CALCULATING PULMONARY-MODE-LETHALITY RISK AVOIDANCE ASSOCIATED WITH RADIONUCLIDE DECORPORATION COUNTERMEASURES RELATED TO A RADIOLOGICAL TERRORISM INCIDENT

Dose-Response, 8:83–96, 2010
Formerly Nonlinearity in Biology, Toxicology, and Medicine

ISSN: 1559-3258
DOI: 10.2203/dose-response.09-026.Scott

International Dose-Response Society
www.Dose-Response.org

CALCULATING PULMONARY-MODE-LETHALITY RISK AVOIDANCE ASSOCIATED WITH RADIONUCLIDE DECORPORATION COUNTERMEASURES RELATED TO A RADIOLOGICAL TERRORISM INCIDENT

Bobby R. Scott □ Lovelace Respiratory Research Institute, Albuquerque, NM

□ Planning for and managing radiological terrorism incidents that involve the release of radionuclides from a dirty bomb requires considering the potential lifesaving impact of protective radionuclide decorporation countermeasures (e.g., lung lavage). Lung lavage therapy could prevent deaths via the pulmonary mode (which involves radiation pneumonitis and fibrosis) by reducing the radiation dose to the lung from inhaled radionuclides. The risk avoidance (*RAV*) assessment framework introduced in a related paper is used to evaluate the pulmonary-lethality-mode *RAV* due to lung lavage and the associated risk avoidance proportion (*RAP*) for hypothetical inhalation-exposure scenarios. The lethality *RAV* is a measure (on a scale from 0 to 1) of the actual risk reduction associated with the applied protective countermeasures. The lethality *RAP* is the lethality *RAV* divided by the lethality risk when no protective countermeasures are employed and is a useful measure of the efficacy of the countermeasures applied. Examples of pulmonary-mode lethality *RAV* and *RAP* calculations are presented for hypothetical scenarios involving lung lavage to remove beta and/or gamma-emitting radionuclides that are inhaled in highly insoluble forms. The approach presented could be used to develop optimal schemes for applying lung lavage therapy following a terrorist incident involving a dirty bomb.

Keywords: Risk, radionuclide, lethality, decorporation, countermeasures

INTRODUCTION

Recent terrorist actions throughout the world underscore the growing threat of radiological terrorism (DHS 2003; CDC 2005; DHHS 2009). This has stimulated research on and development of medical countermeasures for protecting humans against radiation harm, including harm resulting from use by terrorist of a radioactivity dispersal device (RDD) such as a dirty bomb.

During a radiological terrorist incident radionuclides could be inhaled (e.g., after a dirty bomb detonation). Inhaling large quantities of radionuclides could lead to lives lost among the general public from radiation-induced deterministic effects that evolve over time. Deterministic effects are threshold-type effects that include lethal damage to the lung (e.g., radiation-pneumonitis-related). The threshold dose for lethal damage varies for different individuals and depends on how dose rate changes over time (Scott and Hahn 1989). The time to deliver a lethal

Address correspondence to Bobby R. Scott, Lovelace Respiratory Research Institute, 2425 Ridgecrest Drive SE, Albuquerque, NM 87108 USA; Phone: 505-348-9470, Fax: 505-348-8567; E-mail: bscott@LRRI.org

dose increases as dose rate decreases. For long-lived radionuclides inhaled in highly insoluble forms, the accumulation of a lethal radiation dose may require more than a year after inhaling the radioactive material. The effective management of dirty bomb incidents requires careful planning that includes considering the impact of radionuclide decorporation (removal from the body) countermeasures that could be employed to reduce the radiation dose and associated risk of harm to first responders, members of the general public, and others.

Employing lung lavage (bronchoalveolar) is a possible countermeasure to remove excess radioactivity from the respiratory tract in the case of inhalation exposure to airborne radionuclides resulting from a dirty bomb incident (Nolibé et al. 1989; Muggenburg et al. 1990; Breitenstein 2003). The removal leads to a reduction in the committed radiation dose (the dose that builds up over time) and also may reduce the risk of radiation-induced harm depending on the endpoint considered and residual radiation dose (Scott 2005). Pharmaceutical and other products are also being developed for possible employment as radioprotectors and as decorporating agents to facilitate removing radionuclides from the body after uptake into the systemic circulation. However, *the focus here is on scenarios involving inhalation of highly insoluble aerosols that mainly irradiate the respiratory tract.* A related paper addresses ingestion (via a liquid) of highly soluble forms of beta and/or gamma-emitting radionuclides that deposit in the skeleton and irradiate the radiosensitive bone marrow (Scott 2009).

