Mini-Forum of Bioresorbable Vascular Scaffolds

Technology and Biological Implications

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CARDIOVASCULAR SUMMIT TCTAP 2015

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Vascular Healing of BRS

Contributing Technical Factors

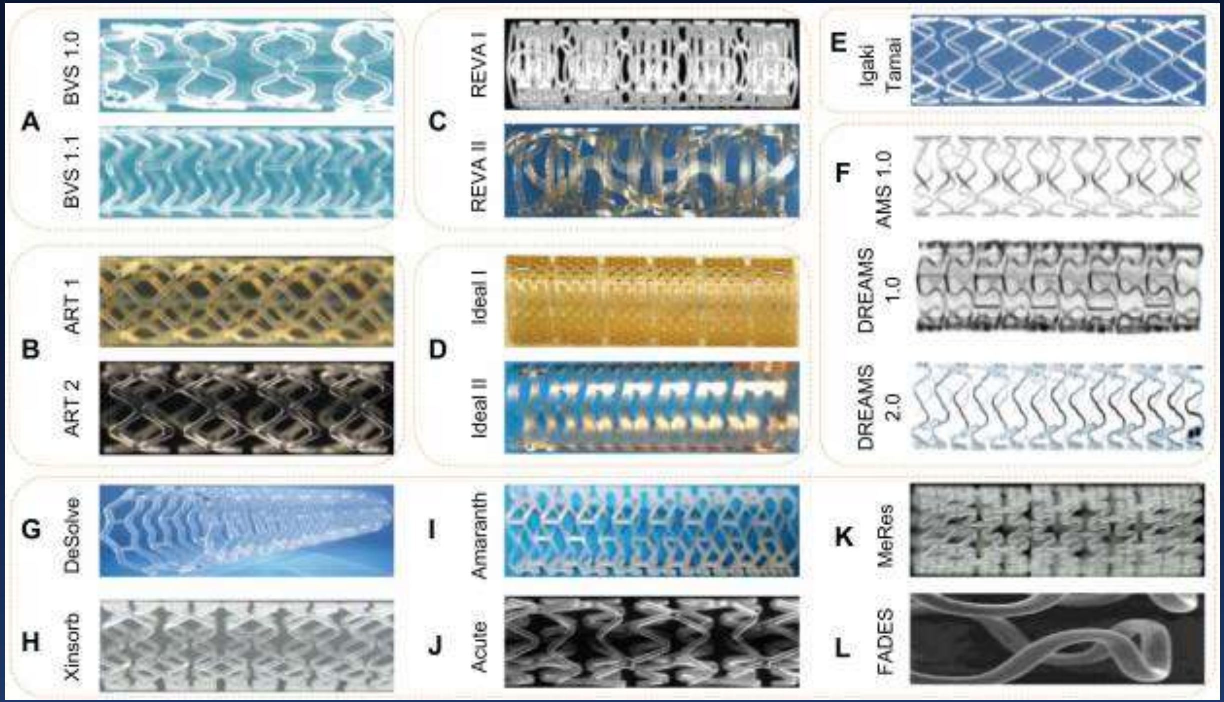


Figure (Left) Med Devices (Auckl). 2013; 6: 37–48

- Polymer Biocompatibility
- Chemical Properties
  - Polymer Crystallinity
- Polymeric Mass
  - Scaffold Design
  - Strut Thickness-Width
- Scaffold Absorption Time
  - Vessel Scaffold Capacity
- Polymer-Drug Interaction
  - Tissue Pharmacokinetics
  - Restenosis Prevention

The resulting vascular healing profile of each individual BRS depends on the interaction of all the material and structural components with the vessel wall at different stages of the healing process

BRS and Vessel Healing

Multifactorial and Time-Dependent Process

ACUTE PHASE

Scaffold Biomechanics: Dilatation and Recoil

↓

Mechanical Impact on Vessel (Injury)

