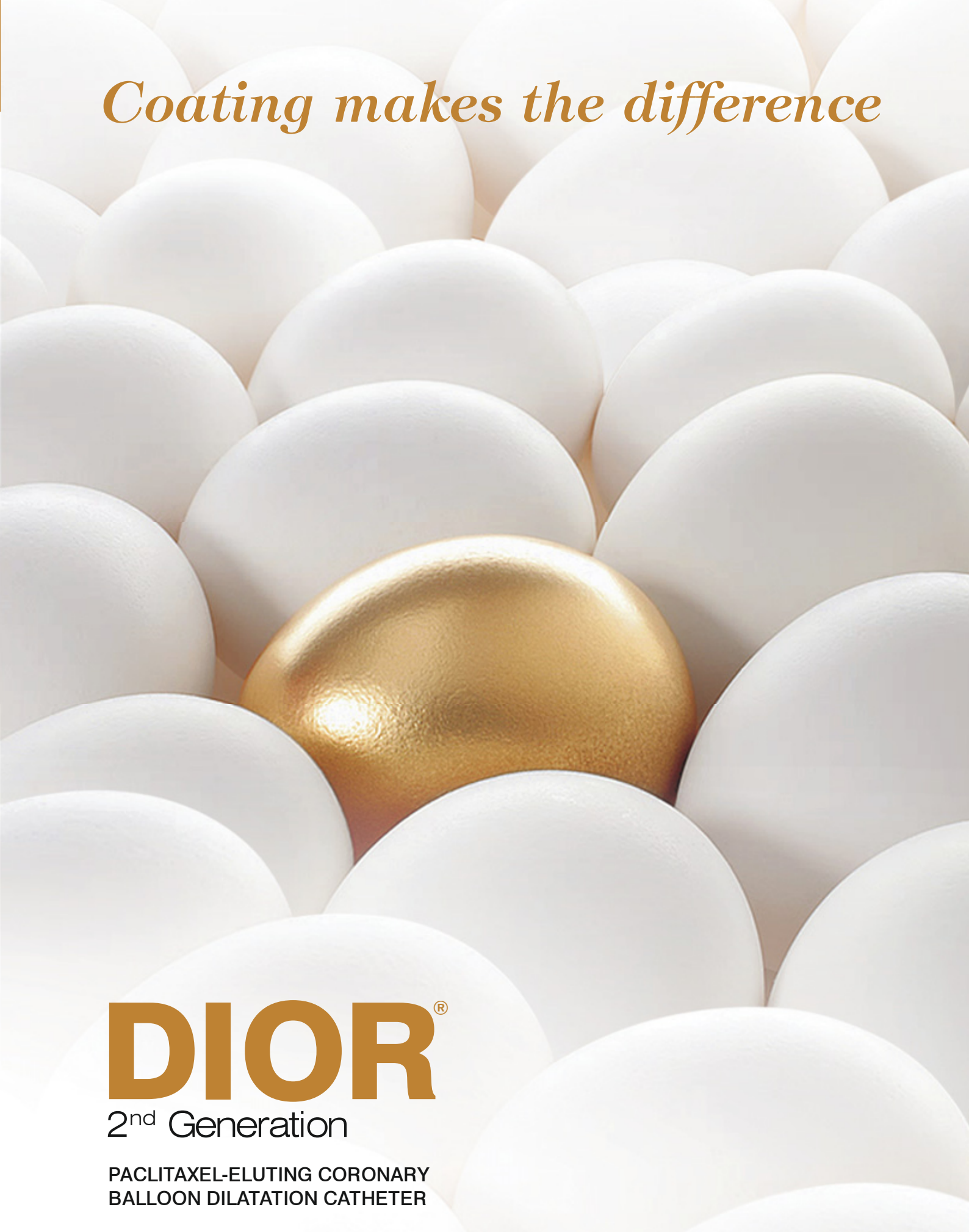
Coating makes the difference



DIOR®

2nd Generation

PACLITAXEL-ELUTING CORONARY
BALLOON DILATATION CATHETER

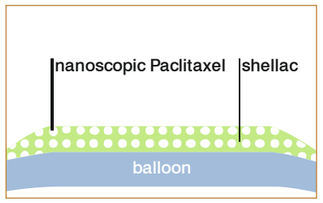
Eurocor

DIOR®
2nd Generation

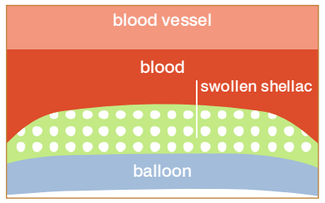
The coating makes the difference

The DIOR® bioshell coating matrix consists of a natural resin, which is EMEA and FDA approved (GRAS) as food additive under E 904.
Shellac is a natural resin composed of shellolic and aleuritic acid.
The excellent film forming properties of shellac are used to coat gastric resistant tablets.

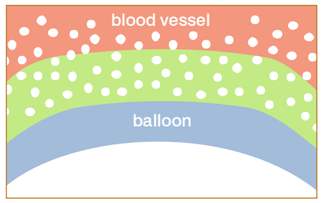
The coating consists of a 1:1 mixture of paclitaxel with shellac applied to the balloon.
In contact with body liquid the hydrophilic shellac-network of the composite swells and opens the structure for the pressure-induced fast release of paclitaxel on the inflated balloon.



coated balloon deflated

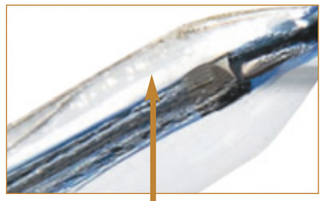


in contact with blood



inflated balloon allows freed paclitaxel to enter the vessel wall

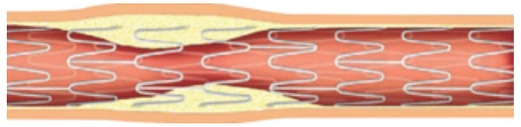

Exclusive bioshell coating

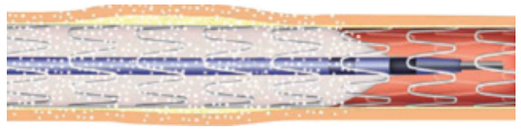

