Yale Cardiovascular Research Group

DOCUMENT APPROVAL FORM

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Accepted for Yale Cardiovascular Research Group	**Accepted for Sponsor Representative of the Trial**
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Yale Cardiovascular Research Group
Yale Echocardiographic Core Lab

Transesophageal Echocardiography (TEE)

Image Acquisition Protocol Guidelines

The CONFORM Pivotal Trial

An Evaluation of the Safety and Effectiveness of the Conformal Left Atrial Appendage Seal for Left Atrial Appendage Occlusion

Sponsor: Conformal Medical, Inc.
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Table of Contents

1.0 General Instructions to Site

The following TEE Imaging Protocol is guidance from the Yale Echocardiographic Core Lab that was written specifically for the CONFORM Trial to visualize the CLAAS device and control devices using transesophageal echocardiography (TEE). In order to obtain complete imaging of the device for patients in this trial, all efforts should be made to obtain images at every angle (0, 45, 90 & 135-degrees), as specified in this protocol.

- Confirm 3-beat loops for subjects in sinus rhythm. 3-second loops for arrhythmias and tachycardia.
- Color Flow Doppler: Optimize frame rate (>=20fps) for temporal resolution. Ensure gain setting is appropriate.
- Spectral Doppler: Sweep speed should be 75-100mm/s. 3-beat spectral acquisition for subjects in sinus rhythm, 5-beat acquisition for arrhythmias.
- Nyquist limit of LAA at 40cm/sec and valvular assessment at 60cm/sec.
- All images for the core lab should be recorded in single-plane, unless otherwise specified.
- **DICOM images *AND* Sonographer Worksheets for Index Procedure and Follow-Up should be uploaded to the EDC.**
- **PLEASE ENSURE ALL PHI HAS BEEN REMOVED FROM IMAGES PRIOR TO UPLOAD!**

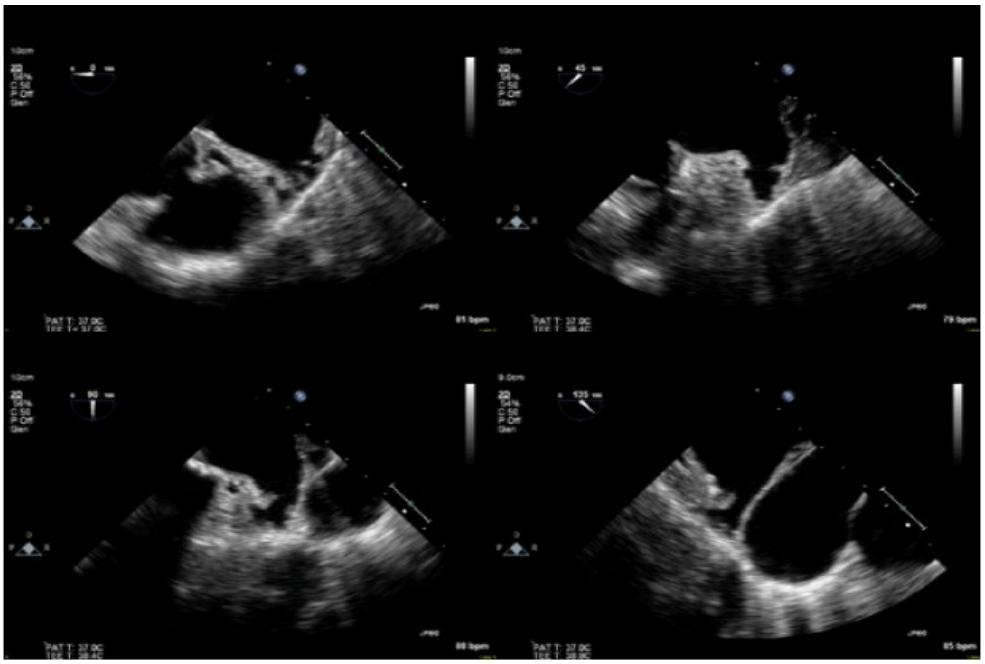
2.0 Two-Dimensional TEE Echocardiography Guide

