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Retrievable scaffold therapy before paclitaxel drug-coated balloon angioplasty in infrapopliteal arteries: one-year outcomes of the DEEPER OUS Study

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Percutaneous transluminal angioplasty (PTA) is a common treatment for infrapopliteal artery disease, but acute elastic recoil and restenosis limit its efficacy. While drug-coated balloons (DCBs) may reduce restenosis by delivering antiproliferative agents to the arterial wall, studies comparing DCBs to PTA have been inconclusive. Retrievable scaffold therapy (RST) utilises a spur stent with microspikes that create microchannels in the arterial wall to enhance DCB drug delivery. The prospective, multicentre, single-arm DEEPER OUS Study (ClinicalTrials.gov: NCT03807531) evaluated RST prior to paclitaxel DCB angioplasty for infrapopliteal disease.

Independent core laboratories evaluated duplex ultrasound and angiographic imaging. An independent clinical events committee adjudicated device-related adverse events, and an independent data safety monitoring board provided study oversight. The study enrolled adults with peripheral artery disease (Rutherford-Becker classification [RBC] 3-5) and infrapopliteal disease with lesion lengths of 30-150 mm and reference vessel diameters of 2.0-4.5 mm **(Supplementary Table 1)**. Patients were treated with RST (Spur Peripheral Retrievable Scaffold System [Reflow Medical]), a temporary self-expanding nitinol stent, prior to DCB angioplasty **(Supplementary Figure 1)**. The primary efficacy endpoint was primary patency at 6 months (duplex ultrasound patency and freedom from clinically driven target lesion revascularisation). The primary efficacy endpoint was compared to a 51% performance goal derived from an infrapopliteal PTA meta-analysis[1]. The primary safety endpoint was freedom from device- or procedure-related death up to 30 days.

Among 107 patients (mean age 76 years [range 49-98 years], 78% male, 69% RBC 5) enrolled at 10 centres between July 2019 and May 2022 **(Supplementary Table 2)**, 169 spur stents were deployed (mean treated length 90 mm) in 106 patients (1 delivery failure), with uncomplicated removal in all cases. Bailout treatment was performed in 2 (1.9%) patients: 1 received stent placement due to residual stenosis >30% in a heavily calcified lesion after DCB angioplasty and 1 received a dissection repair device for type B dissection following DCB angioplasty. Among 84 patients with duplex ultrasound imaging evaluated by the core laboratory at 6 months, primary patency was 85.7% (95% confidence interval: 78.2-93.2%; p<0.001 vs 51% performance goal), with no difference in patients with calcified (Peripheral Arterial Calcium Scoring System [PACSS] score 1-4) versus non-calcified (PACSS score 0) lesions (84.7% vs 88.0%; p=0.70). Freedom from device- or procedure-related death up to 30 days was 100%. Kaplan-Meier estimates at 1 year were 75.7% for primary patency **(Supplementary Figure 2)** (72.7% vs 76.9% in patients with calcified vs non-calcified lesions; p=0.69), 91.7% for freedom from clinically driven target lesion revascularisation **(Supplementary Figure 3)**, and 98.9% for freedom from major amputation. The mean RBC decreased from 4.5±0.8 at baseline to 1.9±2.1 at 1 year, with 69% of patients improving ≥2 categories. The ankle-brachial (0.75±0.28 to 0.94±0.31) and toe-brachial (0.45±0.24 to 0.58±0.24) indices both increased at 1 year (both p<0.001) **(Table 1)**. The composite Wound, Ischemia, foot Infection (WIfI) score decreased from 2.3±1.2 to 1.3±0.7: the wound score decreased from 1.3±0.6 to 0.6±0.6, the ischaemia score decreased from 1.4±0.9 to 0.6±0.9, and the foot infection score decreased from 0.5±0.8 to 0.1±0.4. The median wound area

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Table 1. Clinical outcomes up to 1 year.

