

How should we treat heavily calcified coronary artery disease in contemporary practice?

George Kassimis^{*1,2}, Nestoras Kontogiannis¹, Gopendu Patri¹, Alex Zaphiriou³, Tushar Raina¹, Adrian P. Banning⁴

¹Department of Cardiology, Cheltenham General Hospital, Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, United Kingdom.

²Second Department of Cardiology, Hippokration Hospital, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece.

³Department of Cardiology, University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, United Kingdom.

⁴Oxford Heart Center, John Radcliffe Hospital, Oxford, United Kingdom.

Address for correspondence*:

George Kassimis MD, MSc, PhD

Consultant Interventional Cardiologist

Cheltenham General Hospital

Gloucestershire Hospitals NHS Foundation Trust

Cheltenham

GL53 7AN

United Kingdom

Email: Georgios.Kasimis@nhs.net

Abstract

Heavily calcified and densely fibrotic coronary lesions continue to represent a challenge for percutaneous coronary intervention (PCI), as they are difficult to dilate and it is difficult to deliver and implant drug-eluting stents (DES) properly. Poor stent deployment is associated with high rates of periprocedural complications and suboptimal long-term clinical outcomes. Thanks to the introduction of several adjunctive PCI tools, like cutting and scoring balloons and to atherectomy devices, the treatment of such lesions has become increasingly feasible, predictable and safe. A step-wise progression of strategies is described for coronary plaque modification, from well-recognised techniques to techniques that should only be considered when standard manoeuvres have proven unsuccessful. We highlight these techniques in the setting of clinical examples how best to apply them through better patient and lesion selection, with the main objective of optimising DES delivery and implantation, and subsequent improved outcomes.

Keywords

Calcified lesions; cutting balloon; scoring balloon; atherectomy; lithoplasty

Introduction

Heavily calcified coronary lesions and densely fibrotic coronary artery disease (CAD) remain a real challenge for successful percutaneous coronary intervention (PCI). They are extremely difficult to dilate appropriately with conventional balloons and are frequently associated with either failure to deliver a stent, or stent under-expansion. Revascularisation of such lesions results in significantly increased periprocedural complications, long-term adverse events and high rates of in-stent restenosis (ISR) [1].

Advanced age, renal disease and diabetes have all been associated with coronary artery calcification (CAC), with severe CAC affecting between 6 and 20% of patients treated with PCI [1]. Intravascular imaging has provided insights for adequate vessel preparation before stenting and plays an important role for lesion characterization, CAC extension and fibrotic presence [2]. Intravascular ultrasound (IVUS) has demonstrated that CAC severity is underestimated in nearly half of the cases with coronary angiography (CA) alone [3, 4]. This is especially true in case of fibrotic lesions, where CA depicts coronary artery as a planar silhouette of the contrast-filled lumen and being unable to visualize the vessel wall characteristics [5]. IVUS is the most reliable diagnostic tool to detect endoluminal and deep calcium, but the leading edge of the endoluminal calcium hides in its shadow the actual mass of calcium in the vessel wall. Optical coherence tomography (OCT) has a limited depth penetration but can image superficial calcium and assess the back side of the calcified plaque, rendering possible the measurement of the total calcified mass [6]. Recognition of such calcified anatomy allows appropriate use of ablative techniques for initial lesion modification and vessel preparation prior to drug-eluting stent (DES) implantation. Computed Tomography (CT) CA may have a role here for visualization of CAC, especially for the detection of type I and II calcified plaques, where the ratio of calcified plaque volume to vessel circumference $\leq 25\%$ and 26–50% respectively [7]. Soon, multislice CT could be used

to define the calcium load along the luminal pathway and indicate to the interventional cardiologist the exact plan to follow with the appropriate PCI strategy to use in treating these calcified lesions [8].

In this review, we describe the currently available PCI tools that facilitate lesion crossing and plaque modification through clinical examples (**Table 1**), and we highlight how best to apply them through better patient and lesion selection, with the main objective of optimising DES delivery and implantation, and subsequent improved short and long-term outcomes. To facilitate successful treatment of such lesions, a strategic approach combining understanding of lesion characteristics, coronary and peripheral anatomy and adjunctive techniques should always be used.

1. Methods to facilitate lesion crossing

Large support guide catheters

Catheter support during complex PCI begins with careful selection of the appropriate guide catheter (GC). Proper GC selection ensures coaxial alignment, allowing for delivery of equipment to the lesion, adequate opacification of the coronary arteries and extra support during PCI (**Figure 1 MRN 1201378 GK case**). The GC selected is based on the vascular access used, coronary and aortic anatomy, specific lesion characteristics and finally adjunctive devices planned to be utilized during the intervention. GC size, shape (passive support), sheath length and type, intubation depth of catheter into the vessel (active support) are very important catheter characteristics that should always be considered to enhance catheter support in complex PCI.

