Dosimetry and Radiation Exposure of Patients

7

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7.1 Introduction

Radiosynoviorthesis is a local radionuclide therapy of inflamed synovial membranes involving either Y-90, Er-169, or Re-186. Although the radioactive substance is not supposed to leave the joint after the injection, it might leak to the adjacent lymph nodes and, subsequently, to the remainder of the body. Data on this leakage to regional lymph nodes is provided in various publications [1–5]. Furthermore, since faint uptake in the liver can be seen in some patients, it can be assumed that a fraction of the radioactively labeled colloids reach the blood circulation and are taken up by the reticuloendothelial system.

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The purpose of this chapter is to provide an assessment of leakage rates, absorbed and effective doses to the remainder of the body by leakage, by external irradiation from the joint itself, and absorbed doses to the neighboring lymph nodes.

Due to the low amount of activity injected and the physical properties of the radionuclides used, the exposure of relatives and the public by these patients is extremely low and can be neglected.

7.2 Leakage Rate After Injection

One of the major sources for radiation exposure of the patient is leakage of the radioactive compound from the joint to the adjacent lymph nodes or other organs and tissues. A number of authors reported data on leakage rates.

Gedik et al. [5] determined the leakage rate 48 h after administration of Y-90 or Re-186 in 35 patients with persisting synovitis. The mean leakage of 19 joints treated with Y-90-citrate was 3.2 % (maximum 13 %) and of 21 joints treated with Y-90-silicate 2.3 % (maximum 5 %). There was no statistically significant difference. In addition Gedik et al. [5] observed a mean leakage in 13 patients treated with Re-186-sulfide of 2.5 % (maximum 6 %). Turkmen et al. [6] published leakage data showing that the 50 % percentile of the leakage was 1.8 % and the 84.1 % percentile was 4.8 %. Turkmen et al. [7] determined leakage rates in 20 juvenile hemophilia patients by measuring the uptake with a gamma camera 48 h after injection. The authors observed, in 11 patients, a mean leakage of 0.2 % in lymph nodes and 4.7 % in the liver (maximum, 7.6 %).

Klett et al. [8] measured, for ten patients, the leakage 3 days after injection of 50–60 MBq Re-186. Eight of the ten patients showed a mean leakage of 3.9 % (maximum, 23.4 %) to the axillary lymph nodes. Two patients showed uptake in the liver, one in the spleen.

Van der Zant et al. [4] reported on leakage of Er-169 and Re-186 in 31 patients with arthritis by bremsstrahlung scintigraphy. The mean leakage was 2.1 % for lymph nodes (Re-186, maximum 9.9 %), 0.11 % (Er-169, 1 case), and for liver/spleen 0.5 % (maximum 6.8 %). Van der Zant et al. [9] also determined the leakage from the ankles about 24 h after the injection of 75 MBq Re-186 by imaging. The mean leakage to lymph nodes (2.4 ± 3 %) was higher than to the liver (0.8 ± 1.7 %).

Manil et al. determined the leakage rate from scintigraphic images with the isotope Re-186 using a dual-head gamma camera [3]. Whole body and static images of the injection sites and lymph node chains were obtained. A measurable extra-articular activity was only found in drainage lymph nodes and in the hepatosplenic area. The proportion of the whole body activity in lymph nodes was 4.5 % at 6 h, 4.4 % at 24 h, and 6.0 % at day 7. For the hepatosplenic area, the corresponding results were 0.9 % at 6 h, 1.1 % at 24 h, and 2.1 % at day 7. Van der Zant et al. [9] observed the leakage from the ankles about 24 h after the injection of 75 MBq by Re-186 by imaging. The mean leakage to lymph nodes (2.4 ± 3 %) was higher than to the liver (0.8 ± 1.7 %). The maximal observed leakage to a single lymph node was 4 % and to the liver 5.5 %. For 12 patients with hemophilia, Grmek et al. [2]

calculated leakage rates after the injection of Re-186 colloids. The author observed a mean leakage of 20 ± 10 % (maximum, 40 %). Four of the 12 patients showed uptake in lymph nodes. Overall, leakage rates up to 8 % have been observed.

7.3 Radiation Exposure of Healthy Organs

7.3.1 Generic Model

For calculating the absorbed doses, data on distribution of colloids were taken from the ICRP Publication 53 [10]. In this publication, slightly different data sets are provided for large colloids (diameter 100–1,000 nm) and for small colloids (diameter <100 nm) for the conditions "normal liver."