The related paper (Scott 2009) introduces health risk assessment (HRA) tools that facilitate planning for and managing radiological terrorism incidents such as those that involve an RDD. The indicated HRA tools include analytical functions for evaluating the lethality risk avoidance (*RAV*) due to protective countermeasures and the risk avoidance proportion (*RAP*) (*RAV* divided by the lethality risk in the absence of protective countermeasures). These hazard-function (HF) model-based tools are applied in this paper to hypothetical scenarios that involve humans exposed by inhalation to highly insoluble beta- and/or gamma-emitting aerosols released from a dirty bomb. Examples of pulmonary-mode-lethality *RAV* and *RAP* calculations are provided. The pulmonary mode of lethality (from severe damage to the lung) is considered to be related to radiation pneumonitis and fibrosis (Scott and Hahn 1989).

The hypothetical scenarios considered in the main text involve circumstances where the low linear-energy-transfer (LET) beta/gamma radiation dose rate to the lung (critical target considered) decreases as a single, negative-exponential function of time. The single negative-exponential characterization is used for illustrative purposes to facilitate understanding of how to evaluate the lethality *RAV* and *RAP*. More general relationships that apply to any monotonically decreasing (i.e., steadi-

ly decreasing) dose-rate pattern are presented in the Appendix. Information is also provided in the main text about how to address dose rates that initially increase over time and then steadily decrease.

METHODS

Evaluating Pulmonary Mode Lethality *RAV* and *RAP*

Lethality risks are evaluated based on the HF model (Scott 2004) using the approach described in the cited related paper (Scott 2009). For the HF model and for the pulmonary mode of death, the risk function R (i.e., individual probability of radiation-induced lethal damage to the lung) is given as a function of lethality-mode-specific hazard, H_{pul} (a cumulative hazard function for the pulmonary mode) and survival probability, S, by (Scott and Hahn 1989):

$$R = 1 - S = 1 - \exp(-H_{pul}). \quad (1)$$

The pulmonary-model lethality hazard H_{pul} can be evaluated based on the following equation:

$$H_{pul} = [\ln(2)]X^V, \quad (2)$$

where V (>0) is the shape parameter that determines the steepness of the sigmoid dose-response curve for the lethality risk; X is the *normalized dose* in units of the lethality-mode-specific, median-lethal absorbed dose D_{50}. The value $X = 1$ corresponds to the median lethal absorbed dose D_{50}, which increases as the dose rate decreases. Absorbed dose to the lung is determined by total radiation energy imparted to the lung divided by the mass of the lung and has units such as gray (Gy). A gray equals 1 joule per kilogram of tissue. For high dose rate exposure, D_{50} has been estimated to be 10 Gy (central estimate) (Scott and Hahn 2009).

The normalized dose (i.e., X) is quite useful for addressing subtle changes in dose rate pattern as occur with radionuclide decorporation therapy. For example, the normalized dose increment that occurs before applying lung lavage can be evaluated and added to the additional normalized dose increment that occurs after application of the procedure. Risk is then evaluated based on the sum of the two normalized dose increments (Scott 2009). Evaluating the normalized dose X requires a functional relationship between D_{50} and the organ-specific radiation absorbed dose rate y when held at a given value. For the pulmonary mode of lethality, a functional relationship that has been found to be adequate is given by the following equation (Scott and Hahn 2009):

$$D_{50}(y) = (\theta_1/y) + \theta_\infty. \quad (3)$$

Equation 3 was developed for exposure to low LET beta and/or gamma radiation but was also applied to high-LET alpha radiation via adjusting model parameters (Scott 2007) or via using RBE-weighted dose (Scott and Peterson 2003). For the pulmonary mode of death (radiation pneumonitis and fibrosis related) and for internal low-LET beta/gamma radiation, central estimates for HF model parameters are $V = 5$, $\theta_\infty = 10$ Gy, and $\theta_1 = 30$ Gy^2/h (Scott and Hahn 1989). Uncertainty related to these parameters (i.e., parameter uncertainty) can be addressed *via* subjective lower and upper bounds (Scott and Hahn 1989). Subjective lower and upper bounds for V are 4 and 6, respectively; for θ_∞, 8 and 12 Gy, respectively; for θ_1, 15 and 45 Gy^2/h, respectively. The impact on risk assessment reliability of model parameter uncertainty was address in other publications (USNRC/CEC 1997; Scott and Peterson 2003; Scott 2007).

