The British Journal of Radiology, 81 (2008), 232–243

The Radiation Injury Severity Classification system: an early injury assessment tool for the frontline health-care provider

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ABSTRACT. Our goal was to adapt current diagnostic methods for radiation overexposure patients into a practical system that can be implemented rapidly and reliably by responders unfamiliar with the effects of radiation. Our Radiation Injury Severity Classification (RISC) system uses clinical and haematological parameters from the prodromal phase of the acute radiation syndrome (ARS) to classify acute radiation injury for purposes of managing treatment disposition. Data from well-documented ARS cases were used to test the RISC system. Three-day summaries were generated for each case. These were individually reviewed by the three physicians most involved with the development of the system to establish both a consensus case score (CCS) and disposition category ranges. 30 volunteer raters from varying health disciplines using the RISC system then each independently rated a random selection of 12 cases for injury severity in a self-trained field-simulation exercise. The CCS identified discrete cut-off ranges for the three disposition categories in both manageable and mass casualty events. The group of raters, after a modest period of self-training, achieved overall levels of pairwise agreement with the CCS category of 0.944 for manageable events and 0.947 for mass casualty situations. In conclusion, an early assessment of the severity of the ARS injury is required for an appropriate disposition determination. The RISC system should produce reasonably accurate and reliable assessments of radiation injury severity within 6–12 hours post exposure despite the probable absence of physical dosimetric data.

Received 15 November 2005
Revised 6 May 2007
Accepted 4 June 2007

DOI: 10.1259/bjr/25373719

Acute radiation injuries resulting from exposure to external penetrating whole-body radiation constitute an emergency management problem that is both rare in occurrence and unfamiliar to the broad spectrum of health-care providers [1]. Since 1 December 1990, a total of 33 fatalities have occurred as a result of 259 significant radiation overexposures worldwide. In total, 55% of these fatalities were associated with medical diagnostic and therapeutic procedures [2]. Today, because of the rarity of such radiological events, medical education and training for health professionals and emergency providers in the radiation sciences is minimal.

In an emergency situation involving external radiation overexposure, stabilizing the patient's medical emergency (*e.g.* trauma) always takes precedence over the treatment of the radiation injury. This is because a latent phase occurs in all potentially treatable levels of radiation injury prior to the appearance of clinical manifestations that require medical intervention. Nonetheless, an early assessment tool to classify the severity of acute radiation injury would be a useful adjunct to the conventional triage process used in medical emergencies. At the very least, it would facilitate the acquisition and allocation of necessary treatment resources, as well as help to manage the anxiety of both patients and their caregivers about this relatively unfamiliar toxic agent. This point has become increasingly relevant with the threat of global terrorism and the possibility of radiation-related mass casualties. With such needs in mind, we have developed an efficient early assessment system for acute radiation exposures that can be used on an ''off-the-shelf'' basis and applied effectively by ''frontline health-care providers'' in a pre-hospital

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This work was supported by CDC/NIOSH grant numbers 1-R01-OH007866-01A2 and 1-R01-CCR312952-01A1, and by US Nuclear Regulatory Commission Contract No. 04-97-004. The support of a John M. Arthur/Duquesne Light Company Fellowship in Radiation Health for A Soaita is gratefully acknowledged

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environment or by more highly trained personnel in a hospital setting. These health-care providers are defined as doctors, nurses, emergency medical technicians/paramedics and other emergency medical personnel who are part of the initial assessment process, but who lack a detailed knowledge of the effects of acute radiation exposure.

The purpose of this paper is to introduce the Radiation Injury Severity Classification (RISC) system and to summarize the results of a final classroom field simulation used to demonstrate the overall effective use of the clinical tool after relatively modest self-instruction on its proper application.

Methods

Background to the RISC system

The Thoma–Wald diagnostic classification system [3], which was initially developed in the late 1950s for nuclear industrial accident applications and is still frequently cited in the radiation medicine literature [4–10], was used as the basis for the design of the RISC system. Thoma and Wald designed their system to categorize ARS patients into five prognostic groups (see Figure 1) on the basis of several key prodromal clinical features. One of the primary virtues of their diagnostic classification system was the fact that it did not require knowledge of exposure dose, as dosimetric information is unlikely to be available early after a radiation emergency. However, a limitation of their system when applied to early assessment situations is the requirement of extended periods of observation, sometimes for more than a week, before a patient can be finally assigned to a prognostic group. (For clarity, levels of injury severity in the Thoma–Wald classification model will be referred to as injury *groups*, whereas those in the RISC system will be referred to as disposition *categories*.)

In September 2000, a pilot study was initiated to assess the usefulness of the original Thoma–Wald model as a supplementary emergency triage tool. The results of that pilot study served as the basis for initial modifications to the Thoma–Wald diagnostic classification, which eventually led to the development of the RISC system described in this paper. The present form of the RISC system (see Figure 2) represents the final product of a series of classroom field-simulation exercises using the same set of medically well-documented cases of ARS in 22 Russian nuclear workers [11] and two historical cases from the Western literature [12–14]. Each one of these exercises resulted in subsequent revisions and improvements to the RISC system. The data summarized in this paper focus on the outcome of the most recent of these exercises and, unlike the earlier studies, it includes a combination of the better-documented Russian worker cases and well-documented cases from the open literature [15–25].

Development of the RISC model

The RISC system was developed to provide a simplified and more objective method for early ARS injury assessment. It produces a continuous summary score based on individual ratings for three categories of patients' injury data, *i.e.* haematological, gastrointestinal and neurovascular signs and symptoms. This approach facilitates a more precise definition of components and permits category cut-offs to be set empirically. It also allows separate category cut-offs to be set for what were termed ''manageable'' situations (*i.e.* smaller scale events within the treatment capacity of the medical system) as opposed to ''mass casualty'' situations (*i.e.* large-scale events that initially overwhelm the medical system).

