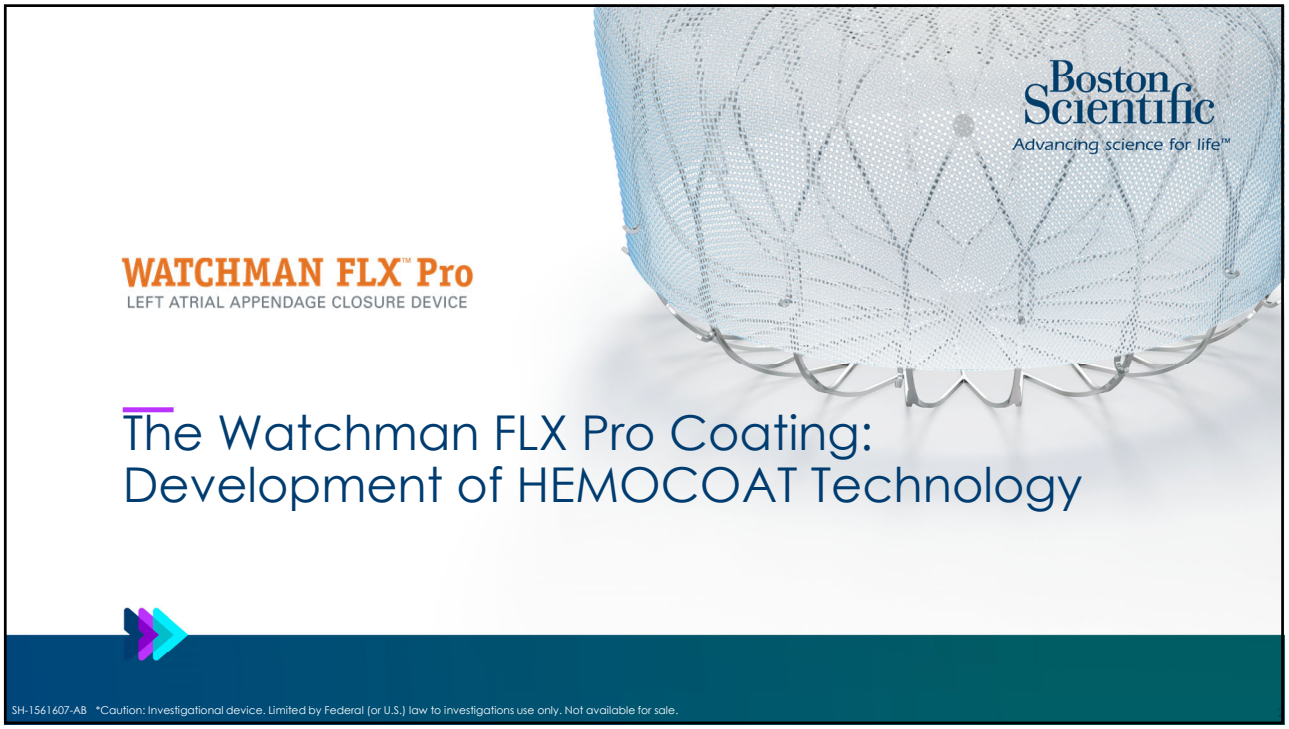

Minneapolis
Heart Institute
Foundation
GRAND ROUNDS

1


Boston
Scientific
Advancing science for life™
WATCHMAN FLX™ Pro
LEFT ATRIAL APPENDAGE CLOSURE DEVICE
The Watchman FLX Pro Coating:
Development of HEMOCOAT Technology
SH-1561607-AB *Caution: Investigational device. Limited by Federal (or U.S.) law to investigations use only. Not available for sale.

2

WATCHMAN FLX Pro Device

Boston Scientific

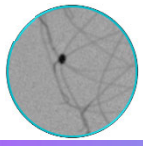
Brian

Built on the proven performance of the WATCHMAN FLX platform, **the Next Gen WATCHMAN FLX** is designed to **improve the healing response, simplify placement,** while further **expanding the treatable patient population.**

Design Goals

Hemocompatible Coating
Reduce the severity of acute foreign body response, encouraging controlled healing

40mm Size
Expand matrix to treat the largest range of patient anatomies



Radiopaque Markers
Increase fluoroscopic visibility for positioning & deployment

SH-1612012

*Concept device or technology. Not available for sale. 3

3

Boston Scientific

Meeting an Unmet Need:

HEMOCOAT™ Intro & Background

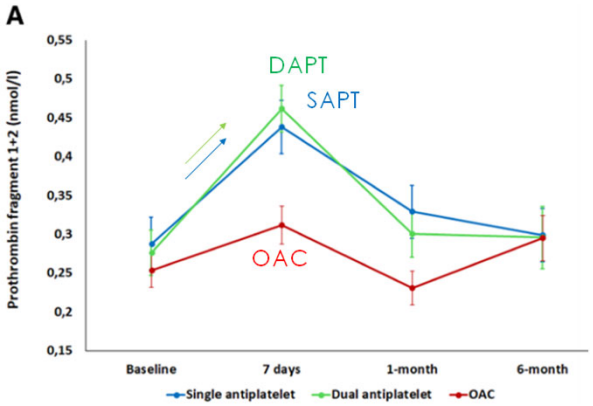
SH-1584802-AA *Caution: Investigational device. Limited by Federal (or U.S.) law to investigations use only. Not available for sale. 4

4

Why coat an LAAC device?

Boston Scientific

Thrombin Generation in LAAC patients



Asmarats et al., 2020, *Circulation: Cardiovasc. Interv.*

5

The HEMOCOAT Story…

Boston Scientific

'What if we coated the WATCHMAN with PVDF?'

Yen-Lane Chen
Corporate Distinguished Fellow (Retired), Boston Scientific

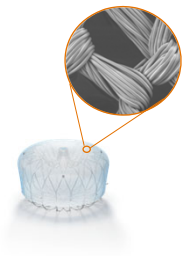
2019

6

HEMOCOAT™ Technology

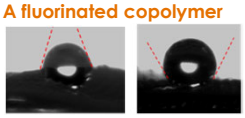
A Teflon-like Polymer Coating

Boston Scientific

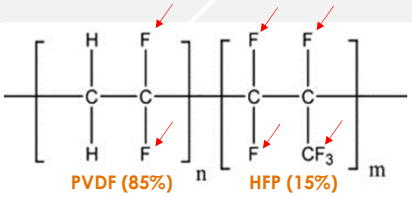


PVDF-HFP:
Poly(vinylidene-fluoride-co-hexafluoropropylene)

A fluorinated copolymer



Uncoated fabric | FLX Pro fabric



Stable

Non-active

Non-eluting

Established

A robust history of safe use on permanently implanted, blood-contacting medical devices[2]

Effective?

Prior to FLX Pro, no data on PVDF-HFP coated devices ***without drug***

1. Boston Scientific Data on File. 2. Wagner et al., Biomaterials Science: An Introduction to Materials in Medicine, 4th Edition, 2020 3. Saliba et al. ESC 2022. 4. Saliba et al. TCT 2022.

SH-1584802-AA *Caution: Investigational device. Limited by Federal (or U.S.) law to investigations use only. Not available for sale.

