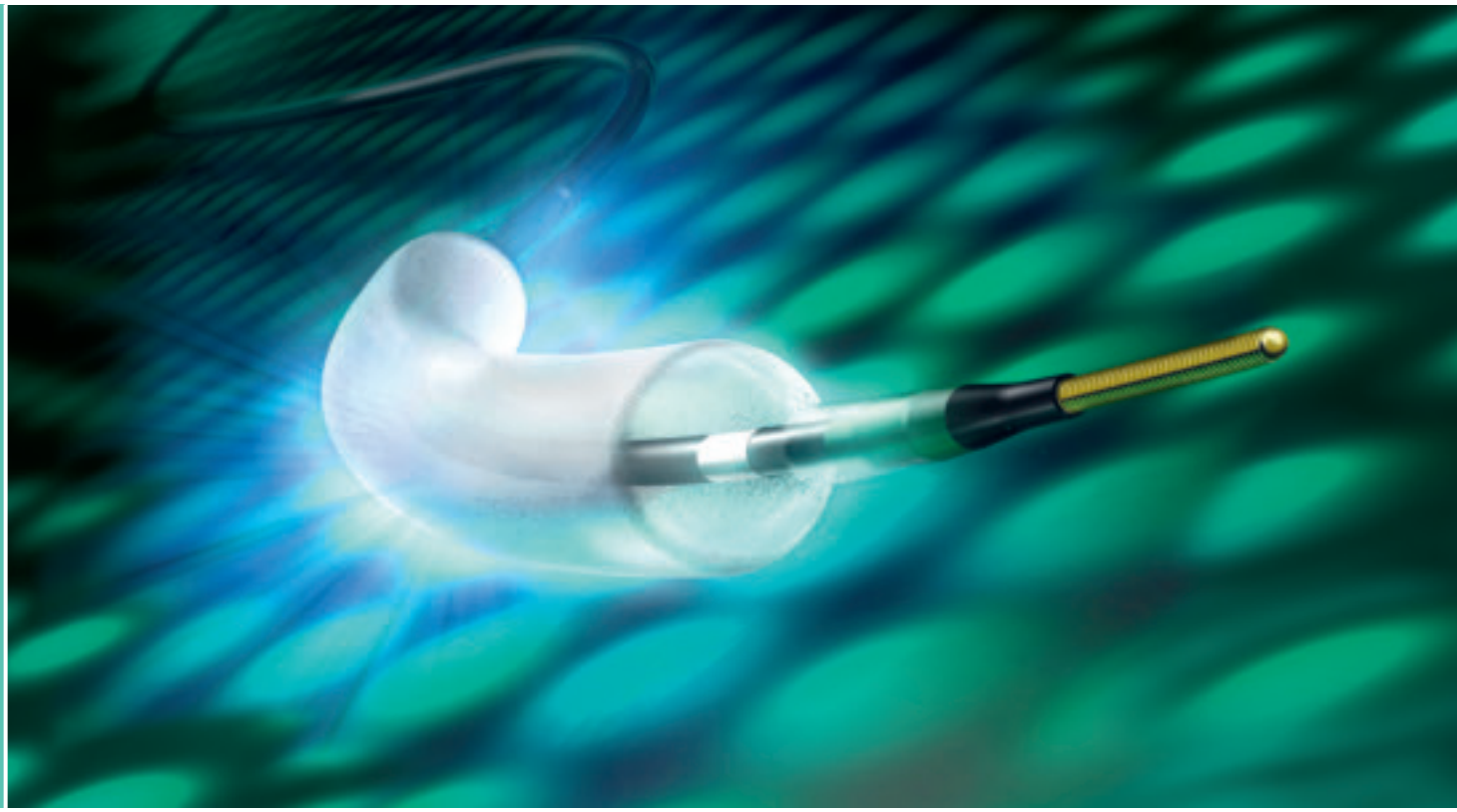
SeQuent® Please

Clinically proven Paclitaxel releasing coronary balloon catheter



Vascular Systems

B BRAUN
SHARING EXPERTISE

SeQuent® PLEASE

PACLITAXEL - RELEASING CORONARY BALLOON CATHETER

Restenosis prevention continues to be a challenge in interventional cardiology. SeQuent® Please is a novel concept of targeted, polymer-free and homogenous drug delivery designed to overcome the limitations of today's treatment options. Clinically proven, it offers completely new procedural solutions combined with a higher safety profile and superior efficacy.

