

ARTIVION™

Formerly CryoLife | Jotec

| INVESTOR & ANALYST DAY

FORWARD-LOOKING STATEMENT

Statements made in this presentation that look forward in time or that express management's beliefs, expectations, or forecasts are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements reflect the views of management at the time such statements are made. These statements include our beliefs that we will deliver double-digit growth from 2022-2024 by focusing globally on cardiac and vascular surgeons who treat patients with aortic disease; we will win through a deep understanding of our customers' most significant clinical challenges and collaborating with them by developing or acquiring simple and elegant solutions that minimize these challenges and reduce healthcare costs; \$700M invested to build leading aortic disease franchise with a total addressable market of \$5.7B; our estimated total addressable market for surgical sealant, heart valves, aortic arch solutions and abdominal aorta stent grafts are \$260M, \$720M, \$2.1B (\$1.4B excluding E-nya), and \$2.6B (\$1.9B excluding E-ventus), respectively; we are and will continue to be a leader in innovation in aortic repair; our key growth drivers will be (a) focus products of On-X and stent grafts (b) international expansion into APAC and LATAM, including estimates of sales force numbers and deadlines for achieving same; (c) regulatory approvals including but not limited to, PerClot PMA and PROACT Mitral and (d) execution on our R&D pipeline, with a total addressable market opportunity of \$1.3B, with market opportunities in the US of \$25M, \$43M, \$610M, \$240M, \$300M and \$100M, for PerClot, PROACT Mitral, PROACT Xa, AMDS, NEXUS and NEO 2.0, respectively; the estimated timelines for FDA approvals of the PMAs for PerClot, PROACT Mitral, PROACT Xa, and NEO 2.0, and for FDA and Japanese approvals of AMDS and NEXUS; our estimates and related assumptions that we will deliver approximately \$330M, \$360M and \$400M in revenue for 2022, 2023, and 2024, respectively, and 68% gross margin and \$75M-\$80M in Adjusted EBIDTA in 2024; our estimates and related assumptions that our net leverage will decrease to 3.0x by 2024; our estimates that we will return 50% of incremental gross margins to shareholders via adjusted EBIDTA in 2024; our estimates compound annual growth rates for stent grafts, On-X heart valves, preservation services, surgical sealants, and other products; our estimates assumptions relating to our projected contributed by adjusted EBIDTA in 2024; the total addressable market for surgical valves for patients 70 years of age and younger \$720M, with \$610M and \$110M for aortic and mitral valves, respectively; the estimated US mechanical aortic valve market share; our belief that we are redefining innovation in valve technology; the estimated percentages of surgical aortic valve replacements, by type, in patients under 70 years of age; our estimates of the total addressable market of \$540M, \$250M, and \$600M, respectively for Acute Type A dissections, dissections and arch aneurysms, and chronic dissections, aneurysms, or PAU involving the Aortic Arch; and our estimates of the total addressable markets for thoracoabdominal, abdominal, and iliac stent grafts is \$480M, \$1.27B, and \$140M, respectively. These risks and uncertainties include the risk factors detailed in our Securities and Exchange Commission filings, including our Form 10-K for the year ended December 31, 2021. These risks and uncertainties also include that our beliefs may be incorrect regarding market opportunities, clinical trial timelines and clearance or approval times for existing or new products or new indications, and our key financial metrics may be incorrect or may change over time. Artivion disclaims any duty to update its forward-looking statements, whether as a result of new information, future events, or otherwise.

COMPANY OVERVIEW

Pat Mackin

Chairman, President and CEO

ON-X HEART VALVES OVERVIEW

John E. Davis

Sr. Vice President, Global Sales and Marketing

Dr. John Alexander

Professor of Medicine/Cardiology, Duke Health

STENT GRAFTS OVERVIEW

Karl Will

Vice President, Sales and Marketing EMEA

Dr. Joerg Kempfert

Professor of Cardiac Surgery, German Heart Center Berlin

Dr. Malakh Shrestha

Professor of Cardiac Surgery, Hannover Medical School

Dr. Tim Resch

Professor of Vascular Surgery, Copenhagen University

PRODUCT PIPELINE OVERVIEW

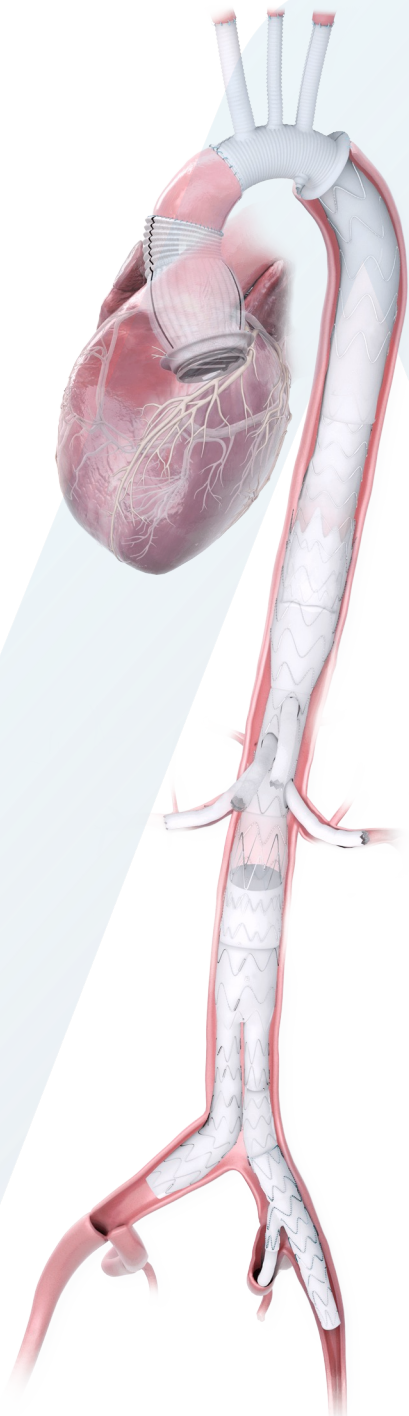
Dr. Marshall Stanton

Sr. Vice President, Clinical Research and Chief Medical Officer

FINANCIAL SUMMARY

Ashley Lee

Executive Vice President, COO & CFO



ARTIVIONTM

Aorta + Innovation + Vision

**Our new name reflects our vision to
deliver innovative technologies for the
treatment of aortic disease.**

1984 – 2015:

\$500M* Total Addressable Market (TAM)



CARDIAC & VASCULAR TISSUE



BioGlue® ACQUIRED 1996



Core Values Power our Culture to Deliver on Our Mission

COLLABORATION



OUR MISSION

We partner with surgeons to restore the health of patients by delivering innovative technologies of unsurpassed quality.



CUSTOMER
FOCUS



RESULTS-
DRIVEN



OUR VISION

To be recognized as a leader in providing technologies for patients with aortic diseases.

OUR STRATEGY

WE WILL DELIVER

Double digit growth from 2022-2024 by focusing globally on cardiac and vascular surgeons who treat patients with aortic disease.

WE WILL WIN

Through a deep understanding of our customer's most significant clinical challenges and collaborating with them by developing or acquiring simple and elegant solutions that minimize these challenges and reduce healthcare costs.

Experienced Leaders

Decades of combined experience and leadership in the medical device industry



Pat Mackin

Chairman, President & CEO

Previously with
Medtronic



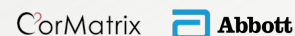
Ashley Lee

EVP, COO & CFO



John Davis

SVP, Global Sales & Marketing



Medtronic



Jean Holloway

SVP, GC, CCO & CS



Medtronic



Marshall Stanton

SVP, Clinical Research
& Chief Medical Officer



Peter Barthold

VP, R&D & Co-GM,
Hechingen



Drew Green

VP, Regulatory Affairs



Dennis Maier

SVP, Operations



Rochelle Maney

VP, Quality



**Invested \$700M
to build a leading
franchise in
aortic disease**



Acquired \$475M of Aortic Technologies in the Past Five Years

\$130M 2016



\$225M 2017

JOTEC®

ARTIVION™

2019 \$20M

ENDOSPAN®

2020 \$100M

ASCYRUS
MEDICAL

MERGERS &
ACQUISITIONS
\$475M

Aortic Disease Franchise: \$5.7B TAM*

Surgical Sealant – \$260M

BioGlue®



Surgical Sealant

Aortic Arch Solutions – \$2.1B

AMDS™



Surgical Acute
Type A Dissection

E-vita® Open Neo



Arch Aneurysm &
Chronic Dissection

NEXUS®



Endovascular
Branched Arch

E-nya™



Endovascular
Descending

Heart Valves – \$720M

On-X®



Mechanical
Valves

CryoValve®



Aortic
Allograft

CryoValve® SG



Pulmonary
Allograft

Abdominal Aorta Stent Grafts – \$2.6B

E-nside™



Thoracoabdominal

E-tegra™



Abdominal

E-liac™



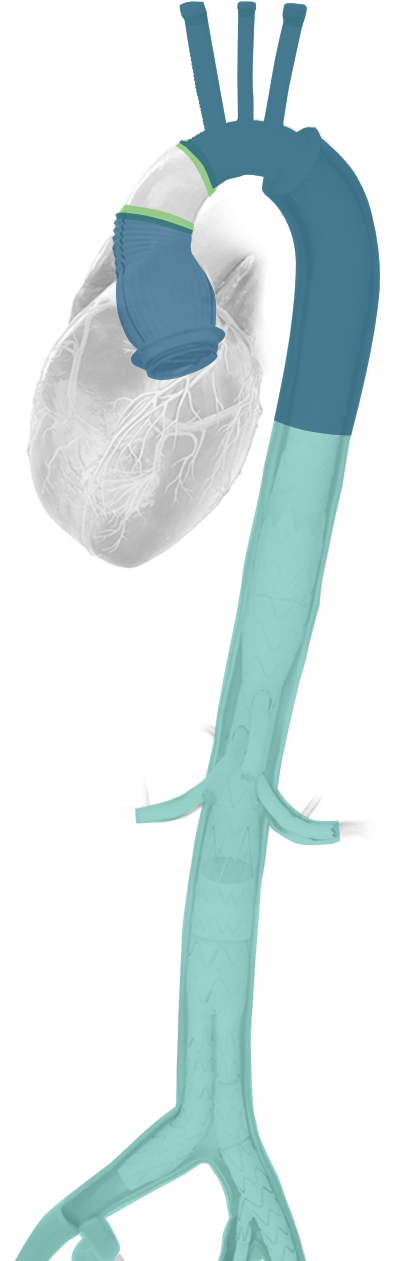
Iliac

E-ventus™






















Peripheral

ARTIVION™



Artivion is Leading Innovation in Aortic Repair

ARTIVION™

Product Groups	Cardiac & Vascular Allografts	Surgical Sealant	Hybrid Acute Type A Dissection (ATAD) Prosthesis	Ascending & Arch Hybrid Frozen Elephant Trunk (FET) System	Endovascular Arch Branch System	Endovascular Thoraco-abdominal System	Aortic and Mitral Heart Valve
Sales %	26%	24%	29%				19%
ARTIVION	CryoValve SG 	BioGlue 	AMDS 	E-vita Open Neo 	NEXUS 	E-nside & Extra Design 	On-X 
							
							
							
							
							
							
							
							
							
							
							
							

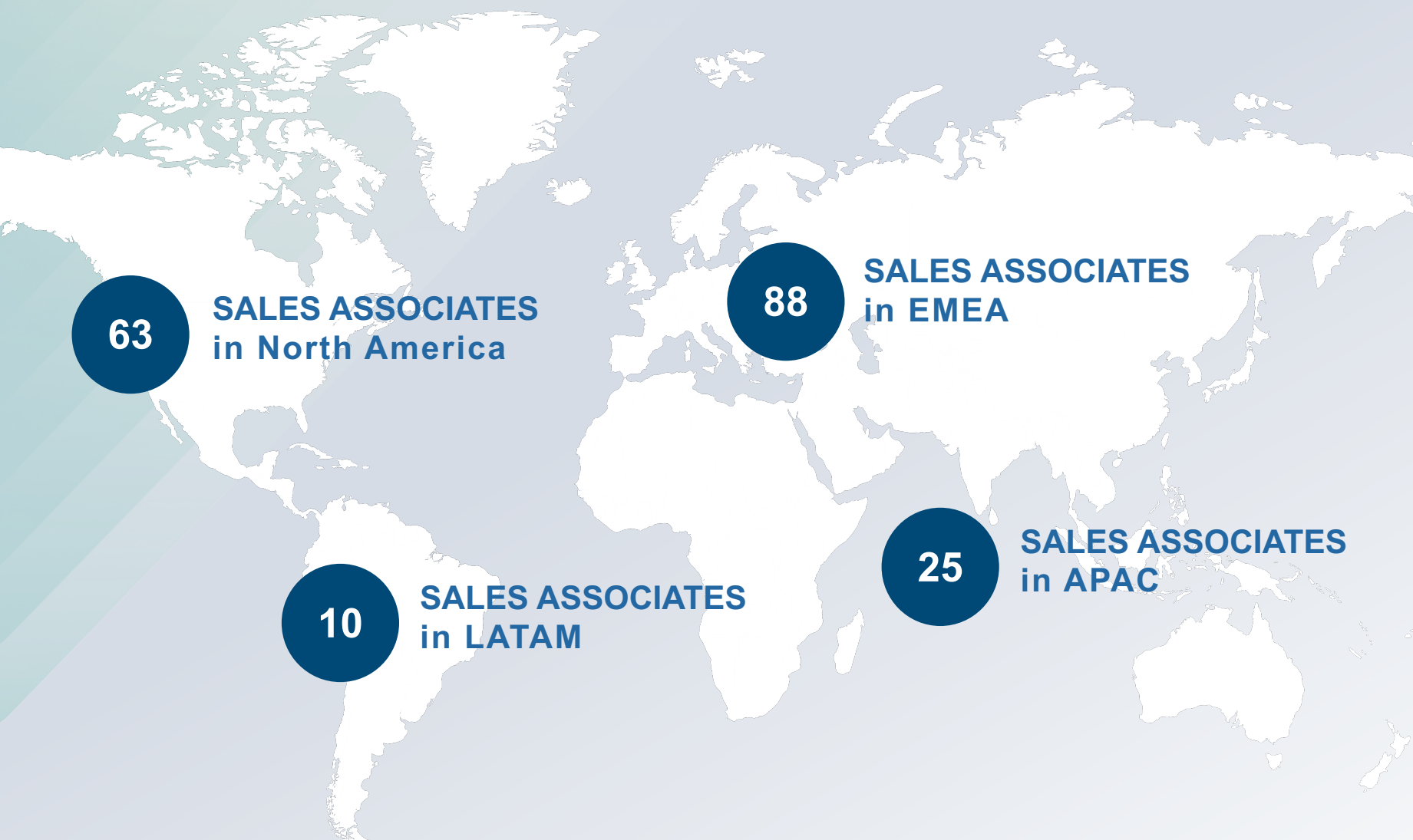
Product Portfolio & Channel Evolution

	1984–1993	1994–2015	2016–2021
Annual Run Rate Revenue	\$21M	\$146M	\$299M
Aortic-Centric Technologies	Allografts	BioGlue®	On-X® Stent Grafts
Direct Sales Channel Added	North America	EMEA	LATAM APAC

1984 – 2021:



Global Sales Channels and Employees



Revenue % by Geography*

57% North America

33% Europe, Middle East, and Africa (EMEA)

7% Asia-Pacific (APAC)

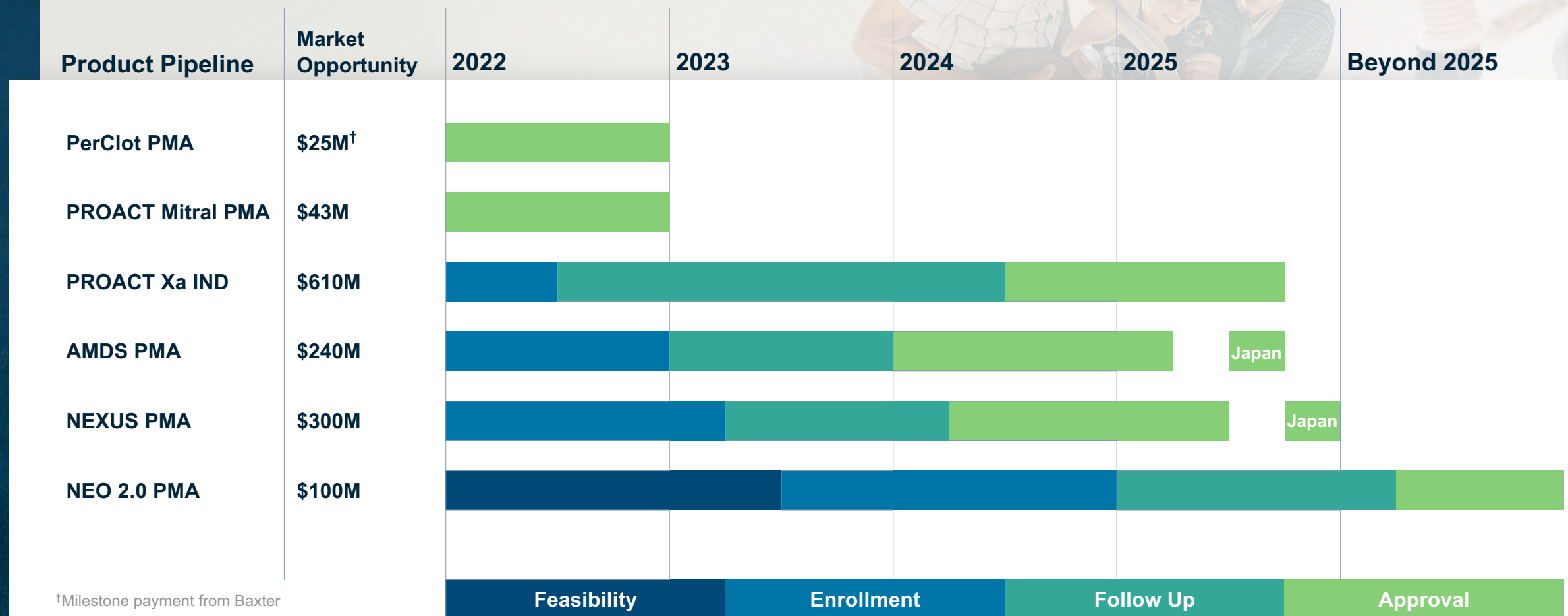
3% Latin America (LATAM)

Employees Worldwide **1,300+**

Number of countries where our products are available **100+**

NYSE Symbol **AORT**

R&D Pipeline Opens \$1.3B Market Opportunity



Manufacturing Locations



ATLANTA, GA • USA

200,000 sq. ft. total
162 dedicated
manufacturing personnel

BioGlue & Tissue



AUSTIN, TX • USA

70,000 sq. ft. total
110 dedicated manufacturing
personnel

On-X Heart Valves



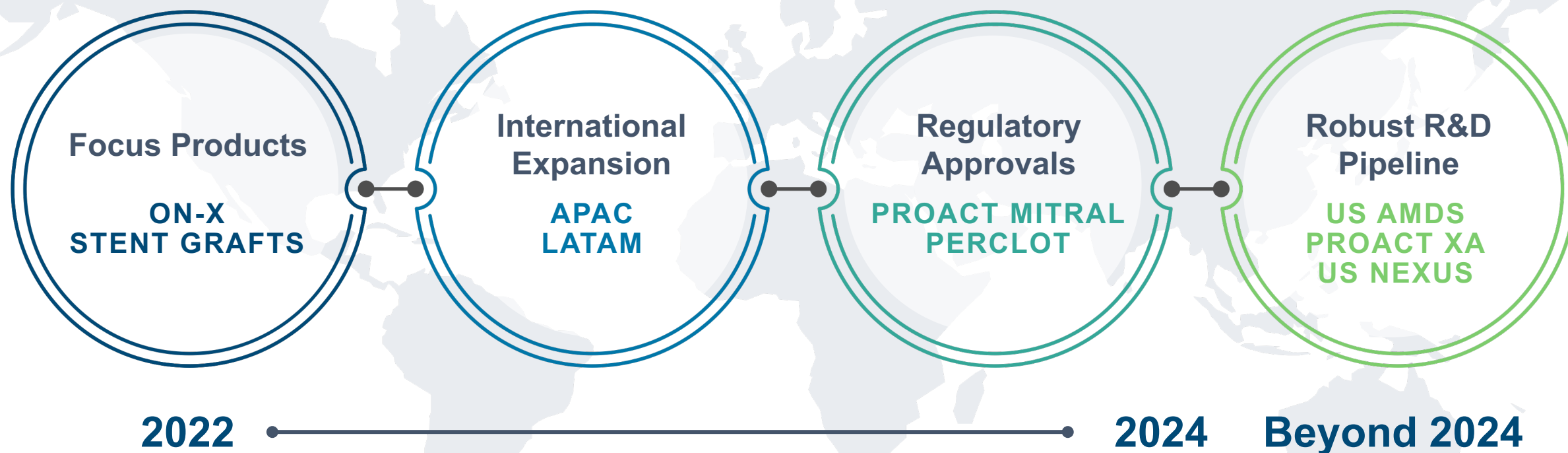
HECHINGEN • GERMANY

156,000 sq. ft. total
325 dedicated
manufacturing personnel

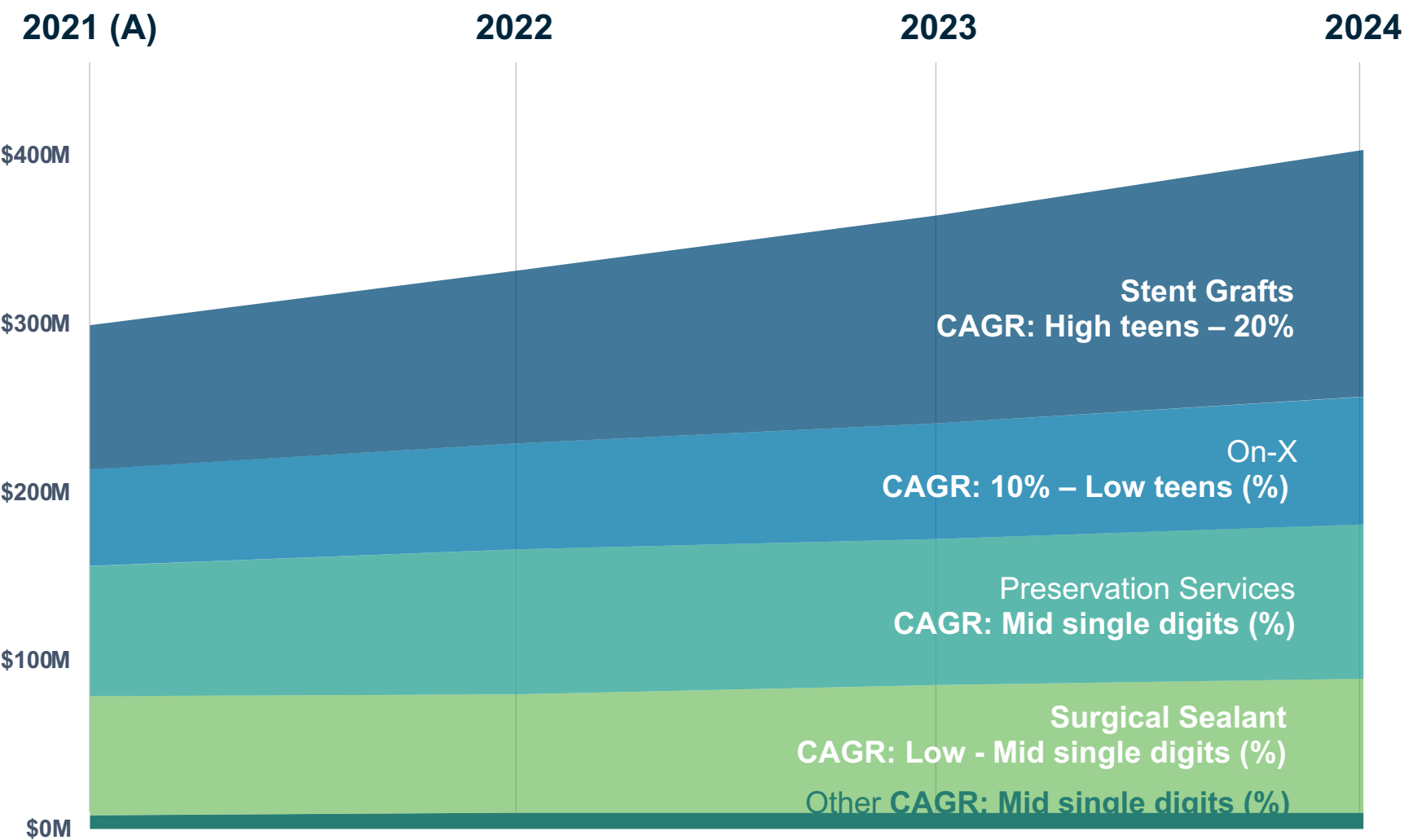
Stent Grafts

Key Growth Drivers

We're poised to deliver double-digit growth in 2022 and beyond.



Double Digit Revenue Growth 2022-2024



Contribution to Adjusted EBITDA – 2024 vs 2021

Return 50% of Incremental Gross Margin to Shareholders via Adjusted EBITDA

INCREMENTAL
REVENUE



INCREMENTAL
GROSS
MARGIN



INCREMENTAL
EXPENSES



INCREMENTAL
ADJUSTED
EBITDA



THREE YEAR ASSUMPTIONS

- ~ 10% revenue growth
- ~ 200 bps gross margin expansion
- ~ \$75M - \$80M Adjusted EBITDA
- ~ Net Leverage from 5.9X to < 3.0X

ARTIVION™



On-X Heart Valves

JOHN DAVIS

Sr. Vice President

Global Sales & Marketing

ARTIVION™

Surgical Valve Replacement <70 Years: \$720M TAM*



Surgical Aortic Valves On-X Aortic Valve



\$610M TAM*

Patients <70 years old requiring
Surgical Aortic Valve Replacement (SAVR)

Surgical Mitral Valves On-X Mitral Valve



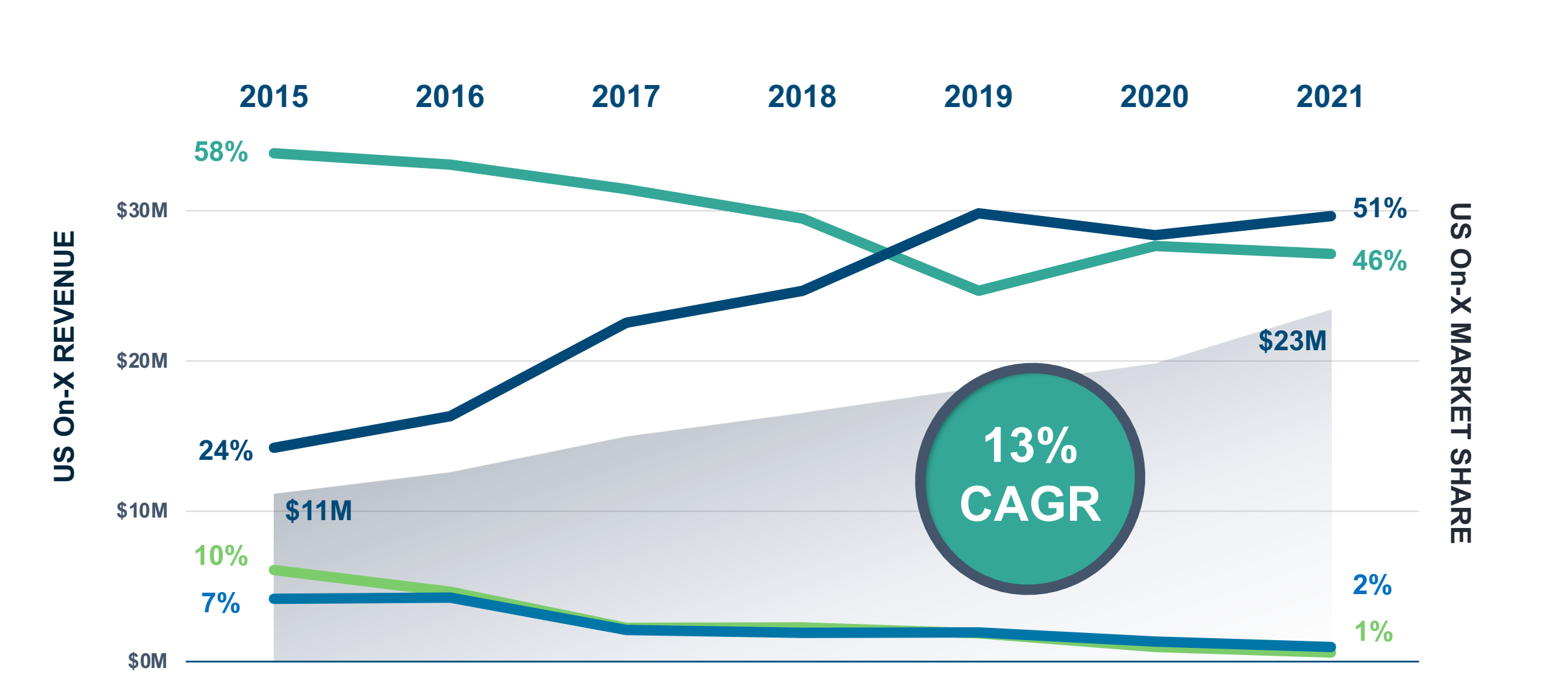
\$110M TAM*

Patients <70 years old requiring
Surgical Mitral Valve Replacement (SMVR)

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US On-X Aortic Valve Revenue and Market Share*

ARTIVION™



ABBOTT ARTIVION CORCYM MEDTRONIC

*Market shares derived from 2021 IQVIA Medical device supply audit and internal sales reports.

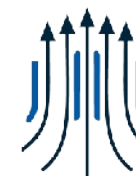
On-X Valve Unique Material and Design



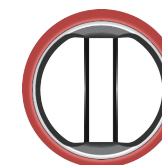
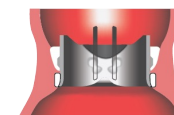
On-X Heart Valves

1 90° leaflets:¹
promoted
laminar flow

90°
Opening

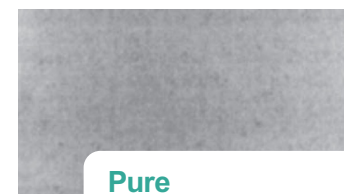


2 Flared inlet:
organizes flow
prevents pannus



Complete Annulus Support

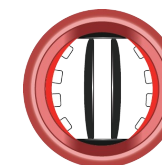
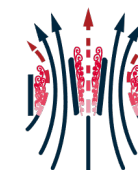
3 Pure pyrolytic
carbon: reduces
thrombogenicity²



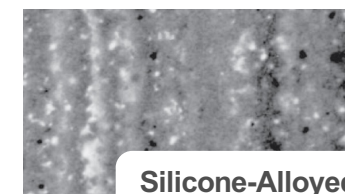
Pure
Pyrolytic Carbon²

All Other Bileaflet Valves

< 90°
Opening



Incomplete Annulus Support



Silicone-Alloyed
Pyrolytic Carbon²

Redefining Innovation in Valve Technology

Improved Anticoagulation vs. Reoperation

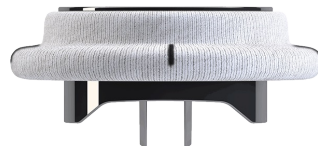
PROACT Aortic



2016

Low INR 1.5-2.0
>60% reduction in bleeding¹

PROACT Mitral



Est 2022

Low INR 2.0-2.5²

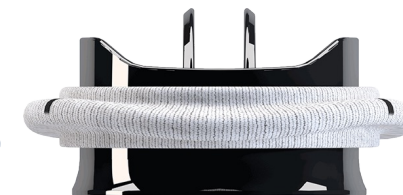
PROACT Xa



Est 2025

No INR³

Same Valve



Advancing
Indications

1. On-X Prosthetic Heart Valve Instructions for Use. 2. Disclaimer: The On-X Mitral valve is not currently approved by the FDA for low INR of 2.0-2.5. 3. Disclaimer: The On-X aortic valve is not currently approved by the FDA for use with apixaban or any other anticoagulation, except vitamin K antagonist. Disclaimer: ELIQUIS® is a registered trademark of the Bristol-Myers Squibb Company. Neither Artivion nor the PROACT Xa Trial are affiliated with, sponsored, or endorsed by the Bristol-Myers Squibb Company.

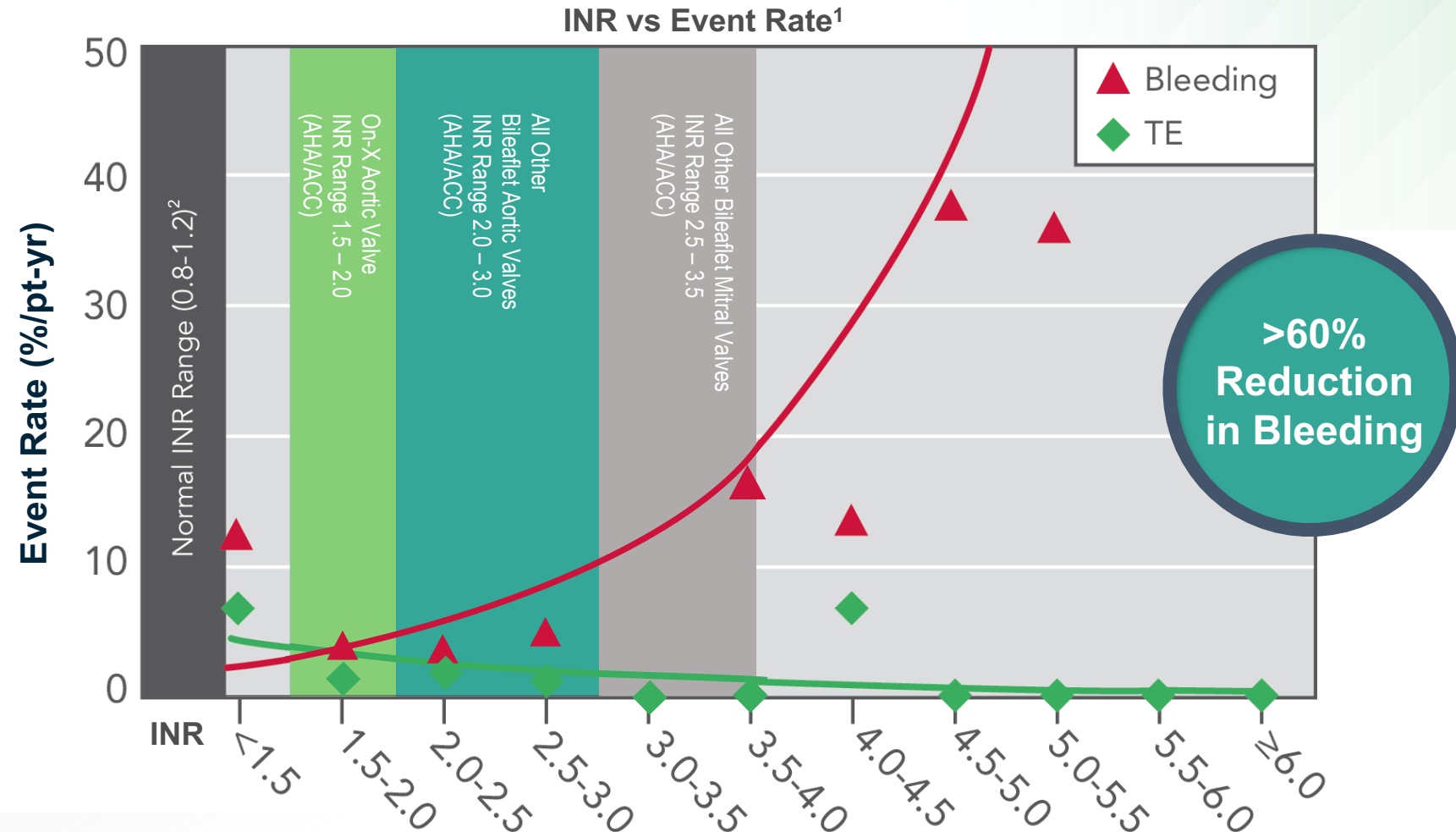
PROACT Aortic Trial Results

ARTIVION™

First and Only FDA
Approved Mechanical
Aortic Valve for
Reduced INR*



Bleeding risk
increases
exponentially with
increase in INR¹



*Reduce INR after 3 months standard therapy

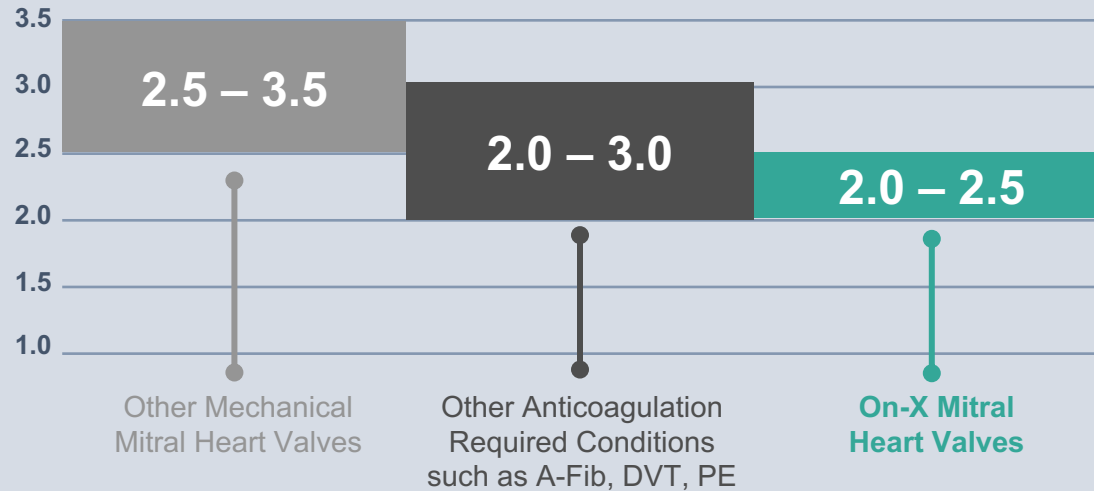
1. Data on file.

