RESPONSE ADAPTED COMBINATION THERAPY (REACT): WHEN AND WHERE TO STENT ? CONCEPT FOR A PILOT STUDY

A/Prof. B. Patrice Mwipatayi

MD, MMed (Surg), MClinEd (Melb), FCS, FRACS

Department of Vascular Surgery,

Royal Perth Hospital, Perth, Australia

University of Western Australia

Director of PIVAR

Disclosure

Speaker name:

Prof Patrice B. Mwipatayi

I have the following potential conflicts of interest to report:

- [X] Consulting : BIOTRONIK
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

REACT.
REsponse Adapted Combination Therapy

RESPONSE ADAPTED COMBINATION THERAPY

PTA

Satisfactory PTA?*

Residual stenosis / flow limiting dissection post-PTA?*

Residual stenosis / flow limiting dissection post-DCB?*

Passeo-18 Lux

BIOLUX P-III (SFA)
fcd TLR 94.5%
PP 84.9%

Passeo-18 Lux
+ Pulsar 18

BIOLUX 4EVER
fTLR 93.6%
PP 89.9%

Pulsar-18

BIOFLEX PEACE
fTLR 97.1%
PP 86.2 %

Pulsar-18
+ Passeo-18 Lux**

DEBAS
fTLR 94.0%
PP 94.0%

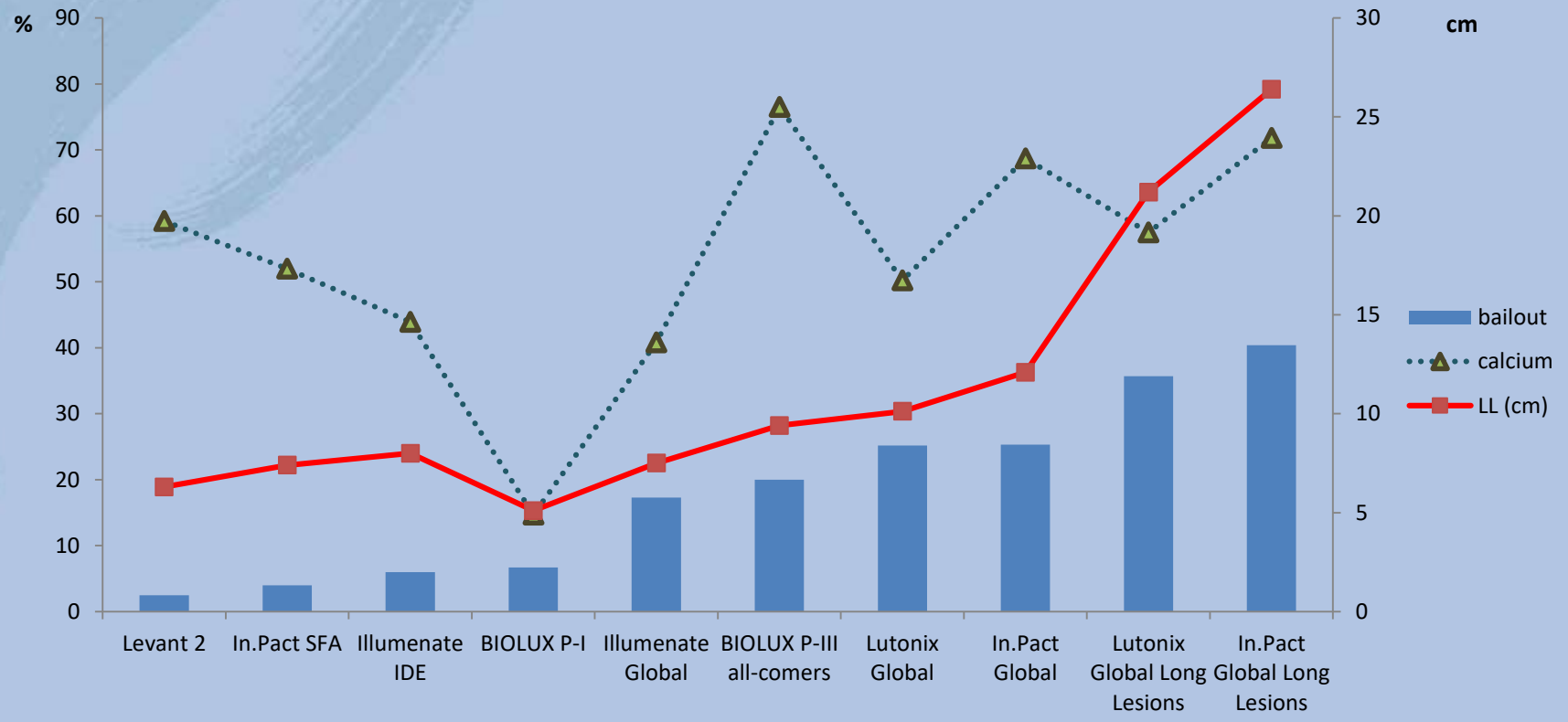
* Rocha-Singh K, Tepe G, Schneider P, Zeller T. Refining Strategies for the SFA: Consensus Panel SFA Treatment Algorithm, Supplement to Endovascular Today Global, Spring 2014: 11.
** The use of Passeo-18 Lux for post-dilatation is not within the indication for the product.
PTA=percutaneous transluminal angioplasty ; PP=Primary Patency; fTLR=freedom from Target Lesion Revascularization for BIOFLEX PEACE and BIOLUX 4EVER freedom from clinically driven TLR for BIOLUX P.III and DEBAS