Compared to competitive products shellac gives the balloon a shiny appearance

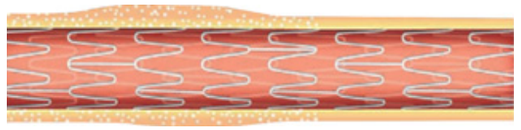
Shellac coating section. Scanned electron microscope image: 2/1000 mm scale*

*Very smooth surface

Paclitaxel eluting PTCA balloon catheter with a bioshell coating matrix with excellent paclitaxel concentration in the arterial tissue

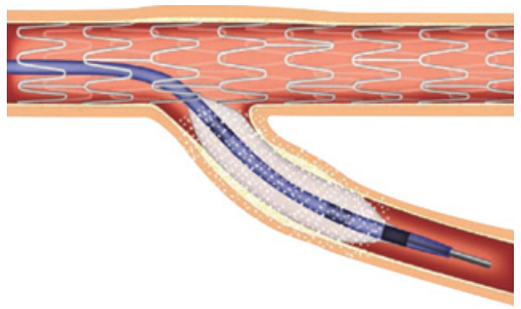

Coronary in-stent restenosis


Dilatation of in-stent restenosis with the new paclitaxel eluting DIOR® Second Generation


Successful treatment with DIOR® Second Generation.
After predilation of ISR, drug delivery with DIOR® the drug eluting balloon

- Low-dose drug application of paclitaxel, reduces smooth muscle cell proliferation for the successful treatment of coronary in-stent restenosis
- Significant reduction of the incidence of recurrent in-stent restenosis
- High effective drug with a short term dilatation of 45 seconds
- Ease of reinvention

The bifurcation strategy


Successful treatment of coronary bifurcation lesions with DIOR®
Provisional stenting of the main branch only and drug eluting balloon dilatation of the side branch enhance a favorable outcome by fewer adverse events and repeat interventions.