In calcified and resistant lesions, PCI can be performed safely through either transfemoral (TF) or transradial (TR) approach. In case of TF access, we recommend the use

of large diameter GC such as 7 or even 8F necessary for better support, easier delivery of equipment to the lesion and adequate coronary vessel opacification. In TR approach, we previously described the feasibility and safety of 7.5F Sheathless (S) GC system for the treatment of complex calcified lesions [9, 10]. SGC systems allow the passage of large-bore catheters with smaller overall diameters at the arterial insertion site, as there is no need for a sheath. The 7.5F SGC Eaucath (ASAHI Eaucath SGC; Vascular Perspectives Ltd., Manchester, UK) has an external diameter smaller than a sheath used for a 6F GC (2.49mm vs. 2.70mm, respectively), but a significantly larger internal lumen (2.06mm vs. 1.78mm, respectively) (**Figure 2 MRN 0201654 GK case**) [9-11]. We rarely recommend the use of 8.5F SGC in selected cases only, where the use of >2mm rota burr size may be necessary for the procedure [9-11]. It is now possible to push the limit of TR complex PCI such that 7F GCs can be advanced and manipulated through a Slender approach when SGC are not available. The 7F Glidesheath slender (Terumo, Tokyo, Japan) is a new dedicated radial sheath with a thinner wall and hydrophilic coating. It combines an inner diameter compatible with any 7F GC and an outer diameter smaller than current 7F sheaths [12, 13].

Anchor balloon support techniques

Anchor balloon support techniques remain a robust method to facilitate balloon crossing of resistant coronary lesions. Typically, proximal anchor balloon inflation in a side-branch (SB) enhances GC stability and increases support prior to crossing the lesion with a microcatheter or balloon [14]. Care should be taken with proximal anchor balloons, and oversizing of the balloon diameter should be avoided to prevent SB disruption or perforation (**Figure 3 MRN 0881536 GK case**). It is also possible to trap a microcatheter (usually a Corsair; Asahi Intecc, Japan) within the main branch (MB) to facilitate extreme support for guidewire advancement through the calcified segment. When 8F GC are used it is possible to use an anchor balloon in the SB as well as the MB with a Corsair, thus providing extreme

support. When a lesion is successfully crossed, balloon inflation distal to, or even within the target lesion can also facilitate delivery of secondary equipment through a different guidewire [15, 16].

Extension catheters

The introduction of extension catheters increased the success rate of lesion crossing by improving GC support. The initial, low-profile Terumo Heartrail II (Terumo, Japan) catheter had relatively limited clinical utility due to its smaller lumen capacity, greater catheter length and subsequent requirement for long wire exchanges. More recently, the GuideLiner™ catheter (Vascular Solutions, Maple Grove, MN) was developed as a monorail or rapid exchange mother and child system. The GuideLiner™ consists of a short guide-catheter extension connected to an introducer rod. The major advantage of the device is that it can be safely engaged very deeply in the distal vessel with (**Figure 4 MRN 0588032 GK case**) or without (**Figure 5 MRN 1191963 TR case**) an anchor balloon to allow balloon and stent delivery, with the greatest benefit seen in those cases with tortuous anatomy and complex, calcified lesions. For this reason, it has become an established treatment modality in contemporary complex PCI. Currently, the Guideliner V3 Catheter in 6, 7 and 8F and the Guideliner XL in 6F allowing 15cm extension from the GC are available [16, 17].

The use of several mother-in-child catheters are currently on the market (like Guidezilla II and Trapliner) which represent alternative valuable devices for balloon and stent delivery in tortuous and calcified lesions. The Guidezilla II 6F, 6F long, 7F and 8F (Boston Scientific, USA) is an evolution of the Guidezilla 6F. Guidezilla™ II 7F and 8Fr extension catheter have a larger inner diameter (1.60mm and 1.83mm) and smaller outer diameter (1.85 mm and 2.11mm) than the respective GuideLiner V3* 7F and 8F (1.57mm and 1.80mm; 1.90mm and 2.16mm) [18].

The TrapLiner Catheter (Vascular Solutions, Maple Grove, MN) is a rapid exchange guide extension catheter that provides backup support with the ability to trap a 0.014" guidewire. This functionality prevents the loss of guidewire position or unintentional guidewire advancement during catheter exchange and eliminates the need for alternative catheter exchange techniques. The straight, flexible extension provides deep-seating for extra backup support and coaxial alignment in challenging anatomies. The integrated balloon adds the ability to trap a guidewire during over-the-wire (OTW) catheter exchanges. This eliminates the extra step of deploying a percutaneous transluminal coronary angioplasty balloon to trap a guidewire when exchanging OTW microcatheters. The primary clinical use for the TrapLiner is during cases in which OTW microcatheters are required to cross calcified lesions in bifurcations or with tortuous anatomy. During these procedures, the TrapLiner not only provides added backup support and deep-seating for the GC, but also allows the operator to maintain guidewire positioning when exchanging the microcatheter. It's offered in 6, 7, and 8F sizes. The TrapLiner Catheter is currently available for sale in the United States and Canada, but not yet in Europe [19].

Microcatheters

Micro-catheters were specifically developed to enhance lesion crossing and can substantially increase the support offered to the guidewire when they are engaged within the calcified lesion. Due to their small profile they can also cross the lesion when small balloons fail to do so. The initial crossing guidewire can then be smoothly exchanged to a different one through this device without losing position. A range of micro-catheters are currently available, but Finecross (Terumo, Japan), Corsair (Vascular Perspectives, United Kingdom) and Tornus (Asahi Intecc, Japan) devices are still the most frequently used in this kind of lesions (**Table 2**).