1: Tepe G. Presented at CIRSE 2017, 12-month All-Comers SFA subset data
2: Deloose K. Presented at CX 2017, 12-month data
3: Nolte-Ernsting C. Presented at CIRSE 2017, 12-month data
4: Mwipatayi P. et al. First-in-man experience of self-expanding nitinol stents combined with drug-coated balloon for the treatment of femoropopliteal occlusive disease. Vascular, Jan 2017 [Epub ahead of print]

LEAVING NOTHING BEHIND DCB ALONE CAN'T FIT ALL

REACT.
REsponse Adapted Combination Therapy

PROVISIONAL STENTING RATE IN DCB TRIAL UP TO 40% IN REAL-WORLD STUDIES



Illumenate Global : Schroë H. et al, Catheter Cardiovasc Interv 2017
BIOLUX P-III all comers: Tepe G, CIRSE 2017
Lutonix Global: Thieme M. et al, JACC: Cardiovascular Interventions 2017
Lutonix Global Long lesions[6]: Thieme M. et al, JACC: Cardiovascular Interventions 2017
In.Pact Global: Jaff MR, VIVA 2016
In.Pact Global Long Lesions: Ansel G. TCT 2015

Levant II : Rosenfield K. et al, N Engl J Med n. 2, 373, pp. 145–153 -
In.Pact SFA: [2], Tepe G. et al, Circulation n. 5, 131, pp. 495–502
Illumenate IDE : [3], Krishnan P. et al, Circulation. 2017;136:1102–1113
Biolux P-I: [4], Scheinert D. et al, J. Endovasc. Ther. 2015;22:14–21

BIOLUX 4EVER

12-months data confirms performance of Passeo-18 Lux and Pulsar

REACT.
REsponse Adapted Combination Therapy

DESIGN:
Physician-Initiated, prospective, multi-center (5), controlled trial Investigating the Efficacy of EV Treatment of Fempop Arterial Stenotic Disease with BIOTRONIK Passeo-18 Lux Drug Releasing Balloon & BIOTRONIK Pulsar-18 Stent.

