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Dosimetry of ^{188}Re and ^{186}Re sources based on Monte Carlo calculations for endovascular brachytherapy after balloon angioplasty

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ABSTRACT

Background: Recent pre-clinical and clinical studies indicate that irradiation in the dose range of 15 to 30 Gy can reduce rate of restenosis in patients who have undergone an angioplasty. The use of filled balloon with radioactive solution was proposed as one of the possible intravascular irradiation techniques.

Materials and Methods: The Monte Carlo N-particle Transport Code (MCNP4b) was used to calculate the dose rate distribution in the tissue equivalent material around the ^{188}Re and ^{186}Re liquid sources. Schematic of Medical Internal Radiation Dose (MIRD) for homogeneous distribution of radio-nuclide in a lesion was used for mean organ absorbed dose calculation due to the internal distribution.

Results: Results indicate that ^{188}Re liquid with 100 mCi/ml and ^{186}Re liquid with 250 mCi/ml can deliver desired dose in the vessel wall to reduce restenosis. The dose ratio in depth of 0.5 mm to surface of vessel wall for ^{188}Re and ^{186}Re were 40% and 18%, respectively. Therefore in case of ^{186}Re, there is a little non-uniformity with respect to the ^{188}Re case. The delivery of form ^{186}Re dose to normal tissue around target tissue is less than ^{188}Re.

Conclusion: Use of the Monte Carlo simulation with ^{188}Re-DTPA and ^{186}Re-DTPA for intra-vascular brachytherapy is a feasible method of delivering a desired dose to the vessel walls. Although^{188}Re-DTPA delivers the desired dose to the target tissue with lower radioactive concentration (mCi/ml), but with the use of ^{186}Re-DTPA, the delivery dose to normal tissue around the target tissue is less. *Iran. J. Radiat. Res., 2004; 2 (2): 89-95*

Keywords: *Dosimetry, Monte-Carlo, ^{188}Re, ^{186}Re, endovascular brachytherapy.*

INTRODUCTION

Recent pre-clinical and clinical studies indicate that irradiation within the dose range of 15 to 30 Gy can reduce the rate of restenosis in patients who have undergone an angioplasty (Nath 1999, King 1998).

Several delivery systems of intravascular brachytherapy have been developed to deliver doses within this rang with minimal normal tissue toxicity. One of the possible intravascular irradiation techniques, introduced by Amols and colleagues, is the use of filled balloon with radioactive solution (Amols *et al.*1996). This method has the advantage of accurate source position and a uniform dose to the vessel wall. However it has a potential of radiological toxicity from the radioactive liquid due to the risk of balloon rupture about 0.1% , (Amols *et al.*1996), since most commonly available beta emitters e.g. ^{90}Y,^{32}P,^{166}Ho are bone seeking compounds , (Amols *et al.*1996) .

^{188}Re ($E_{\beta\text{-max}}$ =2.12 MeV , half-life=16.9h) and ^{186}Re ($E_{\beta\text{-max}}$ =1.07 MeV , half-life=90.6 h) as Perrhenate or DTPA form rapidly excreted

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via the kidneys in the event of the material leaking into the systemic circulation (Lee *et al.* 2002). Therefore the technique utilizing the balloon filled with ^{188}Re or ^{186} Re have been suggested for intravascular brachytherapy.

^{188}Re and ^{186}Re has dominant γ components with 155 keV (abundance 15%) and 137 keV (abundance 9%), respectively. These γ components can be used for imaging purposes.

^{188}Re is supplied as an ^{188}W / ^{188}Re generator, the half life is long enough for experimental purposes (Knapp *et al.* 1999). An ion exchange column-based method used to concentrate ^{188}Re to 100 mCi/ml but ^{188}W production requiring high flux of thermal neutron must be more than 10^{14} n/cm^2 (Hashimoto *et al.* 1999).

^{186}Re with the thermal neutron capture cross section, 112±0.2 barn, is produced by reactors using flux of thermal neutron about 10^{13} n/cm^2, (Hashimoto *et al.* 1999).

Dose distribution of ^{90}Y solution loaded into a balloon of 3mm diameter has been presented by Amols *et al.* (1996), and dosimetry of ^{188}Re-DTPA for endovascular intra-balloon brachytherapy has been performed by Lee *et al.* (2002) .

