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VASCULAR BRACHYTHERAPY USING A BETA EMITTER SOURCE IN DIABETIC PATIENTS WITH IN-STENT RESTENOSIS: ANGIOGRAPHIC AND CLINICAL OUTCOMES

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Purpose: **The management of diabetic patients with restenosis after percutaneous coronary intervention remains a significant challenge. Diabetic patients remain at significant risk of restenosis despite stent implantation. This retrospective analysis was performed to determine the extent to which vascular brachytherapy improves late clinical and angiographic outcomes in diabetic patients compared to conventional therapy and compared to patients' nondiabetic counterparts.**

Methods: **Pooled data from two studies (START [Stents and Radiation Trial] and START-40 trials) of patients (204 diabetic, 477 nondiabetic) receiving vascular brachytherapy (VBT) with a $^{90}Sr/^{90}Y$ source after conventional percutaneous coronary intervention for in-stent restenosis comprise the study population. The radiation delivery system used in both studies was the Beta-Cath system. The prescribed dose at 2 mm from the centerline of the source axis was 18.4 Gy or 23 Gy, depending on vessel diameter. The reference vessel diameter, minimal lumen diameter, and percent diameter stenosis were measured before the intervention, at the conclusion of the procedure, and at the 8-month follow-up examination. The Breslow-Day test was used to formally assess the similarity of treatment effect between diabetic and nondiabetic patients.**

Results: **Target lesion and target vessel revascularization rates and angiographic restenosis rates in diabetic and nondiabetic patients treated with beta radiation or placebo were analyzed. Diabetic patients were more likely to have longer and more complex coronary lesions. In-hospital outcomes in diabetic and nondiabetic patients were similar, irrespective of treatment status. At 8 months, patients treated with beta radiation exhibited less target lesion revascularization (diabetic: 10.9% vs. 22.7%, $p = 0.02$; nondiabetic: 12.8% vs. 22.3%, $p = 0.007$) and less target vessel revascularization (diabetic: 14.7% vs. 25.3%, $p = 0.06$; nondiabetic: 16.6% vs. 23.6%, $p = 0.06$) compared to placebo. In-stent binary angiographic restenosis was lower in irradiated patients (diabetic: 19.4% vs. 37.3% for placebo, $p = 0.01$; nondiabetic: 12.9% vs. 43% for placebo, $p < 0.001$). However, restenosis beyond the stent site reduced the impact of VBT, regardless of diabetic status. The magnitude of the treatment effect for target lesion and target vessel revascularization rates was similar between diabetic and nondiabetic patients.**

Conclusions: **Previously published institutional experiences have suggested that diabetic patients benefit from the use of VBT in the management of in-stent restenosis. This analysis now provides direct evidence to support the role of beta radiation VBT in this patient population. Diabetic patients undergoing this therapy are just as likely to benefit from it as their nondiabetic counterparts.** **© 2003 Elsevier Inc.**

Diabetics, In-stent restenosis, Coronary radiation, Vascular brachytherapy.

INTRODUCTION

Mature data from randomized trials have demonstrated the benefit of placing coronary stents to help reduce the risk of restenosis after angioplasty. Although the rate of restenosis has been decreased by up to 50% with the use of these stents, the incidence of "in-stent" restenosis (ISR) remains a significant problem. On a cellular level, the process of in-stent restenosis results from neointimal hyperplasia. An understanding of this biologic response to vessel wall injury

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associated with coronary angioplasty has led investigators to evaluate the ability of intravascular brachytherapy (VBT) to prevent its occurrence (1–3).

Several randomized clinical trials have shown significant improvements in angiographic and clinical outcomes in patients who received intracoronary brachytherapy after balloon angioplasty (1, 4). The initial studies used a gamma-emitting isotope, ^{192}Ir. The GAMMA-1 multicenter trial reported a significant decrease in angiographic restenosis and major adverse cardiac events in those patients receiving radiation. Recently, similar results were obtained with the use of beta-emitting radioisotopes. The Stents and Radiation Trial (START) documented the safety and efficacy of beta radiation in the prevention of recurrence in patients with in-stent restenosis, and START 40 registry trial helped to confirm these findings (4).

The percutaneous treatment of ISR for the diabetic patient presents a therapeutic challenge, because of high recurrence rates with conventional therapies (5–8). It is well understood that diabetic patients have an exaggerated neointimal response after coronary intervention (9, 10). As a result, this patient population remains at a higher risk of restenosis and adverse clinical outcomes relative to its counterpart nondiabetic population, despite stent implantation (9–13). At the same time, the exaggerated neointimal response after stent implantation may render this population particularly sensitive to the effects of vascular brachytherapy (14).

