# * DOSIMETRY OF $^{131}I$ - HIPPURAN IN URINARY BLADDER

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## ABSTRACT

To illustrate the methodology for estimating the dose commitment to the bladder wall, giving due consideration to its dynamic nature, the dosimetry of $^{131}I$ - Hippuran is examined with reference to the urinary bladder. The general formalism for calculating the cumulated dose for a given filling up time and final volume, from a knowledge of the instantaneous dose rates, is briefly described. For gamma dose estimations these instantaneous dose rates are derived from the results of Monte Carlo calculations for monoenergetic photons by Snyder et al by suitable interpolation and weighting as determined by the decay scheme of $^{131}I$. Instantaneous maximum dose rates from betas are worked out in a spherical geometry so as to ensure its uniformity throughout the internal surface, using the scaled absorbed dose distribution data from MIRD pamphlet No. 7. The total gamma and beta doses are found to be directly proportional to the filling time and smooth functions of the final volume. These revised dose estimates are compared and contrasted with those reported earlier.

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## 1. INTRODUCTION

Although many radionuclides that find their way into the human body are excreted through urine, the dosimetry of the urinary bladder taking into account its dynamic nature is a relatively recent development.[1] As McAFEE[2] points out, the short-lived radiopharmaceuticals that are now injected in millicurie quantities for rapid-sequence imaging of the brain, heart and abdominal organs are frequently selected on the basis of their rapid clearance from the blood stream and this procedure, as a rule, augments the dose commitment to the urinary tract. The MIRD pamphlet No.5[3] which is now widely used for dose calculations in nuclear medicine gives the absorbed fractions for a static bladder plus contents, whereas in reality the bladder wall is the target region, and this has already led to some confusion.[4] The work of Snyder et al[5] has established that the dose to the bladder wall per photon varies almost by an order of magnitude as the bladder fills, being largest for a nearly empty bladder. The corresponding analysis where betas are involved is described in this paper. The general method for determining the total dose commitment to the bladder resulting from the administration of a radionuclide is outlined and illustrated by the calculation of the beta and gamma doses from $^{131}I$ - Hippuran.

## 2. SCHEMA FOR DOSE CALCULATIONS

Let D(V) be the instantaneous dose rate to the bladder wall for unit specific activity of the radionuclide under consideration in urine of volume V. The determination of the function D(V) for beta and gamma radiations is dealt with in sections 3 and 4 and hence D may be assumed to be a known function of V. If C(t) is the specific activity at any

instant and V(t) the volume of contents at that time, the cumulated dose during on filling up of the bladder is given by

$$\tilde{D}(T) = \int_0^T C(t)\, D[V(t)]\, dt \qquad (1)$$

where T is thetime elapsed between the administration of activity and voiding.

Now, since the rate of filling is nearly constant,

$$V(t) = \frac{t}{T} V_T \qquad (2)$$

where $V_T$ is the final volume of urine.

The function C(t) depends on the manner in which the administered activity enters the bladder as well as on the decay constant $\lambda$ of the radionuclide. Two ways of specifying C(t) that have been employed in this work are:

(1) The specific activity, corrected for physical decay, is a constant throughout the period of filling. This means that the activity enters the bladder at a rate equal to that of urine. If the activity remaining at the end of T hr. is $A_T$ uCi,

$$C(t) = \frac{A_T}{V_T} e^{\lambda(T-t)} \quad \mu Ci.g^{-1} \qquad (3)$$

(2) The whole activity enters the bladder at zero time. According to this model,

$$C(t) = \frac{A_T e^{\lambda(T-t)}}{V(t)} \quad \mu Ci.g^{-1} \qquad (4)$$

In general, the expression for C(t) can be derived from the appropriate clearance model.