Previous field-simulation exercises indicated that certain simplifications of the Thoma–Wald classification were necessary to obtain improved field applicability in manageable casualty situations. Thoma–Wald Groups I and II were merged to create an ''outpatient follow up'' disposition category; Groups III and IV were merged to produce an ''inpatient care'' disposition category; and Group V became the ''palliative care'' disposition category (see Figure 3). The term ''palliative care'' is used to mean ''relieving symptoms … without effecting a cure'' [26]. For the purpose of mass casualty situations, Category 2 (inpatient care) was limited to Group III of the Thoma–Wald system and Category 3 (palliative care) was expanded to include Groups IV and V. This reorganization of the assessment categories reflects the still adverse prognosis of Thoma–Wald group IV patients despite intensive medical efforts and the need to focus limited medical resources on those individuals most likely to respond favourably to aggressive treatment in mass casualty situations.

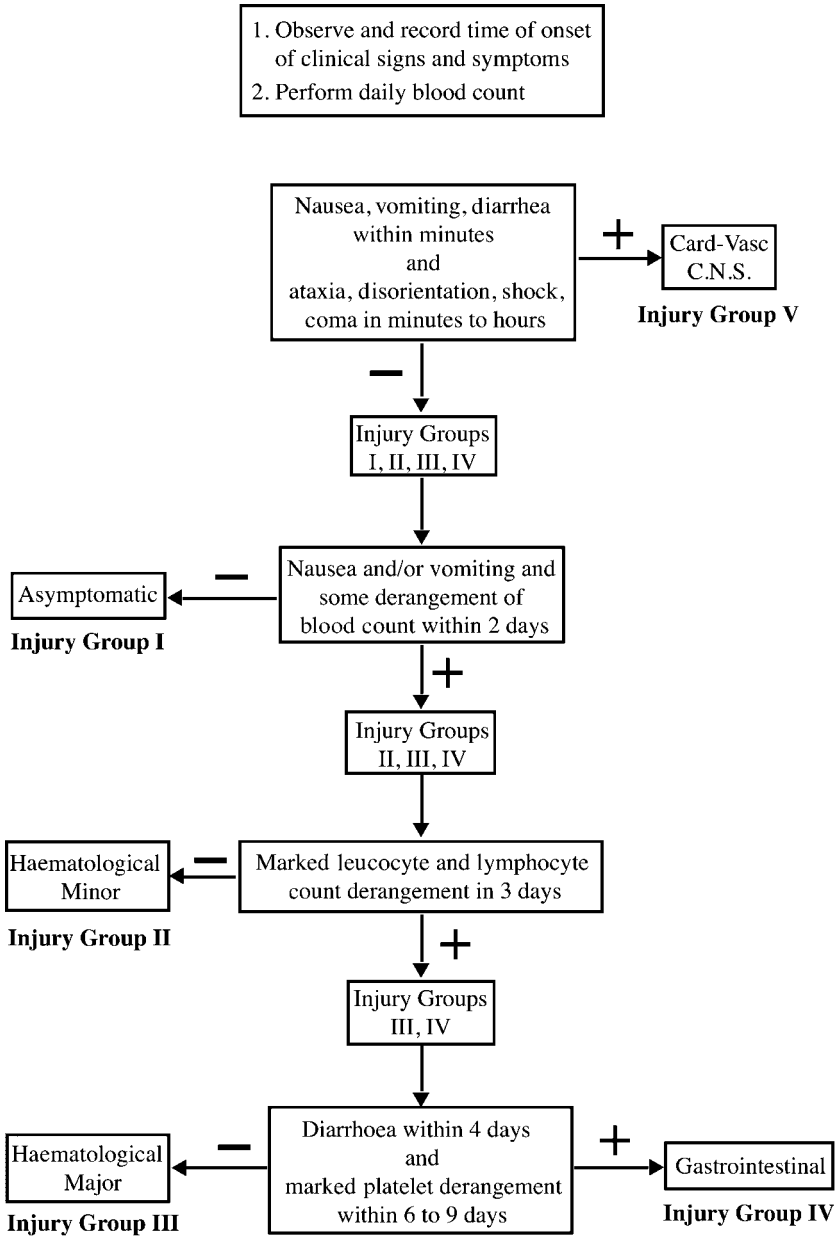
Human subjects protection

All of the work described in this paper was reviewed for human subjects protection and approved by the Institutional Review Boards at the University of Pittsburgh and the Southern Urals Biophysics Institute (SUBI).

Selection of ARS study cases

In January 1996, work began on a joint US–Russian project to test the feasibility of developing a computerized database [11] containing a sample of 14 cases of ARS among nuclear workers employed by the Mayak Production Association (Mayak PA) in Ozyorsk, Russian Federation, between 1948 and 1958. In 1998 the database was expanded to include all 45 of the remaining ARS cases that occurred at Mayak PA. These data were abstracted from the original Russian paper medical records and included a detailed inventory of post-exposure signs and symptoms, as well as the results of haematological and biochemical testing, a summary of the treatment rendered to the patients, and the clinical outcome of each case from time of exposure to time of death or discharge from, typically, 90 days of hospitalization.

From the 59 Russian ARS cases a subset of 22 was selected as appropriate for classroom field-simulation studies of the RISC system. The selection was based entirely on the availability of at least two haematological data points within the first 72 h post exposure. Similarly,



Reproduced with permission. From: Thoma GE, Wald N. The Diagnosis and Management of Accidental Radiation Injury. JOM. 1959;1:437.

