Low-Dose, β-Particle Emission From ‘Stent’ Wire Results in Complete, Localized Inhibition of Smooth Muscle Cell Proliferation

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**Background** Restenosis after catheter-based revascularization has been demonstrated to be primarily caused by medial and/or intimal smooth muscle cell (SMC) proliferation. The objective of this study was to investigate the ability of local emission of β-particles from a 32P-impregnated titanium “stent” wire source to inhibit vascular SMC and endothelial cell proliferation in cell culture and to determine the dose-response characteristics of this inhibition.

**Methods and Results** A series of experiments were performed using 0.20-mm-diameter titanium wires that were impregnated with varying low concentrations of 32P (activity range, 0.002 to 0.06 μCi/cm wire, n = 47) or 35P (nonradioactive control, n = 28) in cultures of rat and human aortic SMCs and in cultured bovine aortic endothelial cells. The zone of complete cell growth inhibition (in millimeters from stent wire) was measured using light microscopy in the cultures exposed to the radioactive (32P) or control (35P) wires at 6 and 12 days after plating. In both rat and human SMC cultures there was a distinct 5.5- to 10.6-mm zone of complete SMC inhibition at wire activity levels ≥0.006 μCi/cm. In contrast, there was no zone of inhibition surrounding the control (32P impregnated) wires (P<.001 versus 32P wires at all wire activities ≥0.006 μCi/cm for human and rat SMCs). Proliferating bovine endothelial cells were more radioresistant than SMCs, with no zone of inhibition observed at wire activity levels up to 0.019 μCi/cm (P<.001 versus SMCs at 0.006 μCi/cm and 0.019 μCi/cm).

**Conclusions** We conclude that very low doses of β-particle emission from a 32P-impregnated stent wire (activity levels as low as 0.006 μCi/cm of wire) completely inhibit the growth and migration of both rat and human SMCs within a range of 5.5 to 10.6 mm from the wire. Endothelial cells appear to be much more radioresistant than SMCs. These data suggest that an intra-arterial stent impregnated with a low concentration of 32P may have a salutary effect on the restenosis process. Whether this approach can be used successfully and safely to inhibit restenosis in vivo and in the clinical setting is under investigation. (Circulation. 1994;90:2956-2963.)

**Key Words** • balloon • angioplasty • restenosis • β-particles • stent

Percutaneous transluminal coronary angioplasty has gained widespread acceptance as a therapeutic option in the treatment of selected patients with obstructive coronary artery disease.1 Restenosis, defined angiographically as the recurrence of a >50% luminal diameter narrowing at the site of prior balloon dilatation, occurs in approximately 40% to 60% of cases after successful percutaneous transluminal coronary angioplasty and is the major problem limiting the long-term efficacy of this therapy.1-5

There is clinical and experimental evidence to suggest that restenosis results primarily from the migration (into the intima) and rapid proliferation of a subset of predominantly medially derived smooth muscle cells after balloon-induced arterial injury.6-8 Smooth muscle cells proliferate in response to mechanical stretch9,10 and stimulation by a variety of growth factors.1,2,11,12 Current concepts of restenosis suggest that these cells stop proliferating within 1 to 2 months after the initial balloon injury but continue to elaborate an extracellular matrix of collagen,8,13,14 elastin,15 and proteoglycans.16 The mass of tissue resulting from the cellular proliferation and the extracellular matrix contribute to the neointimal hyperplasia, which ultimately narrows the arterial lumen in patients who have restenosis.

The efforts to prevent or significantly reduce the incidence of restenosis using a variety of medications, including calcium channel blockers, angiotensin-converting enzyme inhibitors, aspirin, anticoagulant agents, corticosteroids, fish oil, and so on, have been disappointing.3 Likewise, the use of mechanical systems to remove plaque (atherectomy), laser ablative therapy, improved balloon catheters, and mechanical stenting systems have, at best, had a modest impact on the incidence of restenosis. Although there has been great interest in potent platelet inhibitors and specific inhibitors of a number of the myriad of growth factors implicated in the restenosis process, it remains uncertain whether such focused therapies will prove efficacious because the proliferative stimulus is so multifactorial.

