



Take-Home Message: Drug-Eluting Balloon Taken to the World

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9-14-77



9-16-77



10-20-77



9-16-87



Angiograms of the
first person to
undergo balloon
angioplasty:
10-year study

Advantages of Drug-Eluting Balloon

- 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

Not Every Drug-Eluting Balloon Is The Same

Paccocath Technology

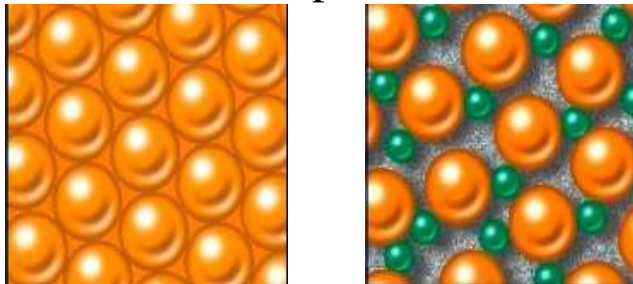
Matrix coating: paclitaxel + hydrophilic spacer (iopromide)



High Tissue Concentration

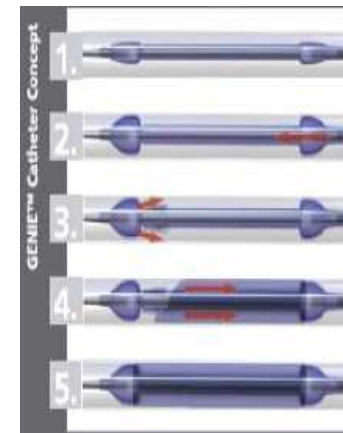
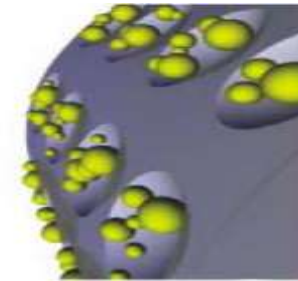
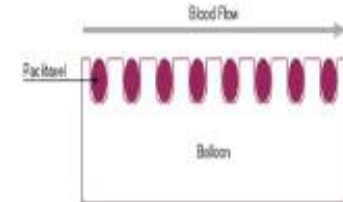
FreePacTechnology

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

- **Eurocor DIOR™ Technology**
Shellac® coating and balloon folds to prevent wash-off. Drug delivery by simple diffusion.
Medium tissue concentration between 50 to 200 $\mu\text{M/L}$
- **Aachen Resonance Elutax Technology**
Drug encased in the surface, 20 % release by diffusion after each inflation.
Tissue concentration??
- **Acrostak Genie Technology**
Liquid drug delivery by operators discretion.
Dosage? Tissue concentration ??



