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EDITORIAL

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# The importance of experimental models in interventional cardiology. An illustration in coronary bifurcation stenting

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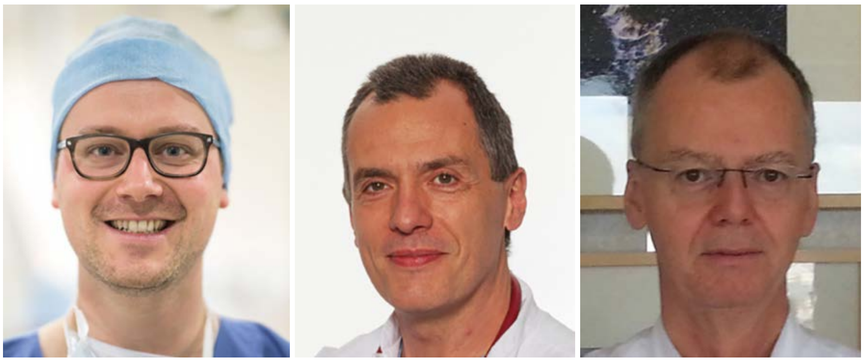
*"All models are wrong, but some are useful."*

[George Box (1919-2013), "Robustness in the Strategy of Scientific Model Building", in Robustness in Statistics (1979)]



Following Vassilev et al. [1], experimental models are increasingly advocated to assess expected mechanical benefit when developing new techniques in interventional cardiology. This experimental and clinical study reports an innovative technique of percutaneous management of coronary bifurcations, proximal optimization with kissing balloon inflation (POKI): a hybrid strategy of proximal optimization technique (POT) and kissing balloon inflation (KBI). It was designed to take into account the various specificities of bifurcations and notably their fractal geometry, deriving from the law of conservation of flow, which underlies a significant difference between up- and down-stream main vessel diameter [2]. The preliminary angiographic results for POKI seemed favorable. The research strategy, moving from theoretical concept to experimental validation, exemplifies scientific method.

In coronary bifurcations, experimental models to address the clinical issue of bifurcation management were introduced in the 1990s. Ormiston et al. [3] reported the first rudimentary bench model analyzing the mechanical consequences of stent post-dilatation in a bifurcation. Subsequently, the interplay of in-vitro and in-vivo studies greatly enhanced knowledge of the anatomic specificities of bifurcations and percutaneous treatment. Bench tests clearly showed the mechanical benefit of the POT sequence [4], first proposed intuitively by Darremont and previously assessed only visually in angiography. POT enables perfect global stent apposition while limiting the metal obstruction in the side-branch ostium [4]. POT thus became the cornerstone of percutaneous bifurcation management, whether complex or not. Likewise, a numeric simulation demonstrated the mechanical benefit of rewiring toward the side branch via the most distal cell: i) balloon opening of the side-branch ostium struts while limiting metal obstruction in the carina, and ii) covering the pro-atheromatous zone lateral to the ostium [5]. In the other direc-

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tion, experimental models enriched clinical findings such as coronary imaging quantification and characterization of the fractal nature of epicardial coronary bifurcations, determining the relative diameters of the 3 vessels [2], which is fundamental to the design of coronary bifurcation bench tests.

Although experimental studies, both bench tests and numerical simulations, have clearly improved management of coronary bifurcations, implementation of models that fail to respect bifurcation physiology can mask the mechanical consequences of certain techniques. Thus, the classical KBI, which was long the sole percutaneous technique for bifurcations, never actually showed any clinical benefit in provisional stenting [6]. KBI can reduce side-branch restenosis, but at the cost of increased proximal mother-vessel restenosis [6]. This clinically adverse outcome could have been expected: proximal juxtaposition of the balloons in KBI obviously incurs a mechanical risk, with 40% overstretch [4]. The bench model initially used to validate KBI [3] by no means matched coronary physiology: it was in plexiglass, which greatly differs from the biomechanical properties of even the most pathological coronary arteries, with a Young's modulus of $3,100\ 10^3$ kPa vs. 500 kPa for a normal artery or 1,500 kPa for a fibrous artery. Moreover, the models did not respect the fractal geometry of bifurcations, but had identical proximal and distal main vessel diameters. Thus, no observation or quantification of any deformation, malapposition or overstretch was possible. In contrast, using a model closer to actual physiology [4], although still imperfect, could have unraveled the drawbacks of KBI and its disappointing clinical results could have been partially anticipated [6]: while KBI does limit side-branch metal obstruction, balloon juxtapositioning leads both to $> 30\%$ elliptic overstretch [4], inducing restenosis [7], and to proximal stent malappositioning [4]. This negative mechanical effect was subsequently confirmed in-vivo on intracoronary imaging [8].

