Each year approximately 200,000 United States patients undergo interventional procedures in which stents are placed in the femoral and popliteal arteries. Multiple studies have shown that nitinol stents improve patency and relieve symptoms more effectively when treating femoral and popliteal obstructions than percutaneous transluminal angioplasty (PTA) alone. Stents in the superficial femoral artery (SFA) and popliteal arteries are subject to external forces such as bending, twisting, elongation, foreshortening, and external compression. It is estimated that approximately 30% to 40% of these stents will develop in-stent restenosis or occlusion within 2 years of implantation. Repeated restenotic events are common. Until late 2014 there were no FDA approved therapies for the treatment of this growing clinical problem. We now have two approved therapies (excimer laser and Viabahn stent grafts). Other therapies are being actively evaluated.

In-stent restenosis (ISR) typically is secondary to neointimal hyperplasia in fully expanded stents. Total occlusions have super-imposed thrombus. ISR is more common when there are stent fractures and with long-segment stenting. Occasionally in-stent restenosis occurs in segments where the stent is compressed, typically in areas of densely calcified plaque. There are many factors to consider when treating ISR including stenosis versus occlusion, acute vs chronic symptoms (suggesting acute thrombus), stent fractures, type of stent, length of lesion, stent compression, type of stent, location of stent, and so on.

The treatment of ISR with standard balloon angioplasty has been associated with poor patency and complications such as embolization and flow-limiting dissections, particularly in long-segment occlusions. Restenosis is common even when initial angiographic results are ideal. Intimal hyperplasia is typically primarily composed of extracellular matrix with high water content and few cells. PTA squeezes the water out of the intimal hyperplasia during the procedure but this rehydrates over time. The stent limits positive vessel remodeling. High-grade stent fractures and compressed stents greatly increase the risk of repeat restenosis. In theory removal of intimal hyperplasia and thrombus may result in better patency. Antiproliferative therapies particularly with cytotoxic drugs may be helpful. Repeat scaffolding may limit elastic recoil and covered stents can provide a physical barrier to intimal ingrowth.

The EXCITE trial utilizing excimer laser followed by PTA demonstrated less complications and improved pa-
tency in the laser plus PTA arm vs PTA-only arm at 6 months and 1 year in a randomized controlled multi-center trial conducted in the United States. This was a “real world” trial with mean lesion lengths in excess of 19 cm. There was no evidence of adverse reactions with the stents. There was less need for stenting and less dis-sections. Laser coupled with PTA was superior to PTA in all lesion subsets. The RELINE randomized controlled multicenter trial utilizing Viabahn stent grafts performed in Europe showed better patency with lower rates of TLR in the stent graft arm than the PTA arm. This trial also included very long lesions.

Siablis demonstrated improved patency utilizing drug-eluting balloons vs PTA in a single-center trial (predominately short lesions) following which a multicenter trial (FAIR trial) demonstrated improved patency in the DEB arm as compared to standard balloon angioplasty. Gandini reported a single-center randomized trial of excimer laser followed by DEB vs DEB alone in which he reported higher patency in the laser plus DEB arm. Drug eluting stents (Zilver PTX; Cook Medical) have shown improved patency in the single arm Zilver PTX trial as compared to the bare metal Zilver stent.

Femoral/popliteal ISR is a growing problem faced by peripheral interventionists. The treatment is in evolution with two therapies that are FDA approved and many other therapies (as sole therapy or in combination) being evaluated. Better stent designs, covered stents, bioabsorbable stents, and drug-eluting stents have the potential to decrease the incidence of femoral/popliteal ISR in the future. Despite potential breakthroughs with stents I suspect ISR will remain a common clinical problem for many years.

References