SELUTION SLR – a Sirolimus DEB: Use of preclinical studies in predicting device safety

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Disclosure

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Employment in industry: No

Honorarium:

Amgen; Abbott Vascular; Biosensors; Boston Scientific; Celonova; Cook Medical; CSI; Lutonix Bard; Sinomed; Terumo Corporation.

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Owner of a healthcare company: No

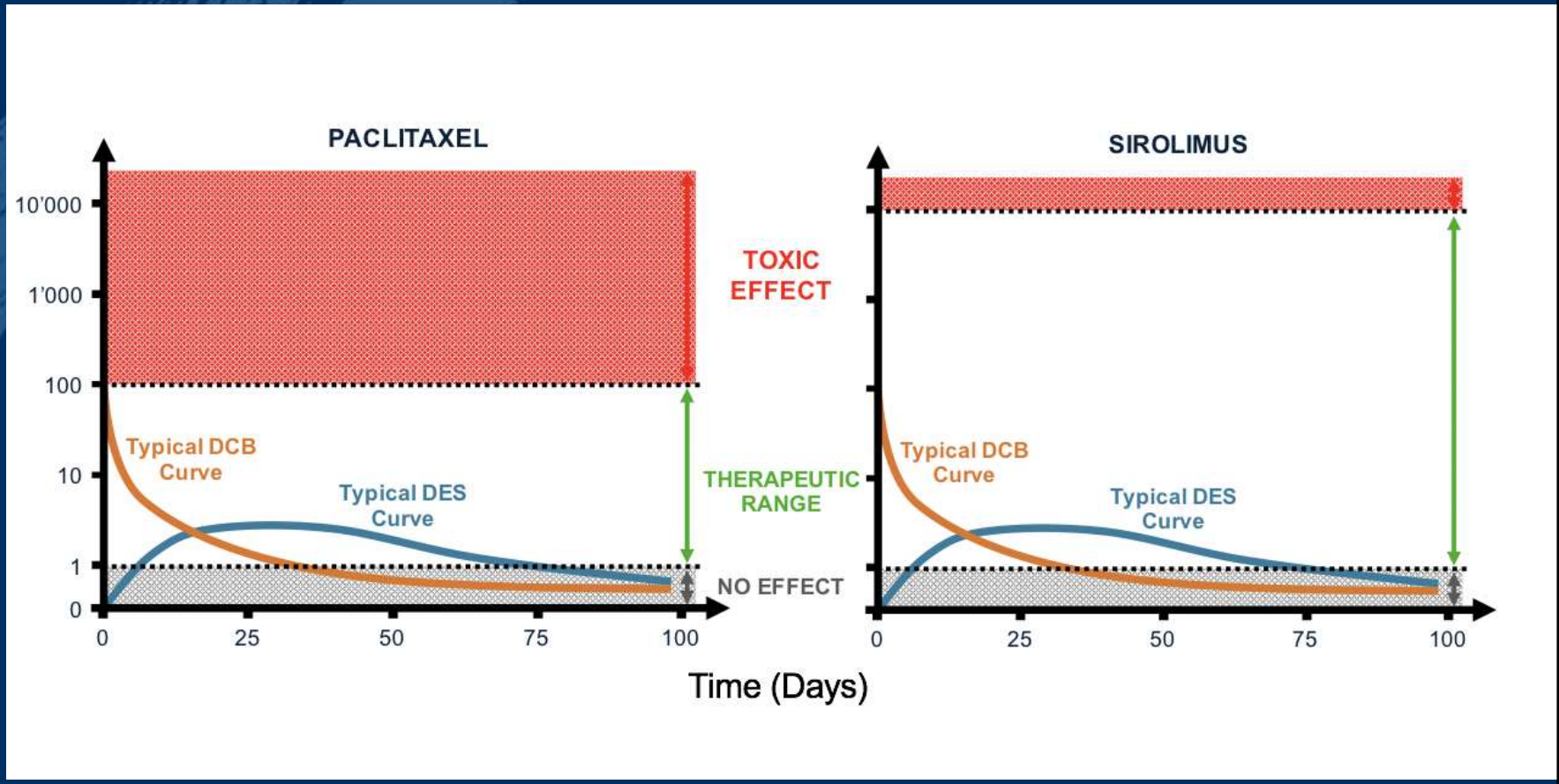
Stockholder of a healthcare company: No

Drug Coated Balloon Devices (Peripheral artery)

