Nuevas evidencias en el tratamiento con balones liberadores de droga

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Endomedical S.R.L.
MEDICINA CARDIOVASCULAR

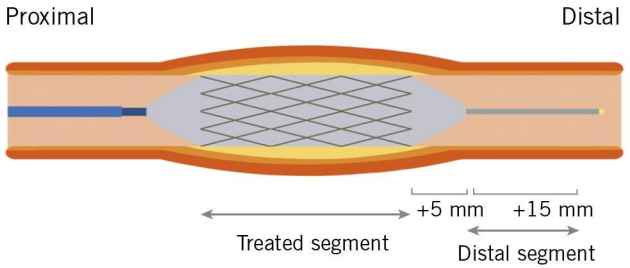
PORQUE USAR BALONES FARMACOLOGICOS?

Stent: disfunción endotelial [1].

Disfuncion Endotelial: eventos cardíacos graves, como infarto de miocardio, arritmia fatal o muerte cardíaca súbita [2].

1. Tsutomu Kawai et al. Eurointervention 2022; e140-e148
2.Brott B.Severe, diffuse coronary artery spasm after drug-eluting stent placement. J Invasive Cardiol. 2006;18:584-92.

Vasomotilidad Coronaria despues del tratamiento con Balon Farmacologico o con Stent Farmacologico



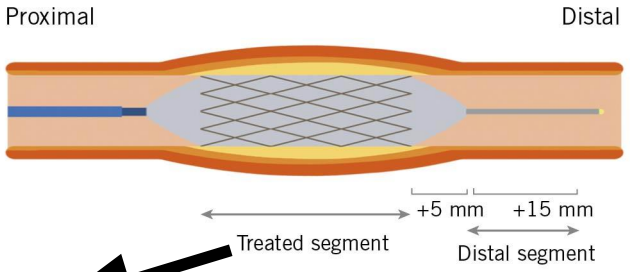
Tsutomu Kawai et al. Eurointervention 2022; e140-e148

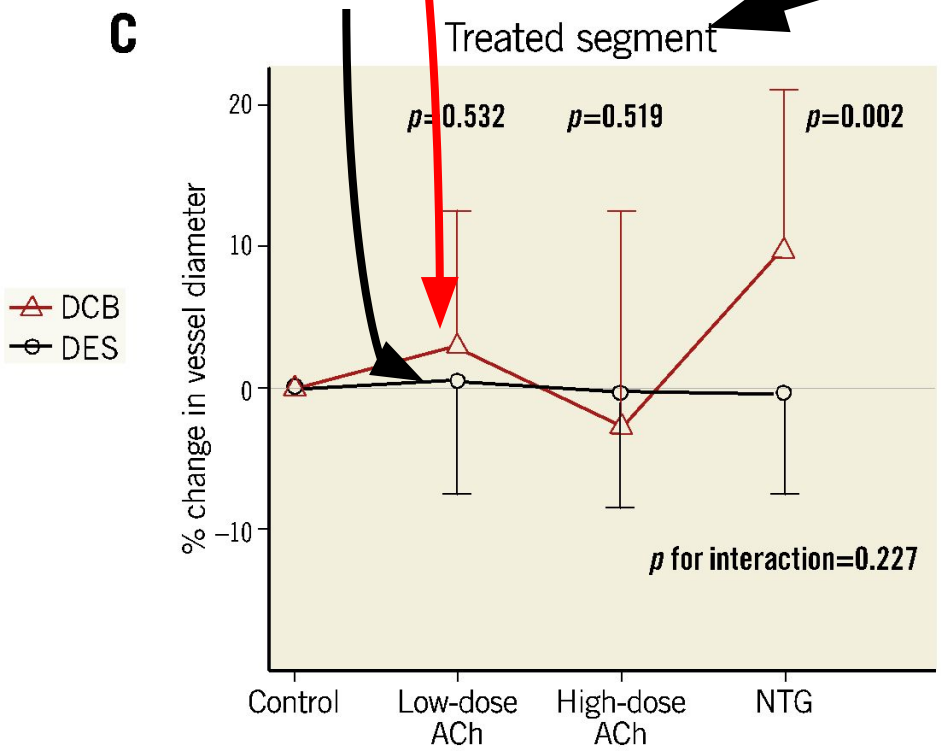
Vasomotilidad Coronaria despues del tratamiento con Balon Farmacologico o con Stent Farmacologico

SEGMENTO TRATADO

DCB: tiene vasomotilidad

DES: no tiene vasomotilidad





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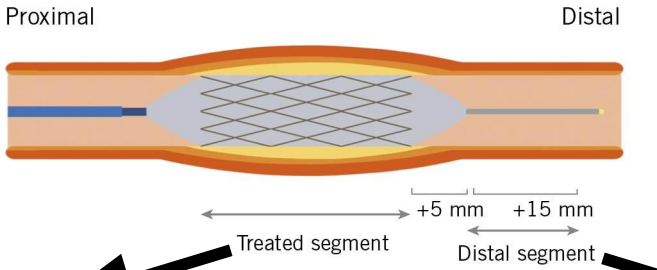


