Nonmyeloablative Iodine-131 Anti-B1 Radioimmunotherapy as Outpatient Therapy

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The expected effective dose equivalent to an individual from contact with ^{131}I anti-B1 radioimmunotherapy (RIT) patients released immediately after therapeutic infusion was estimated. **Methods:** Effective dose equivalents were calculated retrospectively using data acquired on 46 patients treated with ^{131}I anti-B1 RIT as inpatients. Effective dose equivalents to members of the public were estimated using the method published in the Nuclear Regulatory Commission (NRC) Regulatory Guide 8.39, assuming the administered activity, the patient-specific effective half-life, the 0.25 occupancy factor, and no photon attenuation. Effective dose equivalents also were estimated using ionization chamber dose rates, measured immediately after therapeutic infusion and integrated to total decay based on the measured effective half-life. **Results:** For the whole-body treatment absorbed dose limit of 75 cGy (75 rad), the administered ^{131}I activity ranged from 2.1 to 6.5 GBq (56 to 175 mCi), and the measured dose rate at 1 m ranged from 70 to 190 μSv/hr (7 to 19 mrem/hr). The total-body effective half-life for these patients ranged from ~40 to 88 hr. Using the NRC method and not accounting for the attenuation of photons, the mean dose equivalent to the public exposed to an ^{131}I anti-B1 patient discharged without hospitalization was 4.9 ± 0.9 mSv (490 ± 90 mrem). The range was 3.2–6.6 mSv (320 to 660 mrem), where 48% of patients would deliver a dose to another individual that is <5 mSv (500 mrem) (i.e., 48% of the patients would be allowed to return home immediately following the infusion). Using the measured dose rate method, the mean dose equivalent to an individual exposed to the same RIT patients was 2.9 ± 0.4 mSv (290 ± 40 mrem). The range was 2.0–3.7 mSv (200–370 mrem), where 100% of the estimated effective dose equivalents were <5 mSv (500 mrem). **Conclusion:** Based on calculated and patient-specific exposure data, outpatient RIT with nonmyeloablative doses of ^{131}I should be feasible for all patients under current NRC regulations. Implementing outpatient RIT should make the therapy more widely available and more convenient and should lower patient care costs without exceeding accepted limits for public exposure to radiation.

Key Words: radioimmunotherapy; Nuclear Regulatory Commission; patient release; iodine-131 therapy

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Radioimmunotherapy (RIT) with ^{131}I anti-B1 anti-CD20 monoclonal antibody (mAb) is emerging as a safe and effective treatment of chemotherapy-refractory non-Hodgkin's lymphoma (*1,2*). Previous U.S. Nuclear Regulatory Commission (NRC) regulations required patients undergoing ^{131}I therapy to be hospitalized until the dose rate at 1 m from the patient was <5 mrem/hr (0.05 mSv/hr) or the retained radioactivity in the patient was <30 mCi (1.11 GBq) (*3*). In general, to deliver whole-body absorbed doses of 75 cGy (75 rad), which is the maximum tolerated absorbed dose for this treatment, inpatient stays of 3–4 days post-treatment were required (*1,2*). Hospitalization adds expense and inconvenience to this otherwise well-tolerated therapy. The NRC regulations effective May 29, 1997, allow the release from licensee control of patients who are administered activities that are expected to deliver a total effective dose equivalent of no more than 5 mSv (500 mrem) to other individuals exposed to the patient. Guidance on determining when a patient may be released, when written instructions must be given and when records pertaining to the patient's release must be maintained are published in Regulatory Guide 8.39 (*4*). Specifically, for patients administered ^{131}I, the patient may be released immediately without record keeping if the administered activity is <33 mCi (1.4 GBq). For administered ^{131}I activities of >33 mCi (1.4 GBq), documentation that demonstrates that the total effective dose equivalent of individuals exposed to the released patient does not exceed 5 mSv (500 mrem) is required.

The implication of these rules on the release of patients undergoing treatment for non-Hodgkin's lymphoma is examined by retrospective analysis of RIT dose rates and tracer kinetics from patients involved in a Phase I/II clinical trial of ^{131}I anti-B1 RIT. Based on data for radioiodide in thyroid patients and unpublished data on RIT patient room contamination, internal doses to a member of the public due to environmental radioactive contamination are assumed to be negligibly low when compared to the whole-body absorbed dose due to external radiation exposure (*5,6*). Reported effective dose equivalents to members of the public due to contact with RIT patients are based solely on external radiation exposure.

MATERIALS AND METHODS

Treatment Technique

The patients were participants in the dose escalation trial evaluating nonmyeloablative doses of ^{131}I-labeled anti-B1 mAb. Patients who were eligible for the RIT were adults with non-Hodgkin's B-cell lymphoma expressing the CD20 antigen who had failed at least one prior chemotherapy regimen and who had assessable and measurable disease. Detailed patient selection criteria for this RIT trial are described elsewhere (*1,2*).

The anti-B1 mouse immunoglobulin IgG2a mAb was provided by Coulter Pharmaceutical, Inc. (Palo Alto, CA). Radioiodination of the antibody with ^{131}I, purification of the radiolabeled product, verification of its immunoreactivity and testing for its sterility and pyrogenicity were performed at the University of Michigan, as described previously (*1,7,8,9*).

