

# A Mechanistic Look at 0.018 DCBs: Considerations for Efficacy and Durability of Response

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# Disclosures

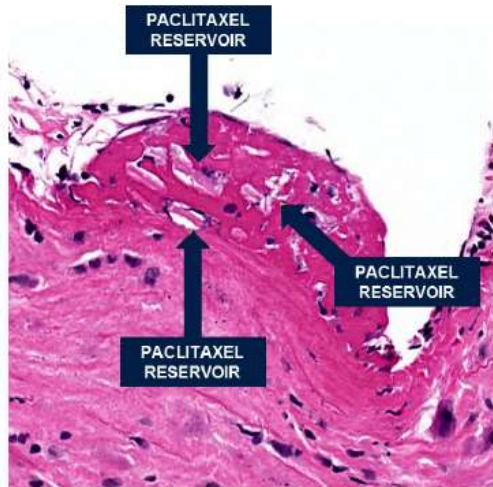
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I have the following potential conflicts of interest to report:

- Consulting
  - Employment in industry
  - Stockholder of a healthcare company
  - Owner of a healthcare company
  - Other(s): Sponsored research, advisory role.
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- I do not have any potential conflict of interest

Acknowledgements: We are grateful for the contributions of Andrew Holden MD for creative input into experimental concept development

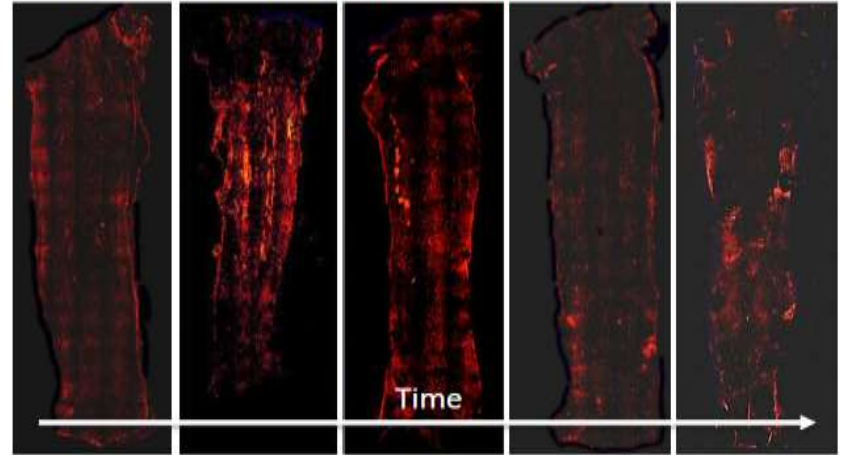
# Paclitaxel Particle Microstructure Affects Drug Tissue Residence



Particle in Solid Phase is Results in the Development of Paclitaxel Reservoirs on the Vessel Surface

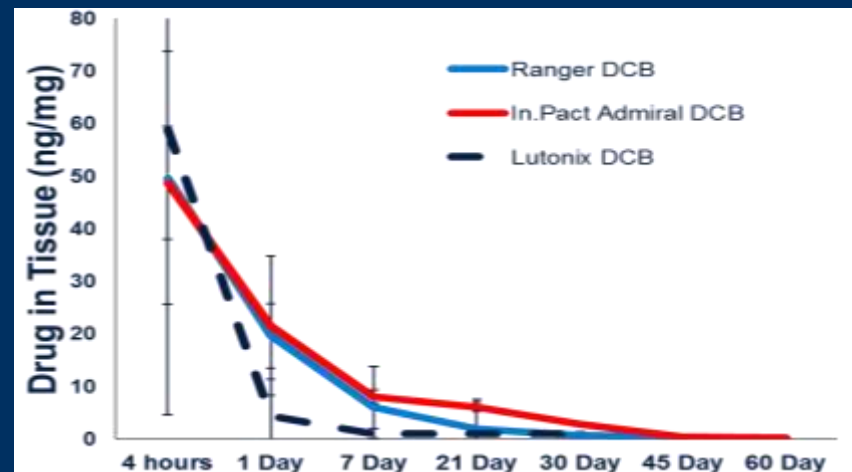
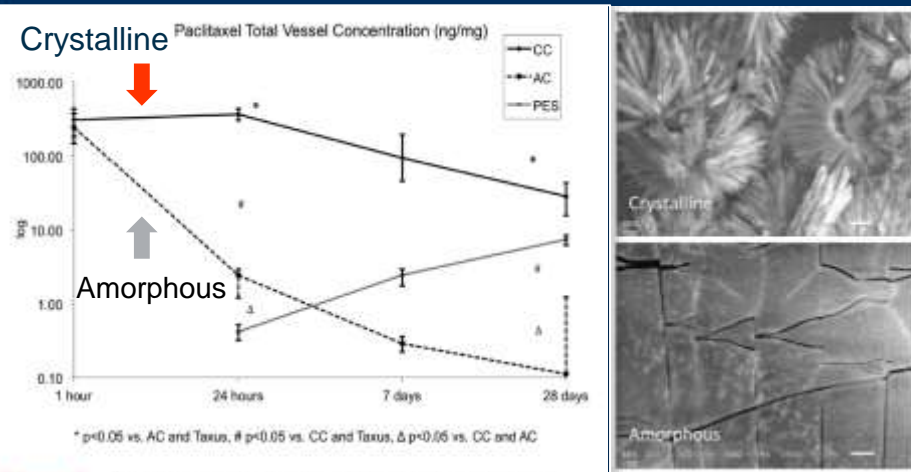
Picture Courtesy of Medtronic

