

Pd-103 Radioactive Stent Dosimetry

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Abstract

“Coronary artery disease is the leading cause of morbidity and mortality in the western world. Approximately 450,000 angioplasties are performed annually in the United States” (5). Angioplasty solves the immediate problem of arterial blockage, but thirty-five to forty percent of those that undergo angioplasty are diagnosed with restenosis, which is the reblocking of the artery. Restenosis results in a societal cost of 800 – 2,000 million dollars per year. Stents have become commonplace in angioplasty procedures. They prevent elastic recoil and can decrease restenosis by twenty-two to thirty-two percent. The main problem is that stents do not prevent neointimal hyperplasia. For this reason, radiation has been researched as a form of treatment. Preclinical trials have shown that using radiation in the dose range of 15-30 Gy can substantially reduce restenosis (5).

Currently only Phosphorus-32 has been used on a stent in clinical trials. These trials concluded that a stent coated with radioactive phosphorus decreased the amount of neointimal hyperplasia along the stent's length but not beyond the stent's ends where the radiation does not reach insignificant enough amounts. The research done for this project proposed using Palladium-103 on the stent instead of P-32. After various computer simulations using the Monte Carlo program MCNP, the results show that a Pd-103 stent's dose is sufficient along the stent in comparison to the P-32 dose and does not decrease as rapidly beyond the end of the stent as the dose from P-32 stent. After several varying trials of point source placements using MCNP, it was shown that palladium should provide a significant improvement over phosphorus.

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Introduction

“Coronary artery disease is the leading cause of morbidity and mortality in the western world” (5). Approximately 450,000 angioplasties are performed each year in the United States alone. About 30%-40% of the patients that undergo angioplasty are diagnosed with restenosis, which is the reblocking of the artery. The use of coronary stents can reduce the rate of restenosis to 22%-32%. The cost to society of this restenosis is estimated to be 0.8 to 2 billion dollars per year. Some preclinical studies have shown that using ionizing radiation in the dose range of 15-30 Gy during or following angioplasty procedures could reduce restenosis to below 10%. (5)

Background

Arteries can be summarized as tubelike structures with several layers. Beginning with the inside most layer, the layers are the endothelium, intima, internal elastic membrane, media, external elastic membrane, and the adventitia. Proximal arteries usually have a diameter in the range of 3–5 mm. (5) Angioplasty is rarely performed in arteries with a normal diameter less than about 1.5 mm, and . . . stents are rarely placed in arteries whose normal diameter is smaller than about 3.0 mm” (5). The lumen of the artery is the area within the tube through which the blood flows.

At times the lumen becomes partially or totally blocked by the formation of plaques called atherosclerosis. The blocking of the lumen compromises blood flow and oxygen delivery. “The plaque begins in the intima by deposits of fatty debris from blood” (5). The build-up of plaque begins a process that eventually causes a complex lesion to develop “as the core of the fibrous atherosclerotic plaque necroses, calcifies, and hemorrhages. This causes reduction in

blood flow, platelet aggregation, and ultimately formation of a thrombosis (blood clot) with consequent myocardial ischemia and/or infarction” (5).

Angioplasty is used to increase the lumen diameter. A catheter is inserted in a distal artery or vein and threaded into the blocked blood vessel. Then either the plaque is cut or ablated away or a balloon is inflated to push the plaque out of the way. The cutting and ablating devices are usually only used when the artery is too blocked for the uninflated balloon to enter or when there is heavy calcification. “In these cases it may be necessary to remove tissue by cutting (atherectomy device), ablating (rotoblator), or vaporizing (laser)” (5). Since these methods can cause damage to the arterial wall, they are not usually used to obtain the final desired lumen diameter. (5) It has become fairly commonplace for an unexpanded stent to also be inserted into the artery with the balloon. The stent is expanded when the balloon is inflated as can be seen in figure 1. The stent remains in the blood vessel. The stent prevents elastic recoil that can be a problem when balloon angioplasty is performed alone without stent implantation since the blood vessels are elastic and tend to return to their original shape after the angioplasty stretches them.

