

**CIRMS 2023 Meeting, Session Title: BIODOSIMETRY –
Joint Medical & RPME Session, 3:30 pm 17 April 2023**

Current Status of Emergency Biodosimetry

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AFRRI



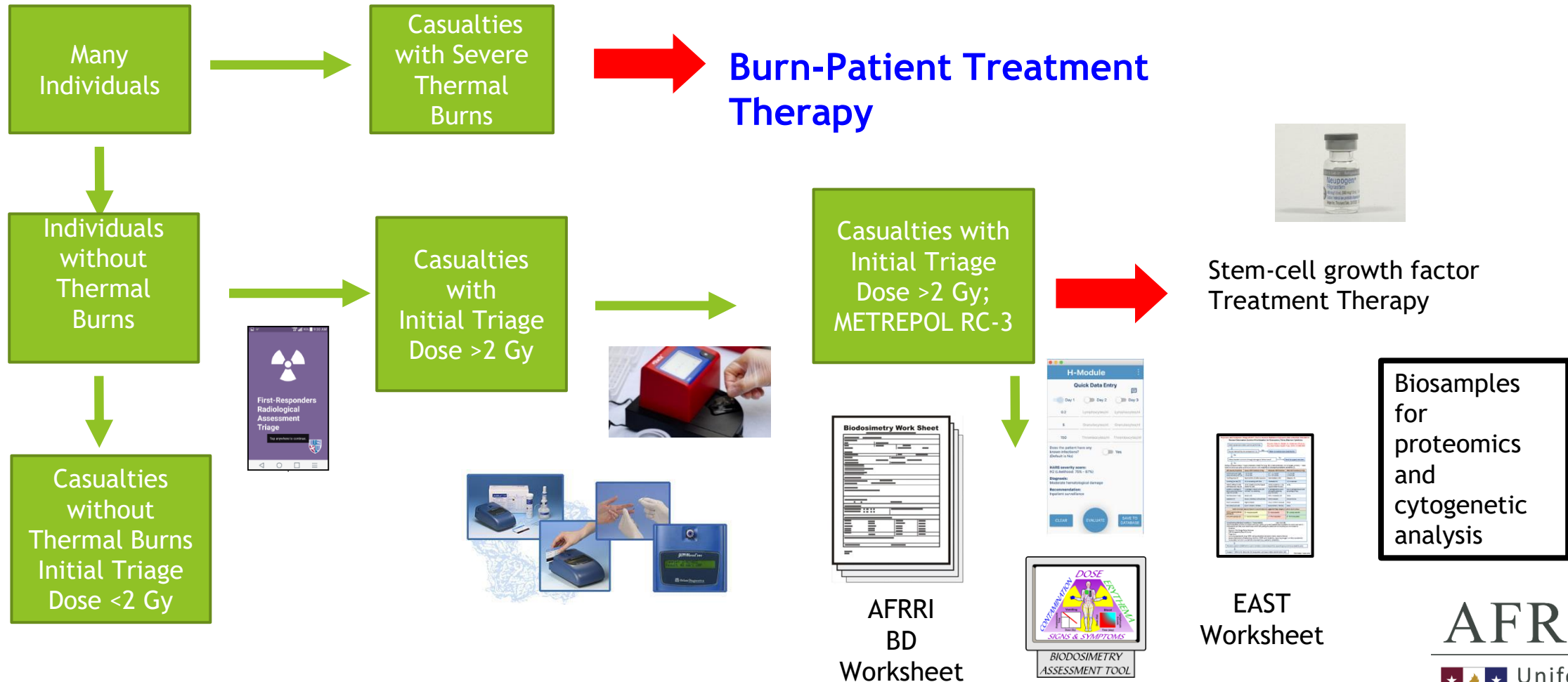
Disclaimer

- ▶ The opinions, conclusions, and recommendations expressed or implied do not necessarily reflect the views of the Department of Defense or any department or agency of the federal government.

Financial Disclosures

- ▶ Biodosimetry panels and methods, US Patent Number US20180246100A1, European(2012), Japan (2017), and United States of America (2018).
- ▶ Biomarker panels for assessing radiation injury and exposure, Patent Number: 8,871,455, issued on October 28, 2014, Institution, United States of America.
- ▶ Radiation injury index algorithm based on hematology changes for rapid early-phase radiological triage applications, US Provisional Patent pending.