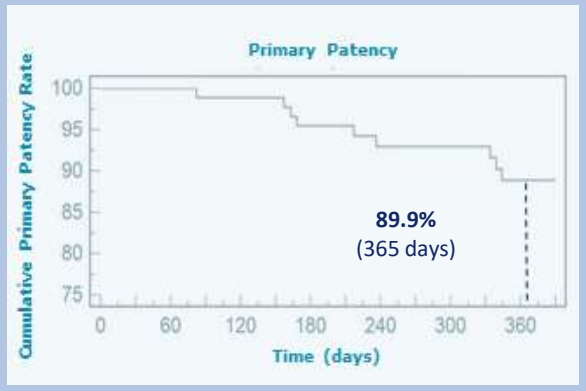
PRINCIPAL INVESTIGATOR:
Dr. Marc Bosiers, AZ Sint-Blasius, Dendermonde, Belgium

PRIMARY ENDPOINT:
Primary patency[1] at 12 months

SECONDARY ENDPOINT:
Primary patency at 6 and 24 months follow-up
F TLR at 6, 12 and 24 months follow-up
Changes in ABI at 12 and 24 months follow-up

Lesion Characteristics	N= 120 /120
Lesion length, mm (min-max ± SD)	83.33 mm (6.0 – 190.0; ±49.49)
Ref. vessel diameter mm (min-max ± SD)	5.26 mm (4.0 – 6.0; ±0.59)
Mean DCB diameter (min – max; ±SD)	5.15 mm (4.0 – 6.0 ; ±0.57)
Mean stent diameter (min – max; ±SD)	5.78 mm (5.0 – 7.0 ; ±0.53)
Occlusions (n, %)	40 (33.33)
Calcified lesions (n, %)	60 (50)

Demographics	N = 120 /120
Male (%)	79 (65.83)
Age (min – max; ±SD)	70.8 (43.7 – 92.4 ±10.5)
Nicotine abuse (n,%)	73 (60.83)
Hypertension (n,%)	76 (63.33)
Diabetes (n,%)	23 (19.17)
Renal insufficiency (n,%)	15 (12.50)
Hyperlipidemia (n,%)	66 (55.00)



(1) defined as freedom from >50% restenosis as indicated by an independently verified duplex ultrasound peak systolic velocity ratio (PSVR) <2.5 in the target vessel with no reintervention
Deloose K., Presented at CX 2017, 12-month data

DEBAS

Intentional use of Pulsar and Passeo-18 Lux is safe and effective

REACT.
REsponse Adapted Combination Therapy

DESIGN:
Physician-Initiated, prospective, multi-center (3), controlled trial Investigating safety and efficacy of BIOTRONIK Pulsar-18/35 Stents combined with BIOTRONIK Passeo-18 Lux Drug Coated Balloon in severe Femoropopliteal Arterial Occlusive Disease.

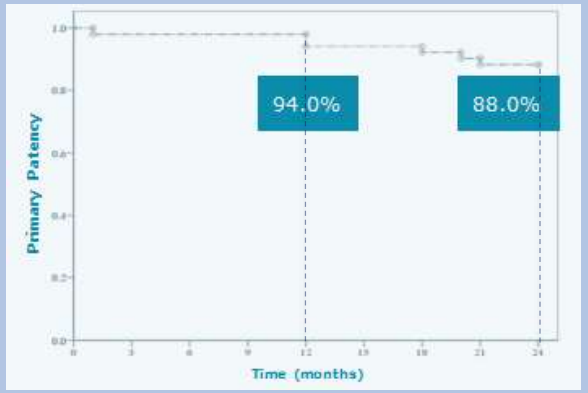
PRINCIPAL INVESTIGATOR:
Dr. Patrice Mwipatayi, Perth, Australia