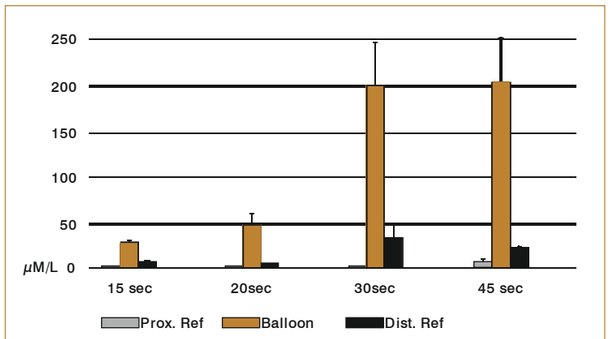
DIOR®
2nd Generation

The coating makes the difference

Bioshell coating for excellent arterial tissue paclitaxel concentration

The DIOR® bioshell coating is a 1:1 mixture of shellac and paclitaxel.
This mixture allows a short and save application of paclitaxel into the arterial tissue.
Paclitaxel dosage: 3µg/mm² balloon surface area

Compared to the first DIOR®, the tissue concentration of paclitaxel in the DIOR® Second Generation is 20 times higher.



Optimal arterial tissue concentration of paclitaxel is achieved by 45 sec. balloon inflatation.

20 porcine arteries were treated with the DIOR® Second Generation balloon in a time-dependent matter. Arteries were dissected and sent to a blinded laboratory for paclitaxel determination.

DIOR® 2nd Generation Paclitaxel-eluting PTCA balloon catheter

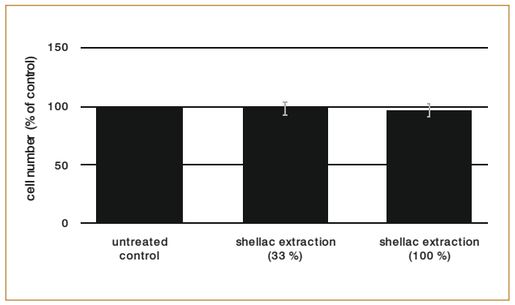
- DIOR® is not an implant. After the treatment you have no material behind.
- DIOR® can eliminate the stent-in-stent reintervention.
- DIOR® prevents additional stiffening of the stented artery.
- DIOR® shortens the antiplatelet therapy up to 3 months.
- DIOR® offers an alternate treatment in bifurcations, by using it in side branches.
- DIOR® has shown excellent clinical outcomes in small vessel without stenting (Spanish Registry with >220 patients).

Advantages of exclusive bioshell coating

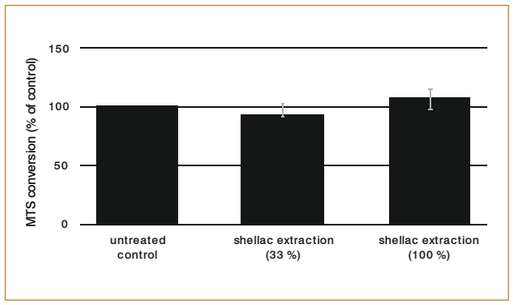
The DIOR® coating shows no signs of cytotoxicity after direct or indirect contact with endothelial cells.
The DIOR® shellac coating allows the adhesion of new endothelial cells.
The DIOR® shellac coating shows no signs of pro-inflammatory activation.

