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The absorbed dose to blood from blood-borne activity

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The absorbed dose to blood from blood-borne activity

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Abstract

The radiation absorbed dose to blood and organs from activity in the blood is relevant for nuclear medicine dosimetry and for research in biodosimetry. The present study provides coefficients for the average absorbed dose rates to the blood from blood-borne activity for radionuclides frequently used in targeted radiotherapy and in PET diagnostics. The results were deduced from published data for vessel radius-dependent dose rate coefficients and reasonable assumptions on the blood-volume distribution as a function of the vessel radius. Different parts of the circulatory system were analyzed separately. Vessel size information for heart chambers, aorta, vena cava, pulmonary artery, and capillaries was taken from published results of morphometric measurements. The remaining blood not contained in the mentioned vessels was assumed to reside in fractal-like vascular trees, the smallest branches of which are the arterioles or venules. The applied vessel size distribution is consistent with recommendations of the ICRP on the blood-volume distribution in the human. The resulting average absorbed dose rates to the blood per nuclear disintegration per milliliter (ml) of blood are (in $10^{-11}$ Gy·s$^{-1}$·Bq$^{-1}$·ml) Y-90: 5.58, I-131: 2.49, Lu-177: 1.72, Sm-153: 2.97, Tc-99m: 0.366, C-11: 4.56, F-18: 3.61, Ga-68: 5.94, I-124: 2.55. Photon radiation contributes $1.1–1.2 \times 10^{-11}$ Gy·s$^{-1}$·Bq$^{-1}$·ml to the total dose rate for positron emitters but significantly less for the other nuclides. Blood self-absorption of the energy emitted by β-particles in the whole blood ranges from 37% for Y-90 to 80% for Tc-99m. The correspondent values in vascular trees, which are important for the absorbed dose to organs, range from 30% for Y-90 to 82% for Tc-99m.

Keywords: absorbed dose to the blood, dosimetry, blood vessel distribution

(Some figures may appear in colour only in the online journal)
1. Introduction

Radioactivity in the blood delivers a radiation absorbed dose to the blood itself as well as extravascular tissues. While penetrating photon radiation emitted by blood-borne activity can be expected to induce approximately a homogeneous absorbed dose distribution in a perfused organ, particle radiation will not. Due to the short range of particles in tissue a major fraction of the emitted energy remains within the lumen of the blood vessel and does not contribute to the exposure of the organ parenchyma. Up to now, the effect is not explicitly considered in dosimetric assessments of blood-borne activity for example the dosimetry of diagnostic radio-pharmaceuticals; instead, ‘the activity in the blood in an organ or tissue is added in that organ or tissue for purposes of dose calculations’ (ICRP106 2008). It has been pointed out in (Hänscheid et al 2014) that neglecting blood self-absorption of radiation leads to an overestimation of the organ absorbed doses for radiopharmaceuticals for which blood is a significant source region.

Blood self-irradiation is also relevant for studies investigating radiation induced physiological changes of blood components such as enhanced formation of micronuclei or of $\gamma$-H2AX and 53BP1 DNA repair foci in blood cells (M’Kacher et al 1996 1997, Monsieurs et al 1999, Watanabe et al 2004, Grawe et al 2005, Lassmann et al 2010, May et al 2012); such studies rely on a correct blood dose estimate.

The fraction of energy deposited within the vessel lumen depends on the kind and energy of the radiation and on the vessel size. While near total absorption within the vessel lumen is expected for particles in vessels with diameters much larger than the typical particle range, the fraction of blood self-absorption decreases with decreasing vessel size. To correctly determine blood self-irradiation it is necessary to calculate the mean absorbed dose to the blood from blood-borne activity based on the actual distribution of vessel diameters. This requires knowledge of both the dose coefficients of blood self-irradiation (the dose rates to the blood from activity in the blood) and the blood-volume distribution as functions of the vessel radius.