↓

Scaffold Material Exposure

Acute Vessel Wall Inflammation

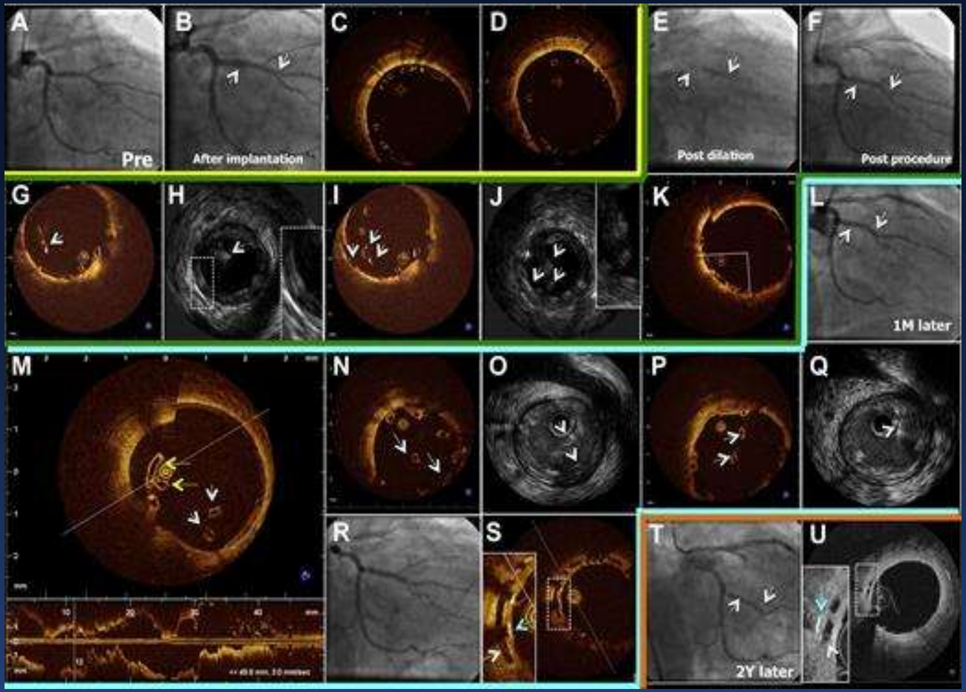
Scaffold Surface Cell Coverage

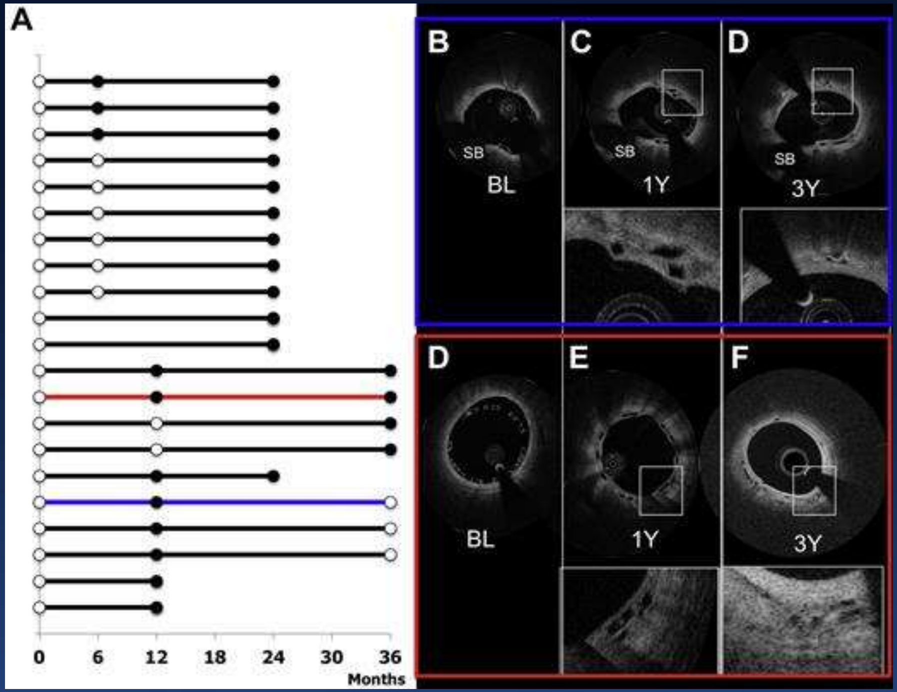
VESSEL PATENCY:
SCAFFOLD BIOMECHANICS
MATERIAL THROMBOGENICITY

In the acute setting; is the biomechanical behavior of BRS comparable to metallic Drug Eluting Stents?

