RCD-22-216-0

Contractor Technical Report

Recommended Ulceration Threshold Dose for Discrete Radioactive Particles

R.R. Benke, D.M. Hamby, C.D. Mangini and C.T. Rose

submitted by:

RCD RADIATION PROTECTION ASSOCIATES

a subsidiary of:

Renaissance Code Development, LLC
310 NW 5th St., Suite 107
P.O. Box 1778
Corvallis, Oregon 97339
(541) 286-4428 (office/fax)
http://www.rcdsoftware.com

September 15, 2022

David M. Hamby, PhD
Managing Partner
david.hamby@rcdsoftware.com
NRC Contract No. 31310019C0036

INTRODUCTION

This technical report recommends an ulceration dose threshold for discrete radioactive particles (DRPs), also referred to as hot particles. The threshold is proposed for a certain averaging area and tissue depths representing target cells at different locations of the human body. The proposed tissue depths and dose threshold are based on scientific committee reports, peer-reviewed publications, emergency response guidance, and comparisons to published DRP irradiation studies.

ULCERATION DOSE THRESHOLD AND JUSTIFICATION

DRPs have the potential to generate ulcers in humans when irradiating tissues of the respiratory tract and the alimentary tract. A literature review began with reports by the National Council on Radiation Protection and Measurements (NCRP) and International Commission on Radiological Protection (ICRP)—NCRP Reports 106 (1989) and 130 (1999) and ICRP Publications 118 (2012), 100 (2006), 66 (1994), 59 (1992) and 41 (1984)—and expanded to include other scientific committee reports, peer-reviewed publications, and emergency response guidance. Suggested and measured thresholds for deterministic effects from ionizing radiation have typically ranged from 1 Gy to more than 50 Gy for a variety of source characteristics, tissue depths, and irradiation cross-sectional areas.

According to 1992 emergency response guidelines by the U.S. Environmental Protection Agency (EPA, 1992, Table B-1), EPA equated doses of 55 Gy and 70 Gy to risks of 5% and 50% for acute skin injuries of ulcers and fibrosis. After initially suggesting 1 Gy for a 1-cm^2 averaging area and 70 μm depth as a threshold for acute ulceration of the skin (ICRP, 1992), ICRP has more recently concluded that higher doses to the skin, ~5 to 10 Gy received in a single exposure represent practical thresholds for developing erythema, desquamation, and necrosis (ICRP, 2012). On the website for Radiation Emergency Medical Management, the U.S. Department of Health and Human Services (HHS, 2022) considers 3.5 to 5 Gy as minimal thresholds for the least severe skin injuries, such as erythema and edema, but does not include thresholds for more severe injuries such as ulceration or necrosis.

In 2020, the International Atomic Energy Agency (IAEA) assigned 25 Gy as the threshold for deep ulceration and necrosis for the medical management of radiation injuries (IAEA, 2020). The Centers for Disease Control and Prevention (CDC) presently indicates a threshold dose of approximately 20 Gy for deep ulceration (CDC, 2022). In a fact sheet for physicians, the CDC explains that ulceration is possible for doses greater than 15 Gy, but doses exceeding 40 Gy can produce ulcers that are extremely difficult to treat and may require months to years to fully heal. Following National Institutes for Health (NIH) clinical ratings (DiCarlo et al. 2020), researchers from NIH, HHS, and the U.S. Food and Drug Administration (FDA) anticipate ulceration at doses greater than 30 Gy with a possibility for necrosis at doses greater than 35 Gy. Similarly in 2022, U.S. researchers at a radiation emergency assistance center reported that the threshold for ulcers and tissue necrosis is at least 25 Gy (Iddins et al., 2022). For deep ulceration, a threshold dose of 25 Gy appears to be the most consistent with available information.

In summary, we recommend a 25-Gy ulceration dose threshold that:

- is consistent with thresholds for severe local radiation injury in recent publications by the IAEA and various researchers at U.S. agencies;
- exceeds similar values suggested by ICRP in 2012 for a range of tissue injuries including less severe reactions; and
- falls below doses indicative of severe tissue injury according to earlier EPA emergency response guidelines.