We have previously demonstrated that relatively low doses of external beam (x-ray) irradiation inhibit arterial smooth muscle cell clonal proliferation in culture17,18 and in an in vivo model of restenosis in the rabbit.19 Although external irradiation may have some ability to inhibit smooth muscle cell proliferation, the use of a very low dose of locally delivered radiation via a radioisotope, β-particle–emitting intravascular stent
may provide a safer and/or more efficacious method of achieving this effect and has not been previously studied.

The objective of the present study was to investigate the ability of very low levels of localized \( \beta \)-particle emission from a \( ^{31} \)P-impregnated titanium stent wire source to inhibit smooth muscle cell proliferation in cell culture and to determine the dose-response characteristics of this inhibition, if present. The effect of local \( \beta \)-particle irradiation on endothelial cell growth was also examined to address the issue of reendothelialization, were a \( ^{31} \)P-impregnated stent implanted after angioplasty.

**Methods**

\( \beta \)-Particle–Emitting Wires

Commercially pure titanium wires (0.2-mm diameter, <0.1% impurities) were cut into 38-mm lengths and successively cleaned in ultrasonic baths of acetone and isopropyl alcohol for 10 minutes each. The wires were then impregnated with an average of 37% (atomic percentage) phosphorous into the first one-third micron of the surface of each wire. Two groups of wires were created. A "high-dose" group of wires were impregnated with \( ^{31} \)P on two sides of the wire, and a "low-dose" group received phosphorous impregnation on only one side.

The phosphorous-impregnated wires were then immersed in a flux of thermal neutrons in a fission reactor. Less than 0.01% of the isotopically stable phosphorus atoms, atomic number 31, absorbed a neutron and were transformed into \( ^{31} \)P, a \( \beta \)-particle emitter (no \( \gamma \)-radiation) with a maximum energy of 1.709 MeV, an average energy of 0.695 MeV, and a half-life of 14.3 days. Spectroscopic measurements indicated that no other long-lived radionuclides were created.

The activity level of each wire specimen was measured using a gas-filled proportion-counting device. In this detection system, the gas that surrounds the specimen is ionized by the \( \beta \)-particles emitted from the activated specimens. The ionized gas creates an electrical pulse that is detected using sensitive electronics. The amplitude of the electrical pulse is dependent on the energy of the detected particle, this enabling the creation of an energy-resolved spectrum.

This detection system was calibrated with sources of known activity before measurements were performed on the specimens used for these tests. Once calibrated, the test specimens were placed into the gas chamber (4\( \pi \)), and the electrical pulses were counted and sorted by energy for several minutes. The counting rate at the energy corresponding to \( ^{31} \)P's 1.7 MeV peak was measured and used to determine the number of microcuries of activity (1 \( \mu \)Ci =3.7\times10\(^{10}\) counts per second) after correction for detector sensitivity. The spectrum collected for each specimen was also searched for emissions from nuclides other than \( ^{31} \)P, and none were detected. With these methods, the high-dose wires were determined to have activities ranging from 0.047 to 0.060 \( \mu \)Ci/cm at the time of initial plating, with the low-dose wires having activities ranging from 0.019 to 0.027 \( \mu \)Ci/cm at the time of initial cell culture plating.

Cell Culture

Rat aortic smooth muscle cells were isolated by collagenase and elastase digestion of thoracic aorta of male Sprague-Dawley rats as previously described.\(^{20,21}\) Human aortic smooth muscle cells were a kind gift from Dr Michael Mendelsohn, Tufts University, Boston, Mass. They were isolated from punch biopsies of human aorta obtained at the time of bypass surgery. The vascular smooth muscle cells from these specimens were isolated by an explant technique. Both types of smooth muscle cells demonstrated fibrillar staining with a specific smooth muscle \( \alpha \)-actin antibody (Boehringer Mannheim). Bovine aortic endothelial cells were a kind gift of Dr Tom Quertermous and were isolated as described by Lee et al.\(^{22}\) All cells were maintained in Dulbecco's modified essential medium with 10% fetal bovine serum.