SeQuent® Please

A new era of treating coronary stenosis

Matrix Coating Technology

Safe and effective local drug delivery

The original clinically proven Drug Eluting Balloon

Superior to existing treatment techniques

A new era of treating coronary stenosis

The proven choice for your solution oriented angioplasty

Advantages and benefits

- Maximum lesion accessibility due to a PTCA balloon-like handling
- Single shot, short-term Paclitaxel delivery for long-term vessel patency
- Targeted drug delivery into the vascular wall
- Bio-absorbable, polymer-free drug coating for the prevention of side effects
- Homogenous and pattern free drug distribution
- No stent related edge effects
- No need for stent-in-stent procedures
- Unlimited treatment options in case of patients' re-intervention
- Reduced duration of antiplatelet therapy
- Single treatment or in combination with a bare metal stent (BMS)

Beyond the standards

Superior clinical patient outcomes in complex lesions

- **ISR** - In-stent restenosis
- **SVD** - Small vessel disease

Advanced interventional options for the most challenging cases

- **CTO** - Chronic Total Occlusion
- **Bifurcations**
- **Diabetic patients**
- **Long lesions**

SeQuent® PLEASE

PACLITAXEL - RELEASING CORONARY BALLOON CATHETER

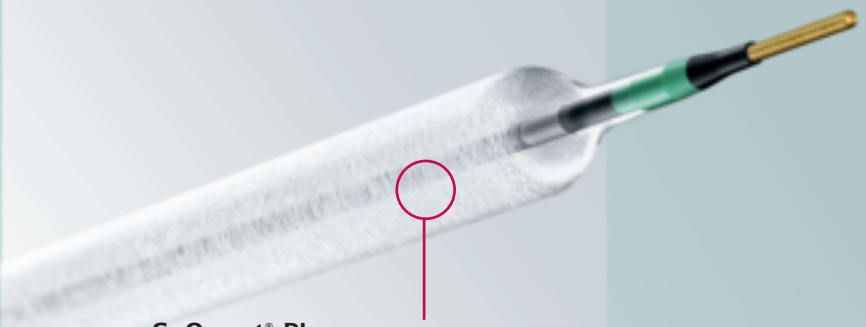
Mode of action

Pure Paclitaxel coating

A short single dose drug application is only possible if Paclitaxel is bioavailable on the balloon surface. Paclitaxel, if applied directly to the balloon surface, needs a matrix, which allows a reliable release and enables an immediate uptake into the vascular wall. If Paclitaxel is applied as a firm compound the required bioavailability is not given.

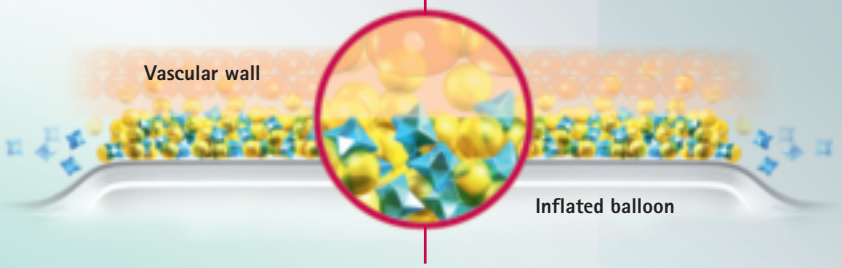
Matrix coating with "spacer"

The SeQuent® Please Matrix Coating is a dispersion of Paclitaxel and Iopromide. Lopromide acts as a "spacer" and thereby makes the coating porous and Paclitaxel bioavailable. The hydrophilic character of Iopromide and the lipophilic properties of Paclitaxel support the release of the drug from the balloon surface and its delivery into the vascular wall.



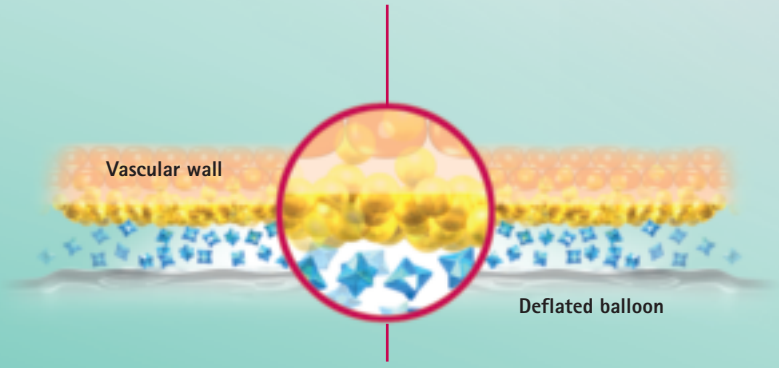
SeQuent® Please

Combines targeted drug delivery with PTCA balloon like flexibility and handling.



Balloon surface in contact with the vascular wall

30-second balloon inflation for effective drug delivery into the vascular wall.