Mass-Casualty Radiological/Nuclear Incident: Biodosimetry Algorithm



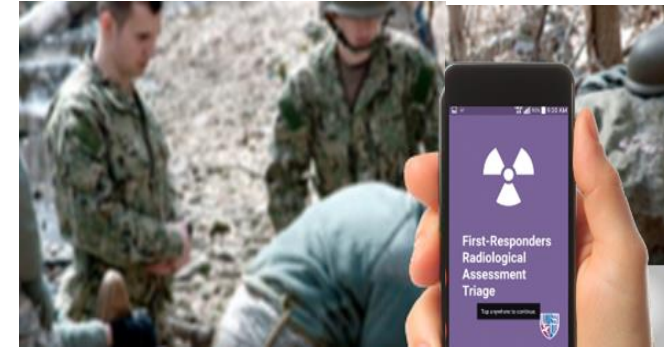
Current Multiple-Parameter Biodosimetry Toolbox

- ▶ mFRAT smartphone apps/WinFRAT software
- ▶ Deployable proteomic device
- ▶ Deployable blood cell counter
- ▶ H-module smartphone app
- ▶ Biodosimetry Worksheet
- ▶ BAT software application
- ▶ EAST tool
- ▶ Cytogenetic biodosimetry

Mobile- or WinFRAT

First-responders Radiological Assessment Triage (for mobile phones) Version 1.0

- ▶ Android version available for download from Play Store
- ▶ <https://play.google.com/store/apps/details?id=edu.usuhs.frat>
- ▶ WinFRAT version available for download at Institute website
- ▶ <https://afrrri.usuhs.edu/research-assessment-of-radiation-injury>



WinFRAT



MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Data Entry and Report

Enter Signs and Symptoms

Enter Lymphocyte Counts and/or Contamination

Enter Dosimetry and/or Contamination

Notes

Display Multiparameter Triage Dose Assessment

Switch Patients

Exit

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Signs and Symptoms

Bold symptoms have a second page

Vomiting Yes No Unknown

Diarrhea Yes No Unknown

Headache Yes No Unknown

Impaired Consciousness Yes No Unknown

Elevated Body Temperature Yes No Unknown

Eyema Yes No Unknown

Tachycardia Yes No Unknown

Weakness Yes No Unknown

Fatigue Yes No Unknown

Data Entry/Report

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Vomiting

Yes No Unknown

Time of onset after exposure:

- Within 30 minutes
- 30-40 minutes
- 40-60 minutes
- 1-1.5 hours
- 1.5-2 hours**
- 2-4.5 hours
- 4.5-9 hours
- More than 9 hours
- Unknown

Vomiting/Nausea Duration:

- Less than 24 hours
- 24-36 hours**
- More than 48 hours
- Unknown

OK

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Dosimetry Information

Yes No Unknown

Enter dosimeter reading:

Enter location-based dose estimate:

Is there evidence that shielding affected the reading or estimate?

Yes No Unknown

OK

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Diarrhea

Yes No Unknown

Time of onset after exposure:

- Less than 1 hour
- 1-3 hours
- 3-6 hours**
- Unknown

Diarrhea severity:

- Mild
- Moderate**
- Severe
- Unknown

OK

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Triage Dose Assessment - 3

Category	Estimated dose (cGy)
Signs and symptoms	535.0
Dosimetry	325.0
Blood lymphocyte counts	
Pooled	472.3
95% Confidence	351.3-593.3

Disclaimer

POOR to MODERATE reliability

Previous Next

MMO Symposium 2013 - WinFRAT (First-Responder Radiological Assessment Triage)