The Finecross MG stainless steel braid construction is designed to provide strength, responsiveness and support for improved pushability to access and cross complex calcified lesions. The distal 13cm is ultra-flexible for improved trackability around tight bends and tortuous anatomy. The floppy distal segment is designed to be atraumatic and provide an optimal balance between trackability and safety while navigating through the tortuous anatomy. It is compatible with 6F GC and additional device use (anchoring, trapping techniques, IVUS or acutely in case of complications). The outer diameter of the stainless-steel shaft tapers from a proximal 2.6F to a distal 1.8F designed for improved crossability and guidewire handling. There are currently in the market 2 catheters one 130cm length and another 150cm. We frequently use this microcatheter to exchange with the rotawire when rotational atherectomy is scheduled [16, 20].

The Tornus was introduced in 2004 to facilitate lesion crossing in those cases where the guidewire had only partially penetrated the lesion cap. The device consists of a stainless steel, wire braided catheter (either 2.1F or 2.6F). It has a tapered steel tip to increase penetration and a silicone coating to increase lubricity. After the Tornus has crossed a lesion even partially, this facilitates successful passage of low profile balloons whilst minimizing the risk of vessel dissection or disruption. It can also be used to increase support to facilitate guidewire advancement [16, 20].

The development of the Corsair micro-catheter has replaced the use of the Tornus in many catheter labs. The Corsair is a braided micro-catheter consisting of 10 interwoven wires which form a polymer-covered metallic tube. The device has a kink resistant, tapered tip to ease access to complex lesions. The device improves wire support and wire manipulation. The Corsair also has the added advantage of allowing contrast injection through the catheter to delineate true lumen presence. The Corsair will also frequently cross resistant lesions with or without balloon anchor support. Corsair is bulkier than Finecross and requires at least a 7F

GC for an additional device use. Corsair may malfunction in very calcified lesions (tip separation, break of the screw head structure) [16, 20].

Over the wire balloons

Historically, the OTW balloon was the first introduced and has remained popular in a few centers. A standard OTW angioplasty balloon catheter has a central lumen throughout the length of the catheter for the guidewire and another, separate lumen for balloon inflation. These balloons are approximately 145 to 155cm long and are designed to be used with guidewires of various dimensions (0.010–0.014 inches). The major OTW advantage is the ability to maintain distal artery access with the balloon beyond the lesion while one guidewire is exchanged for another. The OTW system tracks very well because the whole balloon length has a wire lumen. It permits long guidewire exchanges, and because of the through lumen, it allows for delivery contrast and drugs distally in an artery. To exchange PCI catheters, the balloon is advanced over the wire to a distal position. The standard short (145cm) wire is then removed from the balloon. A longer guidewire (300cm) is then inserted to maintain distal wire position while the balloon catheter is completely withdrawn over the guidewire and another balloon catheter is introduced over the same long guidewire for additional dilatations. OTW catheters can accept multiple guidewires, which allows for exchanging additional devices that may require stronger, stiffer, or specialized guidewires like rotawires [16]. The most frequently used OTW balloons are: Sprinter Legend (Medtronic), Ryujin (Terumo), Emerge (Boston Scientific), Across (Acrostak), Trek and mini Trek (Abbot Vascular), etc.

2. Methods to enhance lesion modification

Non-compliant balloons

The non-compliant (NC) balloons are frequently used for post-dilation of DES to ensure appropriate stent deployment. In addition, they are also used to predilate calcified coronary lesions. NC balloons have little change in volume, even at high pressures concentrating dilating force at the calcified lesion site. Indeed, bench tests and clinical studies have shown that NC balloons exert more dilating force against a lesion than compliant balloons for a given balloon size and inflation pressure. These combined properties allow greater forces to be applied focally without overstretching other parts of the diseased segment. Using a compliant balloon at high pressures, in calcified or very stiff lesions might cause dissection at stent edges and, in small vessels, might facilitate coronary rupture [21, 22].

It is not uncommon in calcified lesions when the arc of calcium/fibrosis extends to a large segment of the circumference of the vessel, the lesion may become resistant to high-pressure dilatation with NC balloons. Unsuccessful lesion expansion may also occur when the wall of the vessel opposite the arc of calcium is very compliant, thus allowing asymmetric balloon expansion, without fracturing the calcification. In these cases, the use of an adjunctive tool is mandatory [21, 22].

High-pressure balloons

In addition to standard NC balloons, ultra NC balloons such as the OPN balloon (SIS Medical, Switzerland) or OPN balloon (Vascular Perspectives), have been developed to deliver high post-dilation pressures of >40 atm. We previously demonstrated their role in severe ISR due to stent under-expansion [23], but in native calcified lesions the operators

must always remember that there is an increased risk of vessel perforation when utilising very high-pressure balloon dilation strategies [16].

Intentional balloon-assisted micro-dissection

The primary intention with balloon-assisted micro-dissection is to cause intentional and controlled vessel dissection while maintaining wire position in the true lumen, thus facilitating delivery of secondary equipment beyond the calcific lesion. This is an ‘off license’ technique which was used a lot in the past and should be regarded as a ‘last resort’ measure where other strategies have failed or are not available in the catheter laboratory especially in emergency out of hours cases. Usually a very small diameter balloon is used, although larger balloons can be required at very resistant lesions (**Figure 6** [MRN 1813839 GK case](#)) [16].