7

7

The Development of HEMOCOAT

Boston Scientific

Coating Technology	***How do we assess the coated device on the bench?***
Animal Study Design	***Does it heal differently?***
Histology	***Why does it heal differently?***

8

The Development of HEMOCOAT

Boston Scientific

Coating Technology

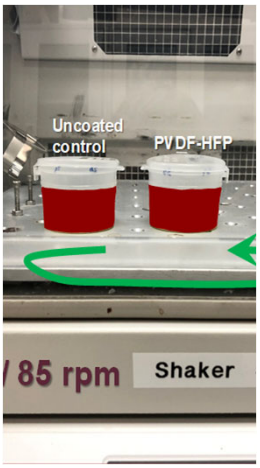
How do we assess the coated device on the bench?

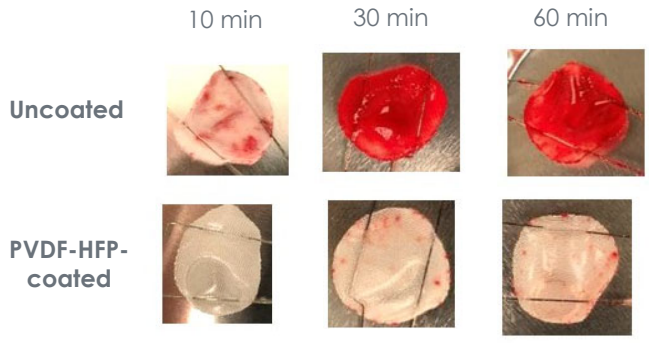
9

How does PVDF-coated Watchman fabric (***without drug***) respond to blood?

Boston Scientific

- Coated and uncoated fabric tested in bovine blood
  - Thrombus growth monitored over time





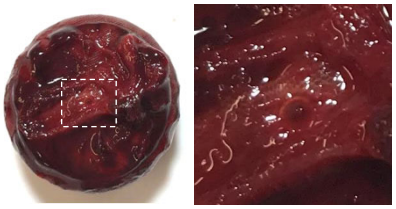
10

Human Blood Flow Loop Results

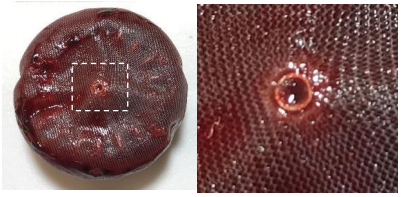
Boston Scientific

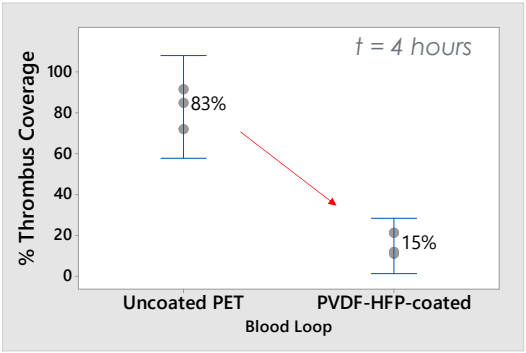
- PVDF-HFP-coated devices developed significantly less thrombus on the proximal surface of the device than uncoated devices

Uncoated



PVDF-HFP-coated





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The Development of HEMOCOAT

Boston Scientific

Coating Technology — *How do we assess the coated device on the bench?*

Animal Study Design — *Does it heal differently?*

12

The Challenge In Vivo Experiment

Boston Scientific

"What if we implant in a thrombogenic animal for 3 days?"

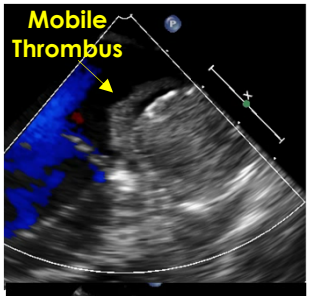
Animal Study Design

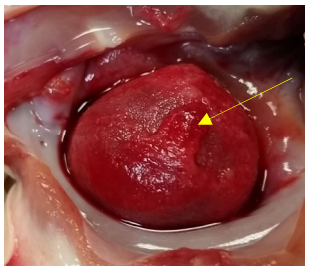
13

3 Day Dog Study (Non-anticoagulated)

Boston Scientific

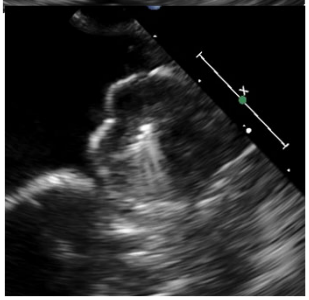
Uncoated

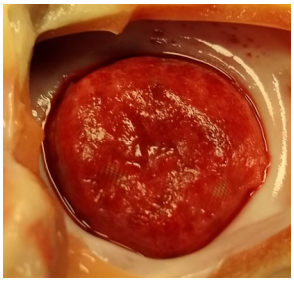




Mobile Thrombus

Coated





Thin, Laminar Thrombus Coverage

14

How does HEMOCOAT impact healing?

Boston Scientific

Coating Technology

How do we assess the coated device on the bench?

Animal Study Design

Does it heal differently?

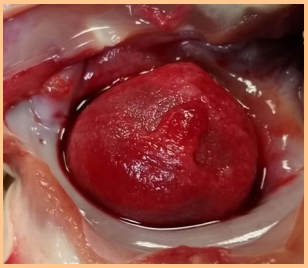
Histology

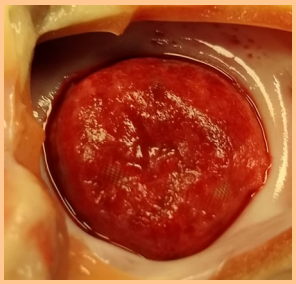
Why does it heal differently?

15

Is all thrombus created equal?

Boston Scientific





Histology

"Is it good thrombus or bad thrombus?"

16

…first, back to the coating process…

Boston Scientific

Coating Technology

Why does the HEMOCOAT work so well with the WATCHMAN fabric?

17

Patented Interaction with Multifilament Polyester Fabric

Boston Scientific

(12) **United States Patent**
Kangas et al.