As suggested in the ICRP Publication 53, immediate uptake by the listed tissues is assumed. Furthermore, it is assumed that the biological half-life in the specified tissues is long compared with the physical half-life of the radionuclide. Under the above assumptions, the residence time in an organ is determined by the physical half-life, the organ uptake, and the percentage of injected activity that leaks out of the joint:

$$\text{Residence time per \% of leakage} = \text{Organ uptake} \times \text{physical half life} / \ln(2) / 100$$

With a half-life of the physical decay of Y-90, Er-169, and Re-186, the resulting residence times per % of leakage were calculated. With these residence times, the absorbed doses to healthy organs and tissues were calculated using software OLINDA/EXM [11]. Organ doses and effective doses as a function of the percentage of leakage are displayed in Table 7.1 for the isotopes under consideration.

7.3.2 Observed Absorbed Doses

According to data on Y-90 published by Klett et al. [12], the median absorbed doses to the liver and spleen were 62 and 62 mGy, respectively. Somewhat higher mean doses for the liver, spleen, and kidneys (265, 119, and 671 mGy) were reported by Gratz et al. [1]. The organ doses to the liver and spleen published by Klett et al. [12] are consistent with mean leakage to the blood system of about 2 %. While the spleen doses reported by Gratz et al. [1] are consistent with 2 % leakage, the liver doses are higher requiring 8 % leakage. The high kidney doses are not consistent with the model assumptions.

Reliable measurements of the whole body activity after administration of Er-169 are not available as almost no direct radiation leaves the body. Manil et al. [3] measured the total blood activity after Er-169 therapy of finger joints in 11 patients and found less than 1 % of the administered activity in all but 1 patient with scintigraphic evidence of extra-articular injection. The effective dose was maximal for this patient and was estimated to be 0.045 mSv/MBq. For Er-169 Gratz et al. [1] estimated the radiation dose to the whole body to be 0.11 mGy/MBq.

Table 7.1 Radiation dose for the reference adult for colloids per % of leakage

	Y-90 labeled colloids		Er-169 labeled colloids		Re-186 labeled colloids	
Target organ	Large colloids (>100 nm) mGy/MBq/ %leakage	Small colloids (<100 nm) mGy/MBq/ %leakage	Large colloids (>100 nm) mGy/MBq/ %leakage	Large colloids (>100 nm) mGy/MBq/ %leakage	Large colloids (>100 nm) mGy/MBq/ %leakage	Small colloids (<100 nm) mGy/MBq/ %leakage
Kidneys	6.76E-04	3.38E-04	2.61E-04	1.31E-04	5.82E-04	4.13E-04
Liver	1.83E-01	1.83E-01	7.05E-02	7.02E-02	9.25E-02	9.25E-02
Ovaries	6.76E-04	3.38E-04	2.61E-04	1.31E-04	3.88E-04	2.19E-04
Red marrow	2.00E-02	2.95E-02	1.06E-02	1.56E-02	1.08E-02	1.59E-02
Osteogenic cells	1.34E-02	1.91E-02	5.47E-03	7.17E-03	7.08E-03	9.86E-03
Spleen	2.64E-01	2.64E-01	1.05E-01	1.05E-01	1.37E-01	1.37E-01
Testes	6.76E-04	3.38E-04	2.61E-04	1.31E-04	3.50E-04	1.76E-04
Uterus	6.76E-04	3.38E-04	2.61E-04	1.31E-04	3.79E-04	2.08E-04
Other organs	6.76E-04	3.38E-04	2.61E-04	1.31E-04	<1E-03	<1E-03
Total body	6.76E-03	6.76E-03	2.61E-03	2.61E-03	3.49E-03	3.48E-03
	mSv/MBq/ % leakage	*mSv/MBq/ % leakage*	*mSv/MBq/ % leakage*	*mSv/MBq/ % leakage*	*mSv/MBq/ % leakage*	*mSv/MBq/ % leakage*
Effective dose	1.88E-02	1.97E-02	7.67E-03	8.20E-03	9.72E-03	1.02E-02

