A DOSIMETRY EVALUATION OF ^{90}Y-STENT IMPLANTATION IN INTRACORONARY RADIATION TREATMENT

by

Alireza KARIMIAN[1*] ***and Somayeh SAGHAMANESH*** [2]

[1]Department of Biomedical Engineering, Faculty of Engineering, University of Isfahan, Isfahan, Iran
[2]Department of Physics, Faculty of Science, University of Isfahan, Isfahan, Iran

Scientific paper
DOI: 10.2298/NTRP1303278K

Ionizing particles have been used for the treatment of atherosclerosis. Internal irradiation is commonly carried out by means of several methods (catheter-based systems, radioactive stents or balloons) to reduce the probability of restenosis. ^{90}Y, due to some of its characteristics, is an appropriate radioisotope for intravascular brachytherapy. However, since there are some critical tissues in the vicinity of the heart like the breast and lymph nodes, it is necessary to perform a dosimetry calculation around the artery under radiotherapy to justify the treatment method. In this study, a 3-D dose distribution was obtained for the coronary vessel and its surrounding tissues for a standard ^{90}Y stent in a MCNPX program. The results were compared with other investigations on restenosis prevention using ^{90}Y-coated stents. The calculations represented a 28-day cumulative dose between 1230 cGy and 2400 cGy at 0.1 mm from the stent surface, while this quantity was about 23.8 cGy at 8.5 mm from the stent surface. An assessment of the dose equivalent and effective dose was also performed at r = 8.5 mm for the mentioned surrounding tissues which may be located in the area, based on the latest changes in ICRP recommendations. Additionally, the dose equivalent calculated within the treatment period for these organs was compared with published dosimetry data for ^{90}Sr/^{90}Y seed sources in order to evaluate radiation protection concerns about these two radiotherapy methods. It has been found that, depending on stent parameters, ^{90}Y stent implantation might increase the unfavorable side effects for the patient, but to a much lesser degree than the other methods.

Key words: intravascular brachytherapy, restenosis, stent, Monte Carlo simulation, ^{90}*Y*

INTRODUCTION

Every year hundreds of people die from atherosclerosis. The disease involves a narrowing of the arteries due to the accumulation of fats and plaques within the artery walls, eventually leading to a full blockage of the vessel and a heart arrest. This occurs particularly in small and narrow vessels. The reoccurrence of the stenosis after an angioplasty procedure is a common event effecting an average of 30%-50% of the patients [1].

Ionizing radiation has been widely used for the control of proliferative tissues in tumors and has proven to be successful [2]. Therefore, the use of radioactive sources to prevent or reduce restenosis seems a rational approach, as it has been examined over two decades. Several methods have been tried, including intravascular brachytherapy (IVBT) and inserting radioactive stents.

IVBT includes catheter-based systems, usually during or after an angioplasty, to send a gamma or beta- emitting source such as a wire, a train of seeds, or liquid- or gas-filled balloons into the vessel in order to irradiate the injury area. On the other hand, radioactive stents are also used during the angioplasty procedure to reduce restenosis. The two methods differ in some aspects, such as the dose rate, treatment period and uniformity of the dose around the device and onto the neointima.

Radioactive stents have certain advantages over catheter-based systems. Stent implantation is performed by means of a well-known procedure of angioplasty and is familiar to cardiologists and easy to apply. The activity of the stent can be as low as possible because the stent is very close to the neointima. Also, stents are permanent implants, not subject to a need for routine procedures such as concerns about the removal and storage of the source and safety matters [3]. However, the procedure has some limitations, including the loss of the adequate dose to the tissues near the stent margins after they have been injured by angioplasty. The result of this is the so-called "candy-wrapper" effect which causes restenosis in the

---

* Corresponding author; e-mail: karimian@eng.ui.ac.ir

artery around 2-3 mm distal and proximal to the stent [4]. Another problem is that due to a high dose delivered near the surface of the stent, we'll have a delayed recovery in that area.