## 3. INSTANTANEOUS AND CUMULATED BETA DOSES

Unlike in the case of photons, for betas there will obviously be

a large difference between the average and maximum doses delivered to the bladder wall, due to the relatively high LET of electrons. In addition, use of the oblate spheroid model suggested by Snyder et al[5] will not result in a constant value for the maximum dose at all points on the inner surface of the wall, whereas a spherical model is free from this inconvenience and can be expected to provide a good estimate of the average value of the maximum dose. Fig.1 represents such a bladder at any instant during itsfilling up. Considering any point P at a depth d in the wall, the portion of the spherical shell of radius $x$ around it that lies within the source region is given by

$$A\,dx = 2\pi x^2 (1 - \cos\theta)\,dx \qquad (5)$$

From geometric considerationbased on Fig.1 it is easily derived that

$$\cos\theta = \frac{2ad + x^2 + d^2}{2(a+d)x} \qquad (6)$$

with the limiting conditions

$$\cos\theta\,[x = d = a] = 0 \quad \text{and} \quad \cos\theta\,[x = d \neq a] = 1$$

Now, in terms of Berger's scaled absorbed dose distribution $F$,[6] the dose rate at a distance $x$ from a point source of strength 1 beta/sec in unit density medium is given by

$$J(x) = 1.6 \times 10^{-8}\ \bar{E}\ \frac{F(x/x_{90})}{4\pi x^2 x_{90}}\ \text{rad.sec}^{-1} \qquad (7)$$

where $x_{90}$ is the 90-percentile distance within which 90% of the emitted energy is absorbed and $\bar{E}$, the average energy of the beta spectrum. The values of $x_{90}$ in water given in ref(6) are related to those in the ICRU tissue[7] by the expression

$$(x_{90})_{\text{Tissue}} = \frac{(x_{90})_{\text{water}}}{0.981}$$

Thus for a specific activity of 1 beta/sec/gm of urine, the dose rate at a depth d in the wall is given by

$$D = 3600 \int_{d}^{x_m} A \cdot J \, dx \quad \text{rad} \cdot \text{hr}^{-1} \qquad (8)$$

where $x_m = 2a+d$ for $(2a+d) \leq R$

$x_m = R$ for $(2a+d) > R$

From eq. (5), (7) and (8),

$$D = \frac{28.8 \bar{E}}{x_{90}} \int_{d}^{x_m} F(1-\cos\theta)\, dx \quad \mu\text{rad} \cdot \text{hr}^{-1} \qquad (9)$$

Putting d = 0, one gets the maximum dose rate to the bladder wall, $D_\beta(V)$, when the volume of contents

$$V = \frac{4}{3}\pi a^3$$

Using equation (3) for C(t), for 1 uCi of activity at the end of T hrs,

$$\tilde{D}(T, V_T) = \frac{37 \eta_\beta e^{\lambda T}}{V_T} \int_0^T e^{-\lambda t} D_\beta\left(\frac{t}{T} V_T\right) \qquad (10)$$

where $\eta_\beta$ is the no. of betas per disintegration.

In the other case, the integrand contains the function $D'_\beta(V) = \frac{D_\beta(V)}{V}$ which does not tend to a finite value as $V \to 0$, thereby presenting difficulties in carrying out numerical integration. We therefore make a change of variable as follows:

If the instantaneous inner radius is r,

$$V = \frac{V_T}{T} t = \frac{4}{3}\pi r^3$$

$$\therefore \quad \tilde{D}_\beta(T, V_T) = 3\eta_\beta e^{\lambda T} \cdot \frac{4\pi}{V_T} \int_0^{r_T} e^{-\lambda t(r)} \cdot D'_\beta \left(\frac{4}{3}\pi r^3\right) r^2 dr \qquad (11)$$

where $t(r) = \frac{4}{3}\pi r^3 \frac{T}{V_T}$ and $r_T = \left(\frac{3V_T}{4\pi}\right)^{1/3}$

This too refers to a final activity of 1 uCi in urine.

Now, as r→o, the volume source reduces to a point source and hence it is readily seen from equation (7) that

$$(4\pi r^2 D'_\beta) \longrightarrow \frac{57.6\,\bar{E}\,F(o)}{x_{90}}$$

(The constant 57.6 appears since $D'_\beta$ is expressed in μrad/hr).

4. GAMMA DOSE ESTIMATION

The problem of determining the average dose rate to the bladder wall due to the presence of a monoenergetic gamma emitter in urine has been tackled by Snyder et al[5] using the Monte Carlo method. Table 19.1 of ref.(5) gives the dose (rads/uCi-hr) for volumes of contents 0, 50, 100, 200, 300, 400 and 500 ml and 12 energies in the range 0.01 - 4.0 MeV. Hence knowing the decay scheme of any radionuclide, the instantaneous dose rate $D_\gamma(V)$ corresponding to it can be calculated by proper interpolation. Then the cumulated dose, when the whole activity enters the bladder at zero time is obtained from

$$\tilde{D}_\gamma(T, V_T) = \int_0^T e^{\lambda(T-t)} D_\gamma\left(\frac{t}{T} V_T\right) dt \qquad (12)$$

This too is normalised to an activity of 1 uCi at T hr.

