Increase of coronary microvascular resistances after recanalization with Drug Eluting Stent

Amedeo Anselmi[1, 2], Majid Harmouche[1, 2], J. Philippe Verhoye[1, 2], Hervé Corbineau[1, 2], Chiara Mariano[3], Mahmoud Maasrani[4], Agnès Drochon[5]

[1] Rennes Hospital Center « PontChaillou »
Department of Thoracic and Cardiovascular Surgery

[2] Inserm Unit 1099 LTSI Rennes1

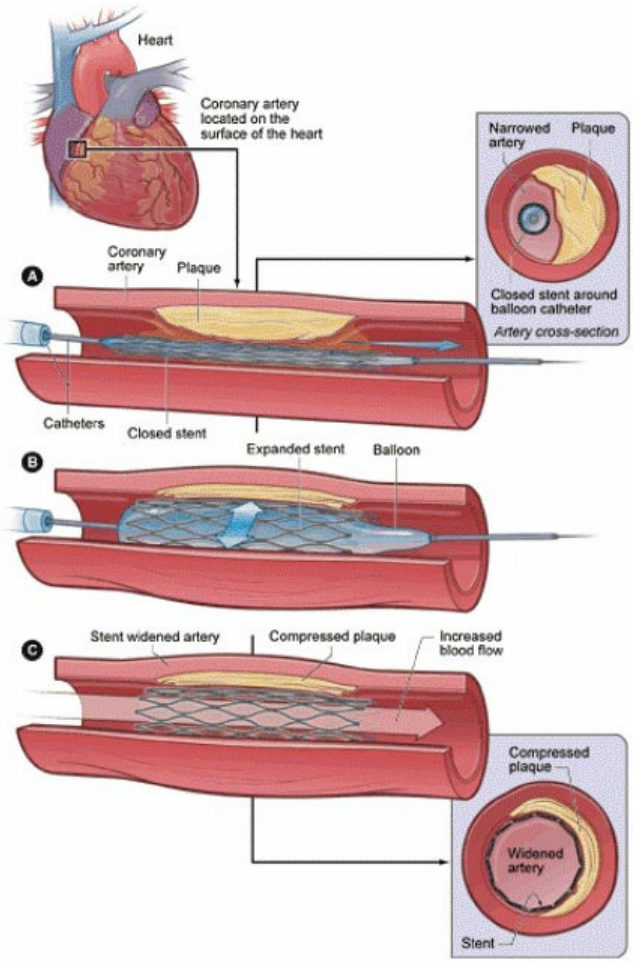
[3] Politecnico di Torino Italy

[4] Faculty of Sciences Lebanese University Tripoli Lebanon

[5] UTC Compiègne UMR CNRS 7338

Context of the study

Diseased coronary artery with atherosclerotic plaque expanded with a stent



First generation: Bare Metal Stents (BMS)

↓

Pb = in 20-30% of cases, cells grow over the wire and the artery re-closes

↓

Solution = to coat the stents with a drug (sirolimus / paclitaxel) that inhibits vascular smooth muscle cells migration and proliferation and inhibits re-endothelialization (DES = Drug Eluting Stent)

↓

2 new problems :

Formation of blood clots in the stent (thrombosis)

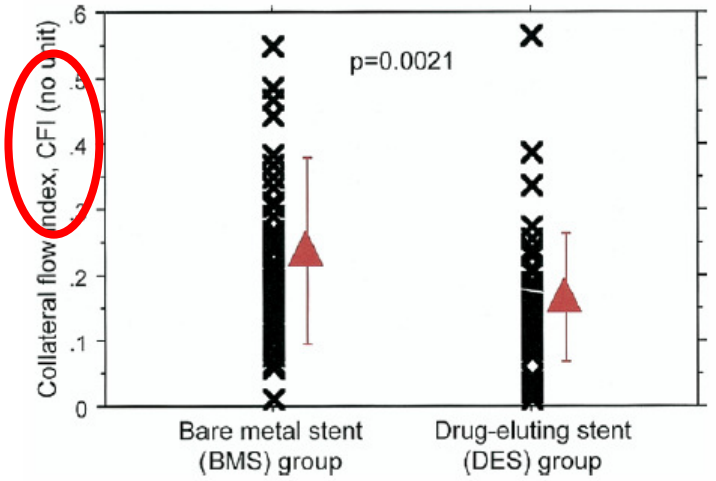
Negative effect on the microvessels around the stent

