PHYSICS AND RADIATION BIOLOGY

Absorbed Doses of Radiation After An Intravenous Injection of N-13 Ammonia in Man: Concise Communication

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Using body distribution data with the MIRD tables and equations, the radiation dose delivered by an i.v. injection of N-13 ammonia has been calculated for several human organs. The liver and the urinary bladder wall receive 0.017 and 0.051 rad/mCi injected respectively; the latter can be reduced by early post-injection voiding. The brain-to-brain absorbed dose is 0.016 rad/mCi injected. The absorbed doses for the whole body, the red marrow, the ovaries, and the testes are, respectively, 0.0055, 0.0054, 0.0098, and 0.0010 rad/mCi injected. Severe liver disease is associated with a reduction in the fraction of the injected N-13 that is excreted in the urine, and thus causes a reduction in the absorbed dose to the urinary bladder wall from the bladder contents. Hepatomegaly increases the fraction of the N-13 ammonia trapped by the liver, and complicates calculation of the absorbed dose of radiation. These data should facilitate the evaluation of the risk from radiation absorption following i.v. injections of N-13 ammonia in humans.

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Ammonia is easily labeled with N-13 and has been used for brain imaging and metabolic studies (*1, 2*). Because of its short half-life (10.0 min), radiation doses absorbed by various organs and the whole body after an i.v. injection of N-13 ammonia have been assumed to be low enough to warrant its use in clinical investigations involving human subjects. This report makes use of recent measurements of the equilibrium distribution of N-13 after i.v. N-13 ammonia (*2*) to calculate absorbed doses for several organs.

METHODS

Calculations of absorbed radiation doses were based on the Medical Internal Radiation Dose (MIRD) model, equations, and tables (*3, 4, 5*). The brain-to-brain absorbed dose was calculated by

$$\bar{D}(r_k \leftarrow r_h) = \frac{\tilde{A}}{m_k} \sum_i \Delta_i \phi_i(r_k \leftarrow r_h), \qquad (1)$$

where

$\bar{D}(r_k \leftarrow r_h)$ = mean absorbed dose (rads) to organ k from a uniformly distributed source in organ h;

$\tilde{A}_h$ = cumulated radioactivity in organ h (μCi-hr);

m_k = mass of organ k (g);

Δ_i = equilibrium dose constant for particles of specified type and energy, i (g-rad/μCi-hr),

Φ_i = absorbed fraction for particle i (dimensionless).

For the brain, ϕ_i was assumed to 1.0 for positrons and 0.16 for the annihilation radiation (*5*). For other organs the calculations were based on the values in the MIRD S table (*4*). In all cases, organ-specific body distribution data of Lockwood et al. were used (*2*). In addition, the following assumptions were made:

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1. After an i.v. injection of N-13 ammonia, the entire dose is instantaneously and uniformly mixed in the vascular compartment for a time equal to the mean transit time for ammonia through the vascular compartment.

2. At the end of the mean transit time, N-13 ammonia instantaneously achieves its equilibrium distribution in body organs as an ammonia metabolite.

3. In the organs, the effective clearance of N-13 is the result of the physical decay of N-13.

4. The absorbed dose to a specific organ is due to: (a) whole-body-to-organ energy absorption during mean transit time through the vascular compartment (assuming a uniform distribution of the emitter in the body), together with (b) the sum of the self-dose to the organ, measured from the end of the mean transit time to infinite time, (c) the radiation from other source organs to the target organ during this same time period, and (d) the absorbed dose to the target organ from the remaining N-13, assumed to be uniformly distributed in the whole body, including the gonads. Gonadal absorbed doses were calculated on this distribution assumption.

The mean transit time for ammonia through the vascular compartment was calculated from the data collected by Lockwood et al. during ammonia clearance measurements (*2*). The methods are described in detail in their report, and the approach and its validity are discussed. The organ-specific N-13 content was measured in all subjects using the method of relative quantitation; appropriate data are included in Table 1 (*2*).

