# Brachytherapy for Refractory Coronary Artery Restenosis

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**ABSTRACT:** a 76-year-old female patient complained of progressive episodes of chest and left arm pain and numbness, accompanied by a burning sensation in the left breast. The symptoms were nitroglycerine responsive and consistent with her prior angina. Cardiac history included an initial percutaneous coronary intervention and 4 subsequent occurrences of restenosis in a stented area of the left anterior descending (LAD) coronary artery. Following a fifth re-stenosis of the LAD, the Novoste™ Beta-Cath™ Brachytherapy System was employed following balloon dilatation of the persistent recurrence. At 10 months post-brachytherapy, angiography revealed a patent LAD with no evidence of in-stent restenosis.

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Vascular disease is the most common cause of morbidity and mortality in the United States,[1] and an atherosclerotic plaque resulting in an occlusive or stenotic process is the most common pathology of vascular disease. Currently, more than 800,000 percutaneous coronary interventions (PCIs) are performed each year in the United States.[2] However, while improved techniques and new, highly sophisticated tools for endovascular intervention continue to improve long-term patency of the treated vessels, long-term outcomes remain handicapped by the phenomenon of restenosis. Approximately 150,000 PCI procedures (20-25% of patients that undergo stent implantation) will experience "in-stent restenosis" and require additional percutaneous or surgical intervention.[3]

Although knowledge about the pathogenesis of post-PCI restenosis is still evolving, the etiology is felt to be a response to vascular injury, essentially a wound healing process. The vessel lumen is reduced by 'scar tissue' formation that often results in recurrence of symptoms, necessitating further therapy. Hypotheses of the etiology of this phenomenon include early failure (i.e., vascular remodeling, recoil, and thrombus formation), and late failure (i.e., intimal/ neointimal hyperplasia). Recent studies also suggest that adventitial fibroblasts may play an important role in the process of geometric remodeling.[4] However, despite progress in the understanding of the disease process, heart disease remains the most common cause of mortality in the United States.

Until recently, physicians had few options for the treatment of these patients apart from serial percutaneous procedures or bypass surgery.[5,6] However, as the concept of cellular hyperplasia bears some resemblance to the neoplastic transformation process, the growth inhibiting properties of radiation stimulated interest in whether intravascular brachytherapy following PCI could be effective in an effort to reduce restenosis.[7,8]

Condado, et al. first reported the feasibility of coronary brachytherapy in 1997.[3] Since that time, the results have been confirmed by a series of clinical trials including SCRIPPS-1, WRIST, GAMMA I, GAMMA II, INHIBIT, START, START 40/20, and others in the setting of in-stent restenosis.[9]

The START trial was a randomized, double-blind, multi-center trial in which 476 patients received either brachytherapy of 16-22 Gray (Gy) prescribed to 2 mm from the center of the Strontium[90] (Sr-90) source in a 30 mm train, or placebo treatment with an inactive source, following PCI on lesions up to 20 mm in length. This trial demonstrated statistically significant reductions in total lesion restenosis (13% treatment group, 22% placebo), total vessel restenosis (16% treatment group, 24% placebo) and major adverse cardiac events (18% treatment group, 26% placebo). Later, in the START 40/20 trial, a 40mm source train was used on patients with similar lesion characteristics as those treated in the START trial. After 207 patients were enrolled in START 40/20, data analysis confirmed the efficacy of using the Novoste™ Beta-Cath™ System in the setting of in-stent restenosis, in addition to demonstrating the importance of treatment with adequate margins beyond the injured segment of the target vessel.[3,10]

