Chapter 5:
Risk of Acute Radiation Syndromes Due to Solar Particle Events

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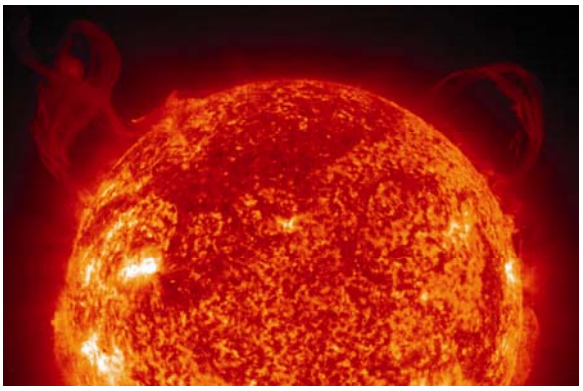
Radiation and synergistic effects of radiation may place the crew at significant risk for acute radiation sickness from a major solar event or artificial event, such that the mission or crew survival may be placed in jeopardy. Crew health and performance may be impacted by acute solar events. Beyond Low Earth Orbit, the protection of the Earth's atmosphere is no longer available, such that increased shielding and protective mechanisms are necessary in order to prevent acute radiation sickness and impacts to mission success or crew survival. The primary data available at present are derived from analysis of medical patients and persons accidentally exposed to high doses of radiation. Data more specific to the spaceflight environment must be compiled to quantify the magnitude of increase of this risk and to develop appropriate protection strategies. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



Research to improve estimates of the risk of acute radiation syndrome resulting from exposure to solar particle events (as pictured here) will help ensure that the risk is sufficiently mitigated through shielding protection, monitoring, and alert systems.

Executive Summary

The foundation of evidence for acute radiation syndrome (ARS) is ground-based observations for humans who were exposed to ionizing radiation, and well-defined dose projections for space explorations missions. Scenarios in which ARS is likely to have a major health impact entail nuclear power plant workers in the event of a nuclear accident; military personnel, in the event of nuclear war; and the general population, should a terrorist attack occur that involves nuclear devices (Waselenko et al., 2004; Pellmar et al., 2005). ARS has been documented in humans who were exposed to gamma or X rays, and these data have been summarized in the literature and in numerous committee reports (e.g., NAS/NRC, 1967; NCRP, 1982; NCRP, 1989; Baum et al., 1984; Evans et al., 1985; ICRP, 2000; ICRP, 2002). NASA has funded several reports from the NAS and the NCRP that provided evidence for the radiation risks in space. Of note, the NCRP is chartered by the United States Congress to guide federal agencies such as NASA on the risk from radiation exposures to their workers. Reports from the NCRP and the NRC on space radiation risks are the foundation of the evidence that is used at NASA for research and operational radiation protection methods and plans.

The risk of ARS from exposure to large SPEs during space missions was identified in the early days of the human space program (NAS/NRC, 1967). The ARS symptoms that appear in the prodromal phase post-exposure (i.e., nausea, vomiting, anorexia, and fatigue) could potentially more significantly affect space mission success because of the lower threshold dose with which these occur compared to other acute risks, as well as the likely dose ranges from SPEs. While ARS has been well defined for gamma- and X-ray exposures, less is known about the acute effects from whole-body exposures to SPE protons, which are characterized by dynamic changes in energy distribution and dose-rates at specific locations in the human body. Protons dominate the dose inside the spacecraft. During EVAs, however, the helium and heavy-ion component of SPEs is also of biological importance. Protons with energies that are above 10 MeV are characterized as low-LET radiation. Inside tissue, a fraction of SPE doses is from high-LET radiation due to the slowing down of higher energy protons, and nuclear reactions producing neutrons and heavy ions. RBE factors for these radiation types are poorly defined. There have also been few investigations of the effectiveness of medical countermeasures for proton, microgravity, or reduced-gravity environments. Improvements in SPE forecasting and alert systems are needed to minimize operational constraints, especially for EVA. While radiation shielding is an effective mitigation to ARS, the high cost of shielding requires precise estimates of the risk to ensure that sufficient protection is provided without overesti-mating shielding requirements, especially in light of the existence of a dose threshold for many ARS components.

Introduction

Description of acute risks of concern to NASA

During an SPE, the sun releases a large amount of energetic particles. Although the composition of the particle type varies slightly from event to event, on average these particles consist of 96% protons, 4% helium-ions, and a small fraction of heavier ions (NCRP, 1989; Cucinotta et al., 1994; Townsend et al., 1994; Kim et al., 1999). The intensity and the energy spectrum of an SPE varies throughout the course of the event, which lasts from a few hours to several days. The intensity of the event can be described by particle fluence, F>E, which is the number of ions per unit area with energy greater than E, expressed as mega electron volts per nucleon (MeV/n). The energies of the protons are important because the range of penetration of these protons increases with energy. Protons with energies above 30 MeV have sufficient range to penetrate an EVA spacesuit, and are used as a simple scaling parameter to compare different SPEs. Each event has distinct temporal and energy characteris-tics, however. The majority of SPEs are relatively harmless to human health, with doses below 10 mGy for

minimal shielding protection; but the SPEs that have the highest fluence of particle of energies above 30 MeV are a major concern for future missions outside the protection of the magnetic field of the Earth.

Figure 5-1 shows data that were collected in the modern era for the F>30 MeV proton fluence (bottom panel) from large SPEs and the solar modulation parameter (Φ) (upper panel). The solar modulation parameter describes the strength of the sun's magnetic field with solar maximum where Φ>1,000 MV. The various SPEs shown in figure 5-1, which are characterized as large SPEs (F>30 MeV > 108 per cm^2), would contribute doses of 10 to 500 mGy for average shielding conditions. Although the dose resulting from the majority of SPEs is small, SPEs nonetheless pose significant operational challenges because the eventual size of an event cannot be predicted until several hours after the particles are initially detected. Extraordinarily large SPEs were recorded in November 1960, August 1972, and October 1989. In general, SPEs occur more often near solar maximum, but, as figure 5-1 shows, the correlation between event frequency and solar conditions is not precise. To date, accurate short- or long-term prediction of SPEs has not been possible.