(10) **Patent No.: US 11,484,320 B2**
(45) **Date of Patent: Nov. 1, 2022**

(54) **LEFT ATRIAL APPENDAGE CLOSURE DEVICE WITH ANTI-THROMBOGENIC COVERING**

(71) Applicant: **BOSTON SCIENTIFIC SCIMED, INC.**, Maple Grove, MN (US)

(72) Inventors: **Steven L. Kangas**, Woodbury, MN (US); **Edward Kopesky**, Mahtomedi, MN (US); **Yen-Lane Chen**, New Brighton, MN (US)

(73) Assignee: **Boston Scientific Scimed, Inc.**, Maple Grove, MN (US)

(56) **References Cited**

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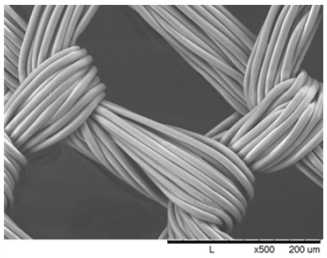
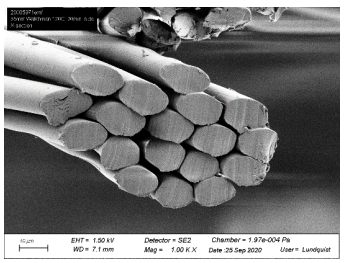
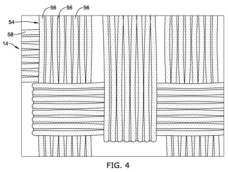
(Continued)







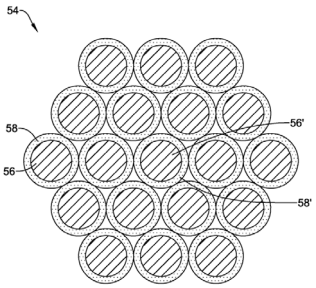


FIG. 6

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More Coated Surface with HEMOCOAT

~4x as much surface area with multifilament structure

Boston Scientific

Monofilament Structure

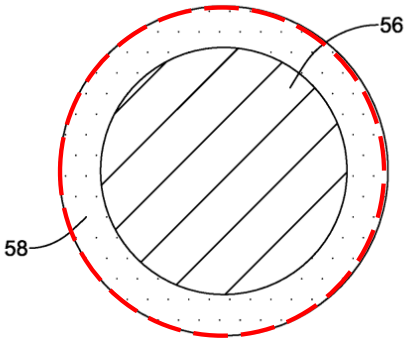

FIG. 5

Multifilament Structure

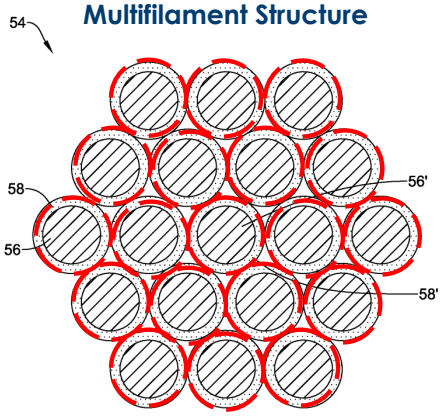

FIG. 6

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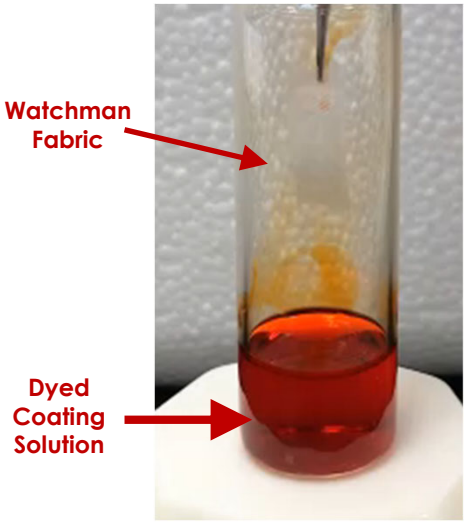
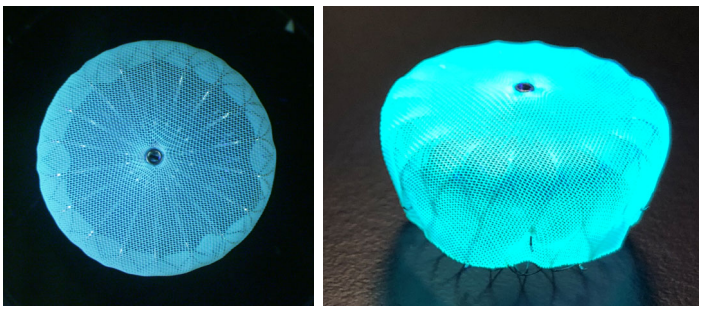
HEMOCOAT Technology in Action

Mulitfilament PET Fabric Causes Coating to Wick In and Coat All Surfaces

Boston Scientific



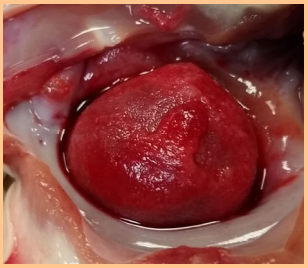
FLX Pro Device with 0.007% Fluorescent Dye

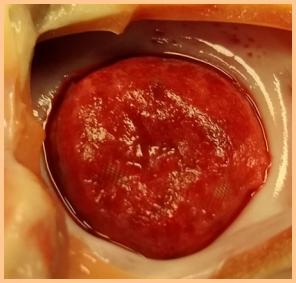


20

Is all thrombus created equal?

Boston Scientific





Histology

"Is it good thrombus or bad thrombus?"

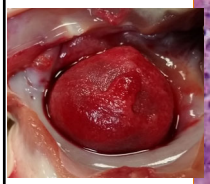
21

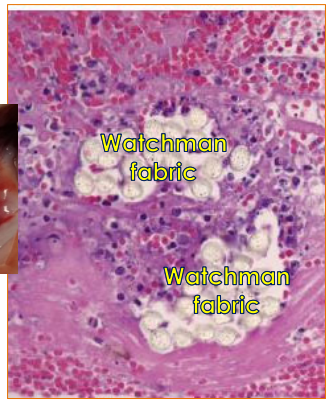
Uncoated vs Coated Histology at 3 days

3 day dog study, no OAC or APT

Boston Scientific

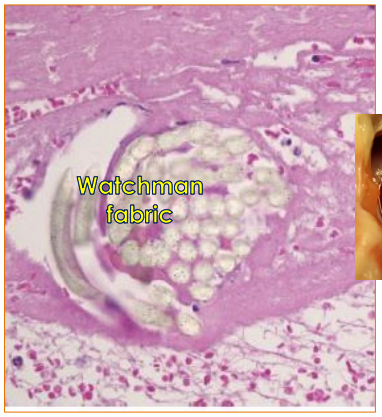
Uncoated

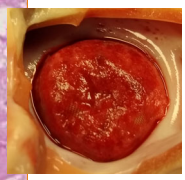




Inflammatory cell nuclei (purple dots) around uncoated fabric bundles

Coated





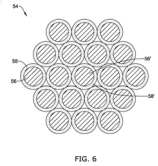


FIG. 6

Minimal inflammatory cells around coated fabric bundles

22

22

Multifilament Structure Amplifies Benefits of HEMOCOAT

Boston Scientific

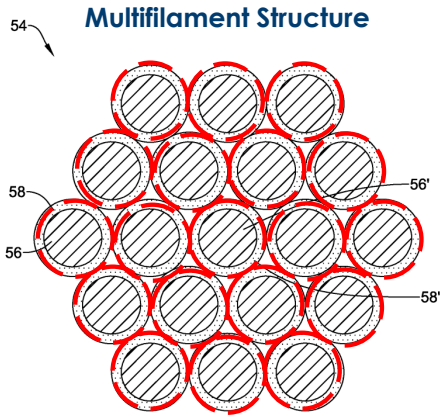
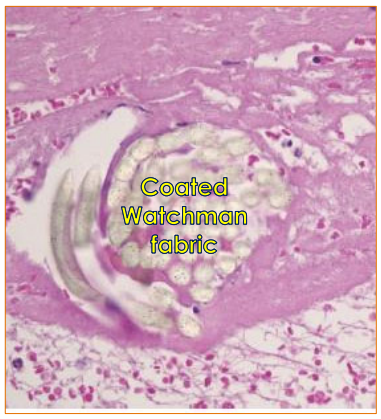


FIG. 6



Minimal inflammatory cells around coated fabric bundles

23

But wait, does it heal completely?