2.1 Pre-Procedural Imaging (TEE 1: Baseline)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

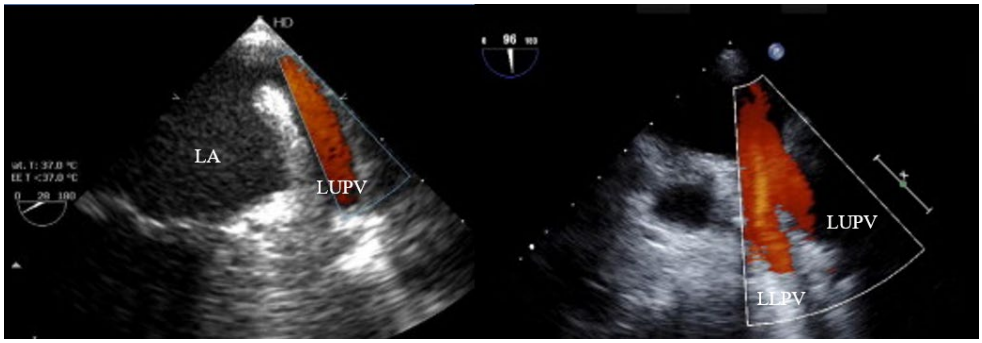
2.1.1 Two-Dimensional Imaging of Left Atrium/Left Atrial Appendage

Two-dimensional imaging of the left atrial appendage is at the level of the aortic valve (AoV). Once the AoV is visualized, anteflexion of the transducer is performed to obtain the LAA and evaluation is done from 0^0 – 180^0. Images of the LAA are acquired at 0^0, 45^0, 90^0, and 135^0.



2.1.2 Pulsed-Wave (PW) and Color Flow Doppler of Left Pulmonary Veins

Assess Left Upper Pulmonary Vein (LUPV) and Left Lower Pulmonary Vein (LLPV).
Increased maximum PV Doppler flow velocity (>1.1m/s) combined with color flow Doppler turbulence may be a reliable index[7] for diagnosing pulmonary vein stenosis.

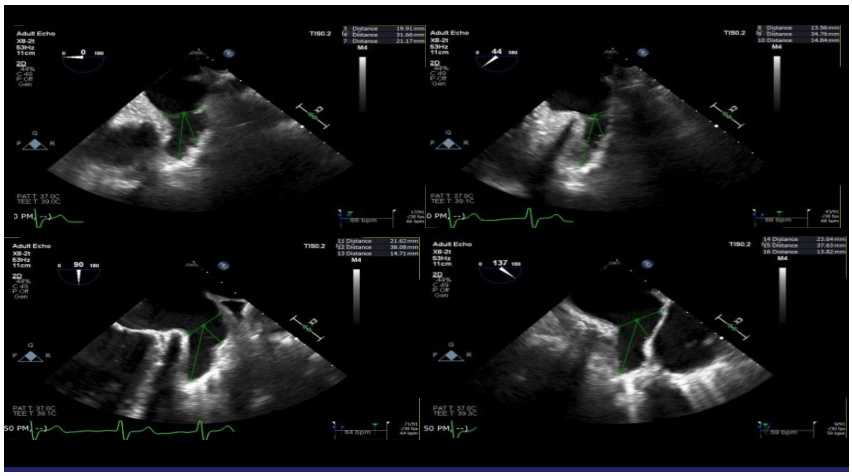


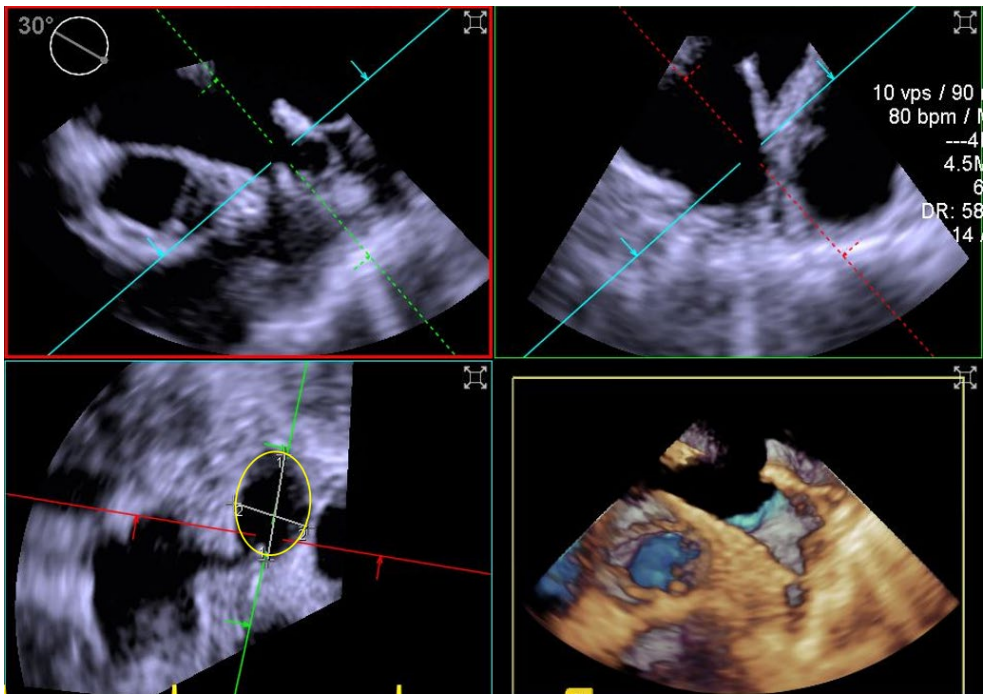
Cartwright, Bruce MBBS, et al Intraoperative Pulmonary Vein Examination by Transesophageal Echocardiography: An Anatomic update and Review of Utility. Journal of Cardiothoracic and Vascular Anesthesia. Volume 27, Issue 1, February 2013, Pages 111-120