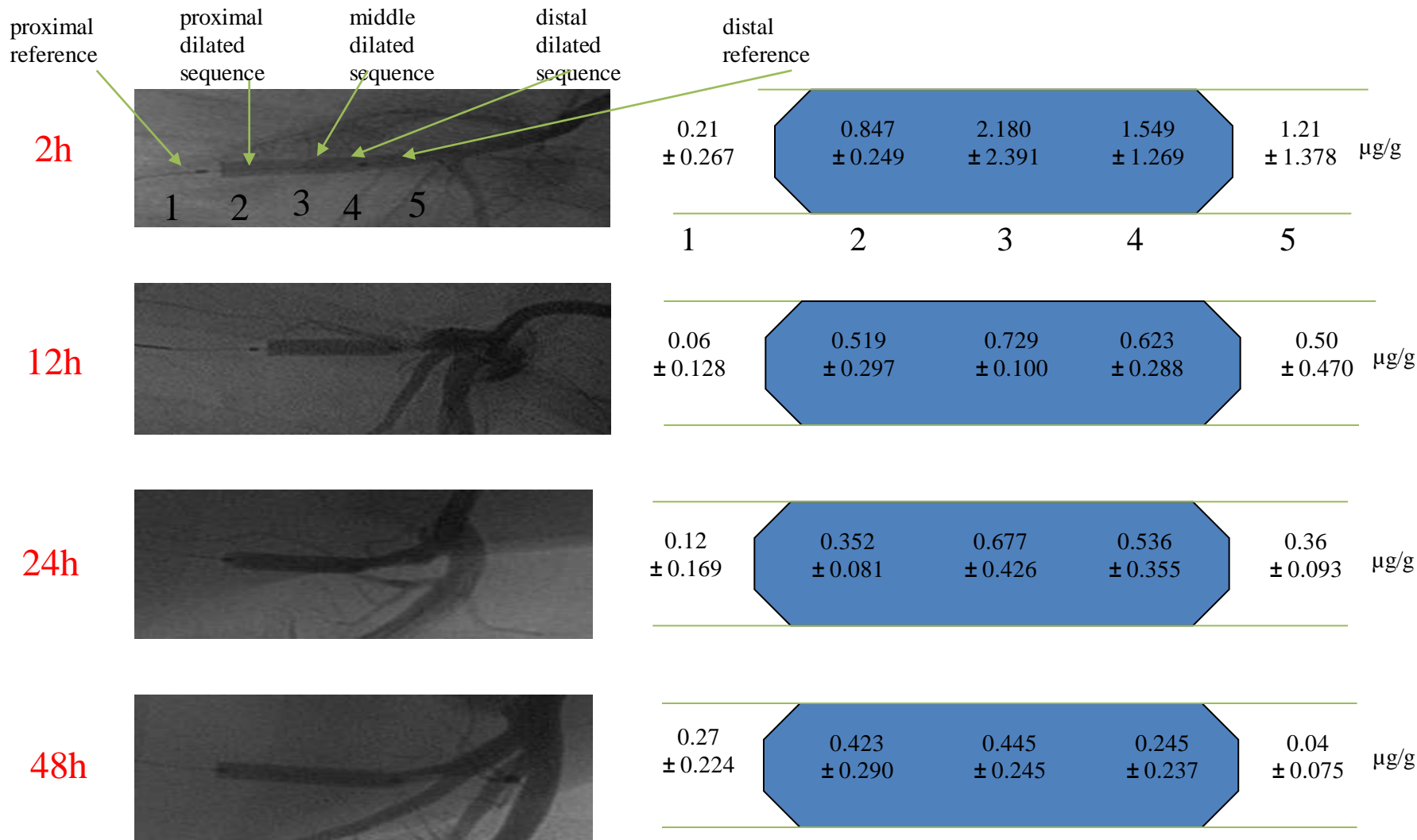
Drug of Choice Must Have Certain Properties