Boston Scientific

Animal Study Design

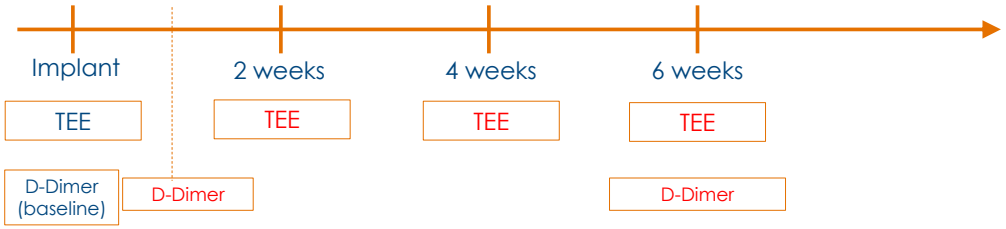
"A nonthrombogenic coating will never heal"
-Management

24

How did we test the coated device? 45 day In Vivo Challenge Animal Model

Boston Scientific

- N = 12 canines received an LAAC device
  - 6 Uncoated
  - 6 Coated
- **No antiplatelets or anticoagulants given to dogs post-implant**
- Intermediate TEE follow-ups at 14 and 28 days to image thrombus on device

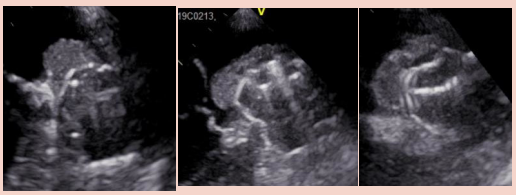
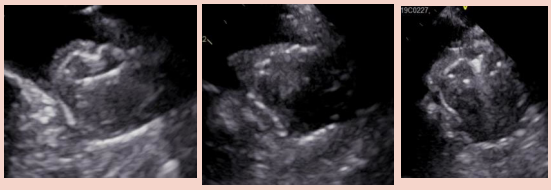
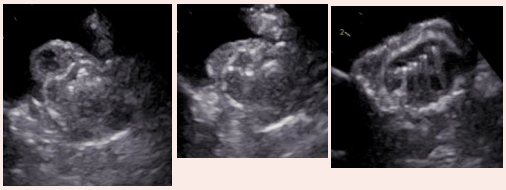
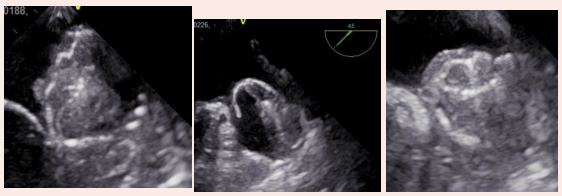


25

25

2 week TEE Follow-Up

Boston Scientific

Uncoated	Coated
	
	

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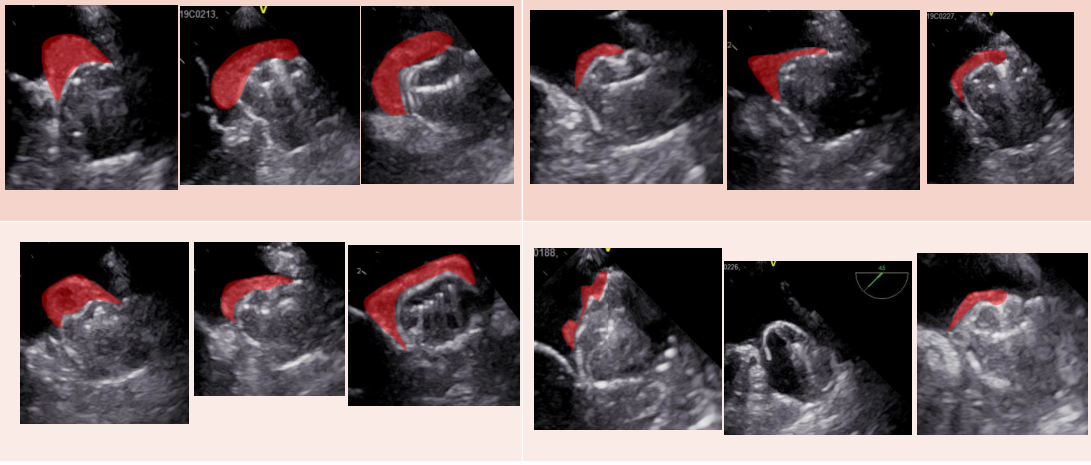
2-week TEE Follow-Up: Raised Thrombus Highlighted (red)

Boston Scientific

Uncoated	Coated
6/6 with DRT > 3 mm	1/6 with DRT > 3 mm

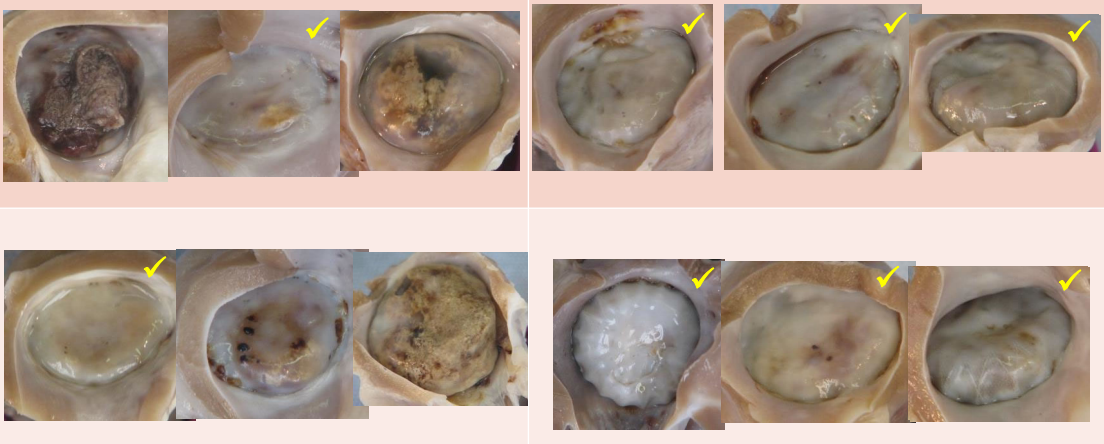


27

45 Day Explants (Post-Fixation)

Boston Scientific

Uncoated	Coated
2/6 exhibit complete coverage/healing	6/6 exhibit complete coverage/healing



