAA Closure or Stroke Reduction
Percutaneous LAA Occlusion Systems

WATCHMAN

Amulet

Lariat

Wavecrest

LAmbre

Occluetech
Percutaneous LAA Occlusion Systems

WATCHMAN

Amulet

Lariat

Wavecrest

LAmbre

Occluetech
Percutaneous LAA Occlusion Systems

WATCHMAN  Amulet  Lariat

Wavecrest  LAmbre  Occluetech
WATCHMAN™ Left Atrial Appendage Closure (LAAC) Device Overview

Nitinol Frame
- Radially expands to maintain position in LAA
- Available sizes:
  - 21, 24, 27, 30, 33 mm (diameter)
- 10 Active fixation anchors around device perimeter engage LAA tissue for stability and retention
- Features an intra-LAA design to avoid contact with Left Atrial wall

160 Micron Membrane
- Polyethylene terephthalate (PET) cap
- Designed to block emboli from exiting the LAA

Designed specifically for the left atrial appendage
WATCHMAN™ Device Clinical Program

- **Pilot**: Early feasibility with >6 years of follow-up
- **PROTECT-AF**: WATCHMAN primary efficacy, CV death, and all-cause mortality superior to warfarin at 4 years¹
- **CAP Registry**: Significantly improved safety results²
- **ASAP**: Expected rate of stroke reduced by 77% in patients contraindicated to warfarin³
- **PREVAIL**: Improved implant success; procedure safety confirmed with new and experienced operators⁴
- **CAP2**: Enrolled up to 1500 patients at ~ 60 sites

Feasibility Trial – First Generation LAA Occluder

- 111 patients – did not receive warfarin
- 97% deployment success
- Leak mild or less in 108
- 1° outcomes measure:

  **Estimated** stroke risk based on CHADS$_2$
  
  **6.3%**

  **Actual** Observed Stroke Rate
  
  **2.2%**

  Ostermayer JACC 2005

  (65% reduction compared to historical control)

  2009 Block et al North American cohort (n=64)  Estimated 6.6%, actual 3.8%
  2010 European PLAATO (n=180)  Estimated 6.6%, actual 2.3%
• 9 procedure related SAEs
  • Pleural effusion, pericardial effusion (2), tamponade (2), hemothorax,
  • DVT, brachial plexus palsy, reintubation
• 7 MAEs
  • 4 cardiac or neurological deaths – non-device related
  • 2 strokes
  • 1 tamponade post transseptal, sternotomy, LAA ligation, DVT, cerebral hemorrhage, death
• 3 TIAs
Pilot Study

- 66 patients implanted at 8 sites in U.S. & Germany – out of 75 attempted
  - 2 procedural – scar in groin, wire malfunction
  - 7 unsuitable anatomy
- 93% complete closure at 45 days
- 333 patient years of follow-up
- Mean follow-up 58 ± 17 months

Courtesy of Dr. Turi
Stroke Rate

• Estimate risk based on CHADS₂ score of 1.9:
  – 4.0 %

• Actual Stroke Rate
  – 0.6 %

(85% reduction compared to historical control)
Complications – Device Version 1.0

- 2 tamponades
- 3 effusions
- 1 air embolism - CPR
- 1 delivery wire fracture – surgical removal
- 2 device embolizations (retrieved)
- 4 thrombus layer at 6 months
  - Anticoagulation – resolved
  - Protocol added clopidogrel at 45 days
- 2 TIAs – 1 with thrombus
- 1 non-device related death at 9 months
WATCHMAN LAA Closure Device for Stroke Prophylaxis and Atrial Fibrillation

PROTECT-AF Trial

Multicenter, prospective, randomized, unblinded trial
The WATCHMAN® Device is an investigational device in the United States and not available for sale.
WATCHMAN LAA Closure Device for Stroke Prophylaxis and Atrial Fibrillation

PROTECT-AF Trial

Multicenter, prospective, randomized, unblinded trial
Anticoagulation and Antiplatelet Therapy

Warfarin INR 2 -3

Aspirin

Clopidogrel

Aspirin

CONTROL

DEVICE

Aspirin

Warfarin

6 weeks

4.5 months
Primary Efficacy Endpoint
(Stroke, Cardiovascular Death, Systemic Embolism)

Days Since Randomization
0 365 730 1095

Probability

Control
Device
244
463
174
332
67
132
17
34

RR = 0.62 (95% CrI 0.35-1.25)
Primary Safety Endpoint
(Hemorrhage, hemorrhagic stroke, procedure related events)

RR = 1.69 (95% CrI 1.01 - 3.19)
RR = 1.53 (95% CrI 0.95 - 2.7)
Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation: A Randomized Clinical Trial

**A** Primary efficacy end point

- HR (95% CI), 0.61 (0.38-0.97)
- \( P = .04 \)

