Left Atrial Appendage Closure: Techniques and Guidelines

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May is Stroke Awareness Month
September is AF Awareness Month
1. Why is Left Atrial Appendage (LAA) closure important?
2. Anatomy of LAA
3. Relationship of LAA to Stroke
4. LAA Closure
   • Devices and procedure
   • Trials on LAA
5. Discussion
6. Conclusion
LAA Closure for Stroke Prevention in AF: Why is it important?

- **700-800,000 Strokes per year in the USA**
- **25% of these are due to embolic events from the left atrium from AF (175-200,000)**
- **Of these 25%, 80-90% originate from the left atrial appendage (160-180,000)**
- **Approximately 15% of patients with AF have left atrial thrombus**
- **Almost 25% of patients who are on warfarin or other oral anticoagulants never took the drug or stopped a medication**
- **Do not underestimate LAA: An underrecognized trigger site of AF. Approximately 20% of AF ablation recurrences are due to the LAA site (Circ 2010;122:109-18)**
Left Atrial Appendage Exclusion
Historical Perspective

• 1949: Adjunct to cardiac surgery
• 1980s: Cox preformed an LAA amputation along with the maze “cut-and-sew” of the left atrium
• 1999: Cox reported 0.6% annualized rate of stroke in patients who were not treated with oral anticoagulants
• 2002: First successful LAA closure device implanted (PLAATO)
• 2005: Watchman device first used and approved in Europe
• 2015: Watchman device approved in United States
• 2003: Blackshear reported on video-assisted thoracoscopic surgical isolation/resection of LAA to prevent stroke
Thromboembolic Stroke

Other Sources of Cardiac Embolism
More than AF and its Type

- Intracranial Atherosclerosis
- Carotid Plaque with Emboli
- Aortic Arch Plaque
- Cardiogenic Emboli
- Small Artery Disease
- Carotid Stenosis
- Atrial Fibrillation
- Patent Foramen Ovale
- Valve Disease
- Ventricular Thrombi

Shenasa 2016
Sources of Cardioembolic Stroke

- Nonvalvular AF: 50%
- Acute MI: 10%
- Ventricular Thrombus: 10%
- Prosthetic Valves: 10%
- Rheumatic Heart Disease: 5%
- Other: 15%
LAA as a Target for Reducing Strokes

Background (1/2)

• One of six strokes occurs in patients with AF
• Among patients in whom a thrombus is found, 90% are located in the LAA
• Antiarrhythmic drugs, even when effective in reducing AF, have not been shown to reduce stroke
• Anticoagulation remains the mainstay to reduce stroke risk in AF; Warfarin reduces the incidence of stroke by 60-70% when compared to no anticoagulation and 30-40% when compared to ASA
LAA as a Target for Reducing Strokes

Background (2/2)

- There are significant limitations with Warfarin use including:
  - Hemorrhagic stroke
  - High prevalence of sub therapeutic anticoagulation
  - Narrow therapeutic window
  - Need for close monitoring
  - Various diet and drug interactions
- Because of this, novel surgical and percutaneous therapies have been developed targeting the LAA

Syed F, et al. Heart Rhythm 2011;8(2)
Questions about LAA Closure

1. Which patient would benefit from a LAA closure device?

2. Are LAA closure devices any better than oral anticoagulants?

3. How to avoid complications during LAA exclusion devices?

3. What are the current guidelines?
Embryology and Morphology of Cardiac Chambers

Pan J, Baker KM. Vitam Horm 2007;75:259
Embryology of LAA

Left Atrium and LAA Anatomy
Left Atrium and LAA Anatomy

(a) [Image of anatomical structures]
(b) [Image of anatomical structures]
(c) [Image of anatomical structures]
(d) [Image of anatomical structures]
(e) [Image of anatomical structures]
Imaging
Thrombogenic Structures

Courtesy of Maxim Didenko
Left Atrial Appendage Closure
LCx artery and LAA
Does the Shape Matter?