Outcome	Baseline	1 month	3 months	6 months	1 year
Primary patency	-	98.9	93.5	85.7*	74.4
Freedom from CD-TLR	-	100	98.0	92.6	89.5
Freedom from major amputation	-	100	98.9	98.9	98.9
Freedom from all-cause death	-	100	98.1	95.3	91.6
Rutherford-Becker class	4.5±0.8	3.5±2.1†	2.7±2.3†	2.1±2.2†	1.9±2.1†
ABI	0.75±0.28	-	-	-	0.94±0.31†
TBI	0.45±0.24	-	-	-	0.58±0.24†

Values are mean±SD or percentages (derived from n/N). *The primary efficacy endpoint was met as the 95% confidence interval lower limit (78.2%) was significantly higher than the performance goal of 51%. †p<0.001 for change from baseline. ABI: ankle-brachial index; CD-TLR: clinically driven target lesion revascularisation; SD: standard deviation; TBI: toe-brachial index

decreased from 200 mm^2 to 2 mm^2, with complete wound healing in 59% of patients. Freedom from a device-related adverse event at 1 year was 95.3%, with only non-flow limiting dissection or vasospasm being reported.

The DEEPER OUS Study demonstrated that RST prior to DCB angioplasty is a safe and effective strategy for treating infrapopliteal artery disease. The primary efficacy endpoint was met, with 6-month primary patency of 85.7% being statistically greater than the 51% performance goal. This outcome favourably compared to typical outcomes with PTA[1-3] or DCB[3,4] **(Supplementary Table 3)**. The sustained effectiveness of this treatment approach was demonstrated by low rates of clinically driven target lesion revascularisation and major amputation at 1 year, with significant improvements in RBC score, wound healing, and limb haemodynamics. Furthermore, a substudy of DEEPER OUS reported elastic recoil in 42.5% of lesions, compared to 97% recoil with PTA[5]. Thus, RST before DCB angioplasty may mitigate the negative impact of arterial recoil, improve intra-arterial drug delivery into complex lesions, and avoid complications associated with permanent metallic stents in infrapopliteal vessels.

Several limitations of this study warrant discussion. First, the 6-month primary patency results were compared to a historical PTA performance goal[1]; however, RST has not been directly compared to PTA or DCB alone in a clinical trial. Second, operators selected DCBs at their discretion, which complicates the evaluation of specific device combinations. Finally, the exclusion of patients with prior bypass surgery, lesion lengths of >150 mm, and severe calcification may limit the generalisability of the findings in these populations.

In conclusion, the DEEPER OUS Study demonstrates that RST prior to paclitaxel DCB angioplasty is a promising treatment strategy for patients with infrapopliteal artery disease. By addressing key limitations of existing endovascular therapies, such as acute vessel recoil and suboptimal drug delivery in calcified lesions, and leaving no permanent implant behind, this combination therapy may represent a significant advancement in the management of infrapopliteal artery disease.

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Conflict of interest statement

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References

1. Romiti M, Albers M, Brochado-Neto FC, Durazzo AE, Pereira CA, De Luccia N. Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia. *J Vasc Surg*. 2008;47:975-81.
2. Snyder DJ, Zilinyi RS, Pruthi S, George S, Tirziu D, Lansky A, Mintz AJ, Sethi SS, Parikh SA. Percutaneous Transluminal Angioplasty for Infrapopliteal Chronic Limb-Threatening Ischemia: A Systematic Review and Meta-analysis of Primary Patency and Binary Restenosis Rates. *J Endovasc Ther.* 2023 Nov 26. [Epub ahead of print].
3. Guo J, Ning Y, Wang H, Li Y, Su Z, Zhang F, Wu S, Guo L, Gu Y. The efficacy and safety of different endovascular modalities for infrapopliteal arteries lesions: A network meta-analysis of randomized controlled trials. *Front Cardiovasc Med*. 2022;9:993290.
4. Giannopoulos S, Ghanian S, Parikh SA, Secemsky EA, Schneider PA, Armstrong EJ. Safety and Efficacy of Drug-Coated Balloon Angioplasty for the Treatment of Chronic Limb-Threatening Ischemia: A Systematic Review and Meta-Analysis. *J Endovasc Ther.* 2020;27:647-57.
5. Zeller T, Zhang Z, Parise H, Mascho C, Holden A, Schmidt A, Thieme M, Piorkowski M, Hertting K, Wissgott C, Andrassy M, Noory E, Weinberg I, Kolluri R. Early Tibial Vessel Recoil Following Treatment With the Bare Temporary Spur Stent System: Results From the DEEPER OUS Vessel Recoil Substudy. *J Endovasc Ther.* 2024 Sep 21. [Epub ahead of print].

