Intravascular Brachytherapy for Native Coronary Ostial In-Stent Restenotic Lesions

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OBJECTIVES
We analyzed the effects of vascular brachytherapy (VBT) on ostial in-stent restenosis (ISR). In-stent restenosis has a high recurrence rate after percutaneous re-intervention. The recurrence rate of ostial ISR lesions and the impact of VBT remain unknown.

METHODS
We evaluated 133 patients with native coronary ostial ISR from a pooled database of 990 patients enrolled in randomized VBT trials. Independent quantitative angiography was performed at baseline and follow-up in 45 gamma, 27 beta, and 61 placebo patients.

RESULTS
Binary restenosis was significantly higher in placebo than radiated patients (75.4% vs. 17.8% in gamma vs. 22.2% in beta, p < 0.0001). The treatment effect of both gamma (odds ratio [OR] 0.06; 95% confidence interval [CI] 0.02 to 0.17) and beta VBT (OR 0.10; 95% CI 0.03 to 0.31) was maintained after controlling for differences in baseline lesion length. Proximal and distal radiation edge restenosis rates were similar among the groups. Vascular brachytherapy with either gamma or beta sources results in significant and similar reductions in restenosis compared with placebo. Similar benefits after VBT prevail in true aorto-ostial lesions. (J Am Coll Cardiol 2003;41:1725–31) © 2003 by the American College of Cardiology Foundation

CONCLUSIONS
Conventional treatment of ostial ISR is associated with a recurrence rate of over 75%. Vascular brachytherapy with either gamma or beta sources results in significant and similar reductions in restenosis compared with placebo. Similar benefits after VBT prevail in true aorto-ostial lesions.

Treatment of ostial lesions is one of the challenges of percutaneous coronary intervention, in part because ostial lesions are technically difficult to treat and in part because restenosis rates are high (1,2). Although stents have improved acute results and long-term outcomes (3,4), in-stent restenosis (ISR) occurs more often after treatment of ostial lesions compared with non-ostial lesions (5). In-stent restenosis lesions are another challenge to conventional percutaneous intervention, primarily because of high recurrence rates (6,7). However, there are few data about the recurrence rate after conventional treatment of ostial ISR lesions. Vascular brachytherapy (VBT) significantly decreases recurrence rates after treatment of ISR (8–12). However, there are also few data about the effect of VBT in ostial ISR lesions. This angiographic study evaluates the effects of gamma or beta VBT in ostial ISR lesions.

METHODS

Study population. From an angiographic database of 990 patients enrolled in several randomized VBT trials for the treatment of ISR, 133 patients were identified with ostial lesions of a native coronary artery. An ostial lesion was any lesion within 3 mm of the origin of a major epicardial native coronary ostium. An aorto-ostial lesion was an ostial lesion located at the origin of the left main or right coronary artery (13). Forty-five lesions were treated with gamma (iridium 92 [192Ir]), 27 lesions were treated with beta VBT (strontium 90/ytrrium 90 [90Sr/90Y]), and 61 lesions did not receive radiation (placebo group). No centering device was used in either the gamma or the beta radiation groups. The different trials had different protocols including dose prescriptions and pre-VBT treatment strategies (Table 1) (8–12). Of importance, the angiographic inclusion criteria were similar among the trials except for lesion length.

Angiographic analysis. Cineangiograms were acquired in multiple, matched projections before percutaneous coronary intervention (PCI), after final treatment of ISR (following VBT), and at six to nine months follow-up, or sooner if recurrent ischemia occurred. Intracoronary nitroglycerin, 50 to 200 mg, was given before angioplasty unless there were clinical contraindications to its use.

