Intracoronary β-Irradiation With a Rhenium-188–Filled Balloon Catheter

A Randomized Trial in Patients With De Novo and Restenotic Lesions

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Background—Restenosis requiring reintervention is the main limitation of coronary angioplasty. Intracoronary irradiation reduces neointimal proliferation. We studied the efficacy of a self-centering liquid rhenium-188–filled balloon catheter for coronary β-brachytherapy.

Methods and Results—After successful coronary angioplasty with or without stenting, 225 patients (71% de novo lesions) were randomly assigned to receive 22.5 Gy intravascular β-irradiation in 0.5-mm tissue depth (n=113) or to receive no additional intervention (n=112). Clinical and procedural data did not differ between the groups except a higher rate of stenting in the control group (63%) compared with the rhenium-188 group (45%, P<0.02). After 6 months of follow-up, late loss was significantly lower in the irradiated group compared with the control group, both of the target lesion (0.11±0.54 versus 0.69±0.81 mm, P<0.0001) and of the total segment (0.22±0.67 versus 0.70±0.82 mm, P<0.0001). This was also evident in the subgroup of patients with de novo lesions and independent from stenting. Binary restenosis rates were significantly lower at the target lesion (6.3% versus 27.5%, P<0.0001) and of the total segment (12.6% versus 28.6%, P<0.007) after rhenium-188 brachytherapy compared with the control group. Target vessel revascularization rate was significantly lower in the rhenium-188 (6.3%) compared with the control group (19.8%, P=0.006).

Conclusions—Intracoronary β-brachytherapy with a rhenium-188 liquid-filled balloon is safe and efficiently reduces restenosis and revascularization rates after coronary angioplasty. (Circulation. 2003;107:3022-3027.)

Key Words: radioisotopes • angioplasty • stents • restenosis • revascularization

Restenosis requiring reintervention is the main limitation of percutaneous coronary revascularization.1,2 Intracoronary brachytherapy with γ- or β-emitters is now a proven concept for treatment of in-stent restenosis,3–6 but its effectiveness for de novo lesions has not been shown. With β-irradiation, a dose-finding study in de novo lesions showed a significant dose-dependent reduction in loss of luminal diameter at 6 months of follow-up.7

Irradiation with a liquid rhenium-188–filled balloon catheter provides a dose-dependent significant antiproliferative effect in vitro8 and in animal models.9,10 The proliferative response was almost completely abolished after balloon denudation and β-radiation with 22.5 Gy in 0.5-mm tissue depth in hypercholesterolemic rabbits.10 In a clinical pilot study, we have shown the safety and feasibility of intracoronary β-irradiation using the liquid rhenium-188–filled balloon.11 After irradiation with 15 Gy in 0.5-mm tissue depth, we revealed a restenosis rate at the target lesion of 12% (n=3 of 26). However, the restenosis rate of the total segment was 46% because of edge stenoses and geographical miss. Other pilot trials with rhenium-188 balloon brachytherapy using 28 Gy (n=11)12 and 30 Gy (n=2613 and n=5014) in 0.5-mm tissue depth to treat in-stent restenosis revealed an angiographic restenosis rate of 10% to 18% at 6 months.

This EndoCoronary-Rhenium-Irradiation-Study (EC-RIS) represents a randomized, controlled trial of β-emitting radiation therapy in a broad spectrum of patients undergoing percutaneous coronary intervention. The objective of our trial was to evaluate the efficacy of β-irradiation with a liquid rhenium-188–filled balloon in patients with de novo or restenotic lesions. To overcome the limitations of our pilot trial,11 a longer irradiation segment exceeding the traumatized area by at least 5 mm at each side and a higher dose of 22.5 Gy in 0.5-mm tissue depth was selected.
Methods

Study Design
The local ethics committee and German radiation authorities approved ECRIS. After successful angioplasty, patients were included on the basis of online quantitative coronary angiography revealing a reference diameter suitable for a 3.0-mm irradiation balloon. Patients were randomized to rhenium-188 β-irradiation with 22.5 Gy in 0.5-mm tissue depth or no additional intervention. Inclusion criteria were successful angioplasty with or without stenting, age 40 to 80 years, ischemia by symptoms or exercise testing, a lesion in a native coronary artery or venous bypass graft, and an ischemic tolerance ≥1 minute during angioplasty. Exclusion criteria were acute myocardial infarction, unprotected main stem disease, strong vessel tortuosity, pregnancy, contraindication to acetylsalicylic acid, ticlopidine, clopidogrel or heparin, and a life expectancy of ≤6 months. Patients scheduled for coronary angioplasty were informed and gave their written consent. Clinical and angiographic follow-up was performed after 6 months. The primary end point was the restenosis rate at the target lesion at 6 months. Secondary end points were the restenosis rate of the total segment including edge stenoses and the incidence of major adverse cardiac events (MACE) defined as cardiac death, myocardial infarction, and repeat revascularization of the target vessel. Analysis was done per protocol and from intention to treat.