Supplementary data

Supplementary Table 1. General and angiographic inclusion/exclusion criteria.

Supplementary Table 2. Patient and procedural characteristics.

Supplementary Table 3. Primary patency with retrievable scaffold therapy compared to meta-analysis-derived estimates with DCB and PTA in infrapopliteal arteries.

Supplementary Figure 1. Retrievable scaffold therapy.

Supplementary Figure 2. Kaplan-Meier estimate of target lesion primary patency up to 12 months.

Supplementary Figure 3. Kaplan-Meier estimate of freedom from clinically driven target lesion revascularisation up to 12 months.

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Supplementary data

Supplementary Table 1. General and angiographic inclusion/exclusion criteria.

General Inclusion Criteria
1. Subject is willing and able to provide informed consent and able to comply with the study protocol.
2. Life expectancy >1 year in the investigator's opinion.
3. Subject is > 18 years of age.
4. Subject is Rutherford class 3-5.
5. For subjects with bilateral disease, planned treatment of the contralateral limb must either be performed ≥ 30 days prior to the index procedure or ≥ 14 days following the index procedure.
Angiographic Inclusion Criteria
1. Stenotic, restenotic, or occlusive lesions located in the infrapopliteal vessels, with target lesion that can be successfully crossed with a guidewire.
2. Target lesion must meet lesion-specific criteria in pre-screening by angiography at time of procedure (pre-screening with Computed Tomography Angiography [CTA], Magnetic Resonance Angiography [MRA], or selective angiography may be performed prior to the index procedure).
3. Target vessel(s) reconstitute(s) at or above the medial malleolus, with the target treated segment extending no more than 10 mm beyond the medial malleolus. Note: If the anterior tibial or posterior tibial arteries are treated, there must be inline flow to the foot. If the peroneal artery is treated, there must be at least one collateral supplying the foot.
4. Target lesion must begin no higher than the tibial trifurcation (popliteal artery excluded).
5. Target vessel reference diameter is measured to be between 2.0 mm to 4.5 mm in diameter, assessed by one of the following methods after successful completion of guidewire crossing of the lesion site: a. Intravascular Ultrasound (IVUS) b. Optical Coherence Tomography (OCT) c. Quantitative Vascular Angiography (QVA)
6. Lesion length must be ≥ 30 mm and ≤ 150 mm
7. Only one limb may be enrolled per subject and only one artery may be treated with the index device. Up to two vessels may be treated per subject; if required, a second modality may be used for treatment in the non-target infrapopliteal vessel.
8. The treated segment is defined as the total length of artery treated with the investigational device. Target treatment length is ≤ 240 mm with a maximum segment of 150 mm separated by 30 mm of healthy tissue between treated lesions.
9. Successful pre-dilatation of the target lesion as outlined in the procedure instructions, defined as resulting in stenosis < 50%, without resulting flow limiting (Type D or greater) dissection, thrombus, or aneurysm by angiography prior to the insertion of the investigative device.
10. Iliac, Superficial Femoral Artery (SFA) and popliteal inflow lesions can be treated using standard angioplasty and/or an approved stent (no atherectomy) during the index procedure or ≥ 30 days prior. Inflow lesions treated intraprocedure must be treated first, prior to