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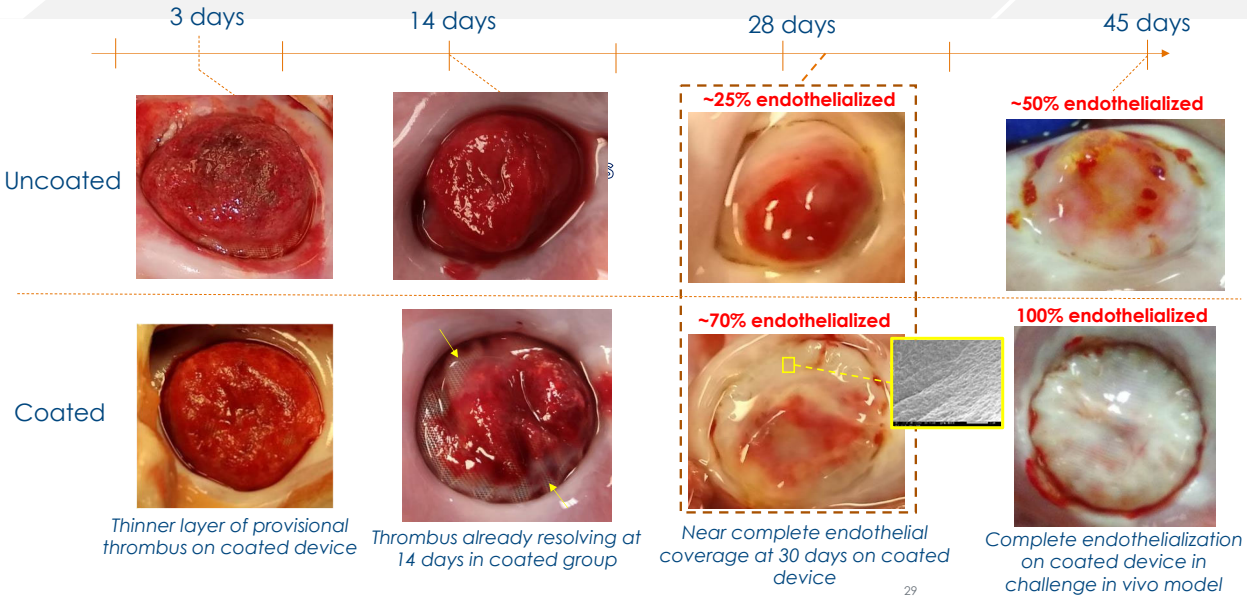
Coated Device: Faster Healing in Challenging In Vivo Model

Canine model (no OAC, no APT)

Boston Scientific



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29

WATCHMAN FLX™ Pro Features HEMOCOAT™ Technology

Designed to Enhance Healing While Reducing DRT

Boston Scientific

Faster, more complete healing may reduce DRT, simplify post-implant drug regimen[1,2]

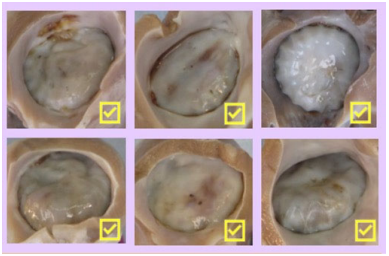
WATCHMAN FLX™ Pro
LEFT ATRIAL APPENDAGE CLOSURE DEVICE

~50%

Increase in endothelial coverage at 45 days.[1]

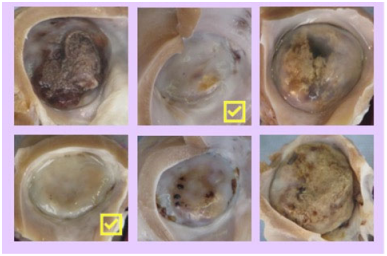
COATED

6/6 exhibit complete coverage/healing at 45 days



UNCOATED

2/6 exhibit complete coverage/healing at 45 days



*Challenged non-anticoagulated canine model. Not representative of clinical results

SH-1584802-AA *Caution: Investigational device. Limited by Federal (or U.S.) law to investigations use only. Not available for sale. 1. Saliba, W. et al. Moderated Poster Presentation, ESC

30

30

The science behind the coating (published May 18, 2023)

Boston Scientific

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Enhanced Thromboresistance and Endothelialization of a Novel Fluoropolymer-Coated Left Atrial Appendage Closure Device GET ACCESS

Original Research Paper

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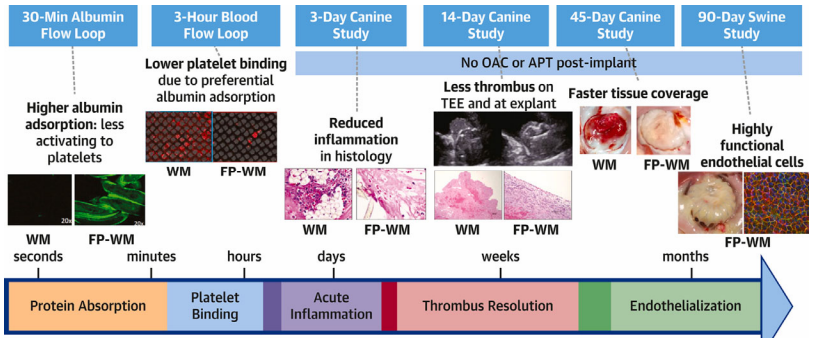

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Device Related Thrombus After Left Atrial Appendage Occlusion

- Jai Parekh

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- Left atrial appendage occlusion (LAAO) has emerged as an attractive alternative to oral anticoagulation in patients with non-valvular atrial fibrillation
- Although many studies have confirmed the safety and efficacy of LAAO, certain issues remain with the procedure
- Device-related thrombus (DRT) continues to represent a conundrum because of the uncertainties surrounding its prediction, detection and management
- There is no unified definition of DRT; a thorough review of the major LAAO trials' protocols reveals no consensus definition of DRT underscoring the ambiguity of its interpretation in literature
- Accurate diagnosis of DRT is critical to avoid thromboembolic complications, whereas overdiagnosis might lead to irrelevant intensified anti-coagulation with an increased risk of bleeding

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Imaging assessment of DRT

In a retrospective study of the PROTECT AF trial, an expert panel developed 5 criteria for the diagnosis of DRT on TEE. These included an echo density on the left atrial aspect of the device

- not explained by imaging artifact
- inconsistent with normal healing or device incorporation
- visible in multiple transesophageal echocardiographic planes
- in contact with the Watchman device
- exhibiting independent motion

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). Main et.al. AJC 2016

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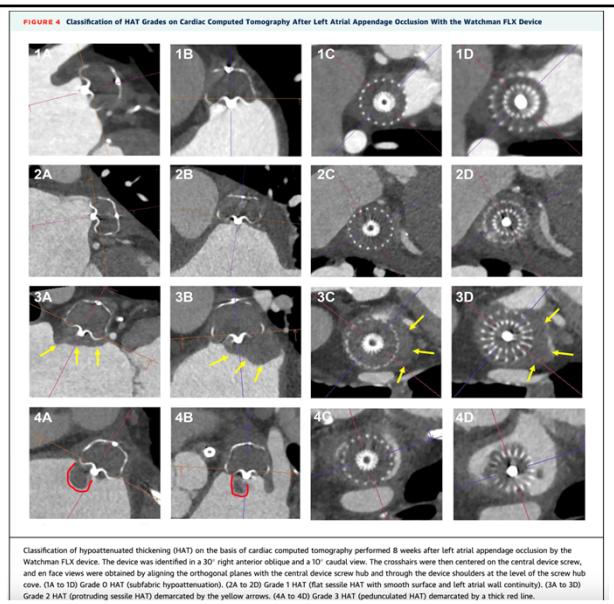
Hypoattenuated thickening (HAT)		Watchman FLX	Amulet
Grade 0	Subfabric		
Grade 1	Sessile ≤3 mm		
	• Sessile ≥3 mm • LA wall continuity • Smooth surface		
Grade 2	• Sessile >3 mm • No LA wall continuity		
	• Sessile >3 mm • Irregular surface		
Grade 3	Pendunculated		



Device-Related Thrombus After Left Atrial Appendage Occlusion. Alkhouli et.al. JACC Nov 2023

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Cardiac CT following Watchman FLX implantation: Device-related thrombus or device healing?

