

Individualised stent therapy 35 years after the first stent implantation

A Viewpoint from the Andreas Grüntzig Heart Catheterization Laboratories

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Introduction

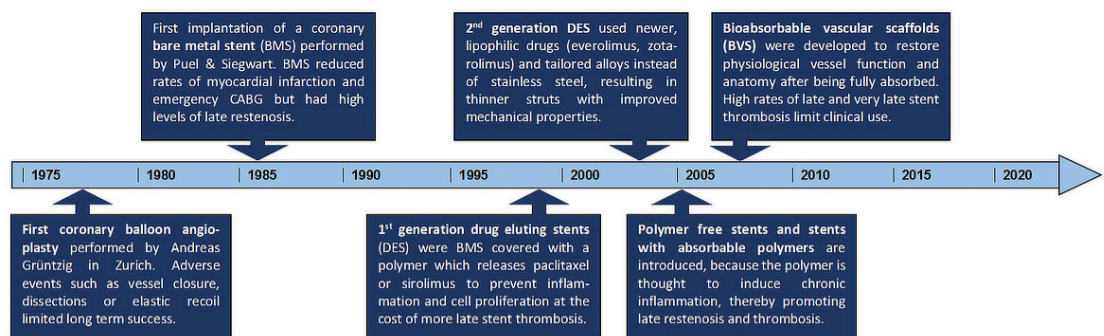
In 1986, Ulrich Sigwart and Jacques Puel implanted the first coronary stents at the Division of Cardiology, CHUV Lausanne and the University Hospital Toulouse, thereby overcoming the limitations of earlier coronary angioplasty, namely acute vessel closure or restenosis due to thrombosis, dissection, elastic recoil, or vascular remodelling [1]. While this innovation improved the success rate of coronary interventions and eliminated the need for surgical standby [2], first-generation bare-metal stents resulted in repeated revascularisation in up to 17% of patients within the first year due to restenosis caused by neointimal hyperplasia [3]. It was not until the development of drug-eluting stents (DES) that the interventional approach proved to be non-inferior to bypass surgery for left main coronary artery disease (CAD) and low-to-intermediate complex multi-vessel CAD [4]. Key to this development were constant refinements in the material, design and drug coating, which led to a broad armamentarium of coronary stents (figure 1 illustrates the milestones in the development of coronary stents). In particular, initial DES types suffered from high rates of late stent thrombosis, which were attributed to delayed endothelialisation caused by the anti-restenotic drugs.

This problem was largely solved with the introduction of custom-made anti-proliferative agents and polymers in the second generation of DES. Simultaneously, increasing economic constraints forced healthcare providers [5] to optimise purchase of supplies, including stents, leading to a reduction in available stent types at some hospitals and consequently limiting the possibility of individualised stent therapy. While many lesions can be successfully treated irrespective of the chosen stent, there are situations in which specific stent properties are essential for a favourable outcome. In this short review, we sought to highlight the four most important areas of individualisation of current stent techniques that should be available at every catheterisation laboratory.

Heavily calcified coronary arteries

Heavily calcified coronary arteries represent one of the most challenging scenarios in which stent deployment is particularly difficult. Not only that extensive lesion calcification increases the risk of target lesion failure, percutaneous coronary intervention (PCI) of calcified lesions is also associated with higher mortality, myocardial infarction and repeated revascularisation when compared with lesions without calcification [6]. The first step to successful intervention of a severely calcified vessel is thorough

Figure 1: Timeline of the milestones and major developments in the evolution of coronary stents for interventional cardiology.