Angioplasty and Irradiation Procedure
Before angioplasty, the patients received 10 000 U heparin, adjusted to the activated clotting time (>280 seconds). Provisional stenting was performed at the operator’s discretion. The irradiation procedure with the liquid rhenium-188–filled balloon catheter has been described previously.11 Rhenium-188 was obtained from a tungsten-rhenium-188 radionuclide generator as a solution of sodium perrhenate in 0.9% chloride (Oak Ridge National Laboratory). The mean activity was 97±28 mCi/mL. The angioplasty balloon was replaced by a noncompliant balloon of the same diameter but at least 10 mm more in length (Tacker, Cordis Europe). To maintain maximum activity, rhenium-188 was not mixed with contrast agent. Exact positioning was accomplished by means of the proximal and distal radio-opaque marker of the irradiation balloon. The target lesion was covered, and the balloon-traumatized area at both sides was overlapped by the irradiation balloon by at least 5 mm. For angiographic analysis, the irradiated segment was identified by contrast injection with the deflated irradiation balloon in place and the same level of inspiration as with the preprocedural and postprocedural angiograms, giving the exact positions of the proximal and distal marker within the vessel. The maximum length of the irradiation balloon was 40 mm. In 4 patients this was not sufficient to cover the target irradiation zone, and the irradiation procedure was done in a sequential positioning technique with careful alignment of the balloon markers. For irradiation, the balloon was manually inflated. Because of the low viscosity of the liquid rhenium-188, manual inflation of the balloon is sufficient to achieve complete filling without bubbles.11 When the irradiation had to be fractionated, the balloon was deflated for about 2 to 5 minutes but left in place across the target lesion to avoid shifts of the balloon and to minimize radiation exposure to other areas. A team composed of 2 cardiologists and 1 nuclear physician performed the procedure. Acetylsalicylic acid 100 mg per day was continued throughout the study. Patients with stents additionally received ticlopidine 250 mg twice daily or clopidogrel 75 mg daily for 4 weeks. From August 1999 on, the combined antiplatelet therapy after irradiation plus stenting was prolonged to 6 months.

Quantitative Coronary Angiography
Coronary angiography of the target lesion before and after angioplasty and at follow-up was performed in the same projections after intracoronary application of glycerol-trinitrate. Angiographic measurements were done with the Pie Medical software 2.1 (Pie Medical Imaging). Quantitative coronary measurements were performed from the target lesion and from the total segment in the same 2 orthogonal views. Data from the target lesion represent the initial stenosis and the segment injured by angioplasty and irradiation. Data from the total segment include the target lesion and the edge zone. The edge zone was defined as the 6-mm segment proximal and the 6-mm segment distal to the target lesion. Restenosis was defined as diameter stenosis of greater than 50%. Restenoses within the edge zones were defined as edge stenoses. Acute gain was calculated as the difference in minimal lumen diameter (MLD) after and before the procedure. Late loss was calculated as the difference between the postprocedural MLD and at 6 months.

Statistical Analysis
Power analysis of ECRIS was done on the assumption of a restenosis rate after angioplasty of 35% and an aimed 50% restenosis reduction by coronary irradiation therapy, resulting in 105 irradiated and 105 control patients required to receive statistical significance (α=0.05, β=0.2). Continuous variables are presented as mean±1 SD. For the comparison of continuous variables, 2-tailed t test was used. Discrete variables were expressed as counts and percentages compared by means of χ² analysis. Survival analysis was performed with the log-rank test. Statistical significance was set at the 5% α-error level (P<0.05).

Results
Clinical and Angioplasty Data
Between January 1999 and August 2001, 225 patients were included; 113 patients were randomized to receive irradiation and 112 patients were randomized to the control group. There was no crossover. Baseline clinical data did not differ between both groups (Table 1). Lesion morphology, the proportion of patients with de novo and restenotic lesions, and procedural parameters were also not different, except the rate of stenting, which was significantly higher in the control group (Table 2).