Acute Scaffold Disruption and Late Structural Discontinuity in BVS

Implications for Clinical Outcomes



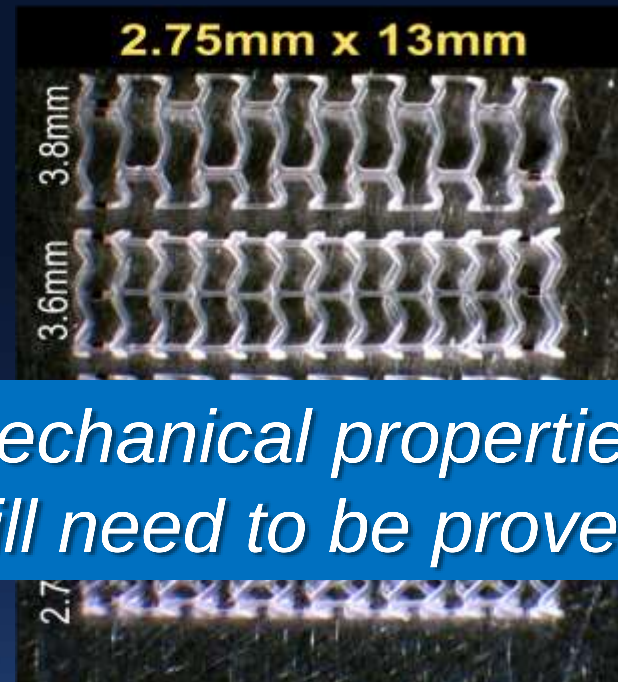


Acute Scaffold Disruption= 2/51 (3.9%)
One TLR Event

Late Discontinuities= 21/49 (42%)
1-Non-Ischemia Driven TLR

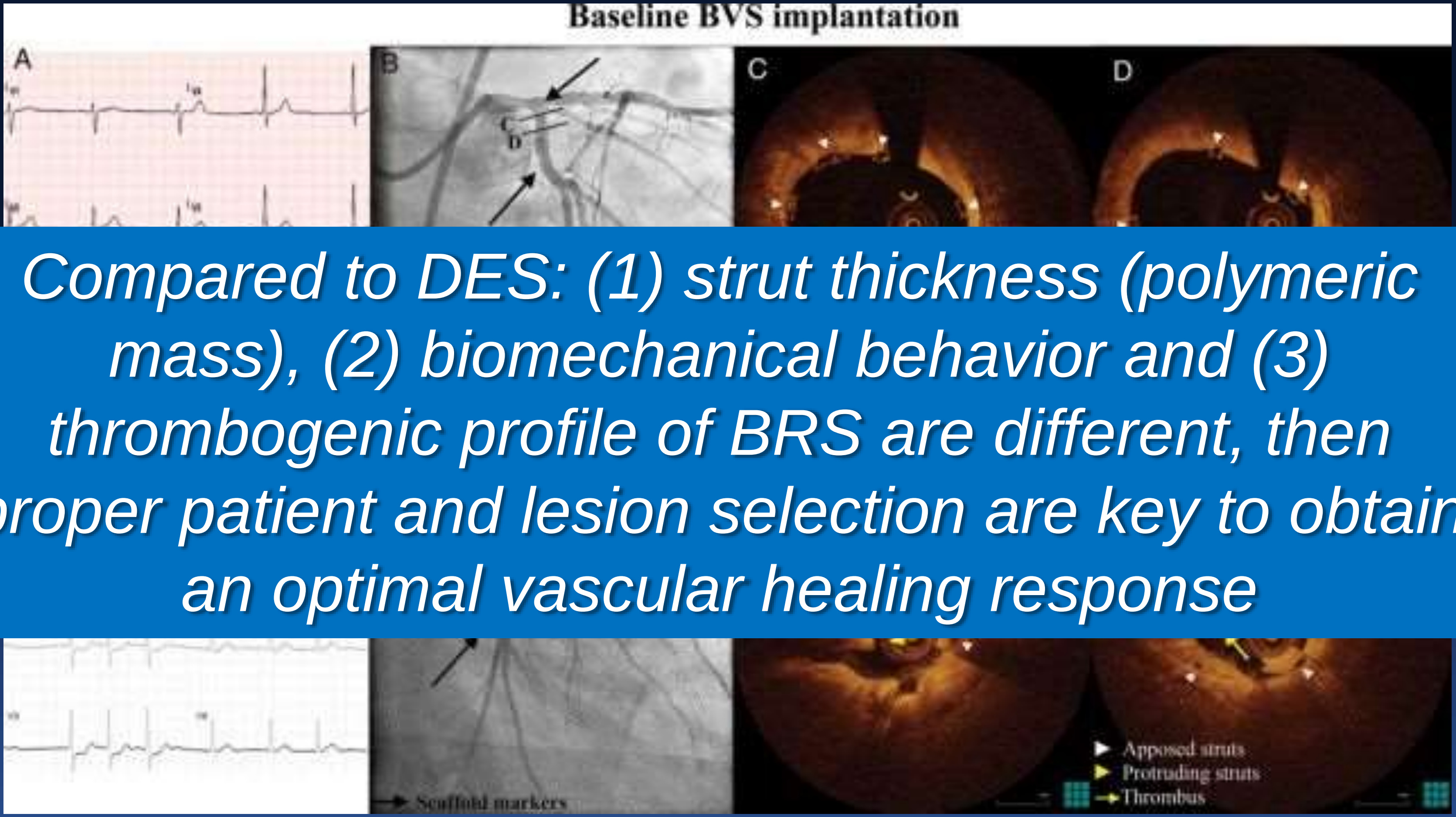
Onuma Y. JACC Cardiovasc Interv. 2014 Dec;7(12):1400-11

BRS: A Huge Win for Polymer Science Research!



For all BRS, comparable biomechanical properties (to DES) below 100 microns will need to be proven!

Very Late BRS Thrombosis After Discontinuation of DATP



Compared to DES: (1) strut thickness (polymeric mass), (2) biomechanical behavior and (3) thrombogenic profile of BRS are different, then proper patient and lesion selection are key to obtain an optimal vascular healing response

Karanasos A. Eur Heart J. 2014 Jul 14; 35(27): 1781

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MATERIAL THROMBOGENICITY

CHRONIC PHASE

Scaffold Material
Coating Absorption
Drug PK

↓

Chronic Vessel Injury & Healing (Inflammatory)

