

The family of drug eluting balloons from Eurocor preclinical results

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Potential conflicts of interest

Speaker's name: Mariann Gyöngyösi

I have the following potential conflicts of interest to report:

- Research contracts
- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

X I do not have any potential conflict of interest

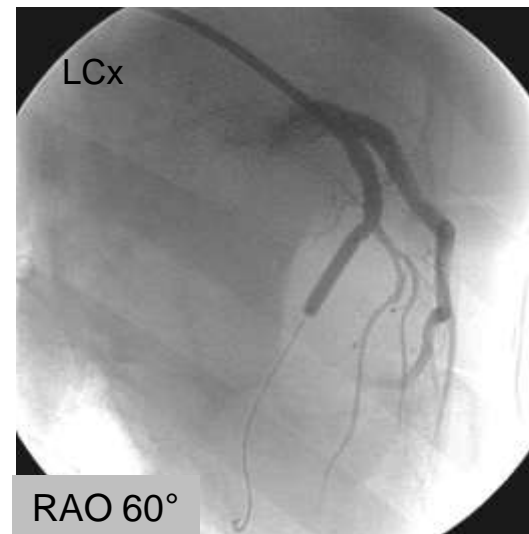
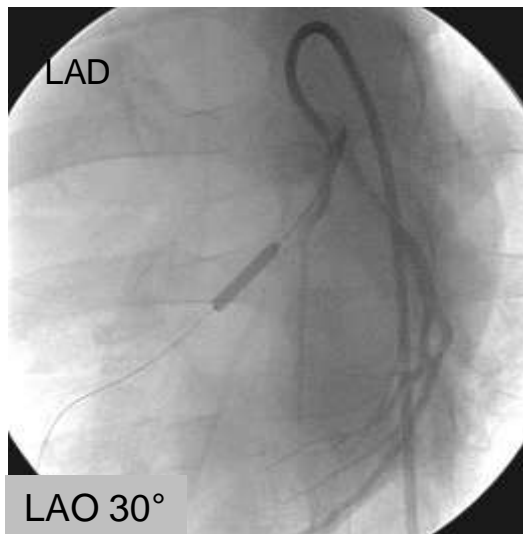
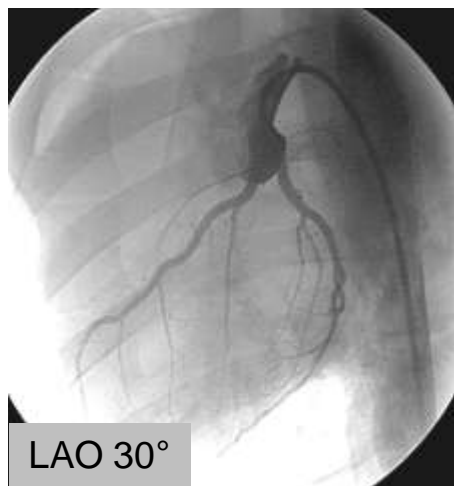
DIOR

The family of drug-eluting balloons of Eurocor:

Preclinical experiments and results

1. 1st Generation DIOR for coronary PCI
2. 2nd Generation DIOR for coronary PCI
3. DEB-Balloon Aortic Valve Valvuloplasty
4. Coated cutting balloon for in-stent restenosis
5. FREEWAY (DEB) for peripheral angioplasty

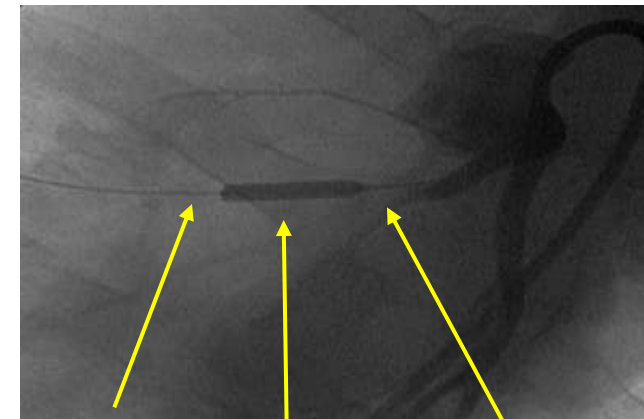
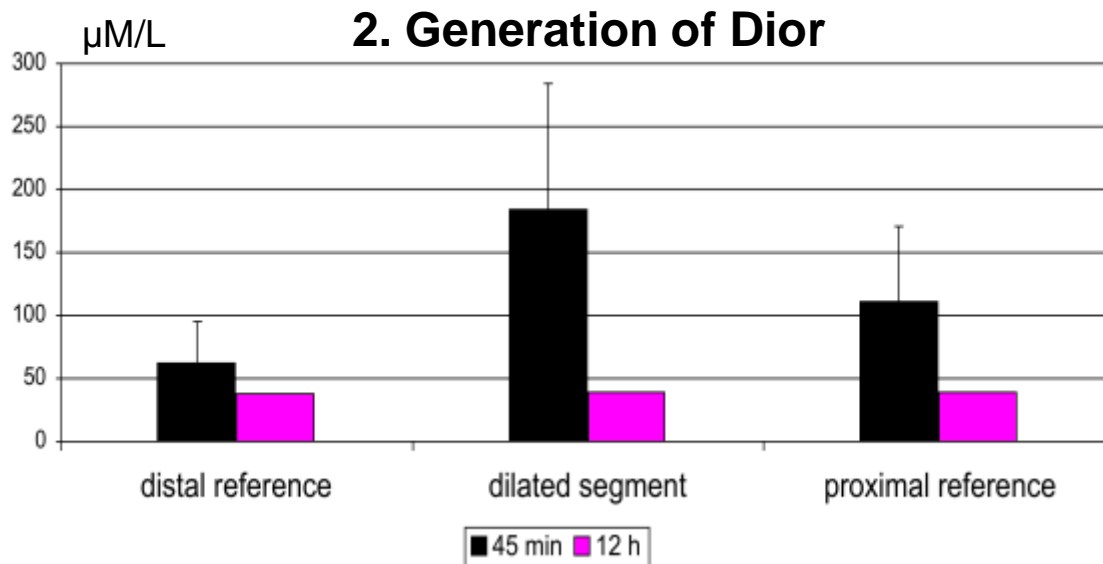
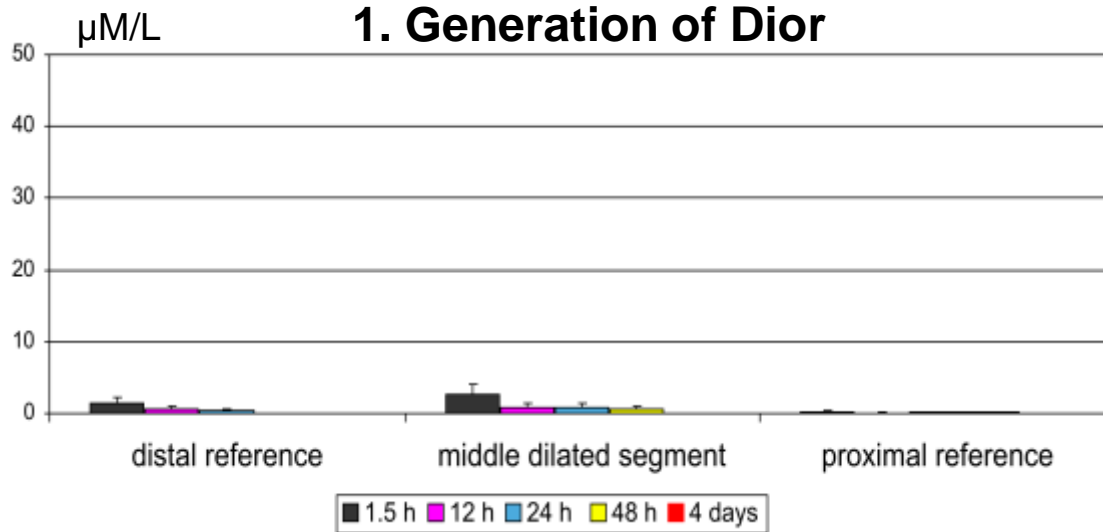
Single vessel Dior
balloon dilatation