**B** Primary safety end point

- HR (95% CI), 1.21 (0.78-1.94)
- \( P = .41 \)

Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation: A Randomized Clinical Trial

**A** Ischemic stroke

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Device</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>463</td>
<td>244</td>
</tr>
<tr>
<td>12</td>
<td>382</td>
<td>220</td>
</tr>
<tr>
<td>24</td>
<td>360</td>
<td>200</td>
</tr>
<tr>
<td>36</td>
<td>336</td>
<td>172</td>
</tr>
<tr>
<td>48</td>
<td>314</td>
<td>144</td>
</tr>
<tr>
<td>60</td>
<td>156</td>
<td>64</td>
</tr>
</tbody>
</table>

RR (95% CI), 1.26 (0.72-3.28)  
*P* = .49

**B** Cardiovascular mortality

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>0</td>
<td>463</td>
<td>244</td>
</tr>
<tr>
<td>12</td>
<td>389</td>
<td>222</td>
</tr>
<tr>
<td>24</td>
<td>372</td>
<td>204</td>
</tr>
<tr>
<td>36</td>
<td>351</td>
<td>176</td>
</tr>
<tr>
<td>48</td>
<td>328</td>
<td>147</td>
</tr>
<tr>
<td>60</td>
<td>165</td>
<td>69</td>
</tr>
</tbody>
</table>

HR (95% CI), 0.40 (0.21-0.75)  
*P* = .005

**C** All-cause mortality

<table>
<thead>
<tr>
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<tbody>
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<td>12</td>
<td>389</td>
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<tr>
<td>24</td>
<td>373</td>
<td>204</td>
</tr>
<tr>
<td>36</td>
<td>352</td>
<td>177</td>
</tr>
<tr>
<td>48</td>
<td>330</td>
<td>150</td>
</tr>
<tr>
<td>60</td>
<td>202</td>
<td>92</td>
</tr>
</tbody>
</table>

HR (95% CI), 0.66 (0.45-0.98)  
*P* = .04
Procedural Complications: Substantial Learning Curve

- Pericardial effusion requiring drainage 5%
  - Rate 50% ↓ > 3 cases
- Periprocedure ischemic stroke 1.1%
  - Air or thromboemboli

All Device and/or procedure-related serious adverse events within 7 Days
Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy

The PREVAIL Trial

David R. Holmes Jr, MD,* Saibal Kar, MD,† Matthew J. Price, MD,‡ Brian Whisenant, MD,§ Horst Sievert, MD,|| Shephal K. Doshi, MD,¶ Kenneth Huber, MD,# Vivek Y. Reddy, MD**
• **First primary endpoint ("primary efficacy"):** the occurrence of stroke (ischemic or hemorrhagic), cardiovascular or unexplained death, and systemic embolism over 18 months.

• **Second primary endpoint ("late ischemic efficacy"):** the occurrence of ischemic stroke and systemic embolism from 8 days after randomization and onward, excluding peri-procedural events in order to evaluate the mechanism of action of stroke prevention over 18 months.

• **Third primary endpoint (mechanistic endpoint):** the occurrence of all-cause death, ischemic stroke, systemic embolism, or device- or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudo-aneurysm repair, arteriovenous fistula repair, or other major endovascular repair occurring between the time of randomization and within 7 days of the procedure or by hospital discharge, whichever was later.
Kaplan-Meier Curve: Freedom From First Primary Endpoint (Intention-to-Treat)

Primary efficacy rates for Watchman (solid line) versus warfarin (dotted line) in the intention-to-treat population show similarly high 18-month event-free rates.
PREVAIL: Warfarin Ischemic Stroke Rate Differs from Other Trials

<table>
<thead>
<tr>
<th>Trial (Warfarin Arm)</th>
<th>Ischemic Stroke Rate per 100 pt-yrs</th>
<th>Mean CHADS$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREVAIL$^1$</td>
<td>0.3</td>
<td>2.6</td>
</tr>
<tr>
<td>PROTECT AF$^1$</td>
<td>1.1</td>
<td>2.2</td>
</tr>
<tr>
<td>RE-LY$^2$</td>
<td>1.2</td>
<td>2.1</td>
</tr>
<tr>
<td>ROCKET AF$^2$</td>
<td>1.42</td>
<td>3.5</td>
</tr>
<tr>
<td>ARISTOTLE$^2$</td>
<td>1.05</td>
<td>2.1</td>
</tr>
<tr>
<td>ENGAGE$^3$</td>
<td>1.25</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Kaplan-Meier Curve: **Freedom From Second Primary Endpoint Event** (Intention-to-Treat)