↓

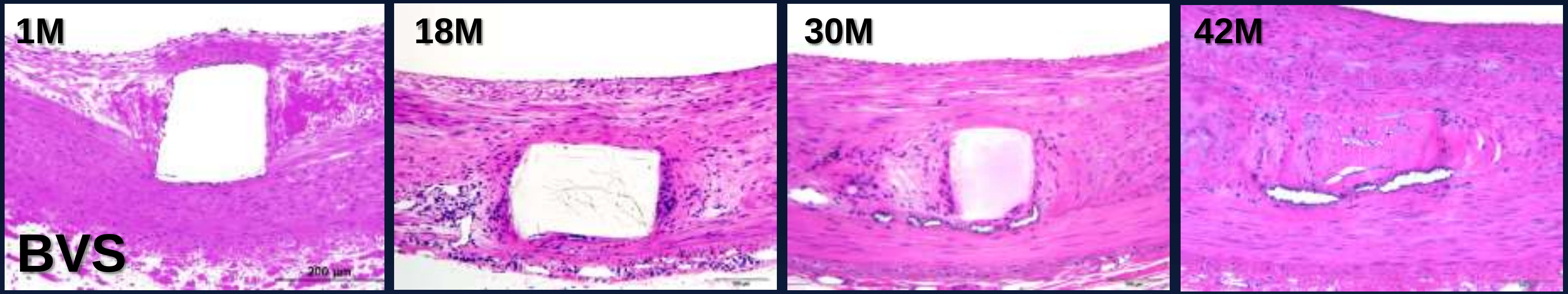
Vessel Wall Healing

↓

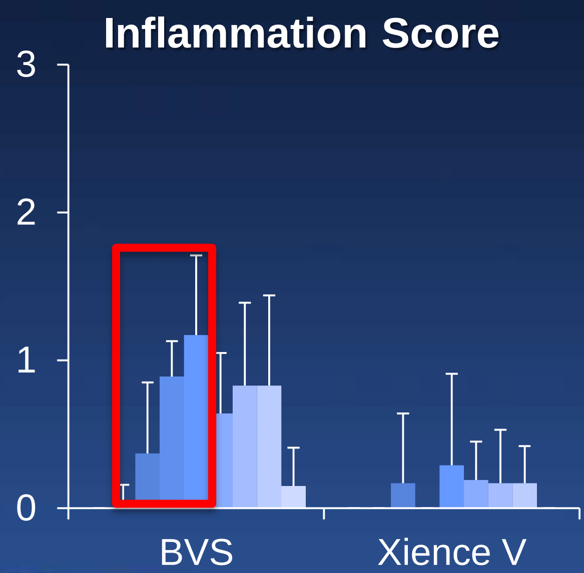
Neointimal Proliferation

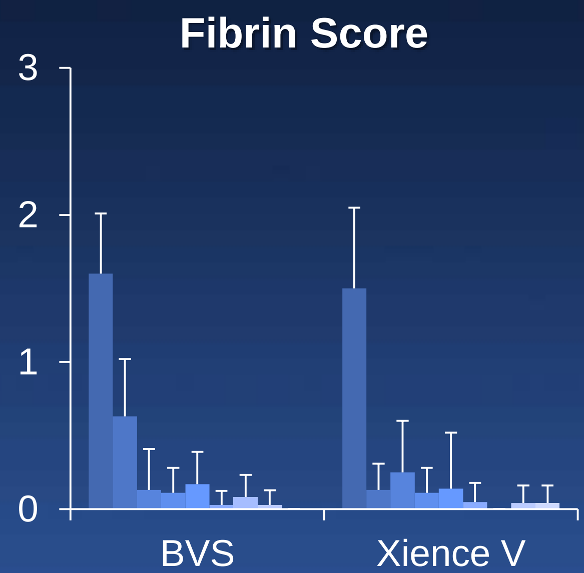
Do BRS induce higher levels of inflammation and neointimal formation compared to metallic DES?

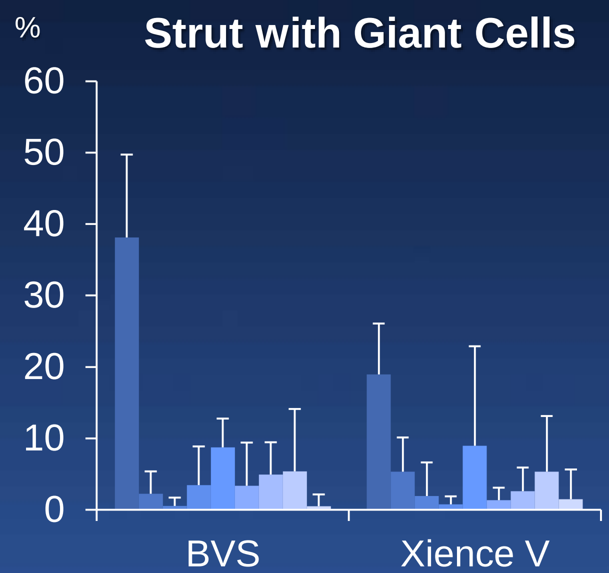
Progression of Para-Strut Inflammation: BVS vs. Xience V



← 1M, 3M, 6M, 12M, 18M, 24M, 30M, 36M, 42M →







Courtesy of Renu Virmani

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Mechanical Impact
on Vessel (Injury)

