Long-Term Coronary Vascular Response to $^{32}$P β-Particle–Emitting Stents in a Canine Model

Allen J. Taylor, MD; Patrick D. Gorman, MD; Andrew Farb, MD; Timothy G. Hoopes, MD; Renu Virmani, MD

Background—The arterial placement of $^{32}$P β-particle–emitting stents in various experimental animal models results in discordant effects on neointimal formation. We studied the vascular effects of β-particle–emitting stents in normal canine coronary arteries because compared with pigs and rabbits, the canine model may more closely mimic the vascular response of humans.

Methods and Results—Thirty stents (control nonradioactive, n=10; low-activity $^{32}$P, 3.5 to 6.0 μCi, n=11; high-activity $^{32}$P, 6.5 to 14.4 μCi, n=8) were implanted in normal canine coronary arteries through the use of a single balloon inflation at nominal pressure. Histological analysis after 15 weeks included the measurement of neointimal and adventitial area and thickness. Neointimal fibrin area was measured with the use of computer-assisted color segmentation on Movat pentachrome sections. Luminal stenosis was significantly increased in $^{32}$P stents compared with control stents (44.6±16.8% versus 32.7±10.8%; P=0.05) and was highest in the high-activity group (45.5±24.3%). No evidence of an “edge effect” was seen in adjacent, nonstented coronary segments. All $^{32}$P stents showed incomplete vascular healing as indicated by a dose-dependent increase in fibrin area with increasing stent activity. Arterial radiation resulted in a decrease in adventitial size, which was maximal for high-activity $^{32}$P stents, indicating an inhibitory effect on the adventitial response to injury.

Conclusions—$^{32}$P β-particle–emitting stents have adverse vascular effects at 15 weeks in the canine normal coronary artery model. Vascular brachytherapy with this device causes increased neointimal formation and prominent, dose-dependent lack of healing. (Circulation. 1999;100:2366-2372.)

Key Words: stents ■ radiotherapy ■ radioisotopes ■ restenosis ■ revascularization

Studies in animals of the use of β-particle–emitting coronary stents have shown variable effects on neointimal formation. In the porcine coronary model, low-dose $^{32}$P β-particle–emitting stents increase neointimal formation between 3 to 6 months after coronary injury. In contrast, higher activities result in a smaller neointimal area but an area that is fibrin rich and immature. In the rabbit iliac model, radioactive stents reduce neointimal accumulation, although delayed healing of the neointima is also evident. The success of β-particle–emitting stents as a method of limiting restenosis hinges on an apparently delicate balance between radiation-related cellular injury and suppression of cellular proliferation and migration.

We chose to study the effects of $^{32}$P β-particle–emitting stents in the canine normal coronary artery model for several reasons. We believed that the canine model would be additive to existing porcine and rabbit data given the variable (large versus small animal) and species-specific response to radioactive stents in these models. Compared with the canine model, the porcine model has an increased tendency for thrombus formation due to reduced intrinsic fibrinolytic capacity and increased adventitial fibrosis and vascularity. These divergent characteristics make the canine model an attractive large animal alternative for the study of the effects of radioactive stents. In particular, dogs may be less prone to the development of the fibrin-rich neointima seen in other models.

We hypothesized that the $^{32}$P β particle–emitting coronary stent would reduce neointimal formation in normal canine coronary arteries.

Methods

This protocol was approved by the Laboratory Care and Use Committee of the Armed Forces Institute of Pathology and was conducted in accordance with regulatory guidelines for the care of laboratory animals. Stainless steel stents (15 mm long, BX design; Isostent, Inc) were made radioactive through the direct implantation of $^{32}$P ions beneath the surface of the metal. Ion implantation is accomplished through the placement of the stent and $^{32}$P in a vacuum apparatus; we then vaporized, ionized, and accelerated the ions with...
a high voltage so the \(^{32}\)P ions became buried beneath the surface of the stent wire.\(^7\) \(^{32}\)P is a pure \(\beta\)-particle emitter with a maximal energy of 1.709 MeV, an average energy of 0.695 MeV, and a half-life of 14.3 days. The activity of each stent was determined through comparison with standard \(^{32}\)P sources; the stent was placed in an acrylic resin shield and sterilized.