File Pocket Guide Help

Patient: MMO Symposium 2013

Triage Dose Assessment - 1

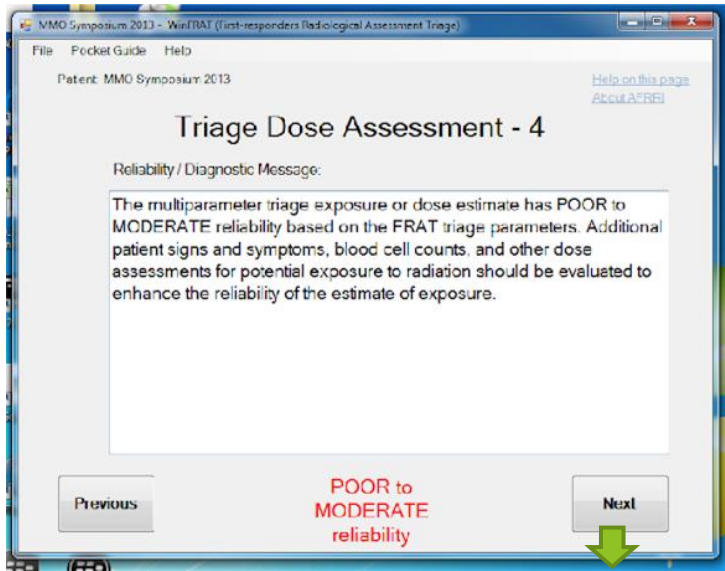
Radiation OVEREXPOSURE – potentially SEVERE medical effect.

All results are based on acute whole-body photon exposures of healthy subjects without medical treatment.

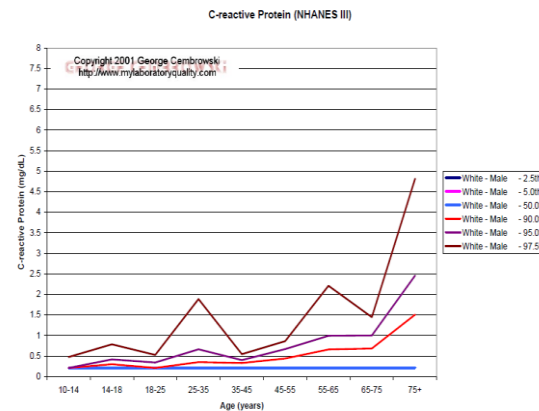
POOR to MODERATE reliability

Next

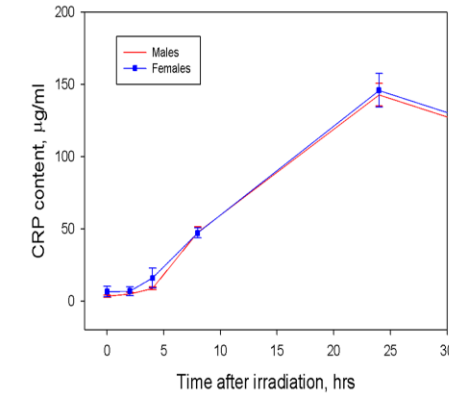
WinFRAT



Low human baseline levels



High signal to noise



Blakely *et al.*, Health Physics, FEB 2010

Rapid FDA Approved Devices



Orion CRP Quick Kit

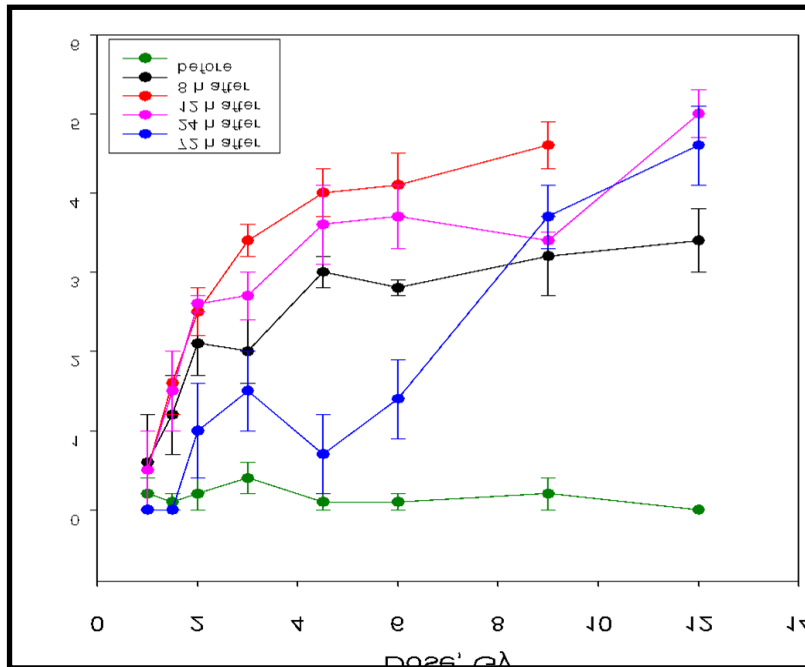


Stanbio Laboratory CRP test kit

Radiological Triage

CRP (Ossetrova and Blakely)

