Left Atrial Appendage Closure

- Indications for percutaneous left atrial appendage (LAA) closure
- Watchman LAA closure procedure and follow up

Atrial Fibrillation is a Prevalent and Growing Condition and a Leading Cause of Stroke

- ~5M people with AF in U.S., expected to more than double by 2050
- 5X increased risk of stroke for AF patients
- 1 in 5 strokes occur in patients with AF
- 47% of AF patients experiencing a stroke will suffer a second stroke within 6 months

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

- Assess stroke risk with CHA$_2$DS$_2$-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

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc Score</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No anticoagulant</td>
</tr>
<tr>
<td>1</td>
<td>Aspirin (81-325 mg daily) or warfarin (INR 2-3)</td>
</tr>
<tr>
<td>2</td>
<td>Oral anticoagulants are recommended (warfarin (INR 2-3), dabigatran, rivaroxaban or apixaban)</td>
</tr>
</tbody>
</table>
Oral Anticoagulation is Standard of Care, but Not Ideal for All

Warfarin
- Bleeding risk
- Daily regimen
- High non-adherence rates
- Regular INR monitoring
- Food and drug interaction issues
- Complicates surgical procedures

Novel Oral Anticoagulants
- Bleeding risk
- Daily regimen
- High non-adherence rates
- Complicates surgical procedures
- Lack of reversal agents
- High cost

Use of OACs in AF Patients peaks at ~50%, use declines with increasing risk

Despite NOAC Adoption and Ability to Switch NOACs, Adherence to Anticoagulation Remains a Challenge

~30% of NOAC patients stop taking any drug at 2 years

Introducing the WATCHMAN™ LAAC Device

A first-of-its-kind, proven alternative to long-term warfarin therapy for stroke risk reduction in patients with non-valvular AF

Most studied LAAC therapy, only one proven with long-term data from randomized trials and multi-center registries

A safe alternative to long-term warfarin therapy which offers comparable stroke risk reduction and enables patients to stop taking warfarin

WATCHMAN™ LAAC Device

- WATCHMAN™ LAAC Device:
  - Reduces risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation

- For patients who:
  - Are at increased risk for stroke or 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
  - 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

WATCHMAN Therapy

Indications for Use

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.
Potential candidates for LAAC

- History of major bleeding while taking anticoagulation therapy
- Patient's prior experience with OAC (if applicable)
- Inability to maintain stable INR
- Inability to comply with regular INR monitoring or unavailability of an approved alternative OAC
- Medication condition, occupation or lifestyle placing patient at high risk of major bleeding secondary to trauma

WATCHMAN™ Left Atrial Appendage Closure (LAAC) Device Procedure

- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite, does not need hybrid OR
- Performed by a Heart Team
  - IC/EP or IC/EP, TEE, General Anesthesia, Surgical Back-up, WATCHMAN Clinical Specialist
- Transfemoral Access: Cath femoral vein
- General anesthesia
  - Does not require open heart surgery
- 1 hour procedure
- 1-2 day hospital stay

WATCHMAN™ LAAC Closure Device

- Minimally Invasive, Local Solution
  - Available sizes: 21, 24, 27, 30, 33 mm diameter
- Intra-LAA design
  - Avoids contact with left atrial wall to help prevent complications
- Nitinol Frame
  - Conforms to unique anatomy of the LAA to reduce embolization risk
  - 10 active fixation anchors - designed to engage tissue for stability
- Proximal Face
  - Minimizes surface area facing the left atrium to reduce post-implant thrombus formation
  - 160 micron membrane PET cap designed to block emboli and promote healing
- Warfarin Cessation
  - 92% after 45 days, >99% after 12 months
  - 95% implant success rate

WATCHMAN Implant Procedure Review

1. Procedure Equipment
2. LAA Anatomy/Assessment
   - Ostium size, LAA type, considerations
3. Transseptal (IAS) Crossing
4. WATCHMAN™ Access Sheath Navigation/Manipulation
5. WATCHMAN™ Device Deployment
7. Device Recapture
8. Final Device Release