2. Levine M et al., Monitoring of international normalized ratios: comparison of community nurses with family physicians. Can Fam Physician 2012;58:e465-71

PROACT Mitral

ARTIVION™

On-X Mitral at a **low-dose warfarin** is consistent with other commonly managed warfarin strategies.



If patients could be managed at a low dose INR of 2.0-2.5* with On-X Mitral Valve:

“Danger Zones” overshoots will be minimized providing patients with greater safety margins

Reduces bleeding risks over the lifetime of the patient.

May allow for no or shorter bridging for routine procedures (colonoscopies, dental procedures, etc.)

PROACT

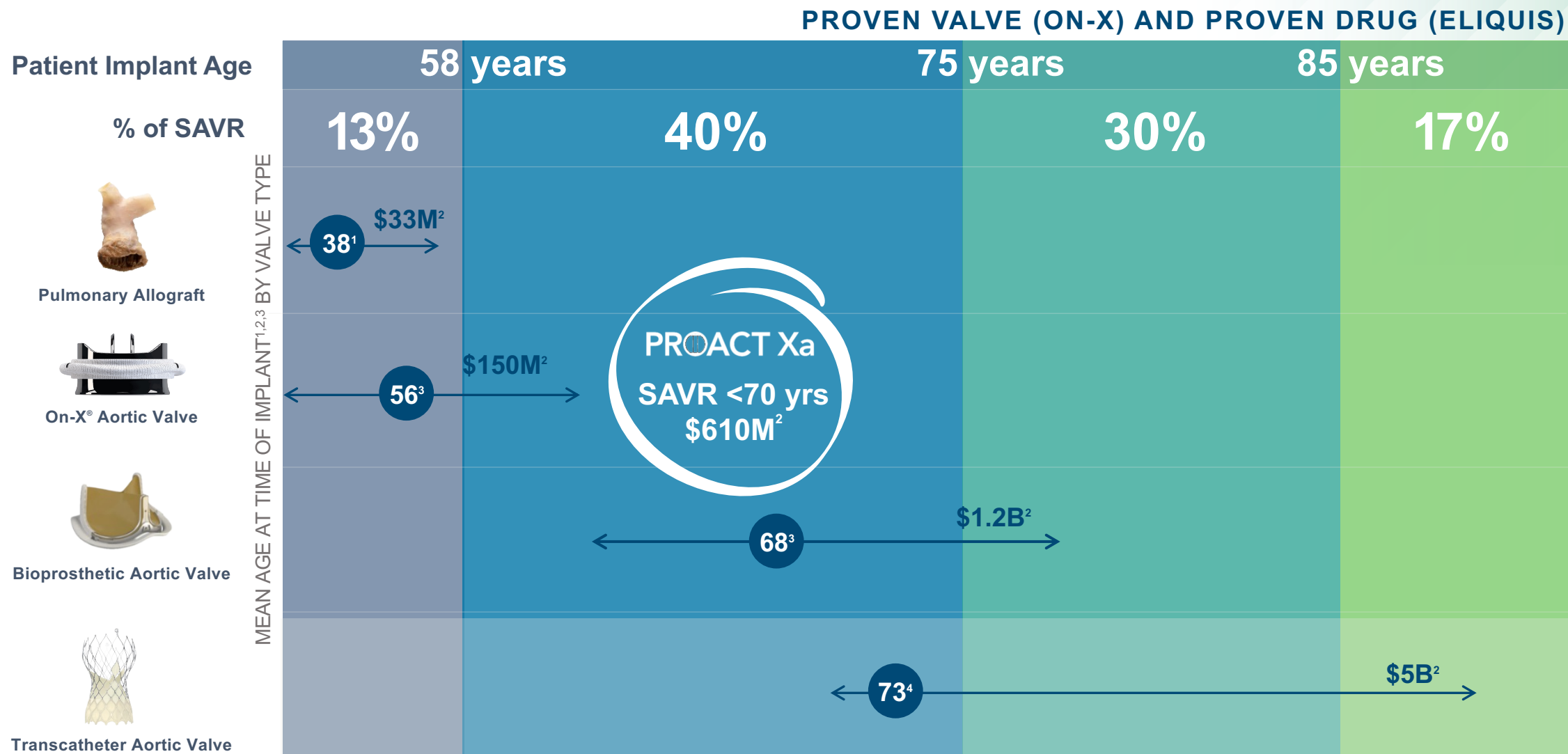


**Estimated Approval
US & EMEA – 2022
Market Opportunity: \$43M**

*Disclaimer: The On-X Mitral valve is not currently approved by the FDA for low INR of 2.0-2.5
1. Data on file.

Expanding Opportunity for SAVR Patients <70 Years of Age

ARTIVION™



1. Mazina A et al., JACC 2018;72(22):2761-77 2. Internal market model for valve replacement technologies 2021 age (yrs): Carroll JD, et al. Ann Thorac Surg. 2020; doi: 10.1016/j.athoracsur.2020.09.002.

3. Weighted national estimates from HCUP National (Nationwide) Inpatient Sample (NIS), 2017 4. 2019 average patient



PROACT Xa US Pivotal Trial

DR. JOHN ALEXANDER

Professor of Medicine/Cardiology
Duke Health

ARTIVION™

Reimagining Prosthetic Valve Antithrombotic Therapy: PROACT Xa



John H. Alexander, MD, MHS

Professor of Medicine/Cardiology
Duke Clinical Research Institute
Duke Health



Duke Clinical Research Institute

FROM THOUGHT LEADERSHIP
TO CLINICAL PRACTICE

Disclosures

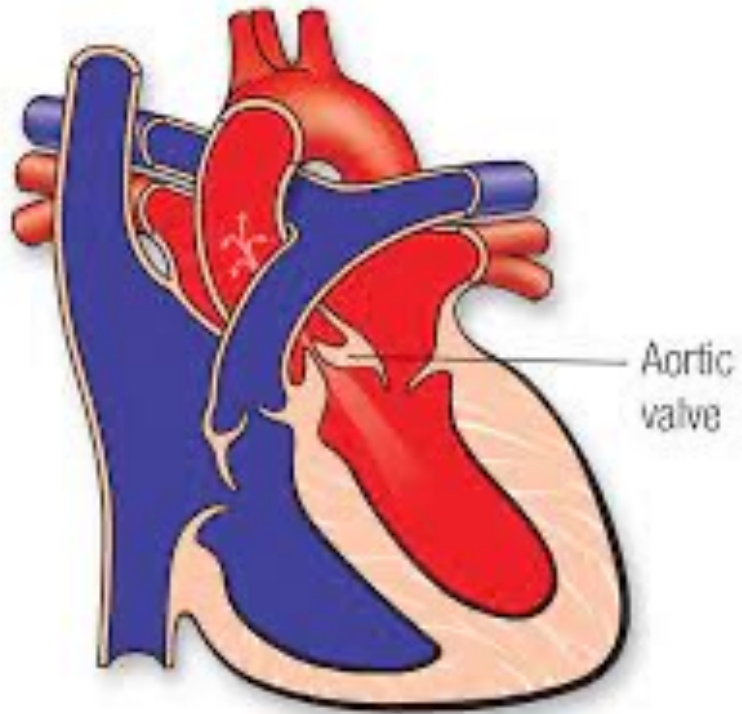
Research Support: Artivion/CryoLife, Bayer, Bristol-Myers Squibb, CSL Behring, Ferring, U.S. FDA, Humacyte, U.S. NIH, XaTek

Consultant: AbbVie, Akros, Artivion/CryoLife, AtriCure, Bristol-Myers Squibb, Ferring, GlaxoSmithKline, Janssen, Pfizer, Portola, Quantum Genomics



Aortic Stenosis

Stenotic Aortic Valve



Mild Stenosis



Moderate Stenosis



Severe Stenosis



Aortic Valve Replacement

Bioprosthetic

- **Transcatheter:**



Transcatheter

- **Bioprosthetic:**



Surgical

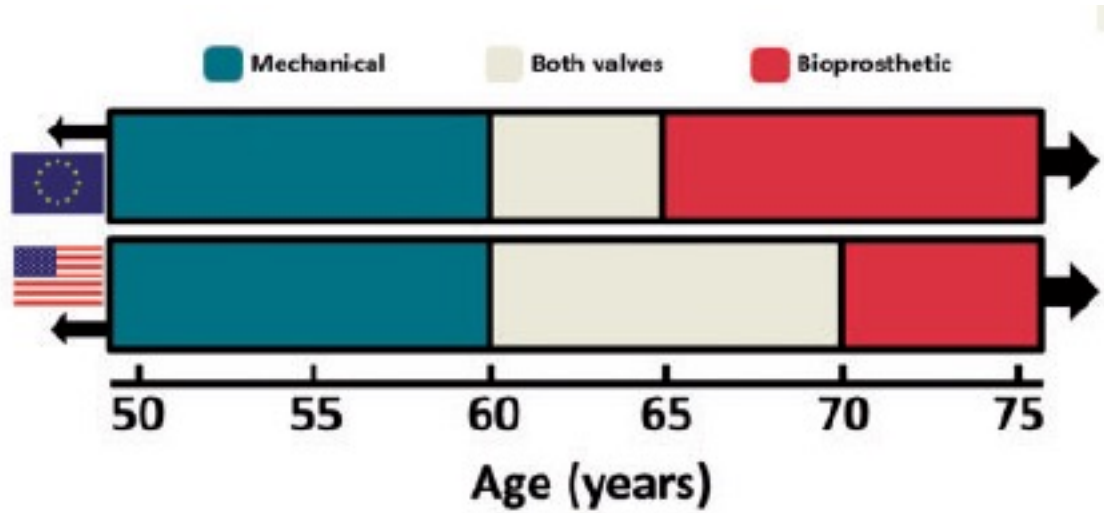
- **Mechanical:**



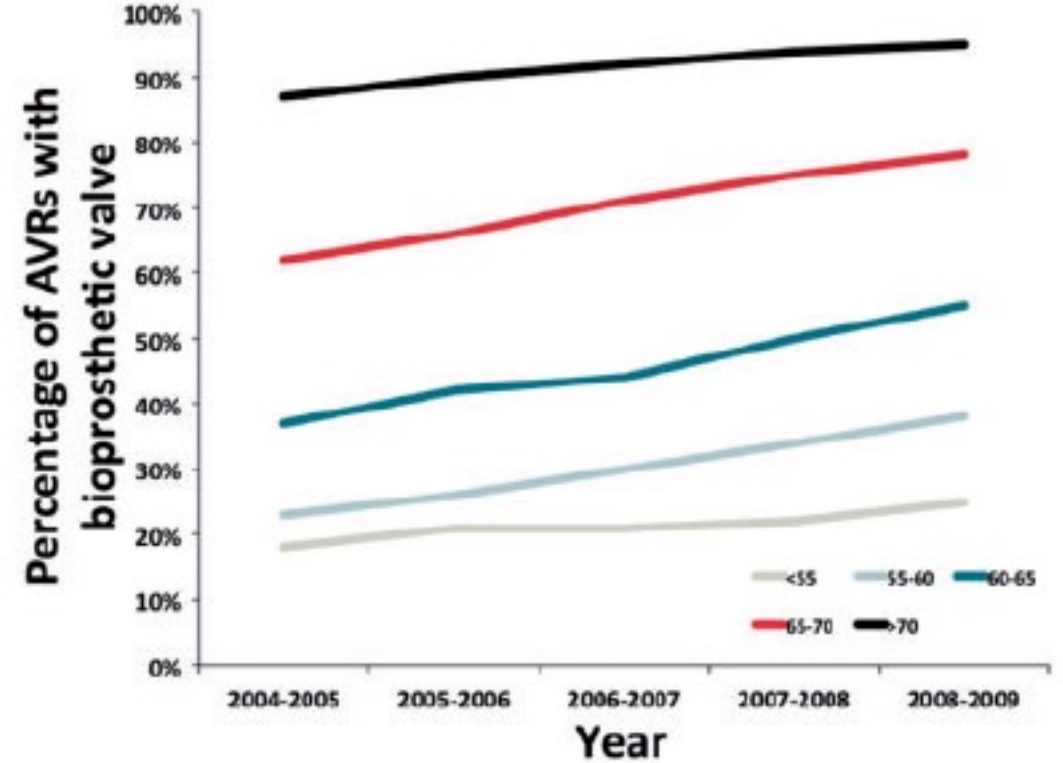
Mechanical



Mechanical vs. Tissue AVR



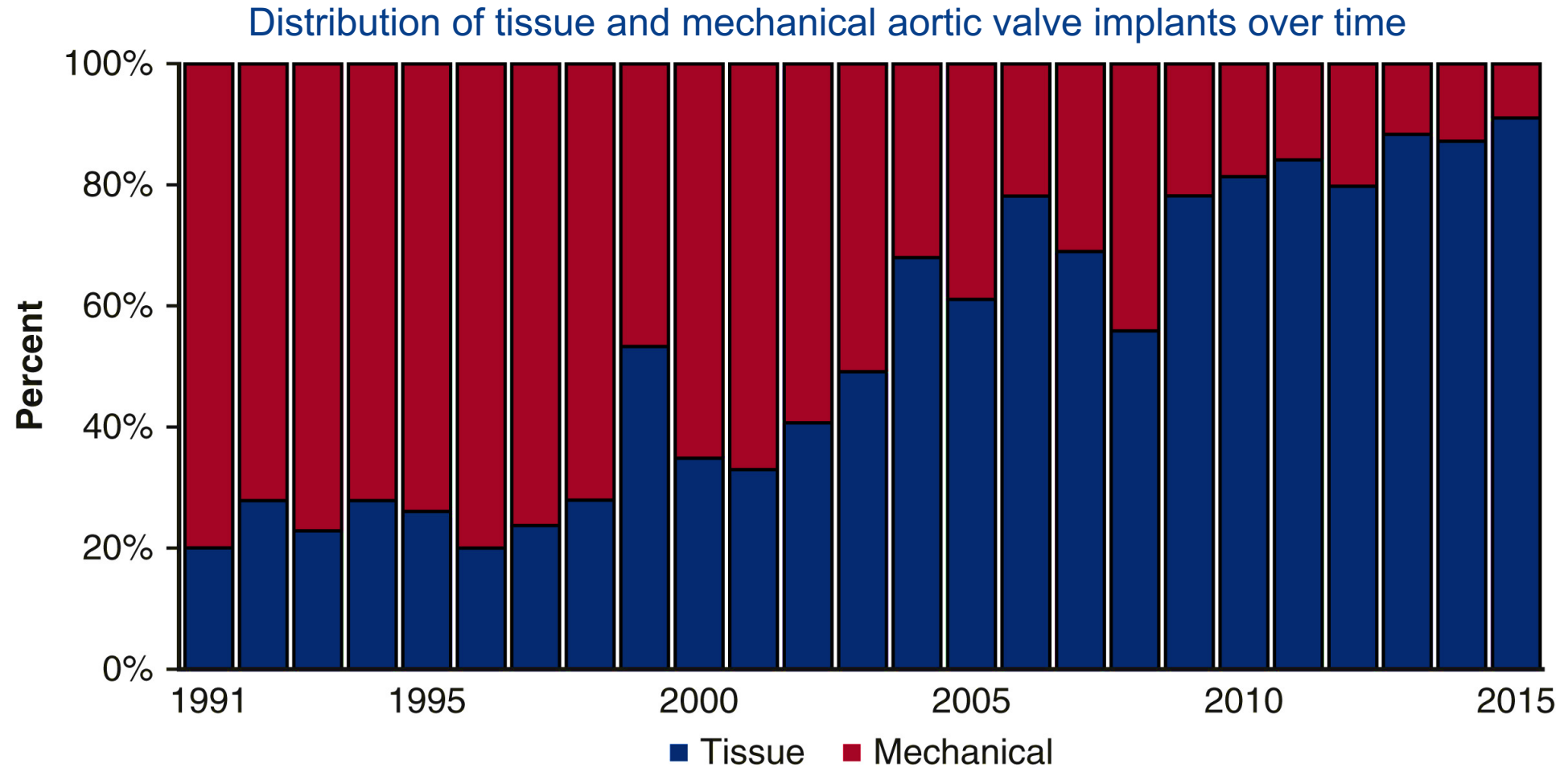
Guidelines
EU and US



Practice
Great Britain and Ireland

Mechanical and Tissue Heart Valves

Patients Aged 50-65 Years



Aortic Valve Replacement and Antithrombotic Therapy

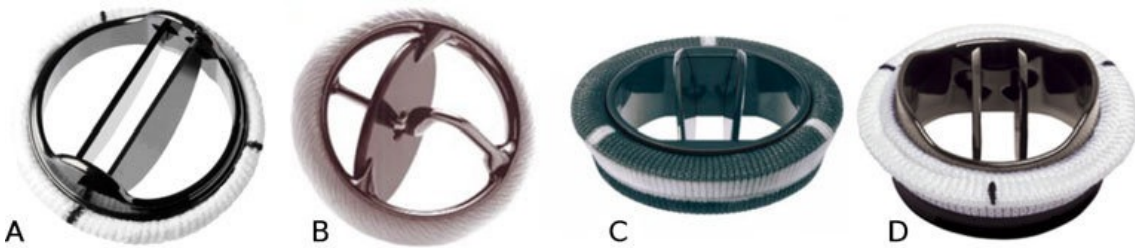
- **Transcatheter:** Aspirin + Clopidogrel



- **Bioprosthetic:** Aspirin \pm Vitamin K Antagonist



- **Mechanical:** Vitamin K Antagonist \pm Aspirin



- FDA device (CDRH) approval = reasonable assurance of safety and effectiveness
- Prosthetic valves developed with an antithrombotic regimen (guess, extrapolation, historical)
- Valve + antithrombotic regimen combination = reasonable assurance of safety and effectiveness
- Typically no systematic evaluation of (or requirement for) an optimal antithrombotic regimen (safety or effectiveness)
- **Antithrombotic options are a major factor in surgeon and patient valve choice**

Mechanical Tissue AVR

- A percutaneous (vs. surgical) option
 - Lets avoid major surgery
- Short term bias
 - Bioprosthetic valves last less long (10-15 years vs. forever)
- Warfarin = Worry
 - Mechanical valves required anticoagulation



Antithrombotic Guideline Recommendations for Patients with Mechanical Prosthetic Aortic Heart Valves

COR	LOE	Recommendation
I	A	In patients with a mechanical prosthetic valve, anticoagulation with a VKA is recommended
I	B-NR	For patients with a mechanical bileaflet or current-generation single-tilting disk AVR and no risk factors for thromboembolism, anticoagulation with a VKA to achieve an INR of 2.5 is recommended
I	B-NR	For patients with a mechanical AVR and additional risk factors for thromboembolism or an older-generation prosthesis, anticoagulation with a VKA to achieve an INR of 3.0 is recommended
IIb	B-R	For patients with a mechanical On-X AVR and no thromboembolic risk factors, use of a VKA targeted to a lower INR (1.5-2.0) may be reasonable starting >3 months after surgery with continuation of aspirin 75-100 mg daily
IIb	B-R	For patients with a mechanical SAVR who are managed with a VKA and have an indication for antiplatelet therapy, addition of aspirin 75-100 mg may be considered when the risk of bleeding is low

COR=Class of Recommendation, LOE = Level of Evidence

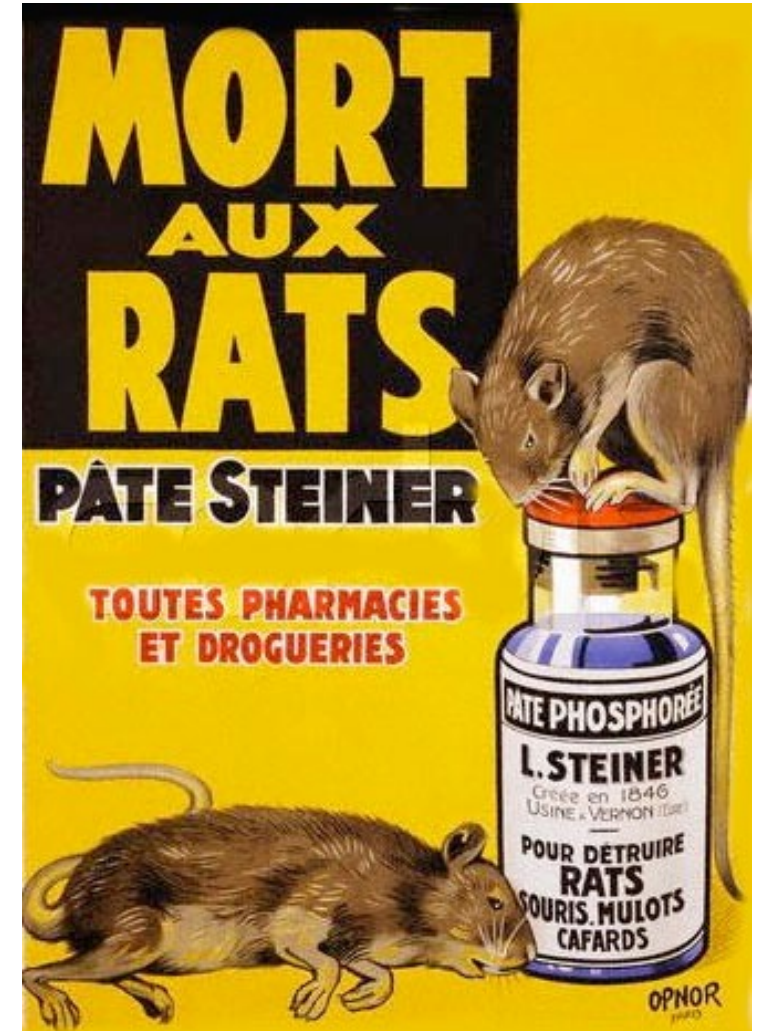


Duke Clinical Research Institute

Otto CM, et al., 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2020;143:e729–e227

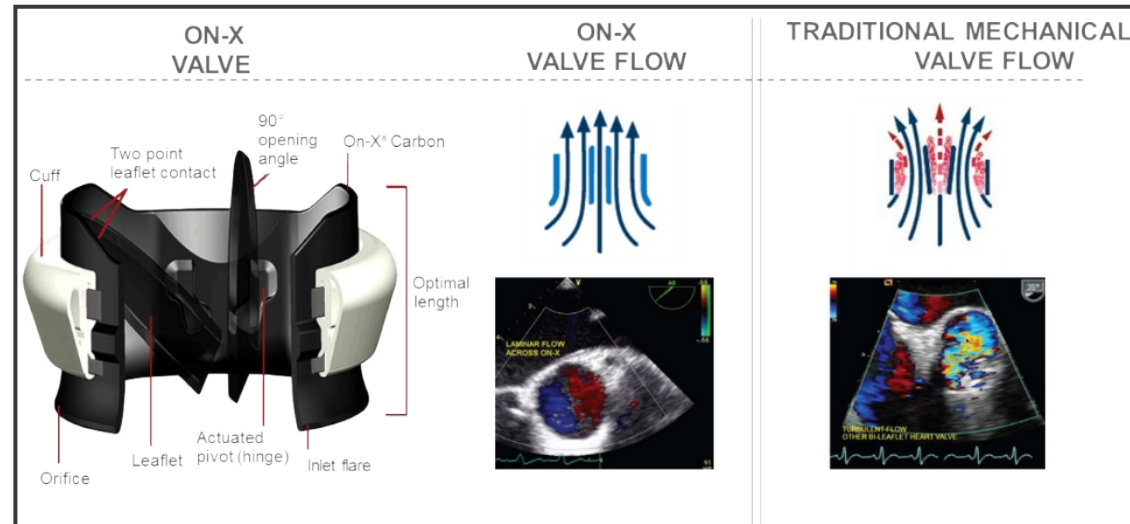
Warfarin = Worry!

- Risk of bleeding
- Narrow therapeutic window
 - \downarrow INR \rightarrow \uparrow risk of embolism
 - \uparrow INR \rightarrow \uparrow risk of bleeding
- Response influenced by diet, concomitant medications, herbal supplements, concomitant illness, etc.
- Requires regular dose-adjustment based on INR
- Slow onset and offset of effect



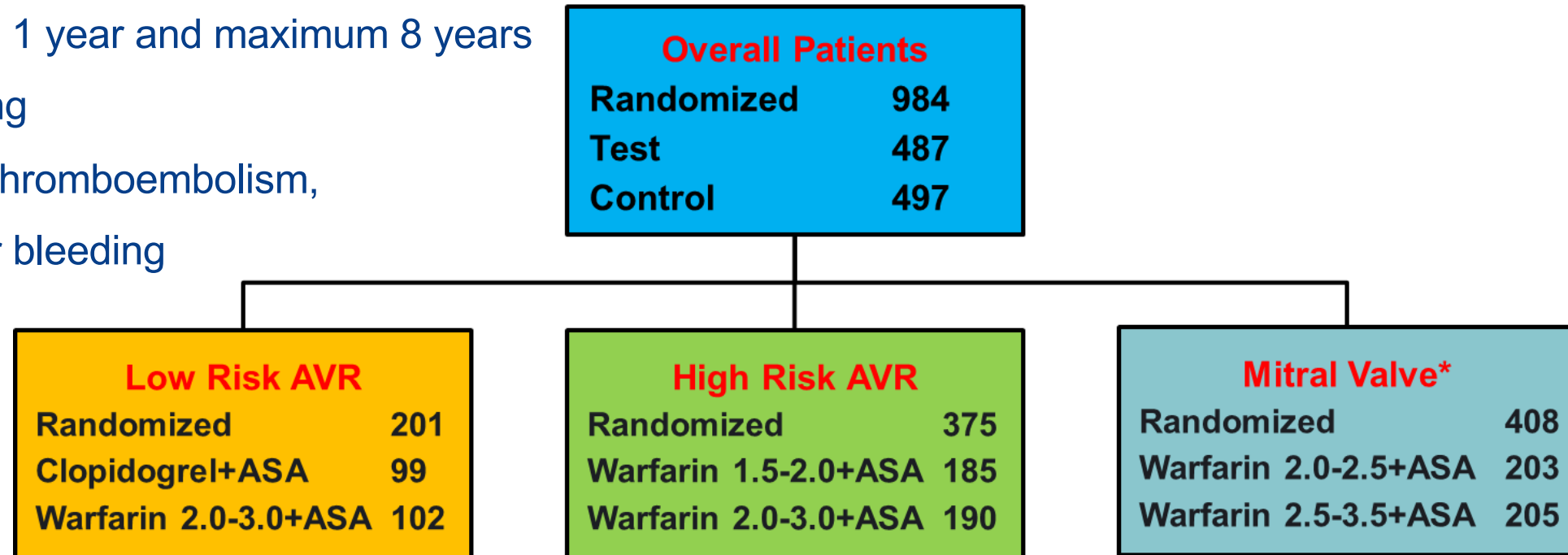
On-X Mechanical Aortic Valve

- Original PMA in 2001 with more than 200,000 implants
- Leaflets are pyrolytic carbon deposited on a graphite substrate
- Orifice inflow area has a flared inlet
- Leaflets form a nominal angle of 90° relative to the orifice plane
- Multiple studies evaluating safety and efficacy of the On-X valve with standard VKA anticoagulation (INR 2-3)

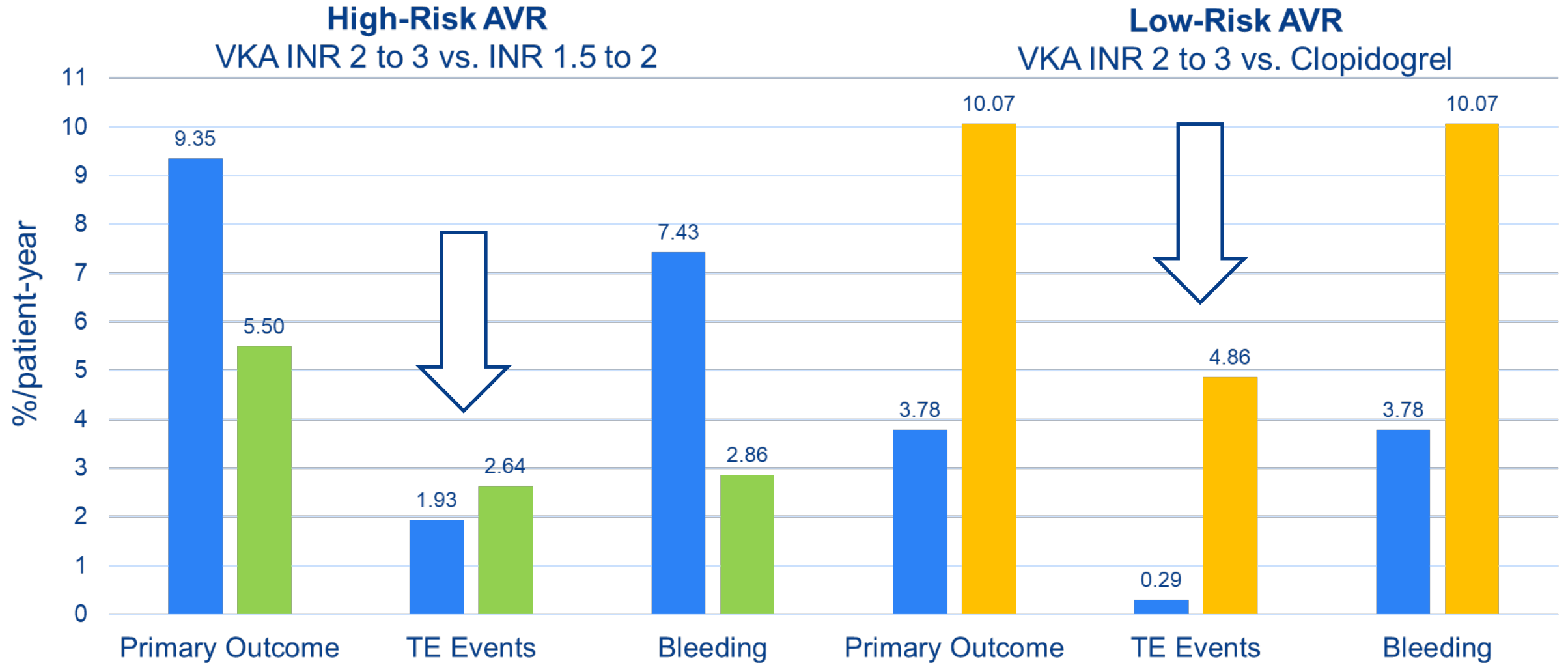


On-X PROACT Trial Design

- PROACT: Prospective Randomized On-X Anticoagulation Clinical Trial
- Multicenter (n=50), Randomized, Non-inferiority study
- 6 Study arms (4 AVR and 2 MVR)
- Patients are randomized ≥ 3 months post-valve implant
- Follow-up: minimum 1 year and maximum 8 years
- Home INR monitoring
- Endpoint (%/pt-yr): thromboembolism, valve thrombosis, or bleeding



PROACT Trial Results



Non-Vitamin K Antagonist Anticoagulants (“NOACs”) in Atrial Fibrillation

	Dabigatran RE-LY	Rivaroxaban ROCKET-AF	Apixaban ARISTOTLE	Edoxaban ENGAGE-AF
Mechanism of action	Selective direct FIIa inhibitor	Selective direct FXa inhibitor	Selective direct FXa inhibitor	Selective direct FXa inhibitor
T_{1/2}	12 - 17 hours	6 - 9 hours	~12 hours	9 - 11 hours
Dosing	110 or 150 mg Twice daily	20 (15) mg Once daily	5 (2.5) mg Twice daily	60/30 mg or 30/15 mg Once daily
N	18,113	14,266	18,201	21,150
Design	Non-inferiority PROBE	Non-inferiority Double-blind	Non-inferiority Double-blind	Non-inferiority Double-blind
Population	AF + CHADS2 ≥ 1	AF + CHADS2 ≥ 2	AF + CHADS2 ≥ 1	AF + CHADS2 ≥ 2
Comparator	Warfarin INR 2-3	Warfarin INR 2-3	Warfarin INR 2-3	Warfarin INR 2-3
Stroke/SE	150 mg = 34% ↓ (Sup) 110 mg = 9% ↓ (NI)	12% ↓ (NI)	21% ↓ (Sup)	60/30 mg = 13% ↓ (NI) 30/15 mg = 13% ↑ (Not NI)
Bleeding	150 mg = 7% ↓ (NS) 110 mg = 20% ↓ (Sup)	3% ↑ (NS)	31% ↓ (Sup)	60/30 mg = 20% ↓ (Sup) 30/15 mg = 53% ↓ (Sup)



Apixaban Versus Warfarin for Mechanical Heart Valve Thromboprophylaxis in a Swine Aortic Heterotopic Valve Model

Patrick A. Lester, Dawn M. Coleman, Jose A. Diaz, Tatum O. Jackson, Angela E. Hawley, Angela R. Mathues, Brandon T. Grant, Robert M. Knabb, Eduardo Ramacciotti, Charles E. Frost, Yan Song, Thomas W. Wakefield, Daniel D. Myers Jr

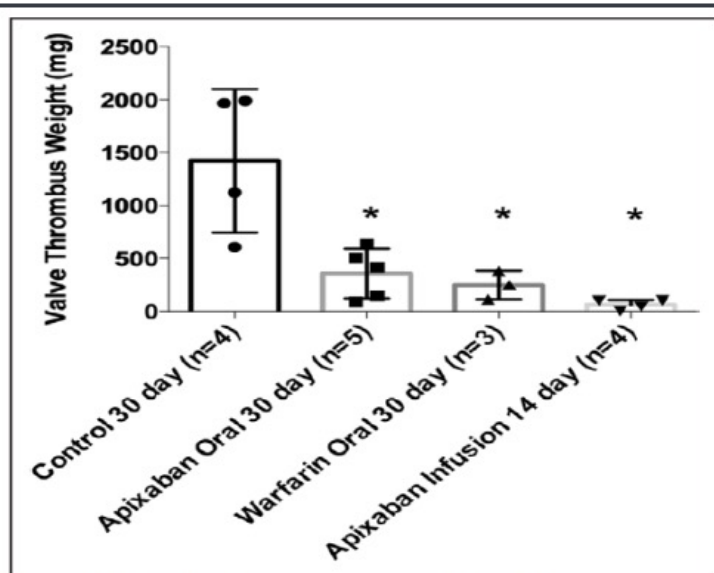
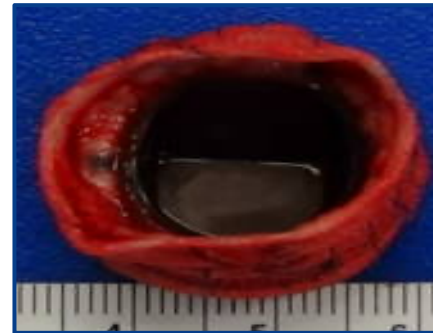
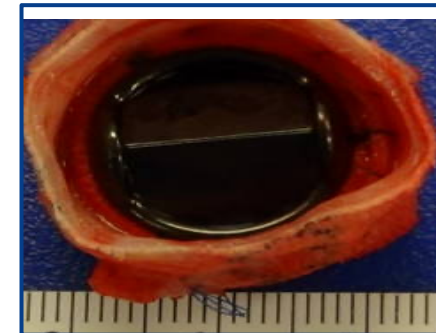


Figure 5. Valve thrombus weight (mean[mg]±SD) for each group. Nontreated control, duration 30 d; oral apixaban 1 mg/kg BID, duration 30 d; oral warfarin, duration 30 d; and apixaban multi-step infusion, duration 14 d. There was a significant difference (*) in control thrombus weights vs apixaban oral, warfarin oral, and apixaban infusion ($P<0.05$).



- Apixaban 30D
- 1 mg/kg PO, BID



- Warfarin 30D
- 2.5-4.5 mg PO, QD
- Average INR = 2.46

PROACT Xa Trial Design

**Patients with On-X aortic valve
replacement >3 months prior (n=1000)**

Randomize

Apixaban 5 mg BID
Apixaban 2.5 mg BID in selected patients

Open
Label

Continued warfarin
INR goal 2.0 – 3.0

2 year follow-up (≥800 patient-years in each arm)

Primary endpoint: composite of valve thrombosis or valve-related thromboembolism

Secondary endpoints: components of primary composite endpoint, major bleeding

Co-Primary Analyses:

- 1) Apixaban non-inferior to warfarin with absolute NI margin of 1.7%/patient-year
- 2) Apixaban primary outcome 95% CI below objective performance criteria (OPC) of 3.4%/patient-year



PROACT Xa Status*

- First participant randomized May 7, 2020 at CHI St. Vincent Medical Center, Little Rock, AR.
- 56 US sites open
 - 52 enrolling
- 627 participants (of 1000) enrolled
 - Median 18 months from AVR
 - 44% 3-12 months post-AVR
 - 56% >12 months post-AVR
- Top enrolling site Mayo Clinic = 73
- Currently 453 (of 1600) patient-years of follow-up
- DSMB Q6 months (November 2021) = “Continue the trial as planned”



Reimagining Prosthetic Valve Antithrombotic Therapy: PROACT Xa

Thank you!