SEGMENTO TRATADO

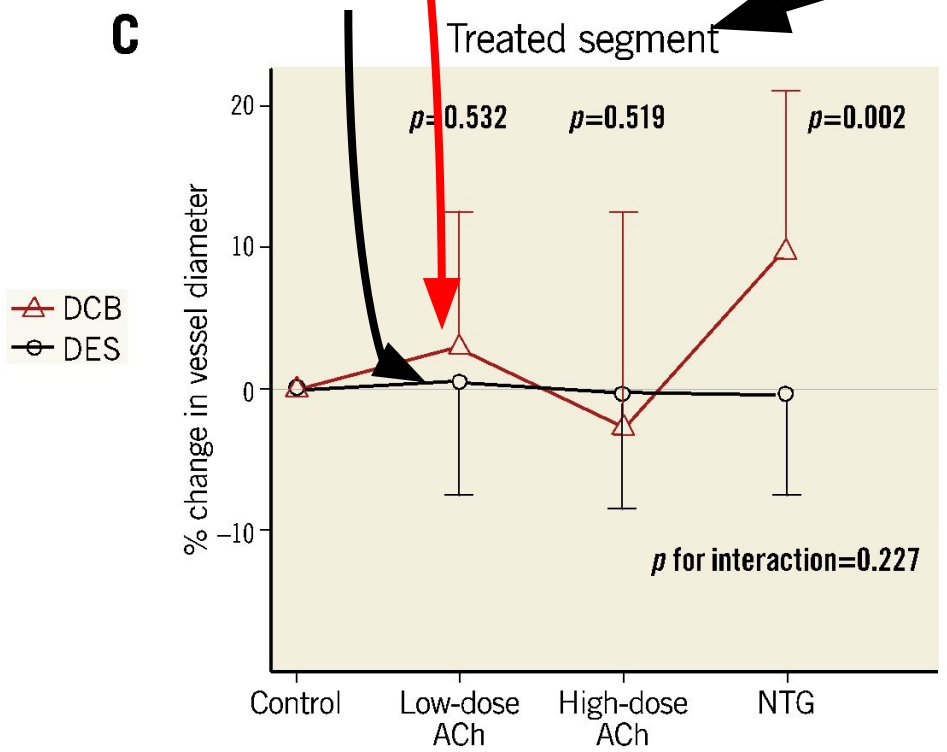
DCB: tiene vasomotilidad

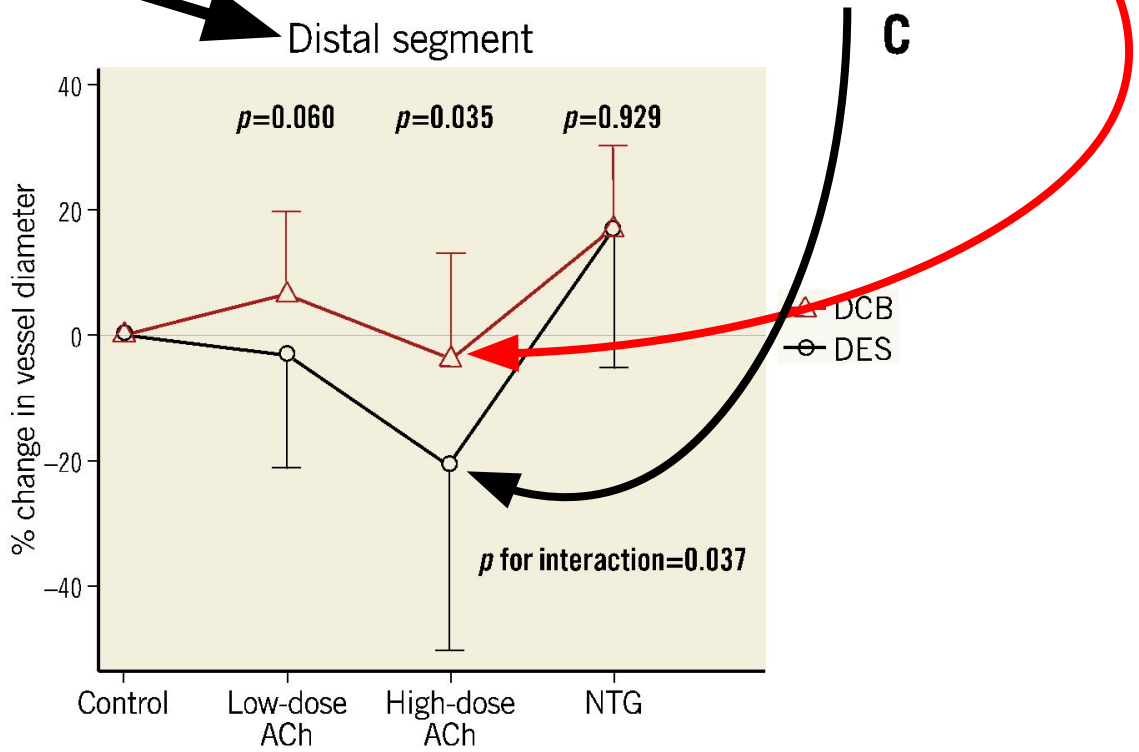
DES: no tiene vasomotilidad

SEGMENTO DISTAL

DCB: tiene normal vasomotilidad

DES: tiene hipersensibilidad en la vasomotilidad



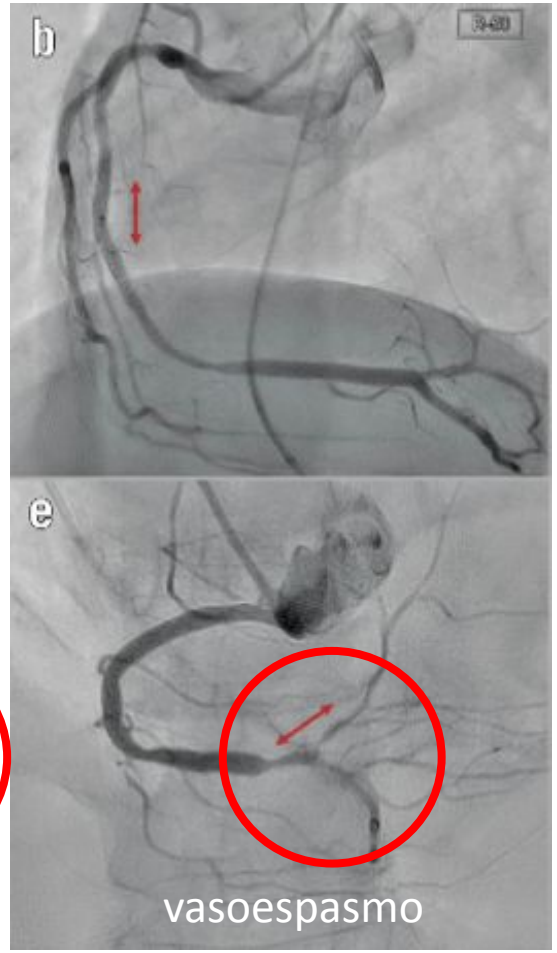


Tsutomu Kawai et al. Eurointervention 2022; e140-e148

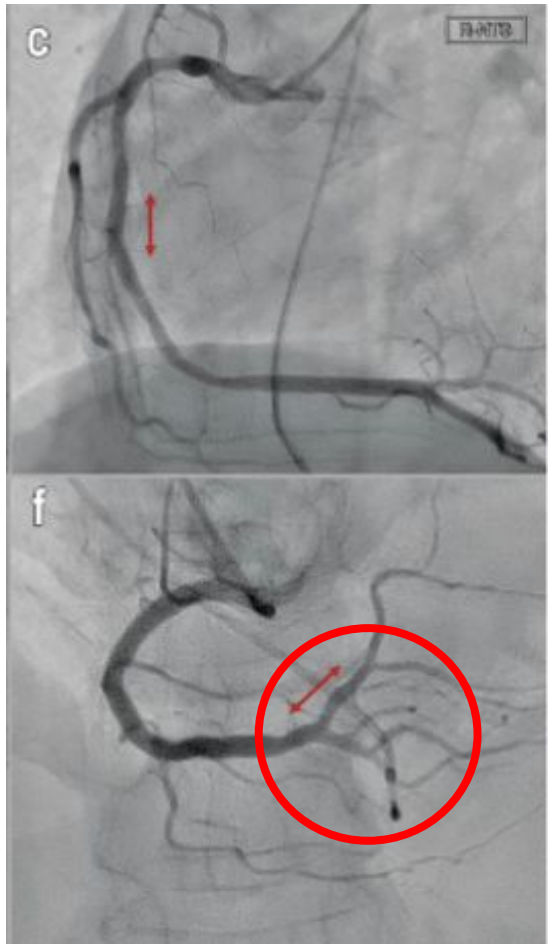
El vasoespasmo se produjo en el segmento distal en un paciente con DES, pero no con DCB. El estiramiento pasivo fuerte y permanente de las capas endoteliales y musculares mediante el stent provocó hipersensibilidad de los segmentos arteriales adyacentes

DCB

DES



AC



NTG

PORQUE USAR BALONES FARMACOLOGICOS?
Para Preservar la Funcion Endotelial

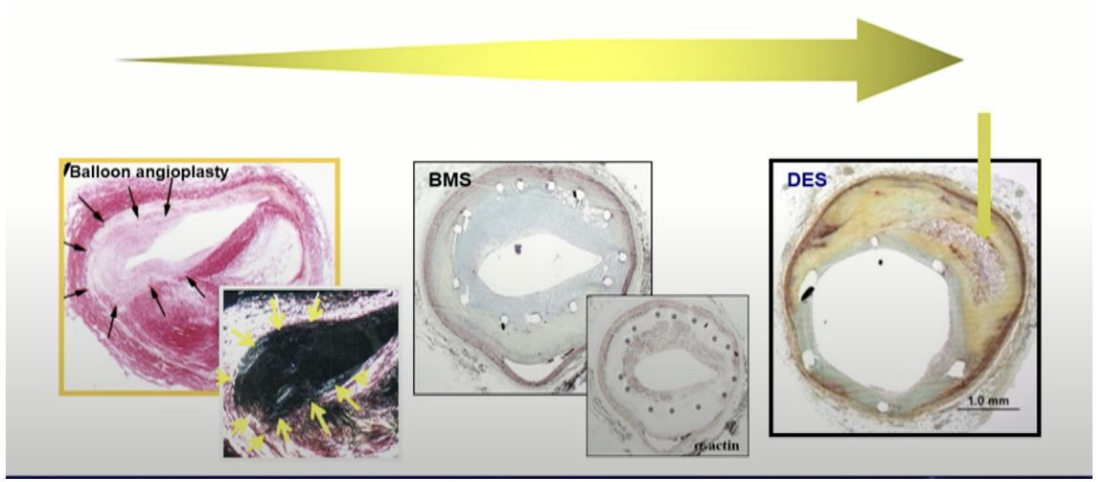
El presente estudio es el primero en revelar que la función endotelial está mejor conservada en los vasos coronarios tratados con DCB que con DES de nueva generación.