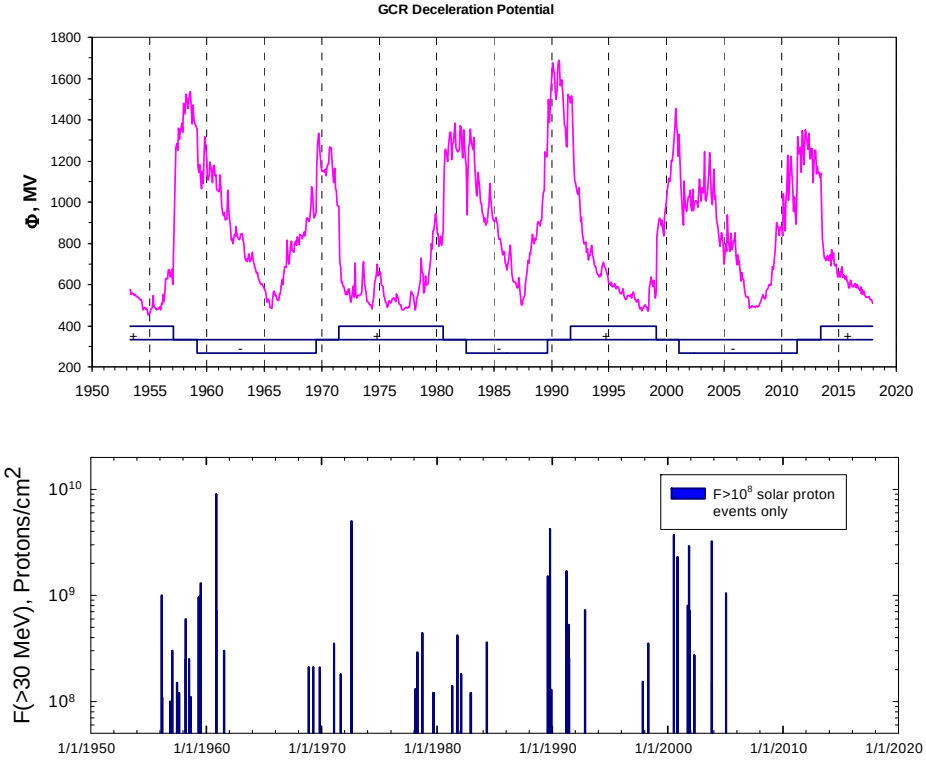


Figure 5-1. ***Historical data on fluence of protons above 30 MeV per cm^2 (F(>30 MeV) from large SPEs relative to solar modulation parameter (Φ). Only events with $F_{>30\ MeV}$ >10^8 particles per cm^2 are shown.***

In contrast to the constant presence of GCRs in space, SPE exposures are sporadic and occur with little warning. Without sufficient shielding protection, a large SPE may result in a whole-body dose of over 0.5 Gy (500 mGy) received over a period of several hours. Humans who are exposed to gamma or X rays at doses above 0.5 Gy are known to experience ARS (Anno et al., 1989). ARS can be classified clinically as hematopoietic syndrome, GI syndrome, and neurovascular syndrome. Based on the time of appearance, ARS can be divided into prodromal phase (0–24 hr), latent phase, manifest illness phase, and recovery phase. The most probable ARS effects from

SPE exposure in space flight that can potentially affect mission success include prodromal effects (nausea, vomiting, anorexia, and fatigue), skin injury, and depletion of the blood-forming organs (BFOs), possibly leading to death. SPEs are of much lower energy than are GCRs and occur at modest dose-rates. Shielding is an effective countermeasure to SPEs inside spacecraft, making ARS extremely unlikely except in EVA or combined EVA and intravehicular activity (IVA) scenarios. The magnitude of ARS risks on the moon has been hypothesized to be increased significantly due to a possible synergistic effect of reduced gravity (Todd et al., 1999) or the background GCR exposure. The operational impacts of ARS on space flight crew members could affect crew performance and lead to the possibility of mission failure. Recovery of ARS can also be hindered by changes of the immune status, including from combined skin burns and blood system depletion, and a slower wound-healing process.

NASA, in past reviews, has included the risks of hereditary, fertility, and sterility effects as part of the collection of risks embodied in the acute radiation effects category. There is no perfect match of these effects with any of the four major identified NASA HRP radiation risks, and, based on past reviews of these effects (NCRP, 1989; 2000), they alone are not likely to rise to the level of a major concern. As SPEs would be the primary cause of fertility and sterility effects, these items are included as part of the acute category of risks.

Current NASA permissible exposure limits

PELs for short-term and career astronaut exposures to space radiation have been approved by the NASA Chief Health and Medical Officer. These PELs provide the basis for setting requirements and standards for mission design and crew selection. Short-term dose limits (i.e., PELs) are imposed to prevent clinically significant deterministic health effects, including performance degradation in flight. Dose limits for deterministic effects, which are given in units of Gray-equivalent, are listed in Table 5-1. The unit of Gray-equivalent is distinct from the unit of Sievert that is used to project cancer risk because distinct radiation quality functions occur for ARS and cancer. The Gray-equivalent is calculated using the RBE values that are described in NCRP Report No. 132 (2000) and Sievert using the LET-dependent radiation quality function. For mission planning, these limits should be applied with a P>0.99 success criteria for a worst-case radiation environment and available mitigation procedures. The basis for the PELs originated in prior reports and recommendations to NASA by the NAS Space Science Board (NAS/NRC, 1967; 1970) and the NCRP (NCRP, 1989; 2000). These reports are summarized below.

Table 5-1. ***Dose Limits (in mGy-Eq or mGy) for Non-cancer Radiation Effects (BFO Refers to the Blood-forming Organs and CNS to the Central Nervous System)***

Organ	30-day limit	1-year limit	Career
Lens*	1,000 mGy-Eq	2,000 mGy-Eq	4,000 mGy-Eq
Skin	1,500 mGy-Eq	3,000 mGy-Eq	6,000 mGy-Eq
BFO	250 mGy-Eq	500 mGy-Eq	Not applicable
Heart**	250 mGy-Eq	500 mGy-Eq	1,000 mGy-Eq
CNS***	500 mGy-Eq	1,000 mGy-Eq	1,500 mGy-Eq
CNS*** (Z≥10)	–	100 mGy	250 mGy

*Lens limits are intended to prevent early (<5 years) severe cataracts (e.g., from an SPE). An additional cataract risk exists at lower doses from cosmic rays for subclinical cataracts, which may progress to severe types after long latency (>5 years) and are not preventable by existing mitigation measures; they are deemed an acceptable risk to the program, however.