2. Methods

2.1. Self-irradiation of the blood

The absorbed dose to the blood originating from activity in the blood $D_{\text{BL} \leftarrow \text{BL}}$ (unit: Gy) can be determined (Akabani and Poston 1991, Hänscheid et al 2014) as the product of the time integrated blood activity concentration $A_{\text{BL}}$ (unit: Bq·s·ml$^{-1}$; unit of the blood activity concentration $A_{\text{BL}}$: Bq·ml$^{-1}$) and the average absorbed dose rate to the blood per nuclear disintegrations per milliliter (ml) of blood $S_{\text{BL} \leftarrow \text{BL}}$ (unit: Gy s$^{-1}$ Bq$^{-1}$·ml):
If the total blood volume \( TBV \) (unit: ml) is partitioned into distinct pools \( i \) with blood volumes \( BV_i \) (such as heart chambers, aorta, capillaries, etc; unit: ml), the coefficient \( S_{BL \leftarrow BL} \) is the weighted mean of the coefficients \( S_i \) (unit: \( \text{Gy} \cdot \text{s}^{-1} \cdot \text{Bq}^{-1} \cdot \text{ml} \)) representative for the pools:

\[
S_{BL \leftarrow BL} = TBV^{-1} \cdot \sum_i BV_i \cdot S_i
\]

As the fraction of energy absorbed within the blood in a vessel increases with increasing radius \( r \) (unit: m) of the vessel lumen, the coefficient \( S_{BL \leftarrow BL} \) valid for the whole pool \( i \) can be determined by averaging radius dependent coefficients \( S_i \) (unit: \( \text{Gy} \cdot \text{s}^{-1} \cdot \text{Bq}^{-1} \cdot \text{ml} \)) weighted by the fraction of blood residing in vessels of radius \( r \):

\[
S_i = BV_i^{-1} \int_r F_i(r) \cdot S_{BL \leftarrow BL}(r) \cdot dr
\]

The parameter \( F_i(r) \) (unit: \( \text{cm}^2 \)) is the total luminal cross-sectional area of all vessels with radius \( r \) in pool \( i \). Integration of the total luminal volume of all vessels with radius \( r \) in pool \( i \), \( F_i(r) \cdot dr \), over the whole range of radii will recover the total volume in the pool, \( BV_i \). It is advisable (Hänscheid et al 2014) to determine \( S_{BL \leftarrow BL} \) as sum of contributions \( S_{BL \leftarrow \beta BL} \) from particles and \( S_{BL \leftarrow \gamma BL} \) from photon radiation by using corresponding radius dependent coefficients \( S_{BL \leftarrow \beta BL}(r) = S_{BL \leftarrow \beta BL}(r) + S_{BL \leftarrow \gamma BL}(r) \). An estimate of the absorbed dose to the blood from blood-borne activity requires the knowledge of the coefficients of self-irradiation from penetrating and particle radiation as well as the blood-volume distribution as functions of the vessel radius.

### 2.2. The blood-volume distribution

The following reference values for the blood-volume distribution are listed in (ICRP89 2002): the typical total volume of blood in the adult male is \( TBV = 5300 \) ml, 9% of which resides in the heart chambers, 10.5% in the pulmonary and 80.5% in the systemic circulation. Seven percent of the blood is attributed to capillaries (2% pulmonary, 5% systemic) with diameters similar to that of erythrocytes (<10 \( \mu \text{m} \)). Of 80.5% of \( TBV \) in the systemic circulation, 6% resides in aorta and large arteries, 10% in small arteries and arterioles, 5% in capillaries, 41.5% in venules and small veins, and 18% in large veins and the venae cavae.