## 5. DOSIMETRY OF $^{131}I$ - HIPPURAN

The practical application of the formalism developed above can be illustrated by considering the case of $^{131}I$ - Hippuran. A detailed study of the retention pattern of this radiopharmaceutical following a single intravenous injection for a routine renogram in man and the resulting doses to the whole body and certain target organs has been reported by Henk *et al*[8]. These authors have come to the conclusion that little or no activity enters the thyroid from the injected Hippuran, most of the activity retained in the thyroid being derived from free-iodide in the injected dose. It is also suggested that for estimating the dose to the urinary bladder, the whole of the administered activity may be assumed to enter the bladder instantly after the injection. This indicates that the appropriate expression for C(t) is that given by equation (4); nevertheless equation (3) has also been employed in the present study in order to assess the implications of the different assumptions.

Computer programs were developed for solving equations (9), (10), (11) and (12). A linear interpolation routine facilitated the use of the scaled absorbed dose functions tabulated in ref.(6). The other parameters used for $^{131}I$ were : $\bar{E}$ = 0.1834 MeV, $(x_{90})_{tissue}$ = 0.08332 cm, $\lambda$ = 0.03509 $hr^{-1}$ and $\eta_\beta$ = 1.003. $D_\beta(V)$ and $D'_\beta(V)$ were evaluated for V = 0.001, 0.01, 0.1, 1.0, 5.0, 10.0, 15.0, 20.0, 25.0, 30.0, 40.0, 50.0, 60.0, 75.0, 100.0, 150.0, 200.0, 250.0, 300.0, 350.0, 400.0 and 450.0 cc. The parameters used to compute $D_\gamma(V)$ are given in Table 1, which is adapted from Lederer *et al*[9]. The cumulated doses were computed for T = 1, 2, 3

and 4.8 hr. and $V_T$ = 82, 100, 120, 140, 164, 175, 220, 280, 360 and 450 cc.

## 6. RESULTS AND DISCUSSION

In this section, some of the results obtained are presented and discussed. Fig.2 shows $\tilde{D}_\beta$ as a function of T for various values of $V_T$. Owing to the small value of $\lambda$, $\tilde{D}_\beta$ is more or less directly proportional to T, although the decay during T hours cannot be ignored. To illustrate, for T = 3 hr and $V_T$ = 82 cc, $D_\beta$ = 7.1 mrad. This is when the final activity is 1 uCi. If, on the other hand, the initial activity had been 1 uCi, $\tilde{D}_\beta = 7.1\ e^{-3} = 6.4$ mrad.

The value of 7.1 mrad is very close to the value of 7.35 mrad computed by Henk et al[8] assuming a static bladder containing 82 g of urine for 3 hours. Thisis because once the bladder has attained a volume of 1 cc, the dose rate $D_\beta(V)$ remains more or less constant. It may also be noted that Henk treats the static model as representing the actual situation when the whole activity enters at zero time and the bladder gets filled to twice the volume taken for computation, i.e. 3 hr. The present calculation shows that this is also equivalent to assuming that the specific activity remains a constant throughout the filling up and that the final volume is half that actually attained.

Another manner in which the bladder dose is likely to be estimated refers to the general schema adopted by the MIRD committee, as exemplified by the calculation reported by Hidalgo.[10] Here the absorbed fraction for betas is assumed to be 1 for self-irradiation, which is adequate only if the source is large enough compared to the beta range. Making

Hidalgo's assumption of a retention time of 30 min and a total bladder mass (wall + contents) 509 g, one estimates the dose from $^{131}I$ as 0.385 mrad/uCi, whereas our calculation for a mass of contents 450 g, keeping the concentration constant as 1/450 uCi/g yields a value of 0.215 mrad. This large difference is, of course, only to be expected since the former calculation gives the dose to the contents rather than the bladder wall.