Duke Clinical Research Institute

FROM THOUGHT LEADERSHIP
TO CLINICAL PRACTICE

PROACT Xa





Stents & Stent Grafts

KARL WILL

Vice President

Sales & Marketing, EMEA

ARTIVION™

Most Comprehensive Endovascular Portfolio

ARTIVION™

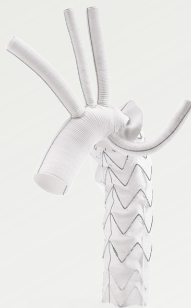


Innovative Aortic Arch Solutions – \$2.1B* TAM

AMDS



E-vita Open Neo



NEXUS



E-nya™



Comprehensive Abdominal Solutions – \$2.6B* TAM

E-nside™



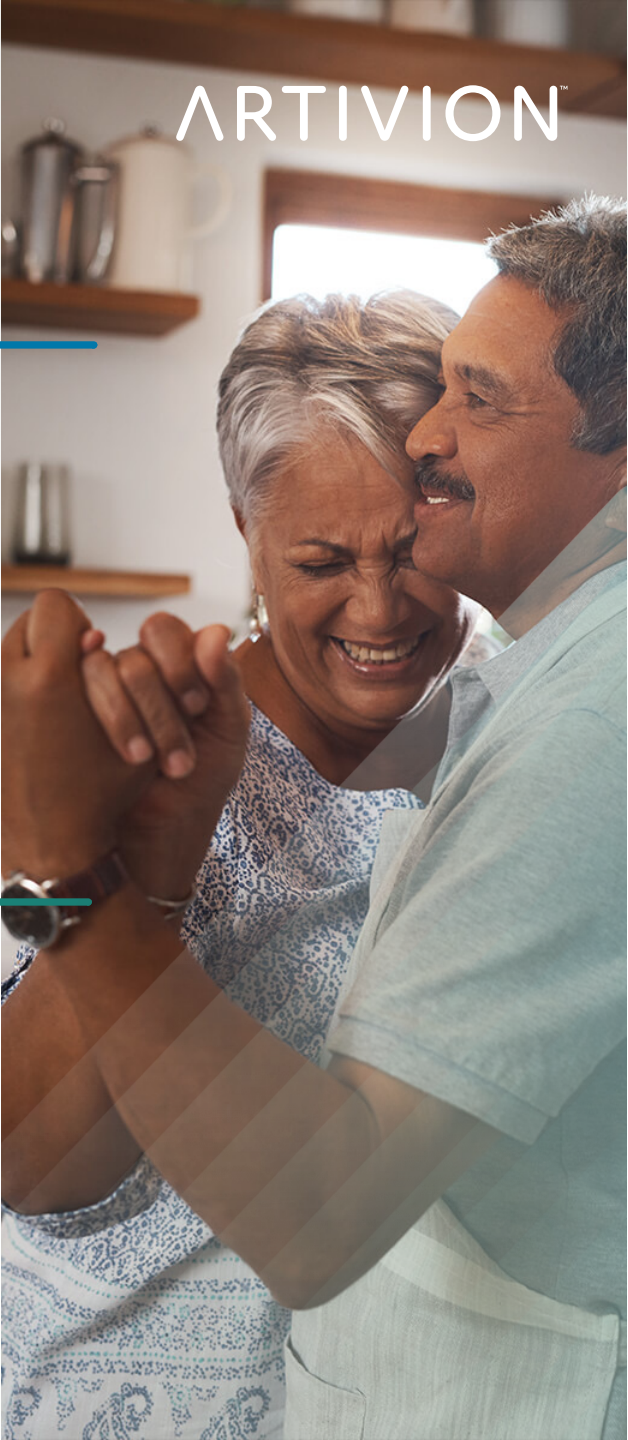
E-tegra



E-liac



E-ventus™

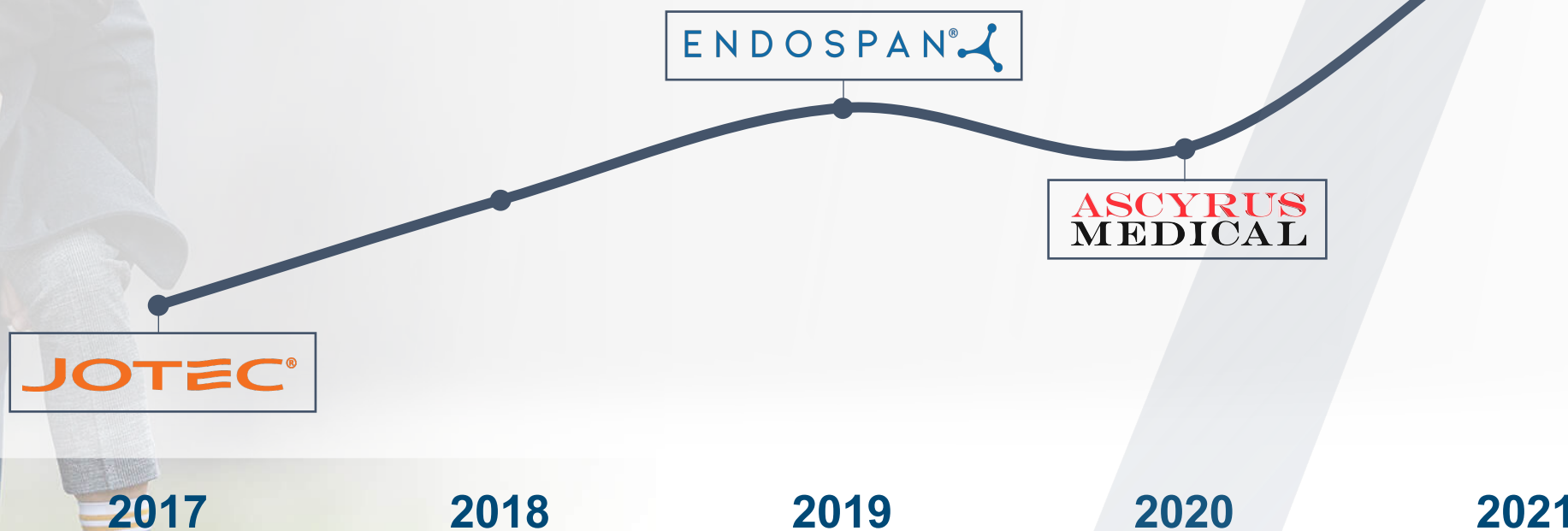


ARTIVION™

Stent Grafts 2017 – 2021 Revenue

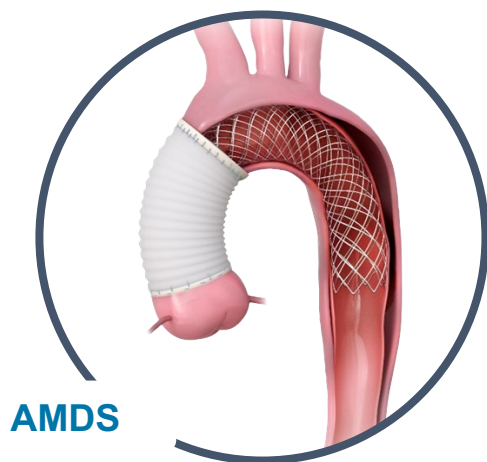
AORTIC-CENTRIC
FRANCHISE DRIVING

12%
CAGR



Aortic Arch Solutions: \$1.4B TAM*

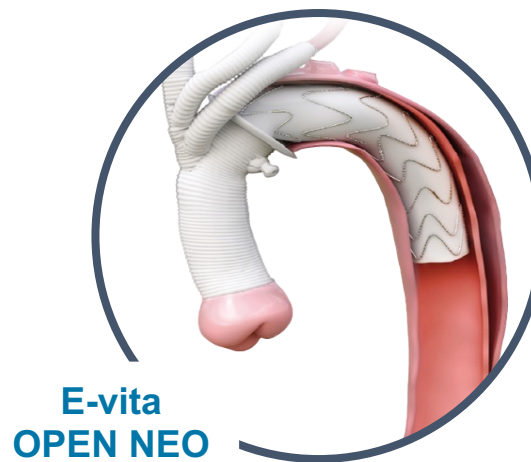
Hybrid Acute Type A Dissection (ATAD) Prosthesis



\$540M TAM*

Acute Type A Dissections (ATAD)

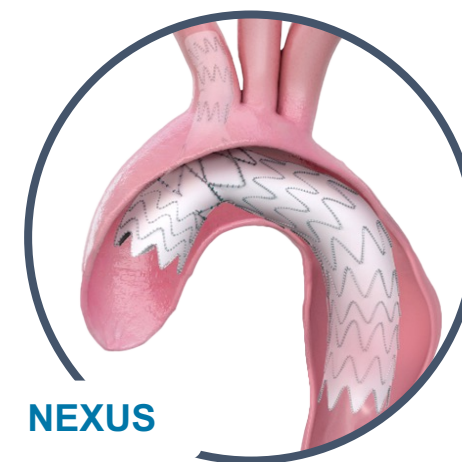
Frozen Elephant Trunk Hybrid System



\$250M TAM*

Dissections & Arch Aneurysms

Endovascular Arch Branch System



\$600M TAM*

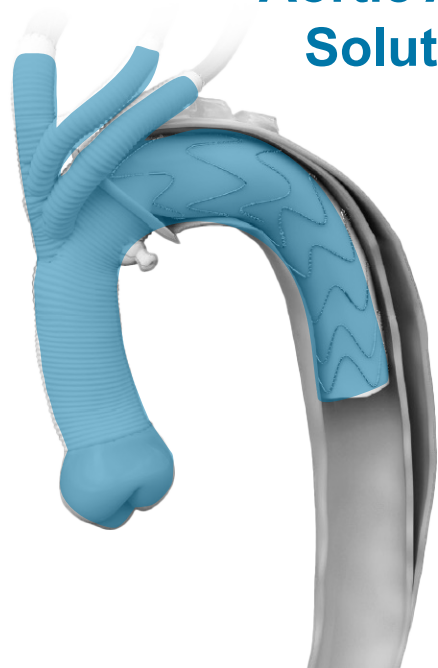
Chronic Dissections, Aneurysms, or PAU** involving the Aortic Arch




*Total available market of referenced portfolios (excluding E-nya) sourced from internal models 2021

**Penetrating atherosclerotic ulcer

Artivion has an Industry Leading & Highly Differentiated **Aortic Arch** Portfolio

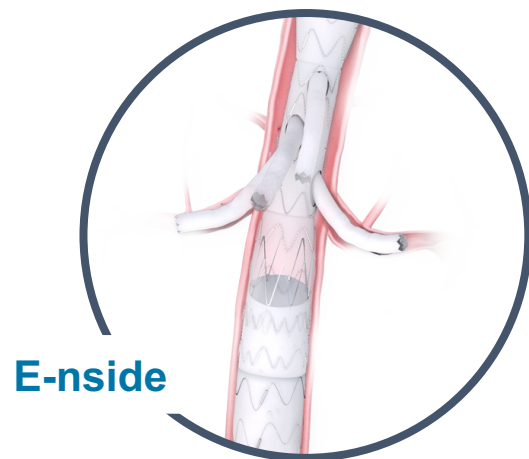
Aortic Arch Solutions



	Hybrid ATAD Prosthesis	Hybrid FET System	Endovascular Arch Branch System
ARTIVION	 AMDS	 E-vita OPEN NEO	 NEXUS
TERUMO		✓	✓
COOK MEDICAL			✓
2021/2020 Growth	58%	60%	85%

Abdominal Stent Grafts by Category: \$1.9B TAM*

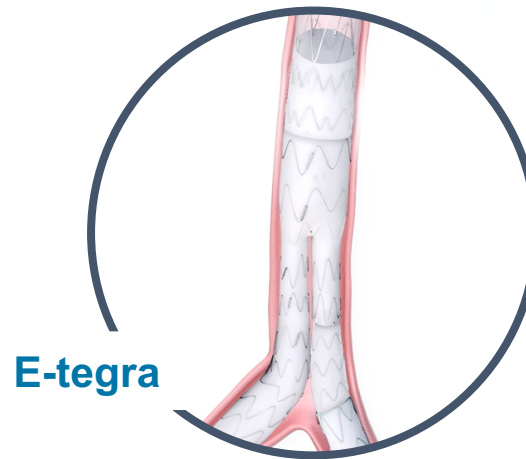
Thoracoabdominal



\$480M TAM*

Crawford I – V

Abdominal



\$1.27B TAM*

Chronic Dissections & Aneurysms

Iliac

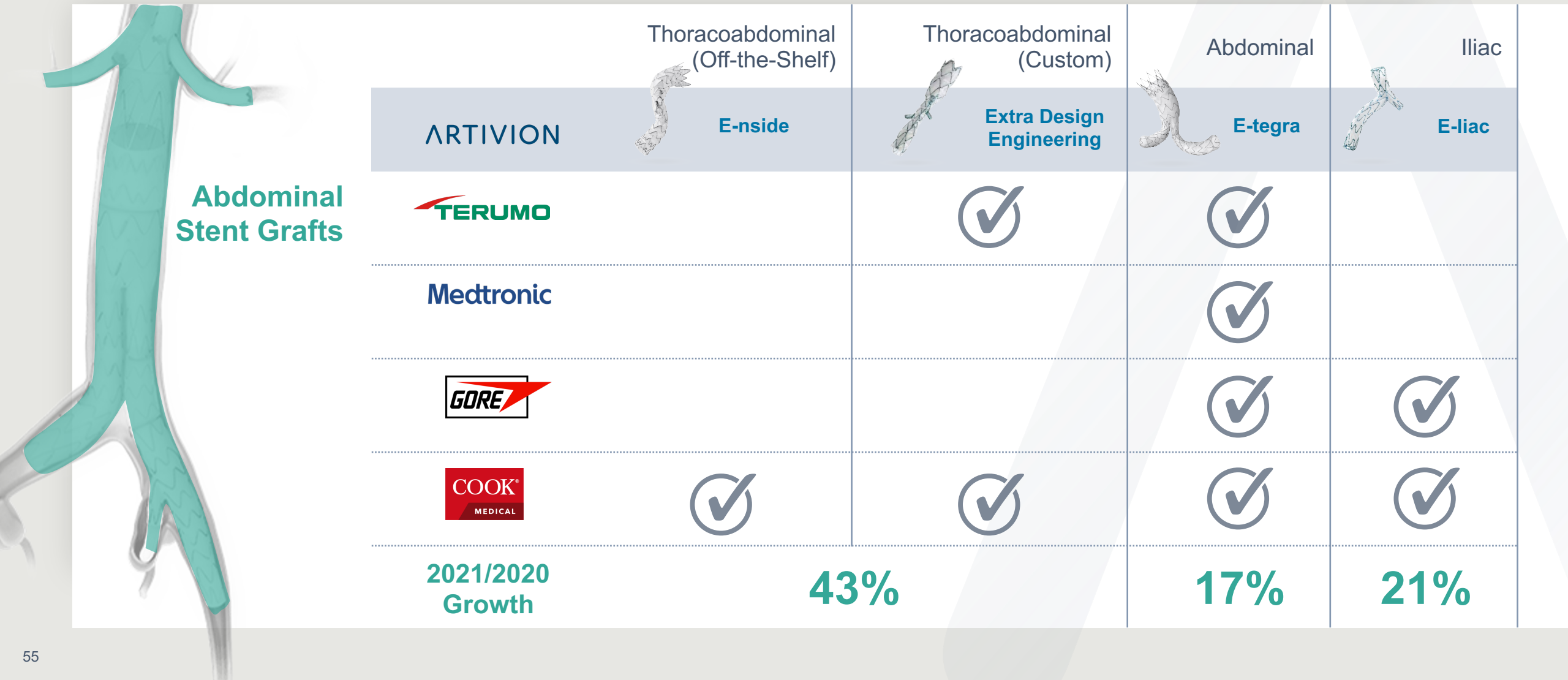


\$140M TAM*

Iliac Aneurysms

Artivion has an Industry Leading & Highly Differentiated **Abdominal Stent Graft Portfolio**

ARTIVION™



Direct Sales Channels EMEA

Artivion's Vascular Solutions offers a complete portfolio of advanced endovascular stent graft technologies to address both **simple** and **complex** anatomy.



32 CARDIAC
Sales Representatives



66 VASCULAR
Sales Representatives





AMDS

Hybrid Prosthesis

DR. JOERG KEMPFERT

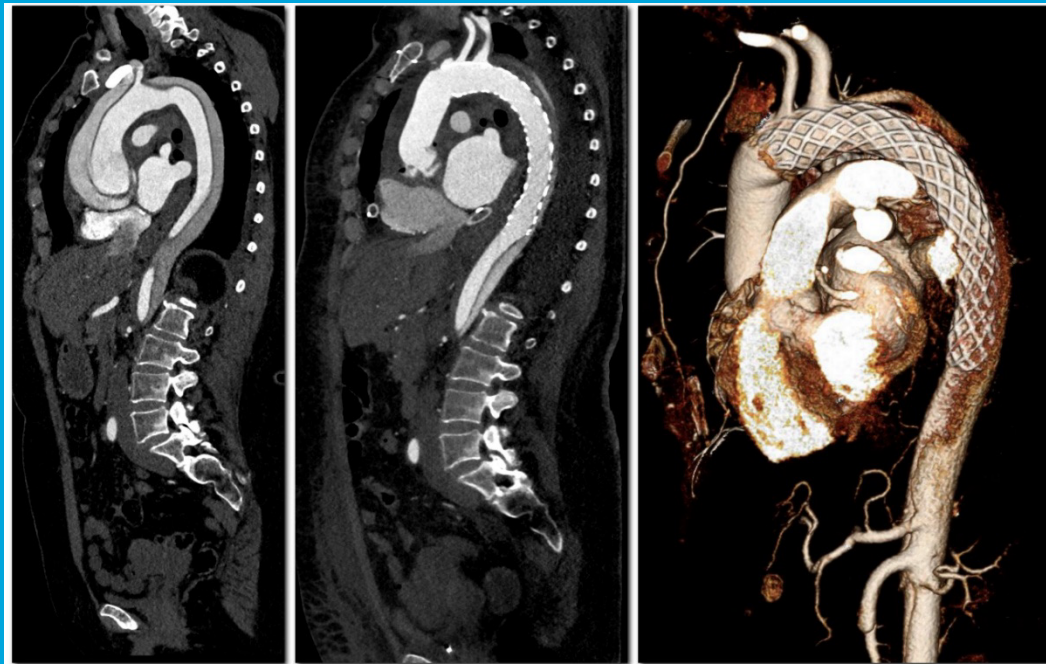
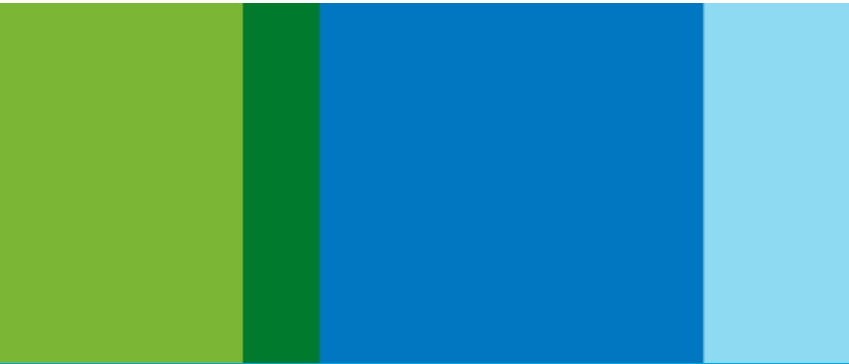
Professor of Cardiac Surgery
German Heart Center Berlin

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STIFTUNG DES BÜRGERLICHEN RECHTS



The AMDS device for acute aortic dissection

Prof. Jörg Kempfert, German Heart Center Berlin, 22.03.2022

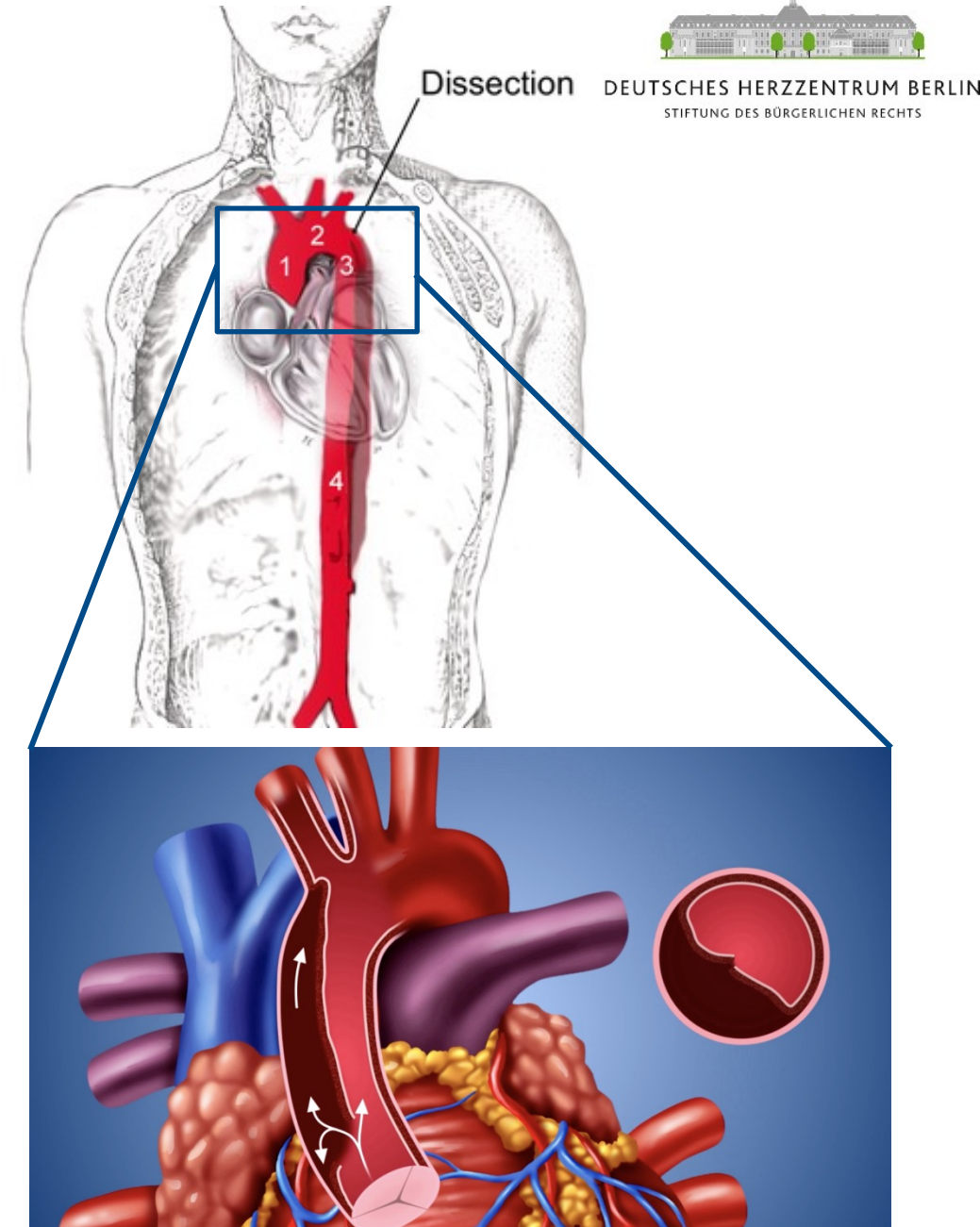


Acute Aortic Dissection

Background

What is an acute aortic dissection?

- Pathology of the **AORTA**,
the main arterial vessel in the human body
- Originates from a **tear** of the inner wall of the vessel
- The blood flowing through the tear disrupts the aortic wall layers, leading to the formation of two parallel flow patterns:
 - Native vessel lumen → **TRUE LUMEN**
 - New lumen in the aortic wall → **FALSE LUMEN**



Incidence of acute aortic dissection

- Reported incidence ranges between 2-16 cases /100,000 persons per year¹⁻¹³
- Acute type A dissections is an EMERGENCY
- Mortality without surgical intervention:
 - 2% per hour¹⁴
 - 50% of patients will die within 48h¹⁵
- CDC reported 12,000 Americans died in 2020 due to an aortic dissection¹⁶

Circulation: Cardiovascular Quality and Outcomes

ORIGINAL ARTICLE

Population-Based Assessment of the Incidence of Aortic Dissection, Intramural Hematoma, and Penetrating Ulcer, and Its Associated Mortality From 1995 to 2015

BACKGROUND: Aortic syndromes (ASs), including aortic dissection, intramural hematoma, and penetrating aortic ulcer, carry significant acute and long-term morbidity and mortality. However, the contemporary incidence and outcomes of AS are unknown.

METHODS AND RESULTS: We used the Rochester Epidemiology Project record linkage system to identify all Olmsted County, MN, residents with AS (1995–2015). Diagnostic imaging, medical records, and death certificates were reviewed to confirm the diagnosis and AS subtype. Age- and sex-adjusted incidence rates were estimated using annual county-level census data. Survival for patients with AS was compared with age- and sex-matched controls using Cox regression to adjust for comorbid conditions. We identified 133 patients with AS (77, aortic dissection; 21, intramural hematoma; and 35, penetrating aortic ulcer). Average age was 71.8 years (SD=14.1), and 57% were men. The age- and sex-adjusted incidence was 7.7 per 100 000 person-years, was higher for men than women (10.2 versus 5.7 per 100 000 person-years), and increased with age. Among subtypes, the incidence of aortic dissection was highest (4.4 per 100 000 person-years), whereas the incidence of penetrating aortic ulcer and intramural hematoma was lower (2.1 and 1.2 per 100 000 person-years). Overall, the incidence of AS was stable over time (P trend=0.33), although the incidence of penetrating aortic ulcer seemed to increase from 0.6 to 2.6 per 100 000 person-years ($P=0.008$) with variability over the study interval. Patients with AS had more than twice the mortality rate at 5, 10, and 20 years when compared with population-based controls (5-, 10-, and 20-year mortality 39%, 57%, and 91% versus 18%, 41%, and 66%; overall adjusted mortality hazards ratio=2.1; $P<0.001$). Survival was lower than expected up to 90 days after AS diagnosis and did not differ significantly by subtype or by 5-year strata of diagnosis.

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Alanna M. Chamberlain, PhD
Salome Weiss, MD
Philip P. Goodney, MD, MS
Veronique Roger, MD, MPH





**King George II
of England
(1683-1760)**



John Ritter



Michael DeBakey



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Princess Diana

Why is acute aortic dissection so deadly?

Aortic rupture

Aortic rupture: the aortic tear becomes transmural:

- the patient will bleed to death within minutes
- and/or will die from „pericardial tamponade“
(blood in the pericardium prevent filling of the heart)



Why is acute aortic dissection (ATAAD) so deadly?

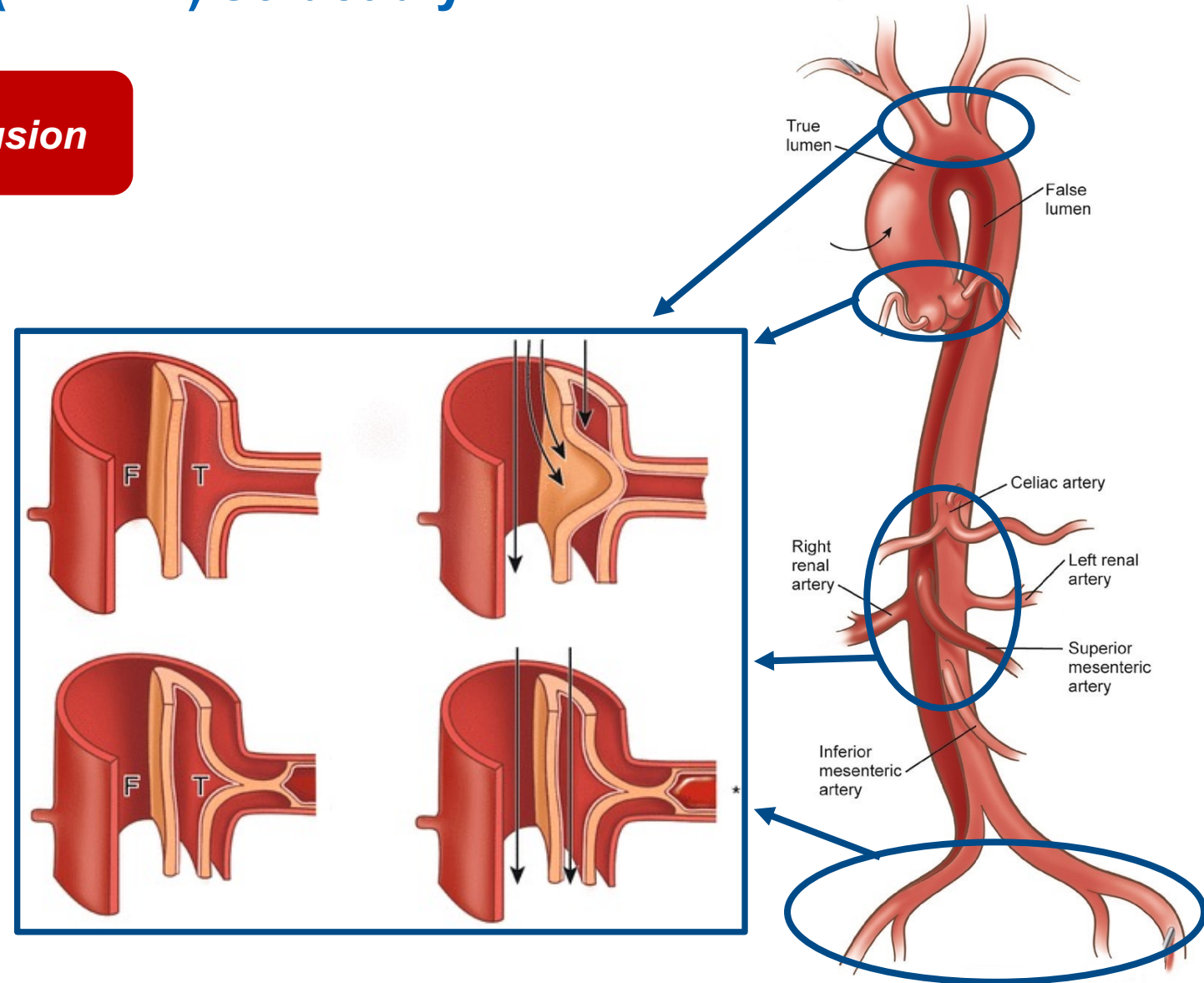
30-55% of all ATAAD¹⁷⁻¹⁹

-> 5x higher mortality¹⁸

Malperfusion

Might involve:

- Coronary arteries - **MI**
- Supraaortic branches - **Stroke**
- Visceral arteries – **Organ Failure**
- Peripheral arteries - **Paresis**



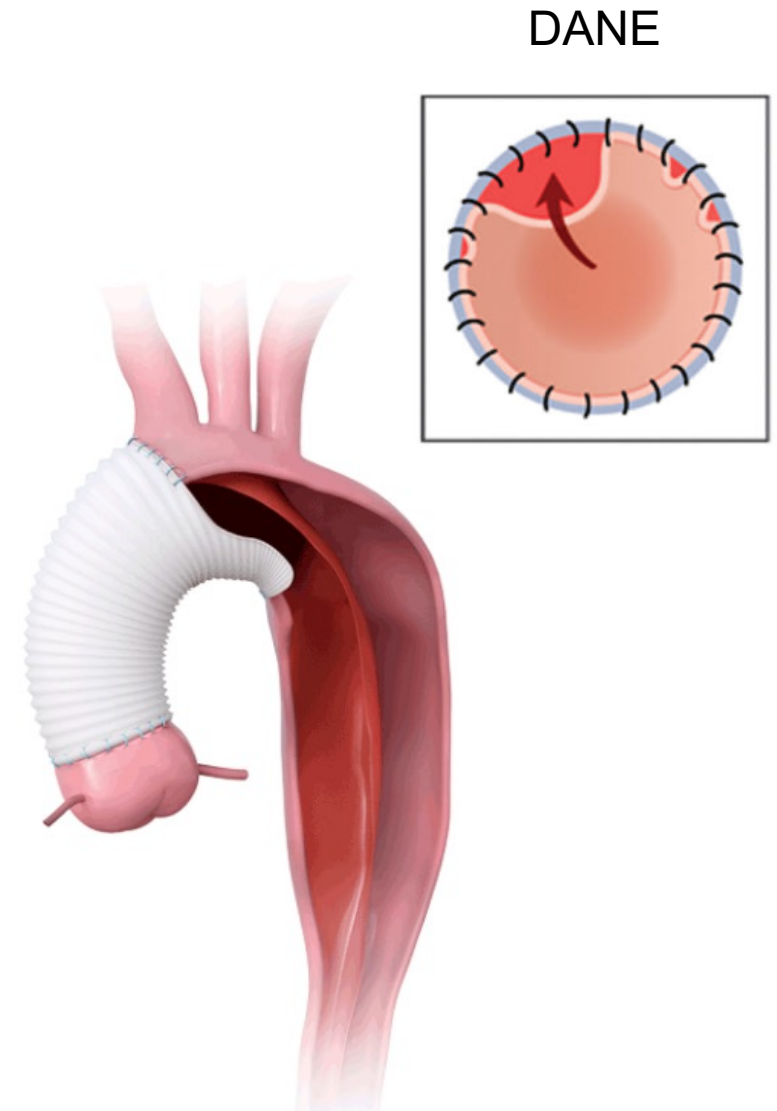


Acute Aortic Dissection

Standard of care

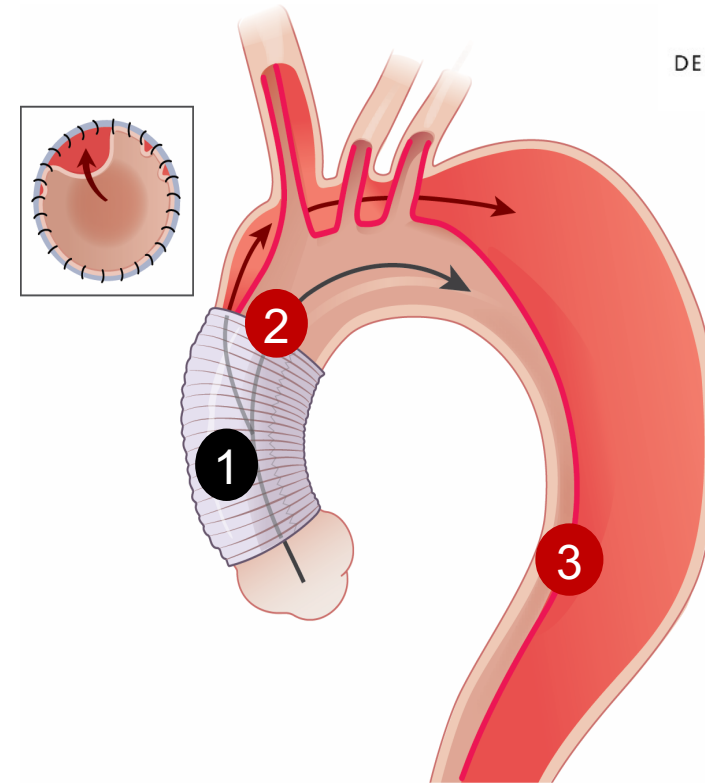
Standard of care: Hemiarch repair

- STS database, the median number of surgical repair for ATAAD performed in an average hospital is **3 per year**. Only 11% of centers performed 10 or more cases.²⁰
- Mortality of ATAAD patients managed surgically range from 17%²⁰ to 26%²¹. There is a correlation between hospital experience and lower mortality.²⁰
- DANE is observed in 40-70% of patients post hemiarch repair.^{22,23} -> Will pressurize FALSE lumen



Pitfalls of standard of care

Patent (pressurized) false lumen leads to **reduced actuarial survival** by over 10% at 5 years and over 30% at 10 years compared to patients with occluded false lumen.²⁴



