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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 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 Medicall), 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-analysis¹. 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 noncalcified 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 anklebrachial $(0.75\pm0.28 \text{ to } 0.94\pm0.31)$ 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

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 mm² to 2 mm², 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 PTA¹⁻³ 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 PTA5. 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 goal¹; 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

M.K.W. Lichtenberg: medical advisory board member for Cook and Philips; clinical investigator for Abbott, Bard/BD, Biotronik, Cagent, Cook, LimFlow, MedAlliance, Penumbra, Philips, Reflow Medical, Shockwave Medical, Terumo, and TriReme Medical. A. Holden: medical advisory board member for Boston Scientific, W. L. Gore & Associates, Medtronic, and Philips; clinical investigator for Abbott, Artivion, Bard/ BD, Biotronik, Boston Scientific, Cagent, Cook, Efemoral, Endospan, Fluidx, W. L. Gore & Associates, LimFlow, MedAlliance, Medtronic, Merit, Nectero, Penumbra, Philips, Reflow Medical, Shape Memory, Shockwave Medical, Terumo, TriReme Medical, and Vesteck. D. Scheinert: consultant or on the advisory board for Abbott, Biotronik, Boston Scientific, Cook Medical, Cordis, CR Bard, Gardia Medical, Medtronic/ Covidien, TriReme Medical, TriVascular, and Upstream Peripheral Technologies. A. Schmidt: consultant for Abbott, Boston Scientific, Cook Medical, Cordis, CR Bard, Reflow Medical, and Upstream Peripheral Technologies. J.C. van den Berg: clinical investigator for Reflow Medical. M. Piorkowski: honoraria received from Abbott, Boston Scientific, Inari Medical, Veryan, and W. L. Gore & Associates; research grants received from Abbott, Bolt Medical, Endologix, Inari Medical, Reflow Medical, Reva Medical, and W. L. Gore & Associates. K. Hertting: honoraria received from Bard-BG and Biosensors. M. Andrassy: honoraria received from Bard-BG and Boston Scientific. C. Wissgott: consultant for Philips and Bard/BD; clinical investigator for InspireMD. L.E. Miller: consultant for Reflow Medical, Micro Medical Solutions, and Shockwave Medical. T. Zeller: honoraria received from: Acotec, Biotronik, Boston Scientific, Cook Medical, Cordis, and Medtronic; consultant for: Acotec, ANT, Boston Scientific, W. L. Gore & Associates, Medtronic, Shockwave Medical, Venture Med, Veryan, and Reflow Medical; institutional grants for research, clinical trial, or drug studies received from: Ablative Solutions, Bard Peripheral Vascular, Boston Scientific, Cook Medical, CSI, W. L. Gore & Associates, Intact Vascular, MedAlliance, Medtronic, Philips, PQ Bypass, Reflow Medical, Shockwave Medical, Surmodics, Terumo, TriReme Medical, University of Jena, and Veryan; stock options: ANT and Cordis/MedAlliance. M. Thieme has no conflicts of interest to declare.

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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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