Bifurcation
Dior balloon
dilatation



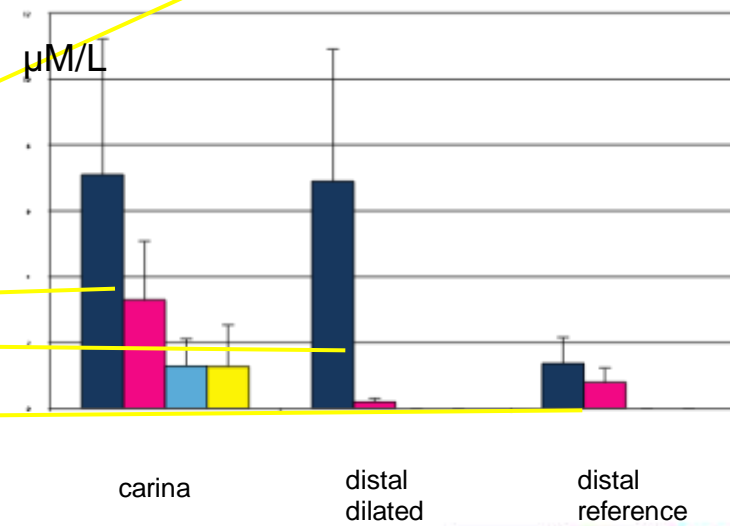
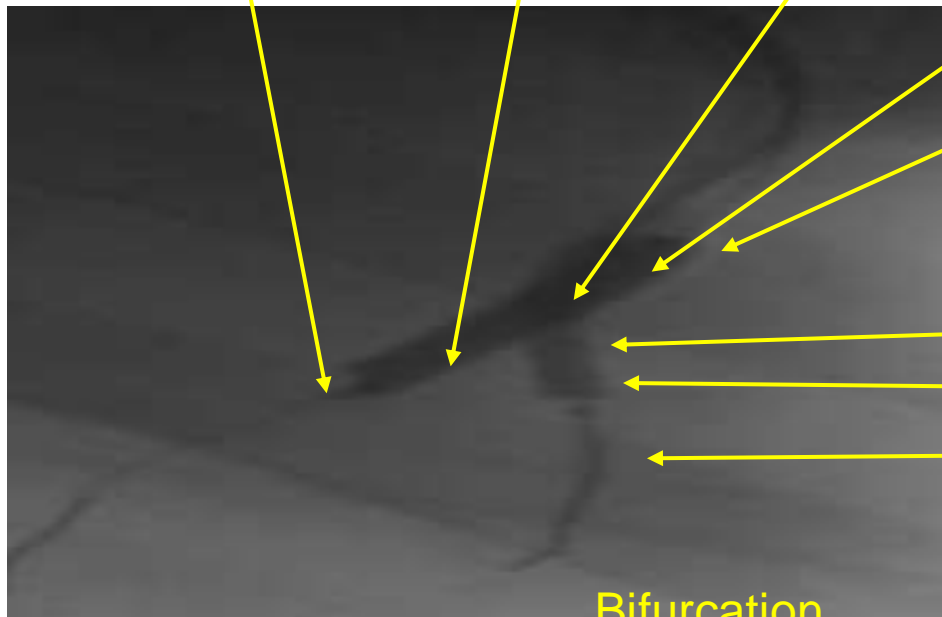
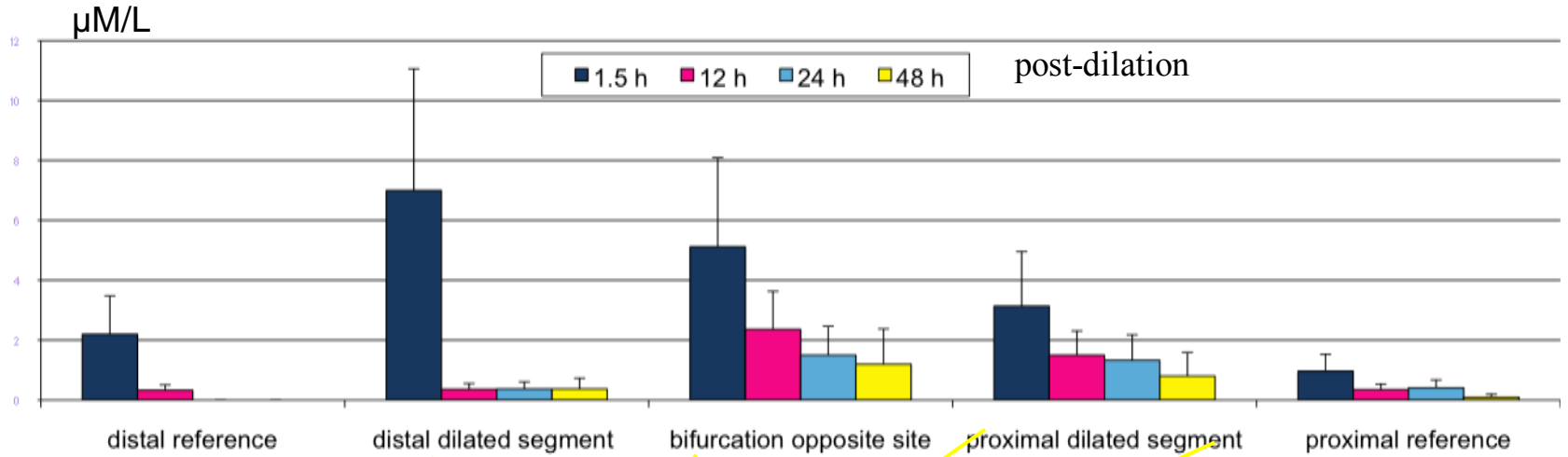
CORONARY ARTERY TISSUE PACLITAXEL CONCENTRATION



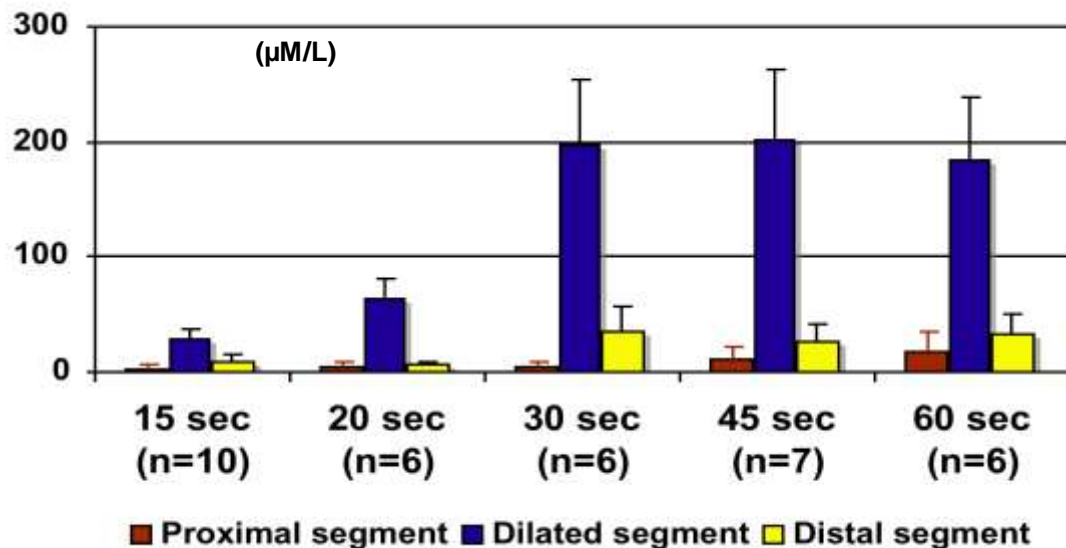
Distal ref. Dilated Proximal ref.