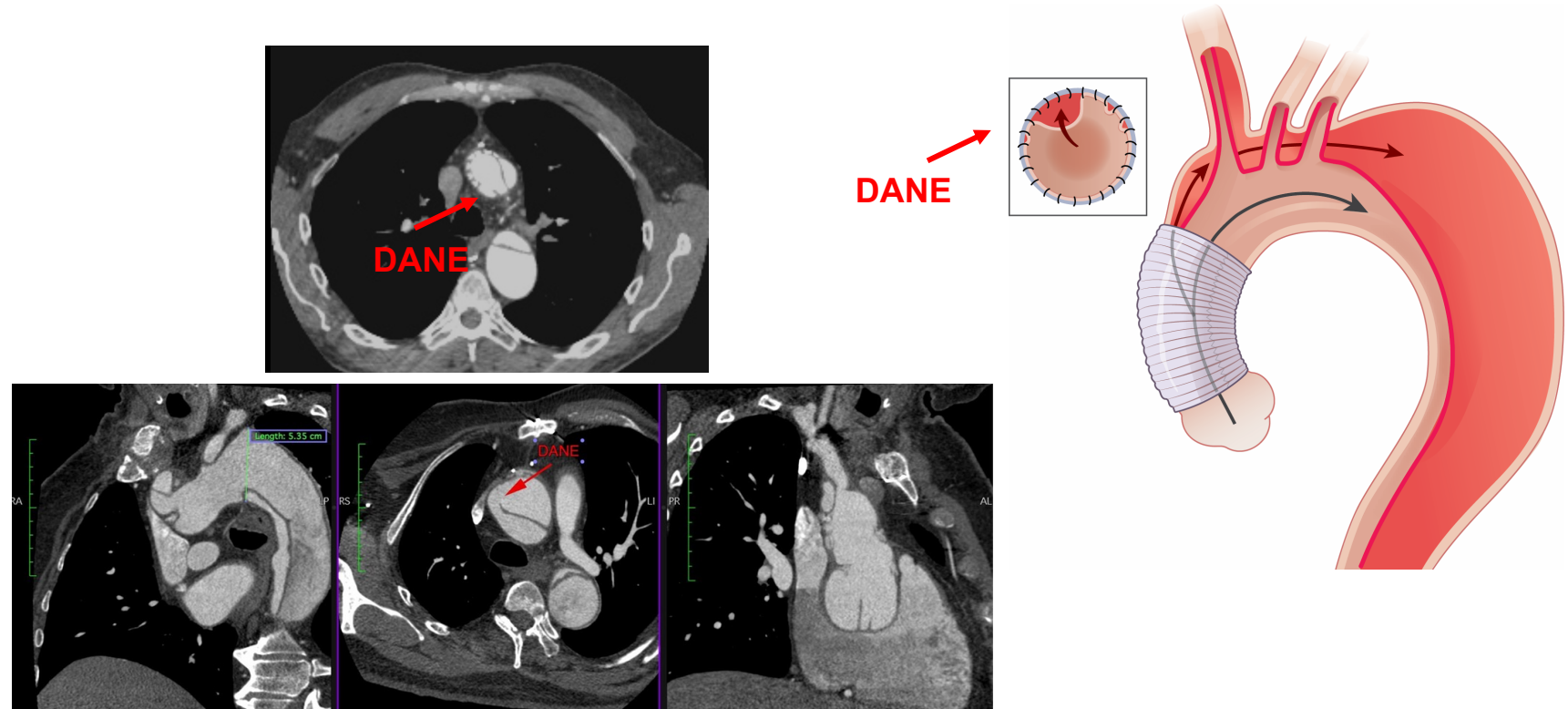
Early: unsolved malperfusion

Late: Aortic Growth (Negative Remodeling)



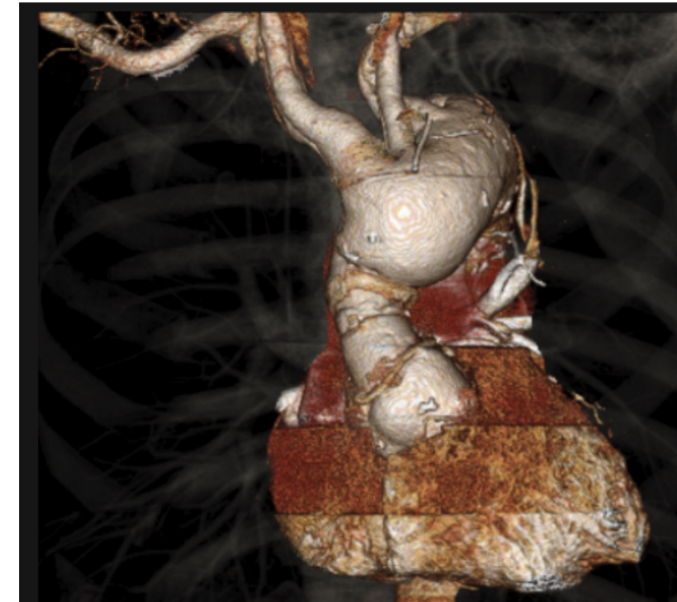
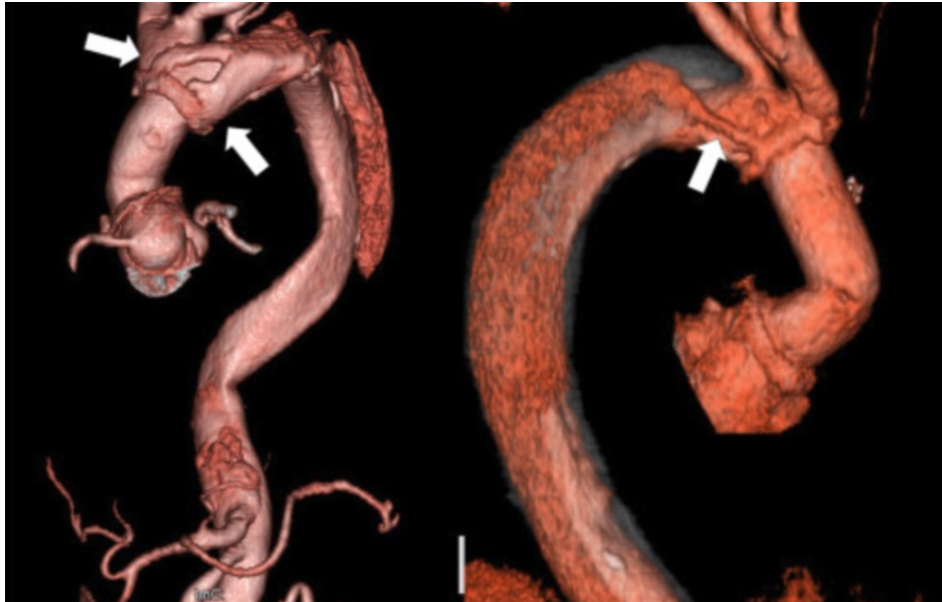
- ***Mortality***
- ***Re-Intervention***

Pitfalls of standard of care: unsolved malperfusion



Actual Standard of Care Cannot Reliably and with Confidence Abolish the Antegrade Pulsatile Flow and Expand the TL

Pitfalls of standard of care: negative remodeling



*In Addition to High Rates of Mortality, Up to 50% of Survivors
Require Reintervention for Malperfusion and Aortic Growth*



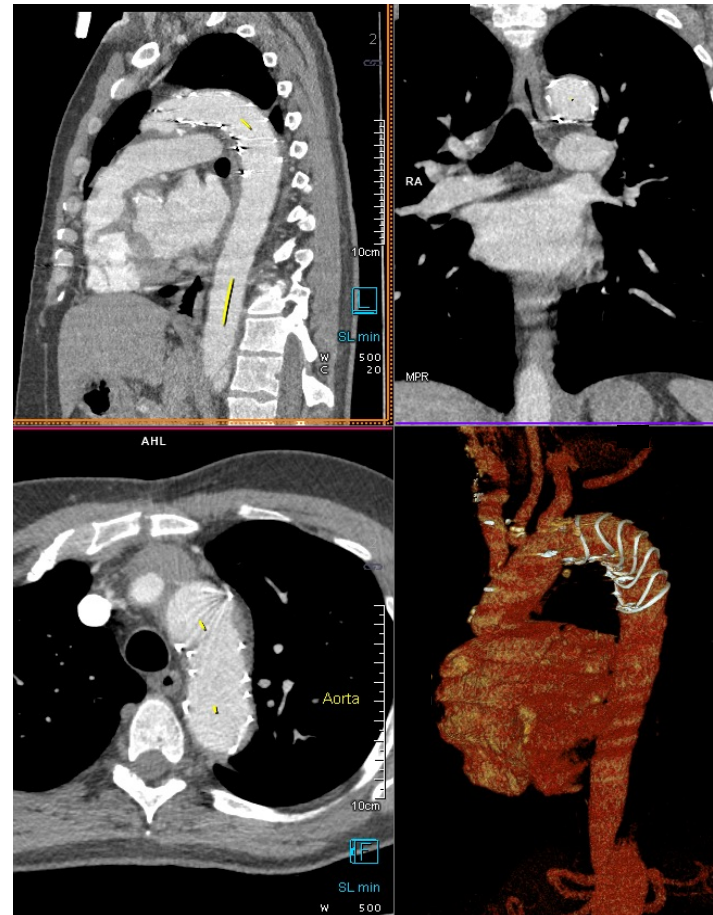
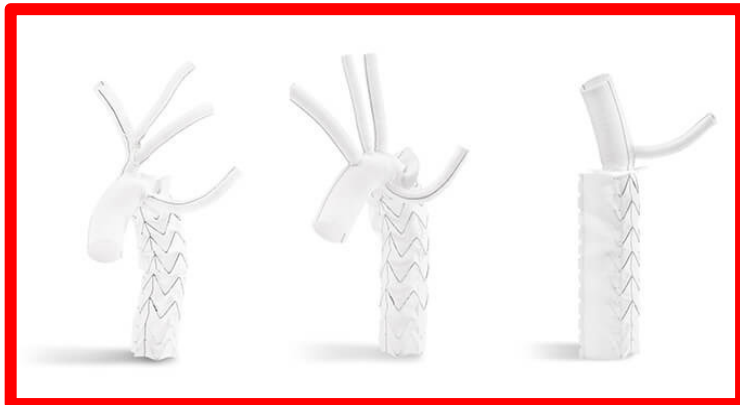
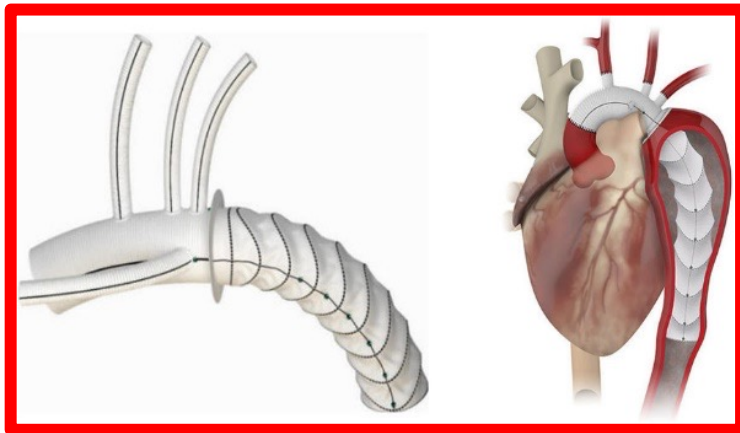
Acute Aortic Dissection

New approaches

Single stage treatment: the Frozen elephant trunk (FET) technique

To overcome pitfalls of standard of care in ATAAD – Surgical Hybrid prosthesis

SINGLE STAGE Total Arch + Proximal Descending Replacement



FET technique (more details follow):

Safety and **reproducibility**

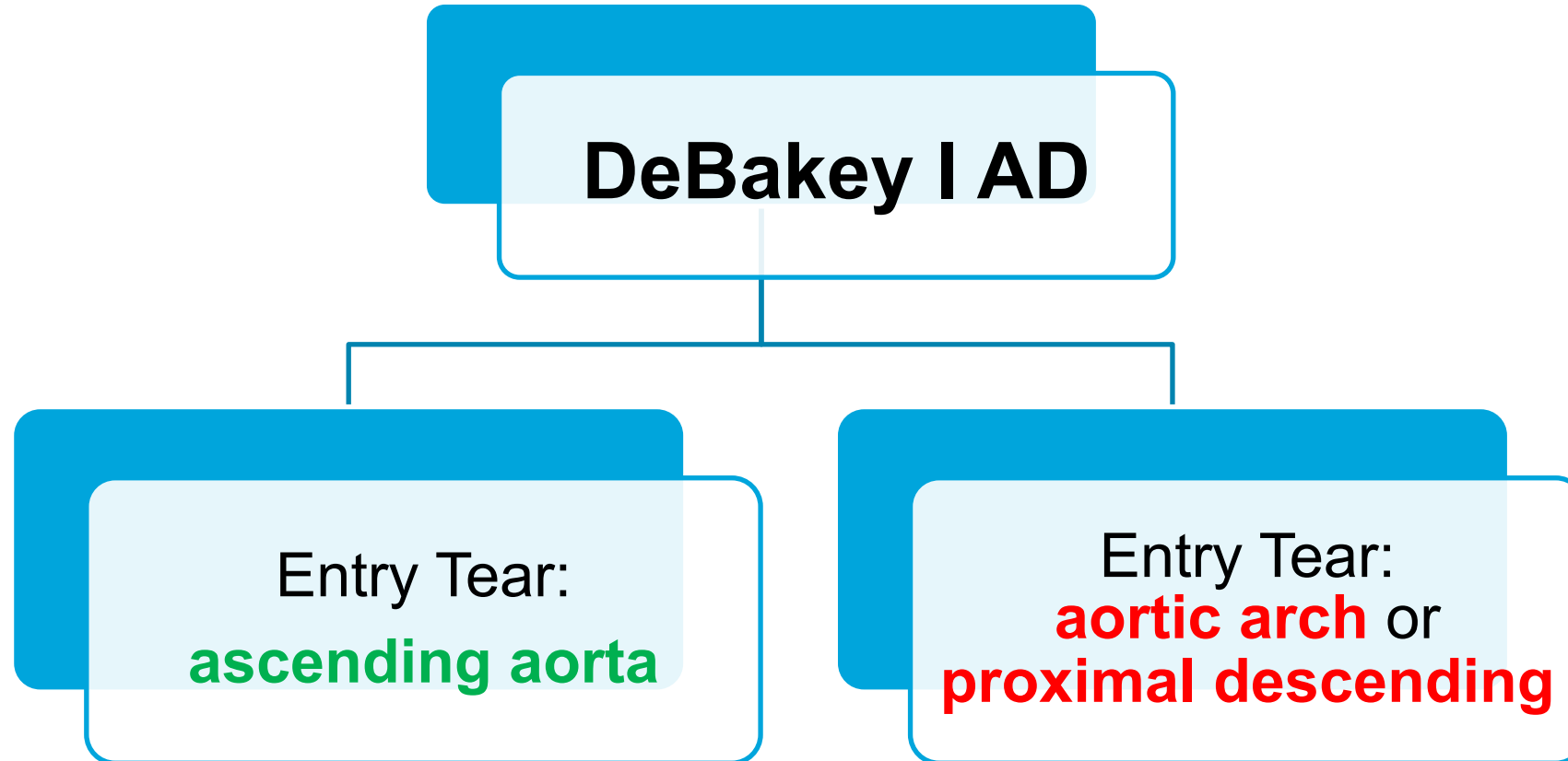
Single stage treatment:

- Resolution of malperfusion
- Prevention of late re-intervention

High **technical complexity**

Use in **high specialized centers only**

Algorithm for DeBakey I acute aortic dissection



* Total arch replacement +/- FET



Ascyrus Medical Dissection Stent (AMDS)

A new tool in the box!

AMDS concept

Secure and expand true lumen flow

- to resolve acute malperfusion

Seal the anastomotic entry tear

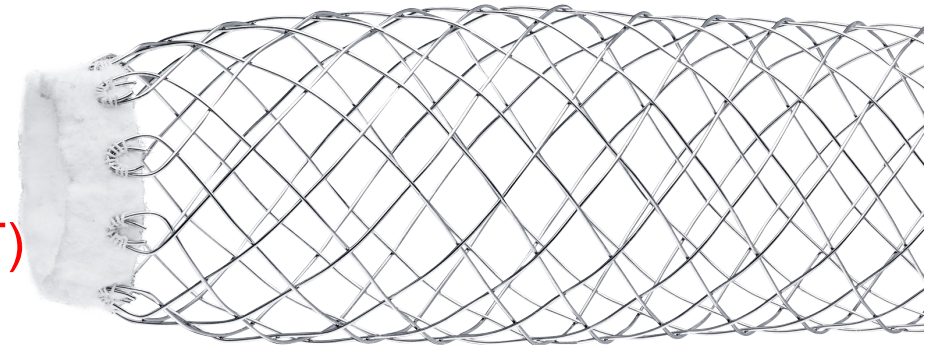
- to avoid DANE

Cut complexity

- to avoid challenging emergent procedures (FET)

Induce positive remodeling

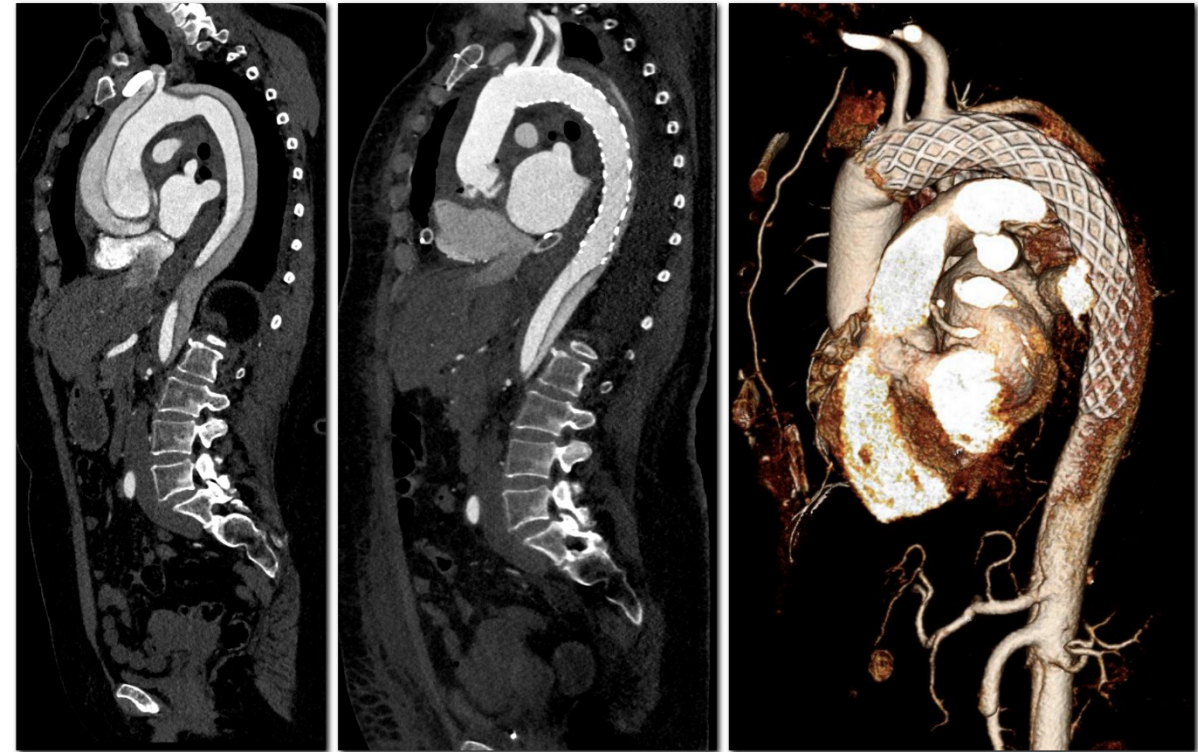
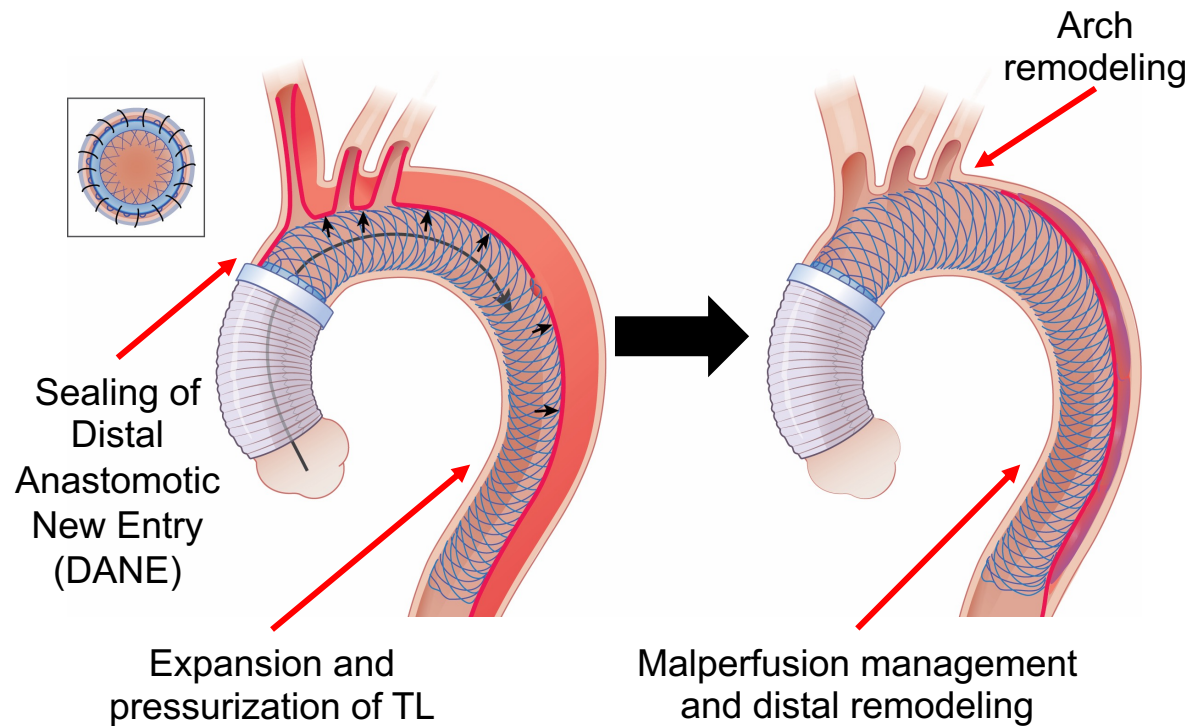
- to avoid aortic growth and negative remodeling



AMDS concept

AMDS Components:

- 1) Super-helical non-covered nitinol stent (arch and descending aorta)
- 2) Proximal PTFE cuff



AMDS concept



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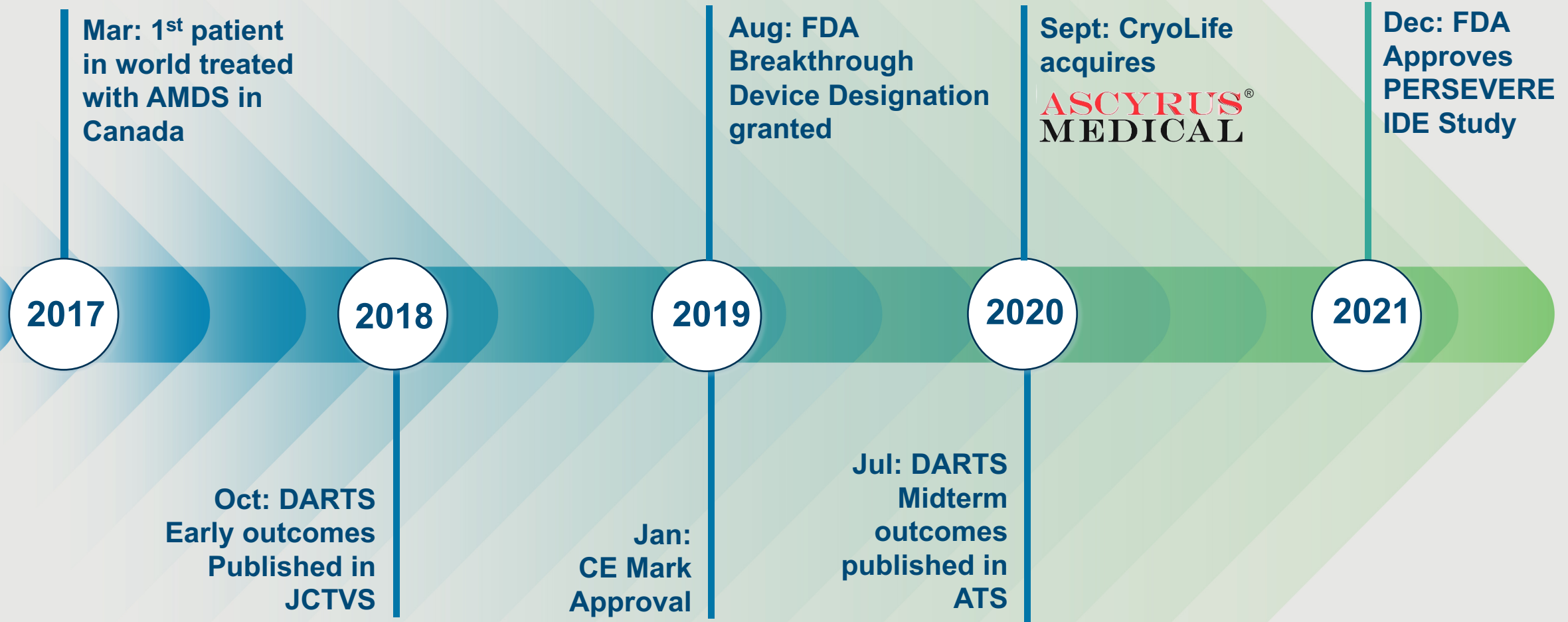
Case Example - Video



Ascyrus Medical Dissection Stent (AMDS)

Clinical evidence

AMDS History



Countries with AMDS use: Australia, Austria, Canada Croatia France, Germany, Hong Kong, Hungary, Italy, Luxembourg, Netherlands, New Zealand, Panama, Poland, Singapore, Slovenia, Spain, Switzerland, United Kingdom

ARTIVION[™]

Standard Surgical Repair vs. Surgical Repair with AMDS



	Standard Surgical Repair	Surgical Repair with AMDS ¹
Pre-Op Malperfusion	33.6% ² – 55.6% ³	56.5%
Overall Operative Mortality	17% ⁴ – 18.7% ⁵	13.0%
Malperfusion Related Mortality	21.3% ² – 47.3% ³	7.7%
One-Stage Malperfusion Resolution	58.1% ⁶	95.5%
Paralysis	2.9% ⁴	0%
New Post-Op Stroke	12.9% ⁷ – 13.6% ⁵	6.5%
Aortic Arch Remodeling (Absence of Aortic Expansion)	24% ⁸	100%

AMDS data – Berlin experience

February 2018 – 2022

- >100 implantations
- **13 surgeons** successfully trained
 - CT-based sizing
 - Standardized surgical technique
- Routine procedure



AMDS – Berlin experience

The New Type A Arch Remodeling Stent for DeBakey I Acute Aortic Dissection: Results and Performance in 100 Implantations

Presented at STS January 2022 - awaiting publication in Annals of Thoracic Surgery

- Key Outcomes:
80% resolution of malperfusion, 76% partial or full false lumen thrombosis
- Hybrid arch AMDS repair - high safety and reproducibility profile
- Does not add technical complexity to standard of care
(adds less than 10 minutes the hemiarch procedure)

Ongoing: DARTS Post Market Registry

- ClinicalTrials.gov reference: NCT03894033
- Observational, prospective study targeting up to 100 patients; sites located in Europe (currently Germany only) and Canada.
- The registry will follow-up all patients through 5-years including CT-imaging
- Endpoints: early (30-days) and late (1+ years) survival, device safety and efficacy profile
image based aortic remodeling during FU

US PIVOTAL STUDY

PERSEVERE

- **IDE study approved by FDA December 2021**
- **Purpose** : To assess the safety and effectiveness of AMDS in ATAAD
- **Study Design** : Prospective, non-randomized, single-arm, multicenter interventional study
- **Investigational Sites** : 25 institutions in the US
 - National PI: Dr. Wilson Szeto (UPenn)
- **Enrollment Target** : 100 patients
- **Objective** :
 - 30-days: to demonstrate a clinically meaningful reduction (31%) in the % of patients who experience at least one of the following MAEs: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, MI, compared to published outcomes after the standard of care (hemiarch procedure).
 - 1-year: to demonstrate a clinically meaningful increase (40%) in the % of patients who have true lumen expansion ≥ 6.0 mm compared to published outcomes after the standard of care (hemiarch procedure).

References

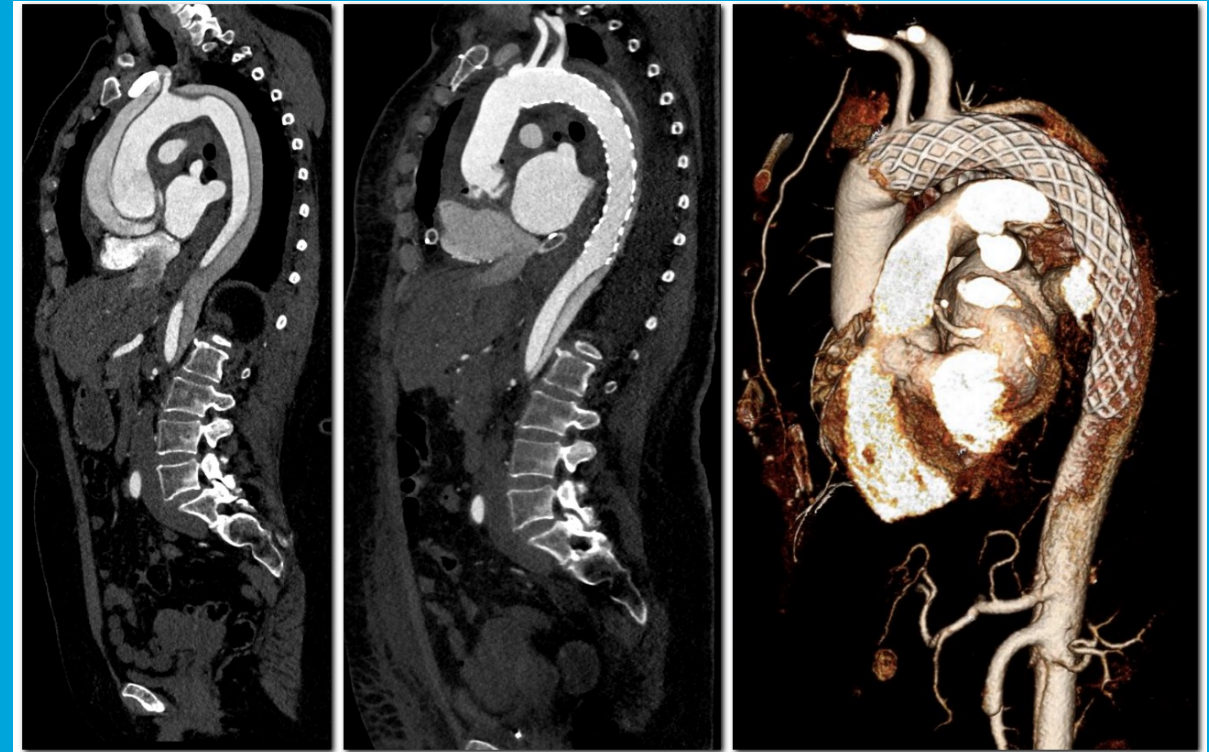
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Thank you for your attention

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E-vita Open Neo Hybrid Stent Graft System

DR. MALAKH SHRESTHA

Professor of Cardiac Surgery
Hannover Medical School

ARTIVION™



**Cardiac, Thoracic, Transplantation
and Vascular Surgery**

E-vita Open Neo Frozen Elephant Trunk Hybrid Graft

Malakh Shrestha

Professor of Cardiac surgery

Director of Aortic Surgery

Vice Chairman

Div. of Cardio-thoracic, Transplantation & Vascular Surgery

Hannover Medical School

Disclosures:

None relevant to this Presentation



At Present:

Professor, Vice Chairman & Director of Aortic Surgery
Program Director for Cardiac Surgery Residency
Div. for Cardio-thoracic, Transplantation- and Vascular Surgery
Hannover Medical University



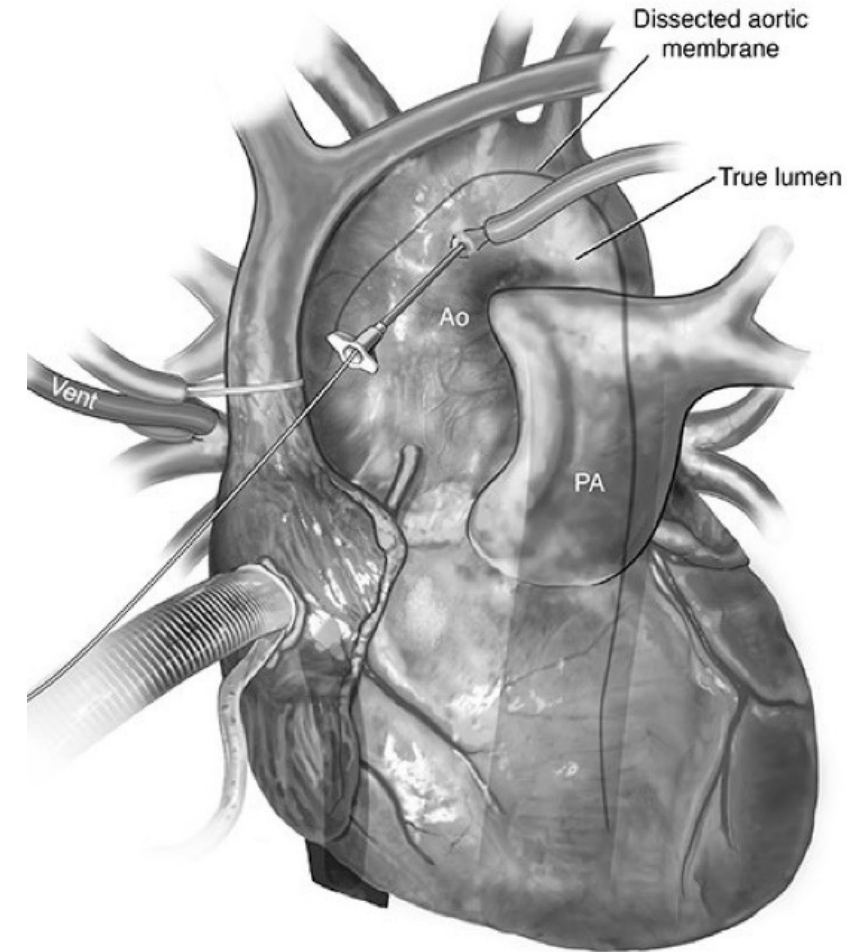
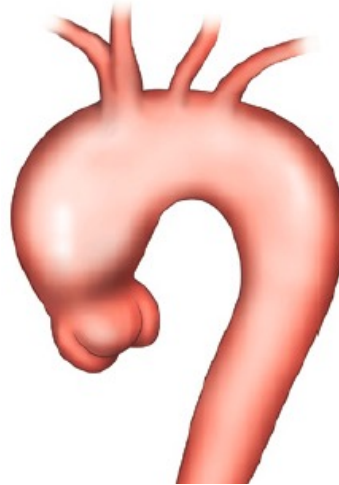
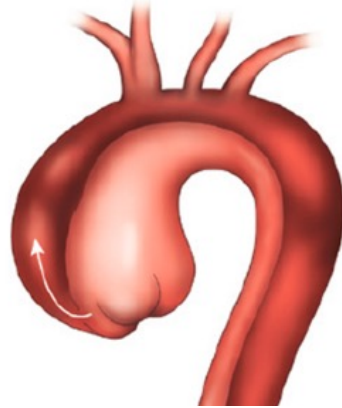
Professor of Surgery
Director of Aortic Surgery



MHH
Cardiac, Thoracic, Transplantation
and Vascular Surgery

Diseases of the Aortic Arch

- Dissections (Tear)
 - Chronic
 - Acute
- Aneurysms (Dilatation)



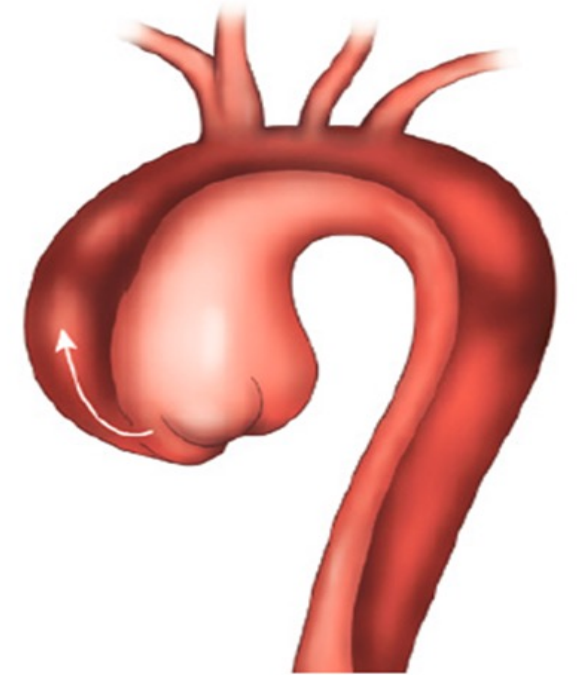
They are three different Diseases!

Indications:

- Acute Dissection (ATAD)
- Chronic Dissections
- Aneurysms



ATAD is more common than previously thought!



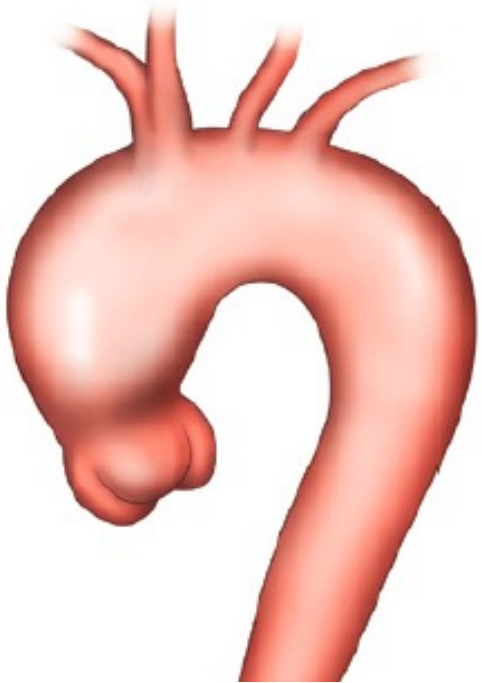
Postmortem CT Scans in Japan showed 8% of out of hospital 'Cardiac arrests' are due to ATAD!