Figure 1. Thoma–Wald Diagnostic Classification System.

the literature was reviewed [12–25] and an additional 13 well-documented cases were identified as being suitable for the purposes of the study. One of the authors (NW) reviewed the cases in their entirety and, based upon all of the available information, assigned each to one of the five prognostic groups previously described by Thoma and Wald. These patient classifications were reviewed and agreed upon by our Russian colleagues, and then used as the ''gold standard'' against which the RISC system and the field-simulation assessments of the medical evaluators were compared.

Vignettes containing the pertinent medical information from the first 72 h post-exposure were constructed by two of us (AZ, MK) for each of the 35 cases and formatted by the co-authors into an easily reviewable clinical summary. To provide a balanced representation among the Thoma–Wald groups (five cases each for Groups I and II, ten cases for Group III, seven for Group IV and three for Group V), six cases were eliminated (because of relatively limited information compared with other cases within a particular group) and a modified case that fulfilled group V criteria was added.

To minimize confusion, conflicting information was conservatively clarified in accordance with instruction on the proper application of the RISC system (see Appendix). For example, several case histories specified an onset of vomiting within 1–4 h, which spans two scoring levels in the gastrointestinal component of the RISC system. Such cases were altered to a conservative higher score by designating the onset as within 2 h.

Gastrointestinal		Neurovascular		Haematological	
No symptoms	0	No symptoms	0	**Within 72 hours** Lymphocyte count (mm^3)>1,250 & neutrophil count (mm^3)<10,000	0
Primarily anorexia/nausea Also other non-specific GI complaintsa within 6 hours NO vomiting	1	**Single** subjective symptoms: possible anxiety, fatigue, weakness or headache	1	**Within 72 hours** Lymphocyte count (mm^3)>1,000 & neutrophil count (mm^3)<10,000 OR Lymphocyte count (mm^3)>1,250 & neutrophil count (mm^3)<10,000	1
Vomiting - onset **within 6 hour**	2	**Multiple** subjective symptoms: anxiety, fatigue, weakness and/or headache [NO objective finding: remains oriented and normotensive (not hypotensive)]	2	**Within 72 hours** Lymphocyte count (mm^3)>500-999 & neutrophil count (mm^3)<10,000	2
Vomiting - onset **within 2 hour**	3	**In addition** to subjective symptom(s): fever, non-symptomatic drop blood pressure and/or mild confusion	3	**Within 72 hours** Lymphocyte count (mm^3)>500 - 1000 & neutrophil count (mm^3)<10,000 OR Lymphocyte count (mm^3)>100 - 499 & neutrophil count (mm^3)<10,000	3
Vomiting - onset **within 1 hour** AND At least one episode of diarrhoea or Abdominal pain **within 48 hours**	4	Objective findings: **symptomatic hypotension[b] mandatory**, Also, probable fever and mild confusion [subjective symptom (s):present and likely more intense and persistent]	4	**Within 72 hours** Lymphocyte count (mm^3)>0 - 499 & neutrophil count (mm^3)<10,000	4
Vomiting - onset **within 30 minutes** AND Recurrent diarrhoea **within 48 hours** or acute abdomen	5	Hypotension - severe but correctable Disorientation Ataxia	5	**Within 48 hours** Lymphocyte count (mm^3)<100 OR **Within 24 hours** Lymphocyte count (mm^3),250	5
		Shock Coma	6	**Within 12 hours** Lymphocyte count (mm^3) < 250 Rapid drop possibly to 0	6

[a] Non-specific GI complaints may include symptoms such as belly ache or feeling sick in children or vague crampy abdominal discomfort, loose bowel movement, etc.
[b] Symptomatic Hypotension implies accompanying symptoms of orthostasis, palor and tachycardia. Transient vasovagal induced hypotension with its associated bradycardia that may be seen with nausea, pain or a state of anxiety does not meet criteria for this level (nor do other obvious causes such as acute blood loss).

Figure 2. Radiation Injury Severity Classification (RISC) system.

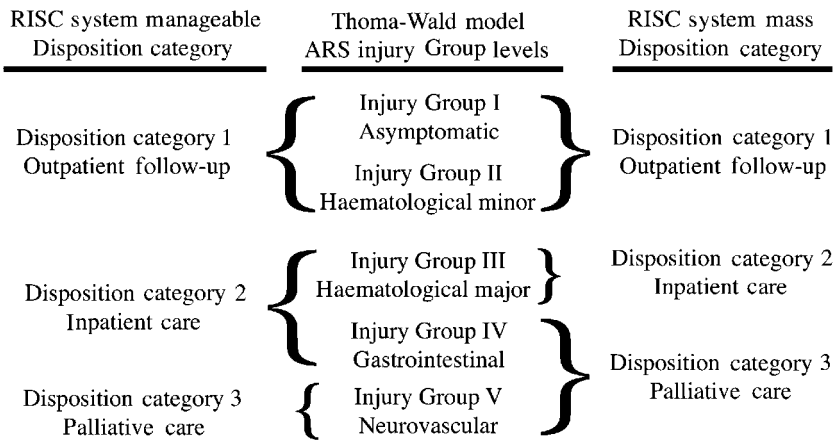


Figure 3. Adaptation of Thoma–Wald Injury Groups to RISC system disposition categories for manageable and mass casualty situations.

Additionally, an interpolated lymphocyte count data point was added to the haematological data in three cases to facilitate the scoring process of study participants. In all cases, the added data point did not affect its Thoma–Wald grouping.