All procedural and follow-up cineangiograms were analyzed independently by a single Angiographic Core Laboratory (Cardiovascular Research Foundation). Analysts were blinded to the treatment strategy. Standard morphologic criteria were used to characterize baseline lesion complexity using the American College of Cardiology/American Heart Association lesion complexity scoring system and to identify the occurrence of angiographic complications. Lesion
length was determined by the “shoulder-to-shoulder” extent of obstruction at baseline and follow-up. Quantitative coronary angiography (QCA) was performed using the CMS-GFT algorithm (MEDIS, Leiden, The Netherlands) guided by analysts’ drawing of the arterial segment and its side branches, demonstrating the precise location of the baseline stenosis, and the positions of the radiation delivery source (14,15). Inter- and intraobserver variability have been reported ranging from 0.07 to 0.10 mm for minimal lumen diameter and 2.7% to 5.1% for percent diameter stenosis even when using the most precise angiographic systems (16–19). The contrast-filled injection catheter was used for image calibration. The minimum lumen diameter (MLD) and the mean reference diameter (RD), obtained from averaging a 5-mm segment proximal and distal to the final ribbon or injured and margin location, were used to calculate the percent diameter stenosis (DS = [1 − MLD/RD] × 100).

A MLD of 0 mm was imputed for total occlusions at baseline or follow-up. Acute gain was defined as the change in the MLD from baseline to the final post-PCI angiogram; late loss was defined as the change in MLD from the final post-PCI angiogram to follow-up. Loss index was calculated as the slope of the best-fit line from regression analysis plotting the late loss versus acute gain. Binary restenosis was defined as a >50% DS at follow-up.

Side branches of main ostial lesions were systematically assessed with electronic handheld calipers before and after each intervention, as well as at follow-up. Only vessels >1.5 mm in diameter measured at the most normal and proximal segment to the main branch were considered as side branches. The side branch percent DS was calculated in relation to the reference size of the side branch.

A decay of the radiation dose occurs at the edges of the source (radiation fall-off). The decrease in dose secondary to radiation fall-off has been implicated in VBT failure. The segments defined as radiation fall-off zones were identified and systematically analyzed (20,21). Radiation fall-off zones were defined as a 10-mm segment, 5 mm immediately inside and 5 mm immediately outside the proximal and distal source markers. The MLD at each fall-off zone was determined. The mean vessel RD was used to calculate the DS percent for proximal and distal radiation dose fall-off. Dose fall-off restenosis was defined by a DS percent in the dose fall-off area >50%.

**Statistical analysis.** Angiographic data were independently analyzed by the Cardiovascular Research Foundation Data Coordinating Center. Statistical analysis was performed using SAS software (SAS Institute Inc., Cary, North Carolina). Categorical data are presented as percent frequencies and compared by chi-square statistics. Continuous variables are presented as mean ± 1 SD and compared across the three treatment groups with one-way analysis of variance; post-hoc comparison between individual groups was performed using the Bonferroni correction where p = 0.0167 is the threshold for significance. Stepwise logistic regression analysis was used to test for a treatment effect while controlling for differences in angiographic and procedure variables including baseline reference vessel diameter, lesion length, final MLD, final %DS, acute gain, stent use, aorto-ostial location, vessel treated, treatment used (gamma VBT vs. placebo, beta VBT vs. placebo), and additional stent use.

**RESULTS**

Baseline angiography and procedure results. Lesion complexity was similar for all three groups. Qualitative and quantitative procedural data are shown in Table 2. Although lesion length was significantly longer in placebo compared with beta VBT groups, baseline reference vessel diameter, MLD, and DS percent were well matched. Restenting was

### Table 1. Protocol Similarities and Differences Among the Analyzed Clinical Trials

<table>
<thead>
<tr>
<th></th>
<th>GAMMA-1</th>
<th>Wrist</th>
<th>Long Wrist</th>
<th>START</th>
<th>START 40/20</th>
</tr>
</thead>
<tbody>
<tr>
<td># of patients (radiated/placebo)</td>
<td>23/12</td>
<td>14/11</td>
<td>8/12</td>
<td>18/26</td>
<td>9/0</td>
</tr>
<tr>
<td>Radiation source</td>
<td>Gamma</td>
<td>Gamma</td>
<td>Gamma</td>
<td>Beta</td>
<td>Beta</td>
</tr>
<tr>
<td>Dose (Gy/depth (mm))</td>
<td>8–30</td>
<td>15/2</td>
<td>15/2</td>
<td>18–23/2</td>
<td>18–23/2</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>&lt;45</td>
<td>&lt;47</td>
<td>36–80</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Vessel size (mm)</td>
<td>2.74–4.0</td>
<td>3.0–5.0</td>
<td>3.0–5.0</td>
<td>2.74–4.0</td>
<td>2.74–4.0</td>
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<tr>
<td>SVG</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Total occlusion</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Plavix/ticlopidine duration (days)</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td>60</td>
<td>60</td>
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<tr>
<td>New stent allowed</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

*The dose in GAMMA-1 was prescribed to the adventitia and the distance measured with intravascular ultrasound.