Cutting balloons

The Flextome™ Cutting Balloon Dilatation Device (Boston Scientific, Marlborough, MA, USA) is a 6, 10 or 15mm-long balloon catheter with three (for 2.0-3.25 mm balloons) or four (on balloon sizes 3.5-4.0mm) micro-blades. These blades, mounted longitudinally on the surface of a NC balloon, are ~0.25mm in height and five times sharper than conventional surgical blades [24]. The cutting balloon should be inflated sequentially first 2 atm, then 4 and finally nominal 6 atm. During dilation, the device creates three or four endovascular radial incisions through the fibrocalcific tissue, thus allowing further expansion with conventional balloons. Additionally, the blades anchor into the intima, thereby preventing balloon slippage, something which is frequently seen in ISR. Furthermore, cutting balloon angioplasty (CBA) achieves significantly larger luminal gain than plain old balloon angioplasty (POBA) in patients with aorto-ostial lesions [26]. This has been linked with the effective fissures created in the muscular layers and elastic fibres around coronary ostia,

which are otherwise prone to acute recoil following conventional angioplasty. An IVUS-based study [24] indicated that CBA achieves larger luminal gain than POBA in calcified lesions. However, in the Cutting Balloon Global Randomized Trial the primary endpoint, six-month binary restenosis, did not differ between CBA and POBA (31% vs. 30%, $p=0.75$) and the rate of perforation was higher with CBA (0.8% vs. 0%, $p=0.03$) [27]. These negative results, together with the difficulties associated with cutting balloon delivery (due to its high crossing profile: 0.041-0.046”), led to the development of alternative balloon-based atherectomy devices, such as scoring balloons.

Scoring balloons

AngioSculpt® (Spectranetics, Colorado Springs, CO, USA) consists of a semi-compliant nylon balloon, surrounded by three external nitinol spiral scoring wires. This device is more flexible and deliverable than the CB (the crossing profile of the smallest device is 0.036”), and is available in lengths of 10, 15, and 20mm, and diameters of 2.0-3.5mm. In the feasibility trial [28], AngioSculpt with routine bare metal stent (BMS) implantation was used for de novo lesions, and AngioSculpt alone was evaluated for the treatment of BMS restenosis. Procedural success was 100%. Two type A dissections following AngioSculpt, and no perforations were reported. The target lesion revascularisation (TLR) rate was 10% at six months. In an observational study [29] including 299 patients undergoing IVUS-guided coronary DES implantation, the AngioSculpt enhanced stent expansion, compared with direct stenting and POBA with semi-compliant balloons. Unfortunately, no randomised comparison exists between cutting and scoring balloons, and any consideration on the comparative performance of these devices is speculative.

In our practice, the CB is preferentially used to treat ISR due to the stability of the device inside the lesion. However, scoring balloons can also be used very effectively to treat

ISR, considering the higher compliance of these devices. We still recommend the use of CBA for proximal focal mildly calcified lesions in relatively big vessels and aorto-ostial disease. Scoring balloons are preferentially utilised in preparing de novo lesions (**figure 5**). We tend to undersize the scoring balloon, inflating it at 20-22 atm. Both balloons are used for the treatment of fibrotic lesions, and mildly to moderately calcified lesions [30].

Lacrosse Non-Slip Element catheter and “leopard-crawl” technique

Calcified lesions are often observed in tortuous vasculature. The design of the Scoreflex catheter is subject to a potential “slacking” phenomenon and is also unable to create multiple scoring effects. The Flextome CB lacks flexibility, with an increased risk for causing vessel perforation. One method for overcoming these obstacles is use of the “leopard-crawl” technique. This technique uses a low inflation pressure to create a wedge into the calcification and then subsequently advances the catheter during balloon deflation to facilitate catheter delivery across the stenosis. This technique is well suited for the Lacrosse Non-Slip Element (NSE) due to the unique catheter design. The Lacrosse NSE catheter (Goodman Co, Ltd) contains three triangular nylon elements (width, 0.014”; height, 0.015”) that are free floating on the outside of the balloon surface and attached proximal and distal beyond (approximately 9mm from marker to location of connection) to a 13mm balloon length. Dilatation using a Lacrosse NSE creates a scoring effect into calcified tissue through a focused transmission of force through the very distal portion of these elements. The Lacrosse NSE elements are attached distal to the balloon location, and for instances whereby the catheter is unable to cross lesion location, a “leopard-crawl” technique can assist in facilitating device delivery. For cases whereby, the Lacrosse NSE catheter is unable to cross the culprit lesion, a low inflation pressure provides for indentation of the calcification, which allows the catheter to be advanced further into the target lesion during balloon deflation. Repeating this process facilitates catheter delivery across the target lesion. This is considered

an effective technique given the preconditions of: (1) a low profile of the distal catheter that allows the tip to be advanced to the lesion location; and (2) a good re-wrap functionality of the balloon [31].