Patients were given unlabeled anti-B1 antibody (685 mg), followed by a tracer dose of ^{131}I-labeled anti-B1 [15–20 mg, 185 MBq (5 mCi)] to assess radiolabeled antibody biodistribution, to measure whole-body clearance rates and to determine the quantity of ^{131}I necessary to deliver a prescribed whole-body absorbed dose for RIT, ranging from 35 to 85 cGy in a dose escalation trial (*1,2*). Following the tracer infusion, serial, conjugate view, whole-body counts recorded by a sodium iodide scintillation probe were

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obtained beginning ~1 hr after the tracer infusion and then daily for 5–7 days postinfusion. The patient voided before the whole-body measurement, with the exception of the first measurement. For normalization of subsequent mean whole-body counts, the mean whole-body counts at 1 hr after the tracer administration were assumed to represent 100% of the administered activity. The effective half-life of the tracer was estimated from analysis of the time-activity curve.

At least 1 wk following the tracer dose, 685 mg of unlabeled antibody were infused, followed by 15–20 mg of anti-B1 labeled with the appropriate ^{131}I activity determined from the tracer whole-body kinetics as the RIT dose. Immediately following the completion of the radioactive infusion, the dose rate was measured using a calibrated analog ionization chamber positioned 1 m from the center line of the patient's thorax. For 29 of the patients, the dose rate also was measured at the patient's bedside (~0.3 m from the patient's liver) with the patient supine. Patients were hospitalized until dose rates at 1 m from the patient's thorax were <5 mrem/hr (0.05 mSv/hr). For a whole-body delivered absorbed dose of 75 cGy (75 rad), the average hospital stay was 3–4 days post-treatment. Patients were instructed on methods of reducing radiation exposure to others. Patient contact restrictions and contamination precautions generally were expected to be followed for at least 1 wk following release from the hospital.

Dose Estimation

Effective dose equivalents to individuals from exposure to the released patient were calculated using data acquired on 46 patients treated with ^{131}I anti-B1 (700 mg) RIT as inpatients at the University of Michigan Hospitals. Dose rates from patients administered ^{131}I activities based on delivered whole-body absorbed doses other than 75 cGy (75 rad) were normalized using the ratio of 75 cGy (75 rad) to the patient-specific delivered whole-body absorbed dose. Effective dose equivalents to hypothetical persons in contact with the RIT patient were calculated using the method published in NRC Regulatory Guide 8.39 (see Eq. 1), assuming the administered activity for the whole-body treatment dose of 75 cGy (75 rad), the patient-specific effective half-life and a 0.25 occupancy factor (*4,5*):

$$D(\infty) = \frac{(346)\Gamma Q_0 T_e(0.25)}{(100\ \text{cm})^2}, \qquad \text{Eq. 1}$$

where $D(\infty)$ = total effective dose equivalent (mSv) from exposure to gamma radiation, Γ = exposure rate constant for a point source of ^{131}I, equal to 2.2 R/mCi · hr at 1 cm, Q_0 = administered activity (mCi) and T_e = patient-specific effective half-life (days) of ^{131}I anti-B1.

Effective dose equivalents to hypothetical persons in contact with the RIT patient also were calculated using patient-specific ionization chamber dose rates, measured immediately after therapeutic infusion, integrated to total decay based on the effective half-life (see Eq. 2) and multiplied by the 0.25 occupancy factor. Because the excretion of this radiopharmaceutical is a monoexponential function, the decay of the measured RIT dose rate is modeled as a monoexponential function of the effective half-life determined from tracer kinetics (*10–12*):

$$D(\infty) = R\tau(0.25), \qquad \text{Eq. 2}$$

where R = measured dose rate (mSv/hr) at 1 m from the patient's thorax immediately after therapy dose infusion and τ = patient-specific whole-body residence time (hr) of ^{131}I anti-B1 = 34.6(T_e).

The mean effective dose equivalent and the associated s.e., maximum effective dose equivalent and minimum effective dose equivalent to a member of the public who may have contact with a released RIT patient are reported for both methods of calculating the effective dose equivalent due to external radiation exposure.

