

Behind DEB Coating Technology Take Home Message

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria

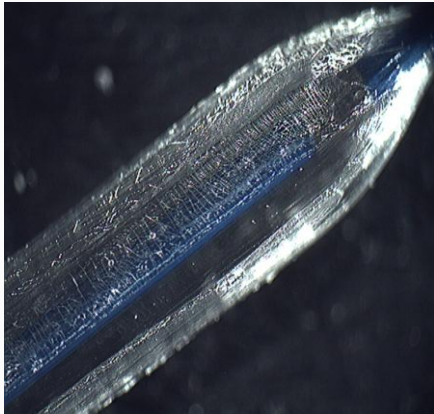
Company

- Medtronic, Boston Scientific, Eurocore, Biotronik
- Eurocore, Cordis, Abbott

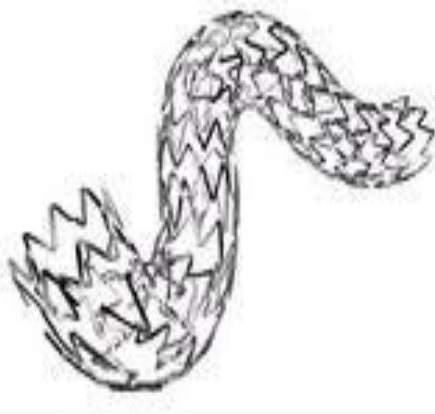
The more we look at the world, the more we may recognize that what one person thinks, may be different to the next



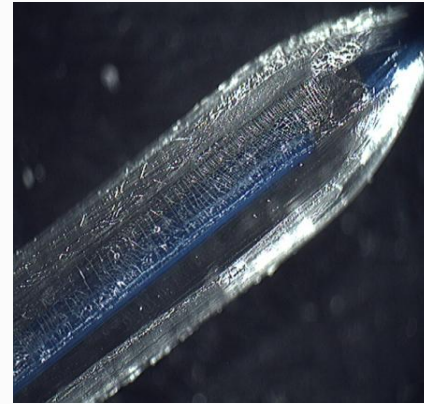
An Open Mind Is the Best Way to Look at the World