1. WATCHMAN Procedure Equipment

- WATCHMAN Delivery System (delivery catheter and pre-loaded LAA closure device)
- Venous Introducer (optional)
- Standard Transseptal Access System
- 0.035" guidewire (exchange length extra support)
- 5F or 6F angiographic pigtail catheter
- WATCHMAN® Access System (which includes the access sheath and dilator)
- TEE
- Heparin – minimum ACT of 200-300sec throughout procedure
- Addl equipment necessary for complex cardiovascular intervention, per hospital procedure
Agenda

- WATCHMAN™ Left Atrial Appendage Closure System Components
  - WATCHMAN™ Implant Procedure
  - WATCHMAN™ Post-Implant Follow-Up

WATCHMAN™ Pre-Loaded Delivery System

WATCHMAN™ Access Sheath

- 14F outer diameter (4.7mm), 12F inner diameter (4mm)
- 75 cm working length

WATCHMAN™ Delivery Sheath

Preformed access sheath curve shapes

guide position in LAA

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2. LAA Anatomy / Assessment

Ostium size and shape

Assess the following through multiple imaging planes (0 - 135 deg sweep):

- LAA size, shape, number of lobes in LAA and location of lobes relative to ostium

Record LAA ostium and LAA length measurements (0 - 135 deg sweep):

- Measure the LAA ostium at approximately these angles:
  - at 0º
  - at 45º
  - at 90º
  - at 135º

- Measure from coronary artery marker to a point 2cm from tip of the "limbus"

- Measure from top of the MV annulus to a point 2cm from tip of the "limbus"

- Measure the approximate LAA usable length from the ostium line to the apex of the LAA
2. LAA Anatomy / Assessment

**Morphology**

| Wind Sock: An anatomy in which one dominant lobe of sufficient length is the primary structure |
| Chicken Wing: An anatomy whose main feature is a sharp bend in the dominant lobe of the LAA at some distance from the perceived LAA ostium |
| Broccoli: An anatomy whose main feature is an LAA that has limited overall length with more complex internal characteristics |

**Absence of Thrombus**

- Use Color Doppler and echo contrast as necessary

**Maximum LAA Ostium (mm) vs. Device Size (mm)**

<table>
<thead>
<tr>
<th>Maximum LAA Ostium (mm)</th>
<th>Device Size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-19</td>
<td>21</td>
</tr>
<tr>
<td>20-22</td>
<td>24</td>
</tr>
<tr>
<td>23-25</td>
<td>27</td>
</tr>
<tr>
<td>26-28</td>
<td>30</td>
</tr>
<tr>
<td>29-31</td>
<td>33</td>
</tr>
</tbody>
</table>

- Maximum LAA ostium and LAA depth measurements determine device size selection
- Maximum LAA ostium size should be \( \geq 17 \text{ mm} \) or \( \leq 31 \text{ mm} \) to accommodate available device sizes

3. Transseptal (IAS) Crossing

- Suggested crossing location – posterior and inferior
- Preferred use of bicaval and short axis views to confirm position in TEE
  - Inferior on short axis, posterior on bicaval
- Preferred exchange of guidewire to WATCHMAN™ Access Sheath in LUPV or left atrium
- Carefully advance 6F pigtail through Access Sheath into distal portion of LAA under fluoroscopy guidance
- Carefully advance Access Sheath over pigtail catheter in multiple angio and echo views

4. WATCHMAN™ Access Sheath Navigation/Manipulation

- Radiopaque marker bands guide initial sheath placement/death in the LAA
- Align radiopaque marker band corresponding to device size until at or just distal to LAA ostium
- To better visualize complex LAA anatomy and verify access sheath tip position:
  - Obtain multiple views with:
    - Angiography (min. RAO cranial/caudal)
    - TEE (min. 0° - 135° sweep)

