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The Dilemma of Repeat in Stent Re-stenosis: Can Intravascular Lithotripsy Provide an Alternative Approach to an Age-Old Problem?

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Abstract

Background: In-stent restenosis (ISR) has always been considered a conundrum for interventional cardiologists. Despite many technical advances in the last 20 years aimed at reducing its occurrence this area of interventional cardiology remains challenging. Here we present a novel use of IVL in a patient with repeat ISR in whom IVL treatment has provided excellent procedural and follow up results.

Case summary: A 79-year-old man with previous in stent restenosis (ISR) to a left circumflex artery stent presented with angina. Elective coronary angiogram confirmed recurrent ISR in the left circumflex artery (LCX). This was treated by Intravascular Lithotripsy (IVL), which provided an excellent procedural result. The patient made an uneventful recovery and was discharged the same day with follow up 90 days post procedure at which point they were asymptomatic from angina.

Conclusion: Despite advances in the development of plaque modifying therapy, management of in-stent restenosis due to heavy calcium burden and fibrotic coronary stenosis, remains difficult, challenging, and often requires adjuvant interventional tools and techniques. However, to date the outcomes of treating in stent re stenosis have been sub optimal and often lead to recurrence of symptoms for the patient. IVL is a relatively simple technique to modify ISR with a short learning curve. This case presentation highlights a novel use of IVL in a sub class of patients that remain challenging for the interventional cardiology community.

Keywords: ***in stent re stenosis, intravascular lithotripsy, calcium, coronary artery disease, IVUS, imaging.***

Introduction

Drug-eluting stents remain a cornerstone in the interventional treatment of coronary artery disease. However, with an ageing population the complexity of coronary artery disease has advanced leading to the need for adjuvant interventional tools in order to achieve satisfactory long-term results. In-stent restenosis (ISR) has always been considered a conundrum for interventional cardiologists. Despite many technical advances in the last 20 years aimed at reducing its occurrence this area of interventional cardiology remains challenging.

Furthermore, ISR is an independent predictor for mortality and to establish the incidence is often complex. The introduction of drug eluting stents (DES) has reduced this number to <10%, rising depending on the complexity of the procedure and patient demographics [1]. However, once in stent restenosis has occurred it is challenging to treat with limited options. Aggressive 1:1 balloon dilatation with non-compliant or high pressure OPN NC balloons is an option but has limited success with the risk of vessel perforation. Excimer laser with contrast (rather than saline) has been reported to be successful in treating under expanded stents. The powerful pressure waves with contrast rather than saline aims to disrupt the plaque under the stent surface. However, again the risk of perforation along with dissection is present along with the need of more experienced operators [2]. The method of using rotational atherectomy through the stent struts in order to disrupt the plaque and allow subsequent modification and use of new stents has been demonstrated in a number of small case series. However, risks including burr entrapment, embolisation of stent material, coronary perforation and slow flow phenomenon make such an intervention unappealing in the first instance [2,3].

The subsequent options after lesion preparation in ISR remain that of further stenting or the deployment of drug eluting balloons within the pre-existing stent (once adequate lesion preparation has been achieved). Use of additional stents in the context of ISR can increase the vulnerabilty of recurrence especially if the underlying aetiology is mechanical (underexpansion or malapposition of stent). Furthermore, small vessel coronary arterties predispose to higher rates of ISR and thus are not an attractive option for repeat stenting. Such concerns paved the way for the introduction of drug eluting balloons (DEB). The fundamental benefit over re stenting lies in the absence of a polymer, stents struts and subsequent longer vascular healing time that predisposes to late stent thrombosis. The use of DEB in ISR has been shown in meta-analysis studies to compare favourable in comparison to balloon only angioplasty and re stenting. However, depsite this the need for repeat vasularisation still exists and thus are more definitive approach is sought after [4,5].

Most recently the use of Intravascular Lithotripsy (IVL) for the treatment of ISR has shown promising results. IVL has been developed to treat calcified lesions in native coronary. A small number of case reports and case series reported its use in more challenging scenarios including in stent restenosis [3]. However, use of Intravascular lithotripsy alone in recurrent coronary in-stent

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restenosis is not evidenced and therefore its use is "off-label"' in this regard.

Along with a favorable risk profile, IVL is an attractive adjuvant technique to conventional angioplasty balloons that has the potential to improve procedural results in patients with ISR due to high calcium burden.

Here we present a novel use of IVL in a patient with repeat ISR in whom IVL treatment has provided excellent procedural result. From our understanding such a use for IVL has not yet been evidenced to provide encouraging medium to long term outcomes.