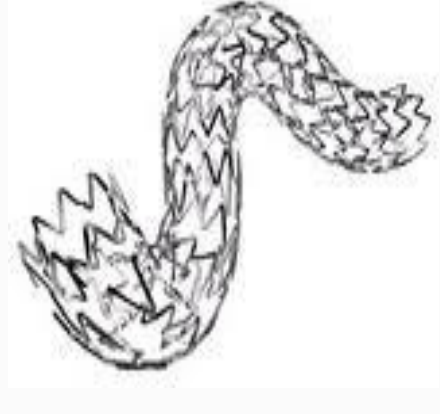
Perfect



Imperfect



Imperfect



Perfect



Local Drug Delivery: **DEB** vs. **DES**

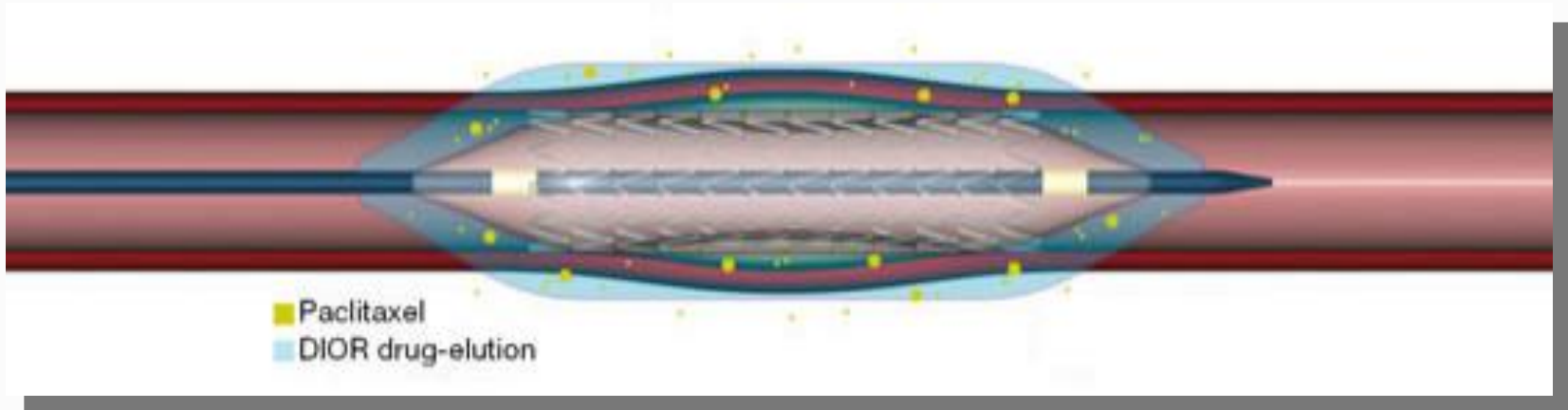


Drug-Eluting Balloon

- Immediate release
- Short-lasting exposure
- ~ 300 - 600 μg dose
- No polymers
- Wiped off the balloon surface
- Premounted stent optional

Drug-Eluting Stent

- Slow release
- Persistent drug exposure
- ~ 100 - 200 μg dose
- Polymer
- Diffusion from stent struts
- Stent mandatory



Advantages of DEB

- Allow homogenous drug transfer to the vessel wall and not only to the areas directly covered by the stent struts
- Drug concentrations at vessel wall highest at the time of injury when neointimal process is most vigorous. Afterwards, absence of drug aids in reendothelialisation and limit risk of late stent thrombosis
- Absence of polymer could decrease the stimulus of chronic inflammation and trigger for late thrombosis
- Absence of stent allows for preservation of original coronary anatomy, notably in cases of bifurcation or small vessels, leaving no scaffold
- Reduce duration of antiplatelet therapy
- Local drug delivery could be applied in situations where stents are not used or undesirable, eg small vessels, in-stent restenosis, or side branch in bifurcation lesions

BACK
TO
THE FUTURE.

The Competitors

| Company | DCB Name | Drug formulation |
|---|--|--|
| Aachen Resonance GmbH (distributed by Biotronik AG in UK, Switzerland, Benelux, Italy and Ireland). | ELUTAX® | Formulated with a matrix of pure Paclitaxel |
| B. Braun Melsungen AG | SeQuant® Please | Paclitaxel with iopirimde formulation (Paccocath® technology) |
| Bayer AG (MEDRAD, Inc.) | Cotavance™ with Paccocath® coating technology | Paclitaxel with iopirimde formulation (Paccocath® technology) |
| Caliber Therapeutics, Inc. | TADD (Targeted Angioplasty Drug Delivery) | Rapalog-based with unknown formulation |
| Cook Group, Inc. | Advance® 18PTX® | Paclitaxel with unknown additive-based formulation |
| Eurocor AG | DIOR® | Paclitaxel without any formulation. (Opto Circuits Ltd. also developing rapamycin- based technology) |
| Invatec s.r.l. | IN.PACT™ Amphirion | Paclitaxel with FreePac™ hydrophilic formulation |
| Lutonix, Inc. | Unknown | Paclitaxel with unknown formulation |

DEBs ARE NOT BORN EQUAL

PEBs Additives

Paccocath Technology

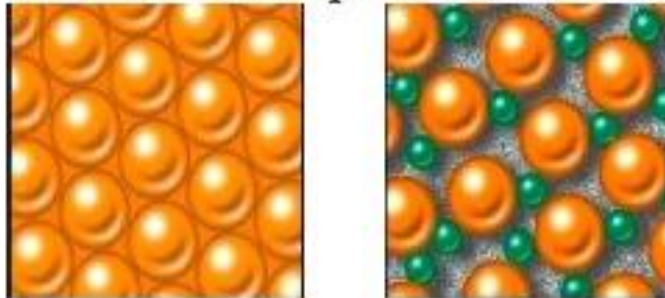
Matrix coating: paclitaxel + hydrophilic pacer (iopromide)