For experimental procedures, the radioactive and control wires were cemented into standard 100-mm tissue culture dishes with surgical bone cement (Howmedica). The dishes were then sterilized with gas, and cells were plated at a density of 5\( \times \)10\(^{3}\) cells per dish. The zone of complete cell growth inhibition was measured at 6 and 12 days after initial plating with a micrometer inserted into the eyepiece of a standard inverted microscope (Olympus). The calibration of the system was confirmed by measuring the titanium wires of known diameter (0.2 mm), mounted in the cell culture dishes. For each wire, the zone of inhibition was defined by the mean of eight determinations (four on each side of the wire at 7-mm intervals, starting 5 mm from each end of the wire). After 12 days, the cells were photographed. In a subset of the cultures (at 12 days), the cells were stained with toluidine blue before photography to allow clear-cut demarcation of the zone of cell growth inhibition at low levels of magnification. After the first cell plating, the wires were removed and then cemented into clean tissue culture dishes and sterilized for a second round of plating. In this manner, the effects of decrementally lower doses of \( \beta \)-particle irradiation on cell growth could be assessed taking advantage of the relatively short half-life of \( ^{31} \)P, 14.3 days. The activity of the wires at the time of the second plating was calculated using the measured initial activity (by date) and the radioactive decay curve for \( ^{31} \)P.

**Statistical Analysis**

All data are expressed as mean±1 SD unless otherwise stated. ANOVA for repeated measures was used to compare the zones of smooth muscle cell and endothelial cell inhibition at varying wire activity levels at 6 and 12 days after plating of the cell cultures. These same methods were used to assess the differences in the zones of smooth muscle cell versus endothelial cell growth inhibition at the same wire activity levels. A value of \( P<.05 \) was considered statistically significant. Statistics were calculated using the software program STATVIEW 512+.
Results

Rat Smooth Muscle Cells

The effect of β-particle irradiation from a 32P-impregnated wire source on the growth and migration of rat vascular smooth muscle cells in culture was studied using a total of 39 wires with activities of 0.002 µCi/cm (of wire) (n=3), 0.006 µCi/cm (n=4), 0.019 µCi/cm (n=8), 0.027 µCi/cm (n=4), 0.047 µCi/cm (n=4), and 0.060 µCi/cm (n=4) and of 0.00 µCi/cm (control, n=12). The dose-response curve describing the relation between wire activity at the time of plating and the zone of complete inhibition of rat smooth muscle cell growth is shown in Fig 1. There appears to be a relatively consistent 5- to 7-mm zone of inhibition at doses between 0.006 and 0.047 µCi/cm of wire. At the highest wire activity level (0.060 µCi/cm), there was inhibition observed as far as 10.6 mm from the wire. There was no inhibition of smooth muscle cell growth near the wires impregnated with 31P, demonstrating that the inhibition of smooth muscle cell growth near the 32P-coated wires was due to β-particle emission rather than any nonspecific inhibitory effect from the titanium wire or phosphorous that was impregnated onto the wires. Fig 2 provides photomicrographs of smooth muscle cells in culture demonstrating a 4- to 5-mm zone of smooth muscle cell inhibition at 12 days after plating around a 0.019 µCi/cm wire (Fig 2B and 2C). In contrast, no inhibition is seen with the control (31P-impregnated) wire (Fig 2A).

Human Smooth Muscle Cells

The effect of β-particle irradiation from a 32P-impregnated wire source on the growth and migration of human aortic vascular smooth muscle cells in culture was studied using a total of 16 wires with activities of 0.019 µCi/cm (n=4), 0.047 µCi/cm (n=4), and 0.00 µCi/cm (control, n=8). The dose-response curve describing the relation between wire activity at the time of plating and the zone of complete inhibition of smooth muscle cell growth is shown in Fig 3. For comparative purposes, the dose response observed with rat smooth muscle cells is also redrawn. Although fewer experiments were performed with the human vascular smooth muscle cells, there appears to be no significant difference in the sensitivity of human compared with rat vascular smooth muscle cells to the inhibitory effects of β-particle irradiation from a 32P wire source (P=NS at equivalent wire activities for human versus rat smooth muscle cells).

Bovine Endothelial Cells

The effect of β-particle irradiation from a 32P-impregnated wire source on the growth and migration of bovine endothelial cells in culture was studied using a total of 20 wires with activities of 0.006 µCi/cm (n=4), 0.019 µCi/cm (n=4), 0.047 µCi/cm (n=4), and 0.00 µCi/cm (control, n=8). The dose-response curve describing the relation between wire activity at the time of plating and the zone of complete inhibition of endothelial cell growth is illustrated in Fig 1. The activity versus response for rat smooth muscle cells is also shown in this figure for comparative purposes. As has been observed in our prior work using external beam irradiation, there was a significant shift to the right of the dose-response curve for the inhibition of the proliferating endothelial cells in culture compared with the vascular smooth muscle cells (P<.001 for comparison of zone of inhibition with endothelial cells versus smooth muscle cells at wire activities of 0.006 µCi/cm and 0.019 µCi/cm of wire). Fig 2 illustrates this diminished sensitivity of endothelial cells (versus smooth muscle cells) to β-particle irradiation in vitro, with endothelial cells growing up to the radioactive wire at a wire activity of 0.019 µCi/cm (Fig 2D) compared with a distinct zone of inhibition of smooth muscle cells around a wire of the same activity (Fig 2C).