Whereas the cardiology community considered these diabetic patients with ISR as an attractive population for VBT, radiation oncologists were concerned about their ability to tolerate radiotherapy, based on the potential risk for increased normal tissue toxicity associated with their endocrine disorder (15). To address these concerns, we performed a retrospective analysis of patients participating in two catheter-based beta radiation trials to determine the extent to which VBT improves late clinical and angiographic outcomes in diabetic patients compared to (*1*) conventional therapy and (*2*) their nondiabetic counterparts.

METHODS

We pooled the results of two separate multicenter studies of catheter-based beta radiation in patients with ISR: the randomized, placebo controlled Stent and Radiation Therapy Trial, START 30 (14), and the START 40 Registry (16). START 30 was a triple-blind, randomized, placebo-controlled trial of beta radiation using a 30-mm radiation source train and consisted of 476 patients with single lesion ($>$50% but $<$100%), single native coronary vessel (2.7 mm to 4.0 mm) ISR. Lesions must have been treatable with a 20-mm balloon. START 40 was a registry comprised of 207 patients with selection criteria identical to those in START 30. However, a 40-mm radiation source train was used.

Study protocols

Devices used during the primary intervention were chosen by the operator and included balloon angioplasty, debulking devices, or a combination thereof. Placement of a new stent was discouraged and used overall in only 18.8% of patients (20% in START 30 and 15.3% in START 40). After successful coronary intervention ($<$30% residual stenosis without complication), patients in START 30 were randomized to beta radiation or placebo. All patients in START 40 received beta radiation. After the procedure, in addition to aspirin, ticlopidine was prescribed for 14 days. In April 1999, a minimum of 90 days of ticlopidine or clopidogrel was recommended after additional stent placement. Clinical follow-up was obtained in 98.2% of patients at 1 month and 91.1% of patients by 240 days. Protocol-required angiography was performed at 8 months in 78.4% of all patients (diabetics, 80.3%; nondiabetics, 77.5%). The study protocols were approved by the appropriate institutional review boards of the participating centers, and written informed consent was obtained from all patients.

Radiation delivery system and dosimetry

The Beta-Cath system (Novoste Corp., Norcross, GA) used for catheter-based VBT has been previously described (17). The radiation source train of the system contains a ^{90}Sr/^{90}Y source (or placebo). The prescribed dose at 2 mm from the centerline of the source axis was 18.4 Gy (for vessels $\geq$2.7–3.3 mm) or 23 Gy (for vessels $>$3.3–4.0 mm), based on the visually determined reference vessel diameter. The treatment times ranged from 2.5 to 4 min. In the patients treated with beta radiation, the dose-equivalent rate during treatment at the patient chest level averaged 6.1 mrem/h; at the groin level, 2.1 mrem/h; and at the position of the cardiologist performing the procedure, 0.68 mrem/h.

Quantitative angiographic analysis

Angiographic core laboratory (Cardiology Research Foundation, Lenox Hill Hospital, New York) personnel who were blinded to treatment assignment performed all angiographic analyses using quantitative computerized analysis. The reference vessel diameter, minimal lumen diameter, and percent diameter stenosis were measured before the intervention, at the conclusion of the procedure, and at the 8-month follow-up examination. Binary restenosis was defined as a lumen diameter stenosis of $>$50%. The acute gain was defined as the difference between the minimum lumen diameter immediately after the procedure minus that before the intervention. Late lumen loss was calculated as the difference between minimum lumen diameter at the conclusion of the procedure and at the 8-month follow-up examination. Late loss index was defined as late loss divided by acute gain. Angiographic variables were assessed in the entire axial length of the original stent (“stent segment”), as well as in the total axial length of vessel exposed to injury and/or radiation (whichever was larger), plus an adjacent 5 mm on proximal and distal ends (“analysis segment”). The details of this analysis have been reported (14). Stent throm-

bosis was defined as angiographic thrombus or subacute closure within the target vessel at the time of (clinically driven) angiographic study. Any death not attributable to a noncardiac source within the first 30 days was considered a surrogate for thrombosis in the absence of angiographic data. Late site thrombosis (>30 days after the index procedure) was defined as myocardial infarction attributable to the target vessel with angiographic documentation of thrombus or total occlusion at the target site.

