

## **RESTENOSIS**

### **MIDWEST INSTITUTE FOR INTERVENTIONAL THERAPY**

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Percutaneous coronary angioplasty is a well-established and increasingly attractive form of therapy to treat patients with symptomatic coronary artery disease. The single most important drawback for angioplasty continues to be a high 30% rate of post angioplasty restenosis. The restenosis process comes from dynamic interplay of vessel elastic recoil, vessel wall remodeling, local thrombus formation and neointimal proliferation. The widespread use of coronary stents virtually eliminated the mechanical components, namely recoil and vascular wall remodeling, of the restenotic process. Local thrombosis can be treated effectively using combination of anti-thrombotic and anti-platelet agents. The neointimal proliferation with aggressive neointimal growth pattern is a frequent and unyielding cause of in-stent restenosis. Numerous clinical trials using pharmacologic therapies including anti-thrombotics, anti-oxydants, vasodilators, lipid lowering agents, growth factor inhibitors, etc thus far brought no clear clinical benefit.

The first effective method to treat neointimal in-stent restenosis came from the application of intracoronary radiation therapy. The intracoronary brachytherapy was shown to reduce the relative risk of in-stent restenosis from 60% to 20%. The latest advances in controlling post angioplasty neointimal growth come from utilization of stents, which are coated with anti-proliferative agents such as Rapamycin, Toxol, Actinomycin, and others. The most recent clinical trials are showing that the stents coated with some of these agents especially Rapamycin coated stents may nearly eliminate the in-stent neointimal hyperplasia. The rate of neointimal proliferation and related restenosis is dramatically reduced not only in the coronary but also in the peripheral circulation. There is unequivocal and sustained reduction in the late luminal loss by 85%, resulting in lowering of in-stent restenosis rate by 94% from 31% restenosis in the placebo group to 2% restenosis in the sirolimus coated stent group ( $P \leq 0.001$ ). The intracoronary radiation caused 6 to 8% of patients who were not on antiplatelet therapy to have late stent thrombosis. There is no late in-stent thrombosis or any other clinical or angiographic pathobiologic responses associated with sirolimus coated stents. Clinically driven target lesion revascularization was markedly reduced (by 72%) from 16.7% with placebo to 4.7% with sirolimus ( $P \leq 0.001$ ). The striking efficacy of sirolimus in virtually eliminating neointimal hyperplasia within the stent was found not only in the coronary arterial tree but also in the peripheral arteries (SFA). Importantly there was a slight increase in neointimal proliferation and restenosis at the stent margins most likely caused by incomplete suppression of neointimal hyperplasia at the site of balloon barotrauma outside the stented sirolimus treatment zone. Thus operator technique and better stent delivery systems to limit the balloon injury zone to match the stented sirolimus treatment zone, avoidance of gaps between stents, and the assurance of complete stent vessel wall apposition with full lesion coverage should further improve the clinical outcomes.