High Tissue Concentration

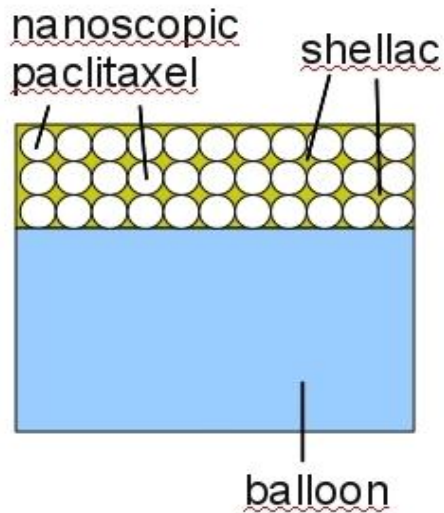
FreePac Technology

Paclitaxel + separator molecule

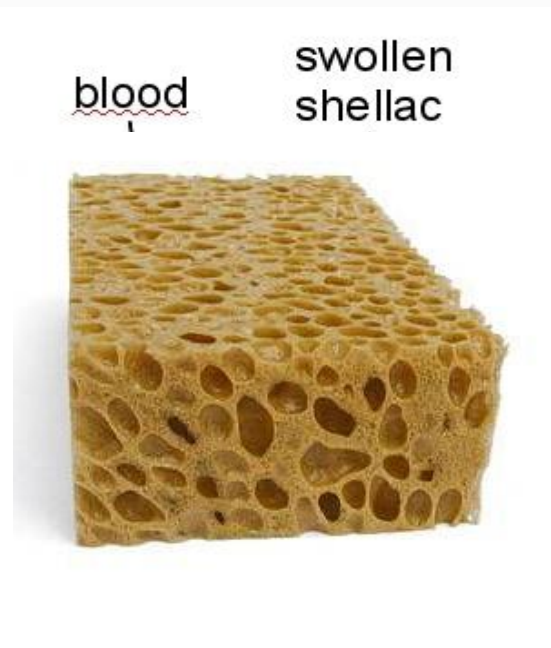


- Porous coating with an high contact surface between the lipophilic drug molecules and vessel wall
- Uniform and complete release of the target dosage at balloon inflation
- High bioavailability of paclitaxel for rapid drug absorption at the level of the vessel wall

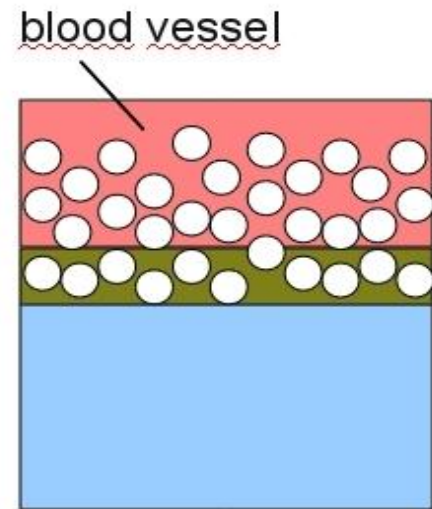
Shellac is not a polymer



coated balloon

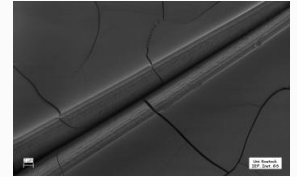


in contact with blood



inflating

Micropipetting technology



Micropipetting ensures the most homogeneous and controllable method of coating application

- ***Coating layer by layer***
- ***Micropipetting allows coating solution to go into pockets under folds***
- ***No-thickening by layer coating***
- ***Only 6 μm layer thickness***

Advantages of the micropipetting technology

- **100% dose control**
- **Homogeneous coating over length and diameter**
- **Reproducibility of appearance, dosage, homogeneity**
- **Balanced adherence and drug transport properties**