The rough subdivision of human blood vessels into capillaries, small vessels, large vessels, etc provided by (ICRP89 2002) is insufficient to generate a reliable blood dose estimate because the coefficient of self-irradiation \( S_{BL \leftarrow BL}(r) \) varies nonlinearly over the range of radii (Hänscheid et al 2014). For our calculations, we consider the six pools, heart chambers, ascending aorta, descending aorta, venae cavae, pulmonary artery, and capillaries, separately and assume that the remaining blood is located in vascular trees. The following assumptions are made:

- the inner diameter of the heart chambers is 50 mm (Kaess et al 2013),
- the ascending aorta is a vessel with a constant lumen diameter of 28 mm containing 40 ml of blood; the descending aorta is a truncated cone with diameters ranging from 15 to 21 mm and with a volume of 100 ml (Kahraman et al 2006, Sugawara et al 2008, Rogers et al 2013),
• the main pulmonary artery, which has a mean outer diameter of 26 mm in men (Truong et al 2012), is approximated by a vessel with 24 mm lumen diameter and 25 ml volume,
• the mean diameter ratio of the vena cava to the aorta is 1.23 (Sridhar et al 2012), suggesting 50% more volume in the vena cava (210 ml), which is approximated by a truncated cone with diameters ranging from 20 to 30 mm,
• the diameter of capillaries is 7 µm (Kassab and Fung 1994, ICRP89 2002),
• local blood transport in organs and tissues takes place in vascular trees with about 10 µm minimum diameter of the pre-capillary arterioles or post-capillary venules (2·r_{min} = 0.01 mm) and 10 mm maximum diameter of the trunk (2·r_{max} = 10 mm).

The resulting blood contents are listed in table 1.

Of 848 ml of blood (16% TBV) in systemic arteries, 530 ml (10% TBV) reside in small arteries (ICRP89 2002) and 140 ml in the aorta. The remaining 178 ml are attributed to large arteries other than the aorta. The fraction of blood in large arteries within the arterial trees is f = 178/(530 + 178) = 25%. The same fraction is analogously derived for the blood in large veins within the venous trees. The assumptions in (ICRP89 2002) regarding the blood contents in large vessels are based on suggestions by (Leggett and Williams 1991) who stated that the related pools are arteries (such as the brachial, iliac, femoral, superior mesenteric, and carotid) and veins (such as the subclavian, femoral, cubital, and superior mesenteric). The diameters of the mentioned vessels are typically larger than 5 mm (Kahraman et al 2006).

2.3. Vascular trees

The blood is pumped by the heart through tree-like branching networks, the arterial trees, presenting an increasing number of vessels of decreasing size and feeding a mesh-like net of capillaries in order to supply the entire volume of the body with oxygen and nutrients. Another branching network, the venous trees, collects the blood and metabolic waste from the capillaries and transports it back to the heart. Arterial and venous trees are considered to be quasi-fractal arborescences with branching geometries optimized for resource distribution (West
et al 1997). A fractal-like tree is characterized by fixed dimensionless scale factors; each tube branches into about the same number $\nu$ of smaller ones and the ratios $\delta$ of the diameters and $\lambda$ of the lengths of the vessel segments from one generation to the next are more or less constant (figure 1).

Although actual vascular trees are not strictly fractal-like and the scale factors have been observed to vary somewhat with the generation number, the entire tree is reasonably approximated by mean values of $\nu$, $\delta$, and $\lambda$ (Kassab 2000). Starting from $r_{\min}$ as the minimum radius of the smallest vessels, the pre-capillary arterioles or post-capillary venules, the radius $r_k$ of vessels after $k$ branches (in generation $k$) is:

$$r_k = r_{\min} \cdot \delta^k$$

(4)

The volume of blood changes by a constant factor from one generation to the next:

$$\beta = \lambda \cdot \delta^2 \cdot \nu^{-1}$$

(5)

As not all pre-capillary arterioles and post-capillary venules have identical radii and the diameter ratio $\delta$ must be considered as a mean value with fluctuations, we approximate the distribution of vessel radii in arterial and venous trees by a continuous function defined by a generation index $x$ (unit: dimensionless):

$$r_x = r_{\min} \cdot \delta^x \Leftrightarrow x = \frac{\ln(r_x / r_{\min})}{\ln(\delta)}$$