SVG = saphenous vein graft.
most frequent in gamma-radiated patients and least frequent in beta-treated patients, as a result of protocol differences. Although final angiographic results were slightly superior in placebo and gamma compared to beta patients, the differences were not significant.

## Angiographic follow-up.
Follow-up QCA results are shown in Table 3. Placebo-treated lesions had a significantly smaller follow-up MLD and higher DS percent compared with both radiation groups. Follow-up QCA measurements of gamma- and beta-irradiated lesions were similar.

Although acute gain was similar among all three groups, late loss was significantly higher in placebo compared to both radiated groups. Consequently, loss index was similar in gamma- and beta-treated lesions and significantly higher in the placebo group. The binary restenosis rate for gamma-irradiated lesions was 17.8% (vs. gamma controls, 77.1%, \( p < 0.0001 \)) and for beta-irradiated lesions was 22.2% (vs. beta controls, 73.1%, \( p = 0.0005 \)). Gamma and beta control patients had similar restenosis rates (77.1% vs. 73.1%, \( p = 0.9 \)). Both control groups combined had a significantly higher restenosis rate compared to gamma- and beta-irradiated lesions (75.4% vs. 17.1% vs. 22.2%, \( p < 0.0001 \)).

Regardless of the source utilized, VBT-treated patients had a 75% relative reduction in binary angiographic restenosis rate compared to placebo. By logistic regression analysis the treatment effect of both gamma (odds ratio [OR] 0.06; 95% confidence interval [CI] 0.02 to 0.17) and beta VBT (OR 0.10; 95% CI 0.03 to 0.31) was maintained after controlling for differences in baseline lesion length of the placebo and VBT groups.

There were 34 true aorto-ostial lesions: 3 in the left main coronary artery and 31 in the right coronary artery. Aorto-ostial lesions showed similar baseline angiographic and final QCA parameters among the three groups. At follow-up, the aorto-ostial lesions of both the gamma and beta controls had the same restenosis rate (83.3%). Both placebo groups combined had a significantly higher restenosis rate compared to either gamma or beta VBT aorto-ostial lesions (83.3% vs. 6.7% vs. 28.6%, \( p = 0.0002 \)). The difference in restenosis rate between gamma and beta aorto-ostial treated lesions was not statistically significant (\( p = 0.46 \)).

### Lesion length.
In general, lesions were shorter at follow-up (Fig. 1). The lesion length reduction from baseline to follow-up was significant for both gamma (14.9 ±

### Table 2. Qualitative and Quantitative Coronary Angiographic Analysis

<table>
<thead>
<tr>
<th>Lesion location (%)</th>
<th>Gamma (n = 45)</th>
<th>Beta (n = 27)</th>
<th>Placebo (n = 61)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>4 (8.9)*</td>
<td>10 (37)*</td>
<td>11 (18)</td>
<td>0.012</td>
</tr>
<tr>
<td>LCX</td>
<td>22 (48.9)</td>
<td>9 (33.3)</td>
<td>34 (55.7)</td>
<td>0.15</td>
</tr>
<tr>
<td>RCA</td>
<td>18 (40)</td>
<td>8 (29.6)</td>
<td>14 (22.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>Left main trunk</td>
<td>1 (2.2)</td>
<td>0 (0)</td>
<td>2 (3.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>Aorto-ostial</td>
<td>15 (33.3)</td>
<td>7 (25.9)</td>
<td>12 (19.6)</td>
<td>0.31</td>
</tr>
<tr>
<td>ACC/AHA ≥ B2 (%)</td>
<td>33 (73.3)</td>
<td>23 (85.1)</td>
<td>52 (85.2)</td>
<td>0.11</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>14.9 ± 9.5†</td>
<td>15.2 ± 8.3‡</td>
<td>19.4 ± 5.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Reference vessel (mm)</td>
<td>2.71 ± 0.39</td>
<td>2.64 ± 0.66</td>
<td>2.61 ± 0.44</td>
<td>0.70</td>
</tr>
<tr>
<td>Pre MLD (mm)</td>
<td>0.92 ± 0.48</td>
<td>0.81 ± 0.25</td>
<td>0.82 ± 0.35</td>
<td>0.31</td>
</tr>
<tr>
<td>Pre DS%</td>
<td>66.0 ± 16.3</td>
<td>68.5 ± 9.6</td>
<td>67.9 ± 13.4</td>
<td>0.70</td>
</tr>
<tr>
<td>Final MLD (mm)</td>
<td>2.03 ± 0.39</td>
<td>2.17 ± 0.54</td>
<td>2.00 ± 0.40</td>
<td>0.23</td>
</tr>
<tr>
<td>Final DS%</td>
<td>26.9 ± 14.5</td>
<td>20.8 ± 13.6</td>
<td>26.9 ± 12.5</td>
<td>0.11</td>
</tr>
<tr>
<td>Acute gain (mm)</td>
<td>1.11 ± 0.53</td>
<td>1.39 ± 0.54</td>
<td>1.17 ± 0.49</td>
<td>0.12</td>
</tr>
<tr>
<td>Stent (%)</td>
<td>27 (60)†</td>
<td>4 (14.8)‡</td>
<td>26 (42.6) &lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

