In-stent restenosis (ISR) occurs in 19% to 37% of treated femoropopliteal (FP) arteries at 1 year.1-4 Treatment of these lesions with balloon angioplasty has a high rate of recurrence and repeat target lesion revascularization (TLR).5-10 FP ISR is predominantly caused by smooth muscle cell proliferation in nonocclusive lesions and smooth muscle cell thrombotic lesions in total occlusions. There is no consensus on the optimal approach for treating FP ISR to reduce intraprocedural complications and improve long-term patency. Tissue reduction while protecting the outflow vessels from distal embolization, coupled with the application of antirestenotic measures, has been described as a strategy that is likely to be successful in achieving safe and durable results in treating FP ISR.11

Tissue reduction in FP ISR may potentially delay the need for frequent repeat revascularization and restenting. Debubbling is best achieved with atherectomy. Small observational series have been reported using debubbling in FP ISR. The following is a summary of the current published data.

**DIRECTIONAL ATERECTOMY WITH SILVERHAWK**

In the instructions for use (IFU), the SilverHawk atherectomy device (Covidien, Mansfield, MA) is contraindicated for FP ISR because of the potential risk of cutter entrapment on the stent with subsequent serious adverse events including perforation, vessel tear, and an inability to retrieve the device, which would require surgical intervention. There are no randomized studies to evaluate SilverHawk atherectomy in the treatment of FP ISR, and it is unlikely that these will be done because of the current IFU label. Limited observational data, however, indicate that SilverHawk atherectomy has high acute procedural success when used by experienced operators, but patency rates at 1 year remain low, and TLR rates are high.

Zeller et al reported a primary patency rate of 49% at 18 months in treating FP ISR (mean lesion length of 111 mm).7 TLR at 12 and 18 months were 47% and 49%, respectively. In addition, Trentmann et al reported an acute procedural...
success rate of 97% in treating FP ISR (mean lesion length of 108 mm).\textsuperscript{6} Adjunct stenting was needed in only 11% of patients. However, patency continued to decline on follow-up from 86.2% at 3 months to 68% at 6 months and 25% at 12 months.

Finally, Shammas et al reported acute procedural success (< 30% angiographic residual narrowing) in 100% of 41 patients who were treated for FP ISR.\textsuperscript{8} The TLR rate was 31.7% at 1 year (lesion length of 126.2 mm). Bailout stenting was performed in 24.4%. An early high success rate was seen at 6 months with SilverHawk atherectomy, which gradually worsened at 1 year.

Similar findings were reported by Brodmann et al in a randomized trial of SilverHawk atherectomy versus percutaneous transluminal angioplasty (PTA) for ISR FP lesions.\textsuperscript{12} In their study, intima media thickness was progressively worse at 2, 6, and after 6 months posttreatment, with no difference in outcome at 1 year between SilverHawk atherectomy and PTA. This aggressive debulking seems to delay the initial need for TLR at 6 months but with a subsequent higher failure rate on further follow-up.\textsuperscript{12,13} The exact mechanism of this delayed progressive TLR is unclear, but it has been observed in other forms of directional atherectomy such as with the use of the Turbo-Tandem laser (Spectranetics Corporation, Colorado Springs, CO) in FP ISR, which was recently reported in the PATENT study.\textsuperscript{14} In summary, SilverHawk atherectomy has high acute procedural success and less need for restenting when treating FP ISR. Its disadvantages, however, are its high TLR rate at 1 year and significant distal embolization.\textsuperscript{15-17} Short runs with frequent packing and emptying of the nose cone of the cutter are essential to reduce this risk. The off-label use of embolic filter protection in FP ISR seems to be effective in capturing debris and reduces the need for treating distal embolization.

**JETSTREAM AHERECTOMY**

Beschorner et al reported data on 40 infrainguinal ISR lesions treated with the Pathway PV atherectomy system (Pathway Medical Technologies, Inc., Kirkland, WA).\textsuperscript{18} Primary patency was 33% after 12 months and 25% after 24 months. Since then, the Pathway PV system has been significantly modified into the Jetstream atherectomy system (Bayer, Indianola, PA). Currently, FP ISR is an off-label application for the Jetstream device.