Establishing a consensus case score

The field-simulation study (described below) asked the participants to designate a *highest* total score for each case reviewed based on the 72 h of information provided in the vignette. To assess the participants' ability to follow the instructions and properly use the RISC system (Figure 2), a consensus case score (CCS) for each component and resulting total score were established (Table 1). This was accomplished by having the three physicians (NW, MK, JS) most involved with the development of the system and most familiar with its proper application carefully review and score each of the 30 selected study vignettes separately. Results were compared and a consensus agreement was reached on the few cases in which findings varied.

Because of a deficiency of information in several cases (*e.g.* a low blood pressure reading but no indication of symptoms), it was recognized that participants in the study would likely have difficulty interpreting the data in those cases and scoring might vary. Such occurrences were primarily limited to the neurovascular component of the RISC system. This was dealt with in the consensus case score by the indication of an acceptable range.

Selection of participants and conduct of field-simulation study

The final field-simulation exercise was conducted over September and October 2006. The main exercise was designed to be self-administered. The participants were volunteers from three health disciplines (physicians (MD), registered nurses (RN) and emergency medical technicians/paramedics (EMT)), contacted through the University of Pittsburgh Medical Center/Presbyterian Hospital emergency department. Participants were randomly provided with a uniquely identified packet containing an introductory letter, a copy of the RISC system table (Figure 2), and separate sections for the training and exercise segments. The training section, which was the same for all participants, provided six pages of instruction on the proper application of the RISC system followed by three example cases with explanation about appropriate scoring.

Table 1. Consensus component scoring by case

Thoma–Wald grouping	RISC system component	Component scoring by case number				
	(Case number)	(1)	(2)	(3)	(4)	(5)
	Gastrointestinal	0	0	0	0	0–1
Group I	Neurovascular	3	0	0	0	1–2
	Haematological	0	0	3	1	1
	Total	3	0	3	1	2–4
	(Case number)	(6)	(7)	(8)	(9)	(10)
	Gastrointestinal	0	1	2	1	2
Group II	Neurovascular	2	3	3	3	2
	Haematological	2	2	1	2	2
	Total	4	6	6	6	6
	(Case number)	(11)	(12)	(13)	(14)	(15)
	Gastrointestinal	3	3	3	3	3
	Neurovascular	2	3	3	2–3	3–4
	Haematological	2	4	2	2	4
	Total	7	10	8	7–8	10–11
Group III	(Case number)	(16)	(17)	(18)	(19)	(20)
	Gastrointestinal	3	3	3	3	4
	Neurovascular	3	3	3–4	3	2
	Haematological	2	2	4	4	2
	Total	8	8	10–11	10	8
	(Case number)	(21)	(22)	(23)	(24)	
	Gastrointestinal	4	4	4	5	
	Neurovascular	3–4	4	5–6	5	
	Haematological	5	4	5	5	
	Total	12–13	12	14–15	15	
Group IV	(Case number)	(25)	(26)	(27)		
	Gastrointestinal	5	4	4		
	Neurovascular	3	4	4–5		
	Haematological	5	5	5		
	Total	13	13	13–14		
	(Case number)	(28)	(29)	(30)		
	Gastrointestinal	5	4–5	5		
Group V	Neurovascular	6	6	6		
	Haematological	5	6	6		
	Total	16	16–17	17		

Table 2. Disposition category cut-offs for manageable and mass exposure events

Disposition category	Category cut-offs			
	Consensus case scoring		Suggested guideline	
	Manageable	Mass exposure	Manageable	Mass exposure
1. Outpatient follow-up	0–6	0–6	0–5	0–6
2. Inpatient care	7–15	7–11	6–15	7–13
3. Palliative care	16–17	12–17	16–17	14–17

The exercise section included a random selection of 12 cases from the pool of 30 potential vignettes. The process for case selection was purposefully designed such that each participant would evaluate four cases from an injury group combining Groups I and II, four cases from Group III and four cases from an injury group combining Groups IV and V. Additionally, with 30 participants, the exercise sections were compiled such that each case would be evaluated 12 times. The exercise section also included a survey for the purpose of assessing health discipline, years of practice, training in and self-assessed knowledge of the evaluation and treatment of radiation injuries. Following the exercise, participants were requested to indicate the approximate amount of time used to complete both the training and the exercise segments of the study.

Participants were asked to complete the exercise by themselves at their leisure. It was requested that they do so at one sitting with an anticipated time for completion of both sections of about 1 h. Upon completion and return of the exercise section a reward valued at US$15 was arranged. No personal identifiers were included in the packets. A deadline was set, unknown to the participants, beyond which additional returns would not be included in the study results.

The results of an earlier pilot study carried out in July 2006 in the same manner as the main exercise, with the exception of being conducted in a classroom setting by three residents of the University of Pittsburgh Occupational Medicine Residency Program and one Family Practice resident, were held in reserve and later included in the analysis to compensate for some physician non-returns in the main exercise. Two EMT volunteers from the Bettis Laboratory, West Mifflin, PA, were recruited to make up the remaining non-returns.

Space was provided on the vignettes for the evaluators to mark a numerical score for each of the three components (haematological, gastrointestinal, neurovascular) of the RISC system and the resulting total score that determined the degree of radiation injury.