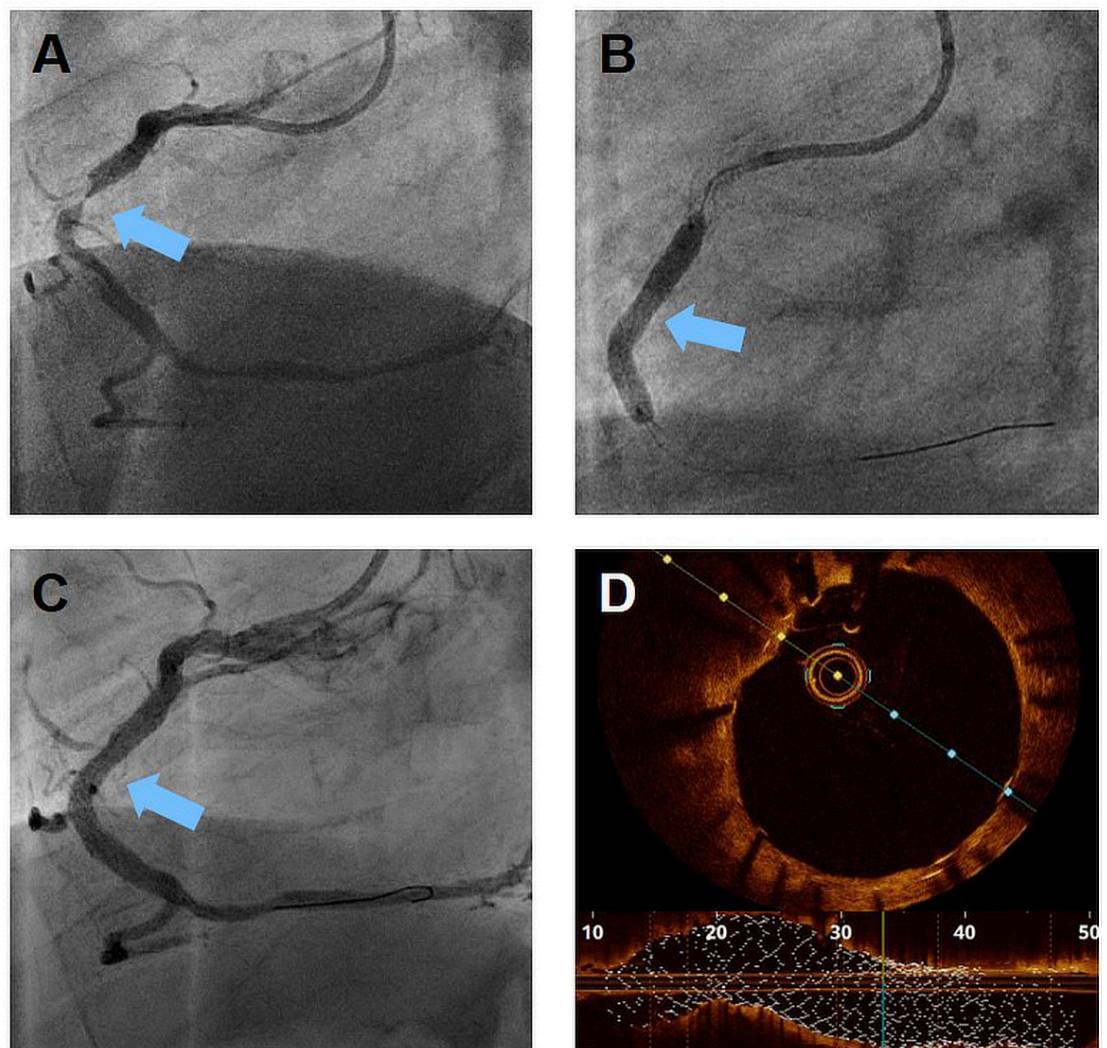
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lesion preparation and pre-dilatation. Common preparation techniques, such as rotational and orbital atherectomy, as well as the recently introduced intravascular coronary lithotripsy, act predominantly by debulking or by modifying plaque composition, with the aim of producing calcium cracks that are associated with improved stent expansion [7, 8]. If stent delivery is still impaired, the use of guide-extension catheters, which are smaller catheters that can be advanced into the coronary artery, can provide additional backup and facilitate stent placement. In these situations, a high radial strength of the stents is essential to resist the recoil forces of these rigid lesions. Radial strength is determined by three factors: the choice of metal alloy, strut thickness and stent architecture. With the majority of stents being made out of cobalt-chrome alloy, it is a combination of strut thickness and stent design that determines the radial strength. Another important stent characteristic for calcified lesions is radio-opacity, which allows precise positioning and post-dilatation of stents. To increase radio-opacity while simultaneously providing a high radial strength, some stents are equipped with a radio dense plat-

inum-iridium core. Figure 2 shows a stent implantation in a patient with severely calcified in-stent restenosis. Particularly in cases of complex or challenging stent implantations, the information provided by coronary angiography may be insufficient and intracoronary imaging is needed. Figure 2D shows an example of intracoronary imaging by optical coherence tomography (OCT), which is one of the two standard methods together with intravascular ultrasound (IVUS). IVUS is a well-established method based on conventional ultrasound and provides a good penetration depth that usually allows to display outer vessel wall structures also. OCT, in contrast, is based on the reflection of infrared light with lower penetration depth and requires the administration of a contrast agent during imaging. In return, it provides an exceptionally high spatial resolution, which allows a detailed analysis of plaque composition or the delineation of individual stent struts.

Figure 2: Representative patient with a severely calcified, subtotal in-stent restenosis of the right coronary artery (A, blue arrow). After extensive lesion preparation including intravascular coronary lithotripsy and the use of high pressure balloons, a stent with superb radial force can be deployed (B). The control coronary angiography shows a good result without residual stenosis (C). With the use of intravascular imaging such as optical coherence tomography (D) an excellent stent expansion and good strut apposition can be confirmed.



Ectatic coronary arteries and bifurcations

Besides calcification, aneurysmal and ectatic transformation is another type of coronary artery degeneration that is prone to thrombotic occlusion and represents a significant challenge for interventional cardiologists. Since stents are usually sized to the often smaller distal landing zone, achieving good stent apposition over the entire length of an ectatic vessel usually requires placement of multiple stents of different diameters, which in turn is associated with an increased risk of stent thrombosis for every overlap with two or more stent layers. An alternative solution is a stent with a high maximum expansion capacity. The over-expansion limit is the maximum size that a stent can be post-dilated to without harming its mechanical integrity. Stents are often produced in a limited number of designs, with each design having a different overexpansion limit. A variety of stent sizes is then achieved by using different sized stent balloons in the same stent design. Thus, knowledge of the different designs and their maximum achievable diameter is critical for stents implanted in segments with marked disparities in diameter [9]. In stents with a large expansion capacity, post-dilatation to ≥ 2 mm above the nominal size can be safely achieved, allowing optimal lesion coverage and good stent apposition with only one or two stents per lesion. Another situation in which the over-expansion limit is of critical importance are bifurcation lesions in which one stent reaches from the distal side branch into a much larger main vessel. As well as an expansion capacity that can bridge this increment in diameter, it is important that stents allow easy access to the overstented side branch. Therefore, a cell design with large, open cells facilitates crossing of struts into the side branch with a guidewire and placement of subsequent balloons or additional stents.