Clinical results

Hypoattenuated thickening (HAT) was seen on 156/244 (64%) of all scans

Subfabric (n=59); flat sessile (n=78); protruding sessile (n=17); pedunculated (n=2)

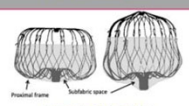
All cases of clinically adjudicated device-related thrombus (n=7) were categorized as **high-grade HAT**

Study cohort

244 Watchman FLX patients

CHA_2DS_2-VASc: 4.0±1.6

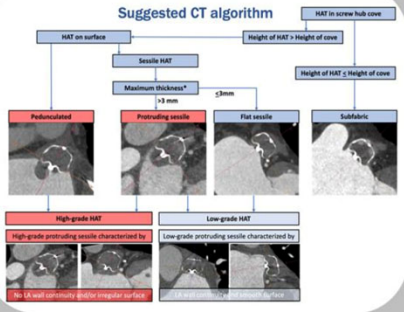
HAS-BLED: 2.5±1.1



Subfabric HAT ≠ DRT

Single-center, retrospective, blinded analysis of eight-week follow-up cardiac CT

Suggested CT algorithm



High-grade HAT might represent device-related thrombus and should warrant further clinical consideration

Preclinical results

Successful Watchman FLX implantation in all canines (n=5)

CT findings corresponding to both flat sessile and subfabric hypoattenuation

Correlated with device healing and neoendothelialization upon explantation

Paired canine imaging and histology

of subfabric hypoattenuation

Low-grade HAT is likely representative of benign device healing and should not be treated as DRT

Cardiac CT following Watchman FLX implantation: device related thrombus or device healing. Kramer et.al. EHJ-Cardiovascular imaging 2023

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Incidence, Predictors & Clinical Impact of DRT

- The incidence of DRT varies considerably among published studies because of the variability in the frequency and standardization of post-LAAO surveillance imaging
- In PROTECT AF and PREVAIL trials, the incidence of DRT was 3.7% (65 of 1,739) at 7,159 patient-years of follow-up
- In the prospective PINNACLE FLX registry, DRT after LAAO with the second-generation Watchman FLX device was diagnosed within 12 months in 7 of 400 patients (1.7%)
- In a meta-analysis of 10,154 patients who underwent post-LAAO surveillance imaging in 66 studies, the pooled incidence of DRT was 3.8% (351 of 10,153)

Device-Related Thrombus After Left Atrial Appendage Closure. Incidence, Predictors, and Outcomes. Dukkipati et.al Circulation 2018

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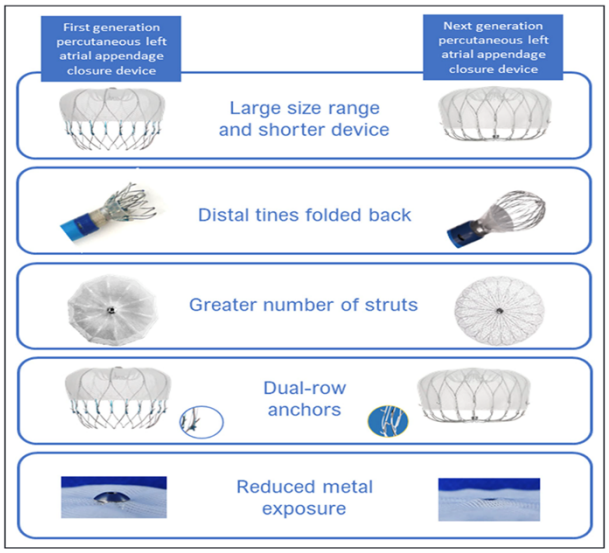

Primary Outcome Evaluation of a Next-Generation Left Atrial Appendage Closure Device. Results From the PINNACLE FLX Trial. Kar et.al Circulation 2021.

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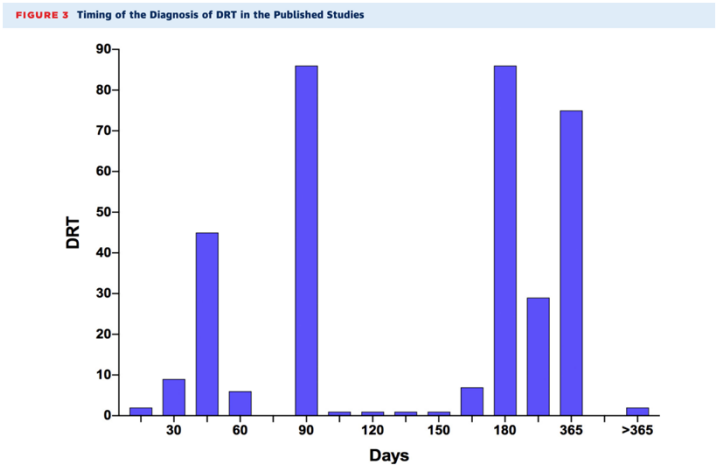
In the meta-analysis by Alkhouli et al involving 66 studies, the DRT diagnosis was made at<90, 90 to 365, and>365 days in 42%, 57%,and 1% of patients, respectively.



- <90 days: 42%
- 90-365 days: 57%
- >365 days: 1%

Incidence and Clinical Impact of Device-Related Thrombus Following Percutaneous Left Atrial Appendage Occlusion. A Meta-Analysis. Alkhouli et.al. JACC EP 2018.

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- The majority of DRTs (85%) were discovered after more than 45 days, suggesting that the currently recommended LAA surveillance at 45 days is inadequate
- In the 2 pivotal WATCHMAN RCTs and their nested registries, 29% of DRTs were detected on unscheduled TEE examinations conducted for other reasons, despite the robust LAA surveillance protocols (routine TEEs at 45, 180, and 365 days in the RCTs and at 45 and 365 days in the continuous access registries)
- This implies that even frequent routine surveillance will likely miss a non-negligible percentage of DRTs and highlights the challenges of determining an optimal surveillance protocol following LAAO

Incidence and Clinical Impact of Device-Related Thrombus Following Percutaneous Left Atrial Appendage Occlusion. A Meta-Analysis. Alkhouli et.al. JACC EP 2018.