Bench tests and numerical models seek to mimic the anatomic and functional reality of coronary bifurcations. The quality of the design is thus essential in order to optimally approximate the real-life physiological data before attempting any clinical translation. In the case of coronary bifurcations, recommendations summarizing the basic points are needed before setting up an experimental model [9]. Respecting fractal geometry and the distributive properties of bifurcations with a model close to real arterial physiology is now indispensable. Likewise, our quantification tools have to be carefully chosen, with resolution 5 to 10 times greater than the parameter to be measured. Presently, it is OCT, with a resolution of 13 $\mu$m, which best meets this metrological requirement [10]. Coronary angiography, with an image based on projection and summation and a resolution of 180 $\mu$m, is insufficiently precise and gives ambiguous images. Exploration of the novel POKI technique in a model closer to physiological reality should be undertaken before moving on to large-scale clinical study.

What is needed, is to proceed rigorously and methodically with the requirement that any new theoretical concept should first undergo experimental validation on bench test and/or numerical simulation before being implemented on a large-scale clinical registry or in randomized controlled trials.

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## References


1. Vassilev D, Mileva N, Panayotov P, et al. A novel technique of proximal optimization with kissing balloon inflation in bifurcation lesions. Cardiol J. 2022; 29(6): 899–905, doi: 10.5603/CJ.a2022.0078, indexed in Pubmed: 35997048.
2. Finet G, Gilard M, Perrenot B, et al. Fractal geometry of arterial coronary bifurcations: a quantitative coronary angiography and intravascular ultrasound analysis. EuroIntervention. 2008; 3(4): 490–498, doi: 10.4244/eijv3i4a87, indexed in Pubmed: 19736093.
3. Ormiston JA, Webster MW, Ruygrok PN, et al. Stent deformation following simulated side-branch dilatation: a comparison of five stent designs. Catheter Cardiovasc Interv. 1999; 47(2): 258–264, doi: 10.1002/(SICI)1522-726X(199906)47:2<258::AID-CCD27>3.0.CO;2-C, indexed in Pubmed: 10376516.
4. Finet G, Derimay F, Motreff P, et al. Comparative analysis of sequential proximal optimizing technique versus kissing balloon inflation technique in provisional bifurcation stenting: fractal coronary bifurcation bench test. JACC Cardiovasc Interv. 2015; 8(10): 1308–1317, doi: 10.1016/j.jcin.2015.05.016, indexed in Pubmed: 26315733.
5. Foin N, Torii R, Alegria E, et al. Location of side branch access critically affects results in bifurcation stenting: Insights from bench modeling and computational flow simulation. Int J Cardiol. 2013; 168(4): 3623–3628, doi: 10.1016/j.ijcard.2013.05.036, indexed in Pubmed: 23714592.
6. Zhong M, Tang B, Zhao Q, et al. Should kissing balloon inflation after main vessel stenting be routine in the one-stent approach? A systematic review and meta-analysis of randomized trials. PLoS One. 2018; 13(6): e0197580, doi: 10.1371/journal.pone.0197580, indexed in Pubmed: 29949587.
7. Russo RJ, Silva PD, Yeager M. Coronary artery overexpansion increases neointimal hyperplasia after stent placement in

a porcine model. Heart. 2007; 93(12): 1609–1615, doi: 10.1136/hrt.2006.105981, indexed in Pubmed: 17639098.

8. Hakim D, Chatterjee A, Alli O, et al. Role of proximal optimization technique guided by intravascular ultrasound on stent expansion, stent symmetry index, and side-branch hemodynamics in patients with coronary bifurcation lesions. Circ Cardiovasc Interv. 2017; 10(10), doi: 10.1161/CIRCINTERVENTIONS.117.005535, indexed in Pubmed: 29038225.
9. Ormiston JA, Kassab G, Finet G, et al. Bench testing and coronary artery bifurcations: a consensus document from the European Bifurcation Club. EuroIntervention. 2018; 13(15): e1794–e1803, doi: 10.4244/EIJ-D-17-00270, indexed in Pubmed: 29131803.
10. Derimay F, Finet G, Souteyrand G, et al. Benefit of a new provisional stenting strategy: the re-Proximal optimizing technique. The rePOT clinical study. EuroIntervention. 2018; 14(3): 325–332.