Inflation time: 2x30 sec

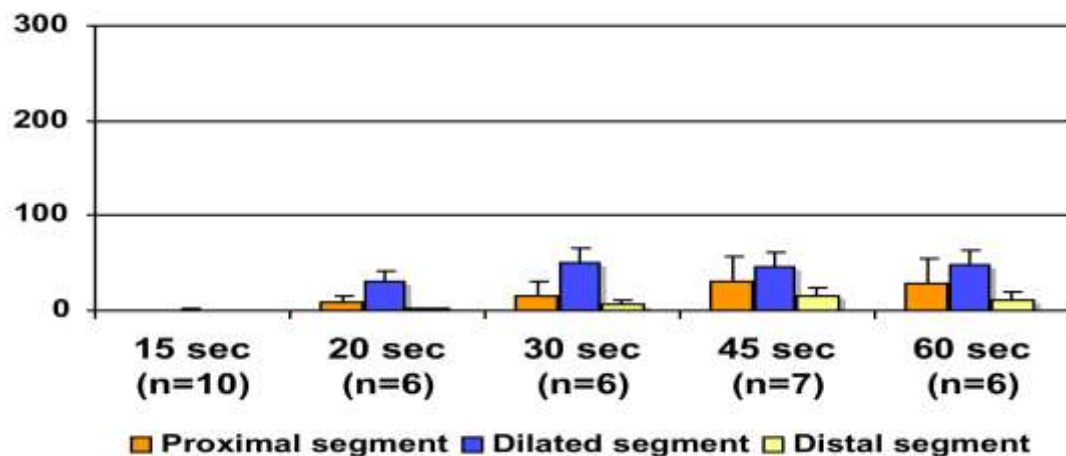
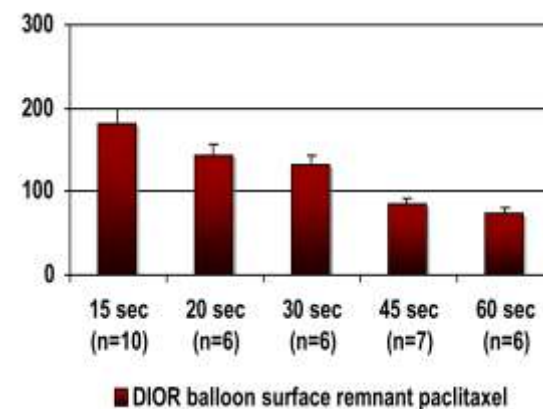
CORONARY ARTERY TISSUE PACLITAXEL CONCENTRATION



INFLATION TIME-DEPENDENT TISSUE PACLITAXEL CONCENTRATION



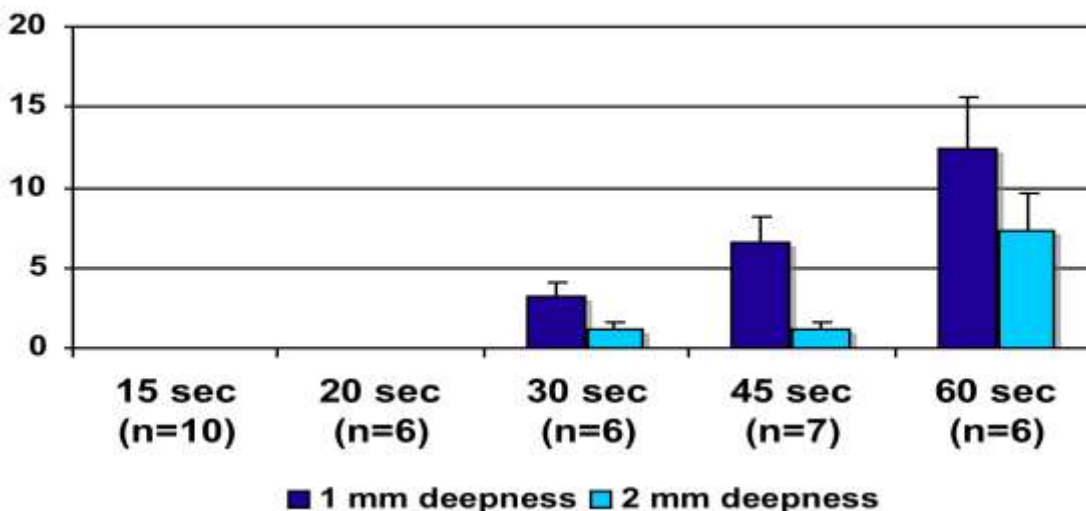
45 min post-dilation



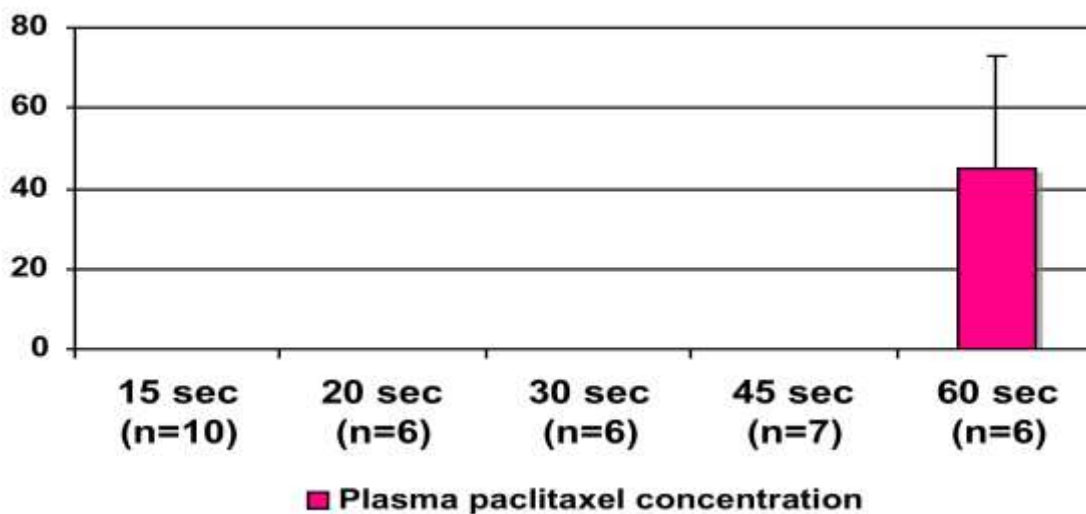
12 h post-dilation

Posa, Gyöngyösi et al.
Catheter Cardiovasc Interv 2010 (in press)