Primary data analysis

The objective of this analysis was to use the case history exercises to measure the mean levels of agreement achieved by our professional raters with the disposition category as derived from the consensus case score assessment provided by the three project clinicians (NW, MK, JS). This design is different from a traditional reliability exercise in that we have a correct answer (*i.e.* disposition category) for each case history and what we wish to determine is the raters' general ability to properly apply the RISC system following their brief review of the self-instructional materials. Given this objective, we have used a simple pairwise agreement coefficient as our primary outcome measure for the study. Mean levels of pairwise agreement were calculated for different professional groups (MD, RN, EMT) and for the overall study, along with standard deviations and 95% confidence intervals. As the primary study outcome measure involves the proper selection of a categorical variable (*i.e.* disposition category), it is possible that chance decisions played a role in the final pairwise results. Given this possibility, mean kappa coefficients [27, 28] were also calculated, along with standard deviations and confidence intervals, as a supplementary measure of agreement, providing an estimate of the possible effects of chance on the primary pairwise coefficients.

Results

Results of the consensus case scoring

Table 1 illustrates the consensus score for the components of the RISC system for each of the 30 cases used in the field-simulation study. The cases are organized according to their ''gold standard'' grouping.

Of particular note is a clear demarcation between the groups of interest: the range of total scores for Groups I and II together does not exceed 6; the range of Group III varies between 7 and 11; Group IV ranges between 12 and 15; and Group V is limited by scores of 16 and 17. These score ranges were used in the assignment of appropriate disposition category ranges for the two levels of casualty events by which the raters would be compared (Table 2).

A closer inspection reveals that the absence of vomiting within 6 h of exposure (as indicated by a score of 0 or 1 in the gastrointestinal component) is an excellent indicator for a favourable outcome. Also, within Group III, the onset of vomiting is not later than 2 h post-exposure. This, however, may not be as reliable a threshold in that, as noted earlier, four of the Group III cases had a range of between 1 and 4 h for onset of vomiting. Generally, an onset of vomiting of less than 1 h is a significant negative prognostic indicator. Results of the haematological component lend confirmatory support to the gastrointestinal component as a prognostic indicator if its score value is approximately the same. Finally, scoring of the neurovascular component also trends upward in agreement with the degree of radiation injury. Although the association is not as strong as with the other two components, it has an important real-world role as will be discussed later.

Table 3. Descriptive information for the 30 acute radiation syndrome (ARS) cases included in the field-simulation exercise

Variables	Thoma–Wald ARS injury classification group					Total
	I	II	III	IV	V[a]	
n (fatalities)	5 (0)	5 (0)	10 (1)	7 (7)	3 (3)	30 (11)
Mean age (SE)	32.2 (5.72)	31.0 (4.20)	31.2 (2.76)	30.4 (1.46)	34.3 (3.18)	31.5 (1.47)
Gender						
Male	5	4	6	6	3	24
Female	0	1	4	1	0	6

[a]Includes one modified case.

Table 4. Characteristics of exercise participants by professional training ($n=30$)

Characteristics	Professional training (mean scores (SE))			
	MDs	RNs	EMTs	All
Professional experience (years)	7.4 (2.6)	13.4 (2.9)	9.0 (1.6)	10.1 (1.42)
ARS knowledge	3.7 (0.9)	3.3 (0.8)	3.3 (0.9)	3.4 (0.5)
Courses/experience	2.3 (0.3)	1.8 (0.3)	2.6 (0.3)	2.2 (0.2)
Training time (min)	27.5 (4.2)	40.5 (10.2)	29.5 (3.8)	32.5 (3.9)
Exercise time (min)	27.5 (4.0)	59.9 (11.5)	37 (7.0)	41.5 (5.2)

ARS, acute radiation syndrome; EMTs, emergency medical technicians/paramedics; MDs, physicians; RNs, registered nurses.

Table 5. Mean levels of agreement between raters and gold standard assignments to disposition categories by professional background

Casualty category	*n*	Coefficient of agreement			
		Pairwise		Kappa	
		Mean (SD)	95% CI	Mean (SD)	95% CI
Manageable[a]					
MD	10	0.975 (0.040)	0.946–1.00	0.963 (0.060)	0.920–1.00
RN	10	0.950 (0.058)	0.908–0.992	0.925 (0.087)	0.863–0.988
EMT	10	0.908 (0.083)	0.849–0.968	0.863 (0.124)	0.775–0.952
Overall	30	0.944 (0.067)	0.919–0.969	0.917 (0.100)	0.880–0.954
Mass exposure[b]					
MD	10	0.967 (0.043)	0.936–0.997	0.950 (0.064)	0.904–0.996
RN	10	0.958 (0.071)	0.907–1.00	0.938 (0.106)	0.862–1.00
EMT	10	0.917 (0.088)	0.854–0.980	0.876 (0.131)	0.782–0.969
Overall	30	0.947 (0.071)	0.921–0.974	0.921 (0.106)	0.882–0.961

CI, confidence interval; EMT, emergency medical technicians/paramedics; MD, physicians; RN, registered nurses.
[a]Test of difference between professional categories: Kruskal–Wallis, $p=0.110$.
[b]Test of difference between professional categories: Kruskal–Wallis, $p=0.323$.

Results of the field-simulation exercise

Table 3 provides basic descriptive information about the 30 ARS cases utilized for the final field-simulation exercise. Table 4 characterizes the raters according to professional training. The results of the exercise are presented in Tables 5–6. Table 5 presents the mean levels of agreement between the rater's total score designation and the ''gold standard'' category assignment by professional background. Table 6 indicates the component of the RISC system that was incorrectly scored (compared with the consensus case score), resulting in a misclassification for the combined manageable and mass category ranges.

Table 5 shows that the overall rates of agreement for both types of casualty situations are in the region of 0.95 for the pairwise coefficient and 0.92 for the kappa coefficient. There are different rates of agreement between the medical disciplines; however, these differences are statistically non-significant.