Los resultados actuales sugieren que el DCB para lesiones coronarias de novo puede preservar el funcionamiento fisiológico de los vasos mejor que el DES de nueva generación, lo que puede ser un efecto beneficioso del concepto de "no dejar nada atrás" del DCB (Leave nothing behind)

Brott B.Severe, diffuse coronary artery spasm after drug-eluting stent placement. J Invasive Cardiol. 2006;18:584-92.

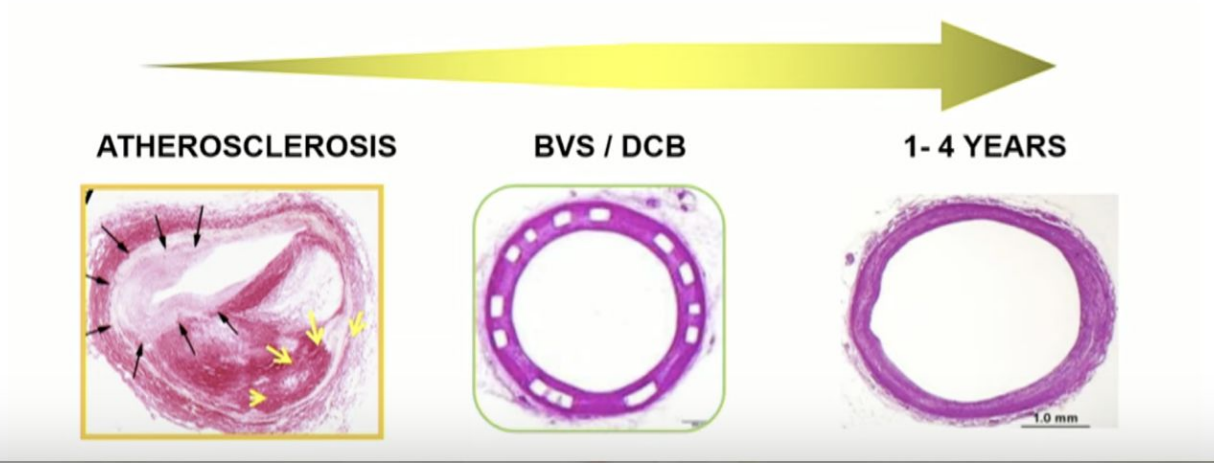
Tsutomu Kawai et al. Eurointervention 2022; e140-e148

"Atherosclerosis PCI = Symptomatic & Palliative Treatment"



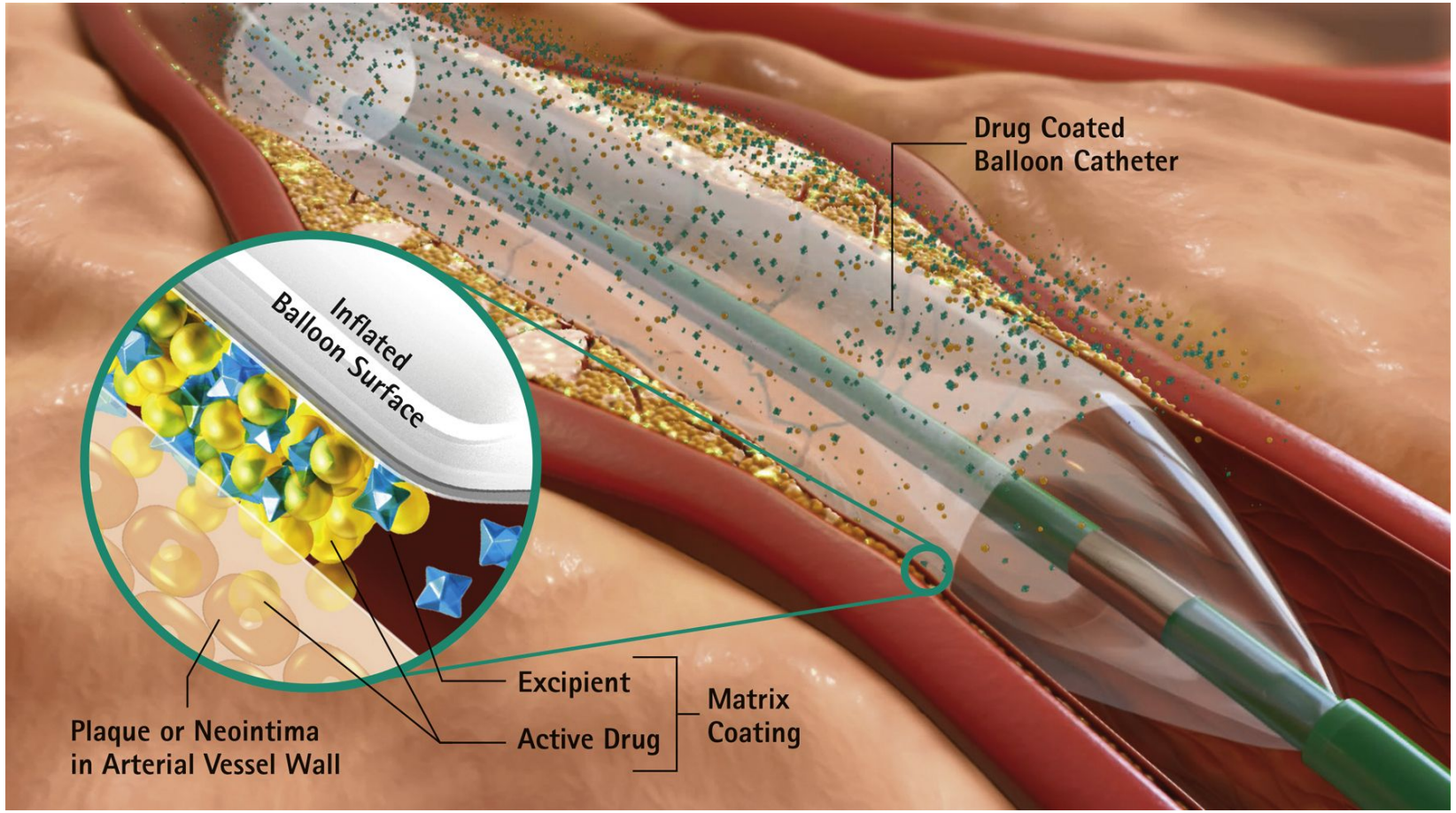
2024 AiCT asia PCR

Atherosclerosis & "Healing Therapy" whilst Leaving nothing behind



BALON CON DROGAS:

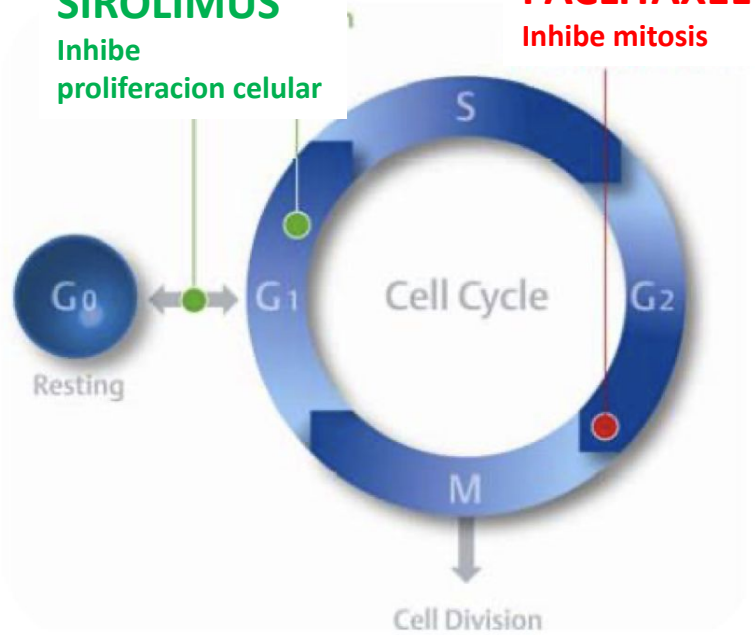
Transferencia Rapida y Homogenea de Farmacos, sin implantes permanentes



MECANISMO DE ACCION

SIROLIMUS
Inhibe proliferacion celular

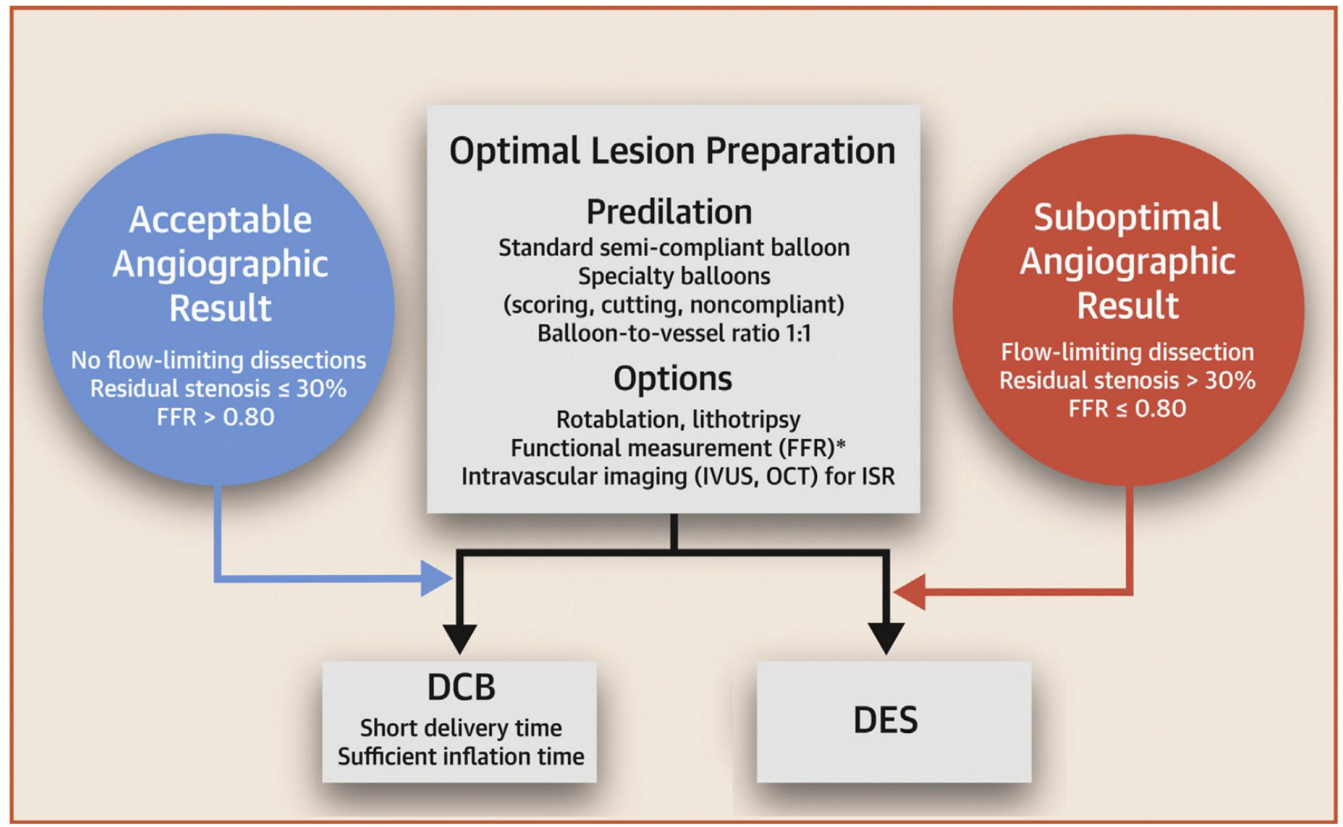
PACLITAXEL
Inhibe mitosis



G1 – cell growth
S – DNA replication
G2 – preparation for Mitosis
M – Cell Division

DCB

Preparacion de la Lesion


Optimal Lesion Preparation
Predilation
Standard semi-compliant balloon
Specialty balloons
(scoring, cutting, noncompliant)
Balloon-to-vessel ratio 1:1
Options
Rotablation, lithotripsy
Functional measurement (FFR)*
Intravascular imaging (IVUS, OCT) for ISR
Acceptable Angiographic Result
No flow-limiting dissections
Residual stenosis ≤ 30%
FFR > 0.80
Suboptimal Angiographic Result
Flow-limiting dissection
Residual stenosis > 30%
FFR ≤ 0.80
DCB
Short delivery time
Sufficient inflation time
DES

Paclitaxel- Choice to Drug In DCB

Protégé
Paclitaxel Coated Balloon Catheter

Why Paclitaxel Is DRUG OF CHOICE ?

- **It has faster action - G1 phase 4 hours after procedure***
- **A highly lipophilic - High absorption into vessel wall****
- **Positive vessel remodeling*****
- **Quicker Vessel Healing & Endothelialization******

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LIMITLESS POSSIBILITIES

* Biomed Res Int. 2015; 2015: 413076 :** 1997 Jul 15;96(2):636-45. doi: 10.1161/01.cir.96.2.636

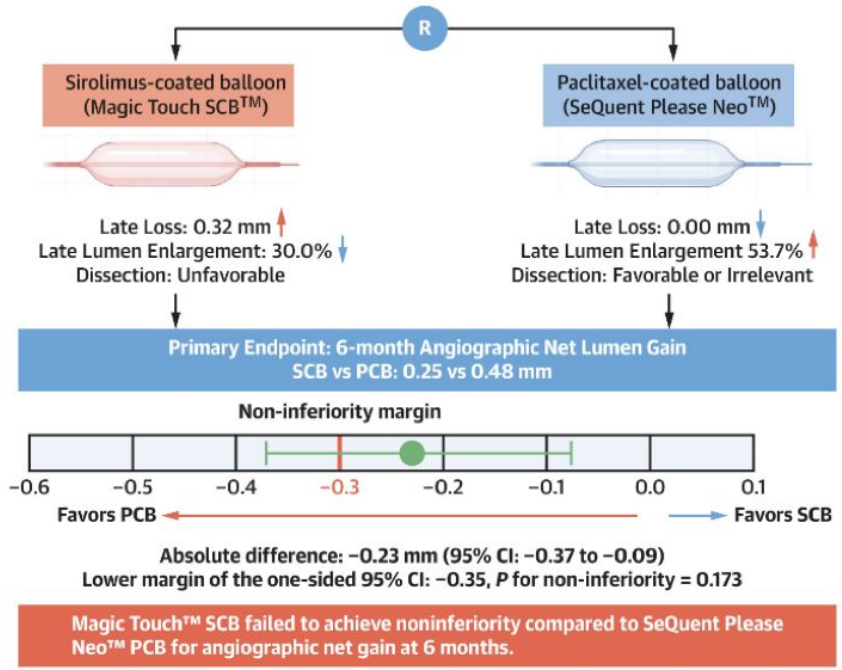
. J Geriatr Cardiol. 2016 Nov; 13(11): 906–913:*https://doi.org/10.1016/S0735-1097(03)01056-8

BLUEMEDICAL

Paclitaxel Vs Sirolimus

Protégé
Paclitaxel Coated Balloon Catheter

CENTRAL ILLUSTRATION: TRANSORM-I Trial: A Prospective, Multicenter, Noninferiority Trial in Patients With De Novo Small Vessel Coronary Artery Disease



Ninomiya K, et al. J Am Coll Cardiol Intv. 2023;■(■):■–■.