The ongoing JetStreamISR registry is currently evaluating the feasibility of the Jetstream Navitus device in treating these lesions. Acute procedural data on the first 11 patients treated as part of the registry were presented at New Cardiovascular Horizons 2013 in New Orleans, Louisiana.\textsuperscript{19} Acute procedural success, defined as ≤ 30% residual stenosis (via quantitative vascular analysis) at the index lesion after Jetstream atherectomy with adjucntive balloon angioplasty and with no occurrence of serious adverse events, was reported in 91% of patients (11/11 patients < 30%, 10/11 patients < 30% and with no adverse events) (Figure 1). Bailout stenting occurred in 9% (1/11 patients). Distal embolization requiring treatment occurred in one patient as a result of the filter wire getting stuck on the Jetstream while being retrieved, requiring pulling out both filter wires and the Jetstream device as one unit. Intermediate-term results are not yet available. Some of the noticeable early advantages of this device appear in its ability to reduce bailout stenting and to minimize distal embolization.

**ORBITAL AHERECTOMY**

Orbital atherectomy is contraindicated in patients with ISR. To our knowledge, there is currently no published data on orbital atherectomy in FP ISR. The safety and effectiveness of this technique have yet to be demonstrated in treating ISR lesions.

**LASER AHERECTOMY IN FP ISR**

Laser photoablation is currently US Food and Drug Administration (FDA) approved for the treatment of de novo coronary artery lesions, de novo peripheral artery lesions, and coronary artery ISR lesions, but not peripheral artery ISR lesions. In fact, there are currently no FDA-approved devices for the treatment of ISR outside the coronary circulation.

There are three distinct mechanisms of action that contribute to laser photoablation: (1) photochemical
disruption of cellular molecular bonds, (2) photothermal heat production that causes steam vapor disruption of cell membranes, and (3) photomechanical kinetic energy that dissipates cellular debris. Each laser pulse has a duration of 125 nanoseconds and a depth of penetration of 100 μm. The physical properties of neointimal hyperplasia are ideal for ablation by excimer laser.

The PATENT study (using the Turbo-Booster device [Spectranetics Corporation]) was a prospective multicenter registry that enrolled 90 patients at five centers in Germany to assess the safety and efficacy of using laser atherectomy for FP ISR. It was designed to be a nonrandomized feasibility study. The average lesion length was 10.9 cm. The angiographic core lab adjudicated pre- and post-laser and post-PTA stenosis percentcs were 87.1%, 32.4%, and 7.5%, respectively, with a technical procedural success rate of 98.8%. The primary safety endpoint of major adverse events at 30 days was 2.2%, consisting of two episodes of stent thrombosis. Freedom from TLR at 6 months was 97.8%, with PTA versus PTA alone (Figure 2), with the goal of obtaining an FDA on-label indication for using laser atherectomy to treat FP ISR. The study will enroll 353 patients at 35 institutions in the United States, with a 2:1 randomization between laser with PTA versus PTA alone. The primary safety endpoint is 30-day freedom from major adverse events (death, major amputation, and TLR). The primary efficacy endpoint is artery patency at 6 months, which is defined as freedom from TLR and a duplex ultrasound peak systolic velocity ratio < 2.5. The study is approximately halfway through the enrollment, and the results are eagerly anticipated.

CONCLUSION

In summary, treatment of FP ISR has a high rate of procedural success, but also a high TLR rate. Aggressive tissue reduction seems to lower the rate of TLR in the first 6 months when compared to the historic control of balloon angioplasty, but with progressive loss of TLR and patency at 1 year, as demonstrated with both SilverHawk atherectomy and the Turbo-Tandem laser. Lack of aggressive initial debulking is associated with a high initial loss of TLR survival, as has predominantly been seen with the Turbo Elite laser. SilverHawk atherectomy is contraindicated per IFU labeling for treating FP ISR, but observational data show a good safety profile with experienced operators. Both Jetstream and the Turbo Elite laser are off label for treating FP ISR. The EXCITE trial is currently ongoing and will evaluate balloon angioplasty with the Turbo-Tandem laser for treating FP ISR.

Nicolas W. Shammas, MD, MS, FACC, is with the Genesis Heart Institute, and is President and Research Director, Midwest Cardiovascular Research Foundation in Davenport, Iowa. He has disclosed that he has received educational and research grants from Medrad, Coviden, CSI, and Spectranetics for the Midwest Cardiovascular Research Foundation. He is also on the Steering Committee of the JET registry and is the Principal Investigator of the Jetstream ISR study. Dr. Shammas may be reached at shammas@mchsi.com.

Eric J. Dippel, MD, FACC, is with the Genesis Heart Institute in Davenport, Iowa. He has disclosed that he is the National Principal Investigator for the EXCITE study, has received research grants from Spectranetics, and is a shareholder of Spectranetics. Dr. Dippel may be reached at dippel@cvmedpc.com.