5. WATCHMAN™ Device Deployment

- Select device based on maximum LAA ostium width recorded; LAA depth must be at least as long as the LAA ostium width
- Confirm distal tip of constrained device aligned with distal marker band of Delivery System
- Maintain fluid to fluid connection when inserting Delivery Sheath into Access Sheath
  - Switch manifold/contrast to delivery system
5. WATCHMAN™ Device Deployment

On fluoro, align most distal marker band on Delivery System with most distal marker band on Access Sheath

Stabilize WATCHMAN Delivery System, retract Access Sheath and snap together

Disconnected

Delivery/Access Sheaths

Connected WATCHMAN System

5. WATCHMAN™ Device Deployment

- Observe distal end of device to ensure no forward motion (or repositioning relative to ostium) has occurred
- Tactile feel may be decreased, risk of complications may be increased
- Loosen hemostasis valve on Delivery System, hold deployment knob stationary, retract Access Sheath/Delivery System assembly to deploy device
- Unsheathe device using slow stable motion for optimal control (at least 3-5 seconds), ensure distal tip remains in desired position


WATCHMAN™ Device features one-step deployment Recapturable and Repositionable

All criteria must be met prior to device release (PASS)

Position – device is at the ostium of the LAA
Anchor – fixation anchors engaged / device is stable
Size – device is compressed 8-20% of original size
Seal – device spans ostium, all lobes of LAA are covered

Device Position: TOO DISTAL

Partial Recapture

Too Distal - possible uncovered lobes, incomplete seal or residual flow in LAA

- Advance tip of Access/Delivery System assembly up to device (do not unsnap)
- Stabilize deployment knob position with right hand and gently advance Access Delivery System over shoulders of device
  - Resistance will be felt as device shoulders collapse
- Continue to advance System up to, but not past, fixation anchors
  - When resistance is felt a second time (anchor contact), stop, tighten hemostasis valve
- Reposition Access/Delivery System assembly proximally and re-deploy by holding deployment knob stationary and retracting Access Sheath

Device Position: TOO PROXIMAL

Full Recapture

Too Proximal - Device protrudes into LA, low compression or unstable device

- Advance tip of Access/Delivery System up to face of device (do not unsnap)
- Stabilize deployment knob position with right hand and gently advance System until device is completely collapsed
  - Resistance will be felt as device shoulders collapse
- Withdraw device until distal anchors are proximal to marker band then tighten hemostasis valve
- Unsheathe and remove Delivery System from Access Sheath while maintaining position within LAA
- Insert pigtail catheter to reposition Access Sheath in LAA
- Repeat implant steps with new Delivery System
6. Device Release Criteria – Anchor

**Tug Test – Pass or Fail**

1. To test stability, gently retract deployment knob and let go, observe device returns to original position
2. If the device moves to where position is no longer acceptable or the compression is no longer sufficient, the device should be recaptured
3. Test stability more than once if device stability is questionable

6. Device Release Criteria – Seal

**Residual flow around the device of ≤ 3mm acceptable**

- If residual jet around device noted - re-assess position, size or device orientation
  - If device not yet released, partial recapture and reposition or full recapture and replacement are possible

8. Final Device Release

- If all four P.A.S.S. release criteria are met, device can be released
- Advance WATCHMAN System to face of device, rotate deployment knob counter clockwise 3-5 full turns
- Perform final check of the following post device release:
  - Device position in all angles
  - Device compression and LAA sealing
- Perform check for pericardial effusion
- Consider performing repeat TTE prior to discharging the patient

**Device Compression Table**

<table>
<thead>
<tr>
<th>Device Size (uncompressed diameter)</th>
<th>Maximum (6%) Compression Measured Diameter</th>
<th>Minimum (8%) Compression Measured Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 mm</td>
<td>21 mm</td>
<td>16.8 mm</td>
</tr>
<tr>
<td>20 mm</td>
<td>24 mm</td>
<td>19.2 mm</td>
</tr>
<tr>
<td>23 mm</td>
<td>27 mm</td>
<td>21.6 mm</td>
</tr>
<tr>
<td>26 mm</td>
<td>30 mm</td>
<td>24.0 mm</td>
</tr>
<tr>
<td>29 mm</td>
<td>33 mm</td>
<td>26.4 mm</td>
</tr>
</tbody>
</table>

Images on file at Boston Scientific Corporation. Results in animal models may not necessarily be indicative of clinical outcomes.
The potential for device embolization exists with cardioversion <30 days following device implantation. Verify device position.