Statistical analysis

Results are summarized as mean ± 1 SD for continuous variables and counts or percentages for categorical variables. Intragroup comparisons were accomplished with a paired *t* test, whereas intergroup comparisons were accomplished using Wilcoxon rank sum statistics. Categorical variables were compared with Chi-square statistics. For all comparisons, a p value <0.05 was considered statistically significant. In view of the post hoc nature of the subgroup analyses, exact p values are reported (except when $p > 0.2$ = NS). The Breslow-Day test was used to formally assess the similarity of treatment effect between diabetic and nondiabetic patients.

RESULTS

Patient characteristics

Baseline clinical and angiographic characteristics of the 204 diabetic patients and the 477 nondiabetic patients are summarized in Tables 1 and 2. Diabetic patients were more often women and had ahigher prevalence of hypertension and peripheral vascular disease. The patient groups were well matched from the standpoint of left ventricular function, anginal status, target lesion location, and number of prior treatments of the target lesion.

Table 1. Baseline clinical characteristics of study population

Characteristic	Diabetic (n = 204)	Non diabetic (n = 477)
Age (yr)	62.3 ± 10	62.2 ± 12
Male gender (%)*	59.3	69
Current smoker (%)†	6.7	11.4
Peripheral vascular disease (%)‡	16.2	9.3
Hypertension (%)§	82.2	69.8
Dyslipidemia (%)	81.6	75.6
Prior myocardial infarction (%)	49.0	44.3
Prior coronary bypass surgery (%)	21.1	22.1
Angina status (%)		
Stable angina	9.3	11.1
Unstable angina	77.9	79.2
Class III or IV	58.6	59.2
Ejection fraction	0.54 ± 0.11	0.55 ± 0.11
Number of prior treatments of target lesion (%)		
None	47.8	51.1
One	40.4	34.8
Two or more	11.8	13.9

* $p = 0.01$.
† $p = 0.06$.
‡ $p = 0.009$.
§ $p < 0.001$.

Table 2. Baseline angiographic characteristics of study population

Characteristic	Diabetic (n = 204)	Non diabetic (n = 477)
No. of diseased coronary arteries (%)		
1	57.6	59.2
2	31.0	26.3
3	11.3	14.5
Location of target lesion (%)		
Left anterior descending	46.8	41.5
Left circumflex	25.6	23.4
Right coronary	27.1	33.1
Left main	0.5	1.3
Saphenous vein graft	0	0.6
Reference vessel diameter (mm)	2.77 ± 0.46	2.76 ± 0.45
Minimum lumen diameter (mm)	0.92 ± 0.39	0.98 ± 0.40
Diameter stenosis (%)*	66.6 ± 13.5	64.2 ± 14.3
Lesion length (mm)†	18.1 ± 7.9	15.8 ± 7.6
Calcification, moderate to severe (%)	25.2	21.8
Complex lesion (%)†	38.6	24.6

* $p = 0.04$.
† $p < 0.001$.

Quantitative coronary angiography

The average lesion length was longer in diabetic patients. The mean baseline percent diameter stenosis was slightly greater in diabetic patients, although the mean reference vessel size and minimum lumen diameter were similar between groups. As expected, postprocedural minimum lumen diameter increased significantly, and percent diameter stenosis decreased significantly in both groups, irrespective of treatment received (Table 3). However, there were no significant differences in these measures between diabetic and nondiabetic patients.

Follow-up angiography was obtained by 240 days in 80.6% (104/129) of diabetic patients receiving radiation and 80% (60/75) of diabetic patients receiving placebo. As seen in Table 3, when compared to placebo, the stent segment binary restenosis rate was significantly lower after radiation, irrespective of diabetic status. The rates of other angiographic measures of restenosis confined to the stented segment (minimum lumen diameter, percent diameter stenosis, late loss, and late loss index) were all significantly reduced after radiation when compared to placebo in both diabetics and nondiabetic patients. Notably, there were no significant