consideration of treatment of infrapopliteal lesions. If pre-screening confirming patent aortoiliac flow with duplex ultrasound (DUS),angiography, CTA, or MRA has been performed ≤ 365 days prior to the procedure, intra-procedure angiography of the aorto-iliac vasculature is not required, however, the femoropopliteal inflow must still be imaged using angiography during the index procedure. Inflow lesions must have a healthy vessel segment of ≥ 30 mm between the study lesion and the treated segment, defined as less than 50% stenosis without aneurysmal segments.
11. Retrograde access (in the infrapopliteal arteries) is permitted for lesion crossing; however, the Bare Temporary Spur Stent System must be deployed from antegrade access.
General Exclusion Criteria
1. Subject unwilling or unlikely to comply with the appropriate follow-up time for the duration of the study in the opinion of the investigator.
2. Subject is pregnant or planning to become pregnant during the course of the trial.
3. Subject has an active infection that is not controlled at the time of the procedure, including septicemia or bacteremia.
4. Subject has osteomyelitis or a heel wound. Osteomyelitis in the digit(s) of the target foot is permitted.
5. Planned major (above the ankle) amputation of the target limb. A planned or previous minor (transmetatarsal amputation or digit amputation) is permitted
6. Recent myocardial infarction or stroke < 90 days prior to the index procedure.
7. Heart failure with Ejection Fraction < 35%.
8. Impaired renal function (estimated glomerular filtration rate ≤ 25 mL/min) within 30days of procedure or end-stage renal disease on dialysis.
9. Subject with vasculitis, systemic Lupus Erythematosus or Polymyalgia Rheumatica.
10. Subject receiving chronic or intravenous corticosteroid therapy.
11. Inability to tolerate dual antiplatelet and oral anticoagulation therapy.
12. Known allergies or sensitivities to heparin, antiplatelet drugs, other anticoagulant therapies which could not be substituted, drug balloon coatings and their excipients, including, but not limited to, paclitaxel, sirolimus, or zotarolimus, or an allergy to contrast media that cannot be adequately pre-treated prior to the index procedure.
13. The subject is currently enrolled in another investigational device or drug trial.
14. Known allergy to nitinol or nickel.
Angiographic Exclusion Criteria
1. Prior stent(s) within the target vessel, or bypass surgery of or within the target vessel(s)
2. Target lesion is located within an aneurysm or associated with an aneurysm in the vessel segment either proximal or distal to the target lesion. Inflow must also be free of aneurysmal segments.
3. Previous treatment failure of inflow arteries (iliac, SFA, and popliteal) which required a surgical procedure. Prior bypass above the level of the infrapopliteal arteries is permitted.
4. Previous treatment of inflow lesions, if not treated during the index procedure, must have been performed ≥ 30 days prior to the index procedure.
5. Previous treatment of the target vessel ≤ 30 days prior to index procedure
6. Angiographic evidence of thrombus within target limb.
7. Inability to obtain antegrade access in the limb from which the investigative device can be deployed.
8. Extremely severe calcification classified as grade 4 as measured by the Peripheral Academic Research Consortium score or the Peripheral Arterial Calcium Scoring System that, in the investigator's opinion, would not be amenable to PTA.

9. Type D dissections or greater incurred during pre-dilation or chronic total occlusion (CTO) crossing.
10. Significant (≥ 50%) stenosis of inflow arteries or unsuccessful treatment of inflow lesions.

Supplementary Table 2. Patient and procedural characteristics.

Characteristic	Value
Demographics	
Age, yrs	76 ± 9
Male sex	77.6% (83/107)
Medical history	
Hypertension	94.4% (101/107)
Hyperlipidemia	84.1% (90/107)
Diabetes mellitus	61.7% (66/107)
Coronary artery disease	35.5% (38/107)
Chronic kidney disease	32.7% (35/107)
Cerebrovascular disease	15.9% (17/107)
Myocardial infarction	13.1% (14/107)
Congestive heart failure	10.3% (11/107)
Planned amputation of index limb/toes	9.3% (10/107)
Previous amputation of index limb/toes	8.4% (9/107)
Osteomyelitis	4.7% (5/107)
Rutherford-Becker classification	
3	20.6% (22/107)
4	10.3% (11/107)
5	69.2% (74/107)
Lesion characteristics	
TASC classification	
A	32.8% (45/137)
B	37.2% (51/137)
C	24.8% (34/137)