Cactus LAA Morphology

Chicken Wing LAA Morphology

Windsock LAA Morphology

Cauliflower LAA Morphology
### Cardiac CCTA Measurements of LAA Anatomic Variation

<table>
<thead>
<tr>
<th>Shapes</th>
<th>Watchman</th>
<th>Amplatzer</th>
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<tbody>
<tr>
<td>Cauliflower</td>
<td><img src="image1" alt="Image" /></td>
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</tr>
<tr>
<td>Windsock</td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
</tr>
<tr>
<td>Chicken Wing</td>
<td><img src="image5" alt="Image" /></td>
<td><img src="image6" alt="Image" /></td>
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<tr>
<td>Cactus</td>
<td><img src="image7" alt="Image" /></td>
<td><img src="image8" alt="Image" /></td>
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</table>

# Dimensions of LAA in Human

<table>
<thead>
<tr>
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<th>Human (n=19)</th>
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<tbody>
<tr>
<td>LAA Length</td>
<td>39.6 ± 6.8</td>
</tr>
<tr>
<td>LAA ostium long-axis diameter</td>
<td>15.3 ± 3.6</td>
</tr>
<tr>
<td>LAA ostium short-axis diameter</td>
<td>8.0 ± 1.8</td>
</tr>
<tr>
<td>Distance from LAA ostium to LCX</td>
<td>2.4 ± 0.8</td>
</tr>
<tr>
<td>Distance from LAA ostium to LAD</td>
<td>10.7 ± 2.0</td>
</tr>
<tr>
<td>Distance from LAA ostium to LSPV</td>
<td>9.5 ± 1.7</td>
</tr>
<tr>
<td>Distance from LAA ostium to MV annulus</td>
<td>10.0 ± 1.8</td>
</tr>
</tbody>
</table>
Prevalence of Prior Stroke/TIA According to Different LAA Morphologies

- **Chicken Wing**: OR 0.2 (0.04-0.8)
- **Windsock**: OR 1.1 (0.4-3.2)
- **Cactus**: OR 2.5 (1.0-6.1)
- **Cauliflower**: OR 2.0 (0.2-7.2)
Multivaraible Analysis

- After controlling for CHADS2 score, gender, and AF type
- **Non Chicken Wing** was found to have prior TIA/ stroke 2.95 (95% CI 1.75-4.99, p=0.041).
- Compared to chicken wing:
  - Cactus had 4 times (OR 4.1, 95%, p= 0.046),
  - Windsock- 5 times (OR 4.8, p=0.038), and
  - Cauliflower 8 times (OR 8.0, p=0.056) **more likely to have prior stroke/TIA**

Di Biase, Natale, Gaita et al JACC 2012
Imaging Techniques for LAA Closure

- Transesophageal Echocardiogram (TOE): Gold standard
- Cardiac CT
- Cardiac MRI
Imaging for LAA Closure
Imaging Conclusions

• 2D and 3D TEE are central imaging tools in patients undergoing LAA obliteration procedures
• Patient selection:
  • LAA morphology and function
  • LAA thrombus and sludge
  • Other potential sources of emboli
• Procedure guidance:
  • Transseptal puncture
  • Catheters and device navigation
  • Device deployment
• Post-procedure:
  • Device stability
  • Demonstration of LAA obliteration
  • Recognition and management of complications
Current Devices for LAA Closure

Watchman

PLAATO

Amplatzer Cardiac Plug

LARIAT
Left Atrial Appendage
Watchman Device Implantation

PROTECT-AF Trial Design: Randomized, non-inferiority trial

- Multicenter, randomized, non-inferiority, 2:1
- Watchman Device

**Inclusion Criteria**
- Nonvalvular AF
- Previous stroke or TIA
- Congestive heart failure
- Diabetes

**Exclusion Criteria**
- Contraindicated to Warfarin
- LAA thrombus
- PFO
- Right to left shunt
- Hypertension
- ≥ 75 years
- INR: 2.0-3.0
- CHADS2 risk score of 1 or more
- Aortic atheroma
- Symptomatic carotid artery disease
PROTECT-AF Trial Design: Randomized, non-inferiority trial