- 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

Arterial Tissue Paclitaxel Concentration After DIOR®

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



Potential Clinical Applications of DEB

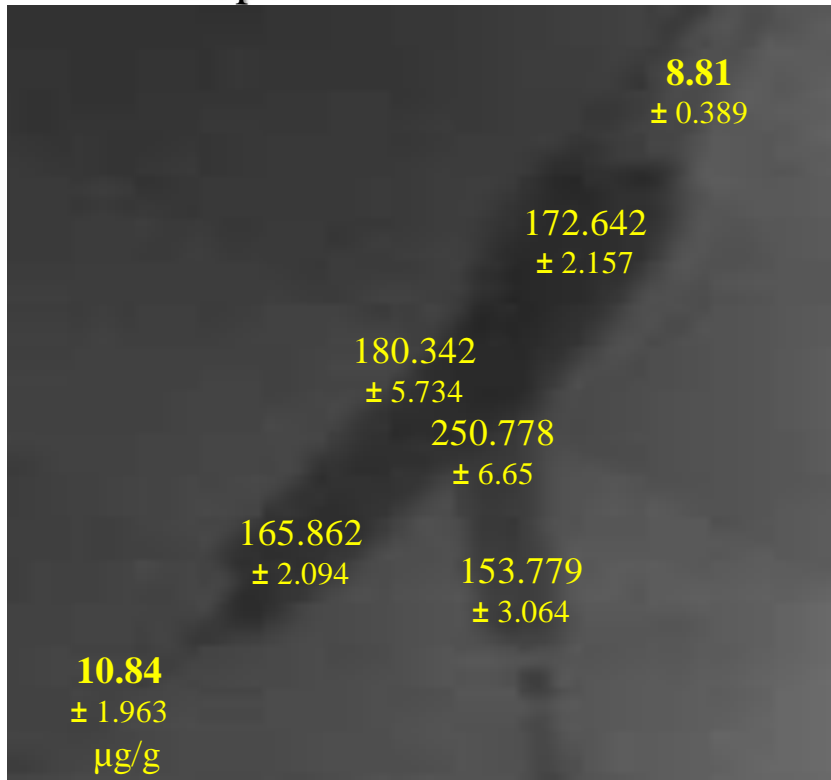
- Recurrent stenosis after balloon or stent PCI (ISR)
- Provisional bifurcation stenting
- Small vessels
- Long lesions
- When prolonged dual antiplatelet therapy is not desirable (eg triple antithrombotic therapy, bleeding diathesis)
- Peripheral intervention