DOSE AVERAGING AREA AND TISSUE DEPTHS

An averaging area of 1 cm^2 for calculating doses from DRP irradiations is proposed based on information in the referenced documents including recent evidence of sparing effects observed for small volumes of irradiation to cell migration from outside of irradiated areas. The averaging area of 1 cm^2 for DRP protection matches the area recommended by the NCRP and ICRP for the same purpose. Additionally, it is consistent with (i) the extent to which surviving cells on the perimeter of an irradiation site will migrate—from diameters up to 15 mm according to ICRP (2012)—toward the central damaged site during tissue response and (ii) observed sizes of DRP-induced ulcers that range from millimeters to a centimeter in diameter (NCRP, 1989).

Anatomical differences among outer tissue of the skin and internal tissue of the respiratory and alimentary tracts justify selecting different depths for target cells in these regions. Target cell depths were determined to be 40–50 µm for extrathoracic surfaces in the upper respiratory tract, 130–150 µm for the small intestine, and 280–300 µm for the large intestine (ICRP, 2006; 1994). Representative depths are therefore recommended for calculating dose to these target cells. The representative depths are: 45 µm for extrathoracic surfaces in the upper respiratory tract, 140 µm for the small intestine, and 290 µm for the large intestine.

Dose calculations for comparison to the ulceration threshold can be averaged over the most highly exposed 1-cm^2 area at the recommended tissue depths:

- 45 µm for the upper respiratory tract,
- 140 µm for the small intestine, and
- 290 µm for the large intestine.

POPULATION VARIABILITY AND RADIATION PROTECTION LIMITS

Considering the reviewed material, an ulceration threshold dose of 25 Gy is roughly compatible with an ulceration incidence of approximately 1 to 10 percent of exposed individuals. This means that individuals with above-average radiological resistance and biologically resiliency could receive doses above the threshold and still not develop ulcers. By establishing an ulceration threshold based on the most radiosensitive individuals, the same threshold remains protective when applied to the entire population. In the context of person-to-person variability for radiosensitivity, the 25-Gy threshold for radiation-induced ulcers is protective. To prevent ulceration from DRP exposure, regulatory authorities can set dose limits at or below this threshold dose.

REFERENCES

Centers for Disease Control and Prevention (CDC). Cutaneous Radiation Injury: Fact Sheet for Physicians. https://www.cdc.gov/nceh/radiation/emergencies/pdf/criphysicianfactsheet.pdf (website accessed on July 30, 2022). 2022.

DiCarlo, AL, AC Bandremer, BA Hollingsworth, S Kasim, A Laniyonu, NF Todd, S-J Wang, ER Wertheimer, CI Rios. Cutaneous Radiation Injuries: Models, Assessment and Treatments. *Radiat Res.* 194(3): 315–344. 2020.

Iddins, CJ, AL DiCarlo, MD Ervin, E Herrera-Reyes, RE Goans. Cutaneous and Local Radiation Injuries. *J Radiol Prot*. 42(1). 2022.

International Atomic Energy Agency (IAEA). Medical Management of Radiation Injuries. Safety Reports Series No. 101. Vienna, Austria. 2020.

International Commission on Radiological Protection (ICRP). ICRP Statement on Tissue Reactions / Early and Late Effects of Radiation in Normal Tissues and Organs ─ Threshold Doses for Tissue Reactions in a Radiation Protection Context. ICRP Publication 118. Ann. ICRP 41(1/2). 2012.

ICRP. Human Alimentary Tract Model for Radiological Protection. ICRP Publication 100. Ann. ICRP 36(1-2). 2006.

ICRP. Human Respiratory Tract Model for Radiological Protection. ICRP Publication 66. Ann. ICRP 24(1-3). 1994.

ICRP. The Biological Basis for Dose Limitation in the Skin. ICRP Publication 59. Ann. ICRP 22(2). 1992.

ICRP. Nonstochastic Effects of Ionizing Radiation. ICRP Publication 41. Ann. ICRP 14(3). 1984.

National Council on Radiation Protection and Measurements (NCRP). Biological Effects and Exposure Limits for "Hot Particles." NCRP Report 130. Bethesda, MD. 1999.

NCRP. Limit for Exposure to "Hot Particles" on the Skin. NCRP Report 106. Bethesda, MD. 1989.

U.S. Department of Health and Human Services (HHS). Radiation Emergency Medical Management (REMM). https://remm.hhs.gov (website last updated on February 17, 2022). 2022.

U.S. Environmental Protection Agency (EPA). Manual of Protective Action Guides and Protective Actions for Nuclear Incidents. EPA 400-R-92-001. Washington, DC. 1992.