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TABLE 1 Independent Predictors of DRT After LAAO

First Author (Year)	Population	Patient Factors	Procedural Factors
Kaneko et al (2017)[34]	Single-center analysis (n = 78)	CHA_2DS_2-VASc score	Deep device implantation
Dukkipati et al (2018)[17]	Ad hoc analysis of PROTECT AF and PREVAIL (n = 1,739)	LAA orifice width, permanent AF, prior TIA, LVEF, vascular disease	
Pracon et al (2018)[33]	Single-center analysis (n = 99)	Prior stroke/TIA, permanent AF, LVEF	Device size, deep device implantation
Fauchier et al (2018)[35]	Multicenter registry (France) (n = 469)	Age, prior stroke/TIA	No OAC or APT post-LAAO
Aminian et al (2019)[9]	Prospective global Amulet registry (n = 1,088)	LAA orifice width	
Simard et al (2021)[7]	Global DRT registry (n = 711)	Hypercoagulopathy, permanent AF, renal insufficiency	Pericardial effusion, deep device implantation
Sedaghat et al (2021)[31]	EWOLUTION prospective Watchman registry (n = 835)	Permanent AF	
Schmidt et al (2022)[6]	Ad hoc analysis of the Amulet IDE trial (n = 1,788)	Age, female, permanent AF	
Vij et al (2022)[32]	Multicenter registry (EUROC-DRT)	Age, prior stroke/TIA, HAS-BLED score, spontaneous echocardiographic contrast	
Freixa et al (2023)[29]	Multicenter registry (Europe and Canada) (n = 1,317)		Deep device implantation, no or single APT post-LAAO

Device-Related Thrombus After Left Atrial Appendage Occlusion. Alkhouli et.al. JACC Nov 2023

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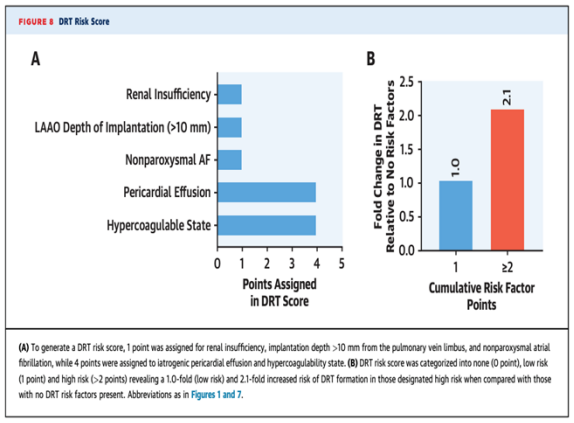

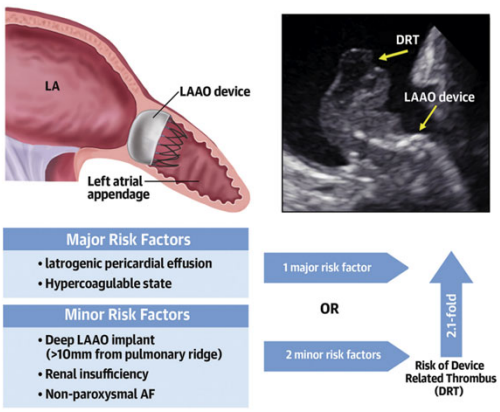

Predictors of Device-Related Thrombus Following Percutaneous Left Atrial Appendage Occlusion. Simard et.al. JACC 2021

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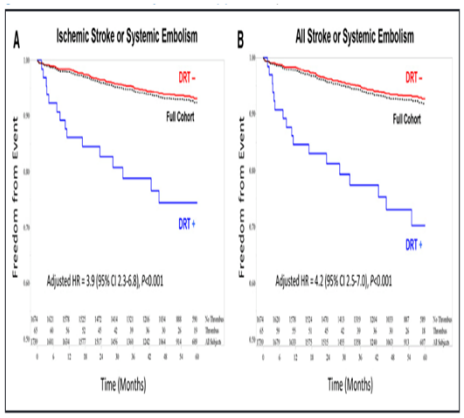

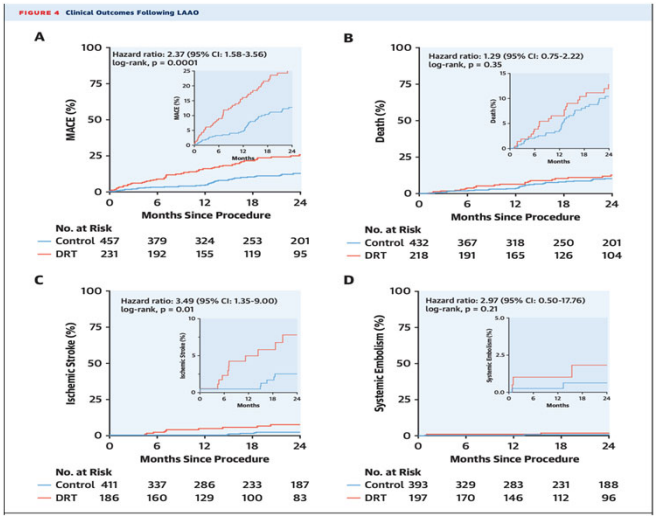

Device-Related Thrombus After Left Atrial Appendage Closure. Incidence, Predictors, and Outcomes. Dukkipati et.al. Circulation 2018

Predictors of Device-Related Thrombus Following Percutaneous Left Atrial Appendage Occlusion. Simard et.al . JACC 2021

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Antithrombotic therapy

The incidence of device-related thrombosis and the anticoagulation protocol in the key trials of the WATCHMAN device

Trial/study	Population	Follow up	Anticoagulation	DRT
PROTECT-AF [8]	707	18 months	Warfarin and aspirin (81 mg) for 45 days, then aspirin (81-325 mg) & Clopidogrel for 6 months followed by aspirin	4.2%
PREVAIL trial [9]	407	18 months		Not reported
CAP [11]	566	50 months		2.6%
CAP2 [11]	578	50 months		3.9%
Dukkipati, Srinivas R et al. [21]	1739	na		3.7%
Kubo, Shunsuke et al. [22]	119	1,456±546 days		3.4%
EWOLUTION [13,14]	1020	24 months	warfarin (16%)	4.1%
			DOACs (11%)	
			DAPT (60%)	
			SAPT (7%)	
			no anticoagulation (6%)	
ASAP [12]	150	14.4±8.6 months	Clopidogrel for 6 months and aspirin for life	4%
Enomoto Y [16]	426		NOAC vs. Warfarin	0.9% vs. 0.5%, P=1
Bösche, Leif I et al. [15]	45	417±323 days	NOAC vs. DAPT	0%

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The WATCHMAN device and post-implantation anticoagulation management. A review of key studies and the risk of device-related thrombosis. Magdi et.al. Am J Cardiovasc Dis 2021