Biochemical Characteristics	Sirolimus	Paclitaxel
Antiproliferative	√	√
Cytostatic	√	√
Cytotoxic	X	√
Apoptotic	X	√
Highly Lipophilic	X	√
Positive Vessel Remodeling	x	√

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LIMITLESS POSSIBILITIES

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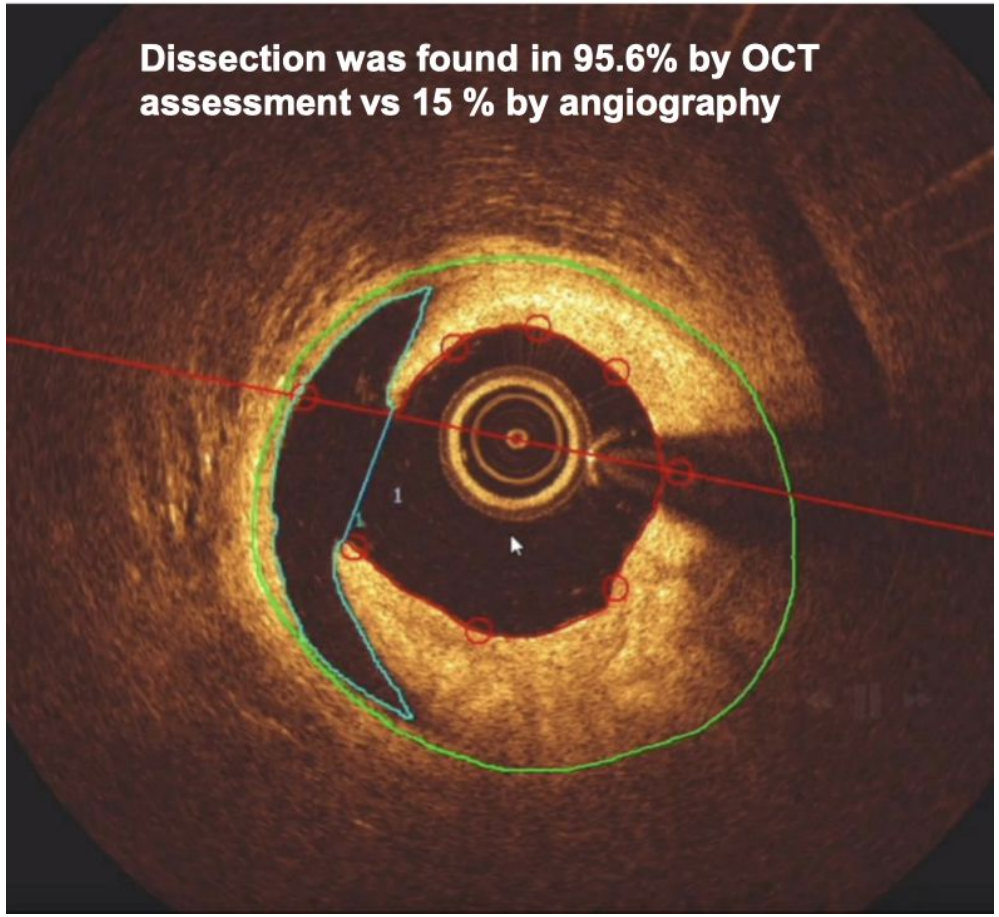
SCB vs PCB: TRANSFORM I

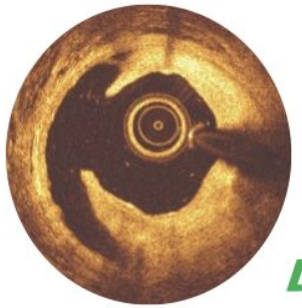


- Con el SCB, la pérdida tardía aumenta en función del volumen de disección, mientras que con el PCB, la pérdida tardía no está relacionada con la disección e incluso disminuye en función del aumento del volumen de disección.

SCB vs PCB: TRANSFORM I

Sirolimus-coated balloon (Magic Touch SCB™)

Late Loss: 0.32mm
Late Lumen Enlargement: 30.0%
Dissection: Unfavorable



Paclitaxel-coated balloon (SeQuent Please Neo™)

Late Loss 0.00mm
Late Lumen Enlargement 53.7%
Dissection: or Irrelevant or Favorable

Primary Endpoint: 6-month Angiographic Net Lumen Gain
SCB vs PCB: 0.25 vs 0.48mm

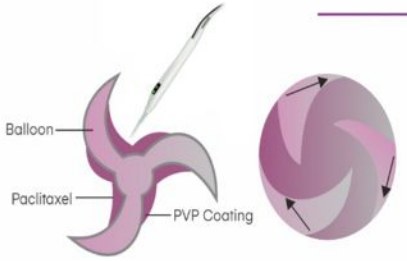
Technology – Minimizing Drug Loss During

02

Loss to circulation (Insertion-Transit-Inflation) & risk of:

- Particulate embolization
- Systemic effects

Unique Drug Application



Unique coating of Paclitaxel is applied within the folds of a PVP-coated (hydrophilic) balloon, reducing exposure and preventing loss prior to inflation

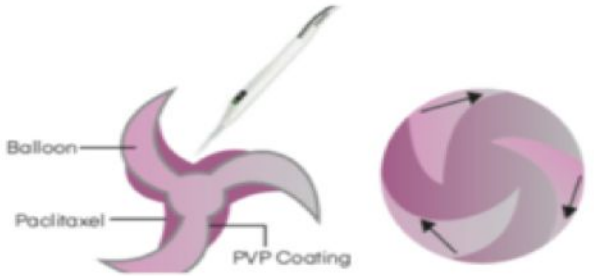
WingSeal Technology

The corrugation increases flexibility of the balloon ensuring better trackability & crossability

Tight wrapping prevents the balloon unfolding during advancement

Unique Drug Application Process

- During the production process the balloon material is inflated & folded



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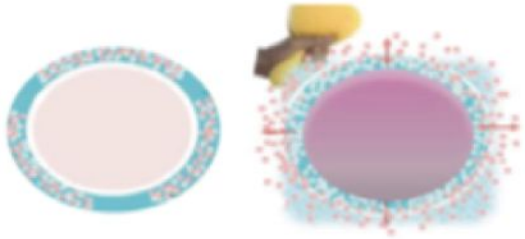

- The coating acts as sponge which elutes the drug only when pressure is applied
- Paclitaxel is released from the coating after first inflation to the target vessel