When instructing the patient on methods to reduce radiation exposure to other individuals, several generic predictions of the patient's lifestyle may be assumed. In Regulatory Guide 8.39, the occupancy factor 0.25 is recommended for calculating the effective dose equivalent to persons who have contact with a released patient undergoing ^{131}I-NaI treatment post-thyroidectomy, who has sole use of a bathroom for at least 2 days, sleeps alone in a room for at least the first night and maintains a prudent distance from others for at least 2 days. When instructing the RIT patient on methods to reduce radiation exposure to other individuals, a restriction time period of 1 or 2 days may not be long enough to maintain effective dose equivalents to others of <5 mSv. To explore this issue, several predictions of the lifestyle and social distances may be assumed. Based on anthropological studies in the U.S., the range of distances involving personal or intimate contact is from 0 to 0.76 m (*13*). For individuals sharing a single bed, the distance may average 0.3 m. The range of distances found among U.S. individuals involved in social contact is from 0.76 to 3.66 m (*13*). For patient contact with family and friends, the average distance is ~1 m. For business contact, the average distance is ~2 m. Because the liver will contain the highest concentration of ^{131}I immediately following the RIT infusion, a conservative estimate of effective dose equivalent to an individual sleeping in the same bed as the patient may be calculated using the dose rate measured at 0.3 m from the patient's liver and the measured dose rate at 1 m from the patient's thorax. For this analysis, two conservative scenarios were considered for occupancy. The first scenario assumes that the patient sleeps alone the first week following treatment and spends no more than 25% of the total time with an individual. Distances between the patient and the other individual are maintained outside of 1 m. After the first week, the patient resumes normal sleeping arrangements (25% of the total time assumed to be at distances of 0.3 m) and socializes with the same individual at distances of >1 m for 25% of the total time. The second scenario assumes the patient waits 2 wk before resuming normal sleeping arrangements. Occupancy factors and distances for measured dose rates are assumed to be the same as those in the first scenario. Equation 3 is used to calculate the dose to the individual who has the most contact with the RIT patient, assuming both scenarios:

$$D(\infty) = (0.25\tau)\left[R_a + R_b\left(\exp\left(\frac{t_{ab}}{\tau}\right)\right)\right], \qquad \text{Eq. 3}$$

where R_a = dose rate (mSv/hr) measured at 1 m, R_b = dose rate (mSv/hr) measured at 0.3 m, t_{ab} = time (hr) patient sleeps alone (either 1 or 2 wk) and τ = patient-specific whole-body residence time (hr).

For the two scenarios described, the mean effective dose equivalent, the s.d. and the effective dose equivalent range of an individual who would most likely spend extended time with the RIT patient are reported using retrospective data from 29 patients who had measured dose rates at bedside and at 1 m.

The time period for limited intimate contact necessary to maintain individual doses less than the specified effective dose equivalent limit of 5 mSv (500 mrem) for NRC-regulated institutions may be calculated on a case-by-case basis. During the limited intimate contact time restriction period, the patient would not have contact with other individuals at distances of <1 m for more than a few minutes a day, but contact involving distances near 1 m or greater would still be allowed. The time period (t_{lic}) for limited intimate contact is given by:

$$t_{lic} = (-\tau)\ln\left[\frac{(D_{limit} - D_{1\,m})}{D_b}\right], \qquad \text{Eq. 4}$$

where τ = patient-specific whole-body residence time of ^{131}I anti-B1, D_{limit} = effective dose equivalent limit set at 5 mSv for

patients in contact with adults, $D_{1\,m}$ = effective dose equivalent to an individual using Equation 2 and the measured dose rate at 1 m from the patient's thorax and D_b = effective dose equivalent to an individual using Equation 2 and the measured dose rate at 0.3 m from the patient's liver.

Because the 0.25 occupancy factor is assumed for the effective dose equivalent calculations, $D_{1\,m}$ may be assumed to be 0 in Equation 4 for cases involving patients who have <6 hr per day (25% of 1 day) of intimate contact with another individual. The derivation of Equation 4 is given in Appendix 1. Using Equation 4, the time period necessary for separate sleeping arrangements involving the RIT patient and another individual are reported using retrospective data from the 29 RIT patients who had measured bedside dose rates.

For patients who may have contact with small children or pregnant women, special instructions to reduce the radiation exposure to this group of individuals could conservatively be viewed as necessary but are not specifically required by the NRC regulations. To protect this group, we are recommending the more conservative effective dose equivalent limit of 1 mSv (100 mrem) rather than the regulatory limit of 5 mSv (500 mrem) (*14,15*). When determining the time restrictions for patient contact with this group of individuals, a distance of 2 m from the patient was considered reasonable to maintain low individual effective dose equivalents and to maintain a reasonable lifestyle (*15–18*). Because the dose rate at 2 m was not measured for the patients in this study, the dose rate was estimated by dividing the measured dose rate at 1 m by 4 (inverse square law). As a more conservative approach at maintaining low effective dose equivalents to children or pregnant women, the time period for no contact with the RIT patient may be calculated. A child or pregnant woman is considered to have no contact with an RIT patient when the distance between the patient and the other individual exceeds 2 m or when distances of <2 m are maintained for time periods that do not exceed a few minutes per day (<5 min/day). By restricting close contact to time periods of <5 min/day, the maximum likely effective dose equivalent to the individual is unlikely to exceed 100 μSv/day (10 mrem/day). A patient is considered to have limited contact with a child or pregnant woman when distances between 1 and 2 m are maintained for a total time exceeding 30 min/day (*17,18*). For limited contact, the maximum likely effective dose equivalent to a child or pregnant woman should not exceed 480 μSv/day (48 mrem/day). Extended periods of close contact, which may include activities such as reading to a small child, were considered to be at distances of 0.3 m. The derivation for the time period for contact restrictions between an RIT patient and a child or pregnant woman is given in Appendix 1. The time period for contact restrictions (no contact or limited contact) with children or pregnant women is given in Equation 5:

$$t_{ab} = (-\tau)\ln\left[\frac{(D_{limit} - D_{2\,m})}{(D_b - D_{2\,m})}\right], \qquad \text{Eq. 5}$$

where τ = patient-specific whole-body residence time of ^{131}I anti-B1; D_{limit} = effective dose equivalent limit set at 1 mSv; $D_{2\,m}$ = effective dose equivalent to an individual using Equation 2 and the estimated dose rate at 2 m from the patient's thorax when considering limited contact (this value is zero when considering no contact with the RIT patient); and D_b = effective dose equivalent to an individual using Equation 2 and the measured dose rate at 0.3 m from the patient's liver.