Table 3. Initial and follow-up quantitative coronary angiography results

	Diabetic			Nondiabetic		
Variable	^{90}Sr $n = 129$	Placebo $n = 75$	p	^{90}Sr $n = 320$	Placebo $n = 157$	
Before procedure						
Lesion length, mm	19.0 ± 8.0	16.7 ± 7.5	0.05	15.9 ± 7.6	15.6 ± 7.6	NS
Reference vessel diameter, mm	2.77 ± 0.49	2.79 ± 0.43	NS	2.77 ± 0.47	2.76 ± 0.43	NS
Minimum lumen diameter, mm	0.90 ± 0.41	0.96 ± 0.35	NS	0.97 ± 0.40	1.0 ± 0.39	NS
Stenosis, %	67.2 ± 14.1	65.5 ± 12.5	NS	64.5 ± 14.8	63.6 ± 13.4	NS
After procedure						
Reference vessel diameter, mm	2.81 ± 0.48	2.80 ± 0.42	NS	2.82 ± 0.46	2.82 ± 0.46	NS
Stent segment						
Minimum lumen diameter, mm	2.13 ± 0.43	2.14 ± 0.39	NS	2.14 ± 0.40	2.16 ± 0.43	NS
Stenosis, %	23.4 ± 14.0	22.9 ± 13.6	NS	23.2 ± 14.7	23.0 ± 12.6	NS
Acute gain, mm	1.23 ± 0.55	1.18 ± 0.47	NS	1.16 ± 0.52	1.16 ± 0.52	NS
Analysis segment						
Minimum lumen diameter, mm	1.88 ± 0.40	1.91 ± 0.42	NS	1.90 ± 0.39	1.96 ± 0.41	NS
Stenosis, %	32.4 ± 12.9	31.8 ± 11.1	NS	32.1 ± 11.9	30.2 ± 11.0	NS
Acute gain, mm	0.98 ± 0.55	0.95 ± 0.46	NS	0.92 ± 0.51	0.96 ± 0.49	NS
At 8 months	$n = 104$	$n = 60$		$n = 242$	$n = 128$	
Reference vessel diameter, mm	2.75 ± 0.50	2.84 ± 0.47	NS	2.78 ± 0.48	2.85 ± 0.43	NS
Stent segment						
Minimum lumen diameter, mm	1.84 ± 0.75	1.51 ± 0.57	0.004	1.95 ± 0.61	1.46 ± 0.62	<0.001
Stenosis, %	33.7 ± 25.4	46.4 ± 20.2	0.001	29.1 ± 21.6	48.6 ± 21.1	<0.001
Late loss, mm	0.3 ± 0.7	0.7 ± 0.6	0.007	0.2 ± 0.6	0.7 ± 0.6	<0.001
Loss index ratio	0.2 ± 0.7	0.6 ± 0.6	0.002	0.1 ± 1.1	0.6 ± 0.6	<0.001
Binary restenosis, %	19.4	37.3	0.012	12.9	43	<0.001
Analysis segment						
Minimum lumen diameter, mm	1.59 ± 0.69	1.42 ± 0.57	NS	1.65 ± 0.58	1.41 ± 0.59	<0.001
Stenosis, %	42.6 ± 23.2	49.5 ± 19.7	0.05	40.4 ± 19.2	50.5 ± 19.7	<0.001
Late loss, mm	0.3 ± 0.6	0.5 ± 0.6	0.01	0.2 ± 0.5	0.6 ± 0.6	<0.001
Loss index ratio	0.3 ± 1.1	0.8 ± 1.9	0.08	0.3 ± 1.1	0.9 ± 3.9	0.03
Binary restenosis, %	32.7	45.0	0.11	25.2	45.3	<0.001

differences in any of these measures between diabetic and nondiabetic patients (all $p > 0.2$) in either placebo or radiated groups.

When the analysis segment was examined, the binary restenosis rate was not significantly reduced in diabetic patients receiving radiation, despite the reductions in percent stenosis, late loss, and late loss index ratio. In nondiabetic patients, all measures of analysis segment restenosis were significantly lower in those receiving radiation (Table 3). However, there were no statistically significant differences in any of these measures between diabetic and nondiabetic patients (all $p > 0.2$) in either placebo or radiated groups.

Clinical outcomes

Combined (in-hospital and out-of-hospital to 240 days) clinical events are summarized in Table 4. Among diabetic patients during the first month after the procedure, there were no deaths, Q-wave myocardial infarctions, or stent thrombosis. There were two periprocedural non–Q wave myocardial infarctions in each treatment arm of the diabetic group. The overall procedural success rate in the diabetic patients was 95.1% and 96.6% in nondiabetic patients ($p =$ NS).