## Paclitaxel Reservoirs Impact Long Term Tissue Levels



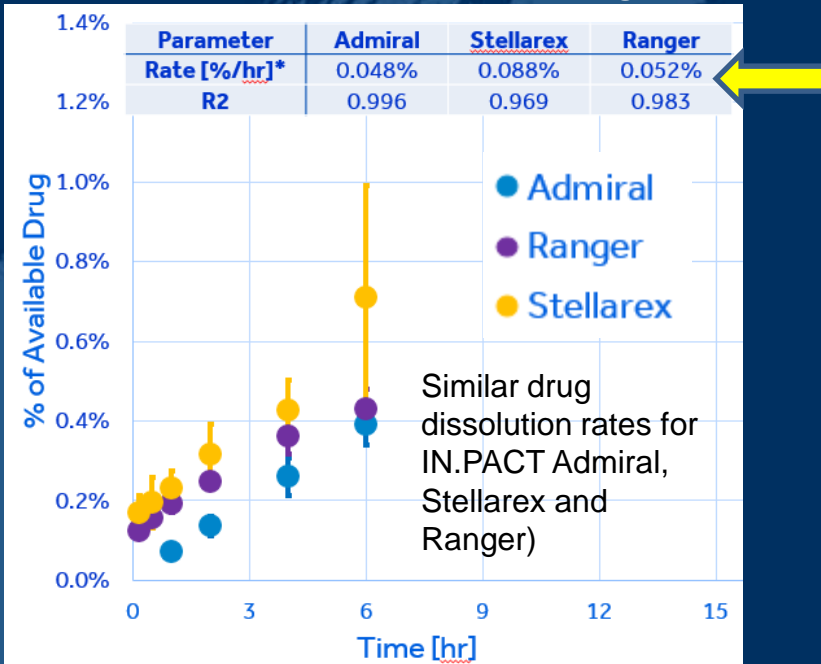
TransPax™ DCB, Picture Courtesy of Boston Scientific