The estimated time period for an RIT patient to minimize contact with a child or a pregnant woman was calculated using retrospective data from the 29 patients who had measured bedside dose rates. The mean time, s.d. and the range of time periods are reported.

TABLE 1
Patient-Specific Parameters Necessary for Determining the Effective Dose Equivalent to an Individual Exposed to a Radioimmunotherapy Patient

	Administered activity (GBq)	Dose rate at 1 m (μSv/hr)	Dose rate at 30 cm (μSv/hr)	Residence time (hr)
Mean ± s.d.	3.5 ± 1.0	120 ± 30	370 ± 140	97 ± 16
Minimum	2.1	72	150	58
Maximum	6.5	190	800	127

RESULTS

For whole-body treatment doses of 75 cGy (75 rad), the projected administered ^{131}I activity ranged from 2.1 to 6.5 GBq (56 to 175 mCi). The measured dose rate at 1 m ranged from 0.072 to 0.19 mSv/hr (7.2 to 19 mrem/hr), and the measured dose rate at 30 cm ranged from 0.15 to 0.80 mSv/hr (15 to 80 mrem/hr). The whole-body effective half-life for these patients ranged from 40 to 88 hr, and hence, the residence time ranged from 58 to 127 hr. Table 1 summarizes the patient-specific parameters necessary for this analysis.

Based on NRC limits for administered activities and measured exposure rates, ^{131}I anti-B1 RIT patients could not be released from the licensee control immediately following the treatment without justification or recordkeeping pertaining to the patient's release. That is, all patients were administered activities of >1.4 GBq (33 mCi).

Examples of justifications for releasing a patient given ^{131}I-NaI are outlined in the Appendix of Regulatory Guide 8.39 (*4*). For releasing patients administered ^{131}I anti-B1, the same guidelines may be assumed when using Equations 1 and 2. Using the NRC method and assuming a point source with no photon attenuation, the mean effective dose equivalent to an individual exposed to an ^{131}I anti-B1 patient discharged without hospitalization is 4.9 ± 0.9 mSv (490 ± 90 mrem). The range was 3.2–6.6 mSv (320–660 mrem), where 48% of patients would be allowed to immediately return home following the infusion [i.e., 48% of the patients would give an effective dose equivalent to an individual member of the public that is predicted to be <5 mSv (500 mrem)].

Using the measured dose rate method, the mean effective dose equivalent to a member of the public exposed to the same set of RIT patients is 2.9 ± 0.4 mSv (290 ± 40 mrem). The range was 2.0–3.7 mSv (200–370 mrem), where 100% of the estimated effective dose equivalents were <5 mSv (500 mrem). The difference between the estimated effective dose equivalents of the two methods is due to the attenuation and distribution of ^{131}I anti-B1 within the patient, which was not considered in the first series of calculations.

Both methods show that all patients would contribute >1 mSv (0.1 rem) to a member of the public, which would require giving special instructions to the patient regarding sleeping arrangements and other methods of reducing the exposure to individuals. Assuming the RIT patient, who is released immediately following the treatment, avoids extended intimate contact for 1 wk, the mean estimated effective dose equivalent to the individual who has the most contact with the patient is 4.5 ± 0.9 mSv (450 ± 90 mrem) and ranges from 2.6 mSv to 6.5 mSv (260 to 650 mrem). Assuming the 1-wk scenario with the measured dose rates, 69% of the patients could resume normal sleeping arrangements with another individual and maintain

doses of <5 mSv (500 mrem). When separate sleeping arrangements are made for 2 wk, the estimated dose is 3.2 ± 0.5 mSv (320 ± 50 mrem), ranging from 2.3 to 4.3 mSv (230 to 430 mrem). The mean time period necessary for separate sleeping arrangements for the RIT patients is 5.9 ± 2.1 days, ranging from 1.5 to 10.5 days. Following 2 wk after the immediate release of an RIT patient, 100% of the patients could resume normal sleeping arrangements while maintaining the dose to the individual in most contact with them at <5 mSv (500 mrem).

For RIT patients who may have contact with small children or pregnant women, the time period for no contact or limited contact assuming the dose limit of 1 mSv (100 mrem) was calculated using Equation 5. The mean time period necessary for no contact was 8.8 ± 2.2 days, ranging from 3.8 to 13.5 days. Because the patient is isolated from their children, this separation period may be too stressful for some families. As an alternative solution, a contact-limiting period also was considered. During the period of limited contact, the patient could have brief periods of close contact, such as hugging or reading to a small child but would keep longer periods of contact at distances of >2 m. To maintain doses of <1 mSv (100 mrem), patient contact with any child must be limited to <30 min/day during the limited contact period. Based on Equation 5 and the estimated dose rate at 2 m, the mean time period for limited contact is 14.2 ± 4.1 days, ranging from 5.8 to 22.8 days. In this series, a RIT patient who was released immediately post-treatment could resume normal contact with a child or a pregnant women within 1–3 wk after their release, using this very conservative approach.

