"The use of low energy photons in brachytherapy : dosimetric and microdosimetric studies around 103Pd and 125I seeds"

Reniers, Brigitte

ABSTRACT

The general context of this work is the use of low energy photon sealed sources in brachytherapy. We have worked in particular on two isotopes: I-125 (mean energy of 27 keV) and Pd-103 (mean energy of 21 keV). The sealed sources are prepared as cylindrical seeds 4.5 mm in length and 0.8 mm in radius. Even if the external dimensions are standard, the internal design can be extremely different from one model to the other as the manufacturers try to improve the dosimetric characteristics of their sources. These isotopes are used mainly as permanent implants for prostate tumours but can also be used in the treatment of eye tumours. Compared to the higher energy photon sources, they offer the physical advantages of a safer manipulation from a radioprotection point of view and of the reduction of the dose to the surrounding healthy tissues. When performing a clinical treatment, it is absolutely mandatory to be able to report very precisely various parameters that can have an impact on the patient treatment outcomes. These parameters are, for example, the prescribed dose, the doses at different organs, the degree of uniformity that has been achieved on the target or some dose-volume information. The brachytherapy treatment planning systems (TPS) also permit more and more to conform the treatment to the patient anatomy, like in external treatments. In the case of prostate tumours, it has been possible for a few years, using ultrasound imaging, to check the positioning of the seeds and to calculate the dose distribution in real time during the implantation procedure. It is clear t...

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II. Theoretical background: definitions and protocols

This chapter is dedicated to the presentation of the physical concepts used in this work. This is intended to present the principal definitions and protocols used in this thesis in order to make the understanding of the results easier even if the reader is not familiar with each topic.

A. Dosimetric quantities

From a practical point of view, the transport of particles must be reduced to statistical values defining the field of radiation or a mean effect on the medium. These values are the basic quantities used in dosimetry and are defined in the following sections (ICRU 33).

1. Fluence and Energy Fluence

The fluence Φ at a given point P in a medium is defined as the ratio dN/da where d*N* is the number of particle incident to a sphere of cross sectional area da, usually expressed in units m^{-2}.

The fluence rate, or flux density, is defined as the time derivative of the fluence:

$$j = \frac{d\Phi}{dt} = \frac{d}{dt}\left(\frac{dN}{da}\right) \qquad \textbf{(1)}$$

The fluence contains only information regarding the number of particles. However, it is often interesting to have details about the field, especially about the energy. The easiest way to obtain such a knowledge is to use the expectation value of the total energy (excluding the rest mass) carried by the *N* particles striking the finite sphere surrounding P, called *radiant energy*, *R*. If the sphere at P is again reduced to an infinitesimal with a sectional area *da,* the *energy fluence* is then defined by:

$$\Psi = \frac{dR}{da} \qquad \textbf{(2)}$$

in units J/m^2.

Like for the fluence rate, the energy flux density or energy fluence rate is defined as:

$$y = \frac{d\Psi}{dt} = \frac{d}{dt}\left(\frac{dR}{da}\right) \qquad \textbf{(3)}$$

in units W/m^2

It is possible to express these quantities as differential distributions. The variables can be either the solid angles, $d\Psi / d\Omega$, or the energy, $d\Psi / dE$. If the energy is chosen, the resulting differential distribution is called the energy spectrum, $\Psi(E)$. In this case, the energy fluence is expressed as:

$$\Psi = \int_{E=0}^{E=E_{\max}} \Psi(E)dE = \int_{E=0}^{E=E_{\max}} E\Phi(E)dE \qquad \textbf{(4)}$$

2. <u>Kerma</u>

The kerma, K, describes the energy transferred to charged particles by uncharged ionising particles per unit mass of the absorbing medium (Kinetic Energy Release in Matter). This nonstochastic quantity is relevant for fields of indirectly ionising radiations (photons or neutrons). It is the quotient of dE_{tr}/dm, where dE_{tr} is the sum of the initial kinetic energies of all the charged ionizing particles liberated by uncharged ionizing particles in a material of mass *dm*:

$$K = \frac{dE_{tr}}{dm} \qquad \textbf{(5)}$$

This quantity is usually expressed in Gray (Gy) = J/kg

The kerma can be related to the energy fluence Ψ of the incident radiation by

$$K = \Psi \cdot \left(\frac{m_{tr}}{r} \right)_{E,Z} \qquad \textbf{(6)}$$

with $(m_{tr} / r)_{E,Z}$ the *mass energy transfer coefficient* for an energy *E* and a material of atomic number *Z*. r is the density of the medium. This coefficient gives the fraction of photon (or neutron) energy transferred into kinetic energy of charged particles per unit thickness of absorber. It includes consequently the energy that these secondary particles will eventually radiate by bremsstrahlung.