In this study, the possibility of using ^{188}Re or ^{186}Re solution for endovascular brachytherapy is investigated and the comparison of dose distributions around balloon that filled with ^{188}Re or ^{186}Re solution were performed using Monte Carlo simulation.

MATERIALS AND METHODS

Dose distribution calculation around the balloon with Monte Carlo simulation

The dose distribution due to a radioactive liquid filled balloon by numeric integration of a Monte Carlo generated point kernel over the volume of the balloon, (Amols *et al.* 1996) is as follows:

$$D(p) = \int k(r')\,(A/v)\,dv; \quad (1)$$

Where D (p) is the dose rate in (Grays per second) at point P.

K(r) is dose point kernel in (Grays per decay), r' is radial distance in cm, A/v is activity per unit volume in (becquerels per cm^3), and k(r') is defined as a dose point kernel, corresponding to the expected value of dose per gram of tissue delivered at point r' by a unit point source of ^{186}Re located at r, (Amols *et al.* 1996).

In figure 1, a schematic diagram of dose calculation for a point P(x, y, z) on a balloon with external radius of R_o and axial length of L which is filled with a β emitter radionuclide is shown. The central channel of catheter contains a lumen of radius R_i to allow passage of guide wire.

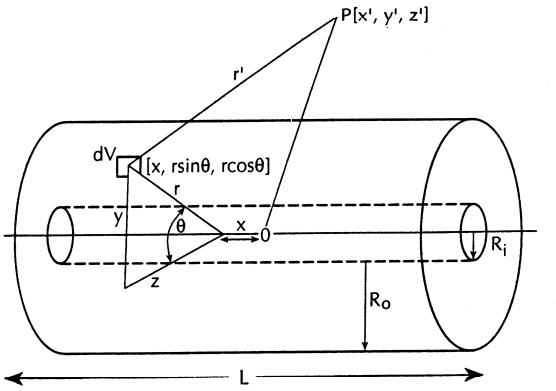

Figure 1. Schematic diagram of dose calculation for a point P (x, y, z) on a balloon with external radius of R_o, internal radius of R_i and axial length of L.

In figure 2, a catheter of balloon angioplasty with a length of 40mm, diameter of 3mm, a lumen to house guide wire and a liquid entrance to send radioactive solution into balloon is shown.

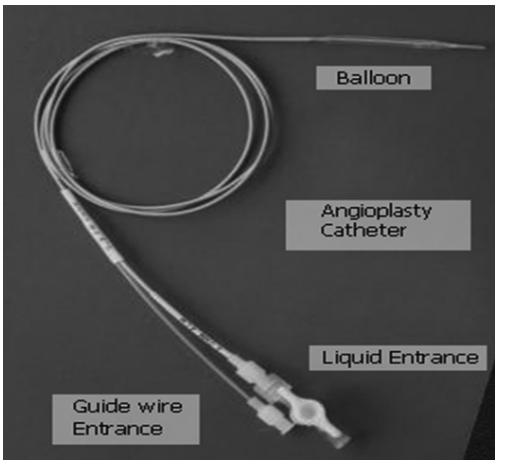

Figure 2. A balloon catheter with four main segments: balloon, catheter body, liquid entrance and guide wire entrance.

The Monte Carlo N-particle Transport Code (MCNP4b) is used to calculate the dose rate distribution in the tissue, equivalent material around the ^{188}Re and ^{186}Re liquid source (Briesmeister 2000). The code is able to consider photoelectric, coherent, Compton and pair production interaction processes. The condensed-history electron transport algorithms in the Monte Carlo code MCNP4c are derived from ITS 3.0, which is a well–validated code for coupled electron photon simulation (Chart 2002). Differences of up to 30% have recently been reported between beta dose distributions calculated with the MCNP4b and two others other codes namely EGS4 and EGSnrc, (Wang and Li 2001). The mass absorption coefficients of Hubbel and Seltzer distributed by NIST are used to obtain the absorbed dose from energy flux (Hubble and Seltzer 1995).

Beta spectrums of ^{188}Re and ^{186}Re for using in INP file of the MCNP code were adopted form Simpkin and Makie (1990).

The source was virtually placed in the center of a cylindrical volume of tissue equivalent phantom. Considering that the source has a symmetric structure, the circular annulus tally cells around the source longitudinal axis were employed to score the eligible events. In this study, up to 1×10^7 betas was involved in each simulation. The statistical uncertainties were found to be less than 5% for all tally points.