**WATCHMAN™ Post**

To prevent damage to the Delivery Catheter or device, do not allow the WATCHMAN Device to protrude beyond the distal tip of the Delivery Catheter when inserting the Delivery System into the Access Sheath.

If a patient remains on warfarin and aspirin 325mg daily and increase aspirin dosage to 300-325mg daily for six months post-implant.

If adequate seal is not demonstrated, term anticoagulation is determined to be contraindicated.

Patients ceasing warfarin should begin clopidogrel 75mg daily and increase aspirin dosage to 300-325mg daily indefinitely.

If LAA closure is satisfactory, patient should remain on 300-325mg aspirin daily indefinitely.

If a patient remains on warfarin and aspirin 81-100mg for at least six months post-implant, and then ceases warfarin, clopidogrel is not required, but aspirin should be increased to 300-325mg daily, taken indefinitely.

**Procedural Success**

Implant success defined as deployment and release of the device into the LAA; no leak ≥ 5mm.
**Favorable Procedural Safety Profile: All Device and/or Procedure-related Serious Adverse Events within 7 Days**

<table>
<thead>
<tr>
<th>Event</th>
<th>PROTECT AF</th>
<th>PREVAIL</th>
<th>CAP</th>
<th>CAP2</th>
<th>EWOLUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embolization related mortality</td>
<td>4.8%</td>
<td>3.8%</td>
<td>4.1%</td>
<td>4.1%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.8%</td>
<td>2.9%</td>
<td>2.8%</td>
<td>3.8%</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

**Favorable Procedural Safety Profile: Major Procedural Complications Across WATCHMAN Studies**

<table>
<thead>
<tr>
<th>Event</th>
<th>PROTECT AF 1st Half</th>
<th>PROTECT AF 2nd Half</th>
<th>CAP</th>
<th>PREVAIL</th>
<th>CAP2</th>
<th>EWOLUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device embolization</td>
<td>15 (0.6%)</td>
<td>5 (0.2%)</td>
<td>5 (0.2%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
<td>7 (0.15%)</td>
</tr>
<tr>
<td>Procedure-related stroke</td>
<td>9 (0.35%)</td>
<td>4 (0.15%)</td>
<td>9 (0.15%)</td>
<td>3 (0.35%)</td>
<td>5 (0.35%)</td>
<td>27 (0.46%)</td>
</tr>
<tr>
<td>Procedure-related mortality</td>
<td>9 (0.35%)</td>
<td>4 (0.15%)</td>
<td>3 (0.35%)</td>
<td>2 (0.35%)</td>
<td>5 (0.35%)</td>
<td>17 (0.32%)</td>
</tr>
</tbody>
</table>

**WATCHMAN Comparable to Warfarin for Ischemic Stroke**

- **Untreated AF:**
  - Ischemic Stroke Risk (events per 100 pt yrs)
- **WATCHMAN Arm:**
  - Ischemic Stroke Risk (events per 100 pt yrs)