^{90}Sr/^{90}Y has some interesting specifications that motivate its application in radiotherapy. It has a much shorter half-life than a common radiotherapy radionuclide such as ^{192}Ir. Also, high-energy negative beta particles of ^{90}Y are more penetrating while having a sharper slope of the depth dose. Because of these features and, due to the high-purity decay of betas, ^{90}Y seems a more suitable radionuclide for an effective treatment. Furthermore, when using radioactive sources, one of the most important concerns in treatment planning is safety. Although there is no dose limit for patients undergoing radiotherapy practices, it is the physician's and physicist's responsibility to deliver an adequate dose to the target while avoiding the normal tissues. Regarding the position of the heart in the vicinity of some critical tissues like the breast or lymph nodes, it seems so important to determine an accurately prescribed dose around the cardiac tissues before making a decision about the treatment procedure.

Dosimetry calculations for intravascular brachytherapy with ^{90}Sr/^{90}Y seed sources have been performed through some experimental works and various simulation programs [1, 2, 5-8].

Arabi *et al.* conducted a dosimetry of renal arteries with a ^{48}V stent [9]. Fischell *et al.* made a review of different methods and sources for application in radiotherapy of coronary arteries [10]. Prestwich *et al.* obtained a dose distribution produced by a ^{32}P-coated stent [11]. McLemore *et al.* calculated the dose distribution around ^{103}Pd stents for IVBT [12].

A limited number of studies have been related to the dosimetry of ^{90}Y-implanted stents. Patel *et al.* calculated dosimetric parameters for a ^{90}Y-coil source by a Monte Carlo method [13]. Carter *et al.* investigated the effects of cumulative dose and dose rate delivery on neointimal formation using ^{32}P and ^{90}Y stents in a porcine model of restenosis, both in an experiment and in a computer-based modeling program [14]. They focused on the morphometry of the vessel after the placement of the radioactive stent. Taylor *et al.* worked on dose response characteristics of a ^{90}Y stent in a canine coronary model [15]. As mentioned, there has been no implicit and precise dosimetry calculation of a cardiovascular system for ^{90}Y stents, while considering the probability of risks involed for surrounding organs.

In this research, dose rates and cumulative doses were calculated using a Monte Carlo method for a ^{90}Y stent implanted into an artery for 28 days. This period was chosen due to the half-life of ^{90}Y after which we will have a relatively full decay of the radioisotope. To validate our calculations, the resulting simulation was compared with other researches. Upon this, calculations were done for the dose equivalent within this period, so as to provide an evaluation of the level of the effective dose for normal tissues which may be situated nearby. The results of these calculations were assessed in comparison to the dosimetry of a train of ^{90}Sr/^{90}Y seed sources in cardiovacular brachytherapy in order to clear some aspects of the radiation safety of the procedures, based on the ICRP103 report [16].

MATERIALS AND METHODS

^{90}Y is a pure negative beta-emitting source. Its half-life is about 64 hours. ^{90}Y has an average and maximum energy of 935 keV and 2.28 MeV, respectively. Its parent, ^{90}Sr, has a maximum energy of 546 keV and a long half-life of 28.8 years. Since ^{90}Y has a short half-life and high energy, it delivers a high initial dose to the tissue and this makes it an appropriate candidate for treatment purposes.

^{90}Y energy spectrum is a complicated one and has been obtained through calculations presented in [17]. Figure 1 shows the calculated energy spectrum for ^{90}Y.

The stent had a meshed cylindrical shape with a length of 15 mm and a diameter of 3 mm. The strut was 0.075 mm thick. The stent was composed of a stainless steel SS316L which consisted of Fe, Cr, Ni, Mn, Si, Mo, P, S, and C, with a density of 8 g/cm^3. The activity of the stent was considered as 1.48 10^5 Bq.

The cardiovascular phantom and surrounding tissues were assumed as a simple cylinder of water with a density of 1 g/cm^3. A cylindrical co-ordinate system was used to mesh the coronary vessel and cardiac phantom and calculate the dose rate at each voxel. The origin of the co-ordinate system was matched to the center of the stent. With an azimuthal symmetry, circular voxels were made as 0.1 mm in the radial direction, up to 10 mm away from the surface, and as 0.2 mm along the cylindrical axis, up to 10 mm from the center (see fig. 2).