Bifurcation Intervention with DIOR™ Balloon

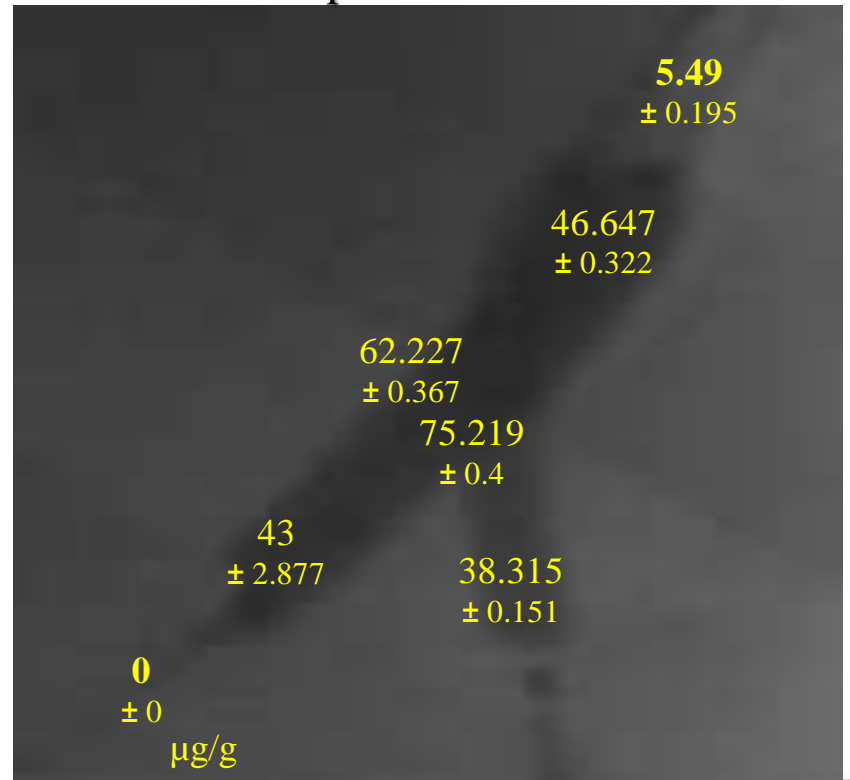


Arterial tissue paclitaxel concentration

2h post-dilatation



12h post-dilatation



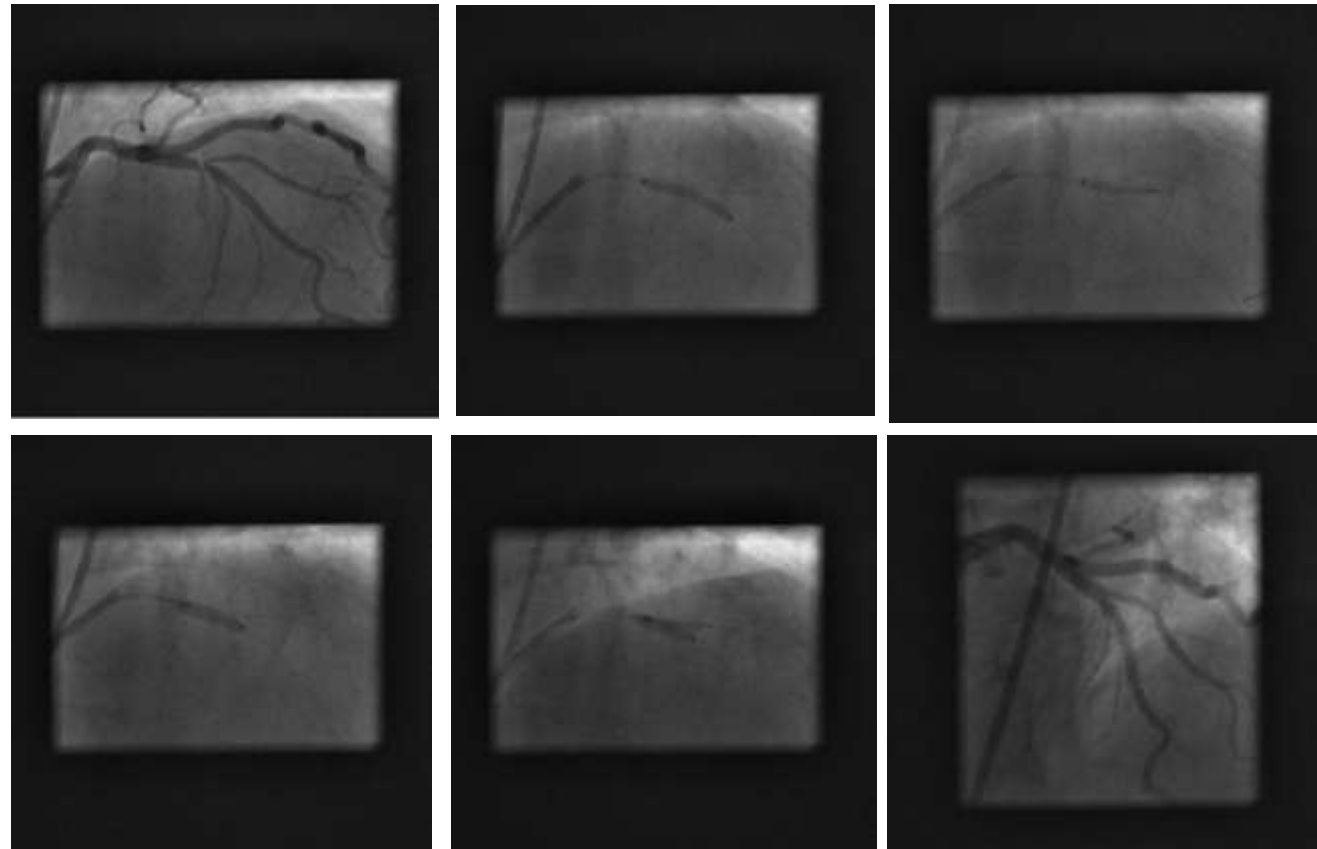
Where Would DEB Fit in Bifurcation Disease ?