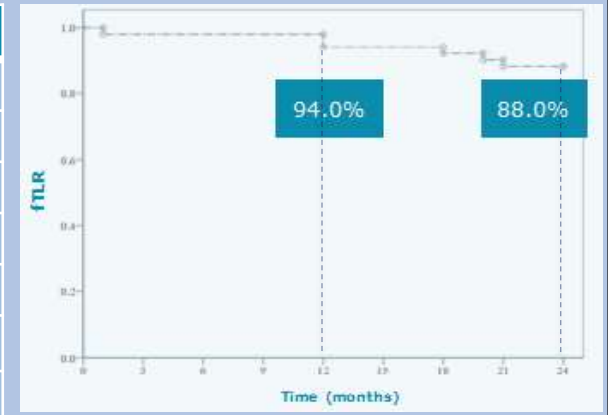
PRIMARY ENDPOINT:
Primary patency[1] at 12 and 24 months,

SECONDARY ENDPOINT:
Freedom from stent occlusion at 12 and 24 months
Freedom from TLR at 12, 18 and 24 months

Lesion Characteristics	N= 51
Lesion length, mm (IQR)	200 mm (140-250)
Ref. vessel diameter mm (min-max ± SD)	6.02 mm +/- 0.33
TASC C (n,%)	23 (45.1)
TASC D (n,%)	26 (51)
Calcified lesion, moderate (n, %)	22 (43.1)
Calcified lesions, severe (n, %)	12 (23.5)

Patients Characteristics	N = 44
Male (%)	32 (72.7)
Age (min – max; ±SD)	67.6 +/- 10.2
Nicotine abuse (n,%)	17 (38.6)
Hypertension (n,%)	31 (70.4)
Diabetes (n,%)	24 (54.6)
CAD (n,%)	16 (36.4)
Hyperlipidemia (n,%)	23 (52.3)