In this simulation by MCNPX codes, all possible interactions of electrons with matter were included and the doses calculated for both electrons and photons.

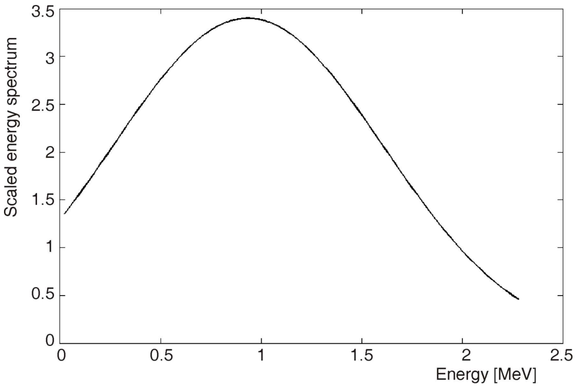

Figure 1. The ^{90}Y energy spectrum according to [17]

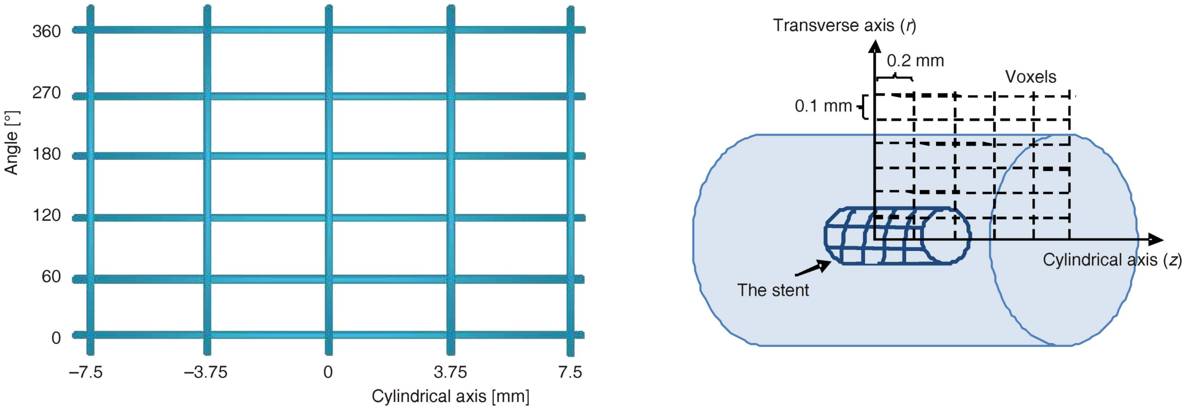

Figure 2. (a) A simple scheme of the extended cylindrical (grid) geometry of the stent and (b) the stent inside the cardiovascular system and surrounding tissues (water) with voxels in a cylindrical co-ordinate system for dose calculations

For scoring the doses and dose rates, a mesh tally (type 3) in MCNPX was used to track the electrons and photons and calculate their energy deposition (and the absorbed dose, upon this) for each voxel in the water.

RESULTS AND DISCUSSION

Depth doses were calculated for all voxels over 28 days in order to ensure a full decay of the radioisotope. These cumulative doses were calculated along the cylindrical axis for various radial distances from the stent surface, as shown in fig. 3. The absorbed dose at 0.1 mm from the surface varies from 2400 cGy over the strut wires to 1230 cGy at the interstices. The values for $r = 0.5$ mm were between 1250 cGy and 650 cGy.

Figure 4 shows the cumulative dose over strut wires at $r = 0.1$ mm throughout 28 days. The ^{90}Y stent delivers 84% of the whole absorbed dose for 28 days in the first 7 days that it shows a high dose percentage. All statistical variances for $r = 0.1$ mm out from the surface were less than 2% and for radial distances up to 10 mm from the surface they were less than 7%.