Common anti-restenotic drug for DCB is **Paclitaxel**

Product	Company	Drug	Drug dose ($\mu g/mm^2$)	Excipient
IN. PACT Admiral	Medtronic, Minneapolis, MN, USA	Paclitaxel	3.5	Urea
Lutonix	C.R. BARD, Murray Hill, NJ, USA	Paclitaxel	2.0	Polysorbate/Sorbitol
Ranger	Boston Scientific, Marlborough, MA, USA	Paclitaxel	2.0	Citrate ester
Stellarex	Philips, Amsterdam, The Netherlands	Paclitaxel	2.0	Polyethylene glycol
SeQuent Please	B. Braun, Melsungen, Germany	Paclitaxel	3.0	Resveratrol
Passeo-18 Lux	Biotronik, Buelach, Switzerland	Paclitaxel	3.0	Butyryl-tri-hexyl citrate
LEGFLOW	Cardionovum GmbH, Bonn, Germany	Paclitaxel	3.0	Shelloic acid
SurVeil	SurModics, Eden Prairie, MN, USA	Paclitaxel	3.2	Proprietary photolink
Lumior	iVascular, Barcelona, Spain	Paclitaxel	3.0	Water reduce ester
SELUTION	**Med Alliance, Irvine, CA, USA**	**Sirolimus**	**1.0**	**Cell adherent techcology**
Magic Touch PTA	Concept Medical, Surat, India	Sirolimus	1.27	Nanolute technology

Sirolimus Coated Balloon benefits



(Presentation Granada at CRT 20140)

Sirolimus Drug Coated Balloons

Sirolimus offers potential benefits over Paclitaxel

Attribute	Sirolimus (or Analogs)	Paclitaxel
Mode of action	Cytostatic	Cytotoxic
Margin of safety	10’000 fold	100 fold
Therapeutic range	Wide	Narrow
Anti-restenotic	Yes – lower late lumen loss	Yes
Anti-inflammatory	Yes	No
Tissue absorption	***Slow***	***Fast***
Tissue retention	***Short***	***Long***

Sirolimus is *drug of choice* for coronary DES supported by solid clinical based evidence.

