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Radiation Dose from Breastfeeding Following Administration of Thallium-201

R. Eugene Johnston, Suresh K. Mukherji, J. Randolph Perry and Michael G. Stabin Department of Radiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina; and Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee

Radiation exposure to a breast feeding infant was estimated when the mother underwent a nuclear medicine procedure using ²⁰¹TI. Methods: A lactating mother was administered 111 MBq of 201 TI for a brain scan. Breast milk samples were collected over a period of three days, and the rate of ²⁰¹Tl secretion was determined. The infant was not breast fed during that time. Based on our data, we determined the time-activity function for radioactivity in the breast milk. From these data, and assuming an intake of 1000 ml/day, we calculated the fraction of administered activity that might be taken in by the infant. We also calculated the intake assuming breastfeeding delays of 2, 24, 48, 72, 96 and 500 hr. Results: We calculated the radiation dose to various organs and the effective dose to an infant and a 1-yr-old for breastfeeding delays of 2 to 500 hr. The effective dose to a 1-yr-old from an administration of 111 MBq of 201 TI to the mother ranged from 0.90 mSv to 0.00072 mSv, and the effective dose to a newborn ranged from 1.6 mSv to 0.0013 mSv depending on delay time. Conclusion: Our estimates of radiation exposure to an infant from breastfeeding indicate that in this case, a 1-yr-old would have received less than the NCRP's proposed limit on annual effective dose to members of the general public of 1 mSv with a 48hr delay and no restrictions on holding the child. A newborn would have received less than the proposed infrequent exposure limit of 5 mSv without any delay or restrictions in breastfeeding.

Key Words: breast milk; radiation dose; radioactivity

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It is generally not desirable to administer radionuclides to patients who are breastfeeding. In those cases, however, where it is deemed necessary for the health of the mother to proceed with a nuclear medicine study, the recommendation often is to stop nursing for some period of time. The ICRP recommendations (1) for cessation of breastfeeding, if any, depend on which of the defined groups the radionuclide falls into. Thallium-201 falls into group 1, for which the recommendation is to stop nursing for a period of 3 wk. This is the most conservative approach, short of complete cessation of breastfeeding, from the viewpoint of radiation safety. It may, however, be highly undesirable for many other reasons. The literature provides limited data on the secretion of radiopharmaceuticals in breast milk (2-4). We measured ²⁰¹Tl excretion in breast milk of a patient after administration of thallous chloride for a brain scan.

MATERIALS AND METHODS

The patient was a 32-yr-old female with a history of a brain tumor which had been treated with multiple surgical resections and radiation therapy. The patient was scheduled in the nuclear medicine clinic for a 201 Tl brain scan which was performed with 111 MBq (3 mCi) to evaluate for abnormal uptake which would indicate residual tumor and serve as a baseline for further imaging. At the time of the study, the patient was breastfeeding. The child was a normal, healthy 5-mo-old. The decision to undergo the study rather than to delay it to a later date was based on the strong desire of the patient and her family to proceed.

The mother was instructed that she should temporarily cease breastfeeding and use a breast pump from the time of administration of the radioactivity until we could make a further evaluation. No restrictions were imposed on holding her infant. Breast milk samples were collected by the patient at the times she would normally have breast fed over a period of three days beginning with the time of administration. Samples from each breast pumping were collected in 20 ml test tubes, labeled with the date and time of expression, and refrigerated. The samples were returned to the nuclear medicine clinic 3 days later. The milk samples and a ²⁰¹Tl standard were counted in a scintillation well counter. The milk sample results were recorded in terms of the radioactive concentration (Bq/ml) and decay corrected to the time of administration. A total of 10 samples were collected over a period of 72 hr from the time of administration. The corrected radioactivity concentration is shown in Table 1.

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For correspondence or reprints contact: R. Eugene Johnston, PhD, Department of Radiology, University of North Carolina School of Medicine, Campus Box 7510, Chapel Hill, NC 27599-7510.

TABLE 1 Thallium-201 Concentration in Breast Milk (Bq/ml)

Date of sample	Time of sample	Elapsed time (hr)	Bq/ml*
12/19	5:30 pm	4	326
12/20	12:15 am	10.75	222
12/20	5:40 am	16.17	199
12/20	6:15 pm	28.75	128
12/21	2:30 am	37	123
12/21	7:00 am	41.5	134
12/21	7:15 pm	53.25	100
12/22	12:15 am	58.25	101
12/22	7:30 am	65.5	115
12/22	1:50 pm	71.83	87

*Corrected for radioactive decay to the time of administration.