Table 6 demonstrates that misclassifications were the result of scoring errors in all components of the RISC system. A χ^2 goodness of fit with two degrees of freedom yields a p-value of 0.038, indicating that a significantly greater number of errors occurred in the neurovascular and haematological components. There was no clear trend identified regarding misclassification tendencies in individual cases. Errors occurred singly in different components by different raters, as demonstrated in case 11, or multiple errors were made by one rater, as in cases 18 and 26. A few cases showed difficulty in the scoring of one component, as was seen with cases 14, 17 and 22.

Discussion

Although the early diagnosis and prognostic evaluation of radiation injuries has been studied in occupational and military medicine for more than 60 years

Table 6. Combined manageable and mass casualty case misclassification analysis of rater scoring error by RISC system subcomponent

Thoma–Wald group	Case number	Misses per case	Rater number (discipline)	RISC component(s) erroneously scored		
				GI	NV	Haem
II	7	1	9 (EMT)			+
II	10	1	5 (EMT)		+	
III	11	3	15 (MD)	+		
			28 (RN)		+	
			30 (MD)			+
III	14	4	2 (MD)			+
			7 (EMT)			+
			14 (EMT)			+
			28 (RN)			+
III	17	2	5 (EMT)		+	
			9 (EMT)		+	
III	18	1	8 (EMT)	+	+	+
IV	21	1	22 (RN)			+
IV	22	3	6 (EMT)		+	
			14 (EMT)		+	
			22 (RN)		+	
IV	23	1	29 (RN)			+
IV	24	2	10 (EMT)		+	+
			27 (RN)		+	
IV	25	1	10 (EMT)		+	+
IV	26	1	14 (EMT)	+	+	+
IV	27	1	3 (MD)		+	+
V	28	3	13 (EMT)		+	
			19 (RN)	+		
			22 (RN)	+		+
V	30	2	14 (EMT)		+	+
			18 (RN)		+	+

EMT, emergency medical technician/paramedic; GI, gastrointestinal; Haem, haematological; MD, physician; NV, neurovascular; RN, registered nurse.

[3, 29–42], there is no widely accepted system specifically designed for the early assessment of acute radiation injuries by health-care providers largely unfamiliar with the effects of radiation injury. As an example, the BAT program [30, 31] was introduced as a tool by the US Armed Forces Radiological Research Institute to ensure adequate documentation of radiation injury. Parameters such as time of onset to vomiting and lymphocyte depletion offer a dose estimate, but with confidence limits that are typically wide. The BAT system was not designed to provide a clinical disposition for the radiation-injured patient. The Medical Treatment Protocols (METROPOL) [34] for radiation accident victims introduces the Response Category (RC) scoring system, to be implemented during what is termed the extended triage. The METROPOL system is intended to provide guidance in the medical management of radiation injuries in an inpatient clinical setting and goes beyond the purview of first responders. The METROPOL system is comparatively more complex than the RISC system and, to be appropriate for use by frontline medical staff, would necessitate extensive training well beyond that required by the self-instructional RISC system.

The RISC system was developed and rigorously tested with the intention of filling a critical niche in the early assessment process of acute radiation injuries, that is as an aid to the frontline health-care provider in recognizing and communicating injury severity levels and as a ready guide in making disposition decisions (*e.g.* watchful waiting as an outpatient for the worried well and those with apparently less-significant injury or more acute management as an inpatient for the more severely injured). It was contemplated as a user-friendly adjunct to existing systems, not as a replacement. Given this intended role, the authors felt it necessary to demonstrate quantitatively the ability of frontline health-care providers to implement the guidelines in the RISC system appropriately following minimal, self-instructional training.

Significant deficiencies still exist in our current capabilities to provide an effective public health response to a large-scale radiological event [43–46]. We believe that this is due, in part, to the relative rarity of radiation emergencies, but is also a function of the inherent difficulties involved in actually producing a valid user-friendly and effective early assessment system.

An effective triage system enhances the allocation of limited health-care resources, while maximizing overall clinical benefits to the injured population. Triage may be carried out by emergency responders at the incident site (pre-hospital) or by health-care providers at the destination hospital. The administration of effective patient triage in both environments has been described as challenging, even in situations with relatively few casualties [47]. The problems associated with rendering an accurate triage assessment, communicating victim status, and making a determination of final disposition for patient care escalate substantially in disaster scenarios with significant mass casualties. Introducing a potential exposure to radiation into such catastrophic events further complicates the triage process as both the

overtly injured and the apparently uninjured require assessment.

The possible severity of acute radiation injuries spans a broad range from being relatively insignificant up to the point at which death ensues within a few hours despite intensive treatment. The phase of clinical manifestations in which treatment is most effective occurs later in the evolution of radiation injuries. For this reason, attention to the radiation injury should never take precedence over other acute medical emergencies. Nonetheless, the provision of an early reliable assessment of the severity of the radiation injury is useful for a number of reasons: (i) to help allay fears in the uninjured population; (ii) to identify the subpopulation that will not require immediate attention but that will require close observation and possible treatment later, thereby helping to minimize loss to follow up; (iii) to alter the timing or treatment direction of non-radiation injuries combined with irradiation; and/or (iv) to limit access to emergency care to the injured populations truly requiring urgent medical attention in mass casualty situations.

The RISC system permits an evaluator without specific training in the effects of radiation injuries to assign an objective numerical score, based on clinical and laboratory findings from the prodromal period, in order to make an early determination of the optimum disposition of a patient who has been acutely exposed to a significant amount of penetrating whole-body radiation.