Analytical Solution for *X* for Single, Negative-Exponential-Decaying Dose Rate

The following analytical solution applies for a single negative-exponential-decaying dose-rate pattern with initial dose rate A and decay parameter λ (Scott and Dillehay 1990; Scott 2009):

$$X\{t, A\} = X_{\max}\{t, A\} - Q\{t, A\}. \tag{4}$$

The terms on the right-hand side of Equation 4 represent the following:

$$X_{\max}\{t, A\} = D\{t, A\})/\theta_\infty \tag{5}$$

and

$$Q\{t, A\} = (\theta_1 \ln\{[A\theta_\infty + \theta_1]/[A\theta_\infty \exp(-\lambda t) + \theta_1]\})/\lambda\theta_\infty{}^2. \tag{6}$$

The function $D\{t, A\}$ is the exposure-time-dependent radiation absorbed dose to the target organ at exposure time t and is evaluated as $(A/\lambda)[1 - \exp(-\lambda t)]$ for the dose rate pattern to the lung considered here. The parameter λ relates to the effective retention halftime ($T_{1/2}$) of the radionuclide in the target organ according to the equation $\lambda = \ln(2)/T_{1/2}$. *Exposure scenarios considered here involve a single, brief inhalation exposure episode rather than chronic intake.*

The function $Q\{t, A\}$ is called the normalized dose adjustment (*NORDA*) (Scott 2009). The adjustment is due to the body's protective measures (e.g., repopulation of lost lung cells and repair of DNA damage) that come into play when the dose rate is low, making the normalized dose shrink from its maximum value $X_{\max}\{t, A\}$ that occurs when dose rate remains high. An equation analogous to Equation 4 is utilized in the

Appendix to obtain results for application to any type of dose rate pattern that monotonically decreases with time.

Asymptotic Solution for Normalized Dose

Over time and for a single, negative-exponential-decaying dose-rate pattern to the lung, $X\{t, A\}$ will approach an asymptotic value $X_\infty\{A\}$ (i.e., *asymptotic normalized dose*) which can be obtained by taking the limit of $X\{t, A\}$ (based on Equation 4) as $t \rightarrow \infty$. This limit is given by the following (Scott 2009):

$$X_\infty\{A\} = (D_\infty\{A\}/\theta_\infty) + Q_\infty\{A\}. \quad (7)$$

where:

$$D_\infty\{A\} = A/\lambda \quad (8)$$

and

$$Q_\infty\{A\} = [\theta_1 \ln\{(A\theta_\infty + \theta_1)/(\theta_1)\}]/\lambda\theta_\infty{}^2. \quad (9)$$

The term $Q_\infty\{A\}$ is the maximum value for the *NORDA* for a single, negative-exponential-decaying dose-rate pattern. The dose $X_\infty\{A\}$ when evaluated according to Equation 7 will be linearly related to $T_{1/2}$ (Scott 2009).

RESULTS AND DISCUSSION

Time Period over which Radiation Dose Should Be Evaluated

Plotting $X\{t, A\}/X_\infty\{A\}$ vs. $t/T_{1/2}$ (normalized time in units of $T_{1/2}$) is a useful way of determining the period over which radiation dose to the lung should be evaluated when assessing lethality risks (or risk avoidance) for single, negative-exponential-decaying dose-rate patterns (Scott 2009). This period will depend on the initial dose rate A, $T_{1/2}$ (which relates to λ), and parameters θ_∞ and θ_1. The ratio $X\{t, A\}/X_\infty\{A\}$ will increase as $t/T_{1/2}$ increases and eventually approach the asymptotic value of 1.0 (Scott 2009). The lethality risk R will be expected to increase so long as $X\{t, A\}/X_\infty\{A\}$ increases.

Table 1 shows calculated values (rounded) of $X\{t, A\}/X_\infty\{A\}$ vs. $t/T_{1/2}$ for different initial dose rates (A = 0.01, 0.02, 0.04, 0.06, 0.08, or 0.1 Gy/h) to the lung of humans after a single inhalation exposure to beta/gamma-emitting radionuclides in highly insoluble forms when dose rate decreases as a single-negative-exponential function of time. Results were obtained based on $T_{1/2}$ = 2000 d. In each case considered, a value of $t/(T_{1/2})$ = 2.2 approximates the normalized time at which 95% of the infi-

TABLE 1. Expected ratio $X\{t, A\}/X_\infty\{A\}$ vs. $t/(T_{1/2})$ for the pulmonary mode of death after single inhalation exposure to highly-insoluble beta/gamma-emitting radionuclides when dose rate decreases as a single-negative-exponential function of time.