Investigation of cytotoxicity

Shellac extraction product
(24 h extraction in cell culture medium)



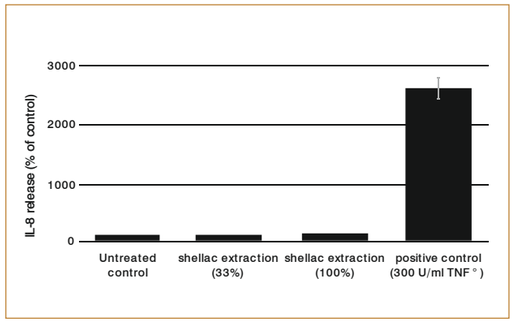
Quantification of cell quantity
Metabolic cell activity (MTS-assay)



No signs of pro-inflammatory activation

IL-8-release
Shellac extraction products (24 h). Exposition of confluent HDMEC with extraction products (24h). Tumour necrosis factor (TNF) as a positive control group.

Peters K., Prinz C, Salamon A., Adam A., Stuhldreier G., Rychly J., Neumann H.-G. Evaluation of she llac as coating of intravascular devices – Testing of in vitro compatibility by endothelial and smooth muscle cells. J ahrestagung der Deutschen Gesellschaft für Biomaterialien, 8.-10.10.2009, Tübingen.



Neither direct contact to shellac-coated materials nor exposure to shellac extraction products impaired HDMEC and hSMC viability and function in vitro.

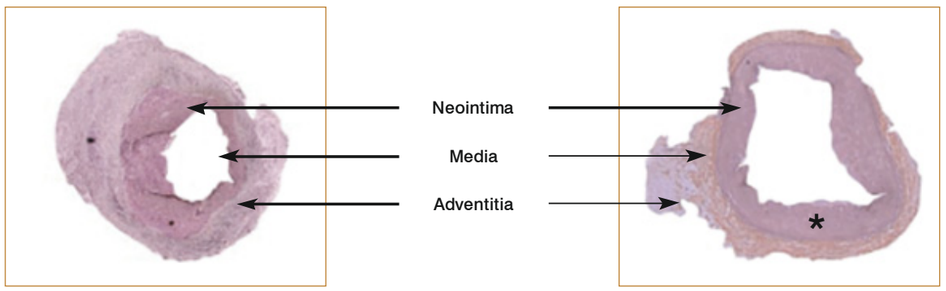
DIOR®
2nd Generation

The coating makes the difference

Excellent clinical efficacy and safety

Histological Evaluation in preclinical setting

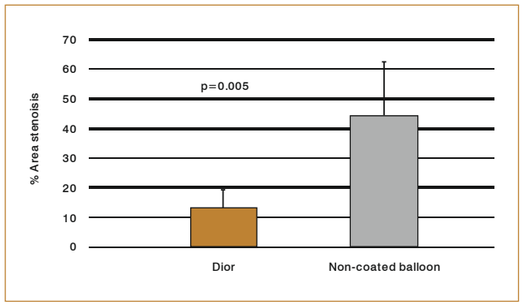
Porcine coronary arteries were dilatated (1.3:1 balloon/artery ratio) with either DIOR® balloon (3µg/mm² Paclitaxel balloon surface) or non coated balloon. Follow up angiography and obduction: 14 days post balloon dilatation.

