Estimation of Absorbed Dose in Japanese Due to the Administration of 18F-FDG in PET Studies

V. 6. Estimation of Absorbed Dose in Japanese Due to the Administration of ^{18}F-FDG in PET Studies

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Introduction

The ^{18}F-labelled 2-fluoro-2-deoxy-glucose in conjunction with the Positron Emission Tomography (PET) is commonly used to measure the metabolic rate of glucose in a tissue that traps 2-^{18}FDG-6-PO_4. Because of the wide potential application of this radiopharmaceutical many investigators are interested in its possible use for a variety of clinical applications. But studies on the internal exposure in human from the administration of ^{18}FDG are very scarce, only one work by Jones et al.[1] is reported.

In this work the absorbed dose in human that results from the administration of this compound is estimated. Time-activity curves were measured in various organs (brain, heart, lungs, liver, pancreas, spleen, kidneys and bladder contents) by PET and using a single CsI detector. The radiation doses were calculated using the MIRD method.[2] The "S" values of MIRD transformed for Japanese physique[3], and mass weight of organs of normal Japanese adult[4] were used to obtain more realistic estimation of the absorbed dose.

Methods and materials

The experimental data of activities cumulated into several source organs were obtained from long-term scanning of the PET system in this center, ECAT II, for normal volunteers, together with their ages, weights, injected activities and so on. The long-term information is limited in its number, since the clinician is often only interested in the initial distribution and metabolism of radiopharmaceuticals. The numbers of data for each source organ are listed in the first column of Table 1.

The time-activity curves for each source organ were derived from sequential PET images, commonly consisting of 5 min. scan. The region of interest was designated on the organs in the PET image, and the average activity was calculated by using a calibration factor that converts the counts/pixel in the image to μCi/g. The time-activity curves were fitted to the function of two exponential terms.

Time-activity curve for bladder contents (urine) was also obtained to estimate the dose to the bladder wall, which is considered to receive the highest absorbed dose from the use of this compound. For this purpose a heavily collimated CsI detector was used to monitor the Fluorine 18 activity in the bladder contents. The 511 keV gamma-ray spectrum was recorded periodically in a multi-channel analyser and stored in a floppy disk for further analysis. Figure 1 shows a schematic diagram of this system. The CsI detector with a 5 cm thick lead collimator is fixed just above the bladder by a flexible support (Fig. 1).

For the calculation of the cumulated activity in bladder contents, the same procedure used by Jones et al.[1] was applied in this work. In this procedure the amount of activity in the bladder at void time A(t), is calculated by measurement of the activity in a urine sample from the total urine volume. The cumulated activity in the bladder contents, $\tilde{A}$, and the area under the time-activity curve, R, are related to the amount of activity in bladder at void time, A(t), and the height of the time-activity curve, H(t), by the proportionality

$$\frac{\tilde{A}}{A(t)} = \frac{R}{H(t)} . \qquad (1)$$

The cumulated activity $\tilde{A}$ in bladder contents can be determined from the measured quantities A(t), R and H(t). R and H(t) are evaluated from the bladder time-activity curve.

The time activity curves corrected for radioactive decay were integrated over all time, $(0,\infty)$, to obtain the cumulated activities in brain, heart, lung, kidneys, liver, pancreas and spleen. The ^{18}F uptake into organs for which time-activity curves were not obtained were calculated using the dog biodistribution data of Gallagher et al.[5] in case of ovaries, and from their relative weights[1] in case of red marrow and testes. The total body uptake was assumed to be 70% of the injected activity according to Ref. (1). Immediate uptake and effective half-life of 1.83 hr was assumed for calculation of the absorbed dose to these organs.

Equation (2) is the basic expression for dose calculation in the MIRD method[2],

$$D(r_k) = \sum_h \tilde{A}_h \, S(r_k \leftarrow r_h) \qquad (2)$$

where, A is the cumulated activity and "S" is the absorbed dose per unit cumulated activity, r is the region and the subscripts h and k refer to the source and target region, respectively. The "S" values transformed for Japanese physique[3] were used for calculation of the absorbed dose except for brain and heart. For these organs the "S" values[2] were calculated from absorbed fractions[6], equilibrium dose constants[7] and masses for normal Japanese adult.[4]

The total dose to target organs was calculated as the sum of the self-dose and the contribution from bladder contents and the rest of the body.

Results and discussion

Typical time-activity curves are shown in Fig. 2 and Fig. 3 for brain, heart, lung, liver, kidney, pancreas and spleen. The activity is expressed as the percentage of injected dose per gram of tissue. These time-activity curves, i.e. the retention functions, are the combined effect of activity uptake and its decay (excretion and physical decay). Fig. 4 shows a typical bladder time-activity curve. Urinary excretion of activity was 12.3% of the injected dose at 60 min after injection. The cumulated activities averaged for number of available data are shown in Table 1. The data are scarce in particular for organs in the abdominal region. Table 2 gives the estimated values of ^{18}F activities in organs, in which the time-activity curves could not be obtained, as described before.