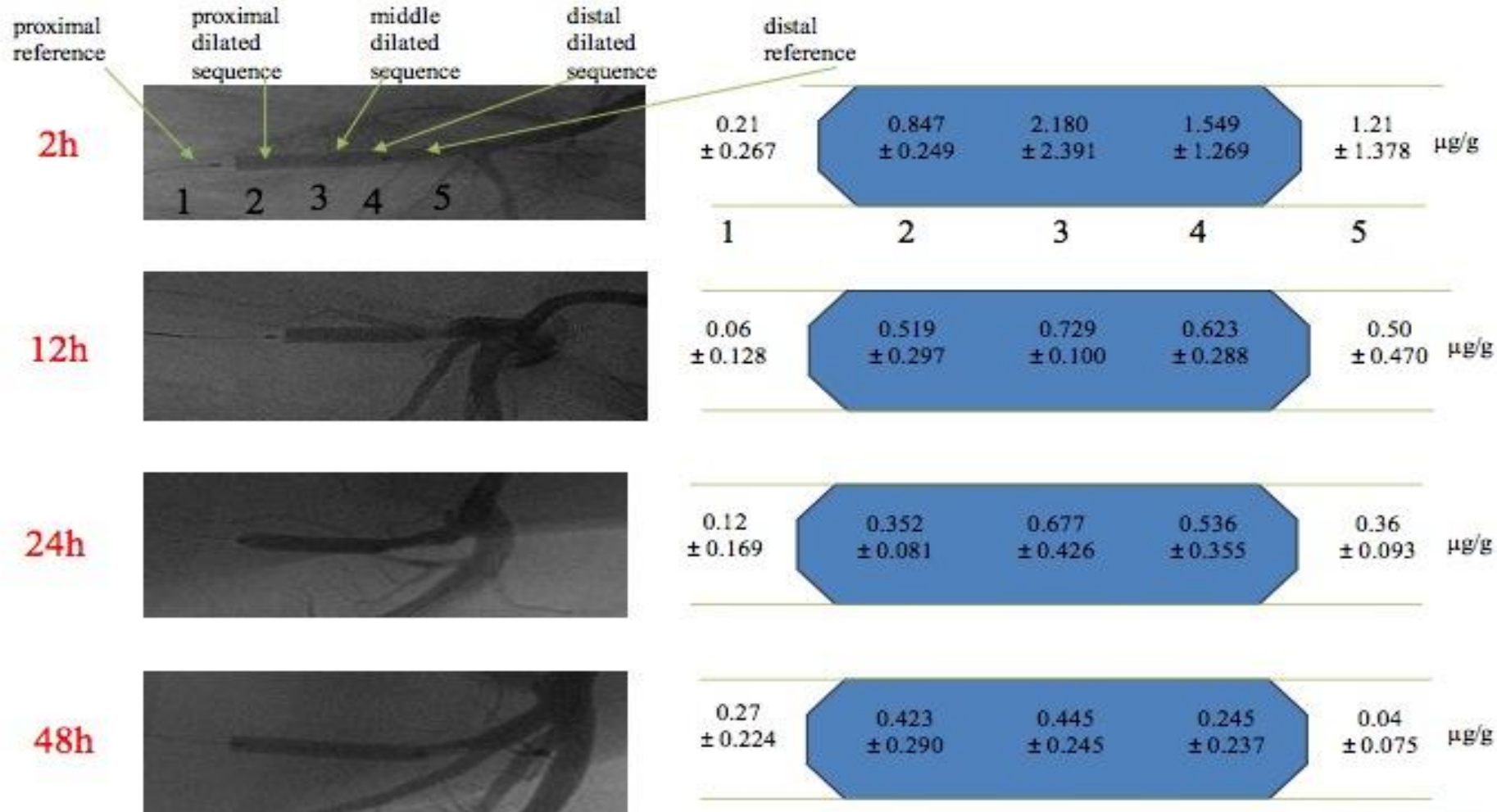
| Requirement | Dose control | Reproducibility | Homogeneity | Effect |
|----------------|------------------|------------------|------------------|-------------|
| Spray coating | Poor | Good | Very good | Mid |
| Dip coating | Very poor | Poor | Poor | Very low |
| Micropipetting | Very good | Very good | Very good | High |

Drug of Choice Should Have Certain Characteristics

- Lipophilic characteristics (efficacy of local drug delivery is 10-20 x higher than hydrophilic drugs)
- High adsorption rates
- Rapid uptake by intima in order to compensate for short contact time
- High retention rate
- Optimal and sustained effect
- Dose dependant effect associated with a large therapeutic window

16 domestic pigs (28±3 kg, 75% male, LAD LCx and RCA; 6 pigs with bifurcation-interv.)