	Initial Dose Rate (Gy/h)					
$t/(T_{1/2})$	0.01	0.02	0.04	0.06	0.08	0.1
0	0	0	0	0	0	0
0.2	0.24	0.24	0.24	0.24	0.24	0.24
0.4	0.43	0.43	0.43	0.42	0.42	0.42
0.6	0.57	0.57	0.56	0.56	0.56	0.56
0.8	0.67	0.67	0.67	0.67	0.67	0.67
1	0.75	0.75	0.75	0.75	0.75	0.75
1.2	0.81	0.81	0.81	0.81	0.81	0.81
1.4	0.86	0.86	0.86	0.86	0.86	0.86
1.6	0.89	0.89	0.89	0.89	0.89	0.89
1.8	0.92	0.92	0.92	0.92	0.92	0.92
2	0.94	0.94	0.94	0.94	0.94	0.94
2.2	0.95	0.95	0.95	0.95	0.95	0.95
2.4	0.97	0.97	0.97	0.97	0.97	0.96
2.6	0.97	0.97	0.97	0.97	0.97	0.97
2.8	0.98	0.98	0.98	0.98	0.98	0.98
3	0.99	0.99	0.99	0.99	0.99	0.99
3.2	0.99	0.99	0.99	0.99	0.99	0.99
3.4	0.99	0.99	0.99	0.99	0.99	0.99
3.6	0.99	0.99	0.99	0.99	0.99	0.99
3.8	1	1	1	1	1	1
4	1	1	1	1	1	1
4.2	1	1	1	1	1	1
4.4	1	1	1	1	1	1
4.6	1	1	1	1	1	1
4.8	1	1	1	1	1	1
5	1	1	1	1	1	1

[a]Values in italics that occur at $t/(T_{1/2}) = 2.2$ are approximately 95% of $X_\infty\{A\}$.

nite normalized dose (i.e., $X_\infty\{A\}$) is achieved. However, for lower initial dose rates, different results may occur. Based on the results presented in Table 1, most of the lethality risk accumulation would be expected to have occurred by the time t for which $t/T_{1/2} = 4$. This time is given by $4T_{1/2}$ which for example would be 4000 d after radionuclide intake when $T_{1/2} = 1000$ d.

For multiple negative exponential decaying dose-rate patterns, $T_{1/2}$ can be evaluated based on the long-term retention component. However, the more involved procedure presented in the Appendix is then needed for evaluating the normalized dose.

Evaluating Lethality Risk Avoidance due to Lung Lavage

Scenarios considered here involve a single application of lung lavage to remove a deposited radionuclide inhaled and deposited as a result of

dirty bomb incident. *It is assumed here and in the Appendix that the lethality risk associated with the lavage procedure itself is negligible.* The dose increment, $X\{t, A\}$, that occurs before application of lung lavage can be evaluated using the following relationship, where $t = T$ is the time at which the single lung lavage treatment is applied (Scott 2009):

$$X\{T, A\} = X_{\max}\{T, A\} - Q\{T, A\}. \tag{10}$$

The normalized dose increment $X\{A_{alt}(T)\}$, that occurs after lung lavage is evaluated, using the asymptotic solution presented in Equation 7; however, A has to be replaced with $A_{alt}(T)$ (Scott 2009). The subscript *alt* stands for altered. The dose rate is evaluated as being reduced (via lavage) on average by a *dose-rate-reduction factor* (*DRRF*) given by $DRRF(T)$, and the pattern of decline in dose rate afterward is presumed to still be a negative exponential but with a possibly modified parameter λ_1 (which can be set equal λ when appropriate). The altered dose rate in the lung just after radiation time $t = T$ is therefore evaluated as follows:

$$A_{alt}(T) = A \exp(-\lambda T)/DRRF(T). \tag{11}$$

For such scenarios, the initial dose rate A in Equation 7 can be replaced by the altered initial dose rate $A_{alt}(T)$ and λ is replaced by λ_1 when evaluating the increment in the normalized dose that occurs after lung lavage treatment. This yields the following results (asymptotic solution) for the indicated increment, $X\{A_{alt}(T)\}$:

$$X_{\infty}\{A_{alt}(T)\} = (D_{\infty}\{A_{alt}(T)\}/\theta_{\infty}) - Q_{\infty}\{A_{alt}(T)\}. \tag{12}$$

Please note that λ_1 now replaces λ when using Equations 8 and 9 to evaluate $D_{\infty}\{A_{alt}(T)\}$and $Q_{\infty}\{A_{alt}(T)\}$. The Appendix provides results that are more general and can be applied to cases where lung lavage is administered multiple times. The increment $X\{T, A\}$, which occurs before lung lavage, is added to the increment $X_{\infty}\{A_{alt}(T)\}$, which occurs after lung lavage, to get the total normalized dose X_{pro} that is used in evaluating lethality risk. The subscript *pro* is used to indicate that protective decorporation measures are accounted for (Scott 2009).