It is also possible to express the kerma by:

$$K = \Psi \cdot \left(\frac{m_{en}}{r} \right)_{E,Z} /(1-g) \qquad \textbf{(7)}$$

where g is the fraction of the electron energy lost into radiative processes and m_{en} / r is the *mass energy absorption coefficient*. Deducing from the previous formula, kerma can be expressed by:

$$K = \Psi \cdot \left(\frac{m_{en}}{r} \right) + \Psi \cdot \left(\frac{m_{en}}{r} \right) \cdot \left(\frac{g}{1-g} \right) = K_{col} + K_{rad} \qquad \textbf{(8)}$$

where K_{coll} is the collisional kerma and K_{rad} is the radiative kerma.

In low atomic number material and for low energy electrons, g is very small and as a result, K_{rad} can be neglected.

For a spectrum of photon energy fluence $\Psi(E)$, the kerma can be expressed as:

$$K = \int_{E=0}^{E=E_{max}} \Psi(E) \cdot \left(\frac{m_{tr}}{r} \right)_{E,Z} dE \qquad \textbf{(9)}$$

3. <u>Absorbed dose</u>

The absorbed dose describes the mean energy imparted to matter per unit mass by all kinds of ionising radiations but delivered by charged particles. The definition of the absorbed dose is the quotient

$$D = d\bar{e} / dm \qquad \textbf{(10)}$$

in units Gy=J/kg

where *m* is the mass of a finite volume of matter *V* and $d\bar{e}$?is the mean energy imparted to a matter of mass *dm*. The *energy imparted* is defined as:

$$e = (R_{in})_u - (R_{out})_u + (R_{in})_c - (R_{out})_c + \sum Q \qquad \textbf{(11)}$$

- $(R_{in})_u$ is the radiant energy of uncharged particle entering the volume *V*
- $(R_{out})_u$ is the radiant energy of uncharged particle leaving the volume *V*
- $(R_{in})_c$ is the radiant energy of charged particle entering the volume *V*
- $(R_{out})_c$ is the radiant energy of charged particle leaving the volume *V*
- $åQ$ is the net energy derived from rest mass in the volume *V*

If each charged particle of a given type and energy leaving the volume is replaced by an identical particle of the same energy entering the volume in term of expectation value, the condition is called *charged particle equilibrium*. In the presence of full charged particle equilibrium, the dose absorbed by a medium can be calculated from the fluence and the weighted mean energy absorption coefficient, $\bar{m}_{en} / r$:

$$D = \Psi \cdot \bar{m}_{en} / r \qquad \textbf{(12)}$$

In the case of low energy photons passing through a low Z material, bremsstrahlung is negligible and with full electronic equilibrium, combining equation (12) and equation (8), the kerma can approximate the absorbed dose.

B. Microdosimetric quantities

1. Linear Energy Transfer: LET

As LET was historically the first quantity that has been used to relate energy deposition with RBE and is still in use, it is defined in this section, even if strictly speaking, it is not a microdosimetric quantity.

Linear energy transfer (*LET* or *L*) is defined as the ratio $L=dE/dx$, where dE is the mean energy loss of a charged particle in electronic collisions along a short section dx of its path. As tracks have lateral extensions due to delta electrons, LET is often replaced by restricted LET, L_Δ, defined as a LET where the energy transfers to the secondary electrons taken into account are limited to a maximum value Δ. A typical value for *D* is 100 eV, roughly corresponding to a residual electron range in water of 5 nm, that in its turn corresponds roughly to the diameter of the DNA helix.

2. Energy deposit ε_i

The energy deposit, e_i, is the energy deposited in a single interaction *i* (J or eV).

$$e_i = T_{in} - T_{out} + Q \qquad \textbf{(13)}$$

- T_{in} is the energy of the incident ionizing particle (excluding rest mass)
- T_{out} is the sum of the energies of all ionizing particles leaving the interaction (excluding rest mass)
- Q are the changes of the rest mass energy of the atom and all particles involved in the interaction (Q>0: decrease of rest mass; Q<0: increase of rest mass)