INFLATION TIME-DEPENDENT VERTICAL PENETRATION OF PACLITAXEL



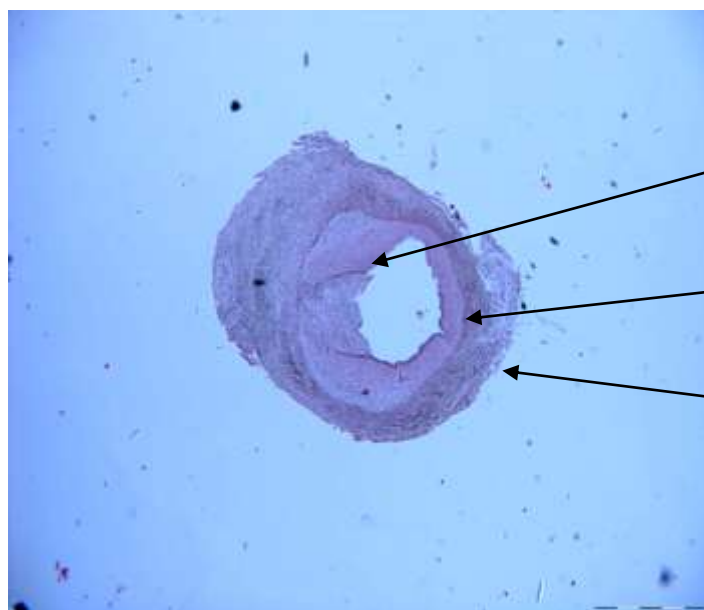
45 min post-dilation



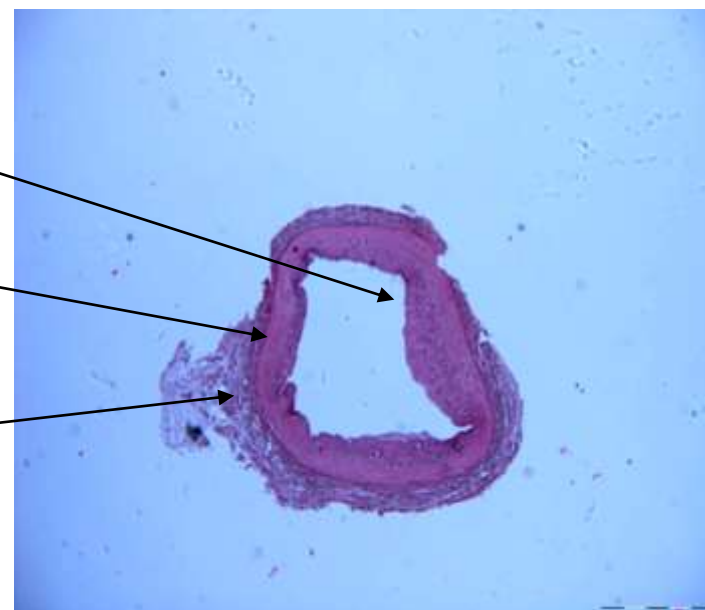
45 min post-dilation

Posa, Gyöngyösi et al.
Catheter Cardiovasc Interv 2010 (in press)

HISTOLOGICAL RESULTS 14 DAYS POST-BALLOON OVERSTRETCH INJURY



Uncoated balloon



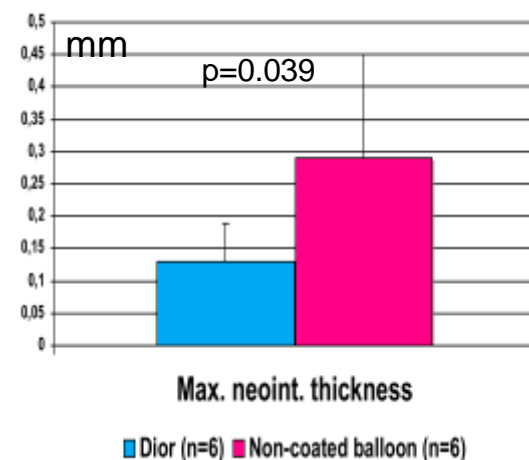
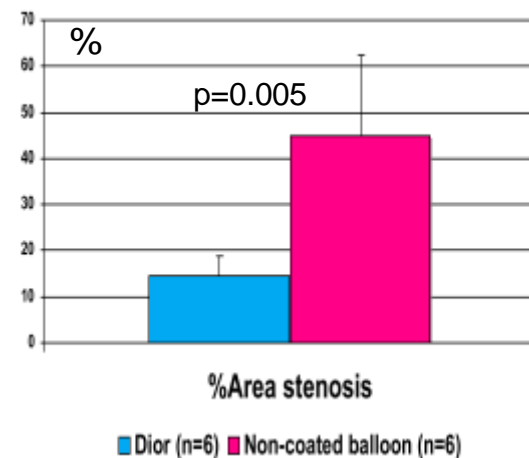
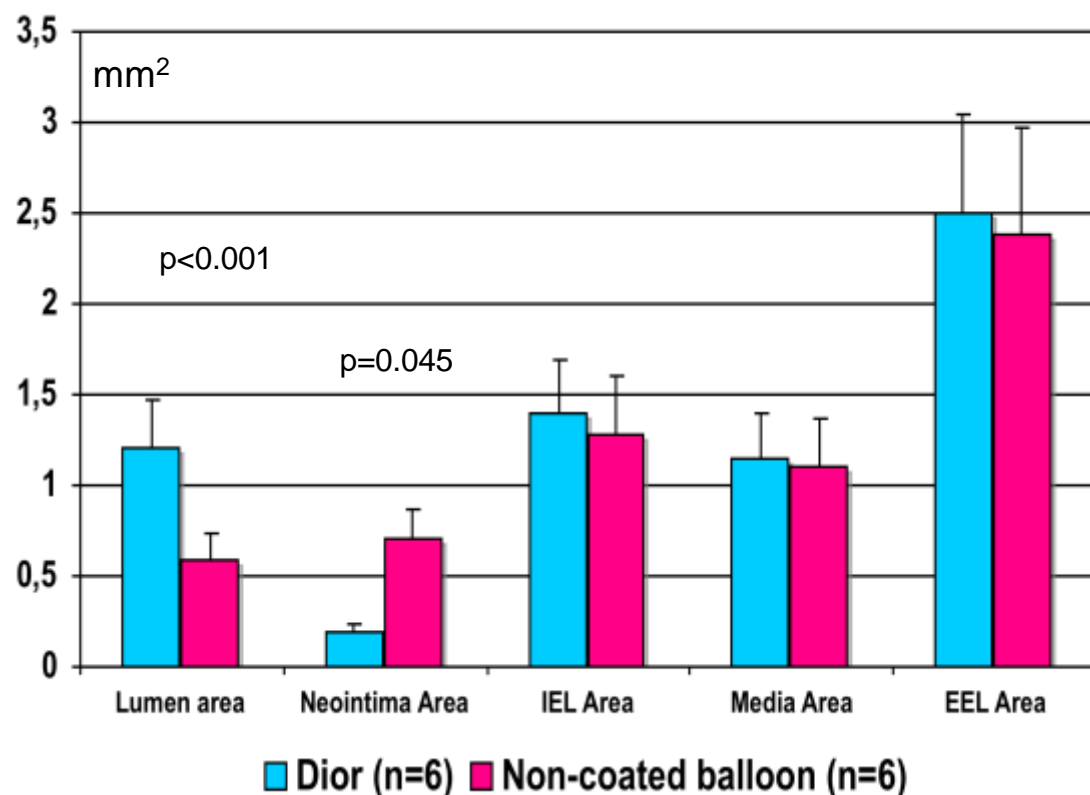
Dior balloon