The total lethality risk (central estimate) without decorporation countermeasures is indicated as R_{unpro} and is given by the following:

$$R_{unpro} = 1 - \exp\{[-\ln(2)]\, X_{\infty}\{A\}^5\}. \tag{13}$$

The subscript *unpro* stands for *unprotected* (e.g., no lavage administered). Table 2 provides risk estimate for R_{unpro} as a function of $X_{\infty}\{A\}$. The corresponding residual risk (Scott 2005) when protective decorporation

TABLE 2. Central estimates of the lethality risk R_{unpro} for the pulmonary mode of death in humans as a function of the asymptotic value of the normalized dose.

Normalized Dose $X_\infty\{A\}$	Lethality Risk
0	0
0.4	$< 10^{-2}$
0.5[a]	0.02
0.6	0.05
0.7	0.11
0.8	0.20
0.9	0.34
1.0	0.50
1.1	0.67
1.2	0.82
1.3	0.92
1.4	0.98
1.5	0.99
1.6	1.00

[a]A value of $X_\infty\{A\} = 0.5$ (lethality risk < 0.025 for the pulmonary mode) has been used as an estimate of the threshold exposure in radiological risk assessment because of the steepness of the dose-response curve for the lethality risk (Scott and Hahn 1989). A value of $X_\infty\{A\} = 0.4$ (lethality risk < 10^{-2}) may be preferred for the threshold estimate for some applications.

countermeasures (lavage considered here) are applied at time T is indicated here as R_{pro} and is given by the following:

$$R_{pro} = 1 - \exp\{[-\ln(2)]\ X_{pro}{}^{5}\}. \quad (14)$$

The shape parameter value of $V = 5$ in Equations 13 and 14 only applies to central risk estimation and only for internal irradiation via radionuclides (Scott and Hahn 1989). For uncertainty characterization, subjective lower and upper bounds of 4 and 6 can be applied (Scott and Hahn 1989). The lethality *RAV* can therefore be evaluated as follows (Scott 2009):

$$RAV = R_{unpro} - R_{pro}. \quad (15)$$

The corresponding equation for the *RAP* is as follows (Scott 2009):

$$RAP = RAV/R_{unpro}. \quad (16)$$

Figure 1 shows the calculated pulmonary-mode-lethality *RAVs* (central estimates) associated with lung lavage when administered to humans 1 h after inhalation exposure to beta- and/or gamma-emitting radionuclides in highly insoluble forms. Essentially the same modeling results (not shown) were obtained for application of lung lavage at 24 h after inhalation exposure. The variable $T_{1/2}$ was assigned the hypothetical

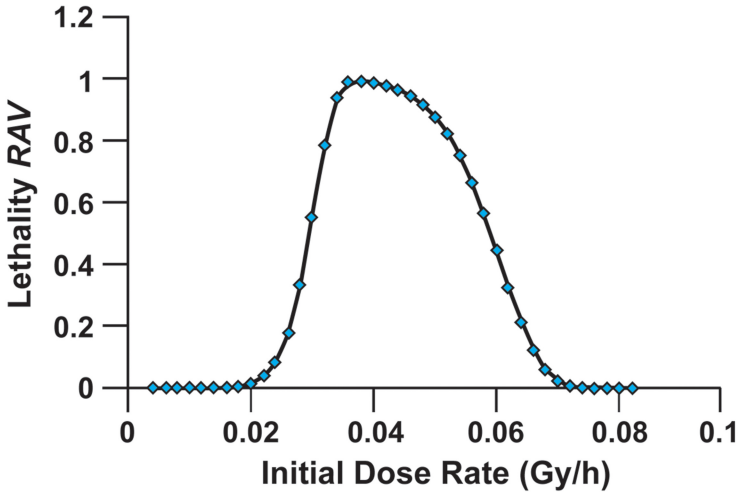

FIGURE 1. Central estimates of the pulmonary-mode-lethality *RAV* associated with lung lavage when administered to humans 1 h after inhalation exposure to beta- and/or gamma-emitting radionuclides in highly insoluble forms. The plotted points correspond to initial dose rates used in the calculations Results apply to $T_{1/2}$ = 2000 d.