For Re-186 the effective dose, according to Manil et al. [3], calculated from the whole body dose due to gamma emission from injection point(s) and uptake foci, as well as from organ doses due to blood activity, was 380 µSv/MBq. According to Manil et al. [3], the radiation dose to the blood ranged between 0.07 and 0.88 mGy/MBq (mean value: 0.34 mGy/MBq). Gratz et al. [1] determined the doses to the hands and other organs by gamma imaging. The authors evaluated whole body and organ time-activity curves using conjugate views to generate residence times. In the 23 cases injected with 74 MBq Re-186 for the ankles ($n=7$), elbows ($n=3$), and wrists ($n=4$) and 111 MBq for shoulders ($n=8$) and hips ($n=1$)], the mean absorbed doses to the whole body, liver, spleen, and kidneys were 53 ± 27 mGy, 100 ± 81 mGy, 203 ± 228 mGy, and 94 ± 113 mGy, respectively. Van der Zant et al. [9] observed an absorbed dose to the liver of 7.5 mGy. Manil et al. [3] and van der Zant et al. [9] have published data of Re-186 uptakes in the hepatosplenic area which are consistent with leakage to the blood system of about 1–2 %. The corresponding values for the mean whole body dose and the organ doses published by Gratz et al. [1] are much higher requiring 50 % leakage or even more.

7.4 Radiation Dose from Penetrating Radiation from the Joint

The mean synovial thickness in joints treated with Y-90 is 6.8 mm [1]. The energy loss of the beta radiation ($E_{max}=2.27$ MeV, range 10 mm in water) is expected to be mainly in the synovia and the production of bremsstrahlung will be similar to that in water. An experimentally verified calculation of the radiation dose from bremsstrahlung of Y-90 has been published by Stabin et al. [13]. Production of bremsstrahlung is proportional to the square of the beta energy. The doses in 5, 10, 20, and 30 cm distance are 0.056, 0.011, 0.0015, and 0.0004 mGy/MBq, respectively.

The dose to organs and gonads from the bremsstrahlung from 200 MBq Y-90 in the knee is less than 0.1 mSv. The gonad dose per % of leakage into the inguinal lymph nodes can be estimated to be less than 0.1 mSv for males and approximately 0.02 mSv for females. The dose from bremsstrahlung from the inguinal lymph nodes to other organs is negligible.

The γ-dose rate constant for the penetrating radiation of Re-186 is 2.4 $\mu Sv \times m^2/h/GBq$. With an attenuation coefficient (energy absorption coefficient) of 0.03/cm the doses in 10, 15, and 30 cm distance are calculated to 0.023, 0.009, and 0.001 mGy/MBq, respectively. The expected radiation dose to the gonads (mean distance 10–15 cm) from a therapy of a hip with 150 MBq Re-186 is between 1.4 and 3.5 mSv. The gonad dose from therapies of other joints with less activity will not exceed 0.1 mSv.

The mean synovial thickness in joints treated with Er-169 is 2.4 mm [1]. The beta radiation ($E_{max}=0.35$ MeV, range 1 mm in water) is expected to be stopped in the synovia and the production of bremsstrahlung will be similar to that in water. Production of bremsstrahlung is proportional to the square of the beta energy. Taking into account the square of the ratio of the mean beta energies and differences in emission probabilities (EP) and residence times (RT) and neglecting differences in the energy absorption coefficient which are expected to be small, the dose per MBq administered is expected to be

$$D_{\text{Er-169}} = D_{\text{Y-90}} \times \left(E_{\text{Er-169}} / E_{\text{Y-90}}\right)^2 \times \text{RT}_{\text{Er-169}} / \text{RT}_{\text{Y-90}} \times \text{EP}_{\text{Er-169}} / \text{EP}_{\text{Y-90}} = 0.04 \times D_{\text{Y-90}}$$

With $D_{\text{Y-90}}$ taken from [13], the dose from Er-169 bremsstrahlung in 10 cm distance is 4×10^{-4} mGy/MBq and, therefore, negligible.

The mean synovial thickness in joints treated with Re-186 is 3.7 mm [1]. The beta radiation ($E_{\text{max}} = 1.05$ MeV, range 4 mm in water) is expected to be stopped in the synovia and the production of bremsstrahlung will be similar to that in water. Taking into account the square of the ratio of the mean beta energies and differences in emission probabilities (EP) and residence times (RT) and neglecting differences in the energy absorption coefficient which are expected to be small, the dose per MBq administered is expected to be

$$D_{\text{Re-186}} = D_{\text{Y-90}} \times \left(E_{\text{Re-186}} / E_{\text{Y-90}}\right)^2 \times \text{RT}_{\text{Re-186}} / \text{RT}_{\text{Y-90}} \times \text{EP}_{\text{Re-186}} / \text{EP}_{\text{Y-90}} = 0.2 \times D_{\text{Y-90}}$$

With $D_{\text{Y-90}}$ taken from Stabin et al. [13], the absorbed doses from bremsstrahlung from Re-186 in 10, 15, and 30 cm distance are 0.002, 0.0006, and 0.0001 mGy/MBq, respectively. The absorbed dose from the bremsstrahlung is an order of magnitude below the dose from the γ-radiation, and the corresponding absorbed dose to the gonads from a therapy of a hip with 150 MBq Re-186 is less than 0.3 mSv.