**Heart doses calculated as average over heart muscle and adjacent arteries.

***CNS limits should be calculated at the hippocampus.

Evidence

Reviews of human data in patients and accident victims

Evidence of ARS in humans from low-LET radiation, such as gamma- or X-ray exposures, has been thoroughly reviewed and documented in the reports that have been generated by regulatory institutes such as NAS, NCRP, the ICRP, and the U.S. Nuclear Regulatory Commission. Data accumulated from the last half-century that were used in the construction of the dose threshold for ARS include: studies on the Japanese atomic-bomb survivors (Ishida and Matsubayashi, 1948; Ohkita, 1975; Oughterson and Warren, 1956); case studies of nuclear accident victims (Blakely, 1968; Vodopick and Andrews, 1974; Gilberti, 1980); and records of total-body therapy patients for cancer and other diseases (Adelstein and Dealy, 1965; Brown, 1953; Warren and Grahn, 1973). More recent events include the Chernobyl accident in 1986 (Bouville et al., 2006); an accident that occurred in Tokai-mura, Japan, in 1999 (Hirama et al., 2003); and the death of a Russian citizen after a possible internal overdose of radioactive materials that was reported in the popular media in 2006.

ARS appears in various forms and has different threshold onset doses for the possible effects. The threshold whole-body dose for ARS is about 0.1 to 0.2 Gy for radiation that is delivered under acute conditions where dose-rates are more than 1 Gy/hr occur. At lower dose-rates, a reduction in effects occur, as described below. At doses that are slightly above this threshold, decreases in sperm counts occur that cause temporary sterility in males (NAS/NRC, 1967; Paulsen, 1973; NCRP, 1989). The dose range and associated patho-physiological events have been summarized previously (Anno et al., 1989). Doses that are in the range of 0.5 to 1 Gy cause minor acute damage to the hemopoietic system and mild prodromal effects (nausea, vomiting, anorexia, and fatigue) in a small number of irradiated persons (Anno et al., 1989). In the dose range of 1 to 2 Gy acute, prodromal effects and injury to the hemopoietic system increase significantly. Most victims will probably survive, however, with only 5% lethality in a population after doses of about 2 Gy (NAS/NRC, 1967; McFarland and Pearson, 1963). Survival is possible within the dose range of 2 to 3.5 Gy; however, prodromal effects become more pronounced, decreasing in latency and increasing in severity. As the dose reaches about 3.25 Gy, 50% may die within 60 days if appropriate medical care is not administered (Lushbaugh, 1969). From 3.5 to 5.5 Gy, symptoms are more severe, affecting nearly all who are exposed. If untreated, 50% to 99% of those who are affected may die primarily because of extensive injury to the hemopoietic system that is manifested by overwhelming infections and bleeding (NAS/NRC, 1967; Lushbaugh, 1969; Messerschmidt, 1979). At this dose range, permanent sterility results in both males and females (Paulsen, 1973; NCRP, 1989).

Responses to doses between 5.5 and 7.5 Gy begin to reflect the combined effects of GI and hemopoietic damage. Survival is almost impossible, short of a compatible bone marrow transplant and/or extensive medical care. Nearly everyone who is irradiated at this level suffers severe prodromal effects during the first day after exposure. When doses range between 7.5 and 10 Gy, injuries are much more severe due to a greater depletion of bone marrow stem cells (Adelstein and Dealy, 1965; Lushbaugh, 1962), increased GI damage, and systemic complications from bacterial endotoxins entering the blood system.

Doses that are between 10 and 20 Gy produce early post-exposure renal failure (Lushbaugh, 1974). Death results in fewer than 2 weeks from septicemia due to severe GI injury, which is complicated by complete bone marrow damage and the cessation of granulocyte production (Lushbaugh 1962). Above approximately 13 Gy, death may occur sooner from electrolyte imbalance and dehydration due to vomiting and diarrhea, especially in hot and humid conditions. Extremely severe GI and cardiovascular damage causes death within 2 to 5 days after doses of 20 to 23 Gy (Lushbaugh, 1969).

Prodromal Effects

Prodromal effects, which have a threshold dose of about 0.5 Gy, are the most likely acute effect to be experienced by crew members after exposure to SPE based on the historical record of SPE fluence and likely shielding conditions. Dose and onset of sickness are inversely correlated, with higher doses producing the shortest time for sickness to occur. The prodromal phase comprises the clinical symptoms (nausea, vomiting, and anorexia) and signs that appear in the first 48 hours after exposure. Prodromal vomiting is of particular importance because it could have catastrophic consequences in space, especially to helmeted individuals (NCRP, 1989), and other symptoms can seriously impair mission success in space. Several sets of data on humans, who are mostly cancer patients, are available to make initial estimates of the likelihood and types of effects (e.g., Lushbaugh et al., 1967; Lushbaugh, 1974). In general, symptoms develop within a few hours of radiation exposure and rarely exceed 24 hours with low-LET radiation (Fajardo et al., 2001). Exposure to higher doses results in greater severity, early onset, and longer duration of the symptoms (Anno et al., 1996). Prodromal effects are not noted below low-LET radiation doses of 0.5 Gy (Mettler and Upton, 1995).

Significantly smaller amounts of data are available for prodromal effects from continuous exposure at lower dose-rates. The current knowledge that has been collected from studies on victims who were exposed to radioactive fallout following the testing of nuclear devices and to other sources (Kumatori et al., 1980; Cronkite et al., 1956) is that dose-rates of perhaps less than a few tens of mGy/h are probably not sufficient to cause ARS. However, continuous dose-rates of around 100 mGy/h are probably high enough to cause significant vomiting within a period of 1 day or so. Accordingly, between a few tens of mGy/h to approximately 100 mGy/h, a considerable amount of uncertainty exists concerning the human response to continuous radiation exposure, which is likely due to variations in the sensitivity of individuals as well as the quality of the very limited amount of existing data.