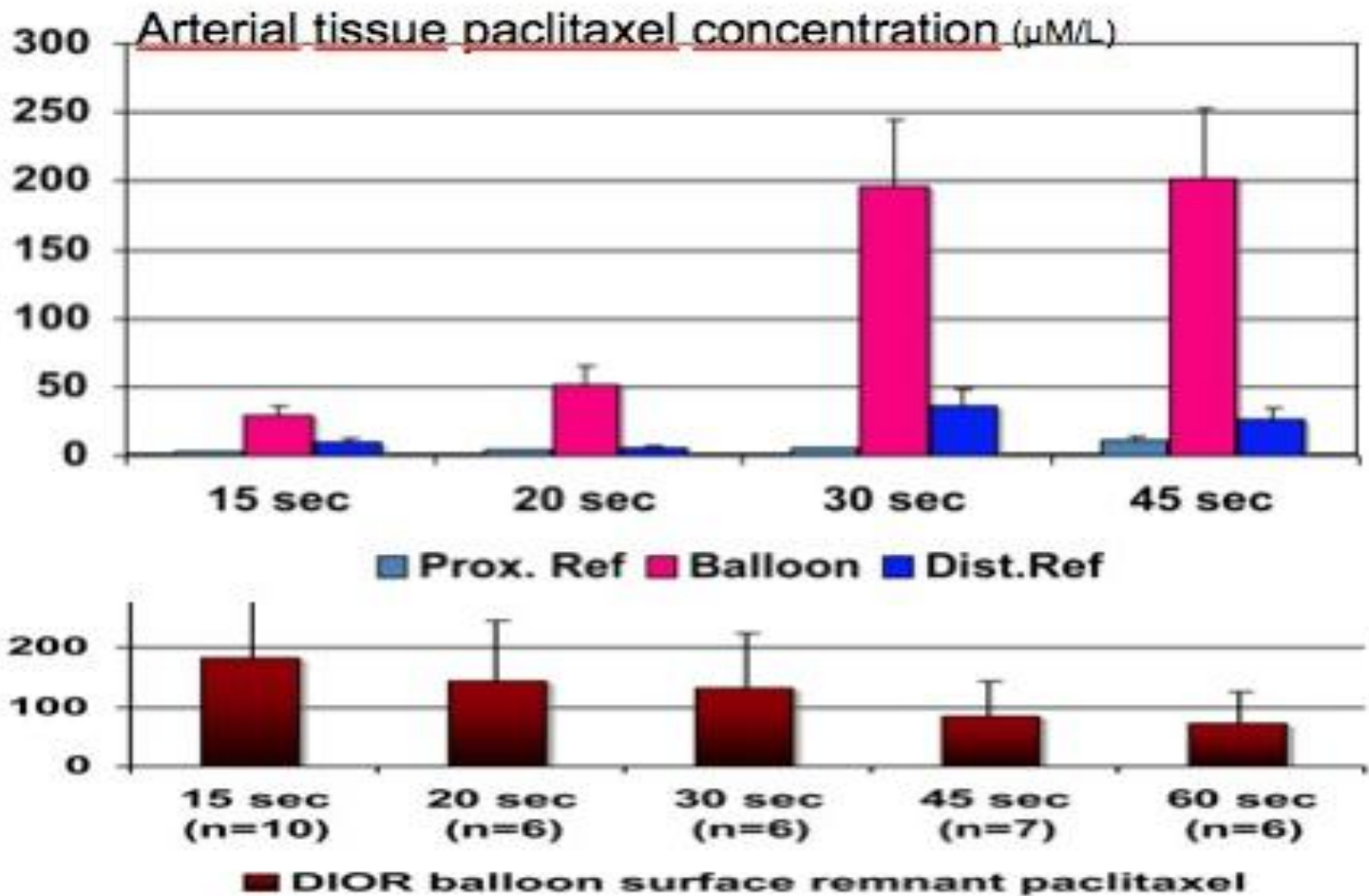
Arterial tissue paclitaxel concentration: 2, 12, 24, 48 h post-dilatation



