Validation of an Analytical Expression for the Absorbed Dose from a Spherical β Source Geometry and Its Application to Micrometastatic Radionuclide Therapy

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Abstract

The purpose of this study was to validate an analytical expression for the absorbed-dose calculation from the spherical source of β-emitting radionuclides and to apply it to micrometastases treated with radiolabeled monoclonal antibodies. The self-absorbed fractions from I-131 and P-32 uniform spherical sources were calculated using the analytical expression introduced by P. K. Leichner (J. Nucl. Med., 35: 1721-1729, 1994). The calculated absorbed fractions were compared with previously reported values and were found to be in reasonable agreement, with a maximum difference of 15% for smaller masses and a long-range β emitter. The expression was subsequently applied to estimate the absorbed dose within spheroid models with nonuniform penetration of radiolabeled antibody. The corresponding absorbed dose for I-131 was compared with reported micro-thermoluminescence dosimeter measurements and found to be in good agreement. This work has independently substantiated the methodology outlined by Leichner and may be reliably incorporated into new software developments for radionuclide dosimetry treatment planning.

Introduction

Radiolabeled monoclonal antibodies have been used in the treatment of micrometastatic tumors (1). The radiation absorbed dose to micrometastases is estimated by modeling micrometastases as a multicell spheroid (2). Because of the small size of micrometastases, the radionuclides of choice are those with α or β emissions. Several calculational schemes have been proposed to compute the absorbed dose for spherical geometry from β emitters based on PSFs (3-7). However, these calculational schemes either approximate the absorbed dose or require sophisticated numerical computations. Therefore, introduction of a simple but accurate formalism is warranted.

An empirical PSF3 for β-particle dosimetry was introduced by Leichner (8) based on Berger’s (9) tabulated dose distributions for point-sources in water. Later, Leichner (10) generalized his formalism to photon emitters as well as β particle emitters and derived an analytical expression for absorbed dose from uniform spherical source distributions. He tested his analytical expression by comparing the results with existing Monte Carlo calculations for photon dose, but he did not make a similar comparison for β emitters.

In this study, we have calculated self-absorbed fractions within a uniform spherical source distribution for medium- and long-range energy β emitters, using Leichner’s analytical expression. The results were compared with values reported by Berger (11). The expression was subsequently applied to estimate the absorbed dose within micrometastases treated with radiolabeled antibodies with various degrees of penetration. The results were compared with micro-TLD measurements performed by Langmuir et al. (12) in a spheroid.

Methods

In accordance with the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine formalism, the absorbed dose rate at point P in Fig. 1 from a volume-containing radionuclide may be written as:

\[ D(s) = A_s \sum \Delta \phi_i(s) \]  

where \( A_s \) is the specific activity (MBq/kg or μCi/g), \( \Delta \) is the energy emitted per disintegration (mGy-kg/MBq-s or radg/μCi-h), and \( \phi_i(s) \) is the dimensionless absorbed fraction for ith radiation component. The absorbed fraction for a β-emitter radionuclide source is derived by Leichner (10) from his PSF, \( G(r) \), as:

\[ \phi(s) = \frac{\int G(r) dv}{4\pi r^2} \]  

where

\[ G(r) = G_0 \{ e^{-\mu r} + \frac{d_1(\mu r) + d_2(\mu r)^2 + d_3(\mu r)^3 + d_4(\mu r)^4}{\mu r} \} \]  

In the above formula, \( d_1, d_2, d_3, \) and \( d_4 \) are Leichner’s fitting parameters to Berger’s point-dose tables and \( \mu \) is the apparent absorption coefficient (cm^2/g) for the radionuclide. The analytical solution to the integral in Eq. B is for points inside of a uniformly distributed sphere is derived as:

\[ \phi(s) = \phi_0(s) + \phi_1(s) + \phi_2(s) + \phi_3(s) \]  

The complete solution can be found in Ref. 10 (Leichner, J. Nucl. Med., 1994; the minus sign inside the parentheses of the first exponential term in Eq. A21 in Ref. 10 should be a plus sign).

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1 The abbreviations used are: PSF, point-source function; TLD, thermoluminescence dosimeter.