Dosimetry

 TABLE 2

 Activity Taken in by the Infant Under Different Interruption Schedules

Interruption time (hr)	Intake (MBq)	Fraction of adm. activity
2	0.442	3.88E - 03
24	0.283	2.35E - 03
48	0.197	1.56E - 03
72	0.140	1.10E - 03
96	0.101	7.83E - 04
500	0.000399	3.08E - 06

from breastfeeding for three days while she collected the milk samples to allow us to determine her secretion rate of 201 Tl. In our case, the radiation dose to the infant from ingested radioactivity did not commence until day three. By day three, the concentration of radioactivity in the milk had decreased by a factor of 4. However, the remaining radioactivity appeared to have a long retention time. We fit a two component exponential equation to our data and obtained the function:

$$A_{milk}(t) = 196 e^{(-0.063 t)} + 109 e^{(-0.019 t)},$$

where $A_{milk}(t)$ is the activity in the breast milk, in Bq/ml, at time t (hr), with effective half-times of 11 hr and 36 hr. We then mathematically sampled this curve every 2 hr, assuming an intake of 83 ml of milk per feeding (following the example of Murphy et al. (2), to represent a daily intake of 1000 ml/day, although starting at 2 hr postadministration rather than at 4 hr) out to the complete radioactive decay of the ²⁰¹Tl. Although the model is not a typical feeding schedule, it represents a reasonable upper limit estimate. From this sampling, we estimated the fraction of the administered

We had the benefit of one previous case reported in detail in the literature by Murphy et al. (2) where a lactating patient had been administered 111 MBq of 201 Tl and breast milk samples collected over some 260 hr. These authors derived a two-component exponential function with effective half-times of 1.13 and 15.1 days describing the secretion rate of 201 Tl into the breast milk. The authors also estimated the amount of radioactivity that would have been ingested by an infant using a model that incorporated assumptions of timing of feeding and amount of milk taken at each feeding.

It has been noted in some summaries of observations of activity excretion in breast milk that the concentrations may vary markedly between individuals or even in the same individual at different times (5). For our particular patient we requested that she refrain

TABLE 3 Radiation Dose Estimates for the One-Year-Old for 111 MBg Thallium-201 Administered to the Mother*

Target organ	Interruption time					
	2 hr	24 hr	48 hr	72 hr	96 hr	500 hr
Adrenals	1.5E – 01	9.3E - 02	6.1E - 02	4.3E - 02	3.1E - 02	1.2E - 04
Brain	4.3E - 02	2.6E - 02	1.7E – 02	1.2E - 02	8.6E - 03	3.4E – 05
Breasts	9.6E - 02	5.8E - 02	3.9E - 02	2.7E – 02	1.9E - 02	7.7E – 05
Gallbladder wali	1.8E – 01	1.1E – 01	7.2E - 02	5.1E - 02	3.6E - 02	1.4E – 04
LLI wali	9.3E - 01	5.6E – 01	3.7E – 01	2.6E - 01	1.9E – 01	7.4E – 04
Sm intestine	1.2E + 00	7.5E – 01	5.0E - 01	3.5E - 01	2.5E - 01	9.9E - 04
Stomach	4.6E - 01	2.8E - 01	1.9E – 01	1.3E – 01	9.3E - 02	3.7E – 04
ULI wali	8.7E – 01	5.3E - 01	3.5E – 01	2.5E - 01	1.8E – 01	7.0E – 04
Heart wall	6.1E – 01	3.7E – 01	2.4E – 01	1.7E – 01	1.2E - 01	4.9E – 04
Kidneys	8.0E - 01	4.8E - 01	3.2E - 01	2.3E - 01	1.6E – 01	6.4E – 04
Liver	2.2E - 01	1.3E – 01	8.7E - 02	6.2E - 02	4.4E - 02	1.7E – 04
Lungs	1.2E – 01	7.4E – 02	4.9E - 02	3.4E - 02	2.5E - 02	9.7E - 05
Muscle	1.2E – 01	7.1E – 02	4.7E – 02	3.3E - 02	2.4E – 02	9.4E - 05
Ovaries	2.2E – 01	1.3E – 01	8.8E - 02	6.2E - 02	4.4E - 02	1.8E – 04
Pancreas	1.7E - 01	1.0E - 01	6.8E - 02	4.8E - 02	3.4E - 02	1.4E – 04
Red marrow	1.1E – 01	6.5E - 02	4.3E - 02	3.0E - 02	2.2E - 02	8.6E - 05
Bone surface	2.2E - 01	1.4E – 01	9.0E - 02	6.3E - 02	4.5E - 02	1.8E – 04
Skin	8.9E - 02	5.4E - 02	3.6E - 02	2.5E - 02	1.8E - 02	7.1E - 05
Spleen	4.3E – 01	2.6E - 01	1.7E – 01	1.2E – 01	8.7E – 02	3.4E - 04
Testes	2.4E + 00	1.4E + 00	9.5E - 01	6.7E – 01	4.8E - 01	1.9E - 03
Thymus	1.1E – 01	7.0E - 02	4.6E - 02	3.2E - 02	2.3E - 02	9.2E - 05
Thyroid	2.6E + 00	1.6E + 00	1.0E + 00	7.3E – 01	5.2E - 01	2.1E - 03
Um bladder wall	1.4E - 01	8.2E - 02	5.4E - 02	3.8E - 02	2.7E - 02	1.1E - 04
Uterus	2.0E - 01	1.2E - 01	8.1E - 02	5.7E - 02	4.1E - 02	1.6E - 04
Total body	1.4E - 01	8.6E - 02	5.7E - 02	4.0E - 02	2.9E - 02	1.1E - 04
Effective dose	9.0E - 01	5.4E - 01	3.6E - 01	2.5E - 01	1.8E - 01	7.2E - 04