Skin Damage

The skin may receive a dose that is up to a magnitude greater than that of internal organs from an SPE during an EVA, when minimal protection is available (Kim et al., 2006a). Risks of concern include erythema, moist desquamation, and epilation (NCRP, 1989). The ED10 (a dose in which 10% of a population receives the effect) has been estimated to be 4 Gy for erythema and 14 Gy for the more serious moist desquamation (Strom, 2003; Haskin et al., 1997). Protraction of exposure increases the dose that is required for a given degree of severity by a factor of about 3. The response of the skin depends on the number of exposures, the total dose, the dose per exposure, and the volume of tissue that is irradiated (Turesson and Notter, 1984). It has been noted that deterministic radiogenic skin injury complicates the treatment of many of the high-dose casualties at Chernobyl (Strom, 2003). Skin doses during an SPE can vary more than five-fold for different regions of the bodydue to the varying energies of solar protons and body self-shielding(Kim et al., 2006a).

Reviews of space flight issues

Past reviews of evidence by the NAS and the NCRP form the basis for the NASA PELs. NAS first reviewed space flight issues in 1967 (NAS, 1967) and conducted a further review in 1970 (NAS, 1970) that led to the dose limits that were used at NASA until 1989. Extensive reviews of humans and experimental radiobiology data for ARS were provided to NASA by reports of the NCRP in 1989, 2000, and 2006 (NCRP, 1989; 2000; 2006). The report of the NAS in 1970 is the basis for the BFO limits that are used at NASA. The rationale for this limit is to protect the hematopoietic system from depletion below a critical limit. Dose limits for the prodromal risks were not advocated by the NAS or the NCRP for NASA missions in the past. The BFO limit likely occurs at doses below that of the threshold for prodromal effects, however.

Acute Risks for Protons, Neutrons, and High-Z High-energy Nuclei

RBE and dose-rate studies in mice, rats, ferrets, and larger species

The data of ARS for high-LET radiation – e.g., neutrons and heavy ions – are collected primarily in animal studies. As mice and rats do not display the prodromal effects such as vomiting, limited research on this particular ARS has been performed on ferrets for particle types of radiation. Rabin et al. (1992; 1994) have studied the dose response of 600 MeV/n ^{56}Fe-ion-induced emesis in ferrets and compared it with the dose response from other radiation types. Over the dose range of 0.2 to 0.5 Gy, fission spectrum neutrons and ^{56}Fe-ions were more effective than Co-60 gamma rays in inducing emesis, and the effects of the ^{56}Fe-ions and fission neutrons could not be distinguished from each other. Co-60 gamma rays were significantly more effective in producing emesis than high-energy electrons or 200-MeV protons. The dose-rates ranged from 0.1 to 1 Gy/min. The relatively large difference in LET between ^{56}Fe-ions and fission neutrons was not associated with any difference in the effectiveness with which the two types of radiation produced emesis.

Relative biological effectiveness and dose-rate studies in cell inactivation

Since some of the ARS effects are related to cell killing or tissue damage, the RBE and dose-rate data for cell inactivation by protons are insightful for ARS that is induced from SPE exposures (Cucinotta, 1999; Yang, 1999). Early results of cell inactivation by charged particles over a wide range of LET have been reviewed by Ainsworth (1986). In general, the RBE for cell inactivation in vitro peaked at LET around 100 keV/micron, and the peak RBE value varied between 1.5 and 5 for different cell types. The maximum RBE for in vivo responses tended to be lower and occurred at a lower LET value in comparison to the in vitro data. The reported RBE-LET relationship for in vitro cell killing showed similar trends as in the early in vivo data (Furusawa et al., 2000).

Factors that determine the dose-rate dependence of ARS include: the kinetics of DNA repair, apoptosis, cell-repopulation and proliferation, and dose distributions across critical organs. Irradiation at reduced dose-rates is known to reduce the probability of lethality of ARS that is induced by low-LET radiation compared to acute irradiation, as illustrated in figure 5-2. Differences between dose-rate effects for protons and X rays or gamma rays may occur due to the heterogeneous dose contribution from slowing protons or recoil nuclei in SPE organ doses. The heterogeneous dose distribution across the bone marrow for protons should lead to a sparing effect that complicates comparisons to gamma rays, where doses are more uniform. The dose distribution across the stomach and other organs in the GI-tract also varies several-fold for SPEs, which complicates the use of gamma-ray data to predict prodromal risks from SPE.

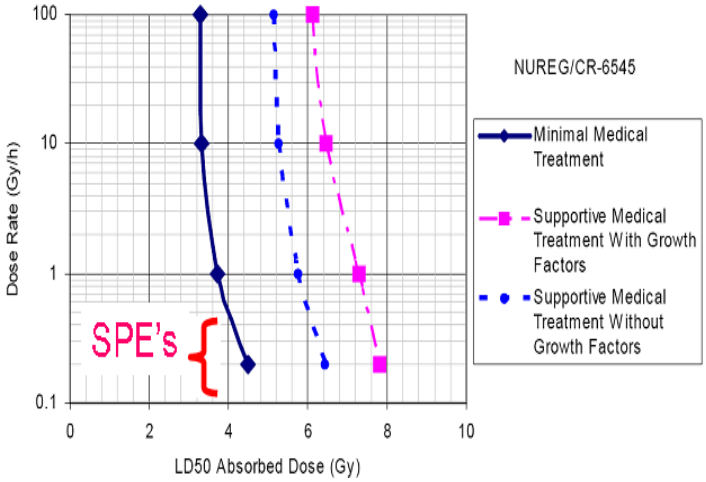


Figure 5-2. ***Effects of medical treatment and dose-rate on the LD50 for gamma radiation; also shows expected region of dose-rates for SPEs during EVA (adapted from Haskin, 1997).***

Models of acute risks

Department of Defense and Nuclear Regulatory Commission Models

The radiation-induced performance decrement from ARS is one of the major concerns for military personnel in a nuclear war scenario. The Defense Nuclear Agency has developed a computer model to calculate the dose and time-dependent human response to ionizing radiation for acute and protracted exposure conditions (Anno et al., 1996). A set of differential equations was mathematically developed to model the ARS for a given dose and the bodily repair and recovery process when the exposure takes place over a period of time. Most of the parameters in the equations were determined from human accident data or data of patients who were receiving whole-body radiation in medical treatment; limited data came from ferrets and other animals for protracted exposures.