**WATCHMAN Significant Reduction in Disabling Strokes (Patient-Level Meta-Analysis)**

- **Disabling/Fatal Strokes**
- **Non-Disabling Strokes**

- **HR 0.45 (0.21 - 0.94)**

- **P=0.03**

**Patient Level Meta-Analysis PROTECT AF, PREVAIL 5 Years**

- **All stroke or SE:**
  - **HR 0.60 (0.40 - 0.90)**
  - **P=0.003**

- **Ischemic stroke or SE:**
  - **HR 0.45 (0.24 - 0.86)**
  - **P=0.03**

- **Hemorrhagic stroke:**
  - **HR 1.50 (0.95 - 2.40)**

- **Hospitalization:**
  - **HR 1.50 (0.95 - 2.40)**

- **Non-Disabling Stroke:**
  - **HR 0.45 (0.24 - 0.86)**

- **Mortality:**
  - **HR 0.60 (0.40 - 0.90)**

- **HR 0.45 (0.24 - 0.86)**

- **P=0.03**

**10 Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. JACC 2017; 70(24): 2964-2975.**

*The EWOLUTION Registry is a European prospective registry which reflects CE Mark indications for use which differ from the FDA indications for use.*
Rate
55% reduction in disabling/fatal stroke, largely driven by
95% implant success rate
>92% warfarin cessation after 45 days, >99% after 1 year

WATCHMAN therapy demonstrated
80% reduction in hemorrhagic stroke
27% reduction in all cause mortality
41% reduction in CV/unexplained mortality

1.5% procedural complication rate
34 successful implants
38 attempted implants

Potential WATCHMAN Patient Populations

Total AFIB Population – 100% – 5,000,000
Non-Valvular AFIB Population – 95%* – 4,750,000

High Risk for Stroke (CHADS2 ≥ 2, CHA2DS2-VASC ≥ 2) – 75%

Cannot take any OAT

Contraindicated
208,600

Meaningless to not be on OAT

Intolerant
1,387,000

No issues with OAT therapy

Tolerant
2,180,900

WATCHMAN™ Clinical Leadership

• WATCHMAN is a safe alternative to long-term warfarin therapy which offers comparable stroke risk reduction and enables patients to stop taking warfarin
  • 95% implant success rate
  • 1.5% procedural complication rate
  • >92% warfarin cessation after 45 days
  • >99% after 1 year

• WATCHMAN therapy demonstrated comparable stroke risk reduction and statistically-significant reductions in disabling/fatal strokes, major non-procedure related bleeding and mortality compared to warfarin:
  • 56% reduction in disabling/fatal stroke, largely driven by
  • 80% reduction in hemorrhagic stroke
  • 72% reduction in major non-procedure related bleeding
  • 27% reduction in all cause mortality, largely driven by
  • 41% reduction in CV/unexplained mortality

Bleeding Outcomes after Left Atrial Appendage Closure Compared with Long-term Warfarin

Freedom of Major Bleeding Over 3 Adjunctive Pharmacotherapy Intervals

WATCHMAN is the Most Studied LAAC Device with Long-term Clinical Data

Results

Safety
WATCHMAN procedure is safe; ~1.5% complication rates

Primary Efficacy
WATCHMAN comparable to warfarin
18% reduction in events (p=0.27)

Stroke
WATCHMAN comparable to warfarin
95% reduction in disabling/fatal stroke (p=0.03), largely driven by
80% reduction in hemorrhagic stroke (p=0.003)

Mortality
WATCHMAN statistically significant to warfarin
27% reduction in all-cause mortality (p=0.04)
41% reduction in CV/unexplained mortality (p=0.03)

Major Bleeding
WATCHMAN statistically significant to warfarin post procedure
72% reduction after 6-months (p=0.001)

Warfarin Cessation
WATCHMAN allows the majority of patients to discontinue warfarin
92% of patients discontinue after 45-days; 99% of patients discontinue after 1 year

Implant Analytics

• 1st Successful Implant 4-9-18
  *Average Procedure Case Time 47 m
• 38 attempted implants
• 34 successful implants
• Total Patients Off OAC: 34
WATCHMAN FLX™: Designed to Broaden Treatment Matrix and Improve Ease of Use

- Designed for greatly enhanced stability and ease-of-use
- Designed for greater apposition to appendage wall
  - New anchor design, additional anchors and reduced main body taper
- Anticipate starting EU and U.S. clinical trials mid-year 2018

Caution: WATCHMAN FLX™ is an Investigational Device. Limited by Federal (or US) law to Investigational use only. Not available for sale.