*Gamma and beta vascular brachytherapy (VBT) versus placebo; \( p = 0.0008 \); †gamma VBT versus placebo and beta VBT versus placebo; \( p < 0.0001 \).

ACC/AHA = American College of Cardiology/American Heart Association; DS% = diameter stenosis percent; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; MLD = minimal lumen diameter; RCA = right coronary artery.

### Table 3. Follow-Up Quantitative Coronary Angiographic Analysis

<table>
<thead>
<tr>
<th>Lesion feature</th>
<th>Gamma (n = 45)</th>
<th>Beta (n = 27)</th>
<th>Placebo (n = 61)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>6.9 ± 3.6*</td>
<td>4.2 ± 2.4‡</td>
<td>16.7 ± 12.1</td>
<td>0.001</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.72 ± 0.62†</td>
<td>1.85 ± 0.77‡</td>
<td>1.07 ± 0.61</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DS%</td>
<td>35.7 ± 22.0†</td>
<td>30.9 ± 24.4‡</td>
<td>61.8 ± 20.1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Restenosis rate (%)</td>
<td>8 (17.8)†</td>
<td>6 (22.2)‡</td>
<td>146 (75.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Total occlusions (%)</td>
<td>2 (4.4)</td>
<td>1 (3.7)</td>
<td>5 (8.2)</td>
<td>0.71</td>
</tr>
<tr>
<td>Late loss (mm)</td>
<td>0.31 ± 0.58‡</td>
<td>0.31 ± 0.60‡</td>
<td>0.94 ± 0.57</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Loss index</td>
<td>0.30 ± 0.78‡</td>
<td>0.23 ± 0.47‡</td>
<td>1.20 ± 2.25</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*There were no statistically significant differences comparing placebo patients from gamma- (n = 35) versus beta-irradiation (n = 26) trials. *Gamma versus placebo; \( p = 0.0001 \); †gamma versus placebo and beta versus placebo; \( p < 0.0001 \); ‡gamma versus placebo and beta versus placebo; \( p = 0.005 \).

Abbreviations as in Table 2.
9.5 to 6.9 ± 3.6, p < 0.001) and beta (15.2 ± 8.3 to 4.2 ± 2.4, p < 0.001) groups; the difference was not significant in placebo-treated lesions (19.4 ± 5.9 to 16.7 ± 12.1, p < 0.18).

Irradiated aorto-ostial lesions presented a trend towards a significant reduction in lesion length from baseline to follow-up (gamma: 12.9 ± 9.6 to 6.1 ± 2.6, p = 0.07; beta: 9.4 ± 6.3 to 3.3 ± 2.1, p = 0.1). Conversely, placebo aorto-ostial lesions presented an increase in the length that was not significant (15.6 ± 12.7 to 18.9 ± 20.4, p = 0.7).