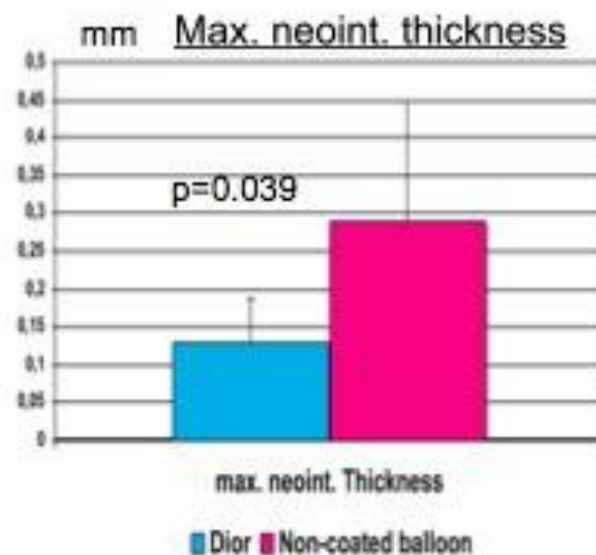
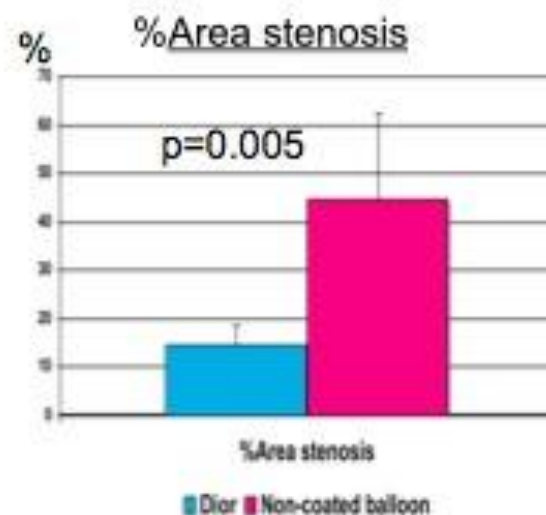
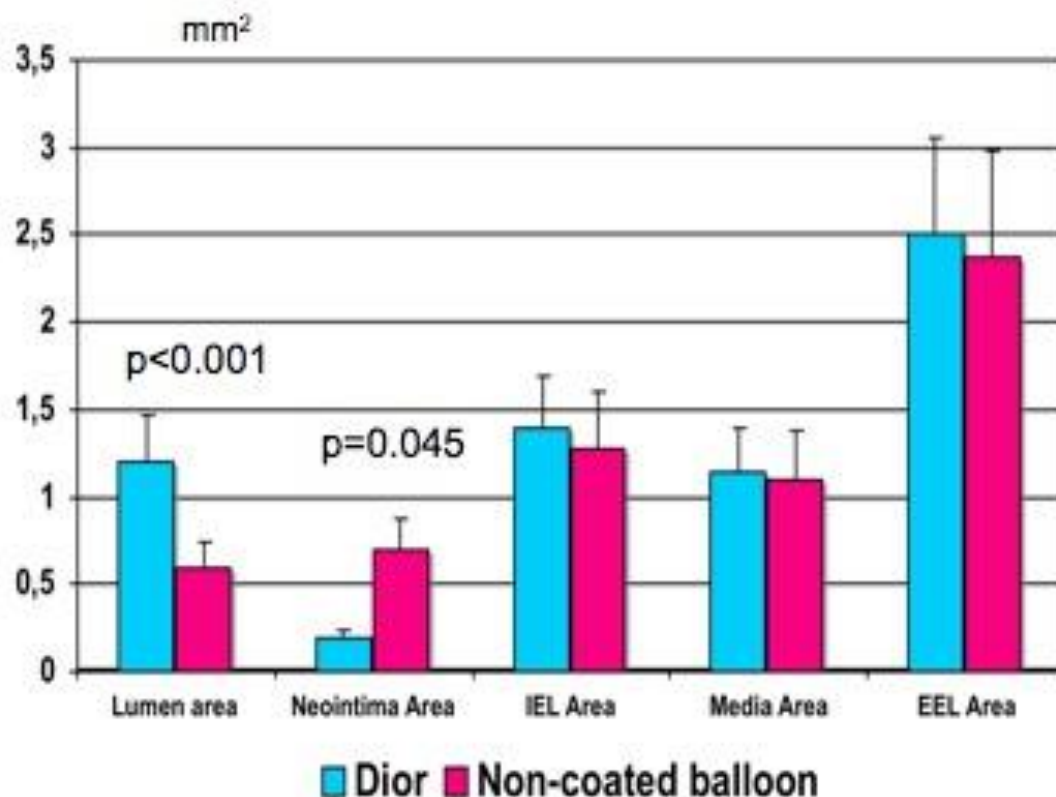
Gyöngyösi et al Coron Artery Dis 2008; 19: 243-7