Morikawa Y, et al. J Emerg Trauma Shock 2013;6:87.54



MTH
Cardiac, Thoracic, Transplantation
and Vascular Surgery

Aortic Arch Aneurysms



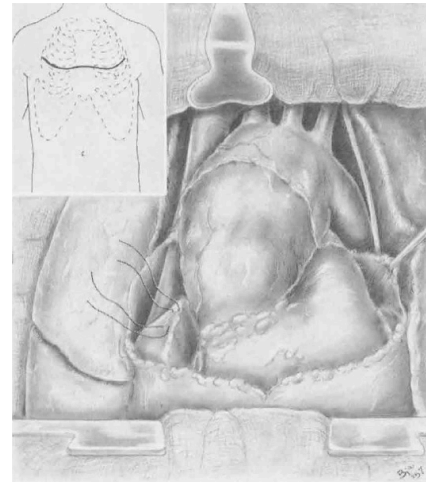
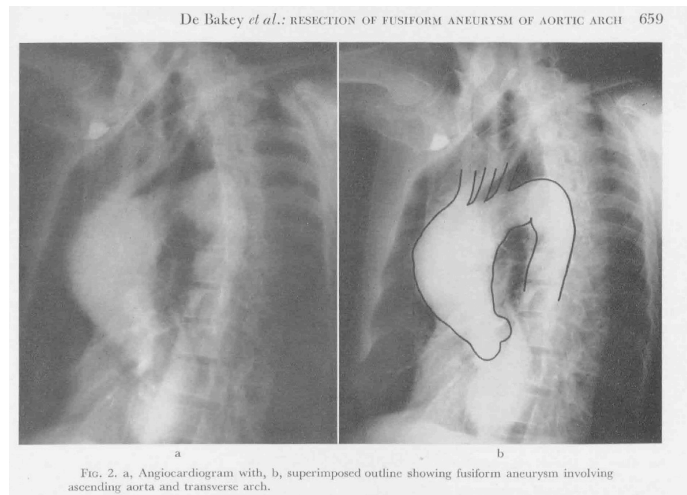
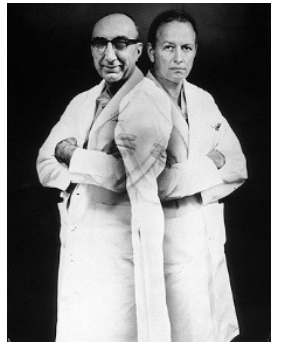
Thoracic aortic aneurysms (TAA) have an estimated incidence of at least 5-10 per 100,000 person-years.

TAAAs are classified into aortic root or ascending aortic aneurysms, which are most common ($\approx 60\%$), followed by aneurysms of the descending aorta ($\approx 35\%$) and aortic arch ($<10\%$).



SUCCESSFUL RESECTION OF FUSIFORM ANEURYSM OF AORTIC ARCH WITH REPLACEMENT BY HOMOGRAFT

MICHAEL E. DE BAKEY, M.D., F.A.C.S., E. STANLEY CRAWFORD, M.D.,
DENTON A. COOLEY, M.D., F.A.C.S., and GEORGE C. MORRIS, JR., M.D.,



SURGERY *DECEMBER 1957*
Gynecology & Obstetrics VOLUME 105
NUMBER 6

Peri-operative Mortality at that time was 50% !!!

Aortic arch surgery remains a challenge!

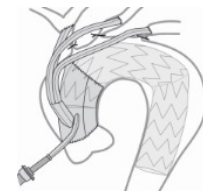
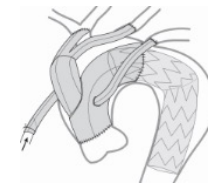
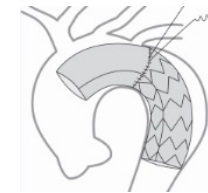
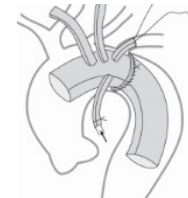
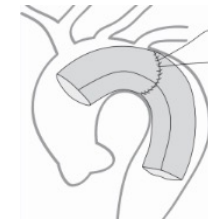
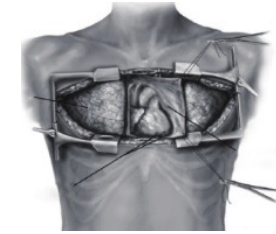
Treatment of complex disease of the aortic arch



Holly Grail?



- Open surgical (Surgical trauma, Bleeding):
- Single Stage
(Clam-shell, Sternotomy+ Thoracotomy)
- Classical two Stage
- “Elephant Trunk Procedure”
- Single/two stage
Frozen elephant trunk
- (Radiation Risks!)
- Hybrid Techniques
- Total Endovascular





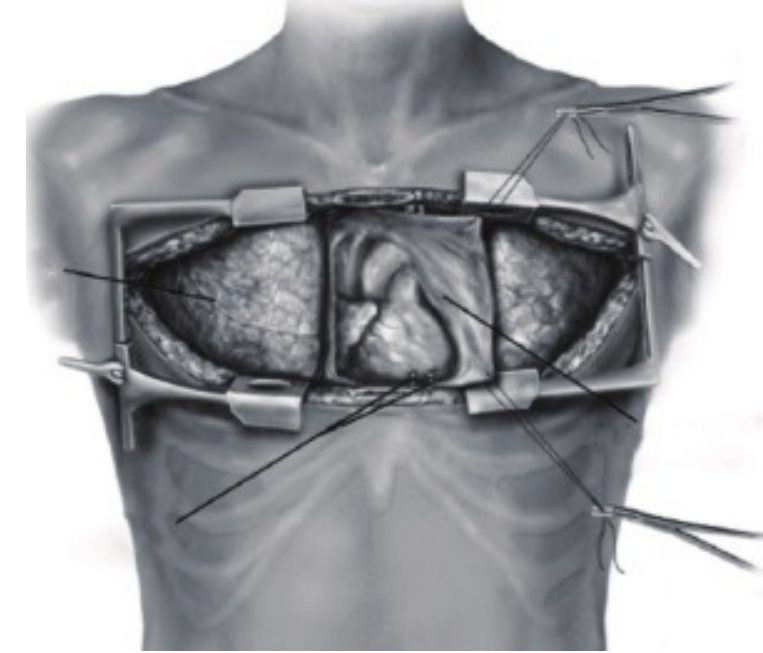
Clinical outcomes and rates of aortic growth and reoperation after 1-stage repair of extensive chronic thoracic aortic dissection.

Kouchoukos NT, Kulik A, Castner CF.

J Thorac Cardiovasc Surg. 2018
May;155(5):1926-1935.

METHODS:

Hospital mortality was 2.5% (2 patients). Stroke occurred in 1 patient (1.2%), spinal cord ischemic injury occurred in 1 patient (1.2%), and renal failure requiring long-term dialysis occurred in 2 patients (2.5%).



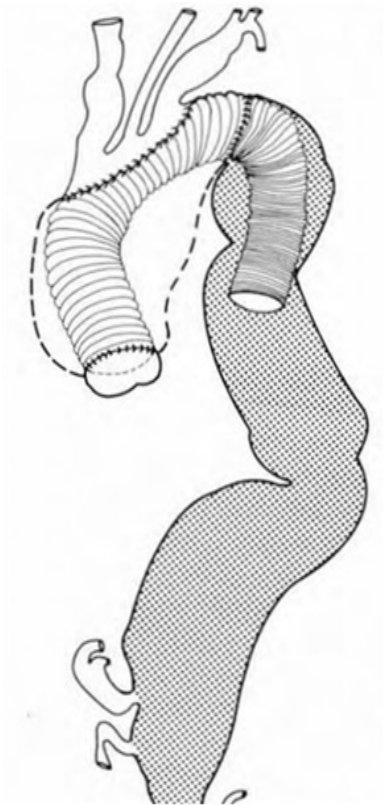
‘1- stage’ Aortic Repair: Results of D Kouchoukos not reproducible by others!



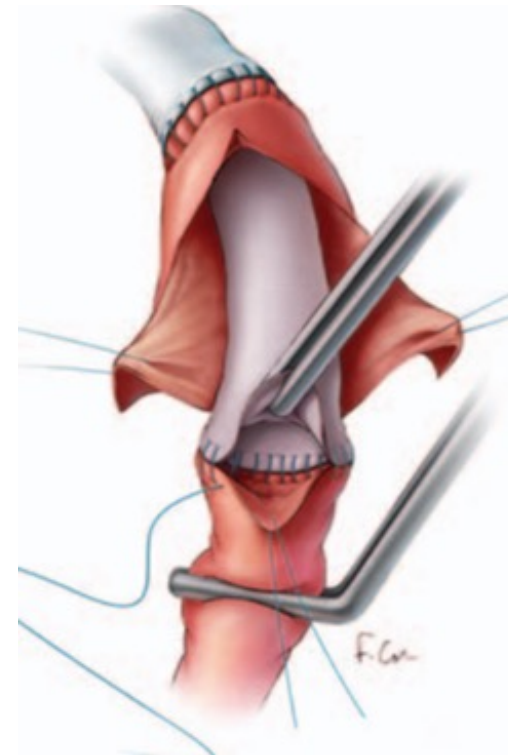


Two Stage: 'Elephant Trunk' Procedure

Stage 1



Stage 2



Borst HG et al.
Extensive aortic replacement using the 'elephant trunk prosthesis'
Thorac Cardiovasc Surg 1983; 31 (1): 37-40



Total aortic arch replacement with the elephant trunk technique: single-centre 30-year results[†]

European Journal of Cardio-Thoracic Surgery 45 (2014) 289–296

Malakh Shrestha*, Andreas Martens, Heike Krüger, Illona Maeding, Fabio Ius,
Felix Fleissner and Axel Haverich

03/1982 – 03/2012, 179 patients

The 30-day mortality during the first-stage operation was **17.3%** (31/179, 15 with AADA). Perioperative stroke was 7.9% (n = 14/176). Postoperative recurrent nerve palsy was present in 18.2% (32/176) and paraplegia in 5.6% (10/176).

50 second stage operations, 50 open surgical, 7 TEVAR

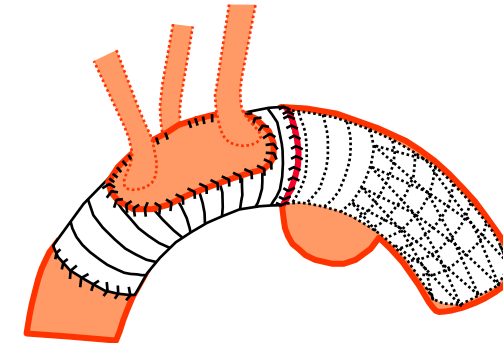
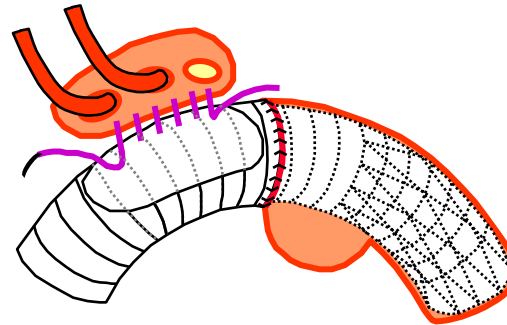
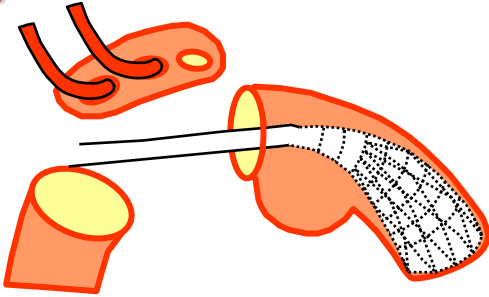
The second stage completion operation was performed as early as possible. Fifty-seven second-stage completion procedures were performed, either surgically (n=50) or through interventional techniques (n=7).

The 30-day mortality after the second-stage completion procedures was **7.0%** (4/57), respectively. The stroke, recurrent nerve palsy and paraplegia rates were 0, 0 and 7% (4/54), respectively.

The second stage completion is inevitable!



'Frozen Elephant Trunk' Procedure



The frozen elephant trunk technique: a new treatment for thoracic aortic aneurysms.
Karck M, Chavan A, Hagl C, Friedrich H, Galanski M, Haverich A.
J Thorac Cardiovasc Surg. 2003 Jun;125(6):1550-3



Single-centre experience with the frozen elephant trunk technique in 251 patients over 15 years[†]

Malakh Shrestha^{a,*}, Andreas Martens^a, Tim Kaufeld^a, Erik Beckmann^a, Sebastian Bertele^a, Heike Krueger^a,
Julia Neuser^a, Felix Fleissner^a, Fabio Ius^a, Firas Abd Alhadi^a, Jasmin Hanke^a, Jan D. Schmitto^a, Serghei Cebotari^a,
Matthias Karck^b, Axel Haverich^a and Ajay Chavan^c

ORIGINAL ARTICLE

European Journal of Cardio-Thoracic Surgery 0 (2017) 1–9

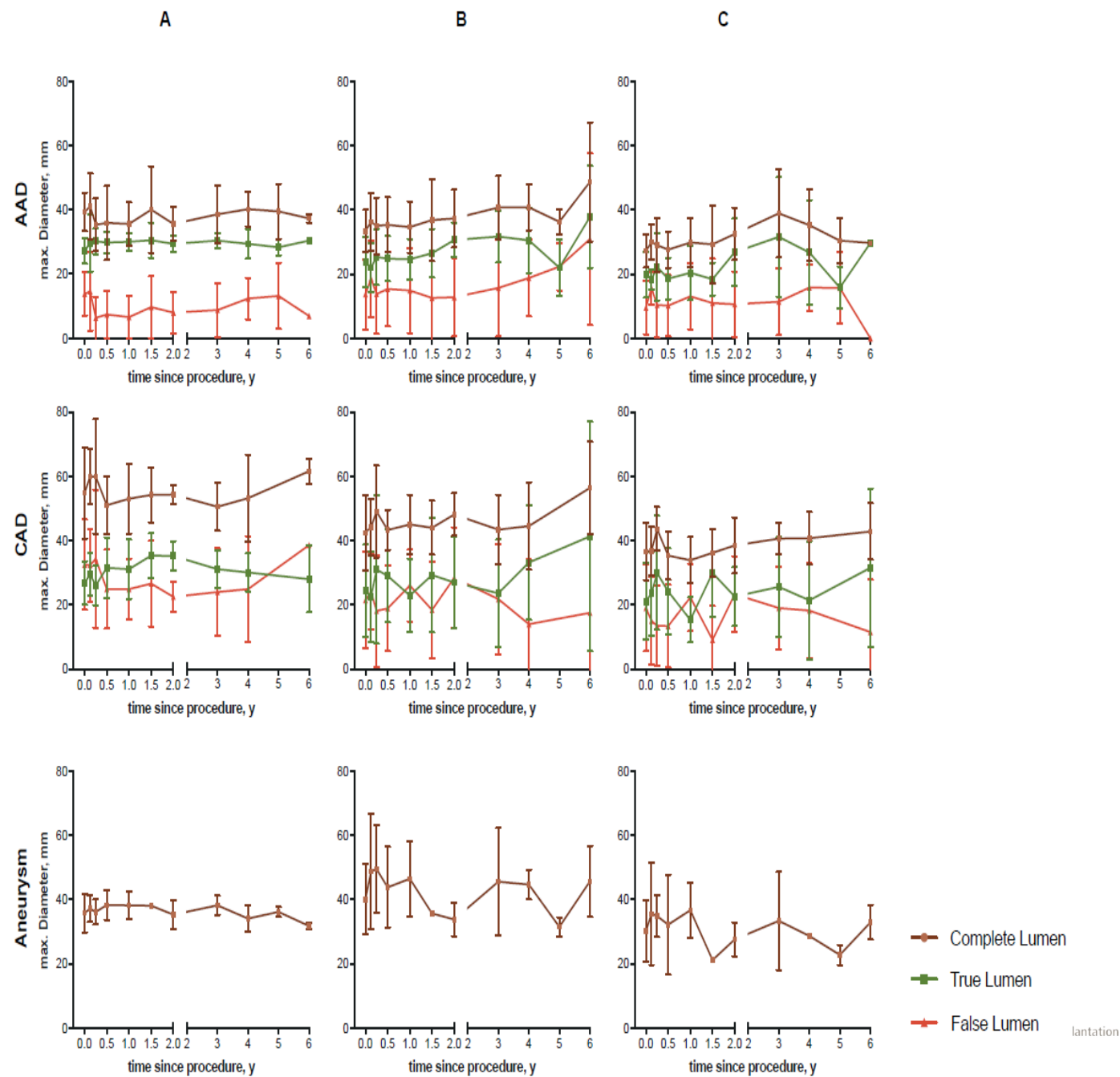
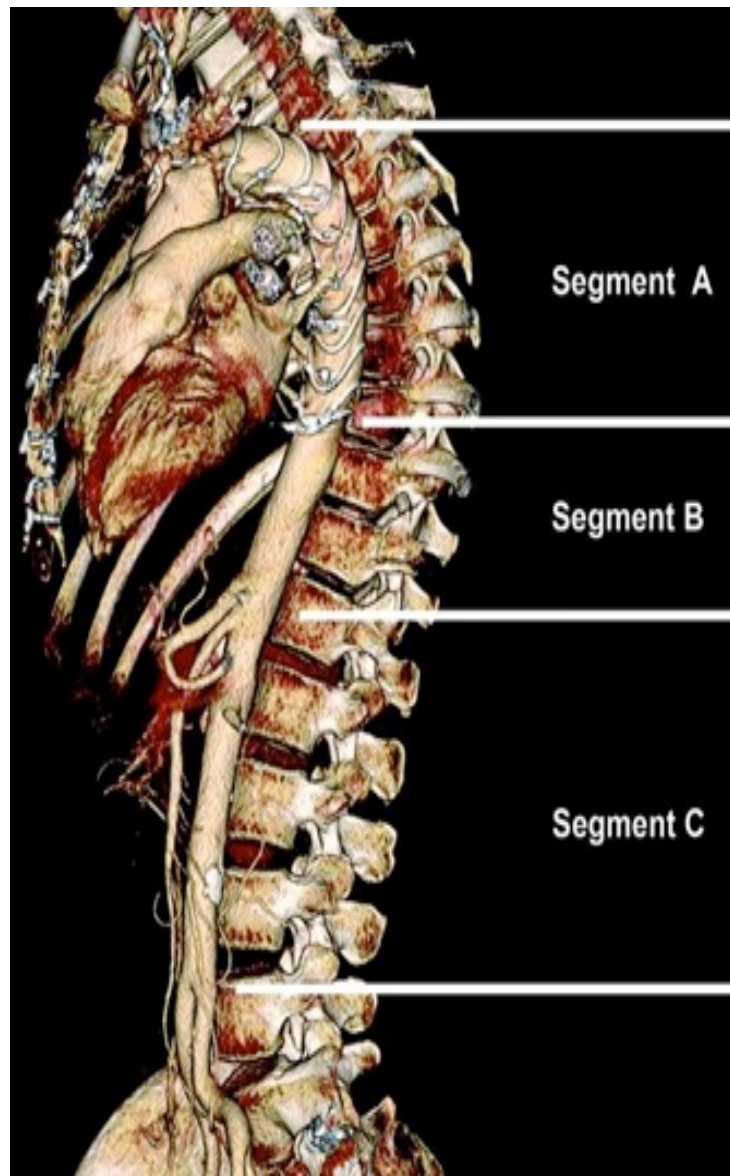
RESULTS:

The in-hospital mortality rate was 11% (in acute aortic dissection type A, 12%).

There were 49 second-stage procedures in the downstream aorta: either open surgical [n = 25] or transfemoral endovascular (n = 23).

Elective thoracic endovascular aneurysm repair was successful in all 23 cases.



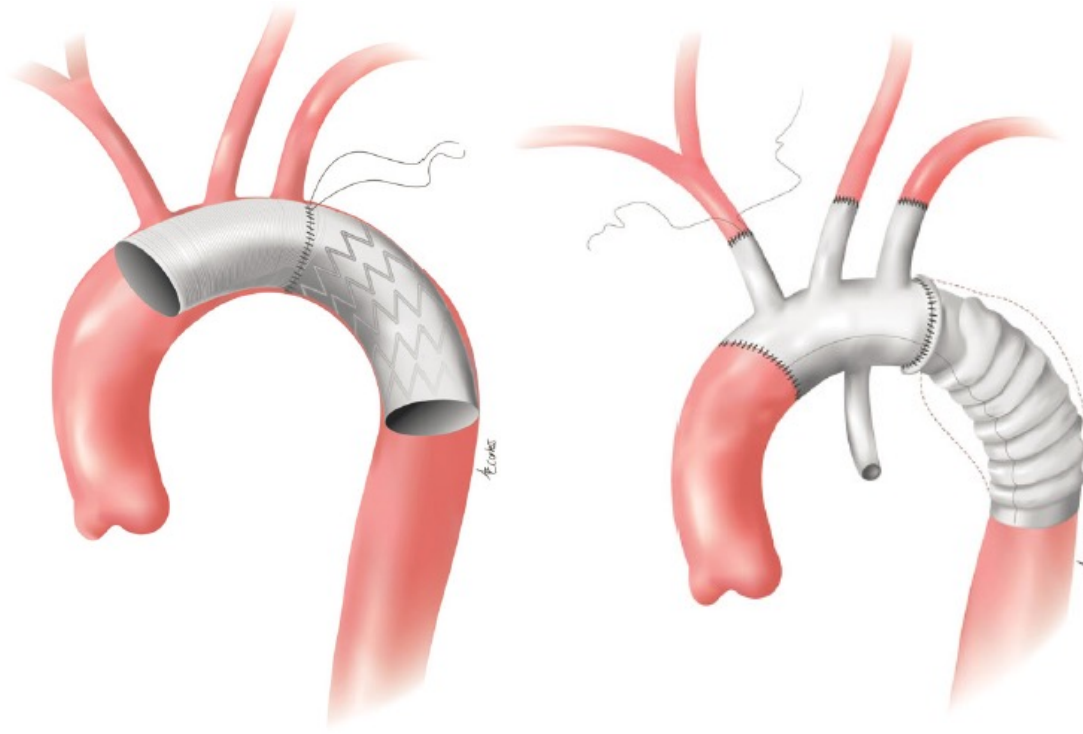


Current status and recommendations for use of the frozen elephant trunk technique: a position paper by the Vascular Domain of EACTS[†]

Malakh Shrestha^a, Jean Bachet^b, Joseph Bavaria^c, Thierry P. Carrel^d, Ruggero De Paulis^e, Roberto Di Bartolomeo^f, Christian D. Etz^g, Martin Grabenwöger^h, Michael Grimmⁱ, Axel Haverich^j, Heinz Jakob^k, Andreas Martens^l, Carlos A. Mestres^{k,l}, Davide Paciniⁱ, Tim Resch^m, Marc Schepensⁿ, Paul P. Urbanski^o and Martin Czerny^{p,q,*}

POSITION STATEMENT

European Journal of Cardio-Thoracic Surgery (2015) 1–11



Recommendation for use

Based on the available literature and on the expert consensus opinion of the authors, the following recommendations can be made:

- (i) The FET technique or an alternative method to close the primary entry tear should be considered in patients with acute type A aortic dissection with a primary entry in the distal aortic arch or in the proximal half of the descending aorta to treat associated malperfusion syndrome or to avoid its postoperative development. Class of recommendation IIa—Level of evidence C [23, 55]
- (ii) The FET technique may be considered for use in patients undergoing surgery for acute type A aortic dissection to prevent mid-term aneurysmal formation in the downstream aorta. Class of recommendation IIb—Level of evidence C [19, 47–49]
- (iii) The FET technique should be considered in patients with complicated acute type B aortic dissection when primary TEVAR is not feasible or the risk of retrograde type A aortic dissection is high. Class of recommendation IIa—Level of evidence C [50]
- (iv) The FET technique should be considered in patients with extensive thoracic or thoraco-abdominal aortic disease when a second procedure, either open surgical or endovascular in downstream aortic segments, can be anticipated. Class of recommendation IIa—Level of evidence C [42, 64]

Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic arch: an expert consensus document of the European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS)

Martin Czerny (EACTS Chairperson)^{a,*†} and Jürg Schmidli (ESVS Chairperson)^{b,‡}

Writing Committee: Sabine Adler^{c,‡}, Jos C. van den Berg^{d,e,‡}, Luca Bertoglio^{f,‡}, Thierry Carrel^{b,†}, Roberto Chiesa^{f,‡}, Rachel E. Clough^{g,‡}, Balthasar Eberle^{h,†}, Christian Etz^{i,†}, Martin Grabenwöger^{j,†}, Stephan Haulon^{k,‡}, Heinz Jakob^{l,†}, Fabian A. Kari^{a,†}, Carlos A. Mestres^{m,†}, Davide Pacini^{n,†}, Timothy Resch^{o,‡}, Bartosz Rylski^{a,†}, Florian Schoenhoff^{b,†}, Malakh Shrestha^{p,†}, Hendrik von Tengg-Kobligh^{q,‡}, Konstantinos Tsagakis^{l,†} and Thomas R. Wyss^{b,‡}

POSITION STATEMENT

European Journal of Cardio-Thoracic Surgery 0 (2018) 1–30

Recommendation 19: the FET technique or TEVAR to close the primary entry tear should be considered in patients with acute type A aortic dissection with a primary entry in the distal aortic arch or in the proximal half of the DTA to treat associated malperfusion syndrome or to avoid its postoperative development.	Class IIA	Level C
Recommendation 20: the FET technique may be considered for use in patients undergoing surgery for acute type A aortic dissection to prevent mid-term aneurysmal formation in the downstream aorta [174].	Class IIB	Level C
Recommendation 21: the FET technique should be considered in patients with complicated acute type B aortic dissection when endovascular interventions are contraindicated [161, 175, 176].	Class IIA	Level C
Recommendation 22: the FET technique should be considered in patients with concomitant distal thoracic and thoraco-abdominal aortic disease that, in a later stage, will or is likely to require either surgical or endovascular treatment.	Class IIA	Level C

DTA: descending thoracic aorta; FET: frozen elephant trunk; TEVAR: thoracic endovascular aortic repair.



2021 The American Association for Thoracic Surgery expert consensus document: Surgical treatment of acute type A aortic dissection

S Christopher Malaisrie ¹, Wilson Y Szeto ², Monika Halas ³, Leonard N Girardi ⁴, Joseph S Coselli ⁵, Thoralf M Sundt 3rd ⁶, Edward P Chen ⁷, Michael P Fischbein ⁸, Thomas G Gleason ⁹, Yutaka Okita ¹⁰, Maral Ouzounian ¹¹, Himanshu J Patel ¹², Eric E Roselli ¹³, Malakh L Shrestha ¹⁴, Lars G Svensson ¹³, Marc R Moon ¹⁵,
AATS Clinical Practice Standards Committee: Adult Cardiac Surgery

Practice Guideline

➤ J Thorac Cardiovasc Surg. 2021 Apr 30;S0022-5223(21)00737-6.

doi: 10.1016/j.jtcvs.2021.04.053. Online ahead of print.

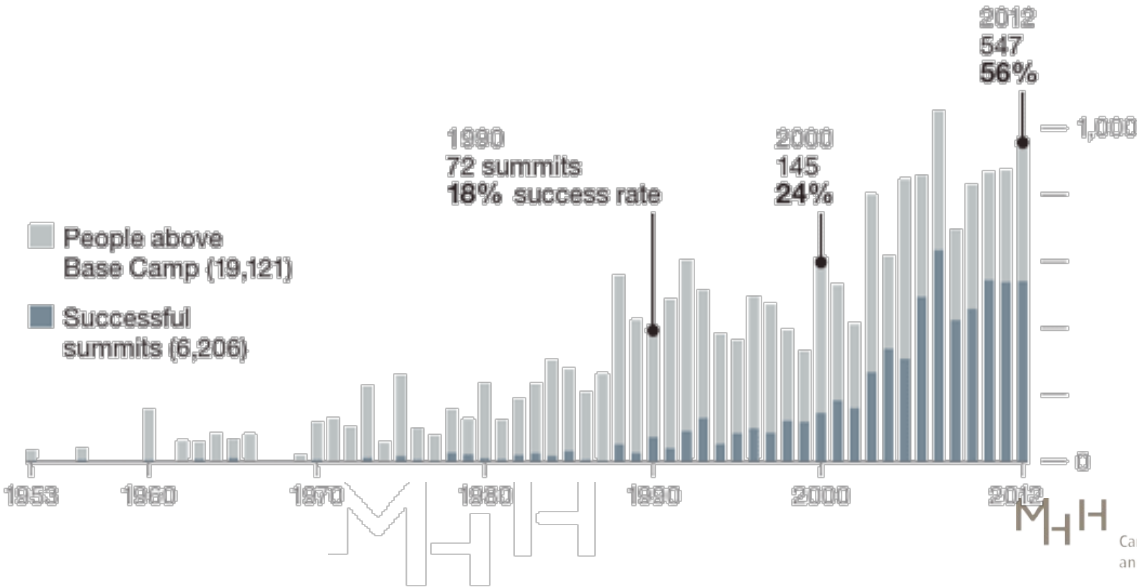
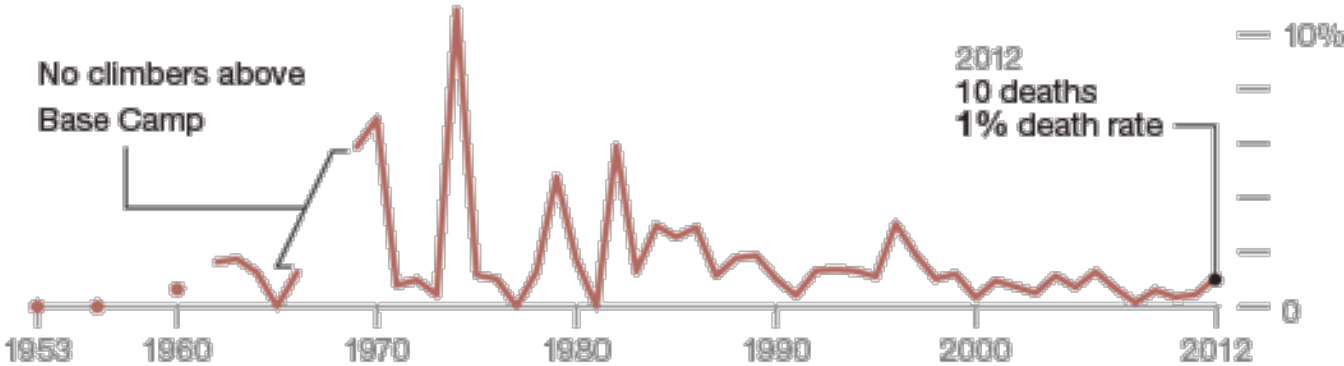


TABLE 7. Management of the Aortic Arch

Recommendations	COR	LOE	References
<i>Aortic Arch Management</i>			
1. Extended aortic arch replacement is reasonable in patients with ATAAD and: <ul style="list-style-type: none">- primary entry tear in the arch or proximal descending thoracic aorta,- brain or peripheral malperfusion,- arch or descending thoracic aortic aneurysm or rupture.	IIa	B	1-9
2. Extended aortic arch replacement with frozen elephant trunk may be reasonable in ATAAD to promote favorable aortic remodeling.	IIb	B	10-23
3. Extended aortic arch replacement may be considered in young patients with Marfan syndrome or hereditary thoracic aortic disorders.	IIb	C	24-30



Kami Rita Sherpa



Evita Neo Hybrid FET Graft (Not yet Available in USA)

- Consists of unstented Dacron & a stented (polyester and nitinol stent) parts
- Un-stented part has 4 'fingers',
- The length of the stented part.
- The proximal unstented & distal stented parts are available in different sizes
- a sewing collar simplifies the suturing of distal anastomosis.
- No Animal Products Used



Best in Class Stent Design
Innovative and simple delivery system



Conclusions

1. In Complex aneurysms Evita Neo FET procedure potentially allows a one stage repair.
IInd Stage procedures, if necessary, are possible (open surgical & endovascular).
3. In AADA, Ideal FET graft due to ease of implantation.
stabilizes the dissecting membrane and favours true lumen expansion.
4. In Chronic dissections, favours false lumen thrombosis & true lumen expansion.
5. Evita Neo has added further to the armamentarium of Surgeons to treat complex aortic arch diseases.