The cylindrical approximation for the individual balloon was made to allow the use of circular symmetry in the Monte Carlo calculation resulting in a reduction in computation time. For calculation we assume that the source was uniformly distributed within the balloon volume.

Absorbed dose calculation by MIRD schema

Schematic of Medical Internal Radiation Dose (MIRD) for homogeneous distribution of radionuclide in a lesion is used for mean organ absorbed dose calculation due to internal distribution (Israel *et al.* 2000). This technique is used to calculate the absorbed doses to the surrounding organs and tissues, when a radionuclide is injected inside the body. These doses are dominated by short-range β particles and conversion electrons.

Source organ is the same as target organ and very low contributions of the γ emissions and X-rays are ignored.

MIRD equation (Israel *et al.* 2000) used in this case is:

$$\check{D}\ (Gy) = C_v . \Sigma\ \Delta_i \quad (2)$$

Where, C_v is an indication of the cumulative concentration in [(MBq/gr) $*$ h], and Δ_i is the mean energy for each type of decay (charge particles or photons) in unite of [(Gy$*$gr)/(MBq$*$h)]. Values of $\Sigma\ \Delta_i$ for the emitted charged particles of ^{186}Re and ^{188}Re are obtained 0.198 and 0.487, respectively from ENSDF Decay Data in the MIRD (USDOE 2004).

RESULTS

Dose Distribution around the balloon

In figure 3, a point kernel dose for ^{188}Re and ^{186}Re point sources in [(cGy/s) per (Bq/ml)] was calculated. The results indicate the effective range of ^{186}Re was about 3mm, but the effective range of ^{188}Re was more than 3mm. The bremesstrahlung dose was less than 1% of beta particle dose for ^{188}Re and ^{186}Re.

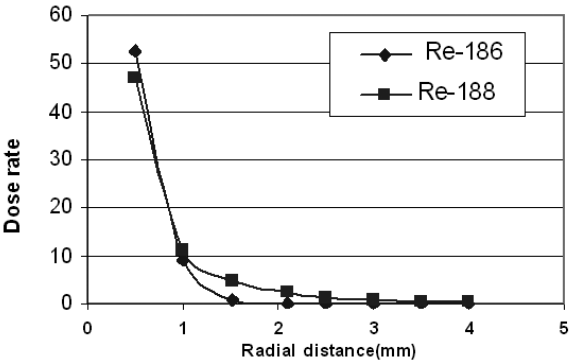

Figure 3. Point kernel dose for ^{188}Re and ^{186}Re point sources in [(cGy/s) per (Bq/ml)].

Depth dose rate distribution in [(cGy/min) per (mCi/ml)] in z=0 plane was calculated for the ^{188}Re and ^{186}Re solution in balloon with the diameter of 3mm and length of 20mm.

The ratio of dose rate of ^{188}Re to ^{186}Re was found to be about 3 in distance of 2mm from the balloon center (distance of 0.5 mm from balloon surface), (figure 4).

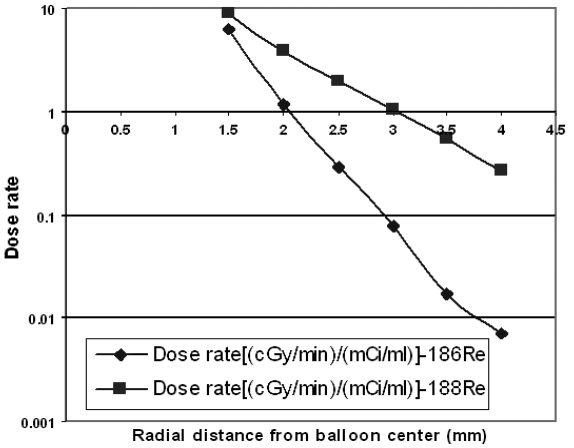

Figure 4. Depth dose rate distribution in [(cGy/min) per (mCi/ml)] in z=0 plane was calculated for ^{188}Re and ^{186}Re solution that balloon had the diameter of 3mm and length of 20mm.

Minimum of required activities of ^{188}Re and ^{186}Re were obtained 100 mCi/ml and 250mCi/ml respectively, because delivery of doses must have been considered between 12 to 20 Gy in 4min time (figure 5).