value of 2000 days for both the pre- and post-lavage periods. Thus $\lambda_1 = \lambda$ for this example. Both *DRRF*(1 h) and *DRRF*(24 h) were assigned the hypothetical value of 2. For the indicated hypothetical scenarios, applying the lung lavage at 24 h after intake would be expected to be as protective as applying the procedure 1 h after intake. However for a scenario for which $T_{1/2}$ = 200 min, this would not be the case as >99% of the radiation dose would have been delivered by 24 h after radionuclide intake. At 1 h after intake, only about 19% of the radiation dose would have been delivered. Applying decorporation therapy at the 1-h time point would therefore be expected to eliminate considerable radioactivity from the body before additional radiation damage is produced. Applying decorporation therapy at 24 h after radionuclide intake would not be expected to provide any real benefit because most of the radiation dose would have already been delivered.

Figure 2 shows corresponding modeling results (central estimates) for the *RAP* for $T_{1/2}$ = 2000 d when lung lavage is applied at 1 h after inhalation exposure. Essentially the same modeling results (not shown) were obtained for application of lung lavage at 24 h after inhalation exposure. For initial dose rates to the lung less than about 0.03 Gy/h, essentially all of the lethality risk would be expected to be avoided as a result of applying the lavage procedure, irrespective of whether given 1 h or 24 h after intake. The dose-rate zone (for initial dose rates) for which all of the lethality risk is avoided by the countermeasures applied is called the *green zone* (Scott 2009). For initial dose rates to the lung greater than about 0.07 Gy/h, no benefit of the lavage therapy (single application)

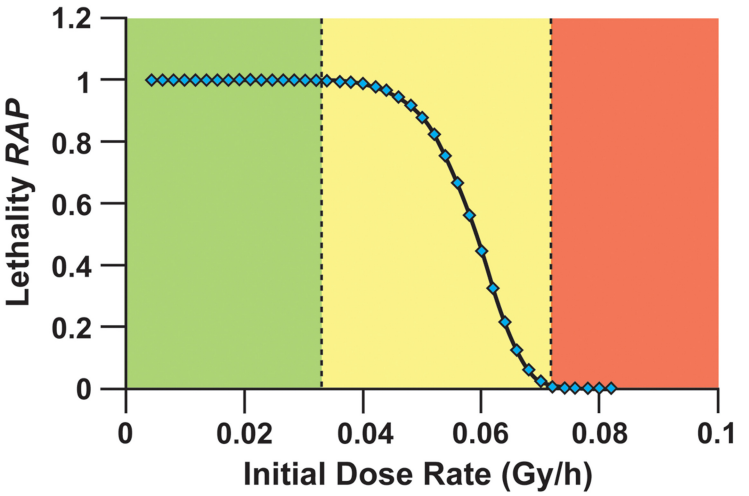

FIGURE 2. Central estimates of the pulmonary-mode-lethality *RAP* associated with lung lavage when administered to humans 1 h after inhalation exposure to beta- and/or gamma emitting radionuclides in highly insoluble forms. The plotted points correspond to initial dose rates used in the calculations. Results apply to $T_{1/2}$ = 2000 d. Dose rate zones (green, yellow, and red) are color coded.

would be expected related to preventing death from radiation-induced damage to the lung. The dose-rate zone for which none of the lethality risk is avoided by the countermeasures applied ($RAP = 0$; $R_{pro} = R_{unpro} = 1$) is called the *red zone* (Scott 2009). The dose-rate zone (initial dose rate) between the green and red zones is where some but not all of the lethality risk is avoided (i.e., $0 < RAP < 1$) and is called the *yellow zone* (Scott 2009). For single lavage scenarios that are associated with the red zone, more intensive countermeasures would be warranted (e.g., multiple lavages and possibly other protective measures).

The dose-rate (initial) boundaries for the green, yellow, and red zones will depend on the radionuclide decorporation therapy scheme and exposure scenario. When the HF-model and countermeasure-related uncertainties are considered, the boundaries will likely become blurred. Zone boundaries should therefore be considered highly uncertain; however, new research is needed to address uncertainty-related issues.

The results presented in figures and tables relate to single, negative-exponential-decaying dose-rate patterns. However, the more general relationships provided in the Appendix can be used to evaluate the lethality *RAV* and *RAP* and associated green, yellow, and red dose-rate zones (based on initial dose rate) for a specified scheme for more complex monotonically decreasing dose rate patterns.