3. Energy imparted ε

The contribution from all energy deposits e_i in a volume of interest *V* is the *energy imparted e* :

$$e = \sum_i e_i \qquad \textbf{(14)}$$

4. Specific energy z

The specific energy, *z*, is the ratio of the energy imparted *e* to the mass *m* of the volume *V* (Gy):

$$z = \frac{e}{m} \qquad \textbf{(15)}$$

z is a stochastic quantity, like e_i and *e*, and can be described by a cumulative probability distribution function *F(z)* and a corresponding probability distribution function *f(z)* related by :

$$f(z) = \frac{dF(z)}{dz} \qquad \textbf{(16)}$$

Some non-stochastic quantities can be described in order to summarize the information like:

- The *mean specific energy* $\bar{z}$ is defined as the expectation value of *z*:

$$\bar{z} = \int_0^\infty z\, f(z) dz \qquad \textbf{(17)}$$

- The *frequency-mean specific energy* in the case where specific energy is deposited in a single event, $\bar{z}_F$:

$$\bar{z}_F = \int_0^\infty z\, f_1(z) dz \qquad \textbf{(18)}$$

with the subscript '1' denoting a single event distribution.

5. Lineal energy y

The lineal energy *y* is defined as the ratio of the imparted energy, ε, to the mean chord length of the target volume V, l:

$$y = \frac{e}{\bar{l}} \qquad \textbf{(19)}$$

This quantity is usually expressed in keV/µm or MeV/cm.

The mean chord length is given by the ratio $\bar{l} = 4V/A$ for a convex body of volume *V* and surface area A. For a sphere with diameter *d* this reduces to $\bar{l} = (2/3)d$.

Like z, y is a stochastic quantity. So the same kind of function and non stochastic quantities can be defined for y:

- The probability distribution function of *y*, *f(y)* known as the lineal energy distribution and its cumulative distribution *F(y)*.
- The expectation value $\bar{y}_F$ known as the *frequency mean lineal energy:*

$$\overline{y}_F = \int_0^{\infty} y \; f(y) dy \qquad \textbf{(20)}$$

- It is also useful to introduce the *dose distribution of* y, *d(y)*, defined as the fraction of the dose delivered with $y \in \{y, y+dy\}$. The expectation value of *y(d)*, $\overline{y}_D$, is known as the *dose mean lineal energy*

$$\overline{y}_D = \int_0^{\infty} y \, d(y) dy \qquad \textbf{(21)}$$

6. Microdosimetric spectra

These statistical distributions are usually called microdosimetric spectra. The lineal energy, however, varies widely for a given radiation type in a site with given dimensions. It is therefore common to plot the data on a logarithmic lineal energy axis. Taking into account the equalities (22) and (23), we see that for these semi-logarithmic plots, the area under the curve delimited by any two values of *y*, gives the *fraction of events* that have lineal energy in that specific *y*-range for equation (22) or the *fractional dose* delivered by particles that have lineal energy in that specific *y*-range for equation (23).

$$\int_{y_1}^{y_2} f(y) dy = \int_{y_1}^{y_2} [y \; f(y)] d \ln(y) \qquad \textbf{(22)}$$

$$\int_{y_1}^{y_2} d(y) dy = \int_{y_1}^{y_2} [y \, d(y)] d \ln(y) \qquad \textbf{(23)}$$

C. Dose Formalism for radioactive seeds : TG-43

The dose distribution around the seed, measured or calculated, has been analyzed using the dose formalism recommended by the AAPM in the report of the TG43 (1995) (Nath et al. 1995). This formalism is described in terms of a polar coordinate system (see Figure 15) where the reference point (r_0, θ_0) is chosen on the transverse axis ($\theta = 90^\circ$) at 1cm from the centre of the source. The reference medium is liquid water.

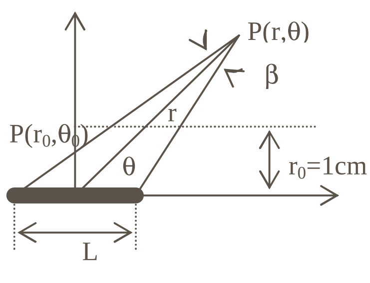

Figure 15: Coordinate system used for TG-43 formalism

In that system, the dose rate at any point $P(r,q)$ around the source can be expressed as:

$$\dot{D}(r,q) = S_k \times \Lambda \times \frac{G(r,q)}{G(r_0,q_0)} \times g(r) \times F(r,q) \qquad \textbf{(24)}$$

where S_k = air kerma strength of the source (m Gy m^2 h^{-1} or cGy cm^2 h^{-1} or U)

Λ = dose rate constant
G(r,θ) = geometry factor
g(r) = radial function
F(r,θ) = anisotropy function

1. <u>Dose rate constant, Λ</u>

The dose rate constant Λ is defined as the dose rate in water at the reference point (r_0,q_0) for a unit air kerma strength source:

$$\Lambda = \frac{\dot{D}(r_0,q_0)}{S_k} \qquad \textbf{(25)}$$

Unlike all the other functions that give only relative data, the dose rate constant is an absolute quantity. The unit is $cGyh^{-1}U^{-1}$. This factor allows transforming the relative information for any point in the space surrounding the source into an absolute dose value. Therefore, it is important to determine this factor as precisely as possible.