Two models were developed separately for upper gastrointestinal distress (UGID) and for fatigue/weakness (FW); these models were based on the postulated pathways. For UGID, the severity of the signs and symptoms was classified in five categories ranging from no noticeable effect (Severity Level 1) to vomiting and retching several times (Severity Level 5). For FW, Severity Level 5 is defined as exhaustion with almost no strength. Outputs of the computer codes are the probability of occurrence of specific symptoms as a function of input dose, dose-rate, and time after exposure. These radiation effects were also related to performance decrement for infantry tasks such as engaging a target with a rifle or walking up a rocky hill. Similar issues will be faced by NASA when astronauts are exposed to SPE on the surface of the moon. The mathematical model applies to gamma- or X-ray exposures only, but it has been adapted to proton effects at NASA (Hu et al., 2009).

Cell Kinetics Models

Cell kinetics models of the relevant cell lineages in the blood system are of interest for describing dose-rate effects. A group at Oak Ridge National Laboratory developed models of the blood system using a linear kinetics formula of cell damage, repair, and repopulation (Morris et al., 1993). The model has been fit to data for mice and larger species. This model, which was applied to study the risk of acute mortality following a large SPE (Wilson et al., 1999), indicates a very small probability for acute death for the largest SPEs, as in the Defense Nuclear Agency model that is described above. In addition, a nonlinear cell population kinetics model of ARS was developed that provides a more realistic simulation of the underlying biology of ARS

(Smirnova and Yonezawa, 2004), including an adaptive response due to simulation of the immune defense mechanisms.

Risk in Context of Exploration Mission Operational Scenarios

Solar particle event environment models and doses

Estimates of likely SPE cumulative doses and dose-rates at critical organs are important for assessing the probability of ARS for specific mission scenarios. Detailed spectra and temporal information are available for most of the SPEs that have occurred since 1955. Analysis of nitrate concentrations in Arctic ice-core samples provides data on integral fluences that are above 30 MeV for SPEs dating back to the 15th century (McKracken et al., 2001). The nitrate core samples indicate that several SPEs that are larger than the August 1972 event, which is considered to be the largest in modern times, have occurred in the past. The nitrate core sample data also allow researchers to estimate their frequency. The prediction of SPEs on Mars, taken from Earth observations, will require improved observational capabilities. Improved knowledge of the physics of these processes can be used to improve the radiation protection of crews.

An understanding of the physical characteristics of solar disturbances is important for protecting the crews that are on Exploration missions. Thus, a summary from the book *Safety design for space systems* (Musgrave et al., 2009, pp. 53–58), is provided here. The solar wind is a plasma that contains both positive and negative particles that are trapped in a magnetic field emanating from the sun. The solar wind is an extension of the solar corona for at least several astronomical units (AUs) from the sun (1 AU $\approx 1.5 \times 10^8$ km). It is composed mostly of protons and persists through variable parts of the sun's output during less active solar phases. The solar wind protons have thermal energies of approximately 1 to 10 keV. Except when the sun is active, the solar wind constitutes the most important particulate solar radiation.

A solar flare is an intense local brightening on the face of the sun close to a sunspot. This solar abnormality results in an alteration of the general outflow of solar plasma at moderate energies and local solar magnetic fields that are carried by that plasma. As the solar plasma envelops the Earth, the magnetic screening effects that are inherent in plasmas act to shield the Earth from GCRs, a process that is known as a Forbush decrease (Forbush, 1937). When the solar plasma interacts with the geomagnetic field, a disturbance or storm occurs. During an intense magnetic disturbance, the magnetic field of the Earth is compressed into the atmosphere in the polar regions of the Earth, and electrons that are trapped in the belt are lost. These auroral electrons, which are observed only in the polar regions, are associated with the coronal mass ejection (CME) that occurs after solar flares.

In association with many of the optical flares that occur from time to time on the solar surface, large fluxes of solar energetic particles are sometimes accelerated and emitted; these emissions of solar cosmic radiation are designated as SPEs. SPEs, with periods of several hours to days, represent one of several short-lived manifestations of the active sun. The solar wind and SPEs are composed of the same types of particles, primarily protons with the next significant component being α-particles. These two groups of particles are distinguished by their numbers as well as their speed or energy. Heavier nuclei, which are mostly in the carbon, nitrogen, and oxygen group (NCRP, 2006), and even heavier particles (atomic charge number, Z, between 22 and 30) have also been observed in major SPEs. Rare clusters of events of high intensity (i.e., of several orders of magnitude) with large numbers of high-energy particles are critical to space flight and EVA because the large events alone determine the yearly fluences of solar particles, and there is a much higher dose-rate effect during the short period of peak intensity (Kim et al., 2006b).

For recent solar cycles 19 through 21 (1955–1986), a list of major SPEs and associated proton fluences has been assembled by Shea and Smart (1990), who place all of the available flux and fluence data in a useful continuous database. From 1986 to the present (solar cycles 22 and 23), both an SPE list and the geostationary operational environmental satellite (GOES) spacecraft measurements of the 5-minute-average integral proton flux can be obtained through direct access to the National Oceanographic and Atmospheric Agency (NOAA) National Geophysical Data Center. Table 5-2 lists the large SPEs that occurred in the past five solar cycles for which the omnidirectional proton fluence with energy above 30 MeV, Φ_{30}, exceeded 10^9 protons/cm^2.

Table 5-2. ***Large SPEs during Solar Cycles 19 through 23 Corresponding to $\Phi_{30} > 10^9$ protons/cm^2***

Solar Cycle	SPE	$\Phi_{>30}$ protons/cm^2
19	11/12/1960	9.00×10^9
20	08/02/1972	5.00×10^9
22	10/19/1989	4.23×10^9
23	07/14/2000	3.74×10^9
23	10/26/2003	3.25×10^9
23	11/04/2001	2.92×10^9
19	07/10/1959	2.30×10^9
23	11/08/2000	2.27×10^9
22	03/23/1991	1.74×10^9
22	08/12/1989	1.51×10^9
22	09/29/1989	1.35×10^9
23	01/16/2005	1.04×10^9
19	02/23/1956	1.00×10^9

In Figure 5-3, the frequency of SPE occurrence that was recorded by the NOAA GOESs for solar cycle 23 is shown for 3-month periods. The monthly mean number of sunspots is included in the figure to show the association between SPE occurrence and solar activity. The times at which the five largest SPEs with $\Phi_{30} > 10^9$ protons/cm^2 occurred are marked with arrows. It is expected that an increase in SPEs occurs with increasing solar activity; however, no recognizable pattern has been identified. Large events have occurred during solar active years, but have not always occurred during months of solar maximal activity. Moreover, large events are more likely to occur in the ascending or declining phases of a solar cycle. This sporadic behavior of SPE occurrence is a major operational problem in planning for missions to the moon and Mars.