"The units of absorbed dose (for the individual organs) are mGy; those of the effective dose are mSv.

 TABLE 4

 Radiation Dose Estimates for the Newborn for 111 MBq Thallium-201 Administered to the Mother*

	Interruption time					
Target organ	2 hr	24 hr	48 hr	72 hr	96 hr	500 hr
Adrenals	3.5E - 01	2.1E - 01	1.4E – 01	1.0E - 01	7.1E – 02	2.8E - 04
Brain	9.5E - 02	5.8E - 02	3.8E - 02	2.7E – 02	1.9E – 02	7.6E – 05
Breasts	2.4E – 01	1.5E – 01	9.8E - 02	6.9E - 02	4.9E - 02	1.9E – 04
Gallbladder wall	4.3E - 01	2.6E - 01	1.7E – 01	1.2E – 01	8.6E - 02	3.4E – 04
LLI wall	2.3E + 00	1.4E + 00	9.3E – 01	6.6E - 01	4.7E – 01	1.9E – 03
Small intestine	3.1E + 00	1.9E + 00	1.2E + 00	8.8E - 01	6.3E - 01	2.5E - 03
Stomach	1.4E + 00	8.4E – 01	5.5E – 01	3.9E – 01	2.8E - 01	1.1E – 03
ULI wall	2.1E + 00	1.3E + 00	8.5E – 01	6.0E - 01	4.3E – 01	1.7E – 03
Heart wall	1.2E + 00	7.2E – 01	4.8E - 01	3.4E – 01	2.4E – 01	9.5E – 04
Kidneys	2.1E + 00	1.3E + 00	8.3E – 01	5.9E – 01	4.2E - 01	1.7E – 03
Liver	4.9E – 01	3.0E – 01	2.0E - 01	1.4E – 01	9.8E - 02	3.9E – 04
Lungs	2.9E - 01	1.8E – 01	1.2E – 01	8.2E - 02	5.8E - 02	2.3E - 04
Muscle	2.9E – 01	1.7E – 01	1.2E – 01	8.1E – 02	5.8E – 02	2.3E – 04
Ovaries	4.8E – 01	2.9E – 01	1.9E – 01	1.4E – 01	9.7E – 02	3.9E - 04
Pancreas	3.8E – 01	2.3E - 01	1.5E – 01	1.1E – 01	7.8E - 02	3.1E – 04
Red marrow	2.6E - 01	1.6E – 01	1.0E – 01	7.3E - 02	5.2E - 02	2.0E - 04
Bone surface	5.2E – 01	3.1E – 01	2.1E – 01	1.5E – 01	1.0E – 01	4.1E – 04
Skin	2.3E – 01	1.4E – 01	9.3E - 02	6.6E - 02	4.7E – 02	1.9E – 04
Spleen	1.1E + 00	6.8E – 01	4.5E – 01	3.2E – 01	2.3E – 01	8.9E – 04
Testes	3.4E + 00	2.1E + 00	1.4E + 00	9.7E – 01	6.9E – 01	2.7E – 03
Thymus	2.8E – 01	1.7E – 01	1.1E – 01	7.9E – 02	5.6E - 02	2.2E - 04
Thyroid	3.6E + 00	2.2E + 00	1.4E + 00	1.0E + 00	7.2E – 01	2.9E - 03
Um bladder wall	2.8E – 01	2.8E - 01	1.1E – 01	7.9E – 02	5.6E – 02	2.2E – 04
Uterus	4.4E – 01	2.7E – 01	1.8E – 01	1.2E – 01	8.9E - 02	3.5E – 04
Total body	3.4E – 01	2.1E – 01	1.4E – 01	9.7E – 02	6.9E - 02	2.7E – 04
Effective dose	1.6E + 00	9.6E - 01	6.3E – 01	4.5E - 01	3.2E – 01	1.3E – 03