neointima

media

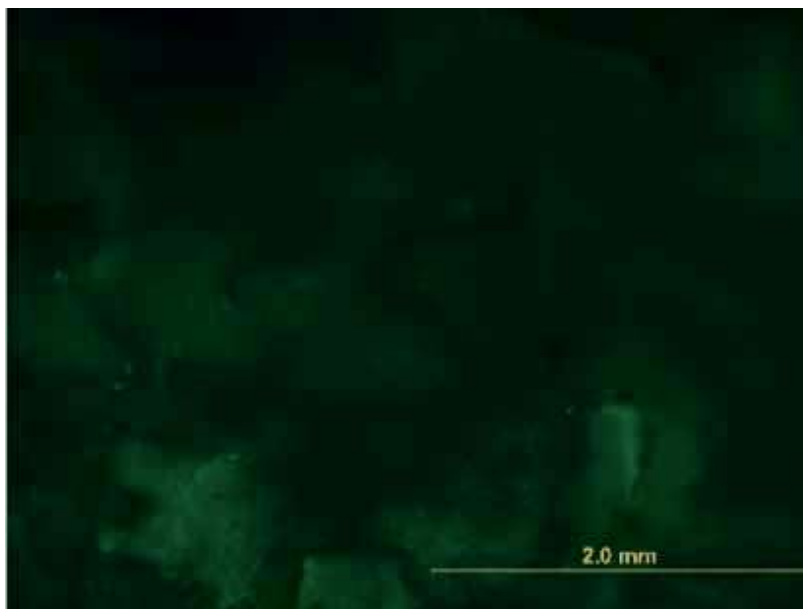
adventitia

QUANTITATIVE HISTOLOGY 14 DAYS POST-BALLOON OVERSTRETCH INJURY

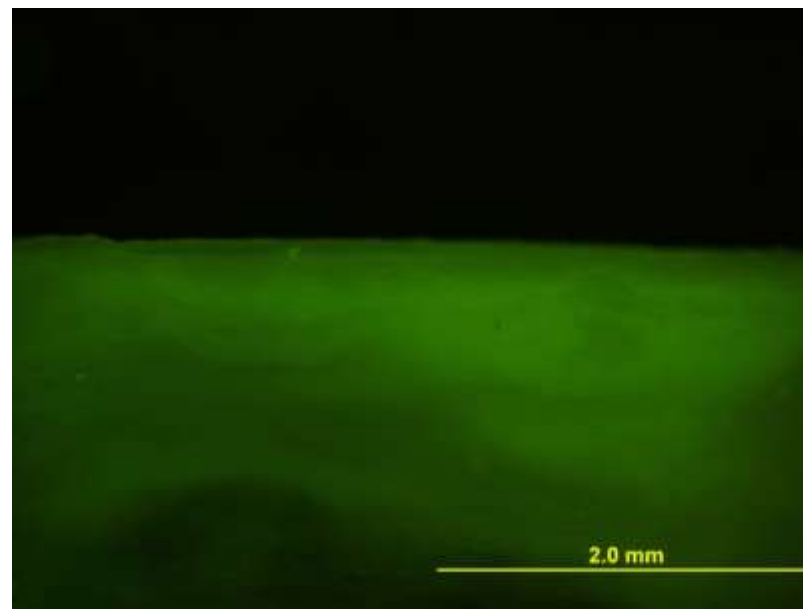


ENDOTHELIAL SURFACE OF PORCINE CORONARY ARTERIES 1H AFTER PCI

Replacing the paclitaxel through fluorescent-conjugated paclitaxel (Oregon green 488)



Artery post-paclitaxel-eluting stent:
small amount of drug penetrated into the
arterial wall, uneven drug distribution

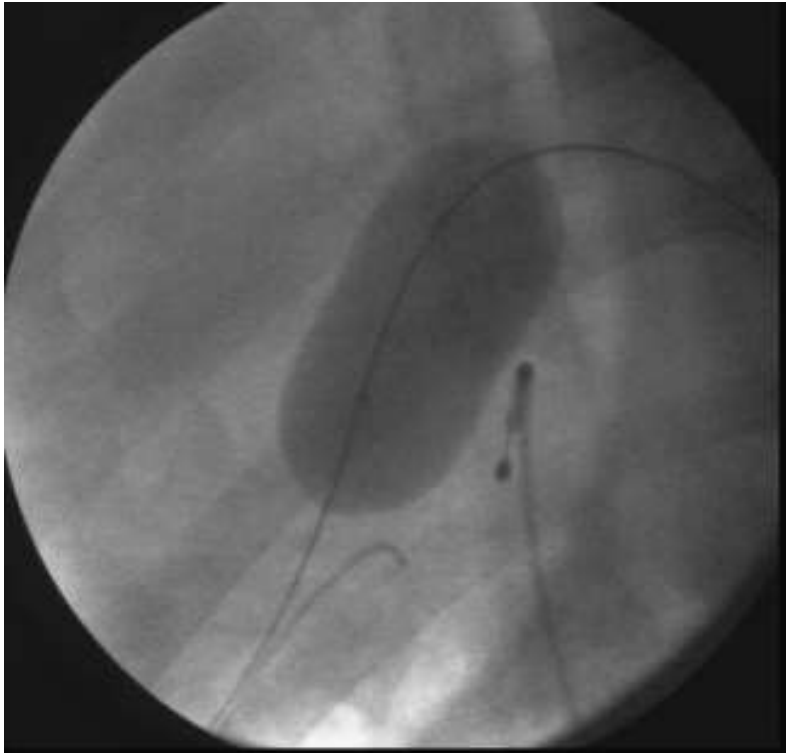


Artery post-paclitaxel-eluting DiOR balloon:
large amount of drug within the arterial wall,
uniform drug distribution

DEB FOR VALVULOPLASTY IN EXPERIMENTAL AORTIC STENOSIS

1. Balloon aortic valve valvuloplasty (BAV) is the choice of therapy, if aortic valve replacement (AVR, surgical or percutaneous) cannot be performed due to serious comorbidity, or as a bridge to surgery in hemodynamically unstable patients who are at high risk for AVR.
2. The drawback of the BAV is the moderate acute success and the lost of the valve area gain within the first 6-12 months, due to hyperplastic reaction of the AV post-BAV (active capillary growth, cellular proliferation with granulation tissue and fibrosis).
3. The use of drug-eluting balloon for BAV might prevent the restenosis of the aortic valve due to inhibition of the active inflammatory processes and cell migration by penetration of the paclitaxel into the valve and aortic ring.