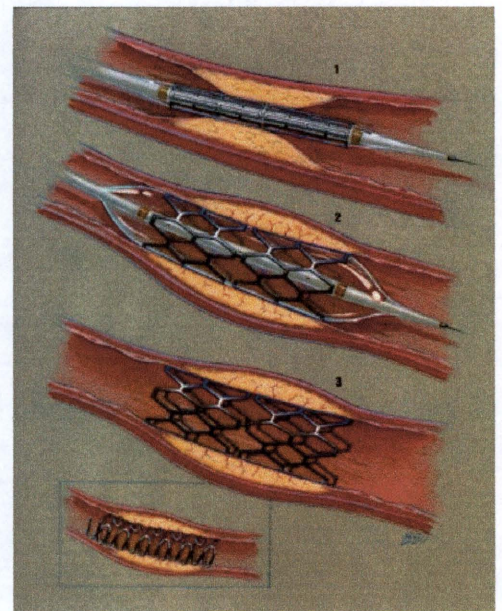


Figure 1: Stent Implantation (6)

Restenosis can also be caused by other means than elastic recoil. One major problem is neointimal hyperplasia. When the balloon is inflated, it stretches the arterial wall and causes lesions of the atherosclerotic plaque, the intima, and sometimes the media. As the body heals the blood vessel, “over weeks the neointima becomes less cellular and the healing site begins to

resemble a fibrous plaque”(5). In most patients the increase in the lumen diameter as a result of the angioplasty outweighs the lumen narrowing caused by the neointimal hyperplasia, but in about 40% of the patients, the neointimal hyperplasia is excessive and causes restenosis within three to six months. (5)

The use of radiation within the blood vessel after balloon angioplasty has been suggested “to inactivate (prevent from dividing) most cells that otherwise could proliferate to produce neointimal formation” (2). It has been reported that approximately a 75% reduction in restenosis can be achieved when stenting is combined with a delivery of 8 to 30 Gy irradiation via an endovascular Iridium-192 sources. (3) These sources were located within a catheter that was inserted after the balloon angioplasty. The catheter based radiation causes some difficulties, including reduced arterial blood flow during the irradiation, and longer treatment times, which increase the risk of complication. Also, the catheter has to be aligned in the center of the blood vessel to provide uniform radiation to the entire vessel wall. Since stents are commonly implanted within the vessel and do not obstruct blood flow, research has been done of the efficacy of inserting a radioactive stent to provide the radiation dose needed. This paper will focus on the use of radioactive stents.

Currently Phosphorus-32 is the only radioactive material that has been used on implanted stents. Albiero *et al.* reported that patients treated with radioactive β -emitting P-32 stents with an initial activity of 0.75 to 12 μCi had no restenosis within the stent. However, more than 40% had restenosis at the edges of the stent. This is most likely a result of the drastic decrease in radioactive activity beyond the end of the stent. (1) “The short range of the beta particles results in a more rapid dose falloff versus . . . gamma sources” (5). Gamma emitters penetrate too far though and would deliver larger doses to normal tissue and staff. (5) “Low-energy x-ray emitters

... reduce these risks” (5). For this reason, the research of this project focused on the radiation dosimetry of a stent irradiated with Palladium-103, an x-ray emitter.

Methods

The goal of this project was to determine the radiation dosimetry of Pd-103. This was done using MCNP4b Monte Carlo simulation code with both electron and photon tallies. Enough histories were performed “to reduce the estimated standard deviation to less than 4% of the mean, except in the bins that were far from the stent” (4). Figure 2 shows the wire frame stent that was used. The stent is composed of 100 micron thick stainless steel with an outer diameter of 3.5 mm and length of 15 mm. There