Discussion

The biological response of arterial wall to acute injury has taken on substantial importance with the increasing use of balloon angioplasty and other catheter-based revascularization techniques as palliative therapy in patients with coronary artery disease. Unfortunately, the response evoked by balloon injury frequently promotes severe neointimal hyperplasia, resulting in clinically important restenosis. The mechanism of neointimal hyperplasia following balloon injury has been
extensively studied and appears to be dependent on the rapid proliferation of smooth muscle cells after arterial trauma. In animal models of balloon-induced arterial injury, neointimal hyperplasia is progressive over the first 4 to 6 weeks. In one study using a rat carotid artery–balloon injury model, maximum DNA synthesis, coincident with active intimal smooth muscle cell proliferation, was seen within the first week after balloon angioplasty. This proliferation started to decrease during the second week and decreased to control levels approximately 28 days after balloon injury. These results suggest that any intervention aimed at reducing neointimal hyperplasia is most likely to have a therapeutic effect if delivered early and continuously within the first several weeks after balloon angioplasty. Although there is optimism regarding the potential for local intra-arterial drug delivery or genetic manipulations to inhibit smooth muscle cell proliferation, this approach may be limited by difficulties in the atraumatic delivery of adequate “inhibitor” to the vessel wall, washout of the active agent, and overly specific rather than nonspecific inhibition of a complex and multifactorial proliferative stimulus.

Irradiation and Neointimal Hyperplasia

The use of irradiation to inhibit smooth muscle cell proliferation after arterial injury represents a reasonable and relatively new approach to inhibit restenosis that is based on the enhanced sensitivity of actively dividing cells (eg, proliferating smooth muscle cells) to the lethal effects of ionizing radiation. There is some precedent for this approach to the problem of restenosis, including the well-documented efficacy of low-dose external irradiation in inhibiting keloid formation after surgery. Fibroblast-mediated obliteration of filtering blebs after glaucoma surgery, and heterotopic ossification after total hip arthroplasty. In all of these settings, radiation has been shown to safely and effectively inhibit a “benign” hyperplastic response of mesenchymal cell growth (ie, fibroblasts and chondroblasts, respectively).

The findings of the present study demonstrate that very low doses of β-particle irradiation emitted from a 32P-impregnated stent wire completely inhibit smooth muscle cell growth within a range of 5.5 to 10.6 mm from the stent wire in cell culture. The observation that there was no inhibition of smooth muscle cell growth with the control (32P) wires demonstrates that the inhibitory effect was due to β-particle irradiation and not nonspecific inhibition from the titanium wire or the inorganic phosphorous impregnated onto the surface of the wire. This has implications regarding the potential efficacy of a β-particle–emitting intra coronary stent as a method of inhibiting neointimal hyperplasia after balloon angioplasty.

These findings are consistent with prior studies that have demonstrated that proliferating smooth muscle cells in vitro are sensitive to relatively low doses (200 to 500 cGy) of external beam (x-ray) irradiation and that externally applied x-ray and β-particle irradiation can inhibit neointimal hyperplasia in vivo. We have previously reported that a single dose of x-ray irradiation as small as 400 to 500 cGy completely inhibited the clonal proliferation of smooth muscle cells in vitro. In a series of parallel experiments, we determined that rapidly growing bovine aortic endothelial cells were significantly more radioreistant than smooth muscle cells. These data are further supported by the results of the present study in which proliferating bovine endothelial cells again appear to be much more resistant to the antiproliferative effects of β-particle irradiation than smooth muscle cells. This suggests that if one were to coat an intra-arterial stent with a radioisotope such as 32P (half-life, 14.3 days), endothelial cell regrowth should occur before the antiproliferative effects of the β-particle emission on smooth muscle cells have been lost.