Late-ischemic events (stroke or systemic embolism >7 days’ post-randomization) for Watchman (solid line) versus warfarin (dotted line) in the intent-to-treat population demonstrated noninferiority for the rate difference endpoint.
Chronic or paroxysmal non-valvular atrial fibrillation (NVAF) CHADS2 ≥2 or CHADS2 score ≥1 with an additional risk factor

Watchman LAA implant group

Aspirin for life, warfarin for 45 days or till closure of LAA, clopidogrel 45 days-6 months

Chronic warfarin group

Warfarin for life Target INR 2-3

LAA occlusion was non-inferior to warfarin for ischemic stroke prevention or systemic embolization (SE) >7 days post procedure
Non-inferiority was not achieved for overall efficacy (stroke, SE, death); event rates were low and numerically similar in both arms.
Procedural success and safety has significantly improved in comparison to previous studies.

The PREVAIL trial provides additional evidence that LAA closure is a safe and effective alternative to coumadin in patients with NVAF

Procedural Complications: Substantial Learning Curve

- Pericardial effusion requiring drainage 5%
  - Rate 50% ↓ > 3 cases
- Periprocedure ischemic stroke 1.1%
  - Air or thromboemboli

All Device and/or procedure-related serious adverse events within 7 Days

Implant Success & Warfarin Cessation

Implant success defined as deployment and release of the device into the left atrial appendage.

**Warfarin Cessation**

<table>
<thead>
<tr>
<th>Study</th>
<th>45-day</th>
<th>12-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECT AF</td>
<td>87%</td>
<td>&gt;93%</td>
</tr>
<tr>
<td>CAP</td>
<td>96%</td>
<td>&gt;96%</td>
</tr>
<tr>
<td>PREVAIL</td>
<td>92%</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

**PREVAIL Implant Success**

No difference between new and experienced operators

- Experienced Operators
  - n=26
  - 96%
- New Operators
  - n=24
  - 93%

p = 0.28

The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on CHADS₂ or CHA₂DS₂-VASc scores and are recommended for anticoagulation therapy;

- Are deemed by their physicians to be suitable for warfarin; and

- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.
CMS will cover percutaneous LAAC implants when specific criteria are met:

- Eligible patients must have a CHADS2 score of >2 or a CHA2DS2-VASc score >3
- Patients must be suitable for short-term warfarin, but deemed unable to take long-term oral anticoagulation
- Documented evidence of a formal shared decision interaction between the patient and an independent non-interventional physician
- Facility requirements: the procedure must be furnished in a hospital with an established structural heart and/or EP program
- Operator requirements: Must be performed by an IC, EP, or cardiovascular surgeon who:
  - has received manufacturer prescribed training on safe and effective use of the device
  - has performed at least 25 TSP through intact septum
  - Must maintain at least 25 TSP over a two year period (at least 12 are LAAC)
- Registry: Patients must be enrolled in a prospective national registry
Appropriate Patients?

- Poor long term candidates for anti-coagulation
  - History of major bleeding
  - Risk of major bleeding (high fall risk)
  - Poor tolerance of anti-coagulation

- Favorable anatomy for LAA closure

- Lifestyle

- Other factors:
  - noncompliance
  - those requiring dual anti-platelet therapy after stenting
Percutaneous LAA Occlusion Systems

WATCHMAN  Amulet  Lariat

Wavecrest  LAmbre  Occluetech
Amulet LAAO

**Lobe**
- Positioned inside the LAA neck
- Designed to conform to different sizes and shapes of LAA anatomy

**Disc**
- Designed to completely seal the LAA at the orifice

**Waist**
- Maintains tension between lobe and disc
- Flexible connection allows device to self-orient

**Stabilizing Wires**
- Engage with the wall of the LAA
- Help hold the device in place
Study Design

• A prospective, randomized, multicenter, active control worldwide trial to evaluate safety and effectiveness of the Amulet device

• Purpose: To evaluate the safety and effectiveness of the Amulet device by demonstrating that the device is non-inferior to the commercially available Boston Scientific LAA closure (LAAC) device (Control) in subjects with non-valvular atrial fibrillation

• Randomization will be 1:1 between Amulet (treatment) and the Boston Scientific LAA closure device (Control)
Study Design

AF Team selects study candidate

Subject signs consent

Baseline TEE (echo done within 90d prior to consent may be used)

Roll-in

Randomization 1:1

Amulet

Control

Amulet
Endpoints

Primary Endpoints

• **Safety**
  – A composite of procedure-related complications, or all-cause death, or major bleeding through 12 months

• **Effectiveness**
  – A composite of ischemic stroke or systemic embolism through 18 months

• **Mechanism of Action**
  ▪ Device closure (defined as residual jet around the device ≤ 5 mm) at the 45-day visit documented by transesophageal echocardiogram (TEE/TOE) defined by Doppler flow
Update in Left Atrial Appendage Occlusion: More Options

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