The shapes of the energy spectra, as well as the total fluence, vary considerably from event to event. Figure 5-4 shows the energy spectra of the January 16, 2005 SPE, which is one of the more recent large events. At that time, there was a sudden increase in proton flux, especially in particles with energies that were greater than 50 MeV. Protons with energies that were greater than 100 MeV increased by as much as four orders of magnitude after they declined following the major pulse. During this sharp commencement, the fluence did not reach the value that was obtained at the major peak intensities; however, this type of sudden increase in high-energy particles may pose a greater threat than the major particle intensities. Total fluence of an SPE is the representative indicator of a large SPE, and the detailed energy spectra for a large SPE – especially at high energies – is the important parameter for assessing the risk of radiation exposure (Kim et al., 2006b).

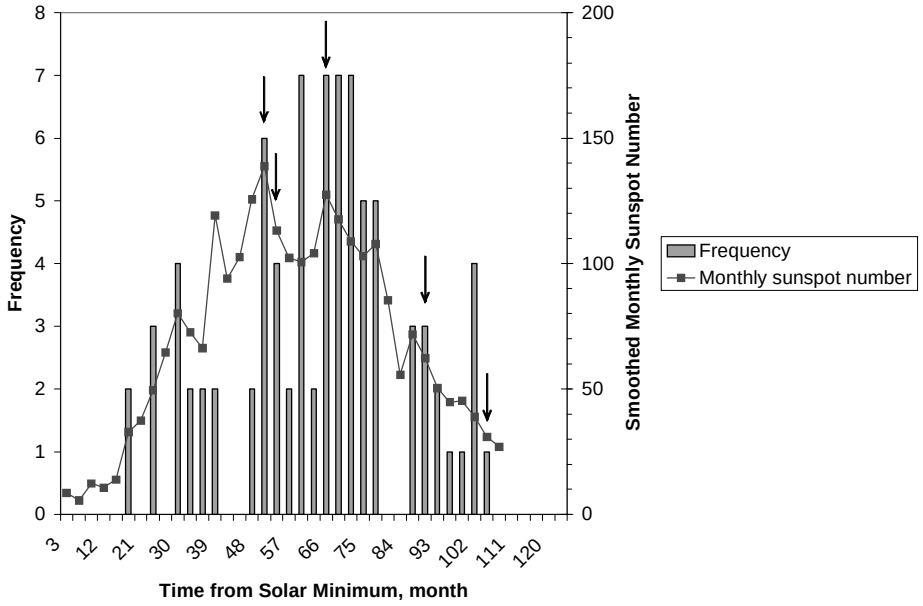


Figure 5-3. ***Frequency of SPE occurrence in 3-month periods of solar cycle 23. The arrows indicate the times at which large SPEs with $\Phi_{30}>10^9$ protons/cm^2 occurred.***

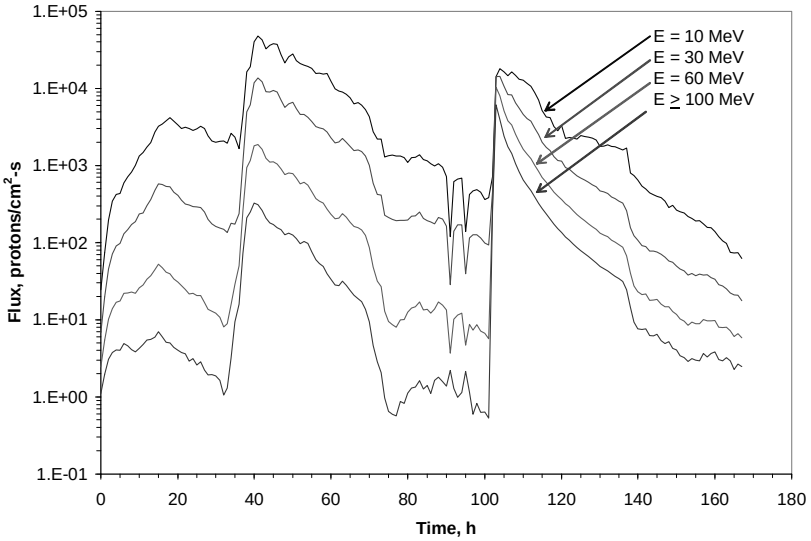


Figure 5-4. ***Hourly-average proton flux from GOES measurements during the SPE of January 16–22, 2005.***

A detailed temporal analysis of dose-rate at the BFOs for the August 1972 SPE is illustrated in figure 5-5. This event, which was one of the largest SPEs in the modern era, had the highest dose-rate at its peak. The temporal behavior that is shown in figure 5-5 suggests that significant biological damage would occur in a crew if adequate shielding is not provided. Figure 5-6 shows the SPE doses during this same event. Estimates for the Φ>30 MeV flux, which were determined from nitrate samples and then scaled to the August 1972 energy

spectra, are also shown. Biological effects are expected to increase significantly for dose-rates that are above 0.05 Gy/h. For an extended EVA, the current recommended 30-day exposure limit for the BFOs, which is 0.25 Gy-Eq (NCRP, 2000), is easily exceeded. The early effects from acute exposure may not be avoided when only a conventional amount of spacecraft material is provided to protect the BFOs from this class of SPE. To avoid placing unrealistic mass on a space vehicle while at the same time increasing safety factors for the astronauts, one solution for shielding against SPEs would be to select optimal materials for the vehicle structure and shielding. To this end it has been shown that materials that have lower atomic mass constituents have better shielding effectiveness (Wilson et al., 1999, Cucinotta, 1999). Overall exposure levels from this specific event have been estimated to be greater than 100 mSv (10 rem) at sensitive sites, while those from other large SPEs that have been recorded in the modern era can be reduced to below 0.1 Sv when heavily shielded "storm shelters" are added to a typical spacecraft (Kim et al., 2006b). Interpretation of this result, however, should be made while keeping in mind the caveat that significant uncertainties are inherent in determining the source spectra of protons (Musgrave et al., 2009.)