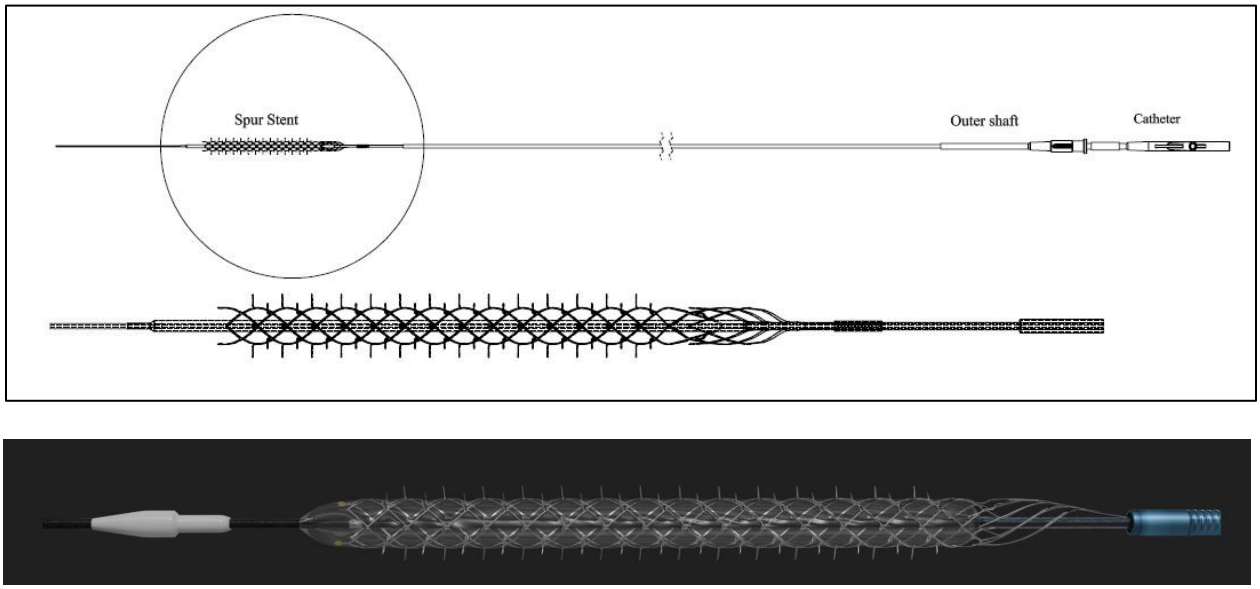
D	5.1% (7/137)
PACSS calcium score	
0	28.8% (40/139)
1	28.1% (39/139)
2	22.3% (31/139)
3	20.1% (28/139)
4	0.7% (1/139)
Lesion length, mm	82 ± 48
Reference vessel diameter, mm	3.1 ± 0.5
Treated artery	
Tibioperoneal trunk	30.8% (33/107)
Peroneal	29.0% (31/107)
Anterior tibial	27.1% (29/107)
Posterior tibial	12.1% (13/107)
Popliteal	0.9% (1/107)
Procedures	
Procedure duration, min	84 ± 45
Fluoroscopy time, min	18 ± 12
Contrast volume, ml	148 ± 94
Spur stent treated length, mm	90 ± 34 *
DCB treated length, mm	97 ± 33 *

Values are mean ± SD or n (%).
*Data from 106 patients with successful predilatation.
DCB = drug-coated balloon; PACSS = Peripheral Arterial Calcium Scoring System; TASC = Trans-Atlantic Inter-Society Consensus.