DRUG DELIVERY AT THE AV TISSUE WITH A PACLITAXEL-ELUTING VALVULOPLASTY BALLOON



Ao root

After 2 inflations: 0.13 ± 0.09 $\mu\text{g}/\text{ml}$

After 4 inflations: 0.32 ± 0.26 $\mu\text{g}/\text{ml}$

AV leaflets

After 2 inflations: 0.34 ± 0.05 $\mu\text{g}/\text{ml}$

After 4 inflations: 1.48 ± 1.86 $\mu\text{g}/\text{ml}$

LVOT

After 2 inflations: 0.06 ± 0.03 $\mu\text{g}/\text{ml}$

After 4 inflations: 0.07 ± 0.01 $\mu\text{g}/\text{ml}$

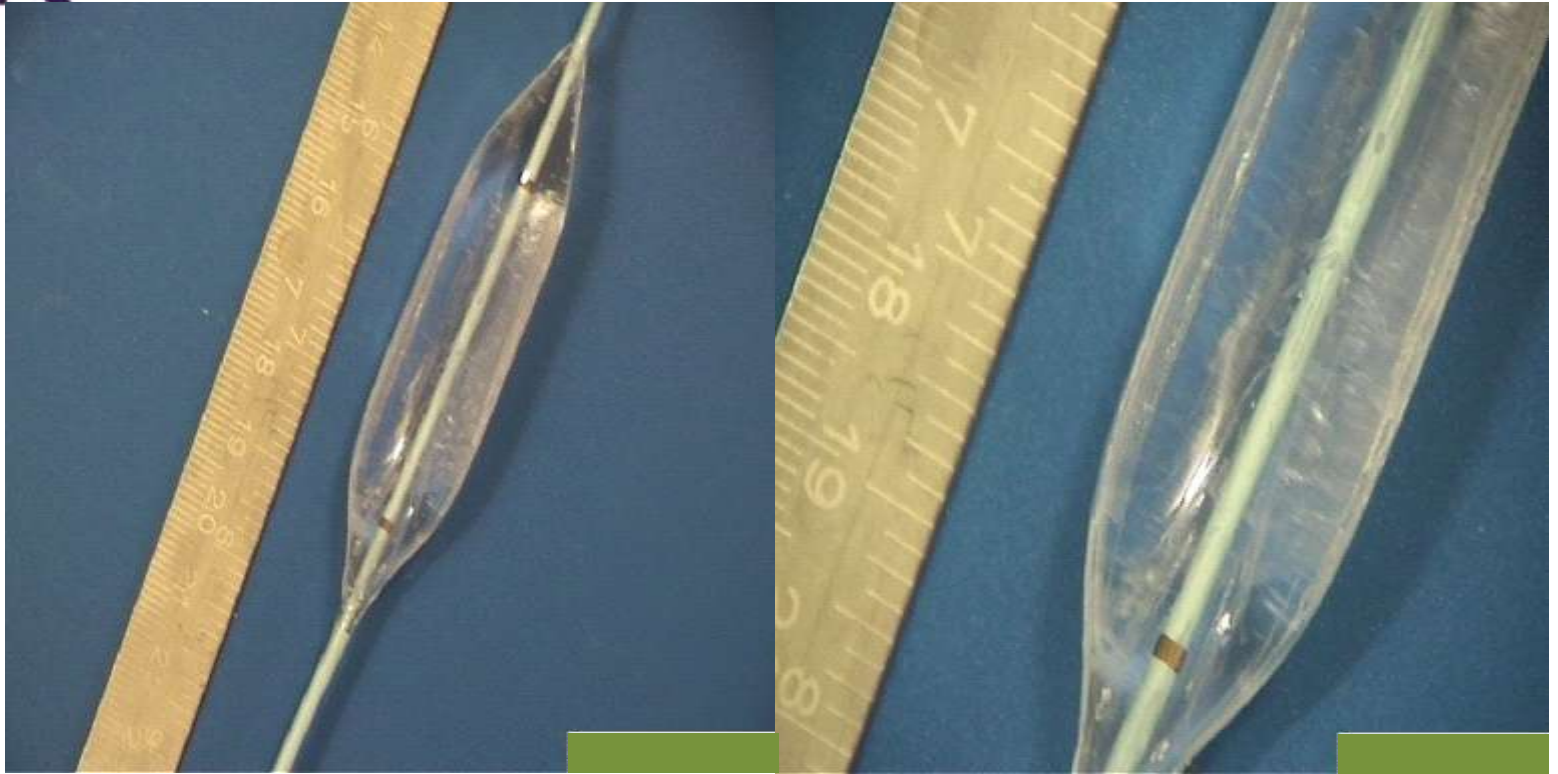
8 healthy domestic pigs

BAV with 22/24 mm paclitaxel-eluting balloons ($2 \mu\text{g}/\text{mm}^2$, DIOR technology)

2 or 4 X 15-second inflations

Spargias K, Athen

Paclitaxel-eluting valvuloplasty balloon



DIOR II™ Technology (Eurocor GmbH)

- Paclitaxel loading/balloon surface: $3 \mu\text{g}/\text{mm}^2$
- Coating method: directly on balloon surface, 1:1 mixture of aleuritic & shellolic acid with Paclitaxel
- Complete drug release @ 30 sec

STUDY PROTOCOL OF AS

- Cholesterol-rich diet (0.5% cholesterol) + 50000 IU/day Vit. D2*



3 months

- General anaesthesia, TTE,
- Access : right carotid artery, Aortography
- Pressure measurements of the ascending aorta and left ventricle
- BAV randomly with coated or uncoated balloon (8.0/20 mm, 3x10 sec)



3 weeks

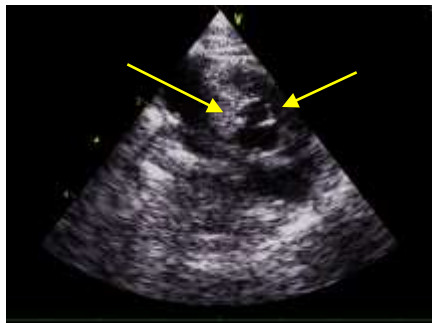
- General anaesthesia, TTE,
- Access: right femoral artery, Aortography
- Pressure measurements of the ascending aorta and left ventricle