These dose calculations show good agreement with the results of [14] at all of the various distances except for the maximum dose over struts at 0.1 mm that Carter *et al.* reported as 3500 cGy for 28 days. This relatively large difference between the values may be due to the setting of the energy spectrum for ^{90}Y. We carefully used a continuous energy spectrum of ^{90}Y ranged from zero to 2.28 MeV, based on [17].

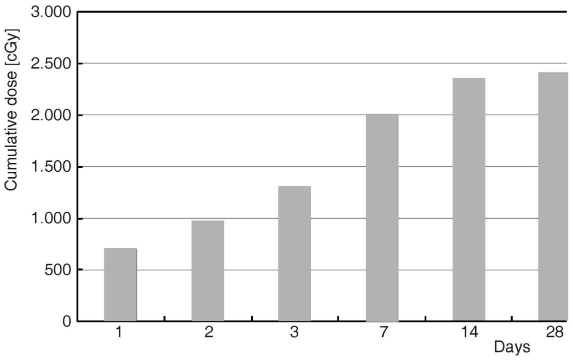

Figure 4. A plot of the maximum cumulative dose over 28 days of radiation treatment for a standard ^{90}Y stent with an activity of 1.48 10^5 Bq

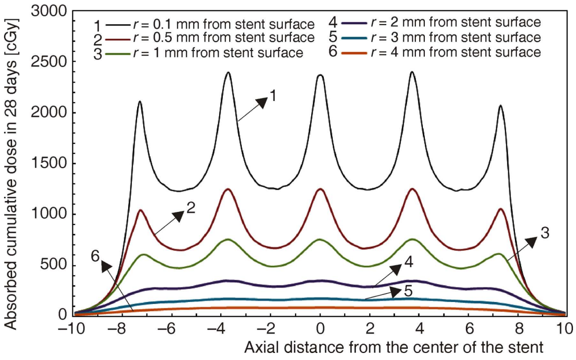

Figure 3. A 2-D cumulative dose distribution around a 4 μCi standard ^{90}Y stent *vs.* the distance from the cylindrical axis of the stent for various radial distances from the stent surface (1 Ci = 3.7 10^{10} Bq)

Furthermore, a Monte Carlo analysis is used in this work, whereas the mentioned authors used a different, numerical approach [18] to simulate and perform the dosimetry procedure which would certainly affect the particle transport method and ,thus, the resulting dose distribution.

Figure 5 represents the dose rates over 28 days at $r = 0.1$ mm and $r = 8.5$ mm out of the surface. This plot indicates that the ^{90}Y stent has a sharp dose gradient and, due to high dose rate decays, faster than other common radioisotopes such as ^{32}P. As shown in fig. 5, the dose rate value is insignificant at the end of 28 days.

In the next step, the focus is on radiation safety of the radioactive stent implantation corresponding to the ICRP103 report.

Considering the increase of the weighting tissue factors for some tissues like the breasts in ICRP103 [16], there seems to be a need for more precise dosime-

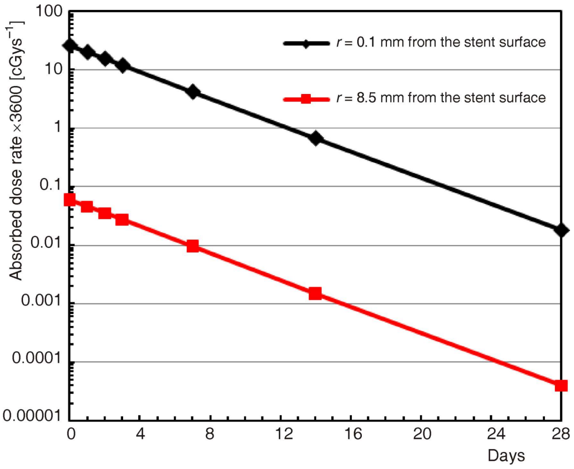

Figure 5. The 28-day dose rate for a 1.48 10^5 Bq standard ^{90}Y stent for two near and far distances out from the stent surface. The absorbed dose rates show a sharp decrease during 28 days after the implant

try calculations before clinical procedures of cardiovascular restenosis using radioactive sources are applied.