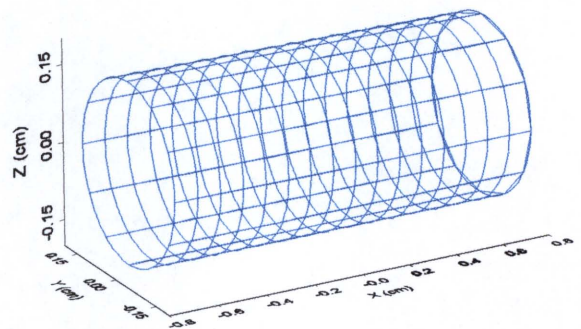
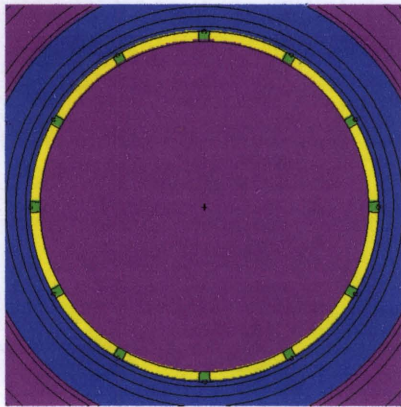


Figure 2: Wire Frame Stent with 192 holes.

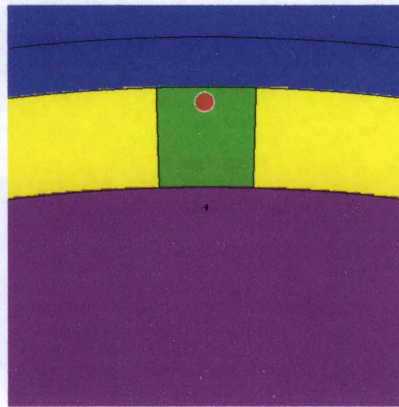
were 192 holes: 12 around and 16 in the axial direction. Point sources were placed at a depth of 0.5 microns into steel (Figure 3b). The point sources were either placed on the inside surface or outside surface of the stent. There were a total of 600-point sources: one at each corner and midway between struts. The stent was then surrounded completely by water. Cylindrical tally cells were then established to determine the dosimetry at various distances from the outer stent surface (Figure 3a). These distances were 0.1, 0.2, 0.5, 1.0, 2.0, 3.0, 4.0, and 5.0 mm from the stent surface.

A program was also designed to determine the dosimetry's angular dependence. The area between struts was divided into tally cells with a middle at the angles of 7.5, 15, 22.5, and 30

degrees as seen in Figure 4. This was only done for the distances from the stent of 0.1 and 0.2 mm since the results from the previous trials showed a uniform dosimetry at 0.5 mm and beyond.



(a)



(b)

Figure 3: Cross-section parallel to the x and z-axes in Figure 2. (a) is the whole stent. (b) is one strut which is nearly a square.

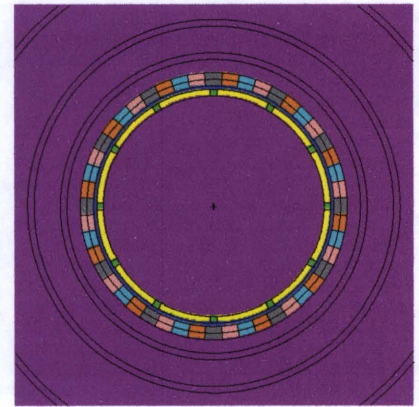


Figure 4: Tally cells for angular dependence.

Results

Figures 5, 6, and 7 show the graphical representation of the dosimetry obtained from MCNP4b. The stent whose dosimetry is shown in figure 5 had point sources located on the outer edge of the stent. The peaks on the graph represent areas directly over a strut containing a point source. The valleys are the holes between the struts. This has an affect until about 0.5 mm when the dosimetry line becomes fairly uniform over the length of the stent. Figure 6 illustrates the affect the stainless steel has on the radiation penetration. Instead of having peaks where the point sources are located, the peaks are flattened the width of each strut. The area between the struts still has a lower radiation dosage than the areas above the point sources. Figure 7 combines the results in figures 5 and 6. There is not as wide a variation in the dose between the

peaks and valleys, but the peak effects from the sources on the outside of the stent are also evident.