## Particle Micro-Structure and Paclitaxel Tissue Levels



# Durability of DCB Therapeutic Response Requires Sustained Drug In Tissue

## In Vitro Dissolution Testing<sup>1</sup>



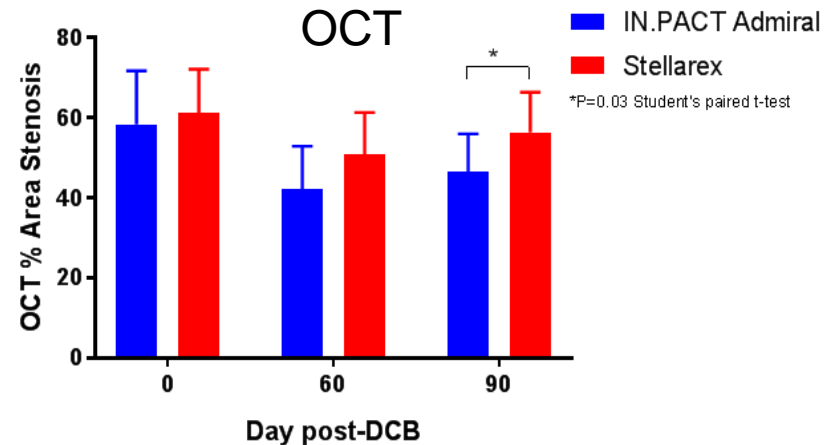
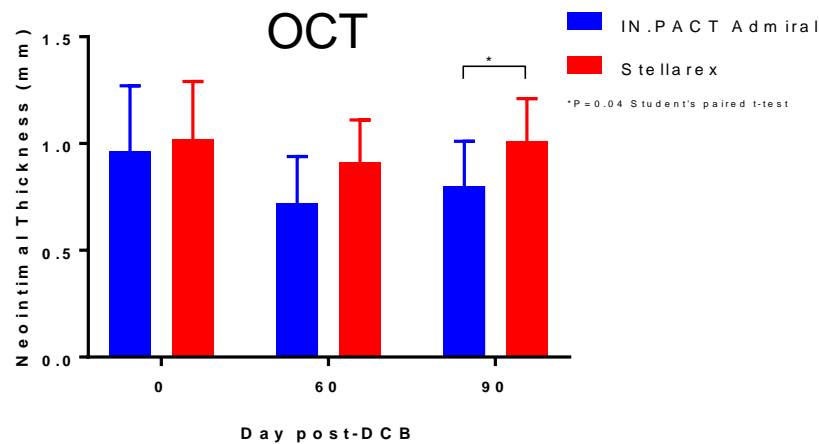
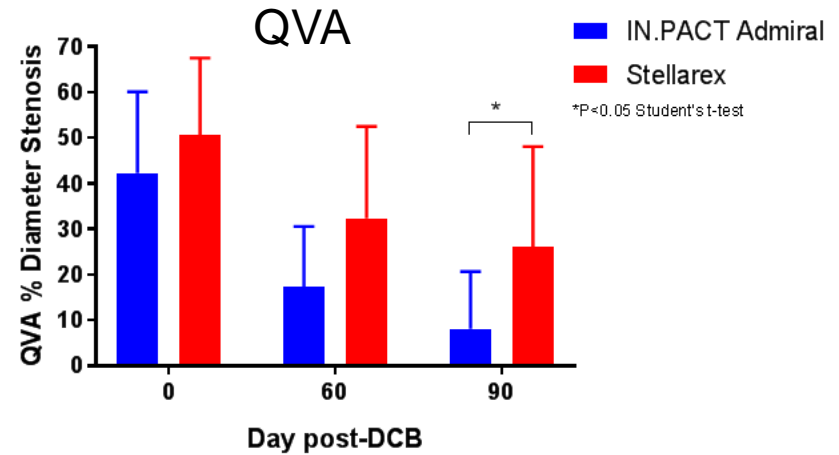
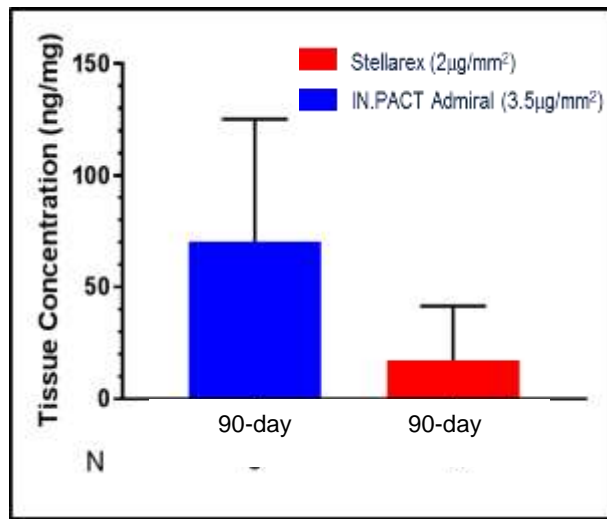
- Bioavailable drug in tissue depends on (a) input dose, (b) drug dissolution rate and (c) local drug clearance
- Drug dissolution rates are similar among different DCB formulations, then, duration of bioavailable drug in tissue is influenced by input drug dose
- Since input dose on different DCBs vary, duration of sustained therapeutic response to drug may also vary accordingly ( $3.5\mu\text{g}/\text{mm}^2$  vs.  $2.0\mu\text{g}/\text{mm}^2$ )
- Hypothesis: a higher input dose provides a therapeutic response at longer timepoints post-treatment

Drug Coated Balloon	Manufacturer	Dose Density
IN.PACT Admiral / Pacific™	Medtronic	$3.5\mu\text{g}/\text{mm}^2$
Stellarex™	Spectranetics	$2.0\mu\text{g}/\text{mm}^2$
Ranger™	Boston Scientific	$2.0\mu\text{g}/\text{mm}^2$

<sup>1</sup>Data on file with Medtronic.