The \(\beta\)-particle–emitting stents were implanted at activities ranging from 3.5 to 14.4 \(\mu\)Ci. For the purpose of analysis, the radioactive stents in this study were divided into 3 groups: (1) control, nonradioactive; (2) low-activity \(^{32}\)P, 3.5 to 6.0 \(\mu\)Ci \((n=11)\); and (3) high-activity \(^{32}\)P, 6.5 to 14.4 \(\mu\)Ci \((n=8)\). The total delivered radiation dose (0.5 mm from a stent wire of a 3-mm stent) was 7894±1251 cGy in the low-activity group and 17 335±3328 cGy in the high-activity group.

**Animal Model**

Eleven male, purpose-bred, mongrel dogs underwent the placement of radioactive stents in the left coronary system (left circumflex and left anterior descending coronary arteries). Animals received aspirin (650 mg) on the evening before the procedure. With the animals under general anesthesia (induction with 0.02 mg/kg buprenorphine IM/SC and 17.5 mg/kg thiopental IV followed by maintenance anesthesia with inhaled isoflurane), an 8F sheath was placed in the left carotid artery, and 50 U/kg heparin was administered. Pre-mounted BX stents (3.0 or 3.5 mm in diameter) were deployed in the proximal or midportions of the left anterior descending coronary artery and in the proximal and distal portion of the left circumflex coronary arteries through a single balloon inflation to nominal pressure (3.0-mm stent at 8 ATM, 3.5-mm stent at 7 ATM) for 45 seconds. One stent was noted to have an associated arterial dissection and was treated with a second balloon inflation at 1 ATM for 90 seconds. This stent (in the high-activity group) was occluded at follow-up angiography (3 months). Stents were placed in arterial locations without major branches and where the stent would be mildly to moderately oversized. One dog died of acute stent thrombosis during stent implantation. The 10 surviving dogs were returned to the animal care facility, where they received 81 mg/d aspirin and a normal diet for 15 weeks. Analgesia (0.01 to 0.02 mg/kg buprenorphine IM/SC) was administered as necessary. At the completion of the study, animals underwent repeat coronary angiography as described above (29 of 30 stents were patent) and then were euthanized with a lethal dose of barbiturate and KCl.

**Histology**

After euthanasia, the hearts were immediately harvested and rinsed with 0.9% Ringer’s lactate followed by perfusion fixation via the aortic stump for 30 minutes at 80 mm Hg and overnight immersion fixation in 10% neutral buffered formalin. Radiographs were taken of the hearts, and the coronary arteries were dissected from the heart. The coronary stented segments were dehydrated in graded series of alcohol and embedded in methyl methacrylate. The stented portion of the artery was sawed into proximal, mid, and distal portions and sectioned at 4 \(\mu\)m with a stainless steel carbide knife. Sections of the nonstented adjacent proximal and distal coronary artery were also submitted for histologic analysis after paraffin embedding. Histologic sections were stained with hematoxylin and eosin and Movat pentachrome for analysis.

**Histological Analysis**

Histological measurements were performed on sections from the proximal, mid, and distal regions of the stent. Adjacent, nonstented coronary segments were examined for any adverse effects, such as neointimal formation (edge effect). All histological analysis was performed by personnel blinded to the stent characteristics (radioactive or control). A vessel injury score was calculated according to the method described by Schwartz et al.\(^8\) The cross-sectional areas (adventitia, external elastic lamina, internal elastic lamina [IEL], and lumen) of each section were measured with digital morphometry (IP Laboratory Spectrum). Neointimal thickness was measured as the distance from the IEL to the luminal border both at and between each stent wire. Percent area stenosis was calculated with the formula \([(\text{Neointimal Area}/\text{IEL Area}) \times 100]\).

Complete neointimal healing was defined as a neointima composed of smooth muscle cells in a proteoglycan and collagen matrix, with no fibrin or inflammatory cell infiltrates. Endothelialization was assessed in the midsten section through manual counting of the total number of endothelial cell nuclei around the neointimal/luminal border. Fibrin within the neointima was quantitatively evaluated with the use of computer-assisted color segmentation. Four digitized regions of interest per stent (1 from each quadrant) were evaluated. For each stent, a neointimal site (midsten section) displaying fibrin was randomly selected for calibration of the computer program. The 4 regions of interest were then interrogated for the percent area of fibrin coverage.