From the above results, as shown in fig. 5, for the ^{90}Y stent at $r = 8.5$ mm out from the stent surface, an initial dose rate of 1.7 10^{-5} cGy/s is obtained, reaching 1.28 10^{-5} cGy/s, 9.72 10^{-6} cGy/s, 7.5 10^{-6} cGy/s, 2.5 10^{-6} cGy/s, 2.8 10^{-7} cGy/s, and 1.1 10^{-8} cGy/s after 1, 2, 3, 7, 14, and 28 days, respectively. Consequently, a cumulative dose and a total dose equivalent of 23.8 cGy and 238 mSv, respectively, may be delivered to such tissues after 28 days (indeed, if those organs just contribute in one voxel row at $r = 8.5$ mm along the z-axis, they may likely overlap for more than one voxel row!). In other words, regarding the weighting factor of 0.12 for breasts [16], the contribution of the breast tissue dose alone in the effective dose will be about 28.56 mSv. This value is relatively high and unfavorable. The weighting factor for lymph nodes and cardiac tissue is about 0.01, so their contribution in the effective dose will be equal to 2.38 mSv. However, these side effects are associated with the activity and design of the stent and the position of the artery. The greater activity, results the higher absorbed dose. The proximity of the treated artery to mentioned organs also increases the risk of undesirable absorbed doses.

Saghamanesh *et al.* worked on safety concerns about cardiovascular brachytherapy with ^{90}Sr/^{90}Y seed sources in [8].

In that research, they calculated the dose rates for the maximum distances of seeds. For a single seed, they obtained an average dose rate of about 9.683 10^{-4} cGy/s (or a dose equivalent of 9.683 10^{-3} mSv/s) for a voxel at $r =$ = 10 mm (that is equivalent to $r = 8.5$ mm from the ^{90}Y-stent surface) [8]. Considering all voxels for a train of 8 seeds and an average time of 5-15 minutes to be taken for the treatment, a cumulative (total) dose of about 56-167 cGy (or a total dose equivalent to 560-1670 mSv) will be calculated. It means that in such a catheter-based system, the contribution of the breast dose in the effective dose (if they overlap in that area) will be about 60-181 mSv. Also, in this method, the contribution of the cardiac tissue and lymph nodes in the effective dose will be 5.6-16.7 mSv.

It is evident that the use of ^{90}Sr/^{90}Y seeds, although taking less time, may deliver a high total dose to the surrounding normal tissues and, consequently, cause more inverse effects on the patient. However, we can also see a more uniform dose profile and endpoint dose in a train of seed sources than in a radioactive stent (see [8] and fig. 3).

Nevertheless, considering the cited calculations, it can be concluded that the total dose rate and cumulative dose in a ^{90}Y-stent implant is much lesser than the high dose rate (HDR) in a catheter-based procedure. In other words, depending on the position of the coronary artery and, also, the activity of the stent, we should consider a higher possibility of risk when using ^{90}Y seed sources.

CONCLUSIONS

A good radioactive stent should have: (1) a short half-life for use in permanent and low-dose-rate irradiation, (2) a good high-energy to penetrate the plaque areas but avoid other tissues, and (3) a high enough activity to prevent restenosis over the entire stent and, in particular, at stent margins.

A Monte Carlo approach was used to calculate a 3-D dose distribution for a standard ^{90}Y stent used in intracoronary radiation treatment. All statistical variances at all distances were less than 7%, verifying the simulation process. The results were in good agreement with a couple of previous works done on the dosimetry of a ^{90}Y stent, except for the maximum cumulative dose. Since we used a realistic continuous energy spectrum and a statistical method to transport particles rather than a numerical method to compute doses, it is expected that a more accurate simulation is provided.