(6)

The volume $V_x$ of vessels representative for generation index $x$ is given by:

$$V_x = V_0 \cdot \beta^x$$

(7)

where $V_0$ (unit: ml) is a constant of proportionality.
The total volume in vessels within a range of generation $x_l$ with radius $r_l$ to generation $x_u$ with radius $r_u$ is

$$V_{r_l,r_u} = \int_{r_l}^{r_u} V_0 \cdot \frac{B^x}{\ln (B)} \cdot \frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} \cdot \frac{\ln\left(\frac{r_l}{r_{\text{min}}}\right)}{\ln\left(\frac{r_u}{r_{\text{min}}}\right)} dx = \frac{V_0}{\ln (B)} \cdot \frac{B^x}{\ln (B)} \cdot \frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} \cdot \frac{\ln\left(\frac{r_l}{r_{\text{min}}}\right)}{\ln\left(\frac{r_u}{r_{\text{min}}}\right)}$$

and the volume of the entire tree is

$$V_{\text{tree}} = \frac{V_0}{\ln (B)} \cdot \left(\frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} - 1\right)$$

where $r_{\text{max}}$ denotes the maximum lumen radius of the largest vessel that is the trunk of the tree.

The fraction of blood residing in vessels with radii ranging from $r_l$ to $r_u$ is

$$f_{V_{r_l,r_u},V_{\text{tree}}} = \left(\frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} - 1\right) \cdot \left(\frac{\ln(r_l)}{\ln(r_{\text{min}})} + \frac{\ln(r_u)}{\ln(r_{\text{min}})} - 1\right)^{-1}$$

The derived representation of the volume distribution in a quasi-fractal vascular tree has the advantage of being independent of explicit values of $\nu$, $\delta$, $\lambda$, and the number of generations in the tree; it is determined solely by the ratio $\ln(\beta)/\ln(\delta)$.

Several groups have performed morphometric measurements on vascular trees in different organs of different mammalian species and the scale factors $\nu$, $\delta$, and $\lambda$ have been deduced (Kassab 2000). These data are overall not conclusive with respect to the scale factors. The $\ln(\beta)/\ln(\delta)$ ratios range from less than −1 to more than +1.4 corresponding to a decreasing or strongly increasing volume with the generation index, respectively. Alternatively, $\ln(\beta)/\ln(\delta)$ can be determined from equation (10) provided that the fraction $f = V_{r_l,r_u}/V_{\text{tree}}$ of blood residing in a range of radii $r_l$ to $r_u$ is known from measurement:

$$f \cdot \left(\frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} - 1\right) - \frac{\ln(r)}{\ln(r_{\text{min}})} + \frac{\ln(r_{\text{max}})}{\ln(r_{\text{min}})} = 0$$

The fraction of $f = 25\%$ of the blood in vascular trees assumed to be located in large vessels (see preceding section) is consistent with a ratio of $\ln(\beta)/\ln(\delta) = 0.38$ if ‘large’ is associated with diameters exceeding 5 mm. The ratios necessary to expect 25% of the blood in large vessels are 0.25 for diameters larger than 4 mm and 0.5 for diameters larger than 5.7 mm.

Additional information is obtained from morphometric studies on human vascular trees. Measurements of complete vascular trees in a human organ have been performed for the lungs by two different groups with consistent results regarding the fraction of blood residing in microvascular structures. The fraction of blood in the smallest vessels integrated up to the generation with mean diameter 0.06 mm was reported to be 7.0% (Horsfield 1978) and 7.8% (Huang et al 1996) in arterioles and 9.1% (Horsfield and Gordon 1981) and 6.4% (Huang et al 1996) in venules. The fraction expected from equation (11) in the diameter range from 0.01 to 0.06 mm is 12.2% with $\ln(\beta)/\ln(\delta) = 0.25$, 7.6% with $\ln(\beta)/\ln(\delta) = 0.38$, and 4.7% with $\ln(\beta)/\ln(\delta) = 0.5$; which supports a value of $\ln(\beta)/\ln(\delta) = 0.38$.