→ Need to redo the revascularization

→ Coronary Artery Bypass Surgery (CABG)

Brief literature review

- Meier et al., « Coronary collateral function long after drug-eluting stent implantation », Jour. Am. Coll. Cardiol., 2007



- Collateral function after coronary stenting is impaired with DES when compared with BMS

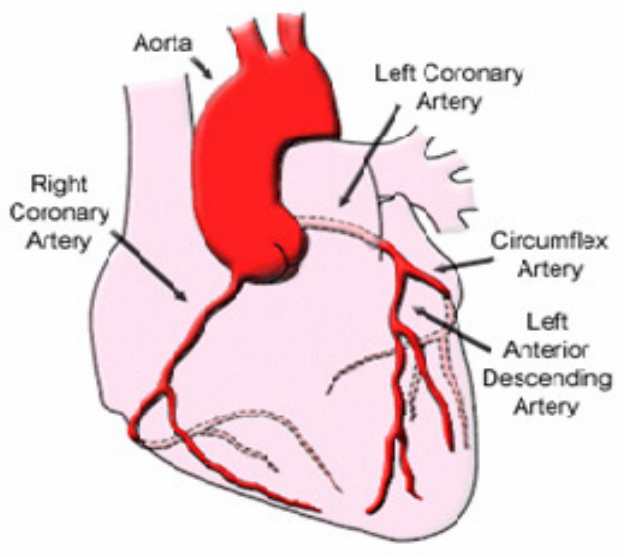
- Considering the protective nature of collateral vessels, this could lead to more serious cardiac events in the presence of an abrupt coronary occlusion

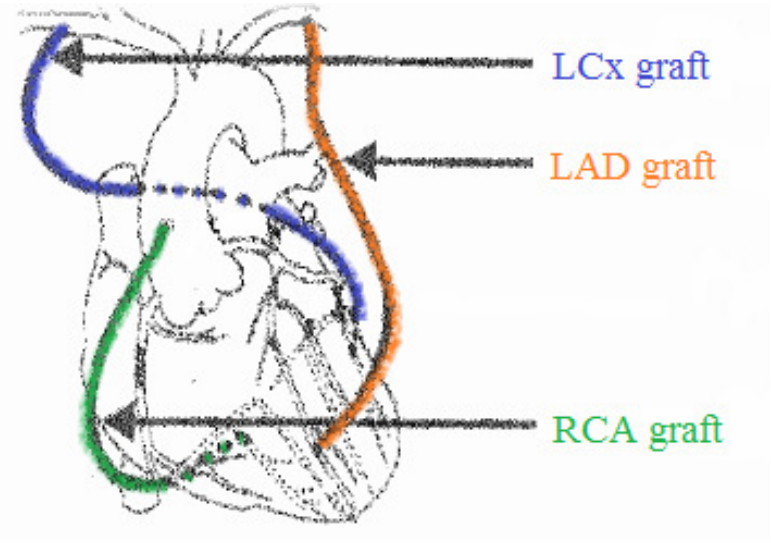
- Kern, « Attenuated coronary collateral function after drug-eluting stent implantation: a new downside of DES? », Jour. Am. Coll. Cardiol., 2007

- Zimarino et al., « Rapid decline of collateral circulation increases susceptibility to myocardial ischemia», Jour. Am. Coll. Cardiol., 2006

→ All these studies remain rather qualitative, using an index based on pressure measurements to provide an estimation of the collateral flow

Our simulating tool for coronary 3 vessel disease (1)