Because the coronary vessel is in the vicinity of sensitive tissue such as the breast and lymph nodes, some of whose tissue weighting factors have been increased in the ICRP103's report (breast), and since we may not have an exact knowledge of the total absorbed dose in the surrounding tissues, we chose the quantity of the "dose equivalent" to evaluate the dose for normal tissues. For a calculated distant point $r = 8.5$ mm out from the stent surface, a total dose equivalent of about 238 mSv was obtained after 28 days. Also, the values of the dose equivalent were compared with those of ^{90}Sr/^{90}Y seed sources for a HDR temporary intravascular brachytherapy. For the same distance away from the seeds, the reference [8] achieved a dose equivalent of about 1670 mSv. Therefore, depending on the position of the coronary artery relative to the breast or lymph nodes and the activity of the stent, we can conclude that possible risks increase when using a ^{90}Sr/^{90}Y seed source, more so than with the implantation of a ^{90}Y radioactive stent. However, it is also obvious that stents with more activity could pose either the same as risks as ^{90}Sr/^{90}Y seeds or even greater ones to normal tissue. Thus, in addition to other medical advantages and disadvantages of using stents, a thorough review of the possibility of side effects of ^{90}Y radioactive stents with different designs and activities is needed before embarking on the treatment procedure. It may be reasonable to consider using ^{90}Sr/^{90}Y seed sources with lower activity for choosing a proper and safe method of reducing restenosis.

AUTHOR CONTRIBUTIONS

The design and theoretical analysis of this research work was carried out by A. Karimian. Monte Carlo simulation and the manuscript, including figures and text, were prepared and written by A. Karimian and S. Saghamanesh.

REFERENCES

[1] Massillon-JL, G., *et al*., The Use of Gel Dosimetry to Measure the 3-D Dose Distribution of a ^{90}Sr/^{90}Y Intravascular Brachytherapy Seed, *Physics in Medicine and Biology, 34* (2009), 6, pp. 1661-1672

[2] Shannon, M., *et al*., Experimental Determination of the Radial Dose Function of ^{90}Sr/^{90}Y IVBT Sources, *Medical Physics, 33* (2006), 9, pp. 3225-3232

[3] Duggan, D. M., *et al*., Radioactive Stents for Intravascular Brachytherapy, Engineering in Medicine and Biology Society, *Proceedings*, 22nd Annual International Conference of the IEEE, Vol. 1572, 2000, pp. 1577-1580

[4] Serruys, P. W., Kaj, I. P., I Like the Candy, I Hate the Wrapper: the (32)P Radioactive Stent, *Circulation Journal of the American Heart Association, 101* (2000), 1, pp. 3-7

[5] Chiu-Tsao, S. T., *et al*., Dose Calculation Formalisms and Consensus Dosimetry Parameters for Intravascular Brachytherapy Dosimetry: Recommendations of the AAPM Therapy Physics Committee Task Group 149, *Medical Physics, 34* (2007), 11, pp. 4126-4157

[6] Wang, R., Li, X. A., A Monte Carlo Calculation of Dosimetric Parameters of ^{90}Sr/^{90}Y and 192 Ir SS Sources for Intravascular Brachytherapy, *Medical Physics, 27* (2000), pp. 2528-2535

[7] Wang, R., Li, X. A., Dosimetric Comparison of Two ^{90}Sr/^{90}Y Sources for Intravascular Brachytherapy: An EGSnrc Monte Carlo Calculation, *Physics in Medicine and Biology, 47* (2002), 23, pp. 4259-4270

[8] Saghamanesh, S., Karimian, A., Abdi, M., Absorbed Dose Assessment of Cardiac and other Tissues around the Cardiovascular System in Brachytherapy with ^{90}Sr/^{90}Y Source by Monte Carlo Simulation, *Radiation Protection Dosimetry*, *147* (2011), 2, pp. 296-299

[9] Arbabi, A., Sadeghi, M., Joharifard, M., Irradiation and Dosimetry of Nitinol Stent for Renal Artery Brachytherapy, *Applied Radiation and Isotopes, 67* (2009), 1, pp.129-132

[10] Fischell, T., Hehrlein, C., The Radioisotope Stent for the Prevention of Restenosis, *Herz, 23* (1998), 6, pp. 373-379