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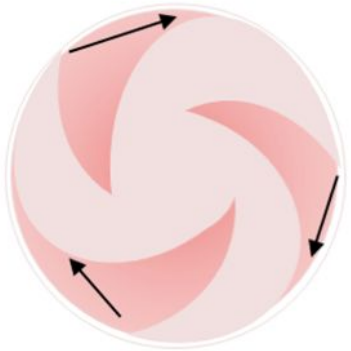
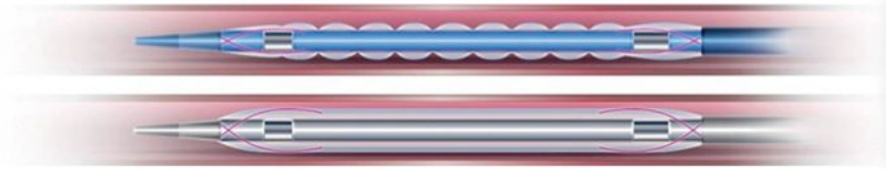
BLUEMEDICAL

Wing Seal Technology

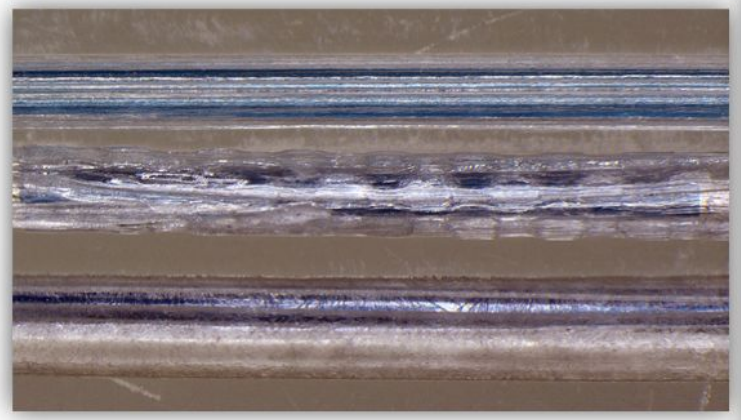


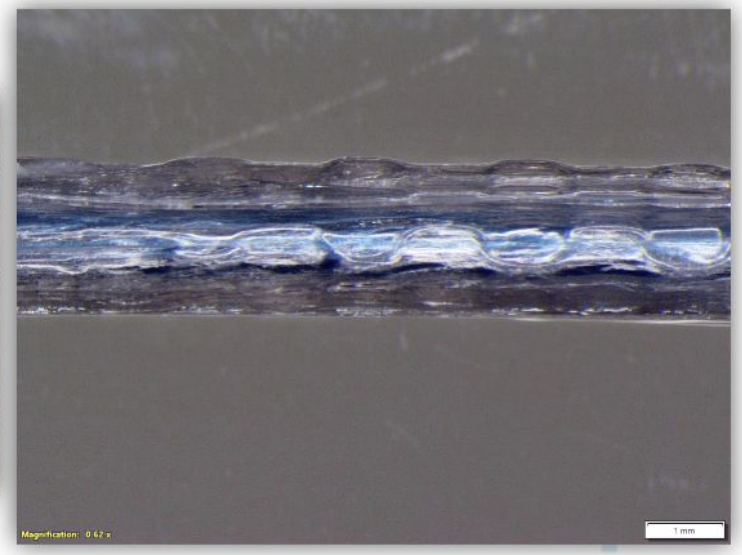


WING SEAL TECHNOLOGY

Advantages

- Prevents unfolding during advancement and minimizes drug loss.
- Creates surface corrugation, which reduces the surface area and consequently reduces frictional abrasion
- Corrugation on surface increases flexibility of the balloon ensuring better Flexibility



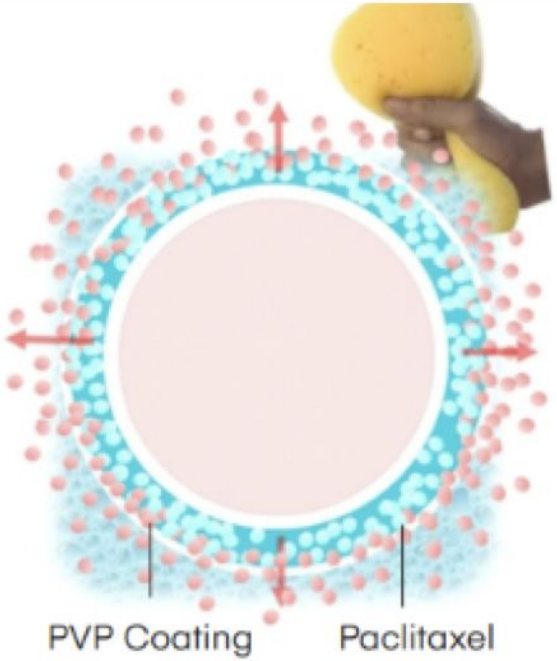


PVP Coating

03

Tissue transfer efficiency

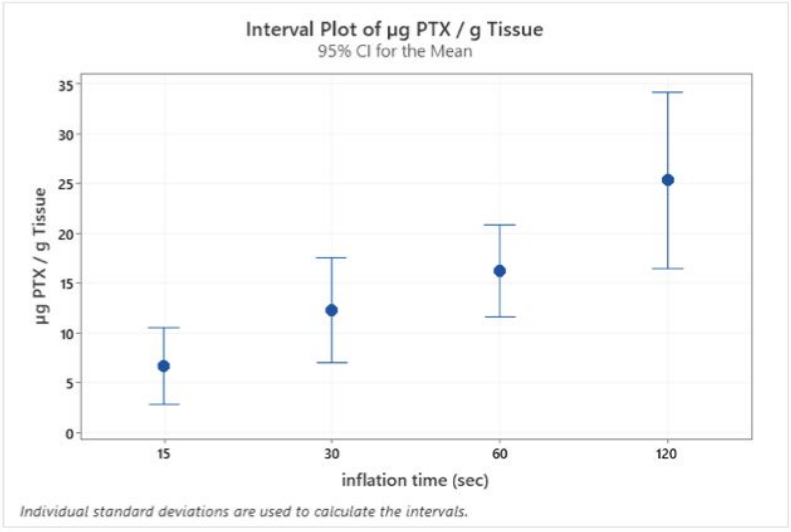
- Coating characteristics (eg,hydrophobicity/ hydrophilicity, crystallinity/amorphous morphology)
- Excipient
- Coating technique



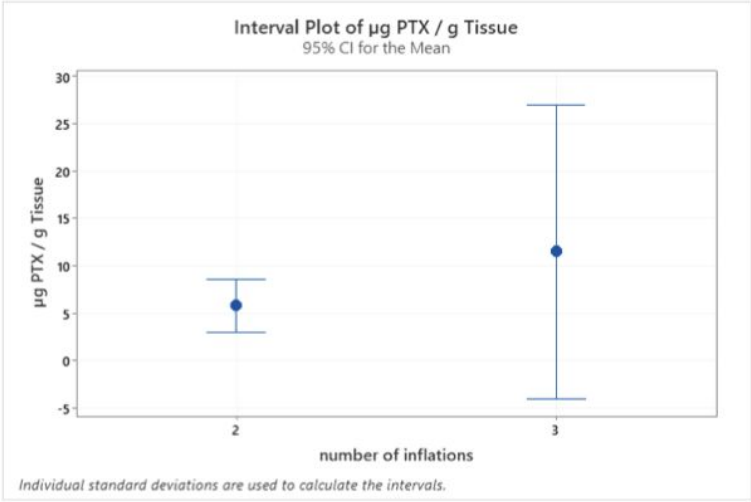
- PVP Coating Acts as a sponge
- Paclitaxel is released once the pressure is applied
- Prevents drug loss transition time

Inflation Time & Drug Release

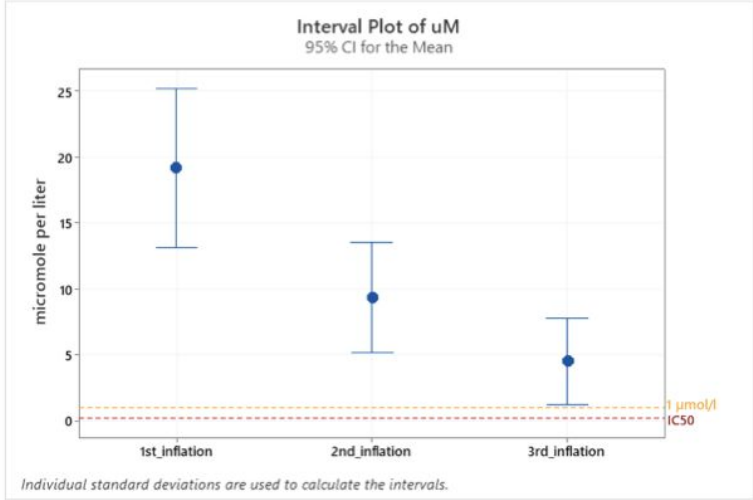
Protégé
Paclitaxel Coated Balloon Catheter



Inflation time can impact the concentration tissue bound paclitaxel, the longer the inflation time the higher the concentration.