2. <u>Geometry factor, *G(r,q)*</u>

The geometry factor takes into account the spatial distribution of the activity within the source ignoring scattering and attenuation in the encapsulating material and in the medium. It is defined as:

$$G(r,q) = \frac{\int_V \left[r(r')dV' / |r' - r|^2 \right]}{\int_V r(r')dV'} \qquad \textbf{(26)}$$

where *r(r)* is the density of radioactivity at the point $p(\vec{r}) = p(r,q)$ within the source and *V* denotes the integration over the source core.

As recommended in TG-43, for a seed, it is possible to use the line source approximation (see equation (27)). This approximation tends to the point source approximation for distances much larger than the dimension of the source:

$$G(r,q) = \frac{b}{L \times r \times \sin q} \xrightarrow{r >> L} \frac{1}{r^2} \qquad \textbf{(27)}$$

where (see Figure 15):

L is the active length of the source, 3.7mm for the IBt source;

β is the angle (given in radians) subtended by the active source with respect to the point $P(r,\theta)$.

3. <u>Radial dose function, g(r)</u>

The radial dose function defines the fall-off of the dose along the transverse axis of the source due to attenuation and scattering in the medium. It is also influenced by the photon filtration in the encapsulation of the source. It is normalized at the reference point (r_0,θ_0) at 1cm from the centre of the source on the transverse axis. This function is mathematically described by:

$$g(r)=\frac{\dot{D}(r,\theta_0)\times G(r_0,\theta_0)}{\dot{D}(r_0,\theta_0)\times G(r,\theta_0)} \qquad \textbf{(28)}$$

4. <u>Anisotropy function, F(r,θ)</u>

The anisotropy function gives the angular variation of the dose rate around the seed due to self-filtration, oblique filtration of the primary photons through the encapsulating material and scattering in the medium. As for the radial dose function, the presence of the geometry factor suppresses the effect of the inverse square law.

$$F(r,\theta)=\frac{\dot{D}(r,\theta)\times G(r,\theta_0)}{\dot{D}(r,\theta_0)\times G(r,\theta)} \qquad \textbf{(29)}$$

For an implant containing a large number, n, of sources randomly oriented, the dose rate to tissue can be approximated using a point source formalism. In this approximation, the dose rate at any point can be expressed using equation (30):

$$\dot{D}(r)=S_k\times\Lambda\times\frac{G_X(r,\theta_0)}{G_X(r_0,\theta_0)}\times g_X(r)\times f_{an}(r) \qquad \textbf{(30)}$$

where f_{an}, the anisotropy factor, is given by the equation (31):

$$f_{an}(r)=\frac{\int_0^{\pi}\dot{D}(r,\theta)\sin\theta\times d\theta}{2\dot{D}(r,\theta_0)} \qquad \textbf{(31)}$$

In the revised TG-43 (Rivard et al. 2004), it is recommended, when using this 1D approximation, to pay attention to the coherence between the geometry factor and the radial function in equation (30). If a point source approximation is assumed, then g(r) must have been calculated in this approximation too. That is the meaning of the subscripts *x* that have been added in the new protocol.

For ^{125}I implants this anisotropy factor varies very little with distance and can be approximated by an average distance-independent factor $\overline{f}_{an}$, called the anisotropy constant. This constant is calculated using equation (32).

$$\overline{f}_{an} = \frac{\sum_{i=1}^{n} f_{an}(r_i)}{n} \qquad \textbf{(32)}$$

This is however no longer recommended in the revision of the TG-43.