DISCUSSION

When patient release is based on biological elimination (i.e., the effective half-life) rather than just the physical half-life of the radionuclide, the equation used to calculate the dose to total decay may need to be modified to account for the uptake and retention of the radionuclide by the patient. A calculation to address this issue is discussed in Appendix B.2 of Regulatory Guide 8.39 (*4*). To conservatively account for the effective dose equivalent to an individual due to holdup of ^{131}I anti-B1 in the urine while in the bladder, 100% of the activity during the first 3 hr following the patient release should be assumed to be removed from the body through physical decay. A detailed discussion of the consequences of Appendix B of Regulatory Guide 8.39 on the RIT patient data is given in Appendix 2. For the RIT patient data presented, the systematic error due to not including this modification results in effective dose equivalent underestimation ranging from 7% to 15%. However, if the patient is instructed to have no contact with another individual for 3–8 hr immediately following the treatment, the effective dose equivalent discrepancy due to biological elimination in the first 3–8 hr following the infusion is negligible. Therefore, an occupancy factor of 0.25 and the effective half-life for the first 3–8 hr following treatment was assumed for effective dose equivalent calculations.

Using measured dose rates and patient-specific kinetics, this analysis demonstrates that all 46 ^{131}I anti-B1 RIT patients treated at 75 cGy (75 rad) whole-body absorbed dose could have been released from the hospital immediately following RIT treatment according to the current NRC requirements. Instead of using Equation 1 or 2 to determine when a patient may be released from licensee control, the administered activity or dose rate limit for a patient may be determined from the residence time using Table 2. The administered activity levels in Table 2 were calculated using Equation 1, which assumes the dose to an individual is due to an ^{131}I point source in air at the distance of 1 m, the 0.25 occupancy factor and the whole-body residence time of ^{131}I anti-B1. The dose rate limits in Table 2 are based on Equation 2, which assumes the 0.25 occupancy factor at a distance of 1 m and the whole-body residence time. Because the measured dose rate at 1 m accounts for the attenuation and distribution of the ^{131}I anti-B1 within the patient, the dose rate limits are less conservative than the administered activity levels. However, the dose rate levels are more representative of the exposure to individuals in contact with the RIT patient.

TABLE 2
Patient Release Limits for the Measured Dose Rate and the Administered Iodine-131 Activity Using the Whole-Body Residence Time, Assuming the Effective Dose Equivalent Limit of 5 mSv

Residence time* (hr)	Releasable activity (mCi)	Releasable dose rate (mSv/hr)
40	227.3	0.50
44	206.6	0.45
48	189.4	0.42
52	174.8	0.38
56	162.3	0.36
60	151.5	0.33
64	142.0	0.31
68	133.7	0.29
72	126.3	0.28
76	119.6	0.26
80	113.6	0.25
84	108.2	0.24
88	103.3	0.23
92	98.8	0.22
96	94.7	0.21
100	90.9	0.20
104	87.4	0.19
108	84.2	0.19
112	81.2	0.18
116	78.4	0.17
120	75.8	0.17
124	73.3	0.16
128	71.0	0.16
132	68.9	0.15
136	66.8	0.15
140	64.9	0.14

*A patient with a given residence time may be released following treatment if either the administered activity or the measured dose rate at 1 m is less than the values given in this table.

Patients would require written instructions describing methods to minimize the radiation exposure to others. Specifically, instructions would need to include sleeping arrangements. For typical American couples, 0.3 m was considered to be the average distance between sleeping couples over a time period of 6–8 hr (*13*). Using this distance as a guide and Equation 4, dose estimates to an individual sharing a bed with a released RIT patient can be used to determine how long the patient should have separate sleeping arrangements. In this series, immediate release from licensee control and 2 wk of separate sleeping arrangements would allow all of the RIT patients who do not have contact with children or pregnant women to be treated as outpatients.

For patients who may have contact with small children or pregnant women, special instructions could be considered necessary to minimize the dose to these individuals due to their higher risk of biological damage from radiation exposure. The

TABLE 3
Suggested Minimum and Maximum Guidelines for Resuming Close Contact with an Immediately Released Iodine-131 Anti-B1 Radioimmunotherapy Patient

Advice	Time
Avoid prolonged contact with pregnant women and small children*	6–23 days
Avoid the workplace, public transportation and other public places*	6–23 days
Make separate sleeping arrangements with another individual†	6–17 days
Avoid long trips in a car (>4 hr)†	6–17 days

Results are based on the patient data from this study.
*Assuming individual effective dose equivalent limit of 1 mSv.
†Assuming individual effective dose equivalent limit of 5 mSv.

most conservative approach to reduce the dose to this group would be to have no contact with the released RIT patient for the time specified by Equation 5. In this series, contact could be resumed for some patients as soon as 4 days post-treatment, but isolation could last as long as 14 days. This may place undue stress on a small child, as well as the family. In cases where extended absences are not feasible, contact time should be limited to brief periods (<30 min/day) of intimate contact, such as reading to a small child, with longer periods of contact at distances >2 m (*16*). Using this method to reduce the dose to the child would allow the child to be with the patient and still maintain a dose of <1 mSv (100 mrem). The time necessary for this arrangement can be determined using Equation 5. In this series, the restrictions may be removed as soon as 6 days but may last as long as 23 days.