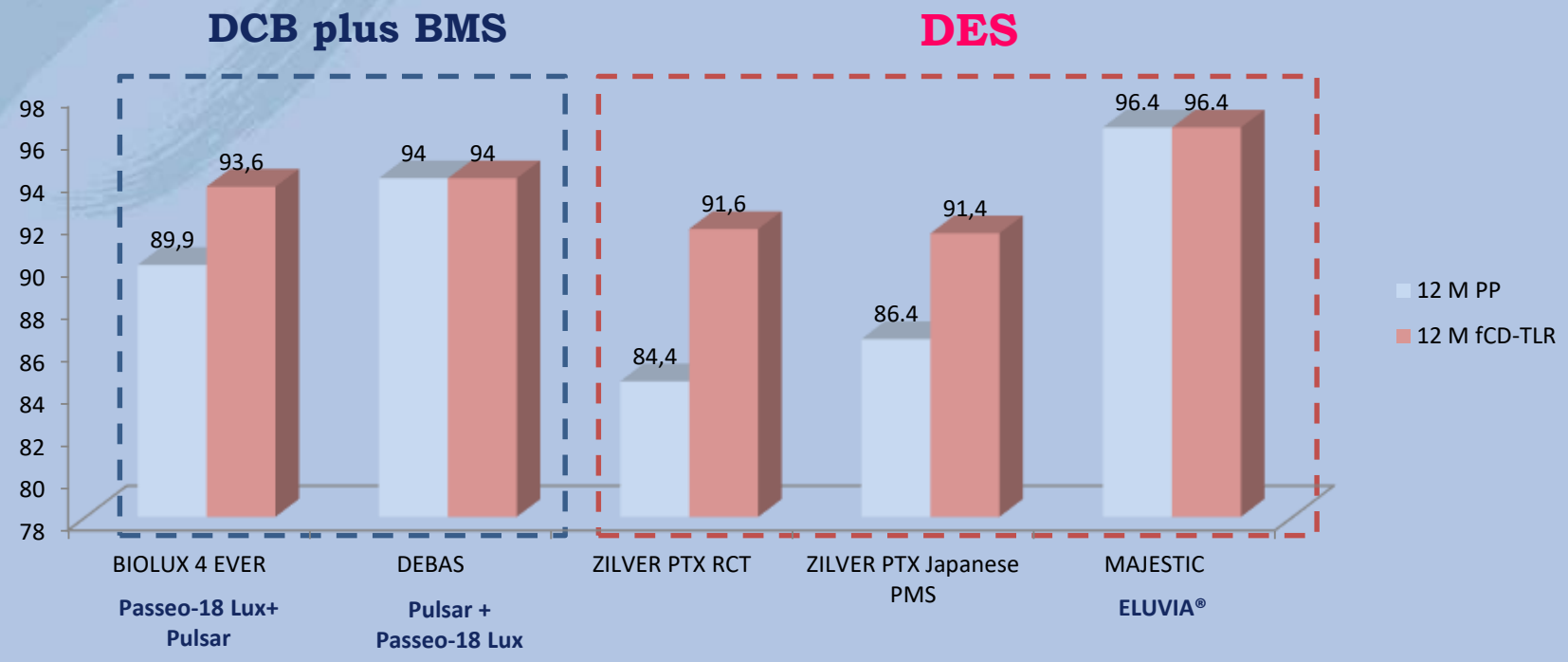




Defined as a PSVR at DUS < 2.5 at the stented target lesion with no clinically-driven reintervention within the stented segment.
DEBAS: Mwipatayi P. et al. First-in-man experience of self-expanding nitinol stents combined with drug-coated balloon for the treatment of femoropopliteal occlusive disease. Vascular, Jan 2017 [Epub ahead of print]
The use of Passeo-18 Lux for post-dilatation is not within the indication for the product.

PASSEO-18 LUX PLUS PULSAR SHOW EXCELLENT OUTCOMES IN SFA WHEN COMPARED TO DES

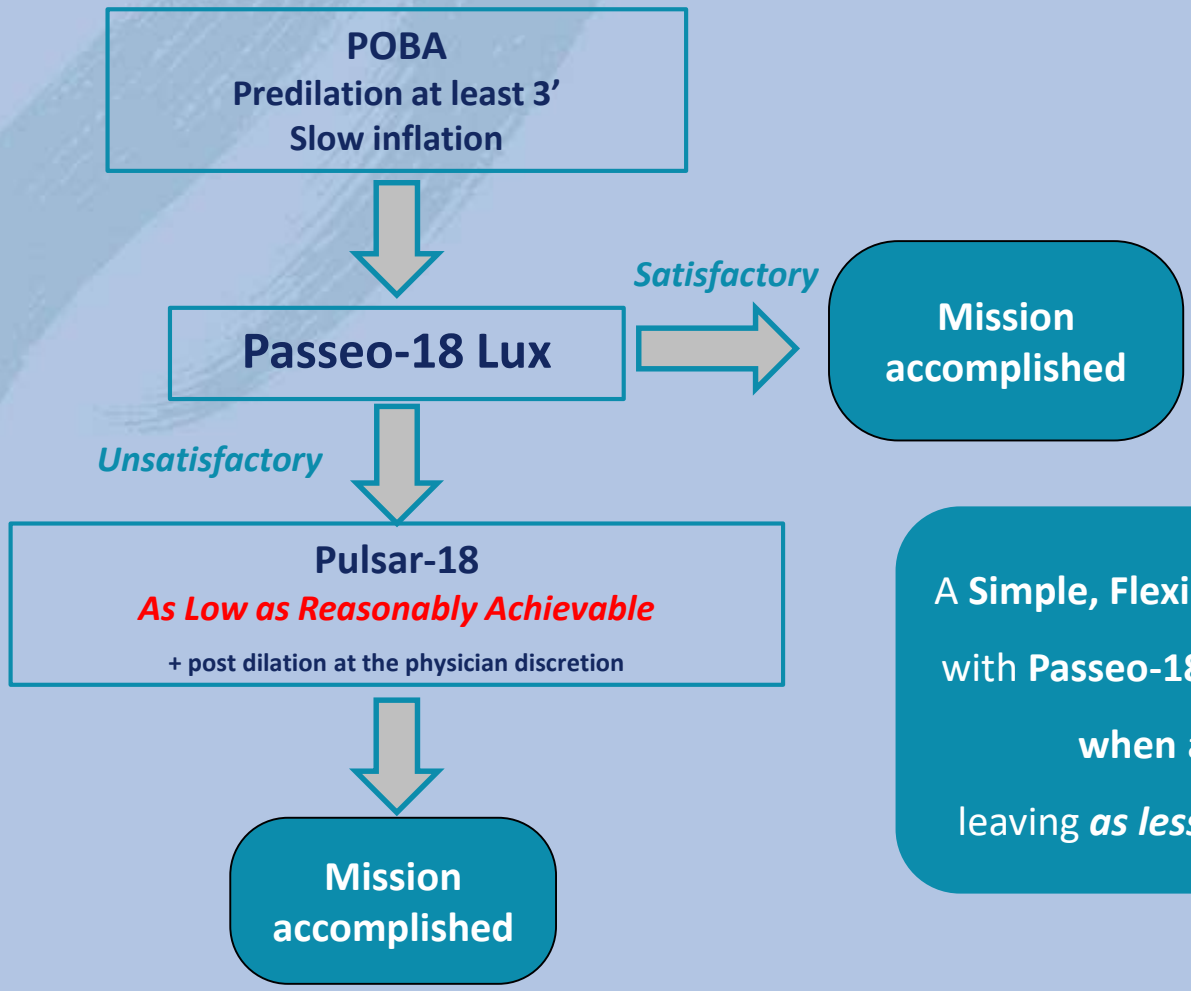
LL (cm)	8.3	**20**	5.5	**14.7**	7
PSVR	2.5	2.5	2	2.4	2.5