Radiation Biomarker



Maltsev *et al.*, [Report of Russian Academia of Sciences] 239(3): 750-2, 1978 (in Russian).

ARS Bioindicator

Prognosis for ARS based on CRP level in serum of blood of people damaged at **Chernobyl NPP accident** during primary reaction (3-9 days after irradiation).

Degree of ARS	CRP level \geq 1 mm	CRP level: 0.5 mm	CRP level 0 mm	Total (row)
3-4	26	9	17	52
2	6	7	19	32
0-1	3	18	23	44
Total (column)	35	34	59	128

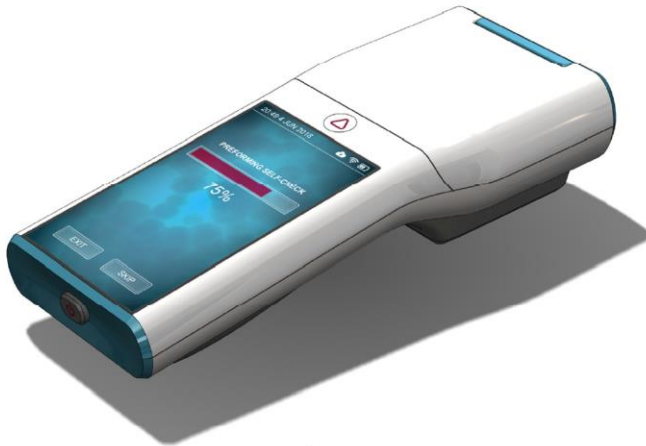
Mal'tsev VN *et al.* [The individual prognosis of the gravity and of the outcome of radiation disease on immunological indexes], Radiation Biology. Radioecology, 46(2), 152-158, 2006 (in Russian).

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Radiological Triage

CellRADx™ - Point of Care Biodosimetry System



MMO Symposium 2013 - WafRAD (First-responders Radiological Assessment Triage)

File Pocket Guide Help
Fetent: MMO Symposium 2013

Lymphocyte Counts

#	Hours post exposure	Count (E+09/L)	Update Row
1	12	1.2	DEL
2	24	1.0	DEL
3	36	0.5	DEL
4	48	0.85	DEL
5			DEL
6			DEL
7			DEL
8			DEL
9			DEL
10			DEL

MMO Symposium 2013 - WafRAD (First-responders Radiological Assessment Triage)

File Pocket Guide Help
Patent MMO Symposium 2013

Triage Dose Assessment - 3

Category	Estimated dose (cCy)
Signs and symptoms	535.8
Dosimetry	325.0
Blood lymphocyte counts	223.4
Pooled	409.6
95% Confidence	279.6-539.6

POOR to MODERATE reliability

ASCELL

Turning Science Into Solutions

Alentic

microscience

Note. At least 3 entities are in various stages of requesting FDA for approval to sell hand-held deployable blood cell counters in US.



H-Module

H-Module

Quick Data Entry

Day 1 Day 2 Day 3

0.2 Lymphocytes/nl Lymphocytes/nl

5 Granulocytes/nl Granulocytes/nl

150 Thrombocytes/nl Thrombocytes/nl

Does the patient have any known infections? (Default is No) Yes

HARS severity score:
H2 (Likelihood: 75% - 87%)