- Ease of the procedure
- No scaffolding of the SB ostium required to prevent restenosis
- “Respecting” original anatomy
- No crushing of DES-material (*polymer/ drug*)
- Dilatation of small diameter coronary artery in SB
- Potential decrease in dual antiplatelet therapy with reduced late thrombosis due to absence of multiple polymers

Safety and Efficacy of Drug-Eluting Balloons in Percutaneous Treatment of Bifurcation Lesions: The DEBIUT (*Drug-Eluting Balloon in Bifurcation UTrecht*) Registry

James C. Fonggiday, MD, Pieter R. Stella,* MD, Siyrous Hoseyni Guyomi, MD, and Pieter A. Doevendans, MD, PhD

Wiring of both branches with a 0.014 coronary guide wire	
Pre-dilation with adequately sized compliant balloon of both main branch and side branch at low pressures (≤ 12 atmospheres)	
Dilatation with DIOR balloon: first main branch, then side branch	
Stent deployment in main vessel	
<i>In case of suboptimal result or dissection in the side branch: stent in side branch</i>	
"Kissing" post-dilatation with normal balloons	



DIOR™ Published or Presented Clinical Studies

Study	Number of patients	Patient selection	Design	Arms (A)	Endpoint	Outcome
DEBIUT DIOR™ balloon	20	De novo coronary bifurcation lesion	Registry single center	—	MACE 4 months	0%
DEB + BMS Registry DIOR™ Balloon	14	De novo coronary lesion	Registry single center	—	MACE 6 months	No
Magical Registry DIOR™ Balloon	22	lesion	center	—	MACE 30 days	No
DIOR™ ISR-Registry	35	DES-ISR	Registry single center	—	TLR 6 months	13.7%
Tuebingen study, GENIE	3	In-stent stenosis of coronary artery bifurcation lesions	Monocenter registry	—	Feasibility	Yes

VALENTINE
 37 countries and 250 pts
 DIOR™ balloon in BMS or DES ISR

ASIAN DIOR REGISTRY

(A multicenter registry with DIOR™ Balloon to prevent restenosis)

Sponsor:

EuroCOR Interventional, Bonn - Germany

Principal Investigator:

Dr Tan Huay Cheem, National University Heart Centre, Singapore

Site PIs:

Dr Praveen Candra (Max Devki Dev Hospital, New Delhi, India)

Dr Tejas Patel (Sal Hospital)

Dr Fazila Malik (Bangladesh)

Dr Yadav Bhatta (Nepal)

Dr Wan Azman (University Malaysia Hospital, Malaysia)

Dr Munawar (Harapan Kita, Indonesia)

Dr Nguyen Quan Tuan (Hanoi)

Dr Vo Thanh Nhan (Cho Ray Hospital, Vietnam)

Dr Michael Lee (Queen Elizabeth Hospital, Hong Kong)

Dr Chan Chi Kin (United Christian Hospital, Hong Kong)

Dr Mishra (SSKM Hosp, Kolkatta, India)

Dr Omar Ismail (Penang General Hospital Malaysia)

New balloon device keeps arteries clear without stent implant

Study shows less chance of arteries re-narrowing; trial to start here this month

BY LEE HUI CHIEH

DOCTORS here will start a trial this month on a new balloon designed to unclog the arteries of heart patients and keep them clear during the critical months after surgery.

The balloon, which was developed in Germany, has shown promise in preventing the arteries from filling with scar tissue in the aftermath of an operation.

From this month, the National Heart Centre will use the new balloon to prevent heart attacks in a trial on 30 patients.

The procedure will involve inserting the tiny balloon capable of delivering an anti-clogging drug into a blocked artery.

This means doctors will no longer need to implant a thin tube of wire mesh coated with the drug, known as a drug-eluting stent, inside the problematic artery.

A study done on 114 patients in Europe showed that 15 per cent of them saw their arteries re-narrow six months after undergoing a procedure with the new balloon, said its author, Dr Martin Unverdorben.

Previous studies have shown the re-narrowing rate of drug-eluting stents to be about 30 per cent,

» HOW THE DRUG-ELUTING BALLOON WORKS

In a balloon angioplasty, a long, flexible tube carrying a deflated balloon is threaded along the artery using a catheter until it reaches the blocked area. The balloon is coated with a drug that prevents the cells in the wall of the artery from growing excessively and causing the artery to narrow again.