Figure 8 illustrates even better the affect the location of the tally cells with respect to the struts has on the magnitude of the dose. The tally cell directly above the strut at 30 degrees has the highest dose. The 15 degree tally cell receives radiation activity from the struts on either side so is higher than that of the 7.5 and 22.5 degree tally cells.

The four graphs also illustrate the rapid dose decay beyond the ends of the stent. The dose decreases by a factor of 100 within 0.5 mm. Figure 9 sums them all up though in comparing stents coated with different radioactive materials. By showing the rate of radioactive activity decrease, the efficacy of the radioactive material in preventing neointimal hyperplasia beyond the end of the stents can more easily be compared. As the graph shows, Pd-103 decreases at a slower rate and can be assumed to prevent the edge restenosis better than P-32 and Cs-131.

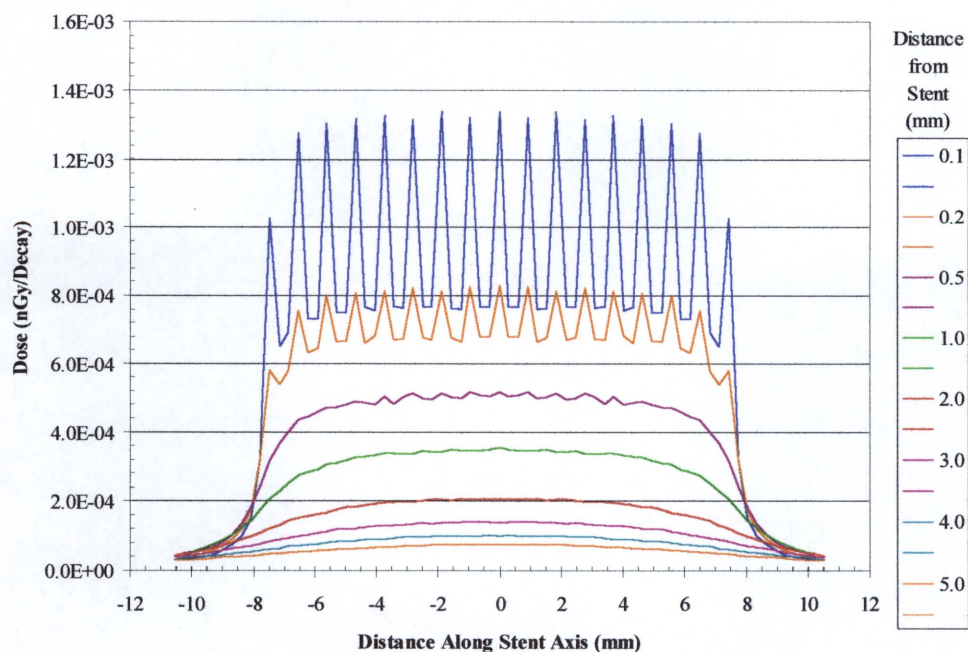


Figure 5: Pd-103 point sources on the outside surface of the stent.