Diagnosis:
Moderate hematological damage

Recommendation:
Inpatient surveillance

CLEAR EVALUATE SAVE TO DATABASE

	Day 1 postirradiation						
	Lymphocytes/nl	Granulocytes/nl	Thrombocytes/nl				
Day 1 postirradiation	0.2	9	300				
Discriminating Prediction (likelihood)	<table border="1"> <tr> <td>Diagnosis</td> <td>Severe to fatal hematological damage</td> </tr> <tr> <td>Actions</td> <td>Specialized hematological facility, ICU, consider SCT</td> </tr> </table>			Diagnosis	Severe to fatal hematological damage	Actions	Specialized hematological facility, ICU, consider SCT
Diagnosis				Severe to fatal hematological damage			
Actions				Specialized hematological facility, ICU, consider SCT			
H0 vs. H1-4:	H1-4 predicted (PPV 75%)						
H0-1 vs. H2-4:	H2-4 predicted (PPV 77%)						
H0-2 vs. H3-4:	H3-4 predicted (PPV 87%)						

Port et al., Rapid prediction of hematologic acute radiation syndrome in radiation injury patients using peripheral blood cell counts. Radiat. Res. 188, 156-168, 2017; Port and Abend, Clinical triage of radiation casualties - The hematological module of the Bundeswehr Institute of Radiobiology, Radiat. Prot. Dosimetry 1-3, 2018.

Radiological Triage



Mobile FRAT

← Data Assessment Results ⓘ

ESTIMATED DOSE

Category	Est. Dose (cGy)*
Signs & Symptoms	553.6
Dosimetry	--
Lymphocyte Counts	--
Pooled	553.6
95% Confidence	403.9 - 703.3

* All results are based on acute whole-body photon exposures of healthy subjects without medical treatment

Disclaimer

Poor Reliability

Assess Support About Us

H-module

Discriminating Prediction (likelihood)	Diagnosis
H0 vs. H1-4: H1-4 predicted (PPV 75%)	Severe to fatal hematological damage
H0-1 vs. H2-4: H2-4 predicted (PPV 77%)	Actions
H0-2 vs. H3-4: H3-4 predicted (PPV 87%)	

Biodosimetry Assessment Tool (BAT)

Summary of Entered Data Screen 14

File Window Help

SUMMARY

Dose estimates and measurements are shown in Red

Patient: MEIR, Scenario, 1
Military unit or organization: United States Army
Filename: MEIR_Scenario_1.mdb

Help on this screen

Prodromal (Gy)

Symptoms Onset of vomiting (h): 7.00
Estimated dose: 1.5 Arthralgia/therapy prior to initial vomiting
95% CL: 1.1-1.9

Radioactive Contamination

Internal Sampling Infection Eryth/Wound
 External Sampling Therapy Wound
 Chelation/Blocking Therapy

Hematology (Photon Equivalent Gy)

Hours: 4.7 95% CL: 3 3.7-5.6 Cytokine therapy

Lymphocyte Cytogenetics

#	Dose (Gy)	95% CL
1		
2		
3		

Physical Dosimetry (Sv)

#	Shallow Dose Equiv	Deep Dose Eq Photon	Deep Dose Eq Neutron	Comm Eff Dose Equiv	Total Eff Dose Equiv
1					
2					
3					

Expert's Assigned Individual Dose: Set 5 Gy

Note: All dose estimates are in sieverts (Sv) or gray (Gy).

Biodosimetry Worksheet

Biodosimetry Work Sheet

Form with multiple sections for data entry, including patient information, symptoms, and dosimetry results.

EAST Worksheet

Appendix with Symptom Triage (EAST) Tool to Assess Radiation Exposure after a Nuclear Disaster

Nuclear Detonation Survivor Prioritization for Evacuation / Bone Marrow Cytokines

Form with decision trees and tables for assessing radiation exposure and determining medical needs.