(*Wessely R, et al. J Am Coll Cardiol. 2006)*

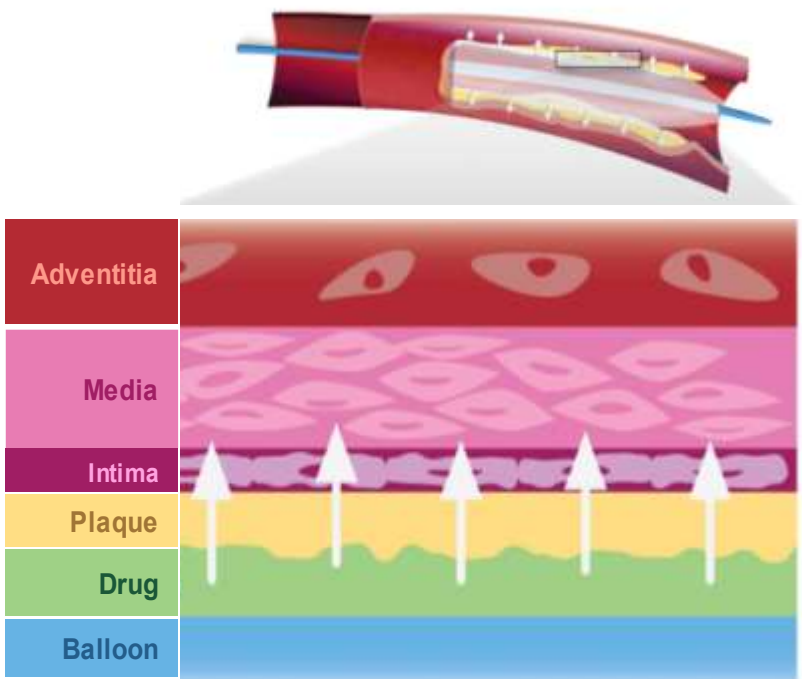
Absorption and Retention

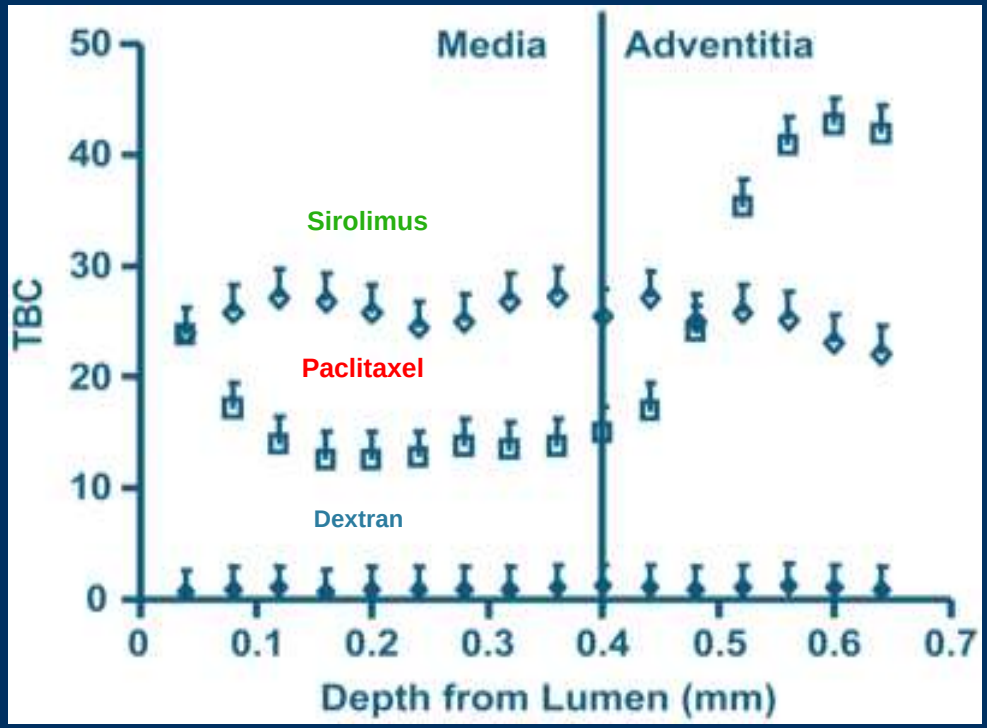
Paclitaxel

- Tends to localize in sub-intimal space and **partitions** significantly in adventitia.

Sirolimus

- Diffuses **slowly** and spreads throughout entire artery where it **dilutes down** to sub-therapeutic levels.



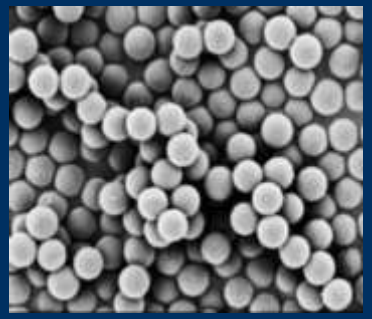


(Tissue Binding Capacity (TBC) of labeled Dextran, Paclitaxel and Sirolimus in 0.040-mm-thick bovine internal carotid tissue segments. Source: PNAS 2004)

Sirolimus DEB SELUTION: MedAlliance

- Micro-reservoirs made out of biodegradable polymer intermixed with Sirolimus:

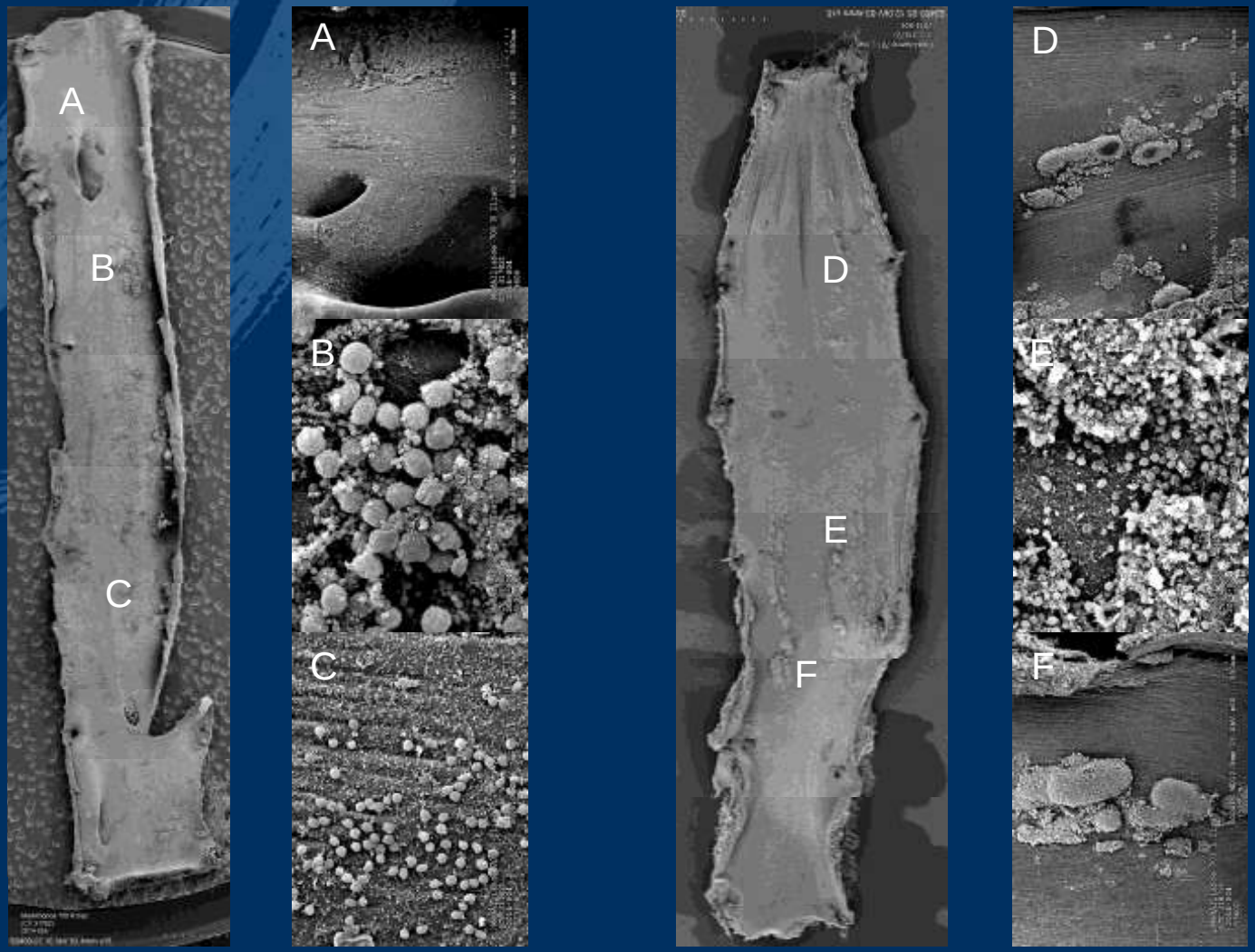
  Controlled and sustained drug release mechanism
  Maintains therapeutic effect in tissue over long period of time



- Novel Cell Adherent Technology – CAT:

  CAT transfer membrane houses and protects micro-reservoirs during balloon insertion, lesion crossing and expansion.
  CAT transfer membrane with embedded micro-reservoirs releases from balloon delivery system and adheres to vessel lumen with short balloon Inflation.

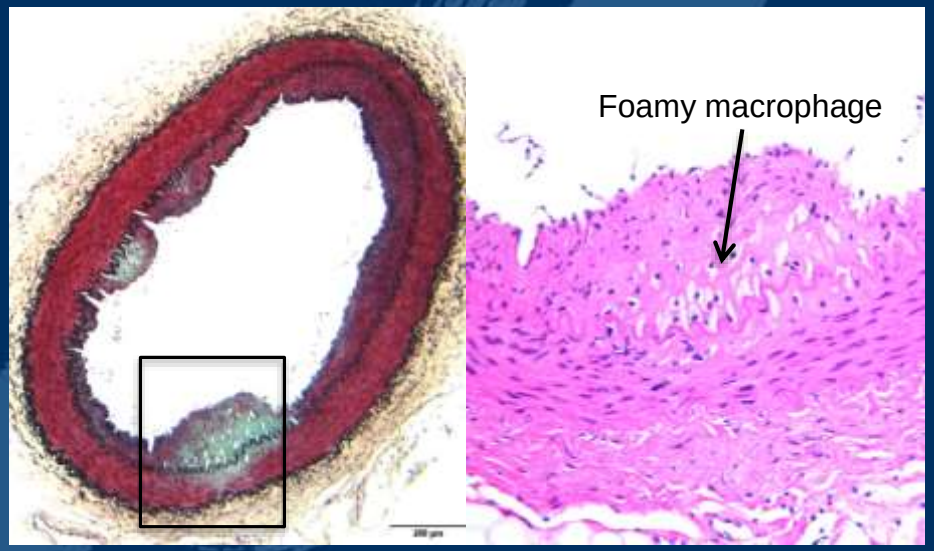
Preclinical Study in Rabbit Iliac Artery Model