Scaffold
Material
Exposure

Acute
Vessel Wall
Inflammation

Scaffold
Surface Cell
Coverage

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CHRONIC PHASE

Scaffold Material
Coating Absorption
Drug PK

Chronic Vessel
Injury & Healing
(Inflammatory)

Vessel
Wall
Healing

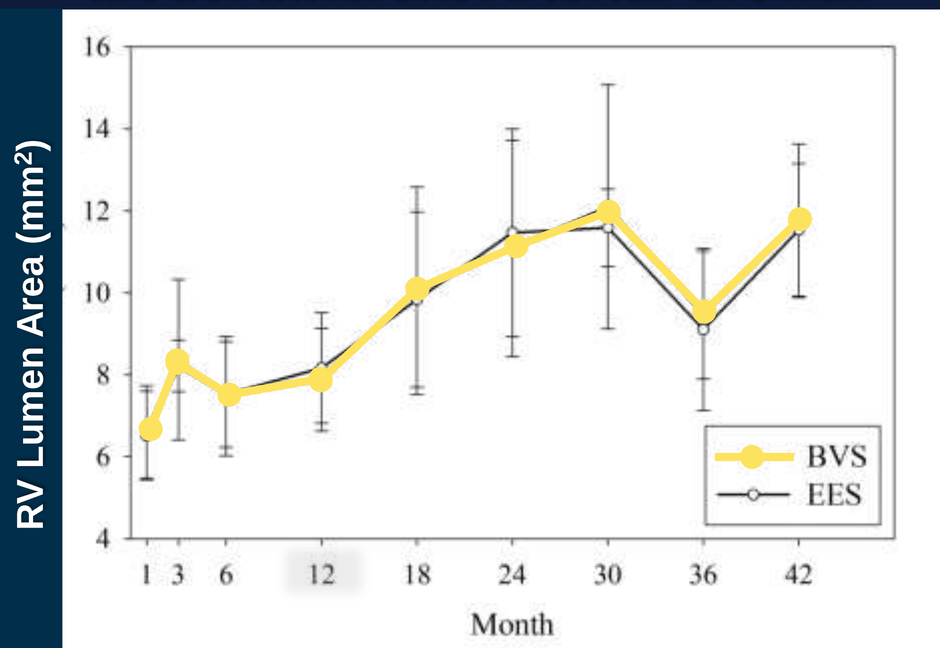
Neointimal
Proliferation

Media
Remodeling

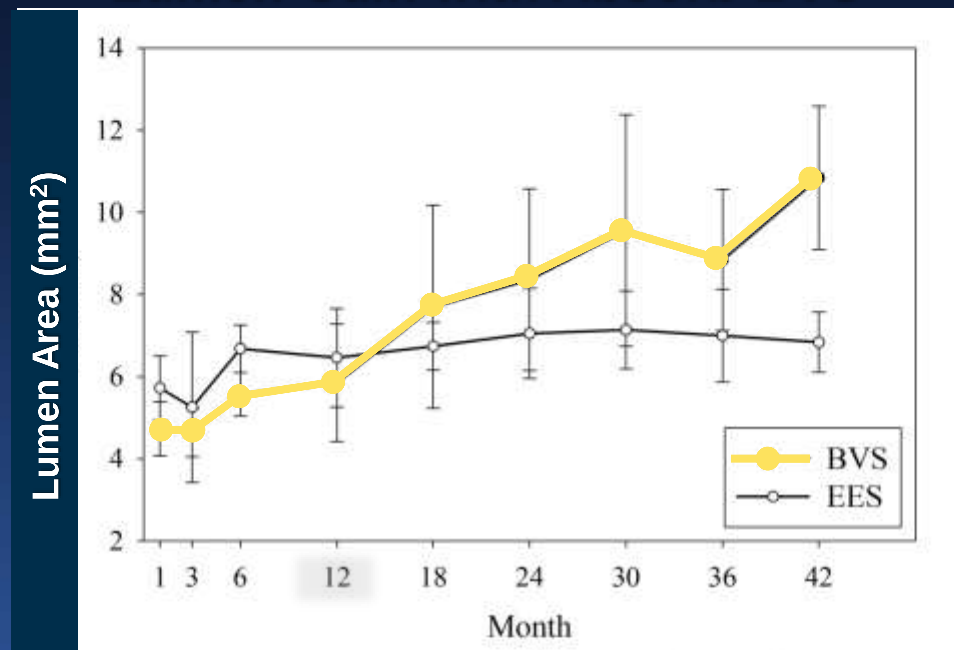
In Vivo (IVUS) Vascular Remodeling in Healthy Swine Coronary Arteries

Porcine coronary arteries 1 to 42 months post-implantation with Absorb BVS. Images on file with Abbott Vascular

Model Inherent Arterial Growth



Lumen Gain with Absorb BVS



Lane, et al, JACC Cardiov Interv. 2014

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Chronic Vessel Injury & Healing (Inflammatory)