The absorbed doses to organs and total body are presented in Table 3. The organ doses ranged from 30 to 110 mrad/mCi. The doses to bladder and heart are 228.9 and 183.3 mrad/mCi, respectively. The absorbed doses to spleen and lungs are lower than the values obtained by Jones et al.[1] of 144 and 60 mrad/mCi, respectively, which used the dog biodistribution data from Gallagher et al.[5] for absorbed dose calculation. For bladder wall, the critical organ for the administration of 2-FDG(F-18), our value obtained for 1 hour void time (228.9 mrad/mCi) is very close to that estimated in human by Jones et al.[4] (220 mrad/mCi) for the same void time.

Conclusion

This work presents the absorbed doses estimated in Japanese due to the administration of ^{18}F-FDG in PET studies. We particularly could give the absorbed dose to bladder wall considered as the critical organ in this kind of procedures. This work may be valuable since the absorbed dose to principal organs was obtained from data in human. This information provides a good guide to the limit of the amount of ^{18}F activity that can be administered in this kind of nuclear medicine procedures in order to keep the absorbed dose to acceptable levels.

References

1) Jones S. C. et al., J. Nucl. Med. 23 (1982) 613.
2) Snyder W. S., Ford M. R., Warner G. G. et al., MIRD Pamphlet 11, New York, Society of Nuclear Medicine, 1975.
3) Yamaguchi H., private communication.
4) Tanaka G., Nippon Act. Radiol. 48,4 (1988) 509.
5) Gallagher B. M. et al., J. Nucl. Med. 18 (1977) 990.
6) Cristy M., Eckerman K. F., ORNL, 1987.
7) Dillman L. T., Von Der Lage F. C., MIRD Pamphlet 10, New York, Society of Nuclear Medicine, 1975.

Table 1. Measured average cumulated activity in source organs.

Organ	Subjects	Cumulated Activity
Bladder Contents	3	80.9
Brain	3	170.4
Heart	4	93.1
Kidneys	2	21.9
Liver	2	80.8
Lungs	4	34.7
Pancreas	2	5.1
Spleen	2	9.7

Table 2. Estimated ^{18}F activities in organs.*

Organ	Activity per organ (μCi/organ)
Red Marrow†	15
Ovaries‡	0.1
Testes†	0.3
Total Body	700

† Estimated based on relative weight[4)]

‡ Based on dog biodistribution data[5)]

* from Reference 4.

Table 3. Radiation doses to various organs and total body in Japanese due to the administration of 2FDG(F-18).

Target Organ	Self Dose (mrad/mCi)	From Bladder (mrad/mCi)	From Rest of the Body (mrad/mCi)	Total Dose (mrad/mCi)
Bladder wall	---	188.5	40.4	228.9*
Brain	108.7	---	---	108.7
Heart	183.3	---	---	183.3
Kidneys	54.0	0.3	21.2	75.5
Liver	44.3	0.2	18.3	62.8
Pancreas	25.5	0.2	24.6	50.3
Lungs	21.5	---	18.4	39.9
Ovaries**	21.5	4.2	22.9	48.6
Red Marrow°	12.3	0.4	31.6	44.3
Spleen	49.0	0.2	20.4	69.6
Testes°	13.1	3.5	28.2	44.8
Total Body	---	5.0	33.3	38.3

* for 1 hour void time
** Estimated based on dog biodistribution data
° Estimated based on relative weight