The balloon is inflated to clear the blockage. At the same time, the drug on the surface of the balloon is pushed into, and absorbed by, the walls of the artery.



and that of bare metal stents to be about 50 per cent.

About 15 per cent of the patients who used the new balloon suffered a heart attack or died after six months.

The rate of heart attacks or deaths was 19 per cent for those on drug-eluting stents, and 27 per cent for those on bare metal stents.

Dr Martin Unverdorben, associate professor of medicine at the Cen-

tre for Cardiovascular Diseases' Clinical Research Institute in Germany, said yesterday: "For it to have such significantly lower rates, there must be something there."

He was speaking at a press conference held during a four-day conference of 1,500 cardiologists at the Singapore International Convention and Exhibition Centre that began yesterday.

In the procedure known as angi-

oplasty - usually used to treat heart disease - a balloon borne on a long flexible tube is threaded through the arteries to the blocked area, and then inflated to clear it.

Often, a stent, placed around the balloon earlier, is left behind in the artery to prop it open after the balloon is removed.

The stent is also often coated with a drug that prevents the artery walls from growing too much

Straits Times 2008

NUH DEB Registry Experience 2007-2010: Patient Clinical Characteristics (n=54)

47 DIOR™ balloon, 7 SEQUENT PLEASE™ balloon

Indications: 50 (92.6%) ISR, 4 (7.4%) Others

Age (years)	60±11
Sex (male)	44 (81.8%)
Diabetes mellitus	27 (50%)
Hypertension	38 (70.3%)
Hyperlipidemia	50 (92.6%)
Smoker	25 (46.3%)
Family history	3 (5.6%)
Previous MI	26 (48.1%)
Presentation	
Stable Angina	9 (16.7%)
Unstable Angina	22 (40.7%)
NSTEMI	6 (11.1%)
STEMI	12 (22.2%)
Objective evidence ischemia	4 (4.7%)
Heart failure	1 (1.9%)

NUH DEB Registry Experience 2007-2010: Angiographic Characteristics (n=54)

Previous Implanted Stent Type

DES	19 (35.2)
BMS	35 (64.8)

Previous Implanted Stent Size

Diameter (mm)	2.9±0.4
Length (mm)	21.6±7.1

Lesion location

LAD	21 (38.9%)
LCX	9 (16.6%)
RCA	16 (29.6%)
D1	3 (5.6%)
OM1	2 (3.7%)
SVG	3 (5.6%)

NUH DEB Registry Experience 2007-2010: Angiographic Characteristics (n=54)

Lesion length (mm)	23.6±11.3
Reference diameter (mm)	
Pre-procedure	2.5±0.6
Post-procedure	2.9±0.4
Minimal luminal diameter (mm)	
Pre-procedure	0.3±0.3
Post-procedure	2.7±0.5
Stenosis (%)	
Pre-procedure	87.0±12.9
Post-procedure	6.8±6.2

NUH DEB Registry Experience 2007-2010: Procedural/Angiographic Characteristics (n=54)

DEB Balloon Diameter (mm)	2.9±0.5
DEB Balloon Length (mm)	23.8±5.7
Additional Stents Implanted	7 (13%)
TIMI flow (Post-procedure)	
Grade 2	1 (1.9%)
Grade 3	53 (98.1%)

NUH DEB Registry Experience 2007-2010: Clinical Outcomes at 1 & 6 Months

	1 mth (n = 50) n (%)	6 mth (n = 32) n (%)
Death	0	1 (3.1%)
MI	0	4 (12.5%)
TVR	1	2 (6.3%)
CABG	0	2 (6.3%)
Stent Thrombosis	0	0 (0.0%)
MACE	1	7 (21.8%)