There were 186 patients (91.2%) in the diabetic group and 434 patients (91.0%) in the nondiabetic group with clinical follow-up data available at 240 days. VBT in the diabetic group reduced target lesion revascularization (10.9% vs. 22.7%, $p = 0.02$) and target vessel revascularization (14.7% vs. 25.3%, $p = 0.06$) rates compared to placebo. Similarly, in the nondiabetic group VBT reduced target lesion (12.8% vs. 22.3%, $p = 0.007$) and target vessel (16.6% vs. 23.6%, $p = 0.07$) revascularization rates. Irrespective of diabetic status, there were favorable, albeit nonstatistically significant, trends toward a lower composite rate of major adverse cardiac events in patients receiving

Table 4. Combined in-hospital and late clinical events through 240 days

Event	Diabetic			Nondiabetic		
	^{90}Sr $n = 129$	Placebo $n = 75$	P	^{90}Sr $n = 320$	Placebo $n = 157$	P
Any major adverse clinical event (death, myocardial infarction, emergent CABG, TVR)	17.1%	28.0%	0.06	19.4%	24.8%	0.17
Death	3.1%	0	NS	1.3%	0.6%	NS
Myocardial infarction						
Q wave	0	0		0.9%	0	NS
Non–Q wave	2.3%	4.0%	NS	2.2%	2.5%	NS
Emergent coronary bypass surgery	0.8%	0	NS	0	0	
Stent thrombosis (to 30 days)	0	0		0	0.6%	NS
Site thrombosis (days 31–240)	0	0		0.6%	0	NS
Target lesion revascularization rate	10.9%	22.7%	0.02	12.8%	22.3%	0.007
Target vessel revascularization rate	14.7%	25.3%	0.06	16.6%	23.6%	0.07

Abbreviations: CABG = coronary artery bypass graft; TVR = target vessel revascularization.

VBT. The magnitude of difference in the respective angiographic and clinical outcomes between patients receiving VBT and those receiving placebo (treatment effect) are summarized in Table 5. VBT resulted in consistent and beneficial changes in each outcome measure. Moreover, the treatment effect was similar in diabetic and nondiabetic subjects.

Late site thrombosis—from Day 31 through 240 days after the procedure—occurred in 2 nondiabetic patients (who received VBT), whereas no events were noted in the diabetic population. Late total occlusion at 8-month follow-up angiography was noted in 9 diabetic patients (5.5%) and 11 nondiabetic patients (3.0%, p = NS). There was no statistically significant difference ($p > 0.2$) in the rate of late total occlusion between patients receiving radiation and those receiving placebo (diabetic patients: radiation 6.7%, placebo 3.3%; nondiabetic patients: radiation 2.5%, placebo 3.9%).

Table 5. Homogeneity of treatment effect between diabetic and nondiabetic patients

	Odds ratio (95% confidence interval)	p value (Breslow-Day)
Stent segment binary restenosis rate		
Diabetic	0.39 (0.17, 0.88)	
Nondiabetic	0.18 (0.10, 0.34)	0.15
Analysis segment binary restenosis rate		
Diabetic	0.59 (0.29, 1.15)	0.35
Nondiabetic	0.41 (0.25, 0.66)	
Target lesion revascularization		
Diabetic	0.42 (0.18, 0.96)	0.65
Nondiabetic	0.51 (0.30, 0.87)	
Target vessel revascularization		
Diabetic	0.55 (0.24, 1.08)	0.59
Nondiabetic	0.65 (0.39, 1.06)	

DISCUSSION

The published data on the use of radiotherapy in the oncologic management of patients with diabetes mellitus have suggested a possible link between impaired normal tissue repair capacity and the endocrine disorder (15). Longstanding diabetes is known to result in microvascular occlusive changes that can include capillary hyalinization, arteriolar obliteration, and atherosclerosis (16–18). These processes can ultimately lead to decreased tissue perfusion and a compromise in oxygenation. Based on this physiologic model, it has been theorized that these patients may in fact be poor VBT candidates because of compromised oxygenation levels that could limit treatment effect and an increased risk for delayed normal tissue damage repair after radiotherapy. So whereas the cardiology community considered these patients to be an attractive group to study given their propensity for an exaggerated proliferative wound healing response, radiation oncologists have been concerned whether an equal treatment benefit would be seen in this population.