The scale factors reported in (Kassab 2000) for the entire trees yield $\ln(\beta)/\ln(\delta)$ ratios of 0.40 (Horsfield 1978) and 0.17 (Huang et al 1996) for pulmonary arteries and 0.42 (Horsfield and Gordon 1981) and 0.27 (Huang et al 1996) for pulmonary veins.
The value of ln(β)/ln(δ) = 0.38 is consistent with the gross distribution suggested in (ICRP89 2002) as well as with the results of the cited morphometric studies of human vascular trees and is, therefore, adopted for our calculations as the most probable ratio. Additional data are generated for ratios 0.25 and 0.5 to show the influence of the parameter on the blood absorbed doses.

2.4. The coefficients of self-irradiation $S_{BL\leftrightarrow BL}(r)$

The radius dependent coefficients $S_{BL\leftrightarrow BL}(r)$ (unit: Gy·s$^{-1}$·Bq$^{-1}$·ml) were approximated as suggested in (Hänscheid et al 2014) by empirical functions of the form

$$S_{BL\leftrightarrow BL}(r) = \frac{E_\beta}{\rho} \left( 1 - \frac{1}{a_\beta \cdot r^b + c_\beta} \right)$$

(12)

for β particles originating from the blood and

$$S_{BL\leftrightarrow BL}(r) = \frac{E_\gamma}{\rho} \left( 1 - \frac{1}{a_\gamma \cdot r + c_\gamma} \right)$$

(13)

for photons. In equations (12) and (13), the lumen radius $r$ is expressed in mm and $\rho$ (unit: g·ml$^{-1}$) is the blood density. $E_\beta$ and $E_\gamma$ (unit: J·Bq$^{-1}$·s$^{-1}$) denote the mean energies emitted per unit transformation by particle and photon radiation, respectively. The constants $a_\beta$, $b_\beta$, $c_\beta$, $a_\gamma$, and $c_\gamma$ were taken from (Hänscheid et al 2014) or, for Sm-153, were deduced as described in (Hänscheid et al 2014). Table 2 lists the values for the constants used in the present calculations.

3. Results

The contributions to the average absorbed dose rates to the blood per nuclear disintegration per ml of blood $S_{\nu\rightarrow BL \leftarrow BL}$ and $S_{\nu\rightarrow BL \leftarrow BL}$ were calculated for the seven pools, heart chambers, ascending aorta, descending aorta, venae cavae, pulmonary artery, vascular trees, and capillaries, according to equation (3) by numerical integration; the total absorbed dose rates $S_{BL\leftrightarrow BL}$ were determined by equation (2) for ratios ln(β)/ln(δ) of 0.38, 0.25, and 0.5 for each nuclide. The total absorbed dose rates are listed in table 3 together with the dose rates from self-absorption of particle radiation in vascular trees $S_{vascular tree \leftrightarrow BL \leftarrow BL}$ which are essential to estimate the energy imparted outside the vessel lumen. In addition, the mean energies emitted by particle radiation per unit transformation $E_\nu$ are shown for comparison.

The highest $S_{BL\leftrightarrow BL}$ rates with values exceeding 5·10$^{-11}$ Gy·s$^{-1}$·Bq$^{-1}$·ml are observed for Ga-68 and Y-90. The other isotopes range from 1 to 5·10$^{-11}$ Gy·s$^{-1}$·Bq$^{-1}$·ml except for Tc-99m for which the coefficient is lower by an order of magnitude. Photon radiation contributes 1.1 to 1.2·10$^{-11}$ Gy·s$^{-1}$·Bq$^{-1}$·ml to the total dose rate for positron emitters but significantly less for the other nuclides. The photon contribution is negligible for Y-90; our Monte-Carlo simulations performed to deduce the S-values (Hänscheid et al 2014) indicated that the contribution from bremsstrahlung is well below 0.1% of the total dose rate.