Careful consideration of both sizing of the Lacrosse NSE and the inflation pressure applied is important. Generally, the Lacrosse NSE can be safely and effectively used for calcified lesions through selection of a catheter size that limits expansion to a smaller size than the adventitia or media. Confirmation of vessel diameter and luminal size of the calcified lesion using IVUS imaging prior to PCI is preferable; however, when IVUS is not undertaken, size selection based on 25%-50% less than the vessel diameter at calcified location determined by CA is considered a safe alternative. Balloon inflation pressure should commence from a low inflation and increase slowly (4 atm to 6 atm to 8 atm). After successfully delivering the Lacrosse NSE to the distal site, dilatation using higher pressure can be performed to treat the target lesion [32].

Atherectomy

A strategy for debulking calcified lesions as part of a bail-out technique to address undilatable stenoses has evolved into a primary approach of lesion preparation by plaque modification. This strategy is associated with decreased procedural and fluoroscopy times, contrast volume, and the number of predilation balloon catheters used when compared to bail-out approach [33]. Atherectomy is currently achieved with either rotational or orbital atherectomy.

Rotational atherectomy

Percutaneous transluminal rotational atherectomy (PTRA) was introduced 30 years ago primarily to achieve mechanical debulking of atherosclerotic plaque [34]. Differential cutting induced by PTRA allows mechanical ablation of inelastic fibrocalcific plaques while sparing

adjacent elastic tissue that deflects away from the ablating burr. PTRAs result in plaque modification with dissections occurring less frequently as compared to POBA. In recent years, PTRAs have been increasingly adopted following the excellent performance of DES. The need for PTRAs before DES implantation stems from a 6% failure rate to deliver and a twofold higher failure rate to deploy DES successfully in heavily calcified stenoses [35]. The latest guidelines reflected the available data [35, 36], granting a Class IIa (level of evidence C) to PTRAs, recommended for the preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilated before planned stenting [37].

Contemporary PTRAs have been refined [38], from the strategy (planned vs bailout) [38], the procedural set-up to the tools and techniques applied. The arterial access that was traditionally a large 8F TF sheath is now a contemporary 6 or 7F TR or TF sheath or STR as we previously described [9, 10]. The wiring technique has been facilitated using a standard workhorse or hydrophilic wire subsequently exchanged over microcatheters or OTW balloons with the rotawire. Fundamental elements of optimal technique include use of a single burr with burr-to-artery ratio of 0.5 to 0.6, rotational speed of about 150,000 rpm, gradual burr advancement using a pecking motion, short ablation runs of 15 to 20s, and avoidance of decelerations >5,000 rpm. The need for a temporary pacemaker has been reconsidered due to significantly lower incidence of transient heart block with smaller burrs and lower speeds, easily manageable with the use of either atropine [9, 10] or aminophylline as recently demonstrated [40]. With adequate training and experience, PTRAs can be a very safe technique.

Orbital atherectomy

The Diamondback 360° Coronary Orbital Atherectomy System (OAS) (Cardiovascular Systems Inc., St. Paul, MN, USA) is a percutaneous device indicated to facilitate stent

delivery in patients with coronary artery disease (CAD) who are candidates for stenting due to de novo, severely calcified CAD. Orbital atherectomy was approved in the USA in 2013, for lesion preparation of severely calcified coronary lesions prior to stent implantation, but not in Europe. Extensive analysis can be found in a review by Barbato et al [41].

Excimer coronary laser atherectomy

Excimer laser coronary atherectomy (ELCA), by means of a photoacoustic mechanism, has been used to treat resistant coronary stenoses (**Figure 7 AZ case**). In contrast to PTR, the use of an excimer laser does not require wire exchange and can be used with high power (80 J/80 Hz). The 0.9 mm X-80 catheter (Spectranetics Corp., Colorado Springs, CO, USA) can cross even heavily calcified lesions creating a “pilot hole” that enables delivery balloons and stents in 93% of all balloon-crossing failures. At the same time pulsed-wave ultraviolet excimer laser light at 308nm vaporises thrombus, suppresses platelet aggregation and enhances thrombolytic and GpIIb/IIIa activity. In centers where it is available this technique is used routinely when the balloon will not cross and it appears to be safe and effective. [42, 43].

Lithoplasty

The Shockwave Medical Coronary Rx Lithoplasty System (Shockwave Medical Inc., Fremont, CA, USA) is a novel balloon catheter-based device that utilises pulsatile mechanical energy to disrupt calcified lesions using technology like lithotripsy for kidney stones. The Coronary Lithoplasty catheter is a single-use, sterile, disposable balloon angioplasty catheter that contains a series of unfocused, electrohydraulic lithotripsy emitters. The emitters convert electrical energy into transient acoustic circumferential pressure pulses that disrupt both superficial and deep calcium within vascular plaque. The balloon catheter is connected via a

patient cable to the generator, which is pre-programmed to deliver the specified dosage of pulses per treatment. The balloon is available in diameters of 2.5-4mm and in only 12mm length [44].