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



6th Asian Interventional Cardiovascular Therapeutics 2010

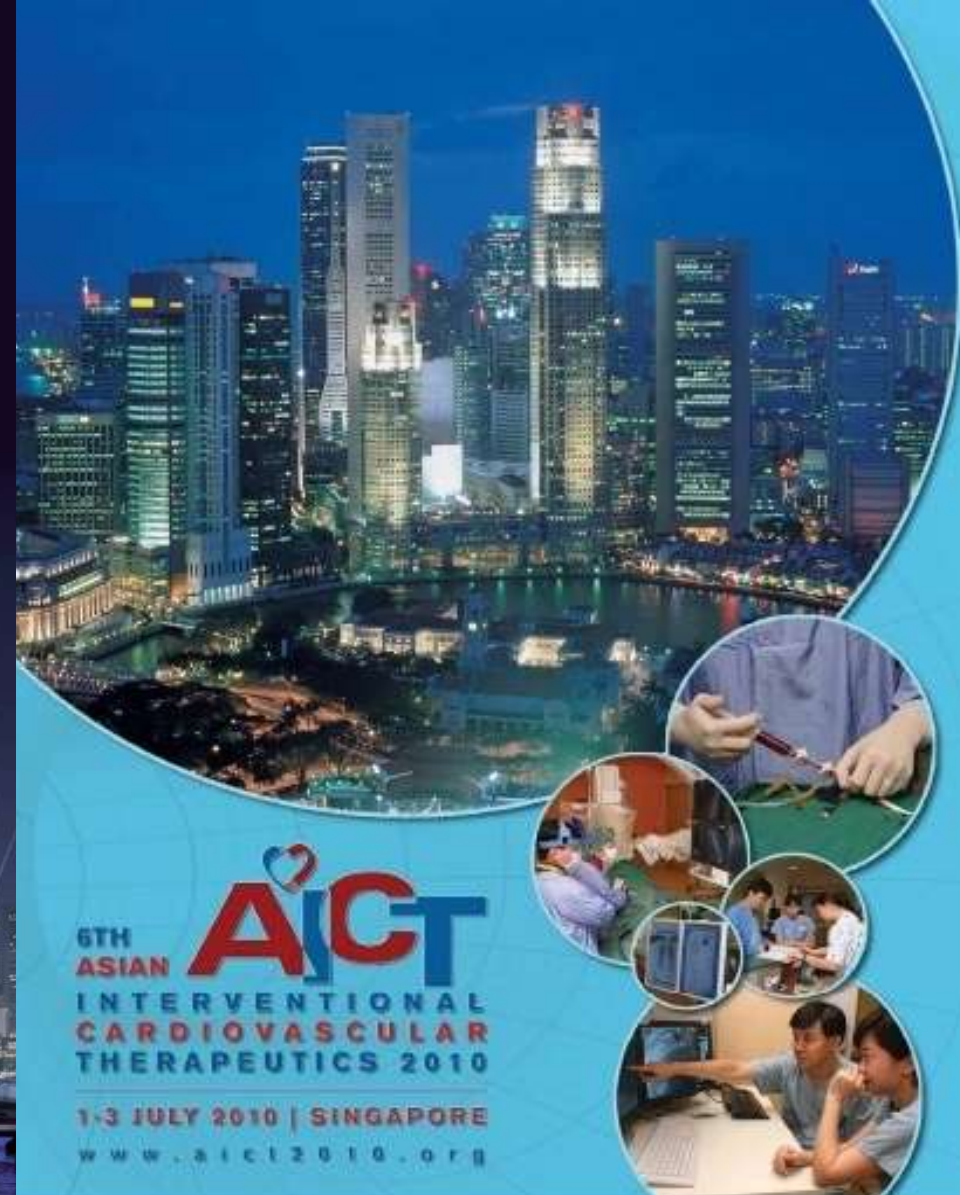
Date: 1 – 3 July 2010

Venue: Marina Bay Sands, Singapore

www.aict2010.org



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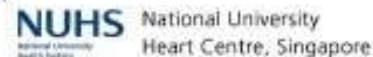
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