Inflating in the same location there is a small average increase in the tissue bound paclitaxel, this is most likely caused by the diffusion characteristics , as when inflating in the same location ensures there to be already tissue bound paclitaxel make the concentration difference smaller.



When multiple inflations were performed at a different location per inflation, the difference in tissue bound paclitaxel was found to be greater. This was attributed to diffusion characteristics,

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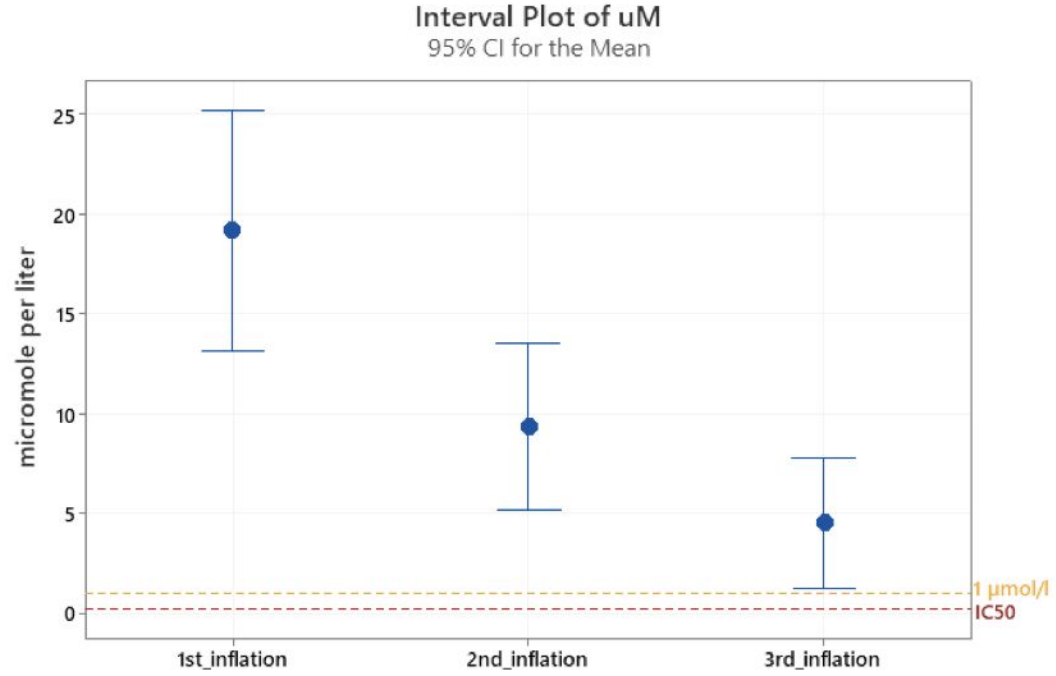
Inflation @ Multiple Location



- For the product to be effective a minimal amount of paclitaxel which is required to inhibit sufficient smooth muscle cells proliferation to reduce the chance on long-term restenosis, this value is define as the IC50 (0.002µmol/l).

- The tissue bound paclitaxel dosage applied by the protégé device is greater that the effective minimal optimal dosage and IC50 value, even at low saturation level(LSL) after 3rd inflation which is 1.28µmol/l (P value <0.05).

Solo DCB Grandes Vasos de NOVO
en Estudios mayores de 100 ptes

TABLE 4 DCB Only in De Novo Lesions of Large Coronary Vessels

Study Name/ First Author et al. (Ref. #)	DCB	n	≥2.75-mm DCB (%)	≥3.0-mm DCB (%)	Bailout Stent (%)	MACE (%)	TLR (%)
					PROMEDIO 9% (0.5-22%)	4.9%.	1,7%
DELUX (70)	Pantera Lux	105		23	22	9.4 (12 months)	3.1 (12 months) (TVR)
FALCON (69)	In.Pact Falcon	326	25		4.8	8.0 (12 months)	4.9 (12 months)
Venetsanos et al. (53)	SeQuent Please, In.Pact Falcon, Pantera Lux	985		6	8		3 (12 months)
Rosenberg et al. (54)	Sequent Please	731	21		6	5.6 (9 months)	2.3 (9 months)
Uskela et al. (68)	Sequent Please	463	79	60	12	6.1 (stable CAD, 12 months)	1.4 (stable CAD, 12 months)
Yu et al.(108)	Sequent Please	595	36		0.5	0 (10 months)	0 (10 months)
DEBUT (57)	Sequent Please vs. BMS (RCT)	103	76	64	2	1.9 (9 months)	0 (9 months)
PEPCAD-NSTEMI (62)	Sequent Please vs. BMS and DES (RCT)	104			17.4	3.8 (9 months)	1.0 (9 months)

Only studies including de novo lesion treatment in 100 patients or more and reporting device diameter are included.
CAD = coronary artery disease; RCT = randomized controlled trial; other abbreviations as in Tables 1 and 2.

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JUNE 22, 2020:1391–40

DCB vs DES en Pequeños Vasos de NOVO

en Estudios Randomizados < 2.75 o 3 mm

Outcome	Events DCB	%	Event DES	%	HR [95% CI]	P
MACE	**103**	**18.5**	**132**	**24.5**	**0.67 [0.47-0.96]**	**0.027**
Death	35	6.3	36	6.7	0.90 [0.56-1.47]	0.682
Cardiac Death	21	3.8	14	2.7	1.78 [0.82-3.88]	0.144
Myocardial Infarction	**25**	**4.7**	**42**	**7.8**	**0.57 [0.35-0.94]**	**0.028**
Target Lesion Thrombosis	**2**	**0.4**	**9**	**1.7**	**0.22 [0.05-1.00]**	**0.051**
Target Lesion Revascularization	41	7.6	52	10.1	0.73 [0.47-1.14]	0.163
Target Vessel Revascularization	**60**	**11.1**	**82**	**15.6**	**0.66 [0.46-0.97]**	**0.032**

Only randomized controlled trials in patients with lesions in native coronary vessels ≤2.75 or 3.0 mm are included. *Only clinically indicated angiography. †Noninferiority.
ZES = zotarolimus-eluting stent; other abbreviations as in Tables 1 and 2.