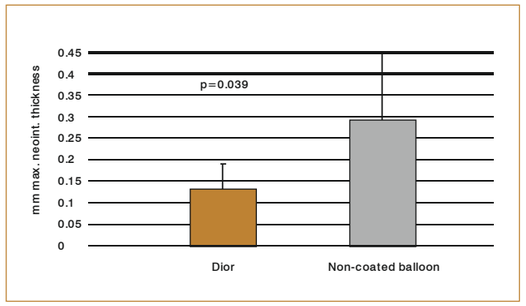


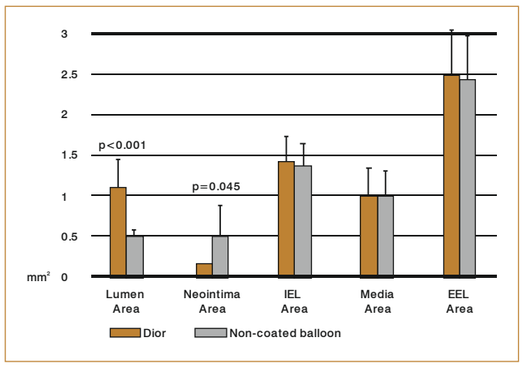
Uncoated balloon dilatation

DIOR® Second Generation with excellent results
*Healthy neointimal formation

Excellent late lumen loss results with 0.13 mm neointima thickness





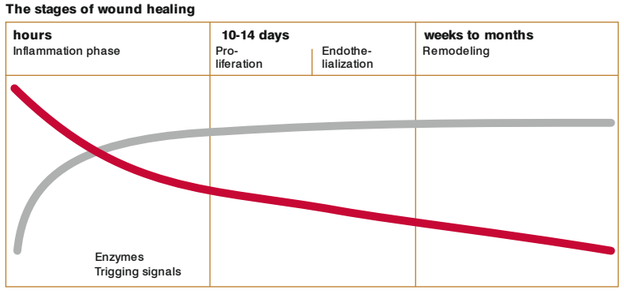


Pósa et al. Optimization of drug-eluting balloon use for safety and efficacy: Evaluation of the second generation paclitaxel-eluting DIOR®-balloon in porcine coronary arteries. CCI 2010; 76(3):395-403

What is most important

Paclitaxel selectively reduces the proliferation of smooth muscle cells. The endothelial cells show a better resistance to paclitaxel than the smooth muscle cells due to the different affinity of the connective structure on the cell surface. Paclitaxel does not influence non-proliferating cells as a result of cytokine and growth factor stimulation. The DIOR® paclitaxel-releasing balloon dilatation catheter enhances a smooth re-endothelialization process.

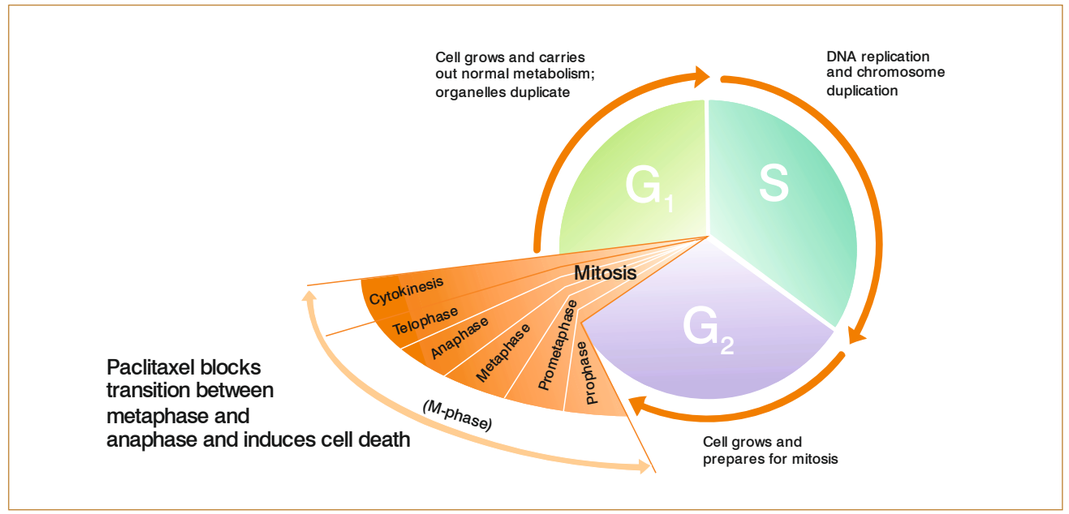
The stages of wound healing



Paclitaxel distribution in tissue after acute dosing using DEB
Paclitaxel distribution in tissue after chronic dosing using DES

Axel et al. Circulation 1997. Paclitaxel reduces arterial smooth muscle cell proliferation and migration in vitro and vivo using local drug delivery. Circulation 1997; 96:636-45

Paclitaxel prevents restenosis by blocking proper microtubal formation, thus it reduces cell division and migration. It inhibits inflammatory processes. After balloon dilatation, injuries to the arterial wall stimulate inflammatory reaction, and the excretion of growth factors occurs as an important process along with the onset of cell division and the migration of smooth muscle cells. Paclitaxel reduces platelet derived growth factor (PDGF) that mediates vascular smooth muscle cell migration to the intima.



