

## **Vascular Brachytherapy in the Prevention of In-Stent Restenosis**

**Ron Waksman, MD, FACC**

**Associate Director Division of Cardiology Washington Hospital Center**

Vascular Brachytherapy delivered by catheter-based system, has been shown effective in the treatment of in-stent restenosis. Single center trials such as SCRIPPS and WRIST and multi center randomized trials such as GAMMA-1 using gamma emitters and START and INHIBIT using beta emitters have shown significant reduction in the recurrence rate and the need for repeat revascularization with the compared to standard therapy. The major adverse event of brachytherapy has been the occurrence of late thrombosis. This was occurred after months after the radiation therapy primarily when new stents were involved in the intervention. The late thrombosis rates reported was up 12% and was associated with Q-wave MI and death. Late thrombosis was nearly eliminated with the use of prolong antiplatelet therapy utilizing Clopidogrel (Table). The required duration of clopidogrel for brachytherapy to prevent late thrombosis has not been determined. Clearly should be longer when stents and radiation are used together. Our own investigation demonstrated that with the use of gamma radiation 12 months will be superior of 6 months in terms of the reduction of major adverse events. Currently the recommendations with beta radiation range from 3-6 months.

Vascular brachytherapy is utilized now in over 300 cath labs in the lab and the potential of patients who would require this treatment in the US will be nearly 120,000 in the year of 2002. In an effort to understand whether brachytherapy will also be helpful in lesions undergoing PTCA without stenting and as adjunct to stenting de-novo lesions, the BETACATH trial was carried out. This trial utilized beta radiation with a 30 mm source train to treat arteries with a strategy of provisional stenting. Arteries were dilated in an adequate result without stenting and then radiation was applied. If there was inadequate luminal enlargement or dissection was present, then stenting was performed at the end of the procedure. Despite effective reduction in restenosis within the irradiated segments, there was excessive renarrowing at the extremities of the radiation source train in segments of the artery that were injured. The trial highlighted the problem of geographic miss and edge effect in radiation therapy. It is apparent that arteries that are injured with balloon dilatation or stenting may be subject to excessive renarrowing in zones that did not receive adequate radiation dose. Nevertheless, radiation therapy has been effective in preventing recurrent restenosis within stents, however, its application to lesions not suitable for stenting remains investigated. With solving complications of late thrombosis utilizing prolonged antiplatelet therapy and edge effect by careful coverage of long lesions vascular brachytherapy remains an excellent tool in the combat against restenosis.

### **References:**

1. Waksman R, White RL, Chan RC, Bass BG, Geirlach L, Mintz GS, Satler LF, Mehran R, Serruys PW, Lansky AJ, Fitzgerald P, Bhargava B, Kent KM, Pichard AD, Leon MB. Intracoronary gamma-radiation therapy after angioplasty inhibits recurrence in patients with in-stent restenosis. *Circulation*. 2000;101:2165-71.
2. Leon MB, Teirstein PS, Moses JW, Tripuraneni P, Lansky AJ, Jani S, Wong SC, Fish D, Ellis S, Holmes DR, Kerieakes D, Kuntz RE. Localized intracoronary gamma-radiation therapy to inhibit the recurrence of restenosis after stenting. *N Engl J Med*. 2001;344:250-6.
3. Verin V, Popowski Y, De Bruyne B, et al. Endoluminal beta radiation therapy for the prevention of coronary restenosis after balloon angioplasty *N Engl J Med* 2001;344-243-9
4. Waksman R, Ajani AE, White RL, Pinnow E, Dieble R, Bui AB, Taaffe M, Gruberg L, Mintz GS, Satler LF, Pichard AD, Kent KK, Lindsay J. Prolonged Antiplatelet Therapy to Prevent Late Thrombosis After Intracoronary gamma-Radiation in Patients With In-Stent Restenosis : Washington Radiation for In-Stent Restenosis Trial Plus 6 Months of Clopidogrel (WRIST PLUS). *Circulation*. 2001;103:2332-5.
5. Teirstein PS, Massulo V, Jani S, et al. Three year clinical and angiographic follow-up after intracoronary radiation results of a randomized clinical trial. *Circulation* 2000;101:360-365.