- **Randomized n=707**
  - **Device n=463**
    - Included in subset n=361
      - Had both baseline and 12 month QOL n=349
      - Died before 12 months n=12
      - Not included n=102
  - **Control N=244**
    - Included in subset n=186
      - Had both baseline and 12 month QOL n=178
      - Died before 12 months n=8
      - Not included n=58

Died before 12 months n=8
Not included n=58
PROTECT-AF Trial Design:
Randomized, non-inferiority trial
Multicenter, randomized, non-inferiority, 2:1

Results
Total Patients: 707

Device
- 463 patients (14 not attempted)
  - 41 unable to implant
  - 408 successful implantation
  - 349 stopped warfarin at 45 days
  - 45-day follow-up 396/408 (92%) able to DC warfarin based on TEE results

Control/warfarin
- 244 patients
  - 3 did not take warfarin
  - 241 randomized

PROTECT-AF Trial Design: Randomized, non-inferiority trial

Multicenter, randomized, non-inferiority, 2:1

Complications

Device
- Pericardial effusion [22 (4.8%)]
- Hemorrhagic stroke
- Death (21)

No deaths were related to LAA closure device
No patients with pericardial effusion died

Control
- Hemorrhagic stroke (6)
- Death (18)

Death was due to hemorrhagic stroke

PROTECT-AF Trial Design: Randomized, non-inferiority trial

Multicenter, randomized, non-inferiority, 2:1

Conclusion

• Efficacy of LAA device was not inferior to that of Warfarin
• Higher rate of safety event observed in intervention group compared to control group
Deployment of Watchman Device

(A) Initial LAA angiogram obtained through a pigtail catheter inserted via a sheath in the LAA.
(B) Sheath advancement into the LAA with the WATCHMAN inside.
(C) Deployment of the WATCHMAN in the LAA.
Deployment of Watchman Device

(D) LAA angiogram to verify position of initial deployment in the LAA neck.
(E) Release of the WATCHMAN.
(F) Final angiogram.
Complications of Watchman Device
Conclusion of PROTECT-AF

1. LAA closure with Watchman device was not inferior to embolic stroke prevention in AF with Warfarin and cardiovascular death.
2. Outside the periprocedural complications of device implantation, mainly pericardial tamponade and procedure-related stroke.
3. The successful deployment of LAA closure device was superior to well-controlled systemic anticoagulation.
4. At this point, the ESC guidelines on LAA closure devices has given a class IIb recommendation.
5. At a 4 year follow-up, there was a 40% relative risk reduction in the Watchman compared to control group.
6. Currently, Watchman is the most studied device for LAA closure.
PREVAIL Trial

Implant – 45 day
Warfarin: dosage to achieve INR 2.0-3.0
Aspirin: 81 mg while on warfarin
Clopidogrel: No

45 day – 6 months
Warfarin: No
Aspirin: 325 mg*
Clopidogrel: Yes

6 months – 5 years
Warfarin: No
Aspirin: 325 mg*
Clopidogrel: No

NO LAA seal per 45 day TEE

NO LAA seal per 45 day TEE

45 day – 6 months
Warfarin: Yes
Aspirin: 81 mg while on warfarin
Clopidogrel: No

45 day – 6 months
Warfarin: No
Aspirin: 325 mg*
Clopidogrel: No

6 months – 5 years
Warfarin: Discontinued when seal is adequate
Aspirin:
On warfarin -81 mg
Off warfarin – 325 mg* indefinitely
Clopidogrel: No
Conclusions

• The Watchman device was not inferior to warfarin for primary efficacy
• The Watchman device was noninferior for occurrence of late ischemic events, such as ischemic stroke, systemic embolism, etc.
• The overall event rates with warfarin were significantly lower
Watchman Device Registry: EWOLUTION