2.1.3 LAA Ostium Diameter and LAA Depth

Sweep through LAA views to ascertain the largest diameter and longest depth of the LAA. Measurements are documented at 0^0, 45^0, 90^0, and 135^0. The 3D image of the LAA should be taken from a wide-angled view at 45^0. The perpendicular depth measurement should be made from the ostial plane to the shortest distance to any anatomic structure. The maximal depth is measured from the ostial plane to the most distal aspect of the LAA.

Implant Size	Mean LAA Ostium Diameter (D_{max} + D_{min}) / 2	LAA Ostium Diameter Range	Minimum Landing Zone
Regular	≤ 25mm	10 – 33mm	10mm
Large	≤ 32mm	20 – 40mm	10mm

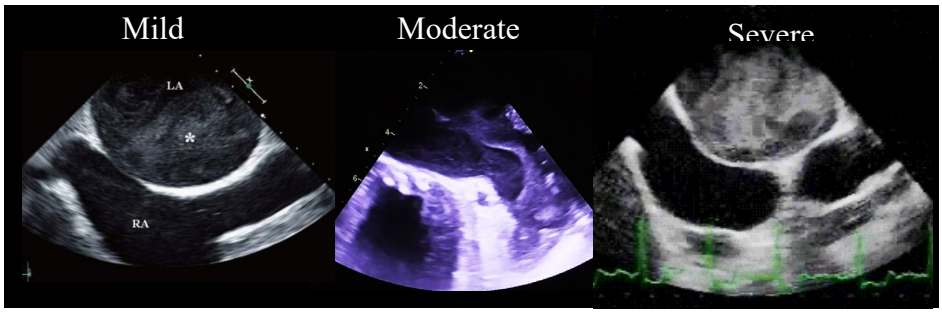




2.1.4 LAA Spontaneous Echocardiographic Contrast (SEC)

Will be assessed from the images acquired. Please optimize gains. The following grading will be used:

a. Absence of echogenicity
b. Mild (minimal echogenicity, only transiently detectable with optimal gain settings during the cardiac cycle)
c. Moderate (dense swirling pattern throughout the cardiac cycle)
d. Severe (intense echo density and very slow swirling patterns in the left atrial appendage, usually with similar density in the left atrium)[6]



Kim, Tae-Seok, MD Role of Echocardiography in Atrial Fibrillation J Cardiovasc Ultrasound. 2011 Jun; 19(2): 51–61.

Echocardiography step by step

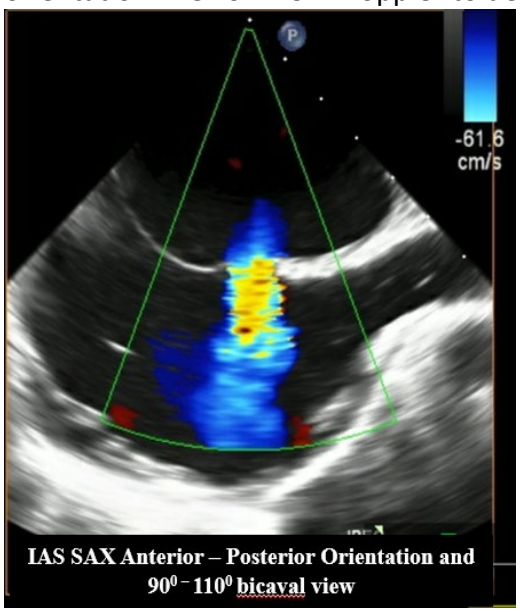
https://drsvenkatesan.com/2011/04/10/a-hurricane-inside-left-atrium/