Five experimental studies and one clinical study have been reported investigating the potential of irradiation to inhibit neointimal hyperplasia after balloon angioplasty. In an earlier investigation, we demonstrated that a single dose of external beam irradiation (1000 cGy) delivered 5 days after balloon injury significantly inhibited neointimal hyperplasia in a nondiseased rabbit iliac model. Similarly, Sheffer et al demonstrated that an externally applied single exposure of β-particle irradiation profoundly inhibited neointimal hyperplasia after balloon injury in a rabbit ear artery model. It is of importance that the inhibition of smooth muscle cell proliferation in their model was critically dependent on the timing of the radiation exposure, with minimal inhibition when radiation was delivered at the time of injury, marked inhibition when radiation was applied at 2 days after injury, and no inhibition when the radiation was applied at 7 days after injury. Waksman et al recently reported the ability of locally delivered arterial radiation from a high-energy iridium source to inhibit intimal hyperplasia in a porcine coronary artery balloon injury model. They also noted improved efficacy in reducing neointimal hyperplasia when the radiation was delivered several days after the balloon injury. Based on these observations, it is possible that the continuous, but decaying, early delivery of radiation from an implanted 32P-impregnated radioisotope stent may represent a superior method of achieving the optimal timing of radiation delivery to inhibit neointimal hyperplasia while minimizing radiation exposure to surrounding normal tissue and the interventionist. The potential efficacy of this approach is further supported by a preliminary report from Hehrlein et al in a nonatherosclerotic rabbit iliac model. This study showed essentially complete inhibition of neointimal hyperplasia at 12 weeks after the implantation of a radioactive stainless steel (Palmaz-Schatz) stent containing multiple γ and β-particle–emitting radioisotopes (55,61,74Co, 51Mg, and 55Fe). This particular radioactive stent, however, has the potential drawbacks of having γ irradiation and multiple radioisotopes, including some with half-lives as long as 2.7 years. Finally, a recently reported clinical experience with endovascular irradiation in the peripheral circulation has suggested that this approach may be very effective in preventing human arterial restenosis.

Contrary to the findings from the experimental studies and the clinical study, Schwartz et al found that x-irradiation modestly increased neointimal hyperplasia in an oversized porcine coronary stent model. These investigators used balloons and stents that were 70% to 100% oversized relative to the reference segment, which may have resulted in a more severe stimulus for neointimal hyperplasia than in the other in vivo
Implications for the Design of a Radioactive Stent

The use of a β-particle-emitting intracoronary stent, using 32P as the sole radioisotope, has several potentially desirable features. First, the radiation is derived exclusively from β-particles, thus greatly limiting the range of radiation delivery. In the clinical setting, the very limited effective range of β-particle irradiation from a 32P source in tissue (≈95% of the β-particles are absorbed within 3 to 4 mm), and the extremely low dose of radiation required to inhibit smooth muscle cell growth and/or migration should help to eliminate concerns regarding the risk of radiation to surrounding cardiac or pulmonary tissue. In contrast, such risks could be of significant concern if one were to use external beam irradiation or catheter-based “afterloading” for the same purposes. With the use of a β-particle-emitting stent, essentially all of the radiation field will be limited to the treated arterial segment. In addition, the short half-life of 32P (14.3 days) may be nearly ideal, since the dose of radiation delivered is relatively high during the critical first second to second week after arterial injury and then falls off quickly to undetectable levels within 3 months.

Finally, the total dose of radiation required from a 32P source to completely inhibit local smooth muscle cell growth appears to be extremely low. If one were to fabricate a 2-cm-long×3-mm-diameter intracoronary stent from a 20-cm length of the wire with the greatest specific activity used in the present study (0.06 mCi/cm), this would result in a dose of approximately 310 rem to an estimated 1.4 g of tissue absorbing the β-particles and would yield a calculated total body dose of radiation of only 10 mrem (see “Appendix”). This radiation dose is estimated to be less than 0.1% of the radiation that a patient is exposed to by x-ray imaging during routine percutaneous transluminal coronary angioplasty (see “Appendix”). The radiation exposure to the interventionist implanting such a device would also be very low, if even measurable (estimated at <5 mrem to operators’ hands using 0.06 μCi/cm wire; see “Appendix”), and would be reduced to essentially zero by providing ½-in Lucite sheathing over the stent wire at the time of stent insertion into the guiding catheter.