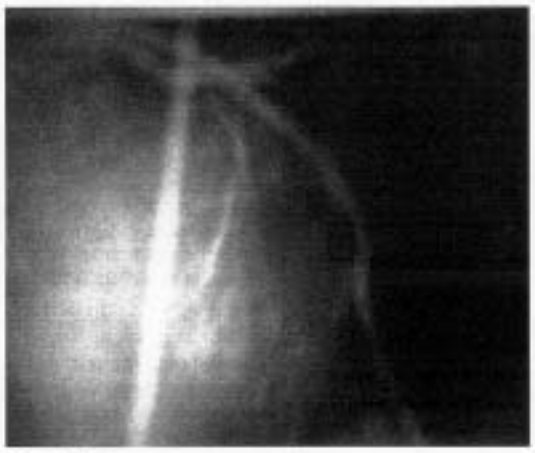

Figure 1. *Pre-treatment coronary angiogram.*

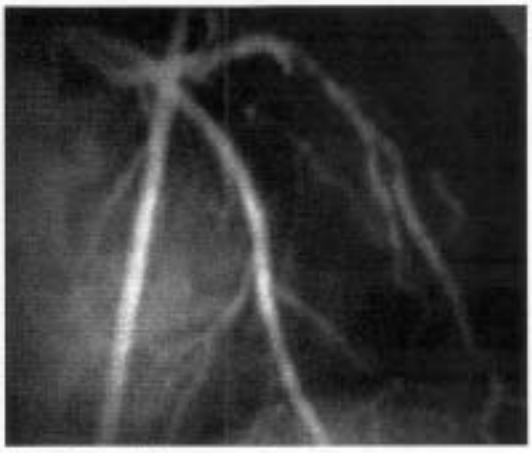

Figure 2. *Post-PCI coronary angiogram.*

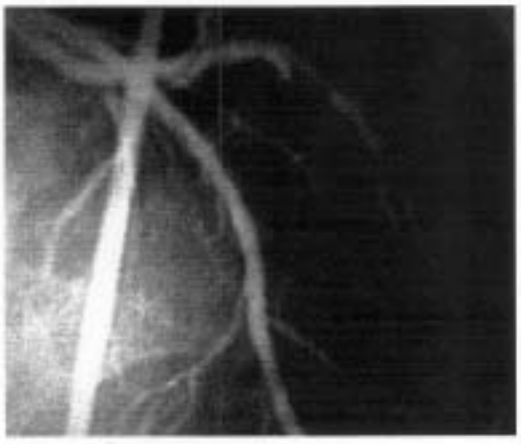

Figure 3. *Follow-up angiogram.*

Debate continues over which isotope (beta vs. gamma) is better suited to coronary brachytherapy. Both isotopes have been shown efficacious, and each has particular advantages and disadvantages.[11] At our institution, we have selected to use beta radiation, primarily for the shorter dwell times and reduced radiation exposure to staff and

physicians. The practicality and ease of use of the Novoste Beta-Cath System have been well received by both the radiation oncologists and cardiologists in our busy clinical practice.

**Case Report.** A 76-year-old female patient presented with patient presented with progressive episodes of chest and left arm pain and numbness, accompanied by a burning sensation in the left breast. The symptoms were nitroglycerine responsive and consistent with her prior angina. Medical history included atherosclerotic heart disease, hypertension, hyperlipidemia and degenerative osteoarthritis. Medications included a calcium channel blocker, beta-blocker, cholesterol lowering statin, diuretic, ASA and sublingual nitroglycerin as needed.

Percutaneous treatment included an initial coronary intervention with stent implantation in the proximal circumflex coronary artery, stent implantation in the left anterior descending (LAD) coronary artery at the level of the first septal perforator, and balloon dilatation of a diffuse narrowing in the right coronary artery. Over the course of the next 3 years, there were 4 subsequent occurrences of restenosis of the stented area of the LAD. Treatment modalities utilized to treat the chronic restenosis included balloon dilatation, cutting balloon atherectomy, excimer laser, and rotational atherectomy.

The patient was admitted for cardiac catheterization and coronary angiography with possible angioplasty on coronary angiography using low-osmolar ionic contrast, the LAD at the level of the first septal perforator appeared to be relatively patent (Figure 1), but upon intravascular ultrasound (IVUS) evaluation the stented segment was found to be focally narrowed as much as 70 percent. Weight-based heparin was administered and this fifth occurrence of restenosis was treated with cutting balloon dilatation. The resultant angiography and IVUS evaluation revealed a patent segment at the treatment site with no residual stenosis (Figure 2).

Quantitative coronary angiography revealed a reference vessel that was 3.4 mm in diameter. The length of the injured segment was less than 20 mm. The Novoste Beta-Cath System was utilized to deliver 23 Gy prescribed 2 mm from the center of the Strontium$^{90}$/Yttrium$^{90}$ source using a 5 French catheter and a 30 mm source train with 12 radioactive seeds. The total dwell time was 243 seconds.

Repeat angiography following brachytherapy demonstrated a widely patent LAD, with no evidence of intimal dissection or impaired distal runoff (TIMI III). Follow-up laboratory results and electrocardiographic recordings were within normal limits, and the patient was discharged the following morning.

Approximately 10 months following brachytherapy, the patient reported some recurrent angina-like symptoms. The chest pain was less frequent and somewhat dissimilar from the prior episodes of angina, however, given her history of chronic restenosis the patient was scheduled for follow-up coronary angiography. Review of follow-up coronary angiography demonstrated that there was no evidence of restenosis within the radiation treated site (Figure 3). There was a minimal narrowing at the edge of the radiation treatment site, but no high-grade obstructive lesions were noted throughout the LAD.

**Conclusions.** While advances in the treatment of in-stent restenosis continue to be made, the option of intracoronary brachytherapy using the Novoste Beta-Cath System is

an important technique that is both effective and FDA approved. In addition, use of intravascular brachytherapy has been shown to be practical in high volume, high quality clinical settings within tertiary and community hospitals.[3] In conjunction with long-term anti-platelet therapy, this technology plays an important role in current treatment options for in-stent restenosis. Ultimately, this treatment advancement translates into enormous clinical, economic and societal benefits.

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