Case presentation

A 79-year-old man was referred to rapid access chest pain clinic with progressive anginal symptoms. He had a history of coronary artery bypass grafting in 2000 (LIMA to LAD, SVG to IM and RCA). 11 years later he underwent native vessel PCI to his LMS, extending into LAD and LCX artery, for recurrent angina symptoms. The first episode of ISR occurred in 2019 to the left circumflex artery stent. OCT confirmed severe fibrotic lesions as the cause of ISR, subsequently being treated with a cutting balloon and deployment of a drug eluting balloon. A further episode of recurrent angina, and subsequently coronary angiogram showed recurrent ISR (Late >6 months) in the LCX 6 months after this event. On this occasion intervention included the use of a cutting balloon and the addition oflaser therapy. 2 years later the patient had recurrence of his angina and underwent a further coronary angiogram. The procedure was carried out through the right radial artery. The left coronary artery system was engaged using a EBU 3.5 guide catheter. Findings confirmed recurrent ISR in left the circumflex artery in a different location to the previously treated ISR (**Figure 1**).

Subsequent IVUS imaging demonstrated the previous stent to be sub optimally expanded (**Figure 2**). Therefore, a decision was made for an attempt of IVL as previous interventions had yielded the patient symptom free for only a short duration of time. The procedure was performed by administering 80 pulses of shockwave (4.0x12 balloon used for 8 cycle), with a 4 × 12 mm noncompliant balloon used for post dilation at a maximum pressure of 20 atmospheres (**Figure 3**).

The final intravascular ultrasound (**Figure 4**), and angiographic result (**Figure 5**) showed calcium augmentation, improvement in mean luminal area, and the absence of vessel perforation or distal dissection.

The patient made an uneventful recovery and was discharged the same day with follow up 90 days post procedure. At this point the patient was well and free of any symptoms suggestive of coronary ischaemia.

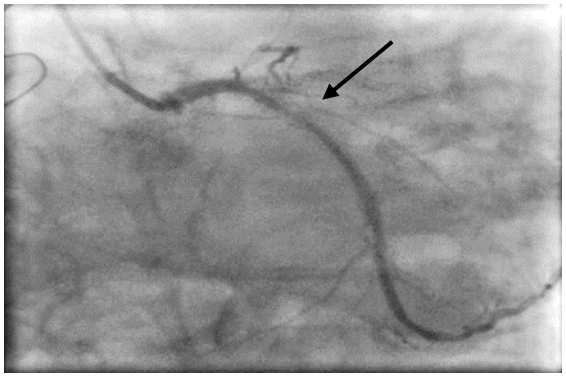
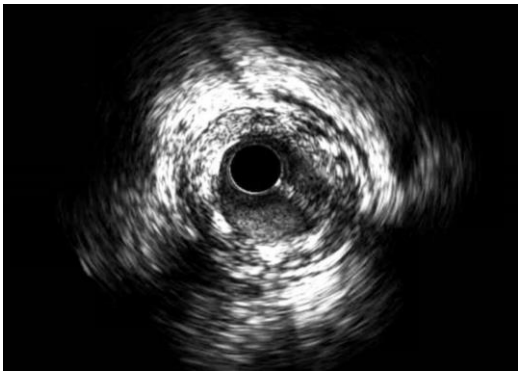


Figure 1



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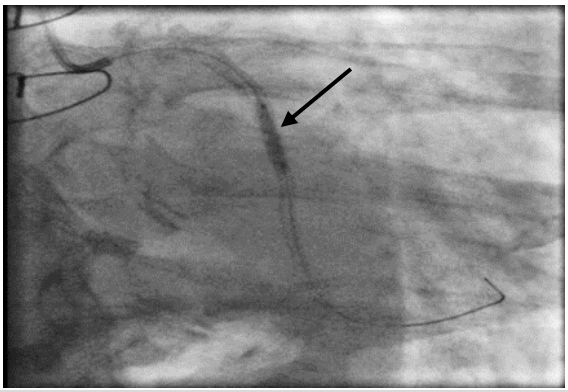

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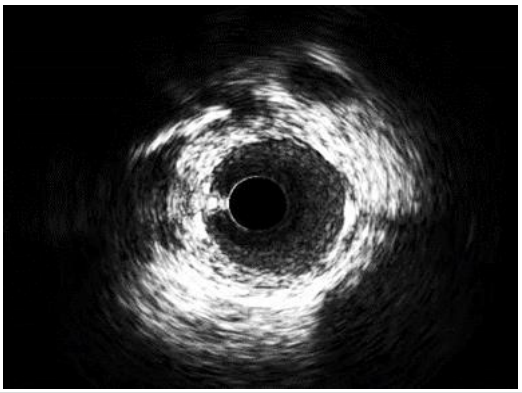