Study Limitations

Despite the intriguing potential of locally delivered low-dose β-particle irradiation to inhibit restenosis, these in vitro data cannot necessarily be extrapolated to an in vivo or clinical setting. There are a number of important unanswered questions regarding the safe application of this technology in the clinical setting. For example, although the data presented suggest that proliferating bovine endothelial cells are much less sensitive to the effects of β-particles than rat or human smooth muscle cells, it is possible that this decreased radiosensitivity may not be observed with human coronary endothelial cells. Thus, the use of a radioisotope stent could delay the reendothelialization process with possible adverse effects. Preliminary in vivo data using a radioactive stent in a rabbit iliac model of restenosis, however, has demonstrated that such a stent was capable of inhibiting neointimal hyperplasia without detectable adverse (e.g., thrombotic) effects. Despite the extremely low doses of localized radiation that could prove effective in preventing restenosis in the clinical setting using a β-particle emitting stent, there will likely be a certain degree of initial resistance among both patients and physicians regarding the application of “radiation” for the prevention of a “nonmalignant” process. This will require careful and objective assessment of risk versus benefit in randomized clinical studies, education regarding the safety of low-dose β-particle irradiation, and the appropriate application of the technology by thoughtful physicians.

Summary

Our findings demonstrate that very low doses of β-particle irradiation (0.006 to 0.060 μCi/cm of wire) emitted from a 32P-impregnated stent wire results in the complete inhibition of smooth muscle cell proliferation within approximately 6.0 mm of the wire in vitro. This inhibition is dose dependent with maximal effects seen at activities as low as 0.006 μCi/cm of wire and minimal or no inhibition at radiation levels of less than 0.002 μCi/cm of wire. These data suggest that an intra-arterial metal or bioabsorbable stent impregnated with a very low concentration of 32P may have a salutary effect on the restenosis process. Whether this approach can be used to successfully and safely inhibit restenosis in vivo and in the clinical setting will require further investigation.

Appendix

Dose in rem to Tissues Directly Adjacent to a 32P Intracoronary Stent

Assumptions

Arterial lumen radius=1.5 mm
Intracoronary stent radius=1.5 mm
Intracoronary stent length=20 mm
Inner radius of tissue cylinder (corresponds to arterial wall)=1.5 mm
Outer radius of tissue cylinder inside of which 90% of the emitted energy is absorbed=5.0 mm
Volume of tissue cylinder (ID=3.0 mm, OD=10 mm, length=20 mm)=1.4 cm³
One half of total energy dissipated by the 32P stent is absorbed by the blood pol
Total activity of 32P in the intracoronary stent=1.2 μCi evenly distributed, using 20 cm of 0.06-μC/cm wire to fabricate the 20-mm-long stent.

Radiation Dose Calculations

According to the Medical Internal Radiation Dose (MIRD) schema, the dose rate (D) to an organ from a beta source of activity, A, inside the organ is:

\[
D = \frac{A}{M} \langle \Delta \rangle \langle \phi \rangle
\]

where M = mass of the organ,
$\Delta = 2.13 \left( \frac{\text{rad/h} \cdot \text{g}}{\mu\text{Ci} \cdot \text{MeV}} \right) \hat{E}_p$

$\hat{E}_p = \text{mean energy of the beta particle} = 0.695 \text{ MeV for } ^{32}\text{P}$

and $\phi = \text{absorbed fraction within the organ} \leq 1.0$.

Substituting $A = 1.2 \text{ } \mu\text{Ci}$,

$\text{mass} = \text{volume of tissue cylinder} \cdot \text{density} = \frac{1.0 \text{ g}}{\text{cm}^3} = 1.4 \text{ g}$

$\phi = 0.50$ in this example, there is normal blood flow through the lumen, and thus the blood pool may absorb up to one half of the total dissipated energy. Then,

$D = \frac{0.63 \text{ rad}}{\text{h}} \cdot \frac{0.01 \text{ rad}}{\text{min}} = \frac{10 \text{ mrad}}{\text{min}}$

The dose equivalent rate (H) is numerically equal to the dose rate, since the quality factor for beta rays is 1.0, so

$\frac{10 \text{ mrem}}{\text{min}} = \text{initial dose rate to surrounding tissue from the stent.}$

Integrating this dose equivalent rate over the lifetime of the $^{32}\text{P}$ activated stent:

$(2) \quad \text{Total dose equivalent} = H = H_0 \int e^{-\lambda t} \text{dt} = H/\lambda$

where $\lambda = \frac{1}{1.44(\text{half-life})}$

which, for a 14.3-day half-life, results in an absorbed dose equivalent of $H = 310 \text{ rem}$.