Technical Data

DIOR® Second Generation	
Catheter design	RX
Catheter shaft	HypoTube shaft
Balloon material	Polyamide blend
Usable catheter length	140 cm
Recommended guide wire	0.014"
Guide wire lumen length	25 cm
Distal tip length	5 mm
Tip profile	0.016"
Proximal shaft diameter	1.9 F
Distal shaft diameter	2.6 F
Average burst pressure (ABP)	22 - 24 bar

Compliance chart

	Bar	Balloon diameter (mm)					
		1,50	2,00	2,50	3,00	3,50	4,00
	2	1,39	1,85	2,32	2,78	3,24	3,71
	4	1,44	1,92	2,40	2,88	3,36	3,84
Nominal pressure	6	1,50	2,00	2,50	3,00	3,50	4,00
	8	1,54	2,05	2,56	3,07	3,58	4,09
	10	1,57	2,09	2,61	3,13	3,65	4,17
	12	1,59	2,12	2,65	3,18	3,71	4,24
	14	1,62	2,16	2,70	3,24	3,78	4,32
Rated burst pressure (RBP)	16	1,65	2,20	2,75	3,30	3,85	4,40
	18	1,68	2,24	2,80	3,36	3,92	4,48

Nominal pressure 6 bar/Rated burst pressure 16 bat (at 37 ° C)
Exception: Balloons at 4 mm and > 20 mm length, rated burst pressure = 14 bar.

DIOR® Product order information

Order Number	Balloon diameter (mm)						
	2,00	2,25	2,50	2,75	3,00	3,50	4,00
Balloon length (mm) 15	Dior 2.00-15	Dior 2.25-15	Dior 2.50-15	Dior 2.75-15	Dior 3.00-15	Dior 3.50-15	Dior 4.00-15
20	Dior 2.00-20	Dior 2.25-20	Dior 2.50-20	Dior 2.75-20	Dior 3.00-20	Dior 3.50-20	Dior 4.00-20
25	Dior 2.00-25	Dior 2.25-25	Dior 2.50-25	Dior 2.75-25	Dior 3.00-25	Dior 3.50-25	Dior 4.00-25
30	Dior 2.00-30	Dior 2.25-30	Dior 2.50-30	Dior 2.75-30	Dior 3.00-30	Dior 3.50-30	Dior 4.00-30

Current DIOR® trials
I. DIOR® dilatation randomized trial (A. Colombo, Multi-Center)
II. DEB-AMI randomized trial (P. Stella, Acute myocardial infarct, Multi-Center)
III. DES-ISR Registry (F. Mauri, Multi-Center)
IV. DIOR®-Registry (Internationales Register)
V. Valentines Trial, weltweites Register (Dres. Silber, Stella, Sangiorgi)
VI. DIOR vs. DES, Multicenter Spain (Dr. Serra)

International Publications
I. Pieter Stella et al., Catheterization and Cardiovascular Interventions, 71:629-635 (2008)
II. Aniko Posa et al., Coronary Artery Disease, 19:243-247 (2008)
III. Ron Waksman et al., Catheterization and Cardiovascular Interventions, 73:643-652 (2009)
IV. Dorothea I. Axel et al., Circulation 1997, Paclitaxel Inhibits Arterial Smooth Muscle Cell Proliferation and Migration In Vitro and In Vivo Using Local Drug Delivery, 96:636-645
V. DEBUIT randomized trial (P. Stella, Bifurcation Study, Multi-Center)
VI. Rembert Pogge v. Strandmann et al., Euro Intervention PCR Supplement (2009)
VII. Kostas Spargias et al., JoIC (2009)

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CE 1434 Rev No. 0111B5 DIOR
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