1 hour post PTA

24 hours post PTA

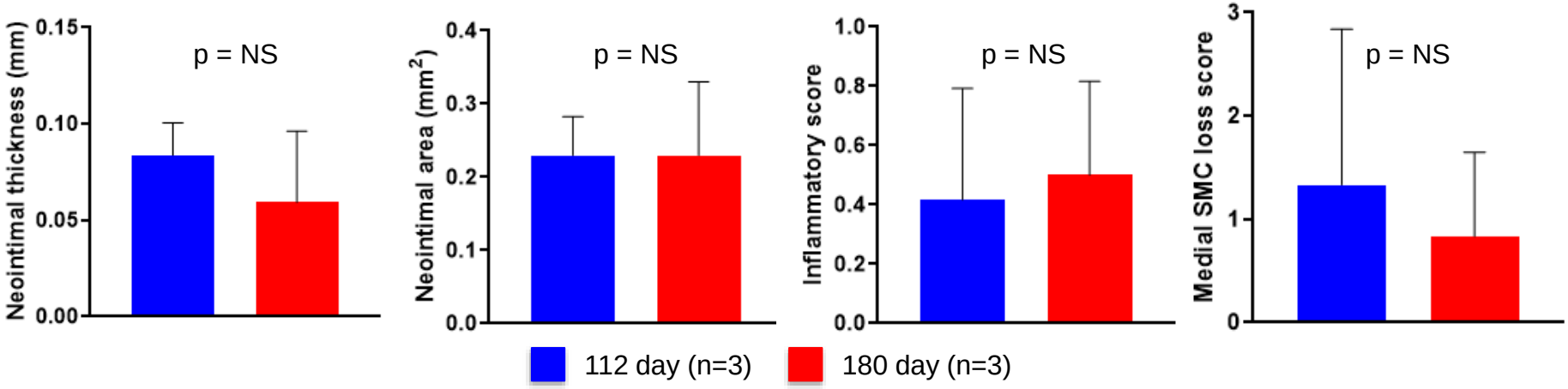
Preclinical Study in Rabbit Iliac Artery Model



112 day

180 day

Morphometry analysis



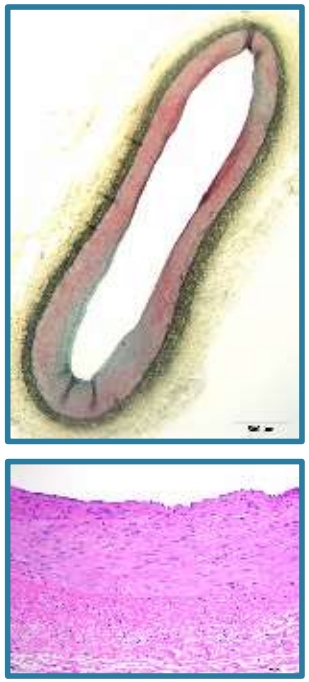
Preclinical Study in Porcine Peripheral Artery Model