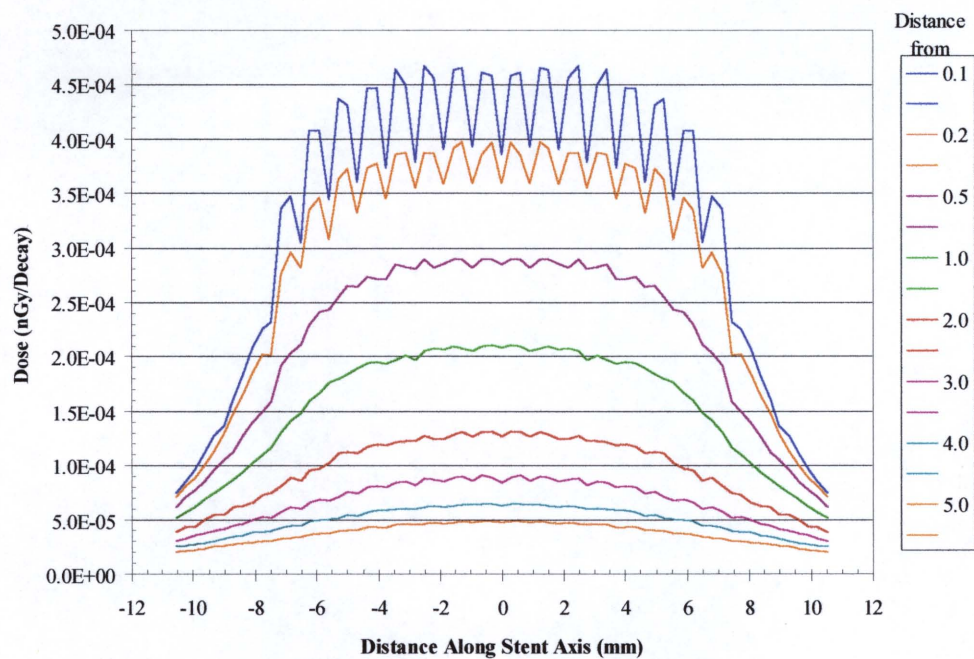


Figure 6: Pd-103 point sources on the inside surface of the stent.

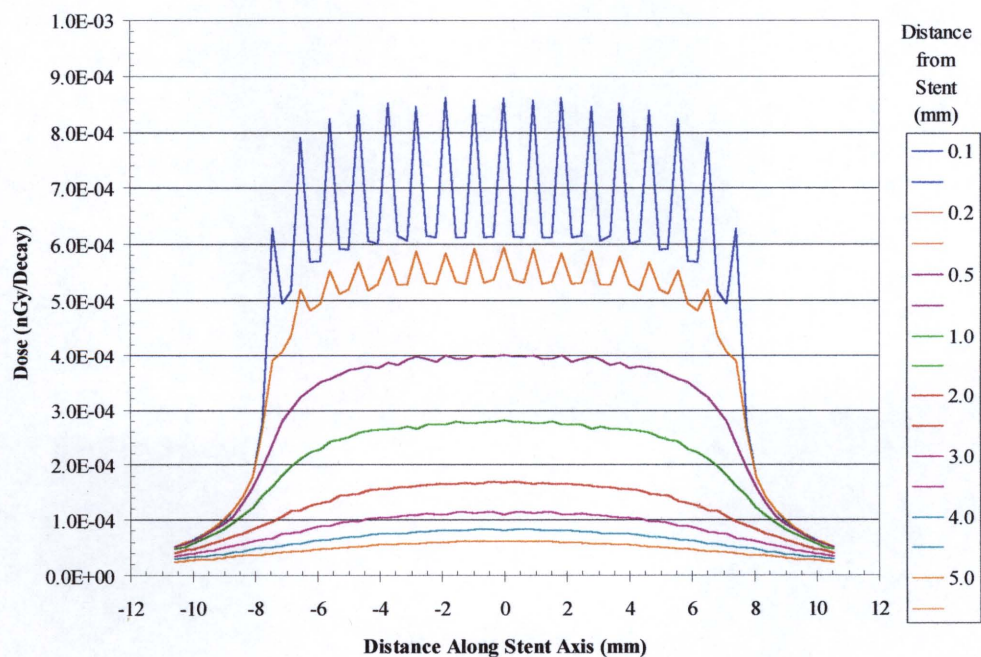


Figure 7: Pd-103 point sources on both surfaces of the stent.