7.5 Radiation Exposure of the Lymph Nodes

7.5.1 Generic Model

For Y-90 the dose to a spherical node with homogeneous activity concentration and a mass of 1 g is 380 mGy per MBq administered activity and per % of the residence time accounting for the node. The correspondent values for nodes with other masses are 2,610 mGy/MBq/% at 0.1 g, 702 mGy/MBq/% at 0.5 g, and 202 mGy/MBq/% at 2 g. Due to the high energy of the beta particles emitted by Y-90, an increasing fraction of the radiation energy is deposited outside the node for decreasing diameters, and the absorbed fraction is shape dependent. The values given above will overestimate the dose in nodes with pronounced nonspherical shapes. Using the same assumptions for the biokinetics as for Re-186, the doses to the affected lymph nodes are 366 mGy/MBq/% if the activity is distributed in a mass of 1 g, 183 mGy/MBq/% if the mass is 2 g, and 91 mGy/MBq/% if the total mass is 4 g.

For Er-169 the dose to a spherical node with homogeneous activity concentration is 190 mGy*g/MBq/%. The dose is dependent on the residence time in the lymph node masses and the total mass of the involved lymph nodes but is almost independent of size and shape of individual lymph nodes. Using the same assumptions for the biokinetics as for Re-186, the doses to the affected lymph nodes are

190 mGy/MBq/% if the activity is distributed in a mass of 1 g, 95 mGy/MBq/% if the mass is 2 g, and 48 mGy/MBq/% if the total mass is 4 g.

For Re-186, according to the sphere model in OLINDA/EXM [11], the dose to a spherical node with homogeneous activity concentration and a mass of 1 g is 234 mGy per MBq administered activity and per % of the residence time accounting for the node. The correspondent values for nodes with other masses are 2,150 mGy/MBq/% at 0.1 g, 458 mGy/MBq/% at 0.5 g, and 119 mGy/MBq/% at 2 g. The product of dose and mass is 225 mGy*g/MBq/% ±5 % for all sizes indicating that the dose is dependent on the residence time in the lymph node masses and on the total mass of the involved lymph nodes but is almost independent of size and shape of individual lymph nodes.

The time-activity function of the activity leaking out of the joint is undefined. Activity release may be limited to a short time interval after the administration; it may occur sporadically after joint movement, or activity may leak out of the joint continuously. With the simplified assumption of a short-term leakage immediately after activity administration and for the worst-case scenario that the activity taken up by the lymph node masses stays there until decay, the percentage of the residence time accounting to the lymph node mass is identical to the uptake in % of the administered activity. The doses to the affected lymph nodes are 225 mGy/MBq/% if the activity is distributed in a mass of 1 g, 113 mGy/MBq/% if the mass is 2 g, and 56 mGy/MBq/% if the total mass is 4 g.

7.5.2 Observed Absorbed Doses

For Er-169 Gratz et al. [1] observed an absorbed dose of 2.3 ± 2 Gy (62 mGy/MBq) for single lymph nodes, van der Zant et al. 3 Gy [4].

For Re-186 Gratz et al. [1] report doses to lymph node masses of 25.9 ± 53.8 Gy (maximum 189 Gy) and to single lymph nodes of 14.7 ± 11.2 (maximum 63 Gy) after the application of 74–111 MBq Re-186. Van der Zant et al. determined the maximal observed dose to a single lymph node to 35 Gy [9]. For 12 patients with hemophilia, Grmek et al. [2] calculated absorbed doses after the injection of Re-186 colloids. The author observed a mean absorbed dose in those lymph nodes of 15 Gy. Van der Zant et al. [11] calculated the doses using the MIRD algorithms and found a maximum absorbed dose of 86 Gy.

Data for Y-90 are not available.

Conclusions

For RSO the exposure to organs/tissues other than the treated joint is negligible if there is no leakage. If there is leakage, the absorbed dose to neighboring lymph nodes could be higher than a few hundred mGy, thus leaving the deterministic range of radiation effects however depending upon the amount of leakage and the size of the lymph node of the individual patient. For the remainder of the body, the highest exposure of much less than one Gray is expected in the liver. The external exposure by the joint itself is low and does not contribute significantly to the patient exposure.

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