Peripheral – 28 days histopathology

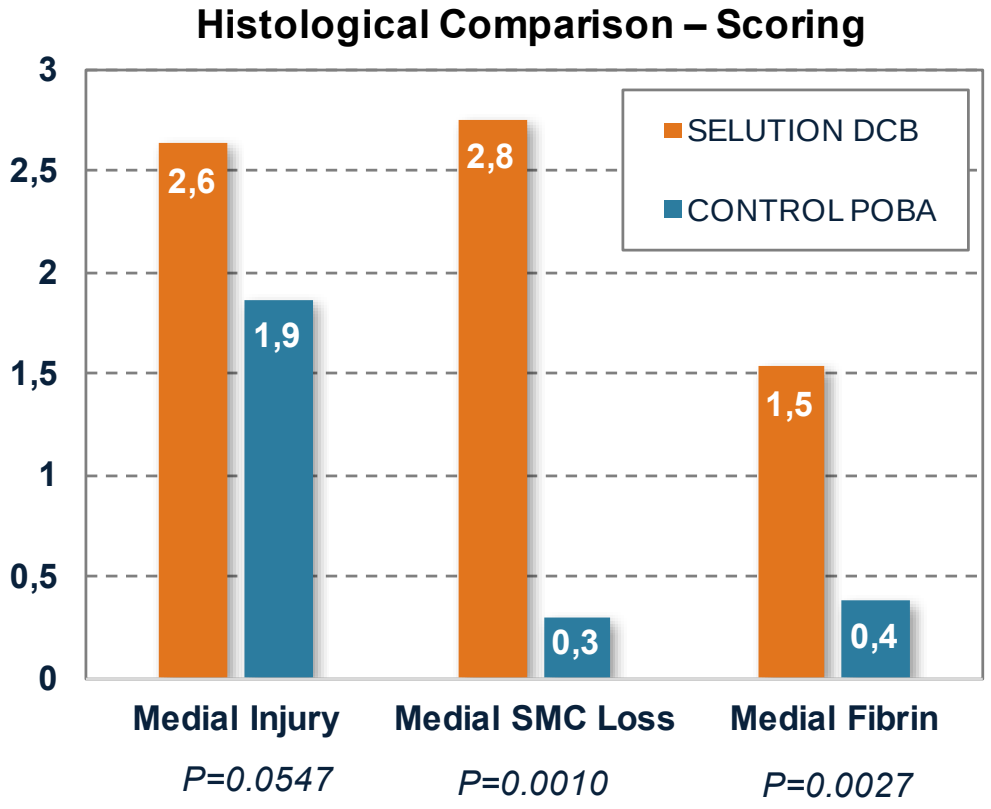
SELUTION DCB

CV33054 30-138E LPFA TR E

CONTROL POBA



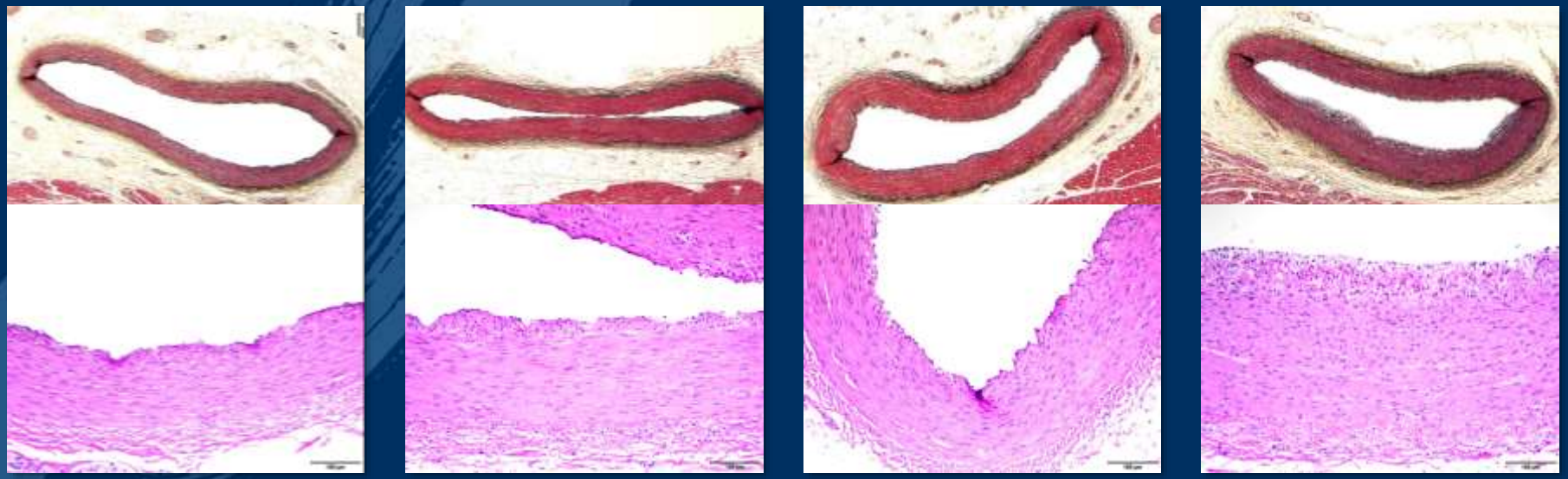
CV33052 30-064E RSFA TR G



P≤0.05 Statistically Significant

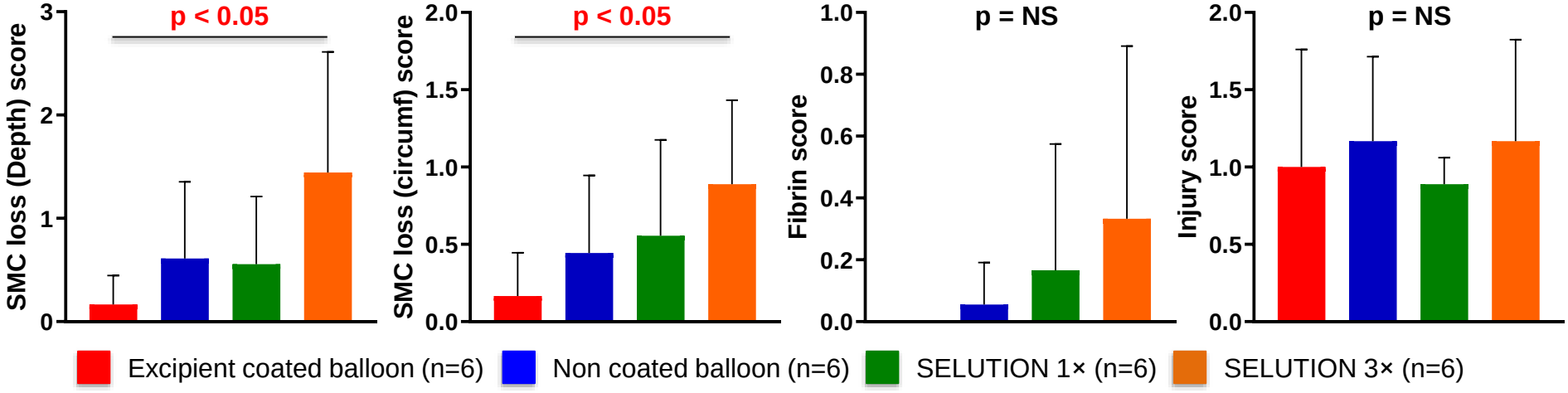
Source: Med Alliance – Histo Study (MEA 439-14).

Preclinical Study (Porcine Coronary Model)



Excipient coated balloon | Non coated balloon | SELUTION 1× | SELUTION 3×

Morphometry analysis



Summary

- Sirolimus has wider therapeutic range and thus higher index as compared to paclitaxel.