Radiological Triage

2015 - NATO EXERCISE

Using Clinical Signs and Symptoms for Medical Management of Radiation Casualties

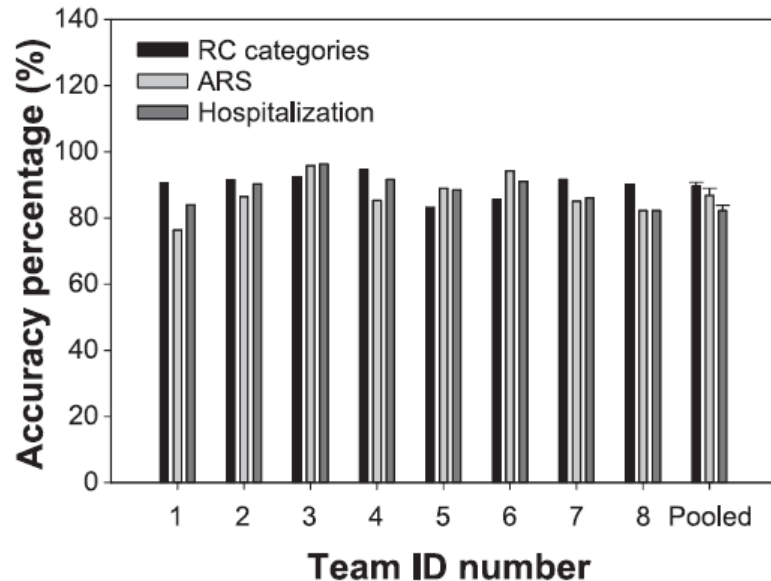
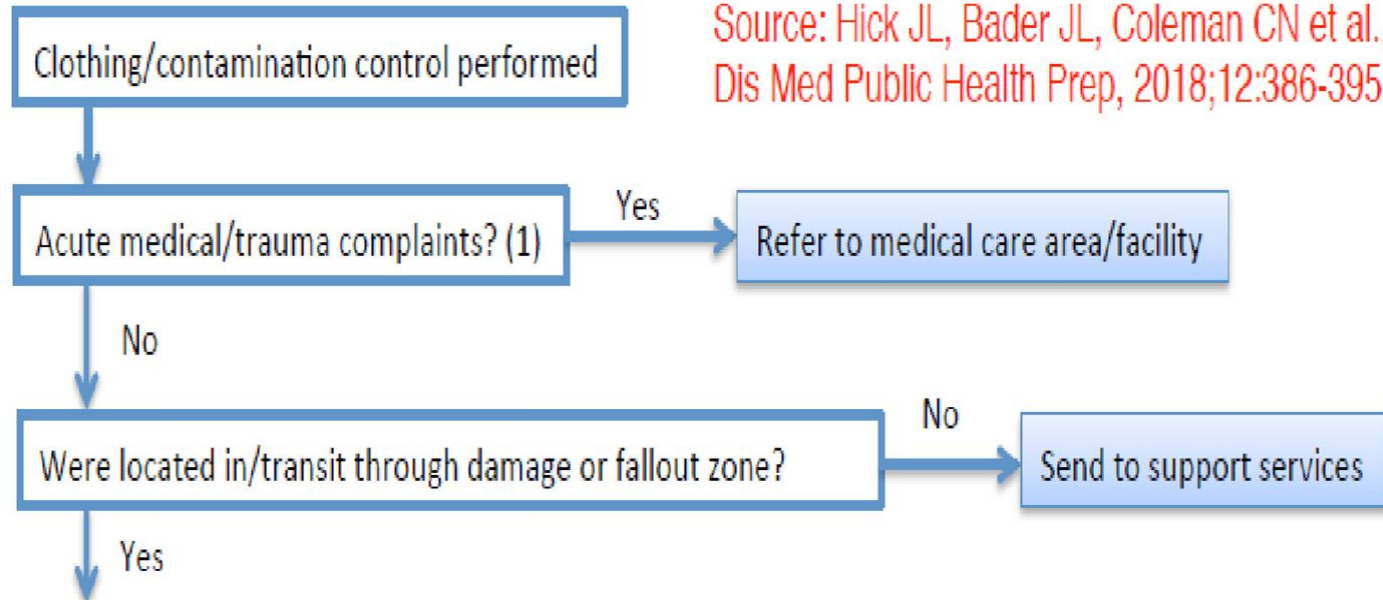
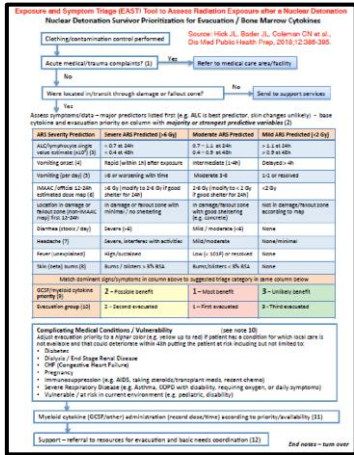


FIG. 2. Percentage of accurate predictions of reported RCs, reported ARS incidence and recommended hospitalizations for each team, based on the overall agreement (true positives + true negatives/191) as shown in Tables 1–3.