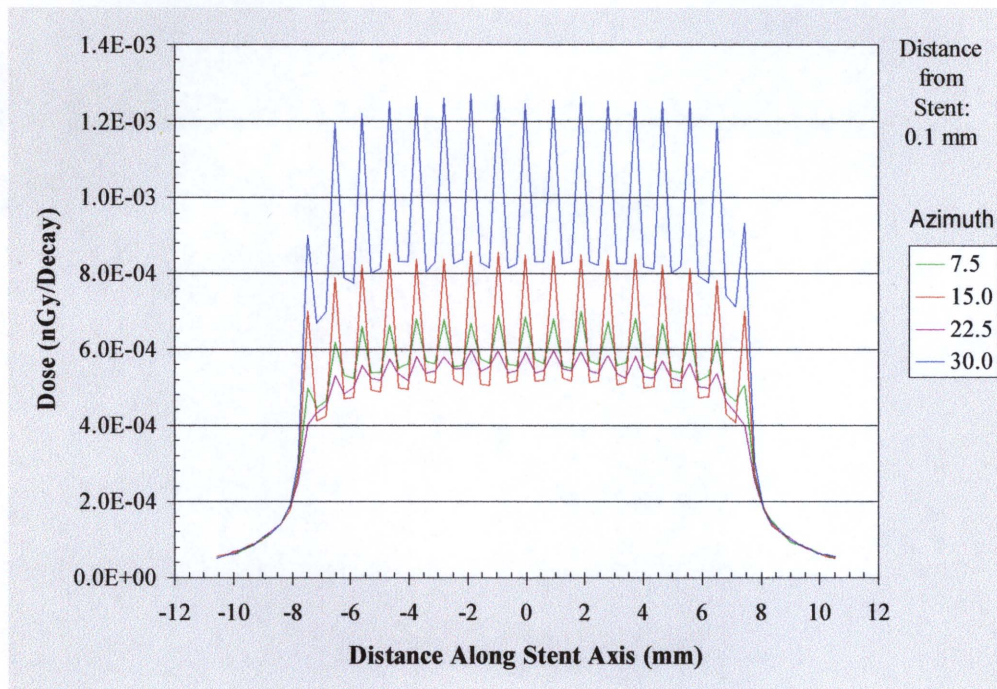


Figure 8: Pd-103 point sources with angular dependence on both surfaces of the stent.

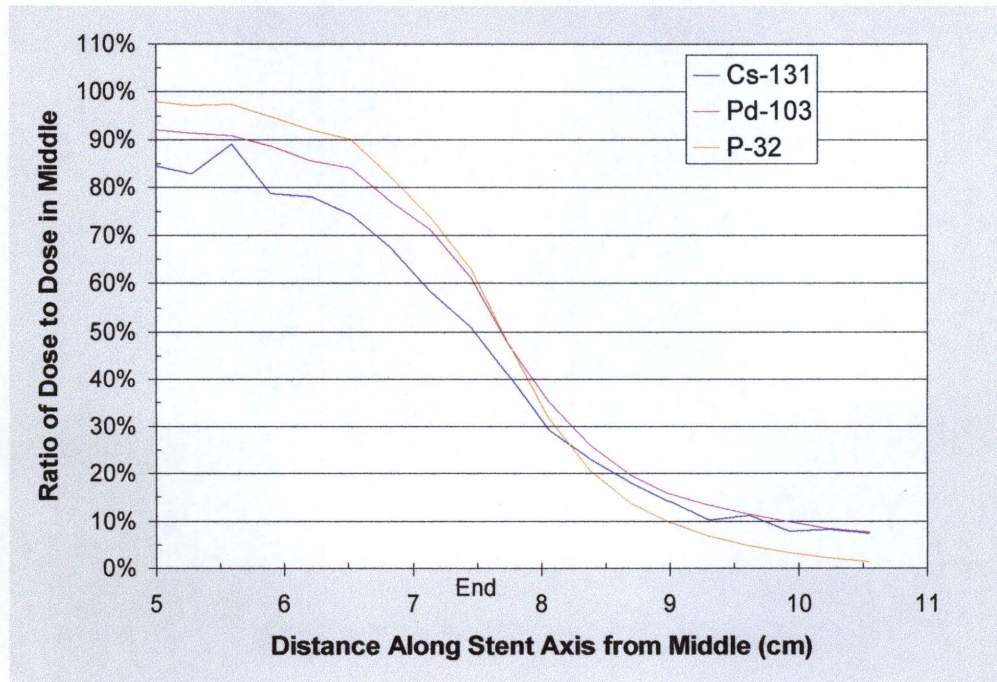


Figure 9: The relative dose at 0.5 mm from the stent surface when the stent is coated on the outside.