- Paclitaxel has faster absorption and longer retention of tissue than sirolimus. On the other hand, sirolimus is absorbed slowly and spreads throughout entire artery.
- Medial SMC loss and fibrin scores were relatively higher in SELUTION groups, suggesting the existence of sirolimus drug effect on the vessels wall healing process and not injury alone.
- Sirolimus is drug of choice and maybe a better choice than paclitaxel for peripheral artery and coronary DCBs.

Acknowledgments

CVPath Institute

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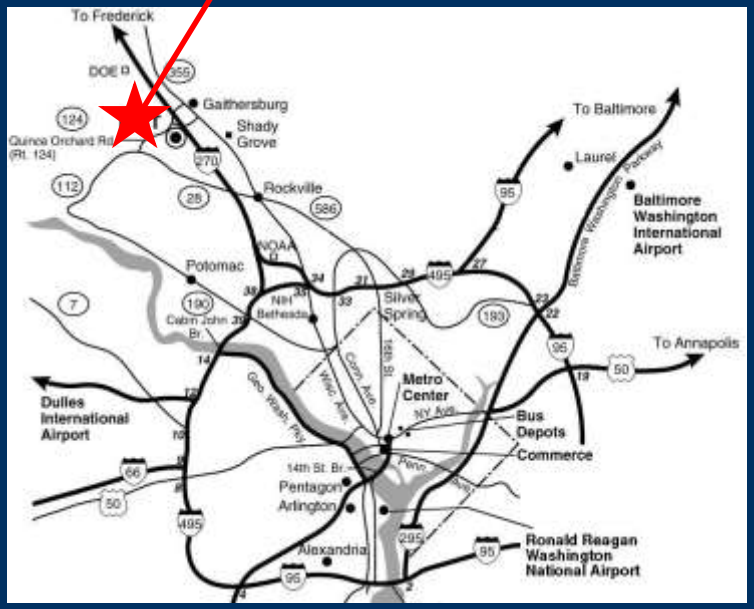

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