The results obtained from using eq. (11), which represents the actual situation closely, are shown in fig.3. Since $V_T$ is the actual volume of the bladder contents just before voiding , for comparison with the results of Henk et al[8], T = 3 hr and $V_T$ = 164 cc. The corresponding cumulated dose is seen to be 22.69 mrad which is 3.1 times that computed by Henk. Thus we find that the static model fails to represent the dynamic bladder adequately for dosimetric purposes. From the data presented in fig.3, $D_\beta$ is again found to be very nearly proportional to T, while its variation with $V_T$ follows an equation of the form

$$\tilde{D}_\beta(V_T) = \alpha V_T^{-\beta} \qquad (13)$$

For T = 1 hr, the best fit is obtained for $\alpha$ = 619 and $\beta$ = 0.866, when $\tilde{D}_\beta$ is in mrad and $V_T$ in cc. The mean deviation of the values calculated using eq. (13) from the actual ones is only 0.23%.

The gamma doses calculated from eq. (12) are given in Table 2. For T = 3 hr and $V_T$ = 164 cc, $\tilde{D}_\gamma$ = 1.62 mrad. This is only 17% higher than the corresponding value calculated by Henk et al[8]. This marked difference in the nature of gamma and beta doses is due to the large difference in their ranges. Owing to the small range of the betas, the volume around the centre

of the bladder at a distance greater than R from the wall is ineffective and this 'dead' volume increases with the total volume. Thus the static model leads to an underestimation of the beta dose.

$\tilde{D}_\gamma$ is found to be inversely proportional to $V_T^{\frac{1}{2}}$ and directly proportional to T. For T = 1 hr, the least squares fit yields

$$\tilde{D}_\gamma \, V_T^{\frac{1}{2}} = 6.845 \qquad (14)$$

when $D_\gamma$ is expressed in mrad and $V_T$ in cc.

## 7. CONCLUDING REMARKS

The methodology developed in this paper is designed to help compute the dose commitment to the urinary bladder following the administration of any radiopharmaceutical, provided, of course, the clearance mechanism of the latter is known. In particular, equations (13) and (14) may be conveniently used to determine the doses from $^{131}I$ - Hippuran. Since the human bladder varies tremendously in size from person to person and with different degree of distention during the time intervals between voiding, the values for T and $V_T$ have to be chosen appropriately for every patient. In our computations, the maximum values used for T and $V_T$, viz. 4.8 hr and 450 cc respectively are those assumed by Snyder[1] in his gamma dose calculations. If one goes by the ICRP recommendation[11] according to which 1400 cc of urine is produced in 24 hr, $V_T$ = 175 cc for T = 3 hr. However, for clinical investigations suitable values have to be chosen depending on the condition of the patient, such as whether he is 'hydrated' or not.

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TABLE - 1

Gamma Radiations from $^{131}I$

| | Gamma-1 | Gamma2 | Gamma-3 | Gamma-4 | Gamma-5 | Gamma-6 | Gamma-7 | Gamma-8 | Gamma-9 |
|---|---|---|---|---|---|---|---|---|---|
| % per disintegration | 5.06 | 0.6 | 0.18 | 5.06 | 0.18 | 85.3 | 0.32 | 6.9 | 1.6 |
| Transition energy (MeV) | 0.0802 | 0.164 | 0.1772 | 0.2843 | 0.3258 | 0.3645 | 0.5030 | 0.6370 | 0.7229 |

TABLE - 2

Cumulated maximum doses $\tilde{D}_\gamma$ to the bladder wall from $^{131}I$ gammas assuming that the whole activity enters at zero time. T is the filling time and $V_T$ the final volume of contents. The doses are normalised to an activity of 1 uCi at T hours.

| | $\tilde{D}_\gamma$ mrads | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| $V_T$ cc → / T hours ↓ | 82 | 100 | 120 | 140 | 164 | 175 | 220 | 280 | 360 | 450 |
| 1 | 0.76 | 0.69 | 0.63 | 0.58 | 0.54 | 0.52 | 0.46 | 0.41 | 0.36 | 0.32 |
| 2 | 1.51 | 1.37 | 1.26 | 1.17 | 1.08 | 1.05 | 0.93 | 0.82 | 0.72 | 0.64 |
| 3 | 2.28 | 2.07 | 1.89 | 1.75 | 1.62 | 1.57 | 1.40 | 1.23 | 1.08 | 0.96 |
| 4.8 | 3.66 | 3.32 | 3.03 | 2.82 | 2.61 | 2.53 | 2.25 | 1.98 | 1.73 | 1.53 |