**Side branch analysis.** Side branches involved in the ostial ISR lesions had similar baseline DS percent (25.6 ± 31.4 vs. 17.4 ± 3.9 vs. 18.8 ± 28.6, p = 0.7) and final DS percent (29.9 ± 31.9 vs. 30.0 ± 36.8 vs. 31.3 ± 39.9, p = 0.4) in the gamma, beta, or placebo groups, respectively. At follow-up, there was an increase in side branch DS percent in irradiated lesions that did not reach statistical significance. There was no increase in side branch DS percent in placebo lesions (Fig. 2).

**Fall-off zones analysis.** From the total group of 133 lesions, only 121 were technically suitable for radiation dose fall-off analysis because of poor acquisition quality in which the fall-off zones were not adequately visualized. In addition, in aorto-ostial lesions as well as in some ostial left anterior descending and left circumflex coronary artery lesions, the proximal edge of the radiation source was located inside the guiding catheter, such that the ostium received the full prescribed dose; as a result, a subtherapeutic fall-off zone was present in 76% of the proximal lesions assessed (Fig. 3). The distal fall-off segment could be analyzed in all lesions at baseline; only 91.4% could be analyzed at follow-up either because of total occlusions or to inadequate contrast filling of the distal arterial segment.

Overall the dose fall-off restenosis rate was significantly higher for placebo compared with beta or gamma VBT-treated patients (30% vs. 11.5% vs. 7.4%, p = 0.009). Proximal and distal radiation dose fall-off restenosis are displayed separately in Figure 4. In the subgroup of aorto-ostial lesions, there was no recurrence located at the proximal or distal dose fall-off of the radiation source.

**DISCUSSION**

Ostial lesions, whether true aorto-ostial or non–aorto-ostial, have higher restenosis rates compared to non-ostial lesions after conventional percutaneous intervention (1,2). Vessel
wall elastic recoil plays an important role in the restenotic process after balloon percutaneous transluminal coronary angioplasty in ostial lesions (22). Because stents have overcome the elastic component, the higher restenosis rates for ostial lesions can only be explained by exaggerated intimal hyperplasia. In-stent restenosis lesions have a higher recurrence rate compared with de novo lesions (6,7). Although angiographic predictors of recurrence after ISR intervention have been reported (7), there are no data regarding the outcome of ostial ISR lesions after percutaneous intervention. In the current report, the data from the placebo patients show that ostial location increases the likelihood of recurrence after an ISR lesion is treated with conventional techniques. The recurrence rate (75%) resembles the high recurrence rates reported in other complex ISR lesion subsets such as proliferative and totally occluded lesions (7,23,24).

Adjunctive VBT has consistently demonstrated significant reductions in restenosis rates compared to conventional PCI for treatment of ISR. The Multicenter trial of localized radiation therapy to inhibit restenosis after stenting (GAMMA-I), SCRIPPS coronary radiation to inhibit proliferation post-stenting trial (SCRIPPS), Intracoronary brachytherapy to prevent recurrence of restenosis following angioplasty in patients with in-stent restenosis (WRIST), Stents and radiation therapy trial (START), Stents and radiation therapy trial 40/20 (START 40/20), and Randomized double-blind sham-controlled evaluation of the Guidant intravascular radiotherapy (INHIBIT) trials showed restenosis rates ranging from 45% to 60% in the placebo arms. Conversely, in the radiated arms restenosis rates ranged between 15% and 32%, representing a relative restenosis reduction of approximately 50% (8,9,12,25,26). In the current analysis, despite an extraordinarily high recurrence rate in placebo patients (75%), recurrence in irradiated patients (18% to 22%) was similar to that observed in most radiation trials enrolling a wide spectrum of patient and lesion subsets. Furthermore, in the ostial lesion subgroup, the reduction in recurrence (~75%) was greater than that observed in each of the overall randomized trials. Thus, radiation therapy appears to mitigate the unfavorable impact of ostial lesion location on restenosis; a finding

**Figure 3.** Frequency of the proximal radiation fall-off zone occurring or not occurring in the analyzed population. According to the location of the proximal edge of the radiation source in relation to the coronary vasculature, the proximal radiation fall-off zone (represented by the ellipse surrounding the proximal source edge) was either present (right) or not present (left).