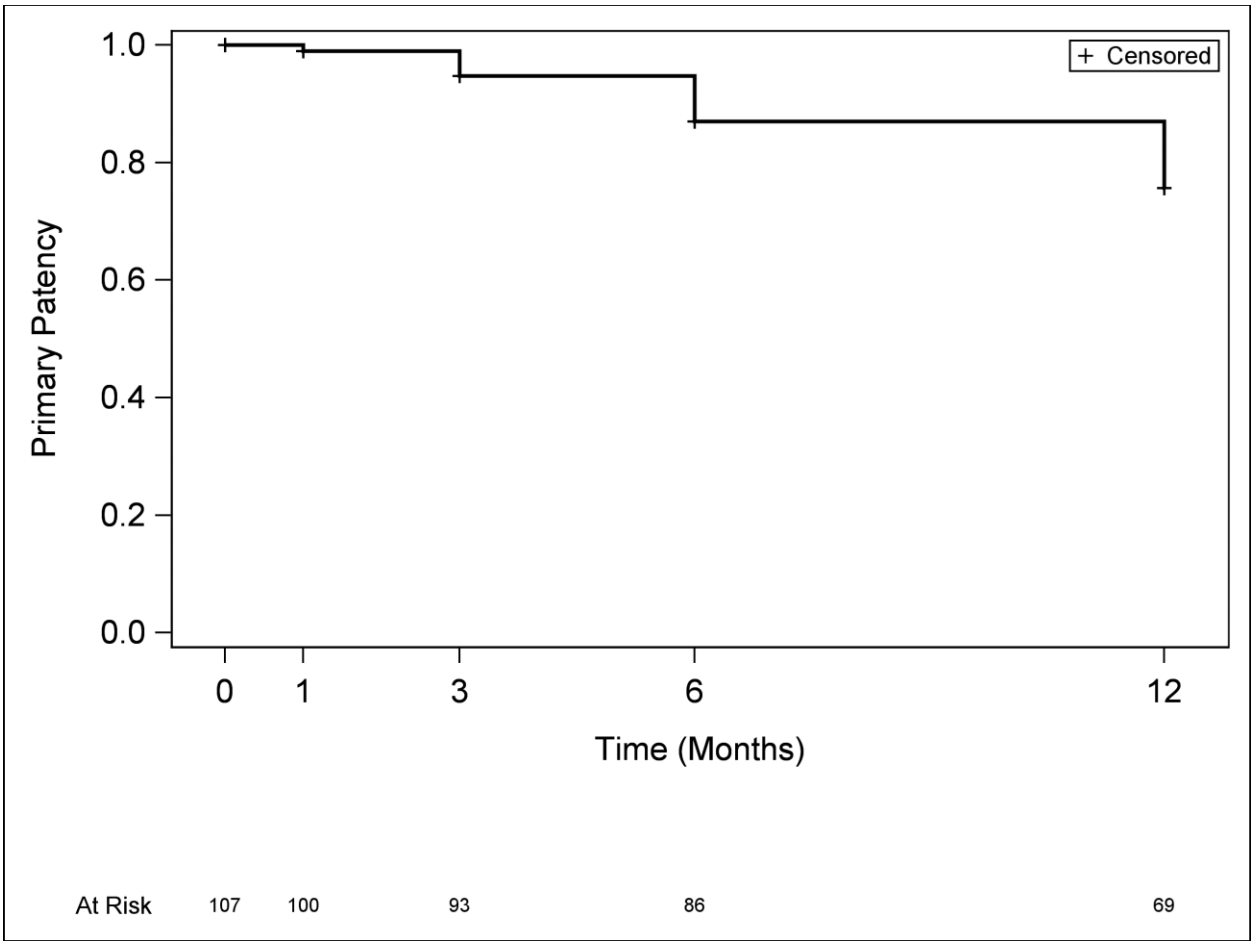
Supplementary Table 3. Primary patency with retrievable scaffold therapy compared to meta-analysis-derived estimates with DCB and PTA in infrapopliteal arteries.

Study	6 months	1 year
Retrievable scaffold therapy		
DEEPER OUS	86%	74%
DCB		
Guo [2022] [3]	68%	74%
Giannopoulos [2020] [4]	*	64%
PTA		
Snyder [2023] [2]	68%	66%
Guo [2022] [3]	35%	27%
Romiti [2008] [1]	65%	58%