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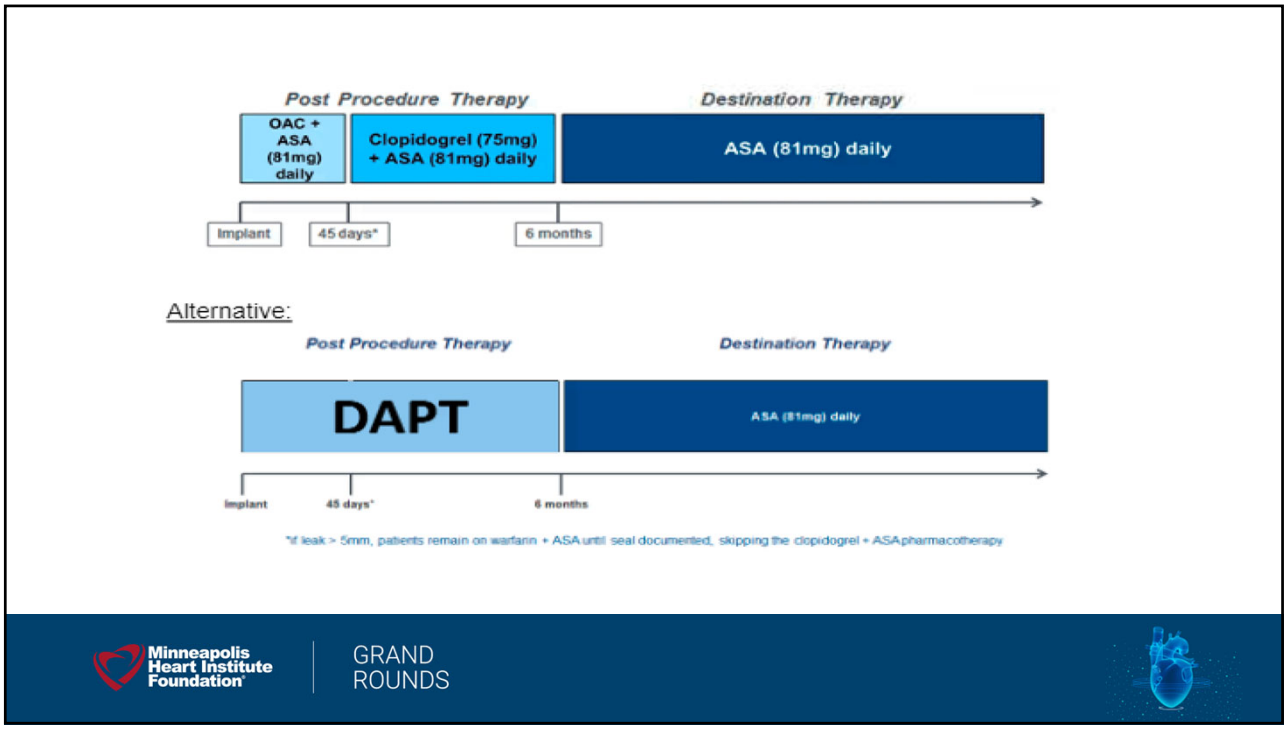
Post Procedure Therapy
Destination Therapy
OAC + ASA (81mg) daily
Clopidogrel (75mg) + ASA (81mg) daily
ASA (81mg) daily
Implant
45 days*
6 months
Alternative:
Post Procedure Therapy
Destination Therapy
DAPT
ASA (81mg) daily
Implant
45 days*
6 months
*if leak > 5mm, patients remain on warfarin + ASA until seal documented, skipping the clopidogrel + ASA pharmacotherapy
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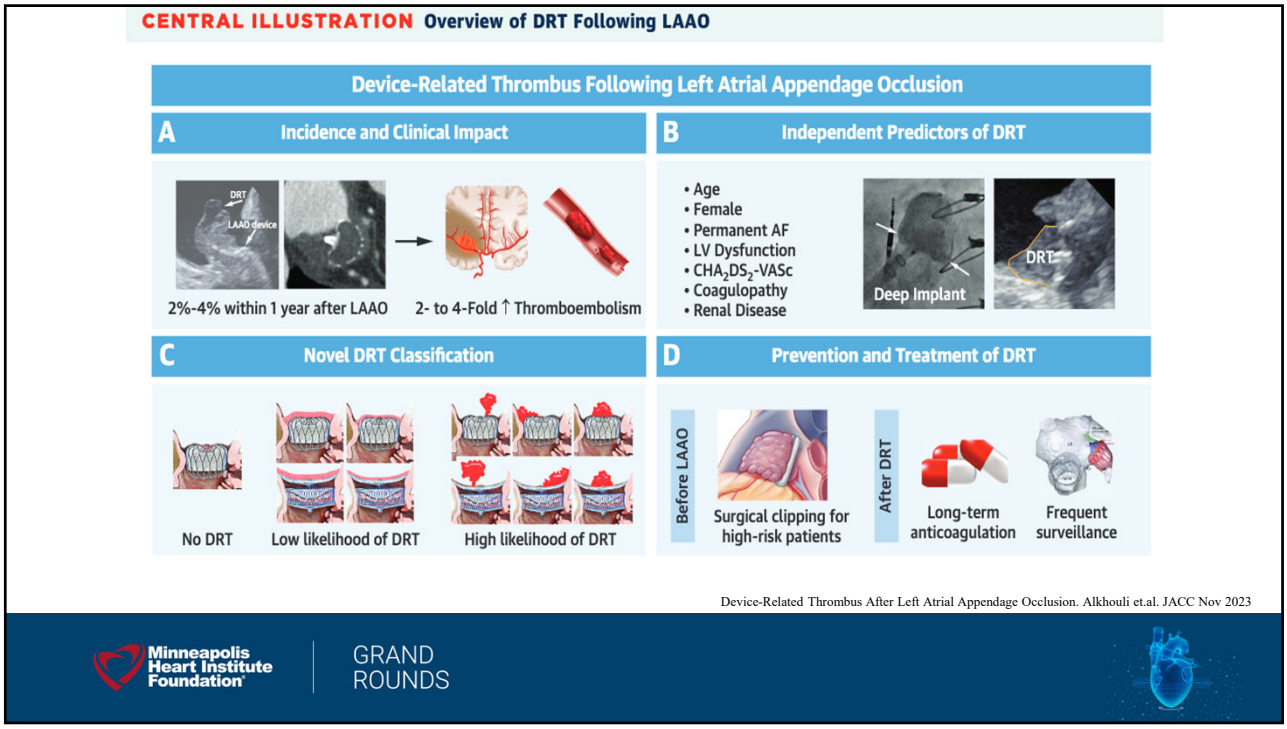
CENTRAL ILLUSTRATION Overview of DRT Following LAAO
Device-Related Thrombus Following Left Atrial Appendage Occlusion
A Incidence and Clinical Impact
DRT
LAAO device
2%-4% within 1 year after LAAO
2- to 4-Fold ↑ Thromboembolism
B Independent Predictors of DRT
• Age
• Female
• Permanent AF
• LV Dysfunction
• CHA2DS2-VASc
• Coagulopathy
• Renal Disease
Deep Implant
DRT
C Novel DRT Classification
No DRT
Low likelihood of DRT
High likelihood of DRT
D Prevention and Treatment of DRT
Before LAAO
Surgical clipping for high-risk patients
After DRT
Long-term anticoagulation
Frequent surveillance
Device-Related Thrombus After Left Atrial Appendage Occlusion. Alkhouli et.al. JACC Nov 2023
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Thank You !

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