Irradiation Data
The length of the irradiated segment varied between 20 (n=2), 30 (n=66), 40 (n=41), 60 (n=2), 80 (n=1), and 90 mm (n=1), with a mean length of 35.0±9.2 mm. The diameter of the liquid rhenium-188–filled balloon varied between 3.0 (n=72), 3.5 (n=30), and 4.0 mm (n=11), with a mean diameter of 3.2±0.3 mm. In all patients, the prescribed dose of 22.5 Gy was delivered. The mean irradiation time was

<table>
<thead>
<tr>
<th>TABLE 1. Baseline Characteristics</th>
<th>Control (n=112)</th>
<th>Rhenium 22.5 Gy (n=113)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.5±10.1</td>
<td>62.5±10.5</td>
<td>NS</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>79</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>Previous infarction, %</td>
<td>68</td>
<td>65</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>70</td>
<td>73</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>79</td>
<td>69</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>59</td>
<td>55</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>25</td>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.6±4.8</td>
<td>27.2±4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Angina pectoris, %</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable</td>
<td>59</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>24</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Silent ischemia, %</td>
<td>17</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>No. diseased vessels</td>
<td>2.0±0.7</td>
<td>1.8±0.7</td>
<td>NS</td>
</tr>
</tbody>
</table>
All myocardial infarctions occurred when the patients took
patient underwent conservative treatment in another hospital.
4 occlusion of the target vessel and received angioplasty, and 1
stent implantation and 2 in patients without a stent on days 77
received an acute myocardial infarction, 3 within 24 hours after
in another hospital. Six of the 7 patients had a newly implanted
139 days. Of the 7 patients, 4 had an angiographically
myocardial infarction, occurring after 6, 8, 45, 59, 70, 77, and
declined to undergo follow-up angiography. Recatheteriza-
dure. Twenty patients who were asymptomatic at 6 months
ventricular fibrillation 97 days after the interventional proce-
died in cardiogenic shock from myocardial infarction 116
There was no in-hospital death. In the control group, 1 patient
Clinical Follow-Up

34), 3 (n=22), 4 (n=12), 5 (n=8), 6 (n=2), and 7
fractions (n=4). There were no adverse effects of the irradia-
tion procedure except anginal pain and ST-segment changes.
No radiation leakage occurred. There were 4 protocol-
vviolating procedures in which the balloon-traumatized zone
of the vessel was clearly not covered by the irradiation
balloon. The 4 patients were excluded from angiographic
analysis per protocol but remained in clinical follow-up and
in the angiographic analysis according to intention to treat.

Clinical Follow-Up
There was no in-hospital death. In the control group, 1 patient
died in cardiogenic shock from myocardial infarction 116
days after the intervention, and 1 patient with history of
myocardial infarction experienced an episode of nonischemic
ventricular fibrillation 97 days after the interventional proce-
dure. Twenty patients who were asymptomatic at 6 months
decided to undergo follow-up angiography. Recatheteriza-
tion was performed in 203 of 225 (90.2%) patients. In the
irradiation group 7 of 113 (6.2%) patients suffered from acute
myocardial infarction, occurring after 6, 8, 45, 59, 70, 77, and
139 days. Of the 7 patients, 4 had an angiographically
documented acute vessel occlusion treated by angioplasty and
3 received thrombolysis without previous angiography in
another hospital. Six of the 7 patients had a newly implanted
stent. In the control group, 5 of 112 (4.5%) patients experi-
enced an acute myocardial infarction, 3 within 24 hours after
stent implantation and 2 in patients without a stent on days 77
and 90. Four patients had an angiographically documented
occlusion of the target vessel and received angioplasty, and 1
patient underwent conservative treatment in another hospital.
All myocardial infarctions occurred when the patients took
only acetylsalicylic acid without additional ticlopidine or
clopidogrel. There was no stent occlusion or myocardial
infarction during prolonged combined antiplatelet therapy
from August 1999. Because the lesion underneath an acute
thrombotic occlusion cannot be measured by angiographic
analysis and based on the different pathomechanism (throm-
bos versus intimal proliferation), the 12 patients with myo-
cardial infarction were excluded from restenosis analysis per
protocol but remained in analysis of MACE and angiographic
analysis by intention to treat.