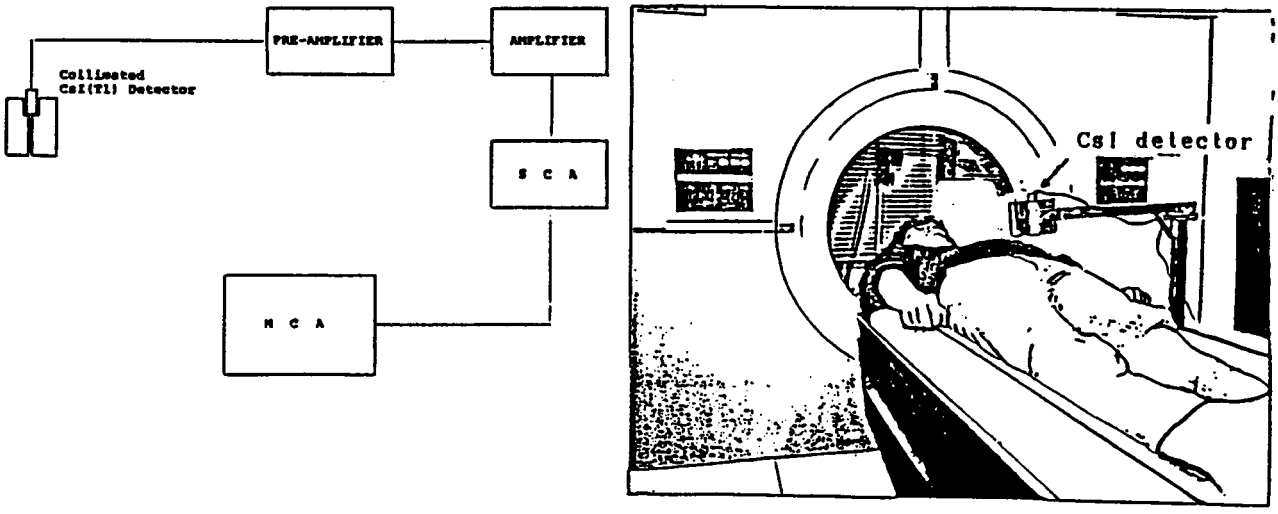

Fig. 1. Schematic diagram of the detection system for bladder time-activity measurements.

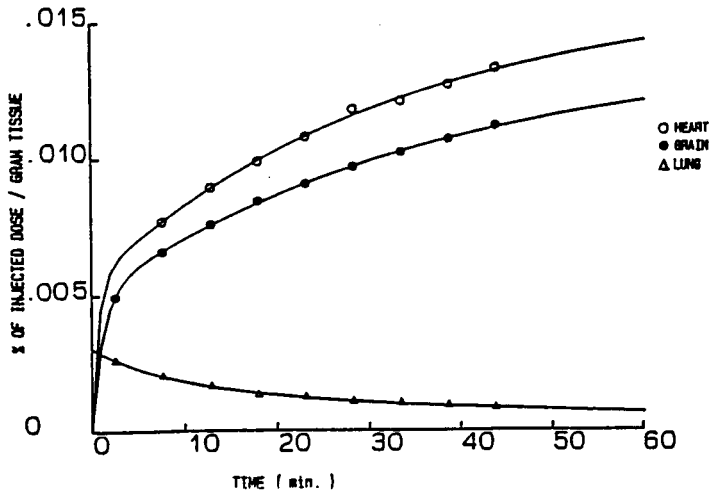

Fig. 2. Time activity curves for heart, brain and lung.

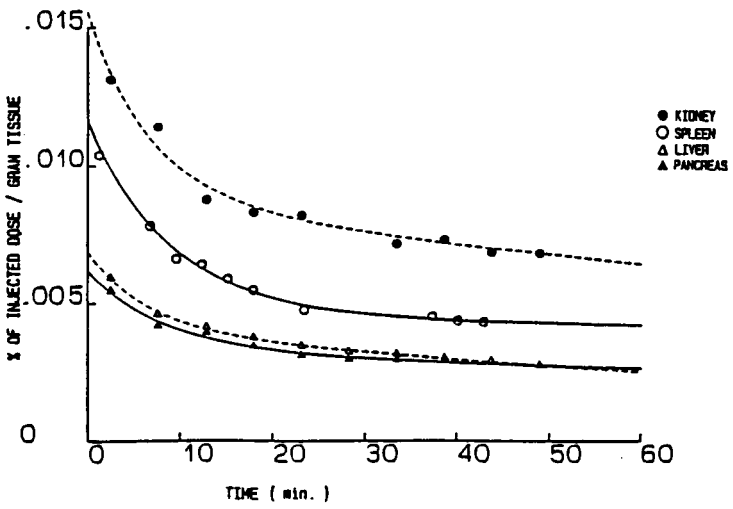

Fig. 3. Time activity curves for kidney, spleen, liver and pancreas.

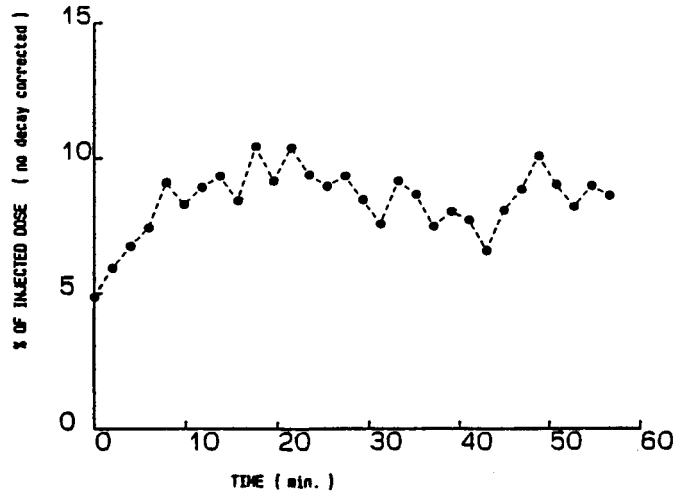

Fig. 4. Bladder time-activity curve.