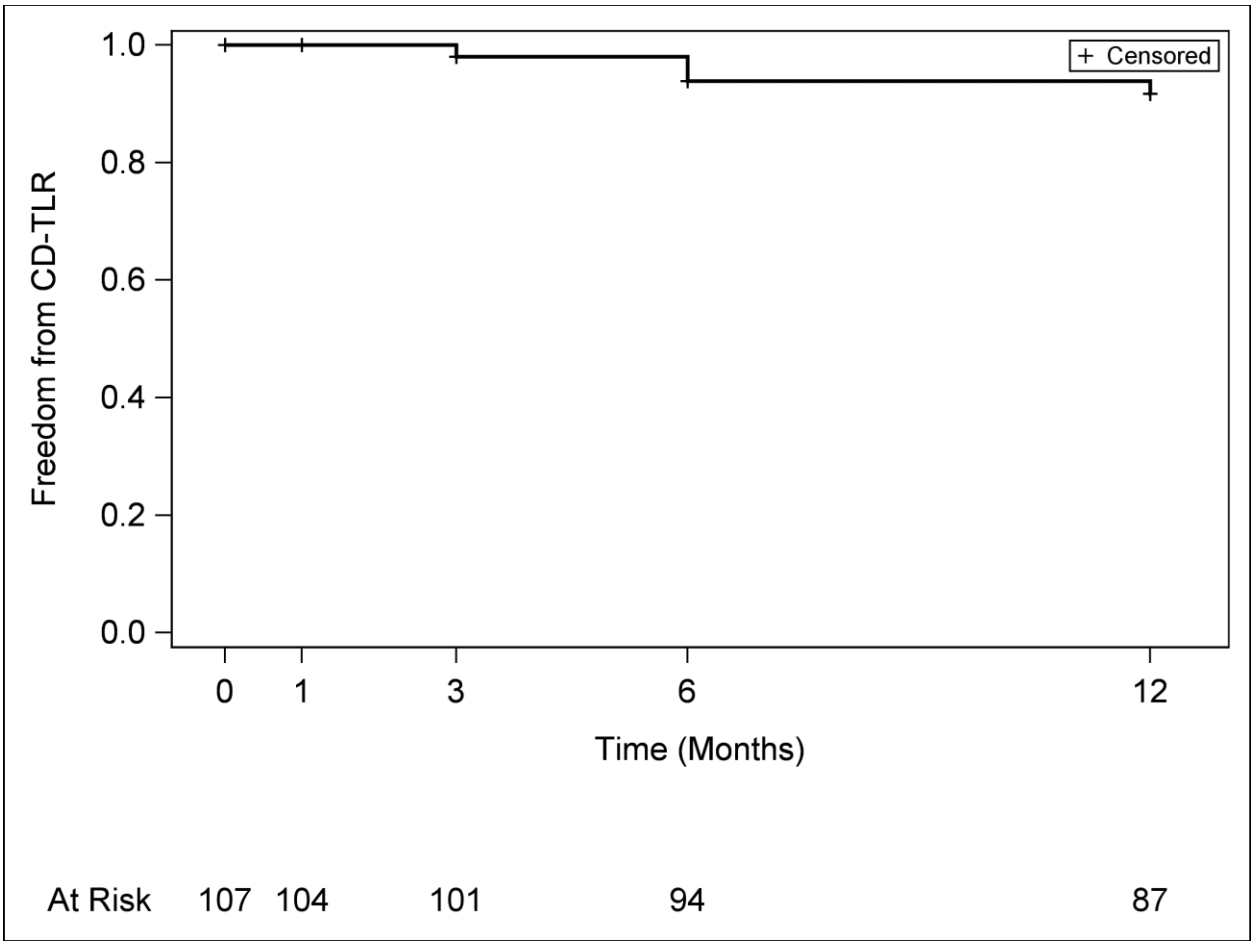
*Values not reported.
DCB = drug-coated balloon; PTA = percutaneous transluminal angioplasty.



Supplementary Figure 1. Retrievable scaffold therapy.
Retrievable scaffold therapy consists of a catheter with a balloon-expandable nitinol stent collapsed and housed within a 5.6Fr outer shaft. The system is advanced to the target lesion where the stent is deployed (top and bottom images), acting as a temporary intra-arterial scaffold. The balloon catheter is then inflated, expanding the stent in a controlled fashion while the circumferential spikes create microchannels in the vessel wall. These microchannels enhance uptake and retention of antiproliferative drugs during subsequent drug-coated balloon angioplasty. The balloon is then deflated, and the stent is recaptured into the outer shaft for complete removal from the vasculature.



Supplementary Figure 2. Kaplan-Meier estimate of target lesion primary patency up to 12 months.



Supplementary Figure 3. Kaplan-Meier estimate of freedom from clinically-driven target lesion revascularisation up to 12 months.