Angiographic Data and Revascularization
Ninety-five patients in the rhenium-188 group and 91 patients
in the control group were included in the angiographic
analysis per protocol. Table 3 lists the results of quantitative
coronary measurements. There was no coronary aneurysm in
both groups at 6 months of follow-up. The MLD before and
after angioplasty did not differ between both groups. At 6
months, the irradiated group compared with the control group
had a significantly lower late loss, a significantly higher
MLD, and a significantly lower percent diameter stenosis
both of the target lesion and the total segment. The binary
restenosis rates of the target lesion and of the total segment
were significantly lower in the rhenium-188–irradiated group
compared with the control group (Table 3). The cumulative
MLD distribution curves of the control group and of the
irradiated group illustrate the striking difference of MLD at
follow-up (Figure 1). Edge stenoses occurred in 6 patients
(6.3%) of the rhenium-188 group and in 1 (1.1%) patient of
the control group (P=0.06). The revascularization rate of the
target lesion was significantly lower in the irradiated group
with 2.1% (n=2 of 95) compared with 18.7% (n=17 of 91)
in the control group (P=0.0002). In addition, the revasculariz-
ation rate of the total segment was significantly lower in the
rhenium-188 group with 6.3% (n=6 of 95) compared with
19.8% (n=18 of 91) in the control group (P=0.006).

In the subgroup of patients with de novo lesions (n=131),
rhenium-188 irradiation resulted in the same significant
reduction of late loss and percent stenosis diameter as in the
whole study group, both for the target lesion and the total
segment (Table 3). The significantly lower late loss in the
irradiated group was independent from stenting. In both
subgroups of patients with stent implantation or balloon
angioplasty alone, late loss of the target lesion and of the total
segment was significantly lower after rhenium-188 irradia-
tion (Figure 2).

Intention-to-Treat Analysis
Table 4 shows the angiographic data from intention-to-treat
analysis, including all lesions with angiographic control
(n=203) and the respective subgroup of de novo lesions
(n=144). Intention-to-treat analysis also revealed a signifi-
cant lower late loss, a lower percent diameter stenosis, and a
significant higher MLD in the irradiated group compared
with the control group. In accordance with the analysis per
protocol, this effect was present at the target lesion and at the
total segment, both with all patients and in the subgroup of
patients with de novo lesions. Even in a worst case scenario,
imputing a 0-mm MLD at follow-up for all 12 patients with

| TABLE 2. Lesion Characteristics and Procedural Data |
|-----------------|-----------------|
| Control (n=112) | Rhenium 22.5 Gy (n=113) | P |
| Target vessel, % | 38 | 38 | NS |
| LAD | 25 | 20 | NS |
| CX | 15 | 38 | NS |
| RCA | 2 | 4 | NS |
| Cabg | 7 | 12 | NS |
| Lesion type, % | 63 | 45 | NS |
| Abciximab during intervention, % | 60 | 40 | NS |
| No. of inflations | 74 | 67 | NS |
| Total inflation time, s | 188±117 | 167±95 | NS |
| Max. inflation pressure, atm | 14.0±3.3 | 13.3±3.5 | NS |
| Max. balloon diameter, mm | 3.2±0.4 | 3.2±0.4 | NS |
| Balloon to artery ratio | 1.1±0.2 | 1.1±0.1 | NS |

6.8±3.6 minutes. Irradiation was performed in 1 (n=31), 2
(n=34), 3 (n=22), 4 (n=12), 5 (n=8), 6 (n=2), and 7
fractions (n=4). There were no adverse effects of the irradia-
tion procedure except anginal pain and ST-segment changes.
No radiation leakage occurred. There were 4 protocol-
vviolating procedures in which the balloon-traumatized zone
of the vessel was clearly not covered by the irradiation
balloon. The 4 patients were excluded from angiographic
analysis per protocol but remained in clinical follow-up and
in the angiographic analysis according to intention to treat.
myocardial infarction, the reduction of late loss of the total segment remained significant (Figure 2).

**Major Adverse Cardiac Events**

Table 5 lists MACEs during 30 days and 6 months of follow-up. MACEs were significantly lower in the irradiated compared with the control group for the subgroup (n=146) of patients included after August 1999 with prescribed combined antiplatelet therapy for 6 months after irradiation and stenting. Because late coronary occlusion may occur after 6 months, clinical follow-up was extended to 12 months. After 6 months there was 1 myocardial infarction from a nontarget vessel in each group and 1 late stent occlusion in the irradiated group. This stent occlusion occurred in a patient without any antiplatelet therapy 10 days after prostatectomy for cancer.