Some exposure scenarios of interest may involve an initial rise in dose rate over time followed by a period of steady decreases in dose rate. For such dose-rate profiles, the increment in the normalized dose that occurs

during the rising dose-rate phase could be evaluated based on taking small time increments over intervals $(t, t + \Delta t)$, with average dose rate calculated for each interval. The increment in the normalize dose for each such interval can be estimated by dividing the interval-specific dose increment by D_{50} (evaluated using Equation 3 with the average dose rate for the interval used in the calculation). The increments in the normalized dose for the rising phase of dose rate would then add to increments that arise from the decaying dose rate phase, which can be evaluated as indicated in the Appendix (or alternatively as indicated for the rising dose-rate phase). Lethality *RAV* and *RAP* can then be evaluated in the same way as outlined above.

The modeling framework presented here could also be applied to inhalation exposure scenarios that involve combined exposure to alpha-, beta-, and gamma-emitting radionuclides provided that absorbed dose was replaced with RBE-weighted dose. Further, competing modes of death (e.g., pulmonary, hematopoietic, and gastrointestinal) could also be included.

The research described here and also in the closely related paper (Scott 2009) is an extension of much earlier research conducted by the author. Unfortunately, support for continuing the earlier research disappeared some years ago and interest in supporting the type of theoretical/modeling research presented in these papers has not increased since that time. Unless more appreciation is develop by the scientific community and funding agencies of the important contributions that theoretical/modeling research (e.g., radionuclide biokinetics/biodistribution, dosimetry and risk modeling) can make to the advancement of scientific knowledge related to planning for and managing radiological terrorism incidents, the next generation of scientist may be devoid of essential knowledge needed for addressing the types of issues that are addressed in this paper.

CONCLUSIONS

A theoretical framework was presented for evaluating both the expected pulmonary mode lethality *RAV* and *RAP* associated with lung lavage therapy for removing inhaled beta/gamma-emitting radionuclides deposited as a result of a terrorist act involving a dirty bomb. The computational tools provided for evaluating the lethality *RAV* and *RAP* should facilitate planning for and managing such radiological terrorism incidents. *RAV* and *RAP* values were evaluated for single-negative exponential decaying dose-rate patterns to the lung from beta/gamma emitting radionuclides that are inhaled in highly insoluble forms. The theoretical framework presented in the Appendix, however, can be applied to any monotonically decreasing dose rate pattern and could be easily incorporated into radiological risk assessment software. The framework could

also be used to design optimal life saving schemes for application of multiple lung lavages; however, new research is needed to address uncertainties associated with *RAV* and *RAP* evaluations.

ACKNOWLEDGMENTS

This research was supported by Lovelace Respiratory Research Institute. I am grateful to Vicki Fisher for editorial assistance and to Wendy Piper for graphics support.

APPENDIX

More Complex, Monotonically Decreasing, Dose-Rate Patterns

A similar approach as described in the main text of this paper can be employed for any monotonically decreasing, dose-rate pattern to the lung using the generalized results presented below, where $y(t)$ is the unmodified dose rate at radiation exposure time t. Relationships are provided that allow for evaluating small increments in the normalized dose over consecutive, relatively short radiation exposure time intervals $(t, t + \Delta t)$. To address departure from a single, negative-exponential-decaying pattern of dose rate, the parameter λ is replaced by a time-dependent function $\lambda(t)$ that allows for a changing rate of radioactivity loss as time increases.

To account for the impact on dose rate of applying single or multiple lung lavages, the dose rate $y(t)$ is adjusted downward by the radiation-exposure-time-dependent $DRRF(t)$, where the altered radiation absorbed dose rate $z(t)$ is given by

$$z(t) = y(t)/DRRF(t). \tag{A1}$$

Prior to application of any lavage therapy, $DRRF(t) = 1$; otherwise $DRRF(t) > 1$. This leads to the following relationships for the exposure-time-dependent increment, $X\{t, \Delta t, z(t)\}$, in the normalized dose over the interval $(t, t + \Delta t)$ (e.g., $\Delta t = 1$ day for long-lived radionuclides):

$$X\{t, \Delta t, z(t)\} = \{z(t)[1 - \exp(-\lambda(t)\Delta t]/[\lambda(t)\theta_\infty]\} -$$

$$(\theta_1/[\lambda(t)\theta_\infty{}^2])\ln\{[z(t)\theta_\infty + \theta_1]/[z(t)\theta_\infty \exp(-\lambda(t)\Delta t) + \theta_1]\}. \tag{A2}$$

The decay function $\lambda(t)$ in the above equation is evaluated as follows:

$$\lambda(t) = -[\ln\{z(t + \Delta t)/z(t)\}]/\Delta t. \tag{A3}$$

The use of the function $DRRF(t)$ as indicated in Equation A1 imposes a constraint on its values (Scott 2009). The constraint is that $DRRF(t_2)$