[11] Prestwich, W. V., Kennet, T. J., Kus, F. W., The Dose Distribution Produced by a [sup 32]P-Coated Stent, *Medical Physics, 22* (1995), 3, pp. 313-320

[12] McLemore, L. B., Horton, J. L., Antolak, J. A., Calculation of the 3-D Dose Distribution Surrounding a ^{103}Pd Stent, *Cardiovascular Radiation Medicine, 2* (2001), 3, pp. 181-190

[13] Patel, N. S., *et al*., Treatment Planning Dosimetric Parameters for a ^{90}Y Coil Source Used in Intravascular Brachytherapy, *Cardiovascular Radiation Medicine, 2* (2001), 2, pp. 83-92

[14] Carter, A. J., *et al*., Dose and Dose Rate Effects of Beta-Particle Emitting Radioactive Stents in a Porcine Model of Restenosis, *Cardiovascular Radiation Medicine, 1* (1999), 4, pp. 327-335

[15] Taylor, A. J., *et al*., The 90-Day Coronary Vascular Response to ^{90}Y-Î² Particle-Emitting Stents in the Canine Model1, *International Journal of Radiation Oncology, Biology, Physics, 46* (2000), 4, pp. 1019-1024

[16] Streffer, C., The ICRP 2007 Recommendations, *Radiation Protection Dosimetry, 127* (2007), 1, pp. 2-7

[17] Prestwich, W. V., Nunes, J, Kwok, C. S., Beta Dose Point Kernels for Radionuclides of Potential Use in Radioimmunotherapy, *Journal of Nuclear Medicine, 30* (1989), 6, pp. 1036-1046

[18] Janicki, C, *et al*., Radiation Dose from a Phosphorous-32 Impregnated Wire Mesh Vascular Stent, *Medical Physics, 24* (1997), 3, pp. 437-445

Received on November 11, 2012
Accepted on September 13, 2013

Алиреза КАРИМИАН, Сомајех САГХАМАНЕШ

ДОЗИМЕТРИЈСКА ПРОЦЕНА ИМПЛАНТАЦИЈЕ ИТРИЈУМСКИХ СТЕНТОВА У ИНТРАКОРОНАРНОМ РАДИЈАЦИОНИМ ЛЕЧЕЊУ

Јонизујуће честице користе се за лечење атеросклерозе. Унутрашње озрачивање обично се изводи различитим методама (поступцима заснованим на катетеру, радиоактивним стентовима, или балонима), како би се умањила вероватноћа рестенозе. Захваљујући својим карактеристикама, ^{90}Y је погодан радионуклид за интраваскуларну брахитерапију. Међутим, пошто се у близини срца налазе нека критична ткива, као што су дојке и лимфни чворови, неопходно је урадити дозиметријске прорачуне у околини артерије како би се оправдала метода лечења. У овом раду, програмским пакетом MCNPX, добијена је 3-D расподела дозе у околини срчане кесе и околних ткива за стандардни ^{90}Y стент. Резултати су упоређени са другим методама спречавања рестенозе коришћењем стентова прекривених ^{90}Y. Прорачуни представљају кумулативну дозу за период од 28 дана у опсегу од 1230 cGy до 2400 cGy на удаљености 0.1 mm од површине стента, док је на 8.5 mm од стента кумулативна доза износила 23.8 cGy. За поменуто околно ткиво, према последњим изменама у ICRP препорукама, процењени су дозни еквивалент и ефективна доза на растојању од 8.5 mm. Дозни еквивалент за ове органе, израчунат за период лечења, упоређен је са објављеним резултатима за ^{90}Sr/^{90}Y изворе како би се процениле последице зрачења код ове две методе радиотерапије. Установљено је да у зависности од карактеристика стента, ^{90}Y стент импланти могу повећати нежељене ефекте за пацијента, али у много мањем обиму него друге методе.

Кључне речи: интраваскуларна брахитерапија, рестеноза, Монте Карло симулација, ^{90}Y