D. <u>Nederlandse Commissie voor Stralingdosimetrie (NCS) protocol for external photon beam dosimetry.</u>

This protocol has been proposed for the calibration of high energy photon beams in 1986 in the report 2 of Nederlandse Commissie voor Stralingdosimetrie (NCS) (Mijnheer et al. 1986). It is recommended by the Belgian Hospital Physicists Association (BHPA) and by the National Medical Physicists Society of the Netherlands (NVKF). Consequently, it has been used in this work for the determination of the absorbed dose in the reference medium (water) for a 6 MV photon beam produced by a linear accelerator. The photon beam was used for the calibration of the TLDs. As the absorbed dose delivered by the linear accelerator is the reference to establish the absolute dose measured by the TLDs, the protocol used for its calibration is a fundamental point in the chain of measurements. That is why it is briefly described here.

This protocol is based on the use of a set of single conversion factors ($C_{w,u}$?values calculated by application of the Bragg-Gray cavity theory) as a function of the energy for recommended ionization chambers. Only three graphite-walled ionization chambers are recommended as reference instrument for their long term stability and because it reduces the uncertainty on the correction factors accounting for the wall effect of the detector. The physical quantities in the user's beam are related to the penetration properties of the photon beam specified as the Quality Index, QI, which is the ratio I_{20}/I_{10} of the ionization at 20 cm and at 10cm depth in water, respectively, at a fixed Source Detector Distance (SDD) at the centre of a 10 x 10 cm² field.

The following list sums up briefly the main features of this protocol:

1. Local standard: cylindrical ionization chamber with a graphite wall;
2. The phantom is water and the absorbed dose is expressed in dose-to-water;
3. Calibration of the local standard (fitted with the build-up cap supplied with the chamber) in air in terms of air kerma at a Standard Laboratory in a beam of ^{60}Co or of 2 MV X-rays;
4. The waterproofing sheath of the ionization chamber in water can not be thicker than 1 mm of PMMA if to be used without correction factor (factor given in the protocol);
5. The radiation quality is represented by the Quality Index;
6. For the determination of the absorbed dose, the chamber will be placed at a depth of 5 cm for beams with a Quality Index up to and including 0.75 and at a depth of 10 cm for photon beams with a Quality Index larger than 0.75;
7. The phantom surface is positioned at the source distance normally used. A field size of 10 cm x 10 cm at either the phantom surface or the chamber centre is used.

Then, for a local standard ionization chamber, the absorbed dose is given by:

$$D_{w,u} = M \cdot N_K \cdot C_{w,u} \qquad \textbf{(33)}$$

where:

- $D_{w,u}$ is the absorbed dose to water in the user's beam at the position of the centre of the ionization chamber when it is replaced by water.
- M is the electrometer reading corrected for the difference between the ambient air conditions affecting the chamber at the time of measurement and the standard ambient air condition for which the calibration factor is applied (air temperature, pressure and humidity), for ion recombination and for polarity effects in the user's beam.
- N_K is the air-kerma calibration factor, given by the Standard Laboratory, which converts the ionization chamber reading to air kerma for the calibration quality and geometry for standard ambient air conditions.
- $C_{w,u}$ is the air-kerma to absorbed dose to water conversion factor, which depends on the chamber type and the radiation Quality Index QI of the user's beam.
- Subscripts w and u indicates water and user's beam, respectively.
- Recommended $C_{w,u}$ values as a function of the Quality Index are provided for a set of ionization chambers.

8. The relative absorbed dose for other field sizes than 10 x 10 cm^2 and other distances are to be obtained by direct measurements at the reference point.
9. Field instruments must be calibrated in term of absorbed dose to water against the local standard at the radiation quality at which they are to be used. The absorbed dose to water calibration factor at the user's quality, $N_{w,u}$ is given by :

$$N_{w,u} = \frac{D_{w,u}}{M_f} = \frac{(M \cdot N_K \cdot C_{w,u})_{local.standard}}{M_f} \qquad \textbf{(34)}$$

where M_f is the reading of the field instrument, corrected in a similar way as M.

10. The absorbed dose at other positions in the phantom are obtained by performing relative measurements with a field instrument and will be matched to the value determined at the reference point. The fact that the effective point of measurement is displaced with regard to the centre of the chamber is already taken into account in the $C_{w,u}$ factors for the local standard ionization chamber. For the field instrument, if it is a cylindrical air chamber, it must be taken at a fraction 0.75 of the chamber radius in front of its centre.

It is a general trend presently to use new recommendations based on ionization chambers calibrated in terms of absorbed dose-to-water. To this end, the IAEA has issued a new protocol (Andreo et al. 2001) for the determination of the absorbed dose to water by means of an ionization chamber calibrated in terms of absorbed dose-to-water. The NCS is preparing a new protocol conform to the IAEA recommendations. These new recommendations were not followed in this work.