Figure 2

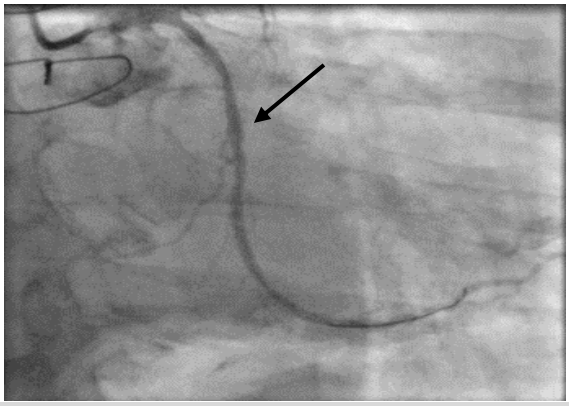

Figure 5

Figure 1: Left coronary angiography showing diffuse in-stent restenosis involving proximal left circumflex artery (Black arrow).
Figure 2: Intravascular Ultrasound showing calcific, neoatherosclerosis involving previous stent.
Figure 3: Initial inflation of the lithotripsy balloon at the proximal stent left circumflex coronary artery, showing adequate expansion of the 3.5 mm × 12 mm lithotripsy balloon at the proximal part of the left circumflex coronary artery (Black arrow)
Figure 4: intravascular ultrasound performed after the lithotripsy showing calcium rupture and absence of vessel perforation or distal dissection.
Figure 5: Final angiographic result of the left circumflex coronary artery was satisfactory, confirmed absence of vessel perforation or distal dissection with good final result (Black arrow).

Timeline

April 2000	CABG(LIMA to LAD,SVG to IM and LCX)
January 2011	PCI to native LMS, LAD, RCA and LCX for ongoing angina
June 2015	Admitted with Angina, coronary angiogram confirmed ISR in the LCX, treated with cutting balloon, DEB.
March 2019	Re-admitted with ISR in LCX, treated with angiosculpt X DCB and laser.
June 2021	Elective coronary angiogram (CA) showed recurrent ISR in left the circumflex artery. IVUS demonstrated the previous stent to be sub optimally expanded. Use of IVL (3.5x12 balloons used for 8 cycles) undertaken. The final IVUS and angiogram images showed calcium augmentation, improvement in mean luminal area, and the absence of vessel perforation or distal dissection. The patient made an uneventful recovery and was discharged the same day
December 2021	Patient was well and free of any symptoms suggestive of coronary ischaemia.

Learning point

1. The use of Intravascular Lithotripsy in recurrent calcium-mediated coronary in-stent restenosis has shown good acute and mid-term procedural and clinical results.
2. The use of IVL in repeat ISR has the potential to provide excellent results in such an area of interventional cardiology where treatment options are limited.

Discussion

Coronary artery calcification is a very strong predictor for the need repeat revascularization due to in-stent restenosis (ILR), stent under expansion, target vessel revascularization (TVR)and stent thrombosis, and overall heavy coronary vessel calcification could lead to a higher risk of stent failure and future adverse events [6].

Despite the development of plaque modifying therapy, management of in-stent restenosis due to heavy calcium burden and fibrotic coronary stenosis, remains difficult, challenging, and often requires adjuvant interventional tools and techniques. For patients with ISR, treatment options are limited and as such this patient population have poorer outcomes vs those with de novo lesions [7]. Furthermore, sub optimal treatment of ISR is associated with poorer patient outcomes with regards to recurrent MI, target vessel revascularisation, cardiovascular death [8]. At present the use of cutting or scoring balloons, laser and rotational atherectomy in the context of ISR has limited efficacy with such techniques carrying heightened procedural complications risk vs use in de novo lesions. Nikolakopoulos el at presented a comprehensive report of first time use of repeated peripheral IVL catheter in combination of brachytherapy to treat recurrent ISR. However, this practice is still off-label, but has been described as effective and safe in management of stent-under-expansion [9]. The evidence for IVL use or its repeated use to treat in-stent restenosis is sparse and is an off-label indication. A small retrospective, single-centre analysis was performed by Brunner FJ, et al of 6 cases with undilatable in-stent restenosis due to calcium-mediated stent under expansion and/ or calcified neointima. Lesions were treated with IVL (Shockwave Medical) and subsequent drug-eluting result has shown acute angiographic success and angina relief were achieved in 5 of 6 cases and sustained during follow-up with no major acute cardiovascular events occurred [10].

IVL therefore offers a simpler technique to modify ISR with a shorter learning curve. Unlike rotational atherectomy IVL can be used in large coronary vessels (largest IVL balloon being 4mm in diameter) and is associated with a lower occurrence of slow or no-reflow phenomenon [11]. This case presentation highlights a novel use of IVL in a sub class of patients that remain challenging for the interventional cardiology community.

Abbreviations

CABG: Coronary artery bypass graft
RCA: Right coronary artery
LAD: Left anterior descending
LCX: Left the circumflex artery
LIMA: Left internal mammary artery
SVG: Saphenous vein graft
IVL: Intravascular lithotripsy therapy
ISR: In-stent restenosis
IVUS: Intravascular ultrasound

Disclosures

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