High absorbed dose rates are mainly due to particle radiation which is locally absorbed. From the total energy emitted by particle radiation, $E_\nu$, the fraction remaining in the blood decreases with increasing mean β-energy. The fraction absorbed in the blood is lowest for Y-90 with 37% of $E_\beta$ and highest for Tc-99m with 80% of $E_\beta$. The correspondent values in vascular trees, which are important for the absorbed dose to organs, range from 30% for Y-90 to 82% for Tc-99m. The rates of absorbed dose in vascular trees, which contribute dominantly
Table 2. Constants used to determine the coefficients for self-irradiation $\widehat{S}_{BL \rightarrow BL}(r)$ and $\widehat{S}_{BL \rightarrow BL}(r)$. The values were taken from Hänscheid et al (2014) or, for Sm-153, deduced as described in Hänscheid et al (2014). The energies $E_{\beta}$ and $E_\gamma$ are from Eckerman and Endo (2008).

<table>
<thead>
<tr>
<th></th>
<th>Y-90</th>
<th>I-131</th>
<th>Lu-177</th>
<th>Sm-153</th>
<th>Tc-99m</th>
<th>C-11</th>
<th>F-18</th>
<th>Ga-68</th>
<th>I-124</th>
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<tbody>
<tr>
<td>$E_{\beta}$ (mJ·Bq$^{-1}$·s$^{-1}$)</td>
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<td>0.0046</td>
<td>0.0046</td>
<td>0.0046</td>
<td>0.0044</td>
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</table>
Table 3. Total absorbed dose rates $\hat{S}_{BL}$ determined for different ratios $\ln(\beta)/\ln(\delta)$ together with the dose rates from self-absorption of particle radiation in vascular trees $\hat{S}_{BL \to \beta BL}$. The mean energies emitted by particle radiation per unit transformation $E_\beta$ are shown for comparison.

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>$\hat{S}_{BL \to BL}$ (Gy·s$^{-1}$·Bq$^{-1}$·ml)</th>
<th>$\hat{S}_{BL \to \beta BL}$ (Gy·s$^{-1}$·Bq$^{-1}$·ml)</th>
<th>$E_\beta$ (mJ·Bq$^{-1}$·s$^{-1}$)</th>
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<tr>
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<td>0.25</td>
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<td>1.72E-11</td>
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<td>Sm-153</td>
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<td>3.14E-11</td>
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<tr>
<td>Tc-99m</td>
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<td>Ga-68</td>
<td>5.94E-11</td>
<td>5.43E-11</td>
<td>6.38E-11</td>
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<td>I-124</td>
<td>2.55E-11</td>
<td>2.41E-11</td>
<td>2.68E-11</td>
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</tbody>
</table>
to the blood volume with about 77% of TBV, increase with increasing ratio \( \ln(\beta)/\ln(\delta) \), that is, decreasing fraction of blood in small vessels. Isotopes with a high contribution from high energy \( \beta \) radiation to the total dose rate are more sensitive to changes in \( \ln(\beta)/\ln(\delta) \) than emitters of low energy particles as those are almost completely absorbed even in small vessels. The largest shift of the mean dose rate due to alteration of \( \ln(\beta)/\ln(\delta) \), from 0.38 down to 0.25 or up to 0.50, is observed for \( {\gamma}-90 \) with relative changes of −10% and +8%, respectively.