Briefly, the lithoplasty balloon, sized 1:1 to the reference artery ratio, is inflated to low pressure (4 atm) with 10 pulses of ultrasound energy of 10s delivered per balloon, followed by further dilatation to nominal pressures. The balloon is then inflated to reference vessel size based on the balloon inflation chart. The procedure is repeated to provide a minimum of 20 pulses in the target lesion, with interval deflation to allow distal perfusion. If the lesion exceeds the 12-mm balloon length, the balloon can be repositioned and the lithoplasty repeated [44, 45].

The Conformité Européenne (CE) mark was granted in May 2017, based on initial results of the DISRUPT CAD I pre-market, prospective, multicentre, single-arm study that was designed to evaluate the safety and efficacy of lithoplasty in 60 patients. High-resolution imaging by OCT delineated calcium modification with fracture as a major mechanism of action of lithoplasty in vivo and demonstrated efficacy in the achievement of significant acute area gain and favourable stent expansion. In particular, OCT imaging identified calcium fracture along the circumference of the lesions and multiple fractures in a single cross section in >25% of lesions, which led to a mean acute area gain of ≈ 2.1 mm. Lithoplasty-induced fractures were independent of calcium depth, with multiple fractures per lesion occurring more frequently as the severity of the underlying calcification increased [45, 46] (**Figure 8 AB case**).

Authors' perspectives and future directions

Lithoplasty preferentially allows calcium modification without affecting the endovascular soft tissue, and subsequently aids stent delivery and optimization. Current

techniques to modify calcific stenoses lead to localized wall injury, which may provide a vascular substrate for restenosis. Furthermore, perforation rates reported in the literature vary from 0.0% to 1.5% with PTRa [36] and from 0.9% to 1.8% with OA [47], whereas no perforations were observed with lithoplasty [45].

Lithoplasty does not rely on mechanical tissue injury by physical interaction, such as atherectomy, cutting or scoring balloon, but rather by a diffuse acoustic pulse through a balloon inflated at low pressure of 4 to 6 atm. By delivering local shockwave energy, lithoplasty does not rely on the high-pressure inflation required with scoring or conventional NC balloons to modify calcium, and its effect is more pronounced with increasing severity of calcification. It provides circumferential plaque modification, as evidenced by the findings of multiple calcium fractures in single cross sections. Such circumferential modification holds the potential advantage of uniform energy distribution and thus uniform plaque modification resulting in enhanced stent apposition and expansion [45].

Moreover, shock-wave pulses affect calcium sheets located within the target field regardless of their depth in the vessel wall, which contrasts with the inefficacy of PTRa or OA to modify deep-seated calcium [48, 49]. Lastly, in contrast to plaque abrasion by PTRa or OA, which generates microparticles that embolize distally, thus impairing microcirculatory function [50], large calcium fragments generated by lithoplasty remain in situ. Indeed, compared with the incidences of 0.0% to 2.5% in contemporary series with PTRa [51], there were no incidents of slow-flow/no-reflow observed with lithoplasty in the current study.

We believe that lithoplasty balloon is going to transform the market, as it is easy to use, with predictable results and in most centers it will replace cutting and scoring balloons for the treatment of calcific disease

Conclusion

The optimal therapy for calcified CAD is multi-adjunctive and several strategies should always be available in the catheter laboratory. The outcome is less favourable compared to non-calcified lesions, but with increased understanding of calcification, more sophisticated, individualized treatment regimens will likely evolve to make optimal use of the variety of dedicated technologies and success. The advent of the lithoplasty balloon may revolutionise this indication but cost-effectiveness of these advanced technologies will need to be considered.

References

1. Généreux P, Madhavan MV, Mintz GS, et al. Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. Pooled analysis from the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) TRIALS. *J Am Coll Cardiol*. 2014; 63: 1845-1854.
2. Witzenbichler B, Maehara A, Weisz G, et al. Relationship between intravascular ultrasound guidance and clinical outcomes after drug-eluting stents: the assessment of dual antiplatelet therapy with drug-eluting stents (ADAPT-DES) study. *Circulation* 2014; 129: 463-470.
3. Mintz GS, Popma JJ, Pichard AD, et al. Patterns of calcification in coronary artery disease. A statistical analysis of intravascular ultrasound and coronary angiography in 1155 lesions. *Circulation* 1995; 91: 1959-1965.

4. Tuzcu EM, Berkalp B, De Franco AC, et al. The dilemma of diagnosing coronary calcification: angiography versus intravascular ultrasound. *J Am Coll Cardiol.* 1996; 27: 832-838.
5. Brugaletta S, Giacchi G, Ortega-Paz L, Garcia-Garcia HM, Sabate M. Stable coronary artery disease. Is it really stable? Lesion morphology interpretation by Grayscale and VH-IVUS in patients with coronary artery disease. *Continuing Cardiology Education* 2016; 2(2), doi: 10.1002/cce2.24.
6. Zeng Y, Tateishi H, Cavalcante R, et al. Serial Assessment of Tissue Precursors and Progression of Coronary Calcification Analyzed by Fusion of IVUS and OCT: 5-Year Follow-Up of Scaffolded and Nonscaffolded Arteries. *JACC Cardiovasc Imaging* 2017; 10: 1151-1161.
7. Qi L, Tang LJ, Xu Y, et al. The Diagnostic Performance of Coronary CT Angiography for the Assessment of Coronary Stenosis in Calcified Plaque. *PLoS One* 2016; 11: e0154852.
8. Serruys PW, Katagiri Y, Onuma Y. Shaking and Breaking Calcified Plaque: Lithoplasty, a Breakthrough in Interventional Armamentarium? *JACC Cardiovasc Imaging.* 2017; 10: 907-911.
9. Kassimis G, Patel N, Kharbanda RK, Channon KM, Banning AP. High-speed rotational atherectomy using the radial artery approach and a sheathless guide: a single-centre comparison with the "conventional" femoral approach. *EuroIntervention* 2014; 10: 694-699.
10. Kassimis G, Weight N, Kontogiannis N, Raina T. Technical considerations in Transradial Unprotected Left Main Stem Rotational Atherectomy-assisted and IVUS-guided Percutaneous Coronary Intervention using the 7.5-Fr Eaucath Sheathless guiding catheter system. *Cardiol Res.* 2018; : .