Small vessel lesions

Different stent properties are required for interventional treatment of small coronary arteries. Often, advancing the stent to the distal lesion can be challenging, in particular through tortuous or calcified vessels. Thus, good stent de-

liverability is of paramount importance. A small crossing profile of the crimped stent and a good transmission of force from the body of the stent to the tip facilitate stent placement in this situation. When successfully implanted, the size of the small vessel is a predictor of early stent thrombosis and the haemodynamic effects as well as acute vessel injury caused by stent struts are of increasing significance. Therefore, stent-specific properties that counteract stent thrombosis such as thinner struts and a small implantation footprint are particularly desirable [10].

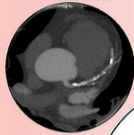
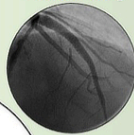

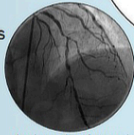

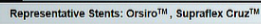
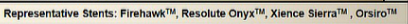
High bleeding risk

An increasingly senior population presenting with acute coronary syndrome equates to a higher burden of comorbidities, which often result in an increased bleeding risk. In such patients, limiting the duration of dual antiplatelet therapy (DAPT) reduces bleeding events. Since DAPT is required to prevent stent thrombosis until the stent is fully endothelialised, any stent properties that enhance endothelialisation also enable a safe reduction in DAPT duration. A major contribution to delayed endothelialisation comes from antiproliferative drugs in the coating of modern DES. While initial stent designs were entirely covered with the antiproliferative drug to prevent restenosis, recent stent designs have shown that focal distribution of smaller amounts of coating are equally able to prevent restenosis but simultaneously allow quicker endothelialisation. Another important way to limit DAPT induced bleeding risks is to avoid unnecessary stent implantation. To this end, hemodynamic measurements such as fractional flow reserve or the instantaneous wave-free ratio can be used to guide stent implantation in angiographically ambiguous cases.

Conclusion

Since 1986, the rapid technological development of coronary stents has revolutionised cardiac care of patients with myocardial infarction and coronary artery disease. Today's stents are mostly designed as all-rounders, but knowledge about specific stent features is essential for a tailored ap-

Figure 3: Comparison of clinical needs and desired stents properties in four different clinical scenarios of challenging coronary artery lesions. A selection of representative stents for the individual clinical scenario is given in the last line of each panel.

Severely Calcified Lesions		Ectatic Coronary Arteries and Bifurcations	
Clinical Need	<ul style="list-style-type: none"> Robust stability against stent recoil Good visibility during stent implantation 	 <p>Coro-CT with showing severe calcification</p>	 <p>Angiography of an ectatic LAD after stenting</p> <ul style="list-style-type: none"> Ability to model the stent over a large range of vessel diameters Easy side branch access
Stent Property	<ul style="list-style-type: none"> Superior radial strength High radiopacity through strut thickness or denser stent material 	 <p>Representative Stents: SYNERGY MEGATRON™, Firehawk™, Xience Sierra™, Resolute Onyx™</p>	<ul style="list-style-type: none"> Wide difference between the nominal size and the overexpansion limit Open cell design
Small Calibre Coronary Arteries		High Bleeding Risk	
Clinical Need	<ul style="list-style-type: none"> Low risk of stent thrombosis High deliverability, also in distal vessels 	 <p>Angiography of stenosis in small calibre vessels</p>	 <p>Head CT showing intracranial hemorrhage</p> <ul style="list-style-type: none"> Rapid and complete endothelialization Option to reduce DAPT duration
Stent Property	<ul style="list-style-type: none"> Small strut thickness Low crossing profile and superior force transmission 	 <p>Representative Stents: Orsiro™, Supralflex Cruz™</p>	<ul style="list-style-type: none"> Reduced drug dose and polymer thickness RCT or CE mark for reduced DAPT duration
		 <p>Representative Stents: Firehawk™, Resolute Onyx™, Xience Sierra™, Orsiro™</p>	

proach to treating challenging coronary lesions (figure 3). Future improvements in coronary angioplasty may be achieved by a stent design that is optimised for lesion-specific characteristics to create purpose-built stents for the next level of individualized stent therapy.

Conflict of interest

Both authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. AG declares no conflict of interest. CT received institutional grants from Abbott Vascular, Medtronic and SMT as well as advisory and consulting grants from Boston Scientific, Biotronik, Microport, Schnell Medical and Schockwave Medical.

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