BIOLUX 4 EVER : Deloose K., Presented at CX 2017, 12-month data (365 days)
DEBAS: Mwipatayi P. et al. First-in-man experience of self-expanding nitinol stents combined with drug-coated balloon for the treatment of femoropopliteal occlusive disease. Vascular, Jan 2017 [Epub ahead of print]. The use of Passeo-18 Lux for post-dilatation is not within the indication for the product.

ZILVER PTX RCT : PMA P100022: FDA Summary of Safety and Effectiveness Data
ZILVER PTX Japan : Hiroyoshi Yokoi, JACC, Volume 9, Issue 3, February 2016
MAJESTIC : Mueller-Huellbeck. S. Presented CIRSE 2015

REACT SFA Treatment Algorithm



A **Simple, Flexible and Dynamic** treatment with **Passeo-18 Lux DCB** & **Pulsar-18 BMS** **when** and **where needed**, leaving ***as less metal as possible behind***

DISSECTION CLASSIFICATION

Type A dissections represent minor radiolucent areas within the coronary lumen during contrast injection with little or no persistence of contrast after the dye has cleared

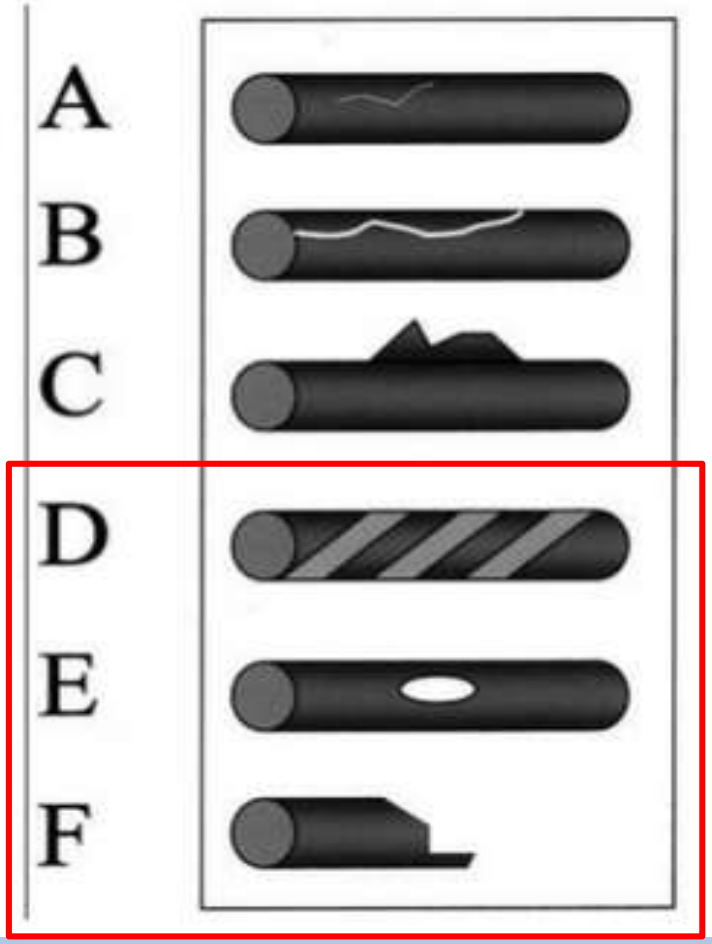
Type B dissections are parallel tracts or a double lumen separated by a radiolucent area during contrast injection, with minimal or no persistence after dye clearance