RESULTS

The average mean transit time in normal subjects was 1.08 min (range 0.99–1.12). Liver disease and mild hyperammonemia had little effect on the mean transit time. During this time period, the injected N-13 decays to 0.93 of the initial amount, measured at the time of the injection. The results of the absorption calculations are shown in the table, and reflect the effects of this delay in organ uptake.

DISCUSSION

The absorbed dose to the urinary bladder wall (0.051 rad/mCi injected) is the highest among the organs for which data are available. Since the N-13 in the urine had to pass through the kidney, the 6.4% of the injected N-13 that was found in the bladder could not have arrived at the end of the mean transit time for ammonia through the vascular compartment. Thus this calculation overestimates the bladder wall's absorbed dose. Early and frequent post-injection urination can reduce the radiation dose absorbed by the bladder. Since accurate estimates for the uptake of N-13 ammonia by the kidneys are not available for humans, the sum of the absorbed doses listed in the table underestimates the true absorbed dose by an amount equal to the renal self-dose. Since the bladder contents came through the kidney, at least 6.4% of the injected N-13 was in the kidney at some time. Monahan et al. have estimated that 10–20% of all N-13 ammonia injected intravenously in dogs is taken up by the kidney and is cleared with a mean half-time of about 9 min (*6*). Since these data are from dogs and not humans, and may not have been corrected for decay, or radioactivity from surrounding tissue, they have not been used in compiling the table.

Liver disease and its associated alterations of am-

TABLE 1. RADIATION ABSORBED DOSES FROM A SINGLE I.V. INJECTION OF N-13 AMMONIA (rad/mCi injected)

Source organ	Equilibrium N-13 content in source organ (% of total injected* r)	Target organ: Brain	Red bone marrow	Liver	Kidney	Urinary bladder	Ovaries	Testes	Total body
Blood, during mean transit	6.4 ± 0.3		0.00032	0.00033	0.00033	0.00033	0.00032	0.00034	0.00030
Brain	6.9 ± 0.5	0.016‡							
Liver	7.1 ± 0.7		0.00013	0.012	0.00012	0.00004	0.00002	0.00001	0.00041
Urinary bladder†	6.4 ± 1.1		0.00013	0.00003	0.00004	0.0458	0.00067	0.00054	0.00023
Ovaries							0.004		
Testes								0.004	
Whole body	(73.2)		0.0048	0.0049	0.0049	0.0049	0.0048	0.0052	0.0046
Sum	100.0	0.016	0.0054	0.017	0.0054	0.051	0.0098	0.0010	0.0055

* Data from Lockwood et al. (*2*); values are for five normal subjects ± s.e.m.

† All N-13 presumed to be in urine.

‡ Absorbed doses from positrons and annihilation radiation are, respectively, 0.012 and 0.004 rad/mCi injected.

monia metabolism affect the radiation doses absorbed by various organs. Lockwood et al. report a 56% reduction in N-13 in the bladder (*2*). Since bladder structure is not affected by liver disease, this reduction in N-13 excretion should produce corresponding reductions in the dose absorbed by the urinary bladder wall. In patients with severe liver disease, the liver N-13 content at equilibrium increases as a linear function of the projected liver area (*2*). In some subjects the N-13 content of the liver was 2 to 3 times normal. Since the MIRD anthropomorphic model and S tables assume a liver mass of 1809 g (*4*), these tables cannot be used for absorbed-dose calculations. Because the liver mass and ϕ_i for that mass cannot be measured directly, Eq. 1 cannot be used for making absorbed-dose calculations, and the absorbed dose for enlarged livers cannot be calculated accurately.

Although any unnecessary radiation exposure should be avoided, these calculations indicate that the absorbed doses of radiation that follow an i.v. injection of N-13 ammonia are low. Since N-13 ammonia is primarily used in clinical investigations, these data should facilitate the evaluation of the risk in such studies, due to the absorption of radiation, both in normal subjects as well as those with severe liver disease and hyperammonemia. The continued development of sensitive positron-emission tomography systems, such as PETT V, a device optimized for cerebral imaging (*7*), will permit studies to be done with minimal radiation exposures.

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