The RISC system is also adaptable to various scenarios. The designation of specific ranges for disposition can be adjusted to fit special needs or incident circumstances. In our RISC application table, initial cut-off scores for two possible triage situations are suggested based on the size of the exposure incident and the number of resulting casualties. The first scenario, termed ''manageable casualties'', implies that relatively few patients have sustained potentially serious radiation injuries. The actual number that can be managed depends on the adequacy of available resources (or time needed to procure them) to render effective treatment. The second scenario, termed ''mass casualties'', assumes a surge of serious radiation injuries that outstrips available or attainable resources.

It is unfortunate that many of the cases used in our field simulations did not have a larger amount of early clinical data. The medical evaluators in our study used 72 h of post-exposure information to render their RISC determination. The choice of this 72 h period was solely dictated by the data available in the case histories, some of which were collected decades ago (*e.g.* the frequency of blood counts), rather than by the actual rate at which the clinical signs and symptoms of ARS develop.

Present-day use of the RISC system can provide valuable information during the triage process, even within the first few hours following a radiation incident. Modern technology has greatly increased the capacity to carry out earlier and more frequent blood counts, for example. Many of the most important ARS prognostic indicators (*e.g.* prompt and progressive lymphopenia) are evident within the first 24 h post exposure, and those related to the most severe clinical outcomes (*e.g.* onset of vomiting, diarrhoea, hypotension) are typically evident within the first 6 h. Thus, any ARS patient likely to attain Category 2 (inpatient care) or Category 3 (palliative care) status would achieve a sufficient RISC score (*e.g.* $\geqslant$5 or 6) within the first 6 h post exposure to ensure that he or she would be held over for further clinical observation or safely discharged with appropriate follow-up instruction. Hence, the RISC system, when applied in present-day potential radiological emergency situations, should be able to produce a reasonably accurate and reliable final patient disposition within 6–12 h post-exposure. The latter time limitation is a function of the latency observed in the appearance of important radiation symptoms and is unlikely to be substantially shortened using any schema dependent upon clinically observable signs and symptoms.

It would be desirable to provide a system that is exclusively objective in its application. The RISC system, however, does require a limited degree of interpretation on the part of the evaluator in its implementation. The inclusion of subjective complaints (*e.g.* anorexia/nausea in the gastrointestinal category and anxiety/fatigue/headache in the neurovascular category) is necessary because within the first few hours post-exposure, especially in the relatively milder cases of ARS, objective findings may not yet be evident. Such cases must be identified as being potentially exposed to ensure adequate follow up outside the emergency treatment setting. Therefore, in the event that occurrence of subjective complaints is the only early finding, patient re-evaluation would be indicated and could be pre-arranged (most appropriately outside the emergency setting) in a well-designed implementation protocol.

Misclassification rates as represented in Table 5 are very respectable, with overall mean agreement rates approximating 0.95 for the pairwise coefficient and 0.92 for the kappa coefficient in both manageable and mass casualty scenarios. This is especially impressive given the mean estimated self-training time of only 32.5 min in a group acknowledging an understanding of ARS of 3.4 out of a possible high of 10 (Table 4). Although not statistically different, physicians as a group performed best (manageable scenario: pairwise coefficient, 0.975; kappa coefficient, 0.963), followed by nurses (manageable scenario: pairwise coefficient, 0.950; kappa coefficient, 0.963). This may reflect relative comfort with terminology used in both the training and exercise vignettes. Not shown is that one of the EMT participants and one of the RN participants misclassified 4 and 3 cases, respectively, accounting for over 25% of the classification errors.

The findings of Table 6 are somewhat surprising. We anticipated that the predominance of scoring errors would occur in the neurovascular component because of its greater subjectivity and the vagueness of some of the available data leading to difficulty in interpretation, *e.g.* a blood pressure reading of 100/60 mmHg with no clear indication of associated symptoms. The haematological component is the most objective and yet it matched the error rate of the neurovascular component. Although overall the participants did very well, this suggests that further emphasis on properly scoring the haematological section during self-training, instituting a training feedback mechanism or employing more traditional face-to-face

instruction may be more effective in further reducing errors.

It was noted that two-thirds of the errors that resulted in misclassifications occurred in cases at the margins of the injury categories, *e.g.* a case that should have been scored a 7 (Category 2) was scored a 6 (Category 1). Although this represents a misapplication of the RISC system in our study it is not unreasonable to anticipate that similar misapplications might occur in real situations. Fortunately, in the evolution of clinical radiation injury, the patients with lesser degrees of injury have a longer latent period so that, with adequate follow up, proper medical management can still be performed.

At the higher end of the RISC system, when a Category 2 patient is misclassified as a Category 3 one, it is likely that the injured individual will be hospitalized, allowing for more specialized attention and reassessment by others before final care disposition. Although our consensus case score delineates clear category cut-offs, we offer cut-off guidelines (see Table 2) as a conservative measure to (i) help deal with misapplications of the RISC system, (ii) bias towards treatment in the borderline cases and (iii) hopefully reduce the frequency of avoidable adverse clinical outcomes.

Based on our experience over the past few years we suspect that it may be difficult to develop an early assessment tool that demonstrates major significant improvements over the misclassification rates observed in the current field-simulation exercise. A number of factors all help to explain this situation, for example the natural delay in the appearance of important clinical radiation symptoms; the necessity of using certain ''subjective'' symptoms (*e.g.* headache, nausea) in the assessment procedure; the tendency of Category 1 patients to report a wide range of non-specific complaints that have an uncertain relationship with their radiation exposure; and the relative inexperience of dealing with radiation emergencies that is characteristic of the physicians and others assessing these case histories. Given all of these inherent difficulties in the development of a practical early assessment system, we have chosen purposely to err on the side of being medically conservative at the expense of the, perhaps, unnecessary utilization of scarce resources. We believe that a significant reduction in the number of inadvertent errors in the use of the RISC system is achievable by reformatting it into a computer programmable form, which is the next planned step in its development.