2.1.5 Intracardiac Thrombus/Vegetation/Mass

A thorough investigation of all cardiac chambers, valves, structures with specific attention to LAA should be performed to rule out intracardiac thrombus, vegetation, or mass.

2.1.6 Atrial Septum

Image atrial septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

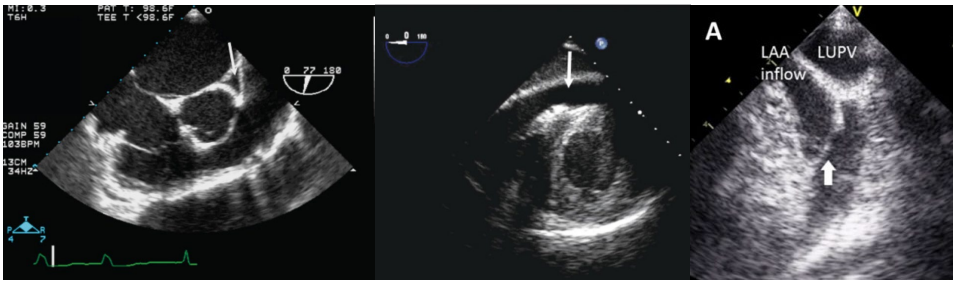


IAS SAX Anterior – Posterior Orientation and $90^0 - 110^0$ bicaval view

2.1.7 Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and <1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width



https://thoracickey.com/wp-content/uploads/2016/06/B9781455707614000232_f23-02-9781455707614.jpg

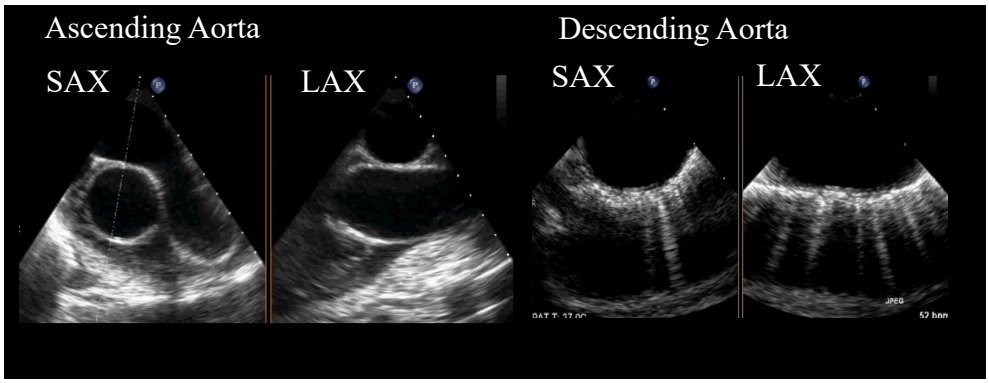
Kamperidis, V et al. "Left Atrial Appendage Pericardial Fluid: Contrast-Enhanced Transesophageal Echocardiography Makes It Visible." Hippokratia20.3 (2016): 235–237. Print.

2.1.8 Mitral Valve

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve. Image from ME4, ME3, and ME2.

2.1.9 Aortic Atheroma/Plaque

Image UE 120-150^0 to assess ascending Ao LAX, UE 0^0 ascending Ao SAX, ME 0^0 descending Ao SAX, ME 90^0 descending Ao LAX Document location and extent of atheroma if present.



2.2 Pre-Release Device Assessment (TEE 2: Pre-Release)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

2.2.1 Assess Device

Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥ 20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.2.1.1 Position

Identify and document the position of the LAAO device, prior to tug test.

Tug Test: Annotate "TUG". Acquire dynamic clip(s) during the tug test showing tether insertion (device apex), in a dedicated viewing angle. Reassess the position of the LAAO device at the conclusion of the tug test.