Paclitaxel migrates into the vascular wall

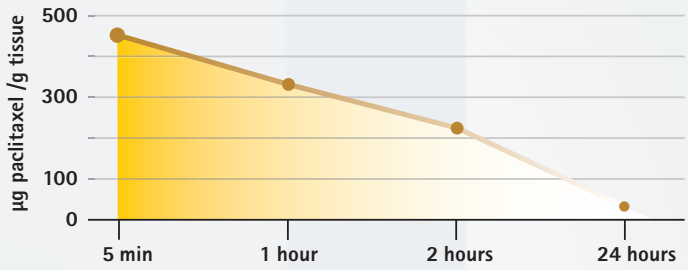
The matrix dissolves. Paclitaxel migrates into the SMC to prevent proliferation without any residues.

Matrix Coating Technology

Safe and effective local drug delivery

Long-term efficacy with short-term release [1]

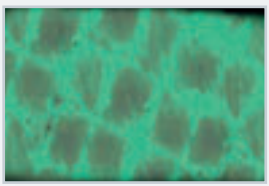
After a "single shot" application of Paclitaxel there is a sustained antiproliferative action on SMC over 14 days in absence of cytotoxic effects. Following such a "single shot" drug delivery the Paclitaxel concentration reaches bottom levels in vascular cells after 24 hours.



Paclitaxel concentration after 24 hours

Effective and homogenous drug delivery into the vascular wall [2] [3] [4]

The SeQuent® Please drug load is 3 µg/mm² balloon surface. A short contact time of only 30 seconds proved to be sufficient to inhibit cell proliferation. Approximately 16 % of the total Paclitaxel dose is transferred into the vascular wall.

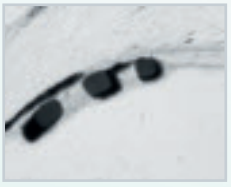


Stent struts of a DES lead to an inhomogenous patterned drug distribution. About 85 % of the vascular wall is not covered by the struts resulting in low drug tissue level.[2]

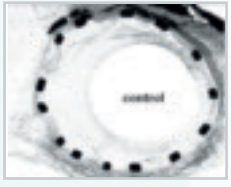
Homogenous drug distribution with SeQuent® Please technology.[4]

Reduction of neointimal proliferation [4] [5]

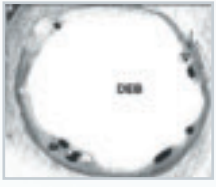
The Matrix Coating Technology clearly demonstrated in pre-clinical studies its benefit in suppressing smooth muscle cell (SMC) proliferation. BMS implantation with SeQuent® Please leads to a rapid stent endothelialization.[4] The SeQuent® Please concept reduces neointimal proliferation up to 4 weeks after intervention (in the porcine model).[5]



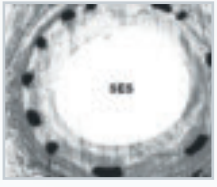
Endothelialization at day 5 in the porcine model



Bare Metal Stent (BMS)



SeQuent® Please Technology



Sirolimus Eluting Stent

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PACLITAXEL - RELEASING CORONARY BALLOON CATHETER

Evaluation of the Matrix Coating Technology

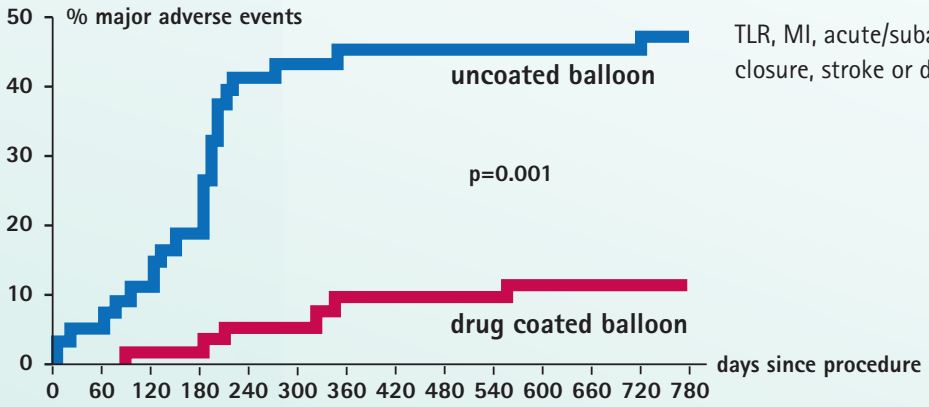
First in man: ISR I/II study [6][7]

Treatment of coronary in-stent restenosis with a Paclitaxel coated balloon catheter - a prospective, randomized trial

In-stent late loss and restenosis at 6 months and MACE at 2-years:

	Uncoated balloon	Paclitaxel-eluting balloon	p-value
In-stent late loss [mm]	0.81 ± 0.79	0.14 ± 0.46	0.001
In-segment late loss [mm]	0.80 ± 0.79	0.11 ± 0.48	0.001
In-stent restenosis	49 %	6 %	0.001
In-segment restenosis	51 %	6 %	0.001
MACE	46%	11%	0.001

Major adverse events at 2 years:



TLR, MI, acute/subacute closure, stroke or death

Conclusion:

- Proven clinical efficacy up to 24 months, safe drug delivery
- No coating-related adverse events, no late thrombosis
- Clopidogrel post PCI follow-up treatment for only one month
- Inhibition of restenosis by drug-coated balloons does not require stent implantation and sustained drug release at the site of injury

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Circulation 1997;96:636-645

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3. **Scheller B, Speck U et al.**
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Circulation 2004;110:810-814

4. **Scheller B, Speck U, Böhm M**
Prevention of restenosis: is angioplasty the answer?
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6. **Scheller B et al.**
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New England Journal of Medicine 2006;355:2113-24

7. **Scheller B, Hehrlein C, Bocksch W, Rutsch W, Haghi D, Dietz U, Böhm M, Speck U**
Two year follow-up after treatment of coronary in-stent restenosis with a paclitaxel-coated balloon catheter
Clin Res Cardiol 97:773-781 (2008)

8. Drug-Eluting Balloons May Be Alternative to Drug-Eluting Stents
FDAnews Device Daily Bulletin Oct. 26, 2007;Vol. 4;No. 211

9. **Unverdorben M et al.**
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Circulation 2009;119:2963-2964

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PACLITAXEL - RELEASING CORONARY BALLOON CATHETER

Balloon diameter	Balloon length	Order number
2.5 mm	10 mm	**5022200**
3.0 mm	10 mm	**5022201**
3.5 mm	10 mm	**5022202**
4.0 mm	10 mm	**5022204**
2.0 mm	15 mm	**5022205**
2.5 mm	15 mm	**5022206**
2.75 mm	15 mm	**5022207**
3.0 mm	15 mm	**5022208**
3.5 mm	15 mm	**5022210**
4.0 mm	15 mm	**5022211**
2.0 mm	17 mm	**5022212**
2.5 mm	17 mm	**5022213**
2.75 mm	17 mm	**5022214**
3.0 mm	17 mm	**5022215**
3.5 mm	17 mm	**5022218**
4.0 mm	17 mm	**5022219**
2.0 mm	20 mm	**5022220**
2.5 mm	20 mm	**5022221**
2.75 mm	20 mm	**5022222**
3.0 mm	20 mm	**5022223**
3.5 mm	20 mm	**5022225**
4.0 mm	20 mm	**5022227**
2.5 mm	26 mm	**5022230**
2.75 mm	26 mm	**5022231**
3.0 mm	26 mm	**5022232**
3.5 mm	26 mm	**5022234**
2.5 mm	30 mm	**5022240**
3.0 mm	30 mm	**5022242**
3.5 mm	30 mm	**5022243**

Order information

The original clinically proven DEB

Superior to existing treatment techniques

B. Braun clinical study program: PEPCAD [8] [9]

PEPCAD I

Treatment of small vessel disease (SVD) in 120 patients. 6-month angiographic data compared to literature data (*Stone G. Jama 2005; 294:1215-23).

	SeQuent® Please	*PES (Paclitaxel eluting stent)
In-segment late loss [mm]	0.16 ± 0.38	0.49 ± 0.61
In-segment restenosis	5.5 %	31.2 %
MACE (after 6 months)	6.1 %	18.9 %
MACE (after 12 months)	6.1 %	

Conclusion:

These results compare very favourably with previously published results on drug eluting stents (DES) in the treatment of small vessel disease (SVD). SeQuent® Please showed a very low binary restenosis rate (5.5 % vs. 31.2 %) and MACE rate (6.1 % vs. 18.9 %) as compared to Paclitaxel eluting stent data.

PEPCAD II

131 patients with in-stent restenosis (ISR) were randomized to either the SeQuent® Please or a Paclitaxel eluting stent (PES) treatment group. 6-month angiographic data and the 12-month MACE rate are shown in the following table:

	SeQuent® Please	PES	p-value
In-segment late loss [mm]	0.18 ± 0.41	0.39 ± 0.63	0.03
In-segment restenosis	6.7 %	20.4 %	0.03
MACE (after 6 months)	4.7 %	18.3 %	<0.02
MACE (after 12 months)	7.7 %	19.0 %	0.04

Conclusion:

Compared to PES, SeQuent® Please was safe and showed clinically superior outcomes after 6 and 12 months.

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