- Total number of patients: 1021
- Average CHADS\textsubscript{2} score 2.8 ± 1.3
- Average CHA\textsubscript{2}DS\textsubscript{2}-VASc: 4.5 ± 1.6
- Average HAS-BLED Score: 2.3 ± 1.2
- Risk Profile (45.4%)
  a. TIA
  b. Ischemic stroke
  c. Hemorrhagic stroke
  d. 62% of patients unsuitable for anticoagulation therapy
- LAA closure device successfully deployed in 98.5%
- Minimal residual flow in 99.3% of patients
- 30 day overall mortality rate was 0.7%
Conclusions

Thromboembolism in AF is a major cause of morbidity and mortality

– Oral anticoagulation is effective, but many cannot tolerate due to bleeding risk

Robust clinical program in place to study Watchman LAA Closure Device

**PROTECT AF**

- WATCHMAN non-inferior to warfarin in patients at high-risk of thromboembolism with a trend toward improved outcomes
- Long-term data showed continued significant reductions in events when compared to warfarin

**PREVAIL trial**

- Despite implantation in higher risk patients, the WATCHMAN device was safely implanted by new operators

**CAP**

- WATCHMAN was deemed to be a viable and novel option for the reduction of stroke in high-risk non-valvular AF patients

1 Reddy, et al., Circulation 2013; 127:720–72
2 PREVAIL results from Holmes, DR Jr et al., CIT 2013
# TEE and Angiogram of LAA Before and After Device Implantation

<table>
<thead>
<tr>
<th>Pre-Implantation</th>
<th>Post-Implantation</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="A" /></td>
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<td><img src="image7.png" alt="G" /></td>
<td><img src="image8.png" alt="H" /></td>
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**Watchman**

**Amplatzer Cardiac Plug**

Watchman Device Implantation

Patient Selection for Watchman Left Atrial Appendage Closure

Non-Valvular AF

- Thromboembolic risk (CHA$_2$DS$_2$-VASc ≥2) AND Bleeding risk (HAS-BLED ≥3)
- Recurrent bleeding on anticoagulant therapy
- Contraindication on anticoagulant therapy
- Intolerant to anticoagulant therapy
- Prior stroke/TIA while on anticoagulant therapy
- Persistent non-compliance to anticoagulant therapy
- Unwilling to take anticoagulant therapy

LAAC Therapy

The LARIAT Device
Fluoroscopic Guidance to Assistant in the Closure of LAA (LARIAT)
LARIAT


Shenasa 2016
Amplatzer Cardiac Plug
Amplatzer Cardiac Plug

Left Atrial Appendage Closure
Amplatzer Cardiac Plug

# Ongoing and Future Trials on LAA Closure

<table>
<thead>
<tr>
<th>Trial</th>
<th>Estimated # Patients</th>
<th>Intervention</th>
<th>Type</th>
<th>Primary Endpoint</th>
<th>Estimated Completion Date</th>
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<tr>
<td>LAAOSIII</td>
<td>4700</td>
<td>LAA suture/surgical stapler</td>
<td>Randomized</td>
<td>Stroke/systemic arterial embolism</td>
<td>May 2019</td>
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<tr>
<td>SELAAOD</td>
<td>850</td>
<td>LARIAT or Watchman</td>
<td>Observational case control</td>
<td>LAA occlusion by LARIAT or Watchman</td>
<td>May 2018</td>
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<tr>
<td>Amplatzer Cardiac Plug Clinical Trial</td>
<td>3000</td>
<td>Amplatzer Cardiac Plug</td>
<td>Randomized</td>
<td>Acute safety; long-term safety</td>
<td>June 2017</td>
</tr>
<tr>
<td>PLACE III</td>
<td></td>
<td>LARIAT</td>
<td></td>
<td>Withdrawn</td>
<td></td>
</tr>
</tbody>
</table>
Recent Device for LAA Closure

WaveCrest
Possible Indications for LAA Closure

Patients with AF at high stroke risk with:

- High risk (or recurrence) of bleeding under (N)OAC due to-
  - Uncontrolled, severe hypertension
  - Coagulopathies, low platelet counts, myelodysplastic syndrome (MDS)
  - Inherited bleeding disorder-Von Willebrand disease, hemophilia
  - Severe hepatic or renal dysfunction-eg, alcoholic liver cirrhosis
  - Vascular disease or malformations-eg, intestinal angiodysplasia, Osler-Weber-Rendu previous intracerebral hemorrhage, cerebral microbleeds (amyloid angiopathy), retinal vasculopathy
- High probability of therapeutic non-compliance to (N)OAC
- Intolerance to (N)OAC drugs-GL intolerance, severe liver/kidney dysfunction, drug interactions
- Insufficiently treatable GI disease with bleeding-eg, neoplastic disease, intestinal angiodysplasia
- Recurrent nephrolithiasis
- High probability of frequent and/or severe traumas-eg, epilepsy, in the elderly

Contraindications for LAA Closure

- Low risk for stroke CHA\textsubscript{2}DS\textsubscript{2}-VASC=0
- Valvular heart disease (i.e. mitral stenosis)
- Other indications for long-term or lifelong OAC-
  mechanical prosthetic valve, pulmonary embolism
  and deep vein thrombosis, thrombi in the left atrium
  or ventricle
- Contraindications for transseptal catheterization-left
  atrial thrombus or tumor, active infection,
  uncooperative patient, (presence of ASD/PFO
  closure device)

ASD-atrial septal defect; LAA-left atrial appendage;
OAC-oral anticoagulants; PFO-patent foramen ovale
Possible Complications for LAA Closure

- Pericardial effusion with tamponade:
  - 5.2% (Watchman)
  - 3.7-10.4 (LARIAT)
- Cardiac perforation
- Device embolization:
  - Incorrect sizing
  - Device deployment
- Device thrombosis (formation):
  - 2-5% of cases
  - Exposure of foreign material
  - 4.2% (PROTECT-AF)
  - 4.8% (LARIAT)
- Stroke/TIA-thromboembolism, air embolism

- Residual flow/leak:
- Incomplete closure
- Chest pain/pericarditis
- Vascular complications
  - Hematoma
  - Bleeding
  - AV fistula formation
- Alteration of neighboring structures
  - LUPV
  - Mitral valve
  - LCX artery
Atrial fibrillation patient with indication for OAC for stroke/embolism prevention (CHA₂DS₂-VASc>1)

- Suitable for OAC
  - OAC, preferable NOAC
    - Mention LAA occlusion
- Increased risk for bleeding
  - HAS-BLED score ≥3
  - Need for a prolonged triple anticoagulation therapy (e.g., recent coronary stents)
  - Increased risk not reflected by the HAS-BLED score (e.g., thrombopenia, cancer, or risk of tumor associated bleeding in case of systemic OAC)
  - Renal failure (severe) as contraindication to NOAC
- Individual risk/benefit evaluation for (N)OAC vs. alternative methods
- Acceptable risk for systemic (N)OAC?
  - No treatment vs. LAA occlusion
- Patient refusal of OAC despite adequate information
- Advise NOAC
  - NOAC
- 1. Contraindication for systemic (N)OAC
  2. Refusing systemic (N)OAC after adequate information and physicians advice
- LAA occlusion (includes the need for antiplatelet therapy)
Guidelines

EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion

SOCIETAL OVERVIEW

2015 ACC/HRS/SCAI Left Atrial Appendage Occlusion Device Societal Overview

A Professional Societal Overview from the American College of Cardiology, Heart Rhythm Society, and Society for Cardiovascular Angiography and Interventions

Frederick A. Masoudi, MD, MSPH, FACC, Chair*
Hugh Calkins, MD, FACC, FHRS, Vice-Chair†
Clifford J. Kavinsky, MD, PhD, FACC, FSCAI, Vice-Chair†
Joseph P. Drozda, Jr, MD, FACC*
Phillip Gainsley§