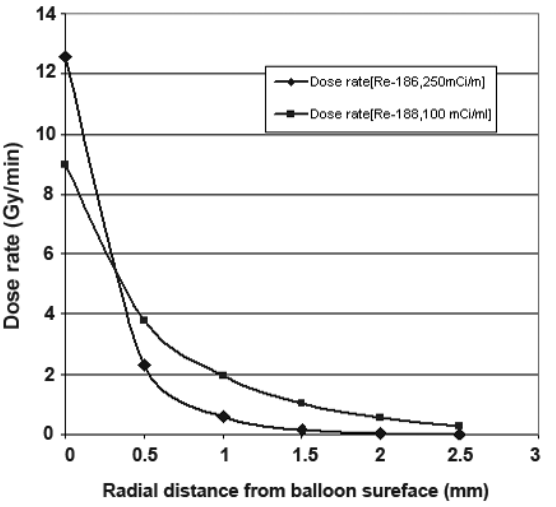

Figure 5. Radial dose rate in (Gy/min) for ^{188}Re and ^{186}Re to be 100 mCi/ml and 250 mCi/ml respectively, with a balloon of the 3mm diameter and length of 20mm.

The effects of variation in balloon diameter to increase dose rate was investigated, (figure 6-a and 6-b). Values of dose rate in depth of 0.5mm for the balloon with 20mm in length and

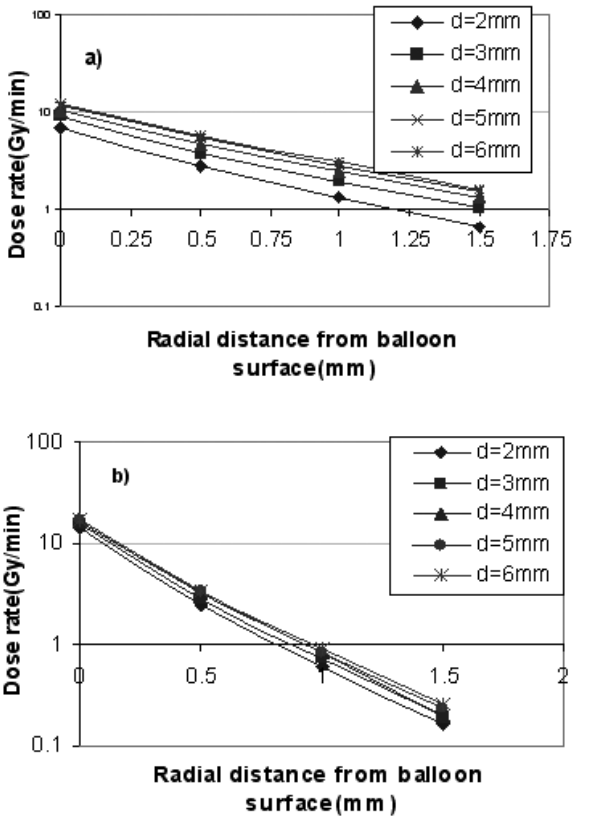

Figure 6. Values of dose rate in depth of 0.5mm for the balloon with 20mm in length and diameters of 2, 3, 4, 5 and 6mm were obtained (**a:**^{188}Re , **b:**^{186}Re).

diameters of 2, 3, 4, 5 and 6mm were obtained, (table 1), and the result of ^{188}Re indicated that the increased percentage of the dose rate due to an increase in balloon diameter was higher than the ^{186}Re case.

Table 1. Values of dose rate in depth of 0.5mm from balloon surface for the balloon with 20mm in length and various diameters.

Diameter of balloon (mm)	2	3	4	5	6
Dose rate (Gy/min) for ^{188}Re (100mCi/ml)	2.75	3.65	4.73	5.33	5.73
Dose rate (Gy/min) for ^{186}Re (250mCi/ml)	2.43	2.88	3.25	3.33	3.45

The effects of various balloon lengths vs. depth dose rate were evaluated (table 2).

Table 2. Dose rate in 0.5mm depth from balloon surface with diameter of 3mm and lengths of 20mm, 40mm.

Liquid source	Re-188, 100mCi/ml		Re-186, 250 mCi/ml	
Balloon specification	L= 20 mm	L= 40 mm	L= 20 mm	L= 40 mm
Dose rate (Gy/min)	2.88	3.11	3.65	3.71

Dose rate in unit of (Gy/min) in depth of 0.5mm from balloon surface was calculated for the balloon with diameter of 3mm and lengths of 20 and 40mm. Results indicate that there was a little increment in dose rate, about 2%, for ^{188}Re and 7% for ^{186}Re when the length of the balloon increased from 20mm to 40mm.