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Fig. 1 Notations used in the derivation of absorbed fraction at point P from spherical source geometry.

where

\[ \phi_b(s) = \frac{1}{4\mu^2 s^2} \{4\mu' s + [1 + \mu' (R - s)]e^{-\mu' (R + s)} \]

\[ - [1 + \mu' (R + s)]e^{-\mu' (R - s)} \}

\[ + \frac{R^2 - s^2}{4s} \{ E_1[\mu' (R - s)] - E_0[\mu' (R + s)] \} \]  

\[ + \frac{R^2 - s^2}{4s} \{ E_1[\mu' (R - s)] - E_0[\mu' (R + s)] \} \]  

\[ - E_1[\mu' (R + s)] \]  

Equations E and F are used for a comparison of the self-absorbed fractions with two different methods.

The above expressions are all based on activity uniformly distributed within the entire sphere volume. In animal and humans, the radionuclide uptake within the tumor is thought to decrease radially toward the center in a linear or exponential fashion. Because the solution of the equations for linear or exponential radionuclide uptake does not yield an analytical expression, it has to be carried out numerically. However, in a special case in which activity is concentrated uniformly within a spherical shell with outer and inner radii \( R_1 \) and \( R_2 \), the self-absorbed fraction can still be obtained from Eq. D by subtracting two concentric spherical terms.

Results

The self-absorbed fractions for sphere radii ranging from 0 to 10 mm, calculated based on Leichner and Berger methods, are presented in Figs. 2 and 3 for P-32 and 1-131, respectively. The distance from a point-source at which 90% of the energy is deposited, \( r_{90} \), is 3.51 and 0.822 mm for P-32 and 1-131, respectively. Therefore, the selected radionuclides encompass medium- to long-range \( \beta \) emissions. As it can be seen, the values are in good agreement with each other, particularly for 1-131. The maximum differences between the two methods are 15% and 10% for P-32 and 1-131, respectively. We also performed the same calculation directly by point-to-point numerical integration using the Leichner PSF, which yielded similar results within 4%, indicating that the steps taken in arriving at Eq. D were correct.

The calculated-dose-rate profiles in a 0.5-mm radius sphere for varying degrees of I-131 penetrations are depicted in Fig. 4. The results can be compared with the Langmuir et al. (12) experiment, in which 0.5-mm-radius LS174T human colon carcinoma spheroids were treated with I-131-labeled antibodies. The radionuclide penetration was estimated by autoradiography to be 0.05 mm. Mini-TLDs—implanted in the spheroids and removed after 36 days—were sectioned and read to obtain the dose profile. The amount of bound I-131 activity at the time of TLD insertion was estimated to be 134 nCi/mm³ spheroid volume. The cumulative mean absorbed dose at 0.025 mm from the surface was measured to be 125 Gy with a SD of 14% of the mean dose. The corresponding calculated dose from Fig. 4 is 125.4 Gy, which is in good agreement with the measurement.
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**Discussion**

This study indicated that self-absorbed fractions for spheres of various sizes computed with the Leichner expression were in reasonable agreement with Berger’s results. Leichner’s analytical PSF reproduced Berger’s tables to better than 3% within $r_{50}$ for P-32. Therefore, the difference between self-absorbed fractions in the two methods can mainly be attributed to different integration processes. Because Leichner used direct-volume element integration, it can be inferred that Berger’s geometrical reduction factor only approximates the electron interactions within the sphere volume. The expression was also used for the first time in comparison with measured data with TLDs within a spheroid. The agreement was very good considering the measurement errors that occur at this small scale.

PSFs are still widely used for absorbed-dose calculations because they can easily be implemented into computational programs. Leichner’s PSF provides considerable calculational advantage for radionuclide dose calculations over other formalisms because it uses the same formalism for both photon and electron sources, and it can be integrated analytically for most regular geometries and source-activity distributions. Another widely used dose-point function has been introduced by Prestwich et al. (13) and is based on an electron-transport equation for selected $\beta$-emitter radionuclides with a controlled cutoff distance. However, Prestwich’s PSF with its complex form cannot be integrated analytically for regular geometries.

The application of Leichner’s expression is not restricted to regular geometries and uniform-source distributions. It can also be used for dosimetry treatment planning of nonuniform activity distributions in which the region of interest is divided into source and target voxels (14). At present, the alternative method of direct Monte Carlo calculation is computationally time consuming (15). Thus, Leichner’s expression may be reliably incorporated into new software developments for radionuclide dosimetry treatment planning.

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