Time-dependent tissue concentrations of paclitaxel from the Dior balloon N=29**



Quantitative histological results N=12 **

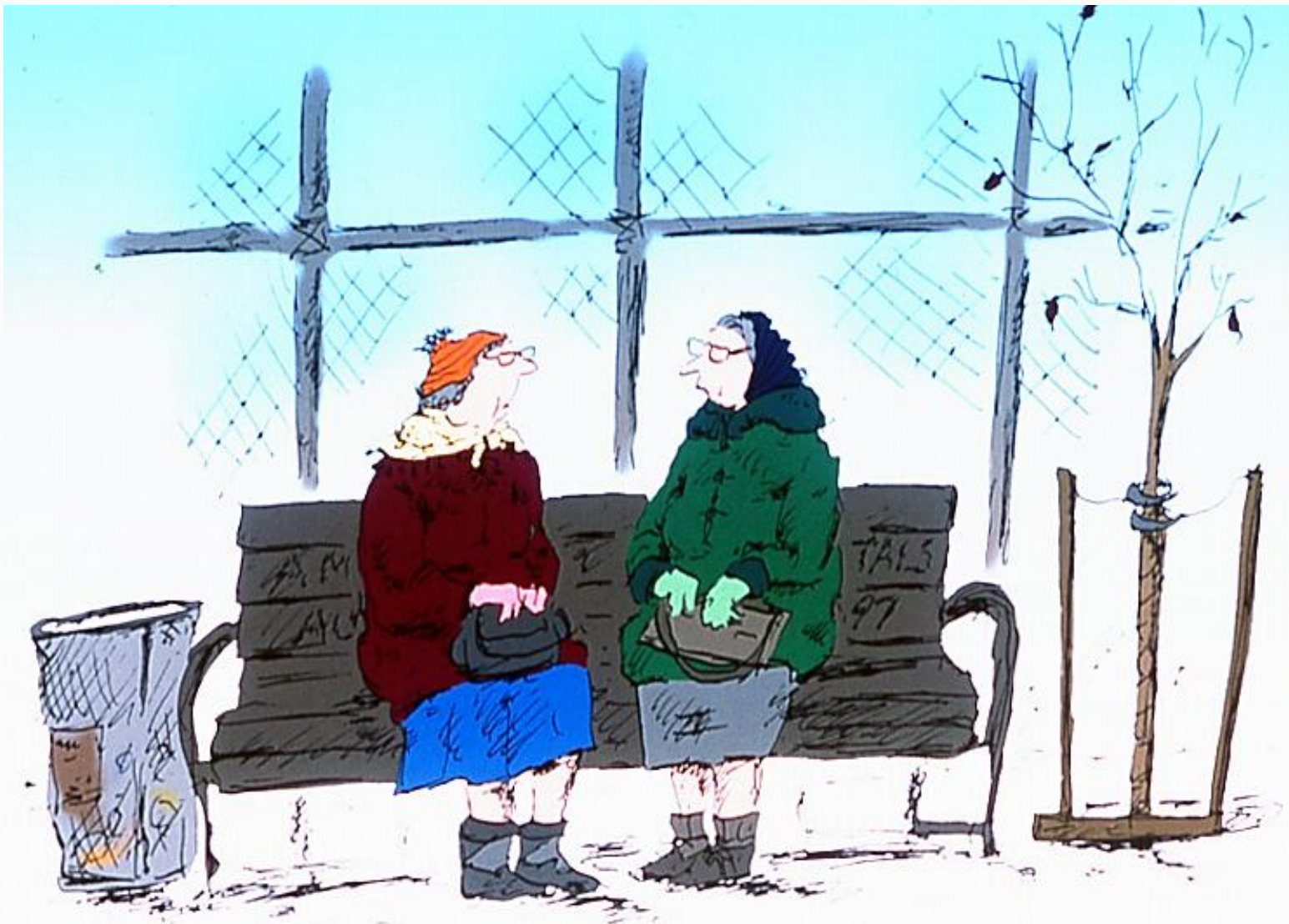




Opportunities
straight ahead

Take Home Messages

- Non stent based drug delivery system especially useful for complex coronary/ peripheral lesions when double/triple layered stent may be avoided
- Early results of DIOR™ DEB have established feasibility, safety and efficacy in the treatment of ISR and bifurcation lesions
- Reduction of dual antiplatelet duration in DEB use provides a useful alternative to situations where DES stent implantation or prolonged dual antiplatelet therapy is not desirable
- Comparative effectiveness between DES remains unknown and it is not likely that same efficacy be obtained with different technology platforms
- More information needed on the ideal tissue concentration and the effective doses of drugs to be delivered via non-stent based system
- Larger randomised studies and registry results needed to fully establish the role of DEB in contemporary PCI practice



“Am I the smart one and you’re the pretty one or is it the other way around?”