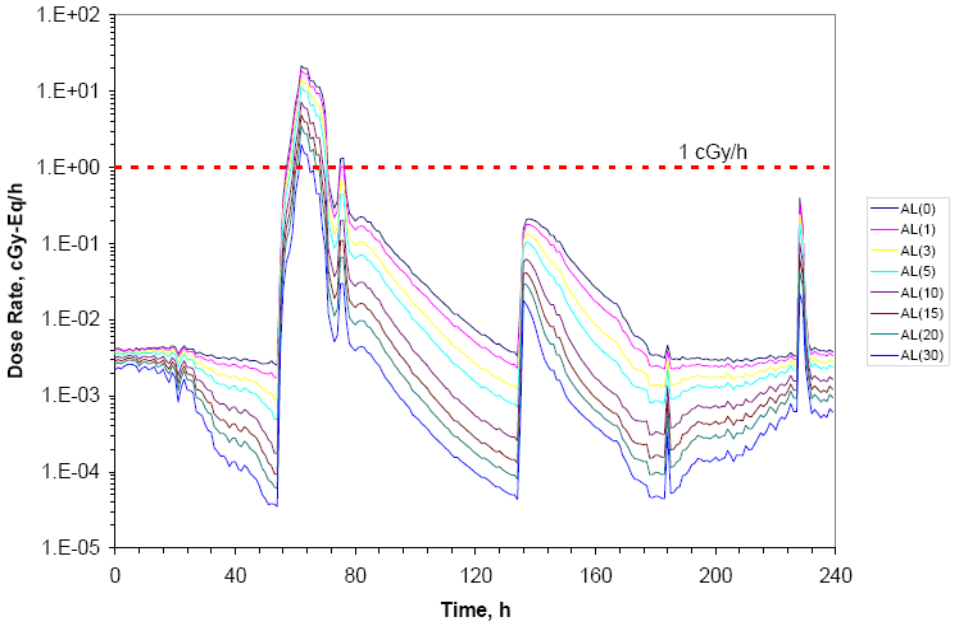


Figure 5-5. Dose-rate to the BFO for increasing levels of aluminum shielding for the large SPE of August 1972 (Kim et al., 2006a).

Solar alert and monitoring

An effective operational procedure requires an SPE warning or alert system. This system, which would be activated at the onset of proton exposure, would include pertinent information concerning the event, such as the fluence or flux and the energy distribution. These capabilities do not exist at the current time, and forecasts from NOAA are limited. New capabilities for deep-space mission forecasting will be needed prior to the Mars mission because the alignment of the Earth and Mars does not allow all SPEs on Mars to be observed from Earth. A recent report by the NRC discussed research approaches in space science that should lead to improved forecasting and alert capabilities for SPEs (NAS/NRC, 2006), including a status of approaches supported by the NASA Science Mission Directorate.

The most likely outcome of an SPE is mission disruption with little or no harm to the crew because, despite the occurrence of some very large SPEs such as the 1972 event described previously, more than 90% of SPEs result in very small radiation doses to critical organs (<10cGy-Eq), as shown in figure 5-6. Mission disruption is likely because the size of the SPE cannot be determined until several hours after its initial onset. Reliable radiation dosimeters that can transmit to Mission Control and provide a self-alert to astronauts are required. Such instrumentation has been available for many years, including during the Apollo missions (NCRP, 1989).

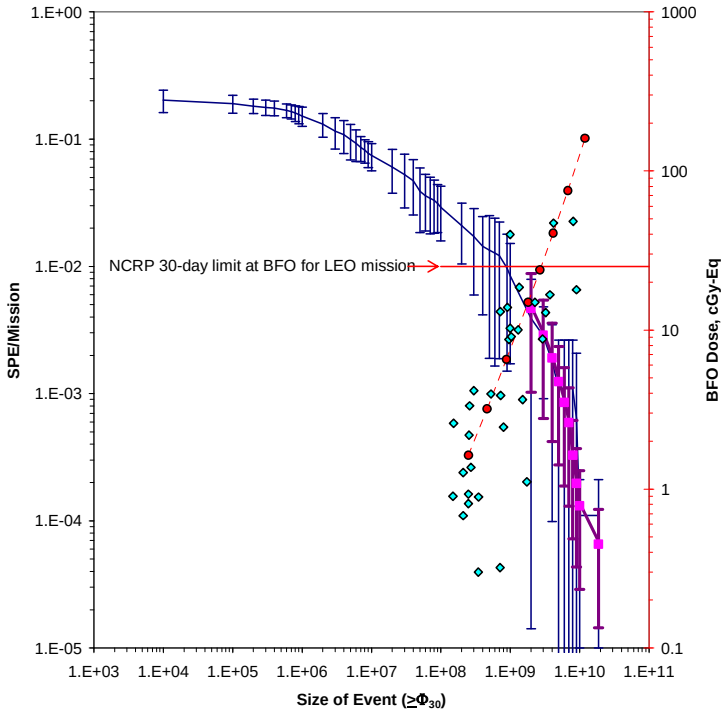


Figure 5-6. ***Probability of SPE in a 1-week mission (thin line: average probability of SPE and statistical fluctuation during space era; thick line: extended average probability including impulsive nitrate events; ■ impulsive nitrate events data) and BFO dose (--●-- BFO dose of the worst-case SPE model scaled by Φ>30 flux to August 1972 SPE; ♦ BFO dose of 34 large SPEs during space era using actual spectra).***

A recent publication (Posner, 2007) provides evidence that detection of relativistic solar electrons may enable as much as a 1-hour warning of proton events as well as prediction of the integral number of protons that can be expected, as illustrated in figure 5-7. The color matrix that is shown provides a code to predict future proton intensity, 1 hour ahead of time, as predicted by relativistic electron measurements. The parameter space is given by the current maximum electron increase parameter, which goes back in time at least 5 minutes and up to 60 minutes, and current relativistic electron intensity. The matrix is derived from the aggregate of all 1998 to 2002 relativistic electron observations and their corresponding 30- to 50-MeV proton intensities that occurred 1 hour later. Data was obtained from the comprehensive suprathermal and energetic particle analyzer (COSTEP) instrument on the solar and heliospheric observatory (SOHO) satellite. The color shows the average for the proton intensity in each locus. Statistical considerations limit the utility of the matrix at the bottom and upper-right ranges. The importance of the findings of Posner (2007) cannot be overestimated as they not only provide up to a 1-hour early detection capability, but also may allow astronauts and Mission Control personnel to predict whether an event will likely be of insignificant size, which is the most likely outcome. Long-term forecasting from hours to days before the onset of an SPE at this time is inherently inaccurate, with a large number of false alarms predicted and many events not predicted at all (NCRP, 2006).