**Discussion**

This randomized trial of a self-centering liquid rhenium-188–filled balloon catheter for coronary β-irradiation showed a

**Figure 1.** Cumulative frequency of the MLD before and after intervention (black) and at 6 months of follow-up (red) of the target lesion in the control (dotted) and the irradiated group (solid). In the rhenium-188 group, the MLDs after intervention and at follow-up are almost superimposed.

**Figure 2.** In the subgroups with de novo lesions, stenting or balloon angioplasty late loss of the total segment was significantly lower in the irradiated compared with the control group. Worst-case analysis includes all patients with angiographic follow-up plus the patients with myocardial infarction or vessel occlusions imputing a 0-mm MLD at follow-up.
TABLE 4. Intention to Treat Analysis at 6 Months of Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>All Lesions</th>
<th>De Novo Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n=96)</td>
<td>Rhenium 22.5 Gy (n=107)</td>
</tr>
<tr>
<td>Minimal lumen diameter, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target lesion</td>
<td>1.83±0.83</td>
<td>2.38±0.90</td>
</tr>
<tr>
<td>Total segment</td>
<td>1.82±0.83</td>
<td>2.21±0.99</td>
</tr>
<tr>
<td>Stenosis, % of luminal diameter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target lesion</td>
<td>38.1±23.9</td>
<td>22.3±25.0</td>
</tr>
<tr>
<td>Total segment</td>
<td>38.6±23.9</td>
<td>28.2±28.1</td>
</tr>
<tr>
<td>Late loss: target lesion, mm</td>
<td>0.71±0.81</td>
<td>0.24±0.78</td>
</tr>
<tr>
<td>Late loss: total segment, mm</td>
<td>0.72±0.82</td>
<td>0.41±0.88</td>
</tr>
</tbody>
</table>

significantly reduced restenosis rate 6 months after irradiation with 22.5 Gy in 0.5-mm tissue depths. The efficacy of rhenium-188 brachytherapy was also evident in de novo lesions and independent from additional stenting. There was no failure of irradiation technique or dose delivery. Our results confirm the positive findings of previous pilot studies with rhenium-188 perrhenate\(^1\)\(^1\)\(^1\)\(^1\) and a nonrandomized series of patients undergoing rhenium-188 mercaptoacetyltriglycine brachytherapy after atherectomy.\(^1\)\(^4\)

Compared with other irradiation devices, the rhenium-188 liquid-filled balloon provides various advantages.\(^1\)\(^5\) The diameter and length of the irradiation balloon can be easily adapted to the individual vessel segment without need for intravascular ultrasound for dosimetry. Furthermore, the irradiation balloon is self-centering, providing a homogeneous dose delivery and a 100% success in dose delivery attributable to the use of a standard monorail balloon catheter technique. \(\beta\)-irradiation compared with \(\gamma\)-irradiation requires less radiation protection and shorter treatment times and is associated with a lower radiation exposure to the medical staff. The initial occurrence of myocardial infarctions attributable to delayed endothelialization, predominantly after stenting, could be solved by prolonging the combined antiplatelet therapy with acetylsalicylic acid and clopidogrel for up to 6 months.

**De Novo Lesions**

Gamma- and \(\beta\)-irradiation has been shown to be effective for the treatment of in-stent restenosis.\(^3\)\(^5\)\(^6\) In de novo lesions, \(\beta\)-irradiation using a strontium-90/yttrium-90 coil source has been shown to result in a dose-dependent decrease of the restenosis rates after 6 months from 28.6% to 15.0% after irradiation with 9, 12, 15, and 18 Gy at 1-mm tissue depth.\(^7\) The rhenium-188–filled balloon, total segment restenosis rate of de novo lesions was 12.5%, despite a 1.6-times lower radiation dose compared with the 18-Gy group from Verin et al\(^7\) (22.5 Gy in 0.5-mm tissue depth corresponds to 11.3 Gy in 1-mm depth). Different from previous randomized studies with \(\beta\)-irradiation of de novo lesions, ECRIS revealed a significant irradiation efficacy both at the target lesion and the total segment. Compared with our pilot trial,\(^1\) edge stenoses decreased from 35% to 6%. The randomized BETACATH trial showed a significant reduction of the restenosis rate at the target lesion (22%) but an unfavorable