David J. Slotwiner, MD, FHRS, FACC†
Zoltan G. Turi, MD, FACC, MSCI‡

*American College of Cardiology representative. †Heart Rhythm Society representative. ‡Society for Cardiovascular Angiography and Interventions representative. §Patient representative.
CLASS IIa

1. For patients with AF or atrial flutter of 48 hours' duration or longer or of unknown duration who have not been anticoagulated for the preceding 3 weeks, it is reasonable to perform transesophageal echocardiography before cardioversion and proceed with cardioversion if no left atrial thrombus is identified, including in the left atrial appendage, provided that anticoagulation is achieved before transesophageal echocardiography and maintained after cardioversion for at least 4 weeks (114). *(Level of Evidence: B)*

3.4. Cardiac Surgery—Left Atrial Appendage Occlusion/Excision: Recommendation

CLASS IIb

1. Surgical excision of the left atrial appendage may be considered in patients undergoing cardiac surgery. *(Level of Evidence: C)*
Potential Patient Selection

• The current ESC guidelines on AF management recommend that percutaneous LAAC “may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.” (Class II b)
## ESC Guidelines for LAA Closure

### Recommendations for LAA closure/occlusion/excision

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref&lt;sup&gt;c&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.</td>
<td>IIb</td>
<td>B</td>
<td>115, 118</td>
</tr>
<tr>
<td>Surgical excision of the LAA may be considered in patients undergoing open heart surgery.</td>
<td>IIb</td>
<td>C</td>
<td></td>
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</tbody>
</table>

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<sup>a</sup> Class of evidence

<sup>b</sup> Level of recommendation

<sup>c</sup> References

Conclusion: Comparison between Watchman and warfarin

1. The use of Watchman device caused fewer hemorrhagic strokes compared to warfarin (p=0.004)
2. BUT; there were more ischemic strokes in the Watchman group compared to chronic warfarin therapy (p=0.005)
3. Patients assigned to Watchman device had fewer cardiovascular deaths (p=0.006)
4. BUT there was no difference in all-cause mortality between the two groups
Left Atrial Appendage Closure for Stroke Prevention in AF:

Cost of Stroke

- In 2007, cost of stroke was $25 billion in the US
- Mean lifetime cost of stroke is $140,000 per patient
- In 2005, cost of stroke was €22 billion in Europe
- In 2015, cost of stroke was $34 billion in the US

New Developments in Stroke Prevention in AF

1. New oral anticoagulants (NOACS)
2. LAA closure devices
Cost-Effectiveness of LAA Closure Devices

- The long-term oral anticoagulation was:
  - $46,560 per quality-adjusted life year with dabigatran
  - $41,565 per quality-adjusted-life year with LAA closure device
- Any cost below $50,000 per quality-adjusted-life year is currently accepted as cost-effective

Risk Benefits

LAA Closure

Benefits
• Less embolic complications
• No adherence required
• Cost-effective

Risks
• Many patients have to continue on OAC

Anticoagulation

Benefits
• Covers other sources of embolic complications

Risks
• Risk of hemorrhagic stroke is higher
• Poor patient compliance

Shenasa 2016

Maisel W. NEJM 2009;360:25
Summary

1. Percutaneous LAA closure has been reported to reduce ischemic stroke rate in high risk AF patients.
2. The results of the randomized controlled PROTECT-AF with the Watchman device suggested that this procedure is noninferior to Warfarin in the prevention of stroke.
3. Careful patient selection and risk benefits as well as cost-effectiveness should be considered when choosing this procedure.

AF Treatment Options

AF

Ablation*

Pacing

Drugs for Rhythm/Rate Control

AND/OR

Embolic Management

Interventions

Surgical Ligation

LAA Clips

Endovascular LAA

Drugs

AND/OR

Drugs (warfarin)

Drugs (dabigatran, rivaroxaban, apixaban)

* BSC currently has no ablation catheters FDA-approved for the treatment of AF
Thank You!