- Histology: leaflet thickness, Masson's trichrom in all, PCNA

*Drolet et al, JACC 2003;41:1211

BAV IN RABBITS



Echocardiography:
thickened sclerotic
aortic valve



Left ventricle Aorta Left ventricle Aorta



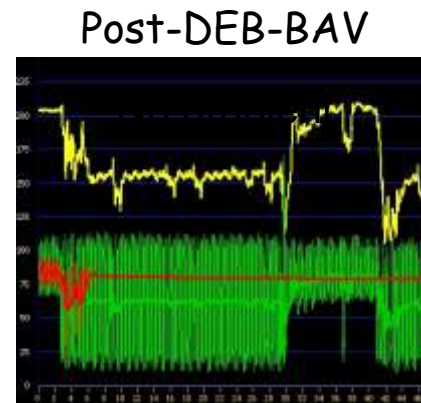
Pre-BAV



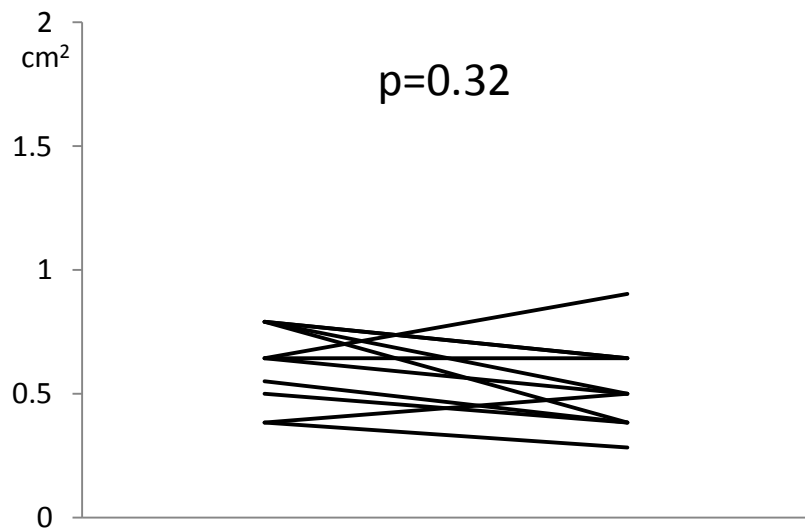
Positioning of
BAV



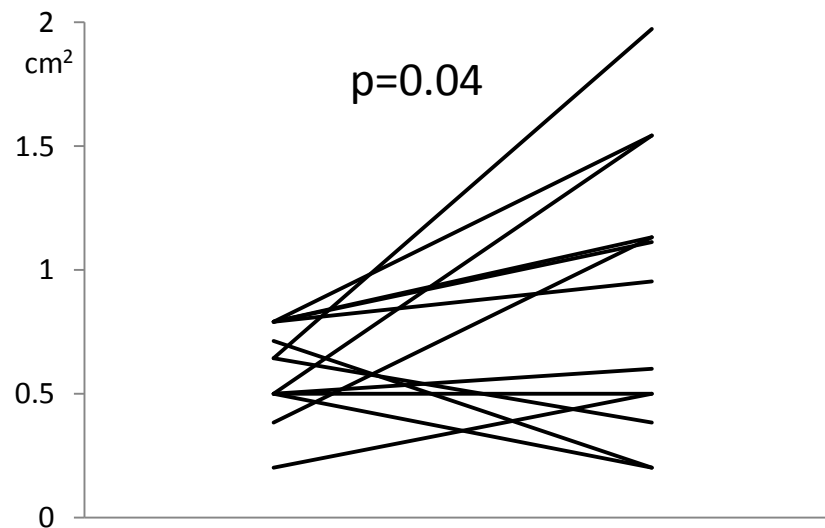
BAV



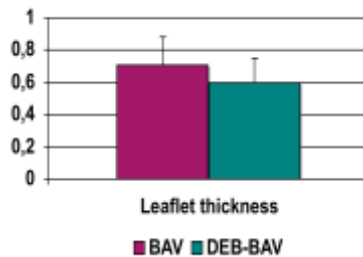
AORTIC VALVE AREA POST-BAV AND AT FOLLOW-UP