Vessel Wall Healing

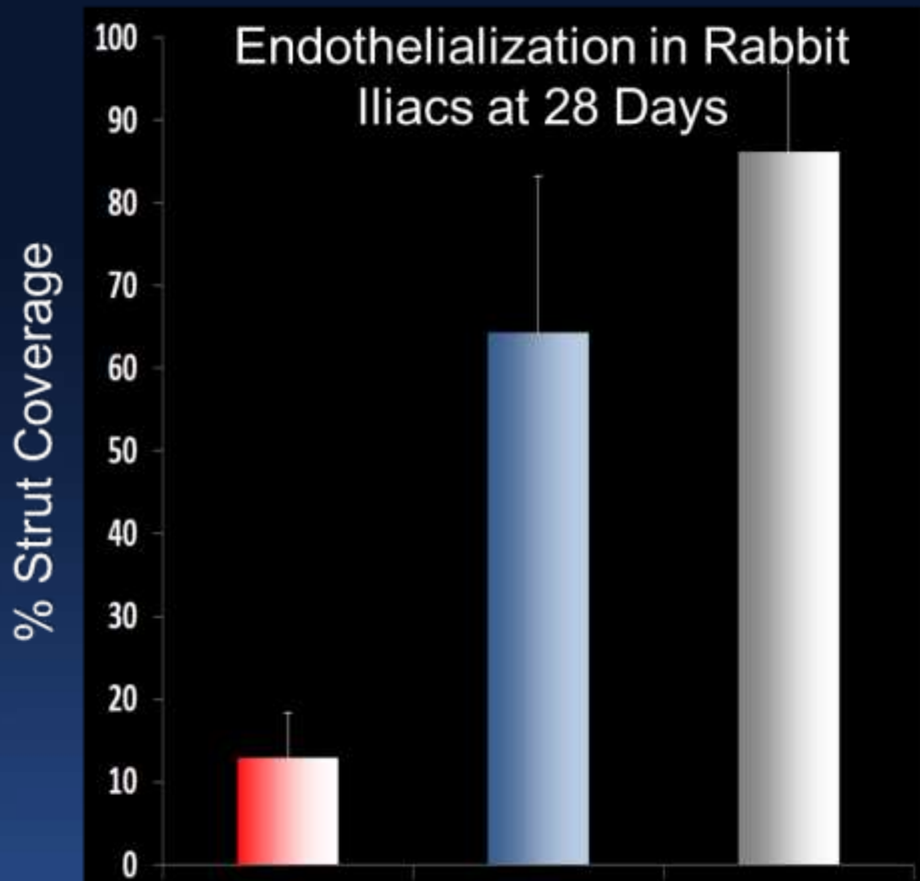
Neointimal Proliferation

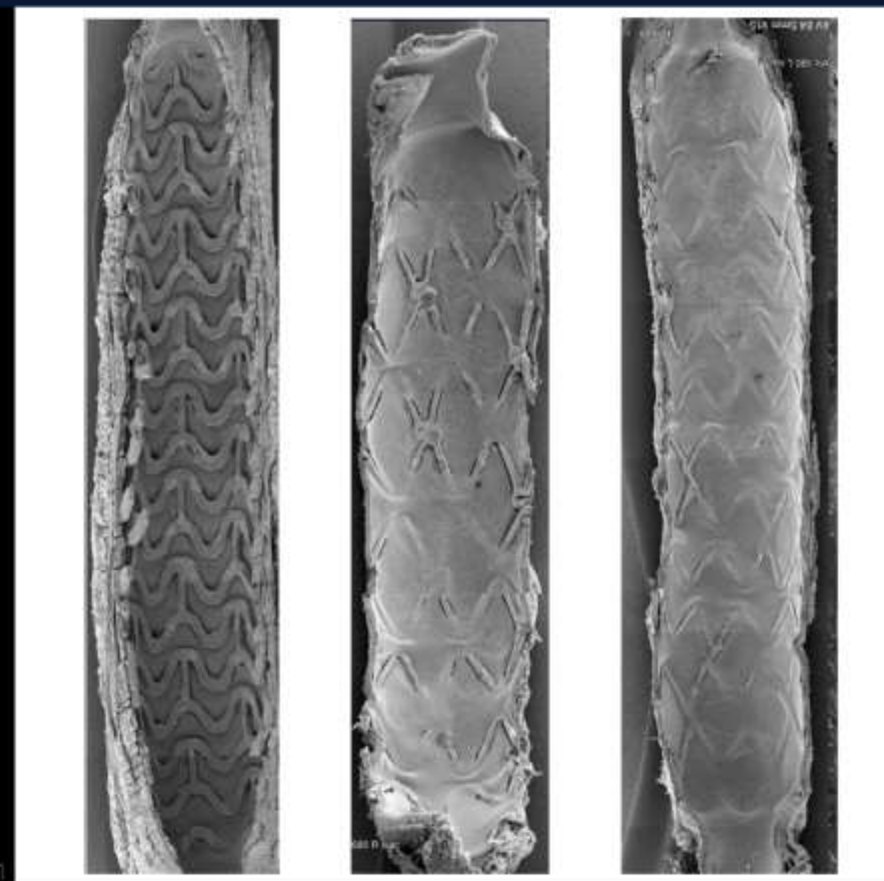
Media Remodeling

Scaffold Surface Coverage

Surface Endothelialization

Impact of Strut Thickness on EC Coverage: BVS vs. Metallic DES





Preliminary Data Presented by Renu Virmani, TCT AP 2014

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Vessel Wall Healing

Scaffold Surface Coverage

Neointimal Proliferation