In summary, the strengths of the RISC system include the following:

(i) The RISC system allows for the rapid assessment of ARS severity, without the availability of dose, while minimizing the necessity of subjective judgments by the evaluators.
(ii) The RISC system cut-off guidelines tend to minimize the misclassification of radiation injuries that would benefit from more immediate medical attention (*i.e.* Category 2 patients).
(iii) The training needs for proper use of the RISC system are minimal and the reliable application of the assessment criteria should be achievable even by first responders with limited experience in radiation emergencies.
(iv) Even if acute radiation exposures remain low-probability events, the re-familiarization of personnel or the training of new personnel with RISC system application requires minimal effort, despite inevitable training lapses.
(v) The RISC system serves as a simple and readily available reference to key ARS clinical findings, allowing for more focused and thorough history and physical examinations.
(vi) The RISC system conveys structure to the assessment process, allaying fears in often already chaotic situations by inducing confidence in the evaluator and providing reassurance to the patient.
(vii) The RISC system may be applied in a variety of care settings as long as complete blood counts are available.
(viii) The RISC system has been empirically tested using actual case vignettes to establish reasonable category cut-off guidelines and to demonstrate ease of use.

The RISC system still has a number of limitations that may affect its usefulness in actual disaster situations:

(i) Use of the RISC system ideally requires 6–12 h of post-exposure time (including an initial assessment followed several hours later by re-assessment) to achieve a more reliable patient disposition for all categories.
(ii) Other potential effects of whole-body radiation injury are ignored (*e.g.* psychological, gonadal, cutaneous radiation syndrome).
(iii) The RISC system does not take into account the impact of non-radiation injuries on the course of ARS (*e.g.* trauma, thermal burns).
(iv) The RISC system has not been tested with patients exposed to whole-body radiation over protracted periods, repetitive low doses or varying dose rates;
(v) The potential significance of coexisting radionuclide contamination, both external and internal, must still be assessed.
(vi) Critical prodromal symptoms of ARS may be masked by medication (*e.g.* antiemetics, analgesics, antipyretics).
(vii) The RISC system may result in the misallocation of a certain portion of clinical resources to cases that do not require immediate treatment.
(viii) The RISC system has not yet been implemented in actual radiation exposure incidents or tested in disaster simulations approximating the chaos inherent to real mass casualty situations.

Despite these limitations, which need to be addressed in future work, we believe that the RISC system has achieved an adequate level of development and that the need for an early radiological assessment tool as an adjunct to the medical triage process has become sufficiently pressing that it is timely to release this system for radiation emergency utilization as well as for further experimentation and review by members of the emergency and radiation medicine communities. To facilitate this process we are making the training section, including the three sample cases used in the field-simulation exercise, available on the internet (http://www.biostat.pitt.edu/bjr_risc/).

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Appendix: Directions for application of the RISC system

Component	Direction
General	1. The RISC system scoring table is organized into three columns representing the three primary biological systems injured in ARS 2. Each column must be assessed separately to give an individual component score. These component scores are then summed for a resultant total score 3. The total score is reflective of the degree of radiation injury and may be utilized for classifying into a prognostic disposition category appropriate to the medical management capabilities available for treating casualties from the radiological event (cut-off guidelines are provided) 4. Interval re-assessment may indicate a higher total score (worsening prognosis). Individual component scores may not be lowered from that of a previous assessment (*e.g.* fever resolution through treatment). Disposition decisions should be based upon the highest score attained 5. When information is conflicting (*e.g.* a range of time to onset of vomiting is provided such that two scores in a component of RISC may be applicable) the more conservative estimate (that which directs towards treatment) should be used
Gastrointestinal	1. Scoring is from 0 to 5 2. A higher score is predicated on fulfilment of criteria of lower levels (*e.g.* an individual with one episode of diarrhoea but no vomiting within 6 hours does not qualify for a score in this component of greater than 1)
Neurovascular	1. Scoring is from 0 to 6 2. A score of 4 or more requires the coexistence of objective finding(s). Note: moderate symptomatic hypotension is required for a minimum designation of a score of 4 3. A fever and/or a non-symptomatic drop in blood pressure in conjunction with at least one subjective complaint may warrant a level 3 score designation 4. Transient vasovagal hypotension with its typically accompanying bradycardia, as might be seen associated with nausea, does not fulfil the criteria for hypotension as indicated under score 4 of this component. Likewise, alternative (non-radiation) reasons for hypotension such as acute blood loss, heart failure or septic shock are excluded from consideration
Haematological	1. Scoring is from 0 to 6 2. This is the most objective of the three components as scoring levels are clearly defined. Working with the lowest lymphocyte count in a series initially to narrow down possible scores and then checking the neutrophil counts (note: if any of the neutrophil counts exceed 10 000 mm^3 in the series then that is the operative count) to finalize the determination is the preferred approach 3. Noting the elapsed time to the blood specimen draw from the acute exposure event is needed for making an accurate assessment in this component 4. An initial baseline complete blood count (CBC) should be determined as soon as reasonable. A minimum of one follow-up CBC at an appropriate re-assessment interval within the first 12 h post exposure enhances reliability in the early time period and guides disposition and subsequent follow up