E-nside TAAA Multibranch Stent Graft System

DR. TIM RESCH

Professor of Vascular Surgery
Copenhagen University

ARTIVION™

Complex Aortic Aneurysms

Timothy Resch

Professor of Vascular Surgery

Copenhagen University Hospital – Rigshospitalet

Denmark



Disclosures

- Artivion – Consulting
- COOK Medical Inc – Consulting, IP
- Bentley Innomed – Consulting
- GORE – Speaker
- Medtronic – Advisory Board

Sleep Summary

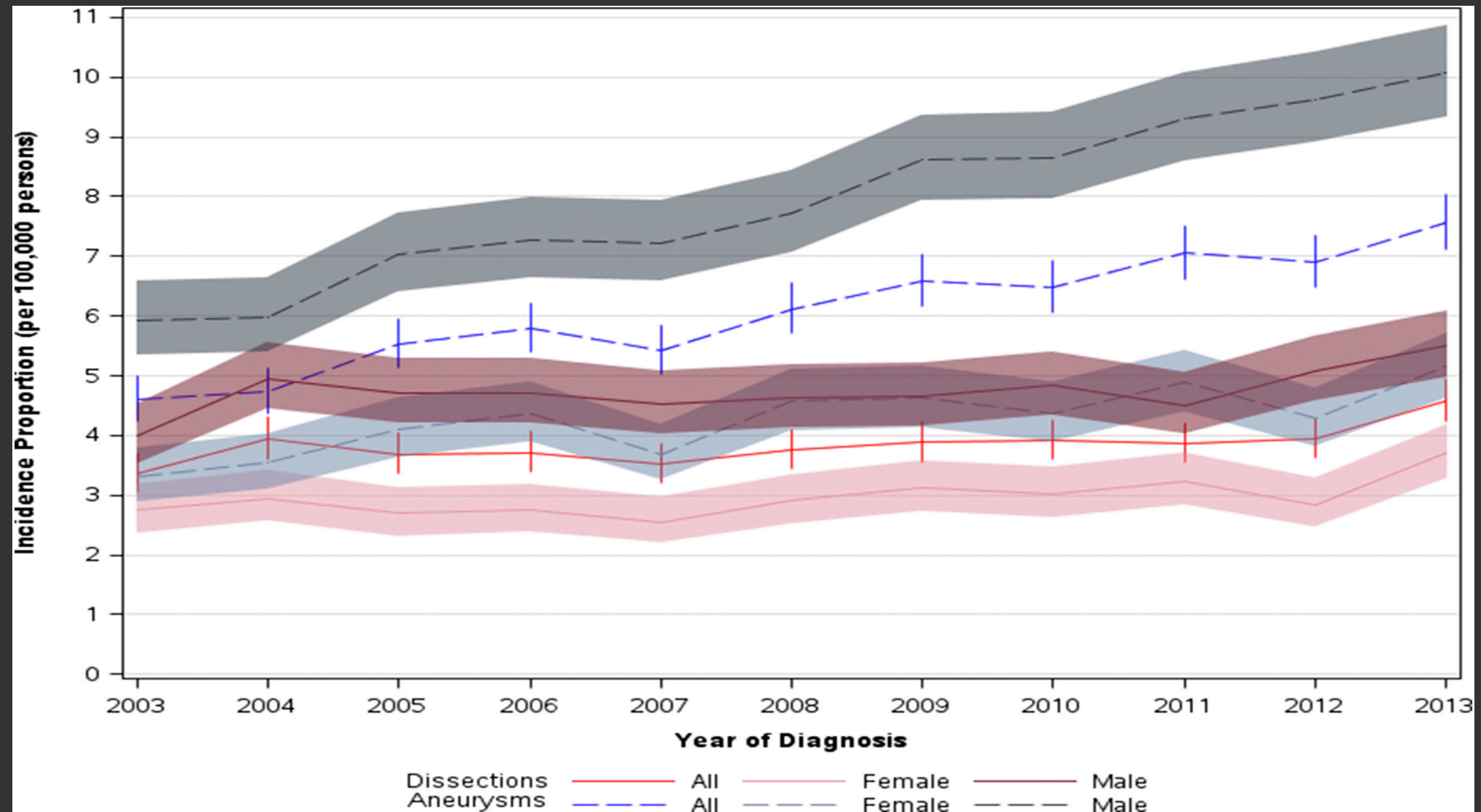
- Complex Aortic Aneurysm Increasing
- Current Surgical Therapies Maximally Invasive
- Minimally Invasive Endovascular Repair Offers Many Benefits
- Off The Shelf Inner Branched Endografts Versatile Solution



- Aneurysm 10/100 000 yearly
 - US 40 000 cases
- 13 th leading Cause of Death
 - US 15 000 deaths yearly
- Rupture Survival 5-10%



Figure 1





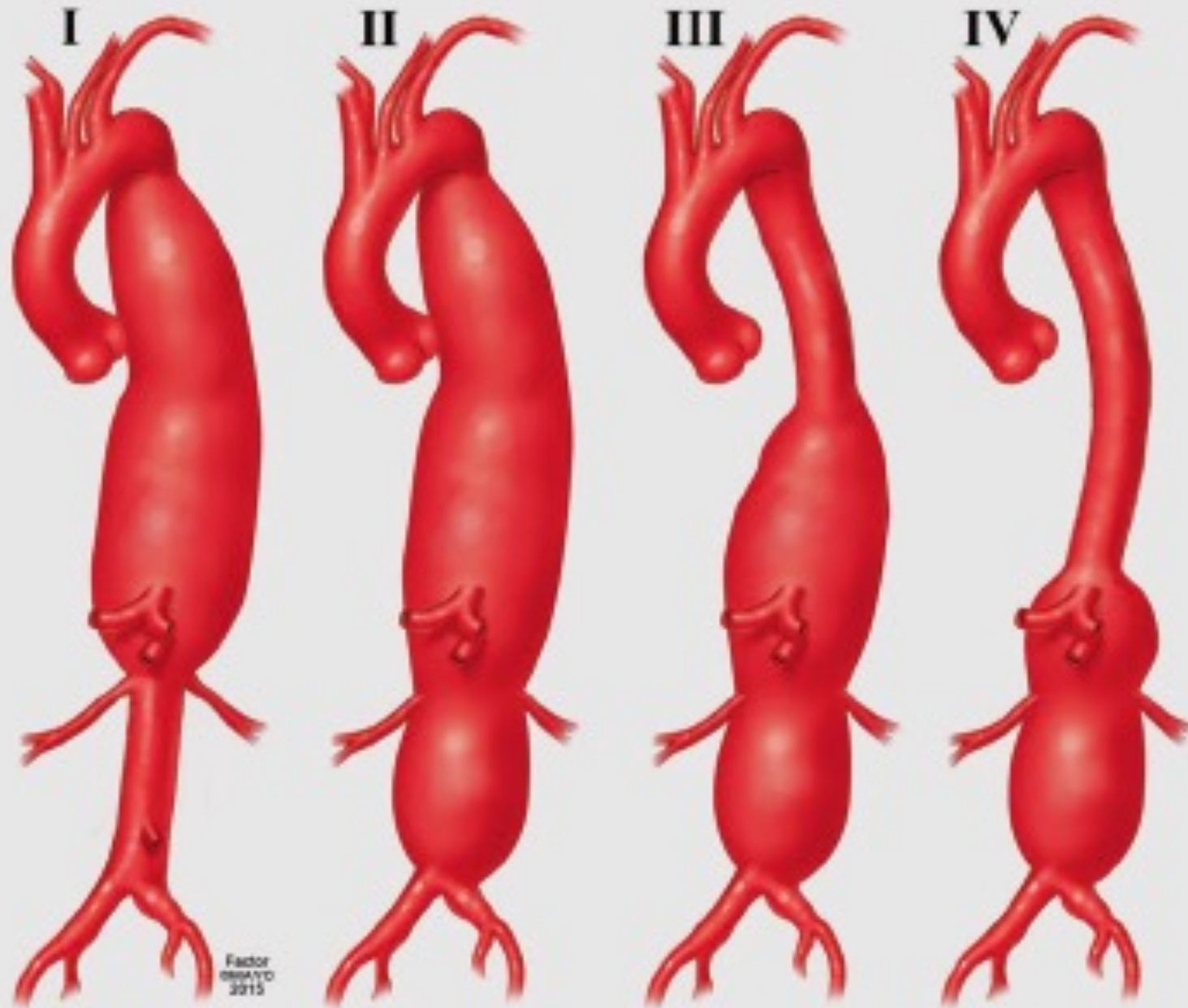
¹**com·plex**



noun

\ˈkām-,pleks\

: a group of things that are connected in complicated ways

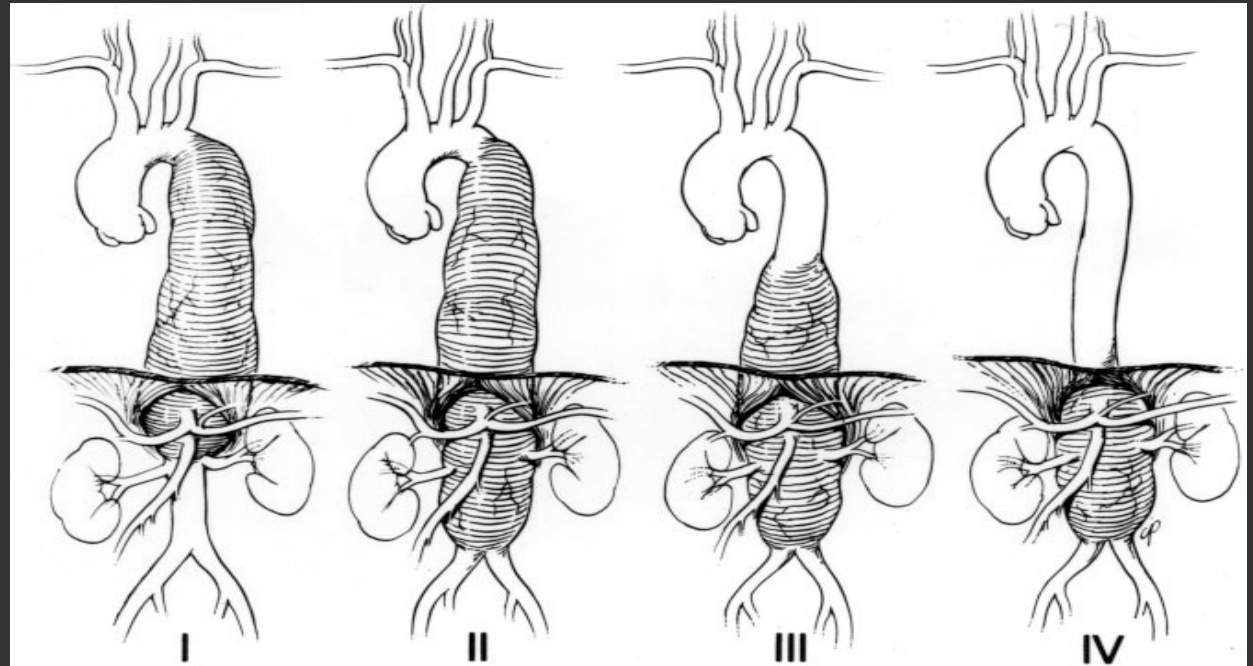


Treatment options for Complex Aneurysm

- Medical Management
- Open Repair
- Endovascular Repair

What effects Treatment Choice?

- Mortality
 - Perioperative
 - Long-term
- Morbidity
- Durability





Best Medical Management

Crawford JVS 1986;3:578

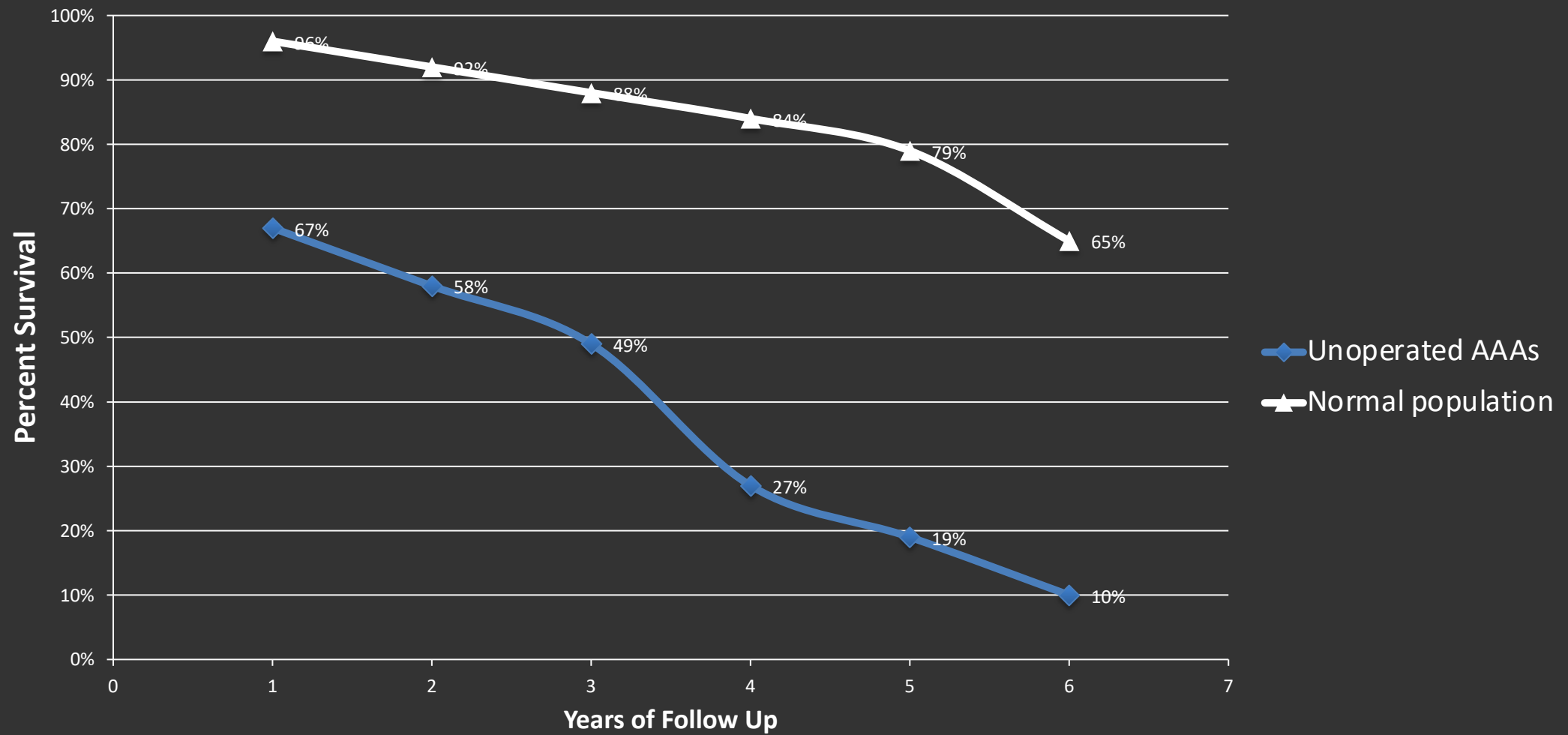
TAAA – Observations regarding the natural history of the disease

- 2 year survival in TAAA patients with conservative Tx is 24%

Hansen et al EJVES 2010

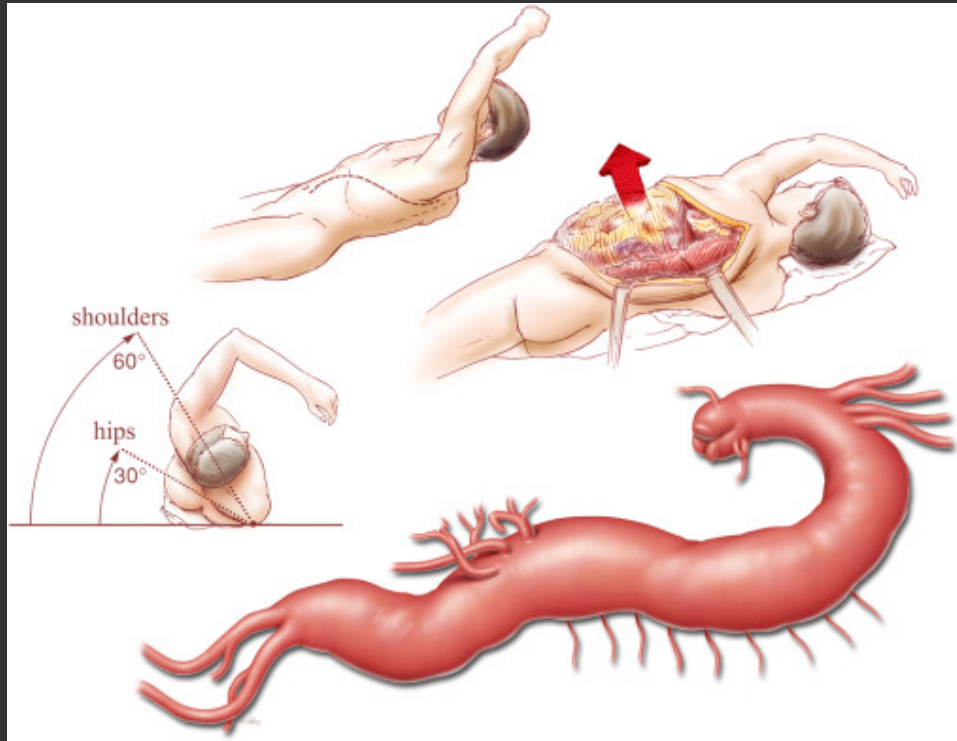
- 201 patients
 - 89(44%) unsuitable for open repair
- Follow Up 6 monthly intervals
 - Median FU 11 months
- 49 Deaths (25%)
 - 23rTAAA

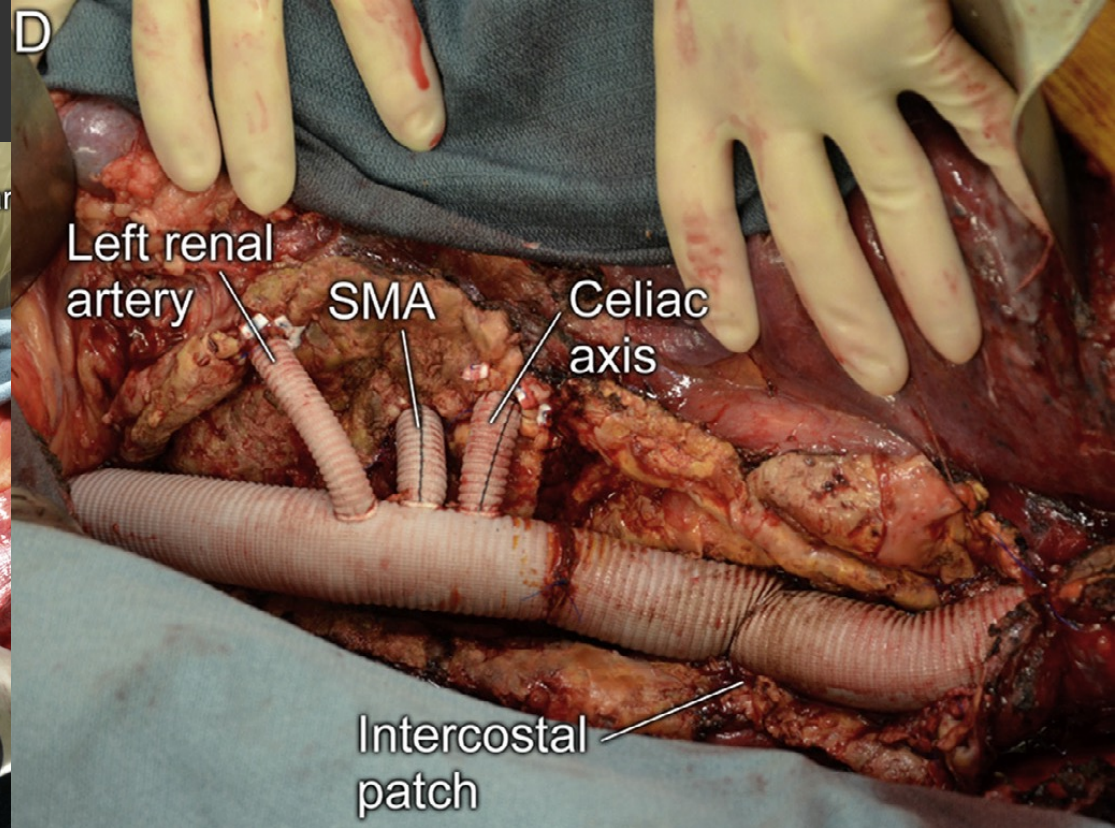
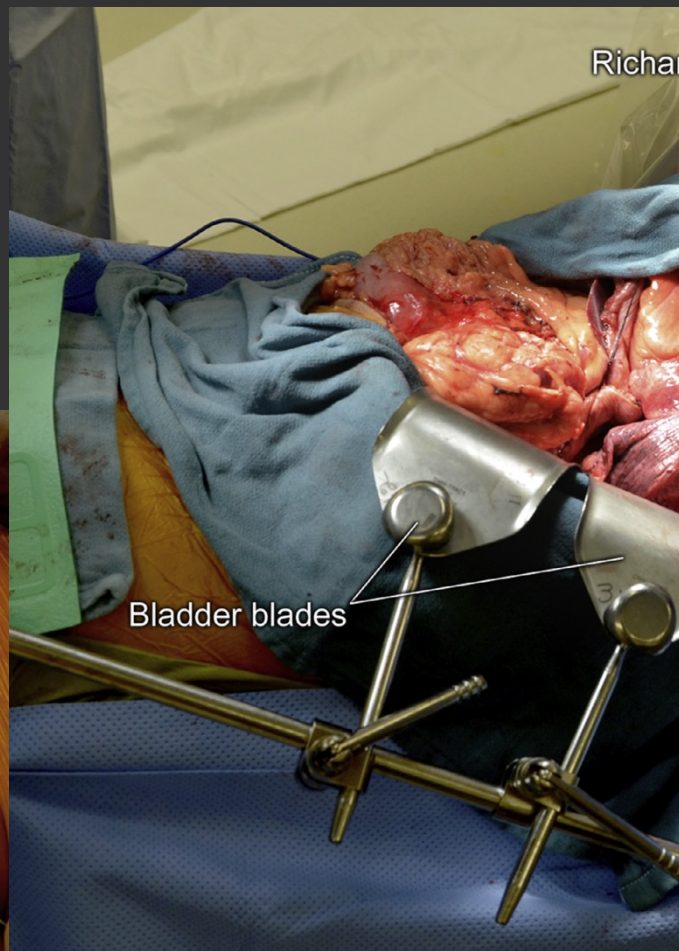
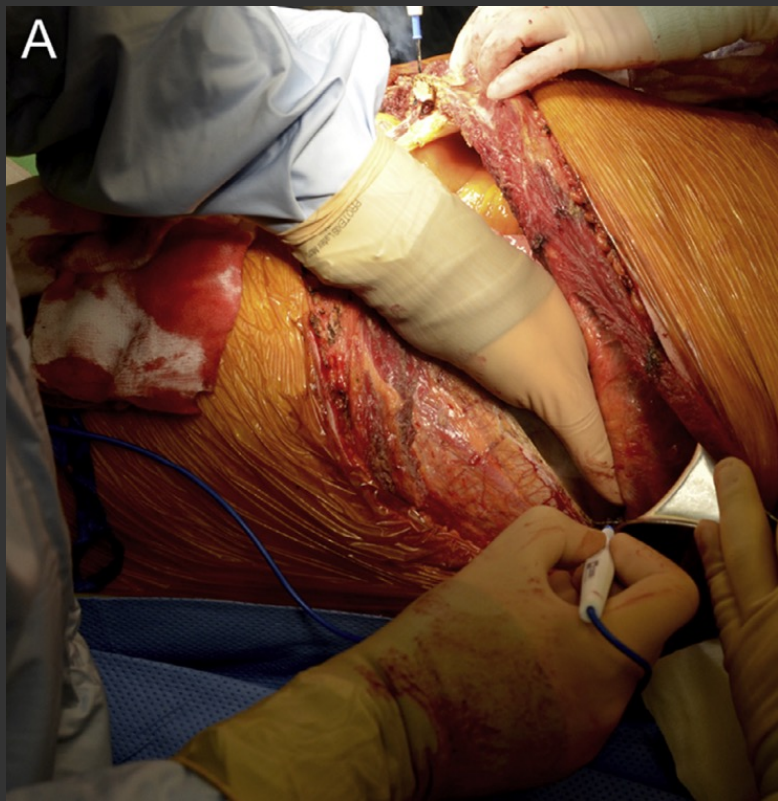
Survival Compared with Matched Cohorts

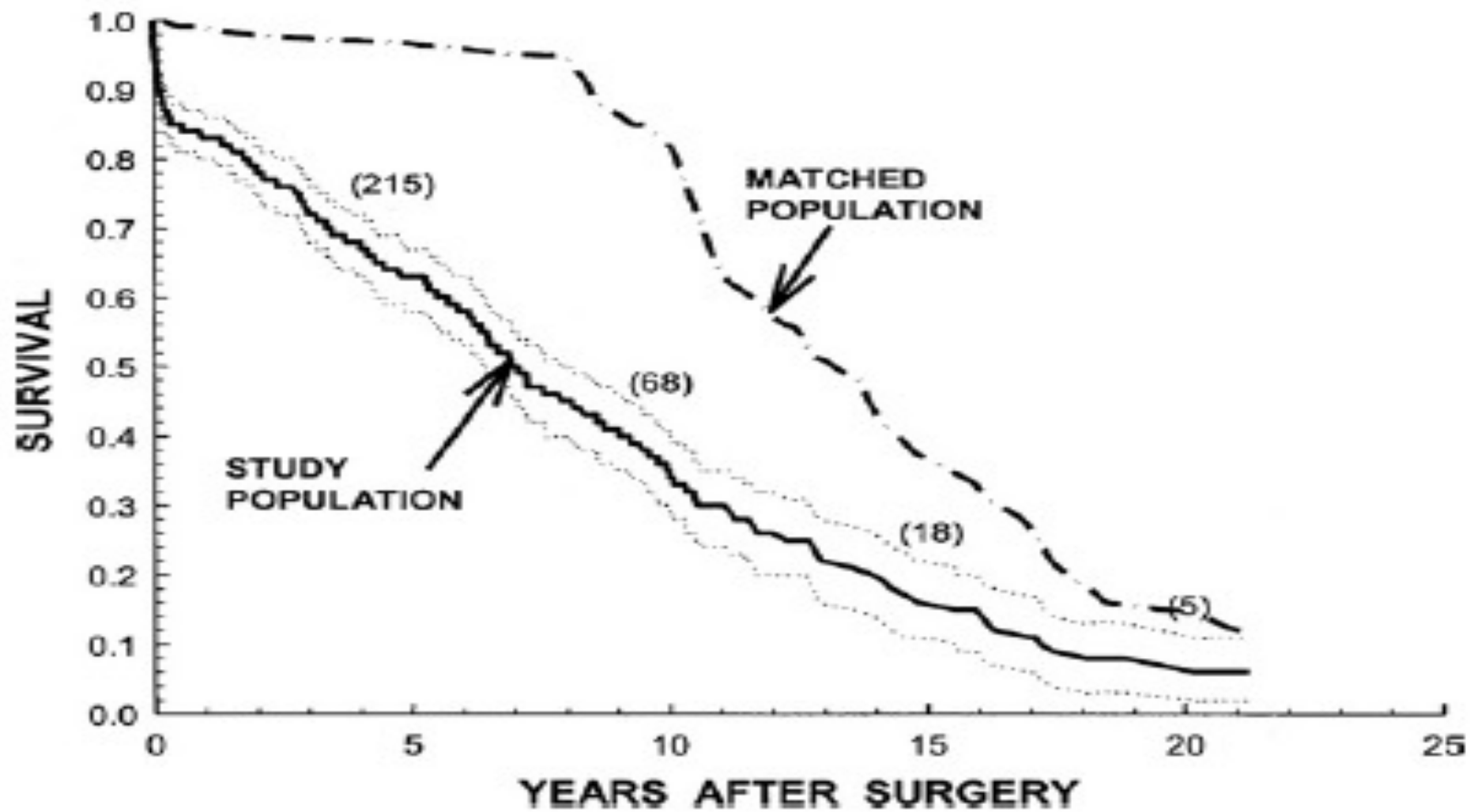




Open Repair







Schepens et al ATS 2007;83



Endovascular Repair

Why do we need EVAR for complex Aneurysms?

- Many patients too high risk for OR
- Surgery has high morbidity and mortality
- Rupture Risk high with medical therapy alone
- EVAR provides:
 - Lesser trauma, lesser ischemia time,
 - Quicker recovery, fewer complications

Endovascular Repair

- Principles
 - Percutaneous
 - No clamping
 - No incision
 - No General Anesthesia
 - Modular systems

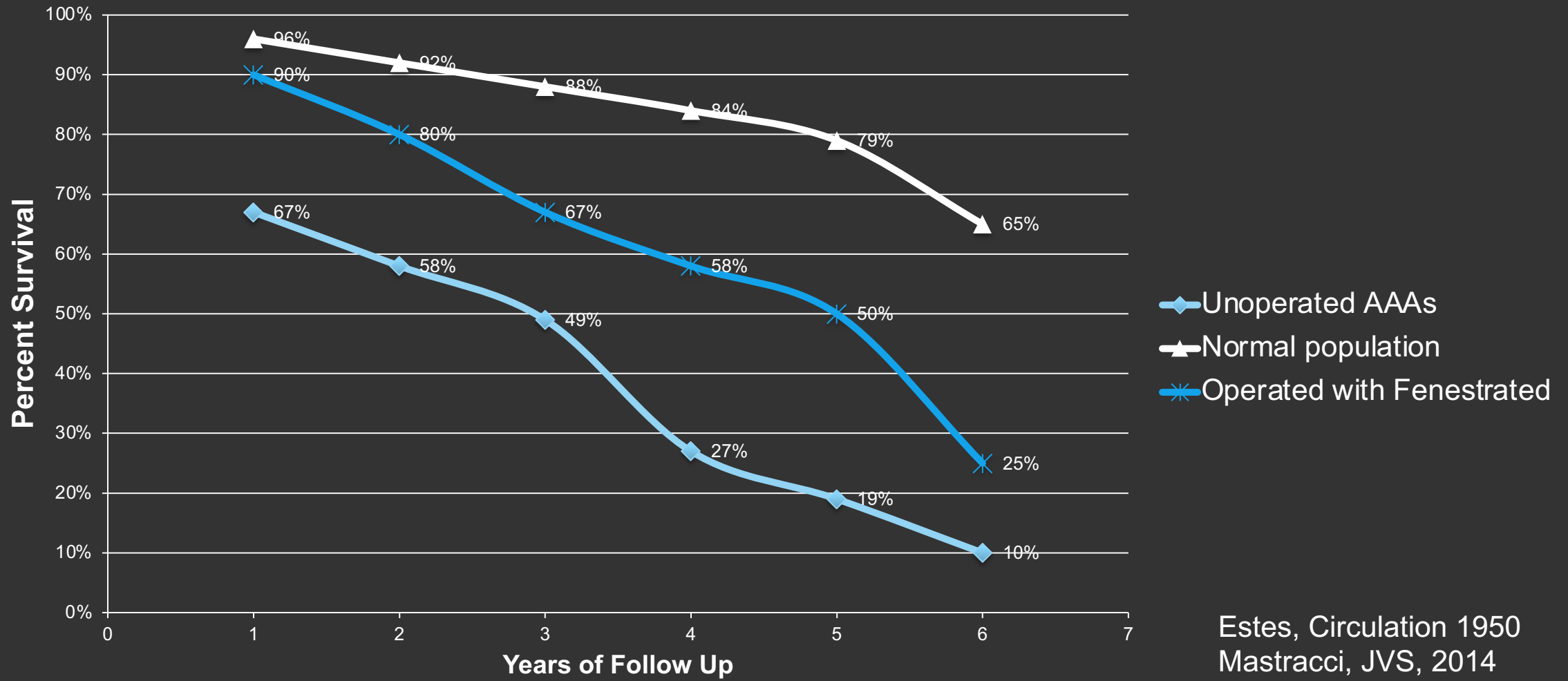
POD 3



4y FU

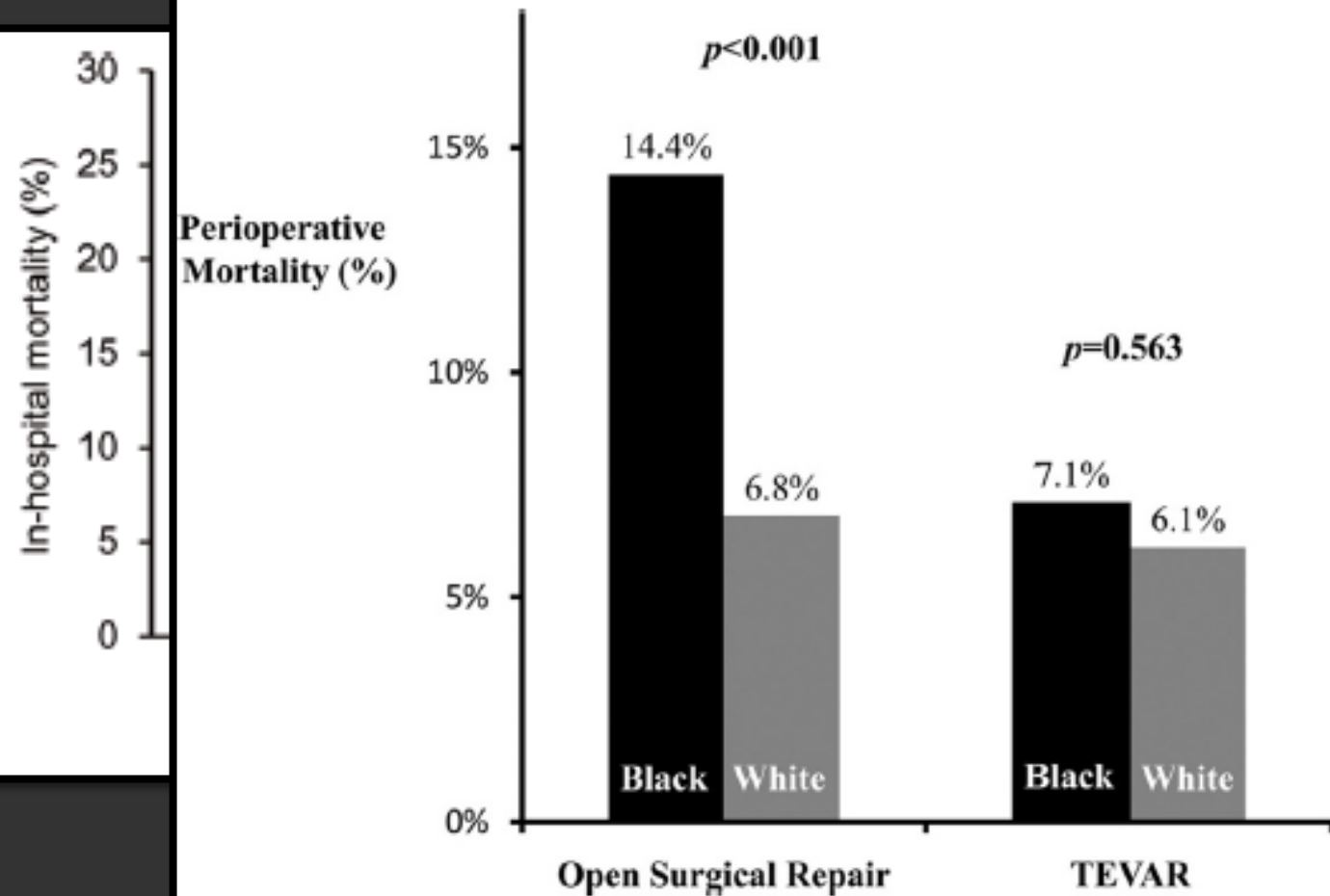


Survival Compared with Matched Cohorts



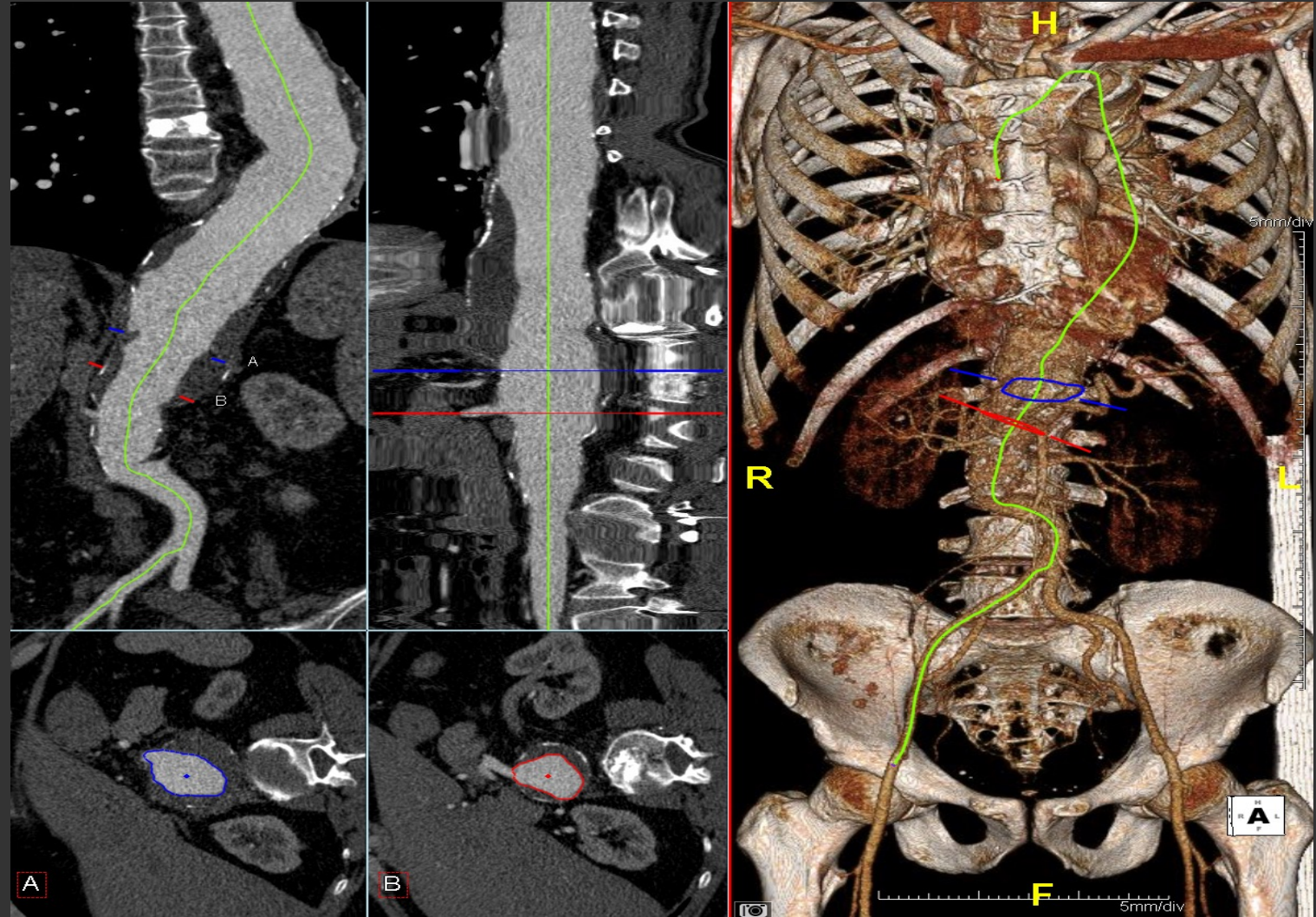


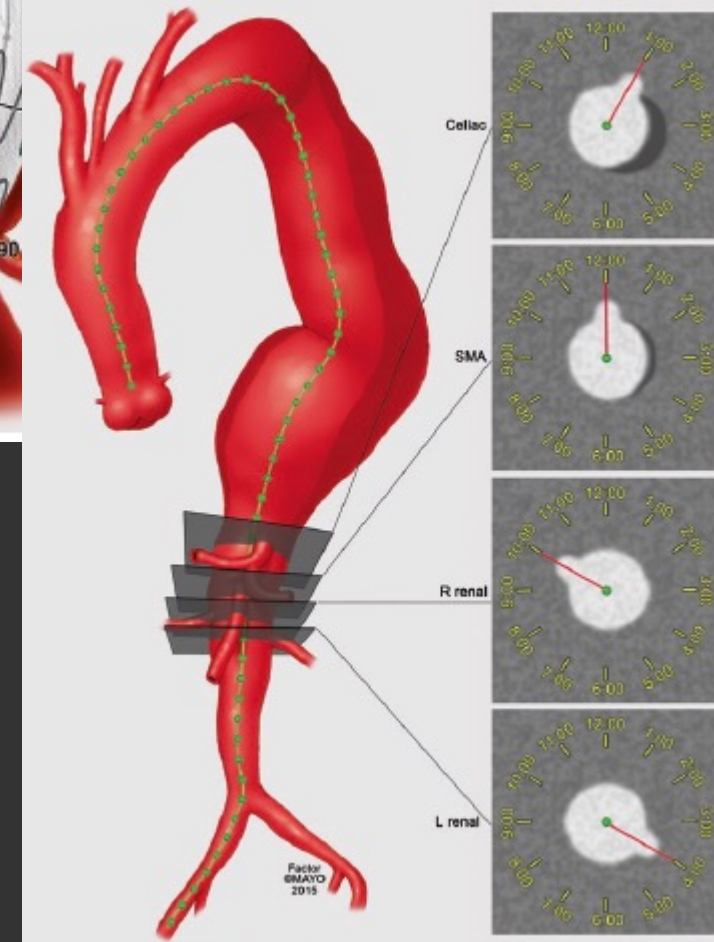
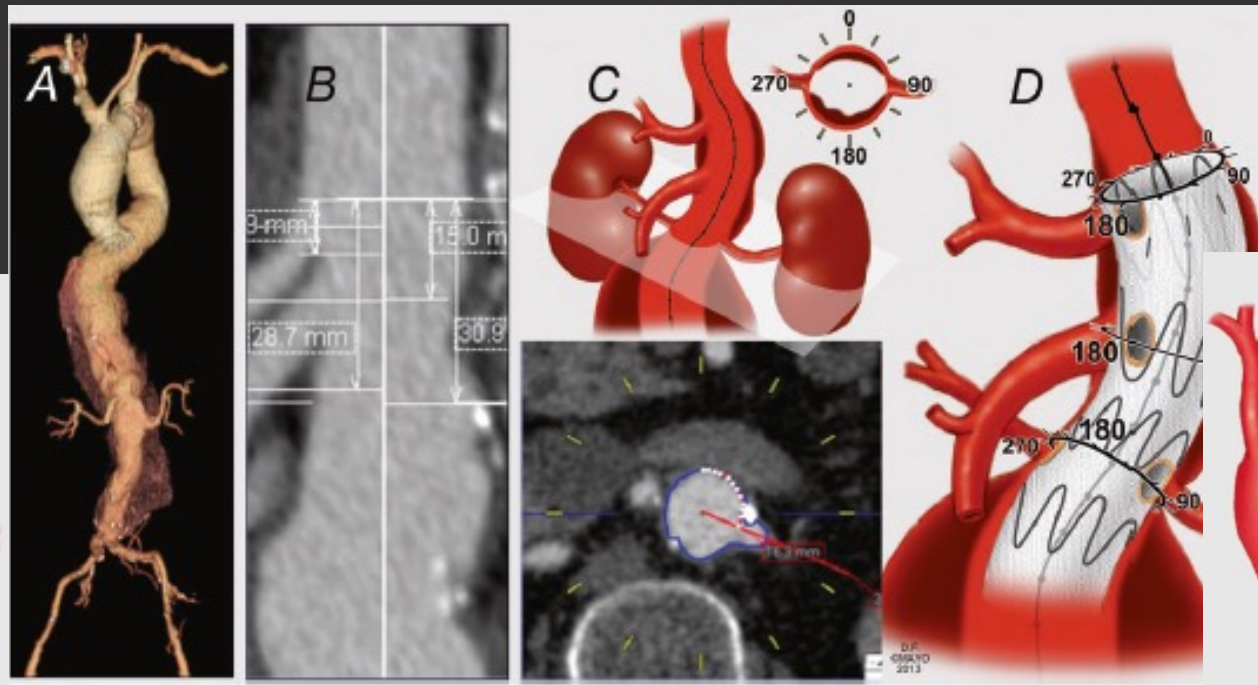
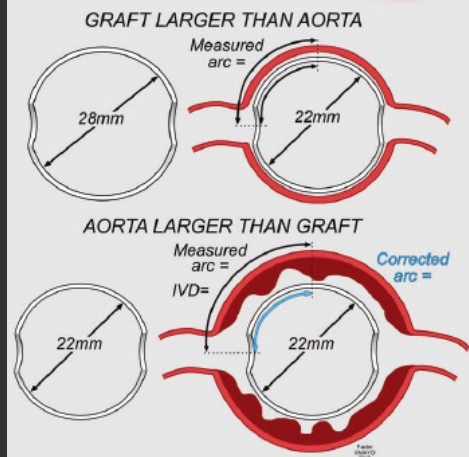
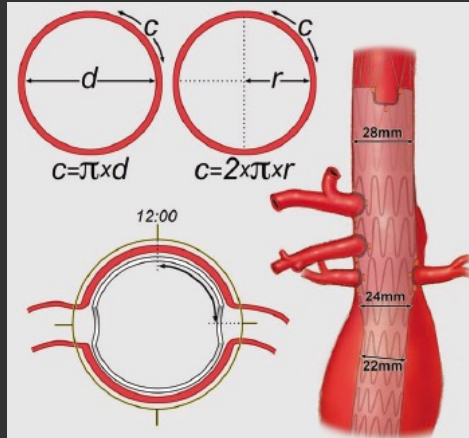
Intervention Impacts survival positively!