**Dose in mrem to a Cardiologist’s Hands From a $^{32}\text{P}$ Intracoronary Stent**

**Assumptions**

- Intracoronary stent radius = 1.5 mm
- Intracoronary stent length = 20 mm
- Total energy absorbed by the hands is confined to a depth of 3.5 mm from the skin surface
- The stent is positioned in air, 10 cm from the hand
- Beta ray dose rate in air can be approximated by the inverse square law
- $^{32}\text{P}$ activity is considered as a point source

Using equation 1, and substituting $\phi = 1.00$,

$D = \frac{1.3 \text{ rad}}{\text{h}} \cdot \frac{0.02 \text{ rad}}{\text{min}} = \frac{20 \text{ mrem}}{\text{min}}$

$H = \frac{20 \text{ mrem}}{\text{min}}$

However, $\phi < 1$, because the beta rays are emitted isotropically and when the stent is held in air 10 cm from the hands, most of the beta rays emitted do not intersect the hands. A conservative estimate of $\phi$ then is the ratio of the surface area subtended by the hand to the total surface area of a 10-cm-radius sphere,

- total surface area of a 10-cm-radius sphere = $4\pi r^2 = 4\pi(10 \text{ cm})^2$
- cross-sectional area of hand = 100 cm$^2$

Therefore, $\phi = \frac{100 \text{ cm}^2}{4\pi(10 \text{ cm})^2} = 0.08$

Hence,

$D @ 10 \text{ cm air} = H @ 10 \text{ cm air} \cdot \phi$

therefore

$H @ 10 \text{ cm air} = \frac{1.6 \text{ mrem}}{\text{min}}$---

**Risk Estimates**

**Patient Total Body Dose From the $^{32}\text{P}$ Stent**

Assuming that the total dissipated energy of the $^{32}\text{P}$ stent (absorbed dose in the tissue cylinder and in the blood pool) could be evenly distributed throughout the total body, the absorbed dose would be

$\frac{620 \text{ rem}}{\text{body mass in grams}}$

Given that the average man is 70 kg, the total absorbed dose and thus the total body dose equivalent is equal to approximately 10 mrem.

**Patient’s Total Body Dose From a PTCA Procedure**

Two recent reports have presented data regarding the average skin entrance exposures, for patients who undergo typical PTCA procedures (69=61R44 and 124 R45). As the data indicate, the entrance exposures may vary widely from patient to patient and institution to institution. Past research efforts have related these skin entrance exposures from standard diagnostic x-ray procedures to the absorbed total body dose equivalents. Gibbs46 has shown using Monte Carlo calculations that the conversion factor to total body dose equivalents for a PA chest x-ray procedure of 16 mR patient skin exposure is 3 mrem. Using this conversion factor, the skin entrance exposure reported for the above PTCA procedure results in total body dose equivalents of 13 to 24 rem.

Relative additional risk. Using the above calculations, the implantation of a 1.2 $\mu\text{Ci}$ $^{32}\text{P}$ stent would increase the total body dose equivalents by $<0.1\%$ as compared to the total dose from a PTCA procedure alone.

**Exposure of the Cardiologist**

$^{32}\text{P}$ stent. Assuming that the dose rate in air at 10 cm distance is 1.6 mrem/min and the cardiologist “inspects” the stent for a total of 2 minutes, the total dose equivalent to the hands would be 3.2 mrem.

PTCA procedure. Jeans et al49 have estimated the dose to a cardiologist’s hands during a PTCA procedure (standing 60 cm from the x-ray table) to be 200 mrem.

Relative additional risk. The additional risk of holding a $^{32}\text{P}$ stent at a distance of 10 cm for 2 minutes adds less than 2% to the dose to the hands of the interventionist during a PTCA procedure.

Actual expected risk. With a transparent Lucite sheathing of at least 3/8-in thickness, there is essentially no detectable radiation emanating from a 1.2-$\mu\text{C}$ $^{32}\text{P}$ stent.

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**References**


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