# Impact of Dose on Long-Term Inhibition of Neointimal Proliferation (90-Days)

Comparison of ISR Responses In Normal Swine Following DCB Treatment<sup>1,2</sup>



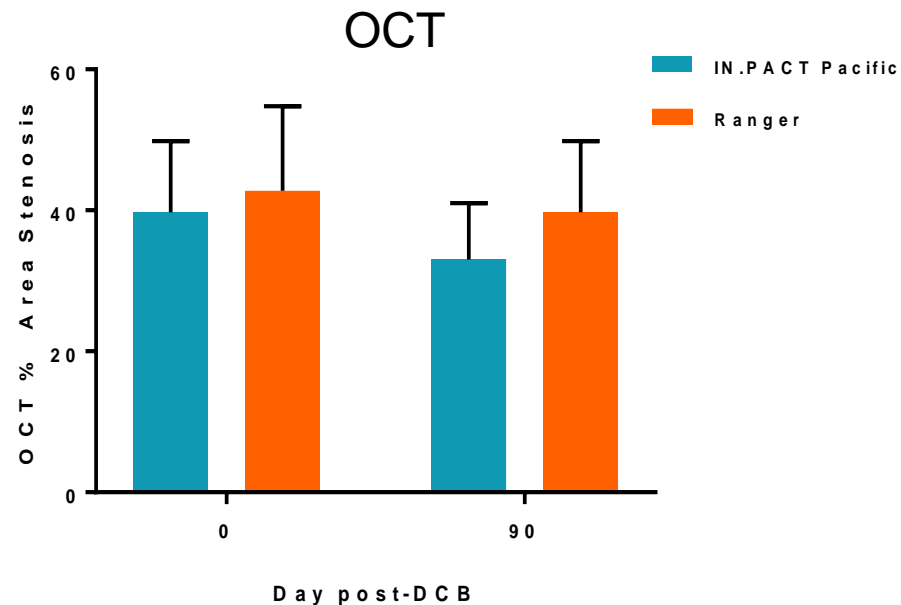
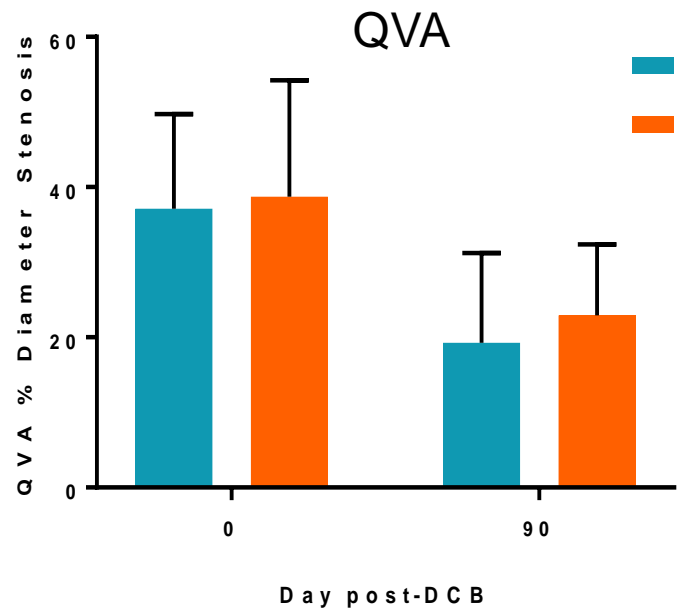
# In.PACT Admiral DCB And Pacific DEB are Closely Similar In Most Attributes (Including Dose Density)

Comparison: IN.PACT Admiral vs. IN.PACT Pacific DCB

	IN.PACT Admiral DCB	IN.PACT Pacific DEB
Drug	Paclitaxel	Paclitaxel
Dose Density	3.5 mg/mm <sup>2</sup>	3.5 mg/mm <sup>2</sup>
Excipient	Urea	Urea
Uncoated PTA	Admiral Extreme	Pacific Extreme
Balloon Platform	0.035"	0.018"
Balloon Diameter	4-12 mm	4-7 mm
Balloon Lengths	40, 60, 80, 120, 150, 200*, 250*mm	40, 60, 80, 120mm