Immunohistochemical staining was performed on selected cases to confirm the presence of fibrin within the sites chosen for calibration of the automated program and to confirm the presence of endothelial cells along the arterial lumen. Slide-mounted arterial sections were pretreated in citrate buffer (100°C for 20 minutes) for antigen recovery, exposed overnight to an antibody to fibrin II \(\beta\) chain (dilution 1:100; Accurate Chemical Co) or factor VIII (dilution 1:1000; DAKO), and developed with the use of a commercially available LSAB kit (DAKO).

**Statistical Analysis**

Values are expressed as mean±SD. Mean values for histological variables were compared between groups with the use of ANOVA or \(t\) tests for analysis of paired or unpaired data as appropriate. A value of \(P<0.05\) was considered statistically significant.

**Results**

Thirty stents from 10 dogs were explanted after a mean of 110±4 days (range 104 to 114 days; 38 days beyond the 5th half-life of \(^{32}\)P decay). Total occlusion occurred in 1 stent (3.3%) in the high-activity group. This stent was treated (see “Methods”) for a presumed arterial dissection at the time of implantation, although a dissection was not present on histology. Control and radioactive stents showed similar injury scores (control stents 1.24±0.19, radioactive stents 1.31±0.31, \(P=0.5\)). The stent-to-artery ratio was similar for control (1.11±0.15) and radioactive (1.09±0.11, \(P=0.58\)) stents.

**Neointimal Growth**

The external elastic lamina, IEL, and lumen areas were similar in control and radioactive stented arteries (Table). Radioactive stents showed a 25% increase in percent luminal stenosis. Luminal stenosis was 44.6±16.8% in \(^{32}\)P stents compared with 32.7±10.8% for controls (\(P=0.05\)). The highest mean value for luminal stenosis was seen in the high-activity group (45.5±24.3%) (Figure 1A). This represented a trend for increased luminal stenosis in the high-activity group (\(P=0.15\) versus control), but there was a large degree of variability (both within and between stents) related to neointimal nonhealing seen in this group. Radioactive stents also resulted in increased neointimal thickness (Table). We tested the possibility that the number or degree of separation of radioactive stent struts was an important variable in the determination of the amount of neointima formation. There was no significant relationship between the number of stent struts per cross section and neointimal thickness (\(r=0.30, P=0.22\)). The neointimal thicknesses over the site of minimum and maximum strut separation within the
midstent section of radioactive stents were similar (0.36±0.17 versus 0.35±0.17 mm, \(P=0.48\)).

Radioactive stents showed significantly increased neointimal area in the proximal stent (3.1±1.6 mm\(^2\)) compared with the middle (2.7±1.3 mm\(^2\), \(P=0.001\)) and distal (2.6±1.4 mm\(^2\), \(P<0.05\)) stent segments. There was no evidence of an edge effect for radioactive stents; arterial sections proximal and distal to the stent showed no significant neointimal accumulation (Figure 1B). Smooth muscle cells and proteoglycan matrix were only focally present in radioactive stents compared with a cellular, proteoglycan-rich neointima in control stents (Figure 2). Radioactive stents showed a significant reduction in the number of endothelial cell nuclei present in the midstent section (Table; \(P=0.028\)).

**Adventitial Effects**

Arteries treated with the use of \(^{32}\)P stents showed a significant, dose-dependent reduction in adventitial thickness (Table). Control stents showed a mean adventitial thickness of 0.19±0.06 mm compared with 0.18±0.04 mm in low-activity stents and 0.14±0.04 mm in high-activity stents (\(P=0.05\)). The ratio of adventitial area to neointimal area was significantly smaller for radioactive stents (\(P=0.027\), ANOVA).

**Neointimal Fibrin and Radioactive Stents**

Extensive fibrin-rich regions within radioactive stents were present 15 weeks after stent implantation, particularly in proximity to stent wires (Figure 3). The neointima of both low- and high-activity \(^{32}\)P stents showed incomplete vascular healing, indicated by large, fibrin-rich, acellular regions (Figure 2). Qualitatively, complete healing was observed in all 10 control stents, in 2 of 11 low-activity stents, and in none of 8 high-activity stents (\(P<0.001\)). Quantitatively, there was a dose-dependent increase in neointimal fibrin in low- and high-activity \(^{32}\)P stents (Figure 1C), up to a maximal value of 23.0±15.4\% of neointimal cross-sectional area (\(P<0.001\), ANOVA). This reflects nonhealing of neointima from persistent radiation effects.