MIRD

Results of calculation for internal dose assessment of ^{186}Re-DTPA from data of Israel *et al.* are shown for the whole body and bladder in table 3. (Israel *et al.* 2000)

Table 3. Estimated absorbed dose from ^{186}Re-DTPA and ^{188}Re-DTPA, and comparison with the estimated radiation dose ^{99m}Tc-DTPA from as reported in the literature.

Organs	**Estimated radiation dose (mGy/MBq)**		
	^{186}Re-DTPA	**^{99m}Tc-DTPA**	**^{188}Re-DTPA**
	Results from data of Israel et al. 2000	Model of Thomas et. al.1984	Animal experiments of Lee et al. 2002
Bladder	1.96	2.71	4.56
Whole body	0.0024	0.012	0.0056

Estimated doses to the whole body and bladder have been measured by Lee and colleagues (Lee *et al.* 2002).

Internal dose of ^{99m}Tc-DTPA model for the whole body and bladder has been found to be 0.012 and 2.71 (mGy/MBq), respectively (Thomas *et al.* 1984).

DISCUSSION

One of the possible intravascular irradiation techniques after Balloon angioplasty is to use a radioactive filled balloon. This method may be a good alternative to the radioactive stent (Prestiwich and Kennet 1995) or radioactive beta-catheter (Verin *et al.* 1997), because it has more dose uniformity around angioplasty balloon to the vessel wall.

^{32}P, ^{90}Y, ^{166}Ho have been tried experimentally using these methods but the three isotopes are inherent bone seekers and thus rupture would be resulted in the outcome radiation damage to adjacent bone marrow (Lee *et al.* 2002).

^{188}Re and ^{186}Re with Perrhenate or DTPA form have been proposed as good candidates, because similar to ^{99m}Tc-Perrhenate, are localized in the thyroid, stomach, kidney and bladder following intravenous injection. DTPA is readily labeled with ^{188}Re and ^{186}Re which ^{188}Re-DTPA and ^{186}Re-DTPA excreted rapidly via the kidneys when injected intravenously. Upon accidental balloon rupture, the gamma ray of ^{188}Re-DTPA (155 keV, 15%) or gamma ray of ^{186}Re-DTPA (137 keV, 9%) would enable imaging in the event of balloon rupture.

The results of calculation for internal dose indicate that the whole body absorbed dose will be about 20 to 30 mGy, if the total amount of 100mCi (3700 MBq) of ^{188}Re-DTPA or 250mCi (9250 MBq) of ^{186}Re-DTPPA leaks into the systemic circulation. However, the probability of a balloon rupture is small, as inflation pressures used for intravascular radiation therapy are lower than those used in the practice of angioplasty, then the risk of internal irradiation dose would be lower than the above calculations in practice.

The calculated activity for the ^{188}Re is in line with the dosimetry results obtained by Lee *et al.* (2002), and there were some differences about 12% in comparison with results reported by Stabin *et al.* (2000). They had been employed the EGS4 code for calculating the beta particles doses in which the calculated activities for delivering a dose of 30 Gy in 5min at 0.5mm

from the vessel surface were ^{186}Re, 17000 MBq/ml (460mCi/ml); ^{188}Re, 7000 MBq/ml (190mCi/ml); (Stabin *et al.* 2000).

It should be noted that there are some uncertainties for using the calculated doses in clinical practice in general. The artery wall was considered as a tissue equivalent material. If the artery was assumed to have a deposition of plaque around the inside wall of artery, doses on the plaque side of the vessel would be lower than on the nonplaque side. Plaque depositions were not generally distributed symmetrically throughout the vessel wall, being irregularly deposited over some or the entire wall; it was not possible to consider plaque geometries in computer simulations.

There was some dose drop-off about 50% near the ends of balloon, so, the length of the balloon must have be selected longer than length of target in artery about 20%.

Finally, it must be noted that, there are certain inevitable limitations of the modeling process in approximating physical realities. In clinical situation, physicians may counter many different artery geometries, plaque deposition configuration, plaque compositions, etc. Therefore, interpreting the results for using in a clinical study should be considered carefully.

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