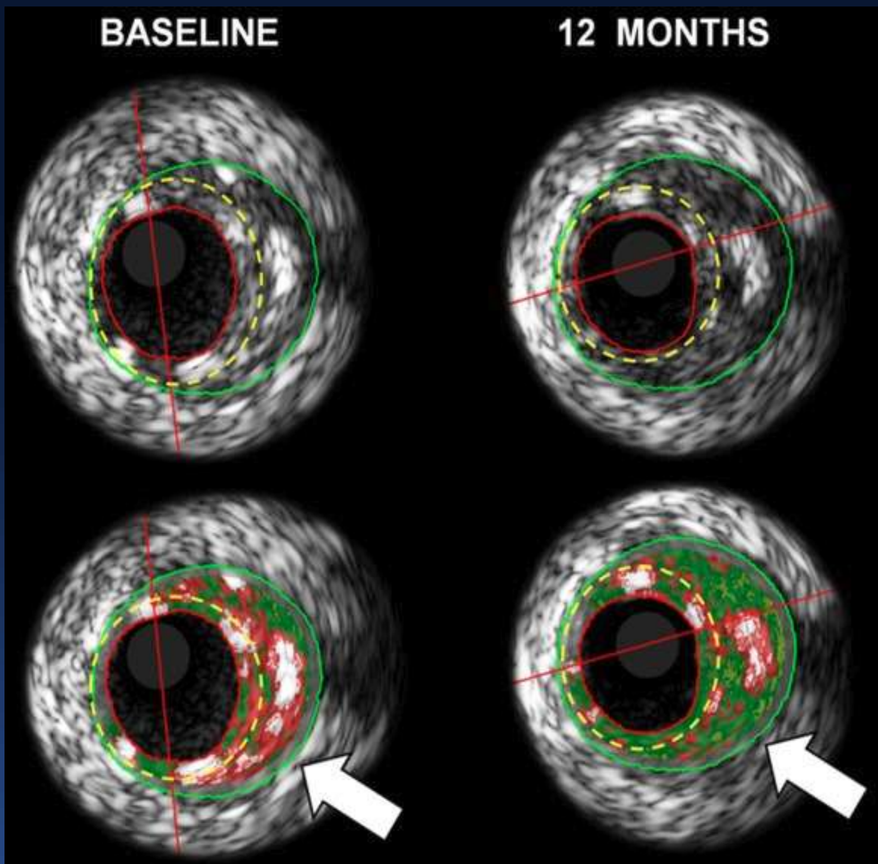
Media Remodeling

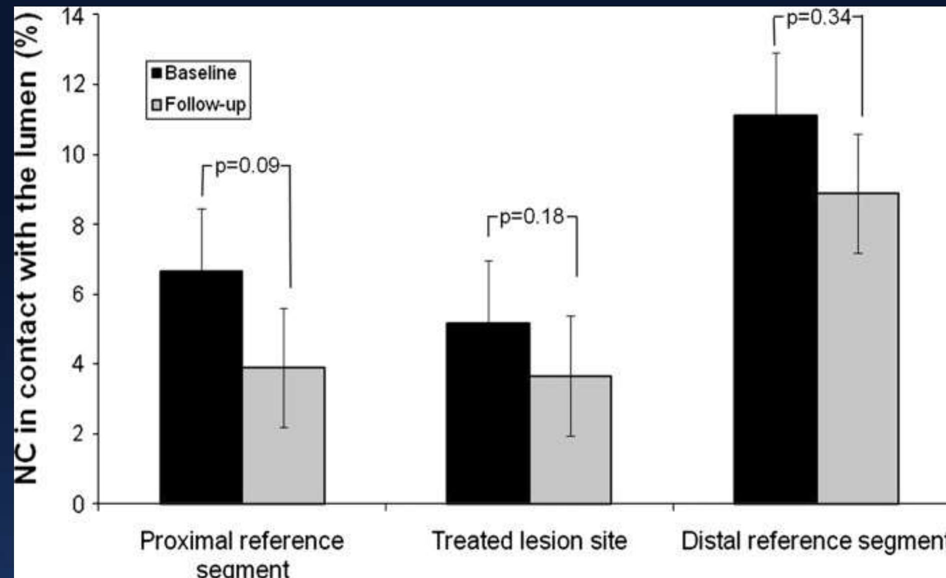
Delayed/Abnormal Surface Healing

RESTENOSIS
NEOATHEROSCLEROSIS

VESSEL PATENCY
VESSEL HEALING & REMODELING

Atherosclerotic Plaque Component Change at 12 Months Following BVS





Increase in mean PBS area (2.39 ± 1.85 mm^2 vs. 2.76 ± 1.79 mm^2, P = 0.078). Significant decrease of 16% and 30% in necrotic core (NC) and dense calcium (DC) content