### TABLE 5. Major Adverse Cardiac Events

<table>
<thead>
<tr>
<th></th>
<th>All Patients (N=225)</th>
<th>6 Months APT (N=146)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n=112)</td>
<td>Rhenium 22.5 Gy (n=113)</td>
</tr>
<tr>
<td>30-Day follow-up, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3 (2.7)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Target lesion rerat</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Target vessel rerat</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6-Month follow-up, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (4.5)</td>
<td>7 (6.2)</td>
</tr>
<tr>
<td>Target lesion rerat</td>
<td>17 (15.2)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Target vessel rerat</td>
<td>18 (16.1)</td>
<td>9 (8.0)</td>
</tr>
<tr>
<td>Total</td>
<td>24 (21.4)</td>
<td>16 (14.2)</td>
</tr>
</tbody>
</table>

APT antiplatelet therapy with acetylsalicylic acid and clopidogrel.

*Patients prematurely stopped their prescribed APT.
restenosis rate of the total segment (39%). Similar results were achieved using a phosphor-32 wire source. In the PREVENT trial, a total of 105 patients with de novo (70%) and restenotic lesions were randomized to receive radiation with 0, 16, 20, or 24 Gy in 1-mm tissue depth. The irradiated patients had a restenosis rate at the target lesion of 8% and at the total segment of 22%.

Differences between BETACATH, PREVENT, and ECRIS include the dose, the length of the irradiated segment and of the edge zones, and the irradiation system. In BETACATH, a noncentered 30-mm radiation source train (strontium-90/ytrrium-90) with an effective irradiation length of 25 mm was used. The dose was 28% lower than in ECRIS (16.1 compared with 22.5 Gy in 0.5-mm tissue depth for a 3.0-mm vessel). The length by which the irradiated segment exceeded the traumatized area at each site was only 0.5 to 2.5 mm in BETACATH, disregarding additional extension of the traumatized area by longitudinal shifts of the balloon, but was ≥5 mm in ECRIS. Especially in the stent group of BETACATH, there was almost no overlap of the irradiated zone, resulting in a 24% rate of edge stenoses. In PREVENT, a centered 27-mm radiation source and a dose 42% to 113% higher than in ECRIS was used. With an effective irradiation segment of 22 mm, the overlap of the irradiation zone over the traumatized area ranged between 0 and 2.5 mm at each site, resulting in 14% edge stenoses. Comparing ECRIS, BETACATH, and PREVENT, the length of the irradiated segment exceeding the full traumatized area and homogeneous dose delivery facilitated by a centered device seems to be critical. Whether compression of the vessel tissue during rhenium-188 balloon brachytherapy and the slightly reduced radiation shielding by intramural calcific deposits or stents struts attributable to the larger diameter of the rhenium-188 balloon source in contrast to a wire source are of additional advantage remains open.

Incorporating prior lesions learned from early brachytherapy trials regarding dosimetry and antiplatelet therapy, our data show that rhenium-188 β-brachytherapy can be applied to a broad spectrum of patients undergoing coronary intervention, including de novo lesions, and could be an alternative to an expensive drug-eluting stent technology.

Limitations

The trial was not designed to study small arteries, because it was limited to vessels suitable for a 3-mm radiation balloon at least. Despite careful randomization and analysis blinded to the operators, stents were used more often in the control group compared with the irradiated group. However, rhenium-188 brachytherapy was effective in the subgroups with and without stenting, and stents were no longer associated with increased late thrombosis after prolonging antiplatelet therapy. Because stenting reduces restenosis rate, the lower stent rate of the irradiated group is even in favor of the control group.

De novo lesions were the largest subgroup (71% of the patients). However, the study was not powered for subgroup analysis. Whether the positive results of rhenium-188 brachytherapy can be expected in patients with diabetes, small vessels, or bypass grafts remains to be determined.

Conclusions

We conclude that intracoronary β-brachytherapy with a rhenium-188 liquid-filled balloon is safe and efficiently reduces restenosis and revascularization rates after coronary angioplasty.

Acknowledgments

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References

Intracoronary β-Irradiation With a Rhenium-188–Filled Balloon Catheter: A Randomized Trial in Patients With De Novo and Restenotic Lesions

Martin Höher, Jochen Wöhrle, Markus Wohlfrom, Joachim Kamenz, Thorsten Nusser, Olaf C. Grebe, Hartmut Hanke, Matthias Kochs, Sven N. Reske, Vinzenz Hombach and Jörg Kotzerke

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