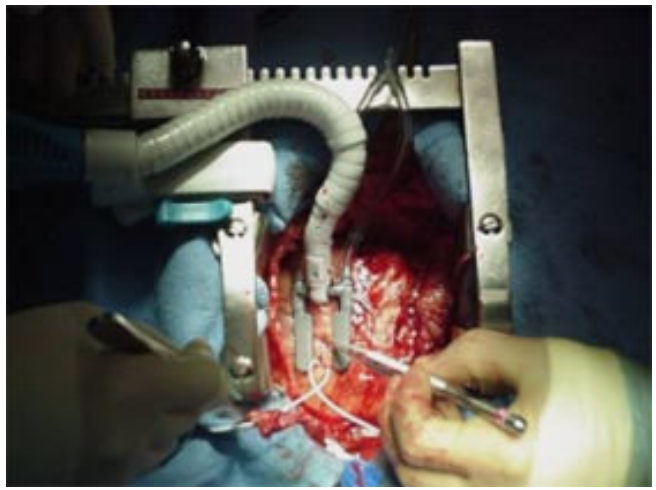




Patients involved in this study show a total occlusion of the right coronary artery (RCA) and serious stenoses on the left main coronary artery (LMCA), the left anterior descending artery (LAD) and the circumflex artery (LCx).

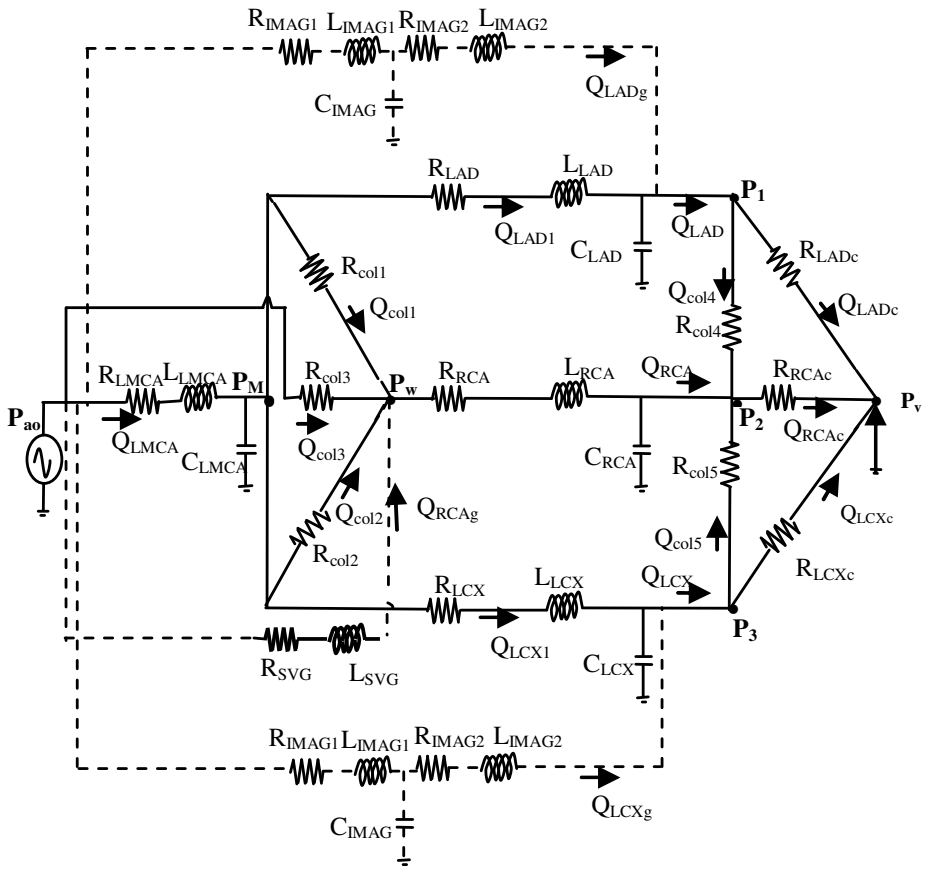
↓

Three bypass grafts



Our simulating tool for coronary 3 vessel disease (2)

Electric analogy



Maasrani et al., Ann. Biomed. Engin., 2008

Maasrani et al., J. Biomed. Science and Engin., 2011

$P \leftrightarrow U$ $\quad$ $Q \leftrightarrow I$

inductance: $U = L\dfrac{dI}{dt}$

compliance: $U = \dfrac{1}{C}\int I\,dt$

resistance: $U = R\,I$

4 situations are considered:

0G (no graft),
1G (right graft only),
2G (left grafts only),
3G (right graft + left grafts)

Our simulating tool for coronary 3 vessel disease (3)

Clinical measurements

→ Percentage stenosis on the left branches
(from Quant. Coro. Angiography)

→ Pressures and flow rates
$P_{ao}, P_v, P_w, Q_{LADg}, Q_{LCxg}, Q_{RCAg}$
(per-operative measurements)
(mean values over the cardiac cycle)