*The units of absorbed dose (for the individual organs) are mGy, those of the effective dose are mSv.

activity which might be taken in by the infant. We also sampled the same curve assuming interruption times of 24, 48, 72, 96 and 500 hr. Table 2 shows the amount of activity which would be taken in by the infant with a 2-hr delay after administration until the first nursing and with longer interruption times.

Using the Medical Internal Radiation Dose (MIRD) technique (6) and pediatric phantoms of Cristy and Eckerman (7), we estimated radiation doses to a newborn and a 1-yr-old from breastfeeding with 2, 24, 48, 72, 96 and 500 hr of delayed breastfeeding following 111 MBq of ²⁰¹Tl administration. Table 3 shows the radiation dose estimates for the 1-yr-old for intake of ²⁰¹Tl under the six scenarios studied and assuming an administration to the mother of 111 MBq. We then used weighting factors from ICRP 60 (8) and recommended by NCRP 116 (9) to determine the effective dose. Table 4 shows the radiation dose estimates for the newborn for the same assumptions as Table 3. It should be noted that our model for ²⁰¹Tl kinetics is different from that assumed by Murphy et al. (2). Our model is based on the more recent biokinetic data of Krahwinkel et al. (10) and the most updated information on testicular uptake of ²⁰¹Tl (Thomas S, personnal communication, 1995). These new data suggest a testicular uptake of only around 0.3%, rather than the 1% published in ICRP 53 (11) and used by Murphy et al., and thus results in a considerably lower testicular and effective dose.

We made the assumption, as did Murphy et al. (2) that activity ingested by the infant passes quickly and completely into the bloodstream. Thus, the dose estimates are identical to those which would be predicted for an intravenous administration directly to the infant and are most likely higher than the actual dose. This model does not make adjustments for any differences in metabolism between infants and adults.

The external radiation exposure, also estimated by Murphy et al.

(2), monitored radiation exposure at chest level for a number of patients who received ²⁰¹Tl. Assuming intimate contact with the mother during nursing, the estimated total radiation exposure to the infant was reported as 8.3 μ C/kg (32 mR) for 111 MBq of ²⁰¹Tl administered to the mother. For the purpose of adding dose and being conservative, we assumed an external radiation absorbed dose to the child's total body to be 0.32 mSv (32 mrem). The total radiation dose to the child is then the sum of the radiation dose from ingested milk and the external radiation exposure.

CONCLUSION

Measurements from a case where 111 MBq of 201 Tl was administered to a lactating mother and breast milk samples were monitored for radioactivity. The estimated effective dose to the child was calculated and found to range from 0.00072 mSv to 1.92 mSv, depending on the age of the child. NCRP radiation safety guidelines state that, for the general public, the annual effective dose limit should be 1 mSv for continuous or frequent exposure (9). For infrequent exposure, the limit is 5 mSv. Our estimates of radiation dose indicate that our 5-mo-old infant would have met the infrequent exposure limit with no interruption of breastfeeding, and a newborn would have met the limit of 1 mSv with a 48-hr interruption period (both cases assumed that the mother was allowed to hold the infant).

Consideration must also be made of the patient and child relationship. If the child is about to cease breastfeeding anyway, then it would seem the best choice to stop breastfeeding from the time of radioactivity administration. If breastfeeding is to be continued, then the choice is complicated by other factors that may be more important to consider than the risk of radiation exposure. A compromise can be made by delaying breastfeeding for a short time to reduce the radiation dose, as shown in Tables 3 and 4.

The data presented provide further information on the secretion rate for ²⁰¹Tl in breast milk and may be helpful in establishing safety guidelines for cases involving ²⁰¹Tl administration to lactating patients.