11. Saito S, Ikei H, Hosokawa G, Tanaka S. Influence of the ratio between radial artery inner diameter and sheath outer diameter on radial artery flow after transradial coronary intervention. *Catheter Cardiovasc Interv.* 1999; 46: 173-178.
12. Sanon S, Gulati R. Slender Approach and Sheathless Techniques. *Interv Cardiol Clin.* 2015; 4: 161-166.
13. Aminian A, Iglesias JF, Van Mieghem C, et al. First prospective multicenter experience with the 7 French Glidesheath slender for complex transradial coronary interventions. *Catheter Cardiovasc Interv.* 2017; 89: 1014-1020.
14. Fujita S, Tamai H, Kyo E, et al. New technique for superior guiding catheter support during advancement of a balloon in coronary angioplasty: The anchor technique. *Catheter Cardiovasc Interv.* 2003; 59: 482-488.
15. Di Mario C, Ramasami N. Techniques to Enhance Guide Catheter Support. *Catheter and Cardiovasc Interv.* 2008; 72: 505-512.
16. Fairley SL, Spratt JC, Rana O, Talwar S, Hanratty C, Walsh S. Adjunctive strategies in the management of resistant, 'undilatable' coronary lesions after successfully crossing a CTO with a guidewire. *Curr Cardiol Rev.* 2014; 10: 145-157.
17. Chan PH, Alegria-Barrero E, Foin N, et al. Extended use of the GuideLiner in complex coronary interventions. *EuroIntervention* 2015; 11: 325-335.
18. Ma J, Hou L, Qian J, et al. The safety and feasibility of guidezilla catheter in complex coronary interventions and an observational study. *Medicine (Baltimore)* 2017; 96: e8172.
19. <https://www.teleflex.com/usa/product-areas/interventional/coronary-interventions/trapliner-catheter/ML3291%20B%20TrapLiner,%20Brochure.pdf>

20. Karalis I, Andreou C, Montero Cabezas JM, Schali J MJ. Microcatheters: A valuable tool in the presence of a challenging coronary anatomy in the setting of acute coronary interventions. Case report and mini review. *Cardiovasc Revasc Med*. 2017; 18: 48-51.
21. Seth A, Gupta S, Pratap Singh V, Kumar V. Expert Opinion: Optimising Stent Deployment in Contemporary Practice: The Role of Intracoronary Imaging and Non-compliant Balloons. *Interv Cardiol*. 2017; 12: 81-84.
22. Romagnoli E, Sangiorgi GM, Cosgrave J, et al. Drug-eluting stenting: The case for post-dilation. *JACC Cardiovascular Interv*. 2008; 1: 22–31.
23. Kassimis G, Patel N, Banning AP. IVUS-guided high-pressure non-compliant balloon dilation to treat in-DES restenosis. *J Invasive Cardiol*. 2014; 26: 348.
24. Barath P, Fishbein MC, Vari S, Forrester JS. Cutting balloon: a novel approach to percutaneous angioplasty. *Am J Cardiol*. 1991; 68: 1249-1252.
25. Kurbaan AS, Kelly PA, Sigwart U. Cutting balloon angioplasty and stenting for aorto-ostial lesions. *Heart* 1997; 77: 350-352.
26. Okura H, Hayase M, Shimodozono S, REDUCE Investigators. Restenosis Reduction by Cutting Balloon Evaluation. Mechanisms of acute lumen gain following cutting balloon angioplasty in calcified and noncalcified lesions: an intravascular ultrasound study. *Catheter Cardiovasc Interv*. 2002; 57:429-436.
27. Mauri L, Bonan R, Weiner BH, et al. Cutting balloon angioplasty for the prevention of restenosis: results of the Cutting Balloon Global Randomized Trial. *Am J Cardiol*. 2002; 90: 1079-1083.
28. Fonseca A, Costa Jde R Jr, Abizaid A, et al. Intravascular ultrasound assessment of the novel AngioSculpt scoring balloon catheter for the treatment of complex coronary lesions. *J Invasive Cardiol*. 2008; 20: 21-27.