\*Not approved OUS

# Comparative Evaluation of ISR Response Following DCB treatment at 90 Days: IN.PACT Pacific 0.018 vs. Ranger DCB

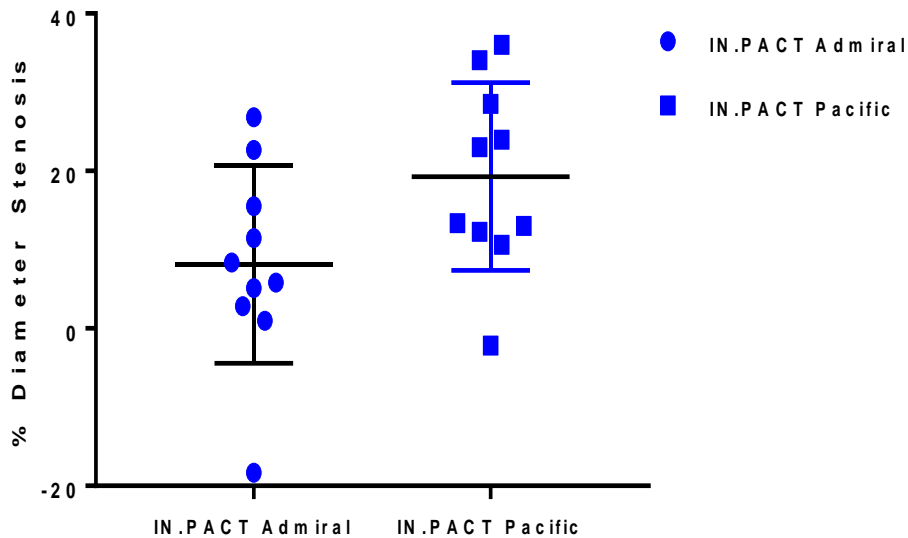


IN.PACT Pacific observed lower % Stenosis by QVA and OCT at 90 days post-treatment relative to Ranger<sup>1</sup> (120 day data pending)

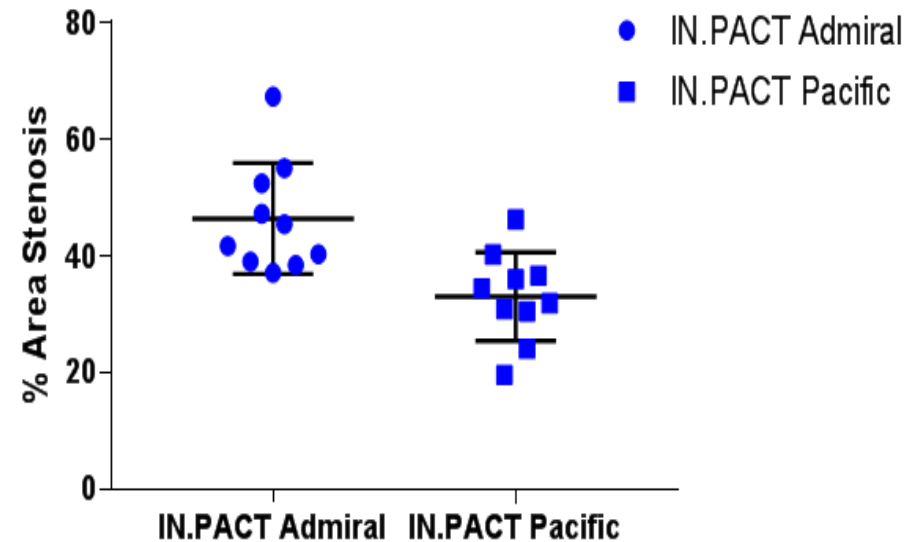
<sup>1</sup>Data on file with Medtronic.

# Comparative Evaluation of ISR Response Following DCB treatment at 90 Days: IN.PACT Pacific 0.018 vs. IN.PACT Admiral

QVA % Diameter of Stenosis at 90 Days



OCT % Diameter of Stenosis at 90 Days



IN.PACT Admiral and IN.PACT Pacific both showed comparable performance in % Stenosis by QVA and OCT at 90 days post – DCB treatment<sup>1</sup>

<sup>1</sup>Data on file with Medtronic; Study PS857 and PS781



# Conclusions

- Paclitaxel particle dissolution and clearance contribute to drug tissue residence time, but these factors being equal, higher input dose provides longer drug tissue availability
- The higher input drug of both IN.PACT Admiral and IN.PACT Pacific 0.018 DCBs may account for their sustained anti-proliferative effect
- 5 Year clinical data<sup>1</sup> has shown a significant difference in the time to CD-TLR for IN.PACT Admiral (808 days for DCB versus 475 days for placebo), supporting this hypothesis
- Experimental comparative evaluation of the of IN.PACT Pacific 0.018 DCB has demonstrated comparable biological performance to the IN.PACT Admiral DCB

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