Uncoated

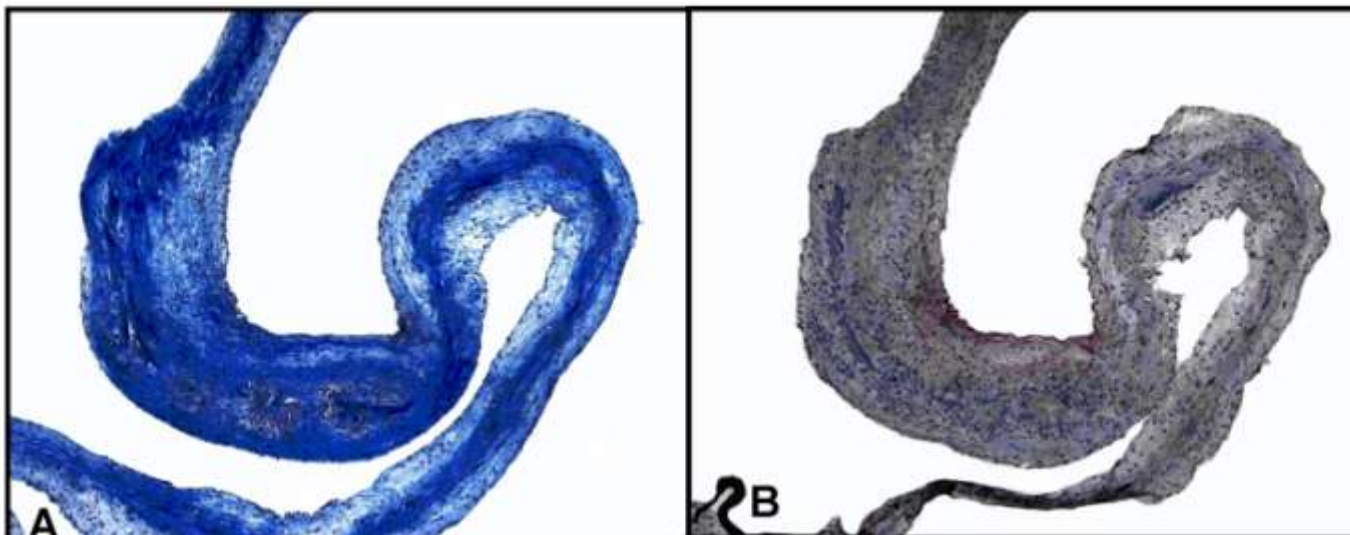


Paclitaxel-coated

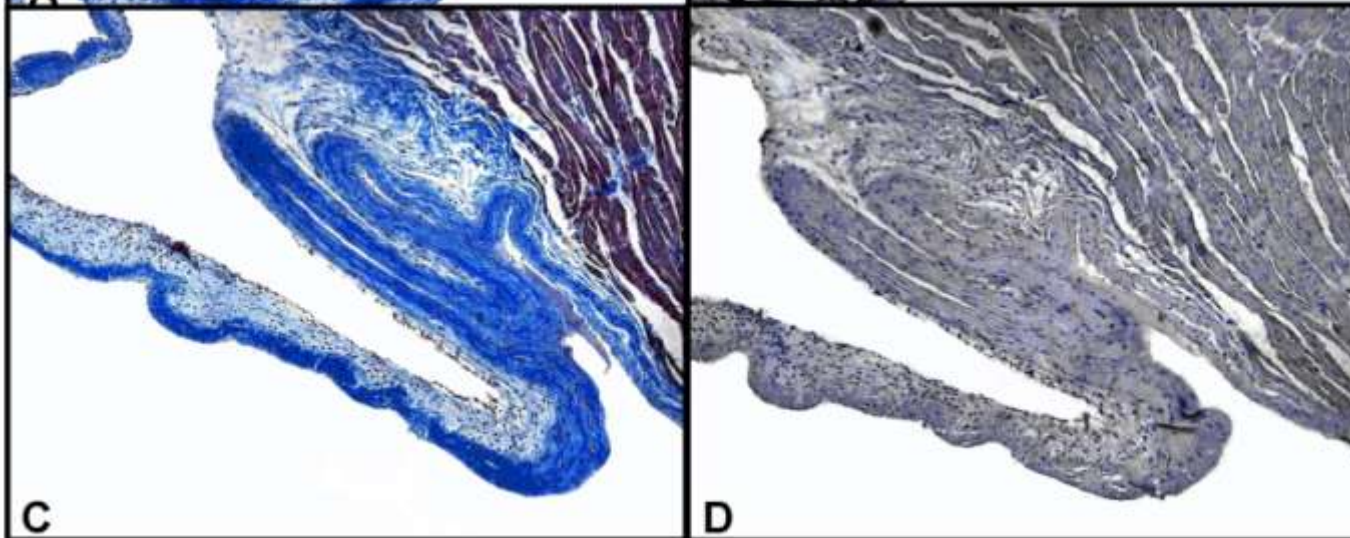


HISTOLOGIC CHANGES OF AORTIC VALVE 1-MONTH POST-BAV

Uncoated



Paclitaxel
coated



Masson's trichrom

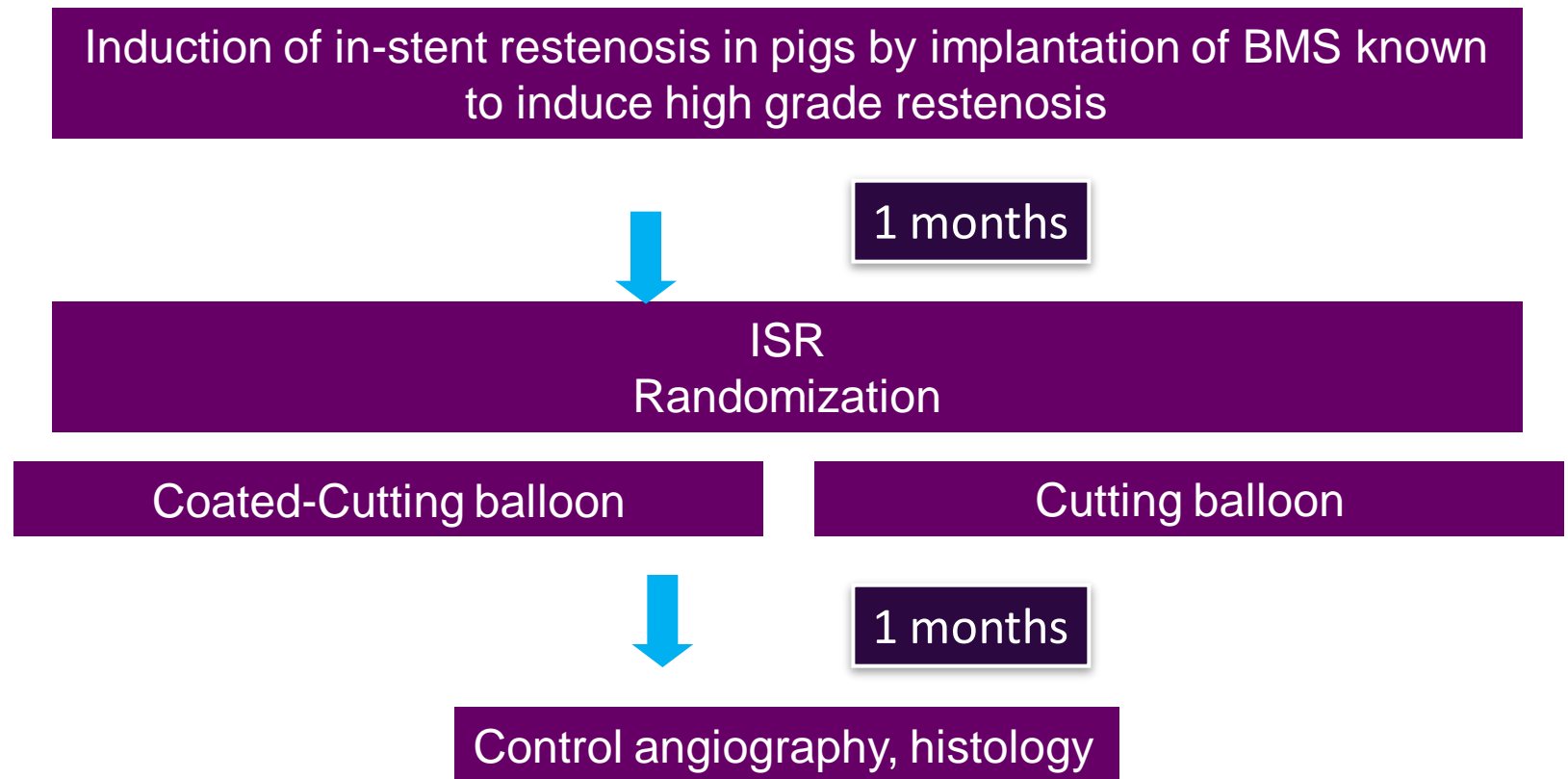
N.Narajam.
Chicago

PCNA

PACLITAXEL-COATED CUTTING BALLOON

for treatment of in-stent restenosis

STUDY DESIGN

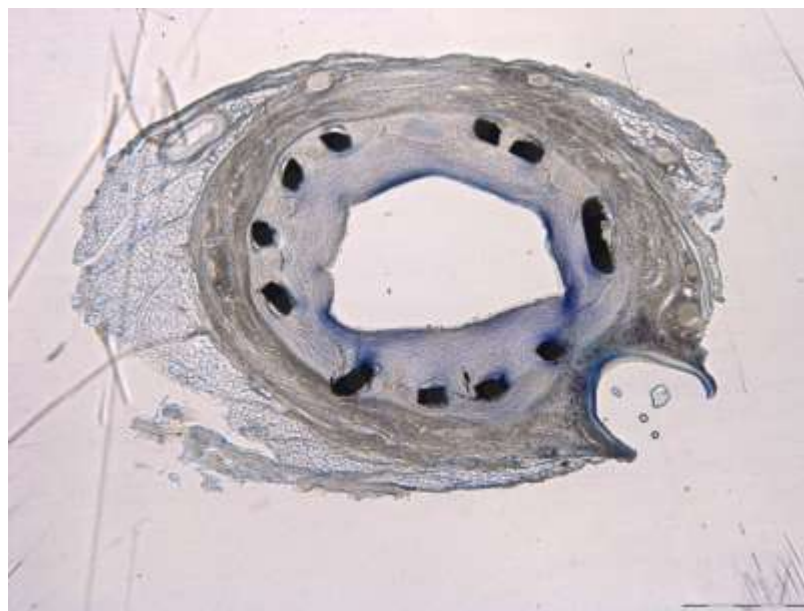


(Sangiorgi G. Italy, Eurocor, Germany)

PACLITAXEL-COATED CUTTING BALLOON for treatment of in-stent restenosis



Coated-Cutting balloon



Cutting balloon

Gyöngyösi et al. ESC Stockholm 2010 accepted abstract



Femoral artery: large elastic artery

Coronary artery: muscular type

Differences:

size

relative compositions of elastic and muscle tissue
in their tunica media

composition of internal and external elastic lamina.

Preclinical Safety study:

measurements of tissue paclitaxel concentration after dilation of the femoral and iliac arteries after use of FREEWAY balloon (Paclitaxel-eluting DEB)

Preclinical Efficacy study:

measurements of neointimal hyperplasia post-overstretch injury after use of FREEWAY (Paclitaxel-eluting DEB) or conventional balloon (randomized)

RESULTS IN PROGRESS

CONCLUSIONS

1. DIOR^{2nd generation} coronary DEB:
 1. a maximal balloon inflation time of 30-45 sec is optimal, reducing effectively the neointimal hyperplasia, and causing less arterial injury and is better tolerated by the patients in clinical scenario.
 2. Longer inflation of the balloon might lead to undesirable release of the drug into the systemic circulation.
 3. Short exposure of paclitaxel to the arterial wall results in penetration of the drug in both longitudinal and vertical directions.
 4. In contrast with DES, the drug delivery is rapid and homogenous using DEB, reaching the maximal tissue drug concentration at the time of the highest level of procedure-induced local tissue injury, which in turn triggers the restenotic and thrombotic cascade.
2. DIOR for DEB-BAV: experimental studies are promising, clinical studies just started
3. Coated cutting balloon using DIOR technology: preclinical results are promising
4. FREEWAY: preclinical results on-going