Type C dissections appear as contrast outside the coronary lumen ("extraluminal cap") with persistence of contrast after dye has cleared from the lumen

Type D dissections represent spiral ("barber shop pole") luminal filling defects, frequently with excessive contrast staining of the dissected false lumen

Type E dissections appear as new, persistent filling defects within the coronary lumen

Type F dissections represent those that lead to total occlusion of the coronary lumen without distal antegrade flow



NHLBI Classification of Coronary Artery Dissection

BIOTRONIK REACT PILOT STUDY RATIONALE

- Consensus on stent requirement to treat elastic recoil and flow limiting dissection
- No clear definition for flow limiting dissection in peripheral artery
- Should a dissection be treated or observed?
- Full lesion stenting or spot stenting?
- Can adjunctive procedural assessments (imaging, ultrasound) improve the stenting approach?

REACT Pilot Study Design: Reflection Questions?

REACT.
REsponse Adapted Combination Therapy

- Evaluate the utility of adjunctive procedural assessments to identify flow limiting dissection
  - Procedural DUS ?
  - IVUS ?
  - Fractional Flow Reserve (FFR)?
- FFR need to be validated
- Feasibility
- Impact on treatment
- Overall impact on procedure costs

REACT Pilot Study Design

REACT.
REsponse Adapted Combination Therapy

Design	**Global Multicenter Prospective Pilot Diagnostic Study**
Objective	Assessing the value of intraoperative **DUS** or **intra-arterial pressure measurement (IAP) or intra-arterial pressure measurement associated to IVUS** to identify flow-limiting dissection when 2 projections angiography is inconclusive
Primary Endpoints	▪ Specificity, Sensitivity, Air Under ROC curves
Secondary Endpoints (selected)	▪ Stenting rate, Nb of stents/lesion, stented length (full, spot) ▪ Primary Patency, cdTLR , MAE
Study duration	▪ Enrolment : 12 months, FUP: 1 month, 6 months and 12 months
Nb of subjects	▪ 150 subjects ≈ 10 sites globally

CONCLUSION

- DCB alone cannot treat all lesions
- The **BIOTRONIK REACT approach** allows physicians to treat SFA with full-lesion paclitaxel coverage offered by a DCB and stenting *when and where needed*, potentially reducing metal burden rather than the one-fits-all with DES
- The **REACT Pilot Study** will be the first study to look beyond full lesion treatment with DCB and BMS but **investigate a treatment algorithm**

RESPONSE ADAPTED COMBINATION THERAPY (REACT): WHEN AND WHERE TO STENT ? CONCEPT FOR A PILOT STUDY

A/Prof. B. Patrice Mwipatayi

MD, MMed (Surg), MClinEd (Melb), FCS, FRACS

Department of Vascular Surgery,

Royal Perth Hospital, Perth, Australia

University of Western Australia

Director of PIVAR