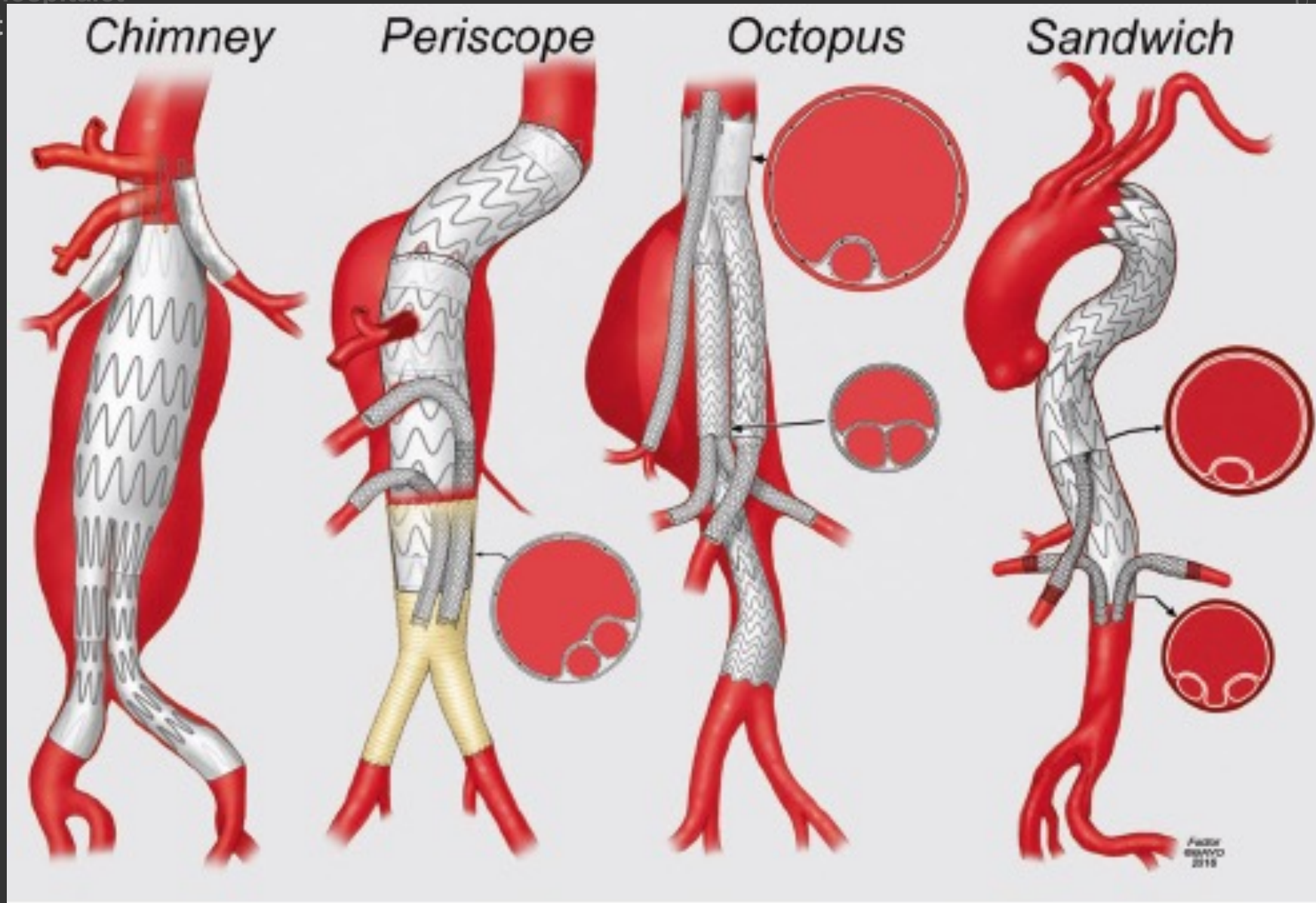


Imaging and Planning

- Preoperative 3D Imaging is critical
- Properly timed contrast
- High-resolution reconstruction
- Understanding of device deployment

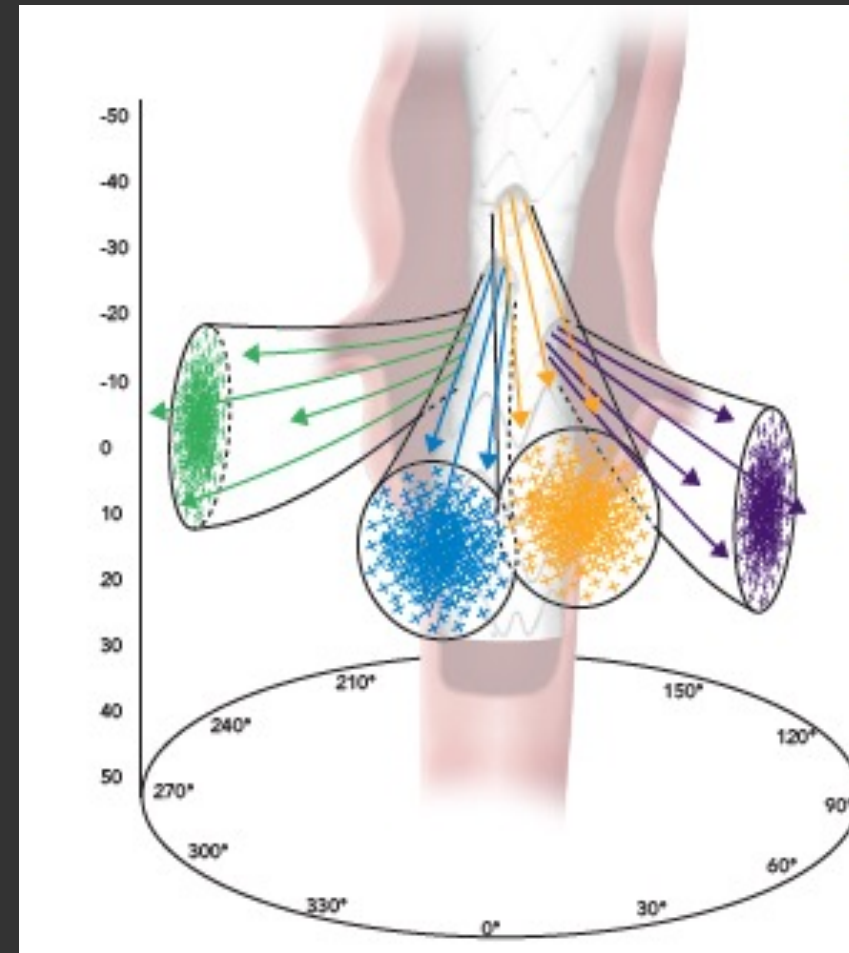
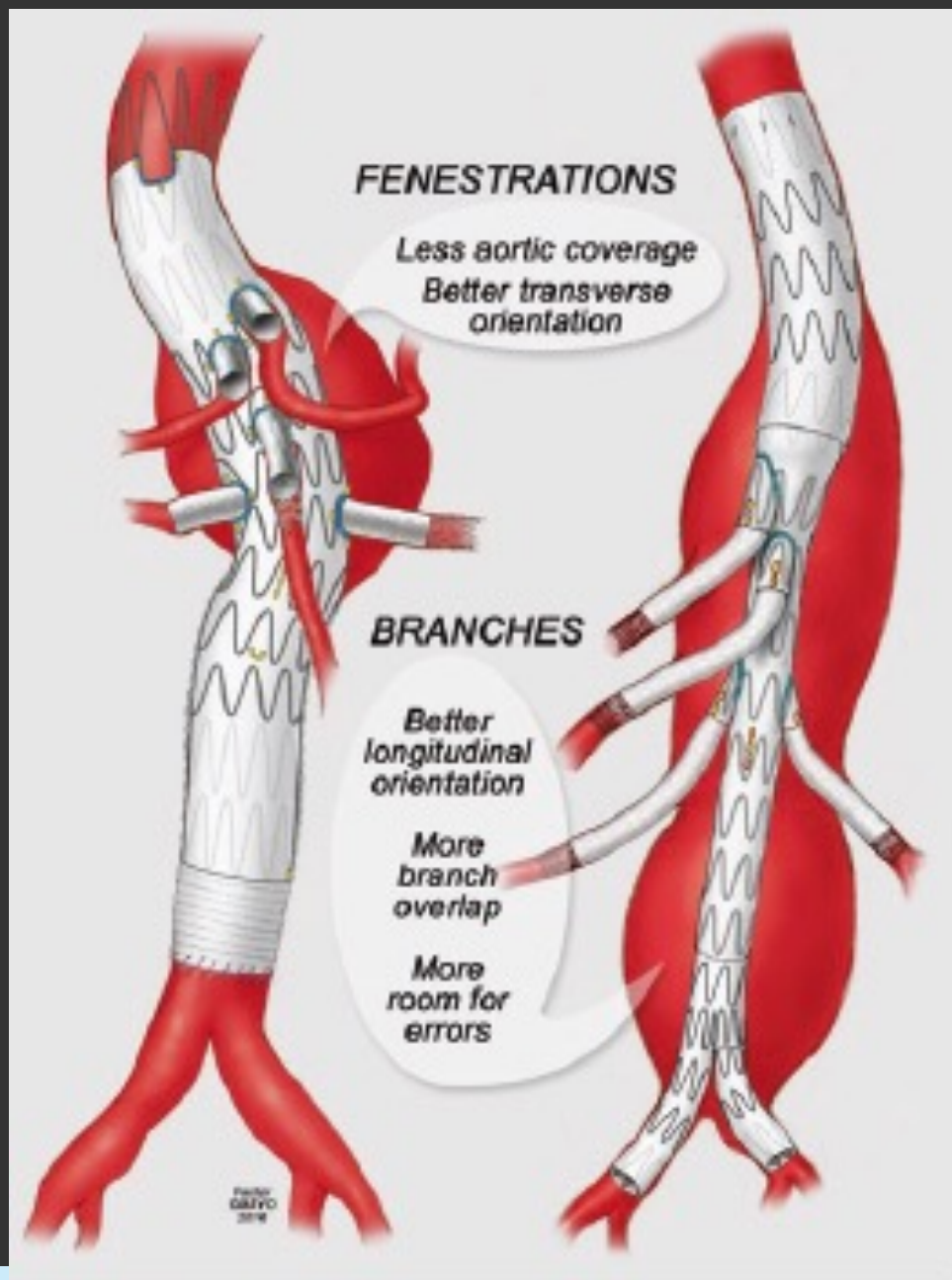


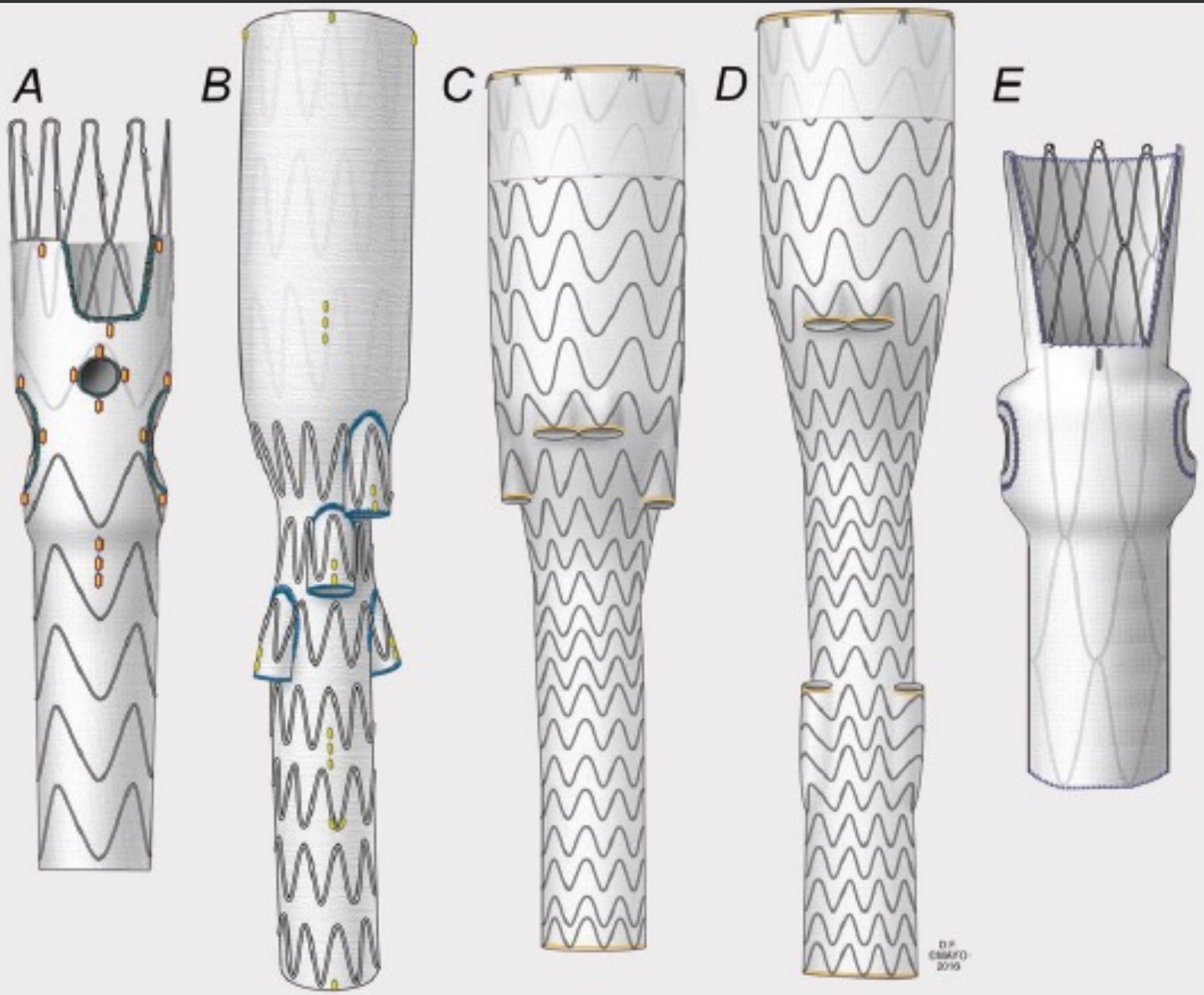


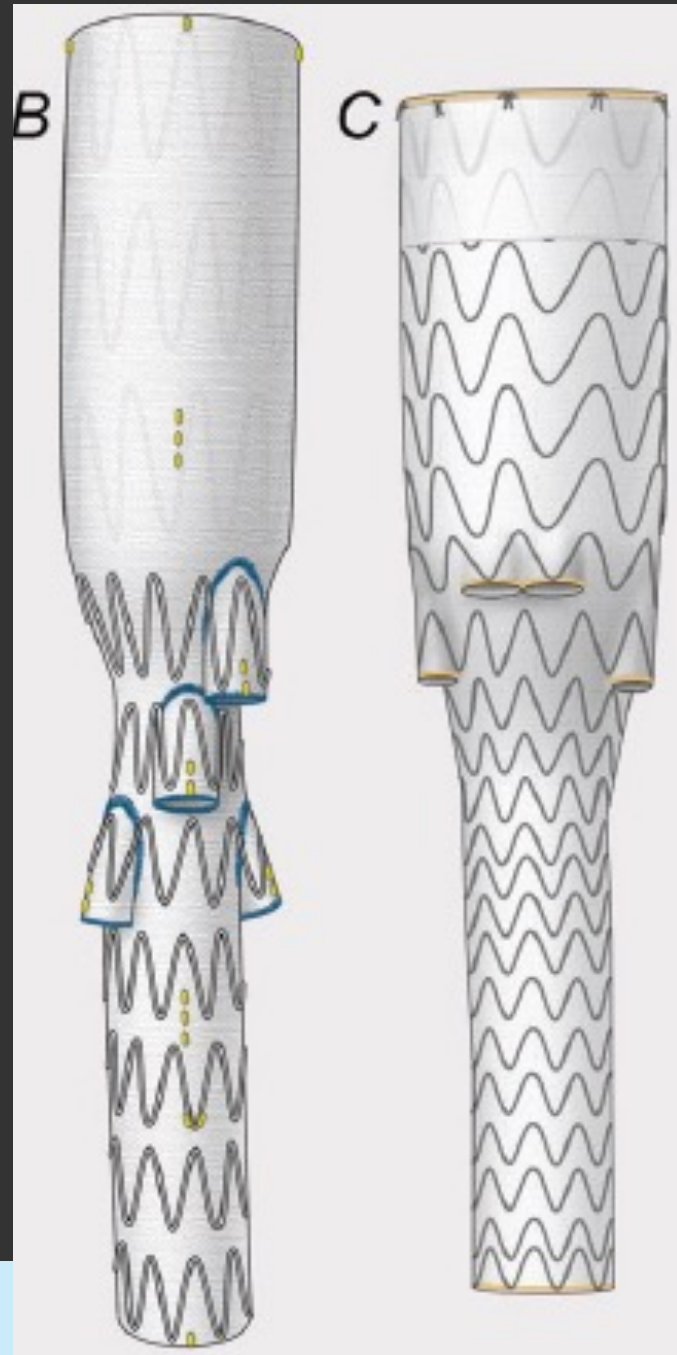


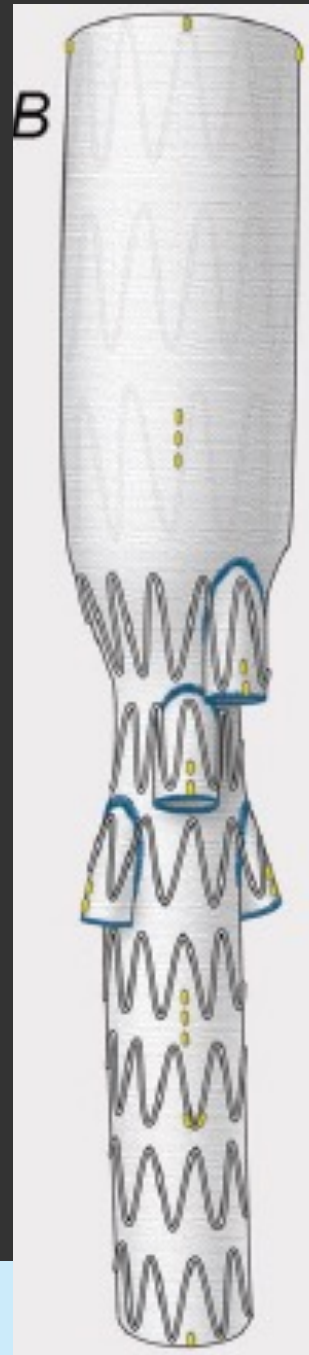
Spandex Rule: "Just Because You Can, Doesn't Mean You should"



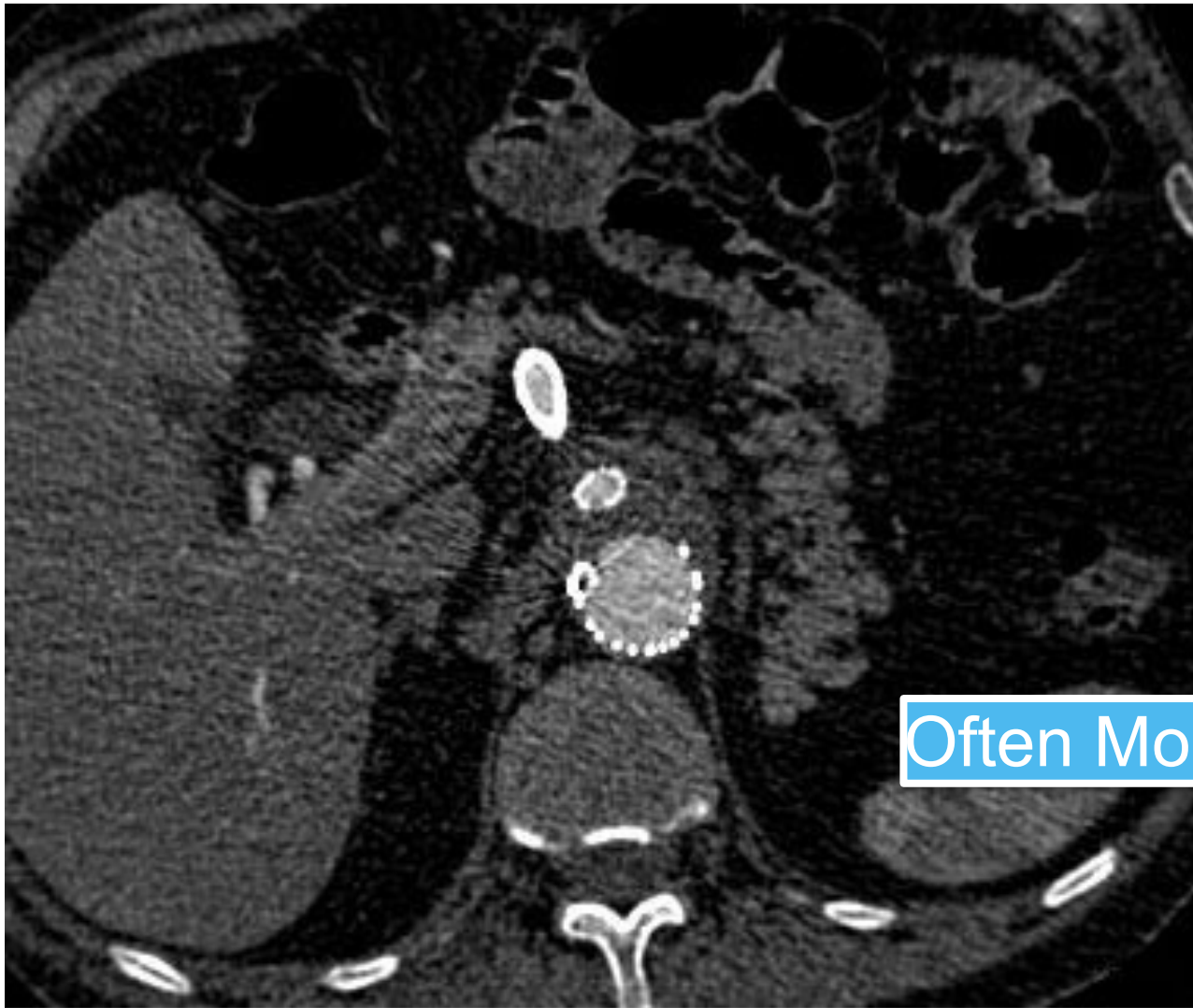






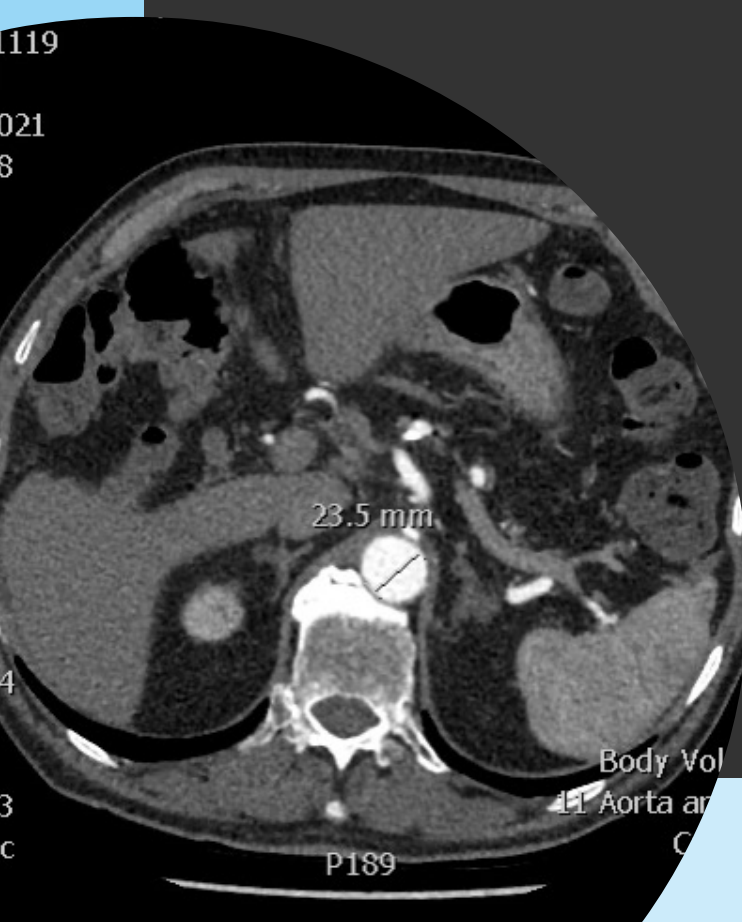
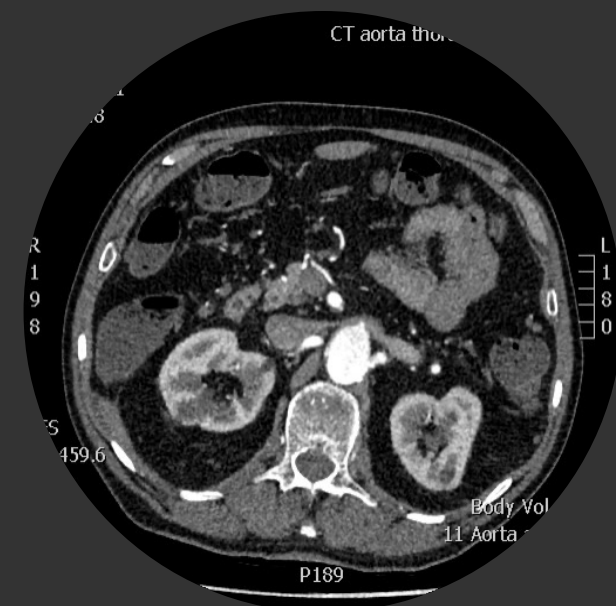
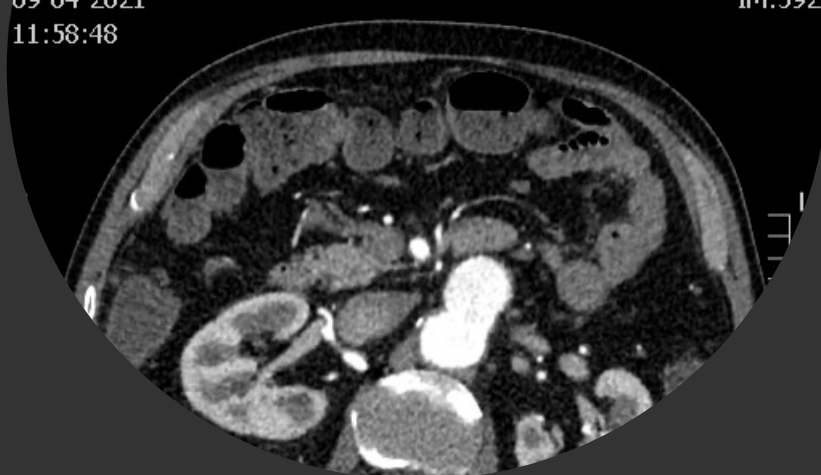


When Might inner Branched Be Better?



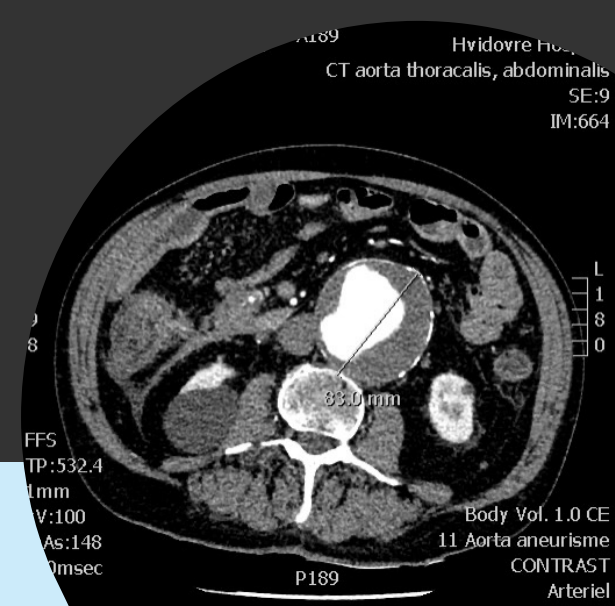
- Narrow Paravisceral Aorta
 - jxAAA, Type IV TAAA
- Angulated Supravisceral Aorta
 - Compression of Branch
- Minimize Coverage of descending Aorta

Often More Compromises in Acute Cases



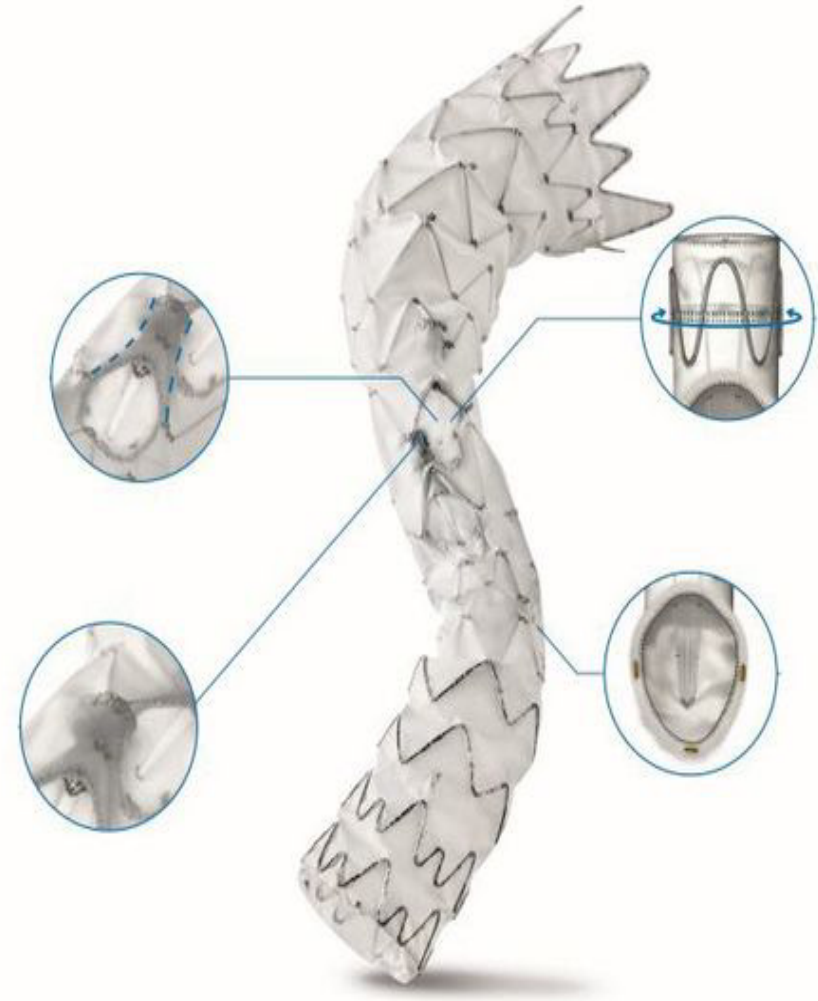
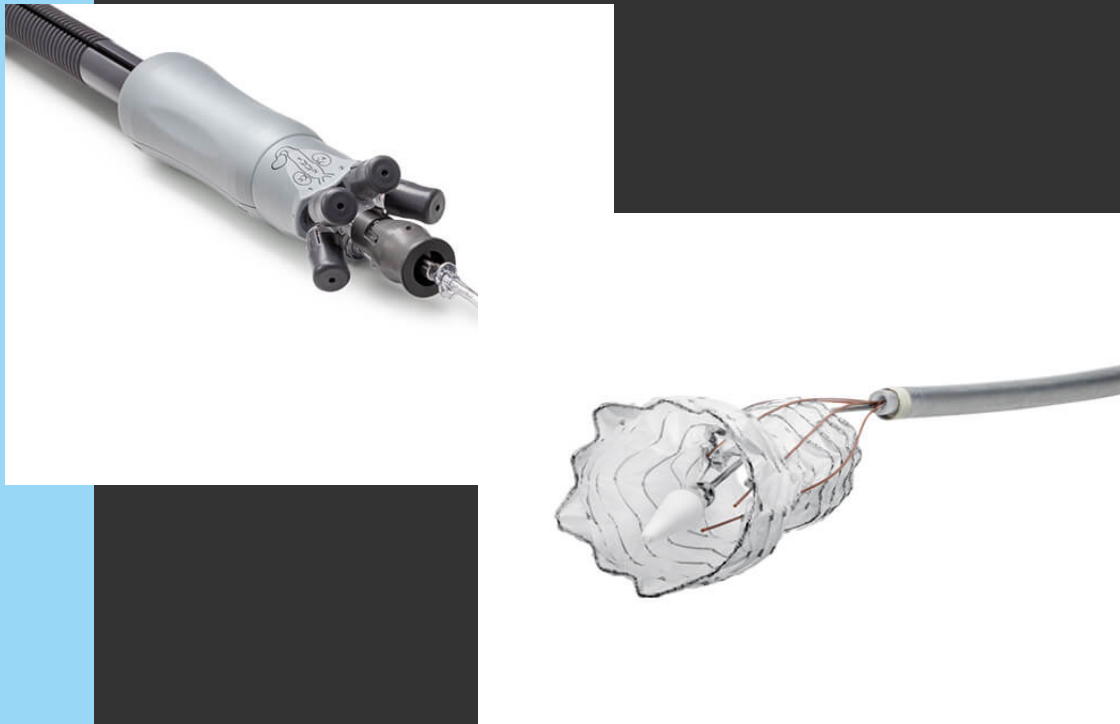
83mm symptomatic AAA