The potential of an internal dose to a member of the public due to radioactive contaminants from an ^{131}I patient was considered to be low when compared to the dose due to external exposure (*6,7*). At the University of Michigan Hospitals, radioactive contamination found in RIT patient rooms were comparable or less than the contamination found in the rooms of patients being treated with ^{131}I-NaI. The primary route of excretion for ^{131}I anti-B1 is similar to that of ^{131}I MB-1, through the kidneys (*unpublished data*) (*1,11*). Generally, the primary source of contamination from an RIT patient would be expected to be found in the bathroom. When good hygiene is observed, an individual's dose due to internal contamination would be minimal. A potential concern would be with small children who tend to place objects into their mouths or play near the same toilet and sink used by the patient. One possible solution to this problem is to have the patient use a separate bathroom that would not be accessible to the small children.

Restricting contact with the patient is the simplest method of reducing radiation exposure to other individuals. The duration of this restriction period can be very long for patients who clear ^{131}I anti-B1 from the body slowly and who have minimal attenuating body mass resulting in high measured dose rates. The time restriction period may be reduced by incorporating detailed instructions for specific activities; however, compliance may become more of an issue (*14,18,19*). In general, prolonged contact with immediately released RIT patients should be avoided for at least 1 wk following the treatment. A summary of minimum and maximum restriction duration based on data from this study is given in Table 3. For more specific time limits for contact restrictions, such as separate sleeping arrangements, a table based on the initial dose rate measured at 30 cm and the whole-body residence time of ^{131}I anti-B1 is shown in Table 4. The time limits shown in Table 4 are based on the NRC intuitive assumption that the dose to another individual is 25% of the dose, assuming constant contact with the patient. Avoidance times are derived using Equation 4, assuming $D_{1\,m}$ is zero and D_b is the dose calculated using the measured dose rate at 30 cm and the patient-specific whole-body residence time. Although many of the avoidance time periods given in Table 4 are <6 hr, it is recommended that the patient avoid intimate contact for a minimum of 6 hr post-therapeutic infusion.

For patients who travel long distances for treatment, close contact with other individuals is often unavoidable, especially when public transportation is involved. However, Barrington et al. (*20*) showed that the relatives of patients given 0.3–0.5 GBq of ^{131}I received 0.002–0.070 mSv for a 1-hr journey using

TABLE 4
Time Period for Separate Sleeping Arrangements with an Immediately Released Iodine-131 Anti-B1 Radioimmunotherapy Patient Based on Patient-Specific Residence Time or the Releasable Dose Rate at 1 m and the Measured Dose Rate at 30 cm

Residence time (hr)	Releasable dose rate at 1 m (mSv/hr)	Avoidance time (hr)*							
		0.5	0.45	0.40	0.35	0.30	0.25	0.20	0.15
55	0.36	18	12	5	0	0	0	0	0
60	0.33	24	18	11	3	0	0	0	0
65	0.31	32	25	17	8	0	0	0	0
70	0.29	39	32	24	14	3	0	0	0
75	0.27	47	39	30	20	9	0	0	0
80	0.25	55	47	38	27	15	0	0	0
85	0.24	64	55	45	34	21	5	0	0
90	0.22	73	64	53	41	27	11	0	0
95	0.21	82	72	61	48	34	16	0	0
100	0.20	92	81	69	56	41	22	0	0
105	0.19	101	90	78	64	48	29	5	0
110	0.18	111	100	87	72	55	35	10	0
115	0.17	121	109	96	80	63	42	16	0
120	0.17	132	119	105	89	71	49	22	0
125	0.16	142	129	115	98	79	56	28	0
130	0.15	153	140	124	107	87	63	34	0

*Numbers represent measured dose rate at 30 cm (mSv/hr).
All calculations are based on the 5-mSv Nuclear Regulatory Commission limit.

private transportation. Patient release dose rates ranged from 0.060 to 0.550 mSv/hr for 0.1 m and from 0.015 to 0.023 mSv/hr for 1-m distances. They concluded that, given appropriate advice, most relatives of patients will not receive >1 mSv. From our study, the dose rate at 1 m ranged from 0.072 to 0.19 mSv/hr. Assuming private transportation places the patient at 1 m from the other passengers, the dose to the other passenger would, therefore, range from 0.072 to 0.190 mSv (*21*). At 30 cm, the dose to another individual traveling with the patient for 1 hr will range from 0.15 to 0.8 mSv. However, these data are skewed by two patients who had dose rates at 30 cm, which were 0.8 mSv/hr. The remaining 27 patients had dose rates at 30 cm that were <0.5 mSv/hr. Assuming adjacent distances for public transportation are at 30 cm rather than 10 cm, which was assumed by Barrington et al. (*20*), the dose to passengers traveling for 1 hr with an RIT patient would have been <1 mSv for most of the individuals.