2.2.1.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.2.1.3 Thrombus

Perform a full cardiac scan to investigate for SEC and/or thrombus with specific attention to the implanted device. If thrombus is suspected, optimize imaging and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.3 Post-Release Device Assessment (TEE 3: Post-Release)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

2.3.1 Assess for Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will

be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and < 1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width

2.3.2 Assess Device

Annotate "POST-RELEASE". Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.3.2.1 Position

Identify and document the position of the LAAO device.

2.3.2.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.3.2.3 Thrombus

Perform a full cardiac scan to investigate for SEC and / or thrombus, with specific attention to the implanted device. If thrombus is suspected, optimize imaging, and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.3.2.4 Assess Device for 3D

The 3D image of the LAAO device should be taken from a wide-angled view at 45^0. If performed per SOC, please provide the 3D raw image file for Core Lab assessment.

2.3.3 Left Pulmonary Vein Assessment

Acquire loops of 2D and color flow Doppler of the LUPV and LLPV. Acquire PW spectral Doppler in the pulmonary vein (1cm inside the PV).

2.3.4 Assess Atrial Septum

Image Atrial Septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

2.3.5 Mitral Valve Assessment

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve.
Image from ME4, ME3, and ME2.

2.4 Follow-Up TEE:

2.4.1 Assess for Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and < 1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width

2.4.2 Assess Device

Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.4.2.1 Position

Identify and document the position of the LAAO device.

2.4.2.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.4.2.3 Thrombus

Perform a full cardiac scan to investigate for SEC and/or thrombus, with specific attention to the implanted device. If thrombus is suspected, optimize imaging and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.4.2.4 Assess Device for 3D

The 3D image of the LAAO device should be taken from a wide-angled view at 45^0. If performed per SOC, please provide the 3D raw image file for Core Lab assessment.

2.4.3 Left Pulmonary Vein Assessment

Acquire loops of 2D and color flow Doppler of the LUPV and LLPV. Acquire PW spectral Doppler in the pulmonary vein (1cm inside the PV).

2.4.4 Assess Atrial Septum

Image atrial septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting (ASD or PFO) in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

2.4.5 Mitral Valve Assessment

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve. Image from ME4, ME3, and ME2.

3.0 Abbreviations

1. **2DE or 2D** - Two-Dimensional Echocardiography
2. **Ao** - Aorta
3. **AoV** - Aortic Valve
4. **ASD** – Atrial Septal Defect
5. **ASE** - American Society of Echocardiography
6. **CLAAS™** - Conformal Left Atrial Appendage Seal
7. **cm** – centimeter
8. **cm/s** – centimeters per second
9. **CW**- Continuous Wave Doppler
10. **DTG** – Deep Transgastric
11. **ePTFE** - expanded polytetrafluoroethylene
12. **fps** – frames per second
13. **IAS** - Interatrial Septum
14. **LA** - Left Atrium
15. **LAA** – Left Atrial Appendage
16. **LAAO** – left Atrial Appendage Occlusion
17. **LAX** – Long Axis
18. **LE** – Lower Esophageal
19. **LLPV** – Left Lower Pulmonary Vein
20. **LUPV** – Left Upper Pulmonary Vein
21. **LV** - Left Ventricle
22. **ME** – Mid Esophageal
23. **mm** – millimeter
24. **m/s** – meters per second
25. **PFO** – Patent Foramen Ovale
26. **PW** - Pulsed Wave Doppler
27. **s** - seconds
28. **SAX** – Short Axis
29. **SEC** – Spontaneous Echocardiographic Contrast
30. **TEE** – Transesophogeal Echocardiography
31. **TG** - Transgastric
32. **UE** – Upper Esophageal
33. **TEE** – Transesophogeal Echocardiography

4.0 References

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2. Rudski, L, et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography. J Am Soc Echocardiogr 2010; 23:685-713.
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7. Pazos-López, Pablo et al. "Pulmonary Vein Stenosis: Etiology, Diagnosis and Management." *World Journal of Cardiology* 8.1 (2016): 81–88. *PMC*. Web. 3 July 2018.
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12. Main, Michael L. et al, Assessment of Device-Related Thrombus and Associated Clinical Outcomes With the WATCHMAN Left Atrial Appendage Closure Device for Embolic Protection in Patients With Atrial Fibrillation (from the PROTECT-AF Trial) American Journal of Cardiology, Volume 117, Issue 7, 1127 - 1134

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CONFORM Pivotal Trial_DAF_TEE Imaging Aquisition Protocol_V6.0_12Mar2024

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