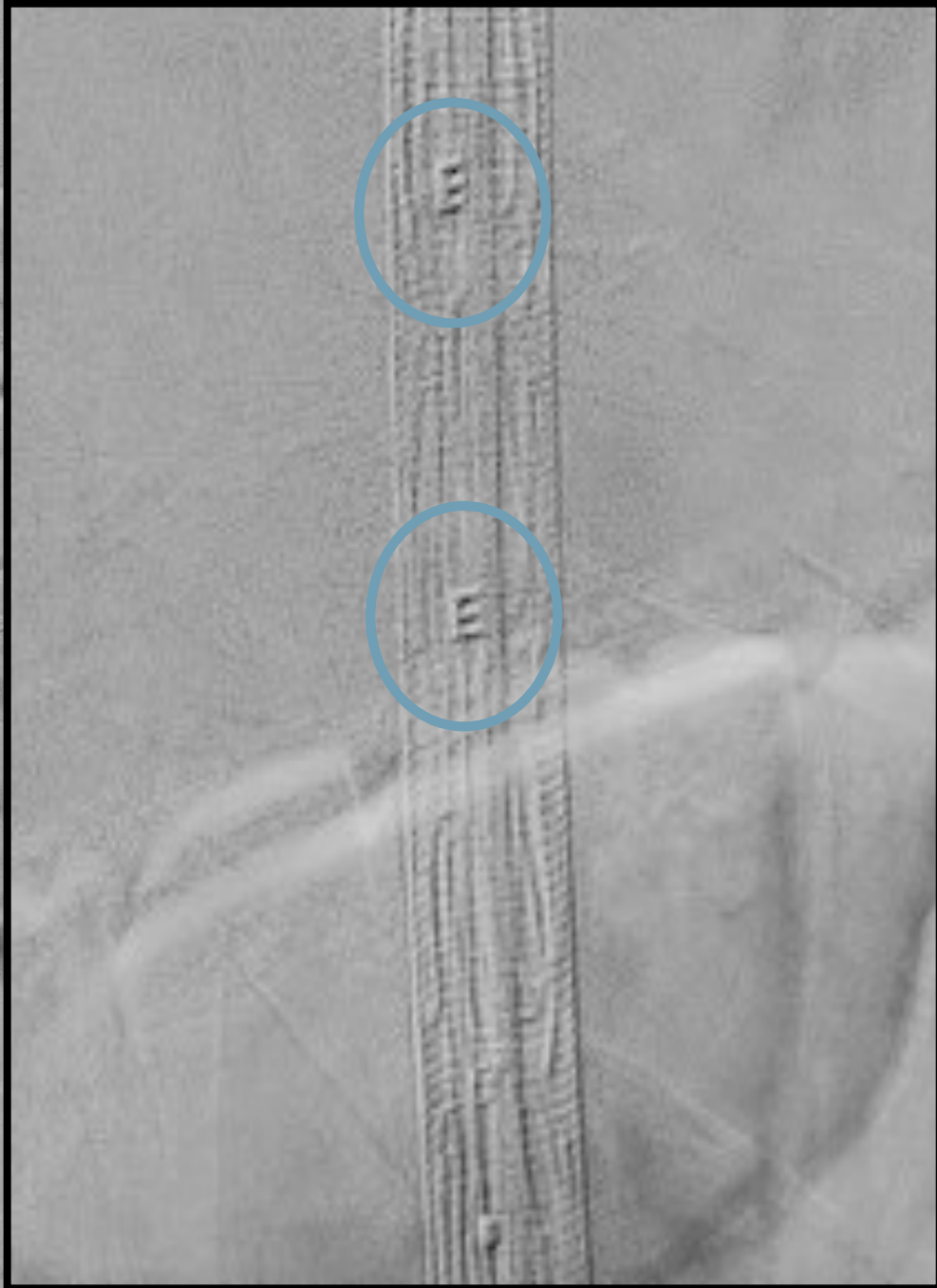
Suprarenal Aorta 23-25mm



Artivion E-nside

- Standard 4 Inner Branch
- Preloaded
- Mates with Any TEVAR EVAR





2021
time08:45:25
31

00
00
54-28

Pelvis

EN, PAUL, HDULER

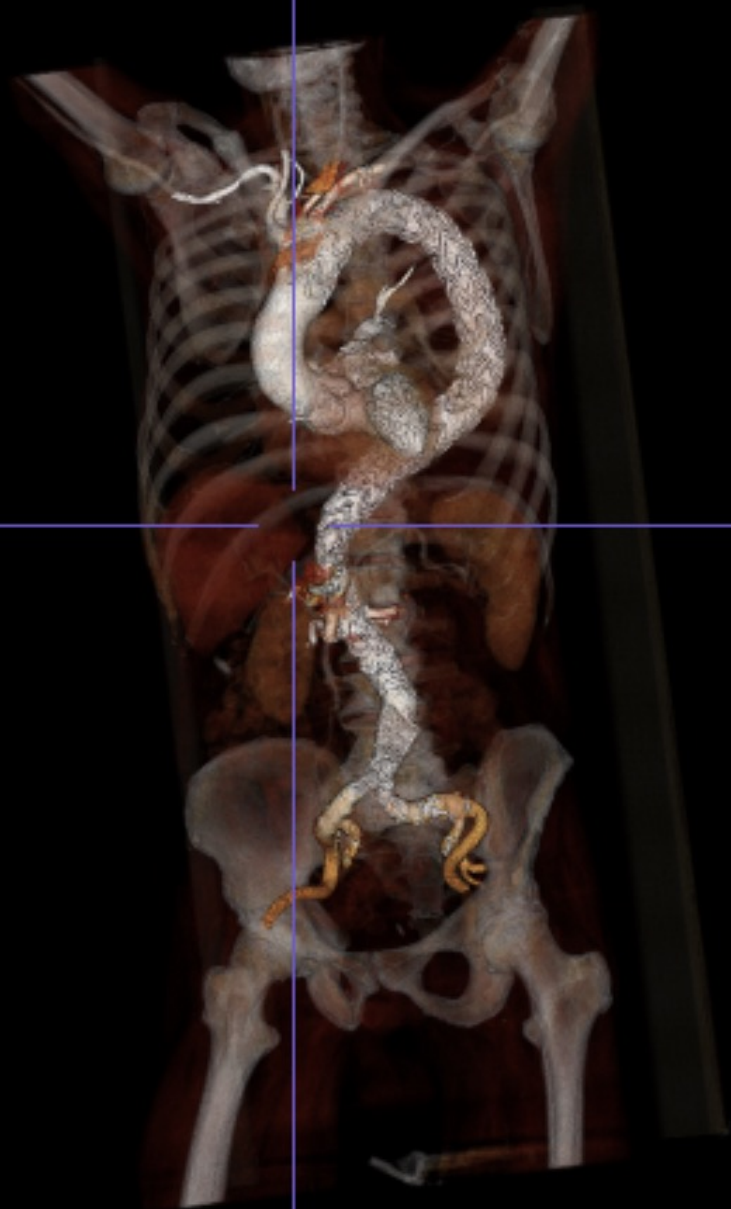
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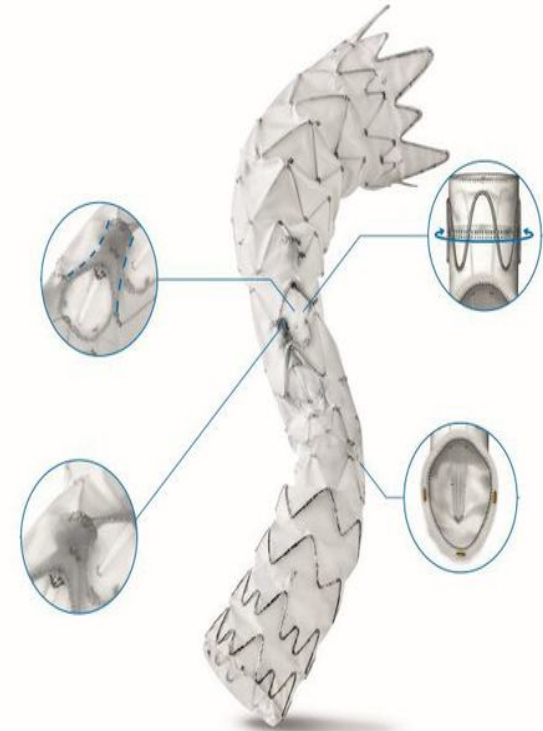
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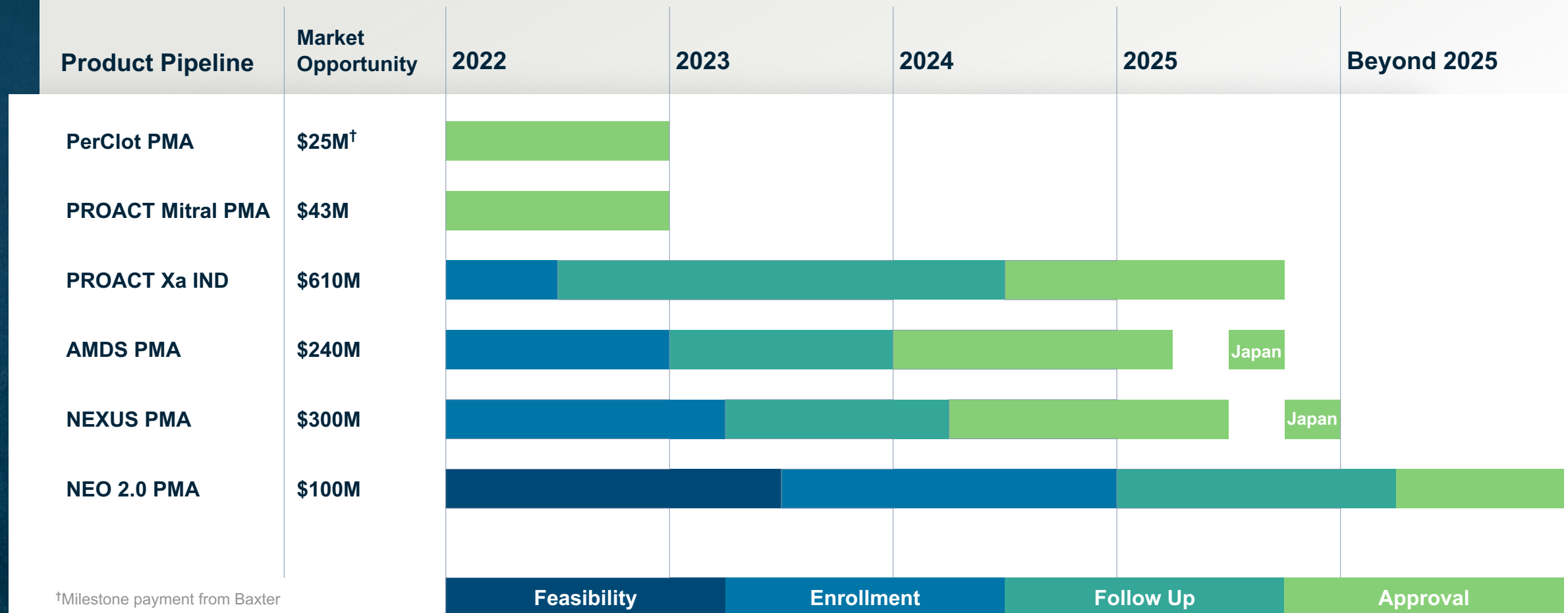
Research & Development Pipeline

MARSHALL STANTON, M.D.

Sr. Vice President, Clinical Research
& Chief Medical Officer

ARTIVION™

R&D Pipeline Opens \$1.3B Market Opportunity



PerClot US Pre-Market Approval Clinical Trial

Strategic Intent: PMA approval triggers \$25M payment from Baxter, if before December 31, 2022.

Product line sold to Baxter International, Inc. Q3 2021.

STUDY DESIGN

Randomized, Non-Inferiority Study vs. Arista™

N = 324 Patients

Cardiac, General, and Urologic Therapeutic Areas

6 Week Follow-Up (24 Months for Oncology Patients)

PRIMARY ENDPOINTS

Primary Efficacy Endpoint: Hemostasis at 7 Minutes

Safety: Comparison of Adverse Events Between Groups

PROJECT STATUS

Enrollment	Complete
Follow Up	Complete
Approval	2022 - Under PMA Review with FDA

CLOT

Prospective, Multicenter, Randomized,
Controlled Clinical Trial



PROACT Mitral US Pivotal Trial

Strategic Intent: Change On-X Mitral Valve labeling to be the only mechanical mitral valve indicated for lower dose Coumadin (warfarin) regimen

STUDY DESIGN

Randomized INR 2.0-2.5 (Test)* vs INR 2.5-3.5 (Control)

N = 401 Patients

1,662 Total Patient-Years Total Follow-Up

PRIMARY ENDPOINTS

Thromboembolism + Thrombosis + Bleeding

PROJECT STATUS

Enrollment	Complete
Follow Up	Complete
Approval	2022 - Under PMA Review with FDA

PROACT

Prospective, Longitudinal, Randomized,
Multi-Center Study



PROACT Xa US Pivotal Trial

Strategic Intent: Expand use of On-X mechanical aortic valve in patients between 60-70 years old by proving that patients can be safely and more simply managed with apixaban rather than warfarin.

Anticoagulation with warfarin is #1 reason people choose tissue rather than mechanical heart valves.

STUDY DESIGN

On-X Aortic Valve or On-X Ascending Aortic Prosthesis
Eliquis (apixaban) 2.5 or 5 mg BID vs Coumadin (warfarin) (INR 2.0-3.0)
1000 Patients randomized; 2 Years Follow-Up

CO-PRIMARY EFFICACY OBJECTIVES

Non-inferiority of apixaban to warfarin for valve thrombosis/thromboembolism
Valve thrombosis/thromboembolism with apixaban <3.4%/pt-yr

PRIMARY SAFETY OBJECTIVE

Determine if apixaban is superior to warfarin for major bleeding

PROJECT STATUS

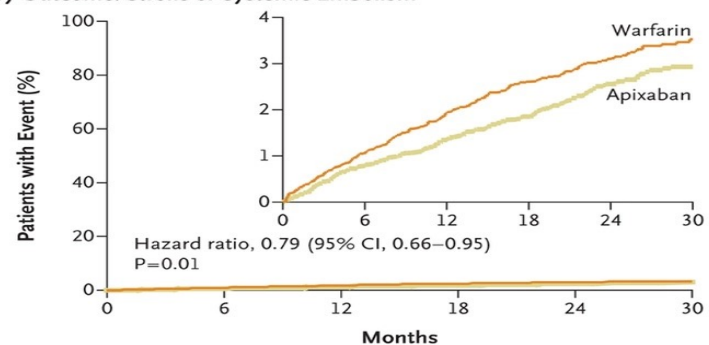
Enrollment	~ 2022	(629 participants randomized to date)
Follow Up	~ 2024	
Approval	~ 2025	

PROACT Xa



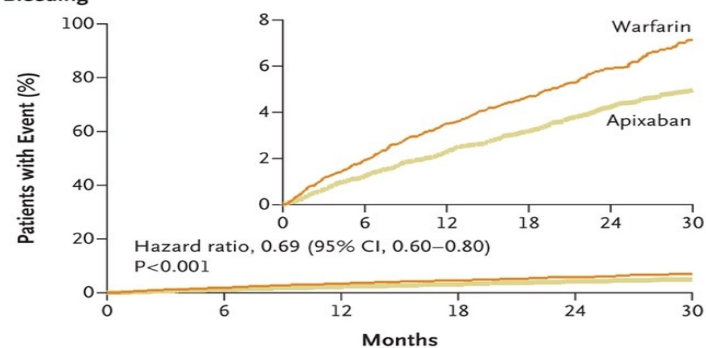
Apixaban's Stroke and Bleeding Reductions Drove Market Share Dominance

A Primary Outcome: Stroke or Systemic Embolism



No. at Risk	0	6	12	18	24	30
Apixaban	9120	8726	8440	6051	3464	1754
Warfarin	9081	8620	8301	5972	3405	1768

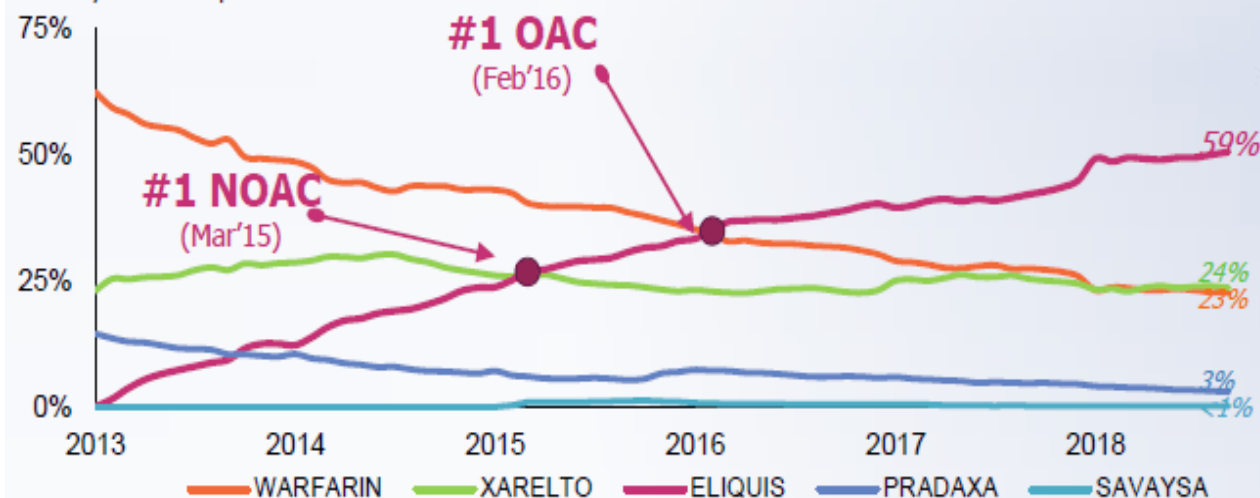
B Major Bleeding



No. at Risk	0	6	12	18	24	30
Apixaban	9088	8103	7564	5365	3048	1515
Warfarin	9052	7910	7335	5196	2956	1491

Evolution of OAC Market Share in Atrial Fibrillation (AF)¹

January 2013 – September 2018



AMDS US Pivotal Trial

Strategic Intent: Bring AMDS to US for treatment of acute aortic dissection; leverage these data for Japan and China approvals.

STUDY DESIGN

Acute DeBakey Type I dissection w/ clinical or radiographic malperfusion
93 Subjects; 25 US Sites; 1 Year Follow Up

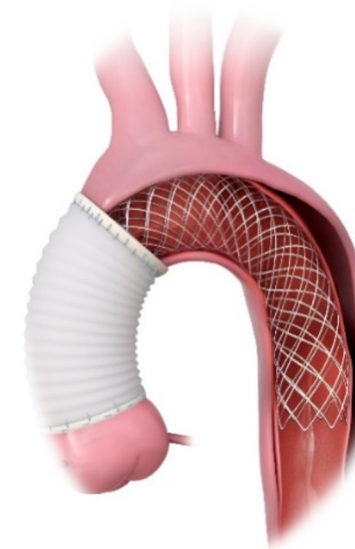
PRIMARY ENDPOINTS

30-day all-cause mortality + new disabling stroke + new renal failure requiring dialysis + MI
c/w published standard of care (hemiarch) outcomes
Maximal true lumen diameter change at 1-yr

PROJECT STATUS

Feasibility	Complete
Enrollment	~ 2022
Follow Up	~ 2023
Approval	~ 2025 (US & Japan)

PERSEVERE



NEXUS by Endospan US Pivotal Trial

Strategic Intent: Fund Endospan's US pivotal clinical trial with option to acquire post-FDA approval.

STUDY DESIGN

Chronic Aortic Arch disease: chronic dissection (n=60), aneurysm (n=20), PAU/IMH** (n=20)
100 Patients; ~30 US sites / 1 Year follow up

PRIMARY ENDPOINTS

30-day clinical outcome: mortality, disabling stroke, permanent paralysis/paraplegia, renal failure, aortic rupture, new dissection in thoracic aorta or brachiocephalic artery
30-day device technical failure

	30 Days	1 Year
First in Man Results* (8 Patients; age 72 +/- 6 yrs)	Mortality	7.1%
	Stroke / TIA	3.6%
	Spinal Cord Ischemia	0.0%

PROJECT STATUS

Feasibility	Complete
Enrollment	~ 2023
Follow Up	~ 2024
Approval	~ 2025 (US & Japan)

TRIOMPHE
S T U D Y



*Planer et al: Annals of Surgery 2021

** Penetrating Aortic Ulcer/Intramural Hematoma

NEO 2.0 US Feasibility + Pivotal Trial

Strategic Intent: Bring novel, 3rd generation aortic arch device to the US for treatment of acute or chronic dissection, or aneurysm involving the Aortic Arch.

STUDY DESIGN

Feasibility Study: 10 patients / 2-3 sites in the US

Pivotal: 110 - 130 patients / 20-25 sites

ANTICIPATED PRIMARY ENDPOINTS (COMPOSITE ENDPOINT THROUGH 1-YEAR)

All-cause mortality

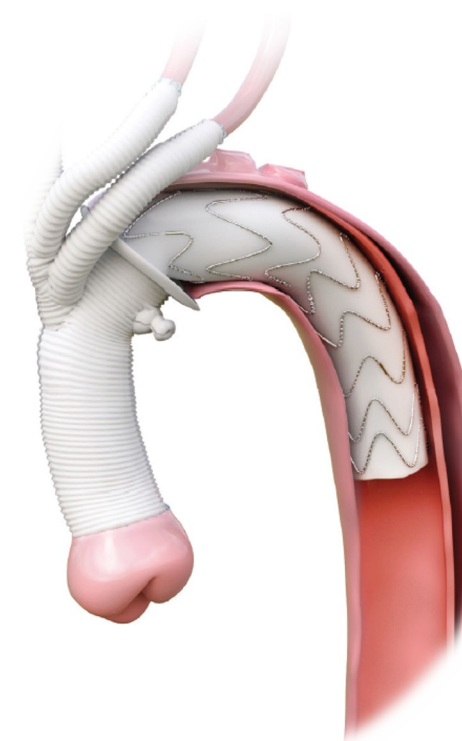
Permanent disabling stroke

Permanent paraplegia/paraparesis

Unanticipated aortic-related reoperation or conversion to open surgery

PROJECT STATUS

Feasibility	~ 2023 - 2024
Enrollment	~ 2025
Follow Up	~ 2026
Approval	~ 2027





Financial Outlook

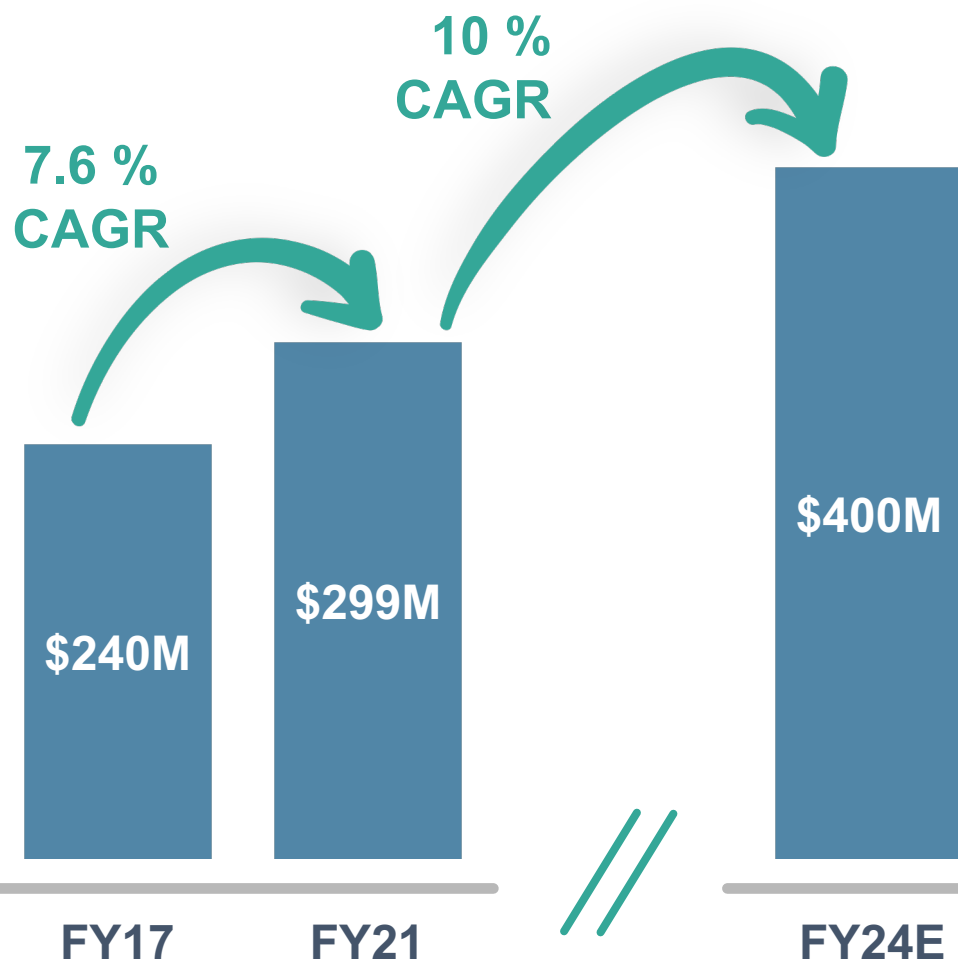
D. ASHLEY LEE, CPA

Executive Vice President &
Chief Financial Officer

ARTIVION™

2022 – 2024 Revenue Expectations

Existing products, OUS investment and regulatory approvals to drive revenue growth



THREE YEAR ASSUMPTIONS

Continued strength in existing products: On-X: Stents
Grafts::AMDS; NEO; E-nside & NEXUS

Accelerating growth in APAC & LATAM

Regulatory approvals: PROACT Mitral & PerClot

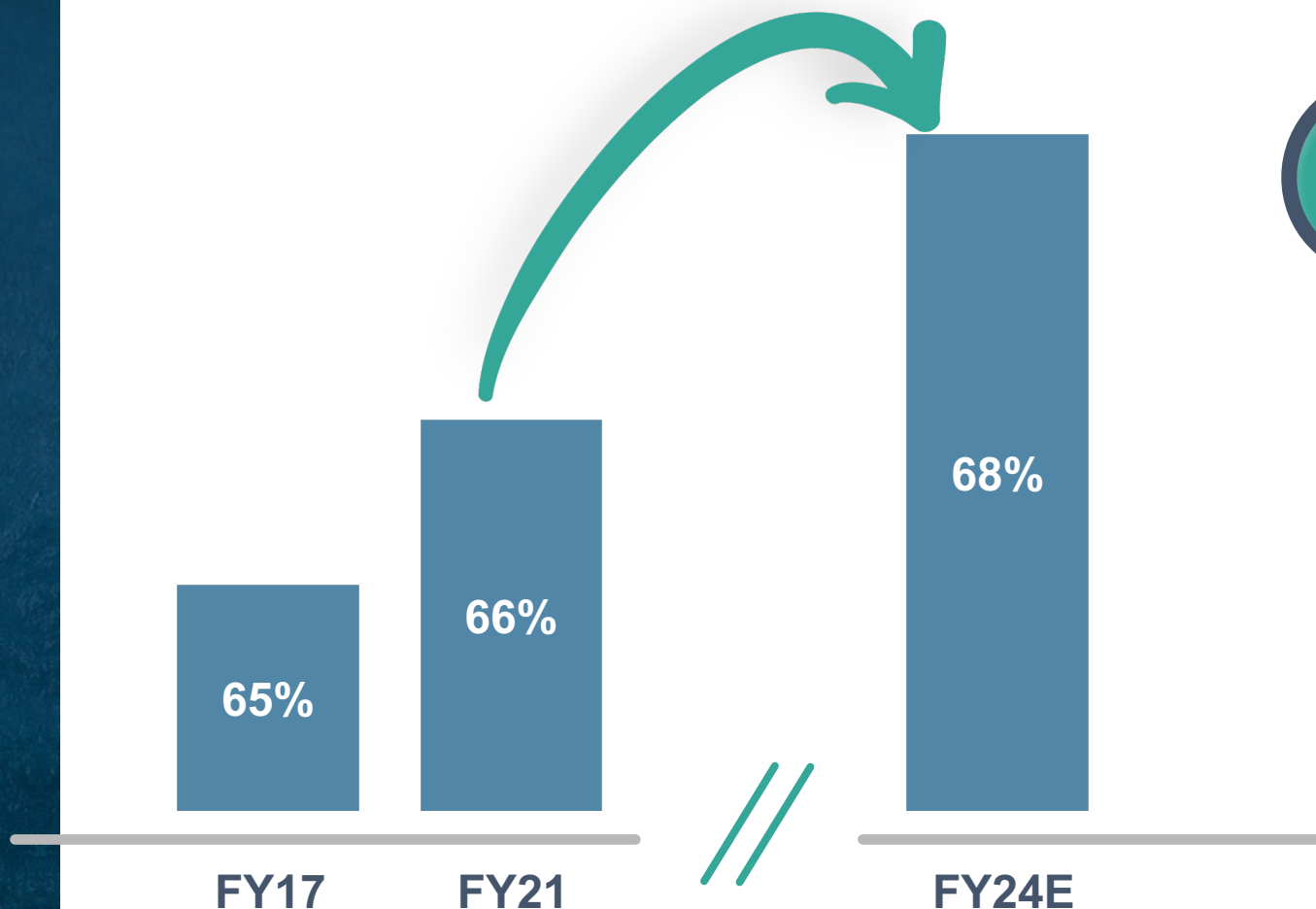
Constant currency growth assumes EUR/USD = 1.13

\$65M revenue contribution from listed initiatives

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2022 – 2024 Gross Margin Expectations

Product mix, channel enhancement and cost-down initiatives to drive gross margin expansion



THREE YEAR ASSUMPTIONS

Revenue mix: accelerating sales of higher margin devices

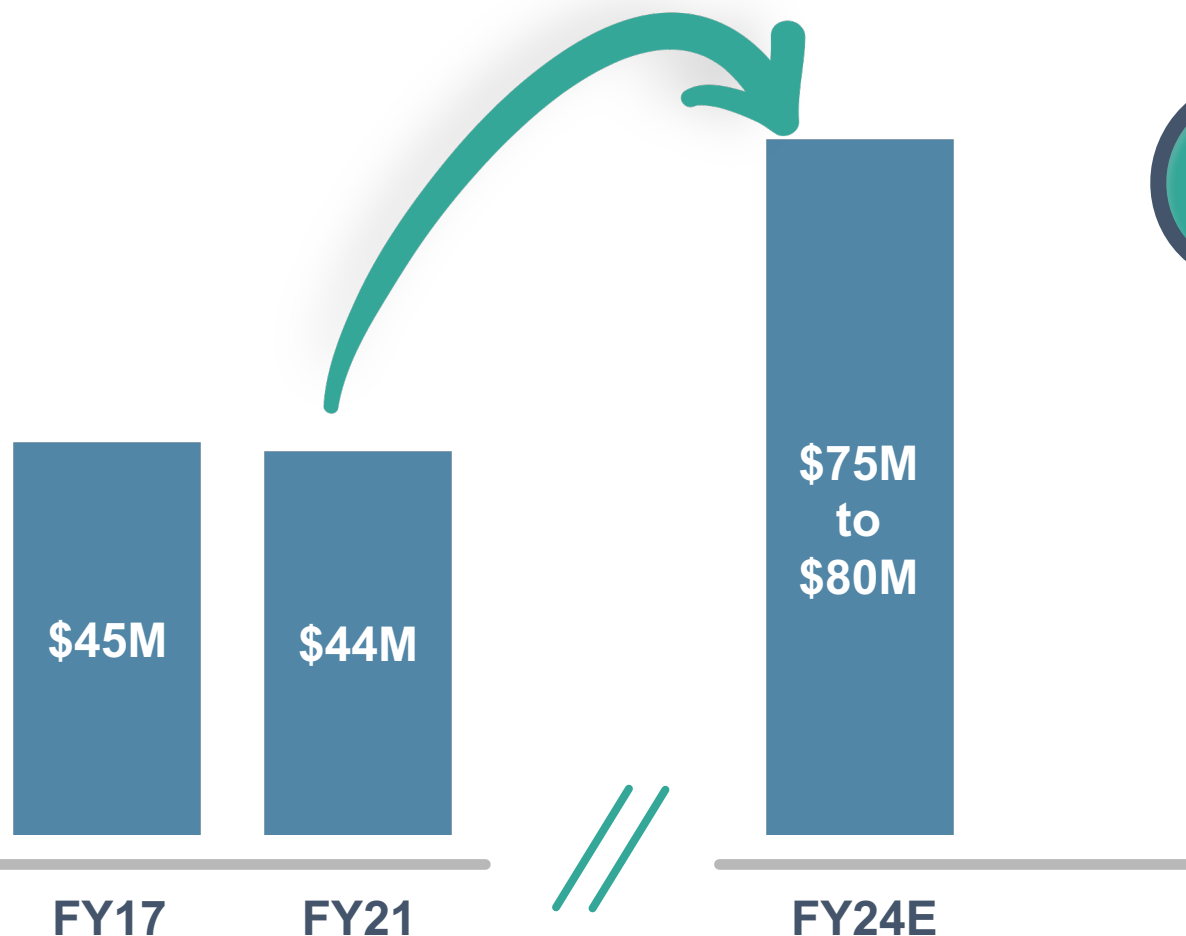
Channel enhancement: direct initiatives and optimization of distributor network

Cost-down initiatives: process improvement, strategic purchasing, and volume increases

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2022 – 2024 Adjusted EBITDA Expectations

Revenue growth and operating leverage to drive EBITDA expansion



THREE YEAR ASSUMPTIONS

Revenue growth and gross margin expansion drives incremental cash flow

Operating leverage accelerates in 2023/2024:

Investment in LATAM / APAC channels moderates

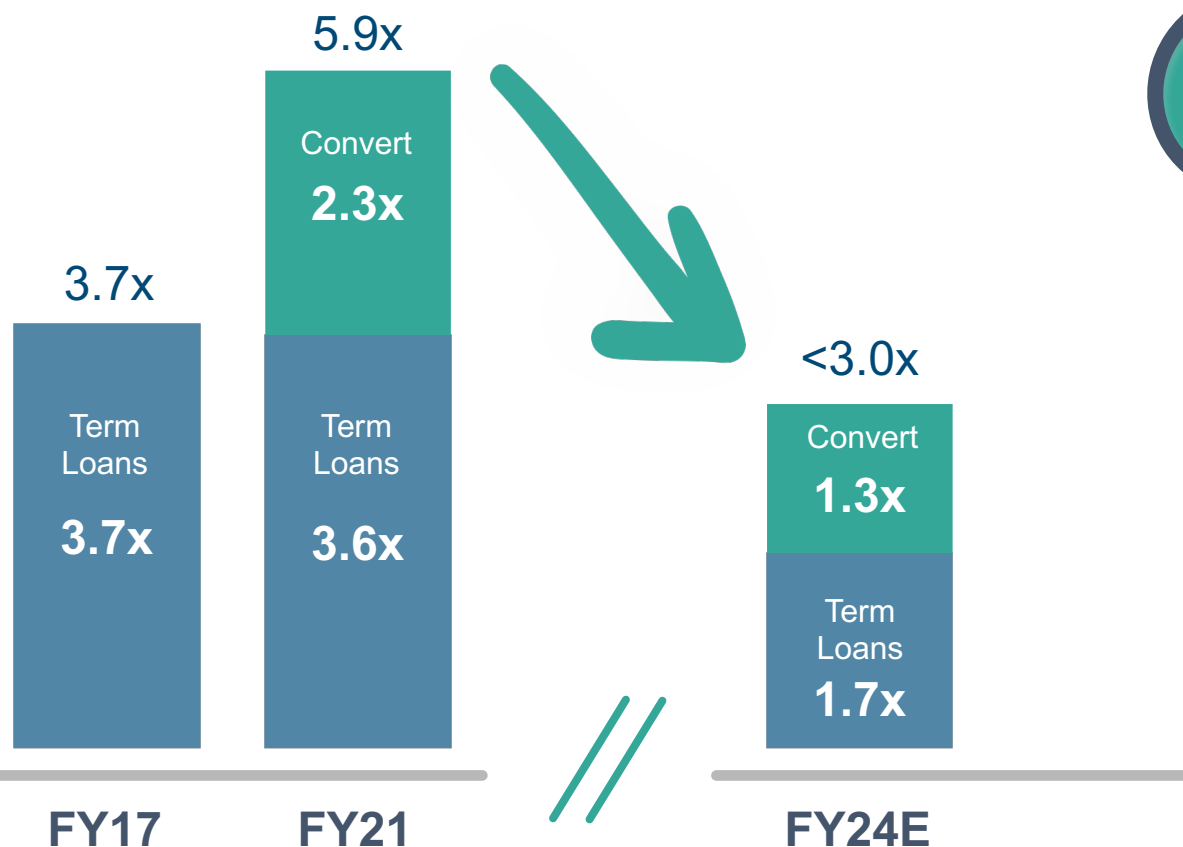
SG&A spending, excluding business development, moderates to mid to high-single digit growth

R&D spending 13% - 11% of revenue

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2022 – 2024 Net Leverage Expectations

Adjusted EBITDA expansion and cash generation to drive down leverage



THREE YEAR ASSUMPTIONS

Existing TLB & convertible notes remain in capital structure in 2024

Adjusted EBITDA expands from \$44M to \$75M - \$80M

Cash balances increase over the forecast period

Net leverage decreases from 5.9x to less than 3.0x adjusted EBITDA

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Contribution to Adjusted EBITDA – 2024 vs 2021

Return 50% of Incremental Gross Margin to Shareholders via Adjusted EBITDA

INCREMENTAL
REVENUE



INCREMENTAL
GROSS
MARGIN



INCREMENTAL
EXPENSES



INCREMENTAL
ADJUSTED
EBITDA



THREE YEAR ASSUMPTIONS

Channel investment decreases after 2024

R&D spending moderates after 2024

PROACT Xa and AMDS approvals position Artivion for accelerated cash flow generation and profitability

ARTIVION™

Summary ~ 2024 and Beyond

Revenue: ~ \$400M → Accelerating Revenue (3 PMAs - \$1.3B)

Gross Margin: ~ 68% → Increasing Gross Margin (3 PMAs - 90%)

EBITDA: ~ \$75M - \$80M → Accelerating EBITDA

- Sales Channel investment made
- R&D spending as % revenue goes down

Net Leverage: <3.0X → Significant drop through





ARTIVION™
Formerly CryoLife | Jotec

Thank you