Gunesekera et al. (*22*) measured the dose to a water-filled human torso due to exposure from a patient administered ^{131}I for thyrotoxicosis. Digital dose meters were placed on the lateral chest wall adjacent to and opposite to the patient. The highest dose measured at the adjacent position was 0.229 mSv per 200 MBq in 1 hr. Assuming the effective dose to be at least one-half of the adjacent dose, they concluded that for a patient administered 400 MBq, an adjacent passenger was unlikely to exceed 0.229 mSv in 1 hr. Assuming a patient is administered 7 GBq and the maximum adjacent dose is 0.229 mSv per 200 MBq in 1 hr, an adjacent passenger might receive an effective dose of 4 mSv in 1 hr. For the RIT patients, the maximum measured dose rate at 30 cm per administered activity is 0.048 mSv/hr per 200 MBq. Assuming that the distance between an RIT patient and an adjacent passenger is 30 cm, the maximum adjacent dose for a passenger beside a patient administered 7 GBq of ^{131}I would be 1.7 mSv in 1 hr. The maximum effective dose to a passenger adjacent to an RIT patient would be 0.850 mSv in 1 hr. Therefore, a passenger adjacent to an RIT patient is unlikely to receive an effective dose in excess of 5 mSv in 1 hr, but they have the potential of receiving entrance doses in excess of 5 mSv in 1 hr. Traveling arrangements requiring >1 hr of travel will most likely result in effective doses to adjacent passengers in excess of 5 mSv. A case-by-case analysis will be necessary to determine the travel restrictions for each patient.

CONCLUSION

Doses to individuals exposed to ^{131}I anti-B1 RIT patients, estimated using patient-specific data, demonstrate that outpatient RIT with ^{131}I at nonmyeloablative doses of 75 cGy (75 rad) to the whole body will be permissible under the current NRC regulations. Written instructions describing methods to reduce radiation exposure to individuals who may contact the patient will be necessary. The time period that the patient will need to restrict contact with other individuals is only a few days longer than the restriction time period recommended to patients who were released at 0.05 mSv/hr (5 mrem/hr). Implementing outpatient RIT will make the therapy more widely available and more convenient for the patient and help lower the cost of patient care.

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APPENDIX 1: DERIVATION OF EFFECTIVE DOSE EQUIVALENT AND RESTRICTION TIME PERIOD FROM MEASURED DOSE RATE

The effective dose equivalent may be determined from the measured exposure rate at 1 m by multiplying 0.25 times the dose rate integrated to total decay. Assuming that the measured dose rate decays monoexponentially with a decay constant equal to $1/\tau$, where τ = whole-body residence time, then the effective dose equivalent is given by the following:

$$\begin{aligned} D(\infty) &= \int_0^{\infty} (0.25Re^{-t/\tau})\,dt \\ &= 0.25R(-\tau)[[e^{-\infty}] - [e^0]] \\ &= 0.25R(-\tau)[0-1] \\ &= R\tau(0.25). \end{aligned} \qquad \text{Eq. 1A}$$

To derive the equation that determines the RIT patient-specific contact restriction period, several assumptions will be necessary. Assume the patient spends time with another individual at distances averaging 1 m for no more than 25% of the total time. The patient also will have contact with the same individual involving distances that average 0.3 m for no more than 25% of the total time. Assuming the measured dose rate at 1 m ($R_{1\,m}$) and 0.3 m (R_b) decay monoexponentially with a decay constant equal to the inverse of the whole-body residence time ($1/\tau$), then the effective dose equivalent to another individual can be written as follows:

$$\begin{aligned} D(\infty) &= (0.25)\left[\int_0^{t_{lic}} R_{1\,m}e^{-t/\tau}\,dt + \left[\int_{t_{lic}}^{\infty} (R_{1\,m} + R_b)e^{-t/\tau}\,dt\right]\right] \\ &= (0.25)[R_{1\,m}\tau(1 - e^{-t_{lic}/\tau}) + (R_{1\,m} + R_b)(\tau)(e^{-t_{lic}/\tau} - 0)] \\ &= 0.25[R_{1\,m}\tau + R_b\tau e^{-t_{lic}/\tau}]. \end{aligned} \qquad \text{Eq. 2A}$$

Assume the following definitions (based on Eq. 1a):

$$D_{1\,m} = 0.25R_{1\,m}\tau$$

and

$$D_b = 0.25R_b\tau.$$

Equation 2a can be written as:

$$D_{limit} = D_{1\,m} + D_b e^{-t_{lic}/\tau}. \qquad \text{Eq. 3A}$$

Solving for t_{lic} gives:

$$t_{lic} = (-\tau)\ln\left[\frac{(D_{limit} - D_{1\,m})}{D_b}\right]. \qquad \text{Eq. 4A}$$