Mechanisms of radiation-induced vomiting

The mechanisms by which radiation induces nausea and vomiting are not well understood. It is known that radiation induces the secretion of serotonin in the GI-tract. In turn, the binding of serotonin to receptors in the brain mediates vomiting. The physiological effects of high-dose radiation are also mediated, in part, by inflammatory responses. Increased secretion of inflammatory cytokines IL-12 and IL-18 was reported in mouse macrophages after irradiation (Shan et al., 2007). Increased production of IL-6 and TNF-α, which are also pro-inflammatory cytokines, has been observed in the lungs of irradiated mice (Fedorocko et al., 2002). Pro-inflammatory cytokines mediate symptoms of nausea, vomiting, anorexia, and cachexia in instances of cancer and other diseases as well as pregnancy. In addition, ionizing radiation directly generates numerous reactive oxygen species. Additional reactive oxygen species are indirectly generated by cellular responses to radiation, initiating long-lasting cascades of inflammatory events. How these molecules interact to induce the symptoms of prodromal syndrome is unknown.

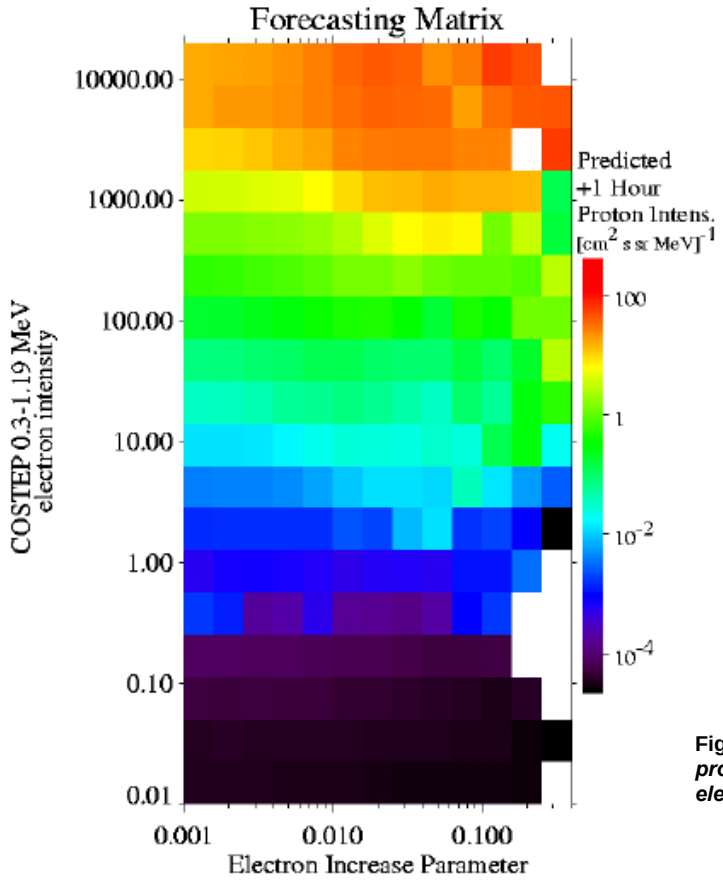


Figure 5-7. ***One-hour lead time prediction of proton spectra that are generated from real-time electron measurements (Posner, 2007).***

Potential for biological countermeasures

Radioprotectors, such as antioxidants, are agents that reduce the damage to various organs by radiation (Gudkow and Komarova, 2005). The likelihood that SPE will produce doses that are above 1 Gy is small, while the occurrence of doses that can induce prodromal risks are quite possible. Although prodromal syndrome may seem more innocuous than the other symptoms of ARS, biological countermeasures for the prodromal risks are a major consideration. Many radioprotectors, including antioxidants and WR-2721, are not expected to coun-

teract prodromal risks such as vomiting or nausea (Harding, 1988). Several classes of drugs have been used to treat the nausea and vomiting that are experienced by patients who are undergoing whole-body radiotherapy (Harding, 1988). While the molecules that regulate vomiting are not well understood, the inhibitors or antagonists of serotonin, dopamine, histamine, and substance P suppress vomiting. Clinical trials have demonstrated that serotonin antagonists were more effective than prochlorperazine or metoclopramide (Franzen et al., 1996; Priestman et al., 1993). Of the 5-HT_3 class drugs, ondansetron has been best studied (Licitra et al., 2002). Studies of the efficacy of combinations of drugs of different classes, such as palonosetron and aprepitant when used with olanzapine or gabapentin, are under way to prevent acute and delayed chemotherapy-induced nausea and vomiting (Navari and Province, 2006). These treatments need to be investigated to determine the efficacy and tolerability for SPE-induced prodromal effects. Cannabinoids, anticholinergics, steroids, benzodiazepides, and plant extracts are also currently being evaluated for their antiemetic properties. Thus, the mechanisms of SPE-induced prodromal symptoms are unclear, but a broad spectrum of potential countermeasures is available for testing.

Conclusion

The biological effects of space radiation, including ARS, are a significant concern. High doses of radiation can induce profound radiation sickness and death. Lower doses of radiation induce symptoms that are much milder physiologically, but that pose operational risks that are equally serious. Both scenarios have the potential to seriously affect crew health and/or prevent the completion of mission objectives. Radiation protection must be provided in the form of predictive models, shielding, and biological countermeasures when traveling outside of the protective magnetosphere of the Earth. Unfortunately, the development of these tools is hindered by a lack of relevant space radiation research. Most radiation studies focus on radiation species and doses that are unlike the radiation that is encountered in space. There is therefore a pressing need for research that accurately reflects the radiation risks that are native to the space environment and that facilitate the development of both improved risk assessment and effective radioprotective strategies.

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