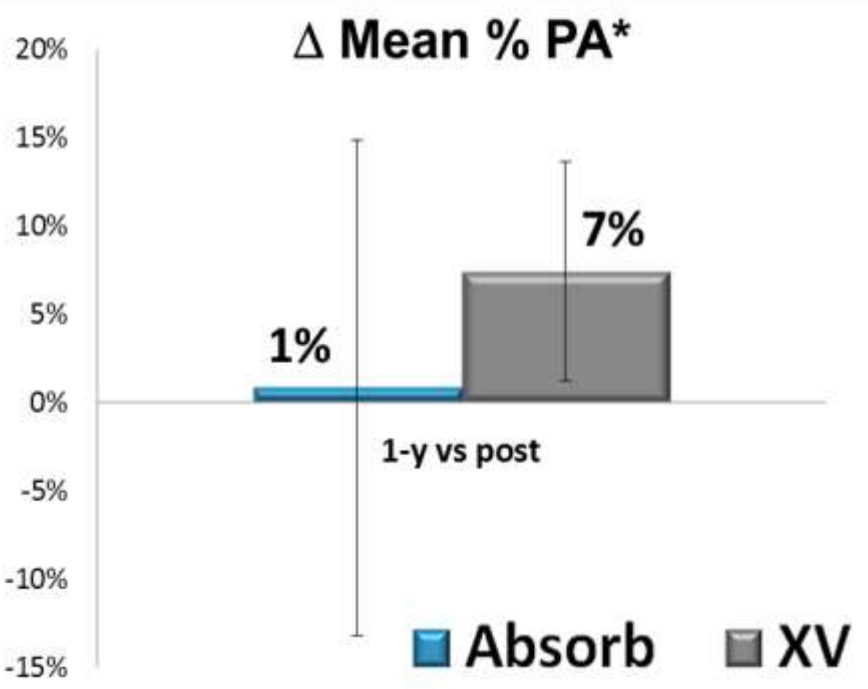
Brugaletta S. Int J Cardiovasc Imaging. 2012 Aug; 28(6): 1307–1314

Absorb BVS in FHS Lesion Model

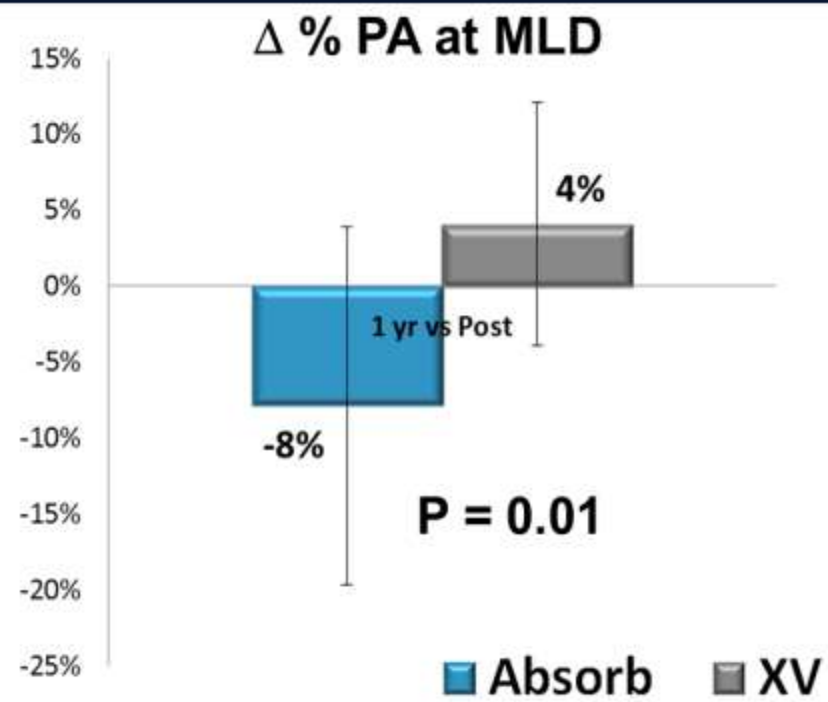
Mean Plaque Progression in Device Segment

Baseline to 1 year Δ % Plaque Area (PA) by IVUS

Vessel Segment*



At MLD Segment



*Values represent the mean of proximal, mid and distal segments

Comparative Vascular Compatibility

BRS versus Metallic DES

BIOLOGICAL VARIABLE	Metallic DES	CURRENT BRS

- In general, BRS display a vascular healing profile comparable to metallic DES, although current structural properties sustain some concerns about higher thrombogenic potential. As with DES, however, prompt improvements are expected as technology advances rapidly (thinner struts etc.)
- Outside this issue, compared to metallic DES:
  - BRS have the potential to achieve higher long term lumen patency rates and lower degrees of plaque progression
  - BRS offer additional biological advantages and have the potential to improve long-term clinical outcomes compared to metallic DES