**Discussion**

This study demonstrates the adverse effects of \(^{32}\)P \(\beta\)--emitting radioactive stents in normal canine coronary arteries. Radioactive stents resulted in a larger neointima and in delayed neointimal healing after 15 weeks. Radioactive stents promoted the persistence of a large, fibrin-rich neointimal area despite also causing a reduction in adventitial size. These data have implications for our understanding of the mechanisms of radioactive stents and for their use in vascular brachytherapy in humans.

**Previous Studies With Radioactive Stents**

\(^{32}\)P \(\beta\)-particle–emitting stents have been studied in the porcine and rabbit models. Laird et al\(^7\) showed reduced neointimal area with complete reendothelialization at 28 days in minimally injured porcine iliac arteries treated with low-activity (0.14 \(\mu\)Ci) versus control stents. A subsequent study by Carter et al\(^1\) in the porcine coronary injury model suggested a complex dose-response relationship, with an increase in neointimal formation seen in 1-\(\mu\)Ci \(^{32}\)P stents at 28 days. Higher activities reduced neointimal formation, but incomplete neointimal healing was present. A subsequent, longer-term porcine coronary study with an atherosclerotic, double-injury model reported a progressive, activity-related increase in neointima formation at 6 months in porcine coronary arteries (atherosclerotic, double-injury model) treated with \(^{3\text{I}}\)P stents (1 to 12 \(\mu\)Ci). Thus, in the porcine model, activities of >1 \(\mu\)Ci result in early (28 days) incomplete neointimal healing and endothelialization,\(^1\) which progress to larger and more complex, atherosclerotic lesions.\(^2\)

Results in the rabbit iliac model\(^3\) differ from those in the porcine model.\(^4\) With the use of \(^{32}\)P \(\beta\)-particle–emitting stents, nonhealing is present at 3 months, but reduced neointimal thickness persists.\(^3\) These data are similar to the 1-month porcine iliac data initially reported by Laird et al.\(^7\)

### Histological Characteristics of Control and Radioactive Stents

<table>
<thead>
<tr>
<th>ROI</th>
<th>Control (n=10)</th>
<th>Low Activity (3.5–6 (\mu)Ci) (n=11)</th>
<th>High Activity (6.5–14.4 (\mu)Ci) (n=8)</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>External elastic lamina area, mm(^2)</td>
<td>7.2±1.1</td>
<td>7.0±2.0</td>
<td>7.9±1.4</td>
<td>0.47</td>
</tr>
<tr>
<td>IEL area, mm(^2)</td>
<td>6.3±1.0</td>
<td>6.0±1.7</td>
<td>6.7±1.1</td>
<td>0.54</td>
</tr>
<tr>
<td>Lumen area, mm(^2)</td>
<td>4.2±0.8</td>
<td>3.4±1.2</td>
<td>3.5±1.6</td>
<td>0.29</td>
</tr>
<tr>
<td>Neointimal area, mm(^2)</td>
<td>2.1±0.9</td>
<td>2.6±0.8</td>
<td>3.1±1.9</td>
<td>0.26</td>
</tr>
<tr>
<td>Neointimal thickness, mm</td>
<td>0.28±0.11</td>
<td>0.35±0.12</td>
<td>0.41±0.20*</td>
<td>0.16</td>
</tr>
<tr>
<td>Luminal stenosis, %</td>
<td>32.7±10.8</td>
<td>43.9±9.6*</td>
<td>45.5±24.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Adventitial thickness, mm</td>
<td>0.19±0.06</td>
<td>0.18±0.04</td>
<td>0.14±0.04*</td>
<td>0.10</td>
</tr>
<tr>
<td>Adventitial area, mm(^2)</td>
<td>2.46±0.96</td>
<td>2.06±0.63</td>
<td>1.79±0.70</td>
<td>0.20</td>
</tr>
<tr>
<td>Adventitia/neointimal area ratio</td>
<td>0.85±0.40</td>
<td>0.56±0.19</td>
<td>0.52±0.09</td>
<td>0.03</td>
</tr>
<tr>
<td>Neointimal fibrin area, % ROI</td>
<td>1.9±3.4</td>
<td>12.4±10.2</td>
<td>23.0±15.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Endothelial cells/vessel</td>
<td>195±27</td>
<td>119±39</td>
<td>101±74</td>
<td>0.028</td>
</tr>
<tr>
<td>Injury score</td>
<td>1.24±0.19</td>
<td>1.41±0.36</td>
<td>1.18±0.17</td>
<td>0.18</td>
</tr>
</tbody>
</table>