**Figure 4.** Rate of restenosis (RS) occurring at the proximal and distal radiation fall-off zones in gamma-, beta-, and placebo-treated patients. The rates of restenosis where a fall-off of the radiation dose occurs (ellipse surrounding each radiation source edge) are shown in the graphic. Black bars = gamma vascular brachytherapy (VBT); striped bars = beta VBT; black bars = placebo.
similar to a previous subgroup analysis which showed an enhanced benefit of brachytherapy in other high-risk groups of patients, such as diabetics, who have exaggerated neointimal hyperplasia (27,28).

One previous report also indicated a higher rate of restenosis after treatment of aorto-ostial lesions compared to the other ostial lesions after conventional PCI (2). Although this previous report did not assess ISR lesions, the current study shows that the VBT treatment effect was similar for aorto-ostial and non–aorto-ostial ISR lesions.

High rates of recurrence located at the fall-off zones have been reported as a limitation for VBT (20,21). Vessel wall injury at the radiations’ fall-off zones or beyond is known as geographic miss (GM) (29). Although GM has been implicated, the specific factors accounting for restenosis occurring in fall-off zones have not yet been defined. However, it is well know that vessel wall injury produces intimal hyperplasia (30); thus, limiting the extent of injury to the lesion proper with or without radiation therapy is generally a valuable practice. The higher restenosis rates observed in the proximal compared with the distal fall-off segments among the three groups likely represent a combination of the higher recoil and more aggressive remodeling associated with the ostial compared to non-ostial location. The higher restenosis in the proximal dose fall-off location of placebo patients can be explained by: 1) a radiation treatment effect, albeit subtherapeutic; and 2) the apparent change in the pattern of restenosis caused by VBT. Placebo patients presented at follow-up a more aggressive and diffuse pattern with long restenotic lesions as in baseline, whereas radiated patients presented a more focal pattern with restenotic lesions significantly shorter than baseline (Fig. 1).

Whether a therapeutic or subtherapeutic radiation dose combined with vessel wall injury could stimulate intimal proliferation in side branches is not well known. The current analysis did not show a significant difference in follow-up side branch diameter stenosis among the three groups; however, although not statistically significant, side branches that received radiation tended to have an increase in DS% whereas placebo-treated vessels tended to show a decrease in DS%. This is consistent with previous reports (31,32).

Study limitations. There are several limitations to this study. This is an angiographic study; therefore, only patients who completed the angiographic follow-up were assessed. (The angiographic follow-up rates were as follows: GAMMA-1, 84.7%; WRIST, 90.7%; Long WRIST, 80.3%; START, 82%; and START 40/20, 81%). Patients from different study protocols were combined; although the inclusion criteria were similar, there were differences with regards to lesion length and treatment strategies allowed. However, across the trials the restenosis rates in the placebo patients ranged from 63% to 92% and in the irradiated patients from 9% to 33%. The number of patients in each group (placebo, gamma-irradiated, and beta-irradiated) is small; this should be considered when interpreting the results. At the time some of the trials were conducted, the importance of limiting vessel injury and GM was not recognized; therefore, the extent of injury was not assessed prospectively and GM was not systematically analyzed. For similar reasons, the quantitative assessment of the dose fall-off zones was a post-hoc analysis. At the time of these trials, the association between new stent deployment during VBT and stent thrombosis and recurrence was not known. Although it is not currently recommended, restenting was allowed in all of these clinical studies. However, the restenting rate in the beta-irradiation trials in the current analysis was 15% versus 60% in the gamma-irradiation trials whereas the late thrombosis and recurrence rates were similar. Finally, a systematic IVUS analysis in all patients would provide the needed data to understand the mechanisms of fall-off segment restenosis, especially in the proximal ostial location; this was not performed.

Conclusions. This post-hoc analysis of patients from multiple VBT trials showed that ostial ISR lesions have a malignant outcome after conventional PCI, with a 75% recurrence rate. Adjunct vascular brachytherapy, with either gamma or beta VBT, equalizes the poor outcome of this complex lesion subset to the outcome of non-ostial ISR lesions treated with brachytherapy. Similar benefits are demonstrated in pure aorto-ostial lesions. More data—ideally, a prospective trial—would help to substantiate these findings as well as to understand the effects of radiation on side branches arising adjacent to ostial lesions.

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REFERENCES