$\geq DRRF(t_1)$ when $t_2 > t_1$. The constraint is necessary because $DRRF(t)$ acts on $y(t)$, which relates to the dose-rate pattern when no lung lavage has been used. Thus, if at time t_1 dose rate is reduced by a factor of 2 because of lung lavage applied, and if at time t_2 the already altered dose rate is reduced also by another factor of 1.5 due to an additional lung lavage, then $DRRF(t_1) = 2$ and $DRRF(t_2) = 2 \times 1.5 = 3$. For this hypothetical example, $z(t_1) = y(t_1)/2$ and $z(t_2) = y(t_2)/3$, where $y(t_1)$ and $y(t_2)$ relate to the unmodified dose-rate patterns at times t_1 and t_2.

It is important that when $z(t)$ is expressed in Gy/h that t be expressed in hours, θ_1 be expressed in Gy^2/h, and θ_∞ be expressed in Grays. For the single, negative-exponential-decaying dose-rate pattern $A \exp(-\lambda t)$, the right-hand side of Equation A3 yields λ.

At the interval for which the last countermeasure is applied at time T, the asymptotic solutions presented in the main text can be used with the dose rate $A_{alt}(T)$ replaced by $z(T)$, which equals $y(T)/DRRF(T)$. The last increment in the normalized dose will then be expressed as $X_\infty\{z(T)\}$. All of the normalized dose increments then can be added to obtain the total normalized dose X_{pro} and applied in Equations 15 and 16 when evaluating the *RAV* and *RAP*. For cases where the long-term retention halftime in the lung is more than 25 years, using the asymptotic solutions may lead to overestimation of risk. In such cases Equations A1, A2, and A3 can be repeatedly used over whatever follow-up time is desired.

REFERENCES

Breitenstein BD. 2003. The medical management of unintentional radionuclide intakes. Radiat Prot Dosim 105(1-4):495-497

CDC (Centers for Disease Control). 2005. Frequently asked questions (FAQs) about dirty bombs. Available at http://www.bt.cdc.gov/radiation/dirtybombs.asp

DHS (Department of Homeland Security). 2003. Radiological dispersion devices fact sheet. Available at http://www.dhs.gov/xnews/releases/press_release_0085.shtm

DHHS (Department of Health & Human Services). 2009. Radiological dispersal devices (RDDs). Available at http://www.remm.nlm.gov/rdd.htm

Muggenburg BA, Boecker BB, Hahn FF, McClellan RO. 1990. Lung lavage therapy to lessen the biological effects of inhaled ^{144}Ce in dogs. Radiat Res 124(2):147-155

Nolibé D, Métivier H, Masse R, Chrétien J. 1989. Benefits and risks of bronchopulmonary lavage: A review. Radiat Prot Dosim 26(1/4):337-343

Scott BR and Hahn FF. 1989. Chapter 2, Early occurring and continuing effects. In: *Health Effects Models for Nuclear Power Plant Accident Consequence Analysis, Low LET Radiation*, Rev. 1, Part II, NUREG/CR-4214, SAND85-7185, U.S. Nuclear Regulatory Commission, Washington, DC

Scott BR, Dillehay LE. 1990. A model for hematopoietic death in man from irradiation of bone marrow during radioimmunotherapy. Br J Radiol 63:863-870

Scott BR, Peterson VL. 2003. Risk estimates for deterministic health effects of inhaled weapons grade plutonium. Health Phys 85(3):280-293

Scott BR. 2004. Health risks from high-level radiation exposures from radiological weapons. Radiat Prot Manage 21(6):9-25

Scott BR. 2005. Evaluating residual risks for lethality from deterministic effects after application of medical countermeasures against damage from inhaled radioactivity dispersal device released gamma-emitting radionuclides. Radiat Prot Manage 22(3):7-26

Scott BR. 2007. Health risk evaluations for ingestion exposure of humans to polonium-210. Dose-Response 5:94-122

Scott 2009. Calculating hematopoietic-mode-lethality risk avoidance associated with radionuclide decorporation countermeasures related to a radiological terrorism incident. Dose-Response (in press)

USNRC/CEC (United States Nuclear Regulatory Commission, Commission of European Communities). 1997. *Probabilistic Accident Consequence Uncertainty Analysis, Early Health Effects Uncertainty Assessment*, Vol. 2 Appendices. Expert B, Report NUREG/CR-6545, Vol. 2, pp. C-31 – C-60, Washington DC