29. de Ribamar Costa J Jr, Mintz GS, Carlier SG, et al. Non-randomized comparison of coronary stenting under intravascular ultrasound guidance of direct stenting without predilation versus conventional predilation with a semi-compliant balloon versus predilation with a new scoring balloon. *Am J Cardiol.* 2007; 100: 812-817.
30. Raina T, Gunn J. The final score: use of a sculpting balloon. *Heart.* 2009; 95: 1448.
31. Ashida K, Hayase T, Shinmura T. Efficacy of lacrosse NSE using the "leopard-crawl" technique on severely calcified lesions. *J Invasive Cardiol.* 2013; 25: 555-564.
32. Taguchi I, Kageyama M, Kanaya T, Abe S, Node K, Inoue T. Clinical significance of non-slip element balloon angioplasty for patients of coronary artery disease: a preliminary report. *J Cardiol.* 2014; 63: 19-23.
33. Kawamoto H, Latib A, Ruparelia N, et al. Planned versus provisional rotational atherectomy for severe calcified coronary lesions: Insights From the ROTATE multi-center registry. *Catheter Cardiovasc Interv.* 2016; 88: 881-889.
34. Fourrier JL, Bertrand ME, Auth DC, Lablanche JM, Gommeaux A, Brunetaud JM. Percutaneous coronary rotational angioplasty in humans: preliminary report. *J Am Coll Cardiol.* 1989; 14: 1278-1282.
35. Benezet J, Diaz de la Llera LS, María Cubero J, Villa M, Fernández-Quero M, Sánchez-González Á. Drug-eluting stents following rotational atherectomy for heavily calcified coronary lesions: long-term clinical outcomes. *J Invasive Cardiol.* 2011; 23: 28-32.
36. Abdel-Wahab M, Richardt G, Joachim Büttner H, et al. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior To

- Taxus Stent Treatment For Complex Native Coronary Artery Disease) trial. JACC Cardiovasc Interv. 2013; 6: 10-19.
37. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J. 2014; 35: 2541-619.
 38. Barbato E, Carrié D, Dardas P, et al; European Association of Percutaneous Cardiovascular Interventions. European expert consensus on rotational atherectomy. EuroIntervention 2015; 11: 30-36.
 39. Allali A, Abdel-Wahab M, Sulimov DS, et al. Comparison of Bailout and Planned Rotational Atherectomy for Heavily Calcified Coronary Lesions: A Single-Center Experience. J Interv Cardiol. 2017; 30: 124-133.
 40. Megaly M, Sandoval Y, Lillyblad MP, Brilakis ES. Aminophylline for Preventing Bradyarrhythmias During Orbital or Rotational Atherectomy of the Right Coronary Artery. J Invasive Cardiol. 2018; 30: 186-189.
 41. Barbato E, Shlofmitz E, Milkas A, Shlofmitz R, Azzalini L, Colombo A. State of the art: evolving concepts in the treatment of heavily calcified and undilatable coronary stenoses - from debulking to plaque modification, a 40-year-long journey. EuroIntervention 2017; 13: 696-705.
 42. Badr S, Ben-Dor I, Dvir D, et al. The state of the excimer laser for coronary intervention in the drug-eluting stent era. Cardiovasc Revasc Med. 2013; 14: 93-98.

43. McKenzie DB, Talwar S, Jokhi PP, O'Kane PD, Osherov A, Strauss B, Dahm J. How should I treat severe coronary artery calcification when it is not possible to dilate a balloon or deliver a RotaWire™? *EuroIntervention* 2011; 6: 779-783.
44. De Silva K, Roy J, Webb I, et al. A Calcific, Undilatable Stenosis: Lithoplasty, a New Tool in the Box? *JACC Cardiovasc Interv.* 2017; 10: 304-306.
45. Ali ZA, Brinton TJ, Hill JM, et al. Optical Coherence Tomography Characterization of Coronary Lithoplasty for Treatment of Calcified Lesions: First Description. *JACC Cardiovasc Imaging* 2017; 10: 897-906.
46. Serruys PW, Katagiri Y, Onuma Y. Shaking and Breaking Calcified Plaque: Lithoplasty, a Breakthrough in Interventional Armamentarium? *JACC Cardiovasc Imaging* 2017; 10: 907-911.
47. Chambers JW, Feldman RL, Himmelstein SI, et al. Pivotal trial to evaluate the safety and efficacy of the orbital atherectomy system in treating de novo, severely calcified coronary lesions (ORBIT II). *J Am Coll Cardiol Interv.* 2014; 7: 510–518.
48. Kini AS, Vengrenyuk Y, Pena J, et al. Optical coherence tomography assessment of the mechanistic effects of rotational and orbital atherectomy in severely calcified coronary lesions. *Catheter Cardiovasc Interv.* 2015; 86: 1024–1032.
49. Karimi Galougahi K, Shlofmitz RA, Ben-Yehuda O, et al. Guiding light: insights into atherectomy by optical coherence tomography. *J Am Coll Cardiol Interv.* 2016; 9: 2362–2363.
50. Karimi Galougahi K, Bhatti N, Shlofmitz R, et al. TCT-236 effects of orbital versus rotational atherectomy facilitated PCI on the coronary microcirculation. *J Am Coll Cardiol.* 2016; 68 Suppl: B96.
51. Tomey MI, Sharma SK. Interventional options for coronary artery calcification. *Curr Cardiol Rep.* 2016; 18: 12.