In the case of pregnant women and children who may have contact with an RIT patient, the dose rate at 2 m was considered more appropriate for providing radiation safety guidelines as a prudent distance. Limited contact was also considered to be ~0.3 m. The dose equation for this situation was derived assuming limited contact during the restriction time period. During the restriction time period, the effective dose equivalent is derived from the dose rates measured at 2 m, assuming the occupancy factor of 0.25. Following the restriction period, normal behavior patterns are resumed, and the effective dose equivalent is derived from the dose rate at 0.3 m assuming the occupancy factor of 0.25. The effective dose equivalent is given by the following:

$$D(\infty) = \int_0^{t_{ab}} 0.25R_{2\,m}e^{-t/\tau}\,dt + \int_{t_{ab}}^{\infty} 0.25R_b e^{-t/\tau}\,dt \qquad \text{Eq. 5A}$$

$$= (0.25R_{2\,m}(-\tau)[-1 + e^{-t_{ab}/\tau}] + 0.25R_b(-\tau)[0 - e^{-t_{ab}/\tau}]).$$

Let:

$$D_{limit} = D(\infty),$$

$$D_b = 0.25R_b\tau$$

and

$$D_{2\,m} = 0.25R_{2\,m}\tau.$$

Equation 5a can be written as:

$$D_{limit} = D_{2\,m} - D_{2\,m}e^{-t_{ab}/\tau} + D_be^{-t_{ab}/\tau}$$

$$D_{limit} = D_{2\,m} + (D_b - D_{2\,m})e^{-t_{ab}/\tau} \qquad \text{Eq. 6A}$$

$$e^{-t_{ab}/\tau} = \frac{D_{limit} - D_{2\,m}}{D_b - D_{2\,m}}$$

$$t_{ab} = (-\tau)\ln\left[\frac{(D_{limit} - D_{2\,m})}{(D_b - D_{2\,m})}\right].$$

APPENDIX 2: PATIENT-SPECIFIC DOSE CALCULATIONS

In the final version of Regulatory Guide 8.39, the NRC introduced an additional component to the equation for calculating the effective dose equivalent to an individual from contact with a patient who received ^{131}I for the treatment of hyperthyroidism or thyroid cancer. This component accounts for the fact that during the initial hours following administration of the radiolabeled material, the patient may not void, and the activity is, therefore, not removed from the body. Failure to account for this contribution to the effective dose equivalent could result in an underestimate of the dose to another individual, as demonstrated in Appendix B of the Regulatory Guide.

The equation to account for this time component is as follows:

$$D(\infty) = \frac{(34.6)\Gamma Q_0}{(100\text{ cm})^2}\,ET_p[1 - e^{-0.693t/T_p}], \qquad \text{Eq. 7A}$$

where E = occupancy factor, T_p = physical half-life of the radionuclide and t = elapsed time.

For ^{131}I-NaI, the NRC assumed that, for the first 8 hr (0.33 days) following administration, 80% of the activity is being removed from the body at a rate determined only by physical decay. The recommended occupancy factor for a time period of <1 day is 0.75, and the physical half-life of ^{131}I is 8.04 days. Inserting these values, Equation 7a becomes:

$$D(\infty) = \frac{(34.6)\Gamma Q_0}{(100\text{ cm})^2}(0.75)(0.8)(8.04)[1 - e^{-0.693(0.33)/8.04}]$$

$$= \frac{(4.68)\Gamma Q_0}{(100\text{ cm})^2}.$$

For ^{131}I anti-B1, it is assumed that the initial void occurs at 3 hr (0.125 days) rather than at 8 hr and that 100% of the activity is being removed from the body at a rate determined only by physical decay. Three hours has been shown to be a conservative estimate for the first or initial voiding time (*23*) and is consistent with the analysis performed on 109 patients following the intravenous administration of ^{131}I anti-B1. For ^{131}I anti-B1, Equation 7a becomes:

$$D(\infty) = \frac{(34.6)\Gamma Q_0}{(100\text{ cm})^2}(0.75)(8.04)[1 - e^{-0.693(0.125)/8.04}]$$

$$= \frac{(2.24)\Gamma Q_0}{(100\text{ cm})^2}.$$

Thus, this component for ^{131}I anti-B1 is ~50% of that for ^{131}I-NaI.

The full equation for total effective dose is the sum of the nonvoided component (Eq. 7a) and the component(s) resulting from exponential elimination. For ^{131}I anti-B1, the equation is as follows:

$$D(\infty) = \frac{\Gamma Q_0}{(100\text{ cm})^2}[2.24 + 34.6ET_{eff}(-e^{-0.693(0.125)/8.04})]. \qquad \text{Eq. 8A}$$

Because the total body residence time, τ (in hr) is equal to 34.6 multiplied by T_{eff} and the recommended occupancy factor for a time period of >1 day is 0.25, Equation 8a becomes:

$$D(\infty) = \frac{\Gamma Q_0}{(100\text{ cm})^2}[2.24 + (0.25)(\tau)(-e^{-0.693(0.125)/8.04})] \qquad \text{Eq. 9A}$$

$$= \frac{0.25\Gamma Q_0}{(100\text{ cm})^2}[8.96 + 0.99(\tau)].$$

In effect, the inclusion of the nonvoided component adds 8.96 hr to the measured total-body residence time. Because the residence time for ^{131}I anti-B1 patients was determined to be in the range of 58–127 hr, the percentage underestimate in this series of patients would range from 7% to 15%.

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