ROI indicates region of interest. \(^*P<0.05\) vs control group.
Hehrlein et al. showed a reduction in neointima formation in the rabbit iliac model with the use of a radioactive stent with a mixture of radioisotopes (predominantly \(^{55}\)Co; \(\beta\), \(\gamma\), and x-irradiation) with stent activities up to 35 \(\mu\)Ci. A second study, in rabbits, by Hehrlein et al. reported inhibition of neointima formation by 13-\(\mu\)Ci, but not 4-\(\mu\)Ci. \(^{32}\)P radioactive stents up to 12 weeks after implantation. Radioactive stents were endothelialized after 4 weeks, but endothelialization was less dense than that in conventional stents. These results are markedly different than those of a similar study in the rabbit model performed in our laboratory in which only one third of the endoluminal surface area of a 6-\(\mu\)Ci stent was endothelialized at 3 months.\(^3\) Thus, the effects of radioactive stents differ for the porcine and rabbit models. The reasons for this are not fully elucidated but likely relate to differences in animal species and age, different time points studied, or differences between peripheral vascular and coronary artery models.

**Present Study**

The canine coronary injury model has been broadly used for the study of coronary stents but not for the study of radioactive stents. In general, the histological response of canine coronary arteries to injury is considered to be very similar to that observed in human coronary arteries. In contrast to pigs, dogs have greater fibrinolytic activity and therefore might be resistant to the development of the fibrin-rich neointima seen in other models. However, in this study, dogs developed a large, fibrin-rich neointima 15 weeks after treatment with \(^{32}\)P \(\beta\)-particle-emitting stents. The adverse effect of radiation on normal canine coronary arteries is consistent with those from previous canine studies in the peripheral (carotid, aortic, and femoral) vasculature.\(^{14,17}\) Our results further illustrate the extreme variability among animal models. Despite the use of \(^{32}\)P radioactive stents with similar activity to those used in the rabbit model of Hehrlein et al.,\(^9\) we found unequivocal evidence of increased neointima formation and delayed neointimal healing in the canine model.

Accumulating data from different large animal coronary models document clear adverse effects of \(^{32}\)P \(\beta\)-particle-emitting stents. Neointimal accumulation is increased, and complete neointimal healing with a \(^{32}\)P stent requires from 3 (present study) to 6 months.\(^2\) In the short term, vascular brachytherapy has both antiproliferative\(^4,7,18–21\) and antimitotic\(^18,20,21\) effects on vascular smooth muscle cells. Thus, long-term, continuous radiation delivered via radioactive stents markedly differs from radiation delivered with \(\gamma\) or \(\beta\) wire devices, despite similarity in the cumulative delivered radiation dose. The mechanisms for this are unclear but are likely complex and multifactorial. The sharp dosimetry peaks of a radioactive stent in the near field lead to extensive heterogeneity in the radiation dose delivered to cellular elements in the vessel wall. This heterogeneity could be particularly deleterious if variable radiation doses induce unique stochastic effects.\(^1,24\) The prolonged dosage rate (longer delivery diminishes the effective dose) with radioactive stents makes the comparison difficult for similar doses delivered across varying lengths of time, with different isotopes and delivery mechanisms. Tissue hypoxia from stent-related compromise of adventitial microvessels can theoretically increase the cellular resistance to radiation by several-fold. Consistent with this hypothesis is the finding that similar doses of radiation have less effect on the prevention of neointimal formation in stented than in balloon-treated arteries.\(^26\)

The effect of radiation on growth factor expression may be another potential explanation for the observed differences between \(\beta\)-particle-emitting stents and \(\beta\) and \(\gamma\) wire devices. For example, radiation enhances the activation of latent transforming growth factor-\(\beta\).\(^{27,28}\) Prolongation of radiation exposure with radioactive stents may enhance exposure to growth factors and influence neointimal growth.\(^29\) The presence of calcification in porcine arteries exposed to continuous...
β-radiation\(^2\) is consistent with the promotion of cartilaginous metaplasia through continuous stimulation with transforming growth factor-β.\(^{29}\)