In this report we demonstrate the safety and efficacy of VBT using a ^{90}Sr/^{90}Y beta-emitter source in reducing clinical and angiographic measures of restenosis in diabetic patients with ISR. Compared to diabetic patients who received conventional catheter-based treatment, diabetic patients who received VBT experienced a 58% reduction in target lesion revascularization and a 45% reduction in target vessel revascularization. All angiographic end points demonstrated a profound inhibition of restenosis within the stented segment with binary restenosis reduced by 48% in diabetic patients. These benefits paralleled those seen in nondiabetic patients. Importantly, we could not detect a differential effect of VBT as a function of the diabetic state; i.e., statistically similar reductions in restenosis rates were noted in both groups.

Although several reports initially suggested a relatively greater treatment effect in subsets of patients with an ag-

gressive proliferative response to injury, e.g., diabetic patients and those with recurrent ISR (19, 20), these studies are limited by the small number of patients in each subgroup. A recent pooled analysis of patients from a single center enrolled in a variety of clinical trials of VBT indicated comparable treatment effects in diabetic and nondiabetic patients (21). This latter study, however, was heavily weighted toward the effects of gamma radiation with only 7% of patients receiving beta radiation. Our analysis of patients participating in two multicenter trials now provides direct evidence to support the role of beta radiation VBT in the diabetic patient population, because they were afforded the same benefits from the addition of radiotherapy as their nondiabetic counterparts.

A highly significant effect of VBT with beta radiation was seen within the stented segment in both diabetic and nondiabetic subjects. When a longer axial segment of the target vessel was analyzed, many patients who received radiation developed restenosis beyond the stented segment, an area where a low(er) dose of radiation may have been administered. This diminished the overall effectiveness of beta radiation in both diabetic and nondiabetic patients (analysis segment binary restenosis rate $>$ stent segment binary restenosis rate). This loss of treatment effect in the analysis segment was more profound in patients receiving radiation compared to controls, irrespective of diabetic status. Similar observations have been made in virtually every VBT trial and may reflect the methodology itself, as well as the biology of this treatment modality (22, 23). Despite this loss of angiographically assessed treatment effect, lower target vessel and target lesion revascularization rates in treated patients support the clinical efficacy of beta radiation in diabetic patients.

An encouraging observation in this cohort is the remarkably low rate of late stent thrombosis. In the present study, late stent thrombosis occurred in only 2 nondiabetic patients treated with beta radiation (0.6%), and no events occurred in the diabetic patients. This incidence needs to be contrasted to the increased risk of late thrombotic occlusion seen in previous VBT trials with reported rates between 6% and 15%. It is generally believed that this high rate of late thrombosis is linked to the frequency of additional stent implantation at the time of the coronary intervention (24). The infrequent placement of new stents in both START populations and the extended use of antiplatelet agents in these patients likely reduced this dire complication of VBT. Finally, in our study the rate of late ($>$30 days) occlusion demonstrated at follow-up angiography was similar between diabetic and nondiabetic patients, as well as patients receiving radiation and those receiving placebo.

The current report is a retrospective subgroup analysis of diabetic patients from 2 separate studies. START 30 was a randomized, placebo-controlled trial, whereas START 40 was an open-label registry. It is important to note that the reductions in target lesion revascularization (radiation, 12.2%; placebo, 22.4%; $p = 0.0005$) and target vessel revascularization (radiation, 16%; placebo, 24.1%; $p < 0.001$) for the entire cohort of patients in both trials were highly statistically significant. Several end points in this analysis, e.g., target vessel revascularization, composite major adverse clinical events, did not meet strict criteria for statistical significance ($p < 0.05$). It must be recalled that subgroup analysis will reduce statistical power. Furthermore, the clinical and angiographic restenosis rates in the diabetic placebo control patients were substantially lower than those reported in the clinical trial literature (1). In our study, in-stent lesion length, a powerful predictor of restenosis, was substantially shorter than the mean lesion length reported in previous VBT trials (1, 3, 25–27). Lower restenosis rates in the placebo control arm, as a consequence of shorter lesion lengths, would further reduce our ability to identify significant differences.

Detailed information about diabetes management was not collected, and the small number of patients on insulin therapy precludes further analysis. The follow-up period in our cohort of patients was limited to 8 months. Late angiographic follow-up was analyzed as part of this study; however, extended follow-up is required to ensure that the observed risk:benefit ratio of VBT with beta radiation is maintained over time (28, 29).

In conclusion, adjuvant intracoronary radiation has now been shown to effectively reduce in-stent restenosis rates after repeat angioplasty. Patients diagnosed with pre-existing diabetes mellitus who undergo this therapeutic intervention are just as likely to benefit from radiation without increased risk of toxicities related to impaired wound healing as their nondiabetic counterparts.

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