4. Discussion

In the present study, we provide estimates of the absorbed dose rates to the blood from blood-borne activity for radionuclides frequently used in nuclear medicine. The results have a major impact on the dosimetric assessment of radiopharmaceuticals for which blood is considered to be a source organ. The total dose rate \( S_{BL \leftarrow BL} \) is dominated by the particle contribution \( S_{BL \leftarrow \beta BL} \) in nuclides with considerable \( e^{-}/\beta \) emission because, due to its short range, a major fraction of the energy emitted by particle radiation remains within the lumen of the blood vessel. This blood self-absorption of radiation should be corrected for in the assessment of radiation absorbed doses from radiopharmaceuticals. A good example is the dosimetry of erythrocytes (RBCs) containing \(^{11}\)CO-labeled hemoglobin (Hänscheid et al 2014). The activity bound to the RBCs remains in the blood and, according to a dose calculation (Hänscheid et al 2014) using OLINDA/EXM (Stabin et al 2005), induces an effective dose of 6 µSv/MBq with 2 µSv/MBq being due to absorption of photons and 4 µSv/MBq being attributed to beta radiation. However, while energy emitted by particles from C-11 in systemic capillaries (5% of TBV) will be almost completely deposited in organ tissue outside the vessel, more than half of the energy emitted in systemic blood in vascular trees (68.9% of TBV; table 1) remains in the blood (\( E_{\beta} = 6.16 \times 10^{-11} \text{mJ} \cdot \text{s}^{-1} \cdot \text{Bq}^{-1}, \tilde{S}_{BL \leftarrow \beta BL} = 3.14 \times 10^{-11} \text{Gy} \cdot \text{s}^{-1} \cdot \text{Bq}^{-1} \cdot \text{ml}; \text{table 3} \)). A major fraction of the energy leaving the lumen will be deposited in the blood vessel walls; this fraction cannot be determined unless the vessel wall thickness as a function of the lumen radius is known. Less than 50% of the particle energy is deposited in organ tissues, the actual absorbed dose by \( \beta \) radiation is less than 2 µSv/MBq. The effective dose from \(^{11}\)CO-labeled RBCs is overestimated by 50% if the activity in the blood is attributed to the organ tissues.

Another simple example is \(^{99m}\)Tc-apcitide, a peptide used for the detection of acute venous thrombosis in the lower extremities. A biokinetic model with distribution in circulating blood and an effective half-time equal to the physical half-time is assumed in (ICRP106 2008). OLINDA/EXM attributes 64% of the effective dose to photon and 36% to beta radiation. The actual beta contribution is much lower because 82% of the energy released by particle radiation is deposited in the blood (see above); the effective dose is overestimated by 42%.

The present findings are also interesting for dosimetry in radionuclide therapy. In their widely used formalism for estimating the patient-specific maximum tolerated activity (corresponding to a 2 Gy blood absorbed dose) for \(^{131}\)I-iodide treatment of metastatic thyroid cancer, (Benua et al 1962) assumed that the \( \beta \)-particle energy emitted by \(^{131}\)I is completely absorbed in blood. Our calculations suggest that only about two thirds of the beta energy from blood-borne \(^{131}\)I is absorbed in blood. However, an exact blood dosimetry of \(^{131}\)I-iodide should take into account that iodide distributes in the pool of exchangeable body water and that beta-radiation from \(^{131}\)I in organs and vessel walls will add to the absorbed dose to the blood. In general, blood self-absorption should be considered for dose estimates in organs and in the blood if the activity concentration in the blood is considerably higher than in the organ parenchyma.

Our results are based on Monte-Carlo calculations of self-irradiation of blood in vessels and assumptions on the blood-volume distribution as a function of the vessel radius. A discussion
of the uncertainties of the vessel radius dependent coefficients of self-irradiation can be found in (Hänscheid et al 2014). The highest uncertainty is introduced by the assumptions regarding the distribution of blood vessels in the entire human body. In order to obtain a reasonable blood-volume distribution we have partitioned the total blood volume into seven separate pools. The error introduced in \(\hat{S}_{BL\leftrightarrow BL}\) from uncertainties in the size of the large vessels, heart chambers, aorta, venae cavae, and pulmonary artery is small because the typical sizes of these pools are well known, the fraction of blood residing in these vessels is only about 16% of TBV, and the vessel diameters are much larger than the typical range of the particle. The values of the \(\hat{S}_{BL\leftrightarrow \beta BL}\) are almost identical with low uncertainties for large vessels with near-total absorption of the \(\beta\) radiation.