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Pharmacokinetics and Dosimetry of Cobalt-55 and Cobalt-57

Hugo M.L. Jansen, Siert Knollema, Lammy Veenma van der Duin, Antoon T.M. Willemsen, Anja Wiersma, Eric J.F. Franssen, Frans G.M. Russel, Jakob Korf and Anne M.J. Paans

Departments of Neurology, Biological Psychiatry, Animal Physiology, Nuclear Medicine and PET Center, University of Groningen; and Department of Pharmacology, University of Nijmegen, The Netherlands

The isotopes ⁵⁵Co and ⁵⁷Co have been evaluated for PET and SPECT imaging in several clinical brain studies. For clinical application of cobalt, it is important to know the delivered radiation dose. The biodistribution of ⁵⁵Co in both rat and humans after intravenous (bolus)-administration was studied. Based on pharmacokinetic data, radiation dose calculations according to the MIRD system are presented. By combining present measurements with literature data on ⁶⁰CoCl₂, the radiation dose delivered by ⁵⁶CoCl₂ (T_{1/2} 78.8 days) and ${}^{57}CoCl_2$ (T_{1/2} = 270 days) could be assessed. Methods: Whole-body Co-PET was performed in two healthy volunteers and one rat after intravenous injection of 37 and 3.7 MBg (1 resp. 0.1 mCi) ⁵⁵Co, respectively. Blood samples were withdrawn during 300 min in humans. In seven rats the 55Co-biodistribution was determined by postmortem analysis. The residence time of the liver (critical organ) was determined in rats and humans. Blood partitiondata of ⁵⁵Co were assessed resulting in basic pharmacokinetic data in humans. Based on these kinetic data, radiation dose was calculated using the MIRD protocol. Results: In both the humans and the rat, the liver and bladder retained the highest fractions of ⁵⁵Co (about 50% resp. 40% of the administered dose). The liver residence time in humans was 8.6 hr. The free fraction ⁵⁵Co in the human plasma was at maximum 12%. The total-body mean transit time was 152 min. The volume of the central compartment = 2.8 liter and the steady-state distribution volume = 48 liter. Conclusion: From these results, according to the WHO recommendations for class II studies, 22.2 MBq (0.6 mCi) ⁵⁵Co and 14.8 MBq (0.4 mCi) ⁵⁷Co (excluding any radionuclide contamination) can be used.

Key Words: cobalt-55; cobalt-57; pharmacokinetics; dosimetry

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In the past, cobalt isotopes have been used for radiotherapy $({}^{60}Co)$ and radio-diagnostic purposes (bleomycine- ${}^{57}Co)$ (1-4).

Presently, the isotopes ⁵⁵Co and ⁵⁷Co are evaluated for brain imaging in several diseases, including stroke, brain trauma and multiple sclerosis (5-8). These studies show the potency of cobalt to detect (small) brain lesions. Because of the limited availability of PET centers, we included both ⁵⁵Co (PET-isotope; $T_{1/2} = 17.5$ hr) and ⁵⁷Co (SPECT-isotope; $T_{1/2} = 270$ days) in our study. Cobalt-55-PET has the advantage of high spatial resolution, absolute quantitation and a relative low radiation dose. The disadvantage is low availability for clinical routine application and logistical problems concerning the relatively short half-life. In contrast, ⁵⁷Co-SPECT has the disadvantage of a lower spatial resolution, a lack of quantitative representation due to the impossibility of attenuation correction and a relatively high radiation dose. The advantage, however, is its wider availability and simple logistics due to a much longer half-life. Cobalt-55 is commonly produced by the ⁵⁶Fe (p,2n)⁵⁵Co nuclear reaction using natural iron as target material (5). Since the 56 Fe(p,n) 56 Co reaction is unavoidable, ⁵⁶Co will always be present as a longer-lived contamination (4.5).

For the clinical applications of these cobalt radionuclides, it is important to estimate the radiation dose to various tissues. To specify such dose commitments, knowledge of excretion, retention and distribution of cobalt in man is essential. Such information in man is limited, except that of cobalt as a complex in vitamin B₁₂ and bleomycine (1,9,10). Virtually all available animal data on free (noncomplexed) cobalt were obtained with ⁶⁰Co in rats (9-16).

In the present study, the in vivo distribution of 55 Co following a (single) intravenous-bolus administration of 55 Co was studied both in healthy volunteers and in rats. Cobalt-55 blood partition-data were determined. Data obtained from biodistribution, in both rat and humans combined with basic pharmacokinetics of cobalt, were used to calculate the absorbed dose of CoCl₂ according to the MIRD formulation (21).

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For correspondence or reprints contact: Anne M.J. Paans, PhD, PET-Center, Groningen University Hospital, P.O. Box 30.001, 9700 RB Groningen, The Netherlands.