**Adventitia as Target Tissue for Vascular Brachytherapy**

After vascular injury, neointimal smooth muscle cells migrate from the adventitia\(^{20,21}\); thus, the adventitia has been postulated as the target tissue for vascular brachytherapy. Both β- and γ-source radiation inhibit smooth muscle cell proliferation and myofibroblast recruitment from the adventitia; however, radiation has well-documented adverse effects on the adventitia. Patients treated with external beam irradiation for thoracic malignancies have increased adventitial thickness and fibrosis.\(^{30}\) In the porcine model, adventitial thickness increases in an activity-dependent manner after vascular brachytherapy.\(^{2,26}\) In our study, we have shown that the adventitial and neointimal effects of vascular brachytherapy can be discordant. Specifically, adventitial thickness was reduced in an activity-dependent manner with the use of radioactive stents, but neointima accumulation was increased. Possible mechanisms for this include the sharp dosimetry gradient of the β-particle emissions and medial “shielding” of the adventitia or differential cellular radiosensitivity of fibroblasts versus smooth muscle cells. Thus, there are additional mechanisms, beyond the beneficial adventitial response to
vascular injury, that prevent radioactive stents from being an effect of antirestenosis therapy.

Current Status of Radioactive Stents

Theoretically, excessive radiation doses to the endothelium will delay reendothelialization and facilitate continued platelet/fibrin deposition, whereas the dosimetry gradient through the arterial wall will decrease the effective radiation dose to pluripotent adventitial myofibroblasts. The result of this paradigm is a larger, fibrin-rich neointima. Thus, the original “electron fence” proposal for the rationale of $^{32}$P stents is, by itself, insufficient.

Trials with the use of $^{32}$P stents in humans are under way. In preliminary results of these feasibility and safety trials (performed without concurrent controls), there has not been an excessive number of early adverse events with radioactive stents, and a beneficial effect on restenosis is, as yet, unproved. Preliminary reports of some angiographic failures of radioactive stents are due to the so-called edge effect (P. W. Serruys, personal communication, 1998). We did not observe evidence of an edge effect in this study; rather, the adverse effect on neointimal accumulation was observed entirely within the stent. The clinical implication of delayed healing of a fibrin-rich neointima is currently uncertain. It seems likely that the persistence of fibrin is at least a marker for continued radiation effects that correlate with delayed reendothelialization (seen in this study). Whether the fibrin contributes to excess thrombosis potential over the risk posed by delayed endothelialization is unknown. Studies in humans have documented that arterial thrombosis is a potential late complication of vascular brachytherapy.

Study Limitations

In the present study, we tested the ability of $\beta$-particle–emitting stents to limit the degree of neointima formation after moderate injury of normal canine coronary arteries. A direct comparison with other animal models is made difficult by the variable, species-specific response to radiation. Even within an animal model, variables such as animal age may affect the vascular response to injury. The effects of radioactive stents in normal and “atherosclerotic” animal arteries are insufficient to predict their effects in heavily atherosclerotic human arteries and thus must await the completion of adequate clinical trials.

Edge effects are an illustration of the differences between results with radioactive stents in animals and humans. We did not observe any evidence of edge effects in this study, but we have observed subtle edge effects in the rabbit model in our laboratory (unpublished observation). In contrast, edge effects are responsible for a large proportion of early failures seen in preliminary human clinical trials (P. W. Serruys, personal communication, 1998). Reasons for this difference are unknown but may relate to differences in stent deployment techniques (multiple, high-pressure balloon inflations in human stenting), the more rapid vascular healing seen in animal models, or the influence of normal versus atherosclerotic tissue in the border zones adjacent the radioactive stent.

Conclusions

The vascular effects of $^{32}$P $\beta$-particle–emitting stents at 15 weeks in normal canine coronary arteries are adverse. Coro- nary vessels irradiated with stent activities ranging from 3.6 to 14.4 $\mu$Ci have more neointima and prominent, dose-dependent lack of healing. The adventitial and neointimal effects of vascular brachytherapy via a $\beta$-particle–emitting stent can be discordant, indicating a failure of the electron fence theory for this device. Ongoing human clinical trials will determine the ultimate role of the $^{32}$P $\beta$-particle–emitting stent in vascular brachytherapy.

Acknowledgments

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References


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