Simulations

→ Simulink (Matlab)
(for each patient and for 0G, 1G, 2G, 3G)

→ Input data:
P_{ao} (t) for each patient

→ Results presented as
mean values over the cardiac cycle

Determination of the model parameters

→ For LAD, LCx, RCA, and the grafts:
R, L, and C taken from Pietrabissa et al.
(*Med. Engin. Physics, 1996*)

→ Influence of the stenosis on R, L, C :

$R = R_0\alpha^{-2}$ $C = C_0\alpha^{3/2}$ $L = L_0\alpha^{-1}$

(α = 1-p, p = % of vessel area reduction)

→ Capillary and collateral resistances:
They are patient- specific;
calculated from clinical measurements
Maasrani et al., Proceedings ICEM-IEEE, 2010

Limiting hypotheses:
- $R_{col\ i\ (i=1à5)}$ all the same
- Influence of cardiac contraction on R_{cap}, R_{col} not taken into account

Case description

A 65 years old man with a severe intra-stent restenosis at the level of the first marginal branch of the LCx, critical stenosis of the first segment of the LAD, and chronic total occlusion of RCA

→ Indication to CABG was posed

Results for this patient

(In italic, mean values obtained for the group of 10 patients studied in Maasrani et al. (2011))

Clinical measurements

	0G	2G	3G
P_{ao}	64 *(75.3 ± 8.0)*	71 *(70.3 ± 10.8)*	71 *(72.2 ± 10.1)*
P_w	22 *(41.4 ± 7.5)*	23 *(39.7 ± 6.6)*	-
Q_{LADg}	-	18 *(28.3 ± 13.1)*	14 *(26.6 ± 13.0)*
Q_{LCxg}	-	4 *(34.1 ± 18.4)*	4 *(27.6 ± 13.4)*
Q_{RCAg}	-	-	18 *(43.6 ± 22.8)*

(Pressures in mmHg and flow rates in ml/min)

Capillary and collateral resistances

(in mmHg.s/ml)

R_{LADc}	R_{LCxc}	R_{RCAc}	R_{coll}
241	808	213	2980
(159 ± 97)	*(125 ± 60)*	*(125 ± 88)*	*(521 ± 282)*

→ Deterioration of the collateral pathways and of the microcirculatory coronary bed distal to the DES

Results for this patient (2)

Simulated values

	0G	2G	3G
Q_{LAD}	11.1 *(28.4 ± 24.1)*	16.7 *(37.4 ± 24.1)*	15.5 *(33.6 ± 23.0)*
Q_{LCx}	4.6 *(31.3 ± 23.5)*	5.7 *(41.3 ± 23.0)*	4.7 *(39.7± 28.8)*
Q_{RCA}	2.5 *(15.6 ± 9.6)*	2.9 *(12.8 ± 6.6)*	18.0 *(44.6 ± 23.2)*
Q_{RCAc}	3.8 *(19.3 ± 10.3)*	4.8 *(20.5 ± 10.3)*	18.0 *(43.6 ± 22.8)*
Q_{col1}	0.8 *(5.0 ± 3.2)*	1.0 *(4.2 ± 2.2)*	0.0 *(-0.1 ± 0.2)*
Q_{col3}	0.8 *(5.6 ± 3.3)*	1.0 *(4.4 ± 2.2)*	0.0 *(0.1 ± 0.1)*
Q_{col4}	0.6 *(1.7 ± 3.6)*	0.9 *(3.9 ± 1.9)*	0.0 *(-0.4 ± 0.4)*
Q_{col5}	0.8 *(2.0 ± 2.1)*	1.0 *(3.9 ± 1.8)*	0.0 *(-0.4 ± 0.4)*

- All the flow rates remain low, even after complete revascularization
- Due to the absence of collateral flow, Q_{RCA} and Q_{RCAc} are dramatically low in the cases (0G) and (2G)
- Q_{LCx} is also quite low, due to the elevated distal resistance

→ This patient is now at risk of future ischemic events

Conclusion

- We confirm (and quantify) the observations published in medical papers: the anti-proliferative drugs released by the DES affect the surrounding microvessels: collateral pathways and capillaries

- Of course, it is necessary to include other similar patients in our study