- Use of early-phase (<3 or <5 d) clinical signs and symptoms
- First verification on the effectiveness of the clinical dosimetry system - METREPOL
- Rapid and accurate prediction of later occurring ARS severity and the development of medical management strategies.

Radiological Triage

Exposure and Symptom Triage (EAST) Tool to Assess Radiation Exposure after a Nuclear Detonation



Source: Hick JL, Bader JL, Coleman CN et al., Dis Med Public Health Prep, 2018;12:386-395.

<https://www.remm.nlm.gov/EAST-tool-notes.htm>

Radiological Triage

Exposure and Symptom Triage (EAST) Tool to Assess Radiation Exposure after a Nuclear Detonation - II

ARS Severity Prediction	Severe ARS Predicted (>6 Gy)	Moderate ARS Predicted	Mild ARS Predicted (<2 Gy)
ALC/lymphocyte single value estimate (x10 ⁹) (3)	< 0.7 at 24h < 0.4 at 48h	0.7 – 1.1 at 24h 0.4 – 0.9 at 48h	> 1.1 at 24h > 0.9 at 48h
Vomiting onset (4)	Rapid (within 1h) after exposure	Intermediate (1-4h)	Delayed > 4h
Vomiting (per day) (5)	>6 or worsening with time	Moderate 3-6	1-2 or resolved
IMAAC /official 12-24h estimated dose map (6)	>6 Gy (modify to 2-6 Gy if good shelter for 24h)	2-6 Gy (modify to < 2 Gy if good shelter for 24h)	<2 Gy
Location in damage or fallout zone (non-IMAAC map) first 12-24h	In damage or fallout zone with minimal / no sheltering	In damage/fallout zone with good sheltering (e.g. concrete)	Not in damage/fallout zone according to map
Diarrhea (stools / day)	Severe (>6)	Mild / moderate (<6)	None
Headache (7)	Severe, interferes with activities	Mild/moderate	None/minimal
Fever (unexplained)	High/sustained	Low (< 101F) or resolved	None
Skin (beta) burns (8)	Burns / blisters > 3% BSA	Burns/blisters < 3% BSA	None
Match dominant signs/symptoms in column above to suggested triage category in same column below			
GCSF/myeloid cytokine priority (9)	2 – Possible benefit	1 – Most benefit	3 – Unlikely benefit
Evacuation group (10)	2 – Second evacuated	1 – First evacuated	3 - Third evacuated

- Hematology
- Clinical signs and symptoms
- Location dosimetry

Hick JL, Bader JL, Coleman CN, Ansari AJ, Chang A, Salame-Alfie A, Hanfling D, Koerner JF. [Proposed "Exposure And Symptom Triage" \(EAST\) Tool to Assess Radiation Exposure After a Nuclear Detonation](#). Disaster Med Public Health Prep. 2018 Jun;12(3):386-395.

Biodosimetry - Input on Identified Diagnostic Gaps

- Establishment of FDA-approved protocols to use national clinical diagnostic laboratories to process biodosimetry assays in a mass-casualty radiological incident
- Integration of the dual-use of dose and injury measures to quantify radiation diagnostics
- Early-phase prognostic test for bone-marrow aplasia to distinguish total vs partial-body exposures
- Diagnostic strategy to identify individuals with severe GI-ARS
- FDA-approved POC device for early-phase radiation diagnostics

WF Blakely, Port M, Abend M.J. Early-response multiple-parameter biodosimetry and dosimetry: risk predictions. *J. Radiol Prot.* 2021 Dec 6;41(4). doi: 10.1088/1361-6498/ac15df.

Abend M, Blakely WF, Ostheim P, Schuele S, Port M. Early molecular markers for retrospective biodosimetry and prediction of acute health effects. *Abend J Radiol Prot.* 2022 Jan 25;42(1). doi: 10.1088/1361-6498/ac2434.