A considerable fraction of TBV resides in small vessels. The total amount of blood in small vessels with diameters less than 5 mm is 3429 ml or about 65% of TBV (7% of TBV in capillaries and 58% of TBV in vascular trees), which is 4.6% of a total body mass of 75 kg.

The constants listed in table 2 used to estimate the dose rate values are deduced from Monte-Carlo calculations for isolated vessels (Hänscheid et al 2014), an assumption which obviously does not hold for small vessels separated by distances smaller than the range of the \(\beta\) radiation. While cross-fire can be neglected for large feeding vessels with near-total absorption of the \(\beta\) radiation, the dose rates for capillaries and small vessels in vascular trees might be significantly underestimated especially for nuclides with high particle energies when cross-fire from other small vessels is neglected. In order to calculate an upper limit for the effect of cross-fire in \(\hat{S}_{BL\leftrightarrow BL}\) we have determined how much energy leaves the small vessels by \(\beta\) radiation. We then assumed that this energy delivers a homogeneous dose rate within the tissue and that 4.6% of the energy is deposited in blood. This approach leads to a very conservative estimate for the maximum contribution from cross-fire because it neglects the decline of the dose rate outside the vessels. The maximum error due to the effect of cross-fire assessed in this way was about 7% of \(\hat{S}_{BL\leftrightarrow BL}\) for Y-90, 5% for Ga-68, and 3% or less for the other nuclides. Our data are not corrected for the effect of cross-fire because the necessary calculations to deduce reliable values depend on assumptions on the spatial distribution of the blood within the tissue, which is beyond the scope of the present study.

Most of the blood in the human, about 77% of TBV, resides in vascular trees with diameters of about 10 mm or less. Therefore, the coefficient \(\hat{S}_{vascular\ tree}\), which depends on the vessel distribution in vascular trees, is of major importance for the estimation of \(\hat{S}_{BL\leftrightarrow BL}\). Up to now, the ICRP has not provided detailed information on the distribution of the total luminal cross-sectional area \(F_{vascular\ tree}(r)\) in vascular trees. Only rough estimates have been suggested on the amounts of blood in large and small vessels (ICRP89 2002), which we used to deduce a value of \(f = 25\%\) for the fraction of blood in the vascular trees assumed to be located in large vessels. As this information is not sufficient for reliable blood dose estimates we have combined it with the assumption that vascular trees are quasi fractal branching networks characterized by the ratio \(\ln(\beta)/\ln(\delta)\). The ratios \(\ln(\beta)/\ln(\delta)\) deduced with \(f = 25\%\) and equation (11) are consistent with results of morphometric studies of vascular trees in the human lung. It is, however, not certain that the same ratio \(\ln(\beta)/\ln(\delta)\) is characteristic for vascular trees in all organs and tissues throughout the body. Provided that the theory is valid, the relative error introduced in \(\hat{S}_{BL\leftrightarrow BL}\) from the uncertainty of \(\hat{S}_{vascular\ tree}\) is expected to be about 10%.

5. Conclusion

A reliable estimate of the absorbed dose rates to the blood originating from activity in the blood must be based on reasonable assumptions on the blood-volume distribution as a function
of the vessel radius. The present study suggests a distribution which is consistent with the gross data provided by (ICRP89 2002) and the theory that vascular trees are quasi fractal branching networks, which is supported by morphometric measurements. The dose rate coefficients deduced from this distribution for radionuclides widely used in nuclear medicine can be used for dosimetric assessments in diagnostics, targeted radionuclide therapy, and for biodosimetric studies.

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