The final figure (figure 10) shows another approach to preventing edge restenosis. By increasing the activity of the radioactive material at the edge of the stent, the radioactive activity magnitude will increase beyond the ends of the stent. Figure 10 illustrates the dosimetry of a P-32 stent with 3 times the activity on the ends than in the middle. One difficulty that may result from this is the increased radiation to which the tissue at the ends of the stent will be exposed.

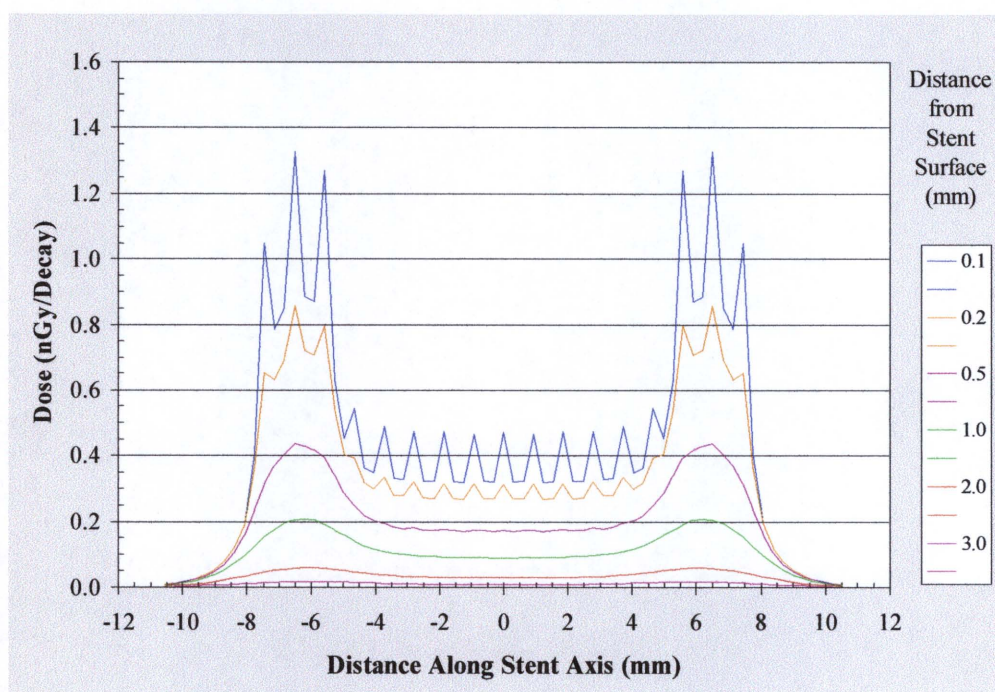


Figure 10: P-32 point sources on the outside surface of the stent with dumbbell loading (3x on ends).

Conclusions

The results of this research show that Pd-103 may prove to be more efficient than P-32 at preventing restenosis beyond the ends of an irradiated stent. More research must be done before this can be concluded with more certainty. Currently, a study with a Pd-103 irradiated stent is being done at Vanderbilt University to verify the above stated dosimetry. Once this is completed, the findings of that study along with the results from this study will be forwarded to a research group in Europe. This group has performed an intravenous ultrasound to determine the thicknesses of the various layers of the vessel walls. With the dosimetries they will be given and the ultrasound, they can determine the dose volume histogram for the real artery and hopefully, obtain results that will support the use of Pd-103 and lead to clinical trials.

Works Cited

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UNIVERSITY HONORS PROGRAM

SENIOR PROJECT - APPROVAL

Name: Dana M. Overman

College: Engineering Department: MAES

Faculty Mentor: Dr. Larry Miller

PROJECT TITLE: Pd-103 Radioactive Stent Dosimetry

I have reviewed this completed senior honors thesis with this student and certify that it is a project commensurate with honors level undergraduate research in this field.

Signed: Lawrence Z Miller, Faculty Mentor

Date: May 3, 2001

Comments (Optional):