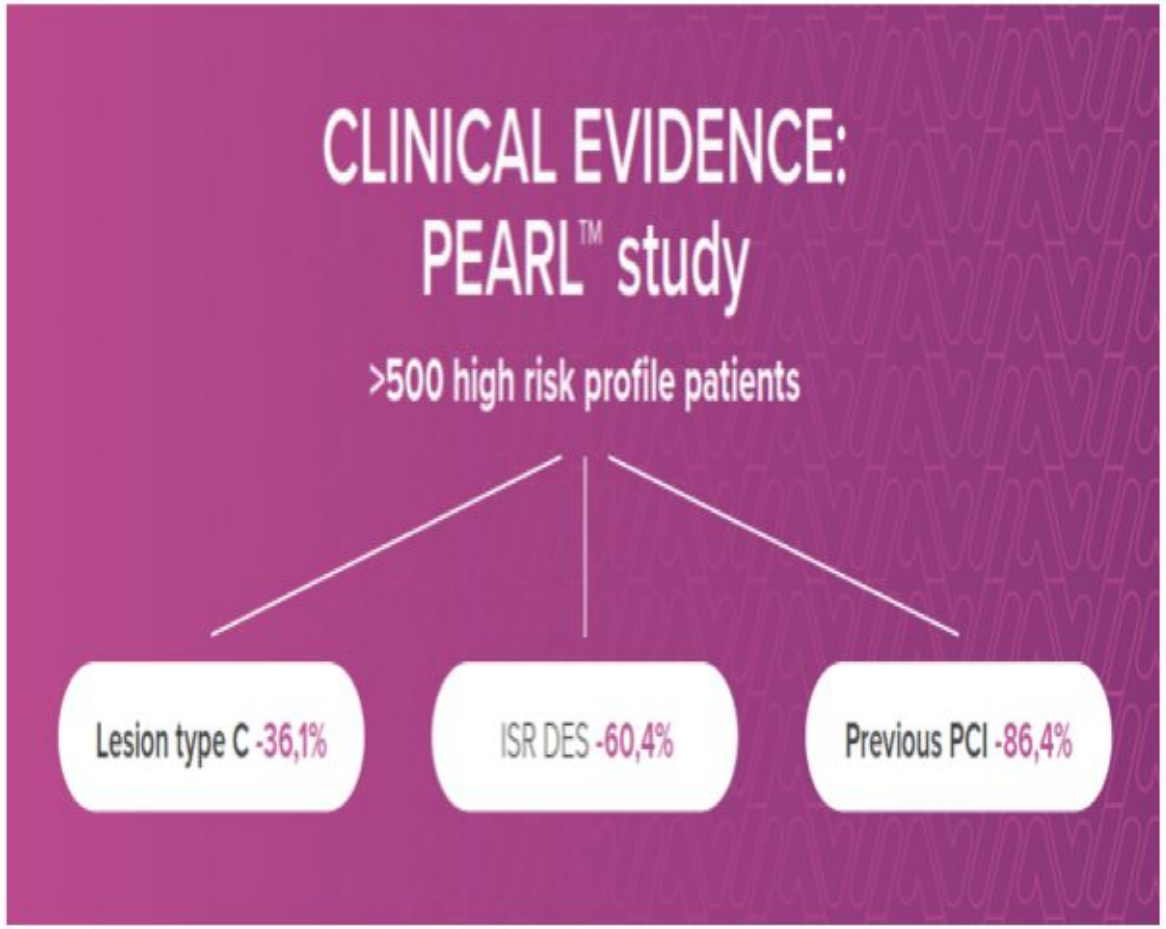
JACC:CARDIOVASCULAR INTERVENTIONS VOL. 13, NO. 12, 2020
JUNE 22, 2020:1391–40

DCB en REESTENOSIS INTRASTENT

Recommendations	Class	Level
Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

2018 ESC/EACTS Guidelines on myocardial revascularisation European Heart Journal (2018) 00, 1-96 - doi:10.1093/eurheartj/ehy394

Protégé : Paclitaxel DCB



https://bit.ly/3x9YfXG

Original Research

Clinical Performance of a Paclitaxel Drug-Coated Balloon in Real-World Percutaneous Coronary Intervention Practice: The PEARL Registry

Selina Vlieger, MSc[1]; Jin M. Cheng, MD, PhD[2]; Rohit M. Oemrawsingh, MD, PhD[1]; Auke P.J.D. Weevers, MD[1]; Jawed Polad, MD[3]; Ben Gho, MD, PhD[4]; Martijn Meuwissen, MD, PhD[2]; Peter den Heijer, MD, PhD[2]; Eric Boersma, PhD[5]; Alexander J.J. IJsselmuiden, MD, PhD[2]

Ref: Cheng et al., 2022, J. Invasive Cardiol. 34(6)- Pearl Registry

Evidencia Clínica Del Registro De Pearl: 2 Años De Seguimiento

- El estudio PEARL muestra que el paclitaxel DCB de Protégé es seguro y efectivo para la ICP de ISR y lesiones de novo. Los 513 pacientes del estudio tenían un alto perfil de riesgo cardiovascular

- La versión no conforme de DCB -Protégé NC- con una presión de ráfaga nominal más alta, se usó más a menudo en ISR.

- El tiempo de inflación de Protégé (NC), múltiples inflaciones usando el mismo Protégé (NC) y la falta de predilación de lesiones no se asociaron con MACE

Pearl Registry Conclusiones:

- En el **estudio Pearl** realizado con PCB protegido en la población de pacientes del mundo real **para lesiones De Novo e ISR con - Protégé Paclitaxel DCB es seguro y efectivo** para PCI de ISR y lesiones de novo.

- La incidencia reportada de TLR en múltiples estudios después de la angioplastia DCB para DES ISR fue de aproximadamente el 15 % a los 2 años. En el estudio PEARL a los 2 años, MACE impulsado por **TLR** en pacientes tratados para ISR fue del 11,7 % y para lesiones **De novo fue del 2,9 %,** que es menor en comparación con lo mismo en otros RCTS.

- La incidencia reportada de MACE durante 1 año de FUP fue del 8 al 9,6 % en otros ECA. En el estudio PEARL, la tasa de **MACE a los 2 años** después de la angioplastia **DCB para lesiones De Novo fue del 9,7 %**

SIZE CATHETER

PROTÉGÉ - DCB CATHETER

L \ Ø	2.00	2.50	3.00	3.50	4.00
10	PRO2010	PRO2510	PRO3010	PRO3510	PRO4010
15	PRO2015	PRO2515	PRO3015	PRO3515	PRO4015
20	PRO2020	PRO2520	PRO3020	PRO3520	PRO4020
30	PRO2030	PRO2530	PRO3030	PRO3530	PRO4030

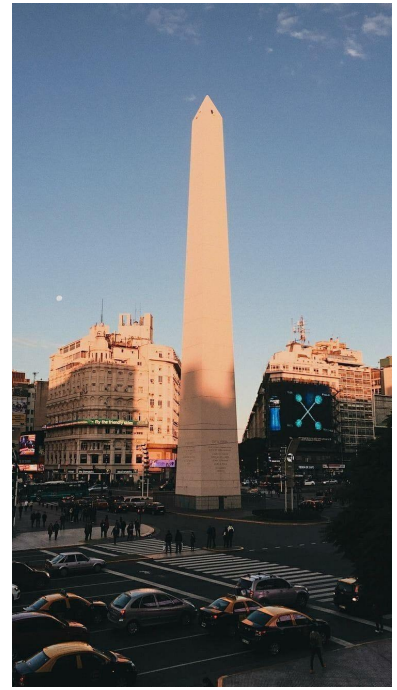
PROTÉGÉ NC - DCB CATHETER

L \ Ø	2.50	2.75	3.00	3.25	3.50	4.00	4.50
10	PNC2510	PNC2710	PNC3010	PNC3210	PNC3510	PNC4010	PNC4510
15	PNC2515	PNC2715	PNC3015	PNC3215	PNC3515	PNC4015	PNC4515
20	PNC2520	PNC2720	PNC3020	PNC3220	PNC3520	PNC4020	PNC4520

(Ø = Diameter, L = Length)

Protégé

Paclitaxel Coated Coronary
Balloon Dilatation Catheter



Buenos Aires

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GRACIAS POR SU ATENCION